



Clinical Development

^{177}Lu -PSMA-617

Clinical Protocol No.: PSMA-617-02

PSMA-Directed Endoradiotherapy of Castration-Resistant Prostate Cancer (RESIST-PC). A Phase 2 Clinical Trial.

Document type: Abbreviated Clinical Study Report

Final

Development phase: Phase 2

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Template version 8.0, effective 20-Sep-2019

1 Study information

Study title: PSMA-directed Endoradiotherapy of Castration-resistant Prostate Cancer (RESIST-PC). A Phase 2 Clinical Trial.

Test drug/investigational product: ^{177}Lu -PSMA-617

Indication studied: metastatic castration-resistant prostate cancer (mCRPC)

Sponsor: Endocyte, Inc., a Novartis Company

Protocol identification: PSMA-617-02

CT.gov Study Number: NCT03042312

IND No.: 133661

Development phase of study: Phase 2

Study initiation date: 05 Jul 2017 (first subject enrolled)

Early termination date: 22 Jun 2018

Last subject last visit: 15 Jan 2020

Study completion date: 08 Jan 2021

Principal Investigators: Johannes Czernin, MD at the University of California, Los Angeles, CA, USA and Ebrahim Delpassand, MD at Excel Diagnostics, Houston, TX, USA.

Company/Sponsor signatory: Rich Messmann, MD, MHS, MSc

Statement: This study was conducted in compliance with Good Clinical Practice (GCP).

Report date: 08 January 2021

Earlier reports from the same study: None.

2 Synopsis

Name of product: ^{177}Lu -PSMA-617

Study number: PSMA-617-02

Title of study: PSMA-Directed Endoradiotherapy of Castration-Resistant Prostate Cancer (RESIST-PC). A Phase 2 Clinical Trial.

Investigators and Study Centers

Principal Investigators: Johannes Czernin, MD at the University of California, Los Angeles, CA, USA and Ebrahim Delpassand, MD at Excel Diagnostics, Houston, TX, USA.

Publication (reference): None

Study period:

Study initiation date: 05 Jul 2017 (first subject enrolled)

Early termination date: 22 Jun 2018

Last subject last visit: 15 Jan 2020

Study completion date: 08 Jan 2021

Phase of development (phase of this clinical study): Phase 2

Objectives:

Primary objectives

1. To assess the clinical safety of ^{177}Lu -PSMA-617 by evaluation of adverse events (AEs) using the Common Terminology Criteria for Adverse Events (CTCAE)
2. To assess the efficacy as defined by proportion of patients with PSA response $\geq 50\%$ decline at 12 weeks from baseline

Secondary objectives for each treatment dose

1. To determine maximum PSA decline from baseline.
2. To determine PSA progression-free survival (PFS), measured from start of study treatment until death or PSA progression.
3. To determine radiographic PFS, measured from start of study treatment until death or radiographic progression using RECIST 1.1/PCWG criteria.
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST V1.1 stable disease (SD), partial response (PR) or complete response (CR).
5. To determine impact on bone pain level.
6. To determine impact on quality of life (QOL).
7. To determine impact on performance status (as measured by the ECOG).

Due to only limited imaging and PSA data being available for the number of actual patients enrolled being 71 as compared with the planned sample size of 200, the efficacy endpoints (i.e., rPFS and DCR, PSA response) were not analyzed as planned in the protocol as described in SAP Version 2.0 dated 15-May-2020. The modeling approaches stated in the protocol could not be carried out as there was insufficient data to perform the analyses that would allow for appropriate evaluation of effectiveness.

However, clinicaltrials.gov requires all available data for primary and secondary endpoints to be disclosed. Therefore, SAP Addendum 1 dated 15-Dec-2020 describes the analyses for clinicaltrials.gov using the

limited data available. Due to only limited imaging and PSA data being available, some secondary endpoints could not be analyzed as planned in the protocol.

Methodology:

This was a 1:1 randomized, open-label, multicenter, prospective trial conducted at 2 treatment centers. Upon meeting the inclusion/exclusion criteria, the patients were randomized into 2 treatment doses. RLT was performed by repeated intravenous (IV) application of 6.0 GBq ($\pm 10\%$) or 7.4 GBq ($\pm 10\%$) ^{177}Lu -PSMA-617 every 8 \pm 1 weeks until reaching 4 cycles or threshold maximum dose to the kidneys of 23 Gy. All doses after labeling were presented in buffered solution for IV injection.

Treatment was continued until either of the following conditions applied:

- PSA/radiographic progression at ≥ 12 weeks
- Completion of 4 cycles of ^{177}Lu -PSMA-617
- 23 Gy kidney dose was exceeded by the next cycle as estimated by dosimetry
- Patient withdrawal (e.g., appearance of intolerable AEs)

Dosimetry data for the first 20 patients in this study (16 from UCLA and 4 from Excel Diagnostics) were analyzed and it was found that the permitted renal dose of 23 Gy was not exceeded in any patient after 4 cycles, demonstrating overall favorable renal dosimetry and dosimetry was no longer required per protocol Amendment 1, Protocol Version 2..

Number of subjects (planned and analyzed):

In total, 200 subjects with histologically proven prostate cancer and mCRPC were scheduled to be enrolled. However, enrollment closed earlier than initially planned, and only 71 patients were enrolled: 28 patients in the ITT population (23 in the Safety population) were enrolled in the ^{177}Lu -PSMA-617 6.0 GBq groups; 43 patients in the ITT population (41 patients in the Safety Population) were enrolled in the ^{177}Lu -PSMA-617 7.4 GBq groups.

Diagnosis and main criteria for inclusion:

In total, 200 subjects with histologically proven prostate cancer and mCRPC were scheduled to be enrolled. However, enrollment closed earlier than initially planned.

The inclusion criteria stayed consistent throughout the study with the exception of removing the dosimetry requirements.

To qualify for enrollment, some of the main study-specific inclusion criteria that subjects were required to meet were:

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy or any equivalent PSMA-directed imaging

To be eligible for the study, a patient must have had a positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy or any equivalent PSMA-directed imaging. To determine eligibility, local readers determined the mean PSMA expression of lesions by visual assessment and assigning a score as defined below, where a score of +, ++, +++ was considered positive and the patient was eligible for the study:

- Score 0, no reported PSMA expression in tumor lesions with uptake below blood pool
- Score +, low reported PSMA expression in tumor lesions with uptake equal to or above blood pool and lower than liver

- Score ++, intermediate reported PSMA expression in tumor lesions with uptake equal to or above liver and lower than salivary glands
 - Score +++, high reported PSMA expression in tumor lesions with uptake equal to or above salivary glands
6. ECOG - Performance Score (PS) of 0 - 2
 7. Sufficient bone marrow capacity as defined by WBC \geq 2500/ μ l, PLT count \geq 100.000/ μ l, Hb \geq 9.9 g/dl, and ANC \geq 1500 mm³ for the first cycle, and WBC \geq 2.000/ μ l, PLT count \geq 75.000/ μ l, Hb \geq 8.9 g/dl, and ANC \geq 1000 mm³ for the subsequent cycles
 8. Patients enrolling in this trial should have received either enzalutamide or abiraterone.

The exclusion criteria were revised during the study with the implementation of Amendment 1, Protocol Version 2 on 07 June 2017.

Patients were excluded from the study if they met any of the following criteria:

1. Less than 6 weeks since their last myelosuppressive therapy (including docetaxel, cabazitaxel, ²²³Ra, ¹⁵³Sm)
2. Glomerular filtration rate (GFR) $<$ 40 ml/min
3. Serum creatinine $>$ 1.5 x upper limit of normal (ULN); AST and ALT $>$ 5 x ULN
4. Urinary tract obstruction or marked hydronephrosis
5. Diffuse bone marrow involvement confirmed by super-scans.

Study Conduct:

The RESIST-PC study (NCT03042312), also identified as PSMA-617-02, began on 05 July 2017 as an Investigator Initiated Trial (sponsored by Drs. Czernin and Delpassand) under US IND 133661 (sponsored by Radiomedix). On 02 October 2017, Endocyte acquired worldwide rights to develop and commercialize PSMA-617. On 31 October 2017 Endocyte and Radiomedix entered into agreement that enabled the transfer of the US IND 133661 from Radiomedix to Endocyte and the IND was transferred from Radiomedix to Endocyte on 14 November 2017. Subsequently, Endocyte submitted a protocol amendment changing the sponsor of the RESIST-PC study to Endocyte on 01 June 2018.

After the acquisition of PSMA-617, Endocyte re-evaluated the clinical development plan for PSMA-617 and the RESIST-PC study was not consistent with the overall strategy of the company. Therefore, Endocyte, in agreement with the two principal investigators, decided to terminate enrollment to the RESIST-PC study prior to enrolling all 200 planned patients. All patients who had been identified to Endocyte as "engaged" as of 22 June 2018 were allowed to continue the screening process through 31 July 2018. All patients that were enrolled in the RESIST-PC study continued to follow the protocol visit schedule through to completion of the study

Test therapies, dose, and mode of administration:

Utilizing published average organ uptake values, the cumulative absorbed dose after 4 cycles of either 6.0 GBq or 7.4 GBq ¹⁷⁷Lu-PSMA-617 was estimated to be 31.2 - 38.5 Gy and 17.8 - 21.9 Gy for the salivary glands and kidneys, respectively. The doses were administered IV in a hospital/clinic setting.

There was no reference therapy given.

Criteria for evaluation

Efficacy:

The efficacy objectives were not examined due to the early ending of enrollment into the study leading to the significantly smaller sample size than the planned 200 patients and the investigator's inconsistency of data collection; the modelling approaches stated in the protocol could not be carried out as there was insufficient data to perform the analyses to draw reliable conclusions.

Safety:

Adverse events (AE) were coded using MedDRA version 22.1, by SOC and PT. Serious AEs were graded according to the NCI CTCAE criteria version 4.0 while AEs were described by severity (i.e., Mild, Moderate, Severe).

In case a patient experienced the same event more than once, the maximum toxicity grade was presented. In all AE tables, multiple occurrences of the same adverse events (AEs) occurring in one individual were counted only once.

Definition of Treatment Emergent Adverse Event (TEAE)

A randomized TEAE was defined as an AE that was not present prior to initiation of randomized treatment, defined as first dose of ¹⁷⁷Lu-PSMA-617, but appeared following treatment, or was present at treatment initiation but worsened during treatment. An AE that was present at treatment initiation but resolved and then reappeared while the patient was on treatment was a TEAE (regardless of the intensity of the AE when the treatment was initiated). Any event that was considered study drug-related (stated as possible, probably, definite relationship, or missing assessment of relatedness), regardless of the start date of the event, or any event that worsened in toxicity grade while on treatment or was subsequently considered study drug-related by the investigator was also defined as a TEAE. The treatment-emergent period was defined as the period from the date of initiation of randomized treatment up to 30 days after date of last administration of study treatment or the day prior to the initiation of subsequent anticancer treatment, whichever occurred first.

Randomized Treatment Adverse Events

A summary table including the number of patients with at least one event, was presented for the AE variables below.

- TEAE^{1, 3}
- Serious TEAE^{1, 2, 3}
- Drug-related TEAE¹
- Serious drug related TEAE¹
- TEAE leading to reduction of ¹⁷⁷Lu-PSMA-617 dose, other than those as allowed by the protocol.¹
- TEAE leading to permanent discontinuation of ¹⁷⁷Lu-PSMA-617 treatment¹
- Fatal TEAE¹

¹AE variables were tabulated by SOC and PT.

²Serious AE variables were tabulated by SOC and PT by CTCAE grade.

³AE variables were tabulated by SOC and PT, CTCAE grade (serious AEs) or severity grade (TEAEs), and cycle.

A listing for each patient included the same variables as mentioned above and included action taken regarding ¹⁷⁷Lu-PSMA-617.

Deaths

All deaths are summarized by treatment groups (6.0 vs. 7.4 GBq ¹⁷⁷Lu-PSMA-617) and overall with the End of Treatment status table; deaths are also listed.

• Safety assessments: Laboratory tests (e.g., CMP, eGFR, CBC)

Laboratory tests were performed at baseline (within 72 hours of the first treatment dose) and every 2 weeks (\pm 3

days) after the first dose of study medication, continued until 12 weeks after the last dose, and every 3 months (\pm 1 week) thereafter, until the end of follow-up visits (24 months from 1st therapy date); or upon disease progression. The CBC, eGFR, and CMP within 2 weeks of each subsequent treatment cycle were used to assess the eligibility of the corresponding treatment cycle.

• **Safety assessments: Telephone follow-up**

Telephone follow-up: 7 days (\pm 3 days) after each of the treatment cycles, and for the follow-up phase every 3 months (\pm 1 month) until the end of the follow-up visits (24 months).

Statistical methods:

Sample size calculations were based on the primary endpoint of this protocol, i.e., baseline to 12-week decline in tumor marker level (PSA) \geq 50% pooling all patients treated with ¹⁷⁷Lu-PSMA-617 regardless of treatment dose of 6.0 GBq or 7.4 GBq. It was estimated that the proportion of patients who would meet the primary endpoint would range between 38% and 65% for both treatment doses. The following null hypothesis was thus defined: Less than 40% of patients would reach the endpoint after ¹⁷⁷Lu-PSMA-617 regardless of the treatment dose of 6.0 GBq or 7.4 GBq. ¹⁷⁷Lu-PSMA-617 would therefore be considered worthy of further study if 50% or more patients met the endpoint and not worthy of further study if 40% and less achieved the endpoint. This rationale was adapted from a single-arm study on patients with mCRPC with the same endpoint definition. A power analysis was performed for the two-sided binomial test (beta 0.2, alpha 0.05) to measure the efficacy of ¹⁷⁷Lu-PSMA-617: it was determined that a sample size of 200 patients achieved 78% power (beta 0.2) at a given alpha of 0.05 to detect a change of 10%, 40% versus 50%, for pooled overall response rate of the two treatment groups.

The final sample size was 71 patients as per changes described previously.

Demographic and background characteristics:

The demographic and baseline characteristics were representative of the mCRPC population and were generally comparable between the ITT Population across the 2 treatment groups and are presented in the following table:

Demographic and Baseline Characteristics (ITT Population)

Study Population: ITT Population	¹⁷⁷ Lu-PSMA-617 6.0 GBq N = 28	¹⁷⁷ Lu-PSMA-617 7.4 GBq N = 43	Overall N = 71
Age (years)			
n	28	43	71
Mean (SD)	72.1 (8.39)	69.1 (8.62)	70.3 (8.60)
Median	72.0	69.0	71.0
Q1; Q3	67.5; 76.0	62.0; 77.0	65.0; 76.0
Min; Max	55; 95	54; 84	54; 95
Age Group n (%)			
n	28	43	71
< 65 years	4 (14.3)	13 (30.2)	17 (23.9)
\geq 65 years	24 (85.7)	30 (69.8)	54 (76.1)
Race			
n	28	43	71
Asian	1 (3.6)	1 (2.3)	2 (2.8)
Black or African American	0	1 (2.3)	1 (1.4)

Study Population: ITT Population	¹⁷⁷ Lu-PSMA-617 6.0 GBq N = 28	¹⁷⁷ Lu-PSMA-617 7.4 GBq N = 43	Overall N = 71
White	26 (92.9)	41 (95.3)	67 (94.4)
Other	1 (3.6)	0	1 (1.4)
Ethnicity			
n	28	43	71
Hispanic or Latino	0	1 (2.3)	1 (1.4)
Not Hispanic or Latino	27 (96.4)	40 (93.0)	67 (94.4)
Not Reported	1 (3.6)	2 (4.7)	3 (4.2)
Weight (kg) at Baseline			
n	23	41	64
Mean (SD)	81.19 (12.101)	85.20; (19.386)	83.76 (17.132)
Median	79.50	79.00	79.25
Q1; Q3	72.20; 92.20	71.30; 99.90	71.45; 96.45
Min; Max	61.2; 104.4	50.4; 125.5	50.4; 125.5
Height (cm) at Baseline			
n	23	41	64
Mean (SD)	176.33 (6.388)	176.63 (8.205)	176.52 (7.551)
Median	175.00	178.00	177.00
Q1; Q3	172.00; 180.30	173.00; 182.00	173.00; 182.00
Min; Max	165.0; 190.0	152.0; 188.0	152.0; 190.0
Pulse Oximetry (%) at Baseline			
n	20	38	58
Mean (SD)	98.20 (1.576)	97.97 (1.652)	98.05 (1.616)
Median	99.00	99.00	99.00
Q1; Q3	98.00; 99.00	97.00; 99.00	97.00; 99.00
Min; Max	94.0; 100.0	94.0; 100.0	94.0; 100.0

Safety results:

An overview of TEAEs, including relationship to study drug (as assessed by the Investigators) is presented in the following table:

Summary Table of Treatment Emergent Adverse Events – Safety Population

	¹⁷⁷ Lu-PSMA-617 6.0 GBq N = 23 n (%)	¹⁷⁷ Lu-PSMA-617 7.4 GBq N = 41 n (%)	Overall N = 64 n (%)
Patients with at least one TEAE	22 (95.7)	39 (95.1)	61 (95.3)
Patients with at least one serious TEAE	4 (17.4)	8 (19.5)	12 (18.8)
Patients with at least one drug-related TEAE	20 (87.0)	37 (90.2)	57 (89.1)
Patients with at least one serious drug-related TEAE	1 (4.3)	4 (9.8)	5 (7.8)
Patients having a TEAE leading to reduction of ¹⁷⁷ Lu-PSMA-617	0	2 (4.9)	2 (3.1)
Patients having a TEAE leading to discontinuation of ¹⁷⁷ Lu-PSMA-617	0	1 (2.4)	1 (1.6)
TEAEs leading to death (during treatment, not counting follow-up)	2 (8.7)	1 (2.4)	3 (4.7)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients. TEAE = is considered study drug-related if relatedness is recorded as possible, probably, definite, or when the value is missing.

- Because of the enrollment closing earlier than initially planned and missing data resulting in a significantly smaller sample size than the initially planned of 200 patients, efficacy endpoints were listed and not summarized other than for clinicaltrials.gov purposes. Specifically, the PSA related efficacy was analyzed with the small sample size and the investigators' inconsistent timing of PSA data collection for clinicaltrials.gov. Limited imaging data were available, and thus the associated endpoints (i.e., radiographic Progression-free survival [rPFS] and disease control rate [DCR]) were not summarized. Summary statistics were presented for EPIC 26 Quality of life (QoL) questionnaire and ECOG performance status. Bone level pain data were only listed due to the nature of the data (i.e., free text pain levels).
- Seven deaths were reported during the study and in the follow-up phase (i.e., from enrollment through the 24 months follow-up); 4/28 (14.3%) and 3/43 (7.0%) subjects died during the study in the 6.0 GBq and 7.4 GBq treatment arms, respectively, 7/71 (9.9%) overall. Three deaths were fatal TEAEs; 3 deaths were fatal, unrelated adverse events occurring more than 30 days after last dose of ¹⁷⁷Lu-PSMA-617; and 1 death occurred in a patient prior to receiving his first dose of ¹⁷⁷Lu-PSMA-617. TEAEs leading to deaths were 2/23 (8.7%) and 1/41 (2.4%) respectively, and 3/64 (4.7%) in the 6.0 and 7.4 GBq arms, overall.
 - There was one death in the 7.4 GBq group determined to be possibly related due to gastrointestinal hemorrhage and unknown causes (72 days after last dose); and one death (94 days after last dose) in the 6.0 GBq group determined to be possibly related due to a subdural hematoma. The third TEAE leading to death was metastases to central nervous system (68 days after last dose) in the 6.0 GBq group, determined to be unrelated to study treatment.
- In general, the patients with any event were comparable in all severity between the groups (95.7% in the 6.0 GBq group compared with 95.1% in the 7.4 GBq group, and the overall group, 95.3%) and slightly higher in the 7.4 GBq group when compared with the 6.0 GBq (17.1% compared with 8.7%, respectively). Overall ¹⁷⁷Lu-PSMA-617 was well tolerated irrespective of the dose.
- The most common TEAEs in the 6.0 GBq treatment arm, the 7.4 GBq treatment arm respectively and overall, were dry mouth (47.8%; 63.4%; 57.8%, respectively), fatigue (56.5%; 51.2%; 53.1%), nausea (52.2%; 43.9%; 46.9%), and diarrhoea (13.0%; 31.7%; 25.0%).
- Older patients aged ≥ 65 years did not have a greater frequency of TEAEs than the patients aged below 65 years.

- There were no clinically significant changes in vital signs in the 2 treatment groups.
- There were no clinically significant findings in ECGs in the 2 treatment groups.
- No trend to creatinine increase was observed during the study. The kidney dosimetry caveat of the dosing procedures were considered unnecessary and deleted from the protocol at the implementation of Study Protocol Amendment 1 on 07 January 2017.
- There were 4 patients with Grade 3 AST and/or ALT levels above the normal ranges that were primarily explained by metastases of the cancer to the liver and were not considered to be related to the study treatment.
- ALP mean values over time during treatment had no substantial change, but individual patients had variable increase or decrease of ALP that was compatible with the disease. During follow up, the number of patients was too small to draw any conclusion.
- There was not a trend of increasing frequency of shifts from normal to abnormal over time for any hematologic parameter.
- These overall hematology findings for the patient population showed no relevant differences between the groups. The data must be interpreted with caution due to the small number of patients with data at some of the timepoints.

Conclusion:

The safety profile of ¹⁷⁷Lu-PSMA-617 in this study was as anticipated based on the mechanism of action and is generally consistent with previous ¹⁷⁷Lu-PSMA-617 experiences as documented in literature in similar populations of patients with mCRPC. There were no efficacy conclusions in this study. Overall, ¹⁷⁷Lu-PSMA-617 was well-tolerated and the safety was manageable with established medical support.

Date of report:

08-Jan-2021

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4

List of abbreviations and definition of terms

ADT	Androgen deprivation therapy
AE	Adverse event
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
ALP	Alkaline phosphatase
AST	Aspartate aminotransferase
BOR	Best overall response
bpm	beats per minute
BUN	Blood urea nitrogen
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CMP	Comprehensive metabolic panel
CR	Complete response
CRF	Case report form
CSR	Clinical Study Report
CT	Computed tomography
DCR	Disease Control Rate
DSMB	Data Safety Monitoring Board
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
eGFR	estimated Glomerular Filtration Rate
EMA	European Medicines Agency
FDA	Food and Drug Administration
GBq	Gigabecquerel
GCP	Good Clinical Practice
GGT	Gamma-glutamyl transferase
GH	Growth hormone
GMP	Good Manufacturing Practices
Hct	Hematocrit
Hb	Hemoglobin
IND	Investigational New Drug (application)

ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intent-to-treat
¹⁷⁷ Lu	Lutetium
mCRPC	metastatic Castration Resistant Prostate Cancer
mo	months
MR	Magnetic resonance
MRI	Magnetic resonance imaging
N/A	Not applicable
NAAD	Novel androgen axis drug
NCI CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NDA	New Drug Application
PD	Progressive disease
PET/CT	Positron Emission Tomography/Computed Tomography
PFS	Progression-free survival
PI	Primary Investigator
PR	Partial response
PSA	Prostate-specific antigen
PSMA	Prostate-specific membrane antigen
PT	Preferred term
QoL	Quality of life
RECIST	Response Evaluation Criteria In Solid Tumors
RLT	Radioligand therapy
rPFS	Radiographic progression-free survival
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Stable disease
SE	Standard error

SOC	System organ class
UCLA	University of California in Los Angeles
ULN	Upper limit of normal
US	United States
WHO-DD	World Health Organization Drug Dictionary

5 Ethics

5.1 Independent Ethics Committee or Institutional Review Board

The study protocol and all amendments have been reviewed by the Institutional Review Board (IRB) for each center as listed in [Appendix 16.1.3](#).

5.2 Ethical conduct of the study

The study was conducted according to ICH E6 Guideline for Good Clinical Practice that have their origin in the Declaration of Helsinki.

5.3 Subject information and consent

Informed consent was obtained from each subject in writing at screening before any study specific procedure was performed. The study was explained to the subject by the Investigator or designee, who answered any questions, and written information was also provided.

Samples of the written information given to each subject and the consent form are presented in [Appendix 16.1.3](#).

6 Investigators and study administrative structure

The administrative structure of the study, including internal and external participants, is described in [Appendix 16.1.4-Section 1](#).

A list of investigators, their affiliations and their qualifications, plus that of other important staff, as well as members of the Data Safety Monitoring Board, are provided in [Appendix 16.1.4-Section 2](#).

The RESIST-PC study (NCT03042312), also identified as PSMA-617-02, began on 05 July 2017 as an Investigator Initiated Trial (sponsored by Drs. Czernin and Delpassand) under US IND 133661 (sponsored by Radiomedix). On 02 October 2017, Endocyte acquired worldwide rights to develop and commercialize PSMA-617 and on 31 October 2017 Endocyte and Radiomedix entered into agreement that enabled the transfer of the US IND 133661 from Radiomedix to Endocyte. Subsequently, Endocyte submitted a protocol amendment changing the sponsor of the RESIST-PC study to Endocyte on 01 June 2018.

After the acquisition of PSMA-617, Endocyte re-evaluated the clinical development plan for PSMA-617 and the RESIST-PC study was not consistent with the overall strategy of the company. Therefore, Endocyte, in agreement with the two principal investigators, decided to terminate enrollment to the RESIST-PC study prior to enrolling all 200 planned patients. All patients who had been identified to Endocyte as “engaged” as of 22 June 2018 were allowed to continue the screening process through 31 July 2018. All patients that were enrolled in the RESIST-PC study continued to follow the protocol visit schedule through to completion of the study.

Endocyte, Inc. is currently a part of Advanced Accelerator Applications (AAA), which is another Novartis company. Endocyte, Inc., AAA, and Novartis staff analyzed this study and authored this report. The signatures of the principal or coordinating Investigators, the Sponsor’s responsible medical officer, and the report authors are provided in [Appendix 16.1.5](#).

7 Introduction

Prostate cancer (PC) is the second leading cause of cancer-related death among men in the United States and the third leading cause of cancer-related death in Europe ([Siegel et al 2020](#) and [Malvezzi et al 2019](#)). At the time of this study conduct, there were four different classes of medical treatments that were shown to prolong survival among patients with mCRPC, including taxanes (docetaxel and cabazitaxel), androgen-signaling-targeted inhibitors (abiraterone and enzalutamide), immunotherapy (sipuleucel-T), and a bone-targeted radionuclide therapy (radium-223 dichloride). The therapeutic landscape is shifting towards treatment with life-extending therapies during all stages of the disease.

Targeted radioligand therapy (RLT) offers the possibility to treat cancer lesions in a specific and tumor-selective manner by exploiting cell surface receptors expressed on malignant cells. The prostate-specific membrane antigen (PSMA) is a potential target for PC therapy because it is highly expressed in PC, including mCRPC. Because of the low and restricted expression levels in normal tissues, PSMA has the potential to be a viable target for RLT with minimized radioactivity-related adverse effects. PSMA-targeted RLT utilizes radiolabeled small-molecule inhibitors of PSMA, which bind with high affinity to PSMA resulting in internalization and

retention within the targeted PC cell ([Ghosh and Heston 2004](#) and [Benešová et al 2015](#)) to identify and treat PSMA-positive mCRPC lesions.

PSMA-617 is a small molecule that is able to bind with high affinity to the extracellular domain of PSMA, has a high tumor uptake, and rapid plasma clearance. It can be labelled with lutetium-177 (^{177}Lu) for RLT. Beta particles emitted from ^{177}Lu have a short-range of ~1 mm, enabling delivery of high doses of radiation to tumors whilst minimizing damage to surrounding normal tissues. Preliminary clinical evidence indicates ^{177}Lu -PSMA-617 may demonstrate clinical benefit in patients with mCRPC in a setting where they had been exposed to chemotherapy and novel androgen axis drug (NAAD). These patients, being in advance stage of the disease, are often on multiple medical therapies for the disease and its complications as there is no recommended standard of care or sequence of treatment to use ([Ahmadzadehfar et al 2016](#), [Baum et al 2016](#), [Kratochwil et al 2016](#), [Rahbar et al 2017](#), [Hofman et al 2018](#), [Hofman et al 2019](#), and [Violet et al 2019](#)).

^{68}Ga -PSMA-11 (also called PSMA-HBED, Glu-CO-Lys(Ahx)-HBED-CC or DKFZ PSMA 11) is constructed using an urea-based targeting ligand and the gallium chelating moiety HBED CC ([Eder et al 2012](#), [Eder et al 2014](#)). The radioisotope gallium-68 (^{68}Ga) utilized with PSMA-11 is a β^+ emitting radionuclide with a 68-minute physical half-life, and a high emission yield, that makes it a suitable PET imaging agent ([Fendler et al 2017b](#)). ^{68}Ga -PSMA PET scanning has been used in the context of imaging diagnosis, patient selection for treatment, staging and biochemical recurrence of prostate cancer ([Fendler et al 2017b](#)) gathered in patients treated on the basis of compassionate use/expanded access and currently ongoing clinical trials listed on trial registries ([Zippel et al 2020](#)).

This randomized, open-label, multicenter, prospective Phase 2 study was designed to assess the efficacy and safety of ^{177}Lu -PSMA-617 in patients with progressive PSMA-positive metastatic Castrate-Resistant Prostate Cancer (mCRPC) in an investigator-initiated trial (IIT) (that was switched to a Sponsored study, as previously explained in [Section 6 Investigators and study administrative structure](#)).

This is an abbreviated CSR (aCSR) because of the enrollment ending earlier with 71 patients enrolled rather than the 200 patients that had been initially planned and therefore limited efficacy data collected during the study. See [Section 9.8.2 Other changes in study conduct](#).

8 Study objectives

8.1 Primary objectives

1. To assess the clinical safety of ^{177}Lu -PSMA-617 by evaluation of adverse events using the Common Terminology Criteria for Adverse Events (CTCAE)
2. To assess the efficacy as defined by proportion of patients with PSA response $\geq 50\%$ decline at 12 weeks from baseline

8.2 Secondary objectives for each treatment dose

1. To determine maximum PSA decline from baseline.
2. To determine PSA progression-free survival (PFS), measured from start of study

treatment until death or PSA progression.

3. To determine radiographic PFS, measured from start of study treatment until death or radiographic progression using RECIST 1.1/PCWG criteria.
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST V1.1 stable disease (SD), partial response (PR) or complete response (CR).
5. To determine impact on bone pain level.
6. To determine impact on quality of life (QOL).
7. To determine impact on performance status (as measured by the ECOG).

9 **Investigational plan**

9.1 **Study design**

This was a 1:1 randomized, open-label, multicenter, prospective trial conducted at 2 treatment centers. Upon meeting the inclusion/exclusion criteria, the patients were randomized into 2 treatment doses. RLT was performed by repeated intravenous (IV) application of 6.0 GBq (\pm 10%) or 7.4 GBq (\pm 10%) ^{177}Lu -PSMA-617 every 8 \pm 1 weeks until reaching 4 cycles or threshold maximum dose to the kidneys of 23 Gy. All doses after labeling were presented in buffered solution for IV injection.

Treatment was continued until either of the following conditions applied:

- PSA/radiographic progression at \geq 12 weeks
- Completion of 4 cycles of ^{177}Lu -PSMA-617
- 23 Gy kidney dose was exceeded by the next cycle as estimated by dosimetry
- Patient withdrawal (e.g., appearance of intolerable AEs)

Dosimetry data for the first 20 patients in this study (16 from UCLA and 4 from Excel Diagnostics) were analyzed and it was found that the permitted renal dose of 23 Gy was not exceeded in any patient after 4 cycles, demonstrating overall favorable renal dosimetry and dosimetry was no longer required per protocol. The change in study conduct is reflected in subsequent protocol amendments (see [Section 9.8 Protocol amendments and other changes in the conduct of the study or planned analyses](#)). Dosimetry was required to be performed in the initial versions of the study according to dosimetry protocol (see Appendix 16.1.1-Protocol-Section 3.1) provided by Prof. [Name] ([Universitätsklinikum Würzburg Germany - Klinik und Poliklinik für Nuklearmedizin](#)) to determine dose to the kidneys.

In total, 200 subjects with histologically proven prostate cancer and mCRPC were scheduled to be enrolled. However, enrollment ended earlier than initially planned. For a complete explanation see [Section 9.8.2 Other changes in study conduct](#).

For information regarding the timing of the efficacy and safety assessments, please refer to the Schedule of Events in the protocol in [Appendix 16.1.1-Protocol-Appendix 2](#).

9.2 Rationale of study design

9.2.1 Rationale for a regimen with multiple therapy cycles

Activity given during targeted radionuclide therapy for different types of cancer was limited by radiation dose to healthy organs. Based on dosimetry that measured the radiation dose to healthy organs, subsequent maximal cumulative activity could be calculated. To obtain optimal safety margin for patients, maximal cumulative activity was not given in one treatment session but approached by application of a defined fraction of this activity in several cycles. The administration of a standard activity over several treatment cycles allowed for early and individual estimation of radiation dose and tolerability.

The efficacy and safety of a sequential approach was proven in patients with ²²³Ra therapy for mCRPC ([Parker et al 2013](#)) and in patients with ¹⁷⁷Lu-DOTATATE therapy for mid-gut NET ([Strosberg et al 2015](#)) each in prospective, double-blind, randomized, international, and multicenter Phase 3 trials. Based on this evidence targeted PSMA RLT was performed by sequential applications of ¹⁷⁷Lu-PSMA-617 with treatment-free intervals.

9.2.2 Rationale for 8-week intervals between dosing

The 8-week interval dosing selected for this study was based on known safety considerations reported previously in other studies for RLT. The highest level of evidence for subacute AEs after radionuclide therapy was published for patients with non-Hodgkin's lymphoma by Witzig et al ([Witzig et al 2002](#)), who analyzed safety and efficacy of ⁹⁰Y-ibritumomab tiuxetan in 73 patients in a prospective Phase 3 randomized trial. This study reported neutrophil, platelet, and hemoglobin nadir approximately 6 weeks after application of the beta emitter RLT. Based on this study, ¹⁷⁷Lu-PSMA-617 RLT was performed by sequential applications with a treatment-free interval of 8 weeks to minimize any potential risk of repeated ¹⁷⁷Lu-PSMA-617 therapy upon hematologic parameters or other organ systems should they occur. This scheme was also supported by safety data from the Phase 3 NETTER-1 trial with ¹⁷⁷Lu- DOTATATE in patients with midgut NET ([Strosberg et al 2015](#)), in which ¹⁷⁷Lu-DOTATATE was administered at 7- to 9-week intervals: the rate of severe AEs was below 10% for 115 patients in the treatment arm.

9.2.3 Rationale for dose regimen

Based on other available data, Ahmadzadehfar et al ([Ahmadzadehfar et al 2016](#)) reported safety and efficacy after application of a mean activity of 6.0 GBq ¹⁷⁷Lu-PSMA-617 in 24 patients with mCRPC. Patients were treated with up to 2 cycles of ¹⁷⁷Lu-PSMA-617 RLT at 8-week intervals. Grade 3 hematotoxicity occurred in 2 patients. No nephrotoxicity or hepatotoxicity grade ≥ 3 was documented. Kratochwil et al ([Kratochwil et al 2016](#)) reported safety and efficacy after repeated application of ¹⁷⁷Lu-PSMA-617 in 30 mCRPC patients: 19 of 30 patients (63%) received 6.0 GBq ¹⁷⁷Lu-PSMA-617 every 2 months. One patient developed grade 3 anemia, and another patient grade 3 thrombocytopenia. Both patients had diffuse pattern of bone marrow infiltration at baseline. Phase 3 data for ¹⁷⁷Lu-DOTATATE, a similar RLT for mid-gut NET patients, demonstrated a rate of severe AEs below 10% after application of 4 cycles of 7.4 GBq in 115 patients ([Strosberg et al 2015](#)). Thus, evidence indicated that repeated applications of 6.0

GBq or 7.4 GBq ^{177}Lu -PSMA-617 RLT would be well-tolerated with low to very low rates of toxicities and SAEs.

The salivary glands and kidneys receive the highest radiation dose following ^{177}Lu -PSMA-617 treatment, according to published dosimetry studies (Kabasakal et al 2015; Delker et al 2016). Utilizing these published average organ uptake values, the cumulative absorbed dose after 4 cycles of either 6.0 GBq or 7.4 GBq ^{177}Lu -PSMA-617 is estimated to be 31.2 – 38.5 Gy and 17.8 – 21.9 Gy for the salivary glands and kidneys, respectively. While the cumulative kidney exposure based on these estimates is below the reported external beam radiation therapy (ERBT) dose limits reported in the literature, the exposure to the salivary glands may exceed the recommended cumulative exposure thresholds (Emami et al 1991; Grundmann et al 2009; Hey et al 2011; Emami et al 2013; Gensheimer et al 2014). However, these dose limits are perhaps overly conservative due to the low-dose rate exposure from systemic radiotherapy compared to high dose ERBT. It has been suggested that a ^{177}Lu -PSMA-617 total cumulative dose of as much as 50 GBq could be administered without long-term salivary gland toxicity (Yadav et al 2017, Kabasakal et al 2017; Virgolini et al 2018). The similarly estimated cumulative absorbed dose to the bone marrow is approximately 0.9 – 1.2 Gy, for 4 cycles of 6.0 or 7.4 GBq respectively, which is below the generally accepted 2 Gy bone marrow radiation threshold (Kwekkeboom et al 2003).

9.3 Study population

In total, 200 patients with histologically proven mCRPC were planned to be enrolled; however, enrollment was stopped at 71 patients that were allowed to continue receiving study treatment as planned (see [9.8.2 Other changes in study conduct](#) for further explanation).

9.3.1 Inclusion criteria

The inclusion criteria stayed consistent throughout the study with the exception of Amendment 3 and are presented in their entirety in the protocol in [Appendix 16.1.1-Protocol-Section 4.2](#).

To qualify for enrollment, some of the main study-specific inclusion criteria that subjects were required to meet were:

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy or any equivalent PSMA-directed imaging

To be eligible for the study, a patient must have had a positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy or any equivalent PSMA-directed imaging. To determine eligibility, local readers determined the mean PSMA expression of lesions by visual assessment and assigning a score as

defined below, where a score of +, ++, +++ was considered positive and the patient was eligible for the study:

- Score 0, no reported PSMA expression in tumor lesions with uptake below blood pool
- Score +, low reported PSMA expression in tumor lesions with uptake equal to or above blood pool and lower than liver
- Score ++, intermediate reported PSMA expression in tumor lesions with uptake equal to or above liver and lower than salivary glands
- Score +++, high reported PSMA expression in tumor lesions with uptake equal to or above salivary glands

6. ECOG – Performance Score (PS) of 0 - 2
7. Sufficient bone marrow capacity as defined by $\text{WBC} \geq 2500/\mu\text{l}$, $\text{PLT count} \geq 100.000/\mu\text{l}$, $\text{Hb} \geq 9.9 \text{ g/dl}$, and $\text{ANC} \geq 1500 \text{ mm}^3$ for the first cycle, and $\text{WBC} \geq 2.000/\mu\text{l}$, $\text{PLT count} \geq 75.000/\mu\text{l}$, $\text{Hb} \geq 8.9 \text{ g/dl}$, and $\text{ANC} \geq 1000 \text{ mm}^3$ for the subsequent cycles
8. Patients enrolling in this trial should have received either enzalutamide or abiraterone.

9.3.2 Exclusion criteria

The exclusion criteria were revised during the study with the implementation of [Amendment 2](#) on 07 June 2017 and are presented in the protocol and protocol amendments in [Appendix 16.1.1-Protocol-Section 4.3](#).

Patients were excluded from the study if they met any of the following criteria:

1. Less than 6 weeks since their last myelosuppressive therapy (including docetaxel, cabazitaxel, ^{223}Ra , ^{153}Sm)
2. Glomerular filtration rate (GFR) $< 40 \text{ ml/min}$
3. Serum creatinine $> 1.5 \times$ upper limit of normal (ULN); AST and ALT $> 5 \times$ ULN
4. Urinary tract obstruction or marked hydronephrosis
5. Diffuse bone marrow involvement confirmed by super-scans.

9.3.3 Treatments administered

9.3.3.1 Method of treatment randomization assignment

Randomization was performed in accordance with [Vickers 2006](#). In order to obtain adequate “allocation concealment” a list of random allocations was created for patients 1 through 200. This list was stored at the Investigators’ sites and was not modified. The list was only accessible for researchers or study personnel not actively involved in the recruitment process.

9.3.3.2 Medication and treatments: $^{177}\text{Lu-PSMA-617}$

Patients were randomized into one of two treatment doses; RLT by repeated IV application of 6.0 GBq ($\pm 10\%$, Arm 1) or 7.4 GBq ($\pm 10\%$, Arm 2) $^{177}\text{Lu-PSMA-617}$ every 8 ± 1 weeks; RLT was administered until completing 4 cycles or reaching threshold maximum dose to the kidneys of 23 Gy as determined by dosimetry. Doses could be modified as necessary, as described per [9.3.3.3 Dose modification](#). This occurred for the first part of the study; however, after Protocol Amendment 4.0 was initiated ([9.8.1 Protocol amendments](#)) mandatory dosimetry was eliminated and no kidney dose was assessed. Cold ice packs in the region of salivary glands was to start 30 minutes prior to administration of $^{177}\text{Lu-PSMA-617}$ and continue for 4 hours. $^{177}\text{Lu-PSMA-617}$ was to be infused over approximately 15-30 minutes using an infusion pump.

9.3.3.3 Dose modification

In some circumstances, it may have been necessary to suspend treatment with $^{177}\text{Lu-PSMA-617}$, adapt the posology (i.e., administer half activity), or even definitively stop administration, as described in the protocol (see [Appendix 16.1.1-Protocol-Section 3.5](#)).

9.4 Concurrent therapies and treatments

9.4.1 Concurrent radiotherapy (Safety Population)

Patients were permitted to receive concurrent radiotherapy as permitted by the protocol (see [Appendix 16.1.1](#)).

9.4.2 Concurrent other treatments (Safety Population)

Patients were permitted to receive concurrent other treatment as permitted by the protocol (see [Appendix 16.1.1](#)).

9.4.3 Early study termination

The investigator may have withdrawn a patient from the study for any of the following reasons:

1. Protocol violation
2. Serious or intolerable AE (that in the opinion of the investigator required the patient's discontinuation)
3. Investigator withdrew the patient (at the investigator's discretion for reasons other than an AE)
4. Sponsor terminated the study
5. Subject requested to be discontinued from the study
6. Subject was lost to follow-up.

During the course of the study patients had the right to withdraw their consent at any time without need for explaining the reason of consent withdrawal to the Investigator or Sponsor. The PIs closely monitored patients during the study and considered terminating investigational product administration or any other trial related procedures in order to maintain the safety of patients, if necessary. In cases of withdrawal either in the patient's favor or the PIs decision due

to safety- or technical issues, withdrawn subjects were replaced (if possible) to maintain data integrity; however, follow-up visits were continued to maintain the safety of patients based on the visits as outlined in the protocol.

Please see [Section 9.8.2 Other changes in study conduct](#) for the description of early study termination.

9.4.3.1 Treatment accountability

Treatment was administered by study staff as described in the protocol in [Appendix 16.1.1-Protocol-Section 5.6](#).

9.4.3.2 Treatment compliance

¹⁷⁷Lu-PSMA-617 was administered only at the investigational site under the direction of the Investigator.

9.5 Study assessments

9.5.1 Visit schedule

The visit schedule is described in the protocol in [Appendix 16.1.1-Protocol-Appendix 2](#).

9.5.2 Efficacy assessments

Additional details are described in the protocol in [Appendix 16.1.1-Protocol-Appendix 2](#) and are not being further discussed in this abbreviated report.

9.5.3 Safety assessments

Additional details are described in the protocol in, see [Appendix 16.1.1](#).

9.5.4 Adverse Events

Adverse events (AE) were coded using MedDRA version 22.1, by SOC and PT. Serious AEs were graded according to the NCI CTCAE criteria version 4.0 while AEs were described by severity (i.e., Mild, Moderate, Severe).

In case a patient experienced the same event more than once, the maximum toxicity grade was presented.

In all AE tables, multiple occurrences of the same adverse events (AEs) occurring in one individual were counted only once.

Definition of Treatment Emergent Adverse Event (TEAE)

A randomized TEAE was defined as an AE that was not present prior to initiation of randomized treatment, defined as first dose of ¹⁷⁷Lu-PSMA-617, but appeared following treatment, or was present at treatment initiation but worsened during treatment. An AE that was present at treatment initiation but resolved and then reappeared while the patient was on treatment was a TEAE (regardless of the intensity of the AE when the treatment was initiated).

Any event that was considered study drug-related (stated as possible, probably, definite relationship, or missing assessment of relatedness), regardless of the start date of the event, or any event that worsened in toxicity grade while on treatment or was subsequently considered study drug-related by the investigator was also defined as a TEAE.

The treatment-emergent period was defined as the period from the date of initiation of randomized treatment up to 30 days after date of last administration of study treatment or the day prior to the initiation of subsequent anticancer treatment, whichever occurred first.

Randomized Treatment Adverse Events

A summary table including the number of patients with at least one event, was presented for the AE variables below:

- TEAE^{1, 3}
- Serious TEAE^{1, 2, 3}
- Drug-related TEAE¹
- Serious drug related TEAE¹
- TEAE leading to reduction of ¹⁷⁷Lu-PSMA-617 dose, other than those as allowed by the protocol.¹
- TEAE leading to permanent discontinuation of ¹⁷⁷Lu-PSMA-617 treatment¹
- Fatal TEAE¹

¹AE variables were tabulated by SOC and PT.

²Serious AE variables were tabulated by SOC and PT by CTCAE grade.

³AE variables were tabulated by SOC and PT, CTCAE grade (serious AEs) or severity grade (TEAEs), and cycle.

A listing for each patient included the same variables as mentioned above and included action taken regarding ¹⁷⁷Lu-PSMA-617.

Deaths

All deaths are summarized by treatment groups (6.0 vs. 7.4 GBq ¹⁷⁷Lu-PSMA-617) and overall with the End of Treatment status table; deaths are also listed in [Section 14.3.3](#).

9.5.4.1 Safety assessments: Laboratory tests (e.g., CMP, eGFR, CBC)

The following laboratory tests were performed at baseline (within 72 hours of the first treatment dose) and every 2 weeks (\pm 3 days) after the first dose of study medication, continued until 12 weeks after the last dose, and every 3 months (\pm 1 week) thereafter, until the end of follow-up visits (24 months from 1st therapy date); or upon disease progression. The CBC, eGFR, and CMP within 2 weeks of each subsequent treatment cycle were used to assess the eligibility of the corresponding treatment cycle.

9.5.4.2 Safety assessments: Telephone follow-up

Telephone follow-up: 7 days (\pm 3 days) after each of the treatment cycles, and for the follow-up phase every 3 months (\pm 1 month) until the end of the follow-up visits (24 months).

9.6 Data quality assurance

9.6.1 Monitoring

The responsibility for site monitoring resided with Pharmtrace throughout the study and was supported by Endocyte as needed once Endocyte became study Sponsor. At a site initiation visit prior to study initiation, Pharmtrace reviewed the protocol and data capture requirements with the investigators and their staff at Study Investigator Meetings where the eCRF manuals were presented and reviewed. During the study, the field monitor visited the site as specified in the Monitoring Plan to check the accuracy and completeness of subject records, the accuracy of entries on the eCRFs, the adherence to the protocol and to Good Clinical Practice, the progress of enrollment, and to ensure that study treatment was being stored, dispensed, and accounted for according to specifications, and to ensure adequate oversight of the study by the investigator. Key study personnel were required to be available to assist the field monitor during these visits. The study followed Pharmtrace SOPs.

The Investigators were required to maintain source documents for each subject in the study, consisting of case and visit notes (hospital or clinic medical records) containing demographic and medical information, laboratory data, electrocardiograms (ECG), and the results of any other tests or assessments. All information on eCRFs was required to be traceable to these source documents in the subject's file. The Investigator was also required to keep the original informed consent forms signed by the subject (a signed copy was given to the subject).

The Investigator provided the monitor access to all relevant source documents to confirm their consistency with the eCRF entries. Source Data Review and Verification was completed in accordance with the study-specific monitoring plan. Information in source documents about the identity of the subjects was not collected to be used in the study.

9.6.2 Data collection

Designated investigator staff entered the data required by the protocol into the electronic data/electronic CRF (eCRF) system; however this system was not available at the start of the study, so data were entered in paper CRFs from 05 Jul 2017 until 13 Dec 2017 until the eCRF system became available. The training materials used during the site initiation visits to train the staff are included in the Trial Master Folder (TMF), staff were not given access to the system until adequately trained. Documented training was completed by the designated investigator site staff before their access was granted.

Automatic validation procedures within the system checked for data discrepancies during and after data entry and, by generating appropriate error messages, allowed the data to be confirmed or corrected online by the designated investigator site staff. The Investigators were responsible for verifying that the data entered into the eCRFs were complete and accurate. After database lock the Investigators received copies of the subjects' data for archiving at the investigational sites.

9.6.3 Database management and quality control

Data for this study were collected across two different data systems/vendors.

- OpenClinica eDC – Site entered all required patient data into this web-based eCRF system. Access for OpenClinica was tracked by Pharmtrace, with defined access and roster review processes. At the start of the study the investigators did their own safety reporting in their own system and reported SUSARs directly to the FDA.
- PrimeVigilance became responsible for the pharmacovigilance safety database for this study once Endocyte became the Sponsor for this study. Previous safety databases were not easily available. Sites faxed or emailed patient SAE forms to PrimeVigilance who entered the data into the safety database. PrimeVigilance used their established data system to enter and review data sent to them by the sites. They followed their own processes for system validation.

Pharmtrace, the data management vendor, performed the UAT/validation testing for the eCRF system.

Data reconciliation across the various data sources was conducted monthly with issues clarified via queries back to the sites.

Medical coding was performed within OpenClinica on an ongoing basis during the study. MedDRA v. 21 was used at the beginning of the study, and the dictionary version was upgraded during the study to MedDRA v 22 then to v.22.1. There was no coding of concomitant medications in this study as directed per the protocol.

9.6.4 Audits and health authority inspections

9.6.4.1 Audits

No investigator site audits were conducted for this study.

9.6.4.2 Health authority inspections

There were no known health authority inspections reflected in the IND records or disclosed by the investigators during the IIT portion of the study. There were no health authority inspections conducted at investigator sites during the Sponsor portion of this study.

9.7 Statistical methods

9.7.1 Data analysis

The planned analyses and statistical methods are described in the final version of the statistical analysis plan that was written and approved prior to database lock in [Appendix 16.1.9](#).

9.7.2 Sample size calculation

Sample size calculations were based on the primary endpoint of this protocol, i.e., baseline to 12-week decline in tumor marker level (PSA) $\geq 50\%$ ([Danila et al 2010](#)) pooling all patients treated with ^{177}Lu -PSMA-617 regardless of treatment dose of 6.0 GBq or 7.4 GBq. Based on a publication ([Rahbar et al 2017](#)), it was estimated that the proportion of patients who would meet the primary endpoint would range between 38% and 65% for both treatment doses. The following null hypothesis was thus defined: Less than 40% of patients would reach the endpoint after ^{177}Lu -PSMA-617 regardless of the treatment dose of 6.0 GBq or 7.4 GBq. ^{177}Lu -PSMA-

617 would therefore be considered worthy of further study if 50% or more patients met the endpoint and not worthy of further study if 40% and less achieved the endpoint. This rationale was adapted from a single-arm study on patients with mCRPC with the same endpoint definition (Danila et al 2010). A power analysis was performed for the two-sided binomial test (beta 0.2, alpha 0.05) to measure the efficacy of ¹⁷⁷Lu-PSMA-617: it was determined that a sample size of 200 patients achieved 78% power (beta 0.2) at a given alpha of 0.05 to detect a change of 10%, 40% versus 50%, for pooled overall response rate of the two treatment groups.

The final sample size was 71 patients as per changes described in [9.8 Protocol amendments and other changes in the conduct of the study or planned analyses](#).

9.8 Protocol amendments and other changes in the conduct of the study or planned analyses

9.8.1 Protocol amendments

The study protocol originated on 28 December 2016 and was amended 4 times (3 times as an IIT and the fourth time as a Sponsored [Endocyte] study, and are presented in [Appendix 16.1.1 Protocol](#)). The previous sections in this report describes the protocol as amended through to the final version ([Protocol Amendment 4, Version 5.0](#)). The key features of each amendment are given in [Table 9-1 Protocol Amendments](#).

Table 9-1 Protocol Amendments

Version and date	Summary of key changes
Amendment 1 07 June 2017	<ul style="list-style-type: none">• Removed the dosimetry requirement.• Revised dose modification criteria.• Revised study procedures.• Updated the Pharmacovigilance Designee for the reporting of safety information.• Updated study activities.• Updated administrative considerations.• Revised the reference section.• Revised the list of appendices.
Amendment 2 29 June 2017	<ul style="list-style-type: none">• Revised exclusion criteria.
Amendment 3 18 September 2017	<ul style="list-style-type: none">• Revised inclusion criteria.• Revised safety assessments.• Revised the investigation plan.• Elaborated on study treatments.• Revised reporting safety information.• Revised study activities and procedures, e.g., acquisition plan for individual dosimetry and ECG procedures.• Revised the Data Safety Monitoring Board and Data Safety Monitoring Plan sections.• Revised the administrative considerations.• Added Appendix V: Dosimetry Protocol and updated of the List of Appendices.

Version and date	Summary of key changes
Amendment 4 01 June 2018	Enrollment was completed under Amendment 4. <ul style="list-style-type: none">• Changed the study Sponsor to Endocyte.• Modified the study identifier from NCT03042312 to PSMA-617-02.• Revised the Pharmacovigilance designee contact.• Revised study activities.• Revised the planned statistical methods.• Revised the administrative considerations.• Revised the references.• Updated the List of Appendices.

9.8.2 Other changes in study conduct

The RESIST-PC study (NCT03042312), also identified as PSMA-617-02, began on 05 July 2017 as an Investigator Initiated Trial (sponsored by Drs. Czernin and Delpassand) under US IND 133661 (sponsored by Radiomedix). On 02 October 2017, Endocyte acquired worldwide rights to develop and commercialize PSMA-617 and on 31 October 2017 Endocyte and Radiomedix entered into agreement that enabled the transfer of the US IND 133661 from Radiomedix to Endocyte. Subsequently, Endocyte submitted a protocol amendment changing the sponsor of the RESIST-PC study to Endocyte on 01 June 2018.

After the acquisition of PSMA-617, Endocyte re-evaluated the clinical development plan for PSMA-617 and the RESIST-PC study was not consistent with the overall strategy of the company. Therefore, Endocyte, in agreement with the two principal investigators, decided to terminate enrollment to the RESIST-PC study prior to enrolling all 200 planned patients. All patients who had been identified to Endocyte as “engaged” as of 22 June 2018 were allowed to continue the screening process through 31 July 2018. All patients that were enrolled in the RESIST-PC study continued to follow the protocol visit schedule through to completion of the study.

9.8.3 Changes in planned analyses

Due to only limited imaging and PSA data being available for the number of actual patients enrolled being 71 as compared with the planned sample size of 200, the efficacy endpoints (i.e., rPFS and DCR, PSA response) were not analyzed as planned in the protocol as described in SAP Version 2.0 dated 15-May-2020. The modeling approaches stated in the protocol could not be carried out as there was insufficient data to perform the analyses that would allow for appropriate evaluation of effectiveness.

However, clinicaltrials.gov requires all available data for primary and secondary endpoints to be disclosed. Therefore, SAP Addendum 1 dated 15-Dec-2020 describes the analyses for clinicaltrials.gov using the limited data available. Due to only limited imaging and PSA data being available, some secondary endpoints could not be analyzed as planned in the protocol and the changes to the analyses are described in the SAP Addendum 1.

The available data in the form of Tables and Listings for primary efficacy results as $\geq 50\%$ decline in PSA at 12-weeks from baseline are presented in [Table 14.2.1.1 Primary Efficacy](#)

($\geq 50\%$ decline in PSA at Week 12) and in Listing 16.2.7.1 Laboratory Results – Chemistry. Other tables for secondary endpoints are in Appendix 16.1.9: Table 14.2.1.2 Maximum PSA response; Table 14.2.1.3 PSA Progression and death; Table 14.2.2.1 RESIST 1.1 Overall response by follow-up assessment; Table 14.2.2.2 RESIST 1.1 Disease control rate by follow-up assessment visit; Table 14.2.3 PCWG3 Bone scan clinical impression by visit.

10 Study patients

10.1 Analysis Sets (All Patients)

A total of 71 patients signed informed consent and were randomized. Patients who failed screening, i.e., were not eligible based on inclusion/exclusion criteria (screen failures) and patients who withdrew consent during the screening period were still randomized (included in the ITT Population) but not treated (included in the Safety Population). According to a Note to File dated 08 Jan 2018 randomization occurred frequently in this study prior to on-site wet ink informed consent but no actual treatment was begun without a patient signed, dated informed consent form (ICF) countersigned by a study physician.

- The ICF was faxed to the patient, protocol events were reviewed with the patient, and the patient was asked if they had any questions and all the questions were answered by a study staff physician via telephone.
- The patient signed the informed consent and faxed it back, and the faxed document was documented in the patient binder. The relevant screening laboratory tests were started locally, if necessary.
- Another original copy was signed when the patient was in the clinic in the presence of a study staff physician. Any additional questions were answered and that original ICF was also stored in the patient's binder.
- Any changes to the ICF requested by the IRB were signed again by the patient even with administrative changes, i.e., Sponsor changes, Principal Investigator Changes.

There were seven patients (9.9%) randomized but not treated; 5 patients discontinued the study due to an occurrence of a condition that prevented the patient's participation in the study (negative PSMA scan [2 patients in 6.0 GBq arm], too weak for treatment [1 patient each in 6.0 GBq and 7.4 GBq arms], low blood counts [1 patient in 7.4 GBq arm]), 1 patient withdrew consent (6.0 GBq arm), and 1 patient died (6.0 GBq arm) (Source: Listing 16.2.1.1).

An imbalance between the arms (i.e., 40% patients assigned to the 6.0 GBq group and 60% assigned to the 7.4 GBq group) was observed that can be attributed to the early termination of the study.

Analysis Sets are presented in Table 10-1 Analysis Sets (All Patients) (Source: Table 14.1.1).

Table 10-1 Analysis Sets (All Patients)

Study Population: All Patients	¹⁷⁷ Lu-PSMA 617 6.0 GBq N = 28 n (%)	¹⁷⁷ Lu-PSMA-617 7.4 GBq N = 43 n (%)	Overall N = 71 n (%)
Patients who signed informed consent	-	-	71 (100)
Patients in the ITT Population ^a	28 (100)	43 (100)	71 (100)
Patients in the Safety Population ^b	23 (82.1)	41 (95.3)	64 (90.1)

^a Intent-to-treat (ITT) population = All randomized patients. Patients were included in the treatment arm to which they were randomized regardless of actual treatment received.

^b Safety population = The subset of patients in the ITT who received at least one dose of randomized therapy. Patients were included in the treatment arm corresponding to the actual treatment received.

Source: [Table 14.1.1](#).

10.2 Patient Disposition (ITT Population)

Patients were to receive up to 4 cycles of ¹⁷⁷Lu-PSMA-617 until one of the following conditions for discontinuation of treatment occurred: completion of 4 RLT cycles, PSA/radiographic progression at \geq 12 weeks, 23 Gy kidney dose was exceeded by the next cycle as estimated by dosimetry, or patient withdrawal (e.g., appearance of intolerable AEs). Patients were then followed for discontinuation from study until one of the following conditions occurred: 24 months after the first treatment, progression by RECIST 1.1/PCWG criteria, or death. Patients who completed the 24 month follow-up were considered as completing follow-up. Patients are noted to have discontinued early from the study for Occurrence of Condition; discontinued early from the study due to occurrence of conditions preventing the patient's participation in the study. One treated patient had ongoing, moderate thrombocytopenia that delayed ¹⁷⁷Lu-PSMA-617 dosing longer than 12 weeks and another 5 patients were never treated with ¹⁷⁷Lu-PSMA-617, as described in [Section 10.1](#). The total number of deaths, from enrollment through the 24 months follow-up, included 7 patients; for 5 of them death was reported as a reason of study completion and 2 patients withdrew consent from the study before their death was reported by the site. (Source: [Listing 16.2.1.1](#)).

- Seven deaths were reported during the study (i.e., from enrollment through the 24 months follow-up); 4/28 (14.3%) and 3/43 (7.0%) subjects died during the study in the 6.0 GBq and 7.4 GBq treatment arms, respectively, 7/71 (9.9%) overall. Three deaths were reported as fatal TEAEs; 3 deaths were reported as unrelated adverse events occurring more than 30 days after last dose of ¹⁷⁷Lu-PSMA-617; and 1 death occurred in a patient prior to receiving his first dose of ¹⁷⁷Lu-PSMA-617. TEAEs leading to deaths were 2/23 (8.7%) and 1/41 (2.4%) respectively, and 3/64 (4.7%) overall. (Sources: [Table 14.3.1.9.1](#), [Listing 16.2.12](#), [Listing 16.2.1.1](#))
 - There was one death in the 7.4 GBq group determined to be possibly related due to gastrointestinal hemorrhage and unknown causes; and one death in the 6.0 GBq group determined to be possibly related due to a subdural hematoma. The third TEAE leading to death was metastases to central nervous system in the 6.0 GBq group determined to be unrelated.

The reasons causing a patient to end treatment in the study are presented in [Table 10-2 Patient Disposition \(ITT Population\)](#) (Source: [Table 14.1.2](#)).

Table 10-2 Patient Disposition (ITT Population)

Study Population: ITT Population	177Lu-PSMA-617 6.0 GBq N = 28 n (%)	177Lu-PSMA-617 7.4 GBq N = 43 n (%)	Overall N = 71 n (%)
Patients who discontinued from 177Lu-PSMA-617	23 (82.1)	41 (95.3)	64 (90.1)
Reason for discontinuation from 177Lu-PSMA-617			
Completion of 4 RLT cycles	10 (35.7)	19 (44.2)	29 (40.8)
Patient withdrawal	6 (21.4)	6 (14.0)	12 (16.9)
PSA/radiographic progression at ≥ 12 weeks	7 (25.0)	16 (37.2)	23 (32.4)
Patients who completed the study	18 (64.3)	31 (72.1)	49 (69.0)
Reason for study completion			
Completed	1 (3.6)	0	1 (1.4)
Death	3 (10.7)	2 (4.7)	5 (7.0)
Progressive disease	14 (50.0)	29 (67.4)	43 (60.6)
Patients who early discontinued from the study	10 (35.7)	12 (27.9)	22 (31.0)
Reason for early discontinuation from the study			
Administrative reason	1 (3.6)	1 (2.3)	2 (2.8)
Adverse event	0	1 (2.3)	1 (1.4)
Lost to follow-up	1 (3.6)	3 (7.0)	4 (5.6)
Occurrence of condition ^a	4 (14.3)	2 (4.7)	6 (8.5)
Patient withdrawal	4 (14.3)	5 (11.6)	9 (12.7)
Total number of deaths	4 (14.3)	3 (7.0)	7 (9.9)

^a Any occurrence of conditions that prevented the patient's participation in the study.

AE = Adverse event; RLT = Radioligand therapy.

Source: [Table 14.1.2](#).

10.3 Protocol deviations (ITT Population)

A total of 31 subjects (43.7%) [45 protocol deviations] experienced important protocol deviations in the overall group: 9 subjects (32.1%) [13 protocol deviations] in the 177Lu-PSMA-617 6.0 GBq group; and 22 subjects (51.2%) [32 deviations] in the 7.4 GBq group. The summary of important protocol deviations is presented in [Table 10-3 Summary of Important Protocol Deviations](#); all protocol deviations are also presented in Source: [Table 14.1.3.1](#). It's

deemed that the occurrence of these PDs did not have an impact on the safety results or conclusions in this study.

As detailed in [Table 14.1.3.1](#), the majority of these protocol deviations include procedures not done or done outside of the protocol required timing [laboratory tests and PSA levels not done or done out of window].

The majority of the trial patient population enrolled at these two clinical sites were patients who were referred specifically for this trial. As such, they were managed locally by their medical oncologist or urologist and visited the trial site mostly for protocol treatment. The required protocol procedures were completed locally when possible or alternatively, completed local to the trial site at the time of patients coming for treatments. Patient compliance was also difficult as patients were not used to the required increased frequency of protocol procedures (laboratory tests and PSA levels) (Source: [Listing 16.2.1.2](#)).

Table 10-3 Summary of Important Protocol Deviations (ITT Population)

Study Population: ITT Population	^{177}Lu-PSMA-617 6.0 GBq N = 28 n (%) [m]	^{177}Lu-PSMA-617 7.4 GBq N = 43 n (%) [m]	Overall N = 71 n (%) [m]
Patient with at least one important protocol deviation	9 (32.1) [13]	22 (51.2) [32]	31 (43.7) [45]
Patient with a procedure violation	8 (28.6) [12]	20 (46.5) [29]	28 (39.4) [41]
Patient with informed consent procedure violation	1 (3.6) [1]	2 (4.7) [2]	3 (4.2) [3]
Inclusion/exclusion criteria violation	0	1 (2.3) [1]	1 (1.4) [1]

n was the number of subjects, m was the number of protocol deviations.

Source: [Table 14.1.3.2](#).

10.4 Demographic and other baseline characteristics

10.4.1 Demographic and baseline characteristics (ITT Population)

The demographic and baseline characteristics were representative of the mCRPC population and were generally comparable between the ITT Population across the 2 treatment groups and are presented in [Table 10-4 Demographic and Baseline Characteristics \(ITT Population\)](#) (Source: [Table 14.1.4.1](#)).

Table 10-4 Demographic and Baseline Characteristics (ITT Population)

Study Population: ITT Population	^{177}Lu-PSMA-617 6.0 GBq N = 28	^{177}Lu-PSMA-617 7.4 GBq N = 43	Overall N = 71
Age (years)			
n	28	43	71
Mean (SD)	72.1 (8.39)	69.1 (8.62)	70.3 (8.60)
Median	72.0	69.0	71.0
Q1; Q3	67.5; 76.0	62.0; 77.0	65.0; 76.0
Min; Max	55; 95	54; 84	54; 95

Study Population: ITT Population	$^{177}\text{Lu-PSMA-617}$ 6.0 GBq N = 28	$^{177}\text{Lu-PSMA-617}$ 7.4 GBq N = 43	Overall N = 71
Age Group n (%)			
n	28	43	71
< 65 years	4 (14.3)	13 (30.2)	17 (23.9)
≥ 65 years	24 (85.7)	30 (69.8)	54 (76.1)
Race			
n	28	43	71
Asian	1 (3.6)	1 (2.3)	2 (2.8)
Black or African American	0	1 (2.3)	1 (1.4)
White	26 (92.9)	41 (95.3)	67 (94.4)
Other	1 (3.6)	0	1 (1.4)
Ethnicity			
n	28	43	71
Hispanic or Latino	0	1 (2.3)	1 (1.4)
Not Hispanic or Latino	27 (96.4)	40 (93.0)	67 (94.4)
Not Reported	1 (3.6)	2 (4.7)	3 (4.2)
Weight (kg) at Baseline			
n	23	41	64
Mean (SD)	81.19 (12.101)	85.20; (19.386)	83.76 (17.132)
Median	79.50	79.00	79.25
Q1; Q3	72.20; 92.20	71.30; 99.90	71.45; 96.45
Min; Max	61.2; 104.4	50.4; 125.5	50.4; 125.5
Height (cm) at Baseline			
n	23	41	64
Mean (SD)	176.33 (6.388)	176.63 (8.205)	176.52 (7.551)
Median	175.00	178.00	177.00
Q1; Q3	172.00; 180.30	173.00; 182.00	173.00; 182.00
Min; Max	165.0; 190.0	152.0; 188.0	152.0; 190.0
Pulse Oximetry (%) at Baseline			
n	20	38	58
Mean (SD)	98.20 (1.576)	97.97 (1.652)	98.05 (1.616)
Median	99.00	99.00	99.00
Q1; Q3	98.00; 99.00	97.00; 99.00	97.00; 99.00
Min; Max	94.0; 100.0	94.0; 100.0	94.0; 100.0

Source: [Table 14.1.4.1.](#)

10.4.2 Baseline disease characteristics (ITT Population)

The baseline disease characteristics were generally comparable between the treatment groups with some minor differences. The study was stopped early and the number of patients is low, so comparisons should not be emphasized.

The baseline disease characteristics for the ITT Population are presented in [Table 10-5 Baseline Disease Characteristics \(ITT Population\)](#) (Source: [Table 14.1.5.1](#)).

Table 10-5 Baseline Disease Characteristics (ITT Population)

Study Population: ITT Population	¹⁷⁷ Lu-PSMA-617 6.0 GBq N = 28	¹⁷⁷ Lu-PSMA-617 7.4 GBq N = 43	Overall N = 71
Time since initial prostate cancer diagnosis (years)			
n	23	41	64
Mean (SD)	8.06 (7.323)	8.06 (7.152)	8.06 (7.156)
Median	4.59	6.00	4.96
Q1; Q3	3.02; 13.73	2.66; 11.99	2.72; 12.17
Min; Max	0.7; 27.2	0.3; 25.9	0.3; 27.2
Initial histopathological classification n (%)			
n	28	43	71
Adenocarcinoma	28 (100)	43 (100)	71 (100)
Other	0	0	0
Unknown	0	0	0
Initial Gleason Score, categorized n (%)			
n	28	43	71
2-3	0	0	0
4-7	7 (25.0)	13 (30.2)	20 (28.2)
8-10	20 (71.4)	26 (60.5)	46 (64.8)
Unknown	1 (3.6)	4 (9.3)	5 (7.0)
Baseline PSA doubling time (months)			
n	26	41	67
Mean (SD)	4.35 (7.131)	3.89 (3.977)	4.07 (5.376)
Median	1.91	2.46	2.07
Q1; Q3	1.18; 3.38	1.41; 4.90	1.22; 4.90
Min; Max	0.0; 31.4	0.0; 20.7	0.0; 31.4
Baseline PSA doubling time (months), Categorized n (%)			
n	26	41	67
≤ 6	21 (80.8)	33 (80.5)	54 (80.6)
> 6	5 (19.2)	8 (19.5)	13 (19.4)
Baseline PSA (ug/L)			
n	12	19	31
Mean (SD)	208.86 (391.804)	287.92 (830.231)	257.32 (686.578)

Table 10-5 Baseline Disease Characteristics (ITT Population)

Study Population: ITT Population	$^{177}\text{Lu-PSMA-617}$ 6.0 GBq N = 28	$^{177}\text{Lu-PSMA-617}$ 7.4 GBq N = 43	Overall N = 71
Median	46.03	19.34	23.66
Q1; Q3	11.28; 99.35	5.34; 68.00	5.59; 93.20
Min; Max	0.6; 1166.0	1.9; 3499.0	0.6; 3499.0

PSA = Prostate-specific antigen.

Source: [Table 14.1.5.1](#).

10.5 Medical history

Medical history for the ITT Population is presented in [Listing 16.2.3.2.1](#).

10.6 Prostate cancer treatment history

10.6.1 Prostate cancer treatment history – chemotherapy (ITT Population)

Previous chemotherapy treatment history was consistent in the ITT Population between the 2 treatment groups, and was considered very similar without any relevant differences for the 2 groups for all parameters included in the table (as seen below). 58 (81.7%) patients in the ITT population had at least one prior chemotherapy treatment for prostate cancer prior to study enrollment. 57 (80.3%) patients had at least one prior taxane; 54 (76.1%) patients had docetaxel and 26 (36.6%) patients had cabazitaxel. Details about the prostate cancer treatment history – previous chemotherapy in the ITT population are presented in [Table 10-6 Prostate Cancer Treatment History – Previous Chemotherapy \(ITT Population\)](#), (Source: [Table 14.1.6.1](#)).

Table 10-6 Prostate Cancer Treatment History – Previous Chemotherapy (ITT Population)

Study Population: ITT Population	^{177}Lu -PSMA-617 6.0 GBq N = 28	^{177}Lu -PSMA-617 7.4 GBq N = 43	Overall N = 71
Number of prior therapies per patient			
n	22	36	58
Mean (SD)	2.5 (1.84)	2.3 (1.28)	2.4 (1.51)
Median	2.0	2.0	2.0
Q1; Q3	1.0; 3.0	1.0; 3.0	1.0; 3.0
Min; Max	1; 7	1; 5	1; 7
Type of prior therapies per patient, n (%)			
Cabazitaxel	9 (32.1)	17 (39.5)	26 (36.6)
Docetaxel	21 (75.0)	33 (76.7)	54 (76.1)
Other	9 (32.1)	18 (41.9)	27 (38.0)
Number of prior taxane-containing therapies per patient			
n	22	35	57
Mean (SD)	1.6 (0.90)	1.5 (0.66)	1.6 (0.75)
Median	1.0	1.0	1.0
Q1; Q3	1.0; 2.0	1.0; 2.0	1.0; 2.0
Min; Max	1; 4	1; 3	1; 4
Number of unique agents per patient			
n	22	36	58
Mean (SD)	2.2 (1.44)	2.2 (1.17)	2.2 (1.26)
Median	2.0	2.0	2.0
Q1; Q3	1.0; 3.0	1.0; 3.0	1.0; 3.0
Min; Max	1; 6	1; 5	1; 6

Source: [Table 14.1.6.1](#).

10.6.2 Prostate cancer treatment history – previous chemotherapy: last therapy (ITT Population)

Details about the last chemotherapy treatment received for prostate cancer prior to study enrollment has a lot of missing data, so this precludes making any conclusions from this data. 50 (70.4%) received taxane as their last therapy and the data in the ITT population are presented in [Table 10-7 Prostate Cancer Treatment History – Previous Chemotherapy: Last Therapy \(ITT Population\)](#), (Source: [Table 14.1.6.3](#)).

Table 10-7 Prostate Cancer Treatment History – Previous Chemotherapy: Last Therapy (ITT Population)

Study Population: ITT Population	¹⁷⁷ Lu-PSMA-617 6.0 GBq N = 28	¹⁷⁷ Lu-PSMA-617 7.4 GBq N = 43	Overall N = 71
Type of last prior therapy n (%)			
n	22	36	58
Docetaxel	13 (59.1)	16 (44.4)	29 (50.0)
Cabazitaxel	7 (31.8)	14 (38.9)	21 (36.2)
Other	2 (9.1)	6 (16.7)	8 (13.8)
Number of cycles per patient			
n	10	18	28
Mean (SD)	5.1 (1.29)	6.2 (2.09)	5.8 (1.89)
Median	5.5	6.0	6.0
Q1; Q3	4.0; 6.0	6.0; 6.0	4.5; 6.0
Min; Max	3; 7	3; 13	3; 13
Best overall response (BOR) to last therapy n (%)			
n	22	36	58
Complete response	0	1 (2.8)	1 (1.7)
Partial response	4 (18.2)	11 (30.6)	15 (25.9)
Stable disease	0	0	0
Progressive disease	6 (27.3)	6 (16.7)	12 (20.7)
Missing	12 (54.5)	18 (50.0)	30 (51.7)

Source: [Table 14.1.6.3](#).

10.6.3 Prostate cancer treatment history – previous other treatment (ITT Population)

71 (100%) patients overall in the ITT population had a history of at least one other treatment for prostate cancer prior to study enrollment, including 67 (94.4%) patients with abiraterone and 55 (77.5%) patients with enzalutamide. These were similar between treatment arms.

Details about the other treatments received for prostate cancer prior to study enrollment in the ITT population are presented in [Table 10-8 Prostate Cancer Treatment History – Other Treatment \(ITT Population\)](#), (Source: [Table 14.1.6.4](#)).

Table 10-8 Prostate Cancer Treatment History – Other Treatment (ITT Population)

Study Population: ITT Population	¹⁷⁷ Lu-PSMA-617 6.0 GBq N = 28	¹⁷⁷ Lu-PSMA-617 7.4 GBq N = 43	Overall N = 71
Patients with at least one prostate cancer-related other treatment n (%)	28 (100)	43 (100)	71 (100)
Type of other treatment n (%)			
Abiraterone	26 (92.9)	41 (95.3)	67 (94.4)
Cryotherapy	0	3 (7.0)	3 (4.2)
Enzalutamide	21 (75.0)	34 (79.1)	55 (77.5)
High-intensity focused ultrasound	0	1 (2.3)	1 (1.4)
Hormonal therapy	22 (78.6)	39 (90.7)	61 (85.9)
Other	20 (71.4)	31 (72.1)	51 (71.8)
Pelvic lymph node resection	1 (3.6)	3 (7.0)	4 (5.6)
Prostatectomy	12 (42.9)	19 (44.2)	31 (43.7)
Salvage lymph node resection	0	2 (4.7)	2 (2.8)
Standard ADT	19 (67.9)	22 (51.2)	41 (57.7)
TURP	2 (7.1)	2 (4.7)	4 (5.6)
Number of other prior treatments per patients			
n	28	43	71
Mean (SD)	6.3 (2.84)	6.4 (2.91)	6.4 (2.86)
Median	7.0	6.0	6.0
Q1; Q3	4.0; 7.5	4.0; 8.0	4.0; 8.0
Min; Max	2; 12	3; 13	2; 13

ADT = Androgen deprivation therapy; TURP = Transurethral resection of the prostate.

Source: [Table 14.1.6.4](#).

10.6.4 Prostate cancer treatment history – radiotherapy (ITT Population)

52 (73.2%) patients in the overall ITT population had a history of at least one prostate cancer-related radiotherapy prior to study enrollment. Almost 10% more of patients in the 7.4 GBq group had some type of radiotherapy compared with the patients in the 6.0 GBq group, but the number of cycles per patient did not differ between the 2 groups. We do not expect that this had any impact on the safety results interpretation or the safety conclusions. Details about the radiotherapy received for prostate cancer prior to study enrollment in the ITT population are presented in [Table 10-9 Prostate Cancer Treatment History – Radiotherapy \(ITT Population\)](#), (Source: [Table 14.1.6.5](#)).

Table 10-9 Prostate Cancer Treatment History – Radiotherapy (ITT Population)

Study Population: ITT Population	¹⁷⁷ Lu-PSMA-617 6.0 GBq N = 28	¹⁷⁷ Lu-PSMA-617 7.4 GBq N = 43	Overall N = 71
Patients with at least one prostate cancer-related radiotherapy	19 (67.9)	33 (76.7)	52 (73.2)
Type of radiotherapy n (%)			
Bone targeted therapy	1 (3.6)	6 (14.0)	7 (9.9)
Other	9 (32.1)	12 (27.9)	21 (29.6)
Primary EBRT	4 (14.3)	10 (23.3)	14 (19.7)
Radium 223*	5 (17.9)	14 (32.6)	19 (26.8)
Salvage EBRT	10 (35.7)	16 (37.2)	26 (36.6)
Number of prior radiotherapies per patients			
n	19	33	52
Mean (SD)	2.3 (1.28)	2.6 (1.76)	2.5 (1.60)
Median	2.0	2.0	2.0
Q1; Q3	1.0; 3.0	1.0; 3.0	1.0; 3.0
Min; Max	1; 5	1; 7	1; 7

* Is a radioligand therapy (RLT). (Was collected on the CRF as a radiotherapy even though it is a RLT.)

EBRT = External beam radiation therapy.

Source: [Table 14.1.6.5](#).

10.7 Concurrent therapies and treatments

10.7.1 Concurrent radiotherapy (Safety Population)

Only 2 patients overall, one patient in each treatment group, received concurrent radiotherapy. Patients who received at least one concurrent radiotherapy are presented in [Table 10-10 Concurrent Radiotherapy \(Safety Population\)](#), (Source: [Table 14.3.6.1.1](#)).

Table 10-10 Concurrent Radiotherapy (Safety Population)

Study Population: Safety Population	$^{177}\text{Lu-PSMA-617}$ 6.0 GBq N = 23 n (%)	$^{177}\text{Lu-PSMA-617}$ 7.4 GBq N = 41 n (%)	Overall N = 64 n (%)
Number of patients with at least one radiotherapy	1 (4.3)	1 (2.4)	2 (3.1)
Type of radiotherapy			
Bone targeted therapy	1 (4.3)	0	1 (1.6)
Salvage EBRT	0	1 (2.4)	1 (1.6)
Number of radiotherapies			
n	1	1	2
Mean (SD)	1.0 (NE)	1.0 (NE)	1.0 (0.00)
Median	1.0	1.0	1.0
Q1; Q3	1.0; 1.0	1.0; 1.0	1.0; 1.0
Min; Max	1; 1	1; 1	1; 1

EBRT = External beam radiation therapy; NE = Not evaluable.

Source: [Table 14.3.6.1.1](#).

10.7.2 Concurrent chemotherapy (Safety Population)

No patients received a concurrent chemotherapy. See Source [Table 14.3.6.3.1](#).

10.7.3 Concurrent other therapies (Safety Population)

The most frequently administered other concurrent therapies overall and for both treatment groups was hormonal therapy: 37 (57.8%) overall, 12 (52.2%) patients in the $^{177}\text{Lu-PSMA-617}$ 6.0 GBq treatment group, and 25 (61.0%) patients in the $^{177}\text{Lu-PSMA-617}$ 7.4 GBq treatment group. Overall patients received abiraterone concurrent therapy 8 (12.5%) and enzalutamide concurrent therapy 9 (14.1%). Patients who received at least one concurrent other treatments are presented in [Table 10-11 Concurrent Other Treatments \(Safety Population\)](#), (Source: [Table 14.3.6.2.1](#)).

Table 10-11 Concurrent Other Treatments (Safety Population)

Study Population: Safety Population	^{177}Lu-PSMA-617 6.0 GBq N = 23 n (%)	^{177}Lu-PSMA-617 7.4 GBq N = 41 n (%)	Overall N = 64 n (%)
Number of patients with at least one other treatment	13 (56.5)	27 (65.9)	40 (62.5)
Type of other treatments			
Abiraterone	3 (13.0)	5 (12.2)	8 (12.5)
Enzalutamide	2 (8.7)	7 (17.1)	9 (14.1)
Hormonal therapy	12 (52.2)	25 (61.0)	37 (57.8)
Other	10 (43.5)	16 (39.0)	26 (40.6)
Standard ADT	1 (4.3)	2 (4.9)	3 (4.7)
Number of other treatments			
n	13	27	40
Mean (SD)	2.8 (1.42)	2.4 (1.39)	2.5 (1.40)
Median	2.0	2.0	2.0
Q1; Q3	2.0; 3.0	1.0; 3.0	1.5; 3.0
Min; Max	1; 6	1; 6	1; 6

ADT = Androgen deprivation therapy.

Source: [Table 14.3.6.2.1](#).

10.8 Measurements of treatment compliance

All study drug administration was administered under the supervision of the Investigators. Details of study drug injections were captured in each patient's source documents. Exposure and compliance are described in [Section 12.1](#) and the extent of ^{177}Lu -PSMA-617 exposure by cycle and overall-Safety Population are presented in [Table 14.3.3.2.1](#).

10.9 Post-treatment therapies and treatments

10.9.1 Post-treatment chemotherapy (Safety Population)

No patients received post-treatment chemotherapy during this study. This information is presented in Source: [Table 14.3.6.3.2](#).

10.9.2 Post-treatment radiotherapy (Safety Population)

Only 2 patients overall, one in each treatment group, received post-treatment radiotherapy. Both patients, one each in the ^{177}Lu -PSMA-617 6.0 GBq group and ^{177}Lu -PSMA-617 7.4 GBq group received salvage external beam radiation therapy (EBRT), and are presented in [Table 10-12 Post-treatment Radiotherapy \(Safety Population\)](#), (Source: [Table 14.3.6.1.2](#)).

Table 10-12 Post-treatment Radiotherapy (Safety Population)

Study Population: Safety Population	^{177}Lu -PSMA-617 6.0 GBq N = 23 n (%)	^{177}Lu -PSMA-617 7.4 GBq N = 41 n (%)	Overall N = 64 n (%)
Patients with at least one post-treatment radiotherapy	1 (4.3)	1 (2.4)	2 (3.1)
Type of therapy			
Salvage EBRT	1 (4.3)	1 (2.4)	2 (3.1)
Number of radiotherapies			
n	1	1	2
Mean (SD)	1.0 (NE)	2.0 (NE)	1.5 (0.71)
Median	1.0	2.0	1.5
Q1; Q3	1.0; 1.0	2.0; 2.0	1.0; 2.0
Min; Max	1; 1	2; 2	1; 2

EBRT = External beam radiation therapy; NE = Not evaluable.

Source: [Table 14.3.6.1.2](#).

10.9.3 Post-treatment – Prostate cancer related other treatment (Safety Population)

Nine patients, overall: 4 patients in the 6.0 GBq ^{177}Lu -PSMA-617 treatment group and 5 patients in the 7.4 GBq ^{177}Lu -PSMA-617 treatment group received at least one post-treatment – other treatment and are presented in [Table 10-13 Post-treatment – Other Treatment \(Safety Population\)](#), (Source: [Table 14.3.6.2.2](#)).

Table 10-13 Post-treatment – Other Treatment (Safety Population)

Study Population: Safety Population	^{177}Lu -PSMA-617 6.0 GBq N = 23 n (%)	^{177}Lu -PSMA-617 7.4 GBq N = 41 n (%)	Overall N = 64 n (%)
Patients with at least one other treatment	4 (17.4)	5 (12.2)	9 (14.1)
Type of other therapy			
Abiraterone	1 (4.3)	2 (4.9)	3 (4.7)
Enzalutamide	1 (4.3)	2 (4.9)	3 (4.7)
Hormonal therapy	3 (13.0)	5 (12.2)	8 (12.5)
Other	1 (4.3)	2 (4.9)	3 (4.7)
Number of other treatments per patient			
n	4	5	9
Mean (SD)	2.0 (0.82)	2.6 (1.82)	2.3 (1.41)
Median	2.0	2.0	2.0
Q1; Q3	1.5; 2.5	1.0; 4.0	1.0; 3.0
Min; Max	1; 3	1; 5	1; 5

Source: [Table 14.3.6.2.2](#).

11 Efficacy results

The efficacy objectives were not examined due to the early ending of enrollment into the study leading to the significantly smaller sample size than the planned 200 patients and the investigator's inconsistency of data collection; the modelling approaches stated in the protocol could not be carried out as there was insufficient data to perform the analyses to draw reliable conclusions. Please see [Section 9.8.3 Changes in planned analyses](#) for efficacy tables created for clinicaltrials.gov.

11.1 Primary efficacy results

11.1.1 $\geq 50\%$ decline in PSA at Week 12 (ITT Population)

The underpowered study with limited and inconsistently collected data do not allow for any robust and reliable conclusions. The protocol-specified primary efficacy analyses were performed with missing and inconsistent data collection. The available data for primary efficacy results as $\geq 50\%$ decline in PSA at 12-weeks from baseline are presented in [Table 14.2.1.1 Primary Efficacy \(\$\geq 50\%\$ decline in PSA at Week 12\)](#) and in [Listing 16.2.7.1 Laboratory Results – Chemistry](#).

11.2 Secondary efficacy results

11.2.1 PSA results and change from baseline during treatment (ITT Population)

The PSA results and change from baseline during treatment in the ITT Population are presented in [Listing 16.2.7.1 Laboratory Results – Chemistry](#).

11.2.2 Quality of Life Questionnaire – EPIC 26 (ITT Population)

Quality of Life (QoL) questionnaire “EPIC 26” individual item responses were transformed into a domain summary score. The domain summary scores at each time point, along with the change from baseline, were summarized as a continuous variable at baseline and at 3, 6, 9, 12, 18, and 24 months after the start of ^{177}Lu -PSMA-617 RLT. Results are presented separately for both treatment groups (6.0 GBq vs. 7.4 GBq ^{177}Lu -PSMA-617), and overall in the Listings for the Quality of Life Questionnaires: EPIC 26 found in [Listings 16.2.5.2.1](#) through [16.2.5.2.5](#).

11.2.3 ECOG – Performance Status (ITT Population)

The changes in ECOG-PS from baseline were evaluated over time at 3, 6, 9, 18, and 24 months after the start of ^{177}Lu -PSMA-617 RLT. Mean baseline values were the same in the two treatment groups, with no relevant change from baseline ([Table 14.2.6.1](#)), with most of the patients remaining in the same category shift tables ([Table 14.2.6.2](#)) were provided for each follow-up time points, and there was no worsening in ECOG performance, with no patients with Grade 3 or Grade 4 in any post baseline visits. Results were presented separately for both treatment groups (6.0 GBq vs. 7.4 GBq ^{177}Lu -PSMA-617) and overall. ECOG-PS results are listed for the ITT Population in [Listing 16.2.5.3](#).

11.3 Statistical and analytical issues

Because the enrollment closed earlier than initially planned and the significantly smaller sample size than the planned 200, efficacy endpoints were listed and the modelling approaches stated in the protocol could not be carried out as there was insufficient data to perform the analyses to draw reliable conclusions. Specifically, the PSA related efficacy was analyzed with the small sample size and the investigator’s inconsistent timing of PSA data collection. Limited imaging data were available, and thus the associated endpoints (i.e., rPFS and DCR) were not summarized. Summary statistics were presented for EPIC 26 QoL questionnaire and ECOG performance status. Bone level pain data were only listed due to the nature of the data (i.e., free text pain levels).

11.3.1 Interim analyses

No interim analyses were planned in the protocol.

11.3.2 Subgroup analyses

All safety endpoints had summary statistics provided by the subgroups of age: < 65-year-old, \geq 65-years old.

11.3.3 Derived data and data sets

11.3.3.1 Rules for incomplete data

Missing data were not replaced. Only partial dates as described in the SAP were imputed for purposes of assignment of AEs to treatment emergent. The imputed dates were not listed.

Rules for incomplete data are described in detail in the SAP, which are presented in full in [Appendix 16.1.9](#).

11.3.3.2 General analyses definitions

The study day describes the day of the event of assessment date, relative to the reference date.

The study day is defined as:

- Study day = Assessment date - Reference date +1 if assessment date was after or on the reference date.
- Study day = Assessment date - Reference date if assessment date was before the reference date.

For visit's assignment during treatment phase for the laboratory tests and PSA, and for EPIC-26, for both treatment and follow-up phases, the reference date was defined as described in the SAP, which is presented in full in [Appendix 16.1.9](#).

Study day definitions and data collected for procedures according to the visit windows are described in detail in the SAP, which are presented in full in [Appendix 16.1.9](#).

A year length was defined as 365.25 days. A month length was 30.4375 days (365.25/12). If duration was reported in months, duration in days was divided by 30.4375; if duration was provided in days, duration in months was multiplied by 30.4375. If duration was reported in years, duration in days was divided by 365.25.

Baseline definitions:

For safety evaluations, the last available assessment on or before the date of start of study treatment was taken as “baseline” assessment. Evaluation of EPIC-26 used safety definition for baseline.

For PSA relevant safety analyses, baseline for safety evaluation definition was used with the Safety population. PSA data were only able to be listed.

ECOG Baseline was defined as last assessment before treatment start date.

12 Safety evaluation

12.1 Randomized treatment exposure

12.1.1 Randomized treatment exposure, summary of cycles (Safety Population)

Exposure to all treatment cycles were similar between both treatment groups.

The duration of study treatment for the mean (SD) number of patients in the ^{177}Lu -PSMA-617 6.0 GBq group was 3.49 (2.37) months; in the ^{177}Lu -PSMA-617 7.4 GBq group was 3.66 (2.01) months; and 3.60 (2.13) months overall. There was good compliance in both groups; patients received their intended dose for each cycle as per the protocol, based on dose and relative dose percentage as expected: cumulative dose for the 6.0 GBq group had a mean dose of 16.9 GBq, which was lower compared with the dose for the 7.4 GBq group, which had a mean dose of 21.4 GBq.

The randomized treatment exposure and summary of cycles is summarized in [Table 12-1 Randomized Treatment Exposure, Summary of Cycles \(Safety Population\)](#), (Source: Table 14.3.3.1.1).

Table 12-1 Randomized Treatment Exposure, Summary of Cycles (Safety Population)

Study Population: Safety Population	¹⁷⁷ Lu-PSMA-617 6.0 GBq N = 23	¹⁷⁷ Lu-PSMA-617 7.4 GBq N = 41	Overall N = 64
Duration of study treatment (months)			
n	23	41	64
Mean (SD)	3.49 (2.37)	3.66 (2.01)	3.60 (2.13)
Median	3.71	3.71	3.71
Q1; Q3	1.87; 5.75	1.87; 5.55	1.87; 5.55
Min; Max	0.0; 6.3	0.0; 7.7	0.0; 7.7
Number of cycles started by patient			
n	23	41	64
Mean (SD)	2.8 (1.23)	3.0 (1.07)	2.9 (1.12)
Median	3.0	3.0	3.0
Q1; Q3	2.0; 4.0	2.0; 4.0	2.0; 4.0
Min; Max	1; 4	1; 4	1; 4
Number of cycles started by patient categories n (%)			
n	23	41	64
1 cycle	5 (21.7)	3 (7.3)	8 (12.5)
2 cycles	4 (17.4)	15 (36.6)	19 (29.7)
3 cycles	4 (17.4)	4 (9.8)	8 (12.5)
4 cycles	10 (43.5)	19 (46.3)	29 (45.3)
Cumulative dose (GBq)			
n	23	41	64
Mean (SD)	16.913 (7.6668)	21.404 (8.0335)	19.790 (8.1376)
Median	18.583	22.287	19.917
Q1; Q3	11.392; 24.169	14.711; 29.454	14.297; 28.394
Min; Max	5.07; 24.91	6.92; 30.59	5.07; 30.59

Duration of study treatment (Months) = (Treatment end date –Treatment start date + 1) / 30.4375

Source: [Table 14.3.3.1.1](#) and [Table 14.3.3.2.1](#).

12.2 Treatment-emergent adverse events (TEAEs)

12.2.1 Overview of treatment emergent adverse events (TEAEs) (Safety Populations)

An overview of TEAEs, including relationship to study drug (as assessed by the Investigators) is presented in [Table 12-2 Summary Table of Adverse Events – Safety Population](#) (Source: [Table 14.3.1.1](#)).

Table 12-2 Summary Table of Treatment Emergent Adverse Events – Safety Population

	¹⁷⁷ Lu-PSMA-617 6.0 GBq N = 23 n (%)	¹⁷⁷ Lu-PSMA-617 7.4 GBq N = 41 n (%)	Overall N = 64 n (%)
Patients with at least one TEAE	22 (95.7)	39 (95.1)	61 (95.3)
Patients with at least one serious TEAE	4 (17.4)	8 (19.5)	12 (18.8)
Patients with at least one drug-related TEAE	20 (87.0)	37 (90.2)	57 (89.1)
Patients with at least one serious drug-related TEAE	1 (4.3)	4 (9.8)	5 (7.8)
Patients having a TEAE leading to reduction of ¹⁷⁷ Lu-PSMA-617	0	2 (4.9)	2 (3.1)
Patients having a TEAE leading to discontinuation of ¹⁷⁷ Lu-PSMA-617	0	1 (2.4)	1 (1.6)
TEAE leading to death	2 (8.7)	1 (2.4)	3 (4.7)

Results given as xx (xx x) where xx = number of patients with adverse events, (xx x) = percentage of patients.

TEAE = is considered study drug-related if relatedness is recorded as possible, probably, definite, or when the value is missing.

Source: [Table 14.3.1.1](#).

12.2.2 Display of TEAEs

12.2.2.1 Display of TEAEs by SOC (Safety Population)

In general, the patients with any event of any severity were comparable in frequency between the groups (95.7% in the 6.0 GBq group compared with 95.1% in the 7.4 GBq group, and the overall group, 95.3%) and the proportion of those with severe events were slightly higher in the 7.4 GBq group when compared with the 6.0 GBq (17.1% compared with 8.7%, respectively). The most frequently occurring TEAEs overall were in the Gastrointestinal disorders and the General disorders and administration site conditions SOCs (81.3% and 59.4% of patients, respectively). The most frequently occurring severe TEAEs were in the 7.4 GBq treatment arm and were in the Gastrointestinal disorders and the Respiratory, thoracic and mediastinal disorders SOCs (each 2 patients, 4.9%). The TEAEs are presented by MedDRA SOC in the Safety Population in [Table 12-3 TEAEs by MedDRA System Organ Class – Safety Population](#).

Table 12-3 TEAEs by MedDRA System Organ Class – Safety Population

	177Lu-PSMA-617 6.0 GBq (N=23) n (%)		177Lu-PSMA-617 7.4 GBq (N=41) n (%)		Overall (N=64) n (%)	
System Organ Class	All severity	Severe	All severity	Severe	All severity	Severe
Patient with Any Event	22 (95.7)	2 (8.7)	39 (95.1)	7 (17.1)	61 (95.3)	9 (14.1)
Gastrointestinal disorders	19 (82.6)	0	33 (80.5)	2 (4.9)	52 (81.3)	2 (3.1)
General disorders and administration site conditions	13 (56.5)	0	25 (61.0)	1 (2.4)	38 (59.4)	1 (1.6)
Musculoskeletal and connective tissue disorders	6 (26.1)	0	10 (24.4)	1 (2.4)	16 (25.0)	1 (1.6)
Nervous system disorders	6 (26.1)	0	10 (24.4)	0	16 (25.0)	0
Blood and lymphatic system disorders	5 (21.7)	0	6 (14.6)	1 (2.4)	11 (17.2)	1 (1.6)
Metabolism and nutrition disorders	2 (8.7)	0	7 (17.1)	0	9 (14.1)	0
Eye disorders	1 (4.3)	0	4 (9.8)	0	5 (7.8)	0
Renal and urinary disorders	1 (4.3)	0	4 (9.8)	0	5 (7.8)	0
Respiratory, thoracic and mediastinal disorders	1 (4.3)	0	4 (9.8)	2 (4.9)	5 (7.8)	2 (3.1)
Infections and infestations	1 (4.3)	0	3 (7.3)	0	4 (6.3)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (8.7)	1 (4.3)	2 (4.9)	0	4 (6.3)	1 (1.6)
Investigations	2 (8.7)	0	1 (2.4)	0	3 (4.7)	0
Skin and subcutaneous tissue disorders	1 (4.3)	0	1 (2.4)	0	2 (3.1)	0
Vascular disorders	0	0	2 (4.9)	0	2 (3.1)	0
Ear and labyrinth disorders	0	0	1 (2.4)	0	1 (1.6)	0
Endocrine disorders	0	0	1 (2.4)	0	1 (1.6)	0
Injury, poisoning and procedural complications	1 (4.3)	1 (4.3)	0	0	1 (1.6)	1 (1.6)
Psychiatric disorders	0	0	1 (2.4)	0	1 (1.6)	0
Reproductive system and breast disorders	0	0	1 (2.4)	0	1 (1.6)	0

Results given as xx (xx x) where xx = number of patients with AEs, (xx x) = percentage of patients. Every patient was counted a single time for each applicable specific AE. A patient with multiple AEs within a SOC was counted a single time for that SOC. All AE tables are coded using MedDRA version 22.1.

System organ classes are sorted in descending frequency of 'All severity' column, as reported in the 'Overall' column.

Source: [Table 14.3.1.2.1](#).

12.2.2.2 Display of TEAEs by MedDRA by Preferred Term (Safety Population)

The most frequently occurring TEAEs (PTs) overall were dry mouth, fatigue, and nausea (57.8%, 53.1%, and 46.9%, respectively). Notably, none of these events was reported to be severe, except one event of nausea in the 7.4 GBq treatment group. Frequencies of individual PTs were comparable between the treatment groups (within 10% difference) with the exceptions of dry mouth (47.8% vs 63.4% in the 6.0 GBq group compared with the 7.4 GBq group, respectively); and diarrhoea (13.0% vs 31.7% in the 6.0 GBq group compared with the 7.4 GBq group, respectively).

The TEAEs by MedDRA by PT in more than 5% of patients in either treatment arm are presented in [Table 12-4 TEAEs by MedDRA by Preferred Term in more than 5% of patients in either treatment arm \(Safety Population\)](#).

Table 12-4 TEAEs by MedDRA by Preferred Term in more than 5% of patients in either treatment arm (Safety Population)

Preferred Term	¹⁷⁷ Lu-PSMA-617 6.0 GBq (N=23) n (%)		¹⁷⁷ Lu-PSMA-617 7.4 GBq (N=41) n (%)		Overall (N=64) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Patient with Any Event	22 (95.7)	2 (8.7)	39 (95.1)	7 (17.1)	61 (95.3)	9 (14.1)
Dry mouth	11 (47.8)	0	26 (63.4)	0	37 (57.8)	0
Fatigue	13 (56.5)	0	21 (51.2)	0	34 (53.1)	0
Nausea	12 (52.2)	0	18 (43.9)	1 (2.4)	30 (46.9)	1 (1.6)
Diarrhoea	3 (13.0)	0	13 (31.7)	0	16 (25.0)	0
Constipation	6 (26.1)	0	9 (22.0)	0	15 (23.4)	0
Vomiting	4 (17.4)	0	8 (19.5)	1 (2.4)	12 (18.8)	1 (1.6)
Taste disorder	4 (17.4)	0	7 (17.1)	0	11 (17.2)	0
Pain	3 (13.0)	0	5 (12.2)	0	8 (12.5)	0
Anaemia	4 (17.4)	0	4 (9.8)	0	8 (12.5)	0
Decreased appetite	1 (4.3)	0	5 (12.2)	0	6 (9.4)	0
Arthralgia	3 (13.0)	0	2 (4.9)	0	5 (7.8)	0
Headache	2 (8.7)	0	2 (4.9)	0	4 (6.3)	0
Dry eye	1 (4.3)	0	3 (7.3)	0	4 (6.3)	0
Back pain	2 (8.7)	0	1 (2.4)	0	3 (4.7)	0
Dyspnoea	0	0	3 (7.3)	1 (2.4)	3 (4.7)	1 (1.6)
Metastases to central nervous system	2 (8.7)	1 (4.3)	0	0	2 (3.1)	1 (1.6)

Results given as xx (xx x) where xx = number of patients with AEs, (xx x) = percentage of patients. Every patient was counted a single time for each applicable specific AE. A patient with multiple AEs within a SOC was counted a single time for that SOC. All AE tables are coded using MedDRA version 22.1.

Preferred terms are sorted in descending frequency of 'All severity' column, as reported in the 'Overall' column.

Source: [Table 14.3.1.2.1](#).

12.2.2.3 Drug-related TEAEs (Safety Population) by age category

Older patients (≥ 65 years old) did not have more frequent drug-related TEAEs as compared with the younger patients (< 65 years old): 15 (93.8%) patients aged < 65 years old compared with 42 (87.5%) patients aged ≥ 65 years old experienced any drug-related TEAEs overall. 4 (100%) patients aged < 65 years and 16 (84.2%) patients aged ≥ 65 years old experienced drug-related TEAEs in the ^{177}Lu -PSMA617 6.0 GBq group; 11 (91.7%) patients aged < 65 years old and 26 (89.7%) patients aged ≥ 65 years old experienced drug-related TEAEs in the ^{177}Lu -PSMA617 7.4 GBq group. These data are presented in Source [Table 14.3.1.5.2](#).

12.2.3 Listing of randomized treatment emergent adverse events (TEAEs) by subject (Safety Population)

Randomized TEAEs by subject are displayed in [Listing 16.2.6.1](#).

12.3 Deaths and other serious or clinically significant adverse events

12.3.1 Deaths by system organ class (Safety Population)

The randomized treatment TEAEs leading to death are summarized by MedDRA SOC and PT in (Source: [Table 14.3.1.10.1](#)).

Table 12-5 Randomized Treatment TEAEs Leading to Death, by MedDRA System Organ Class and Preferred Term (Safety Population)

System organ class Preferred term	^{177}Lu -PSMA-617 6.0 GBq N = 23 n (%)		^{177}Lu -PSMA-617 7.4 GBq N = 41 n (%)		Overall N = 64 n (%)	
	All	Related to treatment	All	Related to treatment	All	Related to treatment
Patient with any event leading to death	2 (8.7)	1 (4.3)	1 (2.4)	1 (2.4)	3 (4.7)	2 (3.1)
General disorders and administration site conditions	0	0	1 (2.4)	1 (2.4)	1 (1.6)	1 (1.6)
Death	0	0	1 (2.4)	1 (2.4)	1 (1.6)	1 (1.6)
Injury, poisoning and procedural complications	1 (4.3)	1 (4.3)	0	0	1 (1.6)	1 (1.6)
Subdural haematoma	1 (4.3)	1 (4.3)	0	0	1 (1.6)	1 (1.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (4.3)	0	0	0	1 (1.6)	0
Metastases to central nervous system	1 (4.3)	0	0	0	1 (1.6)	0

Source: [Table 14.3.1.10.1](#).

12.3.2 Serious TEAEs (Safety Population)

Serious TEAEs were reported for 12 (18.8%) patients overall: 4 (17.4%) in the ¹⁷⁷Lu-PSMA-617 6.0 GBq group and 8 (19.5%) patients in the ¹⁷⁷Lu-PSMA-617 7.4 GBq group.

Overall, the single most commonly reported serious TEAE was metastases to central nervous system, occurring in 2 (3.1%) of patients, both in the 6.0 GBq group. All other SAEs (PTs) occurred only one patient each: 4 patients had SAEs in the Neoplasms benign, malignant and unspecified (including cysts and polyps) SOC, and 2 in the Gastrointestinal disorders SOC.

The serious TEAEs are summarized in [Table 12-6 Serious TEAEs by MedDRA System Organ Class and Preferred Term \(Safety Population\)](#) (Source: [Table 14.3.1.4.1](#)).

Table 12-6 Serious TEAEs by MedDRA System Organ Class and Preferred Term (Safety Population)

System organ class Preferred term	¹⁷⁷ Lu-PSMA-617 6.0 GBq N = 23 n (%)	¹⁷⁷ Lu-PSMA- 617 7.4 GBq N = 41 n (%)	Overall N = 64 n (%)
Patient with any event	4 (17.4)	8 (19.5)	12 (18.8)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (8.7)	2 (4.9)	4 (6.3)
Metastases to central nervous system	2 (8.7)	0	2 (3.1)
Adenocarcinoma of colon	0	1 (2.4)	1 (1.6)
Metastases to meninges	0	1 (2.4)	1 (1.6)
Gastrointestinal disorders	0	2 (4.9)	2 (3.1)
Abdominal pain	0	1 (2.4)	1 (1.6)
Gastrointestinal haemorrhage	0	1 (2.4)	1 (1.6)
Blood and lymphatic system disorders	0	1 (2.4)	1 (1.6)
Anaemia	0	1 (2.4)	1 (1.6)
Thrombocytopenia	0	1 (2.4)	1 (1.6)
General disorders and administration site conditions	0	1 (2.4)	1 (1.6)
Death	0	1 (2.4)	1 (1.6)
Infections and infestations	0	1 (2.4)	1 (1.6)
Pneumonia	0	1 (2.4)	1 (1.6)
Injury, poisoning and procedural complications	1 (4.3)	0	1 (1.6)
Subdural haematoma	1 (4.3)	0	1 (1.6)
Musculoskeletal and connective tissue disorders	1 (4.3)	0	1 (1.6)
Osteoporosis	1 (4.3)	0	1 (1.6)
Renal and urinary disorders	0	1 (2.4)	1 (1.6)
Acute kidney injury	0	1 (2.4)	1 (1.6)
Respiratory, thoracic and mediastinal disorders	0	1 (2.4)	1 (1.6)
Pleural effusion	0	1 (2.4)	1 (1.6)

Results given as xx (xx x) where xx = number of patients with AEs, (xx x) = percentage of patients.

Every patient was counted a single time for each applicable specific AE. A patient with multiple AEs within a SOC was counted a single time for that SOC.

Source: [Table 14.3.1.4.1](#).

12.3.3 Serious drug-related TEAEs (Safety Population)

Serious drug-related TEAEs were reported for 5 (7.8%) patients overall: 1 (4.3%) in the ¹⁷⁷Lu-PSMA-617 6.0 GBq group; and 4 (9.8%) patients in the ¹⁷⁷Lu-PSMA-617 7.4 GBq group.

The patient in the 7.4 GBq treatment arm who died received one full cycle of ¹⁷⁷Lu-PSMA-617, and because of experiencing a Grade 3 hematologic toxicity (i.e., hemoglobin level 7.6 g/dL), his second cycle was reduced to 3.7 GBq (as per the protocol). At the time of the third cycle, the patient was still seen with a Grade 3 hematologic toxicity (i.e., hemoglobin level 7.4 g/dL), so the patient was discontinued from the study; however, he remained in the follow-up phase. On Day 118/55 Days after the last 50% dose of ¹⁷⁷Lu-PSMA-617, the patient was admitted to the hospital due to a gastrointestinal hemorrhage. During that hospitalization, the patient died because of gastrointestinal hemorrhage, and the PI considered the death possibly related to the investigational drug. Scant information is known about this death as medical records were not available from the hospital; available information is presented in the SAE narratives in [Section 14.3.3](#).

The patient in the 6.0 GBq treatment arm who died of a subdural hematoma (primary cause, with mitigating factors of non-STEMI and pneumonia) received 2 full cycles of ¹⁷⁷Lu-PSMA-617; however, prior to the third cycle his PSA-level progression was above protocol-specified limits to continue treatment, but he did continue in the follow-up phase (PSA levels are unknown). He was admitted to the ER on Day 149/92 days after the last day of study drug (while in the Follow-up phase), with complaints of near syncope preceded with moderate nausea and vomiting with headache. On Day 151/94 days after the last days of study drug, the patient died. The Investigator considered the SAE of subdural hematoma as the main cause of death and possibly related to the treatment with ¹⁷⁷Lu-PSMA-617. The Investigator considered that the non-STEMI (Grade 5 severity) and pneumonia (Grade 5 severity) were probably not related to the treatment with ¹⁷⁷Lu-PSMA-617. More information is presented in [Section 14.3.3](#).

The serious drug-related TEAEs are summarized by SOC and PT in [Table 12-7 Serious Drug-related TEAEs by MedDRA System Organ Class and Preferred Term \(Safety Population\)](#) (Source: [Table 14.3.1.6.1](#)).

Table 12-7 Serious Drug-related TEAEs by MedDRA System Organ Class and Preferred Term (Safety Population)

System organ class Preferred term	¹⁷⁷ Lu-PSMA-617 6.0 GBq N = 23 n (%)	¹⁷⁷ Lu-PSMA-617 7.4 GBq N = 41 n (%)	Overall N = 64 n (%)
Patient with any event	1 (4.3)	4 (9.8)	5 (7.8)
Blood and lymphatic system disorders	0	1 (2.4)	1 (1.6)
Anaemia	0	1 (2.4)	1 (1.6)
Thrombocytopenia	0	1 (2.4)	1 (1.6)
Gastrointestinal disorders	0	1 (2.4)	1 (1.6)
Gastrointestinal haemorrhage	0	1 (2.4)	1 (1.6)
General disorders and administration site disorders	0	1 (2.4)	1 (1.6)
Death	0	1 (2.4)	1 (1.6)
Injury, poisoning and procedural complications	1 (4.3)	0	1 (1.6)
Subdural haematoma	1 (4.3)	0	1 (1.6)
Renal and urinary disorders	0	1 (2.4)	1 (1.6)
Acute kidney injury	0	1 (2.4)	1 (1.6)
Respiratory, thoracic and mediastinal disorders	0	1 (2.4)	1 (1.6)
Pleural effusion	0	1 (2.4)	1 (1.6)

Results given as xx (xx x) where xx = number of patients with serious, drug-related TEAEs, (xx x) = percentage of patients
Every patient was counted a single time for each applicable specific serious, drug-related AE with highest severity. A patient
with multiple serious, drug-related TEAEs within a SOC was counted a single time for that SOC with the highest severity.
Source: [Table 14.3.1.6.1](#).

12.3.3.1 Serious TEAEs (Safety Population) – by Age Category

Serious TEAEs by MedDRA System Organ Class and Preferred Term by age category were similar across treatment groups and showed no discernable difference by age category and are presented in Source [Table 14.3.1.4.2](#). These are also described in detail in the narrative [Section 14.3.3](#).

12.3.4 TEAEs leading to discontinuation of ¹⁷⁷Lu-PSMA-617 (Safety Population)

The only TEAE that led to the discontinuation of ¹⁷⁷Lu-PSMA-617 was abdominal pain reported in 1 (2.4%) patient in the ¹⁷⁷Lu-PSMA-617 7.4 GBq group. The patient had only received one cycle and was then hospitalized for right-sided abdominal pain (Day 18). The patient had scans that showed prostate cancer metastases to the liver and bones, and confirmed cancer progression as the cause for pain (see [Section 14.3.3](#)).

The TEAE leading to the discontinuation of ¹⁷⁷Lu-PSMA-617 in the Safety Population was summarized by SOC and PT in Source [Table 14.3.1.8.1](#).

12.3.4.1 TEAEs leading to discontinuation by SOC and preferred term by age category (Safety Population)

The only patient with the TEAE (abdominal pain) that led to the discontinuation of ¹⁷⁷Lu-PSMA-617 was in the ≥ 65 years old age group in the ¹⁷⁷Lu-PSMA-617 7.4 GBq treatment group.

The TEAE leading to the discontinuation of ¹⁷⁷Lu-PSMA-617 in the Safety Population was summarized by SOC and PT in Source [Table 14.3.1.8.2](#).

12.3.5 TEAEs leading to the reduction of ¹⁷⁷Lu-PSMA-617 (Safety Population)

TEAEs leading to the reduction of ¹⁷⁷Lu-PSMA-617 were reported for 2 (4.9%) patients, both events were reported as anaemia and both patients were in the ¹⁷⁷Lu-PSMA-617 7.4 GBq group.

TEAEs leading to the reduction of ¹⁷⁷Lu-PSMA-617 are presented by SOC and PT in Source: [Table 14.3.1.7.1](#).

TEAEs leading to the reduction of ¹⁷⁷Lu-PSMA-617 are presented by SOC and PT – by Age Category are presented in Source [Table 14.3.1.7.2](#).

12.3.6 Specific Adverse Events Questionnaire (Safety Population)

The results of the Specific Adverse Events Questionnaire are presented in [Tables 14.3.1.13.1](#) and [14.3.1.13.2: Listing 16.2.6.2](#).

12.3.7 Listing of deaths (Safety Population)

All subjects who died during the study and the follow-up period are listed in [Listing 16.2.12](#).

12.3.8 Narratives of deaths, other serious adverse events, and certain other clinically significant adverse events (Safety Population)

Narratives are provided for deaths for reasons other than disease progression during study treatment or within 30 days of treatment discontinuation, SAEs occurring during study treatment or within 30 days of treatment discontinuation, and treatment discontinuations due to AEs in [Section 14.3.3](#).

12.4 Clinical laboratory evaluations (Safety Population)

The data must be interpreted with caution because of the small number of patients with data at some of the timepoints.

12.4.1 Hematology (Safety Population)

There were patients with missing data at many time points, so all data must be interpreted with caution. A trend in mild decrease in mean values was observed during treatment for WBCs (all components), RBCs, and platelets. However, during follow-up, the mean values tended to increase again (hematology results and changes from baseline by visit are summarized in source [Table 14.3.2.2](#)). Few patients shifted from normal to low for WBCs and RBCs or from low to normal values. Some patients had an increase in eosinophils above normal during the study at a few timepoint and a higher number of patients had a shift from normal to increased platelet

than from normal to decreased platelet count during the study. There was not a trend of increasing frequency of shifts from normal to abnormal over time for any parameter.

This is overall for the patient population, with no relevant differences between the groups.

The summary of hematology laboratory shifts by visit for is summarized Source [Table 14.3.2.4](#): ([Listing 16.2.7.2](#))

12.4.2 Clinical chemistry (Safety Population)

The summary of chemistry laboratory shifts by visit is summarized in Source: [Table 14.3.2.1](#): ([Listing 16.2.7.1](#))

12.4.2.1 Creatinine

No trend to creatinine increase was observed during the study; with the exception of one patient who had elevated creatinine at several time points throughout the study; however, the patient's creatinine was already elevated at baseline and the creatinine levels decreased close to the baseline at the last assessments. Slight decreases in creatinine levels from baseline were observed in the overall population during treatment with the exception of Week 24 (no difference compared with screening/baseline) with no relevant differences in the behavior between the two groups towards the end of the assessment period. In Follow-up, the number of patients was too small to allow for any conclusions.

12.4.2.2 Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT)

There were 4 patients that, as a course of possible underlying disease, suffered liver metastases and/or liver disease. (Sources: [Listing 16.2.7.1](#), [Listing 16.2.5.4](#), [Listing 16.2.12](#), and [Section 14.3.3](#)) These instances are summarized as follows, with mention of the attendant increases in AST and ALT:

- Patient 673450-118 (29-118) with AST 272 U/L and ALT 172 U/L at follow-up Week 4 died of liver failure shortly thereafter. No information pertaining to liver disease is available at the time of study entry.
- Patient 25-XD-054 had high AST and ALT at follow-up Weeks 4, 6, and 8; however the patient only received one dose of study treatment.
- Patient 860127-714 (60-714) had mostly normal liver enzymes throughout the study or only grade 1 increase above the normal range; a relevant increase was reported at the Month 10 follow-up visit with AST at 557 U/L and ALT at 441 U/L after completion of study treatment. Shortly after that he died following a hip fracture with no laboratory reports or medical records available from the hospitalization. There was no history of liver metastases or liver disease reported in the medical history.
- Patient 808147-323 (20-JR-323) was found with AST increase at follow-up Week 2 (AST of 243 U/L). The patient had right-sided abdominal pain caused by liver and bone metastases reported as unlikely related to study drug, Grade 3 severity SAE on Day 18. He then discontinued from the study because of cancer progression.

12.4.2.3 Alkaline Phosphatase (ALP)

Alkaline phosphatase (ALP) values over time during treatment had no substantial change; but individual patients had variable increase or decrease of ALP that was compatible with the disease. There were no trends observed as substantial changes in the groups. During follow-up, the number of patients was too small to draw any conclusions. Sources: [Table 14.3.2.1: Listing 16.2.7.1.](#)

12.5 Vital signs, physical findings and other observations related to safety

12.5.1 Vital signs (Safety Population)

No clinically significant changes were observed in the mean values during the study when comparing post-baseline values with baseline values and during the cycles when comparing post-treatment values with pretreatment values.

Systolic blood pressure (mmHg), diastolic blood pressure (mmHg), heart rate (bpm), temperature (°C), and respiratory rate (breaths per min) were analyzed descriptively by summary tables noting observed values and change from Baseline. Change from baseline for vital signs are presented in [Table 14.3.4.1.1](#). Transition tables for vitals are provided for the transitions from Baseline to each follow-up time point in [Table 14.3.4.2.1](#); Source: [Listing 16.2.8.](#)

12.5.1.1 Systolic Blood Pressure (SBP)

No findings were found clinically significant. For individual changes from Baseline in vital signs for Systolic Blood Pressure (SBP), there were no increases over 40 mmHg throughout the study. There were 2 episodes of decreases of over 40 mmHg in 2 patients in the Treatment Visit 2 injection +30 min analysis visit timepoint in the ¹⁷⁷Lu-PSMA-617 7.4 GBq treatment arm; 2 decreases of over 40 mmHg at the Treatment Visit 2 injection +60 min analysis visit timepoint, in 1 patient in the ¹⁷⁷Lu-PSMA-617 6.0 GBq treatment arm and 1 in the ¹⁷⁷Lu-PSMA-617 7.4 GBq treatment arm; there was 1 decrease of over 40 mmHg at all remaining analysis visit timepoints in the ¹⁷⁷Lu-PSMA 6.0 GBq treatment arm up to the follow-up Month 3 visit. None of these were considered clinically significant or TEAEs. Source: [Table 14.3.4.2.1, Listing 16.2.6.1.](#)

12.5.1.2 Diastolic Blood Pressure (DBP)

No findings were found clinically significant. For individual changes from Baseline in vital signs for Diastolic Blood Pressure (DBP), there was 1 episode of increase over 30 mmHg at the Treatment Visit 2 injection +30 min analysis visit timepoint in the ¹⁷⁷Lu-PSMA-617 7.4 GBq treatment arm; 1 episode of increase over 30 mmHg in Treatment Visit 3 injection -20 min in the ¹⁷⁷Lu-PSMA-617 6.0 GBq treatment arm; and 2 episodes of increases over 30 mmHg, one in each treatment arm at Treatment Visit 4 injection +60 min. None of these measurements were considered clinically significant or TEAEs. Source: [Table 14.3.4.2.1.](#)

12.5.1.3 Heart Rate

No findings were found clinically significant. For individual changes from Baseline in vital signs for Heart Rate, there was 1 episode of an increase over 30 beats/min at the Treatment Visit 1 injection +30 min analysis visit timepoint, the Treatment Visit 1 injection +60 min analysis timepoint, and the Treatment Visit 2 injection -20 min analysis visit timepoint in one/the same patient in the ¹⁷⁷Lu-PSMA-617 6.0 GBq treatment arm. Other increases over 30 beats/min were noted in 1 patient at the Treatment Visit 4 injection -20 min analysis visit timepoint in the ¹⁷⁷Lu-PSMA-617 7.4 GBq treatment arm, in 2 patients at the Treatment 4 injection +30 min analysis visit timepoint in the ¹⁷⁷Lu-PSMA-617 7.4 GBq treatment arm, and 3 patients at Treatment Visit 4 injection +60 min analysis visit timepoint in the ¹⁷⁷Lu-PSMA-617 7.4 treatment arm. None of these were considered clinically significant or TEAEs.

12.5.2 12-Electrocardiography (Safety Population)

There were no clinically significant abnormalities reported. Overall ECG interpretations were summarized. Heart rate (bpm), pulse rate (msec), QRS (msec), QT (msec) and QTc (msec; measured by both sites as QTcB using Bazett's formula) intervals were summarized as continuous variables. ECG readings at Treatment Visit 1 had no abnormal, clinically significant readings, and 9 (39.1%) abnormal – not clinically significant in the ¹⁷⁷Lu-PSMA-617 6.0 GBq treatment arm and 19 (46.3%) abnormal, not clinically significant in the ¹⁷⁷Lu-PSMA-617 7.4 GBq treatment arm. All other timepoints had no abnormal, clinically significant readings and no more additional abnormal – not clinically significant readings. All ECG variables were also listed. Electrocardiography (ECG) data are presented in [Table 14.3.5.1](#).

12.5.3 Concurrent radiotherapy

Concurrent radiotherapy was summarized and is presented in [Table 14.3.6.1.1](#). Source: [Listing 16.2.11.3](#).

12.5.4 Post-treatment radiotherapy

Post-treatment radiotherapy was summarized and is presented in [Section 10.9.2 Post-treatment radiotherapy \(Safety Population\)](#) and in [Table 14.3.6.1.2](#). Source: [Listing 16.2.11.4](#).

12.5.5 Concurrent other therapy

Concurrent other therapy was summarized and is presented in [Table 10-11 Concurrent Other Treatments \(Safety Population\)](#) and in [Table 14.3.6.2.1](#). Source: [Listing 16.2.11.5](#).

12.5.6 Post-treatment other therapy

Post-treatment other therapy was summarized and is presented in [Table 10-13 Post-treatment – Other Treatment \(Safety Population\)](#) and in [Table 14.3.6.2.2](#). Source: [Listing 16.2.11.6](#).

12.5.7 Concurrent Chemotherapy

Concurrent chemotherapy was summarized and is presented in [Table 14.3.6.3.1](#). Source: [Listing 16.2.11.1](#).

12.5.8 Post-treatment Chemotherapy

Post-treatment chemotherapy was summarized and is presented [10.9.1 Post-treatment chemotherapy \(Safety Population\)](#) in [Table 14.3.6.3.2](#). Source [Listing 16.2.11.2](#).

12.5.9 Pregnancy

No pregnancy was reported in a partner of any patient during the study and up to the 30-day post dose follow-up portion of the study. This was documented in the patient source documents.

12.5.10 Physical examination (Safety Population)

There were no relevant changes observed during the study compared with baseline, other than those noted as a TEAE. Physical examination results are listed for the Safety Population in [Listing 16.2.10](#).

13 Discussion and overall conclusions

Conclusions

- Because of the enrollment closing earlier than initially planned and missing data resulting in a significantly smaller sample size than the initially planned of 200 patients, efficacy endpoints were listed and not summarized other than for clinicaltrials.gov purposes. Specifically, the PSA related efficacy was analyzed with the small sample size and the investigators' inconsistent timing of PSA data collection for clinicaltrials.gov. Limited imaging data were available, and thus the associated endpoints (i.e., radiographic Progression-free survival [rPFS] and disease control rate [DCR]) were not summarized. Summary statistics were presented for EPIC 26 Quality of life (QoL) questionnaire and ECOG performance status. Bone level pain data were only listed due to the nature of the data (i.e., free text pain levels).
- Seven deaths were reported during the study (i.e., from enrollment through the 24 months follow-up); 4/28 (14.3%) and 3/43 (7.0%) subjects died during the study in the 6.0 GBq and 7.4 GBq treatment arms, respectively, 7/71 (9.9%) overall. Three deaths were fatal TEAEs; 3 deaths were fatal, unrelated adverse events occurring more than 30 days after last dose of ¹⁷⁷Lu-PSMA-617; and 1 death occurred in a patient prior to receiving his first dose of ¹⁷⁷Lu-PSMA-617. TEAEs leading to deaths were 2/23 (8.7%) and 1/41 (2.4%) respectively, and 3/64 (4.7%) in the 6.0 and 7.4 GBq arms, overall.
 - There was one death in the 7.4 GBq group determined to be possibly related due to gastrointestinal hemorrhage and unknown causes (72 days after last dose); and one death (94 days after last dose) in the 6.0 GBq group determined to be possibly related due to a subdural hematoma. The third TEAE leading to death was metastases to central nervous system (68 days after last dose) in the 6.0 GBq group, determined to be unrelated to study treatment.
- In general, the patients with any event were comparable in all severity between the groups (95.7% in the 6.0 GBq group compared with 95.1% in the 7.4 GBq group, and the overall group, 95.3%) and slightly higher in the 7.4 GBq group when compared with

the 6.0 GBq (17.1% compared with 8.7%, respectively). Overall PSMA was well tolerated irrespective of the dose.

- The most common TEAEs in the 6.0 GBq treatment arm, the 7.4 GBq treatment arm respectively and overall, were dry mouth (47.8%; 63.4%; 57.8%, respectively), fatigue (56.5%; 51.2%; 53.1%), nausea (52.2%; 43.9%; 46.9%), and diarrhoea (13.0%; 31.7%; 25.0%).
- Older patients aged \geq 65 years did not have a greater frequency of TEAEs than the patients aged below 65 years.
- There were no clinically significant changes in vital signs in the 2 treatment groups.
- There were no clinically significant findings in ECGs in the 2 treatment groups.
- No trend to creatinine increase was observed during the study. The kidney dosimetry caveat of the dosing procedures were considered unnecessary and deleted from the protocol at the implementation of Study Protocol Amendment 1 on 07 January 2017.
- There were 4 patients with Grade 3 AST and/or ALT levels above the normal ranges that were primarily explained by metastases of the cancer to the liver and were not considered to be related to the study treatment.
- ALP mean values over time during treatment had no substantial change, but individual patients had variable increase or decrease of ALP that was compatible with the disease. During follow up, the number of patients was too small to draw any conclusion.
- There was not a trend of increasing frequency of shifts from normal to abnormal over time for any hematologic parameter.
- These overall hematology findings for the patient population showed no relevant differences between the groups. The data must be interpreted with caution due to the small number of patients with data at some of the timepoints.

In Conclusion:

The safety profile of ^{177}Lu -PSMA-617 in this study was as anticipated based on the mechanism of action and is generally consistent with previous ^{177}Lu -PSMA-617 experiences as documented in literature in similar populations of patients with mCRPC. There were no efficacy conclusions in this study. Overall, ^{177}Lu -PSMA-617 was well-tolerated and the safety was manageable with established medical support.

**14 Tables, Figures and Listings referred to but not included
in the text**

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14.1 Demographic data

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Table 14.1.1
Analysis Sets
All Patients

	Lu-PSMA-617 6.0 GBq (N=28)	Lu-PSMA-617 7.4 GBq (N=43)	Overall (N=71)
	n (%)	n (%)	n (%)
Patients who signed informed consent			71 (100)
Patients in the ITT population*	28 (100)	43 (100)	71 (100)
Patients in the Safety Population**	23 (82.1)	41 (95.3)	64 (90.1)

* Intent-to-treat (ITT) population = All randomized patients. Patients are included in the treatment arm to which they were randomized regardless of actual treatment received.

** Safety population = The subset of patients in the ITT population who received at least one dose of randomized therapy. Patients are included in the treatment arm corresponding to the actual treatment received.

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Table 14.1.2
Patient Disposition as per CRF
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)	Lu-PSMA-617 7.4 GBq (N=43)	Overall (N=71)
	n (%)	n (%)	n (%)
Patients who discontinued from Lu-PSMA-617 treatment	23 (82.1)	41 (95.3)	64 (90.1)
Reason for discontinuation from Lu-PSMA-617 treatment			
Completion Of Four RLT Cycles	10 (35.7)	19 (44.2)	29 (40.8)
Patient Withdrawal	6 (21.4)	6 (14.0)	12 (16.9)
PSA/Radiographic Progression At >=12 Weeks	7 (25.0)	16 (37.2)	23 (32.4)
Patients who completed the study	18 (64.3)	31 (72.1)	49 (69.0)
Reason for study completion			
Completed	1 (3.6)	0	1 (1.4)
Death	3 (10.7)	2 (4.7)	5 (7.0)
Progressive Disease	14 (50.0)	29 (67.4)	43 (60.6)
Patients who early discontinued from the study	10 (35.7)	12 (27.9)	22 (31.0)
Reason for early discontinuation from the study			
Administrative Reason	1 (3.6)	1 (2.3)	2 (2.8)
Adverse Event	0	1 (2.3)	1 (1.4)
Lost To Follow-Up	1 (3.6)	3 (7.0)	4 (5.6)
Occurrence Of Condition *	4 (14.3)	2 (4.7)	6 (8.5)
Patient Withdrawal	4 (14.3)	5 (11.6)	9 (12.7)
Total number of deaths	4 (14.3)	3 (7.0)	7 (9.9)

* Any occurrence of conditions which prevented the patient's participation in the study.

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Table 14.1.3.1
Summary of All Protocol Deviations
ITT Population

Protocol Deviation Category	Lu-PSMA-617 6.0 GBq (N=28) n (%) [m]	Lu-PSMA-617 7.4 GBq (N=43) n (%) [m]	Overall (N=71) n (%) [m]
Patient with at least one protocol deviation	19 (67.9) [95]	38 (88.4) [249]	57 (80.3) [344]
PROCEDURE VIOLATION	17 (60.7) [93]	38 (88.4) [239]	55 (77.5) [332]
DRUG DOSING	1 (3.6) [1]	5 (11.6) [7]	6 (8.5) [8]
INFORMED CONSENT PROCEDURE	1 (3.6) [1]	2 (4.7) [2]	3 (4.2) [3]
IN-/EXCLUSION CRITERIA	0	1 (2.3) [1]	1 (1.4) [1]

n is the number of subjects, [m] is the number of protocol deviations

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Table 14.1.3.2
Summary of Important Protocol Deviations
ITT Population

<u>Important Protocol Deviation Category</u>	<u>Lu-PSMA-617</u>	<u>Lu-PSMA-617</u>	<u>Overall</u>
	6.0 GBq (N=28)	7.4 GBq (N=43)	(N=71)
	n (%) [m]	n (%) [m]	n (%) [m]
Patient with at least one important protocol deviation	9 (32.1) [13]	22 (51.2) [32]	31 (43.7) [45]
PROCEDURE VIOLATION	8 (28.6) [12]	20 (46.5) [29]	28 (39.4) [41]
INFORMED CONSENT PROCEDURE	1 (3.6) [1]	2 (4.7) [2]	3 (4.2) [3]
<u>IN-/EXCLUSION CRITERIA</u>	0	1 (2.3) [1]	1 (1.4) [1]

n is the number of subjects, [m] is the number of protocol deviations

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Table 14.1.4.1
Demographic and Baseline Characteristics
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)	Lu-PSMA-617 7.4 GBq (N=43)	Overall (N=71)
Age (years)			
n	28	43	71
Mean (SD)	72.1 (8.39)	69.1 (8.62)	70.3 (8.60)
Median	72.0	69.0	71.0
Q1 ; Q3	67.5 ; 76.0	62.0 ; 77.0	65.0 ; 76.0
Min ; Max	55 ; 95	54 ; 84	54 ; 95
Age Group, n(%)			
n	28	43	71
< 65 years	4 (14.3)	13 (30.2)	17 (23.9)
>= 65 years	24 (85.7)	30 (69.8)	54 (76.1)
Race, n(%)			
n	28	43	71
Asian	1 (3.6)	1 (2.3)	2 (2.8)
Black or African American	0	1 (2.3)	1 (1.4)
White	26 (92.9)	41 (95.3)	67 (94.4)
Other	1 (3.6)	0	1 (1.4)
Ethnicity, n(%)			
n	28	43	71
Hispanic or Latino	0	1 (2.3)	1 (1.4)
Not Hispanic or Latino	27 (96.4)	40 (93.0)	67 (94.4)
Not reported	1 (3.6)	2 (4.7)	3 (4.2)

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Table 14.1.4.1
Demographic and Baseline Characteristics
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)	Lu-PSMA-617 7.4 GBq (N=43)	Overall (N=71)
Weight (kg) at Baseline			
n	23	41	64
Mean (SD)	81.19 (12.101)	85.20 (19.386)	83.76 (17.132)
Median	79.50	79.00	79.25
Q1 ; Q3	72.20 ; 92.20	71.30 ; 99.90	71.45 ; 96.45
Min ; Max	61.2 ; 104.4	50.4 ; 125.5	50.4 ; 125.5
Height (cm) at Baseline			
n	23	41	64
Mean (SD)	176.33 (6.388)	176.63 (8.205)	176.52 (7.551)
Median	175.00	178.00	177.00
Q1 ; Q3	172.00 ; 180.30	173.00 ; 182.00	173.00 ; 182.00
Min ; Max	165.0 ; 190.0	152.0 ; 188.0	152.0 ; 190.0
Pulse Oximetry (%) at Baseline			
n	20	38	58
Mean (SD)	98.20 (1.576)	97.97 (1.652)	98.05 (1.616)
Median	99.00	99.00	99.00
Q1 ; Q3	98.00 ; 99.00	97.00 ; 99.00	97.00 ; 99.00
Min ; Max	94.0 ; 100.0	94.0 ; 100.0	94.0 ; 100.0

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Table 14.1.4.2
Demographic and Baseline Characteristics
Safety Population

	Lu-PSMA-617 6.0 GBq (N=23)	Lu-PSMA-617 7.4 GBq (N=41)	Overall (N=64)
Age (years)			
n	23	41	64
Mean (SD)	71.7 (8.72)	69.4 (8.49)	70.3 (8.57)
Median	72.0	69.0	71.0
Q1 ; Q3	67.0 ; 76.0	64.0 ; 77.0	64.5 ; 76.5
Min ; Max	55 ; 95	54 ; 84	54 ; 95
Age Group, n(%)			
n	23	41	64
< 65 years	4 (17.4)	12 (29.3)	16 (25.0)
>= 65 years	19 (82.6)	29 (70.7)	48 (75.0)
Race, n(%)			
n	23	41	64
Asian	0	1 (2.4)	1 (1.6)
Black or African American	0	1 (2.4)	1 (1.6)
White	23 (100)	39 (95.1)	62 (96.9)
Other	0	0	0
Ethnicity, n(%)			
n	23	41	64
Hispanic or Latino	0	1 (2.4)	1 (1.6)
Not Hispanic or Latino	23 (100)	38 (92.7)	61 (95.3)
Not reported	0	2 (4.9)	2 (3.1)

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Table 14.1.4.2
Demographic and Baseline Characteristics
Safety Population

	Lu-PSMA-617 6.0 GBq (N=23)	Lu-PSMA-617 7.4 GBq (N=41)	Overall (N=64)
Weight (kg) at Baseline			
n	23	41	64
Mean (SD)	81.19 (12.101)	85.20 (19.386)	83.76 (17.132)
Median	79.50	79.00	79.25
Q1 ; Q3	72.20 ; 92.20	71.30 ; 99.90	71.45 ; 96.45
Min ; Max	61.2 ; 104.4	50.4 ; 125.5	50.4 ; 125.5
Height (cm) at Baseline			
n	23	41	64
Mean (SD)	176.33 (6.388)	176.63 (8.205)	176.52 (7.551)
Median	175.00	178.00	177.00
Q1 ; Q3	172.00 ; 180.30	173.00 ; 182.00	173.00 ; 182.00
Min ; Max	165.0 ; 190.0	152.0 ; 188.0	152.0 ; 190.0
Pulse Oximetry (%) at Baseline			
n	20	38	58
Mean (SD)	98.20 (1.576)	97.97 (1.652)	98.05 (1.616)
Median	99.00	99.00	99.00
Q1 ; Q3	98.00 ; 99.00	97.00 ; 99.00	97.00 ; 99.00
Min ; Max	94.0 ; 100.0	94.0 ; 100.0	94.0 ; 100.0

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Table 14.1.5.1
Baseline Disease Characteristics
ITT Population

	Lu-PSMA-617 (N=28)	6.0 GBq	Lu-PSMA-617 (N=43)	7.4 GBq	Overall (N=71)
Time since initial prostate cancer diagnosis (years)					
n		23		41	
Mean (SD)		8.06 (7.323)		8.06 (7.152)	
Median		4.59		6.00	
Q1 ; Q3		3.02 ; 13.73		2.66 ; 11.99	
Min ; Max		0.7 ; 27.2		0.3 ; 25.9	
Initial Histopathological Classification, n(%)					
n		28		43	
Adenocarcinoma		28 (100)		43 (100)	
Other		0		0	
Unknown		0		0	
Initial Gleason score, categorized, n(%)					
n		28		43	
2-3		0		0	
4-7		7 (25.0)		13 (30.2)	
8-10		20 (71.4)		26 (60.5)	
Unknown		1 (3.6)		4 (9.3)	
Baseline PSA doubling time (months)					
n		26		41	
Mean (SD)		4.35 (7.131)		3.89 (3.977)	
Median		1.91		2.46	
Q1 ; Q3		1.18 ; 3.38		1.41 ; 4.90	
Min ; Max		0.0 ; 31.4		0.0 ; 20.7	

Output ID: t-basedis-itt 04JUN20 12:55

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Table 14.1.5.1
Baseline Disease Characteristics
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)	Lu-PSMA-617 7.4 GBq (N=43)	Overall (N=71)
Baseline PSA doubling time (months), categorized, n(%)			
n	26	41	67
<= 6	21 (80.8)	33 (80.5)	54 (80.6)
> 6	5 (19.2)	8 (19.5)	13 (19.4)
Baseline PSA (ug/L)			
n	12	19	31
Mean (SD)	208.86 (391.804)	287.92 (830.231)	257.32 (686.578)
Median	46.03	19.34	23.66
Q1 ; Q3	11.28 ; 99.35	5.34 ; 68.00	5.59 ; 93.20
Min ; Max	0.6 ; 1166.0	1.9 ; 3499.0	0.6 ; 3499.0

Output ID: t-basedis-itt 04JUN20 12:55

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Table 14.1.5.2
Baseline Disease Characteristics
Safety Population

	Lu-PSMA-617 (N=23)	6.0 GBq	Lu-PSMA-617 (N=41)	7.4 GBq	Overall (N=64)
Time since initial prostate cancer diagnosis (years)					
n		18		39	
Mean (SD)		8.62 (7.264)		8.30 (7.247)	
Median		5.77		6.37	
Q1 ; Q3		3.81 ; 13.73		2.66 ; 12.17	
Min ; Max		0.7 ; 27.2		0.3 ; 25.9	
Initial Histopathological Classification, n(%)					
n		23		41	
Adenocarcinoma		23 (100)		41 (100)	
Other		0		0	
Unknown		0		0	
Initial Gleason score, categorized, n(%)					
n		23		41	
2-3		0		0	
4-7		7 (30.4)		13 (31.7)	
8-10		16 (69.6)		24 (58.5)	
Unknown		0		4 (9.8)	
Baseline PSA doubling time (months)					
n		21		39	
Mean (SD)		4.54 (7.838)		3.90 (4.072)	
Median		1.77		2.40	
Q1 ; Q3		1.18 ; 3.22		1.31 ; 4.93	
Min ; Max		0.0 ; 31.4		0.0 ; 20.7	

Output ID: t-basedis-saf 04JUN20 12:56

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Table 14.1.5.2
Baseline Disease Characteristics
Safety Population

	Lu-PSMA-617 6.0 GBq (N=23)	Lu-PSMA-617 7.4 GBq (N=41)	Overall (N=64)
Baseline PSA doubling time (months), categorized, n(%)			
n	21	39	60
<= 6	17 (81.0)	31 (79.5)	48 (80.0)
> 6	4 (19.0)	8 (20.5)	12 (20.0)
Baseline PSA (ug/L)			
n	10	18	28
Mean (SD)	238.04 (426.318)	301.80 (852.029)	279.03 (720.162)
Median	46.03	17.43	19.82
Q1 ; Q3	6.20 ; 105.50	5.34 ; 68.00	5.47 ; 94.90
Min ; Max	0.6 ; 1166.0	1.9 ; 3499.0	0.6 ; 3499.0

Output ID: t-basedis-saf 04JUN20 12:56

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Table 14.1.6.1
Prostate Cancer Treatment History - Previous Chemotherapy
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)	Lu-PSMA-617 7.4 GBq (N=43)	Overall (N=71)
Number of prior therapies per patient			
n	22	36	58
Mean (SD)	2.5 (1.84)	2.3 (1.28)	2.4 (1.51)
Median	2.0	2.0	2.0
Q1 ; Q3	1.0 ; 3.0	1.0 ; 3.0	1.0 ; 3.0
Min ; Max	1 ; 7	1 ; 5	1 ; 7
Type of prior therapies per patient, n(%)			
Cabazitaxel	9 (32.1)	17 (39.5)	26 (36.6)
Docetaxel	21 (75.0)	33 (76.7)	54 (76.1)
Other	9 (32.1)	18 (41.9)	27 (38.0)
Number of prior taxane-containing therapies per patient			
n	22	35	57
Mean (SD)	1.6 (0.90)	1.5 (0.66)	1.6 (0.75)
Median	1.0	1.0	1.0
Q1 ; Q3	1.0 ; 2.0	1.0 ; 2.0	1.0 ; 2.0
Min ; Max	1 ; 4	1 ; 3	1 ; 4
Number of unique agents per patient			
n	22	36	58
Mean (SD)	2.2 (1.44)	2.2 (1.17)	2.2 (1.26)
Median	2.0	2.0	2.0
Q1 ; Q3	1.0 ; 3.0	1.0 ; 3.0	1.0 ; 3.0
Min ; Max	1 ; 6	1 ; 5	1 ; 6

Output ID: t-cancerhist1-itt 04JUN20 12:56

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Table 14.1.6.2
 Prostate Cancer Treatment History - Previous Chemotherapy: Last Taxane Therapy
 ITT Population

	Lu-PSMA-617 (N=28)	6.0 GBq	Lu-PSMA-617 (N=43)	7.4 GBq	Overall (N=71)
Number of cycles per patient					
n		10		18	28
Mean (SD)		4.9 (1.73)		6.2 (2.09)	5.7 (2.03)
Median		5.5		6.0	6.0
Q1 ; Q3		4.0 ; 6.0		6.0 ; 6.0	4.5 ; 6.0
Min ; Max		1 ; 7		3 ; 13	1 ; 13
Best overall response (BOR) to last taxane therapy, n(%)					
n		22		35	57
Complete response		0		1 (2.9)	1 (1.8)
Partial response		4 (18.2)		11 (31.4)	15 (26.3)
Stable disease		0		0	0
Progressive disease		6 (27.3)		7 (20.0)	13 (22.8)
Missing		12 (54.5)		16 (45.7)	28 (49.1)

Output ID: t-cancerhist2-itt 04JUN20 12:56

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Table 14.1.6.3
 Prostate Cancer Treatment History - Previous Chemotherapy: Last Therapy
 ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)	Lu-PSMA-617 7.4 GBq (N=43)	Overall (N=71)
Type of last prior therapy, n(%)			
n	22	36	58
Docetaxel	13 (59.1)	16 (44.4)	29 (50.0)
Cabazitaxel	7 (31.8)	14 (38.9)	21 (36.2)
Other	2 (9.1)	6 (16.7)	8 (13.8)
Number of cycles per patient			
n	10	18	28
Mean (SD)	5.1 (1.29)	6.2 (2.09)	5.8 (1.89)
Median	5.5	6.0	6.0
Q1 ; Q3	4.0 ; 6.0	6.0 ; 6.0	4.5 ; 6.0
Min ; Max	3 ; 13	3 ; 13	3 ; 13
Best overall response (BOR) to last therapy, n(%)			
n	22	36	58
Complete response	0	1 (2.8)	1 (1.7)
Partial response	4 (18.2)	11 (30.6)	15 (25.9)
Stable disease	0	0	0
Progressive disease	6 (27.3)	6 (16.7)	12 (20.7)
Missing	12 (54.5)	18 (50.0)	30 (51.7)

Output ID: t-cancerhist3-itt 04JUN20 12:56

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Table 14.1.6.4
Prostate Cancer Treatment History - Previous Other Treatment
ITT Population

	Lu-PSMA-617 (N=28)	6.0 GBq (N=43)	7.4 GBq (N=71)	Overall (N=71)
Patients with at least one prostate cancer related other treatment, n(%)	28 (100)	43 (100)	71 (100)	
Type of other treatment, n(%)				
ABIRATERONE	26 (92.9)	41 (95.3)	67 (94.4)	
CRYOTHERAPY	0	3 (7.0)	3 (4.2)	
ENZALUTAMIDE	21 (75.0)	34 (79.1)	55 (77.5)	
HIGH-INTENSITY FOCUSED ULTRASOUND	0	1 (2.3)	1 (1.4)	
HORMONAL THERAPY	22 (78.6)	39 (90.7)	61 (85.9)	
OTHER	20 (71.4)	31 (72.1)	51 (71.8)	
PELVIC LYMPH NODE RESECTION	1 (3.6)	3 (7.0)	4 (5.6)	
PROSTATECTOMY	12 (42.9)	19 (44.2)	31 (43.7)	
SALVAGE LYMPH NODE RESECTION	0	2 (4.7)	2 (2.8)	
STANDARD ADT	19 (67.9)	22 (51.2)	41 (57.7)	
TURP	2 (7.1)	2 (4.7)	4 (5.6)	
Number of other prior treatments per patient				
n	28	43	71	
Mean (SD)	6.3 (2.84)	6.4 (2.91)	6.4 (2.86)	
Median	7.0	6.0	6.0	
Q1 ; Q3	4.0 ; 7.5	4.0 ; 8.0	4.0 ; 8.0	
Min ; Max	2 ; 12	3 ; 13	2 ; 13	

Abbreviations: Turp = Transurethral resection of the prostate, ADT = Androgen deprivation therapy.

Output ID: t-cancerhist4-itt 04JUN20 12:56

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Table 14.1.6.5
Prostate Cancer Treatment History - Previous Radiotherapy
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)	Lu-PSMA-617 7.4 GBq (N=43)	Overall (N=71)
Patients with at least one prostate cancer related radiotherapy, n (%)	19 (67.9)	33 (76.7)	52 (73.2)
Type of Radiotherapy, n (%)			
BONE TARGETED THERAPY	1 (3.6)	6 (14.0)	7 (9.9)
OTHER	9 (32.1)	12 (27.9)	21 (29.6)
PRIMARY EBRT	4 (14.3)	10 (23.3)	14 (19.7)
RADIUM223	5 (17.9)	14 (32.6)	19 (26.8)
SALVAGE EBRT	10 (35.7)	16 (37.2)	26 (36.6)
Number of prior radiotherapies per patient			
n	19	33	52
Mean (SD)	2.3 (1.28)	2.6 (1.76)	2.5 (1.60)
Median	2.0	2.0	2.0
Q1 ; Q3	1.0 ; 3.0	1.0 ; 3.0	1.0 ; 3.0
Min ; Max	1 ; 5	1 ; 7	1 ; 7

Abbreviations: EBRT = External beam radiation therapy

Output ID: t-cancerhist5-itt 04JUN20 12:56

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14.2 Efficacy and other non-safety data

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Table 14.2.1.1
 Primary Efficacy (>=50% decline in PSA at Week 12)
 ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)	Lu-PSMA-617 7.4 GBq (N=43)	Overall (N=71)
PSA at Baseline (ug/L)			
n	23	40	63
Mean (SD)	244.70 (386.186)	350.48 (598.458)	311.86 (529.948)
Median	92.77	56.39	65.20
Q1 ; Q3	19.70 ; 296.20	18.30 ; 521.75	19.10 ; 493.20
Min ; Max	1.1 ; 1541.0	0.5 ; 2425.7	0.5 ; 2425.7
PSA at Week 12 (ug/L)			
n	14	26	40
Mean (SD)	308.91 (664.902)	250.66 (658.100)	271.04 (652.520)
Median	28.99	77.22	73.72
Q1 ; Q3	8.10 ; 122.00	23.60 ; 207.36	13.95 ; 202.73
Min ; Max	0.7 ; 2293.0	0.3 ; 3411.0	0.3 ; 3411.0
Percent change in PSA from Baseline to Week 12 (%)¹			
n	14	25	39
Mean (SD)	-22.54 (75.513)	92.15 (301.932)	50.98 (250.268)
Median	-30.57	-17.05	-22.06
Q1 ; Q3	-82.19 ; -1.94	-46.82 ; 60.03	-75.27 ; 43.36
Min ; Max	-96.4 ; 181.1	-86.1 ; 1129.2	-96.4 ; 1129.2
Patients with >=50% decline in PSA compared to baseline at Week 12², n (%)			
n (missing)	14 (0)	25 (1)	39 (1)
<50% Decline	5 (35.7)	8 (32.0)	13 (33.3)
>=50% Decline	6 (42.9)	6 (24.0)	12 (30.8)
Increase from baseline	3 (21.4)	11 (44.0)	14 (35.9)

¹ n is the number of patients who have a baseline and a week 12 valid assessments.

² percentages are based on the number of patients having a valid value at week 12. Patients having a week 12 valid assessment but no baseline are counted in the missing category.

Output ID: t-psadecline-itt 2020-12-03 10:48

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Table 14.2.1.2
Maximum PSA Response
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)	Lu-PSMA-617 7.4 GBq (N=43)	Overall (N=71)
Maximum PSA change (%)			
n	23	40	63
Mean (SD)	-3.63 (95.394)	8.75 (132.954)	4.23 (119.935)
Median	-19.69	-37.69	-37.45
Q1 ; Q3	-82.52 ; 40.73	-79.57 ; 40.23	-80.00 ; 40.50
Min ; Max	-99.9 ; 252.6	-99.1 ; 509.4	-99.9 ; 509.4

Includes all available PSA results, including unscheduled, up to and including the last follow-up visit.

Output ID: t-psamax-itt 2020-12-03 10:48

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Table 14.2.1.3
PSA Progression and Death
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)	Lu-PSMA-617 7.4 GBq (N=43)	Overall (N=71)
Number of events, n (%)			
Number of deaths without PSA progression*	2 (7.1)	2 (4.7)	4 (5.6)
Number of PSA progressions	11 (39.3)	17 (39.5)	28 (39.4)

PSA progression is defined as: (a) For patients with PSA decline: PSA progression is defined as the date that a $\geq 25\%$ increase in PSA and an absolute increase of 2 ng/mL or more from the nadir is documented and confirmed by a second consecutive value obtained 3 or more weeks later. Rises in PSA within the first 12 weeks will be ignored (PCWG3 Guidance), (b) For patients without PSA decline: PSA progression is defined as a $\geq 25\%$ increase from the baseline value along with an increase in absolute value of 2 ng/mL or more after 12 weeks of treatment.

*Deaths only count patients dead without previous PSA progression.

Output ID: t-psaprogr-itt 2020-12-03 10:48

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Table 14.2.2.1

RECIST 1.1 Overall response by follow-up assessment visit
ITT Population

Visit Response	Lu-PSMA-617 6.0 GBq (N=28) n (%)	Lu-PSMA-617 7.4 GBq (N=43) n (%)	Overall (N=71) n (%)
Assessment 1			
CR	1 (3.6)	1 (2.3)	2 (2.8)
PR	3 (10.7)	4 (9.3)	7 (9.9)
SD	1 (3.6)	7 (16.3)	8 (11.3)
PD	6 (21.4)	9 (20.9)	15 (21.1)
Assessment 2			
CR	3 (10.7)	1 (2.3)	4 (5.6)
PR	0	3 (7.0)	3 (4.2)
PD	1 (3.6)	1 (2.3)	2 (2.8)
Assessment 3			
CR	1 (3.6)	0	1 (1.4)
SD	0	1 (2.3)	1 (1.4)
Assessment 4			
PR	1 (3.6)	0	1 (1.4)

CR: Complete response PR: Partial response SD: Stable disease PD: Progressive disease
Investigator assessments (RECIST 1.1) of disease overall response were used.

Output ID: t-radioassess-itt 2020-12-03 10:48

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Table 14.2.2.2
RECIST 1.1 Disease control rate by follow-up assessment visit
ITT Population

Visit	Lu-PSMA-617 6.0 GBq (N=28) n (%)	Lu-PSMA-617 7.4 GBq (N=43) n (%)	Overall (N=71) n (%)
Assessment 1 Disease control	5 (17.9)	12 (27.9)	17 (23.9)
Assessment 2 Disease control	3 (10.7)	4 (9.3)	7 (9.9)
Assessment 3 Disease control	1 (3.6)	1 (2.3)	2 (2.8)
Assessment 4 Disease control	1 (3.6)	0	1 (1.4)

Disease control includes complete response (CR), partial response (PR) and stable disease (SD).

Investigator assessments (RECIST 1.1) of disease overall response were used.

Output ID: t-dcr-itt 2020-12-03 14:06

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Table 14.2.3
PCWG3 Bone scan clinical impression by visit
ITT Population

Visit		Lu-PSMA-617 6.0 GBq (N=28) n (%)	Lu-PSMA-617 7.4 GBq (N=43) n (%)	Overall (N=71) n (%)
Screening	Stable	1 (3.6)	0	1 (1.4)
Week 8	Improved	1 (3.6)	3 (7.0)	4 (5.6)
	Stable	1 (3.6)	2 (4.7)	3 (4.2)
	Progression	0	1 (2.3)	1 (1.4)
Week 10	Improved	0	3 (7.0)	3 (4.2)
	Stable	2 (7.1)	1 (2.3)	3 (4.2)
Week 16	Improved	0	2 (4.7)	2 (2.8)
	Stable	2 (7.1)	0	2 (2.8)
Week 18	Stable	0	3 (7.0)	3 (4.2)
	Progression	1 (3.6)	0	1 (1.4)
Week 22	Stable	0	1 (2.3)	1 (1.4)
Week 24	Stable	0	1 (2.3)	1 (1.4)
Fu Week 4	Progression	0	1 (2.3)	1 (1.4)
Fu Week 6	Progression	0	1 (2.3)	1 (1.4)
Fu Week 8	Stable	1 (3.6)	0	1 (1.4)
	Progression	1 (3.6)	0	1 (1.4)

Clinical impression on bone scan assessments by investigator.

Output ID: t-bonescan-itt 2020-12-03 10:48

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Table 14.2.5.1
Quality of Life Questionnaire - EPIC-26 - Urinary Incontinence
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)		Lu-PSMA-617 7.4 GBq (N=43)		Overall (N=71)	
	Value	Change	Value	Change	Value	Change
Baseline						
n	20		35		55	
Mean (SD)	78.3 (26.87)		77.4 (24.64)		77.7 (25.23)	
Median	86.5		85.5		85.5	
Q1 ; Q3	65.8 ; 100.0		58.5 ; 100.0		64.8 ; 100.0	
Min ; Max	15 ; 100		15 ; 100		15 ; 100	
Month 3						
n	8	8	9	9	17	17
Mean (SD)	87.8 (22.39)	4.9 (12.57)	83.6 (23.33)	9.7 (20.88)	85.6 (22.27)	7.5 (17.12)
Median	100.0	0.0	100.0	0.0	100.0	0.0
Q1 ; Q3	82.4 ; 100.0	0.0 ; 6.3	58.5 ; 100.0	0.0 ; 8.3	73.0 ; 100.0	0.0 ; 8.3
Min ; Max	38 ; 100	-6 ; 33	46 ; 100	0 ; 65	38 ; 100	-6 ; 65
Month 6						
n	3	3	7	7	10	10
Mean (SD)	97.3 (4.76)	11.1 (19.20)	78.0 (23.63)	-6.3 (14.66)	83.8 (21.54)	-1.1 (17.19)
Median	100.0	0.0	79.3	0.0	91.8	0.0
Q1 ; Q3	91.8 ; 100.0	0.0 ; 33.3	73.0 ; 93.8	-20.8 ; 6.3	79.3 ; 100.0	-18.8 ; 6.3
Min ; Max	92 ; 100	0 ; 33	29 ; 100	-25 ; 8	29 ; 100	-25 ; 33
Follow-up Month 3						
n	0	0	3	3	3	3
Mean (SD)			88.9 (10.45)	-2.1 (9.55)	88.9 (10.45)	-2.1 (9.55)
Median			87.5	0.0	87.5	0.0
Q1 ; Q3			79.3 ; 100.0	-12.5 ; 6.3	79.3 ; 100.0	-12.5 ; 6.3
Min ; Max			79 ; 100	-13 ; 6	79 ; 100	-13 ; 6

The response for each numbered question is standardized to a 0 to 100 scale according to the EPIC-26 Scoring Instructions. Higher Score representing higher satisfaction. Domain Summary Scores are calculated using the numbered questions within a specified group identified in the EPIC-26 Scoring Instructions.

If >20% of the items that comprise a domain summary score or subscale score are missing a response, the corresponding domain summary or subscale score cannot be calculated.

Output ID: t-epic26-q1-itt 04JUN20 12:58

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Table 14.2.5.2
Quality of Life Questionnaire - EPIC-26 - Urinary Irritative/Obstructive
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)		Lu-PSMA-617 7.4 GBq (N=43)		Overall (N=71)	
	Value	Change	Value	Change	Value	Change
Baseline						
n	19		35		54	
Mean (SD)	83.2 (20.73)		84.8 (19.13)		84.3 (19.53)	
Median	93.8		93.8		93.8	
Q1 ; Q3	68.8 ; 100.0		75.0 ; 100.0		75.0 ; 100.0	
Min ; Max	31 ; 100		13 ; 100		13 ; 100	
Month 3						
n	7	7	9	9	16	16
Mean (SD)	98.2 (4.72)	17.9 (25.37)	86.8 (15.13)	-1.4 (4.17)	91.8 (12.85)	7.0 (19.08)
Median	100.0	6.3	93.8	0.0	100.0	0.0
Q1 ; Q3	100.0 ; 100.0	0.0 ; 31.3	75.0 ; 100.0	0.0 ; 0.0	84.4 ; 100.0	0.0 ; 3.1
Min ; Max	88 ; 100	0 ; 69	63 ; 100	-13 ; 0	63 ; 100	-13 ; 69
Month 6						
n	3	8	7	7	10	10
Mean (SD)	79.2 (20.09)	2.1 (9.55)	83.0 (14.75)	6.3 (8.84)	81.9 (15.44)	5.0 (8.74)
Median	87.5	0.0	87.5	0.0	87.5	0.0
Q1 ; Q3	56.3 ; 93.8	-6.3 ; 12.5	68.8 ; 100.0	0.0 ; 18.8	68.8 ; 93.8	0.0 ; 12.5
Min ; Max	56 ; 94	-6 ; 13	63 ; 100	0 ; 19	56 ; 100	-6 ; 19
Follow-up Month 3						
n	0	0	3	3	3	3
Mean (SD)			91.7 (14.43)	8.3 (9.55)	91.7 (14.43)	8.3 (9.55)
Median			100.0	6.3	100.0	6.3
Q1 ; Q3			75.0 ; 100.0	0.0 ; 18.8	75.0 ; 100.0	0.0 ; 18.8
Min ; Max			75 ; 100	0 ; 19	75 ; 100	0 ; 19

The response for each numbered question is standardized to a 0 to 100 scale according to the EPIC-26 Scoring Instructions. Higher Score representing higher satisfaction. Domain Summary Scores are calculated using the numbered questions within a specified group identified in the EPIC-26 Scoring Instructions.

If >20% of the items that comprise a domain summary score or subscale score are missing a response, the corresponding domain summary or subscale score cannot be calculated.

Output ID: t-epic26-q2-itt 04JUN20 12:58

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Table 14.2.5.3
Quality of Life Questionnaire - EPIC-26 - Bowel
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)		Lu-PSMA-617 7.4 GBq (N=43)		Overall (N=71)	
	Value	Change	Value	Change	Value	Change
Baseline						
n	20		32		52	
Mean (SD)	90.8 (14.60)		88.4 (14.77)		89.3 (14.61)	
Median	95.8		95.8		95.8	
Q1 ; Q3	89.6 ; 100.0		81.3 ; 100.0		85.4 ; 100.0	
Min ; Max	50 ; 100		50 ; 100		50 ; 100	
Month 3						
n	8	8	9	9	17	17
Mean (SD)	93.8 (8.91)	-1.0 (8.55)	88.7 (11.93)	4.0 (18.57)	91.1 (10.61)	1.6 (14.53)
Median	100.0	0.0	91.7	0.0	95.8	0.0
Q1 ; Q3	85.4 ; 100.0	-6.3 ; 0.0	75.0 ; 100.0	-4.2 ; 12.5	83.3 ; 100.0	-4.2 ; 4.2
Min ; Max	79 ; 100	-13 ; 17	71 ; 100	-29 ; 38	71 ; 100	-29 ; 38
Month 6						
n	3	3	6	6	9	9
Mean (SD)	90.3 (8.67)	-4.2 (8.33)	91.0 (12.48)	4.9 (16.75)	90.7 (10.78)	1.9 (14.60)
Median	87.5	-4.2	93.8	0.0	91.7	-4.2
Q1 ; Q3	83.3 ; 100.0	-12.5 ; 4.2	91.7 ; 100.0	-8.3 ; 20.8	87.5 ; 100.0	-8.3 ; 4.2
Min ; Max	83 ; 100	-13 ; 4	67 ; 100	-13 ; 29	67 ; 100	-13 ; 29
Follow-up Month 3						
n	0	0	3	3	3	3
Mean (SD)			83.3 (28.87)	-8.3 (18.16)	83.3 (28.87)	-8.3 (18.16)
Median			100.0	0.0	100.0	0.0
Q1 ; Q3			50.0 ; 100.0	-29.2 ; 4.2	50.0 ; 100.0	-29.2 ; 4.2
Min ; Max			50 ; 100	-29 ; 4	50 ; 100	-29 ; 4

The response for each numbered question is standardized to a 0 to 100 scale according to the EPIC-26 Scoring Instructions. Higher Score representing higher satisfaction. Domain Summary Scores are calculated using the numbered questions within a specified group identified in the EPIC-26 Scoring Instructions.

If >20% of the items that comprise a domain summary score or subscale score are missing a response, the corresponding domain summary or subscale score cannot be calculated.

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Table 14.2.5.4
Quality of Life Questionnaire - EPIC-26 - Sexual
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)		Lu-PSMA-617 7.4 GBq (N=43)		Overall (N=71)	
	Value	Change	Value	Change	Value	Change
Baseline						
n	20		33		53	
Mean (SD)	8.8 (9.74)		11.7 (19.66)		10.6 (16.57)	
Median	8.3		4.2		5.5	
Q1 ; Q3	0.0 ; 14.6		0.0 ; 16.7		0.0 ; 16.7	
Min ; Max	0 ; 39		0 ; 100		0 ; 100	
Month 3						
n	8	8	9	9	17	17
Mean (SD)	9.5 (7.18)	-4.4 (11.68)	25.0 (30.88)	7.8 (15.76)	17.8 (23.73)	2.1 (14.93)
Median	10.4	0.0	16.7	0.0	13.8	0.0
Q1 ; Q3	2.8 ; 16.7	-6.4 ; 0.0	11.6 ; 16.7	0.0 ; 11.6	5.5 ; 16.7	0.0 ; 0.0
Min ; Max	0 ; 17	-31 ; 8	0 ; 100	-4 ; 46	0 ; 100	-31 ; 46
Month 6						
n	3	3	7	7	10	10
Mean (SD)	2.8 (4.81)	-4.7 (5.02)	12.9 (2.49)	7.3 (5.82)	9.9 (5.75)	3.7 (7.88)
Median	0.0	-4.2	12.5	9.7	12.5	2.1
Q1 ; Q3	0.0 ; 8.3	-10.0 ; 0.0	12.5 ; 13.8	0.0 ; 12.5	8.3 ; 13.8	0.0 ; 12.5
Min ; Max	0 ; 8	-10 ; 0	8 ; 17	0 ; 13	0 ; 17	-10 ; 13
Follow-up Month 3						
n	0	0	3	3	3	3
Mean (SD)			6.0 (7.10)	4.6 (4.85)	6.0 (7.10)	4.6 (4.85)
Median			4.2	4.2	4.2	4.2
Q1 ; Q3			0.0 ; 13.8	0.0 ; 9.7	0.0 ; 13.8	0.0 ; 9.7
Min ; Max			0 ; 14	0 ; 10	0 ; 14	0 ; 10

The response for each numbered question is standardized to a 0 to 100 scale according to the EPIC-26 Scoring Instructions. Higher Score representing higher satisfaction. Domain Summary Scores are calculated using the numbered questions within a specified group identified in the EPIC-26 Scoring Instructions.

If >20% of the items that comprise a domain summary score or subscale score are missing a response, the corresponding domain summary or subscale score cannot be calculated.

Output ID: t-epic26-q4-itt 04JUN20 12:59

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Table 14.2.5.5
Quality of Life Questionnaire - EPIC-26 - Hormonal
ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)		Lu-PSMA-617 7.4 GBq (N=43)		Overall (N=71)	
	Value	Change	Value	Change	Value	Change
Baseline						
n	21		32		53	
Mean (SD)	77.0 (18.19)		73.6 (16.13)		74.9 (16.89)	
Median	80.0		70.0		75.0	
Q1 ; Q3	70.0 ; 90.0		60.0 ; 90.0		60.0 ; 90.0	
Min ; Max	30 ; 100		40 ; 95		30 ; 100	
Month 3						
n	8	8	9	9	17	17
Mean (SD)	81.9 (17.31)	4.4 (16.35)	77.6 (19.73)	10.4 (24.62)	79.6 (18.18)	7.6 (20.73)
Median	87.5	5.0	80.0	10.0	85.0	10.0
Q1 ; Q3	70.0 ; 95.0	-5.0 ; 20.0	65.0 ; 93.8	0.0 ; 20.0	65.0 ; 95.0	0.0 ; 20.0
Min ; Max	50 ; 100	-25 ; 20	40 ; 100	-35 ; 50	40 ; 100	-35 ; 50
Month 6						
n	3	3	7	7	10	10
Mean (SD)	71.7 (7.64)	1.7 (28.87)	75.0 (14.14)	10.0 (10.00)	74.0 (12.20)	7.5 (16.37)
Median	70.0	-15.0	75.0	10.0	72.5	10.0
Q1 ; Q3	65.0 ; 80.0	-15.0 ; 35.0	65.0 ; 80.0	0.0 ; 15.0	65.0 ; 80.0	-5.0 ; 15.0
Min ; Max	65 ; 80	-15 ; 35	55 ; 100	-5 ; 25	55 ; 100	-15 ; 35
Follow-up Month 3						
n	0	0	3	3	3	3
Mean (SD)			71.7 (24.66)	8.3 (7.64)	71.7 (24.66)	8.3 (7.64)
Median			60.0	10.0	60.0	10.0
Q1 ; Q3			55.0 ; 100.0	0.0 ; 15.0	55.0 ; 100.0	0.0 ; 15.0
Min ; Max			55 ; 100	0 ; 15	55 ; 100	0 ; 15

The response for each numbered question is standardized to a 0 to 100 scale according to the EPIC-26 Scoring Instructions. Higher Score representing higher satisfaction. Domain Summary Scores are calculated using the numbered questions within a specified group identified in the EPIC-26 Scoring Instructions.

If >20% of the items that comprise a domain summary score or subscale score are missing a response, the corresponding domain summary or subscale score cannot be calculated.

Output ID: t-epic26-q5-itt 04JUN20 12:59

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Table 14.2.6.1
 Eastern Cooperative Oncology Group (ECOG) Performance Status by Visit
 ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)		Lu-PSMA-617 7.4 GBq (N=43)		Overall (N=71)	
	Value	Change	Value	Change	Value	Change
Baseline						
n	19		33		52	
Mean (SD)	0.9 (0.81)		0.9 (0.61)		0.9 (0.68)	
Median	1.0		1.0		1.0	
Q1 ; Q3	0.0 ; 2.0		1.0 ; 1.0		0.0 ; 1.0	
Min ; Max	0 ; 2		0 ; 2		0 ; 2	
Treatment Visit 1						
n	13	13	28	28	41	41
Mean (SD)	0.7 (0.85)	-0.2 (0.60)	1.0 (0.58)	0.0 (0.54)	0.9 (0.68)	-0.1 (0.57)
Median	0.0	0.0	1.0	0.0	1.0	0.0
Q1 ; Q3	0.0 ; 1.0	0.0 ; 0.0	1.0 ; 1.0	0.0 ; 0.0	0.0 ; 1.0	0.0 ; 0.0
Min ; Max	0 ; 2	-2 ; 0	0 ; 2	-1 ; 2	0 ; 2	-2 ; 2
Treatment Visit 2						
n	16	16	31	31	47	47
Mean (SD)	0.6 (0.72)	-0.3 (0.60)	0.9 (0.62)	-0.1 (0.63)	0.8 (0.66)	-0.1 (0.62)
Median	0.5	0.0	1.0	0.0	1.0	0.0
Q1 ; Q3	0.0 ; 1.0	-0.5 ; 0.0	0.0 ; 1.0	0.0 ; 0.0	0.0 ; 1.0	0.0 ; 0.0
Min ; Max	0 ; 2	-2 ; 0	0 ; 2	-1 ; 2	0 ; 2	-2 ; 2
Treatment Visit 3						
n	13	13	19	19	32	32
Mean (SD)	0.5 (0.66)	-0.2 (0.73)	0.8 (0.63)	-0.2 (0.50)	0.7 (0.64)	-0.2 (0.59)
Median	0.0	0.0	1.0	0.0	1.0	0.0
Q1 ; Q3	0.0 ; 1.0	0.0 ; 0.0	0.0 ; 1.0	0.0 ; 0.0	0.0 ; 1.0	0.0 ; 0.0
Min ; Max	0 ; 2	-2 ; 1	0 ; 2	-1 ; 1	0 ; 2	-2 ; 1

Eastern Cooperative Oncology Group (ECOG) Performance Status. Grade from 0 to 5, higher grade representing worse performance status.

Output ID: t-ecog-q1-itt 04JUN20 12:59

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Table 14.2.6.1
 Eastern Cooperative Oncology Group (ECOG) Performance Status by Visit
 ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)		Lu-PSMA-617 7.4 GBq (N=43)		Overall (N=71)	
	Value	Change	Value	Change	Value	Change
Treatment Visit ⁴						
n	9	9	16	16	25	25
Mean (SD)	0.7 (0.87)	-0.1 (0.93)	0.7 (0.60)	-0.3 (0.48)	0.7 (0.69)	-0.2 (0.66)
Median	0.0	0.0	1.0	0.0	1.0	0.0
Q1 ; Q3	0.0 ; 1.0	0.0 ; 0.0	0.0 ; 1.0	-1.0 ; 0.0	0.0 ; 1.0	-1.0 ; 0.0
Min ; Max	0 ; 2	-2 ; 1	0 ; 2	-1 ; 0	0 ; 2	-2 ; 1
Follow-up Month 3						
n	1	1	0	0	1	1
Mean (SD)	0.0 (NE)	0.0 (NE)	0.0 (NE)	0.0 (NE)	0.0 (NE)	0.0 (NE)
Median	0.0	0.0	0.0	0.0	0.0	0.0
Q1 ; Q3	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0	0.0 ; 0.0
Min ; Max	0 ; 0	0 ; 0	0 ; 0	0 ; 0	0 ; 0	0 ; 0
Follow-up Month 12						
n	0	0	1	1	1	1
Mean (SD)			0.0 (NE)	-1.0 (NE)	0.0 (NE)	-1.0 (NE)
Median			0.0	-1.0	0.0	-1.0
Q1 ; Q3			0.0 ; 0.0	-1.0 ; -1.0	0.0 ; 0.0	-1.0 ; -1.0
Min ; Max			0 ; 0	-1 ; -1	0 ; 0	-1 ; -1
Follow-up Month 15						
n	0	0	1	1	1	1
Mean (SD)			1.0 (NE)	0.0 (NE)	1.0 (NE)	0.0 (NE)
Median			1.0	0.0	1.0	0.0
Q1 ; Q3			1.0 ; 1.0	0.0 ; 0.0	1.0 ; 1.0	0.0 ; 0.0
Min ; Max			1 ; 1	0 ; 0	1 ; 1	0 ; 0

Eastern Cooperative Oncology Group (ECOG) Performance Status. Grade from 0 to 5, higher grade representing worse performance status.

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Table 14.2.6.2
 Eastern Cooperative Oncology Group (ECOG) Performance Status by Visit - Shift Table
 ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)			Lu-PSMA-617 7.4 GBq (N=43)			Overall (N=71)		
	Baseline Grade			Baseline Grade			Baseline Grade		
	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)
Treatment Visit 1									
n*	13			28			41		
Grade 0	6 (46.2)	0	1 (7.7)	3 (10.7)	2 (7.1)	0	9 (22.0)	2 (4.9)	1 (2.4)
Grade 1	0	2 (15.4)	1 (7.7)	1 (3.6)	17 (60.7)	1 (3.6)	1 (2.4)	19 (46.3)	2 (4.9)
Grade 2	0	0	3 (23.1)	1 (3.6)	0	3 (10.7)	1 (2.4)	0	6 (14.6)
Grade 3	0	0	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0	0	0
Treatment Visit 2									
n*	16			31			47		
Grade 0	6 (37.5)	1 (6.3)	1 (6.3)	4 (12.9)	4 (12.9)	0	10 (21.3)	5 (10.6)	1 (2.1)
Grade 1	0	4 (25.0)	2 (12.5)	2 (6.5)	15 (48.4)	2 (6.5)	2 (4.3)	19 (40.4)	4 (8.5)
Grade 2	0	0	2 (12.5)	1 (3.2)	0	3 (9.7)	1 (2.1)	0	5 (10.6)
Grade 3	0	0	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0	0	0
Treatment Visit 3									
n*	13			19			32		
Grade 0	5 (38.5)	1 (7.7)	1 (7.7)	3 (15.8)	3 (15.8)	0	8 (25.0)	4 (12.5)	1 (3.1)
Grade 1	1 (7.7)	3 (23.1)	1 (7.7)	0	10 (52.6)	1 (5.3)	1 (3.1)	13 (40.6)	2 (6.3)
Grade 2	0	0	1 (7.7)	0	1 (5.3)	1 (5.3)	0	1 (3.1)	2 (6.3)
Grade 3	0	0	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0	0	0

n* is the number of patients with both baseline and time point results available, to be used as denominator for the percentage calculation.

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Table 14.2.6.2
 Eastern Cooperative Oncology Group (ECOG) Performance Status by Visit - Shift Table
 ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)			Lu-PSMA-617 7.4 GBq (N=43)			Overall (N=71)		
	Baseline Grade			Baseline Grade			Baseline Grade		
	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)
Treatment Visit 4									
n*	9			16			25		
Grade 0	3 (33.3)	1 (11.1)	1 (11.1)	2 (12.5)	4 (25.0)	0	5 (20.0)	5 (20.0)	1 (4.0)
Grade 1	1 (11.1)	1 (11.1)	0	0	8 (50.0)	1 (6.3)	1 (4.0)	9 (36.0)	1 (4.0)
Grade 2	0	1 (11.1)	1 (11.1)	0	0	1 (6.3)	0	1 (4.0)	2 (8.0)
Grade 3	0	0	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0	0	0
Follow-up Month 3									
n*	1 (100)	0	0	0	0	0	1 (100)	0	0
Grade 0	0	0	0	0	0	0	0	0	0
Grade 1	0	0	0	0	0	0	0	0	0
Grade 2	0	0	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0	0	0
Follow-up Month 12									
n*	0	1	0	1	1 (100)	0	0	1 (100)	0
Grade 0	0	0	0	0	0	0	0	0	0
Grade 1	0	0	0	0	0	0	0	0	0
Grade 2	0	0	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0	0	0

n* is the number of patients with both baseline and time point results available, to be used as denominator for the percentage calculation.

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Table 14.2.6.2
 Eastern Cooperative Oncology Group (ECOG) Performance Status by Visit - Shift Table
 ITT Population

	Lu-PSMA-617 6.0 GBq (N=28)			Lu-PSMA-617 7.4 GBq (N=43)			Overall (N=71)		
	Baseline Grade			Baseline Grade			Baseline Grade		
	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)
Follow-up Month 15									
n*	0	0	0	0	1 (100)	0	0	1 (100)	0
Grade 0	0	0	0	0	0	0	0	1 (100)	0
Grade 1	0	0	0	0	0	0	0	1 (100)	0
Grade 2	0	0	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0	0	0

n* is the number of patients with both baseline and time point results available, to be used as denominator for the percentage calculation.

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14.3 Safety data

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14.3.1 Displays of adverse events

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Table 14.3.1.1
Summary Table of Adverse Events
Safety Population

	Lu-PSMA-617 (N=23) n (%)	6.0 GBq Lu-PSMA-617 (N=41) n (%)	7.4 GBq Overall (N=64) n (%)
Patients with at least one TEAE	22 (95.7)	39 (95.1)	61 (95.3)
Patients with at least one serious TEAE	4 (17.4)	8 (19.5)	12 (18.8)
Patients with at least one drug-related TEAE	20 (87.0)	37 (90.2)	57 (89.1)
Patients with at least one serious drug-related TEAE	1 (4.3)	4 (9.8)	5 (7.8)
Patients having a TEAE leading to reduction of Lu-PSMA-617	0	2 (4.9)	2 (3.1)
Patients having a TEAE leading to discontinuation of Lu-PSMA-617	0	1 (2.4)	1 (1.6)
TEAE leading to death	2 (8.7)	1 (2.4)	3 (4.7)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

TEAE is considered study drug-related if relatedness is recorded as possible, probably, definite, or when the value is missing.

Output ID: t-aesum-saf 04JUN20 12:55

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Table 14.3.1.2.1
TEAEs by Severity, MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)		Lu-PSMA-617 7.4 GBq (N=41) n (%)		Overall (N=64) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Patient with Any Event	22 (95.7)	2 (8.7)	39 (95.1)	7 (17.1)	61 (95.3)	9 (14.1)
Gastrointestinal disorders	19 (82.6)	0	33 (80.5)	2 (4.9)	52 (81.3)	2 (3.1)
Dry mouth	11 (47.8)	0	26 (63.4)	0	37 (57.8)	0
Nausea	12 (52.2)	0	18 (43.9)	1 (2.4)	30 (46.9)	1 (1.6)
Diarrhoea	3 (13.0)	0	13 (31.7)	0	16 (25.0)	0
Constipation	6 (26.1)	0	9 (22.0)	0	15 (23.4)	0
Vomiting	4 (17.4)	0	8 (19.5)	1 (2.4)	12 (18.8)	1 (1.6)
Abdominal pain	1 (4.3)	0	1 (2.4)	1 (2.4)	2 (3.1)	1 (1.6)
Frequent bowel movements	0	0	1 (2.4)	0	1 (1.6)	0
Gastrointestinal haemorrhage	0	0	1 (2.4)	0	1 (1.6)	0
Hyperesthesia teeth	1 (4.3)	0	0	0	1 (1.6)	0
Lip dry	0	0	1 (2.4)	0	1 (1.6)	0
Saliva altered	1 (4.3)	0	0	0	1 (1.6)	0
General disorders and administration site conditions	13 (56.5)	0	25 (61.0)	1 (2.4)	38 (59.4)	1 (1.6)
Fatigue	13 (56.5)	0	21 (51.2)	0	34 (53.1)	0
Pain	3 (13.0)	0	5 (12.2)	0	8 (12.5)	0
Chest pain	1 (4.3)	0	1 (2.4)	0	2 (3.1)	0
Pyrexia	0	0	2 (4.9)	0	2 (3.1)	0
Asthenia	0	0	1 (2.4)	0	1 (1.6)	0
Death	0	0	1 (2.4)	1 (2.4)	1 (1.6)	1 (1.6)
Feeling hot	0	0	1 (2.4)	0	1 (1.6)	0
Oedema peripheral	0	0	1 (2.4)	0	1 (1.6)	0
Musculoskeletal and connective tissue disorders	6 (26.1)	0	10 (24.4)	1 (2.4)	16 (25.0)	1 (1.6)

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.2.1
TEAEs by Severity, MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)		Lu-PSMA-617 7.4 GBq (N=41) n (%)		Overall (N=64) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Musculoskeletal and connective tissue disorders (Continued)						
Arthralgia	3 (13.0)	0	2 (4.9)	0	5 (7.8)	0
Back pain	2 (8.7)	0	1 (2.4)	0	3 (4.7)	0
Bone pain	1 (4.3)	0	2 (4.9)	1 (2.4)	3 (4.7)	1 (1.6)
Pain in extremity	1 (4.3)	0	2 (4.9)	0	3 (4.7)	0
Musculoskeletal chest pain	0	0	2 (4.9)	0	2 (3.1)	0
Musculoskeletal stiffness	0	0	1 (2.4)	0	1 (1.6)	0
Neck pain	0	0	1 (2.4)	0	1 (1.6)	0
Osteoporosis	1 (4.3)	0	0	0	1 (1.6)	0
Nervous system disorders	6 (26.1)	0	10 (24.4)	0	16 (25.0)	0
Taste disorder	4 (17.4)	0	7 (17.1)	0	11 (17.2)	0
Headache	2 (8.7)	0	2 (4.9)	0	4 (6.3)	0
Dizziness	0	0	2 (4.9)	0	2 (3.1)	0
Parosmia	1 (4.3)	0	0	0	1 (1.6)	0
Blood and lymphatic system disorders	5 (21.7)	0	6 (14.6)	1 (2.4)	11 (17.2)	1 (1.6)
Anaemia	4 (17.4)	0	4 (9.8)	0	8 (12.5)	0
Leukopenia	0	0	1 (2.4)	0	1 (1.6)	0
Lymphadenopathy	1 (4.3)	0	0	0	1 (1.6)	0
Lymphopenia	0	0	1 (2.4)	0	1 (1.6)	0
Thrombocytopenia	0	0	1 (2.4)	1 (2.4)	1 (1.6)	1 (1.6)
Metabolism and nutrition disorders	2 (8.7)	0	7 (17.1)	0	9 (14.1)	0
Decreased appetite	1 (4.3)	0	5 (12.2)	0	6 (9.4)	0

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

Output ID: t-aesevx-saf 04JUN20 12:55

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Table 14.3.1.2.1
TEAEs by Severity, MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)		Lu-PSMA-617 7.4 GBq (N=41) n (%)		Overall (N=64) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Metabolism and nutrition disorders (Continued)						
Hyponatraemia	1 (4.3)	0	1 (2.4)	0	2 (3.1)	0
Dehydration	0	0	1 (2.4)	0	1 (1.6)	0
Eye disorders						
Dry eye	1 (4.3)	0	4 (9.8)	0	5 (7.8)	0
Lacration increased	1 (4.3)	0	3 (7.3)	0	4 (6.3)	0
Renal and urinary disorders						
Dysuria	1 (4.3)	0	1 (2.4)	0	2 (3.1)	0
Acute kidney injury	0	0	1 (2.4)	0	1 (1.6)	0
Bladder pain	0	0	1 (2.4)	0	1 (1.6)	0
Pollakiuria	0	0	1 (2.4)	0	1 (1.6)	0
Respiratory, thoracic and mediastinal disorders						
Dyspnoea	1 (4.3)	0	4 (9.8)	2 (4.9)	5 (7.8)	2 (3.1)
Epistaxis	0	0	3 (7.3)	1 (2.4)	3 (4.7)	1 (1.6)
Pleural effusion	1 (4.3)	0	0	0	1 (1.6)	0
Rhinorrhoea	0	0	1 (2.4)	1 (2.4)	1 (1.6)	1 (1.6)
Wheezing	0	0	1 (2.4)	0	1 (1.6)	0
Infections and infestations						
Bronchitis	1 (4.3)	0	3 (7.3)	0	4 (6.3)	0
Herpes zoster	0	0	1 (2.4)	0	1 (1.6)	0
Pneumonia	0	0	1 (2.4)	0	1 (1.6)	0
Urinary tract infection	0	0	1 (2.4)	0	1 (1.6)	0

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.2.1
TEAEs by Severity, MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)		Lu-PSMA-617 7.4 GBq (N=41) n (%)		Overall (N=64) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (8.7)	1 (4.3)	2 (4.9)	0	4 (6.3)	1 (1.6)
Metastases to central nervous system	2 (8.7)	1 (4.3)	0	0	2 (3.1)	1 (1.6)
Adenocarcinoma of colon	0	0	1 (2.4)	0	1 (1.6)	0
Metastases to meninges	0	0	1 (2.4)	0	1 (1.6)	0
Investigations	2 (8.7)	0	1 (2.4)	0	3 (4.7)	0
Blood lactate dehydrogenase increased	1 (4.3)	0	0	0	1 (1.6)	0
Glomerular filtration rate decreased	1 (4.3)	0	0	0	1 (1.6)	0
Weight decreased	0	0	1 (2.4)	0	1 (1.6)	0
Skin and subcutaneous tissue disorders	1 (4.3)	0	1 (2.4)	0	2 (3.1)	0
Dry skin	1 (4.3)	0	0	0	1 (1.6)	0
Pain of skin	0	0	1 (2.4)	0	1 (1.6)	0
Vascular disorders	0	0	2 (4.9)	0	2 (3.1)	0
Haematoma	0	0	2 (4.9)	0	2 (3.1)	0
Ear and labyrinth disorders	0	0	1 (2.4)	0	1 (1.6)	0
Deafness	0	0	1 (2.4)	0	1 (1.6)	0

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.2.1
TEAEs by Severity, MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)		Lu-PSMA-617 7.4 GBq (N=41) n (%)		Overall (N=64) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Endocrine disorders	0	0	1 (2.4)	0	1 (1.6)	0
Hypothyroidism	0	0	1 (2.4)	0	1 (1.6)	0
Injury, poisoning and procedural complications	1 (4.3)	1 (4.3)	0	0	1 (1.6)	1 (1.6)
Subdural haematoma	1 (4.3)	1 (4.3)	0	0	1 (1.6)	1 (1.6)
Psychiatric disorders	0	0	1 (2.4)	0	1 (1.6)	0
Depression	0	0	1 (2.4)	0	1 (1.6)	0
Reproductive system and breast disorders	0	0	1 (2.4)	0	1 (1.6)	0
Prostatic pain	0	0	1 (2.4)	0	1 (1.6)	0

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.2.2.1
TEAEs by Severity, MedDRA System Organ Class and Preferred Term (patients <65 years old)
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=4) n (%)		Lu-PSMA-617 7.4 GBq (N=12) n (%)		Overall (N=16) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Patient with Any Event	4 (100)	1 (25.0)	11 (91.7)	1 (8.3)	15 (93.8)	2 (12.5)
Gastrointestinal disorders	4 (100)	0	10 (83.3)	0	14 (87.5)	0
Nausea	3 (75.0)	0	7 (58.3)	0	10 (62.5)	0
Dry mouth	2 (50.0)	0	5 (41.7)	0	7 (43.8)	0
Vomiting	2 (50.0)	0	3 (25.0)	0	5 (31.3)	0
Constipation	0	0	2 (16.7)	0	2 (12.5)	0
Diarrhoea	1 (25.0)	0	1 (8.3)	0	2 (12.5)	0
Frequent bowel movements	0	0	1 (8.3)	0	1 (6.3)	0
Lip dry	0	0	1 (8.3)	0	1 (6.3)	0
General disorders and administration site conditions	2 (50.0)	0	7 (58.3)	0	9 (56.3)	0
Fatigue	2 (50.0)	0	5 (41.7)	0	7 (43.8)	0
Chest pain	0	0	1 (8.3)	0	1 (6.3)	0
Pain	0	0	1 (8.3)	0	1 (6.3)	0
Pyrexia	0	0	1 (8.3)	0	1 (6.3)	0
Blood and lymphatic system disorders	1 (25.0)	0	3 (25.0)	1 (8.3)	4 (25.0)	1 (6.3)
Anaemia	1 (25.0)	0	3 (25.0)	0	4 (25.0)	0
Thrombocytopenia	0	0	1 (8.3)	1 (8.3)	1 (6.3)	1 (6.3)
Musculoskeletal and connective tissue disorders	1 (25.0)	0	3 (25.0)	0	4 (25.0)	0
Musculoskeletal chest pain	0	0	2 (16.7)	0	2 (12.5)	0
Arthralgia	1 (25.0)	0	0	0	1 (6.3)	0
Bone pain	0	0	1 (8.3)	0	1 (6.3)	0

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.2.2.1
TEAEs by Severity, MedDRA System Organ Class and Preferred Term (patients <65 years old)
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=4) n (%)		Lu-PSMA-617 7.4 GBq (N=12) n (%)		Overall (N=16) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Musculoskeletal and connective tissue disorders (Continued)						
Musculoskeletal stiffness	0	0	1 (8.3)	0	1 (6.3)	0
Nervous system disorders	0	0	4 (33.3)	0	4 (25.0)	0
Taste disorder	0	0	3 (25.0)	0	3 (18.8)	0
Dizziness	0	0	1 (8.3)	0	1 (6.3)	0
Investigations	1 (25.0)	0	1 (8.3)	0	2 (12.5)	0
Glomerular filtration rate decreased	1 (25.0)	0	0	0	1 (6.3)	0
Weight decreased	0	0	1 (8.3)	0	1 (6.3)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (25.0)	1 (25.0)	1 (8.3)	0	2 (12.5)	1 (6.3)
Metastases to central nervous system	1 (25.0)	1 (25.0)	0	0	1 (6.3)	1 (6.3)
Metastases to meninges	0	0	1 (8.3)	0	1 (6.3)	0
Infections and infestations	0	0	1 (8.3)	0	1 (6.3)	0
Pneumonia	0	0	1 (8.3)	0	1 (6.3)	0
Metabolism and nutrition disorders	0	0	1 (8.3)	0	1 (6.3)	0
Decreased appetite	0	0	1 (8.3)	0	1 (6.3)	0
Renal and urinary disorders	0	0	1 (8.3)	0	1 (6.3)	0

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

Output ID: t-aesevx-agea-saf 04JUN20 12:55

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Table 14.3.1.2.2.1
 TEAEs by Severity, MedDRA System Organ Class and Preferred Term (patients <65 years old)
 Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=4) n (%)		Lu-PSMA-617 7.4 GBq (N=12) n (%)		Overall (N=16) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Renal and urinary disorders (Continued)						
Pollakiuria	0	0	1 (8.3)	0	1 (6.3)	0

Numbers (n) represent counts of patients.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.2.2.2
TEAEs by Severity, MedDRA System Organ Class and Preferred Term (patients >=65 years old)
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=19) n (%)		Lu-PSMA-617 7.4 GBq (N=29) n (%)		Overall (N=48) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Patient with Any Event	18 (94.7)	1 (5.3)	28 (96.6)	6 (20.7)	46 (95.8)	7 (14.6)
Gastrointestinal disorders	15 (78.9)	0	23 (79.3)	2 (6.9)	38 (79.2)	2 (4.2)
Dry mouth	9 (47.4)	0	21 (72.4)	0	30 (62.5)	0
Nausea	9 (47.4)	0	11 (37.9)	1 (3.4)	20 (41.7)	1 (2.1)
Diarrhoea	2 (10.5)	0	12 (41.4)	0	14 (29.2)	0
Constipation	6 (31.6)	0	7 (24.1)	0	13 (27.1)	0
Vomiting	2 (10.5)	0	5 (17.2)	1 (3.4)	7 (14.6)	1 (2.1)
Abdominal pain	1 (5.3)	0	1 (3.4)	1 (3.4)	2 (4.2)	1 (2.1)
Gastrointestinal haemorrhage	0	0	1 (3.4)	0	1 (2.1)	0
Hyperaesthesia teeth	1 (5.3)	0	0	0	1 (2.1)	0
Saliva altered	1 (5.3)	0	0	0	1 (2.1)	0
General disorders and administration site conditions	11 (57.9)	0	18 (62.1)	1 (3.4)	29 (60.4)	1 (2.1)
Fatigue	11 (57.9)	0	16 (55.2)	0	27 (56.3)	0
Pain	3 (15.8)	0	4 (13.8)	0	7 (14.6)	0
Asthenia	0	0	1 (3.4)	0	1 (2.1)	0
Chest pain	1 (5.3)	0	0	0	1 (2.1)	0
Death	0	0	1 (3.4)	1 (3.4)	1 (2.1)	1 (2.1)
Feeling hot	0	0	1 (3.4)	0	1 (2.1)	0
Oedema peripheral	0	0	1 (3.4)	0	1 (2.1)	0
Pyrexia	0	0	1 (3.4)	0	1 (2.1)	0
Musculoskeletal and connective tissue disorders	5 (26.3)	0	7 (24.1)	1 (3.4)	12 (25.0)	1 (2.1)
Arthralgia	2 (10.5)	0	2 (6.9)	0	4 (8.3)	0
Back pain	2 (10.5)	0	1 (3.4)	0	3 (6.3)	0

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

Output ID: t-aesevx-ageb-saf 04JUN20 12:55

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Table 14.3.1.2.2.2
TEAEs by Severity, MedDRA System Organ Class and Preferred Term (patients >=65 years old)
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=19) n (%)		Lu-PSMA-617 7.4 GBq (N=29) n (%)		Overall (N=48) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Musculoskeletal and connective tissue disorders (Continued)						
Pain in extremity	1 (5.3)	0	2 (6.9)	0	3 (6.3)	0
Bone pain	1 (5.3)	0	1 (3.4)	1 (3.4)	2 (4.2)	1 (2.1)
Neck pain	0	0	1 (3.4)	0	1 (2.1)	0
Osteoporosis	1 (5.3)	0	0	0	1 (2.1)	0
Nervous system disorders	6 (31.6)	0	6 (20.7)	0	12 (25.0)	0
Taste disorder	4 (21.1)	0	4 (13.8)	0	8 (16.7)	0
Headache	2 (10.5)	0	2 (6.9)	0	4 (8.3)	0
Dizziness	0	0	1 (3.4)	0	1 (2.1)	0
Parosmia	1 (5.3)	0	0	0	1 (2.1)	0
Metabolism and nutrition disorders	2 (10.5)	0	6 (20.7)	0	8 (16.7)	0
Decreased appetite	1 (5.3)	0	4 (13.8)	0	5 (10.4)	0
Hyponatraemia	1 (5.3)	0	1 (3.4)	0	2 (4.2)	0
Dehydration	0	0	1 (3.4)	0	1 (2.1)	0
Blood and lymphatic system disorders	4 (21.1)	0	3 (10.3)	0	7 (14.6)	0
Anaemia	3 (15.8)	0	1 (3.4)	0	4 (8.3)	0
Leukopenia	0	0	1 (3.4)	0	1 (2.1)	0
Lymphadenopathy	1 (5.3)	0	0	0	1 (2.1)	0
Lymphopenia	0	0	1 (3.4)	0	1 (2.1)	0
Eye disorders	1 (5.3)	0	4 (13.8)	0	5 (10.4)	0
Dry eye	1 (5.3)	0	3 (10.3)	0	4 (8.3)	0

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

Output ID: t-aesevx-ageb-saf 04JUN20 12:55

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Table 14.3.1.2.2.2
TEAEs by Severity, MedDRA System Organ Class and Preferred Term (patients >=65 years old)
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=19) n (%)		Lu-PSMA-617 7.4 GBq (N=29) n (%)		Overall (N=48) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Eye disorders (Continued)						
Lacrimation increased	0	0	1 (3.4)	0	1 (2.1)	0
Respiratory, thoracic and mediastinal disorders						
Dyspnoea	0	0	3 (10.3)	1 (3.4)	3 (6.3)	1 (2.1)
Epistaxis	1 (5.3)	0	0	0	1 (2.1)	0
Pleural effusion	0	0	1 (3.4)	1 (3.4)	1 (2.1)	1 (2.1)
Rhinorrhoea	0	0	1 (3.4)	0	1 (2.1)	0
Wheezing	0	0	1 (3.4)	0	1 (2.1)	0
Renal and urinary disorders						
Dysuria	1 (5.3)	0	3 (10.3)	0	4 (8.3)	0
Acute kidney injury	0	0	1 (3.4)	0	1 (2.1)	0
Bladder pain	0	0	1 (3.4)	0	1 (2.1)	0
Infections and infestations						
Bronchitis	1 (5.3)	0	2 (6.9)	0	3 (6.3)	0
Herpes zoster	0	0	1 (3.4)	0	1 (2.1)	0
Urinary tract infection	1 (5.3)	0	0	0	1 (2.1)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)						
Adenocarcinoma of colon	0	0	1 (3.4)	0	1 (2.1)	0
Metastases to central nervous system	1 (5.3)	0	0	0	1 (2.1)	0

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

Output ID: t-aesevx-ageb-saf 04JUN20 12:55

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Table 14.3.1.2.2.2
TEAEs by Severity, MedDRA System Organ Class and Preferred Term (patients >=65 years old)
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=19) n (%)		Lu-PSMA-617 7.4 GBq (N=29) n (%)		Overall (N=48) n (%)	
	All severity	Severe	All severity	Severe	All severity	Severe
Skin and subcutaneous tissue disorders	1 (5.3)	0	1 (3.4)	0	2 (4.2)	0
Dry skin	1 (5.3)	0	0	0	1 (2.1)	0
Pain of skin	0	0	1 (3.4)	0	1 (2.1)	0
Vascular disorders	0	0	2 (6.9)	0	2 (4.2)	0
Haematoma	0	0	2 (6.9)	0	2 (4.2)	0
Ear and labyrinth disorders	0	0	1 (3.4)	0	1 (2.1)	0
Deafness	0	0	1 (3.4)	0	1 (2.1)	0
Endocrine disorders	0	0	1 (3.4)	0	1 (2.1)	0
Hypothyroidism	0	0	1 (3.4)	0	1 (2.1)	0
Injury, poisoning and procedural complications	1 (5.3)	1 (5.3)	0	0	1 (2.1)	1 (2.1)
Subdural haematoma	1 (5.3)	1 (5.3)	0	0	1 (2.1)	1 (2.1)
Investigations	1 (5.3)	0	0	0	1 (2.1)	0
Blood lactate dehydrogenase increased	1 (5.3)	0	0	0	1 (2.1)	0
Psychiatric disorders	0	0	1 (3.4)	0	1 (2.1)	0
Depression	0	0	1 (3.4)	0	1 (2.1)	0

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.2.2.2
TEAEs by Severity, MedDRA System Organ Class and Preferred Term (patients >=65 years old)
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=19) n (%)	All severity	Severe	Lu-PSMA-617 7.4 GBq (N=29) n (%)	All severity	Severe	Overall (N=48) n (%)
Reproductive system and breast disorders	0	0	0	1 (3.4)	0	1 (2.1)	0
Prostatic pain	0	0	0	1 (3.4)	0	1 (2.1)	0

Numbers (n) represent counts of patients.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.3.1
TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Patient with Any Event	22 (95.7)	39 (95.1)	61 (95.3)
Gastrointestinal disorders			
Dry mouth	19 (82.6)	33 (80.5)	52 (81.3)
Nausea	11 (47.8)	26 (63.4)	37 (57.8)
Diarrhoea	12 (52.2)	18 (43.9)	30 (46.9)
Constipation	3 (13.0)	13 (31.7)	16 (25.0)
Vomiting	6 (26.1)	9 (22.0)	15 (23.4)
Abdominal pain	4 (17.4)	8 (19.5)	12 (18.8)
Frequent bowel movements	1 (4.3)	1 (2.4)	2 (3.1)
Gastrointestinal haemorrhage	0	1 (2.4)	1 (1.6)
Hyperaesthesia teeth	0	1 (2.4)	1 (1.6)
Lip dry	1 (4.3)	0	1 (1.6)
Saliva altered	0	1 (2.4)	1 (1.6)
General disorders and administration site conditions			
Fatigue	13 (56.5)	25 (61.0)	38 (59.4)
Pain	13 (56.5)	21 (51.2)	34 (53.1)
Chest pain	3 (13.0)	5 (12.2)	8 (12.5)
Pyrexia	1 (4.3)	1 (2.4)	2 (3.1)
Asthenia	0	2 (4.9)	2 (3.1)
Death	0	1 (2.4)	1 (1.6)
Feeling hot	0	1 (2.4)	1 (1.6)
Oedema peripheral	0	1 (2.4)	1 (1.6)
Musculoskeletal and connective tissue disorders			
Arthralgia	6 (26.1)	10 (24.4)	16 (25.0)
Back pain	3 (13.0)	2 (4.9)	5 (7.8)
	2 (8.7)	1 (2.4)	3 (4.7)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.3.1
TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Musculoskeletal and connective tissue disorders (Continued)			
Bone pain	1 (4.3)	2 (4.9)	3 (4.7)
Pain in extremity	1 (4.3)	2 (4.9)	3 (4.7)
Musculoskeletal chest pain	0	2 (4.9)	2 (3.1)
Musculoskeletal stiffness	0	1 (2.4)	1 (1.6)
Neck pain	0	1 (2.4)	1 (1.6)
Osteoporosis	1 (4.3)	0	1 (1.6)
Nervous system disorders			
Taste disorder	6 (26.1)	10 (24.4)	16 (25.0)
Headache	4 (17.4)	7 (17.1)	11 (17.2)
Dizziness	2 (8.7)	2 (4.9)	4 (6.3)
Parosmia	0	2 (4.9)	2 (3.1)
	1 (4.3)	0	1 (1.6)
Blood and lymphatic system disorders			
Anaemia	5 (21.7)	6 (14.6)	11 (17.2)
Leukopenia	4 (17.4)	4 (9.8)	8 (12.5)
Lymphadenopathy	0	1 (2.4)	1 (1.6)
Lymphopenia	1 (4.3)	0	1 (1.6)
Thrombocytopenia	0	1 (2.4)	1 (1.6)
	0	1 (2.4)	1 (1.6)
Metabolism and nutrition disorders			
Decreased appetite	2 (8.7)	7 (17.1)	9 (14.1)
Hyponatraemia	1 (4.3)	5 (12.2)	6 (9.4)
Dehydration	1 (4.3)	1 (2.4)	2 (3.1)
	0	1 (2.4)	1 (1.6)
Eye disorders	1 (4.3)	4 (9.8)	5 (7.8)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.3.1
TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Eye disorders (Continued)			
Dry eye	1 (4.3)	3 (7.3)	4 (6.3)
Lacrimation increased	0	1 (2.4)	1 (1.6)
Renal and urinary disorders			
Dysuria	1 (4.3)	4 (9.8)	5 (7.8)
Acute kidney injury	0	1 (2.4)	1 (1.6)
Bladder pain	0	1 (2.4)	1 (1.6)
Pollakiuria	0	1 (2.4)	1 (1.6)
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	1 (4.3)	4 (9.8)	5 (7.8)
Epistaxis	0	3 (7.3)	3 (4.7)
Pleural effusion	1 (4.3)	0	1 (1.6)
Rhinorrhoea	0	1 (2.4)	1 (1.6)
Wheezing	0	1 (2.4)	1 (1.6)
Infections and infestations			
Bronchitis	1 (4.3)	3 (7.3)	4 (6.3)
Herpes zoster	0	1 (2.4)	1 (1.6)
Pneumonia	1 (4.3)	0	1 (1.6)
Urinary tract infection	0	1 (2.4)	1 (1.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system	2 (8.7)	2 (4.9)	4 (6.3)
Adenocarcinoma of colon	2 (8.7)	0	2 (3.1)
	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.3.1
TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
(Continued)			
Metastases to meninges	0	1 (2.4)	1 (1.6)
Investigations	2 (8.7) 1 (4.3)	1 (2.4) 0	3 (4.7) 1 (1.6)
Blood lactate dehydrogenase increased	1 (4.3)	0	1 (1.6)
Glomerular filtration rate decreased	1 (4.3)	0	1 (1.6)
Weight decreased	0	1 (2.4)	1 (1.6)
Skin and subcutaneous tissue disorders	1 (4.3) 1 (4.3) 0	1 (2.4) 0 1 (2.4)	2 (3.1) 1 (1.6) 1 (1.6)
Dry skin	1 (4.3)	0	1 (1.6)
Pain of skin	0	1 (2.4)	1 (1.6)
Vascular disorders	0	2 (4.9) 2 (4.9)	2 (3.1) 2 (3.1)
Haematoma	0	2 (4.9)	2 (3.1)
Ear and labyrinth disorders	0	1 (2.4) 1 (2.4)	1 (1.6) 1 (1.6)
Deafness	0	1 (2.4)	1 (1.6)
Endocrine disorders	0	1 (2.4) 1 (2.4)	1 (1.6) 1 (1.6)
Hypothyroidism	0	1 (2.4)	1 (1.6)
Injury, poisoning and procedural complications	1 (4.3) 1 (4.3)	0 0	1 (1.6) 1 (1.6)
Subdural haematoma	1 (4.3)	0	1 (1.6)
Psychiatric disorders	0	1 (2.4) 1 (2.4)	1 (1.6) 1 (1.6)
Depression	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.3.1
TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Reproductive system and breast disorders	0	1 (2.4)	1 (1.6)
Prostatic pain	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.3.2
TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall	
	<65 years (N=4)	>=65 years (N=19)	<65 years (N=12)	>=65 years (N=29)	<65 years (N=16)	>=65 years (N=48)
n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patient with Any Event	4 (100)	18 (94.7)	11 (91.7)	28 (96.6)	15 (93.8)	46 (95.8)
Blood and lymphatic system disorders	1 (25.0)	4 (21.1)	3 (25.0)	3 (10.3)	4 (25.0)	7 (14.6)
Anaemia	1 (25.0)	3 (15.8)	3 (25.0)	1 (3.4)	4 (25.0)	4 (8.3)
Leukopenia	0	0	0	1 (3.4)	0	1 (2.1)
Lymphadenopathy	0	1 (5.3)	0	0	0	1 (2.1)
Lymphopenia	0	0	0	1 (3.4)	0	1 (2.1)
Thrombocytopenia	0	0	1 (8.3)	0	1 (6.3)	0
Ear and labyrinth disorders	0	0	0	1 (3.4)	0	1 (2.1)
Deafness	0	0	0	1 (3.4)	0	1 (2.1)
Endocrine disorders	0	0	0	1 (3.4)	0	1 (2.1)
Hypothyroidism	0	0	0	1 (3.4)	0	1 (2.1)
Eye disorders	0	1 (5.3)	0	4 (13.8)	0	5 (10.4)
Dry eye	0	1 (5.3)	0	3 (10.3)	0	4 (8.3)
Lacrimation increased	0	0	0	1 (3.4)	0	1 (2.1)
Gastrointestinal disorders	4 (100)	15 (78.9)	10 (83.3)	23 (79.3)	14 (87.5)	38 (79.2)
Abdominal pain	0	1 (5.3)	0	1 (3.4)	0	2 (4.2)
Constipation	0	6 (31.6)	2 (16.7)	7 (24.1)	2 (12.5)	13 (27.1)
Diarrhoea	1 (25.0)	2 (10.5)	1 (8.3)	12 (41.4)	2 (12.5)	14 (29.2)
Dry mouth	2 (50.0)	9 (47.4)	5 (41.7)	21 (72.4)	7 (43.8)	30 (62.5)
Frequent bowel movements	0	0	1 (8.3)	0	1 (6.3)	0
Gastrointestinal haemorrhage	0	0	0	1 (3.4)	0	1 (2.1)
Hyperaesthesia teeth	0	1 (5.3)	0	0	0	1 (2.1)
Lip dry	0	0	1 (8.3)	0	1 (6.3)	0
Nausea	3 (75.0)	9 (47.4)	7 (58.3)	11 (37.9)	10 (62.5)	20 (41.7)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.3.2
TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall	
	<65 years (N=4)		>=65 years (N=19)		<65 years (N=16)	
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gastrointestinal disorders (Continued)						
Saliva altered	0	1 (5.3)	0	0	0	1 (2.1)
Vomiting	2 (50.0)	2 (10.5)	3 (25.0)	5 (17.2)	5 (31.3)	7 (14.6)
General disorders and administration site conditions						
Asthenia	0	0	0	1 (3.4)	0	1 (2.1)
Chest pain	0	1 (5.3)	1 (8.3)	0	1 (6.3)	1 (2.1)
Death	0	0	0	1 (3.4)	0	1 (2.1)
Fatigue	2 (50.0)	11 (57.9)	5 (41.7)	16 (55.2)	7 (43.8)	27 (56.3)
Feeling hot	0	0	0	1 (3.4)	0	1 (2.1)
Oedema peripheral	0	0	0	1 (3.4)	0	1 (2.1)
Pain	0	3 (15.8)	1 (8.3)	4 (13.8)	1 (6.3)	7 (14.6)
Pyrexia	0	0	1 (8.3)	1 (3.4)	1 (6.3)	1 (2.1)
Infections and infestations						
Bronchitis	0	1 (5.3)	1 (8.3)	2 (6.9)	1 (6.3)	3 (6.3)
Herpes zoster	0	0	0	1 (3.4)	0	1 (2.1)
Pneumonia	0	1 (5.3)	0	0	0	1 (2.1)
Urinary tract infection	0	0	1 (8.3)	0	1 (6.3)	0
Injury, poisoning and procedural complications						
Subdural haematoma	0	1 (5.3)	0	0	0	1 (2.1)
Investigations						
Blood lactate dehydrogenase increased	1 (25.0)	1 (5.3)	1 (8.3)	0	2 (12.5)	1 (2.1)
	0	1 (5.3)	0	0	0	1 (2.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.3.2
TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall	
	<65 years (N=4)	>=65 years (N=19)	<65 years (N=12)	>=65 years (N=29)	<65 years (N=16)	>=65 years (N=48)
n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Glomerular filtration rate decreased	1 (25.0)	0	0	0	1 (6.3)	0
Weight decreased	0	0	1 (8.3)	0	1 (6.3)	0
Metabolism and nutrition disorders	0	2 (10.5)	1 (8.3)	6 (20.7)	1 (6.3)	8 (16.7)
Decreased appetite	0	1 (5.3)	1 (8.3)	4 (13.8)	1 (6.3)	5 (10.4)
Dehydration	0	0	0	1 (3.4)	0	1 (2.1)
Hyponatraemia	0	1 (5.3)	0	1 (3.4)	0	2 (4.2)
Musculoskeletal and connective tissue disorders	1 (25.0)	5 (26.3)	3 (25.0)	7 (24.1)	4 (25.0)	12 (25.0)
Arthralgia	1 (25.0)	2 (10.5)	0	2 (6.9)	1 (6.3)	4 (8.3)
Back pain	0	2 (10.5)	0	1 (3.4)	0	3 (6.3)
Bone pain	0	1 (5.3)	1 (8.3)	1 (3.4)	1 (6.3)	2 (4.2)
Musculoskeletal chest pain	0	0	2 (16.7)	0	2 (12.5)	0
Musculoskeletal stiffness	0	0	1 (8.3)	0	1 (6.3)	0
Neck pain	0	0	0	1 (3.4)	0	1 (2.1)
Osteoporosis	0	1 (5.3)	0	0	0	1 (2.1)
Pain in extremity	0	1 (5.3)	0	2 (6.9)	0	3 (6.3)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (25.0)	1 (5.3)	1 (8.3)	1 (3.4)	2 (12.5)	2 (4.2)
Adenocarcinoma of colon	0	0	0	1 (3.4)	0	1 (2.1)
Metastases to central nervous system	1 (25.0)	1 (5.3)	0	0	1 (6.3)	1 (2.1)
Metastases to meninges	0	0	1 (8.3)	0	1 (6.3)	0
Nervous system disorders	0	6 (31.6)	4 (33.3)	6 (20.7)	4 (25.0)	12 (25.0)
Dizziness	0	0	1 (8.3)	1 (3.4)	1 (6.3)	1 (2.1)
Headache	0	2 (10.5)	0	2 (6.9)	0	4 (8.3)
Parosmia	0	1 (5.3)	0	0	0	1 (2.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.3.2
TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall	
	<65 years (N=4)	>=65 years (N=19)	<65 years (N=12)	>=65 years (N=29)	<65 years (N=16)	>=65 years (N=48)
n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Nervous system disorders (Continued)						
Taste disorder	0	4 (21.1)	3 (25.0)	4 (13.8)	3 (18.8)	8 (16.7)
Psychiatric disorders						
Depression	0	0	0	1 (3.4)	0	1 (2.1)
	0	0	0	1 (3.4)	0	1 (2.1)
Renal and urinary disorders						
Acute kidney injury	0	1 (5.3)	1 (8.3)	3 (10.3)	1 (6.3)	4 (8.3)
Bladder pain	0	0	0	1 (3.4)	0	1 (2.1)
Dysuria	0	1 (5.3)	0	1 (3.4)	0	2 (4.2)
Pollakiuria	0	0	1 (8.3)	0	1 (6.3)	0
Reproductive system and breast disorders						
Prostatic pain	0	0	0	1 (3.4)	0	1 (2.1)
Respiratory, thoracic and mediastinal disorders						
Dyspnoea	0	0	0	3 (10.3)	0	3 (6.3)
Epistaxis	0	1 (5.3)	0	0	0	1 (2.1)
Pleural effusion	0	0	0	1 (3.4)	0	1 (2.1)
Rhinorrhoea	0	0	0	1 (3.4)	0	1 (2.1)
Wheezing	0	0	0	1 (3.4)	0	1 (2.1)
Skin and subcutaneous tissue disorders						
Dry skin	0	1 (5.3)	0	0	0	1 (2.1)
Pain of skin	0	0	0	1 (3.4)	0	1 (2.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.3.2
 TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
 Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall			
	<65 years (N=4)		>=65 years (N=19)		<65 years (N=16)		>=65 years (N=48)	
	n	(%)	n	(%)	n	(%)	n	(%)
Vascular disorders	0	0	0	0	2	(6.9)	0	2 (4.2)
Haematoma	0	0	0	0	2	(6.9)	0	2 (4.2)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.4.1
Serious TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Patient with Any Event	4 (17.4)	8 (19.5)	12 (18.8)
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	2 (8.7) 2 (8.7)	2 (4.9) 0	4 (6.3) 2 (3.1)
Metastases to central nervous system	0	1 (2.4)	1 (1.6)
Adenocarcinoma of colon	0	1 (2.4)	1 (1.6)
Metastases to meninges	0	1 (2.4)	1 (1.6)
Gastrointestinal disorders	0	2 (4.9)	2 (3.1)
Abdominal pain	0	1 (2.4)	1 (1.6)
Gastrointestinal haemorrhage	0	1 (2.4)	1 (1.6)
Blood and lymphatic system disorders	0	1 (2.4)	1 (1.6)
Anaemia	0	1 (2.4)	1 (1.6)
Thrombocytopenia	0	1 (2.4)	1 (1.6)
General disorders and administration site conditions	0	1 (2.4)	1 (1.6)
Death	0	1 (2.4)	1 (1.6)
Infections and infestations	0	1 (2.4)	1 (1.6)
Pneumonia	0	1 (2.4)	1 (1.6)
Injury, poisoning and procedural complications	1 (4.3) 1 (4.3)	0 0	1 (1.6) 1 (1.6)
Subdural haematoma			
Musculoskeletal and connective tissue disorders	1 (4.3) 1 (4.3)	0 0	1 (1.6) 1 (1.6)
Osteoporosis			

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.4.1
 Serious TEAEs by MedDRA System Organ Class and Preferred Term
 Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Renal and urinary disorders	0	1 (2.4)	1 (1.6)
Acute kidney injury	0	1 (2.4)	1 (1.6)
Respiratory, thoracic and mediastinal disorders	0	1 (2.4)	1 (1.6)
Pleural effusion	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.4.2
Serious TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall	
	<65 years (N=4)	>=65 years (N=19)	<65 years (N=12)	>=65 years (N=29)	<65 years (N=16)	>=65 years (N=48)
n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patient with Any Event	1 (25.0)	3 (15.8)	3 (25.0)	5 (17.2)	4 (25.0)	8 (16.7)
Blood and lymphatic system disorders	0	0	1 (8.3)	0	1 (6.3)	0
Anaemia	0	0	1 (8.3)	0	1 (6.3)	0
Thrombocytopenia	0	0	1 (8.3)	0	1 (6.3)	0
Gastrointestinal disorders	0	0	0	2 (6.9)	0	2 (4.2)
Abdominal pain	0	0	0	1 (3.4)	0	1 (2.1)
Gastrointestinal haemorrhage	0	0	0	1 (3.4)	0	1 (2.1)
General disorders and administration site conditions	0	0	0	1 (3.4)	0	1 (2.1)
Death	0	0	0	1 (3.4)	0	1 (2.1)
Infections and infestations	0	0	1 (8.3)	0	1 (6.3)	0
Pneumonia	0	0	1 (8.3)	0	1 (6.3)	0
Injury, poisoning and procedural complications	0	1 (5.3)	0	0	0	1 (2.1)
Subdural haematoma	0	1 (5.3)	0	0	0	1 (2.1)
Musculoskeletal and connective tissue disorders	0	1 (5.3)	0	0	0	1 (2.1)
Osteoporosis	0	1 (5.3)	0	0	0	1 (2.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (25.0)	1 (5.3)	1 (8.3)	1 (3.4)	2 (12.5)	2 (4.2)
Adenocarcinoma of colon	0	0	0	1 (3.4)	0	1 (2.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.4.2
Serious TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall	
	<65 years (N=4)	>=65 years (N=19)	<65 years (N=12)	>=65 years (N=29)	<65 years (N=16)	>=65 years (N=48)
n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Metastases to central nervous system	1 (25.0)	1 (5.3)	0	0	1 (6.3)	1 (2.1)
Metastases to meninges	0	0	1 (8.3)	0	1 (6.3)	0
Renal and urinary disorders	0	0	0	1 (3.4)	0	1 (2.1)
Acute kidney injury	0	0	0	1 (3.4)	0	1 (2.1)
Respiratory, thoracic and mediastinal disorders	0	0	0	1 (3.4)	0	1 (2.1)
Pleural effusion	0	0	0	1 (3.4)	0	1 (2.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.5.1
Drug-Related TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Patient with Any Event	20 (87.0)	37 (90.2)	57 (89.1)
Gastrointestinal disorders			
Dry mouth	19 (82.6)	33 (80.5)	52 (81.3)
Nausea	11 (47.8)	26 (63.4)	37 (57.8)
Diarrhoea	12 (52.2)	18 (43.9)	30 (46.9)
Constipation	3 (13.0)	12 (29.3)	15 (23.4)
Vomiting	5 (21.7)	9 (22.0)	14 (21.9)
Abdominal pain	4 (17.4)	6 (14.6)	10 (15.6)
Frequent bowel movements	1 (4.3)	0	1 (1.6)
Gastrointestinal haemorrhage	0	1 (2.4)	1 (1.6)
Lip dry	0	1 (2.4)	1 (1.6)
Saliva altered	1 (4.3)	0	1 (1.6)
General disorders and administration site conditions			
Fatigue	12 (52.2)	22 (53.7)	34 (53.1)
Pain	12 (52.2)	21 (51.2)	33 (51.6)
Death	2 (8.7)	5 (12.2)	7 (10.9)
Nervous system disorders			
Taste disorder	5 (21.7)	7 (17.1)	12 (18.8)
Headache	4 (17.4)	6 (14.6)	10 (15.6)
Parosmia	1 (4.3)	1 (2.4)	2 (3.1)
Blood and lymphatic system disorders			
Anaemia	1 (4.3)	0	1 (1.6)
Leukopenia	3 (13.0)	6 (14.6)	9 (14.1)
	3 (18.0)	4 (9.8)	7 (10.9)
	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

TEAE is considered study drug-related if relatedness is recorded as possible, probably, definite, or when the value is missing.
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Table 14.3.1.5.1
Drug-Related TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Blood and lymphatic system disorders (Continued)			
Lymphopenia	0	1 (2.4)	1 (1.6)
Thrombocytopenia	0	1 (2.4)	1 (1.6)
Metabolism and nutrition disorders			
Decreased appetite	2 (8.7) 1 (4.3)	5 (12.2) 5 (12.2)	7 (10.9) 6 (9.4)
Hyponatraemia	1 (4.3)	0	1 (1.6)
Musculoskeletal and connective tissue disorders			
Bone pain	0	2 (4.9)	2 (3.1)
Arthralgia	0	1 (2.4)	1 (1.6)
Back pain	0	1 (2.4)	1 (1.6)
Musculoskeletal chest pain	0	1 (2.4)	1 (1.6)
Pain in extremity	0	1 (2.4)	1 (1.6)
Eye disorders			
Dry eye	1 (4.3) 1 (4.3)	4 (9.8) 3 (7.3)	5 (7.8) 4 (6.3)
Lacrimation increased	0	1 (2.4)	1 (1.6)
Renal and urinary disorders			
Acute kidney injury	0	2 (4.9)	2 (3.1)
Bladder pain	0	1 (2.4)	1 (1.6)
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	0	2 (4.9) 1 (2.4)	2 (3.1) 1 (1.6)
Pleural effusion	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

TEAE is considered study drug-related if relatedness is recorded as possible, probably, definite, or when the value is missing.
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Table 14.3.1.5.1
 Drug-Related TEAEs by MedDRA System Organ Class and Preferred Term
 Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Ear and labyrinth disorders	0	1 (2.4)	1 (1.6)
Deafness	0	1 (2.4)	1 (1.6)
Injury, poisoning and procedural complications	1 (4.3)	0	1 (1.6)
Subdural haematoma	1 (4.3)	0	1 (1.6)
Investigations	1 (4.3)	0	1 (1.6)
Glomerular filtration rate decreased	1 (4.3)	0	1 (1.6)
Skin and subcutaneous tissue disorders	0	1 (2.4)	1 (1.6)
Pain of skin	0	1 (2.4)	1 (1.6)
Vascular disorders	0	1 (2.4)	1 (1.6)
Haematoma	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

TEAE is considered study drug-related if relatedness is recorded as possible, probably, definite, or when the value is missing.

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Table 14.3.1.5.2
Drug-Related TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall	
	<65 years (N=4)	>=65 years (N=19)	<65 years (N=12)	>=65 years (N=29)	<65 years (N=16)	>=65 years (N=48)
n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patient with Any Event	4 (100)	16 (84.2)	11 (91.7)	26 (89.7)	15 (93.8)	42 (87.5)
Blood and lymphatic system disorders	0	3 (15.8)	3 (25.0)	3 (10.3)	3 (18.8)	6 (12.5)
Anaemia	0	3 (15.8)	3 (25.0)	1 (3.4)	3 (18.8)	4 (8.3)
Leukopenia	0	0	0	1 (3.4)	0	1 (2.1)
Lymphopenia	0	0	0	1 (3.4)	0	1 (2.1)
Thrombocytopenia	0	0	1 (8.3)	0	1 (6.3)	0
Ear and labyrinth disorders	0	0	0	1 (3.4)	0	1 (2.1)
Deafness	0	0	0	1 (3.4)	0	1 (2.1)
Eye disorders	0	1 (5.3)	0	4 (13.8)	0	5 (10.4)
Dry eye	0	1 (5.3)	0	3 (10.3)	0	4 (8.3)
Lacrimation increased	0	0	0	1 (3.4)	0	1 (2.1)
Gastrointestinal disorders	4 (100)	15 (78.9)	10 (83.3)	23 (79.3)	14 (87.5)	38 (79.2)
Abdominal pain	0	1 (5.3)	0	0	0	1 (2.1)
Constipation	0	5 (26.3)	2 (16.7)	7 (24.1)	2 (12.5)	12 (25.0)
Diarrhoea	1 (25.0)	2 (10.5)	1 (8.3)	11 (37.9)	2 (12.5)	13 (27.1)
Dry mouth	2 (50.0)	9 (47.4)	5 (41.7)	21 (72.4)	7 (43.8)	30 (62.5)
Frequent bowel movements	0	0	1 (8.3)	0	1 (6.3)	0
Gastrointestinal haemorrhage	0	0	0	1 (3.4)	0	1 (2.1)
Lip dry	0	0	1 (8.3)	0	1 (6.3)	0
Nausea	3 (75.0)	9 (47.4)	7 (58.3)	11 (37.9)	10 (62.5)	20 (41.7)
Saliva altered	0	1 (5.3)	0	0	0	1 (2.1)
Vomiting	2 (50.0)	2 (10.5)	2 (16.7)	4 (13.8)	4 (25.0)	6 (12.5)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

TEAE is considered study drug-related if relatedness is recorded as possible, probably, definite, or when the value is missing.

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Table 14.3.1.5.2
Drug-Related TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall	
	<65 years (N=4)	>=65 years (N=19)	<65 years (N=12)	>=65 years (N=29)	<65 years (N=16)	>=65 years (N=48)
n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
General disorders and administration site conditions	2 (50.0)	10 (52.6)	5 (41.7)	17 (58.6)	7 (43.8)	27 (56.3)
Death	0	0	0	1 (3.4)	0	1 (2.1)
Fatigue	2 (50.0)	10 (52.6)	5 (41.7)	16 (55.2)	7 (43.8)	26 (54.2)
Pain	0	2 (10.5)	1 (8.3)	4 (13.8)	1 (6.3)	6 (12.5)
Injury, poisoning and procedural complications	0	1 (5.3)	0	0	0	1 (2.1)
Subdural haematoma	0	1 (5.3)	0	0	0	1 (2.1)
Investigations	1 (25.0)	0	0	0	1 (6.3)	0
Glomerular filtration rate decreased	1 (25.0)	0	0	0	1 (6.3)	0
Metabolism and nutrition disorders	0	2 (10.5)	1 (8.3)	4 (13.8)	1 (6.3)	6 (12.5)
Decreased appetite	0	1 (5.3)	1 (8.3)	4 (13.8)	1 (6.3)	5 (10.4)
Hyponatraemia	0	1 (5.3)	0	0	0	1 (2.1)
Musculoskeletal and connective tissue disorders	0	0	2 (16.7)	4 (13.8)	2 (12.5)	4 (8.3)
Arthralgia	0	0	0	1 (3.4)	0	1 (2.1)
Back pain	0	0	0	1 (3.4)	0	1 (2.1)
Bone pain	0	0	1 (8.3)	1 (3.4)	1 (6.3)	1 (2.1)
Musculoskeletal chest pain	0	0	1 (8.3)	0	1 (6.3)	0
Pain in extremity	0	0	0	1 (3.4)	0	1 (2.1)
Nervous system disorders	0	5 (26.3)	3 (25.0)	4 (13.8)	3 (18.8)	9 (18.8)
Headache	0	1 (5.3)	0	1 (3.4)	0	2 (4.2)
Parosmia	0	1 (5.3)	0	0	0	1 (2.1)
Taste disorder	0	4 (21.1)	3 (25.0)	3 (10.3)	3 (18.8)	7 (14.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

TEAE is considered study drug-related if relatedness is recorded as possible, probably, definite, or when the value is missing.

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Table 14.3.1.5.2
Drug-Related TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall	
	<65 years (N=4)	>=65 years (N=19)	<65 years (N=12)	>=65 years (N=29)	<65 years (N=16)	>=65 years (N=48)
n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Renal and urinary disorders	0	0	0	2 (6.9)	0	2 (4.2)
Acute kidney injury	0	0	0	1 (3.4)	0	1 (2.1)
Bladder pain	0	0	0	1 (3.4)	0	1 (2.1)
Respiratory, thoracic and mediastinal disorders	0	0	0	2 (6.9)	0	2 (4.2)
Dyspnoea	0	0	0	1 (3.4)	0	1 (2.1)
Pleural effusion	0	0	0	1 (3.4)	0	1 (2.1)
Skin and subcutaneous tissue disorders	0	0	0	1 (3.4)	0	1 (2.1)
Pain of skin	0	0	0	1 (3.4)	0	1 (2.1)
Vascular disorders	0	0	0	1 (3.4)	0	1 (2.1)
Haematoma	0	0	0	1 (3.4)	0	1 (2.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

TEAE is considered study drug-related if relatedness is recorded as possible, probably, definite, or when the value is missing.

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Table 14.3.1.6.1
Serious Drug-Related TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Patient with Any Event	1 (4.3)	4 (9.8)	5 (7.8)
Blood and lymphatic system disorders	0	1 (2.4)	1 (1.6)
Anaemia	0	1 (2.4)	1 (1.6)
Thrombocytopenia	0	1 (2.4)	1 (1.6)
Gastrointestinal disorders	0	1 (2.4)	1 (1.6)
Gastrointestinal haemorrhage	0	1 (2.4)	1 (1.6)
General disorders and administration site conditions	0	1 (2.4)	1 (1.6)
Death	0	1 (2.4)	1 (1.6)
Injury, poisoning and procedural complications	1 (4.3)	0	1 (1.6)
Subdural haematoma	1 (4.3)	0	1 (1.6)
Renal and urinary disorders	0	1 (2.4)	1 (1.6)
Acute kidney injury	0	1 (2.4)	1 (1.6)
Respiratory, thoracic and mediastinal disorders	0	1 (2.4)	1 (1.6)
Pleural effusion	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

TEAE is considered study drug-related if relatedness is recorded as possible, probably, definite, or when the value is missing.

Output ID: t-ae-serrel-saf 04JUN20 12:52

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Table 14.3.1.6.2
Serious Drug-Related TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall	
	<65 years (N=4) n (%)	>=65 years (N=19) n (%)	<65 years (N=12) n (%)	>=65 years (N=29) n (%)	<65 years (N=16) n (%)	>=65 years (N=48) n (%)
Patient with Any Event	0	1 (5.3)	1 (8.3)	3 (10.3)	1 (6.3)	4 (8.3)
Blood and lymphatic system disorders	0	0	1 (8.3)	0	1 (6.3)	0
Anaemia	0	0	1 (8.3)	0	1 (6.3)	0
Thrombocytopenia	0	0	1 (8.3)	0	1 (6.3)	0
Gastrointestinal disorders	0	0	0	1 (3.4)	0	1 (2.1)
Gastrointestinal haemorrhage	0	0	0	1 (3.4)	0	1 (2.1)
General disorders and administration site conditions	0	0	0	1 (3.4)	0	1 (2.1)
Death	0	0	0	1 (3.4)	0	1 (2.1)
Injury, poisoning and procedural complications	0	1 (5.3)	0	0	0	1 (2.1)
Subdural haematoma	0	1 (5.3)	0	0	0	1 (2.1)
Renal and urinary disorders	0	0	0	1 (3.4)	0	1 (2.1)
Acute kidney injury	0	0	0	1 (3.4)	0	1 (2.1)
Respiratory, thoracic and mediastinal disorders	0	0	0	1 (3.4)	0	1 (2.1)
Pleural effusion	0	0	0	1 (3.4)	0	1 (2.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

TEAE is considered study drug-related if relatedness is recorded as possible, probably, definite, or when the value is missing.

Output ID: t-ae-serrelage-saf 04JUN20 12:53

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Table 14.3.1.7.1
TEAEs Leading to Reduction of Lu-PSMA-617 by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Patient with Any Event	0	2 (4.9)	2 (3.1)
Blood and lymphatic system disorders	0	2 (4.9)	2 (3.1)
Anaemia	0	2 (4.9)	2 (3.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

Output ID: t-ae-red-saf 04JUN20 12:52

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Table 14.3.1.7.2
TEAES Leading to Reduction of Lu-PSMA-617 by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall			
	<65 years (N=4)		>=65 years (N=19)		<65 years (N=16)		>=65 years (N=48)	
	n	(%)	n	(%)	n	(%)	n	(%)
Patient with Any Event	0	0	1 (8.3)	1 (3.4)	1 (6.3)	1 (2.1)		
Blood and lymphatic system disorders	0	0	1 (8.3)	1 (3.4)	1 (6.3)	1 (2.1)		
Anaemia	0	0	1 (8.3)	1 (3.4)	1 (6.3)	1 (2.1)		

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

Output ID: t-ae-redage-saf 04JUN20 12:53

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Table 14.3.1.8.1

TEAES Leading to Discontinuation of Lu-PSMA-617 by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Patient with Any Event	0	1 (2.4)	1 (1.6)
Gastrointestinal disorders	0	1 (2.4)	1 (1.6)
Abdominal pain	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.8.2
TEAEs Leading to Discontinuation of Lu-PSMA-617 by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall			
	<65 years (N=4)		>=65 years (N=19)		<65 years (N=16)		>=65 years (N=48)	
	n	(%)	n	(%)	n	(%)	n	(%)
Patient with Any Event	0	0	0	1 (3.4)	0	1 (2.1)		
Gastrointestinal disorders	0	0	0	1 (3.4)	0	1 (2.1)		
Abdominal pain	0	0	0	1 (3.4)	0	1 (2.1)		

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.9.1
Fatal TEAEs by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Patient with Any Event	2 (8.7)	1 (2.4)	3 (4.7)
General disorders and administration site conditions	0	1 (2.4)	1 (1.6)
Death	0	1 (2.4)	1 (1.6)
Injury, poisoning and procedural complications	1 (4.3)	0	1 (1.6)
Subdural haematoma	1 (4.3)	0	1 (1.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (4.3)	0	1 (1.6)
Metastases to central nervous system	1 (4.3)	0	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.9.2
Fatal TEAEs by MedDRA System Organ Class and Preferred Term - by Age Category
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq		Lu-PSMA-617 7.4 GBq		Overall	
	<65 years (N=4)	>=65 years (N=19)	<65 years (N=12)	>=65 years (N=29)	<65 years (N=16)	>=65 years (N=48)
n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Patient with Any Event	1 (25.0)	1 (5.3)	0	1 (3.4)	1 (6.3)	2 (4.2)
General disorders and administration site conditions	0	0	0	1 (3.4)	0	1 (2.1)
Death	0	0	0	1 (3.4)	0	1 (2.1)
Injury, poisoning and procedural complications	0	1 (5.3)	0	0	0	1 (2.1)
Subdural haematoma	0	1 (5.3)	0	0	0	1 (2.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (25.0)	0	0	0	1 (6.3)	0
Metastases to central nervous system	1 (25.0)	0	0	0	1 (6.3)	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class.

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Table 14.3.1.10.1
Randomized Treatment TEAEs leading to Death, by MedDRA System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=23) n (%)		Lu-PSMA-617 7.4 GBq (N=41) n (%)		Overall (N=64) n (%)	
	All	Related to treatment	All	Related to treatment	All	Related to treatment
Patient with Any Event leading to death	2 (8.7)	1 (4.3)	1 (2.4)	1 (2.4)	3 (4.7)	2 (3.1)
General disorders and administration site conditions	0	0	1 (2.4)	1 (2.4)	1 (1.6)	1 (1.6)
Death	0	0	1 (2.4)	1 (2.4)	1 (1.6)	1 (1.6)
Injury, poisoning and procedural complications	1 (4.3)	1 (4.3)	0	0	1 (1.6)	1 (1.6)
Subdural haematoma	1 (4.3)	1 (4.3)	0	0	1 (1.6)	1 (1.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (4.3)	0	0	0	1 (1.6)	0
Metastases to central nervous system	1 (4.3)	0	0	0	1 (1.6)	0

Column <All> represents all TEAEs with fatal outcome regardless of causality to treatment.
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Table 14.3.1.10.2.1
 Randomized Treatment TEAEs leading to Death, by MedDRA System Organ Class and Preferred Term (patients <65 years old)
 Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=4) n (%)		Lu-PSMA-617 7.4 GBq (N=12) n (%)		Overall (N=16) n (%)	
	All	Related to treatment	All	Related to treatment	All	Related to treatment
Patient with Any Event leading to death	1 (25.0)	0	0	0	1 (6.3)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1 (25.0)	0	0	0	1 (6.3)	0
Metastases to central nervous system	1 (25.0)	0	0	0	1 (6.3)	0

Column <All> represents all TEAEs with fatal outcome regardless of causality to treatment.

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Table 14.3.1.10.2.2

Randomized Treatment TEAEs leading to Death, by MedDRA System Organ Class and Preferred Term (patients >=65 years old)
Safety Population

System Organ Class Preferred Term	Lu-PSMA-617 6.0 GBq (N=19) n (%)		Lu-PSMA-617 7.4 GBq (N=29) n (%)		Overall (N=48) n (%)	
	All	Related to treatment	All	Related to treatment	All	Related to treatment
Patient with Any Event leading to death	1 (5.3)	1 (5.3)	1 (3.4)	1 (3.4)	2 (4.2)	2 (4.2)
General disorders and administration site conditions	0	0	1 (3.4)	1 (3.4)	1 (2.1)	1 (2.1)
Death	0	0	1 (3.4)	1 (3.4)	1 (2.1)	1 (2.1)
Injury, poisoning and procedural complications	1 (5.3)	1 (5.3)	0	0	1 (2.1)	1 (2.1)
Subdural haematoma	1 (5.3)	1 (5.3)	0	0	1 (2.1)	1 (2.1)

Column <All> represents all TEAEs with fatal outcome regardless of causality to treatment.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Number of patients with at least one TEAE			22 (95.7)	39 (95.1)	61 (95.3)
Gastrointestinal disorders					
Dry mouth					
Mild	19 (82.6)	33 (80.5)	52 (81.3)		
Moderate	17 (73.9)	24 (58.5)	41 (64.1)		
Severe	2 (8.7)	7 (17.1)	9 (14.1)		
Nausea					
Mild	0	2 (4.9)	2 (3.1)		
Severe	0	0	0		
Diarrhoea					
Mild	12 (52.2)	18 (43.9)	30 (46.9)		
Moderate	11 (47.8)	12 (29.3)	23 (35.9)		
Severe	1 (4.3)	5 (12.2)	6 (9.4)		
Constipation					
Mild	3 (13.0)	13 (31.7)	16 (25.0)		
Moderate	3 (13.0)	12 (29.3)	15 (23.4)		
Severe	0	1 (2.4)	1 (1.6)		
Vomiting					
Mild	6 (26.1)	9 (22.0)	15 (23.4)		
Moderate	6 (26.1)	9 (22.0)	15 (23.4)		
Severe	0	0	0		

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity. Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Gastrointestinal disorders	Vomiting	Mild	3 (13.0)	3 (7.3)	6 (9.4)
		Moderate	1 (4.3)	4 (9.8)	5 (7.8)
		Severe	0	1 (2.4)	1 (1.6)
	Abdominal pain		1 (4.3)	1 (2.4)	2 (3.1)
		Mild	1 (4.3)	0	1 (1.6)
		Moderate	0	0	0
	Frequent bowel movements	Severe	0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
	Gastrointestinal haemorrhage	Severe	0	0	0
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	1 (2.4)	1 (1.6)
Sensory system disorders	Hyperaesthesia teeth		0	1 (2.4)	1 (1.6)
		Mild	1 (4.3)	0	1 (1.6)
		Moderate	1 (4.3)	0	0
		Severe	0	0	0
Skin and appendages disorders	Lip dry		0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Gastrointestinal disorders	Lip dry	Severe	0	0	0
	Saliva altered	Mild	1 (4.3)	0	1 (1.6)
		Moderate	1 (4.3)	0	1 (1.6)
		Severe	0	0	0
General disorders and administration site conditions			13 (56.5)	25 (61.0)	38 (59.4)
	Fatigue	Mild	8 (34.8)	17 (41.5)	25 (39.1)
		Moderate	5 (21.7)	7 (17.1)	12 (18.8)
		Severe	0	1 (2.4)	1 (1.6)
	Pain	Mild	13 (56.5)	21 (51.2)	34 (53.1)
		Moderate	9 (39.1)	17 (41.5)	26 (40.6)
		Severe	4 (17.4)	4 (9.8)	8 (12.5)
			0	0	0
	Chest pain	Mild	3 (13.0)	5 (12.2)	8 (12.5)
		Moderate	1 (4.3)	3 (7.3)	4 (6.3)
		Severe	2 (8.7)	2 (4.9)	4 (6.3)
			0	0	0
	Pyrexia	Mild	1 (4.3)	1 (2.4)	2 (3.1)
		Moderate	1 (4.3)	0	1 (1.6)
		Severe	0	1 (2.4)	1 (1.6)
			0	0	0
			0	2 (4.9)	2 (3.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity. Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
General disorders and administration site conditions	Pyrexia	Mild	0	2 (4.9)	2 (3.1)
		Moderate	0	0	0
		Severe	0	0	0
	Asthenia		0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
	Death	Severe	0	0	0
			0	1 (2.4)	1 (1.6)
		Mild	0	0	0
	Feeling hot	Moderate	0	0	0
		Severe	0	1 (2.4)	1 (1.6)
			0	1 (2.4)	1 (1.6)
Musculoskeletal and connective tissue disorders	Oedema peripheral	Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	1 (2.4)	1 (1.6)
		Severe	0	0	0
	Mild		6 (26.1)	10 (24.4)	16 (25.0)
		Moderate	4 (17.4)	6 (14.6)	10 (15.6)
		Severe	2 (8.7)	3 (7.3)	5 (7.8)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Musculoskeletal and connective tissue disorders		Severe	0	1 (2.4)	1 (1.6)
Arthralgia		Mild	3 (13.0)	2 (4.9)	5 (7.8)
		Moderate	3 (13.0)	0	3 (4.7)
		Severe	0	2 (4.9)	2 (3.1)
			0	0	0
Back pain		Mild	2 (8.7)	1 (2.4)	3 (4.7)
		Moderate	2 (8.7)	1 (2.4)	3 (4.7)
		Severe	0	0	0
			0	0	0
Bone pain		Mild	1 (4.3)	2 (4.9)	3 (4.7)
		Moderate	0	0	0
		Severe	1 (4.3)	1 (2.4)	2 (3.1)
			0	1 (2.4)	1 (1.6)
Pain in extremity		Mild	1 (4.3)	2 (4.9)	3 (4.7)
		Moderate	1 (4.3)	2 (4.9)	3 (4.7)
		Severe	0	0	0
			0	0	0
Musculoskeletal chest pain		Mild	0	2 (4.9)	2 (3.1)
		Moderate	0	2 (4.9)	2 (3.1)
		Severe	0	0	0
			0	0	0
Musculoskeletal stiffness		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
			0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Musculoskeletal and connective tissue disorders	Musculoskeletal stiffness	Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
	Neck pain		0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
	Osteoporosis	Severe	0	0	0
			1 (4.3)	0	1 (1.6)
		Mild	0	0	0
Nervous system disorders	Mild	Moderate	1 (4.3)	0	1 (1.6)
		Severe	0	0	0
	Taste disorder		6 (26.1)	10 (24.4)	16 (25.0)
		Mild	4 (17.4)	8 (19.5)	12 (18.8)
		Moderate	2 (8.7)	2 (4.9)	4 (6.3)
	Headache	Severe	0	0	0
			4 (17.4)	7 (17.1)	11 (17.2)
		Mild	2 (8.7)	7 (17.1)	9 (14.1)
Psychiatric disorders	Moderate	Severe	2 (8.7)	0	2 (3.1)
			0	0	0
		Mild	2 (8.7)	2 (4.9)	4 (6.3)
	Moderate	Moderate	2 (8.7)	1 (2.4)	3 (4.7)
		Severe	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Nervous system disorders	Headache	Severe	0	0	0
	Dizziness		0	2 (4.9)	2 (3.1)
		Mild	0	0	0
		Moderate	0	2 (4.9)	2 (3.1)
		Severe	0	0	0
	Parosmia		1 (4.3)	0	1 (1.6)
		Mild	1 (4.3)	0	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
Blood and lymphatic system disorders					
			5 (21.7)	6 (14.6)	11 (17.2)
		Mild	3 (13.0)	2 (4.9)	5 (7.8)
		Moderate	2 (8.7)	3 (7.3)	5 (7.8)
		Severe	0	1 (2.4)	1 (1.6)
	Anaemia		4 (17.4)	4 (9.8)	8 (12.5)
		Mild	2 (8.7)	0	2 (3.1)
		Moderate	2 (8.7)	4 (9.8)	6 (9.4)
		Severe	0	0	0
	Leukopenia		0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
	Lymphadenopathy		1 (4.3)	0	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity. Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Blood and lymphatic system disorders	Lymphadenopathy	Mild	1 (4.3)	0	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
	Lymphopenia		0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
	Thrombocytopenia		0	1 (2.4)	1 (1.6)
		Mild	0	0	0
		Moderate	0	0	0
Metabolism and nutrition disorders	Decreased appetite		0	1 (2.4)	1 (1.6)
		Mild	2 (8.7)	7 (17.1)	9 (14.1)
		Moderate	1 (4.3)	6 (14.6)	7 (10.9)
		Severe	1 (4.3)	1 (2.4)	2 (3.1)
	Hyponatraemia		0	0	0
		Mild	1 (4.3)	5 (12.2)	6 (9.4)
		Moderate	1 (4.3)	4 (9.8)	5 (7.8)
		Severe	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Metabolism and nutrition disorders	Hyponatraemia	Severe	0	0	0
	Dehydration		0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
Eye disorders			1 (4.3)	4 (9.8)	5 (7.8)
		Mild	1 (4.3)	4 (9.8)	5 (7.8)
		Moderate	0	0	0
		Severe	0	0	0
	Dry eye		1 (4.3)	3 (7.3)	4 (6.3)
		Mild	1 (4.3)	3 (7.3)	4 (6.3)
		Moderate	0	0	0
		Severe	0	0	0
	Lacrimation increased		0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
Renal and urinary disorders			1 (4.3)	4 (9.8)	5 (7.8)
		Mild	1 (4.3)	2 (4.9)	3 (4.7)
		Moderate	0	2 (4.9)	2 (3.1)
		Severe	0	0	0
	Dysuria		1 (4.3)	1 (2.4)	2 (3.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Renal and urinary disorders	Dysuria	Mild	1 (4.3)	1 (2.4)	2 (3.1)
		Moderate	0	0	0
		Severe	0	0	0
	Acute kidney injury		0	1 (2.4)	1 (1.6)
		Mild	0	0	0
		Moderate	0	1 (2.4)	1 (1.6)
	Bladder pain	Severe	0	0	0
			0	1 (2.4)	1 (1.6)
		Mild	0	0	0
	Pollakiuria	Moderate	0	1 (2.4)	1 (1.6)
		Severe	0	0	0
			0	1 (2.4)	1 (1.6)
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Mild	1 (4.3)	4 (9.8)	5 (7.8)
		Moderate	1 (4.3)	1 (2.4)	2 (3.1)
		Severe	0	1 (2.4)	1 (1.6)
			0	2 (4.9)	2 (3.1)
	Dyspnoea		0	3 (7.3)	3 (4.7)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Respiratory, thoracic and mediastinal disorders	Dyspnoea	Severe	0	1 (2.4)	1 (1.6)
	Epistaxis	Mild	1 (4.3)	0	1 (1.6)
		Moderate	1 (4.3)	0	1 (1.6)
		Severe	0	0	0
	Pleural effusion	Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	1 (2.4)	1 (1.6)
	Rhinorrhoea	Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
	Wheezing	Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	1 (2.4)	1 (1.6)
Infections and infestations	Bronchitis	Mild	1 (4.3)	3 (7.3)	4 (6.3)
		Moderate	1 (4.3)	2 (4.9)	3 (4.7)
		Severe	0	1 (2.4)	1 (1.6)
			0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Infections and infestations	Bronchitis	Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
	Herpes zoster		1 (4.3)	0	1 (1.6)
		Mild	1 (4.3)	0	1 (1.6)
		Moderate	0	0	0
	Pneumonia		0	1 (2.4)	1 (1.6)
		Mild	0	0	0
		Moderate	0	1 (2.4)	1 (1.6)
	Urinary tract infection		0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
	Neoplasms benign, malignant and unspecified (incl cysts and polyps)		2 (8.7)	2 (4.9)	4 (6.3)
		Mild	0	0	0
		Moderate	1 (4.3)	2 (4.9)	3 (4.7)
	Metastases to central nervous system	Severe	1 (4.3)	0	1 (1.6)
		Mild	2 (8.7)	0	2 (3.1)
		Moderate	0	0	0
		Moderate	1 (4.3)	0	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Metastases to central nervous system	Severe	1 (4.3)	0	1 (1.6)
	Adenocarcinoma of colon	Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	1 (2.4)	1 (1.6)
	Metastases to meninges	Mild	0	0	0
		Moderate	0	1 (2.4)	1 (1.6)
		Severe	0	0	0
Investigations			2 (8.7)	1 (2.4)	3 (4.7)
		Mild	0	0	0
		Moderate	2 (8.7)	1 (2.4)	3 (4.7)
		Severe	0	0	0
	Blood lactate dehydrogenase increased	Mild	1 (4.3)	0	1 (1.6)
		Moderate	0	0	0
		Severe	1 (4.3)	0	1 (1.6)
		Severe	0	0	0
	Glomerular filtration rate decreased	Mild	1 (4.3)	0	1 (1.6)
		Moderate	0	0	0
		Severe	1 (4.3)	0	1 (1.6)
		Severe	0	0	0
	Weight decreased		0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Investigations	Weight decreased	Mild	0	0	0
		Moderate	0	1 (2.4)	1 (1.6)
		Severe	0	0	0
Skin and subcutaneous tissue disorders	Dry skin		1 (4.3)	1 (2.4)	2 (3.1)
		Mild	1 (4.3)	1 (2.4)	2 (3.1)
		Moderate	0	0	0
Skin and subcutaneous tissue disorders	Pain of skin	Severe	0	0	0
			1 (4.3)	0	1 (1.6)
		Mild	1 (4.3)	0	1 (1.6)
Vascular disorders	Haematoma	Moderate	0	0	0
		Severe	0	0	0
			0	1 (2.4)	1 (1.6)
Vascular disorders	Pain of skin	Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
Vascular disorders	Haematoma		0	2 (4.9)	2 (3.1)
		Mild	0	2 (4.9)	2 (3.1)
		Moderate	0	0	0
Vascular disorders	Haematoma	Severe	0	0	0
			0	2 (4.9)	2 (3.1)
		Mild	0	2 (4.9)	2 (3.1)
Vascular disorders		Moderate	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Vascular disorders	Haematoma	Severe	0	0	0
Ear and labyrinth disorders			0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
	Deafness		0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
Endocrine disorders			0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
	Hypothyroidism		0	1 (2.4)	1 (1.6)
		Mild	0	1 (2.4)	1 (1.6)
		Moderate	0	0	0
		Severe	0	0	0
Injury, poisoning and procedural complications			1 (4.3)	0	1 (1.6)
		Mild	0	0	0
		Moderate	0	0	0
		Severe	1 (4.3)	0	1 (1.6)
	Subdural haematoma		1 (4.3)	0	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.1
TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)	
			6.0 GBq (N=23)	7.4 GBq (N=41)		
Injury, poisoning and procedural complications	Subdural haematoma	Mild	0	0	0	
		Moderate	0	0	0	
		Severe	1 (4.3)	0	1 (1.6)	
Psychiatric disorders	Depression	Mild	0	1 (2.4)	1 (1.6)	
		Moderate	0	1 (2.4)	1 (1.6)	
		Severe	0	0	0	
		Mild	0	1 (2.4)	1 (1.6)	
Reproductive system and breast disorders	Prostatic pain	Moderate	0	0	0	
		Severe	0	0	0	
		Mild	0	1 (2.4)	1 (1.6)	
		Moderate	0	1 (2.4)	1 (1.6)	
		Severe	0	0	0	
		Mild	0	1 (2.4)	1 (1.6)	
		Moderate	0	0	0	
		Severe	0	0	0	

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with

multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.1
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients <65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16) n (%)
			6.0 GBq (N=4) n (%)	7.4 GBq (N=12) n (%)	
Number of patients with at least one TEAE			4 (100)	11 (91.7)	15 (93.8)
Gastrointestinal disorders					
	Mild	4 (100)	10 (83.3)	14 (87.5)	
	Moderate	3 (75.0)	7 (58.3)	10 (62.5)	
	Severe	1 (25.0)	3 (25.0)	4 (25.0)	
		0	0	0	
	Nausea				
	Mild	3 (75.0)	7 (58.3)	10 (62.5)	
	Moderate	3 (75.0)	5 (41.7)	8 (50.0)	
	Severe	0	2 (16.7)	2 (12.5)	
		0	0	0	
	Dry mouth				
	Mild	2 (50.0)	5 (41.7)	7 (43.8)	
	Moderate	2 (50.0)	5 (41.7)	7 (43.8)	
	Severe	0	0	0	
		0	0	0	
	Vomiting				
	Mild	2 (50.0)	3 (25.0)	5 (31.3)	
	Moderate	1 (25.0)	1 (8.3)	2 (12.5)	
	Severe	1 (25.0)	2 (16.7)	3 (18.8)	
		0	0	0	
	Constipation				
	Mild	0	2 (16.7)	2 (12.5)	
	Moderate	0	2 (16.7)	2 (12.5)	
	Severe	0	0	0	
		0	0	0	
	Diarrhoea		1 (25.0)	1 (8.3)	2 (12.5)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity. Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.1
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients <65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16) n (%)
			6.0 GBq (N=4) n (%)	7.4 GBq (N=12) n (%)	
Gastrointestinal disorders	Diarrhoea	Mild	1 (25.0)	1 (8.3)	2 (12.5)
		Moderate	0	0	0
		Severe	0	0	0
	Frequent bowel movements		0	1 (8.3)	1 (6.3)
		Mild	0	1 (8.3)	1 (6.3)
		Moderate	0	0	0
	Lip dry	Severe	0	0	0
			0	1 (8.3)	1 (6.3)
		Mild	0	1 (8.3)	1 (6.3)
General disorders and administration site conditions	General disorders and administration site conditions	Moderate	0	0	0
		Severe	0	0	0
			2 (50.0)	7 (58.3)	9 (56.3)
	Fatigue	Mild	2 (50.0)	4 (33.3)	6 (37.5)
		Moderate	0	3 (25.0)	3 (18.8)
		Severe	0	0	0
	Chest pain		2 (50.0)	5 (41.7)	7 (43.8)
		Mild	2 (50.0)	4 (33.3)	6 (37.5)
		Moderate	0	1 (8.3)	1 (6.3)
		Severe	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.1
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients <65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16) n (%)
			6.0 GBq (N=4) n (%)	7.4 GBq (N=12) n (%)	
General disorders and administration site conditions	Chest pain	Severe	0	0	0
	Pain	Mild	0	1 (8.3)	1 (6.3)
		Moderate	0	0	0
		Severe	0	1 (8.3)	1 (6.3)
	Pyrexia	Mild	0	0	0
		Moderate	0	0	0
		Severe	0	0	0
Blood and lymphatic system disorders			1 (25.0)	3 (25.0)	4 (25.0)
		Mild	1 (25.0)	0	1 (6.3)
		Moderate	0	2 (16.7)	2 (12.5)
		Severe	0	1 (8.3)	1 (6.3)
	Anaemia	Mild	1 (25.0)	3 (25.0)	4 (25.0)
		Moderate	1 (25.0)	0	1 (6.3)
		Severe	0	3 (25.0)	3 (18.8)
	Thrombocytopenia	Mild	0	0	0
		Moderate	0	0	0
		Severe	0	1 (8.3)	1 (6.3)
Musculoskeletal and connective tissue disorders			1 (25.0)	3 (25.0)	4 (25.0)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.1
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients <65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16) n (%)
			6.0 GBq (N=4) n (%)	7.4 GBq (N=12) n (%)	
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders	Mild	1 (25.0)	2 (16.7)	3 (18.8)
		Moderate	0	1 (8.3)	1 (6.3)
		Severe	0	0	0
	Musculoskeletal chest pain		0	2 (16.7)	2 (12.5)
		Mild	0	2 (16.7)	2 (12.5)
		Moderate	0	0	0
	Arthralgia	Severe	0	0	0
			1 (25.0)	0	1 (6.3)
		Mild	1 (25.0)	0	1 (6.3)
Nervous system disorders	Bone pain	Moderate	0	0	0
		Severe	0	0	0
			0	1 (8.3)	1 (6.3)
	Musculoskeletal stiffness	Mild	0	0	0
		Moderate	0	1 (8.3)	1 (6.3)
		Severe	0	0	0
	Nervous system disorders		0	1 (8.3)	1 (6.3)
		Mild	0	3 (25.0)	3 (18.8)
		Moderate	0	1 (8.3)	1 (6.3)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.1
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients <65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16) n (%)
			6.0 GBq (N=4) n (%)	7.4 GBq (N=12) n (%)	
Nervous system disorders		Severe	0	0	0
Taste disorder		Mild	0	3 (25.0)	3 (18.8)
		Moderate	0	3 (25.0)	3 (18.8)
		Severe	0	0	0
Dizziness		Mild	0	1 (8.3)	1 (6.3)
		Moderate	0	0	0
		Severe	0	1 (8.3)	1 (6.3)
				0	0
Investigations		Mild	1 (25.0)	1 (8.3)	2 (12.5)
		Moderate	0	0	0
		Severe	1 (25.0)	1 (8.3)	2 (12.5)
			0	0	0
Glomerular filtration rate decreased		Mild	1 (25.0)	0	1 (6.3)
		Moderate	0	0	0
		Severe	1 (25.0)	0	1 (6.3)
			0	0	0
Weight decreased		Mild	0	1 (8.3)	1 (6.3)
		Moderate	0	0	0
		Severe	0	1 (8.3)	1 (6.3)
			0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			1 (25.0)	1 (8.3)	2 (12.5)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.1
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients <65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16) n (%)
			6.0 GBq (N=4) n (%)	7.4 GBq (N=12) n (%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Metastases to central nervous system	Mild	0	0	0
		Moderate	0	1 (8.3)	1 (6.3)
		Severe	1 (25.0)	0	1 (6.3)
	Metastases to meninges	Mild	1 (25.0)	0	1 (6.3)
		Moderate	0	0	0
		Severe	1 (25.0)	0	1 (6.3)
	Infections and infestations	Mild	0	1 (8.3)	1 (6.3)
		Moderate	0	0	0
		Severe	0	1 (8.3)	1 (6.3)
Metabolism and nutrition disorders	Pneumonia	Mild	0	0	0
		Moderate	0	1 (8.3)	1 (6.3)
		Severe	0	0	0
		Mild	0	1 (8.3)	1 (6.3)
		Moderate	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.1
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients <65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16) n (%)
			6.0 GBq (N=4) n (%)	7.4 GBq (N=12) n (%)	
Metabolism and nutrition disorders		Severe	0	0	0
Renal and urinary disorders	Decreased appetite	Mild	0	1 (8.3)	1 (6.3)
		Moderate	0	0	0
		Severe	0	0	0
		Mild	0	1 (8.3)	1 (6.3)
	Pollakiuria	Moderate	0	0	0
		Severe	0	0	0
		Mild	0	1 (8.3)	1 (6.3)
		Moderate	0	0	0
		Severe	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Number of patients with at least one TEAE			18 (94.7)	28 (96.6)	46 (95.8)
Gastrointestinal disorders		Mild	15 (78.9)	23 (79.3)	38 (79.2)
		Moderate	14 (73.7)	17 (58.6)	31 (64.6)
		Severe	1 (5.3)	4 (13.8)	5 (10.4)
	Dry mouth	Severe	0	2 (6.9)	2 (4.2)
		Mild	9 (47.4)	21 (72.4)	30 (62.5)
		Moderate	9 (47.4)	19 (65.5)	28 (58.3)
		Severe	0	2 (6.9)	2 (4.2)
	Nausea	Severe	0	0	0
		Mild	9 (47.4)	11 (37.9)	20 (41.7)
		Moderate	8 (42.1)	7 (24.1)	15 (31.3)
		Severe	1 (5.3)	3 (10.3)	4 (8.3)
		Severe	0	1 (3.4)	1 (2.1)
	Diarrhoea	Mild	9 (47.4)	11 (37.9)	15 (31.3)
		Moderate	2 (10.5)	1 (3.4)	4 (8.3)
		Severe	0	0	0
		Mild	2 (10.5)	12 (41.4)	14 (29.2)
		Moderate	2 (10.5)	11 (37.9)	13 (27.1)
		Severe	0	1 (3.4)	1 (2.1)
	Constipation	Severe	0	0	0
		Mild	6 (31.6)	7 (24.1)	13 (27.1)
		Moderate	6 (31.6)	7 (24.1)	13 (27.1)
		Severe	0	0	0
	Vomiting	Severe	0	0	0
		Mild	2 (10.5)	5 (17.2)	7 (14.6)
		Moderate	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity. Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Gastrointestinal disorders	Vomiting	Mild	2 (10.5)	2 (6.9)	4 (8.3)
		Moderate	0	2 (6.9)	2 (4.2)
		Severe	0	1 (3.4)	1 (2.1)
	Abdominal pain		1 (5.3)	1 (3.4)	2 (4.2)
		Mild	1 (5.3)	0	1 (2.1)
		Moderate	0	0	0
	Gastrointestinal haemorrhage	Severe	0	1 (3.4)	1 (2.1)
		Mild	0	0	0
		Moderate	0	1 (3.4)	1 (2.1)
	Hyperaesthesia teeth	Severe	0	0	0
		Mild	1 (5.3)	0	1 (2.1)
		Moderate	0	0	0
	Saliva altered	Severe	0	0	0
		Mild	1 (5.3)	0	1 (2.1)
		Moderate	0	0	0
General disorders and administration site conditions			11 (57.9)	18 (62.1)	29 (60.4)
		Mild	6 (31.6)	13 (44.8)	19 (39.6)
		Moderate	5 (26.3)	4 (13.8)	9 (18.8)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients ≥ 65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
General disorders and administration site conditions	Severe	0	1 (3.4)	1 (2.1)	
Fatigue	Mild	11 (57.9) 7 (36.8)	16 (55.2) 13 (44.8)	27 (56.3) 20 (41.7)	
	Moderate	4 (21.1)	3 (10.3)	7 (14.6)	
	Severe	0	0	0	
Pain	Mild	3 (15.8) 1 (5.3)	4 (13.8) 3 (10.3)	7 (14.6) 4 (8.3)	
	Moderate	2 (10.5)	1 (3.4)	3 (6.3)	
	Severe	0	0	0	
Asthenia	Mild	0	1 (3.4)	1 (2.1)	
	Moderate	0	1 (3.4)	1 (2.1)	
	Severe	0	0	0	
Chest pain	Mild	1 (5.3) 1 (5.3)	0	1 (2.1)	
	Moderate	0	0	0	
	Severe	0	0	0	
Death	Mild	0	1 (3.4)	1 (2.1)	
	Moderate	0	0	0	
	Severe	0	1 (3.4)	1 (2.1)	
Feeling hot		0	1 (3.4)	1 (2.1)	

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2

TEAES by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
General disorders and administration site conditions	Feeling hot	Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
		Severe	0	0	0
	Oedema peripheral	Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
		Severe	0	0	0
	Pyrexia	Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
		Severe	0	0	0
Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders	Mild	5 (26.3)	7 (24.1)	12 (25.0)
		Moderate	3 (15.8)	4 (13.8)	7 (14.6)
		Severe	2 (10.5)	2 (6.9)	4 (8.3)
	Arthralgia	Mild	0	1 (3.4)	1 (2.1)
		Moderate	2 (10.5)	2 (6.9)	4 (8.3)
		Severe	2 (10.5)	0	2 (4.2)
	Back pain	Mild	0	2 (6.9)	2 (4.2)
		Moderate	0	0	0
		Severe	2 (10.5)	1 (3.4)	3 (6.3)
		Mild	2 (10.5)	1 (3.4)	3 (6.3)
		Moderate	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Musculoskeletal and connective tissue disorders	Back pain	Severe	0	0	0
	Pain in extremity		1 (5.3)	2 (6.9)	3 (6.3)
		Mild	1 (5.3)	2 (6.9)	3 (6.3)
		Moderate	0	0	0
		Severe	0	0	0
	Bone pain		1 (5.3)	1 (3.4)	2 (4.2)
		Mild	0	0	0
		Moderate	1 (5.3)	0	1 (2.1)
		Severe	0	1 (3.4)	1 (2.1)
	Neck pain		0	1 (3.4)	1 (2.1)
		Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
		Severe	0	0	0
	Osteoporosis		1 (5.3)	0	1 (2.1)
		Mild	0	0	0
		Moderate	1 (5.3)	0	1 (2.1)
		Severe	0	0	0
Nervous system disorders			6 (31.6)	6 (20.7)	12 (25.0)
		Mild	4 (21.1)	5 (17.2)	9 (18.8)
		Moderate	2 (10.5)	1 (3.4)	3 (6.3)
		Severe	0	0	0
	Taste disorder		4 (21.1)	4 (13.8)	8 (16.7)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.
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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Nervous system disorders	Taste disorder	Mild	2 (10.5)	4 (13.8)	6 (12.5)
		Moderate	2 (10.5)	0	2 (4.2)
		Severe	0	0	0
	Headache	Mild	2 (10.5)	2 (6.9)	4 (8.3)
		Moderate	2 (10.5)	1 (3.4)	3 (6.3)
		Severe	0	1 (3.4)	1 (2.1)
	Dizziness	Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
		Severe	0	1 (3.4)	0
	Parosmia	Mild	1 (5.3)	0	1 (2.1)
		Moderate	1 (5.3)	0	1 (2.1)
		Severe	0	0	0
Metabolism and nutrition disorders	Hypoglycemia	Mild	2 (10.5)	6 (20.7)	8 (16.7)
		Moderate	1 (5.3)	5 (17.2)	6 (12.5)
		Severe	1 (5.3)	1 (3.4)	2 (4.2)
		Severe	0	0	0
	Decreased appetite	Mild	1 (5.3)	4 (13.8)	5 (10.4)
		Moderate	1 (5.3)	3 (10.3)	4 (8.3)
		Moderate	0	1 (3.4)	1 (2.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Metabolism and nutrition disorders	Decreased appetite	Severe	0	0	0
	Hyponatraemia	Mild	1 (5.3)	1 (3.4)	2 (4.2)
		Moderate	0	1 (3.4)	1 (2.1)
		Severe	1 (5.3)	0	1 (2.1)
			0	0	0
	Dehydration	Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	1 (3.4)	1 (2.1)
		Severe	0	0	0
Blood and lymphatic system disorders					
	Anaemia	Mild	4 (21.1)	3 (10.3)	7 (14.6)
		Moderate	2 (10.5)	2 (6.9)	4 (8.3)
		Severe	2 (10.5)	1 (3.4)	3 (6.3)
			0	0	0
	Anaemia	Mild	3 (15.8)	1 (3.4)	4 (8.3)
		Moderate	1 (5.3)	0	1 (2.1)
		Severe	2 (10.5)	1 (3.4)	3 (6.3)
			0	0	0
	Leukopenia	Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	1 (3.4)	1 (2.1)
		Severe	0	0	0
	Lymphadenopathy		1 (5.3)	0	1 (2.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity. Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Blood and lymphatic system disorders	Lymphadenopathy	Mild	1 (5.3)	0	1 (2.1)
		Moderate	0	0	0
		Severe	0	0	0
	Lymphopenia		0	1 (3.4)	1 (2.1)
		Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
Eye disorders	Dry eye		1 (5.3)	4 (13.8)	5 (10.4)
		Mild	1 (5.3)	4 (13.8)	5 (10.4)
		Moderate	0	0	0
	Lacrimation increased	Severe	0	0	0
			1 (5.3)	3 (10.3)	4 (8.3)
		Mild	1 (5.3)	3 (10.3)	4 (8.3)
Respiratory, thoracic and mediastinal disorders	Lacrimation increased	Moderate	0	0	0
		Severe	0	0	0
			0	1 (3.4)	1 (2.1)
	Respiratory, thoracic and mediastinal disorders	Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
		Severe	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Respiratory, thoracic and mediastinal disorders		Severe	0	2 (6.9)	2 (4.2)
	Dyspnoea		0	3 (10.3)	3 (6.3)
		Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	1 (3.4)	1 (2.1)
		Severe	0	1 (3.4)	1 (2.1)
	Epistaxis		1 (5.3)	0	1 (2.1)
		Mild	1 (5.3)	0	1 (2.1)
		Moderate	0	0	0
		Severe	0	0	0
	Pleural effusion		0	1 (3.4)	1 (2.1)
		Mild	0	0	0
		Moderate	0	0	0
		Severe	0	1 (3.4)	1 (2.1)
	Rhinorrhoea		0	1 (3.4)	1 (2.1)
		Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
		Severe	0	0	0
	Wheezing		0	1 (3.4)	1 (2.1)
		Mild	0	0	0
		Moderate	0	1 (3.4)	1 (2.1)
		Severe	0	0	0
Renal and urinary disorders			1 (5.3)	3 (10.3)	4 (8.3)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Renal and urinary disorders		Mild	1 (5.3)	1 (3.4)	2 (4.2)
		Moderate	0	2 (6.9)	2 (4.2)
		Severe	0	0	0
Dysuria		Mild	1 (5.3)	1 (3.4)	2 (4.2)
		Moderate	0	0	0
		Severe	0	0	0
Acute kidney injury		Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	1 (3.4)	1 (2.1)
		Severe	0	0	0
Bladder pain		Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
		Severe	0	1 (3.4)	1 (2.1)
Infections and infestations		Mild	1 (5.3)	2 (6.9)	3 (6.3)
		Moderate	1 (5.3)	2 (6.9)	3 (6.3)
		Severe	0	0	0
Bronchitis		Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	1 (3.4)	1 (2.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Infections and infestations	Bronchitis	Severe	0	0	0
	Herpes zoster	Mild	1 (5.3)	0	1 (2.1)
		Moderate	1 (5.3)	0	1 (2.1)
		Severe	0	0	0
	Urinary tract infection	Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	1 (3.4)	1 (2.1)
		Severe	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		Mild	1 (5.3)	1 (3.4)	2 (4.2)
		Moderate	0	0	0
		Severe	1 (5.3)	1 (3.4)	2 (4.2)
	Adenocarcinoma of colon	Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
		Severe	0	1 (3.4)	1 (2.1)
			0	0	0
	Metastases to central nervous system	Mild	1 (5.3)	0	1 (2.1)
		Moderate	0	0	0
		Severe	1 (5.3)	0	1 (2.1)
			0	0	0
Skin and subcutaneous tissue disorders			1 (5.3)	1 (3.4)	2 (4.2)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity. Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Skin and subcutaneous tissue disorders		Mild	1 (5.3)	1 (3.4)	2 (4.2)
		Moderate	0	0	0
		Severe	0	0	0
	Dry skin		1 (5.3)	0	1 (2.1)
		Mild	1 (5.3)	0	1 (2.1)
		Moderate	0	0	0
		Severe	0	0	0
	Pain of skin		0	1 (3.4)	1 (2.1)
		Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
		Severe	0	0	0
Vascular disorders			0	2 (6.9)	2 (4.2)
		Mild	0	2 (6.9)	2 (4.2)
		Moderate	0	0	0
		Severe	0	0	0
	Haematoma		0	2 (6.9)	2 (4.2)
		Mild	0	2 (6.9)	2 (4.2)
		Moderate	0	0	0
		Severe	0	0	0
Ear and labyrinth disorders			0	1 (3.4)	1 (2.1)
		Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19)	7.4 GBq (N=29)	
Ear and labyrinth disorders	Severe	0	0	0	0
	Deafness		0	1 (3.4)	1 (2.1)
	Mild	0	1 (3.4)	1 (2.1)	
	Moderate	0	0	0	
	Severe	0	0	0	
Endocrine disorders	Severe	0	1 (3.4)	1 (2.1)	
	Mild	0	1 (3.4)	1 (2.1)	
	Moderate	0	0	0	
	Severe	0	0	0	
	Hypothyroidism		0	1 (3.4)	1 (2.1)
	Mild	0	1 (3.4)	1 (2.1)	
	Moderate	0	0	0	
	Severe	0	0	0	
Injury, poisoning and procedural complications	Severe	1 (5.3)	0	1 (2.1)	
	Mild	0	0	0	
	Moderate	0	0	0	
	Severe	1 (5.3)	0	1 (2.1)	
Subdural haematoma	Severe	1 (5.3)	0	1 (2.1)	
	Mild	0	0	0	
	Moderate	0	0	0	
	Severe	1 (5.3)	0	1 (2.1)	
Investigations		1 (5.3)	0	1 (2.1)	

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.

Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2
 TEAEs by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Investigations	Blood lactate dehydrogenase increased	Mild	0	0	0
		Moderate	1 (5.3)	0	1 (2.1)
		Severe	0	0	0
Psychiatric disorders	Depression		1 (5.3)	0	1 (2.1)
		Mild	0	0	0
		Moderate	1 (5.3)	0	1 (2.1)
		Severe	0	0	0
Reproductive system and breast disorders	Prostatic pain		0	1 (3.4)	1 (2.1)
		Mild	0	1 (3.4)	1 (2.1)
		Moderate	0	0	0
		Severe	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
 Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
 Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.11.2.2

TEAES by MedDRA System Organ Class, Preferred Term, and Severity Grade (patients >=65 years old)
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617 6.0 GBq (N=19)	Lu-PSMA-617 7.4 GBq (N=29)	Overall (N=48)
		n (%)	n (%)	n (%)	n (%)
Reproductive system and breast disorders	Prostatic pain	Severe	0	0	0

Results given as xx' (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.
Every patient is counted a single time for each applicable specific adverse event with highest severity. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest severity.
Coded using MedDRA version 22.1. Severity (mild, moderate and severe) is assessed independently by investigators.

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Table 14.3.1.12.1
 Serious TEAEs by MedDRA System Organ Class, Preferred Term and NCI CTCAE Grade
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Number of patients with at least one TEAE			4 (17.4)	8 (19.5)	12 (18.8)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			2 (8.7) 1 (4.3) Grade 3 Grade 4 Grade 5	2 (4.9) 2 (4.9) 0 0 0	4 (6.3) 3 (4.7) 0 1 (1.6)
Metastases to central nervous system			2 (8.7) 1 (4.3) Grade 3 Grade 4 Grade 5	0 0 0	2 (3.1) 1 (1.6) 0
Adenocarcinoma of colon			0 0 0 Grade 3 Grade 4 Grade 5	1 (2.4) 1 (2.4) 0 0	1 (1.6) 1 (1.6) 0
Metastases to meninges			0 0 0 Grade 3 Grade 4 Grade 5	1 (2.4) 1 (2.4) 0 0	1 (1.6) 1 (1.6) 0
Gastrointestinal disorders			0 0 0 Grade 3 Grade 4 Grade 5	2 (4.9) 2 (4.9) 0 0	2 (3.1) 2 (3.1) 0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest grade. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest grade.

Coded using MedDRA version 22.1 and NCI CTCAE version 4.03

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Table 14.3.1.12.1
 Serious TEAEs by MedDRA System Organ Class, Preferred Term and NCI CTCAE Grade
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Gastrointestinal disorders	Abdominal pain		0	1 (2.4)	1 (1.6)
	Grade 3	0	1 (2.4)	1 (1.6)	
	Grade 4	0	0	0	
	Grade 5	0	0	0	
	Gastrointestinal haemorrhage		0	1 (2.4)	1 (1.6)
	Grade 3	0	1 (2.4)	1 (1.6)	
	Grade 4	0	0	0	
	Grade 5	0	0	0	
Blood and lymphatic system disorders			0	1 (2.4)	1 (1.6)
		Grade 3	0	0	0
		Grade 4	0	1 (2.4)	1 (1.6)
		Grade 5	0	0	0
	Anaemia		0	1 (2.4)	1 (1.6)
	Grade 3	0	1 (2.4)	1 (1.6)	
	Grade 4	0	0	0	
	Grade 5	0	0	0	
	Thrombocytopenia		0	1 (2.4)	1 (1.6)
	Grade 3	0	0	0	
	Grade 4	0	1 (2.4)	1 (1.6)	
	Grade 5	0	0	0	
General disorders and administration site conditions			0	1 (2.4)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest grade. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest grade.

Coded using MedDRA version 22.1 and NCI CTCAE version 4.03

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Table 14.3.1.12.1
 Serious TEAEs by MedDRA System Organ Class, Preferred Term and NCI CTCAE Grade
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
General disorders and administration site conditions	Grade 3	0	0	0	0
	Grade 4	0	0	0	0
	Grade 5	0	1 (2.4)	1 (1.6)	1 (1.6)
Death	Grade 3	0	1 (2.4)	1 (1.6)	1 (1.6)
	Grade 4	0	0	0	0
	Grade 5	0	1 (2.4)	1 (1.6)	1 (1.6)
Infections and infestations	Grade 3	0	1 (2.4)	1 (1.6)	1 (1.6)
	Grade 4	0	0	0	0
	Grade 5	0	0	0	0
Pneumonia	Grade 3	0	1 (2.4)	1 (1.6)	1 (1.6)
	Grade 4	0	0	0	0
	Grade 5	0	0	0	0
Injury, poisoning and procedural complications	Grade 3	1 (4.3)	0	1 (1.6)	1 (1.6)
	Grade 4	0	0	0	0
	Grade 5	1 (4.3)	0	1 (1.6)	1 (1.6)
Subdural haematoma	Grade 3	1 (4.3)	0	1 (1.6)	1 (1.6)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest grade. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest grade.

Coded using MedDRA version 22.1 and NCI CTCAE version 4.03

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Table 14.3.1.12.1
 Serious TEAEs by MedDRA System Organ Class, Preferred Term and NCI CTCAE Grade
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Injury, poisoning and procedural complications	Subdural haematoma	Grade 4	0	0	0
		Grade 5	1 (4.3)	0	1 (1.6)
Musculoskeletal and connective tissue disorders			1 (4.3)	0	1 (1.6)
		Grade 3	1 (4.3)	0	1 (1.6)
		Grade 4	0	0	0
		Grade 5	0	0	0
Osteoporosis			1 (4.3)	0	1 (1.6)
		Grade 3	1 (4.3)	0	1 (1.6)
		Grade 4	0	0	0
		Grade 5	0	0	0
Renal and urinary disorders			0	1 (2.4)	1 (1.6)
		Grade 3	0	1 (2.4)	1 (1.6)
		Grade 4	0	0	0
		Grade 5	0	0	0
Acute kidney injury			0	1 (2.4)	1 (1.6)
		Grade 3	0	1 (2.4)	1 (1.6)
		Grade 4	0	0	0
		Grade 5	0	0	0
Respiratory, thoracic and mediastinal disorders			0	1 (2.4)	1 (1.6)
		Grade 3	0	1 (2.4)	1 (1.6)
		Grade 4	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest grade. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest grade.

Coded using MedDRA version 22.1 and NCI CTCAE version 4.03

Output ID: t-ae-ctc-saf 04JUN20 12:53

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Table 14.3.1.12.1
 Serious TEAEs by MedDRA System Organ Class, Preferred Term and NCI CTCAE Grade
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Respiratory, thoracic and mediastinal disorders		Grade 5	0	0	0
	Pleural effusion		0	1 (2.4)	1 (1.6)
		Grade 3	0	1 (2.4)	1 (1.6)
		Grade 4	0	0	0
		Grade 5	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest grade. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest grade.

Coded using MedDRA version 22.1 and NCI CTCAE version 4.03

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Table 14.3.1.12.2.1

Serious TEAEs by MedDRA System Organ Class, Preferred Term and NCI CTCAE Grade (patients <65 years old)
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16) n (%)
			6.0 GBq (N=4) n (%)	7.4 GBq (N=12) n (%)	
Number of patients with at least one TEAE			1 (25.0)	3 (25.0)	4 (25.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)		Grade 3	1 (25.0) 0	1 (8.3) 1 (8.3)	2 (12.5) 1 (6.3)
		Grade 4	0	0	0
		Grade 5	1 (25.0)	0	1 (6.3)
Metastases to central nervous system		Grade 3	1 (25.0) 0	0	1 (6.3) 0
		Grade 4	0	0	0
		Grade 5	1 (25.0)	0	1 (6.3)
Metastases to meninges		Grade 3	0	1 (8.3) 1 (8.3)	1 (6.3) 1 (6.3)
		Grade 4	0	0	0
		Grade 5	0	0	0
Blood and lymphatic system disorders		Grade 3	0	1 (8.3) 0	1 (6.3) 0
		Grade 4	0	1 (8.3)	1 (6.3)
		Grade 5	0	0	0
Anaemia		Grade 3	0	1 (8.3) 1 (8.3)	1 (6.3) 1 (6.3)
		Grade 4	0	0	0
		Grade 5	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest grade. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest grade.

Coded using MedDRA version 22.1 and NCI CTCAE version 4.03

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Table 14.3.1.12.2.1

Serious TEAEs by MedDRA System Organ Class, Preferred Term and NCI CTCAE Grade (patients <65 years old)
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16) n (%)	
			6.0 GBq (N=4) n (%)	7.4 GBq (N=12) n (%)		
Blood and lymphatic system disorders	Thrombocytopenia		0	1 (8.3)	1 (6.3)	
		Grade 3	0	0	0	
		Grade 4	0	1 (8.3)	1 (6.3)	
		Grade 5	0	0	0	
Infections and infestations	Pneumonia		0	1 (8.3)	1 (6.3)	
		Grade 3	0	1 (8.3)	1 (6.3)	
		Grade 4	0	0	0	
		Grade 5	0	0	0	
			0	1 (8.3)	1 (6.3)	
		Grade 3	0	1 (8.3)	1 (6.3)	
		Grade 4	0	0	0	
		Grade 5	0	0	0	

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest grade. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest grade.

Coded using MedDRA version 22.1 and NCI CTCAE version 4.03

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Table 14.3.1.12.2.2
 Serious TEAEs by MedDRA System Organ Class, Preferred Term and NCI CTCAE Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Number of patients with at least one TEAE			3 (15.8)	5 (17.2)	8 (16.7)
Gastrointestinal disorders			0	2 (6.9)	2 (4.2)
	Grade 3	0	2 (6.9)	2 (4.2)	
	Grade 4	0	0	0	
	Grade 5	0	0	0	
Abdominal pain			0	1 (3.4)	1 (2.1)
	Grade 3	0	1 (3.4)	1 (2.1)	
	Grade 4	0	0	0	
	Grade 5	0	0	0	
Gastrointestinal haemorrhage			0	1 (3.4)	1 (2.1)
	Grade 3	0	1 (3.4)	1 (2.1)	
	Grade 4	0	0	0	
	Grade 5	0	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			1 (5.3)	1 (3.4)	2 (4.2)
	Grade 3	1 (5.3)	1 (3.4)	2 (4.2)	
	Grade 4	0	0	0	
	Grade 5	0	0	0	
Adenocarcinoma of colon			0	1 (3.4)	1 (2.1)
	Grade 3	0	1 (3.4)	1 (2.1)	
	Grade 4	0	0	0	
	Grade 5	0	0	0	

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest grade. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest grade.

Coded using MedDRA version 22.1 and NCI CTCAE version 4.03

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Table 14.3.1.12.2.2
 Serious TEAEs by MedDRA System Organ Class, Preferred Term and NCI CTCAE Grade (patients >=65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Metastases to central nervous system	Grade 3	1 (5.3)	0	1 (2.1)
		Grade 4	1 (5.3)	0	1 (2.1)
		Grade 5	0	0	0
General disorders and administration site conditions		Grade 3	0	1 (3.4)	1 (2.1)
		Grade 4	0	0	0
		Grade 5	0	0	0
		Death	0	1 (3.4)	1 (2.1)
Injury, poisoning and procedural complications		Grade 3	0	0	0
		Grade 4	0	0	0
		Grade 5	1 (5.3)	0	1 (2.1)
		Subdural haematoma	1 (5.3)	0	1 (2.1)
Musculoskeletal and connective tissue disorders		Grade 3	0	0	0
		Grade 4	0	0	0
		Grade 5	1 (5.3)	0	1 (2.1)
			1 (5.3)	0	1 (2.1)

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest grade. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest grade.

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Table 14.3.1.12.2.2
 Serious TEAEs by MedDRA System Organ Class, Preferred Term and NCI CTCAE Grade (patients ≥ 65 years old)
 Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Musculoskeletal and connective tissue disorders	Grade 3	Grade 3	1 (5.3)	0	1 (2.1)
		Grade 4	0	0	0
		Grade 5	0	0	0
	Osteoporosis	Grade 3	1 (5.3)	0	1 (2.1)
			1 (5.3)	0	1 (2.1)
			0	0	0
			0	0	0
	Renal and urinary disorders	Grade 3	0	1 (3.4)	1 (2.1)
			0	1 (3.4)	1 (2.1)
			0	0	0
			0	0	0
Acute kidney injury	Grade 3	Grade 3	0	1 (3.4)	1 (2.1)
			0	1 (3.4)	1 (2.1)
			0	0	0
			0	0	0
	Respiratory, thoracic and mediastinal disorders	Grade 3	0	1 (3.4)	1 (2.1)
			0	1 (3.4)	1 (2.1)
			0	0	0
			0	0	0
Pleural effusion	Grade 3	0	1 (3.4)	1 (2.1)	
		0	1 (3.4)	1 (2.1)	

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest grade. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest grade.

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Table 14.3.1.12.2.2

Serious TEAEs by MedDRA System Organ Class, Preferred Term and NCI CTCAE Grade (patients ≥ 65 years old)
Safety Population

System Organ Class	Preferred Term	Severity	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48) n (%)
			6.0 GBq (N=19) n (%)	7.4 GBq (N=29) n (%)	
Respiratory, thoracic and mediastinal disorders	Pleural effusion	Grade 4	0	0	0
		Grade 5	0	0	0

Results given as xx (xx.x) where xx = number of patients with adverse events, (xx.x) = percentage of patients.

Every patient is counted a single time for each applicable specific adverse event with highest grade. A patient with multiple adverse events within a system organ class is counted a single time for that system organ class with highest grade.

Coded using MedDRA version 22.1 and NCI CTCAE version 4.03

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Table 14.3.1.13.1
Specific Adverse Events (AES) Questionnaire
Safety Population

Visit	Question	Answer	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Cycle 1 Pre-dose	NAUSEA	NAUSEA WITH LOSS OF APPETITE ONLY	1 (4.3)	0	1 (1.6)
		NO NAUSEA	11 (47.8)	12 (29.3)	23 (35.9)
	VOMITING	NO VOMITING	12 (52.2)	11 (26.8)	23 (35.9)
		DRY MOUTH	1 (4.3)	1 (2.4)	2 (3.1)
	DRY MOUTH	DRY OR THICK SALIVA	10 (43.5)	11 (26.8)	21 (32.8)
		NO DRY MOUTH			
	TASTE	ALTERED TASTE BUT NO CHANGE IN DIET	1 (4.3)	1 (2.4)	2 (3.1)
		NORMAL TASTE	10 (43.5)	11 (26.8)	21 (32.8)
	FATIGUE	FATIGUE RELIEVED BY REST	2 (8.7)	4 (9.8)	6 (9.4)
		NO FATIGUE	9 (39.1)	8 (19.5)	17 (26.6)
Cycle 1 Post-dose	HEMATOMA	NO HEMATOMA	12 (52.2)	12 (29.3)	24 (37.5)
		NO FEVER	12 (52.2)	12 (29.3)	24 (37.5)
	URINARY RETENTION	ABLE TO VOID NORMALLY	12 (52.2)	12 (29.3)	24 (37.5)
		NORMAL BOWEL MOVEMENTS	11 (47.8)	12 (29.3)	23 (35.9)
	DIARRHEA	YES	3 (13.0)	1 (2.4)	4 (6.3)
		NO			
	OTHER	NAUSEA WITH EATING/DRINKING LESS THAN USUAL	1 (4.3)	0	1 (1.6)
		NAUSEA WITH LOSS OF APPETITE ONLY	7 (30.4)	9 (22.0)	16 (25.0)
		NO NAUSEA	15 (65.2)	30 (73.2)	45 (70.3)
	VOMITING	1-2 EPISODES PER DAY	4 (17.4)	1 (2.4)	5 (7.8)
		3-5 EPISODES PER DAY	0	2 (4.9)	2 (3.1)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.1
Specific Adverse Events (AES) Questionnaire
Safety Population

Visit	Question	Answer	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Cycle 1 Post-dose	VOMITING	NO VOMITING	19 (82.6)	37 (90.2)	56 (87.5)
	DRY MOUTH	DRY OR THICK SALIVA	4 (17.4)	14 (34.1)	18 (28.1)
		NO DRY MOUTH	19 (82.6)	25 (61.0)	44 (68.8)
	TASTE	ALTERED TASTE BUT NO CHANGE IN DIET	0	6 (14.6)	6 (9.4)
		ALTERED TASTE WITH CHANGE IN DIET	1 (4.3)	0	1 (1.6)
		NORMAL TASTE	22 (95.7)	33 (80.5)	55 (85.9)
	FATIGUE	FATIGUE NOT RELIEVED BY REST, LIMITING WORK	3 (13.0)	2 (4.9)	5 (7.8)
		FATIGUE RELIEVED BY REST	8 (34.8)	24 (58.5)	32 (50.0)
		NO FATIGUE	12 (52.2)	14 (34.1)	26 (40.6)
	HEMATOMA	NO HEMATOMA	21 (91.3)	38 (92.7)	59 (92.2)
		OCCURENCE OF HEMATOMA WITHOUT KNOWN EVENT	0	1 (2.4)	1 (1.6)
	FEVER	NO FEVER	22 (95.7)	38 (92.7)	60 (93.8)
	URINARY RETENTION	ABLE TO VOID NORMALLY	18 (78.3)	33 (80.5)	51 (79.7)
		ABLE TO VOID WITH SOME PRESSURE	1 (4.3)	1 (2.4)	2 (3.1)
	DIARRHEA	INCREASE BY 4-6 STOOLS PER DAY	0	2 (4.9)	2 (3.1)
		INCREASE BY<4 STOOLS PER DAY	1 (4.3)	6 (14.6)	7 (10.9)
		NORMAL BOWEL MOVEMENTS	20 (87.0)	30 (73.2)	50 (78.1)
	OTHER	YES	9 (39.1)	15 (36.6)	24 (37.5)
Cycle 2 Pre-dose	NAUSEA	NAUSEA WITH LOSS OF APPETITE ONLY	0	1 (2.4)	1 (1.6)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.1
Specific Adverse Events (AES) Questionnaire
Safety Population

Visit	Question	Answer	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Cycle 2 Pre-dose	NAUSEA	NO NAUSEA	6 (26.1)	7 (17.1)	13 (20.3)
	VOMITING	NO VOMITING		7 (17.1)	13 (20.3)
	DRY MOUTH	DRY OR THICK SALIVA		1 (4.3)	1 (2.4)
		NO DRY MOUTH		5 (21.7)	7 (17.1)
	TASTE	NORMAL TASTE		8 (19.5)	14 (21.9)
	FATIGUE	FATIGUE RELIEVED BY REST		1 (4.3)	3 (7.3)
		NO FATIGUE		5 (21.7)	4 (9.8)
	HEMATOMA	NO HEMATOMA		8 (19.5)	14 (21.9)
	FEVER	NO FEVER		8 (19.5)	14 (21.9)
Cycle 2 Post-dose	NAUSEA	ABLE TO VOID NORMALLY	5 (21.7)	8 (19.5)	13 (20.3)
		INCREASE BY<4 STOOLS PER DAY		1 (4.3)	2 (3.1)
		NORMAL BOWEL MOVEMENTS		5 (21.7)	7 (17.1)
		HAD TO GO TO HOSPITAL FOR NAUSEA		0	1 (2.4)
	VOMITING	NAUSEA WITH EATING/DRINKING LESS THAN USUAL	0	1 (2.4)	1 (1.6)
		NAUSEA WITH LOSS OF APPETITE ONLY		5 (21.7)	7 (17.1)
		NO NAUSEA		10 (43.5)	23 (56.1)
	VOMITING	1-2 EPISODES PER DAY	0	2 (4.9)	2 (3.1)
		3-5 EPISODES PER DAY		0	1 (2.4)
		MORE THAN 5 EPISODES PER DAY		0	1 (2.4)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.1
Specific Adverse Events (AES) Questionnaire
Safety Population

Visit	Question	Answer	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Cycle 2 Post-dose	VOMITING	NO VOMITING	15 (65.2)	27 (65.9)	42 (65.6)
	DRY MOUTH	DRY OR THICK SALIVA	3 (13.0)	14 (34.1)	17 (26.6)
		NO DRY MOUTH	11 (47.8)	17 (41.5)	28 (43.8)
		NO DRY MOUTH DRY OR THICK SALIVA	1 (4.3)	0	1 (1.6)
	TASTE	NORMAL TASTE	15 (65.2)	31 (75.6)	46 (71.9)
	FATIGUE	FATIGUE NOT RELIEVED BY REST, LIMITING WORK	0	1 (2.4)	1 (1.6)
		FATIGUE RELIEVED BY REST	8 (34.8)	14 (34.1)	22 (34.4)
		FATIGUE RELIEVED BY REST FATIGUE NOT RELIEVED BY REST, LIMITING WORK	0	1 (2.4)	1 (1.6)
		NO FATIGUE	7 (30.4)	15 (36.6)	22 (34.4)
		NO FATIGUE FATIGUE RELIEVED BY REST	0	1 (2.4)	1 (1.6)
	HEMATOMA	NO HEMATOMA	15 (65.2)	28 (68.3)	43 (67.2)
		OCCURENCE OF HEMATOMA WITHOUT KNOWN EVENT	0	1 (2.4)	1 (1.6)
	FEVER	NO FEVER	15 (65.2)	31 (75.6)	46 (71.9)
	URINARY RETENTION	ABLE TO VOID NORMALLY	14 (60.9)	29 (70.7)	43 (67.2)
	DIARRHEA	INCREASE BY<4 STOOLS PER DAY	1 (4.3)	2 (4.9)	3 (4.7)
		NORMAL BOWEL MOVEMENTS	14 (60.9)	27 (65.9)	41 (64.1)
	OTHER	NO	0	1 (2.4)	1 (1.6)
		YES	8 (34.8)	13 (31.7)	21 (32.8)
Cycle 3 Pre-dose	NAUSEA	NAUSEA WITH LOSS OF APPETITE ONLY	1 (4.3)	0	1 (1.6)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.1
Specific Adverse Events (AES) Questionnaire
Safety Population

Visit	Question	Answer	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Cycle 3 Pre-dose	NAUSEA	NO NAUSEA	2 (8.7)	5 (12.2)	7 (10.9)
	VOMITING	NO VOMITING	3 (13.0)	5 (12.2)	8 (12.5)
	DRY MOUTH	DRY OR THICK SALIVA	1 (4.3)	0	1 (1.6)
		NO DRY MOUTH	2 (8.7)	5 (12.2)	7 (10.9)
	TASTE	NORMAL TASTE	3 (13.0)	5 (12.2)	8 (12.5)
	FATIGUE	FATIGUE NOT RELIEVED BY REST, LIMITING WORK	0	1 (2.4)	1 (1.6)
		FATIGUE RELIEVED BY REST	1 (4.3)	0	1 (1.6)
		NO FATIGUE	2 (8.7)	4 (9.8)	6 (9.4)
	HEMATOMA	NO HEMATOMA	3 (13.0)	4 (9.8)	7 (10.9)
	FEVER	NO FEVER	3 (13.0)	4 (9.8)	7 (10.9)
	URINARY RETENTION	ABLE TO VOID NORMALLY	2 (8.7)	3 (7.3)	5 (7.8)
	DIARRHEA	INCREASE BY<4 STOOLS PER DAY	1 (4.3)	0	1 (1.6)
		NORMAL BOWEL MOVEMENTS	2 (8.7)	5 (12.2)	7 (10.9)
Cycle 3 Post-dose	NAUSEA	NAUSEA WITH LOSS OF APPETITE ONLY	2 (8.7)	2 (4.9)	4 (6.3)
		NO NAUSEA	8 (34.8)	16 (39.0)	24 (37.5)
	VOMITING	1-2 EPISODES PER DAY	0	1 (2.4)	1 (1.6)
		NO VOMITING	10 (43.5)	17 (41.5)	27 (42.2)
	DRY MOUTH	DRY OR THICK SALIVA	2 (8.7)	7 (17.1)	9 (14.1)
		NO DRY MOUTH	8 (34.8)	11 (26.8)	19 (29.7)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.1
Specific Adverse Events (AES) Questionnaire
Safety Population

Visit	Question	Answer	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Cycle 3 Post-dose	TASTE	ALTERED TASTE BUT NO CHANGE IN DIET	0	1 (2.4)	1 (1.6)
		ALTERED TASTE WITH CHANGE IN DIET	1 (4.3)	0	1 (1.6)
		NORMAL TASTE	7 (30.4)	16 (39.0)	23 (35.9)
	FATIGUE	FATIGUE NOT RELIEVED BY REST, LIMITING WORK	2 (8.7)	2 (4.9)	4 (6.3)
		FATIGUE RELIEVED BY REST	4 (17.4)	6 (14.6)	10 (15.6)
		NO FATIGUE	4 (17.4)	10 (24.4)	14 (21.9)
	HEMATOMA	NO HEMATOMA	9 (39.1)	18 (43.9)	27 (42.2)
	FEVER	NO FEVER	9 (39.1)	18 (43.9)	27 (42.2)
	URINARY RETENTION	ABLE TO VOID NORMALLY	9 (39.1)	15 (36.6)	24 (37.5)
	DIARRHEA	NORMAL BOWEL MOVEMENTS	8 (34.8)	18 (43.9)	26 (40.6)
Cycle 4 Pre-dose	OTHER	YES	6 (26.1)	6 (14.6)	12 (18.8)
		NAUSEA WITH LOSS OF APPÉTITE ONLY	2 (8.7)	0	2 (3.1)
	NAUSEA	NO NAUSEA	1 (4.3)	3 (7.3)	4 (6.3)
		VOMITING	3 (13.0)	3 (7.3)	6 (9.4)
	DRY MOUTH	NO DRY MOUTH	3 (13.0)	3 (7.3)	6 (9.4)
	TASTE	NORMAL TASTE	3 (13.0)	3 (7.3)	6 (9.4)
	FATIGUE	FATIGUE RELIEVED BY REST	2 (8.7)	0	2 (3.1)
		NO FATIGUE	1 (4.3)	3 (7.3)	4 (6.3)
	HEMATOMA	NO HEMATOMA	3 (13.0)	3 (7.3)	6 (9.4)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.1
Specific Adverse Events (AES) Questionnaire
Safety Population

Visit	Question	Answer	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Cycle 4 Pre-dose	FEVER	NO FEVER	3 (13.0)	3 (7.3)	6 (9.4)
	URINARY RETENTION	ABLE TO VOID NORMALLY	3 (13.0)	3 (7.3)	6 (9.4)
	DIARRHEA	NORMAL BOWEL MOVEMENTS	3 (13.0)	3 (7.3)	6 (9.4)
Cycle 4 Post-dose	NAUSEA	NAUSEA WITH LOSS OF APPETITE ONLY	0	2 (4.9)	2 (3.1)
		NO NAUSEA	5 (21.7)	9 (22.0)	14 (21.9)
	VOMITING	MORE THAN 5 EPISODES PER DAY	0	1 (2.4)	1 (1.6)
		NO VOMITING	5 (21.7)	10 (24.4)	15 (23.4)
	DRY MOUTH	DRY OR THICK SALIVA	2 (8.7)	5 (12.2)	7 (10.9)
		NO DRY MOUTH	3 (13.0)	6 (14.6)	9 (14.1)
	TASTE	ALTERED TASTE BUT NO CHANGE IN DIET	1 (4.3)	0	1 (1.6)
		NORMAL TASTE	4 (17.4)	11 (26.8)	15 (23.4)
	FATIGUE	FATIGUE NOT RELIEVED BY REST, LIMITING WORK	0	1 (2.4)	1 (1.6)
		FATIGUE RELIEVED BY REST	3 (13.0)	3 (7.3)	6 (9.4)
		NO FATIGUE	2 (8.7)	7 (17.1)	9 (14.1)
	HEMATOMA	NO HEMATOMA	5 (21.7)	9 (22.0)	14 (21.9)
	FEVER	NO FEVER	5 (21.7)	11 (26.8)	16 (25.0)
	URINARY RETENTION	ABLE TO VOID NORMALLY	5 (21.7)	11 (26.8)	16 (25.0)
	DIARRHEA	NORMAL BOWEL MOVEMENTS	5 (21.7)	10 (24.4)	15 (23.4)
	OTHER	YES	1 (4.3)	4 (9.8)	5 (7.8)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.1
Specific Adverse Events (AES) Questionnaire
Safety Population

Visit	Question	Answer	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Follow-up Month 3	NAUSEA	NO NAUSEA	2 (8.7)	3 (7.3)	5 (7.8)
	VOMITING	NO VOMITING	2 (8.7)	3 (7.3)	5 (7.8)
	DRY MOUTH	DRY OR THICK SALIVA	2 (8.7)	2 (4.9)	4 (6.3)
		NO DRY MOUTH	0	1 (2.4)	1 (1.6)
		NORMAL TASTE	2 (8.7)	3 (7.3)	5 (7.8)
	FATIGUE	FATIGUE RELIEVED BY REST	2 (8.7)	1 (2.4)	3 (4.7)
		NO FATIGUE	0	2 (4.9)	2 (3.1)
		NO HEMATOMA	2 (8.7)	3 (7.3)	5 (7.8)
	FEVER	38.0-39.0C (100.4-102.2F)	1 (4.3)	0	1 (1.6)
		NO FEVER	1 (4.3)	3 (7.3)	4 (6.3)
	URINARY RETENTION	ABLE TO VOID NORMALLY	2 (8.7)	3 (7.3)	5 (7.8)
	DIARRHEA	INCREASE BY<4 STOOLS PER DAY	0	1 (2.4)	1 (1.6)
		NORMAL BOWEL MOVEMENTS	2 (8.7)	2 (4.9)	4 (6.3)
	OTHER	YES	2 (8.7)	2 (4.9)	4 (6.3)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.2
Specific Adverse Events (AEs) Questionnaire - by Age Category
Safety Population

Visit	Question	Answer	Lu-PSMA-617		Lu-PSMA-617		Overall	
			<65 years (N=4) n (%)	>=65 years (N=19) n (%)	<65 years (N=12) n (%)	>=65 years (N=29) n (%)	<65 years (N=16) n (%)	>=65 years (N=48) n (%)
Cycle 1 Pre-dose	NAUSEA	NAUSEA WITH LOSS OF APPETITE ONLY	0	1 (5.3)	0	0	0	1 (2.1)
		NO NAUSEA	3 (75.0)	8 (42.1)	5 (41.7)	7 (24.1)	8 (50.0)	15 (31.3)
	VOMITING	NO VOMITING	3 (75.0)	9 (47.4)	5 (41.7)	6 (20.7)	8 (50.0)	15 (31.3)
	DRY MOUTH	DRY OR THICK SALIVA	0	1 (5.3)	1 (8.3)	0	1 (6.3)	1 (2.1)
		NO DRY MOUTH	3 (75.0)	7 (36.8)	4 (33.3)	7 (24.1)	7 (43.8)	14 (29.2)
	TASTE	ALTERED TASTE BUT NO CHANGE IN DIET	0	1 (5.3)	0	1 (3.4)	0	2 (4.2)
		NORMAL TASTE	2 (50.0)	8 (42.1)	5 (41.7)	6 (20.7)	7 (43.8)	14 (29.2)
	FATIGUE	FATIGUE RELIEVED BY REST	0	2 (10.5)	1 (8.3)	3 (10.3)	1 (6.3)	5 (10.4)
		NO FATIGUE	2 (50.0)	7 (36.8)	4 (33.3)	4 (13.8)	6 (37.5)	11 (22.9)
	HEMATOMA	NO HEMATOMA	3 (75.0)	9 (47.4)	5 (41.7)	7 (24.1)	8 (50.0)	16 (33.3)
Cycle 1 Post-dose	FEVER	NO FEVER	3 (75.0)	9 (47.4)	5 (41.7)	7 (24.1)	8 (50.0)	16 (33.3)
	URINARY RETENTION	ABLE TO VOID NORMALLY	3 (75.0)	9 (47.4)	5 (41.7)	7 (24.1)	8 (50.0)	16 (33.3)
	DIARRHEA	NORMAL BOWEL MOVEMENTS	3 (75.0)	8 (42.1)	5 (41.7)	7 (24.1)	8 (50.0)	15 (31.3)
	OTHER	YES	0	3 (15.8)	0	1 (3.4)	0	4 (8.3)
	NAUSEA	NAUSEA WITH EATING/DRINKING LESS THAN USUAL	0	1 (5.3)	0	0	0	1 (2.1)
		NAUSEA WITH LOSS OF APPETITE ONLY	1 (25.0)	6 (31.6)	4 (33.3)	5 (17.2)	5 (31.3)	11 (22.9)

A patient may have multiple answers for a question; these are combined using " | "

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Table 14.3.1.13.2
Specific Adverse Events (AEs) Questionnaire - by Age Category
Safety Population

Visit	Question	Answer	Lu-PSMA-617		Lu-PSMA-617		Overall	
			6.0 GBq <65 years (N=4) n (%)	>=65 years (N=19) n (%)	<65 years (N=12) n (%)	>=65 years (N=29) n (%)	<65 years (N=16) n (%)	>=65 years (N=48) n (%)
Cycle 1 Post-dose	NAUSEA	NO NAUSEA	3 (75.0)	12 (63.2)	6 (50.0)	24 (82.8)	9 (56.3)	36 (75.0)
	VOMITING	1-2 EPISODES PER DAY	2 (50.0)	2 (10.5)	1 (8.3)	0	3 (18.8)	2 (4.2)
		3-5 EPISODES PER DAY	0	0	0	2 (6.9)	0	2 (4.2)
		NO VOMITING	2 (50.0)	17 (89.5)	10 (83.3)	27 (93.1)	12 (75.0)	44 (91.7)
	DRY MOUTH	DRY OR THICK SALIVA	0	4 (21.1)	3 (25.0)	11 (37.9)	3 (18.8)	15 (31.3)
		NO DRY MOUTH	4 (100)	15 (78.9)	7 (58.3)	18 (62.1)	11 (68.8)	33 (68.8)
	TASTE	ALTERED TASTE BUT NO CHANGE IN DIET	0	0	2 (16.7)	4 (13.8)	2 (12.5)	4 (8.3)
		ALTERED TASTE WITH CHANGE IN DIET	0	1 (5.3)	0	0	0	1 (2.1)
		NORMAL TASTE	4 (100)	18 (94.7)	8 (66.7)	25 (86.2)	12 (75.0)	43 (89.6)
	FATIGUE	FATIGUE NOT RELIEVED BY REST, LIMITING WORK	0	3 (15.8)	0	2 (6.9)	0	5 (10.4)
		FATIGUE RELIEVED BY REST	2 (50.0)	6 (31.6)	7 (58.3)	17 (58.6)	9 (56.3)	23 (47.9)
		NO FATIGUE	2 (50.0)	10 (52.6)	4 (33.3)	10 (34.5)	6 (37.5)	20 (41.7)
	HEMATOMA	NO HEMATOMA	4 (100)	17 (89.5)	10 (83.3)	28 (96.6)	14 (87.5)	45 (93.8)
		OCCURRENCE OF HEMATOMA WITHOUT KNOWN EVENT	0	0	0	1 (3.4)	0	1 (2.1)
	FEVER	NO FEVER	4 (100)	18 (94.7)	11 (91.7)	27 (93.1)	15 (93.8)	45 (93.8)
	URINARY RETENTION ABLE TO VOID NORMALLY		3 (75.0)	15 (78.9)	7 (58.3)	26 (89.7)	10 (62.5)	41 (85.4)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.2
Specific Adverse Events (AEs) Questionnaire - by Age Category
Safety Population

Visit	Question	Answer	Lu-PSMA-617		Lu-PSMA-617		Overall	
			6.0 GBq <65 years (N=4) n (%)	>=65 years (N=19) n (%)	7.4 GBq <65 years (N=12) n (%)	>=65 years (N=29) n (%)	<65 years (N=16) n (%)	>=65 years (N=48) n (%)
Cycle 1	URINARY RETENTION Post-dose	ABLE TO VOID WITH SOME PRESSURE	0	1 (5.3)	0	1 (3.4)	0	2 (4.2)
	DIARRHEA	INCREASE BY 4-6 STOOLS PER DAY	0	0	0	2 (6.9)	0	2 (4.2)
		INCREASE BY <4 STOOLS PER DAY	0	1 (5.3)	0	6 (20.7)	0	7 (14.6)
		NORMAL BOWEL MOVEMENTS	4 (100)	16 (84.2)	11 (91.7)	19 (65.5)	15 (93.8)	35 (72.9)
	OTHER	YES	0	9 (47.4)	2 (16.7)	13 (44.8)	2 (12.5)	22 (45.8)
Cycle 2	NAUSEA Pre-dose	NAUSEA WITH LOSS OF APPETITE ONLY	0	0	0	1 (3.4)	0	1 (2.1)
		NO NAUSEA	3 (75.0)	3 (15.8)	3 (25.0)	4 (13.8)	6 (37.5)	7 (14.6)
	VOMITING	NO VOMITING	3 (75.0)	3 (15.8)	3 (25.0)	4 (13.8)	6 (37.5)	7 (14.6)
	DRY MOUTH	DRY OR THICK SALIVA	0	1 (5.3)	1 (8.3)	0	1 (6.3)	1 (2.1)
		NO DRY MOUTH	3 (75.0)	2 (10.5)	2 (16.7)	5 (17.2)	5 (31.3)	7 (14.6)
	TASTE	NORMAL TASTE	3 (75.0)	3 (15.8)	3 (25.0)	5 (17.2)	6 (37.5)	8 (16.7)
	FATIGUE	FATIGUE RELIEVED BY REST	0	1 (5.3)	1 (8.3)	2 (6.9)	1 (6.3)	3 (6.3)
		NO FATIGUE	3 (75.0)	2 (10.5)	2 (16.7)	2 (6.9)	5 (31.3)	4 (8.3)
	HEMATOMA	NO HEMATOMA	3 (75.0)	3 (15.8)	3 (25.0)	5 (17.2)	6 (37.5)	8 (16.7)
	FEVER	NO FEVER	3 (75.0)	3 (15.8)	3 (25.0)	5 (17.2)	6 (37.5)	8 (16.7)
	URINARY RETENTION	ABLE TO VOID NORMALLY	2 (50.0)	3 (15.8)	3 (25.0)	5 (17.2)	5 (31.3)	8 (16.7)

A patient may have multiple answers for a question; these are combined using " | "

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Table 14.3.1.13.2
Specific Adverse Events (AEs) Questionnaire - by Age Category
Safety Population

Visit	Question	Answer	Lu-PSMA-617		Lu-PSMA-617		Overall	
			6.0 GBq <65 years (N=4) n (%)	>=65 years (N=19) n (%)	<65 years (N=12) n (%)	>=65 years (N=29) n (%)	<65 years (N=16) n (%)	>=65 years (N=48) n (%)
Cycle 2 Pre-dose	DIARRHEA	INCREASE BY<4 STOOLS PER DAY	1 (25.0)	0	1 (8.3)	0	2 (12.5)	0
		NORMAL BOWEL MOVEMENTS	2 (50.0)	3 (15.8)	2 (16.7)	5 (17.2)	4 (25.0)	8 (16.7)
Cycle 2 Post-dose	NAUSEA	HAD TO GO TO HOSPITAL FOR NAUSEA	0	0	0	1 (3.4)	0	1 (2.1)
		NAUSEA WITH EATING/DRINKING	0	0	0	1 (3.4)	0	1 (2.1)
	VOMITING	LESS THAN USUAL						
		NAUSEA WITH LOSS OF APPETITE ONLY	2 (50.0)	3 (15.8)	2 (16.7)	5 (17.2)	4 (25.0)	8 (16.7)
	DRY MOUTH	NO NAUSEA	1 (25.0)	9 (47.4)	7 (58.3)	16 (55.2)	8 (50.0)	25 (52.1)
		1-2 EPISODES PER DAY	0	0	1 (8.3)	1 (3.4)	1 (6.3)	1 (2.1)
	TASTE	3-5 EPISODES PER DAY	0	0	0	1 (3.4)	0	1 (2.1)
		MORE THAN 5 EPISODES PER DAY	0	0	0	1 (3.4)	0	1 (2.1)
	FATIGUE	NO VOMITING	3 (75.0)	12 (63.2)	8 (66.7)	19 (65.5)	11 (68.8)	31 (64.6)
		DRY OR THICK SALIVA	1 (25.0)	2 (10.5)	3 (25.0)	11 (37.9)	4 (25.0)	13 (27.1)
	TASTE	NO DRY MOUTH	2 (50.0)	9 (47.4)	6 (50.0)	11 (37.9)	8 (50.0)	20 (41.7)
		NO DRY MOUTH DRY OR THICK SALIVA	0	1 (5.3)	0	0	0	1 (2.1)
	FATIGUE	NORMAL TASTE	3 (75.0)	12 (63.2)	9 (75.0)	22 (75.9)	12 (75.0)	34 (70.8)
		FATIGUE NOT RELIEVED BY REST, LIMITING WORK	0	0	0	1 (3.4)	0	1 (2.1)
	FATIGUE	FATIGUE RELIEVED BY REST	2 (50.0)	6 (31.6)	5 (41.7)	9 (31.0)	7 (43.8)	15 (31.3)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.2
Specific Adverse Events (AEs) Questionnaire - by Age Category
Safety Population

Visit	Question	Answer	Lu-PSMA-617		Lu-PSMA-617		Overall	
			6.0 GBq <65 years (N=4) n (%)	>=65 years (N=19) n (%)	<65 years (N=12) n (%)	>=65 years (N=29) n (%)	<65 years (N=16) n (%)	>=65 years (N=48) n (%)
Cycle 2	FATIGUE Post-dose	FATIGUE RELIEVED BY REST FATIGUE NOT RELIEVED BY REST, LIMITING WORK	0	0	0	1 (3.4)	0	1 (2.1)
		NO FATIGUE	1 (25.0)	6 (31.6)	4 (33.3)	11 (37.9)	5 (31.3)	17 (35.4)
		NO FATIGUE FATIGUE RELIEVED BY REST	0	0	0	1 (3.4)	0	1 (2.1)
	HEMATOMA	NO HEMATOMA OCCURENCE OF HEMATOMA WITHOUT KNOWN EVENT	3 (75.0) 0	12 (63.2) 0	8 (66.7) 0	20 (69.0) 1 (3.4)	11 (68.8) 0	32 (66.7) 1 (2.1)
	FEVER	NO FEVER	3 (75.0)	12 (63.2)	9 (75.0)	22 (75.9)	12 (75.0)	34 (70.8)
	URINARY RETENTION	ABLE TO VOID NORMALLY	3 (75.0)	11 (57.9)	9 (75.0)	20 (69.0)	12 (75.0)	31 (64.6)
	DIARRHEA	INCREASE BY<4 STOOLS PER DAY NORMAL BOWEL MOVEMENTS	1 (25.0) 2 (50.0)	0 12 (63.2)	1 (8.3) 7 (58.3)	1 (3.4) 20 (69.0)	2 (12.5) 9 (56.3)	1 (2.1) 32 (66.7)
	OTHER	NO YES	0 1 (25.0)	0 7 (36.8)	0 3 (25.0)	1 (3.4) 10 (34.5)	0 4 (25.0)	1 (2.1) 17 (35.4)
Cycle 3	NAUSEA Pre-dose	NAUSEA WITH LOSS OF APPETITE ONLY	0	1 (5.3)	0	0	0	1 (2.1)
		NO NAUSEA	1 (25.0)	1 (5.3)	3 (25.0)	2 (6.9)	4 (25.0)	3 (6.3)
	VOMITING	NO VOMITING	1 (25.0)	2 (10.5)	3 (25.0)	2 (6.9)	4 (25.0)	4 (8.3)
	DRY MOUTH	DRY OR THICK SALIVA NO DRY MOUTH	0 1 (25.0)	1 (5.3) 1 (5.3)	0 3 (25.0)	0 2 (6.9)	0 4 (25.0)	1 (2.1) 3 (6.3)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.2
Specific Adverse Events (AEs) Questionnaire - by Age Category
Safety Population

Visit	Question	Answer	Lu-PSMA-617		Lu-PSMA-617		Overall	
			6.0 GBq <65 years (N=4) n (%)	>=65 years (N=19) n (%)	<65 years (N=12) n (%)	>=65 years (N=29) n (%)	<65 years (N=16) n (%)	>=65 years (N=48) n (%)
Cycle 3 Pre-dose	TASTE	NORMAL TASTE	1 (25.0)	2 (10.5)	3 (25.0)	2 (6.9)	4 (25.0)	4 (8.3)
	FATIGUE	FATIGUE NOT RELIEVED BY REST, LIMITING WORK	0	0	1 (8.3)	0	1 (6.3)	0
		FATIGUE RELIEVED BY REST	0	1 (5.3)	0	0	0	1 (2.1)
		NO FATIGUE	1 (25.0)	1 (5.3)	2 (16.7)	2 (6.9)	3 (18.8)	3 (6.3)
	HEMATOMA	NO HEMATOMA	1 (25.0)	2 (10.5)	2 (16.7)	2 (6.9)	3 (18.8)	4 (8.3)
	FEVER	NO FEVER	1 (25.0)	2 (10.5)	3 (25.0)	1 (3.4)	4 (25.0)	3 (6.3)
	URINARY RETENTION	ABLE TO VOID NORMALLY	0	2 (10.5)	2 (16.7)	1 (3.4)	2 (12.5)	3 (6.3)
	DIARRHEA	INCREASE BY<4 STOOLS PER DAY	1 (25.0)	0	0	0	1 (6.3)	0
		NORMAL BOWEL MOVEMENTS	0	2 (10.5)	3 (25.0)	2 (6.9)	3 (18.8)	4 (8.3)
Cycle 3 Post-dose	NAUSEA	NAUSEA WITH LOSS OF APPETITE ONLY	1 (25.0)	1 (5.3)	1 (8.3)	1 (3.4)	2 (12.5)	2 (4.2)
		NO NAUSEA	1 (25.0)	7 (36.8)	2 (16.7)	14 (48.3)	3 (18.8)	21 (43.8)
	VOMITING	1-2 EPISODES PER DAY	0	0	1 (8.3)	0	1 (6.3)	0
		NO VOMITING	2 (50.0)	8 (42.1)	2 (16.7)	15 (51.7)	4 (25.0)	23 (47.9)
	DRY MOUTH	DRY OR THICK SALIVA	1 (25.0)	1 (5.3)	1 (8.3)	6 (20.7)	2 (12.5)	7 (14.6)
		NO DRY MOUTH	1 (25.0)	7 (36.8)	2 (16.7)	9 (31.0)	3 (18.8)	16 (33.3)
	TASTE	ALTERED TASTE BUT NO CHANGE IN DIET	0	0	0	1 (3.4)	0	1 (2.1)

A patient may have multiple answers for a question; these are combined using "|"

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Table 14.3.1.13.2
Specific Adverse Events (AEs) Questionnaire - by Age Category
Safety Population

Visit	Question	Answer	Lu-PSMA-617		Lu-PSMA-617		Overall	
			<65 years (N=4) n (%)	>=65 years (N=19) n (%)	<65 years (N=12) n (%)	>=65 years (N=29) n (%)	<65 years (N=16) n (%)	>=65 years (N=48) n (%)
Cycle 3 Post-dose	TASTE	ALTERED TASTE WITH CHANGE IN DIET	0	1 (5.3)	0	0	0	1 (2.1)
		NORMAL TASTE	2 (50.0)	5 (26.3)	3 (25.0)	13 (44.8)	5 (31.3)	18 (37.5)
	FATIGUE	FATIGUE NOT RELIEVED BY REST, LIMITING WORK	0	2 (10.5)	1 (8.3)	1 (3.4)	1 (6.3)	3 (6.3)
		FATIGUE RELIEVED BY REST	1 (25.0)	3 (15.8)	1 (8.3)	5 (17.2)	2 (12.5)	8 (16.7)
		NO FATIGUE	1 (25.0)	3 (15.8)	1 (8.3)	9 (31.0)	2 (12.5)	12 (25.0)
	HEMATOMA	NO HEMATOMA	2 (50.0)	7 (36.8)	3 (25.0)	15 (51.7)	5 (31.3)	22 (45.8)
	FEVER	NO FEVER	2 (50.0)	7 (36.8)	3 (25.0)	15 (51.7)	5 (31.3)	22 (45.8)
	URINARY RETENTION	ABLE TO VOID NORMALLY	2 (50.0)	7 (36.8)	2 (16.7)	13 (44.8)	4 (25.0)	20 (41.7)
	DIARRHEA	NORMAL BOWEL MOVEMENTS	1 (25.0)	7 (36.8)	3 (25.0)	15 (51.7)	4 (25.0)	22 (45.8)
	OTHER	YES	2 (50.0)	4 (21.1)	1 (8.3)	5 (17.2)	3 (18.8)	9 (18.8)
Cycle 4 Pre-dose	NAUSEA	NAUSEA WITH LOSS OF APPETITE ONLY	0	2 (10.5)	0	0	0	2 (4.2)
		NO NAUSEA	1 (25.0)	0	2 (16.7)	1 (3.4)	3 (18.8)	1 (2.1)
	VOMITING	NO VOMITING	1 (25.0)	2 (10.5)	2 (16.7)	1 (3.4)	3 (18.8)	3 (6.3)
	DRY MOUTH	NO DRY MOUTH	1 (25.0)	2 (10.5)	2 (16.7)	1 (3.4)	3 (18.8)	3 (6.3)
	TASTE	NORMAL TASTE	1 (25.0)	2 (10.5)	2 (16.7)	1 (3.4)	3 (18.8)	3 (6.3)
	FATIGUE	FATIGUE RELIEVED BY REST	0	2 (10.5)	0	0	0	2 (4.2)

A patient may have multiple answers for a question; these are combined using " | "

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Table 14.3.1.13.2
Specific Adverse Events (AEs) Questionnaire - by Age Category
Safety Population

Visit	Question	Answer	Lu-PSMA-617		Lu-PSMA-617		Overall	
			6.0 GBq <65 years (N=4) n (%)	>=65 years (N=19) n (%)	<65 years (N=12) n (%)	>=65 years (N=29) n (%)	<65 years (N=16) n (%)	>=65 years (N=48) n (%)
Cycle 4 Pre-dose	FATIGUE	NO FATIGUE	1 (25.0)	0	2 (16.7)	1 (3.4)	3 (18.8)	1 (2.1)
	HEMATOMA	NO HEMATOMA	1 (25.0)	2 (10.5)	2 (16.7)	1 (3.4)	3 (18.8)	3 (6.3)
	FEVER	NO FEVER	1 (25.0)	2 (10.5)	2 (16.7)	1 (3.4)	3 (18.8)	3 (6.3)
	URINARY RETENTION	ABLE TO VOID NORMALLY	1 (25.0)	2 (10.5)	2 (16.7)	1 (3.4)	3 (18.8)	3 (6.3)
	DIARRHEA	NORMAL BOWEL MOVEMENTS	1 (25.0)	2 (10.5)	2 (16.7)	1 (3.4)	3 (18.8)	3 (6.3)
Cycle 4 Post-dose	NAUSEA	NAUSEA WITH LOSS OF APPETITE ONLY	0	0	1 (8.3)	1 (3.4)	1 (6.3)	1 (2.1)
		NO NAUSEA	1 (25.0)	4 (21.1)	1 (8.3)	8 (31.0)	2 (12.5)	12 (25.0)
	VOMITING	MORE THAN 5 EPISODES PER DAY	0	0	1 (8.3)	0	1 (6.3)	0
		NO VOMITING	1 (25.0)	4 (21.1)	1 (8.3)	9 (31.0)	2 (12.5)	13 (27.1)
	DRY MOUTH	DRY OR THICK SALIVA	0	2 (10.5)	0	5 (17.2)	0	7 (14.6)
		NO DRY MOUTH	1 (25.0)	2 (10.5)	2 (16.7)	4 (13.8)	3 (18.8)	6 (12.5)
	TASTE	ALTERED TASTE BUT NO CHANGE IN DIET	0	1 (5.3)	0	0	0	1 (2.1)
		NORMAL TASTE	1 (25.0)	3 (15.8)	2 (16.7)	9 (31.0)	3 (18.8)	12 (25.0)
	FATIGUE	FATIGUE NOT RELIEVED BY REST, LIMITING WORK	0	0	0	1 (3.4)	0	1 (2.1)
		FATIGUE RELIEVED BY REST	0	3 (15.8)	0	3 (10.3)	0	6 (12.5)
		NO FATIGUE	1 (25.0)	1 (5.3)	2 (16.7)	5 (17.2)	3 (18.8)	6 (12.5)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.1.13.2
Specific Adverse Events (AEs) Questionnaire - by Age Category
Safety Population

Visit	Question	Answer	Lu-PSMA-617		Lu-PSMA-617		Overall	
			6.0 GBq <65 years (N=4) n (%)	>=65 years (N=19) n (%)	<65 years (N=12) n (%)	>=65 years (N=29) n (%)	<65 years (N=16) n (%)	>=65 years (N=48) n (%)
Cycle 4 Post-dose	HEMATOMA	NO HEMATOMA	1 (25.0)	4 (21.1)	2 (16.7)	7 (24.1)	3 (18.8)	11 (22.9)
	FEVER	NO FEVER	1 (25.0)	4 (21.1)	2 (16.7)	9 (31.0)	3 (18.8)	13 (27.1)
	URINARY RETENTION ABLE TO VOID NORMALLY		1 (25.0)	4 (21.1)	2 (16.7)	9 (31.0)	3 (18.8)	13 (27.1)
	DIARRHEA	NORMAL BOWEL MOVEMENTS	1 (25.0)	4 (21.1)	2 (16.7)	8 (27.6)	3 (18.8)	12 (25.0)
	OTHER	YES	0	1 (5.3)	1 (8.3)	3 (10.3)	1 (6.3)	4 (8.3)
Follow-up Month 3	NAUSEA	NO NAUSEA	0	2 (10.5)	1 (8.3)	2 (6.9)	1 (6.3)	4 (8.3)
	VOMITING	NO VOMITING	0	2 (10.5)	1 (8.3)	2 (6.9)	1 (6.3)	4 (8.3)
	DRY MOUTH	DRY OR THICK SALIVA NO DRY MOUTH	0 0	2 (10.5) 0	0 1 (8.3)	2 (6.9) 0	0 1 (6.3)	4 (8.3) 0
	TASTE	NORMAL TASTE	0	2 (10.5)	1 (8.3)	2 (6.9)	1 (6.3)	4 (8.3)
	FATIGUE	FATIGUE RELIEVED BY REST NO FATIGUE	0 0	2 (10.5) 0	0 1 (8.3)	1 (3.4) 1 (3.4)	0 1 (6.3)	3 (6.3) 1 (2.1)
	HEMATOMA	NO HEMATOMA	0	2 (10.5)	1 (8.3)	2 (6.9)	1 (6.3)	4 (8.3)
	FEVER	38.0-39.0C (100.4-102.2F) NO FEVER	0 0	1 (5.3) 1 (5.3)	0 1 (8.3)	0 2 (6.9)	0 1 (6.3)	1 (2.1) 3 (6.3)
	URINARY RETENTION ABLE TO VOID NORMALLY		0	2 (10.5)	1 (8.3)	2 (6.9)	1 (6.3)	4 (8.3)

A patient may have multiple answers for a question; these are combined using " | "

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Table 14.3.1.13.2
Specific Adverse Events (AEs) Questionnaire - by Age Category
Safety Population

Visit	Question	Answer	Lu-PSMA-617		Lu-PSMA-617		Overall	
			6.0 GBq <65 years (N=4) n (%)	>=65 years (N=19) n (%)	<65 years (N=12) n (%)	>=65 years (N=29) n (%)	<65 years (N=16) n (%)	>=65 years (N=48) n (%)
Follow-up Month 3	DIARRHEA	INCREASE BY<4 STOOLS PER DAY	0	0	0	1 (3.4)	0	1 (2.1)
		NORMAL BOWEL MOVEMENTS	0	2 (10.5)	1 (8.3)	1 (3.4)	1 (6.3)	3 (6.3)
	OTHER	YES	0	2 (10.5)	0	2 (6.9)	0	4 (8.3)

A patient may have multiple answers for a question; these are combined using "!"

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)	Baseline	n	21		37		58
		Mean	76.810	83.379			81.000
		SD	24.9111	17.4272			20.4866
		Median	79.000	87.000			86.500
		Q1	60.000	78.000			68.000
		Q3	89.000	94.000			93.000
		Min	35.00	50.00			35.00
		Max	147.00	118.00			147.00
	Week 2	n	14	14	32	32	46
		Mean	76.714	-0.071	84.313	2.750	82.000
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)		SD	17.0313	27.9600	15.4051	10.7366	16.1176
		Median	83.500	5.500	87.000	1.500	86.500
		Q1	66.000	-8.000	77.000	-2.300	72.000
		Q3	89.000	15.000	93.000	10.500	91.000
		Min	42.00	-87.00	54.00	-24.00	42.00
		Max	94.00	32.00	119.00	27.00	119.00
	Week 4	n	15	15	29	29	44
		Mean	74.531	-0.469	84.037	1.864	80.796
		SD	15.2944	27.3960	19.8136	17.3698	18.7768
		Median	73.000	3.000	87.000	2.000	83.000

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)	Week 6	n	16	31	31	47	47
		Mean	73.563	-2.188	83.015	-1.792	79.797
		SD	15.8070	28.9418	18.2305	13.5531	17.8528
		Median	72.000	4.500	88.000	0.000	85.000
		Q1	60.000	-12.500	73.000	-5.000	63.000
		Q3	84.500	14.000	93.000	3.000	92.000
		Min	49.00	-84.00	39.00	-58.00	39.00
		Max	101.00	37.00	119.00	21.00	119.00
		n	12	22	22	34	34
		Mean	82.250	3.750	85.699	0.226	84.482
	Week 8	SD	14.0203	29.2237	23.7791	16.4397	20.6918
		Median	86.000	7.500	88.000	1.500	87.500
		Q1	73.000	0.000	82.000	-2.000	76.000
		Q3	91.500	19.500	100.000	11.000	97.000
		Min	52.00	-80.00	23.00	-56.00	23.00
		Max	101.00	37.00	135.00	24.00	135.00
		n	13	22	22	35	35
		Mean	74.692	-0.462	81.127	-1.919	78.737
		SD	20.2624	27.8227	15.1275	16.1415	17.2104
		Median	84.000	4.000	82.000	-2.500	83.000

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)	Week 12	n	11	11	20	20	31
		Mean	80.091	9.182	89.601	5.850	86.226
		SD	32.3031	24.7217	13.7285	13.1412	22.1040
		Median	89.000	8.000	88.500	1.500	89.000
		Q1	54.000	-15.000	84.000	-2.390	83.000
		Q3	97.000	25.000	95.065	11.000	96.000
		Min	28.00	-32.00	51.00	-14.00	28.00
		Max	144.00	57.00	126.70	43.00	144.00
		n	12	12	20	20	32
		Mean	76.667	2.250	85.716	0.116	82.323
	Week 14	SD	29.8491	33.5183	14.5946	17.2757	21.5989
		Median	70.500	-0.500	87.765	1.000	85.500
		Q1	56.000	-7.500	79.850	-4.000	67.500
		Q3	90.500	19.500	94.000	8.500	94.000
		Min	42.00	-79.00	52.00	-58.00	42.00
		Max	152.00	65.00	115.00	23.00	152.00
		n	11	11	15	15	26
		Mean	79.000	1.000	88.400	0.333	84.423
		SD	21.3260	29.0069	6.5688	13.7486	15.1166
		Median	78.000	6.000	88.000	-2.000	87.000
	Week 16	Q1	67.000	-6.000	83.000	-7.000	79.000
		Q3	97.000	17.000	92.000	4.000	92.000
		Min	45.00	-75.00	79.00	-14.80	45.00
		Max	119.00	32.00	101.00	44.00	119.00
		n	11	11	15	15	26
		Mean	79.000	1.000	88.400	0.333	84.423
		SD	21.3260	29.0069	6.5688	13.7486	15.1166
		Median	78.000	6.000	88.000	-2.000	87.000
		Q1	67.000	-6.000	83.000	-7.000	79.000
		Q3	97.000	17.000	92.000	4.000	92.000
		Min	45.00	-75.00	79.00	-14.80	45.00
		Max	119.00	32.00	101.00	44.00	119.00

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)	Week 18	n	7	7	12	12	19
		Mean	87.714	0.286	83.335	-1.083	84.948
		SD	9.9115	32.2992	10.1099	15.8846	9.9959
		Median	89.000	11.000	84.000	-2.500	84.000
		Q1	76.000	2.000	81.300	-11.000	81.000
		Q3	97.000	17.000	87.210	9.500	92.000
		Min	75.00	-71.00	60.00	-28.41	60.00
		Max	99.00	25.00	102.00	27.00	102.00
		n	7	7	14	14	21
		Mean	89.429	13.000	85.131	5.344	86.563
	Week 20	SD	17.4151	15.6098	12.1993	16.0941	13.8575
		Median	83.000	13.000	88.265	0.500	88.000
		Q1	79.000	-1.000	79.000	-0.300	79.000
		Q3	97.000	25.000	89.300	9.000	92.000
		Min	69.00	-5.00	59.00	-17.41	59.00
		Max	123.00	36.00	111.00	51.00	123.00
		n	7	7	13	13	20
		Mean	89.714	4.286	79.075	0.490	82.799
		SD	25.2502	42.0940	11.3956	11.2522	17.6200
		Median	86.000	20.000	84.000	0.000	84.500
	Week 22	Q1	68.000	-8.000	75.000	-5.030	72.000
		Q3	99.000	27.000	88.000	5.000	88.485
		Min	62.00	-79.00	55.00	-14.60	55.00
		Max	138.00	51.00	89.00	27.00	138.00
		n	7	7	13	13	20
		Mean	89.714	4.286	79.075	0.490	82.799
		SD	25.2502	42.0940	11.3956	11.2522	17.6200
		Median	86.000	20.000	84.000	0.000	84.500
		Q1	68.000	-8.000	75.000	-5.030	72.000

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)	Week 24	n	6	6	8	8	14
		Mean	80.667	-7.333	83.829	-4.746	82.474
		SD	20.9730	39.6619	8.0127	9.8908	14.3662
		Median	74.000	-2.500	84.315	-3.500	82.500
		Q1	64.000	-5.000	78.000	-10.985	73.000
		Q3	91.000	19.000	87.000	2.500	88.000
		Min	64.00	-83.00	73.00	-22.00	64.00
		Max	117.00	30.00	99.00	8.00	117.00
		n	3	3	3	6	6
		Mean	88.333	13.000	77.667	-16.667	83.000
	Week 26	SD	5.6862	13.0000	19.7569	19.2180	14.2548
		Median	90.000	20.000	74.0000	-20.000	86.000
		Q1	82.000	-2.000	60.000	-34.000	74.000
		Q3	93.000	21.000	99.000	4.000	93.000
		Min	82.00	-2.00	60.00	-34.00	60.00
		Max	93.00	21.00	99.00	4.00	99.00
		n	1	1	2	3	3
		Mean	93.000	6.000	75.500	-15.500	81.333
		SD	NE	NE	21.9203	26.1630	18.5023
		Median	93.000	6.000	75.500	-15.500	91.000

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)	Week 30	n	0	1	1	1	1
		Mean		59.900	-34.100	59.900	-34.100
		SD		NE	NE	NE	NE
		Median		59.900	-34.100	59.900	-34.100
		Q1		59.900	-34.100	59.900	-34.100
		Q3		59.900	-34.100	59.900	-34.100
		Min		59.90	-34.10	59.90	-34.10
		Max		59.90	-34.10	59.90	-34.10
	Week 32	n	0	1	1	1	1
		Mean		60.000	-34.000	60.000	-34.000
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)		SD		NE	NE	NE	NE
		Median		60.000	-34.000	60.000	-34.000
		Q1		60.000	-34.000	60.000	-34.000
		Q3		60.000	-34.000	60.000	-34.000
		Min		60.00	-34.00	60.00	-34.00
		Max		60.00	-34.00	60.00	-34.00
	Week 34	n	0	1	1	1	1
		Mean		60.000	-34.000	60.000	-34.000
		SD		NE	NE	NE	NE
		Median		60.000	-34.000	60.000	-34.000

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)	Follow-up Week 2	n 14 Mean 83.357 SD 23.5196 Median 84.500 Q1 78.000 Q3 92.000 Min 40.00 Max 135.00	n 14 Mean 9.429 SD 17.2569 Median 7.000 Q1 -5.000 Q3 20.000 Min -12.00 Max 40.00	n 21 Mean 82.828 SD 22.8994 Median 86.020 Q1 68.000 Q3 99.000 Min 33.00 Max 129.00	n 21 Mean 0.999 SD 17.7133 Median 5.000 Q1 -6.000 Q3 7.000 Min -50.00 Max 44.00	n 35 Mean 83.040 SD 22.8043 Median 85.000 Q1 68.000 Q3 99.000 Min 33.00 Max 135.00	n 35 Mean 4.371 SD 17.7760 Median 5.000 Q1 -6.000 Q3 14.000 Min -50.00 Max 44.00
	Follow-up Week 4	n 11 Mean 88.818 SD 20.1882 Median 87.000 Q1 85.000 Q3 98.000 Min 50.00 Max 128.00	n 11 Mean 12.455 SD 14.6654 Median 9.000 Q1 -1.000 Q3 24.000 Min -9.00 Max 36.00	n 19 Mean 78.105 SD 23.5332 Median 82.000 Q1 57.000 Q3 88.000 Min 44.00 Max 122.00	n 19 Mean -0.947 SD 10.5478 Median 0.000 Q1 -6.000 Q3 7.000 Min -25.00 Max 15.00	n 30 Mean 82.033 SD 22.6242 Median 84.745 Q1 67.000 Q3 91.000 Min 44.00 Max 128.00	n 30 Mean 3.967 SD 13.6516 Median 2.000 Q1 -4.000 Q3 11.000 Min -25.00 Max 36.00
	Follow-up Week 6	n 9 Mean 78.111 SD 19.0882 Median 87.000 Q1 71.000 Q3 93.000 Min 41.00 Max 97.00	n 9 Mean 7.444 SD 14.7403 Median 2.000 Q1 -1.000 Q3 17.000 Min -8.00 Max 37.00	n 15 Mean 88.446 SD 24.0530 Median 84.000 Q1 74.680 Q3 99.000 Min 48.01 Max 148.00	n 15 Mean 4.246 SD 16.7711 Median 7.000 Q1 -8.000 Q3 12.000 Min -20.00 Max 32.00	n 24 Mean 84.570 SD 22.4725 Median 84.000 Q1 72.000 Q3 94.000 Min 41.00 Max 148.00	n 24 Mean 5.445 SD 15.7888 Median 3.000 Q1 -6.500 Q3 14.500 Min -20.00 Max 37.00

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)	Follow-up Week 8	n 6 Mean 61.333 SD 26.1508 Median 65.000 Q1 47.000 Q3 78.000 Min 19.00 Max 94.00	n 6 Mean -8.000 SD 25.8070 Median -3.000 Q1 -29.000 Q3 12.000 Min -47.00 Max 22.00	n 5 Mean 82.330 SD 5.0739 Median 84.000 Q1 79.650 Q3 85.000 Min 75.00 Max 88.00	n 5 Mean -0.870 SD 9.7486 Median 0.000 Q1 -5.000 Q3 3.000 Min -14.35 Max 12.00	n 11 Mean 70.877 SD 21.7363 Median 78.000 Q1 60.000 Q3 85.000 Min 19.00 Max 94.00	n 11 Mean -4.759 SD 19.6183 Median 0.000 Q1 -14.350 Q3 12.000 Min -47.00 Max 22.00
	Follow-up Week 10	n 2 Mean 69.000 SD 18.3848 Median 69.000 Q1 56.000 Q3 82.000 Min 56.00 Max 82.00	n 2 Mean -0.500 SD 17.6777 Median -0.500 Q1 -13.000 Q3 12.000 Min -13.00 Max 12.00	n 9 Mean 82.667 SD 11.8743 Median 82.0000 Q1 78.000 Q3 93.000 Min 60.00 Max 96.00	n 9 Mean 2.778 SD 20.1232 Median 1.000 Q1 -5.000 Q3 16.000 Min -34.00 Max 36.00	n 11 Mean 80.182 SD 13.3103 Median 82.000 Q1 73.000 Q3 93.000 Min 56.00 Max 96.00	n 11 Mean 2.182 SD 18.8935 Median 1.000 Q1 -11.000 Q3 16.000 Min -34.00 Max 36.00
	Follow-up Week 12	n 3 Mean 70.667 SD 11.9304 Median 67.000 Q1 61.000 Q3 84.000 Min 61.00 Max 84.00	n 3 Mean 6.333 SD 20.7926 Median -2.000 Q1 -9.000 Q3 30.000 Min -9.00 Max 30.00	n 1 Mean 65.000 SD NE Median 65.000 Q1 65.000 Q3 65.000 Min 65.00 Max 65.00	n 1 Mean 8.000 SD NE Median 8.000 Q1 8.000 Q3 8.000 Min 8.00 Max 8.00	n 4 Mean 69.250 SD 10.1448 Median 66.000 Q1 63.000 Q3 75.500 Min 61.00 Max 84.00	n 4 Mean 6.750 SD 16.9975 Median 3.000 Q1 -5.500 Q3 19.000 Min -9.00 Max 30.00

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)	Follow-up Month 6	n	1	1	2	2	3
		Mean	81.000	11.000	75.000	-19.500	77.000
		SD	NE	NE	21.2132	20.5061	15.3948
		Median	81.000	11.000	75.000	-19.500	81.000
		Q1	81.000	11.000	60.000	-34.000	60.000
		Q3	81.000	11.000	90.000	-5.000	90.000
		Min	81.00	11.00	60.00	-34.00	60.00
		Max	81.00	11.00	90.00	-5.00	90.00
	Follow-up Month 9	n	1	1	0	0	1
		Mean	67.000	-3.000	NE	NE	67.000
		SD	NE	NE	NE	NE	NE
		Median	67.000	-3.000	NE	NE	67.000
		Q1	67.000	-3.000	NE	NE	67.000
		Q3	67.000	-3.000	NE	NE	67.000
		Min	67.00	-3.00	NE	NE	67.00
		Max	67.00	-3.00	NE	NE	67.00
	Follow-up Month 12	n	1	1	0	0	1
		Mean	82.000	12.000	NE	NE	82.000
		SD	NE	NE	NE	NE	NE
		Median	82.000	12.000	NE	NE	82.000
		Q1	82.000	12.000	NE	NE	82.000
		Q3	82.000	12.000	NE	NE	82.000
		Min	82.00	12.00	NE	NE	82.00
		Max	82.00	12.00	NE	NE	82.00

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value	Change
Glomerular Filtration Rate, Estimated (mL/min/1.73m ²)	Follow-up Month 15	n	1	1	0	0	0	1	1
		Mean	75.000	5.000				75.000	5.000
		SD	NE					NE	NE
		Median	75.000	5.000				75.000	5.000
		Q1	75.000	5.000				75.000	5.000
		Q3	75.000	5.000				75.000	5.000
		Min	75.00	5.00				75.00	5.00
		Max	75.00	5.00				75.00	5.00
	Follow-up Month 18	n	1	1	0	0	0	1	1
		Mean	74.000	4.000				74.000	4.000
Bilirubin (umol/L)	Baseline	n	23		41			64	
		Mean	8.825		8.333			8.510	
		SD	5.6154		3.7306			4.4614	
		Median	6.840		8.210			6.840	
		Q1	5.130		5.130			5.130	
		Q3	8.550		10.260			10.260	
		Min	3.42		1.71			1.71	
		Max	25.65		22.23			25.65	

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Bilirubin (umol/L)	Week 2	n	18	34	34	52	52
		Mean	8.075	-0.541	8.052	0.116	8.060
		SD	4.0553	3.9523	3.4782	3.2130	3.6483
		Median	6.840	0.000	8.550	-1.625	6.840
		Q1	5.130	0.000	5.130	-1.710	5.130
		Q3	8.550	0.000	10.260	1.710	10.260
		Min	3.42	-14.87	3.42	-5.13	3.42
		Max	17.10	5.13	17.10	8.55	17.10
	Week 4	n	16	34	34	50	50
		Mean	7.588	-0.321	8.986	0.949	8.539
		SD	3.5852	2.2702	4.8530	4.1806	4.4978
		Median	6.840	0.000	8.465	0.000	6.840
		Q1	5.130	-1.710	6.840	-1.710	5.130
		Q3	8.550	0.855	10.260	3.420	10.260
		Min	3.42	-5.13	3.42	-4.79	3.42
		Max	18.81	3.42	29.07	15.39	29.07
	Week 6	n	18	32	32	50	50
		Mean	7.118	-1.498	8.098	0.136	7.745
		SD	4.0780	3.8489	3.8385	3.1768	3.9137
		Median	5.985	-1.710	6.840	0.000	6.840
		Q1	5.130	-1.710	5.130	-1.710	5.130
		Q3	8.550	0.000	10.260	1.710	10.260
		Min	3.42	-15.00	2.29	-3.42	2.29
		Max	20.52	3.42	20.52	10.26	20.52

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall		
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change	
Bilirubin (umol/L)	Week 8	n	13	24	24	37	37	
		Mean	8.014	-1.154	8.108	0.000	8.075	-0.405
		SD	3.7279	4.4435	3.9261	3.2540	3.8056	3.6957
		Median	6.840	0.000	6.840	-0.170	6.840	0.000
		Q1	5.130	-1.710	5.130	-1.710	5.130	-1.710
		Q3	10.260	0.000	9.405	2.565	10.260	1.710
		Min	5.00	-15.00	3.42	-6.84	3.42	-15.00
		Max	17.10	3.42	17.10	6.84	17.10	6.84
	Week 10	n	14	24	24	38	38	
		Mean	7.656	-1.224	8.443	-0.093	8.153	-0.509
		SD	3.3292	3.8843	2.9651	5.1796	3.0834	4.7206
		Median	6.840	-1.710	8.125	0.000	7.270	0.000
		Q1	5.130	-1.710	6.840	-1.710	5.130	-1.710
		Q3	10.260	1.710	11.115	1.710	10.260	1.710
		Min	3.42	-12.00	3.42	-17.10	3.42	-17.10
		Max	15.39	5.13	15.39	13.68	15.39	13.68
	Week 12	n	12	20	20	32	32	
		Mean	7.125	-0.998	8.854	0.748	8.205	0.093
		SD	2.9916	2.1206	3.3367	3.4188	3.2745	3.0817
		Median	6.840	0.000	8.550	0.000	6.840	0.000
		Q1	5.130	-2.565	6.840	-1.710	5.130	-1.710
		Q3	7.695	0.000	11.800	2.565	10.815	1.710
		Min	3.42	-5.13	3.42	-5.13	3.42	-5.13
		Max	13.68	1.71	15.39	10.26	15.39	10.26

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Bilirubin (umol/L)	Week 14	n	13	22	22	35	35
		Mean	8.485	-0.551	8.559	0.568	8.531
		SD	6.1498	4.7265	4.2267	4.6738	4.9380
		Median	6.840	0.000	8.550	0.000	6.840
		Q1	5.130	-1.710	6.000	-1.710	5.130
		Q3	8.550	1.710	10.260	0.000	10.260
		Min	1.71	-14.00	3.42	-5.97	1.71
		Max	25.65	6.84	20.52	17.10	25.65
	Week 16	n	12	17	17	29	29
		Mean	8.053	-1.309	7.997	-0.432	8.020
		SD	4.3508	4.6401	4.0598	3.3258	4.1055
		Median	6.840	0.000	6.840	0.000	6.840
		Q1	5.565	-2.565	5.130	-1.710	5.130
		Q3	8.550	1.710	10.260	1.710	10.260
		Min	3.42	-14.00	3.42	-8.55	3.42
		Max	20.52	3.42	17.10	5.13	20.52
	Week 18	n	8	14	14	22	22
		Mean	5.755	-2.089	7.573	-0.098	6.912
		SD	1.5748	5.4079	3.0526	4.3931	2.7196
		Median	5.130	-0.855	7.695	0.000	6.840
		Q1	5.065	-1.710	5.130	-1.710	5.130
		Q3	6.840	0.855	8.550	0.000	8.550
		Min	3.42	-15.00	3.42	-8.55	3.42
		Max	8.55	1.71	13.68	10.26	13.68

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Bilirubin (umol/L)	Week 20	n	8	8	15	15	23
		Mean	7.695	0.000	8.049	0.091	7.926
		SD	4.7495	1.5832	3.4097	3.5389	3.8217
		Median	6.840	0.000	8.550	-0.680	6.840
		Q1	5.130	-0.855	5.130	-1.710	5.130
		Q3	7.695	0.000	10.260	0.000	8.550
		Min	3.42	-1.71	3.42	-4.79	3.42
		Max	18.81	3.42	15.39	8.55	18.81
	Week 22	n	8	8	15	15	23
		Mean	7.590	-1.750	9.143	1.277	8.603
		SD	3.0795	5.7319	3.9005	5.6470	3.6429
		Median	6.420	0.000	8.550	0.000	8.550
		Q1	5.130	-3.420	6.840	-1.710	5.130
		Q3	9.405	0.855	10.260	1.710	10.260
		Min	5.13	-14.00	5.13	-6.84	5.13
		Max	13.68	5.13	20.52	18.81	20.52
	Week 24	n	8	8	8	8	16
		Mean	5.130	-2.714	7.888	0.620	6.509
		SD	1.8281	5.7396	3.1537	3.5258	2.8685
		Median	5.130	0.000	6.840	0.770	6.840
		Q1	3.420	-2.565	6.840	-2.565	5.130
		Q3	5.985	0.000	7.610	2.565	6.840
		Min	3.42	-16.58	5.13	-3.42	3.42
		Max	8.55	0.00	15.39	6.84	15.39

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Bilirubin (umol/L)	Week 26	n	3	3	3	6	6
		Mean	13.110	1.710	6.270	-0.570	9.690
		SD	8.0811	2.9618	0.9873	0.9873	6.3677
		Median	10.260	3.420	6.840	0.000	6.840
		Q1	6.840	-1.710	5.130	-1.710	6.840
		Q3	22.230	3.420	6.840	0.000	10.260
		Min	6.84	-1.71	5.13	-1.71	5.13
		Max	22.23	3.42	6.84	0.00	22.23
	Week 28	n	1	1	2	3	3
		Mean	6.840	-1.710	5.985	-1.710	6.270
		SD	NE	NE	1.2092	2.4183	0.9873
		Median	6.840	-1.710	5.985	-1.710	6.840
		Q1	6.840	-1.710	5.130	-3.420	5.130
		Q3	6.840	-1.710	6.840	0.000	6.840
		Min	6.84	-1.71	5.13	-3.42	5.13
		Max	6.84	-1.71	6.84	0.00	6.84
	Week 30	n	0	0	1	1	1
		Mean	NE	NE	3.420	-1.710	3.420
		SD	NE	NE	NE	NE	NE
		Median	3.420	-1.710	3.420	-1.710	3.420
		Q1	3.420	-1.710	3.420	-1.710	3.420
		Q3	3.420	-1.710	3.420	-1.710	3.420
		Min	3.42	-1.71	3.42	-1.71	3.42
		Max	3.42	-1.71	3.42	-1.71	3.42

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Bilirubin (umol/L)	Week 32	n	0	1	1	1	1
		Mean		3.420	-1.710	3.420	-1.710
		SD		NE	NE	NE	NE
		Median		3.420	-1.710	3.420	-1.710
		Q1		3.420	-1.710	3.420	-1.710
		Q3		3.420	-1.710	3.420	-1.710
		Min		3.42	-1.71	3.42	-1.71
		Max		3.42	-1.71	3.42	-1.71
	Week 34	n	0	1	1	1	1
		Mean		3.420	-1.710	3.420	-1.710
		SD		NE	NE	NE	NE
		Median		3.420	-1.710	3.420	-1.710
		Q1		3.420	-1.710	3.420	-1.710
		Q3		3.420	-1.710	3.420	-1.710
		Min		3.42	-1.71	3.42	-1.71
		Max		3.42	-1.71	3.42	-1.71
Follow-up	n	17	17	22	22	39	39
Week 2	Mean	8.248	-0.604	7.715	-0.508	7.948	-0.550
	SD	4.0662	3.7240	3.6826	4.7786	3.8115	4.2966
	Median	8.550	0.000	6.840	0.000	8.550	0.000
	Q1	5.130	-1.710	5.130	-1.710	5.130	-1.710
	Q3	8.550	1.710	8.550	1.710	8.550	1.710
	Min	3.42	-11.97	3.42	-17.10	3.42	-17.10
	Max	18.81	5.13	18.81	8.55	18.81	8.55

Output ID: t-lb-chemchg-saf 04JUN20 13:03

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value
Bilirubin (umol/L)	Follow-up Week 4	n	11	11	21	21	32	32	32
		Mean	10.726	1.088	7.964	-0.586	8.913	-0.011	
		SD	7.1367	2.0623	3.9175	4.5011	5.3017	3.8853	
		Median	8.550	1.710	6.840	-1.710	7.695	0.000	
		Q1	5.130	0.000	5.130	-1.710	5.130	-1.710	
		Q3	15.390	3.420	10.260	1.710	11.115	1.710	
		Min	3.42	-3.42	1.71	-15.39	1.71	-15.39	
		Max	25.65	3.42	17.10	6.84	25.65	6.84	
	Follow-up Week 6	n	10	10	16	16	26	26	26
		Mean	10.089	1.197	8.361	0.666	9.026	0.870	
Bilirubin (umol/L)		SD	8.9564	3.0215	4.6275	5.9196	6.5163	4.9377	
		Median	5.985	0.000	7.180	-0.140	6.840	0.000	
		Q1	3.420	-1.710	5.130	-2.565	5.130	-1.710	
		Q3	15.390	3.420	9.405	2.050	10.260	3.420	
		Min	3.42	-1.71	3.42	-8.55	3.42	-8.55	
		Max	27.36	6.84	20.52	15.39	27.36	15.39	
	Follow-up Week 8	n	6	6	9	9	15	15	15
		Mean	10.830	2.850	10.446	1.326	10.599	1.935	
		SD	9.8924	11.3772	5.1479	4.7858	7.0803	7.7404	
		Median	5.985	-1.710	10.260	-1.710	8.550	-1.710	

Output ID: t-lb-chemchg-saf 04JUN20 13:03

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Bilirubin (umol/L)	Follow-up Week 10	n	3	n	9	n	12
	Mean	11.400	1.710	9.120	0.950	9.690	1.140
	SD	7.8982	0.0000	2.4183	4.1103	4.0815	3.5221
	Median	6.840	1.710	8.550	0.000	8.550	0.855
	Q1	6.840	1.710	8.550	-1.710	6.840	-1.710
	Q3	20.520	1.710	10.260	1.710	10.260	1.710
	Min	6.84	1.71	5.13	-3.42	5.13	-3.42
	Max	20.52	1.71	13.68	8.55	20.52	8.55
	Follow-up Week 12	n	4	n	2	n	6
	Mean	14.108	4.703	7.270	-3.845	11.828	1.853
	SD	8.5357	6.1457	4.2285	5.4377	7.7304	6.9324
	Median	14.535	2.565	7.270	-3.845	9.405	0.855
	Q1	6.840	0.855	4.280	-7.690	5.130	0.000
	Q3	21.375	8.550	10.260	0.000	20.520	3.420
	Min	5.13	0.00	4.28	-7.69	4.28	-7.69
	Max	22.23	13.68	10.26	0.00	22.23	13.68
	Follow-up Month 6	n	3	n	3	n	6
	Mean	9.120	-1.710	9.690	1.710	9.405	0.000
	SD	5.4969	1.7100	4.9363	5.9236	4.6830	4.3260
	Median	6.840	-1.710	6.840	-1.710	6.840	-1.710
	Q1	5.130	-3.420	6.840	-1.710	6.840	-1.710
	Q3	15.390	0.000	15.390	8.550	15.390	0.000
	Min	5.13	-3.42	6.84	-1.71	5.13	-3.42
	Max	15.39	0.00	15.39	8.55	15.39	8.55

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Bilirubin (umol/L)	Follow-up Month 9	n	2	n	1	n	3
	Mean	13.680	0.855	8.550	-1.710	11.970	0.000
	SD	4.8366	3.6275	NE	NE	4.5242	2.9618
	Median	13.680	0.855	8.550	-1.710	10.260	-1.710
	Q1	10.260	-1.710	8.550	-1.710	8.550	-1.710
	Q3	17.100	3.420	8.550	-1.710	17.100	3.420
	Min	10.26	-1.71	8.55	-1.71	8.55	-1.71
	Max	17.10	3.42	8.55	-1.71	17.10	3.42
	Follow-up Month 12	n	1	n	1	n	2
	Mean	18.810	0.000	6.840	0.000	12.825	0.000
	SD	NE	NE	NE	NE	8.4641	0.0000
	Median	18.810	0.000	6.840	0.000	12.825	0.000
	Q1	18.810	0.000	6.840	0.000	6.840	0.000
	Q3	18.810	0.000	6.840	0.000	18.810	0.000
	Min	18.81	0.00	6.84	0.00	6.84	0.00
	Max	18.81	0.00	6.84	0.00	18.81	0.00
	Follow-up Month 15	n	2	n	0	n	2
	Mean	10.260	-2.565	0	0	10.260	-2.565
	SD	4.8366	3.6275	0	0	4.8366	3.6275
	Median	10.260	-2.565	0	0	10.260	-2.565
	Q1	6.840	-5.130	0	0	6.840	-5.130
	Q3	13.680	0.000	0	0	13.680	0.000
	Min	6.84	-5.13	0	0	6.84	-5.13
	Max	13.68	0.00	0	0	13.68	0.00

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value	Change
Bilirubin (umol/L)	Follow-up Month 18	n	1	1	0	0	0	1	1
		Mean	18.810	0.000	NE	NE	NE	18.810	0.000
		SD	NE	NE	NE	NE	NE	NE	NE
		Median	18.810	0.000	18.6199	18.810	0.000	18.810	0.000
		Q1	18.810	0.000	18.6199	18.810	0.000	18.810	0.000
		Q3	18.810	0.000	18.6199	18.810	0.000	18.810	0.000
		Min	18.81	0.00	18.6199	18.81	0.00	18.81	0.00
Creatinine (umol/L)	Baseline	n	23	41	64	85.285	21.4111	85.285	21.4111
		Mean	91.454	81.824	81.824	80.000	71.600	71.600	95.475
		SD	24.9063	18.6199	24.9063	50.39	50.39	50.39	50.39
		Median	83.100	78.680	78.680	123.76	144.09	123.76	144.09
		Q1	75.140	67.180	67.180	144.09	144.09	67.180	144.09
		Q3	116.690	88.400	88.400	144.09	144.09	88.400	144.09
		Min	53.04	50.39	50.39	144.09	144.09	50.39	144.09
Week 2		Max	144.09	123.76	123.76	144.09	144.09	123.76	144.09
		n	18	36	54	54	54	54	54
		Mean	90.167	-4.689	76.589	-6.090	81.115	-5.623	81.115
		SD	20.2221	15.5465	14.6534	8.7628	17.7400	11.3436	17.7400
		Median	84.860	-6.185	76.025	-4.865	79.560	-5.305	79.560
		Q1	78.680	-15.030	68.065	-11.490	69.840	-14.150	69.840
		Q3	96.360	7.070	83.980	0.000	88.400	2.650	88.400
Output ID: t-lb-chemchg-saf 04JUN20 13:03 \AAA.LOCAL\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\RESIST\FINAL ANALYSIS\PRODUCTION\TLF\PGM\t-lbchg.sas	Min	64.53	-38.01	53.04	-26.52	53.04	-38.01	53.04	-38.01
	Max	135.25	17.28	107.85	8.84	135.25	17.28	135.25	17.28

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Creatinine (umol/L)	Week 4	n	17	36	36	53	53
		Mean	89.464	-6.552	78.686	-2.668	-3.913
		SD	13.3117	19.5395	20.4422	12.5685	15.0714
		Median	88.400	-7.070	76.465	-2.655	-4.420
		Q1	77.790	-17.680	63.650	-11.045	-12.370
		Q3	98.120	6.190	88.845	3.095	3.540
		Min	70.72	-44.20	45.97	-26.52	-44.20
		Max	114.04	29.17	132.60	30.05	30.05
	Week 6	n	18	34	34	52	52
		Mean	88.785	-6.071	78.818	-1.133	-2.842
		SD	18.0218	20.0188	22.4941	14.6064	16.6511
		Median	85.305	-7.960	76.465	-1.765	-2.215
		Q1	71.600	-17.680	65.420	-8.840	-10.610
		Q3	102.540	7.070	83.100	5.310	5.750
		Min	61.88	-48.62	46.85	-35.36	-48.62
		Max	124.64	26.00	159.12	38.01	38.01
	Week 8	n	14	25	25	39	39
		Mean	84.183	-9.929	83.800	2.507	-1.957
		SD	15.3705	18.7935	41.5886	36.5470	31.6377
		Median	81.770	-8.840	73.370	-4.420	-4.420
		Q1	69.840	-25.630	68.070	-8.840	-13.260
		Q3	93.000	1.770	83.100	0.880	1.770
		Min	68.07	-47.74	48.62	-30.94	-47.74
		Max	118.46	21.00	256.36	167.96	167.96

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Creatinine (umol/L)	Week 10	n	14	24	24	38	38
		Mean	93.316	-2.626	77.277	-4.973	83.186
		SD	27.3122	19.1008	16.8336	14.9833	22.3545
		Median	83.980	-3.530	77.790	-3.540	80.000
		Q1	74.260	-15.030	63.650	-12.370	68.950
		Q3	98.000	6.180	87.960	7.075	92.820
		Min	64.53	-34.48	49.50	-44.20	49.50
		Max	160.00	37.12	112.27	18.56	160.00
	Week 12	n	12	21	21	33	33
		Mean	96.209	0.589	76.858	-5.313	83.895
		SD	42.1726	31.5015	12.7604	12.7132	28.3285
		Median	85.750	-4.860	72.490	-1.770	78.680
		Q1	72.045	-25.635	67.180	-7.070	68.070
		Q3	105.195	14.145	83.100	0.880	86.630
		Min	49.50	-28.29	61.88	-44.20	49.50
		Max	206.86	83.98	119.34	15.74	206.86
	Week 14	n	13	22	22	35	35
		Mean	92.554	-4.989	76.594	-4.414	82.522
		SD	25.0463	17.7268	15.0501	12.5668	20.5554
		Median	87.520	0.000	75.140	-3.455	79.560
		Q1	79.560	-19.450	67.180	-11.490	69.840
		Q3	100.780	5.300	83.100	5.300	88.400
		Min	55.69	-33.59	53.04	-35.36	53.04
		Max	147.63	24.75	123.76	17.68	147.63

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Creatinine (umol/L)	Week 16	n	12	17	17	29	29
		Mean	89.461	-4.277	76.908	0.728	82.102
		SD	22.0679	16.9206	9.4593	17.3595	16.7940
		Median	85.050	-2.210	77.790	1.770	81.330
		Q1	74.695	-20.775	73.370	-4.420	73.370
		Q3	97.240	11.035	82.210	7.070	84.860
		Min	58.34	-28.29	58.34	-53.04	58.34
		Max	137.90	16.79	95.47	28.29	137.90
	Week 18	n	8	14	14	22	22
		Mean	77.338	-7.576	77.981	-1.896	77.747
		SD	11.8708	14.4406	12.6555	18.2374	12.0922
		Median	80.395	-5.745	75.140	-0.440	76.905
		Q1	70.720	-19.005	70.720	-16.800	70.720
		Q3	86.190	4.415	85.750	14.140	85.750
		Min	54.81	-30.94	53.92	-35.36	53.92
		Max	89.28	11.00	106.96	27.40	106.96
	Week 20	n	8	15	15	23	23
		Mean	82.875	-3.426	78.617	-6.483	80.098
		SD	17.6392	18.4541	11.8857	13.4458	13.8995
		Median	83.095	-0.890	79.560	-3.540	80.440
		Q1	71.605	-16.350	72.490	-15.910	72.490
		Q3	91.050	2.655	82.210	0.000	88.400
		Min	56.58	-30.06	56.58	-35.36	56.58
		Max	114.92	31.82	105.20	13.26	114.92

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Creatinine (umol/L)	Week 22	n	8	8	15	15	23
		Mean	81.873	-4.036	82.978	-2.712	82.593
		SD	17.4603	19.6756	11.9669	13.7782	13.7267
		Median	84.420	1.325	80.440	-1.770	81.330
		Q1	71.160	-22.100	72.490	-9.730	72.490
		Q3	95.005	11.930	89.280	3.530	91.000
		Min	51.27	-33.60	66.30	-35.36	51.27
		Max	102.54	19.00	111.38	24.75	111.38
	Week 24	n	8	8	8	16	16
		Mean	96.468	2.935	76.908	3.203	86.688
		SD	25.3160	15.3347	11.9537	9.7074	21.6285
		Median	97.240	3.095	79.560	0.440	83.095
		Q1	80.885	-7.070	67.625	-4.865	74.695
		Q3	105.200	12.820	86.190	13.260	97.240
		Min	59.23	-18.57	57.46	-7.96	57.46
		Max	145.86	24.36	91.05	15.91	145.86
	Week 26	n	3	3	3	6	6
		Mean	79.267	-5.600	68.360	0.290	73.813
		SD	5.3243	14.3171	19.9698	22.2288	14.3716
		Median	78.680	1.760	66.300	-8.840	76.470
		Q1	74.260	-22.100	49.500	-15.920	66.300
		Q3	84.860	3.540	89.280	25.630	84.860
		Min	74.26	-22.10	49.50	-15.92	49.50
		Max	84.86	3.54	89.28	25.63	89.28

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Creatinine (umol/L)	Week 28	n	1	2	2	3	3
		Mean	63.650	11.490	61.880	-7.515	62.470
		SD	NE	NE	6.2508	0.6293	4.5366
		Median	63.650	-11.490	61.880	-7.515	63.650
		Q1	63.650	-11.490	57.460	-7.960	57.460
		Q3	63.650	-11.490	66.300	-7.070	66.300
		Min	63.65	-11.49	57.46	-7.96	57.46
		Max	63.65	-11.49	66.30	-7.07	66.30
	Week 30	n	0	0	1	1	1
		Mean	NE	NE	59.230	-6.190	59.230
		SD	NE	NE	NE	NE	NE
		Median	59.230	59.230	59.230	-6.190	59.230
		Q1	59.230	59.230	59.230	-6.190	59.230
		Q3	59.230	59.230	59.230	-6.190	59.230
		Min	59.23	59.23	59.23	-6.19	59.23
		Max	59.23	59.23	59.23	-6.19	59.23
	Week 32	n	0	0	1	1	1
		Mean	NE	NE	54.810	-10.610	54.810
		SD	NE	NE	NE	NE	NE
		Median	54.810	54.810	54.810	-10.610	54.810
		Q1	54.810	54.810	54.810	-10.610	54.810
		Q3	54.810	54.810	54.810	-10.610	54.810
		Min	54.81	54.81	54.81	-10.61	54.81
		Max	54.81	54.81	54.81	-10.61	54.81

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall				
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value	Change
Creatinine (umol/L)	Week 34	n	0	0	1	1	1	1	1	1
		Mean			54.810	-10.610	54.810	-10.610	NE	NE
		SD			NE	NE	NE	NE	NE	NE
		Median			54.810	-10.610	54.810	-10.610	54.810	-10.610
		Q1			54.810	-10.610	54.810	-10.610	54.810	-10.610
		Q3			54.810	-10.610	54.810	-10.610	54.810	-10.610
		Min			54.81	-10.61	54.81	-10.61	54.81	-10.61
		Max			54.81	-10.61	54.81	-10.61	54.81	-10.61
Follow-up	Week 2	n	17	17	24	24	41	41	41	41
		Mean	85.175	-4.839	82.135	-1.846	83.395	-3.087	82.135	-1.846
		SD	25.0869	20.1549	28.5534	19.2083	26.8856	19.4131	28.5534	19.2083
		Median	78.680	-2.650	76.905	-4.860	77.790	-4.420	76.905	-4.860
		Q1	68.950	-10.610	65.415	-9.280	68.950	-9.720	65.415	-9.280
		Q3	83.980	3.530	91.935	1.320	90.170	1.760	91.935	1.320
		Min	53.92	-50.39	38.90	-53.04	38.90	-53.04	38.90	-53.04
		Max	137.90	40.66	183.87	62.76	183.87	62.76	183.87	62.76
Follow-up	Week 4	n	12	12	21	21	33	33	33	33
		Mean	79.119	-7.588	87.674	1.757	84.563	-1.641	87.674	1.757
		SD	19.7763	16.7289	27.6573	13.3512	25.0995	15.1144	27.6573	13.3512
		Median	75.585	-3.980	80.440	0.000	79.560	-1.770	80.440	0.000
		Q1	68.950	-14.140	72.490	-5.300	70.720	-7.960	72.490	-5.300
		Q3	83.100	2.655	106.080	4.420	95.470	4.420	106.080	4.420
		Min	56.58	-45.97	41.55	-17.68	41.55	-45.97	41.55	-17.68
		Max	129.95	15.91	152.05	45.97	152.05	45.97	152.05	45.97

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Creatinine (umol/L)	Follow-up Week 6	n	10	16	16	26	26
	Mean	89.460	-1.682	76.626	-2.328	81.562	-2.080
	SD	25.1505	21.5418	21.6091	16.0360	23.4187	17.9291
	Median	82.215	5.300	73.815	-3.095	74.700	0.385
	Q1	70.720	-12.380	61.880	-13.260	66.300	-12.380
	Q3	106.080	10.610	88.400	5.305	93.700	7.950
	Min	64.53	-48.62	39.78	-35.36	39.78	-48.62
	Max	142.32	22.98	121.00	24.75	142.32	24.75
	Follow-up Week 8	n	6	9	9	15	15
	Mean	119.782	26.077	79.759	-2.356	95.768	9.017
	SD	81.0981	76.5635	19.8112	12.2880	54.6358	48.8642
	Median	82.210	3.090	72.490	-0.880	82.210	-0.880
	Q1	79.560	-21.210	70.720	-6.190	70.720	-16.800
	Q3	122.880	18.560	88.400	3.540	90.170	7.070
	Min	70.72	-25.64	52.16	-21.21	52.16	-25.64
	Max	281.11	178.57	122.00	20.33	281.11	178.57
	Follow-up Week 10	n	3	9	9	12	12
	Mean	103.130	16.200	76.517	-5.893	83.170	-0.370
	SD	10.6925	7.9714	10.0798	16.0283	15.4775	17.2695
	Median	106.960	16.790	74.260	-5.300	82.655	4.415
	Q1	91.050	7.950	68.070	-8.840	70.280	-7.515
	Q3	111.380	23.860	86.630	8.840	90.610	9.725
	Min	91.05	7.95	61.88	-35.36	61.88	-35.36
	Max	111.38	23.86	90.17	10.61	111.38	23.86

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Creatinine (umol/L)	Follow-up Week 12	n	4	n	2	n	6
	Mean	95.030	0.660	101.660	2.650	97.240	1.323
	SD	20.6508	31.5236	6.2508	41.2526	16.5955	30.6212
	Median	88.400	-0.885	101.660	2.650	96.800	-0.885
	Q1	80.000	-19.895	97.240	-26.520	80.440	-26.520
	Q3	110.060	21.215	106.080	31.820	106.080	31.820
	Min	79.56	-36.25	97.24	-26.52	79.56	-36.25
	Max	123.76	40.66	106.08	31.82	123.76	40.66
	Follow-up Month 6	n	3	n	3	n	6
	Mean	94.293	-6.483	74.257	-1.180	84.275	-3.832
	SD	21.6955	16.4253	8.7086	4.3615	18.4134	11.1339
	Median	82.210	-1.770	76.910	0.880	81.330	-0.445
	Q1	81.330	-24.750	64.530	-6.190	76.910	-6.190
	Q3	119.340	7.070	81.330	1.770	82.210	1.770
	Min	81.33	-24.75	64.53	-6.19	64.53	-24.75
	Max	119.34	7.07	81.33	1.77	119.34	7.07
	Follow-up Month 9	n	2	n	1	n	3
	Mean	88.400	9.280	79.560	15.910	85.453	11.490
	SD	8.7540	3.1254	NE	NE	8.0228	4.4200
	Median	88.400	9.280	79.560	15.910	82.210	11.490
	Q1	82.210	7.070	79.560	15.910	79.560	7.070
	Q3	94.590	11.490	79.560	15.910	94.590	15.910
	Min	82.21	7.07	79.56	15.91	79.56	7.07
	Max	94.59	11.49	79.56	15.91	94.59	15.91

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Creatinine (umol/L)	Follow-up Month 12	n	1	n	1	n	2
	Mean	80.440	-2.660	60.110	-11.490	70.275	-7.075
	SD	NE	NE	NE	NE	14.3755	6.2438
	Median	80.440	-2.660	60.110	-11.490	70.275	-7.075
	Q1	80.440	-2.660	60.110	-11.490	60.110	-11.490
	Q3	80.440	-2.660	60.110	-11.490	80.440	-2.660
	Min	80.44	-2.66	60.11	-11.49	60.11	-11.49
	Max	80.44	-2.66	60.11	-11.49	80.44	-2.66
	Follow-up Month 15	n	2	n	0	n	2
	Mean	80.445	1.325	80.445	1.325	80.445	1.325
	SD	8.7469	3.1183	8.7469	3.1183	8.7469	3.1183
	Median	80.445	1.325	80.445	1.325	80.445	1.325
	Q1	74.260	-0.880	74.260	-0.880	74.260	-0.880
	Q3	86.630	3.530	86.630	3.530	86.630	3.530
	Min	74.26	-0.88	74.26	-0.88	74.26	-0.88
	Max	86.63	3.53	86.63	3.53	86.63	3.53
	Follow-up Month 18	n	1	n	0	n	1
	Mean	87.520	4.420	87.520	4.420	87.520	4.420
	SD	NE	NE	NE	NE	NE	NE
	Median	87.520	4.420	87.520	4.420	87.520	4.420
	Q1	87.520	4.420	87.520	4.420	87.520	4.420
	Q3	87.520	4.420	87.520	4.420	87.520	4.420
	Min	87.52	4.42	87.52	4.42	87.52	4.42
	Max	87.52	4.42	87.52	4.42	87.52	4.42

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value	Change
Sodium (mmol/L)	Baseline	n	23		41			64	
		Mean	138.78		138.83			138.81	
		SD	4.210		3.185			3.554	
		Median	140.00		139.00			140.00	
		Q1	137.00		136.00			137.00	
		Q3	141.00		141.00			141.00	
		Min	126.0		132.0			126.0	
		Max	145.0		146.0			146.0	
	Week 2	n	17	17	36	36	53	53	
		Mean	139.12	0.12	139.00	-0.28	139.04	-0.15	
		SD	3.967	3.180	3.103	2.062	3.365	2.451	
		Median	139.00	-1.00	139.00	0.00	139.00	0.00	
		Q1	138.00	-2.00	137.50	-1.00	138.00	-2.00	
		Q3	141.00	2.00	141.00	1.00	141.00	1.00	
		Min	130.0	-5.0	132.0	-5.0	130.0	-5.0	
		Max	146.0	8.0	145.0	3.0	146.0	8.0	
	Week 4	n	17	17	36	36	53	53	
		Mean	139.41	0.41	139.17	0.14	139.25	0.23	
		SD	2.830	3.083	2.923	3.035	2.868	3.023	
		Median	140.00	0.00	139.00	0.50	139.00	0.00	
		Q1	138.00	-2.00	138.00	-1.50	138.00	-2.00	
		Q3	141.00	3.00	141.00	2.00	141.00	2.00	
		Min	132.0	-5.0	131.0	-9.0	131.0	-9.0	
		Max	144.0	6.0	145.0	5.0	145.0	6.0	

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Sodium (mmol/L)	Week 6	n	18	34	34	52	52
		Mean	140.28	139.21	0.38	139.58	0.63
		SD	2.986	2.694	2.283	2.817	2.385
		Median	141.00	139.50	0.50	140.00	1.00
		Q1	139.00	137.00	-2.00	138.00	-1.00
		Q3	142.00	141.00	2.00	141.00	2.00
		Min	132.0	133.0	-4.0	132.0	-4.0
		Max	144.0	145.0	4.0	145.0	6.0
	Week 8	n	14	26	26	40	40
		Mean	138.57	138.85	-0.19	138.75	-0.30
		SD	5.598	3.120	2.173	4.087	2.574
		Median	139.00	139.00	0.00	139.00	0.00
		Q1	138.00	138.00	-1.00	138.00	-1.50
		Q3	141.00	141.00	1.00	141.00	1.00
		Min	121.0	132.0	-6.0	121.0	-6.0
		Max	144.0	146.0	6.0	146.0	7.0
	Week 10	n	14	23	23	37	37
		Mean	140.07	138.39	0.13	139.03	0.00
		SD	2.759	3.448	2.849	3.270	2.698
		Median	139.50	140.00	0.00	140.00	0.00
		Q1	138.00	137.00	-1.00	138.00	-1.00
		Q3	142.00	140.00	2.00	141.00	1.00
		Min	137.0	129.0	-6.0	129.0	-6.0
		Max	145.0	144.0	6.0	145.0	6.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Sodium (mmol/L)	Week 12	n	12	20	20	32	32
		Mean	140.17	-0.08	139.95	1.00	140.03
		SD	2.209	2.193	2.781	2.026	2.546
		Median	140.00	0.00	141.00	1.00	141.00
		Q1	138.00	-2.00	138.50	0.00	138.00
		Q3	142.00	1.50	142.00	2.00	142.00
		Min	137.0	-3.0	134.0	-4.0	134.0
		Max	143.0	4.0	143.0	5.0	143.0
	Week 14	n	13	22	22	35	35
		Mean	140.38	-0.08	139.68	0.68	139.94
		SD	3.097	3.904	2.644	2.147	2.796
		Median	141.00	-1.00	140.00	1.00	141.00
		Q1	138.00	-3.00	139.00	0.00	138.00
		Q3	141.00	3.00	141.00	2.00	141.00
		Min	135.0	-6.0	133.0	-6.0	133.0
		Max	147.0	6.0	143.0	4.0	147.0
	Week 16	n	12	17	17	29	29
		Mean	138.92	-1.58	139.41	0.24	139.21
		SD	2.234	3.175	3.589	2.463	3.063
		Median	139.50	-1.00	139.00	0.00	139.00
		Q1	137.00	-4.00	138.00	-1.00	137.00
		Q3	140.50	0.50	142.00	2.00	142.00
		Min	136.0	-8.0	131.0	-5.0	131.0
		Max	142.0	3.0	145.0	4.0	145.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Sodium (mmol/L)	Week 18	n	8	14	14	22	22
		Mean	138.88	-0.75	138.57	0.57	138.68
		SD	2.031	2.915	3.155	2.344	2.750
		Median	139.00	-1.00	139.00	0.50	139.00
		Q1	138.00	-3.00	137.00	0.00	138.00
		Q3	140.00	0.50	142.00	2.00	140.00
		Min	135.0	-4.0	131.0	-4.0	131.0
		Max	142.0	5.0	142.0	4.0	142.0
	Week 20	n	8	15	15	23	23
		Mean	140.88	0.75	138.33	-0.73	139.22
		SD	1.126	2.493	3.498	2.658	3.118
		Median	141.00	0.50	138.00	-1.00	140.00
		Q1	140.00	-1.50	137.00	-3.00	138.00
		Q3	142.00	2.50	141.00	1.00	142.00
		Min	139.0	-2.0	130.0	-5.0	130.0
		Max	142.0	5.0	143.0	4.0	143.0
	Week 22	n	8	14	14	22	22
		Mean	140.38	0.00	139.57	0.93	139.86
		SD	4.502	3.891	3.502	3.385	3.808
		Median	143.00	0.00	139.50	2.00	141.00
		Q1	135.50	-4.00	136.00	-1.00	136.00
		Q3	144.00	3.00	143.00	3.00	143.00
		Min	134.0	-4.0	134.0	-6.0	134.0
		Max	144.0	6.0	145.0	5.0	145.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Sodium (mmol/L)	Week 24	n	8	n	8	Value	16
		Mean	139.63	Value	138.75	Change	16
		SD	1.923	Change	-0.88	Value	-0.25
		Median	139.50	Value	2.605	2.504	2.490
		Q1	138.00	Value	-1.00	1.00	-0.50
		Q3	141.50	Value	139.50	-0.50	138.00
		Min	137.0	Value	136.50	2.00	138.00
		Max	142.0	Value	-5.0	-5.0	-1.00
				Value	140.50	1.50	1.50
				Change	-5.0	135.0	-5.0
				Value	135.0	3.0	142.0
				Change	4.0	142.0	4.0
	Week 26	n	3	n	3	Value	6
		Mean	142.33	Value	139.67	Change	6
		SD	1.155	Value	2.082	0.33	0.50
		Median	143.00	Value	2.082	1.528	1.643
		Q1	141.00	Value	0.00	0.00	0.00
		Q3	143.00	Value	139.00	-1.00	-1.00
		Min	141.0	Value	138.00	2.00	139.00
		Max	143.0	Value	142.00	-1.0	-1.0
				Value	138.0	2.0	143.00
				Change	142.0	3.0	3.0
	Week 28	n	1	n	2	Value	3
		Mean	140.00	Value	138.50	Change	3
		SD	NE	Value	-1.50	139.00	-1.67
		Median	140.00	Value	0.707	0.707	0.577
		Q1	140.00	Value	0.707	-1.50	1.000
		Q3	140.00	Value	138.50	-2.00	-2.00
		Min	140.0	Value	138.00	-1.00	138.00
		Max	140.0	Value	139.00	-2.0	-2.0
				Value	138.0	-1.0	140.0
				Change	139.00	-1.0	-1.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Sodium (mmol/L)	Week 30	n	0	n	1	1	1
		Mean		144.00	5.00	144.00	5.00
		SD		NE	NE	NE	NE
		Median		144.00	5.00	144.00	5.00
		Q1		144.00	5.00	144.00	5.00
		Q3		144.00	5.00	144.00	5.00
		Min		144.0	5.0	144.0	5.0
		Max		144.0	5.0	144.0	5.0
	Week 32	n	0	n	1	1	1
		Mean		138.00	-1.00	138.00	-1.00
		SD		NE	NE	NE	NE
		Median		138.00	-1.00	138.00	-1.00
		Q1		138.00	-1.00	138.00	-1.00
		Q3		138.00	-1.00	138.00	-1.00
		Min		138.0	-1.0	138.0	-1.0
		Max		138.0	-1.0	138.0	-1.0
	Week 34	n	0	n	1	1	1
		Mean		138.00	-1.00	138.00	-1.00
		SD		NE	NE	NE	NE
		Median		138.00	-1.00	138.00	-1.00
		Q1		138.00	-1.00	138.00	-1.00
		Q3		138.00	-1.00	138.00	-1.00
		Min		138.0	-1.0	138.0	-1.0
		Max		138.0	-1.0	138.0	-1.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Sodium (mmol/L)	Follow-up Week 2	n	17	23	23	40	40
		Mean	137.76	-0.53	138.09	-0.13	137.95
		SD	4.161	3.204	3.566	2.735	3.782
		Median	139.00	-1.00	139.00	0.00	139.00
		Q1	136.00	-2.00	135.00	-2.00	135.50
		Q3	140.00	1.00	140.00	2.00	140.00
		Min	127.0	-8.0	133.0	-6.0	127.0
		Max	142.0	5.0	145.0	5.0	145.0
	Follow-up Week 4	n	11	21	21	32	32
		Mean	139.82	1.64	138.71	0.43	139.09
		SD	4.332	2.618	2.849	2.619	3.402
		Median	141.00	1.00	139.00	0.00	139.00
		Q1	139.00	0.00	137.00	-1.00	137.00
		Q3	143.00	3.00	140.00	2.00	142.00
		Min	128.0	-1.0	134.0	-5.0	128.0
		Max	143.0	8.0	143.0	5.0	143.0
	Follow-up Week 6	n	10	16	16	26	26
		Mean	138.30	0.30	138.69	0.75	138.54
		SD	4.644	2.946	3.807	3.044	4.062
		Median	139.00	0.00	139.00	1.00	139.00
		Q1	136.00	-2.00	136.50	-0.50	136.00
		Q3	141.00	2.00	142.00	2.00	142.00
		Min	128.0	-4.0	129.0	-6.0	128.0
		Max	145.0	5.0	143.0	6.0	145.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Sodium (mmol/L)	Follow-up Week 8	n	6	n	8	n	14
		Mean	138.50	Value	140.00	Change	139.36
		SD	4.848	Value	2.726	Change	3.692
		Median	140.50	Value	141.00	Change	141.00
		Q1	134.00	Value	138.00	Change	138.00
		Q3	142.00	Value	142.00	Change	142.00
		Min	131.0	Value	135.0	Change	131.0
		Max	143.0	Value	143.0	Change	143.0
	Follow-up Week 10	n	3	n	9	n	12
		Mean	141.00	Value	138.56	Change	139.17
		SD	4.583	Value	3.167	Change	3.512
		Median	142.00	Value	138.00	Change	138.50
		Q1	136.00	Value	136.00	Change	136.00
		Q3	145.00	Value	142.00	Change	142.00
		Min	136.0	Value	134.0	Change	134.0
		Max	145.0	Value	143.0	Change	145.0
	Follow-up Week 12	n	4	n	2	n	6
		Mean	134.75	Value	142.00	Change	137.17
		SD	9.287	Value	5.188	Change	8.134
		Median	137.00	Value	141.414	Change	140.50
		Q1	128.00	Value	142.00	Change	140.50
		Q3	141.50	Value	141.00	Change	-2.50
		Min	122.0	Value	143.00	Change	-4.00
		Max	143.0	Value	141.0	Change	-4.00
				Value	143.0	Change	143.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Sodium (mmol/L)	Follow-up Month 6	n	3	3	3	6	6
		Mean	138.33	-4.00	137.00	-1.00	137.67
		SD	3.512	5.292	3.000	4.359	3.011
		Median	138.00	-2.00	137.00	1.00	137.50
		Q1	135.00	-10.00	134.00	-6.00	135.00
		Q3	142.00	0.00	140.00	2.00	140.00
		Min	135.0	-10.0	134.0	-6.0	134.0
		Max	142.0	0.0	140.0	2.0	142.0
	Follow-up Month 9	n	2	2	1	3	3
		Mean	146.00	5.00	135.00	-3.00	142.33
		SD	4.243	0.000	NE	NE	7.024
		Median	146.00	5.00	135.00	-3.00	143.00
		Q1	143.00	5.00	135.00	-3.00	135.00
		Q3	149.00	5.00	135.00	-3.00	149.00
		Min	143.0	5.0	135.0	-3.0	135.0
		Max	149.0	5.0	135.0	-3.0	149.0
	Follow-up Month 12	n	1	1	1	2	2
		Mean	146.00	2.00	136.00	1.00	141.00
		SD	NE	NE	NE	NE	7.071
		Median	146.00	2.00	136.00	1.00	141.00
		Q1	146.00	2.00	136.00	1.00	136.00
		Q3	146.00	2.00	136.00	1.00	146.00
		Min	146.0	2.0	136.0	1.0	136.0
		Max	146.0	2.0	136.0	1.0	146.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value
Sodium (mmol/L)	Follow-up Month 15	n	2	2	0	0	0	2	2
	Mean	143.00	2.00			143.00	2.00	143.00	2.00
	SD	0.000	4.243			0.000	4.243	0.000	4.243
	Median	143.00	2.00			143.00	2.00	143.00	2.00
	Q1	143.00	-1.00			143.00	-1.00	143.00	-1.00
	Q3	143.00	5.00			143.00	5.00	143.00	5.00
	Min	143.0	-1.0			143.0	-1.0	143.0	-1.0
	Max	143.0	5.0			143.0	5.0	143.0	5.0
	Follow-up Month 18	n	1	1	0	0	0	1	1
	Mean	146.00	2.00			146.00	2.00	146.00	2.00
Urea Nitrogen (mmol/L)	Baseline	n	23		40			63	
	Mean	6.877		6.907		6.896		6.896	
	SD	2.8778		2.6200		2.6939		2.6939	
	Median	6.430		6.250		6.430		6.430	
	Q1	4.280		5.000		5.000		5.000	
	Q3	8.570		7.675		8.210		8.210	
	Min	3.57		2.86		2.86		2.86	
	Max	13.57		16.07		16.07		16.07	

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Urea Nitrogen (mmol/L)	Week 2	n	18	34	34	52	52
		Mean	6.585	6.578	-0.036	6.580	0.052
		SD	1.9299	2.2079	1.4011	2.0966	1.5562
		Median	6.250	6.140	-0.180	6.140	0.000
		Q1	5.360	4.640	-0.710	4.640	-0.720
		Q3	7.850	8.210	0.360	8.030	0.895
		Min	3.21	3.93	-3.57	3.21	-3.57
		Max	10.71	12.50	2.86	12.50	4.28
		n	16	34	34	50	50
		Mean	6.538	6.679	-0.092	6.634	0.002
	Week 4	SD	2.3744	2.5822	1.7895	2.4942	1.7982
		Median	6.425	6.070	-0.350	6.070	0.000
		Q1	4.460	4.640	-1.430	4.640	-1.430
		Q3	8.030	8.210	1.070	8.210	1.070
		Min	2.86	3.57	-3.21	2.86	-3.21
		Max	11.07	13.92	3.57	13.92	3.57
		n	17	33	33	50	50
		Mean	6.491	7.099	0.534	6.892	0.360
		SD	2.9451	2.6876	2.2161	2.7629	2.0885
		Median	6.070	6.430	0.000	6.250	0.360

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Urea Nitrogen (mmol/L)	Week 8	n	13	13	25	25	38
		Mean	6.509	0.275	7.354	0.344	7.065
		SD	3.5759	1.4817	3.0623	2.2512	3.2241
		Median	5.000	0.360	7.140	0.330	6.415
		Q1	4.640	-0.720	4.640	-1.780	4.640
		Q3	8.210	0.720	8.930	1.780	8.570
		Min	3.21	-1.79	2.86	-2.50	2.86
		Max	16.42	2.86	13.92	5.71	16.42
		n	13	23	23	36	36
		Mean	7.744	0.851	7.371	0.667	7.506
	Week 10	SD	4.2164	2.5959	3.2935	3.0259	3.5981
		Median	6.430	0.710	6.430	0.350	6.430
		Q1	5.710	0.000	5.000	-1.070	5.360
		Q3	7.850	2.140	8.930	2.140	8.390
		Min	2.50	-3.93	3.57	-6.07	2.50
		Max	19.99	6.42	14.64	7.64	19.99
		n	12	12	19	19	31
		Mean	7.915	1.102	6.852	0.165	7.263
		SD	4.3800	2.8385	2.4613	1.6485	3.3085
		Median	6.070	0.715	6.430	0.000	6.430
	Week 12	Q1	5.180	-0.535	5.360	-1.430	5.360
		Q3	8.745	2.860	8.210	1.430	8.210
		Min	5.00	-3.57	3.93	-1.78	3.93
		Max	19.28	5.71	14.64	3.21	19.28

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Urea Nitrogen (mmol/L)	Week 14	n	12	21	21	33	33
		Mean	7.319	6.792	0.113	6.984	0.148
		SD	3.0272	2.0520	2.0794	2.5394	2.0377
		Median	6.250	6.430	0.000	6.430	0.000
		Q1	5.360	-1.075	5.360	-1.080	5.360
		Q3	8.210	1.435	7.850	1.500	7.850
		Min	4.64	-2.86	3.21	-3.57	3.21
		Max	14.28	3.93	12.50	4.64	14.28
		n	11	17	17	28	28
		Mean	6.847	6.825	0.864	6.834	0.588
	Week 16	SD	2.8299	1.6720	2.3924	2.1964	2.5215
		Median	6.430	6.430	0.350	6.430	0.355
		Q1	4.640	-0.720	5.710	-0.360	5.355
		Q3	8.930	1.430	8.570	2.500	8.750
		Min	3.21	-3.22	3.21	-2.15	3.21
		Max	13.21	2.15	11.07	6.07	13.21
		n	7	13	13	20	20
		Mean	6.173	-0.304	7.086	0.637	6.767
		SD	1.3136	1.7321	1.8368	2.6008	1.6957
		Median	6.070	-0.360	6.780	0.710	6.605

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Urea Nitrogen (mmol/L)	Week 20	n	8	8	14	14	22
		Mean	6.783	-0.001	7.879	1.074	7.480
		SD	1.8301	2.1024	2.4712	2.0771	2.2778
		Median	7.140	-0.715	7.320	0.890	7.140
		Q1	5.000	-1.610	6.780	-0.360	5.710
		Q3	8.210	1.430	9.640	2.860	8.930
		Min	4.28	-2.15	3.57	-2.86	3.57
	Week 22	Max	9.28	3.93	13.21	4.35	13.21
		n	7	7	14	14	21
		Mean	6.271	-0.870	7.269	0.331	6.936
	Week 24	SD	2.3046	1.6862	2.0791	2.1902	2.1529
		Median	4.640	-0.720	7.140	0.180	6.780
		Q1	4.280	-1.790	5.710	-0.710	5.000
		Q3	8.930	0.710	8.570	2.140	8.570
		Min	4.28	-3.93	3.93	-4.29	3.93
		Max	9.28	0.72	11.78	4.28	11.78
		n	8	8	8	8	16
		Mean	8.658	1.249	7.454	1.205	8.056
		SD	4.7306	2.7376	1.1030	1.5942	3.3760
		Median	7.320	0.895	7.320	1.785	7.320

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Urea Nitrogen (mmol/L)	Week 26	n	3	3	3	6	6
		Mean	7.857	1.310	7.140	0.830	7.498
		SD	2.4711	1.1495	1.0700	3.0353	1.7477
		Median	6.430	1.780	7.140	-0.360	6.785
		Q1	6.430	0.000	6.070	-1.430	6.430
		Q3	10.710	2.150	8.210	4.280	8.210
		Min	6.43	0.00	6.07	-1.43	6.07
		Max	10.71	2.15	8.21	4.28	10.71
		n	1	1	2	2	3
		Mean	6.780	-1.790	6.605	-0.535	6.663
	Week 28	SD	NE	NE	2.7789	2.2698	1.9676
		Median	6.780	-1.790	6.605	-0.535	6.780
		Q1	6.780	-1.790	4.640	-2.140	4.640
		Q3	6.780	-1.790	8.570	1.070	8.570
		Min	6.78	-1.79	4.64	-2.14	4.64
		Max	6.78	-1.79	8.57	1.07	8.57
		n	0	0	1	1	1
		Mean	9.640	2.140	9.640	2.140	9.640
		SD	NE	NE	NE	NE	NE
		Median	9.640	2.140	9.640	2.140	9.640

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Urea Nitrogen (mmol/L)	Week 32	n	0	n	1	1	1
		Mean	0	8.930	1.430	8.930	1.430
		SD	0	NE	NE	NE	NE
		Median	0	8.930	1.430	8.930	1.430
		Q1	0	8.930	1.430	8.930	1.430
		Q3	0	8.930	1.430	8.930	1.430
		Min	0	8.93	1.43	8.93	1.43
		Max	0	8.93	1.43	8.93	1.43
		n	0	n	1	1	1
		Mean	0	8.930	1.430	8.930	1.430
Follow-up	Week 34	SD	0	NE	NE	NE	NE
		Median	0	8.930	1.430	8.930	1.430
		Q1	0	8.930	1.430	8.930	1.430
		Q3	0	8.930	1.430	8.930	1.430
		Min	0	8.93	1.43	8.93	1.43
		Max	0	8.93	1.43	8.93	1.43
		n	17	n	23	n	40
		Mean	6.805	Mean	8.246	Mean	7.634
		SD	2.2321	SD	4.0874	SD	3.4625
		Median	7.500	Median	6.780	Median	6.960
		Q1	5.000	Q1	6.070	Q1	5.180
		Q3	7.850	Q3	8.930	Q3	8.570
		Min	3.21	Min	3.93	Min	3.21
		Max	12.14	Max	5.36	Max	20.35
				Change	0.596	Change	0.271
					3.0055		2.8933
					0.000		0.000
					-1.080		-1.605
					1.430		1.255
					-3.57		-3.93
					8.57		8.57

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Urea Nitrogen (mmol/L)	Follow-up Week 4	n 12	n 21	n 21	n 33	33	33
	Mean	6.219	-1.398	8.230	1.089	7.499	0.185
	SD	1.9229	1.8930	3.0131	2.1961	2.8125	2.3922
	Median	6.070	-1.070	8.210	1.070	7.140	-0.360
	Q1	4.105	-2.855	6.430	-0.710	5.710	-1.070
	Q3	8.035	-0.360	8.930	2.150	8.570	2.140
	Min	3.93	-5.00	4.28	-2.50	3.93	-5.00
	Max	8.93	1.79	16.78	5.73	16.78	5.73
	Follow-up Week 6	n 10	n 15	n 15	n 25	25	25
	Mean	7.677	0.357	7.507	0.795	7.575	0.620
	SD	2.8573	1.9513	2.0662	3.4270	2.3578	2.8856
	Median	8.035	0.000	7.140	1.070	7.140	0.000
	Q1	4.640	-1.070	6.430	-1.430	5.360	-1.070
	Q3	10.710	1.070	9.000	3.210	9.280	2.860
	Min	3.93	-1.79	4.28	-7.50	3.93	-7.50
	Max	11.07	4.29	11.42	6.42	11.42	6.42
	Follow-up Week 8	n 5	n 8	n 8	n 13	13	13
	Mean	10.494	3.282	6.294	0.446	7.909	1.537
	SD	3.9820	3.0378	1.5483	1.7888	3.3478	2.6466
	Median	9.280	3.570	6.430	0.535	7.500	1.070
	Q1	7.850	0.350	5.000	-1.070	6.430	0.000
	Q3	11.780	4.640	7.675	1.430	8.210	3.570
	Min	6.78	0.35	3.93	-1.79	3.93	-1.79
	Max	16.78	7.50	8.21	3.57	16.78	7.50

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Urea Nitrogen (mmol/L)	Follow-up Week 10	n	3	n	8	n	11
	Mean	9.043	2.140	6.695	1.116	7.335	1.395
	SD	3.0787	0.7100	1.8778	2.2300	2.3595	1.9521
	Median	9.640	2.140	6.785	0.895	7.500	1.430
	Q1	5.710	1.430	5.175	-0.180	5.710	0.350
	Q3	11.780	2.850	8.390	2.855	8.930	2.850
	Min	5.71	1.43	3.93	-2.50	3.93	-2.50
	Max	11.78	2.85	8.93	4.29	11.78	4.29
	Follow-up Week 12	n	4	n	2	n	6
	Mean	7.855	1.428	9.995	3.570	8.568	2.142
	SD	2.7180	0.7684	2.0153	2.5173	2.5429	1.6869
	Median	7.675	1.605	9.995	3.570	9.105	1.785
	Q1	5.535	0.895	8.570	1.790	5.710	1.430
	Q3	10.175	1.960	11.420	5.350	10.710	2.140
	Min	5.36	0.36	8.57	1.79	5.36	0.36
	Max	10.71	2.14	11.42	5.35	11.42	5.35
	Follow-up Month 6	n	3	n	3	n	6
	Mean	7.853	-1.073	7.023	0.833	7.438	-0.120
	SD	1.7850	2.8600	1.3515	3.2967	1.4872	2.9512
	Median	7.850	-1.080	6.430	-1.070	7.140	-1.070
	Q1	6.070	-3.930	6.070	-1.070	6.070	-1.080
	Q3	9.640	1.790	8.570	4.640	8.570	1.790
	Min	6.07	-3.93	6.07	-1.07	6.07	-3.93
	Max	9.64	1.79	8.57	4.64	9.64	4.64

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Urea Nitrogen (mmol/L)	Follow-up Month 9	n	2	2	1	1	3
	Mean	10.175	3.570	5.710	0.710	8.687	2.617
	SD	3.2880	0.0000	NE	NE	3.4715	1.6512
	Median	10.175	3.570	5.710	0.710	7.850	3.570
	Q1	7.850	3.570	5.710	0.710	5.710	0.710
	Q3	12.500	3.570	5.710	0.710	12.500	3.570
	Min	7.85	3.57	5.71	0.71	5.71	0.71
	Max	12.50	3.57	5.71	0.71	12.50	3.57
	Follow-up Month 12	n	1	1	1	1	2
	Mean	10.350	1.420	7.140	4.280	8.745	2.850
Urea Nitrogen (mmol/L)	SD	NE	NE	NE	NE	2.2698	2.0223
	Median	10.350	1.420	7.140	4.280	8.745	2.850
	Q1	10.350	1.420	7.140	4.280	7.140	1.420
	Q3	10.350	1.420	7.140	4.280	10.350	4.280
	Min	10.35	1.42	7.14	4.28	7.14	1.42
	Max	10.35	1.42	7.14	4.28	10.35	4.28
	Follow-up Month 15	n	2	2	0	0	2
	Mean	8.570	1.965	8.570	8.570	1.965	0.2616
	SD	3.0264	0.2616	3.0264	3.0264	0.2616	0.2616
	Median	8.570	1.965	8.570	8.570	1.965	0.2616

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Urea Nitrogen (mmol/L)	Follow-up Month 18	n	1	1	0	0	1
		Mean	10.350	1.420			10.350
		SD	NE	NE			NE
		Median	10.350	1.420			10.350
		Q1	10.350	1.420			10.350
		Q3	10.350	1.420			10.350
		Min	10.35	1.42			10.35
		Max	10.35	1.42			10.35
Chloride (mmol/L)	Baseline	n	22	41			63
		Mean	102.9	102.9			102.9
		SD	4.40	3.75			3.95
		Median	102.5	103.0			103.0
		Q1	101.0	101.0			101.0
		Q3	105.0	105.0			105.0
		Min	93	94			93
		Max	112	111			112
Week 2	n	16	16	36	36	52	52
	Mean	101.7	-0.7	102.7	-0.8	102.4	-0.7
	SD	3.72	3.82	3.63	2.41	3.65	2.88
	Median	102.0	-1.0	104.0	-1.0	103.0	-1.0
	Q1	100.5	-3.0	100.0	-2.0	100.0	-2.0
	Q3	103.5	0.5	105.0	1.0	105.0	1.0
	Min	93	-6	94	-6	93	-6
		Max	109	11	109	4	109

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Chloride (mmol/L)	Week 4	n	15	36	36	51	51
		Mean	103.0	103.0	-0.3	103.0	0.1
		SD	4.46	3.59	2.45	4.05	2.84
		Median	103.0	103.0	-1.0	103.0	0.0
		Q1	101.0	101.0	-2.0	101.0	-2.0
		Q3	106.0	105.0	1.5	105.0	2.0
		Min	93	94	-5	93	-6
		Max	110	112	5	112	8
	Week 6	n	16	34	34	50	50
		Mean	103.3	102.8	-0.2	103.0	0.1
		SD	4.19	3.84	3.04	3.86	3.30
		Median	103.0	103.5	-1.0	103.5	-0.5
		Q1	99.5	101.0	-2.0	100.0	-2.0
		Q3	106.0	105.0	2.0	106.0	3.0
		Min	96	93	-5	93	-6
		Max	111	111	8	111	9
	Week 8	n	13	26	26	39	39
		Mean	101.5	103.2	0.0	102.6	-0.2
		SD	4.48	3.26	4.54	4.53	3.36
		Median	101.0	103.0	0.0	102.0	0.0
		Q1	101.0	100.0	-3.0	100.0	-3.0
		Q3	104.0	106.0	1.0	106.0	1.0
		Min	91	95	-5	91	-5
		Max	109	113	9	113	9

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Chloride (mmol/L)	Week 10	n	13	23	23	36	36
		Mean	103.0	102.1	-0.7	102.4	-0.6
		SD	3.24	3.84	3.61	3.76	3.64
		Median	104.0	-1.0	103.0	-1.0	103.0
		Q1	100.0	-2.0	100.0	-3.0	100.0
		Q3	105.0	1.0	105.0	2.0	105.0
		Min	98	-6	93	-7	93
		Max	109	10	109	8	109
		n	12	20	20	32	32
		Mean	103.4	104.0	0.7	103.8	0.5
Chloride (mmol/L)	Week 12	SD	4.83	4.17	2.43	4.36	2.54
		Median	104.0	1.0	105.0	0.0	105.0
		Q1	99.0	-2.0	100.0	-1.0	100.0
		Q3	107.0	2.5	107.5	2.0	107.0
		Min	96	-5	98	-3	96
		Max	111	4	112	6	112
		n	12	22	22	34	34
		Mean	103.4	103.7	0.3	103.6	0.2
		SD	4.06	3.67	3.85	3.86	3.29
		Median	104.0	0.5	104.5	0.5	104.5
Chloride (mmol/L)	Week 14	Q1	99.5	-3.0	102.0	-2.0	101.0
		Q3	106.5	1.5	107.0	2.0	107.0
		Min	98	-5	94	-6	94
		Max	110	9	110	8	110

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall		
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value
Chloride (mmol/L)	Week 16	n	11	11	17	17	28	28
		Mean	103.4	-0.6	103.2	-0.2	103.3	-0.4
		SD	4.50	2.58	4.02	2.59	4.13	2.54
		Median	102.0	-1.0	103.0	0.0	102.5	-1.0
		Q1	100.0	-3.0	101.0	-1.0	101.0	-2.0
		Q3	109.0	1.0	106.0	1.0	106.0	1.0
		Min	97	-4	93	-6	93	-6
		Max	110	5	110	4	110	5
	Week 18	n	7	7	14	14	21	21
		Mean	103.1	0.0	102.1	-0.2	102.5	-0.1
		SD	4.10	5.54	4.54	3.26	4.32	4.02
		Median	103.0	-1.0	102.5	0.0	103.0	0.0
		Q1	100.0	-3.0	101.0	-1.0	101.0	-1.0
		Q3	104.0	3.0	104.0	1.0	104.0	1.0
		Min	98	-8	90	-9	90	-9
		Max	111	10	110	5	111	10
	Week 20	n	8	8	15	15	23	23
		Mean	104.0	0.8	102.5	-0.8	103.0	-0.3
		SD	4.04	4.13	4.90	3.12	4.58	3.49
		Median	104.5	0.5	103.0	-1.0	104.0	0.0
		Q1	100.0	-1.0	101.0	-3.0	101.0	-2.0
		Q3	107.5	4.0	106.0	2.0	106.0	2.0
		Min	99	-7	93	-6	93	-7
		Max	109	6	110	5	110	6

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Chloride (mmol/L)	Week 22	n	7	14	14	21	21
		Mean	103.0	-0.1	104.6	1.6	104.1
		SD	4.73	4.56	3.32	3.71	3.81
		Median	102.0	-1.0	105.0	1.5	104.0
		Q1	98.0	-4.0	102.0	0.0	102.0
		Q3	107.0	3.0	106.0	5.0	107.0
		Min	97	-5	99	-5	97
		Max	109	8	112	7	112
	Week 24	n	8	8	8	16	16
		Mean	102.4	-0.9	103.0	0.5	102.7
		SD	3.78	4.39	3.66	2.20	3.61
		Median	101.5	-1.5	103.5	0.0	103.0
		Q1	100.0	-3.0	101.0	-0.5	100.0
		Q3	104.0	1.5	106.0	2.0	105.0
		Min	98	-8	96	-3	96
		Max	110	7	107	4	110
	Week 26	n	3	3	3	6	6
		Mean	107.3	0.7	105.3	2.3	106.3
		SD	2.52	2.52	4.04	3.06	3.20
		Median	107.0	1.0	103.0	3.0	106.0
		Q1	105.0	-2.0	103.0	-1.0	103.0
		Q3	110.0	3.0	110.0	5.0	110.0
		Min	105	-2	103	-1	103
		Max	110	3	110	5	110

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Chloride (mmol/L)	Week 28	n	1	2	2	3	3
		Mean	106.0	-2.0	103.5	0.5	104.3
		SD	NE	0.71	3.54	1.53	2.89
		Median	106.0	-2.0	103.5	0.5	104.0
		Q1	106.0	-2.0	103.0	-2.0	103.0
		Q3	106.0	-2.0	104.0	3.0	106.0
		Min	106	-2	103	-2	103
		Max	106	-2	104	3	106
	Week 30	n	0	0	1	1	1
		Mean		110.0	10.0	110.0	10.0
		SD		NE	NE	NE	NE
		Median		110.0	10.0	110.0	10.0
		Q1		110.0	10.0	110.0	10.0
		Q3		110.0	10.0	110.0	10.0
		Min		110	10	110	10
		Max		110	10	110	10
	Week 32	n	0	0	1	1	1
		Mean		107.0	7.0	107.0	7.0
		SD		NE	NE	NE	NE
		Median		107.0	7.0	107.0	7.0
		Q1		107.0	7.0	107.0	7.0
		Q3		107.0	7.0	107.0	7.0
		Min		107	7	107	7
		Max		107	7	107	7

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall				
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value	Change
Chloride (mmol/L)	Week 34	n	0	0	1	1	1	1	1	1
		Mean			107.0	7.0	107.0	7.0		
		SD			NE	NE	NE	NE		
		Median			107.0	7.0	107.0	7.0		
		Q1			107.0	7.0	107.0	7.0		
		Q3			107.0	7.0	107.0	7.0		
		Min			107	7	107	7		
		Max			107	7	107	7		
	Follow-up Week 2	n	16	16	23	23	39	39		
		Mean	100.9	-1.6	101.5	-0.9	101.3	-1.2		
		SD	4.33	4.32	4.48	2.58	4.38	3.37		
		Median	103.0	-2.0	103.0	0.0	103.0	0.0		
		Q1	98.0	-4.5	99.0	-2.0	99.0	-4.0		
		Q3	103.0	0.5	104.0	1.0	104.0	1.0		
		Min	90	-9	93	-7	90	-9		
		Max	107	10	111	2	111	10		
	Follow-up Week 4	n	11	11	21	21	32	32		
		Mean	102.5	0.3	102.5	0.0	102.5	0.1		
		SD	4.50	3.44	3.82	2.56	3.99	2.84		
		Median	104.0	1.0	103.0	1.0	103.5	1.0		
		Q1	101.0	-2.0	100.0	-2.0	100.5	-2.0		
		Q3	106.0	2.0	105.0	1.0	105.0	2.0		
		Min	91	-6	96	-5	91	-6		
		Max	108	7	112	4	112	7		

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Chloride (mmol/L)	Follow-up Week 6	n	10	16	16	26	26
	Mean	101.1	-1.1	102.3	-0.3	101.8	-0.6
	SD	5.17	4.12	4.14	2.24	4.51	3.05
	Median	103.0	-1.5	102.0	0.0	102.5	0.0
	Q1	98.0	-3.0	99.0	-2.0	99.0	-3.0
	Q3	105.0	0.0	105.0	1.0	105.0	1.0
	Min	92	-7	97	-4	92	-7
	Max	107	8	111	3	111	8
	Follow-up Week 8	n	6	8	8	14	14
	Mean	103.3	-1.3	102.3	-1.4	102.7	-1.4
Chloride (mmol/L)	SD	4.63	3.27	2.66	1.92	3.52	2.47
	Median	104.5	-1.5	102.5	-1.5	103.5	-1.5
	Q1	100.0	-3.0	100.5	-3.0	100.0	-3.0
	Q3	106.0	1.0	104.0	0.5	105.0	1.0
	Min	96	-6	98	-4	96	-6
	Max	109	3	106	1	109	3
	Follow-up Week 10	n	3	9	9	12	12
	Mean	102.0	2.7	103.1	-0.8	102.8	0.1
	SD	2.65	4.73	3.86	2.44	3.51	3.29
	Median	101.0	1.0	102.0	0.0	101.5	0.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Chloride (mmol/L)	Follow-up Week 12	n	4	2	2	6	6
		Mean	97.8	0.0	110.0	2.5	101.8
		SD	8.34	6.83	0.00	4.95	9.04
		Median	100.0	-1.0	110.0	2.5	103.5
		Q1	92.0	-5.0	110.0	-1.0	98.0
		Q3	103.5	5.0	110.0	6.0	110.0
		Min	86	-7	110	-1	86
		Max	105	9	110	6	110
	Follow-up Month 6	n	3	3	3	6	6
		Mean	100.3	-3.3	101.0	-2.3	100.7
		SD	5.69	5.13	4.36	5.86	4.55
		Median	102.0	-2.0	103.0	0.0	102.5
		Q1	94.0	-9.0	96.0	-9.0	96.0
		Q3	105.0	1.0	104.0	2.0	104.0
		Min	94	-9	96	-9	94
		Max	105	1	104	2	105
	Follow-up Month 9	n	2	1	1	3	3
		Mean	108.0	4.0	99.0	-3.0	105.0
		SD	1.41	1.41	NE	NE	5.29
		Median	108.0	4.0	99.0	-3.0	107.0
		Q1	107.0	3.0	99.0	-3.0	99.0
		Q3	109.0	5.0	99.0	-3.0	109.0
		Min	107	3	99	-3	99
		Max	109	5	99	-3	109

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Chloride (mmol/L)	Follow-up Month 12	n	1	1	1	2	2
	Mean	108.0	4.0	99.0	0.0	103.5	2.0
	SD	NE	NE	NE	NE	6.36	2.83
	Median	108.0	4.0	99.0	0.0	103.5	2.0
	Q1	108.0	4.0	99.0	0.0	99.0	0.0
	Q3	108.0	4.0	99.0	0.0	108.0	4.0
	Min	108	4	99	0	99	0
	Max	108	4	99	0	108	4
	Follow-up Month 15	n	2	0	0	2	2
	Mean	105.0	1.0			105.0	1.0
	SD	0.00	0.00			0.00	0.00
	Median	105.0	1.0			105.0	1.0
	Q1	105.0	1.0			105.0	1.0
	Q3	105.0	1.0			105.0	1.0
	Min	105	1			105	1
	Max	105	1			105	1
	Follow-up Month 18	n	1	0	0	1	1
	Mean	106.0	2.0			106.0	2.0
	SD	NE	NE			NE	NE
	Median	106.0	2.0			106.0	2.0
	Q1	106.0	2.0			106.0	2.0
	Q3	106.0	2.0			106.0	2.0
	Min	106	2			106	2
	Max	106	2			106	2

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Aspartate Aminotransferase (U/L)	Baseline	n	23		41		64
		Mean	32.5	26.0		28.4	
		SD	38.97	18.34		27.46	
		Median	22.0	20.0		21.0	
		Q1	15.0	16.0		16.0	
		Q3	26.0	30.0		29.0	
		Min	9	7		7	
		Max	172	118		172	
	Week 2	n	18	18	34	34	52
		Mean	23.4	-7.0	24.7	0.1	24.3
Aspartate Aminotransferase (U/L)		SD	9.94	38.45	17.05	14.59	14.88
		Median	21.0	0.5	21.0	-1.0	21.0
		Q1	15.0	-2.0	14.0	-4.0	14.0
		Q3	25.0	6.0	26.0	1.0	25.5
		Min	13	-159	9	-41	9
		Max	48	15	82	64	82
	Week 4	n	16	16	34	34	50
		Mean	22.5	-0.1	25.6	-0.4	24.6
		SD	9.07	3.47	14.26	16.02	12.82
		Median	21.0	-0.5	22.0	0.0	21.5

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Aspartate Aminotransferase (U/L)	Week 6	n	18	34	34	52	52
		Mean	25.1	25.1	-0.4	25.1	-2.1
		SD	9.06	37.51	16.26	11.87	25.41
		Median	22.5	1.5	0.5	22.0	1.0
		Q1	20.0	-2.0	-3.0	17.5	-2.5
		Q3	28.0	7.0	6.0	29.5	6.5
		Min	12	-154	-78	11	-154
		Max	46	16	37	79	37
		n	13	24	24	37	37
		Mean	22.3	-11.2	4.5	24.5	-1.0
	Week 8	SD	7.13	43.42	18.07	15.80	29.92
		Median	21.0	-1.0	0.5	21.0	0.0
		Q1	19.0	-3.0	-4.0	17.0	-3.0
		Q3	26.0	2.0	5.5	27.0	5.0
		Min	10	-155	-11	10	-155
		Max	40	11	83	101	83
		n	14	24	24	38	38
		Mean	22.2	-9.0	-3.1	22.6	-5.3
		SD	7.51	42.20	12.65	10.93	29.35
		Median	21.0	1.0	0.0	19.5	1.0
	Week 10	Q1	17.0	-4.0	-4.5	15.0	-4.0
		Q3	25.0	5.0	3.0	26.0	4.0
		Min	12	-154	-84	8	-154
		Max	38	15	63	63	23

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Aspartate Aminotransferase (U/L)	Week 12	n	12	20	20	32	32
		Mean	20.6	21.4	-5.6	21.1	-3.5
		SD	5.53	4.84	7.98	7.07	14.95
		Median	21.5	0.5	19.0	-2.0	20.5
		Q1	17.0	-2.0	15.5	-6.0	16.5
		Q3	24.5	3.0	25.0	3.0	24.5
		Min	10	-11	12	-80	10
		Max	29	5	38	9	38
		n	13	22	22	35	35
		Mean	22.0	-10.5	22.0	-3.7	22.0
	Week 14	SD	5.76	43.91	10.71	19.83	9.09
		Median	23.0	0.0	20.0	0.0	22.0
		Q1	19.0	-3.0	16.0	-4.0	16.0
		Q3	24.0	3.0	24.0	2.0	24.0
		Min	11	-156	9	-86	9
		Max	33	9	56	28	56
		n	12	17	17	29	29
		Mean	19.5	-13.3	20.8	-4.7	20.3
		SD	5.07	45.38	9.40	20.53	7.81
		Median	20.0	-1.0	18.0	0.0	19.0
	Week 16	Q1	14.5	-2.0	13.0	-3.0	14.0
		Q3	23.0	0.5	31.0	4.0	25.0
		Min	11	-157	9	-81	9
		Max	28	6	37	10	-157
						37	10

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Aspartate Aminotransferase (U/L)	Week 18	n	8	14	14	22	22
		Mean	18.6	-19.6	20.4	-7.4	19.7
		SD	6.93	55.59	7.42	22.44	7.13
		Median	16.5	-0.5	18.5	-1.5	18.0
		Q1	13.5	-4.0	16.0	-8.0	14.0
		Q3	25.5	2.5	24.0	2.0	24.0
		Min	10	-157	7	-83	7
		Max	28	4	35	9	35
		n	8	15	15	23	23
		Mean	21.5	1.8	19.8	-6.1	20.4
	Week 20	SD	6.09	3.96	5.98	21.80	5.94
		Median	22.0	1.0	18.0	-1.0	20.0
		Q1	17.5	-1.0	15.0	-6.0	15.0
		Q3	25.0	5.0	23.0	2.0	23.0
		Min	12	-4	14	-83	12
		Max	31	8	35	10	35
		n	8	14	14	22	22
		Mean	20.5	-19.0	23.4	-4.1	22.3
		SD	5.58	55.14	15.07	28.97	12.37
		Median	19.0	0.0	18.5	-4.0	18.5
	Week 22	Q1	17.0	-5.5	16.0	-7.0	16.0
		Q3	25.0	3.5	27.0	2.0	27.0
		Min	13	-155	11	-87	11
		Max	29	7	71	56	71
		n	8	14	14	22	22
		Mean	20.5	-19.0	23.4	-4.1	22.3
		SD	5.58	55.14	15.07	28.97	12.37
		Median	19.0	0.0	18.5	-4.0	18.5
		Q1	17.0	-5.5	16.0	-7.0	16.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Aspartate Aminotransferase (U/L)	Week 24	n	8	8	8	16	16
		Mean	25.0	-14.1	21.9	7.6	23.4
		SD	9.74	57.35	13.46	13.45	41.78
		Median	22.5	0.0	16.0	4.0	19.0
		Q1	19.0	-3.0	13.5	-2.0	14.5
		Q3	32.0	12.5	26.5	12.5	31.0
		Min	12	-154	13	-3	12
		Max	41	22	50	35	50
		n	3	3	3	6	6
		Mean	24.0	2.7	13.7	-0.3	18.8
Aspartate Aminotransferase (U/L)	Week 26	SD	10.82	6.66	2.31	3.21	9.00
		Median	21.0	1.0	15.0	1.0	15.0
		Q1	15.0	-3.0	11.0	-4.0	15.0
		Q3	36.0	10.0	15.0	2.0	21.0
		Min	15	-3	11	-4	11
		Max	36	10	15	2	36
		n	1	1	2	3	3
		Mean	18.0	3.0	12.0	0.5	14.0
		SD	NE	NE	2.83	0.71	4.00
		Median	18.0	3.0	12.0	0.5	14.0
Aspartate Aminotransferase (U/L)	Week 28	Q1	18.0	3.0	10.0	0.0	10.0
		Q3	18.0	3.0	14.0	1.0	18.0
		Min	18	3	10	0	10
		Max	18	3	14	1	18
		n	1	1	2	3	3
		Mean	18.0	3.0	12.0	0.5	14.0
		SD	NE	NE	2.83	0.71	4.00
		Median	18.0	3.0	12.0	0.5	14.0
		Q1	18.0	3.0	10.0	0.0	10.0
		Q3	18.0	3.0	14.0	1.0	18.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall				
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value	Change
Aspartate Aminotransferase (U/L)	Week 30	n	0	0	1	1	1	1	1	1
		Mean			13.0	4.0	13.0		4.0	
		SD			NE	NE	NE		NE	
		Median			13.0	4.0	13.0		4.0	
		Q1			13.0	4.0	13.0		4.0	
		Q3			13.0	4.0	13.0		4.0	
		Min			13	4	13		4	
		Max			13	4	13		4	
		n	0	0	1	1	1	1	1	
		Mean			15.0	6.0	15.0		6.0	
Aspartate Aminotransferase (U/L)	Week 32	SD			NE	NE	NE		NE	
		Median			15.0	6.0	15.0		6.0	
		Q1			15.0	6.0	15.0		6.0	
		Q3			15.0	6.0	15.0		6.0	
		Min			15	6	15		6	
		Max			15	6	15		6	
		n	0	0	1	1	1	1	1	
		Mean			15.0	6.0	15.0		6.0	
		SD			NE	NE	NE		NE	
		Median			15.0	6.0	15.0		6.0	
Aspartate Aminotransferase (U/L)	Week 34	Q1			15.0	6.0	15.0		6.0	
		Q3			15.0	6.0	15.0		6.0	
		Min			15	6	15		6	
		Max			15	6	15		6	

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Aspartate Aminotransferase (U/L)	Follow-up Week 2	n	17	17	23	23	40
		Mean	33.2	4.5	42.3	14.7	38.4
		SD	35.57	10.26	48.95	45.36	35.07
		Median	25.0	3.0	29.0	6.0	27.5
		Q1	19.0	-2.0	20.0	0.0	19.5
		Q3	30.0	8.0	37.0	16.0	34.5
	Follow-up Week 4	Min	10	-12	14	-88	10
		Max	166	34	243	182	243
		n	11	11	21	21	32
		Mean	55.5	24.0	39.6	10.9	45.0
Creatinine (mg/dL)	Follow-up Week 6	SD	77.57	48.50	33.65	31.87	52.25
		Median	27.0	4.0	32.0	6.0	27.0
		Q1	17.0	-3.0	19.0	-1.0	18.0
		Q3	45.0	19.0	39.0	20.0	42.0
		Min	12	-7	10	-82	10
		Max	272	140	147	86	272
	Follow-up Week 8	n	10	10	16	16	26
		Mean	54.7	33.3	34.9	5.8	42.5
		SD	78.34	76.86	31.49	36.26	53.85
		Median	25.5	3.0	26.0	1.0	26.0
Urea (mg/dL)	Follow-up Week 10	Q1	18.0	1.0	17.0	-3.5	17.0
		Q3	39.0	17.0	32.0	13.5	33.0
		Min	15	-6	10	-90	10
		Max	270	244	130	90	270
		n	10	10	16	16	26
		Mean	54.7	33.3	34.9	5.8	42.5
		SD	78.34	76.86	31.49	36.26	53.85
		Median	25.5	3.0	26.0	1.0	26.0
		Q1	18.0	1.0	17.0	-3.5	17.0
		Q3	39.0	17.0	32.0	13.5	33.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Aspartate Aminotransferase (U/L)	Follow-up Week 8	n	6	n	9	9	15
	Week 8	Mean	48.8	Value	33.4	15.4	39.6
		SD	63.62	Change	28.5	26.95	20.7
		Median	24.5		31.18	45.41	42.14
		Q1	18.0		17.0	2.0	2.0
		Q3	33.0		16.0	1.0	1.0
		Min	15		32.0	17.0	33.0
		Max	178		-3	-3	17.0
					152	12	-3
					95	79	178
Aspartate Aminotransferase (U/L)	Follow-up Week 10	n	3	n	9	9	12
	Week 10	Mean	19.7	Value	-3.7	19.2	19.3
		SD	2.08	Change	3.21	-9.2	-7.8
		Median	19.0		8.60	27.90	7.39
		Q1	18.0		15.0	-1.0	23.97
		Q3	22.0		-6.0	18.5	-2.0
		Min	18		13.0	-6.0	-6.0
		Max	22		22.0	2.0	1.5
					-82	22.0	-82
					36	11	12
Aspartate Aminotransferase (U/L)	Follow-up Week 12	n	4	n	2	2	6
	Week 12	Mean	31.3	Value	4.0	33.5	-43.0
		SD	17.35	Change	9.93	9.19	32.0
		Median	24.0		1.0	49.50	-11.7
		Q1	21.0		33.5	-43.0	33.74
		Q3	41.5		-3.0	-78.0	14.10
		Min	20		11.0	-8.0	26.5
		Max	57		-4	22.0	-3.0
					27	40.0	-8.0
					40	20	-8.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Aspartate Aminotransferase (U/L)	Follow-up Month 6	n	3	3	3	6	6
	Mean	22.3	22.7	23.3	7.3	22.8	5.0
	SD	10.07	8.14	12.10	9.71	9.97	8.41
	Median	21.0	-1.0	19.0	5.0	20.0	2.0
	Q1	13.0	-3.0	14.0	-1.0	14.0	-1.0
	Q3	33.0	12.0	37.0	18.0	33.0	12.0
	Min	13	-3	14	-1	13	-3
	Max	33	12	37	18	37	18
	Follow-up Month 9	n	2	1	1	3	3
	Mean	17.0	-2.0	15.0	4.0	16.3	0.0
Month 12	SD	5.66	1.41	NE	NE	4.16	3.61
	Median	17.0	-2.0	15.0	4.0	15.0	-1.0
	Q1	13.0	-3.0	15.0	4.0	13.0	-3.0
	Q3	21.0	-1.0	15.0	4.0	21.0	4.0
	Min	13	-3	15	4	13	-3
	Max	21	-1	15	4	21	4
	Follow-up Month 12	n	1	1	1	2	2
	Mean	21.0	-3.0	21.0	2.0	21.0	-0.5
	SD	NE	NE	NE	NE	0.00	3.54
	Median	21.0	-3.0	21.0	2.0	21.0	-0.5

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value
Aspartate Aminotransferase (U/L)	Follow-up Month 15	n	2	2	0	0	2	2	2
		Mean	18.0	-1.0			18.0	-1.0	
		SD	5.66	1.41			5.66	1.41	
		Median	18.0	-1.0			18.0	-1.0	
		Q1	14.0	-2.0			14.0	-2.0	
		Q3	22.0	0.0			22.0	0.0	
		Min	14	-2			14	-2	
		Max	22	0			22	0	
		n	1	1	0	0	1	1	
		Mean	22.0	-2.0			22.0	-2.0	
Alanine Aminotransferase (U/L)	Baseline	SD	NE	NE			NE	NE	
		Median	22.0	-2.0			22.0	-2.0	
		Q1	22.0	-2.0			22.0	-2.0	
		Q3	22.0	-2.0			22.0	-2.0	
		Min	22	-2			22	-2	
		Max	22	-2			22	-2	
		n	23	41			64		
		Mean	29.7	22.0			24.7		
		SD	43.81	21.91			31.45		
		Median	17.0	16.0			16.0		

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Alanine Aminotransferase (U/L)	Week 2	n	18	34	34	52	52
		Mean	21.8	18.4	-2.9	19.6	-2.9
		SD	11.37	34.16	8.77	15.20	20.94
		Median	19.5	0.5	-0.5	15.5	0.0
		Q1	11.0	-4.0	-4.0	10.0	-4.0
		Q3	28.0	8.0	1.0	24.5	2.0
		Min	6	-133	-35	5	-133
		Max	45	37	8	98	37
		n	16	35	35	51	51
		Mean	19.4	0.8	0.2	21.5	0.4
	Week 4	SD	9.51	5.62	13.15	15.97	11.27
		Median	18.0	0.0	0.0	17.0	0.0
		Q1	12.0	-3.5	-3.0	11.0	-3.0
		Q3	24.0	2.5	5.0	26.0	4.0
		Min	7	-6	-38	3	-38
		Max	40	15	42	88	42
		n	18	34	34	52	52
		Mean	21.7	-3.1	-0.4	21.8	-1.3
		SD	9.01	32.84	12.59	14.81	21.53
		Median	23.0	2.0	0.0	18.0	1.0
	Week 6	Q1	14.0	-4.0	-5.0	11.5	-4.5
		Q3	29.0	7.0	7.0	29.0	7.0
		Min	9	-130	-45	6	-130
		Max	37	21	22	98	22

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Alanine Aminotransferase (U/L)	Week 8	n	14	24	24	38	38
		Mean	16.8	-9.0	17.8	17.4	-2.7
		SD	7.23	35.21	10.98	9.67	22.35
		Median	16.5	-1.5	14.5	16.0	-1.0
		Q1	11.0	-4.0	10.0	10.0	-4.0
		Q3	21.0	3.0	23.5	21.0	3.0
		Min	6	-129	5	5	-129
		Max	30	20	43	43	23
		n	14	24	24	38	38
		Mean	16.9	-9.4	20.0	18.8	-4.7
	Week 10	SD	6.93	34.56	24.37	19.71	30.94
		Median	17.5	-2.0	13.0	13.5	-2.0
		Q1	11.0	-4.0	11.0	11.0	-6.0
		Q3	20.0	1.0	18.0	19.0	2.0
		Min	9	-128	5	5	-128
		Max	34	11	122	122	107
		n	12	20	20	32	32
		Mean	19.5	2.4	20.1	19.8	-2.3
		SD	8.42	8.16	13.27	11.54	15.06
		Median	19.5	0.0	15.5	17.0	0.0
	Week 12	Q1	13.5	-3.0	11.5	12.0	-4.0
		Q3	22.0	8.0	20.5	22.0	4.5
		Min	10	-8	9	9	-66
		Max	42	19	60	60	19

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Alanine Aminotransferase (U/L)	Week 14	n	13	22	22	35	35
		Mean	19.5	-8.1	20.0	-3.3	19.8
		SD	7.25	37.24	17.55	17.87	14.45
		Median	19.0	1.0	12.0	-2.5	15.0
		Q1	15.0	-5.0	10.0	-5.0	11.0
		Q3	23.0	5.0	20.0	2.0	23.0
		Min	8	-129	5	-52	5
		Max	33	19	74	43	74
		n	12	17	17	29	29
		Mean	15.7	-12.0	19.6	-6.1	18.0
	Week 16	SD	6.51	38.23	16.16	17.36	13.03
		Median	15.5	-1.0	14.0	-2.0	14.0
		Q1	10.0	-7.5	12.0	-7.0	11.0
		Q3	20.5	2.0	17.0	3.0	20.0
		Min	7	-132	5	-56	5
		Max	28	10	70	16	70
		n	8	14	14	22	22
		Mean	17.5	-13.0	20.3	-1.4	19.3
		SD	7.19	47.93	12.24	13.61	10.57
		Median	18.0	-1.0	16.5	-3.0	16.5
	Week 18	Q1	11.0	-4.0	13.0	-5.0	13.0
		Q3	21.5	9.0	22.0	9.0	22.0
		Min	9	-130	5	-36	5
		Max	30	18	49	19	49
		n	8	14	14	22	22
		Mean	17.5	-13.0	20.3	-1.4	19.3
		SD	7.19	47.93	12.24	13.61	10.57
		Median	18.0	-1.0	16.5	-3.0	16.5
		Q1	11.0	-4.0	13.0	-5.0	13.0
		Q3	21.5	9.0	22.0	9.0	22.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall		
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value
Alanine Aminotransferase (U/L)	Week 20	n	8	8	15	15	23	23
		Mean	18.0	2.4	15.3	-3.7	16.3	-1.6
		SD	4.66	5.90	9.98	12.13	8.48	10.66
		Median	20.0	1.0	13.0	-2.0	13.0	0.0
		Q1	13.5	-1.5	11.0	-9.0	11.0	-5.0
		Q3	21.5	7.0	15.0	0.0	20.0	2.0
		Min	11	-5	5	-38	5	-38
		Max	23	11	47	19	47	19
		n	8	8	14	14	22	22
		Mean	17.3	-14.6	25.4	2.9	22.5	-3.5
	Week 22	SD	4.17	46.32	24.43	27.80	19.79	35.60
		Median	18.0	-3.5	15.5	-2.5	16.0	-3.0
		Q1	14.0	-5.0	13.0	-6.0	13.0	-5.0
		Q3	20.0	8.5	31.0	4.0	21.0	5.0
		Min	11	-128	12	-43	11	-128
		Max	23	11	104	86	104	86
		n	8	8	8	8	16	16
		Mean	20.5	-11.8	21.3	10.1	20.9	-0.8
		SD	11.87	46.70	15.97	13.92	13.60	35.15
		Median	15.5	-1.0	17.5	8.0	16.5	2.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Alanine Aminotransferase (U/L)	Week 26	n	3	3	3	6	6
		Mean	15.3	-3.7	13.0	6.0	14.2
		SD	4.73	5.03	3.00	3.46	3.76
		Median	17.0	-3.0	13.0	8.0	14.5
		Q1	10.0	-9.0	10.0	2.0	10.0
		Q3	19.0	1.0	16.0	8.0	17.0
		Min	10	-9	10	2	10
		Max	19	1	16	8	19
		n	1	1	2	3	3
		Mean	8.0	-2.0	13.0	5.0	11.3
Alanine Aminotransferase (U/L)	Week 28	SD	NE	NE	1.41	5.66	3.06
		Median	8.0	-2.0	13.0	5.0	12.0
		Q1	8.0	-2.0	12.0	1.0	8.0
		Q3	8.0	-2.0	14.0	9.0	14.0
		Min	8	-2	12	1	8
		Max	8	-2	14	9	14
		n	0	0	1	1	1
		Mean		13.0	8.0	13.0	8.0
		SD		NE	NE	NE	NE
		Median		13.0	8.0	13.0	8.0
Alanine Aminotransferase (U/L)	Week 30	Q1		13.0	8.0	13.0	8.0
		Q3		13.0	8.0	13.0	8.0
		Min		13	8	13	8
		Max		13	8	13	8

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall				
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value	Change
Alanine Aminotransferase (U/L)	Week 32	n	0	0	1	1	1	1	1	1
		Mean			12.0	7.0	12.0	12.0	7.0	7.0
		SD			NE	NE	NE	NE	NE	NE
		Median			12.0	7.0	12.0	12.0	7.0	7.0
		Q1			12.0	7.0	12.0	12.0	7.0	7.0
		Q3			12.0	7.0	12.0	12.0	7.0	7.0
		Min			12	7	12	12	7	7
		Max			12	7	12	12	7	7
		n	0	0	1	1	1	1	1	1
		Mean			12.0	7.0	12.0	12.0	7.0	7.0
Follow-up	Week 34	SD			NE	NE	NE	NE	NE	NE
		Median			12.0	7.0	12.0	12.0	7.0	7.0
		Q1			12.0	7.0	12.0	12.0	7.0	7.0
		Q3			12.0	7.0	12.0	12.0	7.0	7.0
		Min			12	7	12	12	7	7
		Max			12	7	12	12	7	7
		n	17	17	23	23	40	40	40	40
		Mean	26.9	-0.5	23.0	3.8	24.7	24.7	2.0	2.0
		SD	35.68	9.78	14.04	16.26	25.24	25.24	13.89	13.89
		Median	18.0	0.0	20.0	4.0	19.0	19.0	1.5	1.5
		Q1	16.0	-7.0	10.0	-5.0	14.0	14.0	-5.0	-5.0
		Q3	21.0	9.0	29.0	12.0	24.5	24.5	11.0	11.0
		Min	12	-24	7	-44	7	7	-44	-44
		Max	164	11	60	34	164	164	34	34

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall		
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value
Alanine Aminotransferase (U/L)	Follow-up Week 4	n	11	11	21	21	32	32
		Mean	33.3	1.8	24.0	2.0	27.2	1.9
		SD	46.50	9.78	13.35	11.29	28.86	10.63
		Median	19.0	4.0	19.0	3.0	19.0	3.5
		Q1	16.0	-6.0	14.0	-4.0	14.5	-5.5
		Q3	25.0	10.0	35.0	7.0	32.5	8.5
	Follow-up Week 6	Min	10	-16	9	-22	9	-22
		Max	172	15	63	27	172	27
		n	10	10	16	16	26	26
		Mean	48.8	32.9	23.6	-0.1	33.3	12.6
Creatinine (mg/dL)	Follow-up Week 8	SD	78.99	77.99	12.55	18.49	49.97	51.61
		Median	18.0	3.5	21.0	0.0	19.0	2.0
		Q1	15.0	-5.0	15.5	-6.5	15.0	-5.0
		Q3	25.0	16.0	30.0	8.5	30.0	11.0
		Min	11	-9	7	-39	7	-39
		Max	265	244	54	33	265	244
	Follow-up Week 12	n	6	6	9	9	15	15
		Mean	54.5	36.2	20.0	4.7	33.8	17.3
		SD	75.84	74.86	12.43	12.14	49.48	48.38
		Median	23.5	10.5	17.0	3.0	22.0	6.0
Urea (mg/dL)	Follow-up Week 16	Q1	21.0	-2.0	10.0	-2.0	11.0	-2.0
		Q3	32.0	16.0	33.0	15.0	33.0	16.0
		Min	18	-6	7	-11	7	-11
		Max	209	188	39	25	209	188
		n	10	10	16	16	26	26
		Mean	48.8	32.9	23.6	-0.1	33.3	12.6
	Follow-up Week 20	SD	78.99	77.99	12.55	18.49	49.97	51.61
		Median	18.0	3.5	21.0	0.0	19.0	2.0
		Q1	15.0	-5.0	15.5	-6.5	15.0	-5.0
		Q3	25.0	16.0	30.0	8.5	30.0	11.0
Urea (mmol/L)	Follow-up Week 24	Min	11	-9	7	-39	7	-39
		Max	265	244	54	33	265	244
		n	6	6	9	9	15	15
		Mean	54.5	36.2	20.0	4.7	33.8	17.3
		SD	75.84	74.86	12.43	12.14	49.48	48.38
		Median	23.5	10.5	17.0	3.0	22.0	6.0
	Follow-up Week 28	Q1	21.0	-2.0	10.0	-2.0	11.0	-2.0
		Q3	32.0	16.0	33.0	15.0	33.0	16.0
		Min	18	-6	7	-11	7	-11
		Max	209	188	39	25	209	188

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Alanine Aminotransferase (U/L)	Follow-up Week 10	n	3	3	9	9	12
	Mean	17.7	-0.3	18.1	-4.1	18.0	-3.2
	SD	3.79	3.51	14.07	24.88	12.11	21.34
	Median	16.0	0.0	12.0	-3.0	14.5	-1.5
	Q1	15.0	-4.0	9.0	-10.0	9.5	-8.0
	Q3	22.0	3.0	22.0	3.0	22.0	3.0
	Min	15	-4	7	-55	7	-55
	Max	22	3	50	42	50	42
	Follow-up Week 12	n	4	4	2	2	6
	Mean	17.5	-1.0	45.0	-21.5	26.7	-7.8
Month 6	SD	3.70	3.74	18.38	7.78	16.66	11.51
	Median	17.0	-0.5	45.0	-21.5	20.5	-3.5
	Q1	14.5	-3.5	32.0	-27.0	15.0	-16.0
	Q3	20.5	1.5	58.0	-16.0	32.0	0.0
	Min	14	-6	32	-27	14	-27
	Max	22	3	58	-16	58	3
	Follow-up Month 6	n	3	3	3	3	6
	Mean	24.3	7.0	66.0	54.7	45.2	30.8
	SD	6.03	9.00	84.92	87.78	58.48	61.61
	Median	25.0	7.0	20.0	6.0	22.5	6.5

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Alanine Aminotransferase (U/L)	Follow-up Month 9	n	2	2	1	1	3
		Mean	25.0	10.5	31.0	20.0	27.0
		SD	4.24	12.02	NE	NE	4.58
		Median	25.0	10.5	31.0	20.0	28.0
		Q1	22.0	2.0	31.0	20.0	22.0
		Q3	28.0	19.0	31.0	20.0	31.0
		Min	22	2	31	20	22
		Max	28	19	31	20	31
		n	1	1	1	1	2
		Mean	18.0	-2.0	29.0	6.0	23.5
Alanine Aminotransferase (U/L)	Follow-up Month 12	SD	NE	NE	NE	NE	7.78
		Median	18.0	-2.0	29.0	6.0	23.5
		Q1	18.0	-2.0	29.0	6.0	18.0
		Q3	18.0	-2.0	29.0	6.0	29.0
		Min	18	-2	29	6	18
		Max	18	-2	29	6	29
		n	2	2	0	0	2
		Mean	24.0	9.5	0	0	24.0
		SD	0.00	7.78	0	0	0.00
		Median	24.0	9.5	0	0	24.0
Alanine Aminotransferase (U/L)	Follow-up Month 15	Q1	24.0	4.0	0	0	24.0
		Q3	24.0	15.0	0	0	24.0
		Min	24	4	0	0	24
		Max	24	15	0	0	24
		n	2	2	0	0	2
		Mean	24.0	9.5	0	0	24.0
		SD	0.00	7.78	0	0	0.00
		Median	24.0	9.5	0	0	24.0
		Q1	24.0	4.0	0	0	24.0
		Q3	24.0	15.0	0	0	24.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Alanine Aminotransferase (U/L)	Follow-up Month 18	n	1	0	0	1	1
		Mean	26.0	6.0		26.0	6.0
		SD	NE	NE		NE	NE
		Median	26.0	6.0		26.0	6.0
		Q1	26.0	6.0		26.0	6.0
		Q3	26.0	6.0		26.0	6.0
		Min	26	6		26	6
		Max	26	6		26	6
Alkaline Phosphatase (U/L)	Baseline	n	23	41		64	
		Mean	188.52	117.56		143.06	
		SD	192.415	75.726		133.219	
		Median	103.00	94.00		97.00	
		Q1	69.00	70.00		69.50	
		Q3	282.00	125.00		182.00	
		Min	40.0	42.0		40.0	
		Max	903.0	379.0		903.0	
Week 2	n	18	18	34	34	52	52
	Mean	113.61	-32.00	93.94	-8.50	100.75	-16.63
	SD	71.771	105.241	44.567	29.632	55.601	66.238
	Median	100.00	0.00	78.00	-6.00	80.00	-5.00
	Q1	50.00	-29.00	63.00	-18.00	61.00	-18.00
	Q3	163.00	16.00	110.00	5.00	136.00	8.00
	Min	42.0	-381.0	30.0	-137.0	30.0	-381.0
		Max	283.0	71.0	197.0	48.0	71.0

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Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Alkaline Phosphatase (U/L)	Week 4	n	16	35	35	51	51
		Mean	130.19	-0.19	126.63	5.29	127.75
		SD	90.235	61.406	83.420	44.104	84.720
		Median	89.50	3.50	104.00	-2.00	103.00
		Q1	56.00	-14.50	64.00	-14.00	61.00
		Q3	186.50	16.50	166.00	21.00	168.00
		Min	44.0	-181.0	42.0	-121.0	42.0
		Max	318.0	106.0	372.0	122.0	372.0
	Week 6	n	18	34	34	52	52
		Mean	151.22	5.61	160.68	41.65	157.40
		SD	115.314	129.067	179.411	137.972	158.999
		Median	104.50	19.00	102.50	3.50	103.00
		Q1	51.00	-18.00	71.00	-9.00	65.00
		Q3	228.00	77.00	196.00	42.00	205.00
		Min	43.0	-384.0	34.0	-97.0	34.0
		Max	392.0	182.0	1030.0	758.0	1030.0
	Week 8	n	13	24	24	37	37
		Mean	153.00	-13.38	156.63	38.96	155.35
		SD	122.797	147.150	152.652	116.014	141.129
		Median	88.00	11.00	89.00	-1.50	88.00
		Q1	59.00	-10.00	71.50	-10.00	66.00
		Q3	204.00	88.00	197.00	26.00	199.00
		Min	42.0	-381.0	37.0	-124.0	37.0
		Max	413.0	136.0	731.0	459.0	731.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Alkaline Phosphatase (U/L)	Week 10	n	13	24	24	37	37
		Mean	97.79	-10.82	161.63	38.83	139.20
		SD	65.016	88.911	157.872	116.821	135.228
		Median	71.30	2.00	88.50	-1.50	82.00
		Q1	45.00	-13.70	68.50	-21.50	68.00
		Q3	105.00	24.00	153.50	16.50	153.00
		Min	42.0	-278.0	29.0	-125.0	29.0
		Max	230.0	73.0	576.0	321.0	576.0
	Week 12	n	12	20	20	32	32
		Mean	104.08	-6.50	136.95	18.20	124.63
		SD	80.826	103.114	169.703	127.705	142.234
		Median	64.00	1.00	75.50	-8.00	72.00
		Q1	47.00	-24.50	65.00	-18.00	55.50
		Q3	147.50	51.50	129.50	3.00	129.50
		Min	41.0	-290.0	42.0	-132.0	41.0
		Max	257.0	105.0	782.0	510.0	782.0
	Week 14	n	12	22	22	34	34
		Mean	150.42	36.08	122.64	11.50	132.44
		SD	129.173	154.141	119.832	77.285	121.990
		Median	73.00	7.00	75.50	-2.00	75.50
		Q1	56.00	-18.00	64.00	-18.00	61.00
		Q3	274.50	122.00	125.00	8.00	126.00
		Min	48.0	-307.0	31.0	-130.0	31.0
		Max	375.0	290.0	475.0	257.0	475.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Alkaline Phosphatase (U/L)	Week 16	n	11	17	17	28	28
		Mean	113.36	27.55	128.53	1.24	122.57
		SD	100.012	68.547	110.967	80.272	105.159
		Median	64.00	6.00	83.00	-2.00	80.50
		Q1	49.00	-25.00	71.00	-25.00	58.00
		Q3	147.00	44.00	124.00	7.00	135.50
		Min	44.0	-54.0	57.0	-155.0	44.0
		Max	314.0	160.0	467.0	264.0	467.0
	Week 18	n	8	14	14	22	22
		Mean	109.38	-59.88	105.21	6.14	106.73
		SD	84.520	183.713	96.281	62.786	90.133
		Median	78.50	9.00	75.00	-4.00	75.00
		Q1	54.50	-176.00	62.00	-26.00	59.00
		Q3	130.00	35.50	105.00	5.00	105.00
		Min	50.0	-378.0	42.0	-32.0	42.0
		Max	299.0	162.0	420.0	217.0	420.0
	Week 20	n	8	15	15	23	23
		Mean	106.38	-18.75	106.80	-11.53	106.65
		SD	89.511	131.292	86.616	65.224	85.578
		Median	81.00	7.50	80.00	-13.00	80.00
		Q1	49.00	-42.00	57.00	-26.00	55.00
		Q3	115.50	17.50	126.00	-5.00	122.00
		Min	44.0	-295.0	30.0	-164.0	30.0
		Max	316.0	179.0	376.0	173.0	376.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Alkaline Phosphatase (U/L)	Week 22	n	8	8	15	15	23
		Mean	122.38	-51.75	103.07	-6.00	109.78
		SD	96.536	188.728	82.056	62.706	85.664
		Median	78.00	-17.00	80.00	-12.00	80.00
		Q1	68.50	-171.50	55.00	-24.00	63.00
		Q3	165.50	71.50	109.00	3.00	109.00
		Min	40.0	-358.0	47.0	-149.0	40.0
		Max	315.0	178.0	370.0	167.0	370.0
	Week 24	n	8	8	8	16	16
		Mean	135.75	-37.13	117.00	-0.38	126.38
		SD	97.375	185.897	100.566	82.446	96.116
		Median	95.00	3.50	76.50	7.50	85.50
		Q1	78.50	-157.50	61.00	-15.50	70.00
		Q3	165.50	65.00	130.50	14.50	146.50
		Min	61.0	-329.0	53.0	-160.0	53.0
		Max	347.0	210.0	347.0	144.0	347.0
	Week 26	n	3	3	3	6	6
		Mean	65.00	-7.33	141.33	27.67	103.17
		SD	36.373	24.090	138.074	66.576	99.514
		Median	44.00	4.00	83.00	24.00	63.50
		Q1	44.00	-35.00	42.00	-37.00	44.00
		Q3	107.00	9.00	299.00	96.00	107.00
		Min	44.0	-35.0	42.0	-37.0	42.0
		Max	107.0	9.0	299.0	96.0	299.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Alkaline Phosphatase (U/L)	Week 28	n	1	n	2	n	3
		Mean	124.00	21.00	80.00	25.50	94.67
		SD	NE	NE	26.870	20.506	31.723
		Median	124.00	21.00	80.00	25.50	99.00
		Q1	124.00	21.00	61.00	11.00	61.00
		Q3	124.00	21.00	99.00	40.00	124.00
		Min	124.0	21.0	61.0	11.0	61.0
		Max	124.0	21.0	99.0	40.0	124.0
	Week 30	n	0	n	1	n	1
		Mean	101.00	101.00	42.00	42.00	101.00
		SD	NE	NE	NE	NE	NE
		Median	101.00	101.00	42.00	42.00	101.00
		Q1	101.00	101.00	42.00	42.00	101.00
		Q3	101.00	101.00	42.00	42.00	101.00
		Min	101.0	101.0	42.0	42.0	101.0
		Max	101.0	101.0	42.0	42.0	101.0
	Week 32	n	0	n	1	n	1
		Mean	102.00	102.00	43.00	43.00	102.00
		SD	NE	NE	NE	NE	NE
		Median	102.00	102.00	43.00	43.00	102.00
		Q1	102.00	102.00	43.00	43.00	102.00
		Q3	102.00	102.00	43.00	43.00	102.00
		Min	102.0	102.0	43.0	43.0	102.0
		Max	102.0	102.0	43.0	43.0	102.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall				
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value	Change
Alkaline Phosphatase (U/L)	Week 34	n	0	0	1	1	1	1	1	1
		Mean			102.00	43.00	102.00	43.00		
		SD			NE	NE	NE	NE		
		Median			102.00	43.00	102.00	43.00		
		Q1			102.00	43.00	102.00	43.00		
		Q3			102.00	43.00	102.00	43.00		
		Min			102.0	43.0	102.0	43.0		
		Max			102.0	43.0	102.0	43.0		
	Follow-up Week 2	n	17	17	23	23	40	40		
		Mean	288.94	80.94	151.91	29.78	210.15	51.53		
		SD	346.666	182.852	121.500	108.494	249.674	144.958		
		Median	239.00	30.00	129.00	0.00	132.50	8.50		
		Q1	73.00	7.00	70.00	-32.00	71.50	-18.00		
		Q3	353.00	136.00	183.00	70.00	285.50	107.50		
		Min	42.0	-310.0	26.0	-155.0	26.0	-310.0		
		Max	1515.0	612.0	540.0	326.0	1515.0	612.0		
	Follow-up Week 4	n	11	11	21	21	32	32		
		Mean	327.73	93.27	196.57	66.33	241.66	75.59		
		SD	561.160	342.089	171.274	158.047	352.863	232.453		
		Median	107.00	9.00	126.00	13.00	118.50	12.00		
		Q1	77.00	-23.00	84.00	-17.00	80.50	-18.50		
		Q3	363.00	73.00	251.00	91.00	275.00	82.00		
		Min	38.0	-306.0	57.0	-123.0	38.0	-306.0		
		Max	1966.0	1063.0	762.0	548.0	1966.0	1063.0		

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Alkaline Phosphatase (U/L)	Follow-up Week 6	n	10	16	16	26	26
		Mean	284.90	98.40	206.25	70.44	236.50
		SD	235.416	210.951	245.867	212.914	240.301
		Median	229.50	47.00	124.00	13.50	124.00
		Q1	71.00	0.00	67.50	-20.50	71.00
		Q3	488.00	309.00	252.50	79.50	345.00
		Min	44.0	-312.0	34.0	-96.0	34.0
		Max	617.0	387.0	1050.0	836.0	1050.0
	Follow-up Week 8	n	6	9	9	15	15
		Mean	195.17	90.83	120.78	23.00	150.53
		SD	305.905	219.033	60.520	45.692	192.189
		Median	74.00	12.00	106.00	10.00	95.00
		Q1	49.00	-16.00	82.00	-10.00	53.00
		Q3	113.00	37.00	172.00	33.00	172.00
		Min	44.0	-35.0	51.0	-27.0	44.0
		Max	817.0	535.0	234.0	109.0	817.0
	Follow-up Week 10	n	3	9	9	12	12
		Mean	205.33	5.67	122.33	-3.56	143.08
		SD	262.392	345.979	84.688	38.965	138.359
		Median	66.00	-37.00	93.00	-3.00	92.50
		Q1	42.00	-317.00	71.00	-31.00	64.50
		Q3	508.00	371.00	114.00	21.00	187.00
		Min	42.0	-317.0	33.0	-63.0	33.0
		Max	508.0	371.0	271.0	57.0	508.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Alkaline Phosphatase (U/L)	Follow-up Week 12	n 4	4	n 2	2	n 6	6
	Mean	250.50	26.25	116.50	-1.00	205.83	17.17
	SD	229.141	288.427	9.192	35.355	190.548	224.415
	Median	212.50	17.00	116.50	-1.00	116.50	-0.50
	Q1	61.00	-170.00	110.00	-26.00	68.00	-26.00
	Q3	440.00	222.50	123.00	24.00	357.00	59.00
	Min	54.0	-315.0	110.0	-26.0	54.0	-315.0
	Max	523.0	386.0	123.0	24.0	523.0	386.0
	Follow-up Month 6	n 3	3	n 3	3	n 6	6
	Mean	44.00	-18.67	66.67	-51.33	55.33	-35.00
	SD	4.000	17.616	25.697	65.501	20.607	46.480
	Median	44.00	-21.00	81.00	-42.00	46.00	-28.00
	Q1	40.00	-35.00	37.00	-121.00	40.00	-42.00
	Q3	48.00	0.00	82.00	9.00	81.00	0.00
	Min	40.0	-35.0	37.0	-121.0	37.0	-121.0
	Max	48.0	0.0	82.0	9.0	82.0	9.0
	Follow-up Month 9	n 2	2	n 1	1	n 3	3
	Mean	46.00	-13.50	62.00	5.00	51.33	-7.33
	SD	1.414	26.163	NE	NE	9.292	21.362
	Median	46.00	-13.50	62.00	5.00	47.00	5.00
	Q1	45.00	-32.00	62.00	5.00	45.00	-32.00
	Q3	47.00	5.00	62.00	5.00	62.00	5.00
	Min	45.0	-32.0	62.0	5.0	45.0	-32.0
	Max	47.0	5.0	62.0	5.0	62.0	5.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Alkaline Phosphatase (U/L)	Follow-up Month 12	n	1	1	1	1	2
		Mean	44.00	-35.00	104.00	-21.00	74.00
		SD	NE	NE	NE	NE	9.899
		Median	44.00	-35.00	104.00	-21.00	74.00
		Q1	44.00	-35.00	104.00	-21.00	44.00
		Q3	44.00	-35.00	104.00	-21.00	104.00
		Min	44.0	-35.0	104.0	-21.0	44.0
		Max	44.0	-35.0	104.0	-21.0	104.0
	Follow-up Month 15	n	2	2	0	0	2
		Mean	45.00	-14.50			45.00
		SD	1.414	28.991			1.414
		Median	45.00	-14.50			45.00
		Q1	44.00	-35.00			44.00
		Q3	46.00	6.00			46.00
		Min	44.0	-35.0			44.0
		Max	46.0	6.0			46.0
	Follow-up Month 18	n	1	1	0	0	1
		Mean	39.00	-40.00			39.00
		SD	NE	NE			NE
		Median	39.00	-40.00			39.00
		Q1	39.00	-40.00			39.00
		Q3	39.00	-40.00			39.00
		Min	39.0	-40.0			39.0
		Max	39.0	-40.0			39.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value
Prostate Specific Antigen (ug/L)	Baseline	n	23		40			63	
		Mean	244.6978		350.4760			311.8586	
		SD	386.18626		598.45804			529.94827	
		Median	92.7700		56.3850			65.2000	
		Q1	19.7000		18.3000			19.1000	
		Q3	296.2000		521.7500			493.2000	
		Min	1.080		0.500			0.500	
		Max	1541.000		2425.700			2425.700	
	Week 6	n	19	19	33	33	52	52	
		Mean	222.5963	31.5200	217.5053	-144.3053	219.3655	-80.0614	
		SD	484.95955	117.16543	416.02731	321.57259	437.73426	277.55738	
		Median	35.4400	1.6900	38.9700	-0.4000	38.1750	0.0000	
		Q1	13.5000	-10.6600	25.1000	-60.8000	16.5350	-23.6600	
		Q3	155.0000	27.0400	207.8000	14.0300	205.9000	14.7050	
		Min	0.030	-162.100	0.060	-1360.764	0.030	-1360.764	
		Max	1984.000	443.000	2158.000	104.600	2158.000	443.000	
	Week 12	n	14	14	25	25	39	39	
		Mean	308.9064	63.6279	254.9506	-157.2578	274.3194	-77.9655	
		SD	664.90178	247.01798	671.29844	521.61576	660.71635	451.92826	
		Median	28.9900	-9.7500	76.8300	-1.1000	70.6000	-6.0500	
		Q1	8.1000	-28.1500	23.6000	-75.5000	13.9000	-51.6000	
		Q3	122.0000	-1.8000	207.3600	25.6900	207.3600	25.6900	
		Min	0.740	-285.400	0.300	-1669.614	0.300	-1669.614	
		Max	2293.000	752.000	3411.000	985.300	3411.000	985.300	

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Prostate Specific Antigen (ug/L)	Week 18	n	11	11	11	22	22
		Mean	241.6982	26.7436	87.4736	-381.5409	164.5859
		SD	634.81943	215.58549	141.10923	584.30678	455.64679
		Median	21.1000	-6.6200	20.5000	-8.6000	20.8000
		Q1	5.7000	-52.3800	2.1800	-829.1000	3.5000
		Q3	117.0000	33.3800	71.7500	-0.2000	71.7500
		Min	0.680	-290.500	0.060	-1424.740	0.060
		Max	2144.000	603.000	439.400	37.500	2144.000
	Week 24	n	8	8	11	19	19
		Mean	25.0288	-62.5238	141.4427	-376.8836	92.4263
		SD	29.60304	99.45381	234.63885	567.01356	185.51077
		Median	15.8600	-45.8600	20.5000	-58.6000	20.5000
		Q1	2.6400	-66.9000	6.6000	-651.5000	3.1800
		Q3	37.5500	-0.9250	221.6000	-4.8600	40.9800
		Min	0.530	-294.100	0.090	-1458.550	0.090
		Max	87.600	21.280	617.000	3.000	617.000
	Week 30	n	2	2	1	3	3
		Mean	15.4800	-2.5450	21.4000	3.9000	17.4533
		SD	21.76475	19.39594	NE	NE	15.76497
		Median	15.4800	-2.5450	21.4000	3.9000	21.4000
		Q1	0.0900	-16.2600	21.4000	3.9000	0.0900
		Q3	30.8700	11.1700	21.4000	3.9000	30.8700
		Min	0.090	-16.260	21.400	3.900	0.090
		Max	30.870	11.170	21.400	3.900	30.870

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Prostate Specific Antigen (ug/L)	Follow-up Week 6	n 10 Mean 562.6096 SD 797.23704 Median 185.2500 Q1 0.3000 Q3 1019.1300 Min 0.006 Max 2337.000	n 10 Mean 295.2796 SD 480.23467 Median 122.4630 Q1 -16.2800 Q3 525.9300 Min -72.680 Max 1487.100	n 13 Mean 115.4515 SD 268.10338 Median 21.8000 Q1 4.2000 Q3 65.7000 Min 0.100 Max 977.400	n 13 Mean -212.2431 SD 581.16718 Median -2.7700 Q1 -38.7000 Q3 -0.4000 Min -1477.900 Max 466.400	n 23 Mean 309.8681 SD 592.10676 Median 21.9000 Q1 0.6000 Q3 343.4000 Min 0.006 Max 2337.000	n 23 Mean 8.4190 SD 587.15703 Median -1.8600 Q1 -38.7000 Q3 246.0000 Min -1477.900 Max 1487.100
	Follow-up Month 3	n 7 Mean 47.7514 SD 94.18922 Median 10.4000 Q1 0.0500 Q3 32.9000 Min 0.020 Max 259.000	n 7 Mean 118.41659 SD 133.52419 Median 10.9200 Q1 -62.4900 Q3 -1.0600 Min -285.800 Max 106.600	n 11 Mean 55.5627 SD 611.59979 Median -15.2200 Q1 0.8600 Q3 33.7800 Min -1478.440 Max 454.000	n 11 Mean -238.5736 SD 116.76466 Median 10.6600 Q1 -26.8200 Q3 1.6000 Min 0.020 Max 365.910	n 18 Mean 52.5250 SD 483.61898 Median 10.6600 Q1 0.8600 Q3 32.9000 Min 0.020 Max 454.000	n 18 Mean -165.4111 SD 483.61898 Median -15.8500 Q1 -59.4000 Q3 -0.3700 Min -1478.440 Max 365.910
	Follow-up Month 6	n 3 Mean 0.5667 SD 0.73935 Median 0.2600 Q1 0.0300 Q3 1.4100 Min 0.030 Max 1.410	n 3 Mean -19.4000 SD 14.15361 Median -16.3200 Q1 -34.8400 Q3 -7.0400 Min -34.840 Max -7.040	n 3 Mean 44.5700 SD 76.85116 Median 0.3000 Q1 0.1000 Q3 133.3100 Min 0.100 Max 133.310	n 3 Mean -462.0300 SD 778.35958 Median -25.0000 Q1 -1360.6900 Q3 -0.4000 Min -1360.690 Max -0.400	n 6 Mean 22.5683 SD 54.25446 Median 0.2800 Q1 0.1000 Q3 1.4100 Min 0.030 Max 133.310	n 6 Mean -240.7150 SD 548.81142 Median -20.6600 Q1 -34.8400 Q3 -7.0400 Min -1360.690 Max -0.400

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Prostate Specific Antigen (ug/L)	Follow-up Month 9	n	2	n	3	n	5
		Mean	0.2700	Value	3.3967	Change	-7.4233
		SD	0.36770	Value	4.39359	Change	2.1460
		Median	0.2700	Value	1.5000	Change	3.55224
		Q1	0.0100	Value	0.2700	Change	-6.7700
		Q3	0.5300	Value	8.4200	Change	0.2700
		Min	0.010	Value	0.270	Change	-16.3400
		Max	0.530	Value	8.420	Change	-4.0000
	Follow-up Month 12	n	1	n	2	n	3
		Mean	0.0100	Value	0.2600	Change	-2.1250
		SD	NE	Value	0.22627	Change	0.1767
		Median	0.0100	Value	0.2600	Change	0.21548
		Q1	0.0100	Value	0.1000	Change	8.38636
		Q3	0.0100	Value	0.4200	Change	-3.8500
		Min	0.010	Value	0.100	Change	0.1000
		Max	0.010	Value	0.420	Change	-16.3400
	Follow-up Month 15	n	2	n	1	n	3
		Mean	1.3350	Value	0.1160	Change	-0.3840
		SD	1.87383	Value	NE	Change	0.9287
		Median	1.3350	Value	0.1160	Change	8.26234
		Q1	0.0100	Value	0.1160	Change	-0.1160
		Q3	2.6600	Value	0.1160	Change	-4.6400
		Min	0.010	Value	0.116	Change	0.0100
		Max	2.660	Value	0.116	Change	-16.3400
							-0.384

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value
Prostate Specific Antigen (ug/L)	Follow-up Month 18	n	1	1	0	0	0	1	1
		Mean	0.0100	-16.3400	NE	NE	NE	0.0100	-16.3400
		SD	NE	NE	NE	NE	NE	NE	NE
		Median	0.0100	-16.3400	0.0100	-16.3400	0.0100	-16.3400	-16.3400
		Q1	0.0100	-16.3400	0.0100	-16.3400	0.0100	-16.3400	-16.3400
		Q3	0.0100	-16.3400	0.0100	-16.3400	0.0100	-16.3400	-16.3400
		Min	0.010	-16.340	0.010	-16.340	0.010	-16.340	-16.340
		Max	0.010	-16.340	0.010	-16.340	0.010	-16.340	-16.340
Albumin (g/L)	Baseline	n	22	37	38.25	37	59	38.04	38.04
		Mean	37.68	38.25	4.730	4.730	5.094	5.094	5.094
		SD	5.752	4.730	5.752	5.752	5.752	5.752	5.752
		Median	38.00	37.00	37.00	37.00	37.00	37.00	37.00
		Q1	34.00	35.00	35.00	35.00	35.00	35.00	35.00
		Q3	42.00	42.00	42.00	42.00	42.00	42.00	42.00
		Min	26.0	29.4	29.4	29.4	26.0	26.0	26.0
		Max	48.0	50.0	50.0	50.0	50.0	50.0	50.0
Week 2	n	16	16	28	28	44	44	44	44
	Mean	40.25	1.63	37.89	-0.69	38.75	0.15	38.75	0.15
	SD	5.040	4.689	4.685	3.012	4.895	3.826	4.895	3.826
	Median	41.00	1.00	38.00	0.00	38.00	0.30	38.00	0.30
	Q1	36.00	-1.50	35.00	-2.50	35.50	-2.00	35.50	-2.00
	Q3	45.00	4.00	41.00	1.50	43.00	2.00	43.00	2.00
	Min	31.0	-5.0	25.0	-7.0	25.0	-7.0	25.0	-7.0
	Max	47.0	13.0	48.0	4.0	48.0	13.0	48.0	13.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Albumin (g/L)	Week 4	n	15	15	28	28	43
		Mean	39.20	0.13	37.32	-0.91	37.98
		SD	4.263	3.114	5.683	4.355	5.258
		Median	40.00	1.00	37.50	0.00	39.00
		Q1	36.00	-3.00	35.00	-4.00	35.00
		Q3	44.00	3.00	42.00	2.00	42.00
		Min	31.0	-5.0	24.0	-11.0	24.0
		Max	44.0	5.0	46.0	7.0	46.0
	Week 6	n	17	17	29	29	46
		Mean	40.59	2.18	38.72	0.33	39.41
		SD	3.906	5.187	4.659	3.704	4.445
		Median	42.00	2.00	39.00	1.00	40.00
		Q1	38.00	-2.00	36.00	-3.00	36.00
		Q3	44.00	3.00	42.00	3.00	42.00
		Min	33.0	-5.0	25.0	-6.0	25.0
		Max	46.0	14.0	47.0	8.0	47.0
	Week 8	n	13	13	20	20	33
		Mean	40.62	2.46	38.50	-0.57	39.33
		SD	3.070	6.091	4.718	4.798	4.225
		Median	42.00	1.00	39.00	-1.00	39.00
		Q1	38.00	-2.00	36.00	-3.00	37.00
		Q3	43.00	7.00	42.00	2.50	42.00
		Min	36.0	-5.0	31.0	-10.0	31.0
		Max	45.0	16.0	47.0	8.6	47.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Albumin (g/L)	Week 10	n	13	13	20	20	33
		Mean	41.08	3.00	39.80	1.75	40.30
		SD	3.427	5.701	3.778	3.998	3.644
		Median	42.00	3.00	39.00	2.00	40.00
		Q1	40.00	-1.00	38.00	-1.00	38.00
		Q3	43.00	5.00	43.00	3.50	43.00
		Min	35.0	-5.0	33.0	-4.0	33.0
		Max	45.0	15.0	47.0	9.0	47.0
	Week 12	n	11	11	17	17	28
		Mean	41.36	1.91	39.00	0.33	39.93
		SD	3.443	4.085	4.822	4.530	4.422
		Median	42.00	2.00	38.00	1.00	40.00
		Q1	39.00	-1.00	35.00	-1.00	37.50
		Q3	45.00	4.00	43.00	3.00	43.50
		Min	35.0	-5.0	31.0	-10.0	31.0
		Max	46.0	10.0	46.0	7.0	46.0
	Week 14	n	12	12	19	19	31
		Mean	40.25	2.42	38.05	-0.44	38.90
		SD	4.751	6.829	4.441	3.439	4.614
		Median	42.00	1.00	38.00	0.00	38.00
		Q1	38.00	-2.50	34.00	-2.00	36.00
		Q3	43.50	7.00	41.00	1.00	43.00
		Min	29.0	-6.0	31.0	-9.0	29.0
		Max	45.0	17.0	47.0	6.6	47.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Albumin (g/L)	Week 16	n	11	15	15	26	26
		Mean	38.00	-0.55	39.00	0.04	38.58
		SD	5.657	8.847	3.982	4.292	4.683
		Median	40.00	-2.00	39.00	-1.00	39.50
		Q1	37.00	-4.00	36.00	-2.00	37.00
		Q3	40.00	6.00	41.00	3.00	41.00
		Min	22.0	-19.0	31.0	-10.0	22.0
		Max	44.0	14.0	46.0	8.6	46.0
	Week 18	n	7	13	13	20	20
		Mean	40.14	3.00	39.54	0.89	39.75
		SD	2.911	6.377	4.054	4.894	3.626
		Median	40.00	1.00	40.00	0.00	40.00
		Q1	37.00	-3.00	37.00	-2.00	37.00
		Q3	43.00	7.00	42.00	5.00	42.00
		Min	37.0	-4.0	31.0	-8.0	31.0
		Max	44.0	14.0	46.0	7.6	46.0
	Week 20	n	7	13	13	20	20
		Mean	41.43	2.00	39.69	0.97	40.30
		SD	4.036	5.099	3.545	4.459	3.715
		Median	43.00	2.00	40.00	2.00	40.50
		Q1	37.00	-3.00	37.00	-1.00	37.00
		Q3	45.00	8.00	42.00	4.00	43.00
		Min	36.0	-4.0	33.0	-9.0	33.0
		Max	46.0	9.0	46.0	7.6	46.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Albumin (g/L)	Week 22	n	7	7	13	13	20
		Mean	39.29	2.00	40.23	0.38	39.90
		SD	2.870	6.532	2.976	3.280	2.900
		Median	39.00	0.00	40.00	0.00	39.50
		Q1	37.00	-5.00	39.00	-2.00	37.50
		Q3	42.00	7.00	43.00	3.00	42.50
		Min	35.0	-5.0	36.0	-6.0	35.0
		Max	43.0	13.0	45.0	6.0	45.0
	Week 24	n	7	7	8	8	15
		Mean	41.71	6.57	38.38	0.25	39.93
		SD	4.821	4.429	3.739	3.991	4.464
		Median	43.00	6.00	38.50	1.00	40.00
		Q1	40.00	3.00	37.00	-1.00	38.00
		Q3	45.00	9.00	41.00	3.00	43.00
		Min	32.0	2.0	31.0	-8.0	31.0
		Max	47.0	15.0	43.0	4.0	47.0
	Week 26	n	3	3	3	3	6
		Mean	40.67	0.33	37.00	0.33	38.83
		SD	2.082	2.082	3.606	2.517	3.312
		Median	40.00	1.00	38.00	0.00	39.50
		Q1	39.00	-2.00	33.00	-2.00	38.00
		Q3	43.00	2.00	40.00	3.00	40.00
		Min	39.0	-2.0	33.0	-2.0	33.0
		Max	43.0	2.0	40.0	3.0	43.0

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Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Albumin (g/L)	Week 28	n	1	1	2	3	3
		Mean	42.00	1.00	36.50	0.50	38.33
		SD	NE	NE	4.950	3.536	4.726
		Median	42.00	1.00	36.50	0.50	40.00
		Q1	42.00	1.00	33.00	-2.00	33.00
		Q3	42.00	1.00	40.00	3.00	42.00
		Min	42.0	1.0	33.0	-2.0	33.0
		Max	42.0	1.0	40.0	3.0	42.0
	Week 30	n	0	0	1	1	1
		Mean	34.00	NE	34.00	-1.00	34.00
		SD	NE	NE	NE	NE	NE
		Median	34.00	NE	34.00	-1.00	34.00
		Q1	34.00	NE	34.00	-1.00	34.00
		Q3	34.00	NE	34.00	-1.00	34.00
		Min	34.0	NE	34.0	-1.0	34.0
		Max	34.0	NE	34.0	-1.0	34.0
	Week 32	n	0	0	1	1	1
		Mean	33.00	NE	33.00	-2.00	33.00
		SD	NE	NE	NE	NE	NE
		Median	33.00	NE	33.00	-2.00	33.00
		Q1	33.00	NE	33.00	-2.00	33.00
		Q3	33.00	NE	33.00	-2.00	33.00
		Min	33.0	NE	33.0	-2.0	33.0
		Max	33.0	NE	33.0	-2.0	33.0

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Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall				
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value	Change
Albumin (g/L)	Week 34	n	0	0	1	1	1	1	1	1
		Mean			33.00	-2.00	33.00	-2.00	33.00	-2.00
		SD			NE	NE	NE	NE	NE	NE
		Median			33.00	-2.00	33.00	-2.00	33.00	-2.00
		Q1			33.00	-2.00	33.00	-2.00	33.00	-2.00
		Q3			33.00	-2.00	33.00	-2.00	33.00	-2.00
		Min			33.0	-2.0	33.0	-2.0	33.0	-2.0
		Max			33.0	-2.0	33.0	-2.0	33.0	-2.0
	Follow-up	n	16	16	19	19	35	35	35	35
	Week 2	Mean	39.19	0.00	37.79	0.35	38.43	0.19	38.43	0.19
		SD	4.415	3.559	5.534	4.105	5.031	3.813	5.031	3.813
		Median	40.50	-0.50	38.00	1.00	40.00	0.00	40.00	0.00
		Q1	36.50	-3.00	35.00	-3.00	35.00	-3.00	35.00	-3.00
		Q3	42.00	1.50	42.00	3.00	42.00	2.00	42.00	2.00
		Min	31.0	-5.0	26.0	-7.0	26.0	-7.0	26.0	-7.0
		Max	45.0	8.0	50.0	8.0	50.0	8.0	50.0	8.0
	Follow-up	n	11	11	20	20	31	31	31	31
	Week 4	Mean	38.27	-0.73	37.45	0.05	37.74	-0.23	37.74	-0.23
		SD	5.405	5.042	5.907	4.807	5.657	4.822	5.657	4.822
		Median	39.00	-3.00	38.00	1.00	38.00	1.00	38.00	1.00
		Q1	35.00	-5.00	33.00	-3.50	33.00	-4.00	33.00	-4.00
		Q3	43.00	4.00	42.00	4.00	43.00	4.00	43.00	4.00
		Min	28.0	-7.0	27.0	-11.0	27.0	-11.0	27.0	-11.0
		Max	45.0	7.0	47.0	7.0	47.0	7.0	47.0	7.0

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Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Albumin (g/L)	Follow-up Week 6	n	9	n	14	14	23
		Mean	39.44	0.56	38.07	-0.29	38.61
		SD	4.362	4.419	6.427	5.090	5.639
		Median	40.00	0.00	39.50	0.50	40.00
		Q1	39.00	-3.00	34.00	-3.00	34.00
		Q3	42.00	5.00	42.00	4.00	42.00
		Min	31.0	-6.0	23.0	-13.0	23.0
		Max	45.0	6.0	46.0	5.0	46.0
	Follow-up Week 8	n	6	n	8	8	14
		Mean	36.83	-0.33	36.75	-2.25	36.79
		SD	2.927	5.241	8.697	7.686	6.635
		Median	37.50	-2.00	38.50	-2.50	37.50
		Q1	34.00	-3.00	31.00	-10.00	33.00
		Q3	39.00	2.00	43.50	5.00	41.00
		Min	33.0	-6.0	21.0	-11.0	21.0
		Max	40.0	9.0	47.0	8.0	47.0
	Follow-up Week 10	n	2	n	8	8	10
		Mean	39.50	0.50	40.63	0.13	40.40
		SD	0.707	4.950	3.739	3.871	3.340
		Median	39.50	0.50	39.50	-0.50	39.50
		Q1	39.00	-3.00	37.50	-2.00	38.00
		Q3	40.00	4.00	43.50	1.50	42.00
		Min	39.0	-3.0	37.0	-5.0	37.0
		Max	40.0	4.0	47.0	8.0	47.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Albumin (g/L)	Follow-up Week 12	n 3	3	n 2	2	5	5
	Mean	41.33	-0.67	38.00	-2.50	40.00	-1.40
	SD	1.155	6.110	4.243	3.536	2.915	4.775
	Median	42.00	-2.00	38.00	-2.50	41.00	-2.00
	Q1	40.00	-6.00	35.00	-5.00	40.00	-5.00
	Q3	42.00	6.00	41.00	0.00	42.00	0.00
	Min	40.0	-6.0	35.0	-5.0	35.0	-6.0
	Max	42.0	6.0	41.0	0.0	42.0	6.0
	Follow-up Month 6	n 3	3	n 3	3	6	6
	Mean	36.33	-0.33	40.00	2.00	38.17	0.83
	SD	4.726	3.786	1.000	2.000	3.656	2.994
	Median	38.00	-2.00	40.00	2.00	39.50	1.00
	Q1	31.00	-3.00	39.00	0.00	38.00	-2.00
	Q3	40.00	4.00	41.00	4.00	40.00	4.00
	Min	31.0	-3.0	39.0	0.0	31.0	-3.0
	Max	40.0	4.0	41.0	4.0	41.0	4.0
	Follow-up Month 9	n 2	2	n 1	1	3	3
	Mean	41.00	-0.50	34.00	-5.00	38.67	-2.00
	SD	0.000	0.707	NE	NE	4.041	2.646
	Median	41.00	-0.50	34.00	-5.00	41.00	-1.00
	Q1	41.00	-1.00	34.00	-5.00	34.00	-5.00
	Q3	41.00	0.00	34.00	-5.00	41.00	0.00
	Min	41.0	-1.0	34.0	-5.0	34.0	-5.0
	Max	41.0	0.0	34.0	-5.0	41.0	0.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Albumin (g/L)	Follow-up Month 12	n	1	1	1	2	2
	Mean	40.00	-2.00	34.00	-8.00	37.00	-5.00
	SD	NE	NE	NE	NE	4.243	4.243
	Median	40.00	-2.00	34.00	-8.00	37.00	-5.00
	Q1	40.00	-2.00	34.00	-8.00	34.00	-8.00
	Q3	40.00	-2.00	34.00	-8.00	40.00	-2.00
	Min	40.0	-2.0	34.0	-8.0	34.0	-8.0
	Max	40.0	-2.0	34.0	-8.0	40.0	-2.0
	Follow-up Month 15	n	2	0	0	2	2
	Mean	39.50	-2.00	39.50	0.707	39.50	-2.00
	SD	0.707	1.414	0.707	1.414	0.707	1.414
	Median	39.50	-2.00	39.50	0.707	39.50	-2.00
	Q1	39.00	-3.00	39.00	0.707	39.00	-3.00
	Q3	40.00	-1.00	40.00	0.707	40.00	-1.00
	Min	39.0	-3.0	39.0	0.707	39.0	-3.0
	Max	40.0	-1.0	40.0	0.707	40.0	-1.0
	Follow-up Month 18	n	1	0	0	1	1
	Mean	39.00	-3.00	39.00	39.00	39.00	-3.00
	SD	NE	NE	NE	NE	NE	NE
	Median	39.00	-3.00	39.00	39.00	39.00	-3.00
	Q1	39.00	-3.00	39.00	39.00	39.00	-3.00
	Q3	39.00	-3.00	39.00	39.00	39.00	-3.00
	Min	39.0	-3.0	39.0	39.0	39.0	-3.0
	Max	39.0	-3.0	39.0	39.0	39.0	-3.0

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value	Change
Potassium (mmol/L)	Baseline	n	23		41			64	
		Mean	4.37		4.35			4.35	
		SD	0.440		0.470			0.456	
		Median	4.40		4.30			4.35	
		Q1	4.10		4.10			4.10	
		Q3	4.60		4.50			4.60	
		Min	3.2		3.4			3.2	
		Max	5.1		5.6			5.6	
	Week 2	n	17	17	36	36	53	53	
		Mean	4.68	0.32	4.45	0.13	4.53	0.19	
		SD	0.490	0.647	0.499	0.459	0.503	0.528	
		Median	4.70	0.20	4.35	0.10	4.50	0.20	
		Q1	4.40	-0.10	4.20	-0.10	4.20	-0.10	
		Q3	5.00	0.80	4.75	0.40	4.80	0.50	
		Min	3.7	-0.1	3.5	-1.1	3.5	-1.1	
		Max	5.4	1.6	6.0	1.1	6.0	1.6	
	Week 4	n	17	17	36	36	53	53	
		Mean	4.52	0.15	4.32	-0.03	4.38	0.03	
		SD	0.323	0.495	0.496	0.486	0.454	0.492	
		Median	4.60	0.10	4.30	0.00	4.40	0.00	
		Q1	4.20	-0.20	4.05	-0.30	4.10	-0.30	
		Q3	4.70	0.40	4.65	0.30	4.70	0.30	
		Min	3.9	-0.5	3.4	-1.2	3.4	-1.2	
		Max	5.1	1.4	5.6	0.7	5.6	1.4	

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Potassium (mmol/L)	Week 6	n	18	34	34	52	52
		Mean	4.61	0.27	4.38	0.01	4.46
		SD	0.440	0.545	0.405	0.485	0.427
		Median	4.65	0.20	4.45	0.10	4.50
		Q1	4.20	-0.20	4.20	-0.30	4.20
		Q3	5.00	0.70	4.70	0.30	4.80
		Min	3.6	-0.6	3.5	-1.0	3.5
		Max	5.3	1.4	5.0	0.9	5.3
	Week 8	n	13	26	26	39	39
		Mean	4.39	0.04	4.46	0.08	4.44
		SD	0.563	0.659	0.466	0.433	0.494
		Median	4.40	0.20	4.50	0.10	4.50
		Q1	4.20	-0.30	4.10	-0.10	4.10
		Q3	4.50	0.30	4.70	0.30	4.70
		Min	3.5	-1.0	3.6	-1.0	3.5
		Max	5.8	1.3	5.4	1.1	5.8
	Week 10	n	14	23	23	37	37
		Mean	4.57	0.29	4.30	0.01	4.41
		SD	0.476	0.481	0.579	0.480	0.551
		Median	4.45	0.15	4.20	0.00	4.40
		Q1	4.40	0.00	3.90	-0.30	4.00
		Q3	4.90	0.70	4.60	0.20	4.60
		Min	3.7	-0.3	3.3	-1.0	3.3
		Max	5.5	1.2	5.9	1.0	5.9

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Potassium (mmol/L)	Week 12	n	12	20	20	32	32
		Mean	4.50	0.12	4.36	0.03	0.06
		SD	0.527	0.641	0.562	0.480	0.538
		Median	4.40	0.10	4.35	0.05	0.05
		Q1	4.10	-0.45	3.90	-0.25	-0.30
		Q3	4.85	0.55	4.80	0.30	0.45
		Min	3.8	-0.7	3.3	-1.0	-1.0
		Max	5.5	1.3	5.4	1.0	1.3
	Week 14	n	13	22	22	35	35
		Mean	4.68	0.40	4.44	0.10	0.21
		SD	0.510	0.619	0.547	0.529	0.539
		Median	4.80	0.30	4.35	0.20	0.20
		Q1	4.50	0.10	4.10	-0.10	-0.10
		Q3	4.90	0.80	4.80	0.30	0.60
		Min	3.6	-0.9	3.5	-1.3	-1.3
		Max	5.4	1.3	5.7	1.0	1.3
	Week 16	n	12	17	17	29	29
		Mean	4.39	0.12	4.42	0.08	0.10
		SD	0.483	0.646	0.485	0.433	0.476
		Median	4.25	0.10	4.40	0.10	0.10
		Q1	4.05	-0.30	4.20	-0.10	-0.20
		Q3	4.65	0.20	4.70	0.40	0.40
		Min	3.8	-0.7	3.6	-0.8	-0.8
		Max	5.4	1.6	5.6	0.8	1.6

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Potassium (mmol/L)	Week 18	n	8	8	14	14	22
		Mean	4.49	0.26	4.41	0.01	4.44
		SD	0.309	0.663	0.564	0.467	0.480
		Median	4.60	0.25	4.45	0.05	4.50
		Q1	4.30	-0.15	3.90	-0.20	4.00
		Q3	4.70	0.75	4.90	0.20	4.80
		Min	3.9	-0.8	3.6	-0.7	3.6
		Max	4.8	1.2	5.2	0.8	5.2
	Week 20	n	8	8	15	15	23
		Mean	4.80	0.39	4.27	-0.02	4.45
		SD	0.404	0.629	0.403	0.489	0.472
		Median	4.70	0.30	4.20	0.20	4.40
		Q1	4.45	-0.10	4.00	-0.50	4.10
		Q3	5.10	0.85	4.60	0.30	4.80
		Min	4.4	-0.4	3.6	-1.0	3.6
		Max	5.5	1.4	5.0	0.6	5.5
	Week 22	n	8	8	14	14	22
		Mean	4.43	0.15	4.51	0.16	4.48
		SD	0.282	0.593	0.502	0.420	0.429
		Median	4.55	0.20	4.55	0.10	4.55
		Q1	4.25	-0.25	4.10	-0.10	4.10
		Q3	4.60	0.60	4.90	0.40	4.70
		Min	3.9	-0.8	3.7	-0.5	3.7
		Max	4.7	0.9	5.3	1.0	5.3

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Potassium (mmol/L)	Week 24	n	8	8	8	16	16
		Mean	4.75	0.45	4.35	0.06	4.55
		SD	0.438	0.481	0.578	0.490	0.537
		Median	4.90	0.50	4.35	0.00	4.45
		Q1	4.50	0.40	4.15	-0.10	4.25
		Q3	5.00	0.65	4.45	0.50	4.95
		Min	3.9	-0.6	3.4	-0.9	3.4
		Max	5.3	1.1	5.5	0.6	5.5
	Week 26	n	3	3	3	6	6
		Mean	4.23	-0.23	4.27	0.13	4.25
		SD	0.473	0.404	0.208	0.153	0.327
		Median	4.40	-0.30	4.20	0.10	4.30
		Q1	3.70	-0.60	4.10	0.00	4.10
		Q3	4.60	0.20	4.50	0.30	4.50
		Min	3.7	-0.6	4.1	0.0	3.7
		Max	4.6	0.2	4.5	0.3	4.6
	Week 28	n	1	1	2	3	3
		Mean	4.10	0.30	4.25	0.00	4.20
		SD	NE	NE	0.212	0.000	0.173
		Median	4.10	0.30	4.25	0.00	4.10
		Q1	4.10	0.30	4.10	0.00	4.10
		Q3	4.10	0.30	4.40	0.00	4.40
		Min	4.1	0.3	4.1	0.0	4.1
		Max	4.1	0.3	4.4	0.0	4.4

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall				
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value	Change
Potassium (mmol/L)	Week 30	n	0	0	1	1	1	1	1	1
		Mean			4.00	-0.10	4.00	4.00	-0.10	
		SD			NE	NE	NE	NE	NE	
		Median			4.00	-0.10	4.00	4.00	-0.10	
		Q1			4.00	-0.10	4.00	4.00	-0.10	
		Q3			4.00	-0.10	4.00	4.00	-0.10	
		Min			4.0	-0.1	4.0	4.0	-0.1	
		Max			4.0	-0.1	4.0	4.0	-0.1	
	Week 32	n	0	0	1	1	1	1	1	1
		Mean			4.10	0.00	4.10	4.10	0.00	
		SD			NE	NE	NE	NE	NE	
		Median			4.10	0.00	4.10	4.10	0.00	
		Q1			4.10	0.00	4.10	4.10	0.00	
		Q3			4.10	0.00	4.10	4.10	0.00	
		Min			4.1	0.0	4.1	4.1	0.0	
		Max			4.1	0.0	4.1	4.1	0.0	
	Week 34	n	0	0	1	1	1	1	1	1
		Mean			4.10	0.00	4.10	4.10	0.00	
		SD			NE	NE	NE	NE	NE	
		Median			4.10	0.00	4.10	4.10	0.00	
		Q1			4.10	0.00	4.10	4.10	0.00	
		Q3			4.10	0.00	4.10	4.10	0.00	
		Min			4.1	0.0	4.1	4.1	0.0	
		Max			4.1	0.0	4.1	4.1	0.0	

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall		
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value
Potassium (mmol/L)	Follow-up Week 2	n	17	17	23	23	40	40
		Mean	4.67	0.30	4.40	0.03	4.51	0.15
		SD	0.513	0.501	0.427	0.484	0.479	0.503
		Median	4.60	0.30	4.30	0.10	4.45	0.20
		Q1	4.30	0.10	4.10	-0.40	4.10	-0.20
		Q3	5.00	0.70	4.80	0.40	4.90	0.50
		Min	3.9	-0.7	3.7	-0.9	3.7	-0.9
		Max	5.6	1.0	5.2	0.8	5.6	1.0
	Follow-up Week 4	n	11	11	21	21	32	32
		Mean	4.70	0.16	4.45	0.09	4.53	0.11
Potassium (mmol/L)		SD	0.562	0.631	0.427	0.403	0.484	0.484
		Median	4.70	0.40	4.40	0.10	4.50	0.10
		Q1	4.30	-0.40	4.10	-0.10	4.15	-0.20
		Q3	5.10	0.70	4.70	0.30	4.95	0.50
		Min	3.8	-0.8	3.8	-0.8	3.8	-0.8
		Max	5.6	1.0	5.1	0.8	5.6	1.0
	Follow-up Week 6	n	10	10	16	16	26	26
		Mean	4.64	0.16	4.38	-0.04	4.48	0.03
		SD	0.384	0.433	0.796	0.689	0.671	0.602
		Median	4.65	0.10	4.40	0.00	4.50	0.10

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Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Potassium (mmol/L)	Follow-up Week 8	n	6	8	8	14	14
	Mean	4.53	0.08	4.45	0.05	4.49	0.06
	SD	0.489	0.655	0.558	0.652	0.511	0.628
	Median	4.45	-0.15	4.40	0.05	4.45	0.00
	Q1	4.40	-0.40	4.00	-0.30	4.20	-0.40
	Q3	4.60	0.30	5.00	0.35	4.90	0.30
	Min	3.9	-0.4	3.7	-1.0	3.7	-1.0
	Max	5.4	1.3	5.1	1.2	5.4	1.3
	Follow-up Week 10	n	3	9	9	12	12
	Mean	4.90	0.33	4.44	0.20	4.56	0.23
	SD	0.436	0.493	0.513	0.570	0.518	0.533
	Median	4.70	0.10	4.30	0.30	4.55	0.25
	Q1	4.60	0.00	4.20	0.00	4.25	0.00
	Q3	5.40	0.90	4.60	0.30	4.85	0.55
	Min	4.6	0.0	3.7	-0.8	3.7	-0.8
	Max	5.4	0.9	5.4	1.1	5.4	1.1
	Follow-up Week 12	n	4	2	2	6	6
	Mean	4.95	0.25	4.25	0.00	4.72	0.17
	SD	0.332	0.569	0.495	0.707	0.496	0.557
	Median	4.85	0.25	4.25	0.00	4.70	0.25
	Q1	4.70	-0.20	3.90	-0.50	4.60	-0.40
	Q3	5.20	0.70	4.60	0.50	5.00	0.50
	Min	4.7	-0.4	3.9	-0.5	3.9	-0.5
	Max	5.4	0.9	4.6	0.5	5.4	0.9

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Potassium (mmol/L)	Follow-up Month 6	n	3	n	3	n	6
	Mean	4.43	-0.20	4.60	0.20	4.52	0.00
	SD	0.473	0.265	0.458	0.557	0.426	0.447
	Median	4.60	-0.30	4.70	0.10	4.65	-0.10
	Q1	3.90	-0.40	4.10	-0.30	4.10	-0.30
	Q3	4.80	0.10	5.00	0.80	4.80	0.10
	Min	3.9	-0.4	4.1	-0.3	3.9	-0.4
	Max	4.8	0.1	5.0	0.8	5.0	0.8
	Follow-up Month 9	n	2	n	1	n	3
	Mean	4.90	0.40	4.10	0.10	4.63	0.30
	SD	0.849	0.566	NE	NE	0.757	0.436
	Median	4.90	0.40	4.10	0.10	4.30	0.10
	Q1	4.30	0.00	4.10	0.10	4.10	0.00
	Q3	5.50	0.80	4.10	0.10	5.50	0.80
	Min	4.3	0.0	4.1	0.1	4.1	0.0
	Max	5.5	0.8	4.1	0.1	5.5	0.8
	Follow-up Month 12	n	1	n	1	n	2
	Mean	5.40	0.70	4.60	-0.10	5.00	0.30
	SD	NE	NE	NE	NE	0.566	0.566
	Median	5.40	0.70	4.60	-0.10	5.00	0.30
	Q1	5.40	0.70	4.60	-0.10	4.60	-0.10
	Q3	5.40	0.70	4.60	-0.10	5.40	0.70
	Min	5.4	0.7	4.6	-0.1	4.6	-0.1
	Max	5.4	0.7	4.6	-0.1	5.4	0.7

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Table 14.3.2.1
Chemistry Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value
Potassium (mmol/L)	Follow-up Month 15	n	2	2	0	0	0	2	2
	Mean	4.10		-0.40				4.10	-0.40
	SD	0.566		0.283				0.566	0.283
	Median	4.10		-0.40				4.10	-0.40
	Q1	3.70		-0.60				3.70	-0.60
	Q3	4.50		-0.20				4.50	-0.20
	Min	3.7		-0.6				3.7	-0.6
	Max	4.5		-0.2				4.5	-0.2
	Follow-up Month 18	n	1	1	0	0	0	1	1
	Mean	4.60		-0.10				4.60	-0.10

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value	Change
Basophils (10E9/L)	Baseline	n	21		40			61	
		Mean	0.0271		0.0252			0.0259	
		SD	0.02411		0.01880			0.02060	
		Median	0.0200		0.0300			0.0200	
		Q1	0.0100		0.0100			0.0100	
		Q3	0.0300		0.0400			0.0400	
		Min	0.000		0.000			0.000	
		Max	0.100		0.060			0.100	
	Week 2	n	13	13	35	35	48	48	
		Mean	0.0146	-0.0146	0.0209	-0.0051	0.0192	-0.0076	
		SD	0.02066	0.02025	0.02582	0.02637	0.02448	0.02502	
		Median	0.0000	-0.0100	0.0200	-0.0100	0.0100	-0.0100	
		Q1	0.0000	-0.0200	0.0000	-0.0200	0.0000	-0.0200	
		Q3	0.0200	0.0000	0.0300	0.0100	0.0300	0.0000	
		Min	0.000	-0.050	0.000	-0.052	0.000	-0.052	
		Max	0.060	0.010	0.100	0.100	0.100	0.100	
	Week 4	n	15	15	33	33	48	48	
		Mean	0.0173	-0.0120	0.0270	0.0016	0.0240	-0.0026	
		SD	0.02404	0.02808	0.03046	0.02875	0.02871	0.02895	
		Median	0.0000	-0.0100	0.0200	0.0000	0.0150	0.0000	
		Q1	0.0000	-0.0200	0.0000	-0.0100	0.0000	-0.0100	
		Q3	0.0400	0.0100	0.0400	0.0100	0.0400	0.0100	
		Min	0.000	-0.100	0.000	-0.052	0.000	-0.100	
		Max	0.070	0.010	0.100	0.100	0.100	0.100	

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Basophils (10E9/L)	Week 6	n	15	35	35	50	50
		Mean	0.0100	-0.0167	0.0166	-0.0091	0.0146
		SD	0.01254	0.02870	0.02057	0.01787	0.01865
		Median	0.0100	-0.0100	0.0100	-0.0100	0.0100
		Q1	0.0000	-0.0200	0.0000	-0.0200	0.0000
		Q3	0.0200	0.0000	0.0300	0.0000	0.0200
		Min	0.000	-0.100	0.000	-0.052	0.000
		Max	0.040	0.010	0.100	0.040	0.100
	Week 8	n	11	24	24	35	35
		Mean	0.0155	-0.0127	0.0233	-0.0047	0.0209
		SD	0.01508	0.03133	0.02259	0.02020	0.02063
		Median	0.0100	0.0000	0.0200	0.0000	0.0200
		Q1	0.0000	-0.0200	0.0100	-0.0200	0.0100
		Q3	0.0300	0.0000	0.0300	0.0000	0.0300
		Min	0.000	-0.100	0.000	-0.052	0.000
		Max	0.040	0.010	0.100	0.040	0.100
	Week 10	n	13	22	22	35	35
		Mean	0.0146	-0.0138	0.0255	-0.0017	0.0214
		SD	0.01664	0.02902	0.04206	0.04358	0.03491
		Median	0.0100	0.0000	0.0200	-0.0100	0.0100
		Q1	0.0000	-0.0200	0.0000	-0.0200	0.0000
		Q3	0.0200	0.0000	0.0300	0.0000	0.0300
		Min	0.000	-0.100	0.000	-0.050	0.000
		Max	0.060	0.010	0.200	0.180	0.200

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Basophils (10E9/L)	Week 12	n	11	20	20	31	31
		Mean	0.0100	-0.0091	0.0235	-0.0026	0.0187
		SD	0.01000	0.01446	0.02477	0.02206	0.02156
		Median	0.0100	0.0000	0.0200	-0.0050	0.0100
		Q1	0.0000	-0.0200	0.0000	-0.0150	0.0000
		Q3	0.0200	0.0000	0.0300	0.0000	0.0300
		Min	0.000	-0.040	0.000	-0.030	0.000
		Max	0.030	0.010	0.080	0.070	0.080
	Week 14	n	12	21	21	33	33
		Mean	0.0117	-0.0175	0.0138	-0.0122	0.0130
		SD	0.01801	0.02927	0.01465	0.01339	0.01571
		Median	0.0050	-0.0100	0.0100	-0.0100	0.0100
		Q1	0.0000	-0.0200	0.0000	-0.0200	0.0000
		Q3	0.0150	0.0000	0.0300	0.0000	0.0300
		Min	0.000	-0.100	0.000	-0.052	0.000
		Max	0.060	0.010	0.040	0.000	0.060
	Week 16	n	10	10	17	27	27
		Mean	0.0120	-0.0140	0.0200	-0.0116	0.0170
		SD	0.01033	0.03169	0.02525	0.02172	0.02109
		Median	0.0100	-0.0100	0.0100	-0.0100	0.0100
		Q1	0.0000	-0.0100	0.0000	-0.0200	0.0000
		Q3	0.0200	0.0000	0.0300	0.0000	0.0300
		Min	0.000	-0.100	0.000	-0.052	0.000
		Max	0.030	0.010	0.100	0.040	0.100

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Basophils (10E9/L)	Week 18	n	8	8	14	-0.0026	22
		Mean	0.0125	-0.0238	0.0257	0.0209	-0.0103
		SD	0.01488	0.03335	0.02738	0.02408	0.02959
		Median	0.0100	-0.0100	0.0250	0.0000	-0.0100
		Q1	0.0000	-0.0300	0.0000	-0.0100	-0.0200
		Q3	0.0200	-0.0050	0.0400	0.0000	0.0300
		Min	0.000	-0.100	0.000	-0.052	0.000
		Max	0.040	0.000	0.100	0.050	0.100
	Week 20	n	9	9	15	-0.0115	24
		Mean	0.0156	-0.0067	0.0147	0.0150	-0.0097
		SD	0.01424	0.01803	0.02356	0.02022	0.02271
		Median	0.0200	0.0000	0.0000	-0.0100	-0.0100
		Q1	0.0000	-0.0200	0.0000	-0.0300	-0.0200
		Q3	0.0200	0.0000	0.0300	0.0000	0.0250
		Min	0.000	-0.040	0.000	-0.052	0.000
		Max	0.040	0.020	0.080	0.050	0.080
	Week 22	n	8	8	15	-0.0080	23
		Mean	0.0088	-0.0263	0.0200	0.0161	-0.0143
		SD	0.01126	0.03204	0.02646	0.01897	0.02271
		Median	0.0050	-0.0150	0.0100	0.0000	-0.0100
		Q1	0.0000	-0.0300	0.0000	-0.0200	-0.0200
		Q3	0.0150	-0.0100	0.0300	0.0000	0.0300
		Min	0.000	-0.100	0.000	-0.040	0.000
		Max	0.030	0.000	0.100	0.040	0.100

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Basophils (10E9/L)	Week 24	n	8	n	6	n	14
		Mean	0.0163	Value	0.0250	Value	0.0200
		SD	0.01408	Change	-0.0175	Change	-0.0082
		Median	0.0150	Value	0.01643	Value	0.01519
		Q1	0.0050	Change	-0.02375	Change	0.02569
		Q3	0.0250	Value	0.0250	Value	-0.0025
		Min	0.000	Change	-0.0150	Value	0.0200
		Max	0.040	Value	0.0200	Change	-0.0100
				0.0200	Change	0.0100	-0.0100
				-0.0100	Value	0.0100	-0.0200
				0.0100	Change	0.0100	-0.0000
				0.0300	Value	0.0300	0.0000
				0.000	Change	0.000	-0.070
				0.050	Value	0.050	0.050
					Change	Change	Change
	Week 26	n	3	n	3	n	6
		Mean	0.0167	Value	0.0100	Value	0.0133
		SD	0.0057	Change	0.0000	Change	-0.0067
		Median	0.0200	Value	0.0100	Value	0.00816
		Q1	0.0100	Change	0.0000	Value	0.01211
		Q3	0.0200	Value	0.0100	Change	0.0000
		Min	0.010	Change	-0.0000	Value	0.0150
		Max	0.020	Value	0.0200	Change	-0.0300
				0.000	Value	0.0200	0.0000
				0.020	Change	0.020	-0.030
					Value	0.020	0.000
					Change	0.020	0.000
	Week 28	n	1	n	2	n	3
		Mean	0.0100	Value	0.0250	Value	0.0200
		SD	NE	Change	-0.0100	Change	-0.0133
		Median	0.0100	Value	0.03536	Value	0.02646
		Q1	0.0100	Change	-0.0100	Value	0.01528
		Q3	0.0100	Value	0.0250	Change	0.0100
		Min	0.010	Change	-0.0100	Value	-0.0100
		Max	0.010	Value	0.000	Change	-0.0300
				0.050	Value	0.0500	0.0000
				0.000	Change	0.000	-0.030
				0.000	Value	0.000	0.000

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Basophils (10E9/L)	Week 30	n	0	n	1	1	1
		Mean		0.0000	-0.0300	0.0000	-0.0300
		SD		NE	NE	NE	NE
		Median		0.0000	-0.0300	0.0000	-0.0300
		Q1		0.0000	-0.0300	0.0000	-0.0300
		Q3		0.0000	-0.0300	0.0000	-0.0300
		Min		0.000	-0.030	0.000	-0.030
		Max		0.000	-0.030	0.000	-0.030
	Week 32	n	0	n	1	1	1
		Mean		0.0000	-0.0300	0.0000	-0.0300
		SD		NE	NE	NE	NE
		Median		0.0000	-0.0300	0.0000	-0.0300
		Q1		0.0000	-0.0300	0.0000	-0.0300
		Q3		0.0000	-0.0300	0.0000	-0.0300
		Min		0.000	-0.030	0.000	-0.030
		Max		0.000	-0.030	0.000	-0.030
	Week 34	n	0	n	1	1	1
		Mean		0.0000	-0.0300	0.0000	-0.0300
		SD		NE	NE	NE	NE
		Median		0.0000	-0.0300	0.0000	-0.0300
		Q1		0.0000	-0.0300	0.0000	-0.0300
		Q3		0.0000	-0.0300	0.0000	-0.0300
		Min		0.000	-0.030	0.000	-0.030
		Max		0.000	-0.030	0.000	-0.030

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Basophils (10E9/L)	Follow-up Week 2	n	14	21	21	35	35
		Mean	0.0071	-0.0129	0.0205	-0.0025	0.0151
		SD	0.01139	0.01267	0.02397	0.02998	0.02077
		Median	0.0000	-0.0150	0.0200	0.0000	0.0100
		Q1	0.0000	-0.0200	0.0000	-0.0200	0.0000
		Q3	0.0100	0.0000	0.0300	0.0000	0.0200
		Min	0.000	-0.040	0.000	-0.052	0.000
		Max	0.030	0.010	0.100	0.100	0.100
	Follow-up Week 4	n	10	19	19	29	29
		Mean	0.0160	-0.0050	0.0237	-0.0050	0.0210
		SD	0.02797	0.03274	0.02140	0.02267	0.02366
		Median	0.0050	-0.0150	0.0200	-0.0050	0.0100
		Q1	0.0000	-0.0200	0.0100	-0.0200	0.0000
		Q3	0.0200	0.0000	0.0400	0.0000	0.0300
		Min	0.000	-0.040	0.000	-0.030	0.000
		Max	0.090	0.080	0.060	0.060	0.090
	Follow-up Week 6	n	9	14	14	23	23
		Mean	0.0100	-0.0122	0.0221	0.0004	0.0174
		SD	0.01323	0.01481	0.02940	0.02590	0.02472
		Median	0.0000	-0.0100	0.0100	-0.0050	0.0100
		Q1	0.0000	-0.0200	0.0000	-0.0200	0.0000
		Q3	0.0200	0.0000	0.0300	0.0100	0.0300
		Min	0.000	-0.040	0.000	-0.040	0.000
		Max	0.030	0.010	0.100	0.060	0.100

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Basophils (10E9/L)	Follow-up Week 8	n	7	7	8	8	15
		Mean	0.0043	-0.0157	0.0238	-0.0025	0.0147
		SD	0.00787	0.01618	0.01847	0.02375	0.01727
		Median	0.0000	-0.0200	0.0300	-0.0100	0.0100
		Q1	0.0000	-0.0300	0.0050	-0.0200	0.0000
		Q3	0.0100	0.0000	0.0350	0.0050	0.0300
		Min	0.000	-0.040	0.000	-0.020	0.000
		Max	0.020	0.000	0.050	0.050	0.050
	Follow-up Week 10	n	4	4	9	9	13
		Mean	0.1375	0.1125	0.0156	-0.0050	0.0531
		SD	0.24226	0.24541	0.02186	0.01414	0.13573
		Median	0.0250	0.0000	0.0000	0.0000	0.0100
		Q1	0.0050	-0.0150	0.0000	-0.0100	0.0000
		Q3	0.2700	0.2400	0.0300	0.0000	0.0400
		Min	0.000	-0.030	0.000	-0.030	0.000
		Max	0.500	0.480	0.050	0.015	0.500
	Follow-up Week 12	n	4	4	2	2	6
		Mean	0.0300	0.0100	0.0600	0.0100	0.0400
		SD	0.02582	0.02708	0.05657	0.04243	0.03578
		Median	0.0300	0.0000	0.0600	0.0100	0.0300
		Q1	0.0100	-0.0050	0.0200	-0.0200	0.0200
		Q3	0.0500	0.0250	0.1000	0.0400	0.0600
		Min	0.000	-0.010	0.020	-0.020	0.000
		Max	0.060	0.050	0.100	0.040	0.100

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Basophils (10E9/L)	Follow-up Month 6	n	3	n	3	n	6
	Mean	0.0100	0.0000	0.0000	-0.0133	0.0050	-0.0067
	SD	0.00000	0.01000	0.00000	0.01528	0.00548	0.01366
	Median	0.0100	0.0000	0.0000	-0.0100	0.0050	-0.0050
	Q1	0.0100	-0.0100	0.0000	-0.0300	0.0000	-0.0100
	Q3	0.0100	0.0100	0.0000	0.0000	0.0100	0.0000
	Min	0.010	-0.010	0.000	-0.030	0.000	-0.030
	Max	0.010	0.010	0.000	0.000	0.010	0.010
	Follow-up Month 9	n	2	n	1	n	3
	Mean	0.0100	-0.0050	0.0300	-0.0050	0.0167	-0.0050
	SD	0.00000	0.00707	NE	NE	0.01155	0.00500
	Median	0.0100	-0.0050	0.0300	-0.0050	0.0100	-0.0050
	Q1	0.0100	-0.0100	0.0300	-0.0050	0.0100	-0.0100
	Q3	0.0100	0.0000	0.0300	-0.0050	0.0300	0.0000
	Min	0.010	-0.010	0.030	-0.005	0.010	-0.010
	Max	0.010	0.000	0.030	-0.005	0.030	0.000
	Follow-up Month 12	n	1	n	1	n	2
	Mean	0.0100	0.0000	0.0400	-0.0100	0.0250	-0.0050
	SD	NE	NE	NE	NE	0.02121	0.00707
	Median	0.0100	0.0000	0.0400	-0.0100	0.0250	-0.0050
	Q1	0.0100	0.0000	0.0400	-0.0100	0.0100	-0.0100
	Q3	0.0100	0.0000	0.0400	-0.0100	0.0400	0.0000
	Min	0.010	0.000	0.040	-0.010	0.010	-0.010
	Max	0.010	0.000	0.040	-0.010	0.040	0.000

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall		
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value
Basophils (10E9/L)	Follow-up Month 15	n	2	2	1	1	3	3
		Mean	0.0100	-0.0050	0.0000	-0.0600	0.0067	-0.0233
		SD	0.00000	0.00707	NE	NE	0.00577	0.03215
		Median	0.0100	-0.0050	0.0000	-0.0600	0.0100	-0.0100
		Q1	0.0100	-0.0100	0.0000	-0.0600	0.0000	-0.0600
		Q3	0.0100	0.0000	0.0000	-0.0600	0.0100	0.0000
		Min	0.010	-0.010	0.000	-0.060	0.000	-0.060
		Max	0.010	0.000	0.000	-0.060	0.010	0.000
	Follow-up Month 18	n	1	1	0	0	1	1
		Mean	0.0100	0.0000	NE	NE	0.0100	0.0000
		SD	NE	NE	NE	NE	NE	NE
		Median	0.0100	0.0000	0.0000	0.0100	0.0100	0.0000
		Q1	0.0100	0.0000	0.0000	0.0100	0.0100	0.0000
		Q3	0.0100	0.0000	0.0000	0.0100	0.0100	0.0000
		Min	0.010	0.000	0.000	0.010	0.010	0.000
		Max	0.010	0.000	0.000	0.010	0.010	0.000
Eosinophils (10E9/L)	Baseline	n	22	40	62	62	62	62
		Mean	0.1386	0.1552	0.1493	0.1493	0.1493	0.1493
		SD	0.16985	0.14853	0.15524	0.15524	0.15524	0.15524
		Median	0.0950	0.1200	0.1050	0.1050	0.1050	0.1050
		Q1	0.0300	0.0700	0.0400	0.0400	0.0400	0.0400
		Q3	0.1900	0.1950	0.1900	0.1900	0.1900	0.1900
		Min	0.000	0.000	0.000	0.000	0.000	0.000
		Max	0.780	0.630	0.780	0.780	0.780	0.780

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Eosinophils (10E9/L)	Week 2	n	14	35	35	49	49
		Mean	0.1000	-0.0443	0.1243	-0.0437	0.1173
		SD	0.11388	0.10566	0.10051	0.12462	0.10388
		Median	0.0850	-0.0200	0.1000	-0.0100	0.1000
		Q1	0.0500	-0.0500	0.0600	-0.0600	0.0600
		Q3	0.1000	0.0300	0.1800	0.0200	0.1400
		Min	0.000	-0.310	0.000	-0.390	0.000
		Max	0.470	0.060	0.500	0.160	0.500
	Week 4	n	16	33	33	49	49
		Mean	0.1356	-0.0113	0.1358	-0.0336	0.1357
		SD	0.11972	0.11575	0.11742	0.11241	0.11692
		Median	0.1000	-0.0050	0.1000	-0.0100	0.1000
		Q1	0.0650	-0.0700	0.0800	-0.0600	0.0800
		Q3	0.1850	0.0450	0.1900	0.0200	0.1900
		Min	0.000	-0.300	0.000	-0.370	0.000
		Max	0.480	0.200	0.580	0.200	0.580
	Week 6	n	16	35	35	51	51
		Mean	0.1000	-0.0031	0.1463	-0.0180	0.1318
		SD	0.08278	0.08340	0.11988	0.12860	0.11090
		Median	0.0900	-0.0050	0.1000	0.0000	0.1000
		Q1	0.0400	-0.0450	0.1000	-0.0800	0.0700
		Q3	0.1400	0.0450	0.1800	0.0500	0.1800
		Min	0.000	-0.180	0.000	-0.350	0.000
		Max	0.300	0.200	0.500	0.290	0.500

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value	Change
Eosinophils (10E9/L) Week 8									
n		12	12		24	24		36	36
Mean		0.1025	-0.0075		0.1996	0.0295		0.1672	0.0171
SD		0.06797	0.08519		0.41688	0.41100		0.34323	0.33704
Median		0.0800	0.0100		0.0900	-0.0200		0.0900	0.0000
Q1		0.0500	-0.0300		0.0550	-0.1050		0.0500	-0.0850
Q3		0.1550	0.0450		0.1800	0.0150		0.1700	0.0200
Min		0.030	-0.200		0.000	-0.300		0.000	-0.300
Max		0.230	0.100		2.100	1.880		2.100	1.880
Week 10									
n		13	13		22	22		35	35
Mean		0.1108	-0.0477		0.1382	-0.0259		0.1280	-0.0340
SD		0.14291	0.11882		0.15234	0.18457		0.14739	0.16168
Median		0.0900	-0.0200		0.1000	-0.0100		0.1000	-0.0100
Q1		0.0400	-0.0500		0.0600	-0.1100		0.0400	-0.1100
Q3		0.1000	0.0200		0.1700	0.0200		0.1300	0.0200
Min		0.000	-0.290		0.000	-0.460		0.000	-0.460
Max		0.550	0.100		0.680	0.580		0.680	0.580
Week 12									
n		11	11		20	20		31	31
Mean		0.0945	0.0055		0.1900	0.0419		0.1561	0.0289
SD		0.05222	0.08347		0.22773	0.16006		0.18950	0.13734
Median		0.0900	0.0200		0.1000	0.0000		0.1000	0.0100
Q1		0.0600	-0.0300		0.0350	-0.0650		0.0500	-0.0500
Q3		0.1000	0.0600		0.2400	0.0950		0.2000	0.0900
Min		0.020	-0.200		0.000	-0.130		0.000	-0.200
Max		0.200	0.100		0.780	0.600		0.780	0.600

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Eosinophils (10E9/L)	Week 14	n	13	21	21	34	34
		Mean	0.1462	-0.0185	0.1862	0.0515	0.1709
		SD	0.14286	0.11718	0.25533	0.18403	0.21754
		Median	0.1000	0.0000	0.1100	0.0000	0.1000
		Q1	0.0600	-0.0900	0.0800	-0.0400	0.0600
		Q3	0.1800	0.0600	0.1900	0.0200	0.1900
		Min	0.000	-0.240	0.000	-0.160	0.000
		Max	0.540	0.200	1.120	0.530	1.120
	Week 16	n	11	17	17	28	28
		Mean	0.0800	-0.0136	0.1488	0.0218	0.1218
		SD	0.04000	0.06903	0.16530	0.16025	0.13400
		Median	0.0900	0.0100	0.1000	0.0000	0.0950
		Q1	0.0400	-0.0400	0.0700	-0.0400	0.0600
		Q3	0.1000	0.0300	0.2000	0.0100	0.1700
		Min	0.020	-0.200	0.000	-0.120	0.000
		Max	0.160	0.050	0.700	0.600	0.700
	Week 18	n	8	14	14	22	22
		Mean	0.0750	-0.0425	0.1700	0.0358	0.1355
		SD	0.04721	0.08714	0.23658	0.19410	0.19385
		Median	0.0700	-0.0350	0.1200	-0.0100	0.1000
		Q1	0.0350	-0.0900	0.0000	-0.0400	0.0300
		Q3	0.1000	0.0250	0.1800	0.0200	0.1500
		Min	0.030	-0.200	0.000	-0.093	0.000
		Max	0.160	0.060	0.900	0.690	0.900

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Eosinophils (10E9/L)	Week 20	n	9	9	15	15	24
		Mean	0.0867	0.0011	0.1360	-0.0129	0.1175
		SD	0.05362	0.04936	0.12275	0.17451	0.10377
		Median	0.0700	0.0000	0.1000	0.0000	0.1000
		Q1	0.0700	-0.0200	0.0600	-0.0400	0.0600
		Q3	0.1000	0.0300	0.1700	0.0600	0.1600
		Min	0.030	-0.080	0.000	-0.530	0.000
		Max	0.210	0.070	0.400	0.300	0.400
	Week 22	n	8	8	15	15	23
		Mean	0.0950	-0.0275	0.1560	-0.0100	0.1348
		SD	0.06047	0.08137	0.15009	0.18272	0.12799
		Median	0.1000	-0.0050	0.1100	0.0000	0.1000
		Q1	0.0600	-0.0600	0.0900	-0.0900	0.0900
		Q3	0.1000	0.0250	0.2200	0.0600	0.2000
		Min	0.020	-0.200	0.000	-0.500	0.000
		Max	0.220	0.060	0.600	0.390	0.600
	Week 24	n	8	8	7	7	15
		Mean	0.1063	-0.0100	0.0991	-0.0103	0.1029
		SD	0.06632	0.07368	0.05445	0.05094	0.05902
		Median	0.1000	0.0050	0.1100	0.0000	0.1100
		Q1	0.0550	-0.0750	0.0600	-0.0700	0.0600
		Q3	0.1550	0.0450	0.1300	0.0340	0.1300
		Min	0.020	-0.120	0.000	-0.080	0.000
		Max	0.210	0.090	0.170	0.060	0.210

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Eosinophils (10E9/L)							
Week 26	n	3	3	3	3	6	6
	Mean	0.0700	0.0100	0.0867	-0.0233	0.0783	-0.0067
	SD	0.03000	0.04359	0.01528	0.02317	0.02317	0.03445
	Median	0.0700	-0.0100	0.0900	-0.0200	0.0800	-0.0150
	Q1	0.0400	-0.0200	0.0700	-0.0400	0.0700	-0.0200
	Q3	0.1000	0.0600	0.1000	-0.0100	0.1000	-0.0100
	Min	0.040	-0.020	0.070	-0.040	0.040	-0.040
	Max	0.100	0.060	0.100	-0.010	0.100	0.060
Week 28	n	1	1	2	2	3	3
	Mean	0.0200	-0.0600	0.0850	-0.0100	0.0633	-0.0267
	SD	NE	NE	0.02121	0.04243	0.04041	0.04163
	Median	0.0200	-0.0600	0.0850	-0.0100	0.0700	-0.0400
	Q1	0.0200	-0.0600	0.0700	-0.0400	0.0200	-0.0600
	Q3	0.0200	-0.0600	0.1000	0.0200	0.1000	0.0200
	Min	0.020	-0.060	0.070	-0.040	0.020	-0.060
	Max	0.020	-0.060	0.100	0.020	0.100	0.020
Week 30	n	0	0	1	1	1	1
	Mean	NE	NE	0.1000	-0.0400	0.1000	-0.0400
	SD	NE	NE	NE	NE	NE	NE
	Median	0.1000	-0.0400	0.1000	-0.0400	0.1000	-0.0400
	Q1	0.1000	-0.0400	0.1000	-0.0400	0.1000	-0.0400
	Q3	0.1000	-0.0400	0.1000	-0.0400	0.1000	-0.0400
	Min	0.100	-0.040	0.100	-0.040	0.100	-0.040
	Max	0.100	-0.040	0.100	-0.040	0.100	-0.040

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall		
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value	
Eosinophils (10E9/L)	Week 32	n	0	1	1	1	1	
		Mean		0.1000	-0.0400	0.1000	-0.0400	
		SD		NE	NE	NE	NE	
		Median		0.1000	-0.0400	0.1000	-0.0400	
		Q1		0.1000	-0.0400	0.1000	-0.0400	
		Q3		0.1000	-0.0400	0.1000	-0.0400	
		Min		0.100	-0.040	0.100	-0.040	
		Max		0.100	-0.040	0.100	-0.040	
	Week 34	n	0	1	1	1	1	
		Mean		0.1000	-0.0400	0.1000	-0.0400	
		SD		NE	NE	NE	NE	
		Median		0.1000	-0.0400	0.1000	-0.0400	
		Q1		0.1000	-0.0400	0.1000	-0.0400	
		Q3		0.1000	-0.0400	0.1000	-0.0400	
		Min		0.100	-0.040	0.100	-0.040	
		Max		0.100	-0.040	0.100	-0.040	
	Follow-up Week 2	n	15	15	21	36	36	
		Mean	0.0940	-0.0107	0.1010	-0.0516	0.0981	-0.0345
		SD	0.08441	0.05922	0.08037	0.12990	0.08095	0.10707
		Median	0.1000	-0.0100	0.1000	-0.0200	0.1000	-0.0200
		Q1	0.0200	-0.0200	0.0500	-0.0700	0.0200	-0.0550
		Q3	0.1500	0.0200	0.1300	0.0000	0.1400	0.0135
		Min	0.000	-0.160	0.000	-0.530	0.000	-0.530
		Max	0.280	0.100	0.300	0.100	0.300	0.100

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Eosinophils (10E9/L)	Follow-up Week 4	n	10	10	19	19	29
		Mean	0.0750	-0.0200	0.1384	-0.0556	0.1166
		SD	0.06433	0.05578	0.10976	0.16535	0.10008
		Median	0.0750	-0.0150	0.1300	-0.0200	0.1000
		Q1	0.0200	-0.0400	0.0400	-0.1000	0.0300
		Q3	0.1000	0.0000	0.2500	0.0600	0.1500
		Min	0.000	-0.150	0.000	-0.570	0.000
		Max	0.200	0.060	0.320	0.110	0.320
	Follow-up Week 6	n	10	10	15	15	25
		Mean	0.0930	-0.0290	0.1453	-0.0071	0.1244
		SD	0.07987	0.08452	0.15524	0.15593	0.13090
		Median	0.1000	-0.0150	0.1000	0.0000	0.1000
		Q1	0.0300	-0.1200	0.0100	-0.0900	0.0300
		Q3	0.1000	0.0000	0.2200	0.0600	0.1900
		Min	0.000	-0.150	0.000	-0.400	0.000
		Max	0.290	0.120	0.500	0.290	0.500
	Follow-up Week 8	n	7	7	8	8	15
		Mean	0.0557	-0.0643	0.1725	0.0038	0.1180
		SD	0.04962	0.12475	0.15636	0.17087	0.13007
		Median	0.0800	-0.0400	0.1350	-0.0300	0.1000
		Q1	0.0000	-0.2200	0.0650	-0.0900	0.0100
		Q3	0.1000	0.0600	0.2350	0.0150	0.1700
		Min	0.000	-0.250	0.010	-0.160	0.000
		Max	0.100	0.060	0.500	0.400	0.500

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Eosinophils (10E9/L)	Follow-up Week 10	n	4	4	9	9	13
	Mean	0.2675	0.1100	0.1178	-0.0073	0.1638	0.0288
	SD	0.30956	0.40620	0.07759	0.07706	0.18205	0.21997
	Median	0.1750	-0.0150	0.1000	0.0000	0.1000	-0.0100
	Q1	0.0450	-0.1250	0.0800	-0.0400	0.0700	-0.0400
	Q3	0.4900	0.3450	0.1800	0.0500	0.2000	0.0500
	Min	0.020	-0.230	0.000	-0.130	0.000	-0.230
	Max	0.700	0.700	0.250	0.100	0.700	0.700
Eosinophils (10E9/L)	Follow-up Week 12	n	4	4	2	2	6
	Mean	0.1275	0.0250	0.3300	0.1600	0.1950	0.0700
	SD	0.14315	0.08660	0.24042	0.18385	0.18652	0.12696
	Median	0.0950	0.0350	0.3300	0.1600	0.1550	0.0350
	Q1	0.0200	-0.0300	0.1600	0.0300	0.0400	0.0300
	Q3	0.2350	0.0800	0.5000	0.2900	0.3200	0.1200
	Min	0.000	-0.090	0.160	0.030	0.000	-0.090
	Max	0.320	0.120	0.500	0.290	0.500	0.290
Eosinophils (10E9/L)	Follow-up Month 6	n	3	3	3	3	6
	Mean	0.0567	-0.0033	0.1000	-0.0300	0.0783	-0.0167
	SD	0.04509	0.03215	0.10000	0.07000	0.07333	0.05086
	Median	0.0600	0.0100	0.1000	0.0000	0.0800	0.0050
	Q1	0.0100	-0.0400	0.0000	-0.1100	0.0100	-0.0400
	Q3	0.1000	0.0200	0.2000	0.0200	0.1000	0.0200
	Min	0.010	-0.040	0.000	-0.110	0.000	-0.110
	Max	0.100	0.020	0.200	0.020	0.200	0.020

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Eosinophils (10E9/L)							
Follow-up Month 9	n	2	2	1	1	3	3
Mean	Value	0.0550	Change	-0.0150	0.0900	-0.0960	0.0667
SD	Value	0.03536	Change	0.00707	NE	NE	0.03215
Median	Value	0.0550	Change	-0.0150	0.0900	-0.0960	0.0800
Q1	Value	0.0300	Change	-0.0200	0.0900	-0.0960	0.0300
Q3	Value	0.0800	Change	-0.0100	0.0900	-0.0960	0.0900
Min	Value	0.030	Change	-0.020	0.090	-0.096	0.030
Max	Value	0.080	Change	-0.010	0.090	-0.096	0.090
Follow-up Month 12	n	1	1	1	1	2	2
Mean	Value	0.0700	Change	-0.0200	0.3100	-0.1100	0.1900
SD	Value	NE	Change	NE	NE	NE	0.16971
Median	Value	0.0700	Change	-0.0200	0.3100	-0.1100	0.1900
Q1	Value	0.0700	Change	-0.0200	0.3100	-0.1100	0.0700
Q3	Value	0.0700	Change	-0.0200	0.3100	-0.1100	0.3100
Min	Value	0.070	Change	-0.020	0.310	-0.110	0.070
Max	Value	0.070	Change	-0.020	0.310	-0.110	0.310
Follow-up Month 15	n	2	2	1	1	3	3
Mean	Value	0.0400	Change	-0.0300	0.3000	0.0900	0.1267
SD	Value	0.02828	Change	0.00000	NE	NE	0.15144
Median	Value	0.0400	Change	-0.0300	0.3000	0.0900	0.0600
Q1	Value	0.0200	Change	-0.0300	0.3000	0.0900	0.0200
Q3	Value	0.0600	Change	-0.0300	0.3000	0.0900	0.3000
Min	Value	0.020	Change	-0.030	0.300	0.090	0.020
Max	Value	0.060	Change	-0.030	0.300	0.090	0.300

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value
Eosinophils (10E9/L) Follow-up Month 18	n	1	1	0	0	1	1	0.0500	-0.0400
	Mean	0.0500	-0.0400	NE	NE	NE	NE	NE	NE
	SD	NE	NE	NE	NE	NE	NE	NE	NE
	Median	0.0500	-0.0400	0.0500	-0.0400	0.0500	-0.0400	0.0500	-0.0400
	Q1	0.0500	-0.0400	0.0500	-0.0400	0.0500	-0.0400	0.0500	-0.0400
	Q3	0.0500	-0.0400	0.0500	-0.0400	0.0500	-0.0400	0.0500	-0.0400
	Min	0.050	-0.040	0.050	-0.040	0.050	-0.040	0.050	-0.040
	Max	0.050	-0.040	0.050	-0.040	0.050	-0.040	0.050	-0.040
Ery. Mean Corpuscular Hemoglobin (pg)	Baseline	n	22	38	60	60	60	30.54	2.270
	Mean	30.47	30.57	30.57	30.57	30.57	30.57	30.45	30.45
	SD	2.082	2.698	2.698	2.698	2.698	2.698	2.270	2.270
	Median	30.35	30.70	30.70	30.70	30.70	30.70	29.25	29.25
	Q1	29.10	29.30	29.30	29.30	29.30	29.30	31.95	31.95
	Q3	31.30	32.40	32.40	32.40	32.40	32.40	24.1	24.1
	Min	27.0	24.1	24.1	24.1	24.1	24.1	35.0	35.0
	Max	35.0	34.9	34.9	34.9	34.9	34.9		
	Week 2	n	17	34	51	51	51		
	Mean	30.36	-0.02	30.75	-0.03	30.62	-0.03		
	SD	2.060	1.045	2.320	0.779	2.223	0.866		
	Median	29.90	0.00	30.65	-0.05	30.20	0.00		
	Q1	28.70	-0.80	29.30	-0.50	29.00	-0.60		
	Q3	31.50	0.70	32.20	0.50	32.20	0.70		
	Min	27.3	-2.6	25.8	-1.4	25.8	-2.6		
	Max	34.5	1.4	35.6	2.4	35.6	2.4		

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Ery. Mean Corpuscular Hemoglobin (pg)	Week 4	n 16	16	32	32	48	48
		Mean 30.59	0.25	30.33	-0.13	30.42	0.00
		SD 2.078	1.058	2.237	0.736	2.166	0.864
		Median 30.00	0.00	30.50	-0.15	30.30	-0.10
		Q1 29.00	-0.55	29.20	-0.65	29.15	-0.60
		Q3 32.00	1.05	32.00	0.35	32.00	0.55
		Min 28.4	-1.3	23.5	-1.5	23.5	-1.5
		Max 34.3	2.1	34.1	1.4	34.3	2.1
	Week 6	n 17	17	34	34	51	51
		Mean 30.54	0.15	30.82	0.15	30.72	0.15
		SD 1.959	1.239	2.102	1.380	2.040	1.322
		Median 30.60	0.20	31.00	0.15	30.90	0.20
		Q1 28.90	-0.50	29.70	-0.60	29.40	-0.50
		Q3 31.40	1.00	32.20	0.60	32.00	0.80
		Min 28.1	-3.0	26.7	-2.6	26.7	-3.0
		Max 34.9	1.9	35.9	5.0	35.9	5.0
	Week 8	n 14	14	23	23	37	37
		Mean 30.50	0.32	30.56	0.18	30.54	0.24
		SD 2.340	1.127	2.187	1.464	2.214	1.332
		Median 30.15	0.10	30.80	0.10	30.40	0.10
		Q1 28.60	-0.20	29.50	-0.50	29.20	-0.30
		Q3 32.00	1.10	32.50	1.20	32.10	1.10
		Min 27.8	-2.2	25.2	-2.6	25.2	-2.6
		Max 35.8	2.7	34.3	3.9	35.8	3.9

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Ery. Mean Corpuscular Hemoglobin (pg)	Week 10	n	14	23	23	37	37
		Mean	30.51	30.78	0.55	30.68	0.39
		SD	2.183	1.439	2.037	2.286	1.823
		Median	30.10	0.55	0.50	30.90	0.50
		Q1	29.00	-0.90	-0.90	29.20	-0.90
		Q3	32.00	0.80	1.30	31.90	1.10
		Min	27.4	-3.1	-3.1	25.9	-3.1
		Max	34.8	2.3	5.4	36.3	5.4
		n	12	20	20	32	32
		Mean	30.68	0.50	0.62	30.98	0.57
	Week 12	SD	2.033	1.436	2.202	2.364	1.925
		Median	30.70	0.90	0.35	31.10	0.55
		Q1	29.10	0.05	-0.75	29.25	-0.50
		Q3	32.40	1.35	0.95	32.70	1.15
		Min	27.4	-3.1	-2.9	25.3	-3.1
		Max	34.0	2.2	6.3	37.2	6.3
		n	13	21	21	34	34
		Mean	30.85	0.42	0.53	30.88	0.49
		SD	2.096	1.485	2.244	2.319	1.964
		Median	30.10	0.80	0.30	30.60	0.60
	Week 14	Q1	29.30	-0.60	-0.70	29.10	-0.70
		Q3	32.70	1.30	0.90	32.70	1.10
		Min	27.4	-3.1	-4.1	24.9	-4.1
		Max	33.9	2.6	5.7	36.6	5.7

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Ery. Mean Corpuscular Hemoglobin (pg)	Week 16	n 12	12	n 17	17	29	29
		Mean 30.87	0.83	Mean 30.71	0.76	30.78	0.79
		SD 2.277	1.701	SD 2.959	2.225	2.655	1.992
		Median 31.00	1.30	Median 30.60	0.10	30.60	0.90
		Q1 29.35	0.90	Q1 29.30	-0.60	29.30	-0.10
		Q3 32.70	1.60	Q3 33.00	1.10	32.80	1.50
		Min 26.2	-4.3	Min 24.3	-2.2	24.3	-4.3
		Max 33.8	2.1	Max 37.4	6.5	37.4	6.5
	Week 18	n 8	8	n 14	14	22	22
		Mean 31.23	1.61	Mean 31.40	0.84	31.34	1.12
		SD 1.677	0.958	SD 2.469	2.191	2.172	1.850
		Median 31.15	1.95	Median 30.95	0.75	30.95	1.00
		Q1 29.95	0.90	Q1 29.80	-0.30	29.80	0.40
		Q3 32.55	2.25	Q3 33.20	1.80	32.60	2.20
		Min 28.9	-0.1	Min 27.1	-3.8	27.1	-3.8
		Max 33.6	2.8	Max 36.5	5.6	36.5	5.6
	Week 20	n 9	9	n 15	15	24	24
		Mean 31.67	1.63	Mean 31.38	0.48	31.49	0.91
		SD 1.506	0.841	SD 3.135	2.438	2.606	2.047
		Median 32.00	1.80	Median 31.80	0.10	31.90	1.40
		Q1 30.40	1.50	Q1 30.10	-0.60	30.25	-0.05
		Q3 32.70	2.30	Q3 33.00	1.60	32.90	2.10
		Min 29.5	-0.1	Min 23.9	-4.3	23.9	-4.3
		Max 33.6	2.5	Max 36.6	5.7	36.6	5.7

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Ery. Mean Corpuscular Hemoglobin (pg)	Week 22	n	8	15	15	23	23
		Mean	31.79	1.78	31.08	0.43	31.33
		SD	1.916	0.916	3.039	2.014	2.677
		Median	31.70	1.75	31.30	0.40	31.30
		Q1	29.95	1.50	29.30	-0.70	29.90
		Q3	33.50	2.35	33.20	1.70	33.20
		Min	29.6	0.0	23.5	-3.0	23.5
		Max	34.4	3.0	35.7	4.8	35.7
	Week 24	n	8	7	7	15	15
		Mean	31.35	1.88	30.81	1.34	31.10
		SD	1.500	0.933	2.662	1.793	2.058
		Median	31.10	1.90	30.20	0.80	30.30
		Q1	29.95	1.80	29.00	0.10	29.70
		Q3	32.90	2.45	32.90	2.50	32.90
		Min	29.7	-0.2	28.1	-0.2	28.1
		Max	33.2	2.9	35.8	4.9	35.8
	Week 26	n	3	3	3	6	6
		Mean	31.87	2.00	31.77	2.20	31.82
		SD	2.272	0.721	4.537	3.081	3.210
		Median	31.50	1.80	31.10	1.00	31.30
		Q1	29.80	1.40	27.60	-0.10	29.80
		Q3	34.30	2.80	36.60	5.70	34.30
		Min	29.8	1.4	27.6	-0.1	27.6
		Max	34.3	2.8	36.6	5.7	36.6

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Ery. Mean Corpuscular Hemoglobin (pg)	Week 28	n	1	1	2	2	3
		Mean	31.70	0.60	32.45	0.85	32.20
		SD	NE	NE	1.485	0.636	1.136
		Median	31.70	0.60	32.45	0.85	31.70
		Q1	31.70	0.60	31.40	0.40	31.40
		Q3	31.70	0.60	33.50	1.30	33.50
		Min	31.7	0.6	31.4	0.4	31.4
		Max	31.7	0.6	33.5	1.3	33.5
	Week 30	n	0	0	1	1	1
		Mean	31.40	NE	31.40	1.30	31.40
		SD	NE	NE	NE	NE	NE
		Median	31.40	1.30	31.40	1.30	31.40
		Q1	31.40	1.30	31.40	1.30	31.40
		Q3	31.40	1.30	31.40	1.30	31.40
		Min	31.4	1.3	31.4	1.3	31.4
		Max	31.4	1.3	31.4	1.3	31.4
	Week 32	n	0	0	1	1	1
		Mean	31.50	NE	31.50	1.40	31.50
		SD	NE	NE	NE	NE	NE
		Median	31.50	1.40	31.50	1.40	31.50
		Q1	31.50	1.40	31.50	1.40	31.50
		Q3	31.50	1.40	31.50	1.40	31.50
		Min	31.5	1.4	31.5	1.4	31.5
		Max	31.5	1.4	31.5	1.4	31.5

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall				
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value	Change
Ery. Mean Corpuscular Hemoglobin (pg)	Week 34	n	0	0	1	1	1	1	1	1
		Mean			31.50	1.40	31.50	1.40	31.50	1.40
		SD			NE	NE	NE	NE	NE	NE
		Median			31.50	1.40	31.50	1.40	31.50	1.40
		Q1			31.50	1.40	31.50	1.40	31.50	1.40
		Q3			31.50	1.40	31.50	1.40	31.50	1.40
		Min			31.5	1.4	31.5	1.4	31.5	1.4
		Max			31.5	1.4	31.5	1.4	31.5	1.4
	Follow-up Week 2	n	16	16	21	21	37	37	37	37
		Mean	31.40	0.88	30.88	0.28	31.10	0.54	31.10	0.54
		SD	2.469	1.526	2.534	1.895	2.485	1.749	2.485	1.749
		Median	31.10	1.15	31.10	-0.10	31.10	0.50	31.10	0.50
		Q1	29.80	0.15	30.10	-0.50	30.00	-0.30	30.00	-0.30
		Q3	32.95	1.80	32.40	0.80	32.60	1.40	32.60	1.40
		Min	26.9	-3.6	23.8	-2.7	23.8	-3.6	23.8	-3.6
		Max	35.6	2.7	36.2	5.3	36.2	5.3	36.2	5.3
	Follow-up Week 4	n	10	10	19	19	29	29	29	29
		Mean	31.42	0.70	31.31	0.59	31.34	0.63	31.34	0.63
		SD	2.802	2.030	2.081	2.010	2.304	1.981	2.304	1.981
		Median	30.90	1.20	31.50	0.30	31.30	0.90	31.30	0.90
		Q1	29.30	0.20	30.20	-1.00	29.90	-0.30	29.90	-0.30
		Q3	34.40	2.00	32.40	1.50	32.70	1.60	32.70	1.60
		Min	27.6	-4.3	27.1	-3.0	27.1	-4.3	27.1	-4.3
		Max	35.2	2.9	36.4	5.5	36.4	5.5	36.4	5.5

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Ery. Mean Corpuscular Hemoglobin (pg)	Follow-up Week 6	n	10	16	16	26	26
		Mean	31.08	0.45	31.01	0.19	31.03
		SD	1.974	1.227	2.838	2.152	2.497
		Median	30.75	0.20	31.15	0.50	31.15
		Q1	29.30	-0.10	29.55	-1.35	29.40
		Q3	32.90	1.70	32.75	1.25	32.90
		Min	28.7	-1.4	23.6	-2.9	23.6
		Max	34.6	2.3	36.9	6.0	36.9
	Follow-up Week 8	n	7	8	8	15	15
		Mean	31.76	1.77	33.03	0.96	32.43
Follow-up Week 10		SD	2.771	1.141	2.197	2.544	2.476
		Median	31.60	1.90	33.10	1.05	32.60
		Q1	29.50	1.10	31.00	0.05	30.50
		Q3	34.60	2.50	34.55	1.70	34.60
		Min	27.7	-0.3	30.4	-3.5	27.7
		Max	35.4	3.3	36.5	5.6	36.5
		n	4	9	9	13	13
		Mean	33.40	1.30	31.13	0.58	31.83
		SD	2.741	0.876	3.621	2.257	3.436
		Median	33.30	1.25	31.10	0.70	31.80

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Ery. Mean	Follow-up Week 12	n	5	5	2	2	7
Corpuscular Hemoglobin (pg)		Mean	33.12	0.82	31.20	-0.70	32.57
		SD	3.371	2.556	0.141	0.707	2.908
		Median	32.10	0.80	31.20	-0.70	31.30
		Q1	30.50	0.60	31.10	-1.20	30.50
		Q3	35.20	2.30	31.30	-0.20	35.20
		Min	29.9	-3.2	31.1	-1.2	29.9
		Max	37.9	3.6	31.3	-0.2	37.9
	Follow-up Month 6	n	3	3	3	3	6
		Mean	31.20	0.80	32.23	2.90	31.72
		SD	3.032	1.000	4.272	2.862	3.361
		Median	29.50	0.80	30.50	1.40	30.00
		Q1	29.40	-0.20	29.10	1.10	29.40
		Q3	34.70	1.80	37.10	6.20	34.70
		Min	29.4	-0.2	29.1	1.1	29.1
		Max	34.7	1.8	37.1	6.2	37.1
	Follow-up Month 9	n	2	2	1	1	3
		Mean	30.25	-1.05	29.00	0.40	29.83
		SD	6.293	4.031	NE	NE	4.508
		Median	30.25	-1.05	29.00	0.40	29.00
		Q1	25.80	-3.90	29.00	0.40	25.80
		Q3	34.70	1.80	29.00	0.40	34.70
		Min	25.8	-3.9	29.0	0.4	25.8
		Max	34.7	1.8	29.0	0.4	34.7

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Ery. Mean	Follow-up Month 12	n	1	1	1	2	2
Corpuscular Hemoglobin (pg)	Mean	35.30	2.40	34.30	2.90	34.80	2.65
	SD	NE	NE	NE	NE	0.707	0.354
	Median	35.30	2.40	34.30	2.90	34.80	2.65
	Q1	35.30	2.40	34.30	2.90	34.30	2.40
	Q3	35.30	2.40	34.30	2.90	35.30	2.90
	Min	35.3	2.4	34.3	2.9	34.3	2.4
	Max	35.3	2.4	34.3	2.9	35.3	2.9
	Follow-up Month 15	n	2	2	1	3	3
	Mean	34.40	3.10	30.00	-1.30	32.93	1.63
	SD	0.849	1.414	NE	NE	2.610	2.730
	Median	34.40	3.10	30.00	-1.30	33.80	2.10
	Q1	33.80	2.10	30.00	-1.30	30.00	-1.30
	Q3	35.00	4.10	30.00	-1.30	35.00	4.10
	Min	33.8	2.1	30.0	-1.3	30.0	-1.3
	Max	35.0	4.1	30.0	-1.3	35.0	4.1
	Follow-up Month 18	n	1	1	0	1	1
	Mean	34.50	1.60	NE	NE	34.50	1.60
	SD	NE	NE	NE	NE	NE	NE
	Median	34.50	1.60	NE	NE	34.50	1.60
	Q1	34.50	1.60	NE	NE	34.50	1.60
	Q3	34.50	1.60	NE	NE	34.50	1.60
	Min	34.5	1.6	NE	NE	34.5	1.6
	Max	34.5	1.6	NE	NE	34.5	1.6

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Ery. Mean Corpuscular Volume (fL)	Baseline	n	23		40		63
		Mean	93.48	92.37		92.77	
		SD	5.050	6.110		5.729	
		Median	94.00	92.20		93.10	
		Q1	88.80	88.35		88.40	
		Q3	96.10	97.00		96.80	
		Min	84.0	75.3		75.3	
		Max	103.0	105.9		105.9	
	Week 2	n	18	35	35	53	53
		Mean	93.03	-0.35	93.14	0.06	93.10
Week 4		SD	4.931	2.377	5.211	2.806	5.070
		Median	93.50	-0.70	93.90	0.30	93.50
		Q1	90.30	-2.00	89.10	-1.30	89.40
		Q3	95.70	0.10	97.00	1.70	96.00
		Min	84.0	-3.70	82.2	-6.3	82.2
		Max	102.2	6.0	103.0	7.9	103.0
	Week 4	n	17	35	35	52	52
		Mean	92.59	-0.71	90.56	-1.55	91.23
		SD	5.131	2.564	11.514	11.139	9.878
		Median	92.30	-1.10	92.20	0.00	92.25

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Ery. Mean Corpuscular Volume (fL)	Week 6	n	18	35	35	53	53
		Mean	93.12	92.79	0.23	92.90	0.06
		SD	5.253	5.352	4.328	5.270	3.838
		Median	94.00	93.00	0.80	93.10	-0.30
		Q1	88.50	88.70	-3.00	88.70	-2.00
		Q3	95.00	97.00	2.80	96.00	1.80
	Week 8	Min	84.0	80.3	-9.9	80.3	-9.9
		Max	102.0	105.0	12.6	105.0	12.6
		n	14	24	24	38	38
		Mean	91.74	92.25	0.54	92.06	-0.13
Week 10	Week 8	SD	5.014	5.664	3.633	5.370	3.350
		Median	92.20	92.70	0.95	92.35	-0.10
		Q1	87.00	89.80	-1.65	89.40	-2.00
		Q3	94.30	95.60	2.60	95.20	1.80
		Min	84.0	77.8	-9.0	77.8	-9.0
		Max	99.8	103.9	9.0	103.9	9.0
	Week 10	n	14	23	23	37	37
		Mean	92.57	93.12	1.07	92.91	0.44
		SD	5.722	5.725	5.760	5.651	4.794
		Median	93.30	93.60	1.40	93.30	-0.20

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Ery. Mean Corpuscular Volume (fL)	Week 12	n	12	21	21	33	33
		Mean	92.37	-0.54	94.06	1.27	93.44
		SD	5.080	3.928	6.126	5.919	5.745
		Median	92.90	-1.40	94.80	0.00	93.50
		Q1	90.35	-2.60	91.50	-1.20	91.50
		Q3	95.10	2.05	97.00	2.10	96.70
		Min	83.0	-8.5	80.0	-10.8	80.0
		Max	100.0	5.8	107.5	17.2	107.5
		n	13	22	22	35	35
		Mean	93.50	0.22	93.23	1.18	93.33
	Week 14	SD	6.947	4.169	6.238	5.934	6.410
		Median	94.40	0.30	93.35	0.05	93.70
		Q1	88.00	-1.80	89.00	-1.50	89.00
		Q3	95.60	3.60	97.00	3.60	97.00
		Min	82.5	-9.8	79.1	-13.4	79.1
		Max	106.6	6.5	106.4	14.0	106.6
		n	12	17	17	29	29
		Mean	92.71	0.53	92.96	1.98	92.86
		SD	5.445	3.743	7.095	5.192	6.358
		Median	94.40	1.10	94.00	2.10	94.30
	Week 16	Q1	87.50	-0.35	88.90	-2.00	88.00
		Q3	95.90	2.55	96.70	3.30	96.60
		Min	83.3	-9.0	76.9	-4.3	76.9
		Max	101.2	6.5	105.8	13.4	105.8

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Ery. Mean Corpuscular Volume (fL)	Week 18	n	8	8	14	14	22
		Mean	93.48	2.25	93.23	1.01	93.32
		SD	4.481	2.938	5.582	6.024	5.099
		Median	93.80	1.55	91.50	1.20	93.20
		Q1	90.50	0.10	90.10	0.30	90.10
		Q3	95.50	4.70	97.90	4.00	95.80
		Min	87.0	-1.2	83.3	-16.0	83.3
		Max	101.2	6.5	103.2	10.8	103.2
		n	9	9	15	15	24
		Mean	96.14	2.70	93.99	-0.23	94.80
	Week 20	SD	3.995	3.203	7.546	5.670	6.430
		Median	95.70	0.80	96.00	0.00	95.85
		Q1	94.80	0.60	90.40	-3.40	90.80
		Q3	97.30	4.00	98.00	3.30	97.65
		Min	88.0	-0.6	76.2	-13.8	76.2
		Max	101.7	8.5	106.0	9.2	106.0
		n	8	8	15	15	23
		Mean	95.55	3.10	93.23	0.39	94.04
		SD	5.331	2.996	7.066	4.799	6.488
		Median	96.00	2.20	93.00	0.70	94.30
	Week 22	Q1	91.65	1.30	90.40	-1.40	90.40
		Q3	99.15	5.65	99.00	2.60	99.00
		Min	88.0	-1.0	75.5	-10.4	75.5
		Max	102.8	7.5	103.9	11.5	103.9
		n	8	8	15	15	23
		Mean	95.55	3.10	93.23	0.39	94.04
		SD	5.331	2.996	7.066	4.799	6.488
		Median	96.00	2.20	93.00	0.70	94.30
		Q1	91.65	1.30	90.40	-1.40	90.40
		Q3	99.15	5.65	99.00	2.60	99.00
		Min	88.0	-1.0	75.5	-10.4	75.5
		Max	102.8	7.5	103.9	11.5	103.9

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Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Ery. Mean Corpuscular Volume (fL)	Week 24	n	8	n	7	Value	15
		Mean	94.86	Mean	92.76	3.47	93.88
		SD	3.718	SD	5.701	2.941	4.693
		Median	95.20	Median	92.40	3.00	93.50
		Q1	93.10	Q1	89.20	1.20	91.40
		Q3	96.80	Q3	98.30	5.10	97.20
	Week 26	Min	88.0	Min	84.0	0.4	84.0
		Max	100.7	Max	101.3	8.9	101.3
		n	3	n	3	Value	6
		Mean	95.47	Mean	93.03	3.93	94.25
Week 28	Week 26	SD	8.719	SD	9.050	5.036	8.059
		Median	94.80	Median	93.00	1.70	93.90
		Q1	87.10	Q1	84.00	0.40	87.10
		Q3	104.50	Q3	102.10	9.70	102.10
		Min	87.1	Min	84.0	0.4	84.0
		Max	104.5	Max	102.1	9.7	104.5
	Week 28	n	1	n	2	Value	3
		Mean	95.00	Mean	94.65	0.45	94.77
		SD	NE	SD	2.333	1.768	1.662
		Median	95.00	Median	94.65	0.45	95.00

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Ery. Mean Corpuscular Volume (fL)	Week 30	n	0	n	1	1	1
		Mean		94.00	2.70	94.00	2.70
		SD		NE	NE	NE	NE
		Median		94.00	2.70	94.00	2.70
		Q1		94.00	2.70	94.00	2.70
		Q3		94.00	2.70	94.00	2.70
		Min		94.0	2.7	94.0	2.7
		Max		94.0	2.7	94.0	2.7
		n	0	n	1	1	1
		Mean		95.00	3.70	95.00	3.70
	Week 32	SD		NE	NE	NE	NE
		Median		95.00	3.70	95.00	3.70
		Q1		95.00	3.70	95.00	3.70
		Q3		95.00	3.70	95.00	3.70
		Min		95.0	3.7	95.0	3.7
		Max		95.0	3.7	95.0	3.7
		n	0	n	1	1	1
		Mean		95.00	3.70	95.00	3.70
		SD		NE	NE	NE	NE
		Median		95.00	3.70	95.00	3.70
	Week 34	Q1		95.00	3.70	95.00	3.70
		Q3		95.00	3.70	95.00	3.70
		Min		95.0	3.7	95.0	3.7
		Max		95.0	3.7	95.0	3.7

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Ery. Mean Corpuscular Volume (fL)	Follow-up Week 2	n 17	17	n 22	22	39	39
		Mean 94.11	0.88	Mean 93.20	1.38	93.60	1.16
		SD 6.329	5.065	SD 6.360	4.873	6.279	4.898
		Median 94.00	0.30	Median 93.20	1.35	93.40	1.00
		Q1 91.00	-0.60	Q1 91.00	-1.60	91.00	-1.60
		Q3 98.00	3.00	Q3 97.00	5.10	97.50	3.80
		Min 80.5	-11.8	Min 75.1	-7.2	75.1	-11.8
		Max 103.9	10.0	Max 105.0	11.1	105.0	11.1
	Follow-up Week 4	n 10	10	n 20	20	30	30
		Mean 96.20	2.30	Mean 93.89	1.39	94.66	1.69
		SD 5.473	2.702	SD 4.856	4.398	5.097	3.889
		Median 96.65	2.10	Median 93.15	1.15	94.55	1.75
		Q1 94.10	-0.10	Q1 91.45	-1.25	91.80	-0.60
		Q3 101.40	3.30	Q3 97.65	4.20	97.80	3.80
		Min 87.0	-0.6	Min 84.0	-5.6	84.0	-5.6
		Max 103.5	8.6	Max 102.6	10.2	103.5	10.2
	Follow-up Week 6	n 10	10	n 16	16	26	26
		Mean 96.19	2.47	Mean 93.33	1.15	94.43	1.66
		SD 5.518	3.398	SD 6.081	4.430	5.931	4.045
		Median 96.55	2.50	Median 93.20	2.35	94.85	2.35
		Q1 94.00	0.90	Q1 90.35	-3.00	90.70	-1.40
		Q3 98.30	4.00	Q3 98.40	3.60	98.30	3.80
		Min 87.3	-2.6	Min 78.2	-6.8	78.2	-6.8
		Max 104.8	9.5	Max 102.9	10.5	104.8	10.5

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Ery. Mean Corpuscular Volume (fL)	Follow-up Week 8	n 7	7	n 8	8	Value 15	Value 15
		Mean 95.99	3.34	Mean 98.75	2.51	Mean 97.46	Mean 2.90
		SD 7.069	3.561	SD 6.135	4.852	SD 6.502	SD 4.170
		Median 94.30	2.90	Median 98.15	2.15	Median 96.30	Median 2.50
		Q1 89.00	0.70	Q1 94.50	0.20	Q1 94.00	Q1 0.70
		Q3 104.50	5.80	Q3 103.60	5.35	Q3 104.50	Q3 5.80
		Min 87.1	-2.2	Min 89.5	-5.6	Min 87.1	Min -5.6
		Max 105.5	8.7	Max 108.0	10.3	Max 108.0	Max 10.3
	Follow-up Week 10	n 4	4	n 9	9	Value 13	Value 13
		Mean 99.85	2.03	Mean 93.39	1.30	Mean 95.38	Mean 1.52
		SD 7.371	4.654	SD 7.862	4.680	SD 8.027	SD 4.487
		Median 100.30	2.15	Median 94.40	1.00	Median 95.80	Median 1.10
		Q1 93.70	-1.30	Q1 89.40	-3.20	Q1 91.60	Q1 -3.20
		Q3 106.00	5.35	Q3 98.90	2.70	Q3 99.70	Q3 3.20
		Min 91.6	-3.7	Min 77.3	-3.9	Min 77.3	Min -3.9
		Max 107.2	7.5	Max 103.0	10.6	Max 107.2	Max 10.6
	Follow-up Week 12	n 5	5	n 2	2	Value 7	Value 7
		Mean 98.86	0.66	Mean 93.40	-0.15	Mean 97.30	Mean 0.43
		SD 11.046	10.390	SD 4.525	7.142	SD 9.584	SD 8.979
		Median 97.90	2.40	Median 93.40	-0.15	Median 96.60	Median 2.40
		Q1 91.60	-3.70	Q1 90.20	-5.20	Q1 90.20	Q1 -5.20
		Q3 104.00	3.20	Q3 96.60	4.90	Q3 104.00	Q3 4.90
		Min 86.2	-13.5	Min 90.2	-5.2	Min 86.2	Min -13.5
		Max 114.6	14.9	Max 96.6	4.9	Max 114.6	Max 14.9

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Ery. Mean Corpuscular Volume (fL)	Follow-up Month 6	n	3	3	3	3	6
		Mean	97.87	1.33	94.80	7.03	96.33
		SD	6.104	1.201	9.704	5.894	7.443
		Median	97.60	1.40	89.50	5.30	94.75
		Q1	91.90	0.10	88.90	2.20	89.50
		Q3	104.10	2.50	106.00	13.60	104.10
		Min	91.9	0.1	88.9	2.2	88.9
		Max	104.1	2.5	106.0	13.6	106.0
	Follow-up Month 9	n	2	2	1	1	3
		Mean	94.35	-2.35	89.20	2.10	92.63
		SD	13.930	7.000	NE	NE	10.289
		Median	94.35	-2.35	89.20	2.10	89.20
		Q1	84.50	-7.30	89.20	2.10	84.50
		Q3	104.20	2.60	89.20	2.10	104.20
		Min	84.5	-7.3	89.2	2.1	84.5
		Max	104.2	2.6	89.2	2.1	104.2
	Follow-up Month 12	n	1	1	1	1	2
		Mean	105.30	3.70	103.40	6.60	104.35
		SD	NE	NE	NE	NE	1.344
		Median	105.30	3.70	103.40	6.60	104.35
		Q1	105.30	3.70	103.40	6.60	103.40
		Q3	105.30	3.70	103.40	6.60	105.30
		Min	105.3	3.7	103.4	6.6	103.4
		Max	105.3	3.7	103.4	6.6	105.3

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall		
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value
Ery. Mean Corpuscular Volume (fL)	Follow-up Month 15	n	2	2	1	1	3	3
		Mean	101.75	5.05	93.00	1.30	98.83	3.80
		SD	7.000	0.071	NE	NE	7.073	2.166
		Median	101.75	5.05	93.00	1.30	96.80	5.00
		Q1	96.80	5.00	93.00	1.30	93.00	1.30
		Q3	106.70	5.10	93.00	1.30	106.70	5.10
		Min	96.8	5.0	93.0	1.3	93.0	1.3
		Max	106.7	5.1	93.0	1.3	106.7	5.1
	Follow-up Month 18	n	1	1	0	0	1	1
		Mean	107.30	5.70	NE	NE	107.30	5.70
Erythrocytes Distribution Width (%)		SD	NE	NE	NE	NE	NE	NE
		Median	107.30	5.70	107.30	107.30	107.30	5.70
		Q1	107.30	5.70	107.30	107.30	107.30	5.70
		Q3	107.30	5.70	107.30	107.30	107.30	5.70
		Min	107.3	5.7	107.3	107.3	107.3	5.7
		Max	107.3	5.7	107.3	107.3	107.3	5.7
	Baseline	n	23	39	62	62	62	62
		Mean	14.50	14.48	14.49	14.49	14.49	14.49

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Erythrocytes	Week 2	n	18	35	35	53	53
Distribution Width (%)	Week 2	Mean	14.70	0.41	15.69	1.32	15.35
	SD	1.514	0.964	6.065	5.957	5.002	4.868
	Median	14.35	0.25	14.30	0.30	14.30	0.30
	Q1	13.60	-0.10	13.40	-0.30	13.40	-0.30
	Q3	15.90	0.80	15.80	1.30	15.80	1.10
	Min	12.5	-1.7	12.2	-3.9	12.2	-3.9
	Max	17.6	2.6	48.6	34.9	48.6	34.9
	Week 4	n	17	32	32	49	49
	SD	14.89	0.57	15.09	0.71	15.02	0.66
	Median	1.704	1.316	2.519	1.693	2.252	1.560
	Q1	14.90	0.30	14.15	0.50	14.40	0.40
	Q3	13.50	0.10	13.00	-0.25	13.00	-0.10
	Min	15.70	0.90	16.50	1.90	15.70	1.30
	Max	12.3	-1.9	12.3	-4.9	12.3	-4.9
	Week 6	n	18	33	33	51	51
	SD	15.03	0.73	15.25	0.72	15.17	0.72
	Median	1.408	1.011	2.771	1.979	2.366	1.689
	Q1	15.25	0.55	14.40	0.30	14.60	0.50
	Q3	13.80	0.20	13.40	-0.30	13.40	0.10
	Min	16.00	1.20	15.80	1.40	16.00	1.40
	Max	12.9	-1.1	12.2	-5.1	12.2	-5.1
			17.1	3.4	23.8	6.0	23.8

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Erythrocytes	Week 8	n	14	23	23	37	37
Distribution Width (%)	Week 8	Mean	15.24	0.85	16.72	2.32	16.16
	SD	1.369	1.394	7.668	7.515	6.094	5.978
	Median	15.10	0.95	14.50	0.30	14.80	0.40
	Q1	14.20	0.10	13.10	-0.80	13.50	-0.40
	Q3	16.10	1.80	17.60	2.80	16.10	2.00
	Min	13.2	-1.8	12.0	-1.5	12.0	-1.8
	Max	17.5	3.6	49.5	35.8	49.5	35.8
	Week 10	n	14	22	22	36	36
	SD	15.26	0.90	15.27	0.57	15.27	0.70
	Median	1.410	1.508	2.495	2.140	2.115	1.902
	Q1	15.10	0.60	14.80	0.80	15.00	0.80
	Q3	14.60	-0.20	13.10	-1.00	13.75	-0.40
	Min	14.60	2.20	16.30	1.80	16.20	1.95
	Max	13.1	-1.3	11.9	-4.7	11.9	-4.7
	Week 12	n	12	19	19	31	31
	SD	15.09	0.74	14.16	0.11	14.52	0.35
	Median	1.177	1.399	1.906	1.896	1.702	1.724
	Q1	14.70	0.60	13.60	0.50	14.10	0.50
	Q3	14.30	-0.30	12.90	-0.50	13.30	-0.30
	Min	15.75	2.00	15.80	1.20	15.80	1.60
	Max	13.6	-1.7	11.7	-4.5	11.7	-4.5
	Week 12	n	17.6	3.1	19.4	2.7	19.4

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Erythrocytes	Week 14	n	13	13	20	20	33
Distribution Width (%)	Week 14	Mean	15.05	0.74	14.19	-0.04	14.53
		SD	0.969	1.295	1.655	1.933	1.470
		Median	15.20	1.00	13.85	0.40	14.40
		Q1	14.40	0.00	12.85	-0.55	13.30
		Q3	15.70	1.40	15.80	1.20	15.70
		Min	13.2	-2.1	11.6	-5.1	11.6
		Max	16.4	2.8	17.4	2.8	17.4
	Week 16	n	12	12	16	16	28
		Mean	14.74	0.18	14.31	-0.27	14.49
		SD	1.289	1.549	1.728	2.146	1.544
		Median	15.05	0.45	14.15	0.15	14.20
		Q1	13.65	-0.55	12.80	-1.35	13.15
		Q3	15.80	1.05	15.90	1.40	15.90
		Min	12.7	-3.6	11.8	-5.4	11.8
		Max	16.5	2.4	17.4	1.9	17.4
	Week 18	n	8	8	14	14	22
		Mean	14.51	-0.25	13.76	-0.41	14.03
		SD	1.170	1.296	1.168	2.141	1.200
		Median	14.50	-0.15	13.55	0.40	13.75
		Q1	13.70	-0.90	12.80	-0.80	13.30
		Q3	15.30	0.60	14.30	1.10	14.80
		Min	12.7	-2.6	12.3	-5.5	12.3
		Max	16.4	1.5	16.4	1.9	16.4

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Erythrocytes	Week 20	n	8	8	14	14	22
Distribution Width (%)	Week 20	Mean	14.06	-0.39	13.88	-0.46	13.95
	Week 20	SD	0.930	1.191	1.302	2.169	1.160
	Week 20	Median	13.95	-0.50	14.05	0.05	13.95
	Week 20	Q1	13.30	-1.15	12.90	-1.10	13.10
	Week 20	Q3	14.90	0.70	14.90	0.70	14.90
	Week 20	Min	12.8	-2.3	12.0	-5.7	12.0
	Week 20	Max	15.4	1.1	16.0	1.9	16.0
	Week 22	n	8	8	14	14	22
	Week 22	Mean	14.09	-0.53	14.03	0.05	14.05
	Week 22	SD	0.757	1.268	1.644	2.318	1.365
	Week 22	Median	14.30	-0.55	13.40	0.65	13.55
	Week 22	Q1	13.30	-1.75	12.90	-0.90	13.10
	Week 22	Q3	14.70	0.70	14.80	1.70	14.80
	Week 22	Min	13.1	-2.1	12.2	-5.2	12.2
	Week 22	Max	15.0	1.1	17.7	2.4	17.7
	Week 24	n	8	8	7	7	15
	Week 24	Mean	14.29	-0.50	14.21	-0.51	14.25
	Week 24	SD	0.804	1.128	1.833	2.564	1.328
	Week 24	Median	14.25	-0.35	13.60	-0.80	14.20
	Week 24	Q1	13.70	-1.40	12.40	-1.40	13.20
	Week 24	Q3	14.80	0.45	16.10	1.70	15.00
	Week 24	Min	13.2	-2.2	12.3	-5.4	12.3
	Week 24	Max	15.6	0.8	17.0	2.2	17.0

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Erythrocytes	Week 26	n	3	n	3	Value	6
Distribution Width (%)	Week 26	Mean	13.40	Value	-1.70	Change	-1.27
		SD	0.300	14.83	-0.83	14.12	2.247
		Median	13.40	1.662	3.190	1.326	-0.95
		Q1	13.10	14.60	0.70	13.55	-3.20
		Q3	13.70	13.30	-4.50	13.30	0.70
		Min	13.1	16.60	1.30	14.60	-4.5
		Max	13.7	-3.2	-4.5	13.1	1.3
	Week 28	n	1	n	2	Value	3
		Mean	13.10	14.60	0.40	14.10	0.03
		SD	NE	3.677	2.121	2.740	1.629
		Median	13.10	14.60	0.40	13.10	-0.70
		Q1	13.10	12.00	-1.10	12.00	-1.10
		Q3	13.10	17.20	1.90	17.20	1.90
		Min	13.1	12.0	-1.1	12.0	-1.1
		Max	13.1	17.2	1.9	17.2	1.9
	Week 30	n	0	n	1	Value	1
		Mean	17.60	17.60	2.30	17.60	2.30
		SD	NE	NE	NE	NE	NE
		Median	17.60	2.30	17.60	2.30	2.30
		Q1	17.60	2.30	17.60	2.30	2.30
		Q3	17.60	2.30	17.60	2.30	2.30
		Min	17.6	2.3	17.6	2.3	2.3
		Max	17.6	2.3	17.6	2.3	2.3

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Erythrocytes	Week 32	n	0	1	1	1	1
Distribution Width (%)		Mean		16.30	1.00	16.30	1.00
		SD		NE	NE	NE	NE
		Median		16.30	1.00	16.30	1.00
		Q1		16.30	1.00	16.30	1.00
		Q3		16.30	1.00	16.30	1.00
		Min		16.3	1.0	16.3	1.0
		Max		16.3	1.0	16.3	1.0
	Week 34	n	0	1	1	1	1
		Mean		16.30	1.00	16.30	1.00
		SD		NE	NE	NE	NE
		Median		16.30	1.00	16.30	1.00
		Q1		16.30	1.00	16.30	1.00
		Q3		16.30	1.00	16.30	1.00
		Min		16.3	1.0	16.3	1.0
		Max		16.3	1.0	16.3	1.0
	Follow-up	n	17	22	22	39	39
	Week 2	Mean	14.88	0.40	16.53	1.72	15.81
		SD	1.611	1.255	7.333	7.560	5.612
		Median	14.30	0.30	14.55	0.65	14.50
		Q1	13.80	-0.40	13.50	-0.20	13.60
		Q3	15.70	0.80	16.20	1.50	16.00
		Min	12.9	-2.3	12.5	-4.9	12.5
		Max	19.0	2.9	48.2	34.5	48.2

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Erythrocytes	Follow-up Week 4	n	10	19	19	29	29
Distribution Width (%)		Mean	14.92	0.44	16.78	1.82	16.14
		SD	2.170	1.683	7.884	8.036	6.503
		Median	14.25	0.60	14.10	0.70	14.20
		Q1	13.50	-0.90	13.00	-0.40	13.00
		Q3	15.80	1.20	17.00	1.50	16.60
		Min	13.0	-2.1	11.8	-4.8	11.8
		Max	19.9	3.8	47.7	34.0	47.7
	Follow-up Week 6	n	10	16	16	26	26
		Mean	15.35	0.41	17.48	2.56	16.66
		SD	2.107	1.973	8.561	8.913	6.833
		Median	14.40	-0.10	15.20	1.25	15.05
		Q1	13.70	-0.60	13.55	-0.20	13.70
		Q3	17.80	1.10	16.95	2.10	17.80
		Min	13.3	-1.7	12.9	-4.8	12.9
		Max	18.8	4.7	48.6	34.9	48.6
	Follow-up Week 8	n	7	8	8	15	15
		Mean	15.47	0.39	13.80	-0.30	14.58
		SD	2.476	2.316	1.719	2.099	2.202
		Median	14.50	-0.20	13.00	0.10	13.80
		Q1	13.70	-1.80	12.65	-0.65	12.90
		Q3	18.90	3.10	15.10	0.65	15.60
		Min	13.6	-2.0	12.0	-4.9	12.0
		Max	19.2	3.6	16.9	2.3	19.2

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Erythrocytes	Follow-up Week 10	n	4	4	9	9	13
Distribution Width (%)	Mean	14.70	0.80	14.13	-0.49	14.31	-0.09
	SD	1.445	1.501	1.770	2.653	1.638	2.375
	Median	14.70	0.50	13.10	0.10	13.50	0.10
	Q1	13.45	-0.40	12.90	-0.80	13.00	-0.50
	Q3	15.95	2.00	15.40	1.10	15.90	1.30
	Min	13.4	-0.5	12.1	-4.9	12.1	-4.9
	Max	16.0	2.7	17.1	2.3	17.1	2.7
	Follow-up Week 12	n	5	5	2	2	7
	Mean	15.88	2.14	13.00	-1.75	15.06	1.03
	SD	2.359	2.567	0.283	4.031	2.387	3.271
	Median	17.20	2.60	13.00	-1.75	13.60	1.10
	Q1	13.60	-0.20	12.80	-4.60	13.10	-0.80
	Q3	17.20	4.10	13.20	1.10	17.20	4.10
	Min	13.1	-0.8	12.8	-4.6	12.8	-4.6
	Max	18.3	5.0	13.2	1.1	18.3	5.0
	Follow-up Month 6	n	3	3	3	3	6
	Mean	14.60	-0.17	14.57	-0.20	14.58	-0.18
	SD	1.758	1.305	1.358	2.066	1.405	1.546
	Median	13.90	-0.60	15.30	0.40	14.60	-0.10
	Q1	13.30	-1.20	13.00	-2.50	13.30	-1.20
	Q3	16.60	1.30	15.40	1.50	15.40	1.30
	Min	13.3	-1.2	13.0	-2.5	13.0	-2.5
	Max	16.6	1.3	15.4	1.5	16.6	1.5

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Erythrocytes	Follow-up Month 9	n	2	2	1	1	3
Distribution Width (%)	Mean	14.70	0.20	14.10	-1.70	14.50	-0.43
	SD	1.838	0.990	NE	NE	1.345	1.301
	Median	14.70	0.20	14.10	-1.70	14.10	-0.50
	Q1	13.40	-0.50	14.10	-1.70	13.40	-1.70
	Q3	16.00	0.90	14.10	-1.70	16.00	0.90
	Min	13.4	-0.5	14.1	-1.7	13.4	-1.7
	Max	16.0	0.9	14.1	-1.7	16.0	0.9
	Follow-up Month 12	n	1	1	1	2	2
	Mean	13.30	-0.60	12.50	-0.40	12.90	-0.50
	SD	NE	NE	NE	NE	0.566	0.141
	Median	13.30	-0.60	12.50	-0.40	12.90	-0.50
	Q1	13.30	-0.60	12.50	-0.40	12.50	-0.60
	Q3	13.30	-0.60	12.50	-0.40	13.30	-0.40
	Min	13.3	-0.6	12.5	-0.4	12.5	-0.6
	Max	13.3	-0.6	12.5	-0.4	13.3	-0.4
	Follow-up Month 15	n	2	2	1	1	3
	Mean	13.40	-1.10	14.20	2.50	13.67	0.10
	SD	0.849	1.697	NE	NE	0.757	2.400
	Median	13.40	-1.10	14.20	2.50	14.00	0.10
	Q1	12.80	-2.30	14.20	2.50	12.80	-2.30
	Q3	14.00	0.10	14.20	2.50	14.20	2.50
	Min	12.8	-2.3	14.2	2.5	12.8	-2.3
	Max	14.0	0.1	14.2	2.5	14.2	2.5

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Erythrocytes Distribution Width (%)	Follow-up Month 18	n	1	1	0	0	1
		Mean	13.20	-0.70	NE	NE	13.20
		SD	NE	NE	NE	NE	NE
		Median	13.20	-0.70	13.20	-0.70	13.20
		Q1	13.20	-0.70	13.20	-0.70	13.20
		Q3	13.20	-0.70	13.20	-0.70	13.20
		Min	13.2	-0.7	13.2	-0.7	13.2
Erythrocytes (10E12/L)	Baseline	n	23	40	63	63	3.832
		Mean	3.853	3.820	3.832	3.832	0.5352
		SD	0.5382	0.5400	0.5352	0.5352	0.5352
		Median	3.890	3.770	3.830	3.830	3.830
		Q1	3.420	3.385	3.410	3.410	3.410
		Q3	4.260	4.225	4.260	4.260	4.260
		Min	2.80	2.92	2.80	2.80	2.80
Week 2		Max	4.80	5.08	5.08	5.08	5.08
		n	18	18	36	54	54
		Mean	3.874	-0.015	3.820	-0.048	3.838
		SD	0.4209	0.3719	0.5507	0.2624	0.5077
		Median	4.065	-0.070	3.805	-0.015	3.840
		Q1	3.710	-0.200	3.450	-0.170	3.600
		Q3	4.100	0.250	4.280	0.110	4.150
Output ID: t-lb-hemchg-saf 04JUN20 13:05 \AAA.LOCAL\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\RESIST\FINAL ANALYSIS\PRODUCTION\TLF\PGM\t-lbchg.sas		Min	2.58	-0.95	2.66	-0.66	2.58
		Max	4.35	0.75	4.96	0.40	4.96

Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Erythrocytes (10E12/L)	Week 4	n	17	35	35	52	52
		Mean	3.776	-0.168	3.781	-0.106	-0.126
		SD	0.4117	0.3316	0.5780	0.3282	0.3274
		Median	3.900	-0.100	3.850	-0.110	-0.105
		Q1	3.600	-0.390	3.470	-0.340	-0.345
		Q3	4.000	0.080	4.070	0.190	0.170
		Min	2.51	-0.93	2.57	-0.87	-0.93
	Week 6	Max	4.21	0.36	5.09	0.39	0.39
		n	18	35	35	53	53
		Mean	3.859	-0.030	3.759	-0.082	-0.064
White Blood Cells (10E9/L)	Week 8	SD	0.4180	0.4319	0.5641	0.3398	0.3703
		Median	3.940	0.020	3.790	-0.070	-0.030
		Q1	3.620	-0.290	3.470	-0.330	-0.290
		Q3	4.190	0.280	4.160	0.160	0.200
		Min	2.61	-1.03	2.33	-1.06	-1.06
		Max	4.38	0.90	4.90	0.55	0.90
		n	14	25	25	39	39
	Week 12	Mean	3.751	-0.049	3.700	-0.149	-0.113
		SD	0.4172	0.3329	0.4742	0.2957	0.3090
		Median	3.875	-0.145	3.740	-0.200	-0.190
Platelets (10E9/L)	Week 16	Q1	3.580	-0.290	3.390	-0.290	-0.290
		Q3	3.970	0.170	4.020	0.120	0.120
		Min	2.57	-0.43	2.77	-0.83	-0.83
		Max	4.20	0.75	4.64	0.44	0.75
		n	16	35	35	54	54
		Mean	3.751	-0.049	3.700	-0.149	-0.113
		SD	0.4172	0.3329	0.4742	0.2957	0.3090
	Week 20	Median	3.875	-0.145	3.740	-0.200	-0.190
		Q1	3.580	-0.290	3.390	-0.290	-0.290
		Q3	3.970	0.170	4.020	0.120	0.120
		Min	2.57	-0.43	2.77	-0.83	-0.83
		Max	4.20	0.75	4.64	0.44	0.75

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Erythrocytes (10E12/L)	Week 10	n	14	14	23	23	37
		Mean	3.816	-0.163	3.729	-0.011	3.762
		SD	0.3255	0.3776	0.5443	0.3677	0.4703
		Median	3.805	-0.110	3.740	0.040	3.800
		Q1	3.700	-0.330	3.280	-0.380	3.480
		Q3	4.000	0.060	4.070	0.220	4.000
		Min	3.21	-1.00	2.67	-0.57	2.67
	Week 12	Max	4.45	0.34	4.85	0.63	4.85
		n	12	12	21	21	33
		Mean	3.838	-0.118	3.776	-0.010	3.799
Week 14	Week 14	SD	0.3571	0.4504	0.5093	0.2859	0.4548
		Median	3.750	-0.130	3.760	0.000	3.760
		Q1	3.615	-0.370	3.360	-0.200	3.410
		Q3	4.005	0.215	4.080	0.180	4.010
		Min	3.35	-1.07	2.93	-0.48	2.93
		Max	4.64	0.58	4.68	0.50	4.68
		n	13	13	22	22	35
	Week 16	Mean	3.880	-0.076	3.805	-0.054	3.833
		SD	0.4589	0.5533	0.5381	0.2958	0.5045
		Median	3.840	-0.190	3.800	0.000	3.800

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Erythrocytes (10E12/L)	Week 16	n	12	12	17	29	29
		Mean	3.719	-0.318	3.797	-0.099	-0.189
		SD	0.3867	0.4139	0.5435	0.3361	0.3793
		Median	3.785	-0.320	3.910	-0.100	-0.110
		Q1	3.395	-0.560	3.390	-0.270	-0.440
		Q3	3.900	-0.045	4.210	0.090	0.070
		Min	3.08	-1.07	2.91	-0.84	2.91
	Week 18	Max	4.54	0.43	4.61	0.46	4.61
		n	8	8	14	22	22
		Mean	3.668	-0.243	3.857	-0.049	-0.120
Week 20	Week 20	SD	0.2461	0.5645	0.5054	0.3763	0.4325
		Median	3.665	-0.140	3.930	-0.050	-0.110
		Q1	3.450	-0.765	3.400	-0.300	-0.380
		Q3	3.850	0.190	4.310	0.340	0.340
		Min	3.36	-1.03	3.12	-0.79	3.12
		Max	4.05	0.52	4.50	0.41	4.50
		n	9	9	15	24	24
	Week 22	Mean	3.724	-0.204	3.635	-0.016	-0.087
		SD	0.1885	0.5634	0.5213	0.3266	0.4240
		Median	3.640	-0.210	3.440	-0.060	-0.115

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Erythrocytes (10E12/L)	Week 22	n	8	8	15	15	23
		Mean	3.633	-0.276	3.662	-0.183	3.652
		SD	0.2367	0.5936	0.5154	0.3743	0.4325
		Median	3.615	-0.340	3.640	-0.100	3.630
		Q1	3.510	-0.605	3.200	-0.540	3.300
		Q3	3.855	0.105	3.970	0.190	3.900
		Min	3.20	-1.17	2.97	-0.79	2.97
	Week 24	Max	3.90	0.64	4.78	0.32	4.78
		n	8	8	7	7	15
		Mean	3.610	-0.291	3.789	-0.077	3.693
	Week 26	SD	0.3100	0.7341	0.4565	0.3852	0.3819
		Median	3.650	-0.305	3.960	0.060	3.700
		Q1	3.370	-0.700	3.340	-0.530	3.340
		Q3	3.890	0.020	4.160	0.250	3.960
		Min	3.10	-1.36	3.20	-0.58	3.10
		Max	3.96	1.00	4.30	0.38	4.30
		n	3	3	3	3	6
		Mean	3.797	-0.443	3.360	-0.070	3.578
		SD	0.0586	0.0153	0.5003	0.0872	0.3984
		Median	3.820	-0.440	3.340	-0.030	3.775

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Erythrocytes (10E12/L)	Week 28	n	1	2	2	3	3
		Mean	3.200	0.240	3.600	0.035	3.467
		SD	NE	NE	0.6505	0.3465	0.5147
		Median	3.200	0.240	3.600	0.035	3.200
		Q1	3.200	0.240	3.140	-0.210	3.140
		Q3	3.200	0.240	4.060	0.280	4.060
		Min	3.20	0.24	3.14	-0.21	3.14
		Max	3.20	0.24	4.06	0.28	4.06
		n	0	0	1	1	1
		Mean	NE	3.080	-0.270	3.080	NE
Erythrocytes (10E12/L)	Week 30	SD	NE	NE	NE	NE	NE
		Median	3.080	-0.270	3.080	-0.270	3.080
		Q1	3.080	-0.270	3.080	-0.270	3.080
		Q3	3.080	-0.270	3.080	-0.270	3.080
		Min	3.08	-0.27	3.08	-0.27	3.08
		Max	3.08	-0.27	3.08	-0.27	3.08
		n	0	0	1	1	1
		Mean	NE	2.910	-0.440	2.910	NE
		SD	NE	NE	NE	NE	NE
		Median	2.910	-0.440	2.910	-0.440	2.910
Erythrocytes (10E12/L)	Week 32	Q1	2.910	-0.440	2.910	-0.440	2.910
		Q3	2.910	-0.440	2.910	-0.440	2.910
		Min	2.91	-0.44	2.91	-0.44	2.91
		Max	2.91	-0.44	2.91	-0.44	2.91

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall				
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value	Change
Erythrocytes (10E12/L)	Week 34	n	0	0	1	1	1	1	1	1
		Mean			2.910	-0.440	2.910	-0.440	2.910	-0.440
		SD			NE	NE	NE	NE	NE	NE
		Median			2.910	-0.440	2.910	-0.440	2.910	-0.440
		Q1			2.910	-0.440	2.910	-0.440	2.910	-0.440
		Q3			2.910	-0.440	2.910	-0.440	2.910	-0.440
		Min			2.91	-0.44	2.91	-0.44	2.91	-0.44
		Max			2.91	-0.44	2.91	-0.44	2.91	-0.44
	Follow-up	n	17	17	22	22	39	39	39	39
	Week 2	Mean	3.572	-0.185	3.495	-0.184	3.529	-0.184	3.529	-0.184
		SD	0.6456	0.5719	0.5397	0.3545	0.5813	0.4552	0.5813	0.4552
		Median	3.540	-0.190	3.400	-0.205	3.450	-0.190	3.450	-0.190
		Q1	3.140	-0.520	3.070	-0.410	3.070	-0.490	3.070	-0.490
		Q3	3.930	0.300	3.800	0.100	3.930	0.180	3.930	0.180
		Min	2.19	-1.26	2.56	-0.86	2.19	-1.26	2.19	-1.26
		Max	4.68	0.97	4.78	0.44	4.78	0.97	4.78	0.97
	Follow-up	n	10	10	20	20	30	30	30	30
	Week 4	Mean	3.380	-0.589	3.475	-0.309	3.443	-0.402	3.443	-0.402
		SD	0.7284	0.4509	0.6220	0.4406	0.6482	0.4564	0.6482	0.4564
		Median	3.390	-0.630	3.430	-0.395	3.390	-0.490	3.390	-0.490
		Q1	2.900	-0.880	3.075	-0.570	3.070	-0.640	3.070	-0.640
		Q3	3.630	-0.470	3.890	0.090	3.840	0.040	3.840	0.040
		Min	2.02	-1.35	2.40	-0.96	2.02	-1.35	2.02	-1.35
		Max	4.67	0.15	5.15	0.58	5.15	0.58	5.15	0.58

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Erythrocytes (10E12/L)	Follow-up Week 6	n	10	16	16	26	26
		Mean	3.351	-0.347	3.396	-0.366	3.379
		SD	0.6132	0.5373	0.7740	0.4420	0.7038
		Median	3.375	-0.470	3.240	-0.460	3.275
		Q1	2.800	-0.620	2.745	-0.720	2.760
		Q3	3.790	0.100	3.895	-0.130	3.810
		Min	2.41	-1.25	2.12	-0.89	2.12
		Max	4.50	0.47	4.92	0.57	4.92
	Follow-up Week 8	n	7	8	8	15	15
		Mean	3.710	-0.493	3.504	-0.304	3.600
		SD	0.5088	0.6377	0.5475	0.4179	0.5217
		Median	3.810	-0.450	3.550	-0.305	3.600
		Q1	3.260	-0.770	3.065	-0.600	3.170
		Q3	3.860	-0.330	3.900	-0.145	3.860
		Min	3.08	-1.54	2.70	-0.85	2.70
		Max	4.64	0.61	4.30	0.52	4.64
	Follow-up Week 10	n	4	9	9	13	13
		Mean	3.278	-0.413	3.729	-0.199	3.590
		SD	0.5491	0.5770	0.7064	0.4228	0.6745
		Median	3.435	-0.320	3.830	-0.260	3.570
		Q1	2.900	-0.845	3.080	-0.400	3.080
		Q3	3.655	0.020	4.340	0.080	4.140
		Min	2.50	-1.17	2.80	-0.82	2.50
		Max	3.74	0.16	4.60	0.57	4.60

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Erythrocytes (10E12/L)	Follow-up Week 12	n 5	5	n 2	2	7	7
	Mean	3.078	-0.454	3.900	-0.270	3.313	-0.401
	SD	0.6000	0.5088	0.3111	0.9758	0.6457	0.5825
	Median	2.800	-0.480	3.900	-0.270	3.670	-0.480
	Q1	2.610	-0.620	3.680	-0.960	2.610	-0.960
	Q3	3.670	-0.290	4.120	0.420	3.780	0.260
	Min	2.53	-1.14	3.68	-0.96	2.53	-1.14
	Max	3.78	0.26	4.12	0.42	4.12	0.42
	Follow-up Month 6	n 3	3	n 3	3	6	6
	Mean	3.640	-0.603	3.777	-0.033	3.708	-0.318
	SD	0.2623	0.2371	0.1872	0.7032	0.2171	0.5637
	Median	3.600	-0.670	3.700	0.090	3.670	-0.505
	Q1	3.400	-0.800	3.640	-0.790	3.600	-0.790
	Q3	3.920	-0.340	3.990	0.600	3.920	0.090
	Min	3.40	-0.80	3.64	-0.79	3.40	-0.80
	Max	3.92	-0.34	3.99	0.60	3.99	0.60
	Follow-up Month 9	n 2	2	n 1	1	3	3
	Mean	3.655	-0.610	4.800	-0.080	4.037	-0.433
	SD	0.5020	0.5091	NE	NE	0.7504	0.4725
	Median	3.655	-0.610	4.800	-0.080	4.010	-0.250
	Q1	3.300	-0.970	4.800	-0.080	3.300	-0.970
	Q3	4.010	-0.250	4.800	-0.080	4.800	-0.080
	Min	3.30	-0.97	4.80	-0.08	3.30	-0.97
	Max	4.01	-0.25	4.80	-0.08	4.80	-0.08

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Erythrocytes (10E12/L)	Follow-up Month 12	n	1	1	1	1	2
		Mean	4.000	-0.260	3.800	-0.300	3.900
		SD	NE	NE	NE	NE	0.1414
		Median	4.000	-0.260	3.800	-0.300	3.900
		Q1	4.000	-0.260	3.800	-0.300	3.800
		Q3	4.000	-0.260	3.800	-0.300	4.000
		Min	4.00	-0.26	3.80	-0.30	3.80
		Max	4.00	-0.26	3.80	-0.30	4.00
	Follow-up Month 15	n	2	2	1	1	3
		Mean	3.770	-0.495	4.670	-0.410	4.070
		SD	0.0424	0.0354	NE	NE	0.5205
		Median	3.770	-0.495	4.670	-0.410	3.800
		Q1	3.740	-0.520	4.670	-0.410	3.740
		Q3	3.800	-0.470	4.670	-0.410	4.670
		Min	3.74	-0.52	4.67	-0.41	3.74
		Max	3.80	-0.47	4.67	-0.41	4.67
	Follow-up Month 18	n	1	1	0	0	1
		Mean	3.680	-0.580	NE	NE	3.680
		SD	NE	NE	NE	NE	NE
		Median	3.680	-0.580	NE	NE	3.680
		Q1	3.680	-0.580	NE	NE	3.680
		Q3	3.680	-0.580	NE	NE	3.680
		Min	3.68	-0.58	NE	NE	3.68
		Max	3.68	-0.58	NE	NE	3.68

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value	Change
Hematocrit (L/L)	Baseline	n	23		41			64	
		Mean	0.359		0.351			0.354	
		SD	0.0503		0.0482			0.0487	
		Median	0.360		0.350			0.355	
		Q1	0.330		0.320			0.320	
		Q3	0.400		0.390			0.390	
		Min	0.26		0.26			0.26	
		Max	0.44		0.47			0.47	
	Week 2	n	18	18	37	37	55	55	
		Mean	0.362	0.001	0.353	-0.005	0.356	-0.003	
		SD	0.0396	0.0349	0.0471	0.0271	0.0447	0.0297	
		Median	0.360	-0.010	0.360	0.000	0.360	-0.010	
		Q1	0.350	-0.020	0.320	-0.020	0.330	-0.020	
		Q3	0.390	0.020	0.390	0.010	0.390	0.020	
		Min	0.26	-0.06	0.24	-0.06	0.24	-0.06	
		Max	0.42	0.07	0.43	0.05	0.43	0.07	
	Week 4	n	17	17	36	36	53	53	
		Mean	0.349	-0.017	0.349	-0.007	0.349	-0.010	
		SD	0.0393	0.0339	0.0522	0.0261	0.0481	0.0289	
		Median	0.350	-0.010	0.360	-0.010	0.350	-0.010	
		Q1	0.340	-0.040	0.315	-0.020	0.330	-0.030	
		Q3	0.360	0.000	0.385	0.010	0.380	0.010	
		Min	0.25	-0.08	0.21	-0.07	0.21	-0.08	
		Max	0.43	0.05	0.44	0.03	0.44	0.05	

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Hematocrit (L/L)	Week 6	n	18	35	35	53	53
		Mean	0.358	-0.004	0.347	-0.008	0.351
		SD	0.0377	0.0399	0.0473	0.0286	0.0442
		Median	0.355	-0.010	0.350	-0.010	0.350
		Q1	0.340	-0.030	0.320	-0.030	0.320
		Q3	0.390	0.020	0.380	0.010	0.380
		Min	0.26	-0.08	0.21	-0.09	0.21
		Max	0.43	0.08	0.43	0.04	0.43
	Week 8	n	14	26	26	40	40
		Mean	0.344	-0.008	0.340	-0.013	0.341
		SD	0.0348	0.0340	0.0430	0.0227	0.0399
		Median	0.345	-0.015	0.335	-0.010	0.340
		Q1	0.320	-0.030	0.310	-0.020	0.320
		Q3	0.360	0.020	0.380	0.000	0.375
		Min	0.26	-0.05	0.25	-0.07	0.25
		Max	0.40	0.07	0.41	0.04	0.41
	Week 10	n	14	23	23	37	37
		Mean	0.353	-0.016	0.347	0.003	0.349
		SD	0.0307	0.0337	0.0452	0.0332	0.0400
		Median	0.350	-0.015	0.350	0.000	0.350
		Q1	0.340	-0.040	0.330	-0.030	0.330
		Q3	0.370	0.020	0.370	0.020	0.370
		Min	0.30	-0.08	0.24	-0.06	0.24
		Max	0.40	0.03	0.43	0.07	0.43

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Hematocrit (L/L)	Week 12	n	12	21	21	33	33
		Mean	0.356	-0.012	0.353	0.354	-0.003
		SD	0.0320	0.0364	0.0409	0.0374	0.0300
		Median	0.355	-0.015	0.350	0.350	-0.010
		Q1	0.340	-0.035	0.320	0.330	-0.030
		Q3	0.380	0.020	0.380	0.380	0.020
		Min	0.30	-0.08	0.29	0.29	-0.08
		Max	0.40	0.04	0.44	0.44	0.04
	Week 14	n	13	22	22	35	35
		Mean	0.363	-0.005	0.353	0.357	-0.003
		SD	0.0368	0.0418	0.0414	0.0396	0.0327
		Median	0.360	0.000	0.350	0.350	0.000
		Q1	0.350	-0.030	0.320	0.330	-0.030
		Q3	0.380	0.020	0.390	0.390	0.020
		Min	0.30	-0.07	0.27	0.27	-0.07
		Max	0.43	0.07	0.44	0.44	0.07
	Week 16	n	12	17	17	29	29
		Mean	0.344	-0.026	0.349	0.347	-0.014
		SD	0.0334	0.0380	0.0440	0.0394	0.0353
		Median	0.345	-0.030	0.340	0.340	-0.020
		Q1	0.325	-0.040	0.330	0.330	-0.030
		Q3	0.365	-0.005	0.380	0.380	0.010
		Min	0.29	-0.09	0.26	0.26	-0.09
		Max	0.40	0.04	0.41	0.41	0.05

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hematocrit (L/L)	Week 18	n	8	14	14	22	22
		Mean	0.343	-0.010	0.359	-0.001	0.353
		SD	0.0183	0.0431	0.0420	0.0351	0.0356
		Median	0.345	-0.005	0.360	-0.010	0.350
		Q1	0.325	-0.050	0.320	-0.020	0.320
		Q3	0.355	0.030	0.400	0.030	0.380
		Min	0.32	-0.07	0.30	-0.07	0.30
		Max	0.37	0.04	0.42	0.05	0.42
	Week 20	n	9	15	15	24	24
		Mean	0.358	-0.009	0.339	-0.005	0.346
		SD	0.0205	0.0504	0.0302	0.0316	0.0281
		Median	0.350	-0.010	0.340	-0.010	0.350
		Q1	0.340	-0.050	0.310	-0.040	0.325
		Q3	0.360	0.040	0.370	0.020	0.365
		Min	0.34	-0.07	0.30	-0.05	0.30
		Max	0.40	0.06	0.39	0.04	0.40
	Week 22	n	8	15	15	23	23
		Mean	0.346	-0.011	0.339	-0.017	0.341
		SD	0.0262	0.0458	0.0334	0.0361	0.0306
		Median	0.345	-0.020	0.330	-0.020	0.340
		Q1	0.325	-0.035	0.310	-0.050	0.320
		Q3	0.355	0.015	0.360	0.020	0.360
		Min	0.32	-0.08	0.28	-0.08	0.28
		Max	0.40	0.07	0.39	0.04	0.40

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hematocrit (L/L)	Week 24	n	8	8	7	7	15
		Mean	0.343	-0.013	0.350	0.004	0.346
		SD	0.0255	0.0580	0.0420	0.0288	0.0331
		Median	0.345	-0.010	0.350	0.010	0.350
		Q1	0.320	-0.045	0.310	-0.020	0.310
		Q3	0.360	0.005	0.390	0.030	0.370
		Min	0.31	-0.10	0.30	-0.04	0.30
		Max	0.38	0.10	0.41	0.04	0.41
	Week 26	n	3	3	3	3	6
		Mean	0.363	-0.027	0.310	0.003	0.337
		SD	0.0351	0.0058	0.0200	0.0058	0.0388
		Median	0.360	-0.030	0.310	0.000	0.330
		Q1	0.330	-0.030	0.290	0.000	0.310
		Q3	0.400	-0.020	0.330	0.010	0.360
		Min	0.33	-0.03	0.29	0.00	0.29
		Max	0.40	-0.02	0.33	0.01	0.40
	Week 28	n	1	1	2	2	3
		Mean	0.310	0.030	0.340	0.000	0.330
		SD	NE	NE	0.0707	0.0283	0.0529
		Median	0.310	0.030	0.340	0.000	0.310
		Q1	0.310	0.030	0.290	-0.020	0.290
		Q3	0.310	0.030	0.390	0.020	0.390
		Min	0.31	0.03	0.29	-0.02	0.29
		Max	0.31	0.03	0.39	0.02	0.39

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value
Hematocrit (L/L)	Week 30	n	0	0	1	1	1	1	1
		Mean		0.290	-0.020	0.290	-0.020	0.290	-0.020
		SD		NE	NE	NE	NE	NE	NE
		Median		0.290	-0.020	0.290	-0.020	0.290	-0.020
		Q1		0.290	-0.020	0.290	-0.020	0.290	-0.020
		Q3		0.290	-0.020	0.290	-0.020	0.290	-0.020
		Min		0.29	-0.02	0.29	-0.02	0.29	-0.02
		Max		0.29	-0.02	0.29	-0.02	0.29	-0.02
	Week 32	n	0	0	1	1	1	1	1
		Mean		0.280	-0.030	0.280	-0.030	0.280	-0.030
		SD		NE	NE	NE	NE	NE	NE
		Median		0.280	-0.030	0.280	-0.030	0.280	-0.030
		Q1		0.280	-0.030	0.280	-0.030	0.280	-0.030
		Q3		0.280	-0.030	0.280	-0.030	0.280	-0.030
		Min		0.28	-0.03	0.28	-0.03	0.28	-0.03
		Max		0.28	-0.03	0.28	-0.03	0.28	-0.03
	Week 34	n	0	0	1	1	1	1	1
		Mean		0.280	-0.030	0.280	-0.030	0.280	-0.030
		SD		NE	NE	NE	NE	NE	NE
		Median		0.280	-0.030	0.280	-0.030	0.280	-0.030
		Q1		0.280	-0.030	0.280	-0.030	0.280	-0.030
		Q3		0.280	-0.030	0.280	-0.030	0.280	-0.030
		Min		0.28	-0.03	0.28	-0.03	0.28	-0.03
		Max		0.28	-0.03	0.28	-0.03	0.28	-0.03

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hematocrit (L/L)	Follow-up Week 2	n	17	23	23	40	40
		Mean	0.335	-0.015	0.320	-0.017	0.327
		SD	0.0541	0.0552	0.0430	0.0341	0.0480
		Median	0.340	-0.020	0.330	-0.010	0.330
		Q1	0.300	-0.070	0.290	-0.040	0.295
		Q3	0.390	0.020	0.350	0.000	0.360
		Min	0.22	-0.09	0.23	-0.08	0.22
		Max	0.43	0.11	0.39	0.05	0.43
	Follow-up Week 4	n	10	20	20	30	30
		Mean	0.325	-0.047	0.328	-0.022	0.327
		SD	0.0654	0.0380	0.0555	0.0365	0.0579
		Median	0.325	-0.050	0.320	-0.030	0.320
		Q1	0.280	-0.080	0.290	-0.050	0.290
		Q3	0.370	-0.040	0.365	0.010	0.370
		Min	0.21	-0.09	0.22	-0.07	0.21
		Max	0.45	0.02	0.45	0.04	0.45
	Follow-up Week 6	n	10	17	17	27	27
		Mean	0.320	-0.026	0.312	-0.032	0.315
		SD	0.0519	0.0435	0.0623	0.0368	0.0577
		Median	0.330	-0.040	0.320	-0.040	0.330
		Q1	0.270	-0.060	0.270	-0.060	0.270
		Q3	0.350	0.000	0.360	-0.020	0.360
		Min	0.23	-0.08	0.19	-0.08	0.19
		Max	0.39	0.05	0.41	0.04	0.41

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hematocrit (L/L)	Follow-up Week 8	n	7	8	8	15	15
	Mean	0.356	-0.034	0.343	-0.021	0.349	-0.027
	SD	0.0331	0.0500	0.0399	0.0356	0.0362	0.0418
	Median	0.350	-0.040	0.345	-0.030	0.350	-0.040
	Q1	0.330	-0.060	0.320	-0.040	0.330	-0.050
	Q3	0.400	0.000	0.360	0.000	0.370	0.000
	Min	0.32	-0.11	0.28	-0.07	0.28	-0.11
	Max	0.40	0.05	0.41	0.04	0.41	0.05
	Follow-up Week 10	n	4	9	9	13	13
	Mean	0.328	-0.035	0.344	-0.014	0.339	-0.021
	SD	0.0492	0.0473	0.0445	0.0403	0.0446	0.0417
	Median	0.325	-0.020	0.350	-0.020	0.330	-0.020
	Q1	0.295	-0.070	0.300	-0.030	0.300	-0.040
	Q3	0.360	0.000	0.390	0.000	0.390	0.000
	Min	0.27	-0.10	0.28	-0.07	0.27	-0.10
	Max	0.39	0.00	0.40	0.05	0.40	0.05
	Follow-up Week 12	n	5	2	2	7	7
	Mean	0.304	-0.044	0.365	-0.025	0.321	-0.039
	SD	0.0623	0.0336	0.0495	0.0636	0.0623	0.0389
	Median	0.290	-0.050	0.365	-0.025	0.330	-0.050
	Q1	0.270	-0.060	0.330	-0.070	0.270	-0.070
	Q3	0.340	-0.040	0.400	0.020	0.390	0.010
	Min	0.23	-0.08	0.33	-0.07	0.23	-0.08
	Max	0.39	0.01	0.40	0.02	0.40	0.02

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hematocrit (L/L)	Follow-up Month 6	n	3	n	3	n	6
	Mean	0.357	-0.053	0.360	0.027	0.358	-0.013
	SD	0.0462	0.0306	0.0300	0.0850	0.0349	0.0720
	Median	0.330	-0.060	0.360	0.030	0.345	-0.040
	Q1	0.330	-0.080	0.330	-0.060	0.330	-0.060
	Q3	0.410	-0.020	0.390	0.110	0.390	0.030
	Min	0.33	-0.08	0.33	-0.06	0.33	-0.08
	Max	0.41	-0.02	0.39	0.11	0.41	0.11
	Follow-up Month 9	n	2	n	1	n	3
	Mean	0.350	-0.060	0.430	0.000	0.377	-0.040
	SD	0.0990	0.0707	NE	NE	0.0839	0.0608
	Median	0.350	-0.060	0.430	0.000	0.420	-0.010
	Q1	0.280	-0.110	0.430	0.000	0.280	-0.110
	Q3	0.420	-0.010	0.430	0.000	0.430	0.000
	Min	0.28	-0.11	0.43	0.00	0.28	-0.11
	Max	0.42	-0.01	0.43	0.00	0.43	0.00
	Follow-up Month 12	n	1	n	1	n	2
	Mean	0.420	-0.010	0.390	0.000	0.405	-0.005
	SD	NE	NE	NE	NE	0.0212	0.0071
	Median	0.420	-0.010	0.390	0.000	0.405	-0.005
	Q1	0.420	-0.010	0.390	0.000	0.390	-0.010
	Q3	0.420	-0.010	0.390	0.000	0.420	0.000
	Min	0.42	-0.01	0.39	0.00	0.39	-0.01
	Max	0.42	-0.01	0.39	0.00	0.42	0.00

Output ID: t-lb-hemchg-saf 04JUN20 13:05

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hematocrit (L/L)	Follow-up Month 15	n	2	1	1	3	3
		Mean	0.385	-0.025	0.430	-0.040	0.400
		SD	0.0212	0.0071	NE	NE	0.0300
		Median	0.385	-0.025	0.430	-0.040	0.400
		Q1	0.370	-0.030	0.430	-0.040	0.370
		Q3	0.400	-0.020	0.430	-0.040	0.430
		Min	0.37	-0.03	0.43	-0.04	0.37
		Max	0.40	-0.02	0.43	-0.04	0.43
	Follow-up Month 18	n	1	0	0	1	1
		Mean	0.400	-0.030	NE	0.400	-0.030
		SD	NE	NE	NE	NE	NE
		Median	0.400	-0.030	NE	0.400	-0.030
		Q1	0.400	-0.030	NE	0.400	-0.030
		Q3	0.400	-0.030	NE	0.400	-0.030
		Min	0.40	-0.03	NE	0.40	-0.03
		Max	0.40	-0.03	NE	0.40	-0.03
Hemoglobin (g/L)	Baseline	n	23	41	64	116.71	116.71
		Mean	116.91	116.60	116.422	116.422	116.422
		SD	16.312	16.684	116.00	116.00	116.00
		Median	117.00	115.00	105.00	105.00	105.00
		Q1	102.00	105.00	83.0	83.0	83.0
		Q3	127.00	132.00	159.0	159.0	159.0
		Min	87.0	83.0	83.0	83.0	83.0
		Max	143.0	159.0	159.0	159.0	159.0

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Hemoglobin (g/L)	Week 2	n	18	37	37	55	55
		Mean	117.78	116.59	-2.10	116.98	-1.37
		SD	12.469	16.380	8.462	15.104	9.600
		Median	119.00	119.00	-1.00	119.00	-1.00
		Q1	111.00	104.00	-7.00	107.00	-7.00
		Q3	124.00	129.00	4.00	127.00	5.00
		Min	89.0	80.0	-26.0	80.0	-31.0
		Max	141.0	146.0	10.0	146.0	25.0
	Week 4	n	17	36	36	53	53
		Mean	115.29	114.42	-3.88	114.70	-3.88
		SD	13.275	18.520	8.929	16.889	9.434
		Median	114.00	120.00	-2.80	116.00	-3.00
		Q1	112.00	99.00	-10.50	106.00	-10.00
		Q3	120.00	128.50	3.00	124.00	3.00
		Min	86.0	64.0	-30.0	64.0	-30.0
		Max	143.0	142.0	11.0	143.0	13.0
	Week 6	n	18	35	35	53	53
		Mean	117.56	115.23	-2.56	116.02	-1.73
		SD	11.289	13.033	9.540	14.745	10.789
		Median	117.00	118.00	-2.00	118.00	-1.00
		Q1	110.00	105.00	-9.00	108.00	-7.00
		Q3	127.00	129.00	3.00	128.00	4.00
		Min	91.0	72.0	-28.0	72.0	-32.0
		Max	137.0	141.0	16.0	141.0	29.0

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hemoglobin (g/L)	Week 8	n	14	26	26	40	40
		Mean	113.93	-0.07	112.12	-4.72	112.75
		SD	10.866	10.565	14.787	8.393	13.427
		Median	113.50	-2.50	114.00	-4.50	114.00
		Q1	110.00	-7.00	100.00	-9.00	103.50
		Q3	119.00	5.00	124.00	-1.00	121.00
		Min	92.0	-14.0	81.0	-28.0	81.0
		Max	135.0	27.0	140.0	15.0	140.0
	Week 10	n	14	23	23	37	37
		Mean	116.14	-4.00	114.22	1.10	114.95
		SD	9.272	12.070	14.881	11.587	12.933
		Median	115.00	-4.50	115.00	1.00	115.00
		Q1	108.00	-11.00	105.00	-9.00	108.00
		Q3	122.00	6.00	122.00	10.00	122.00
		Min	105.0	-30.0	80.0	-21.0	80.0
		Max	139.0	13.0	144.0	21.0	144.0
	Week 12	n	12	21	21	33	33
		Mean	117.50	-1.75	116.95	0.83	117.15
		SD	8.576	13.081	13.592	9.532	11.867
		Median	117.00	-1.00	116.00	1.00	117.00
		Q1	112.00	-10.00	108.00	-3.00	109.00
		Q3	121.00	7.00	126.00	5.00	123.00
		Min	103.0	-29.0	93.0	-18.0	93.0
		Max	136.0	17.0	143.0	16.0	143.0

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Hemoglobin (g/L)	Week 14	n	13	22	22	35	35
		Mean	119.23	-0.38	117.05	-0.53	-0.47
		SD	10.418	14.558	14.927	11.033	12.247
		Median	117.00	-4.00	115.50	-0.30	-1.00
		Q1	114.00	-8.00	108.00	-8.00	-8.00
		Q3	127.00	9.00	128.00	4.00	9.00
		Min	105.0	-27.0	85.0	-19.0	-27.0
		Max	141.0	26.0	146.0	21.0	26.0
	Week 16	n	12	17	17	29	29
		Mean	114.42	-6.08	115.41	-1.68	-3.50
		SD	9.986	12.703	14.782	12.188	12.375
		Median	112.50	-5.00	116.00	-1.00	-4.00
		Q1	110.00	-15.00	107.00	-10.00	-12.00
		Q3	120.50	2.00	127.00	6.00	5.00
		Min	98.0	-28.0	85.0	-28.0	-28.0
		Max	136.0	18.0	138.0	23.0	23.0
	Week 18	n	8	14	14	22	22
		Mean	114.25	-0.25	120.43	0.60	0.29
		SD	4.301	14.568	12.930	12.449	12.917
		Median	114.50	4.00	117.00	-0.80	1.00
		Q1	111.00	-10.00	113.00	-5.00	-6.00
		Q3	117.00	10.50	133.00	9.00	9.00
		Min	108.0	-27.0	100.0	-26.0	-27.0
		Max	121.0	16.0	142.0	20.0	20.0

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hemoglobin (g/L)	Week 20	n	9	15	15	24	24
		Mean	117.67	-0.11	112.93	-0.11	114.71
		SD	7.000	15.831	10.409	10.868	9.406
		Median	117.00	2.00	115.00	-2.60	115.00
		Q1	115.00	-12.00	101.00	-7.00	107.50
		Q3	119.00	12.00	121.00	9.00	119.00
		Min	108.0	-27.0	99.0	-16.0	99.0
		Max	134.0	23.0	134.0	21.0	134.0
	Week 22	n	8	15	15	23	23
		Mean	115.25	-0.88	112.67	-4.80	113.57
		SD	8.779	16.435	10.959	12.090	10.126
		Median	114.00	-2.00	112.00	-3.00	112.00
		Q1	110.00	-9.00	104.00	-14.00	106.00
		Q3	117.50	8.00	118.00	6.00	118.00
		Min	105.0	-28.0	97.0	-25.0	97.0
		Max	134.0	27.0	134.0	15.0	134.0
	Week 24	n	8	6	6	14	14
		Mean	112.88	-0.88	118.50	2.00	115.29
		SD	10.006	20.343	12.276	11.950	10.964
		Median	113.00	-0.50	118.50	5.50	116.50
		Q1	105.50	-11.50	108.00	-12.00	108.00
		Q3	118.50	5.50	126.00	12.00	120.00
		Min	99.0	-32.0	103.0	-13.0	99.0
		Max	130.0	38.0	137.0	14.0	137.0

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hemoglobin (g/L)	Week 26	n	3	n	3	n	6
		Mean	121.00	Value	105.33	Change	113.17
		SD	10.000	Value	3.512	Change	7.062
		Median	121.00	Value	-6.00	Change	109.00
		Q1	111.00	Value	-9.00	Change	105.00
		Q3	131.00	Value	-2.00	Change	121.00
		Min	111.0	Value	104.0	Change	104.0
		Max	131.0	Value	107.0	Change	131.0
	Week 28	n	1	n	2	n	3
		Mean	102.00	Value	10.00	Change	112.00
		SD	NE	Value	NE	Change	20.881
		Median	102.00	Value	10.00	Change	102.00
		Q1	102.00	Value	10.00	Change	98.00
		Q3	102.00	Value	10.00	Change	136.00
		Min	102.0	Value	10.0	Change	98.0
		Max	102.0	Value	10.0	Change	136.0
	Week 30	n	0	n	1	n	1
		Mean	96.00	Value	-5.00	Change	96.00
		SD	NE	Value	NE	Change	NE
		Median	96.00	Value	-5.00	Change	96.00
		Q1	96.00	Value	-5.00	Change	96.00
		Q3	96.00	Value	-5.00	Change	96.00
		Min	96.0	Value	-5.0	Change	96.0
		Max	96.0	Value	-5.0	Change	96.0

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hemoglobin (g/L)	Week 32	n	0	n	1	1	1
		Mean		92.00	-9.00	92.00	-9.00
		SD		NE	NE	NE	NE
		Median		92.00	-9.00	92.00	-9.00
		Q1		92.00	-9.00	92.00	-9.00
		Q3		92.00	-9.00	92.00	-9.00
		Min		92.0	-9.0	92.0	-9.0
		Max		92.0	-9.0	92.0	-9.0
	Week 34	n	0	n	1	1	1
		Mean		92.00	-9.00	92.00	-9.00
		SD		NE	NE	NE	NE
		Median		92.00	-9.00	92.00	-9.00
		Q1		92.00	-9.00	92.00	-9.00
		Q3		92.00	-9.00	92.00	-9.00
		Min		92.0	-9.0	92.0	-9.0
		Max		92.0	-9.0	92.0	-9.0
Follow-up	Week 2	n	17	n	23	n	40
		Mean	110.71	Value	105.91	Value	40
		SD	16.419	Change	-6.42	Change	-5.29
		Median	111.00	17.704	14.110	11.328	15.122
		Q1	99.00	-3.00	110.00	-7.00	14.239
		Q3	124.00	-18.00	114.00	-15.00	-7.00
		Min	78.0	9.00	74.0	-2.00	99.00
		Max	144.0	-30.0	130.0	-23.0	-15.00
					24.0	74.0	2.50
						144.0	-30.0
							35.0

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hemoglobin (g/L)	Follow-up Week 4	n	10	20	20	30	30
		Mean	107.10	-14.40	107.95	-7.85	107.67
		SD	20.529	12.721	19.135	13.307	19.257
		Median	108.00	-14.50	108.00	-10.50	108.00
		Q1	94.00	-25.00	94.00	-20.50	94.00
		Q3	118.00	-7.00	121.00	1.50	121.00
		Min	71.0	-34.0	74.0	-25.0	71.0
		Max	144.0	5.0	146.0	18.0	146.0
	Follow-up Week 6	n	10	17	17	27	27
		Mean	104.20	-8.50	103.41	-11.29	103.70
		SD	18.268	15.284	20.761	13.251	19.517
		Median	107.00	-12.00	111.00	-13.00	108.00
		Q1	87.00	-20.00	86.00	-18.00	86.00
		Q3	111.00	4.00	120.00	-6.00	120.00
		Min	80.0	-30.0	66.0	-27.0	66.0
		Max	132.0	16.0	135.0	22.0	135.0
	Follow-up Week 8	n	7	9	9	16	16
		Mean	117.43	-8.43	110.44	-7.00	113.50
		SD	11.208	17.653	18.656	13.574	15.769
		Median	115.00	-8.00	113.00	-10.00	113.50
		Q1	109.00	-17.00	108.00	-16.00	108.50
		Q3	132.00	1.00	117.00	-4.00	121.00
		Min	103.0	-38.0	75.0	-23.0	75.0
		Max	133.0	20.0	140.0	15.0	140.0

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hemoglobin (g/L)	Follow-up Week 10	n	4	n	9	n	13
	Mean	108.75	-10.00	114.33	-4.44	112.62	-6.15
	SD	16.132	18.055	14.697	14.063	14.706	14.848
	Median	107.00	-6.00	115.00	-7.00	109.00	-7.00
	Q1	98.00	-22.50	106.00	-13.00	105.00	-13.00
	Q3	119.50	2.50	124.00	0.00	124.00	0.00
	Min	91.0	-35.0	91.0	-24.0	91.0	-35.0
	Max	130.0	7.0	135.0	21.0	135.0	21.0
	Follow-up Week 12	n	5	n	2	n	7
	Mean	101.80	-12.40	121.50	-11.00	107.43	-12.00
	SD	21.312	14.943	9.192	28.284	20.231	16.813
	Median	96.00	-17.00	121.50	-11.00	112.00	-17.00
	Q1	90.00	-18.00	115.00	-31.00	90.00	-30.00
	Q3	112.00	-7.00	128.00	9.00	128.00	9.00
	Min	78.0	-30.0	115.0	-31.0	78.0	-31.0
	Max	133.0	10.0	128.0	9.0	133.0	10.0
	Follow-up Month 6	n	3	n	3	n	6
	Mean	113.67	-15.67	121.33	10.00	117.50	-2.83
	SD	19.502	10.116	11.930	30.050	15.057	24.490
	Median	105.00	-21.00	116.00	8.00	114.50	-11.50
	Q1	100.00	-22.00	113.00	-19.00	105.00	-21.00
	Q3	136.00	-4.00	135.00	41.00	135.00	8.00
	Min	100.0	-22.0	113.0	-19.0	100.0	-22.0
	Max	136.0	-4.0	135.0	41.0	136.0	41.0

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Hemoglobin (g/L)	Follow-up Month 9	n	2	2	1	1	3
		Mean	112.00	-21.50	140.00	1.00	121.33
		SD	38.184	28.991	NE	NE	31.470
		Median	112.00	-21.50	140.00	1.00	139.00
		Q1	85.00	-42.00	140.00	1.00	85.00
		Q3	139.00	-1.00	140.00	1.00	140.00
		Min	85.0	-42.0	140.0	1.0	85.0
		Max	139.0	-1.0	140.0	1.0	140.0
	Follow-up Month 12	n	1	1	1	1	2
		Mean	141.00	1.00	130.00	3.00	135.50
		SD	NE	NE	NE	NE	7.778
		Median	141.00	1.00	130.00	3.00	135.50
		Q1	141.00	1.00	130.00	3.00	130.00
		Q3	141.00	1.00	130.00	3.00	141.00
		Min	141.0	1.0	130.0	3.0	130.0
		Max	141.0	1.0	130.0	3.0	141.0
	Follow-up Month 15	n	2	2	1	1	3
		Mean	129.50	-4.00	140.00	-19.00	133.00
		SD	2.121	7.071	NE	NE	6.245
		Median	129.50	-4.00	140.00	-19.00	131.00
		Q1	128.00	-9.00	140.00	-19.00	128.00
		Q3	131.00	1.00	140.00	-19.00	140.00
		Min	128.0	-9.0	140.0	-19.0	128.0
		Max	131.0	1.0	140.0	-19.0	140.0

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Hemoglobin (g/L)	Follow-up Month 18	n	1	1	0	0	1
		Mean	127.00	-13.00			127.00
		SD	NE	NE			NE
		Median	127.00	-13.00			127.00
		Q1	127.00	-13.00			127.00
		Q3	127.00	-13.00			127.00
		Min	127.0	-13.0			127.0
		Max	127.0	-13.0			127.0
Leukocytes (10E9/L)	Baseline	n	23	41			64
		Mean	6.260	5.768			5.945
		SD	3.0300	2.3452			2.5990
		Median	6.100	5.400			5.550
		Q1	4.000	3.800			3.900
		Q3	8.200	6.900			7.150
		Min	2.60	2.80			2.60
		Max	15.90	14.83			15.90
	Week 2	n	18	37	37	55	55
		Mean	5.816	0.051	5.149	-0.429	5.367
		SD	2.2540	1.9916	2.0678	1.2363	2.1330
		Median	4.900	0.130	4.800	-0.300	4.900
		Q1	4.300	-1.300	3.600	-1.300	3.800
		Q3	8.300	1.200	6.300	0.500	6.640
		Min	2.30	-4.20	2.70	-3.34	2.30
		Max	9.71	4.90	13.00	1.44	13.00

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Leukocytes (10E9/L)	Week 4	n	17	36	36	53	53
		Mean	5.214	-0.685	4.978	-0.674	5.054
		SD	2.2874	1.8568	1.6408	1.7116	1.8532
		Median	4.400	-0.140	4.900	-0.385	4.900
		Q1	3.870	-1.500	3.520	-1.050	3.700
		Q3	6.800	0.200	6.250	0.215	6.300
		Min	2.60	-4.50	2.60	-8.42	2.60
		Max	11.30	2.90	8.43	1.60	11.30
	Week 6	n	18	35	35	53	53
		Mean	4.833	-0.932	4.956	-0.733	4.915
		SD	1.7413	1.6071	1.6161	1.4302	1.6439
		Median	4.300	-0.950	5.100	-0.480	4.500
		Q1	3.600	-1.700	3.600	-1.240	3.600
		Q3	6.800	0.560	6.000	0.100	6.000
		Min	2.40	-4.24	2.50	-7.03	2.40
		Max	8.47	1.03	7.80	1.40	8.47
	Week 8	n	14	26	26	40	40
		Mean	4.420	-1.129	4.896	-0.733	4.730
		SD	1.5921	1.9337	1.6064	1.2203	1.5975
		Median	4.000	-0.950	4.950	-0.850	4.800
		Q1	3.260	-1.810	3.600	-1.800	3.600
		Q3	5.400	0.660	6.000	0.300	5.950
		Min	2.50	-5.20	2.32	-3.50	2.32
		Max	7.32	1.10	9.28	1.60	9.28

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Leukocytes (10E9/L)	Week 10	n	14	23	23	37	37
		Mean	4.985	-0.828	4.915	-0.592	4.942
		SD	1.6957	1.9504	1.6556	1.5866	1.6476
		Median	4.600	-0.450	4.810	-0.600	4.750
		Q1	4.000	-1.800	3.500	-0.950	3.700
		Q3	5.500	0.260	6.100	0.200	5.900
		Min	2.80	-4.90	2.40	-5.80	2.40
		Max	8.82	1.79	9.00	2.20	9.00
	Week 12	n	12	21	21	33	33
		Mean	5.290	-0.058	4.860	-0.374	5.017
		SD	2.6887	1.6819	1.6323	1.3211	2.0480
		Median	4.450	0.310	5.300	-0.400	4.840
		Q1	3.600	-0.900	3.300	-0.700	3.300
		Q3	5.700	0.900	5.620	0.500	5.620
		Min	3.24	-4.28	2.30	-4.66	2.30
		Max	12.61	2.50	7.80	1.60	12.61
	Week 14	n	13	22	22	35	35
		Mean	4.718	-1.072	4.798	-0.504	4.768
		SD	1.2449	2.0430	1.5221	1.5203	1.4069
		Median	4.600	-0.900	5.150	-0.350	4.600
		Q1	3.900	-2.500	3.510	-1.200	3.600
		Q3	5.300	0.800	5.800	0.410	5.800
		Min	3.24	-4.30	2.20	-5.50	2.20
		Max	6.90	1.30	7.40	2.30	7.40

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Leukocytes (10E9/L)	Week 16	n	12	17	17	29	29
		Mean	4.433	-0.815	5.004	-0.562	-0.667
		SD	1.4187	2.0192	1.2982	1.4181	1.3550
		Median	4.050	-0.500	5.300	-0.120	4.400
		Q1	3.610	-1.650	4.100	-1.200	3.900
		Q3	4.750	0.530	5.800	0.400	5.700
		Min	2.90	-5.00	2.98	-3.20	2.90
		Max	8.37	1.80	7.20	1.55	8.37
	Week 18	n	8	14	14	22	22
		Mean	4.329	-2.280	4.826	-0.424	4.645
		SD	1.2667	1.9395	1.5944	0.8026	1.4726
		Median	4.150	-2.150	5.050	-0.200	4.550
		Q1	3.505	-3.800	3.300	-0.700	3.300
		Q3	4.900	-1.000	5.900	0.200	5.900
		Min	2.70	-5.10	2.90	-2.30	2.70
		Max	6.82	0.76	7.30	0.37	7.30
	Week 20	n	9	15	15	24	24
		Mean	4.369	-1.283	4.484	-0.311	4.441
		SD	1.1380	1.9606	1.5096	1.1623	1.3568
		Median	4.000	-1.000	4.400	-0.270	4.200
		Q1	3.600	-2.700	3.200	-0.900	3.350
		Q3	5.100	0.000	5.500	0.220	5.240
		Min	3.01	-4.51	2.60	-2.50	2.60
		Max	6.71	1.10	7.80	1.60	7.80

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Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Leukocytes (10E9/L)	Week 22	n	8	8	15	15	23
		Mean	4.504	-1.843	4.861	-0.074	4.737
		SD	1.5117	2.6437	1.5432	1.2053	1.5076
		Median	4.050	-1.600	4.600	-0.100	4.500
		Q1	3.250	-4.100	3.500	-0.850	3.400
		Q3	5.905	-0.300	6.500	0.300	6.500
		Min	2.92	-5.30	2.90	-1.60	2.90
		Max	6.70	2.56	7.20	3.60	7.20
	Week 24	n	8	8	7	7	15
		Mean	4.354	-1.855	4.776	0.119	4.551
		SD	0.7225	2.3763	1.1266	1.2518	0.9232
		Median	4.200	-1.800	4.500	0.030	4.300
		Q1	4.000	-4.100	3.800	-1.100	4.000
		Q3	4.500	0.230	5.700	1.200	5.700
		Min	3.50	-4.90	3.13	-1.20	3.13
		Max	5.93	1.40	6.20	2.10	6.20
	Week 26	n	3	3	3	3	6
		Mean	4.167	-1.567	3.467	-0.367	3.817
		SD	0.9292	0.8505	1.4572	0.4619	1.1583
		Median	3.900	-1.900	3.000	-0.100	3.650
		Q1	3.400	-2.200	2.300	-0.900	3.000
		Q3	5.200	-0.600	5.100	-0.100	5.100
		Min	3.40	-2.20	2.30	-0.90	2.30
		Max	5.20	-0.60	5.10	-0.10	5.20

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Leukocytes (10E9/L)	Week 28	n	1	2	2	3	3
		Mean	2.900	-0.600	4.450	0.200	3.933
		SD	NE	NE	0.9192	0.4243	1.1060
		Median	2.900	-0.600	4.450	0.200	3.800
		Q1	2.900	-0.600	3.800	-0.100	2.900
		Q3	2.900	-0.600	5.100	0.500	5.100
		Min	2.90	-0.60	3.80	-0.10	2.90
		Max	2.90	-0.60	5.10	0.50	5.10
	Week 30	n	0	0	1	1	1
		Mean	NE	NE	4.400	-0.800	4.400
		SD	NE	NE	NE	NE	NE
		Median	4.400	4.400	-0.800	4.400	-0.800
		Q1	4.400	4.400	-0.800	4.400	-0.800
		Q3	4.400	4.400	-0.800	4.400	-0.800
		Min	4.40	4.40	-0.80	4.40	-0.80
		Max	4.40	4.40	-0.80	4.40	-0.80
	Week 32	n	0	0	1	1	1
		Mean	NE	NE	4.100	-1.100	4.100
		SD	NE	NE	NE	NE	NE
		Median	4.100	4.100	-1.100	4.100	-1.100
		Q1	4.100	4.100	-1.100	4.100	-1.100
		Q3	4.100	4.100	-1.100	4.100	-1.100
		Min	4.10	4.10	-1.10	4.10	-1.10
		Max	4.10	4.10	-1.10	4.10	-1.10

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall		
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value	
Leukocytes (10E9/L)	Week 34	n	0	1	1	1	1	
		Mean		4.100	-1.100	4.100	-1.100	
		SD		NE	NE	NE	NE	
		Median		4.100	-1.100	4.100	-1.100	
		Q1		4.100	-1.100	4.100	-1.100	
		Q3		4.100	-1.100	4.100	-1.100	
		Min		4.10	-1.10	4.10	-1.10	
		Max		4.10	-1.10	4.10	-1.10	
Follow-up	Week 2	n	17	23	23	40	40	
		Mean	4.810	-1.182	4.719	-0.870	4.758	-1.003
		SD	2.1009	2.2855	2.1732	1.4768	2.1159	1.8433
		Median	4.200	-1.200	4.000	-1.000	4.150	-1.045
		Q1	3.400	-2.200	3.100	-1.850	3.200	-1.915
		Q3	5.500	0.400	6.090	0.000	5.650	0.150
		Min	2.50	-6.70	2.10	-4.10	2.10	-6.70
		Max	9.60	2.00	9.70	2.70	9.70	2.70
Follow-up	Week 4	n	10	20	20	30	30	
		Mean	3.972	-2.330	5.203	-1.028	4.792	-1.462
		SD	2.2217	1.9794	1.4482	2.1879	1.8039	2.1777
		Median	3.650	-2.050	5.330	-0.500	4.200	-0.950
		Q1	2.900	-3.400	3.850	-1.560	3.600	-2.100
		Q3	3.900	-1.100	6.200	0.165	5.700	-0.070
		Min	2.50	-5.80	3.13	-9.18	2.50	-9.18
		Max	10.10	0.80	8.50	1.20	10.10	1.20

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Leukocytes (10E9/L)	Follow-up Week 6	n	10	16	16	26	26
		Mean	4.176	-1.749	4.644	-1.183	4.464
		SD	1.2792	1.2039	2.1219	2.7103	1.8288
		Median	3.950	-1.650	4.325	-0.350	4.095
		Q1	3.000	-2.500	3.200	-1.705	3.200
		Q3	4.600	-1.000	5.700	-0.170	5.400
		Min	2.90	-3.50	1.59	-10.07	1.59
		Max	6.76	0.46	9.80	2.80	9.80
	Follow-up Week 8	n	7	9	9	16	16
		Mean	4.886	-0.400	4.103	-0.889	4.466
		SD	1.4311	1.1690	1.9983	1.5292	1.7634
		Median	4.100	-0.700	3.600	-1.290	4.050
		Q1	4.000	-1.100	3.500	-1.700	3.550
		Q3	6.000	1.100	4.340	0.300	5.050
		Min	3.60	-2.00	1.25	-3.15	1.25
		Max	7.60	1.20	8.60	1.30	8.60
	Follow-up Week 10	n	4	9	9	13	13
		Mean	3.763	-2.050	4.529	-0.463	4.293
		SD	1.3413	2.2807	1.7325	0.9224	1.6082
		Median	3.850	-1.750	4.280	-0.600	4.280
		Q1	2.750	-3.880	3.100	-1.100	3.100
		Q3	4.775	-0.220	6.000	0.200	5.250
		Min	2.10	-4.86	2.40	-1.92	2.10
		Max	5.25	0.16	7.50	0.70	7.50

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Leukocytes (10E9/L)	Follow-up Week 12	n	5	n	2	n	7
		Mean	5.120	Value	7.350	Change	0.293
		SD	1.8458	Change	-0.350	Value	5.757
		Median	5.500	Value	2.3817	Change	2.3066
		Q1	3.400	Value	-0.700	Value	6.500
		Q3	6.700	Value	-2.000	Value	0.900
		Min	3.00	Value	1.360	Value	3.400
		Max	7.00	Value	-3.11	Value	-2.000
				Value	8.200	Value	2.700
				Value	6.50	Value	3.00
				Value	2.900	Value	-3.11
				Value	8.20	Value	2.90
	Follow-up Month 6	n	3	n	3	n	6
		Mean	3.967	Value	-0.367	Value	4.100
		SD	0.2309	Value	4.233	Value	-0.333
		Median	4.100	Value	1.6010	Value	1.2420
		Q1	3.700	Value	-0.300	Value	3.900
		Q3	4.100	Value	-2.000	Value	-0.050
		Min	3.70	Value	1.200	Value	3.600
		Max	4.10	Value	-2.00	Value	-1.600
				Value	7.500	Value	0.500
				Value	1.60	Value	4.100
				Value	-1.60	Value	0.500
				Value	0.50	Value	-2.00
				Value	7.50	Value	1.20
	Follow-up Month 9	n	2	n	1	n	3
		Mean	4.300	Value	-0.750	Value	4.800
		SD	0.1414	Value	5.800	Value	-0.867
		Median	4.300	Value	1.3435	Value	0.9713
		Q1	4.200	Value	-0.750	Value	0.8718
		Q3	4.400	Value	-1.700	Value	4.400
		Min	4.20	Value	0.200	Value	-1.100
		Max	4.40	Value	-1.70	Value	-1.700
				Value	5.800	Value	0.200
				Value	5.80	Value	-1.10
				Value	-1.10	Value	4.20
				Value	5.80	Value	-1.70
				Value	0.20	Value	5.80

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Leukocytes (10E9/L)	Follow-up Month 12	n	1	1	1	1	2
		Mean	3.700	-0.300	5.100	-1.900	4.400
		SD	NE	NE	NE	NE	0.9899
		Median	3.700	-0.300	5.100	-1.900	4.400
		Q1	3.700	-0.300	5.100	-1.900	3.700
		Q3	3.700	-0.300	5.100	-1.900	5.100
		Min	3.70	-0.30	5.10	-1.90	3.70
		Max	3.70	-0.30	5.10	-1.90	5.10
	Follow-up Month 15	n	2	2	1	1	3
		Mean	4.500	-0.550	4.600	-1.000	4.533
		SD	1.4142	0.0707	NE	NE	1.0017
		Median	4.500	-0.550	4.600	-1.000	4.600
		Q1	3.500	-0.600	4.600	-1.000	3.500
		Q3	5.500	-0.500	4.600	-1.000	5.500
		Min	3.50	-0.60	4.60	-1.00	3.50
		Max	5.50	-0.50	4.60	-1.00	5.50
	Follow-up Month 18	n	1	1	0	0	1
		Mean	3.500	-0.500	NE	NE	3.500
		SD	NE	NE	NE	NE	NE
		Median	3.500	-0.500	NE	NE	3.500
		Q1	3.500	-0.500	NE	NE	3.500
		Q3	3.500	-0.500	NE	NE	3.500
		Min	3.50	-0.50	NE	NE	3.50
		Max	3.50	-0.50	NE	NE	3.50

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Lymphocytes (10E9/L)	Baseline	n	22		40		62
		Mean	1.2264		1.0028		1.0821
		SD	0.89622		0.52854		0.68319
		Median	0.9700		0.9850		0.9850
		Q1	0.6100		0.6050		0.6100
		Q3	1.6000		1.2765		1.4300
		Min	0.300		0.300		0.300
		Max	4.250		2.800		4.250
	Week 2	n	14	14	35	35	49
		Mean	0.8714	-0.1071	0.8749	-0.1807	0.8739
		SD	0.60944	0.44398	0.46148	0.22391	0.50144
		Median	0.6750	-0.1150	0.7700	-0.1400	0.7000
		Q1	0.4600	-0.3800	0.5100	-0.3200	0.5100
		Q3	1.1100	0.2600	1.1000	-0.0800	1.1000
		Min	0.290	-1.110	0.220	-0.700	0.220
		Max	2.570	0.560	2.310	0.320	2.570
	Week 4	n	16	16	34	34	50
		Mean	1.0906	-0.0988	0.8629	-0.1898	0.9358
		SD	0.90472	0.56725	0.42578	0.26089	0.61981
		Median	0.7000	-0.0500	0.7900	-0.1100	0.7250
		Q1	0.5000	-0.1550	0.6000	-0.3500	0.6000
		Q3	1.4450	0.0000	1.0000	0.0000	1.0800
		Min	0.300	-1.240	0.280	-0.770	0.280
		Max	3.290	1.380	2.090	0.200	3.290

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Lymphocytes (10E9/L)	Week 6	n	17	35	35	52	52
		Mean	1.1341	-0.0406	0.9414	-0.0947	1.0044
		SD	0.92117	0.46231	0.57996	0.27880	0.70625
		Median	0.7000	-0.1300	0.8000	-0.0800	0.7950
		Q1	0.6000	-0.3400	0.5300	-0.2000	0.5650
		Q3	1.2400	0.1300	1.2000	0.0900	1.2000
		Min	0.300	-0.900	0.220	-0.800	0.220
		Max	3.780	1.180	3.270	0.470	3.780
	Week 8	n	12	24	24	36	36
		Mean	0.9717	-0.1600	0.8446	-0.2546	0.8869
		SD	0.91258	0.58695	0.47432	0.24072	0.64286
		Median	0.5750	-0.0900	0.7200	-0.2500	0.7050
		Q1	0.4500	-0.2200	0.5450	-0.4400	0.5100
		Q3	1.0300	0.1200	1.0500	-0.1200	1.0500
		Min	0.300	-1.360	0.200	-0.630	0.200
		Max	2.890	0.780	2.440	0.220	2.890
	Week 10	n	13	22	22	35	35
		Mean	1.2369	-0.0069	0.7491	-0.2370	0.9303
		SD	0.95721	0.91672	0.33881	0.34474	0.67192
		Median	0.9200	-0.1200	0.6250	-0.1000	0.6500
		Q1	0.5300	-0.3200	0.4800	-0.4800	0.4800
		Q3	1.3000	0.1000	1.0200	0.0000	1.1000
		Min	0.340	-1.370	0.300	-1.260	0.300
		Max	3.000	2.600	1.540	0.300	3.000

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Lymphocytes (10E9/L)	Week 12	n	11	20	20	31	31
		Mean	1.4727	0.1755	0.7805	-0.1740	1.0261
		SD	1.35695	0.46481	0.36359	0.35148	0.90047
		Median	0.9000	0.0600	0.7350	-0.0950	0.8400
		Q1	0.5800	-0.0400	0.5000	-0.3200	0.5000
		Q3	1.7000	0.5400	0.9800	0.0000	1.1500
		Min	0.420	-0.580	0.250	-1.150	0.250
		Max	4.790	1.230	1.650	0.400	4.790
	Week 14	n	13	21	21	34	34
		Mean	1.0623	-0.2708	0.9138	-0.1082	0.9706
		SD	0.79191	0.57206	0.44554	0.27308	0.59474
		Median	0.7000	-0.1500	0.9000	-0.0600	0.8800
		Q1	0.5400	-0.6100	0.5000	-0.2200	0.5000
		Q3	1.0000	0.1000	1.2000	0.0400	1.2000
		Min	0.310	-1.290	0.300	-0.930	0.300
		Max	2.960	0.410	1.870	0.200	2.960
	Week 16	n	11	11	17	28	28
		Mean	0.7800	-0.1991	0.8624	-0.1837	0.8300
		SD	0.57154	0.38526	0.51320	0.33045	0.52795
		Median	0.6200	-0.1200	0.7300	-0.1100	0.6750
		Q1	0.4000	-0.3200	0.5000	-0.3500	0.4900
		Q3	0.9000	0.0000	1.0000	0.0300	0.9500
		Min	0.200	-1.150	0.200	-0.780	0.200
		Max	2.230	0.220	2.020	0.390	2.230

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Lymphocytes (10E9/L) Week 18							
n		8	8	14	14	22	22
Mean		1.2275	-0.1988	0.7621	-0.2116	0.9314	-0.2070
SD		1.04004	0.54257	0.39404	0.20806	0.71356	0.35350
Median		0.7100	-0.1200	0.7650	-0.1600	0.7650	-0.1600
Q1		0.5350	-0.5000	0.4800	-0.3200	0.5000	-0.3200
Q3		1.9800	0.1400	0.8000	-0.1000	1.0500	-0.0500
Min		0.300	-1.180	0.300	-0.620	0.300	-1.180
Max		3.070	0.550	1.760	0.110	3.070	0.550
Week 20							
n		9	9	15	15	24	24
Mean		1.3133	-0.1767	0.7080	-0.1993	0.9350	-0.1908
SD		0.97081	0.73268	0.36064	0.39480	0.70470	0.53077
Median		0.9000	-0.2600	0.6000	-0.1000	0.6700	-0.1550
Q1		0.6000	-0.3400	0.4700	-0.4200	0.5100	-0.4050
Q3		1.5000	-0.0100	0.9000	0.1000	1.0500	0.0900
Min		0.480	-1.580	0.200	-1.120	0.200	-1.580
Max		3.160	1.150	1.680	0.400	3.160	1.150
Week 22							
n		8	8	15	15	23	23
Mean		1.2838	-0.2313	0.9573	-0.0740	1.0709	-0.1287
SD		0.96587	0.70756	0.53697	0.34107	0.71105	0.48907
Median		1.0200	-0.1950	0.8200	-0.0400	0.8400	-0.1100
Q1		0.5600	-0.4450	0.6000	-0.2200	0.6000	-0.3100
Q3		2.0600	0.1400	1.3000	0.0500	1.4000	0.0500
Min		0.200	-1.630	0.400	-0.770	0.200	-1.630
Max		2.790	0.780	2.400	0.650	2.790	0.780

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Lymphocytes (10E9/L)	Week 24	n	8	8	7	7	15
		Mean	1.1113	-0.3288	0.7454	-0.0221	0.9405
		SD	0.86303	0.80577	0.26120	0.27546	0.66131
		Median	0.8050	-0.1400	0.7980	0.0880	0.7980
		Q1	0.4400	-0.5350	0.5900	-0.2600	0.5900
		Q3	1.7900	0.1200	0.8400	0.1100	1.1600
		Min	0.260	-2.070	0.300	-0.463	0.260
		Max	2.560	0.550	1.160	0.370	2.560
	Week 26	n	3	3	3	3	6
		Mean	1.0800	-0.0233	0.6933	-0.0133	0.8867
		SD	0.46936	0.25580	0.36350	0.27062	0.43108
		Median	1.3100	-0.1400	0.5800	0.0500	0.8400
		Q1	0.5400	-0.2000	0.4000	-0.3100	0.5400
		Q3	1.3900	0.2700	1.1000	0.2200	1.3100
		Min	0.540	-0.200	0.400	-0.310	0.400
		Max	1.390	0.270	1.100	0.220	1.390
	Week 28	n	1	1	2	2	3
		Mean	0.4800	-0.4600	1.0350	0.2650	0.8500
		SD	NE	NE	0.37477	0.02121	0.41581
		Median	0.4800	-0.4600	1.0350	0.2650	0.7700
		Q1	0.4800	-0.4600	0.7700	0.2500	0.4800
		Q3	0.4800	-0.4600	1.3000	0.2800	1.3000
		Min	0.480	-0.460	0.770	0.250	0.480
		Max	0.480	-0.460	1.300	0.280	1.300

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value	Change
Lymphocytes (10E9/L)	Week 30	n	0	0	1	1	1	1	1
		Mean			1.1000	0.0500	1.1000	0.0500	
		SD			NE	NE	NE	NE	
		Median			1.1000	0.0500	1.1000	0.0500	
		Q1			1.1000	0.0500	1.1000	0.0500	
		Q3			1.1000	0.0500	1.1000	0.0500	
		Min			1.100	0.050	1.100	0.050	
		Max			1.100	0.050	1.100	0.050	
	Week 32	n	0	0	1	1	1	1	1
		Mean			1.2000	0.1500	1.2000	0.1500	
		SD			NE	NE	NE	NE	
		Median			1.2000	0.1500	1.2000	0.1500	
		Q1			1.2000	0.1500	1.2000	0.1500	
		Q3			1.2000	0.1500	1.2000	0.1500	
		Min			1.200	0.150	1.200	0.150	
		Max			1.200	0.150	1.200	0.150	
	Week 34	n	0	0	1	1	1	1	1
		Mean			1.2000	0.1500	1.2000	0.1500	
		SD			NE	NE	NE	NE	
		Median			1.2000	0.1500	1.2000	0.1500	
		Q1			1.2000	0.1500	1.2000	0.1500	
		Q3			1.2000	0.1500	1.2000	0.1500	
		Min			1.200	0.150	1.200	0.150	
		Max			1.200	0.150	1.200	0.150	

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Lymphocytes (10E9/L)	Follow-up Week 2	n	16	22	22	38	38
		Mean	0.9806	-0.3994	0.7364	-0.2559	0.8392
		SD	0.76014	0.66618	0.40368	0.30145	0.58453
		Median	0.8750	-0.1900	0.6050	-0.2150	0.6550
		Q1	0.4400	-0.7650	0.5100	-0.4900	0.5000
		Q3	1.2250	-0.1000	0.8600	0.0000	1.0000
		Min	0.280	-1.860	0.230	-0.880	0.230
		Max	2.970	0.960	1.920	0.230	2.970
Lymphocytes (10E9/L)	Follow-up Week 4	n	10	19	19	29	29
		Mean	0.7770	-0.3750	0.8384	-0.1491	0.8172
		SD	0.44813	0.47273	0.41521	0.34865	0.41984
		Median	0.7950	-0.2350	0.7100	-0.2000	0.7100
		Q1	0.2900	-0.7800	0.6000	-0.3900	0.5500
		Q3	1.0000	-0.1200	1.0900	0.1600	1.0300
		Min	0.270	-1.060	0.050	-0.960	0.050
		Max	1.550	0.450	1.750	0.400	1.750
Lymphocytes (10E9/L)	Follow-up Week 6	n	10	16	16	26	26
		Mean	1.1920	-0.4730	0.8419	-0.2164	0.9765
		SD	0.62804	0.69921	0.54770	0.29216	0.59343
		Median	1.1000	-0.3400	0.7650	-0.1950	0.9850
		Q1	0.7000	-0.7500	0.4000	-0.3850	0.5100
		Q3	1.2000	0.0200	1.1000	0.0150	1.2000
		Min	0.450	-2.010	0.200	-0.810	0.200
		Max	2.300	0.290	2.170	0.150	2.300

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Lymphocytes (10E9/L)	Follow-up Week 8	n	7	7	8	8	15
		Mean	1.2114	-0.2086	0.7588	-0.0738	0.9700
		SD	0.47562	0.54404	0.37407	0.35661	0.47070
		Median	1.2900	-0.0500	0.7050	-0.1150	0.9000
		Q1	0.7000	-0.7800	0.6150	-0.2300	0.6900
		Q3	1.7000	0.0500	0.9150	0.2050	1.3000
		Min	0.690	-1.050	0.140	-0.710	0.140
		Max	1.900	0.580	1.460	0.400	1.900
Lymphocytes (10E9/L)	Follow-up Week 10	n	4	4	9	9	13
		Mean	1.5800	-0.8350	0.9622	-0.1737	1.1523
		SD	0.59705	1.05105	0.47468	0.46308	0.57219
		Median	1.5750	-0.6300	1.0000	-0.0030	1.1000
		Q1	1.0700	-1.6050	0.7000	-0.2900	0.7300
		Q3	2.0900	-0.0650	1.2600	0.1000	1.3000
		Min	0.990	-2.250	0.250	-0.980	0.250
		Max	2.180	0.170	1.820	0.340	2.180
Lymphocytes (10E9/L)	Follow-up Week 12	n	5	5	2	2	7
		Mean	1.6520	-0.3660	0.8000	-0.4150	1.4086
		SD	1.12777	1.14505	0.14142	0.16263	1.01197
		Median	1.1000	-0.7500	0.8000	-0.4150	0.9000
		Q1	0.7700	-0.8500	0.7000	-0.5300	0.7000
		Q3	2.4900	0.3400	0.9000	-0.3000	2.4900
		Min	0.700	-1.760	0.700	-0.530	0.700
		Max	3.200	1.190	0.900	-0.300	3.200

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Lymphocytes (10E9/L)	Follow-up Month 6	n	3	n	3	n	6
	Mean	0.8733	-0.1400	0.6667	-0.0567	0.7700	-0.0983
	SD	0.43501	0.05292	0.28868	0.17898	0.34906	0.12656
	Median	0.6900	-0.1600	0.5000	-0.1000	0.6250	-0.1300
	Q1	0.5600	-0.1800	0.5000	-0.2100	0.5000	-0.1800
	Q3	1.3700	-0.0800	1.0000	0.1400	1.0000	-0.0800
	Min	0.560	-0.180	0.500	-0.210	0.500	-0.210
	Max	1.370	-0.080	1.000	0.140	1.370	0.140
Lymphocytes (10E9/L)	Follow-up Month 9	n	2	n	1	n	3
	Mean	1.0000	-0.0950	0.9500	-0.3130	0.9833	-0.1677
	SD	0.72125	0.21920	NE	NE	0.51082	0.19967
	Median	1.0000	-0.0950	0.9500	-0.3130	0.9500	-0.2500
	Q1	0.4900	-0.2500	0.9500	-0.3130	0.4900	-0.3130
	Q3	1.5100	0.0600	0.9500	-0.3130	1.5100	0.0600
	Min	0.490	-0.250	0.950	-0.313	0.490	-0.313
	Max	1.510	0.060	0.950	-0.313	1.510	0.060
Lymphocytes (10E9/L)	Follow-up Month 12	n	1	n	1	n	2
	Mean	1.4100	-0.0400	0.9200	-0.0500	1.1650	-0.0450
	SD	NE	NE	NE	NE	0.34648	0.00707
	Median	1.4100	-0.0400	0.9200	-0.0500	1.1650	-0.0450
	Q1	1.4100	-0.0400	0.9200	-0.0500	0.9200	-0.0500
	Q3	1.4100	-0.0400	0.9200	-0.0500	1.4100	-0.0400
	Min	1.410	-0.040	0.920	-0.050	0.920	-0.050
	Max	1.410	-0.040	0.920	-0.050	1.410	-0.040

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Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Lymphocytes (10E9/L)	Follow-up Month 15	n	2	1	1	3	3
		Mean	1.0050	-0.0900	0.8000	-0.6300	0.9367
		SD	0.00707	0.49497	NE	NE	0.11846
		Median	1.0050	-0.0900	0.8000	-0.6300	1.0000
		Q1	1.0000	-0.4400	0.8000	-0.6300	0.8000
		Q3	1.0100	0.2600	0.8000	-0.6300	1.0100
		Min	1.000	-0.440	0.800	-0.630	0.800
		Max	1.010	0.260	0.800	-0.630	1.010
	Follow-up Month 18	n	1	0	0	1	1
		Mean	0.9800	-0.4700	NE	0.9800	-0.4700
		SD	NE	NE	NE	NE	NE
		Median	0.9800	-0.4700	NE	0.9800	-0.4700
		Q1	0.9800	-0.4700	NE	0.9800	-0.4700
		Q3	0.9800	-0.4700	NE	0.9800	-0.4700
		Min	0.980	-0.470	NE	0.980	-0.470
		Max	0.980	-0.470	NE	0.980	-0.470
Monocytes (10E9/L)	Baseline	n	22	40	62		
		Mean	0.5945	0.5016	0.5345		
		SD	0.31606	0.21110	0.25474		
		Median	0.4900	0.4700	0.4800		
		Q1	0.4000	0.3400	0.3600		
		Q3	0.7000	0.5900	0.6100		
		Min	0.290	0.270	0.270		
		Max	1.500	1.270	1.500		

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	7.4 GBq (N=41)	6.0 GBq (N=23)	7.4 GBq (N=41)	Value	Change
Monocytes (10E9/L)	Week 2	n	14	35	35	49	49
		Mean	0.5043	-0.0843	0.5311	0.0262	0.5235
		SD	0.27895	0.21622	0.18632	0.11741	0.21404
		Median	0.3900	-0.0950	0.5000	0.0400	0.5000
		Q1	0.3400	-0.1900	0.3900	-0.0630	0.3900
		Q3	0.5900	0.0900	0.6000	0.1000	0.6000
		Min	0.200	-0.460	0.300	-0.300	0.200
		Max	1.140	0.250	1.060	0.200	1.140
	Week 4	n	16	34	34	50	50
		Mean	0.5294	-0.0769	0.4459	-0.0565	0.4726
		SD	0.27103	0.15611	0.15482	0.19113	0.20045
		Median	0.4100	-0.0500	0.4000	-0.0200	0.4000
		Q1	0.3450	-0.1850	0.3100	-0.1000	0.3300
		Q3	0.6400	0.0300	0.5300	0.0300	0.5300
		Min	0.260	-0.410	0.200	-0.870	0.200
		Max	1.090	0.150	0.900	0.200	1.090
	Week 6	n	16	35	35	51	51
		Mean	0.4481	-0.1131	0.4574	-0.0515	0.4545
		SD	0.18677	0.21669	0.16470	0.15333	0.17009
		Median	0.3950	-0.0850	0.4300	-0.0400	0.4100
		Q1	0.3150	-0.2600	0.3200	-0.1000	0.3200
		Q3	0.5350	0.0650	0.5100	0.0500	0.5100
		Min	0.300	-0.550	0.200	-0.510	0.200
		Max	0.950	0.210	0.800	0.240	0.950

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Monocytes (10E9/L)	Week 8	n	12	24	24	36	36
		Mean	0.4458	-0.1250	0.4588	-0.0501	0.4544
		SD	0.16952	0.28852	0.14290	0.11837	0.14996
		Median	0.4000	-0.0600	0.4150	-0.0665	0.4050
		Q1	0.3300	-0.2200	0.3450	-0.1550	0.3450
		Q3	0.5100	0.0900	0.5650	0.0300	0.5650
		Min	0.270	-0.870	0.260	-0.250	0.260
		Max	0.860	0.130	0.710	0.170	0.860
	Week 10	n	13	22	22	35	35
		Mean	0.4846	-0.0338	0.4182	-0.0542	0.4429
		SD	0.16210	0.15180	0.20437	0.21762	0.19009
		Median	0.4500	0.0100	0.3950	-0.0165	0.4000
		Q1	0.4000	-0.1400	0.3300	-0.1600	0.3500
		Q3	0.5800	0.0700	0.4700	0.0700	0.5500
		Min	0.270	-0.300	0.100	-0.650	0.100
		Max	0.890	0.160	1.140	0.430	1.140
	Week 12	n	11	20	20	31	31
		Mean	0.4336	-0.0218	0.4330	-0.0517	0.4332
		SD	0.10754	0.16431	0.17101	0.16324	0.14959
		Median	0.4000	0.0300	0.3650	0.0000	0.4000
		Q1	0.3900	-0.1200	0.3050	-0.0900	0.3100
		Q3	0.5200	0.0900	0.5500	0.0150	0.5200
		Min	0.230	-0.360	0.200	-0.440	0.200
		Max	0.600	0.180	0.780	0.220	0.780

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Monocytes (10E9/L)	Week 14	n	13	21	21	34	34
		Mean	0.4531	-0.1423	0.4657	-0.0201	0.4609
		SD	0.24119	0.29917	0.15468	0.17223	0.18893
		Median	0.4000	0.0000	0.4500	0.0000	0.4000
		Q1	0.3100	-0.2600	0.3300	-0.0600	0.3100
		Q3	0.4600	0.0900	0.5400	0.1000	0.5400
		Min	0.200	-0.860	0.270	-0.500	0.200
		Max	1.150	0.120	0.860	0.170	1.150
	Week 16	n	11	17	17	28	28
		Mean	0.4609	-0.1018	0.4818	0.0016	0.4736
		SD	0.19160	0.20454	0.13282	0.08298	0.15543
		Median	0.4300	-0.0600	0.4700	0.0000	0.4300
		Q1	0.3400	-0.2500	0.4000	-0.0600	0.4000
		Q3	0.5000	0.0800	0.6000	0.0700	0.5700
		Min	0.270	-0.520	0.260	-0.163	0.260
		Max	0.980	0.140	0.700	0.120	0.980
	Week 18	n	8	14	14	22	22
		Mean	0.4525	-0.0575	0.5293	0.0249	0.5014
		SD	0.13424	0.19948	0.15692	0.07571	0.15060
		Median	0.4850	-0.0950	0.5050	0.0385	0.5000
		Q1	0.3100	-0.2200	0.4000	0.0000	0.3900
		Q3	0.5750	0.0950	0.6300	0.0700	0.6000
		Min	0.280	-0.280	0.300	-0.190	0.280
		Max	0.600	0.260	0.810	0.120	0.810

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Monocytes (10E9/L)	Week 20	n	9	9	15	15	24
		Mean	0.4733	-0.0178	0.4467	0.0158	0.4567
		SD	0.12659	0.17740	0.17162	0.16823	0.15387
		Median	0.5000	0.0000	0.5000	0.0000	0.5000
		Q1	0.4100	-0.0500	0.3000	-0.0600	0.3200
		Q3	0.5200	0.0900	0.5300	0.1700	0.5250
		Min	0.240	-0.320	0.200	-0.360	0.200
		Max	0.700	0.240	0.840	0.200	0.840
	Week 22	n	8	8	15	15	23
		Mean	0.5025	-0.0150	0.5300	0.0533	0.5204
		SD	0.13740	0.22722	0.14871	0.10621	0.14233
		Median	0.5100	0.0200	0.5000	0.0600	0.5000
		Q1	0.3900	-0.1950	0.4000	0.0000	0.4000
		Q3	0.6100	0.1700	0.6200	0.1000	0.6200
		Min	0.300	-0.370	0.320	-0.200	0.300
		Max	0.700	0.260	0.800	0.300	0.800
	Week 24	n	8	8	7	7	15
		Mean	0.4488	-0.0588	0.4983	-0.0187	0.4719
		SD	0.09717	0.16128	0.14998	0.21090	0.12254
		Median	0.4300	0.0100	0.5100	-0.0490	0.5000
		Q1	0.3900	-0.1650	0.4200	-0.2100	0.3900
		Q3	0.5250	0.0550	0.6000	0.1300	0.5300
		Min	0.300	-0.360	0.228	-0.290	0.228
		Max	0.600	0.090	0.710	0.300	0.710

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Monocytes (10E9/L)	Week 26	n	3	3	3	6	6
		Mean	0.4067	-0.1300	0.4333	-0.0300	0.4200
		SD	0.13796	0.10817	0.14224	0.14000	0.12617
		Median	0.4600	-0.1000	0.5000	-0.0900	0.4800
		Q1	0.2500	-0.2500	0.2700	-0.1300	0.2700
		Q3	0.5100	-0.0400	0.5300	0.1300	0.5100
		Min	0.250	-0.250	0.270	-0.130	0.250
		Max	0.510	-0.040	0.530	0.130	0.530
	Week 28	n	1	1	2	2	3
		Mean	0.3300	0.0200	0.4900	-0.0100	0.4367
		SD	NE	NE	0.01414	0.16971	0.09292
		Median	0.3300	0.0200	0.4900	-0.0100	0.4800
		Q1	0.3300	0.0200	0.4800	-0.1300	0.3300
		Q3	0.3300	0.0200	0.5000	0.1100	0.5000
		Min	0.330	0.020	0.480	-0.130	0.330
		Max	0.330	0.020	0.500	0.110	0.500
	Week 30	n	0	0	1	1	1
		Mean	NE	NE	0.5000	-0.1300	0.5000
		SD	NE	NE	NE	NE	NE
		Median	0.5000	0.5000	-0.1300	0.5000	-0.1300
		Q1	0.5000	0.5000	-0.1300	0.5000	-0.1300
		Q3	0.5000	0.5000	-0.1300	0.5000	-0.1300
		Min	0.500	0.500	-0.130	0.500	-0.130
		Max	0.500	0.500	-0.130	0.500	-0.130

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall		
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value	
Monocytes (10E9/L)	Week 32	n	0	1	1	1	1	
		Mean		0.5000	-0.1300	0.5000	-0.1300	
		SD		NE	NE	NE	NE	
		Median		0.5000	-0.1300	0.5000	-0.1300	
		Q1		0.5000	-0.1300	0.5000	-0.1300	
		Q3		0.5000	-0.1300	0.5000	-0.1300	
		Min		0.500	-0.130	0.500	-0.130	
		Max		0.500	-0.130	0.500	-0.130	
	Week 34	n	0	1	1	1	1	
		Mean		0.5000	-0.1300	0.5000	-0.1300	
		SD		NE	NE	NE	NE	
		Median		0.5000	-0.1300	0.5000	-0.1300	
		Q1		0.5000	-0.1300	0.5000	-0.1300	
		Q3		0.5000	-0.1300	0.5000	-0.1300	
		Min		0.500	-0.130	0.500	-0.130	
		Max		0.500	-0.130	0.500	-0.130	
	Follow-up	n	15	15	21	36	36	
	Week 2	Mean	0.4887	-0.0500	0.4652	-0.0335	0.4750	-0.0404
		SD	0.23185	0.17092	0.21979	0.15960	0.22191	0.16220
		Median	0.4000	-0.0100	0.4100	-0.0200	0.4050	-0.0150
		Q1	0.3000	-0.1000	0.3000	-0.1400	0.3000	-0.1250
		Q3	0.6000	0.0500	0.6700	0.0100	0.6350	0.0150
		Min	0.200	-0.500	0.100	-0.300	0.100	-0.500
		Max	1.000	0.190	0.900	0.270	1.000	0.270

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Monocytes (10E9/L)	Follow-up Week 4	n	10	10	19	19	29
		Mean	0.4230	-0.0730	0.4563	-0.0910	0.4448
		SD	0.13013	0.13953	0.16415	0.23593	0.15174
		Median	0.4050	-0.0600	0.4800	-0.0200	0.4400
		Q1	0.3500	-0.1500	0.3100	-0.0900	0.3500
		Q3	0.5000	0.0600	0.5300	0.0700	0.5300
		Min	0.220	-0.340	0.090	-0.790	0.090
		Max	0.650	0.110	0.800	0.130	0.800
	Follow-up Week 6	n	10	10	16	16	26
		Mean	0.4510	-0.0750	0.3775	-0.1612	0.4058
		SD	0.17521	0.21532	0.16819	0.28116	0.17133
		Median	0.4100	-0.0200	0.3700	-0.0495	0.4000
		Q1	0.3900	-0.1900	0.3000	-0.2400	0.3000
		Q3	0.6000	0.0800	0.5000	0.0250	0.5000
		Min	0.100	-0.480	0.000	-0.970	0.000
		Max	0.700	0.220	0.730	0.100	0.730
	Follow-up Week 8	n	7	7	8	8	15
		Mean	0.4700	-0.0229	0.4413	-0.0638	0.4547
		SD	0.18877	0.19704	0.23991	0.16053	0.21040
		Median	0.5000	0.0200	0.3900	-0.0150	0.4500
		Q1	0.2400	-0.2400	0.2650	-0.1550	0.2400
		Q3	0.6000	0.0800	0.5450	0.0400	0.6000
		Min	0.200	-0.260	0.200	-0.360	0.200
		Max	0.700	0.300	0.930	0.110	0.930

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Monocytes (10E9/L)	Follow-up Week 10	n	4	4	9	9	13
		Mean	0.3550	-0.0825	0.3844	-0.0843	0.3754
		SD	0.17464	0.17727	0.08002	0.20943	0.10997
		Median	0.4100	-0.0300	0.4000	0.0000	0.4000
		Q1	0.2300	-0.2100	0.3100	-0.0590	0.3100
		Q3	0.4800	0.0450	0.4000	0.0000	0.4700
		Min	0.110	-0.330	0.280	-0.600	0.110
		Max	0.490	0.060	0.500	0.070	0.500
	Follow-up Week 12	n	5	5	2	2	7
		Mean	0.4460	0.0160	0.6000	0.1100	0.4900
		SD	0.25066	0.27682	0.14142	0.12728	0.22554
		Median	0.5000	-0.0600	0.6000	0.1100	0.5000
		Q1	0.3000	-0.1400	0.5000	0.0200	0.3000
		Q3	0.6700	0.2100	0.7000	0.2000	0.6700
		Min	0.090	-0.310	0.500	0.020	0.090
		Max	0.670	0.380	0.700	0.200	0.700
	Follow-up Month 6	n	3	3	3	3	6
		Mean	0.4700	-0.0433	0.4333	-0.1533	0.4517
		SD	0.24269	0.24583	0.32146	0.05033	0.25553
		Median	0.5400	-0.0200	0.3000	-0.1600	0.4200
		Q1	0.2000	-0.3000	0.2000	-0.2000	0.2000
		Q3	0.6700	0.1900	0.8000	-0.1000	0.6700
		Min	0.200	-0.300	0.200	-0.200	0.200
		Max	0.670	0.190	0.800	-0.100	0.800

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Monocytes (10E9/L)	Follow-up Month 9	n	2	2	1	1	3
	Mean	0.3550	-0.1750	0.4700	-0.0890	0.3933	-0.1463
	SD	0.17678	0.13435	NE	NE	0.14154	0.10719
	Median	0.3550	-0.1750	0.4700	-0.0890	0.4700	-0.0890
	Q1	0.2300	-0.2700	0.4700	-0.0890	0.2300	-0.2700
	Q3	0.4800	-0.0800	0.4700	-0.0890	0.4800	-0.0800
	Min	0.230	-0.270	0.470	-0.089	0.230	-0.270
	Max	0.480	-0.080	0.470	-0.089	0.480	-0.080
	Follow-up Month 12	n	1	1	1	2	2
	Mean	0.5000	-0.0600	0.5700	-0.0500	0.5350	-0.0550
	SD	NE	NE	NE	NE	0.04950	0.00707
	Median	0.5000	-0.0600	0.5700	-0.0500	0.5350	-0.0550
	Q1	0.5000	-0.0600	0.5700	-0.0500	0.5000	-0.0600
	Q3	0.5000	-0.0600	0.5700	-0.0500	0.5700	-0.0500
	Min	0.500	-0.060	0.570	-0.050	0.500	-0.060
	Max	0.500	-0.060	0.570	-0.050	0.570	-0.050
	Follow-up Month 15	n	2	2	1	3	3
	Mean	0.3850	-0.1450	0.8000	0.3200	0.5233	0.0100
	SD	0.07778	0.03536	NE	NE	0.24583	0.26963
	Median	0.3850	-0.1450	0.8000	0.3200	0.4400	-0.1200
	Q1	0.3300	-0.1700	0.8000	0.3200	0.3300	-0.1700
	Q3	0.4400	-0.1200	0.8000	0.3200	0.8000	0.3200
	Min	0.330	-0.170	0.800	0.320	0.330	-0.170
	Max	0.440	-0.120	0.800	0.320	0.800	0.320

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value
Monocytes (10E9/L)	Follow-up Month 18	n	1	1	0	0	0	1	1
		Mean	0.4600	-0.1000	NE	NE	NE	0.4600	-0.1000
		SD	NE	NE	NE	NE	NE	NE	NE
		Median	0.4600	-0.1000	0.09518	0.09518	0.09518	0.4600	-0.1000
		Q1	0.4600	-0.1000	3.4800	3.4800	3.4800	0.4600	-0.1000
		Q3	0.4600	-0.1000	2.5200	2.5200	2.5200	0.4600	-0.1000
		Min	0.460	-0.100	4.9400	4.9400	4.9400	0.460	-0.100
		Max	0.460	-0.100	1.700	1.700	1.700	0.460	-0.100
Neutrophils (10E9/L)	Baseline	n	21	41	62	62	62	4.1271	4.1271
		Mean	4.2571	4.0604	4.0604	4.0604	4.0604	2.37124	2.37124
		SD	2.88843	2.09518	2.09518	2.09518	2.09518	3.4500	3.4500
		Median	3.3100	3.4800	3.4800	3.4800	3.4800	2.3500	2.3500
		Q1	2.1500	2.5200	2.5200	2.5200	2.5200	4.9700	4.9700
		Q3	5.3700	4.9400	4.9400	4.9400	4.9400	1.510	1.510
		Min	1.510	1.700	1.700	1.700	1.700	14.200	14.200
		Max	14.200	11.550	11.550	11.550	11.550		
	Week 2	n	13	36	36	49	49	49	49
		Mean	4.0077	3.6464	-0.1972	3.7422	3.7422	-0.0453	-0.0453
		SD	2.12422	1.78705	1.22101	1.86619	1.86619	1.49877	1.49877
		Median	3.7100	3.2500	0.1000	3.4000	3.4000	0.1200	0.1200
		Q1	2.6800	2.4650	-0.8950	2.5800	2.5800	-0.7400	-0.7400
		Q3	4.2100	4.4500	0.6900	4.4000	4.4000	0.8000	0.8000
		Min	1.230	1.300	-3.600	1.230	1.230	-3.790	-3.790
		Max	8.370	11.290	1.580	11.290	11.290	5.050	5.050

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Neutrophils (10E9/L)	Week 4	n	15	15	35	35	50
		Mean	3.2893	-0.5813	3.5594	-0.3708	3.4784
		SD	1.99619	1.91232	1.40757	1.58195	1.59025
		Median	2.8500	-0.5100	3.3000	-0.1200	3.2500
		Q1	2.1000	-1.8700	2.4000	-0.9000	2.1700
		Q3	3.5000	0.4200	4.2000	0.5400	4.1300
		Min	1.130	-4.200	1.570	-6.250	1.130
		Max	9.570	3.250	7.000	2.580	9.570
	Week 6	n	16	16	35	35	51
		Mean	2.8913	-0.8719	3.3711	-0.5362	3.2206
		SD	1.19158	1.53685	1.32722	1.29810	1.29397
		Median	2.7100	-0.6450	3.2000	-0.2600	3.0200
		Q1	1.9950	-1.6800	2.1200	-1.1000	2.0900
		Q3	3.6800	0.2250	4.2800	0.1900	3.9000
		Min	1.130	-4.020	1.530	-5.350	1.130
		Max	6.020	1.130	6.200	2.200	6.200
	Week 8	n	11	11	25	25	36
		Mean	2.7409	-0.8936	3.5496	-0.3536	3.3025
		SD	1.15179	1.91388	1.35005	1.17677	1.33101
		Median	2.5000	-0.2800	3.5400	-0.2000	3.3250
		Q1	1.9000	-1.4200	2.8000	-0.9300	2.3150
		Q3	3.5500	0.3500	4.1000	0.6900	4.0200
		Min	1.530	-4.700	1.250	-3.230	1.250
		Max	5.480	1.170	7.630	1.240	7.630

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Neutrophils (10E9/L)	Week 10	n	13	22	22	35	35
		Mean	3.0462	-0.6462	3.4582	-0.3085	3.3051
		SD	1.14789	1.85261	1.38729	1.33089	1.30176
		Median	3.0000	-0.1200	3.2950	-0.3940	3.1000
		Q1	2.1900	-0.6300	2.6000	-0.7600	2.2000
		Q3	3.5700	0.3000	4.3000	0.2500	4.2900
		Min	1.240	-4.400	1.200	-4.800	1.200
		Max	5.270	2.060	6.800	1.530	6.800
	Week 12	n	11	20	20	31	31
		Mean	3.0064	-0.2345	3.5094	-0.1752	3.3309
		SD	1.55835	1.57297	1.31419	1.21572	1.40113
		Median	2.4600	-0.0500	3.6385	-0.0400	3.1900
		Q1	2.1900	-0.9700	2.5000	-0.5900	2.3000
		Q3	3.8000	0.5500	4.2900	0.8450	4.2200
		Min	1.330	-3.920	1.500	-4.173	1.330
		Max	7.120	2.150	6.230	1.020	7.120
	Week 14	n	12	21	21	33	33
		Mean	2.8275	-0.7733	3.3176	-0.3804	3.1394
		SD	0.79390	2.01708	1.17817	1.49297	1.06842
		Median	2.8100	-0.4900	3.4000	-0.0800	2.9000
		Q1	2.4300	-2.5100	2.2900	-0.7000	2.3600
		Q3	3.2700	0.6400	4.3000	0.2900	3.8700
		Min	1.240	-3.900	1.300	-5.200	1.240
		Max	4.200	2.290	5.300	2.140	5.300

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Neutrophils (10E9/L)	Week 16	n	10	10	17	17	27
		Mean	2.8330	-0.7940	3.4653	-0.4081	3.2311
		SD	0.91037	2.05189	0.94851	1.22966	0.96817
		Median	2.7950	-0.3900	3.3000	-0.1700	3.1000
		Q1	2.5100	-2.7100	2.9000	-1.3700	2.6900
		Q3	3.5000	0.5900	4.1000	0.6000	4.0400
		Min	1.290	-4.400	1.760	-2.500	1.290
		Max	4.460	1.700	5.400	1.200	5.400
	Week 18	n	8	8	14	14	22
		Mean	2.5275	-1.9738	3.3293	-0.2720	3.0377
		SD	0.74206	1.75686	1.16558	0.65969	1.09978
		Median	2.4500	-1.4200	2.9200	-0.1100	2.7500
		Q1	1.9400	-3.5200	2.3700	-0.5200	2.3000
		Q3	2.8650	-0.5700	4.3000	0.1600	4.1000
		Min	1.720	-4.700	1.680	-2.060	1.680
		Max	3.990	-0.070	5.590	0.470	5.590
	Week 20	n	9	9	15	15	24
		Mean	2.4678	-1.0800	3.1827	-0.0893	2.9146
		SD	0.83368	1.65311	1.27776	1.11980	1.16642
		Median	2.3000	-0.4600	3.0900	0.0000	2.4700
		Q1	2.0000	-1.8900	2.2000	-0.5500	2.1000
		Q3	2.5400	-0.1600	3.7000	0.7900	3.6000
		Min	1.510	-4.110	1.660	-2.570	1.510
		Max	4.330	1.030	6.150	1.500	6.150

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Neutrophils (10E9/L)	Week 22	n	8	8	15	15	23
		Mean	2.6075	1.5338	3.2107	-0.0160	3.0009
		SD	0.68222	2.24784	1.38687	1.16255	1.20763
		Median	2.5500	-1.0700	2.8600	-0.0100	2.8000
		Q1	2.0350	-3.5550	2.0300	-0.3000	2.0300
		Q3	3.1800	0.0700	4.0700	0.3800	3.5900
		Min	1.730	-4.700	1.540	-1.650	1.540
		Max	3.600	1.540	6.200	3.400	6.200
	Week 24	n	8	8	6	6	14
		Mean	2.6525	-1.4388	3.1400	-0.1580	2.8614
		SD	0.63209	2.07511	0.99312	0.71467	0.81065
		Median	2.8550	-1.3200	3.0050	-0.5400	2.8550
		Q1	2.6000	-3.0650	2.5800	-0.6200	2.6000
		Q3	2.9850	0.0500	4.1200	0.5600	3.1700
		Min	1.170	-4.500	1.750	-0.738	1.170
		Max	3.170	1.660	4.380	0.930	4.380
	Week 26	n	3	3	3	3	6
		Mean	2.5867	-1.4367	2.2100	-0.3167	2.3983
		SD	0.91741	0.94236	0.95221	0.23288	0.86133
		Median	3.0500	-1.7400	1.7900	-0.4200	2.4200
		Q1	1.5300	-2.1900	1.5400	-0.4800	1.5400
		Q3	3.1800	-0.3800	3.3000	-0.0500	3.1800
		Min	1.530	-2.190	1.540	-0.480	1.530
		Max	3.180	-0.380	3.300	-0.050	3.300

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Neutrophils (10E9/L)	Week 28	n	1	1	2	2	3
		Mean	2.0600	-0.0900	2.8150	-0.0350	2.5633
		SD	NE	NE	0.54447	0.16263	0.58158
		Median	2.0600	-0.0900	2.8150	-0.0350	2.4300
		Q1	2.0600	-0.0900	2.4300	-0.1500	2.0600
		Q3	2.0600	-0.0900	3.2000	0.0800	3.2000
		Min	2.060	-0.090	2.430	-0.150	2.060
		Max	2.060	-0.090	3.200	0.080	3.200
	Week 30	n	0	0	1	1	1
		Mean	NE	NE	2.7000	-0.6500	2.7000
		SD	NE	NE	NE	NE	NE
		Median	2.7000	-0.6500	2.7000	2.7000	-0.6500
		Q1	2.7000	-0.6500	2.7000	2.7000	-0.6500
		Q3	2.7000	-0.6500	2.7000	2.7000	-0.6500
		Min	2.700	-0.650	2.700	2.700	-0.650
		Max	2.700	-0.650	2.700	2.700	-0.650
	Week 32	n	0	0	1	1	1
		Mean	2.3000	-1.0500	2.3000	-1.0500	-1.0500
		SD	NE	NE	NE	NE	NE
		Median	2.3000	-1.0500	2.3000	2.3000	-1.0500
		Q1	2.3000	-1.0500	2.3000	2.3000	-1.0500
		Q3	2.3000	-1.0500	2.3000	2.3000	-1.0500
		Min	2.300	-1.050	2.300	2.300	-1.050
		Max	2.300	-1.050	2.300	2.300	-1.050

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall				
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Overall (N=64)	Value	Change
Neutrophils (10E9/L)	Week 34	n	0	0	1	1	1	1	1	1
		Mean			2.3000	-1.0500	2.3000	-1.0500	NE	NE
		SD			NE	NE	NE	NE	SD	SD
		Median			2.3000	-1.0500	2.3000	-1.0500	2.3000	-1.0500
		Q1			2.3000	-1.0500	2.3000	-1.0500	2.3000	-1.0500
		Q3			2.3000	-1.0500	2.3000	-1.0500	2.3000	-1.0500
		Min			2.300	-1.050	2.300	-1.050	2.300	-1.050
		Max			2.300	-1.050	2.300	-1.050	2.300	-1.050
Follow-up	Week 2	n	15	15	22	22	37	37		
		Mean	2.9013	-0.9867	3.4891	-0.4627	3.2508	-0.6751		
		SD	1.60653	2.14349	2.03953	1.28882	1.87503	1.68040		
		Median	2.2900	-0.8400	2.5250	-0.4150	2.4400	-0.5100		
		Q1	1.9000	-1.4100	2.3100	-1.0300	2.1000	-1.2800		
		Q3	3.5000	0.4800	4.6500	0.2400	3.9000	0.2400		
		Min	1.410	-6.700	1.100	-2.980	1.100	-6.700		
		Max	7.500	2.550	8.640	2.700	8.640	2.700		
Follow-up	Week 4	n	10	10	19	19	29	29		
		Mean	2.6530	-1.8640	3.6500	-0.6046	3.3062	-1.0389		
		SD	1.90765	2.10949	1.41554	1.97067	1.64026	2.07317		
		Median	2.1650	-1.0300	3.2900	-0.2200	2.7800	-0.4780		
		Q1	1.7900	-3.3700	2.5300	-0.6500	2.2300	-1.0800		
		Q3	2.5200	-0.8100	4.4100	0.5400	3.6900	0.2500		
		Min	1.290	-6.290	1.730	-7.860	1.290	-7.860		
		Max	7.910	0.600	6.800	1.000	7.910	1.000		

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Neutrophils (10E9/L)	Follow-up Week 6	n	10	16	16	26	26
		Mean	2.3950	1.1650	3.2088	-0.7711	2.8958
		SD	0.87232	0.97005	1.99916	2.22463	1.68372
		Median	2.1700	-0.9950	2.8600	-0.4400	2.7000
		Q1	1.7500	-1.4800	1.8350	-1.2700	1.7500
		Q3	2.7000	-0.4800	3.9850	0.1500	3.4900
		Min	1.480	-3.470	0.880	-7.650	0.880
		Max	4.100	-0.060	9.200	3.260	9.200
Follow-up Week 8	n	7	7	8	8	15	15
	Mean	3.1186	-0.0829	2.9988	-0.5163	3.0547	-0.3140
	SD	1.28531	1.42382	1.51745	1.37134	1.36497	1.36352
	Median	3.1100	-0.1900	2.6650	-0.4000	2.8700	-0.2800
	Q1	1.9000	-1.6700	1.9650	-1.3250	1.9300	-1.4300
	Q3	3.7000	0.9900	3.2850	0.4400	3.6800	0.7700
	Min	1.720	-1.680	1.750	-2.970	1.720	-2.970
	Max	5.500	2.320	6.410	1.410	6.410	2.320
Follow-up Week 10	n	4	4	9	9	13	13
	Mean	1.6925	-1.0650	2.7267	-0.5198	2.4085	-0.6875
	SD	0.58008	1.13044	1.46656	1.38300	1.32846	1.28965
	Median	1.6750	-0.7850	2.7600	-0.2700	1.9000	-0.2700
	Q1	1.3350	-1.9450	1.6000	-0.7700	1.6000	-1.1000
	Q3	2.0500	-0.1850	3.1400	0.4000	2.8000	-0.1400
	Min	1.000	-2.550	1.040	-3.818	1.000	-3.818
	Max	2.420	-0.140	5.700	0.700	5.700	0.700

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Neutrophils (10E9/L)	Follow-up Week 12	n	5	2	2	7	7
		Mean	2.8340	-0.0200	5.5000	1.9400	3.5957
		SD	1.68970	2.06509	1.41421	1.21622	1.98217
		Median	2.1900	-0.8400	5.5000	1.9400	3.4600
		Q1	1.5200	-1.0500	4.5000	1.0800	1.5200
		Q3	3.4600	-0.2900	6.5000	2.8000	5.5000
		Min	1.500	-1.510	4.500	1.080	1.500
		Max	5.500	3.590	6.500	2.800	6.500
	Follow-up Month 6	n	3	3	3	6	6
		Mean	2.5333	-0.2033	3.0000	-0.0767	2.7667
		SD	0.80749	1.33538	2.30651	0.99470	1.56657
		Median	2.6600	-0.2400	2.8000	0.4000	2.7300
		Q1	1.6700	-1.5200	0.8000	-1.2200	1.6700
		Q3	3.2700	1.1500	5.4000	0.5900	3.2700
		Min	1.670	-1.520	0.800	-1.220	0.800
		Max	3.270	1.150	5.400	0.590	5.400
	Follow-up Month 9	n	2	2	1	3	3
		Mean	2.8750	-0.4750	4.1800	-0.6780	3.3100
		SD	1.05359	0.98288	NE	NE	1.05958
		Median	2.8750	-0.4750	4.1800	-0.6780	3.6200
		Q1	2.1300	-1.1700	4.1800	-0.6780	2.1300
		Q3	3.6200	0.2200	4.1800	-0.6780	4.1800
		Min	2.130	-1.170	4.180	-0.678	2.130
		Max	3.620	0.220	4.180	-0.678	4.180

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Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		Statisti cs	Value	Change	Value	Change	Value
Neutrophils (10E9/L)	Follow-up Month 12	n	1	1	1	1	2
		Mean	1.7500	-0.1600	3.2800	-1.6200	2.5150
		SD	NE	NE	NE	NE	1.08187
		Median	1.7500	-0.1600	3.2800	-1.6200	2.5150
		Q1	1.7500	-0.1600	3.2800	-1.6200	1.7500
		Q3	1.7500	-0.1600	3.2800	-1.6200	3.2800
		Min	1.750	-0.160	3.280	-1.620	1.750
		Max	1.750	-0.160	3.280	-1.620	3.280
Follow-up Month 15	n	2	2	1	1	3	3
		Mean	3.0450	-0.3050	2.7000	-0.7200	2.9300
		SD	1.56271	0.47376	NE	NE	1.12281
		Median	3.0450	-0.3050	2.7000	-0.7200	2.7000
		Q1	1.9400	-0.6400	2.7000	-0.7200	1.9400
		Q3	4.1500	0.0300	2.7000	-0.7200	4.1500
		Min	1.940	-0.640	2.700	-0.720	1.940
		Max	4.150	0.030	2.700	-0.720	4.150
Follow-up Month 18	n	1	1	0	0	1	1
		Mean	2.0200	0.1100	NE	NE	2.0200
		SD	NE	NE	NE	NE	NE
		Median	2.0200	0.1100	2.0200	0.1100	2.0200
		Q1	2.0200	0.1100	2.0200	0.1100	2.0200
		Q3	2.0200	0.1100	2.0200	0.1100	2.0200
		Min	2.020	0.110	2.020	0.110	2.020
		Max	2.020	0.110	2.020	0.110	2.020

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall			
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value	Change
Platelets (10E9/L)	Baseline	n	23		41			64	
		Mean	229.3		228.1			228.5	
		SD	101.34		85.00			90.41	
		Median	197.0		219.0			216.5	
		Q1	159.0		160.0			160.0	
		Q3	308.0		255.0			263.5	
		Min	115		136			115	
		Max	503		531			531	
	Week 2	n	18	18	37	37	55	55	
		Mean	248.4	12.1	226.6	3.2	233.7	6.1	
		SD	99.59	55.92	64.62	55.98	77.55	55.60	
		Median	213.5	7.0	218.0	7.0	216.0	7.0	
		Q1	175.0	-20.0	177.0	-6.0	175.0	-13.0	
		Q3	356.0	48.0	258.0	25.0	276.0	29.0	
		Min	121	-107	134	-222	121	-222	
		Max	439	121	462	116	462	121	
	Week 4	n	17	17	36	36	53	53	
		Mean	187.7	-55.8	184.9	-41.9	185.8	-46.4	
		SD	71.53	55.76	55.07	63.45	60.14	60.90	
		Median	179.0	-43.0	181.0	-25.5	179.0	-34.0	
		Q1	140.0	-80.0	139.0	-64.0	140.0	-66.0	
		Q3	204.0	-19.0	225.0	-6.5	224.0	-10.0	
		Min	91	-198	103	-307	91	-307	
		Max	378	41	347	50	378	50	

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Platelets (10E9/L)	Week 6	n	18	35	35	53	53
		Mean	205.4	-31.0	199.4	-25.8	201.5
		SD	70.71	58.94	51.87	73.65	58.33
		Median	206.0	-15.5	198.0	-9.0	205.0
		Q1	154.0	-50.0	161.0	-45.0	161.0
		Q3	219.0	-5.0	239.0	15.0	238.0
		Min	106	-165	91	-333	91
		Max	394	57	282	81	394
	Week 8	n	14	26	26	40	40
		Mean	201.4	-34.6	211.0	-28.4	207.6
		SD	96.50	55.81	69.44	53.37	78.85
		Median	192.0	-25.0	208.5	-14.0	205.5
		Q1	158.0	-59.0	167.0	-43.0	163.0
		Q3	209.0	-6.0	244.0	3.0	235.0
		Min	84	-171	72	-183	72
		Max	494	35	443	49	494
	Week 10	n	14	23	23	37	37
		Mean	205.7	-18.6	211.3	-10.7	209.2
		SD	75.55	56.58	69.96	54.80	71.13
		Median	200.0	-9.0	214.0	-4.0	201.0
		Q1	171.0	-44.0	160.0	-24.0	164.0
		Q3	225.0	14.0	252.0	19.0	238.0
		Min	104	-173	96	-161	96
		Max	436	56	430	66	436

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Platelets (10E9/L)	Week 12	n	12	21	21	33	33
		Mean	169.9	-34.3	179.4	-28.9	175.9
		SD	27.27	67.33	44.92	41.96	39.22
		Median	182.0	-30.0	162.0	-19.0	165.0
		Q1	148.5	-43.0	145.0	-31.0	147.0
		Q3	192.5	2.5	210.0	-7.0	201.0
		Min	126	-198	128	-184	126
		Max	201	77	279	5	279
	Week 14	n	13	22	22	35	35
		Mean	190.3	-34.4	182.3	-23.0	185.3
		SD	53.82	62.43	48.31	50.18	49.79
		Median	180.0	-28.0	172.5	-8.5	179.0
		Q1	163.0	-55.0	141.0	-35.0	142.0
		Q3	200.0	4.0	223.0	4.0	223.0
		Min	125	-190	125	-193	125
		Max	325	64	307	41	325
	Week 16	n	12	17	17	29	29
		Mean	175.3	-32.7	190.4	-20.1	184.1
		SD	38.03	61.68	46.66	36.41	43.23
		Median	181.0	-26.5	196.0	-8.0	182.0
		Q1	150.5	-41.0	153.0	-26.0	153.0
		Q3	200.0	5.5	233.0	-1.0	211.0
		Min	105	-197	128	-135	105
		Max	231	44	272	19	272

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Platelets (10E9/L)	Week 18	n	8	14	14	22	22
		Mean	172.9	-65.8	194.9	-7.9	186.9
		SD	30.90	72.51	52.35	47.44	46.18
		Median	179.0	-46.5	182.0	-10.0	179.5
		Q1	160.0	-94.5	159.0	-22.0	159.0
		Q3	193.5	-23.5	219.0	-3.0	209.0
		Min	109	-214	129	-126	109
		Max	209	17	298	69	298
	Week 20	n	9	15	15	24	24
		Mean	166.0	-43.8	182.0	-11.5	176.0
		SD	24.89	71.06	50.22	37.38	42.58
		Median	174.0	-25.0	179.0	-4.0	174.5
		Q1	172.0	-56.0	142.0	-33.0	145.5
		Q3	175.0	-18.0	221.0	16.0	204.5
		Min	108	-205	111	-96	108
		Max	189	58	279	50	279
	Week 22	n	8	15	15	23	23
		Mean	169.4	-62.3	178.7	-22.5	175.5
		SD	26.14	88.52	51.39	29.27	43.80
		Median	172.0	-31.5	167.0	-25.0	167.0
		Q1	144.0	-115.0	147.0	-36.0	147.0
		Q3	189.5	5.0	233.0	-14.0	193.0
		Min	138	-237	103	-63	103
		Max	206	22	268	51	268

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617 6.0 GBq (N=23)		Lu-PSMA-617 7.4 GBq (N=41)		Overall (N=64)	
		Statistic	Value	Change	Value	Change	Value
Platelets (10E9/L)	Week 24	n	8	8	7	7	15
		Mean	165.6	-61.3	170.3	-22.4	167.8
		SD	32.39	101.35	52.82	42.41	41.55
		Median	163.5	-17.5	159.0	-19.0	162.0
		Q1	141.5	-124.5	154.0	-70.0	148.0
		Q3	196.5	16.5	189.0	17.0	190.0
		Min	116	-261	95	-71	95
		Max	206	22	271	42	271
	Week 26	n	3	3	3	3	6
		Mean	180.3	-24.7	150.0	-48.7	165.2
		SD	30.66	14.22	59.03	28.54	45.23
		Median	190.0	-18.0	152.0	-47.0	171.0
		Q1	146.0	-41.0	90.0	-78.0	146.0
		Q3	205.0	-15.0	208.0	-21.0	205.0
		Min	146	-41	90	-78	90
		Max	205	-15	208	-21	208
	Week 28	n	1	1	2	2	3
		Mean	101.0	-15.0	156.0	-49.5	137.7
		SD	NE	NE	9.90	44.55	32.52
		Median	101.0	-15.0	156.0	-49.5	149.0
		Q1	101.0	-15.0	149.0	-81.0	101.0
		Q3	101.0	-15.0	163.0	-18.0	163.0
		Min	101	-15	149	-81	101
		Max	101	-15	163	-18	163

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Platelets (10E9/L)	Week 30	n	0	n	1	1	1
		Mean		145.0	-85.0	145.0	-85.0
		SD		NE	NE	NE	NE
		Median		145.0	-85.0	145.0	-85.0
		Q1		145.0	-85.0	145.0	-85.0
		Q3		145.0	-85.0	145.0	-85.0
		Min		145	-85	145	-85
		Max		145	-85	145	-85
	Week 32	n	0	n	1	1	1
		Mean		158.0	-72.0	158.0	-72.0
		SD		NE	NE	NE	NE
		Median		158.0	-72.0	158.0	-72.0
		Q1		158.0	-72.0	158.0	-72.0
		Q3		158.0	-72.0	158.0	-72.0
		Min		158	-72	158	-72
		Max		158	-72	158	-72
	Week 34	n	0	n	1	1	1
		Mean		158.0	-72.0	158.0	-72.0
		SD		NE	NE	NE	NE
		Median		158.0	-72.0	158.0	-72.0
		Q1		158.0	-72.0	158.0	-72.0
		Q3		158.0	-72.0	158.0	-72.0
		Min		158	-72	158	-72
		Max		158	-72	158	-72

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Platelets (10E9/L)	Follow-up Week 2	n	17	23	23	40	40
		Mean	183.4	-14.1	191.0	-40.0	187.8
		SD	60.13	55.54	62.74	65.84	60.98
		Median	184.0	-10.0	208.0	-32.0	196.0
		Q1	137.0	-47.0	132.0	-77.0	134.5
		Q3	220.0	12.0	239.0	-2.0	238.5
		Min	88	-109	78	-222	78
		Max	302	115	282	79	302
	Follow-up Week 4	n	10	20	20	30	30
		Mean	133.2	-69.3	156.4	-90.1	148.6
		SD	49.53	91.14	42.49	101.64	45.47
		Median	141.0	-50.0	153.5	-58.5	153.5
		Q1	83.0	-96.0	140.0	-129.0	128.0
		Q3	172.0	-17.0	172.5	-24.0	172.0
		Min	61	-249	48	-356	48
		Max	193	78	252	29	252
	Follow-up Week 6	n	10	16	16	26	26
		Mean	145.2	-64.5	149.5	-102.0	147.8
		SD	59.24	53.87	71.57	124.63	65.89
		Median	157.0	-54.0	155.0	-42.0	157.0
		Q1	77.0	-98.0	108.5	-143.0	102.0
		Q3	183.0	-27.0	191.0	-26.0	184.0
		Min	64	-184	19	-429	19
		Max	247	0	266	30	266

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Platelets (10E9/L)	Follow-up Week 8	n	7	9	9	16	16
		Mean	187.0	-13.9	139.4	-51.7	160.3
		SD	64.58	42.10	62.02	64.97	65.68
		Median	182.0	-25.0	135.0	-32.0	171.5
		Q1	151.0	-49.0	97.0	-55.0	101.0
		Q3	226.0	34.0	195.0	-17.0	201.0
		Min	83	-56	39	-216	39
		Max	293	53	223	6	293
	Follow-up Week 10	n	4	9	9	13	13
		Mean	129.5	-58.0	170.9	-20.9	158.2
		SD	51.80	49.13	44.39	28.84	48.78
		Median	144.0	-45.5	160.0	-19.0	153.0
		Q1	98.5	-96.0	143.0	-47.0	142.0
		Q3	160.5	-20.0	198.0	-7.0	179.0
		Min	55	-123	118	-50	55
		Max	175	-18	246	29	246
	Follow-up Week 12	n	5	2	2	7	7
		Mean	112.4	-66.2	204.5	-20.0	138.7
		SD	71.10	46.47	95.46	16.97	83.12
		Median	148.0	-62.0	204.5	-20.0	148.0
		Q1	62.0	-93.0	137.0	-32.0	62.0
		Q3	167.0	-30.0	272.0	-8.0	172.0
		Min	13	-130	137	-32	13
		Max	172	-16	272	-8	272

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall	
		6.0 GBq (N=23)	Value	7.4 GBq (N=41)	Value	Change	Value
Platelets (10E9/L)	Follow-up Month 6	n	3	3	3	6	6
	Mean	170.0	0.0	155.3	-42.3	162.7	-21.2
	SD	25.98	25.71	42.91	11.02	32.73	29.16
	Median	155.0	-9.0	176.0	-43.0	165.5	-25.5
	Q1	155.0	-20.0	106.0	-53.0	155.0	-43.0
	Q3	200.0	29.0	184.0	-31.0	184.0	-9.0
	Min	155	-20	106	-53	106	-53
	Max	200	29	184	-31	200	29
	Follow-up Month 9	n	2	2	1	3	3
	Mean	189.0	-3.0	195.0	-13.0	191.0	-6.3
	SD	50.91	11.31	NE	NE	36.17	9.87
	Median	189.0	-3.0	195.0	-13.0	195.0	-11.0
	Q1	153.0	-11.0	195.0	-13.0	153.0	-13.0
	Q3	225.0	5.0	195.0	-13.0	225.0	5.0
	Min	153	-11	195	-13	153	-13
	Max	225	5	195	-13	225	5
	Follow-up Month 12	n	1	1	1	2	2
	Mean	149.0	-15.0	194.0	-44.0	171.5	-29.5
	SD	NE	NE	NE	NE	31.82	20.51
	Median	149.0	-15.0	194.0	-44.0	171.5	-29.5
	Q1	149.0	-15.0	194.0	-44.0	149.0	-44.0
	Q3	149.0	-15.0	194.0	-44.0	194.0	-15.0
	Min	149	-15	194	-44	149	-44
	Max	149	-15	194	-44	194	-15

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Table 14.3.2.2
Hematology Results and Changes from Baseline by Visit
Safety Population

Parameter	Analysis Visit	Lu-PSMA-617		Lu-PSMA-617		Overall		
		6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	Value
Platelets (10E9/L)	Follow-up Month 15	n	2	2	1	1	3	3
	Mean	170.5	-21.5	279.0	-1.0	206.7	-14.7	
	SD	36.06	3.54	NE	NE	67.63	12.10	
	Median	170.5	-21.5	279.0	-1.0	196.0	-19.0	
	Q1	145.0	-24.0	279.0	-1.0	145.0	-24.0	
	Q3	196.0	-19.0	279.0	-1.0	279.0	-1.0	
	Min	145	-24	279	-1	145	-24	
	Max	196	-19	279	-1	279	-1	
	Follow-up Month 18	n	1	1	0	0	1	1
	Mean	138.0	-26.0	NE	NE	138.0	-26.0	
	SD	NE	NE	NE	NE	NE	NE	
	Median	138.0	-26.0	NE	NE	138.0	-26.0	
	Q1	138.0	-26.0	NE	NE	138.0	-26.0	
	Q3	138.0	-26.0	NE	NE	138.0	-26.0	
	Min	138	-26	NE	NE	138	-26	
	Max	138	-26	NE	NE	138	-26	

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
GFR _e (mL/min/1.73m ²)	Week 2	Any	14		32			46		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (7.1)	2 (14.3)	7 (21.9)	5 (15.6)	0	8 (17.4)	7 (15.2)
		Low	0	2 (14.3)	9 (64.3)	3 (9.4)	17 (53.1)	0	5 (10.9)	26 (56.5)
	Week 4	Any	15		29			44		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	2 (13.3)	7 (24.1)	6 (20.7)	0	7 (15.9)	8 (18.2)
		Low	0	3 (20.0)	10 (66.7)	2 (6.9)	14 (48.3)	0	5 (11.4)	24 (54.5)
	Week 6	Any	16		31			47		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	3 (18.8)	8 (25.8)	3 (9.7)	0	8 (17.0)	6 (12.8)
		Low	0	3 (18.8)	10 (62.5)	4 (12.9)	16 (51.6)	0	7 (14.9)	26 (55.3)
	Week 8	Any	12		22			34		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (8.3)	4 (33.3)	6 (27.3)	4 (18.2)	0	7 (20.6)	8 (23.5)
		Low	0	2 (16.7)	5 (41.7)	3 (13.6)	9 (40.9)	0	5 (14.7)	14 (41.2)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
GFR _e (mL/min/1.73m ²)	Any	13			22			35		
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (7.7)	3 (23.1)	0	5 (22.7)	2 (9.1)	0	6 (17.1)	5 (14.3)
	Low	0	1 (7.7)	8 (61.5)	0	2 (9.1)	13 (59.1)	0	3 (8.6)	21 (60.0)
Week 10	Any	11			20			31		
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (9.1)	4 (36.4)	0	4 (20.0)	3 (15.0)	0	5 (16.1)	7 (22.6)
	Low	0	0	6 (54.5)	0	2 (10.0)	11 (55.0)	0	2 (6.5)	17 (54.8)
Week 12	Any	12			20			32		
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (8.3)	2 (16.7)	0	3 (15.0)	3 (15.0)	0	4 (12.5)	5 (15.6)
	Low	0	1 (8.3)	8 (66.7)	0	4 (20.0)	10 (50.0)	0	5 (15.6)	18 (56.3)
Week 14	Any	11			15			26		
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (9.1)	2 (18.2)	0	3 (20.0)	4 (26.7)	0	4 (15.4)	6 (23.1)
	Low	0	1 (9.1)	7 (63.6)	0	3 (20.0)	5 (33.3)	0	4 (15.4)	12 (46.2)
Week 16	Any	11			15			26		
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (9.1)	2 (18.2)	0	3 (20.0)	4 (26.7)	0	4 (15.4)	6 (23.1)
	Low	0	1 (9.1)	7 (63.6)	0	3 (20.0)	5 (33.3)	0	4 (15.4)	12 (46.2)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
GFR _e (mL/min/1.73m ²)	Week 18	Any 7	0	0	12	0	0	0	19	0
	High 0	0	0	3 (42.9)	0	2 (16.7)	0	0	2 (10.5)	3 (15.8)
	Normal 0	0	3 (42.9)	0	2 (16.7)	8 (66.7)	0	3 (15.8)	11 (57.9)	0
	Low 0	1 (14.3)	3 (42.9)	0	2 (16.7)	8 (66.7)	0	3 (15.8)	11 (57.9)	0
	Week 20	Any 7	0	0	14	0	0	0	21	0
	High 0	0	0	3 (42.9)	0	1 (7.1)	2 (14.3)	0	1 (4.8)	5 (23.8)
	Normal 0	0	3 (42.9)	0	2 (14.3)	9 (64.3)	0	2 (9.5)	13 (61.9)	0
	Low 0	0	4 (57.1)	0	2 (14.3)	9 (64.3)	0	2 (9.5)	13 (61.9)	0
	Week 22	Any 7	0	0	13	0	0	0	20	0
	High 0	0	0	3 (42.9)	0	0	0	0	0	0
	Normal 0	0	3 (42.9)	0	3 (23.1)	10 (76.9)	0	4 (20.0)	13 (65.0)	0
	Low 0	1 (14.3)	3 (42.9)	0	3 (23.1)	10 (76.9)	0	4 (20.0)	13 (65.0)	0
	Week 24	Any 6	0	0	8	0	0	0	14	0
	High 0	0	0	2 (33.3)	0	1 (12.5)	0	0	1 (7.1)	2 (14.3)
	Normal 0	0	2 (33.3)	0	2 (25.0)	5 (62.5)	0	3 (21.4)	8 (57.1)	0
	Low 0	1 (16.7)	3 (50.0)	0	2 (25.0)	5 (62.5)	0	3 (21.4)	8 (57.1)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
GFR _e (mL/min/1.73m ²)	Week 26	Any	3	0	0	3	0	0	6	0
		High	0	0	0	0	0	0	0	0
		Normal	0	2 (66.7)	0	1 (33.3)	0	0	1 (16.7)	2 (33.3)
		Low	0	1 (33.3)	0	2 (66.7)	0	0	2 (33.3)	1 (16.7)
	Week 28	Any	1	0	0	2	0	0	3	0
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (100)	0	0	1 (50.0)	0	0	2 (66.7)
		Low	0	0	0	1 (50.0)	0	0	1 (33.3)	0
	Week 30	Any	0	0	0	1	0	0	1	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	0	0	1 (100)	0	0	1 (100)	0
	Week 32	Any	0	0	0	1	0	0	1	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	0	0	1 (100)	0	0	1 (100)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
GFR _e (mL/min/1.73m ²)	Week 34	Any 0	0	0	1	0	0	0	1	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	1 (100)	0	0	1 (100)	0
FU W 2	Any 14	0	0	0	21	0	0	0	35	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 0	3 (21.4)	3 (21.4)	0	6 (28.6)	4 (19.0)	0	0	9 (25.7)	7 (20.0)
	Low 0	1 (7.1)	7 (50.0)	0	2 (9.5)	9 (42.9)	0	0	3 (8.6)	16 (45.7)
FU W 4	Any 11	0	0	0	19	0	0	0	30	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 0	2 (18.2)	3 (27.3)	0	3 (15.8)	1 (5.3)	0	0	5 (16.7)	4 (13.3)
	Low 0	1 (9.1)	5 (45.5)	0	2 (10.5)	13 (68.4)	0	0	3 (10.0)	18 (60.0)
FU W 6	Any 9	0	0	0	15	0	0	0	24	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 0	1 (11.1)	3 (33.3)	0	4 (26.7)	2 (13.3)	0	0	5 (20.8)	5 (20.8)
	Low 0	0	5 (55.6)	0	2 (13.3)	7 (46.7)	0	0	2 (8.3)	12 (50.0)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
GFR _e (mL/min/1.73m ²) FU W 8	Any	6			5				11	
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (16.7)	0	0	0	0	0	0	1 (9.1)
	Low	0	5 (83.3)	0	1 (20.0)	4 (80.0)	0	1 (9.1)	9 (81.8)	
FU W 10	Any	2			9				11	
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	1 (11.1)	2 (22.2)	0	1 (9.1)	2 (18.2)	
	Low	0	2 (100)	0	1 (11.1)	5 (55.6)	0	1 (9.1)	7 (63.6)	
FU W 12	Any	3			1				4	
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	0	0	0	0	0	0
	Low	0	3 (100)	0	0	1 (100)	0	0	4 (100)	
FU M 6	Any	1			2				3	
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	1 (50.0)	0	0	1 (33.3)	0	
	Low	0	1 (100)	0	1 (50.0)	0	0	1 (33.3)	1 (33.3)	

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
GFR _e (mL/min/1.73m ²)	FU M 9	Any 1	0	0	0	0	0	0	1	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 0	0	0	0	0	0	0	0	0	0
	Low 0	0	1 (100)	0	0	0	0	0	0	1 (100)
FU M 12	Any 1	0	0	0	0	0	0	0	1	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 0	0	0	0	0	0	0	0	0	0
	Low 0	0	1 (100)	0	0	0	0	0	0	1 (100)
FU M 15	Any 1	0	0	0	0	0	0	0	1	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 0	0	0	0	0	0	0	0	0	0
	Low 0	0	1 (100)	0	0	0	0	0	0	1 (100)
FU M 18	Any 1	0	0	0	0	0	0	0	1	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 0	0	0	0	0	0	0	0	0	0
	Low 0	0	1 (100)	0	0	0	0	0	0	1 (100)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Bilirubin (umol/L)	Week 2	Any 18			34			52		
		High 0	0	0	0	0	0	0	0	0
		Normal 0	16 (88.9)	0	0	25 (73.5)	3 (8.8)	0	41 (78.8)	3 (5.8)
		Low 0	1 (5.6)	1 (5.6)	0	5 (14.7)	1 (2.9)	0	6 (11.5)	2 (3.8)
	Week 4	Any 16			34			50		
		High 0	0	0	0	1 (2.9)	0	0	1 (2.0)	0
		Normal 0	15 (93.8)	0	0	26 (76.5)	3 (8.8)	0	41 (82.0)	3 (6.0)
		Low 0	0	1 (6.3)	0	3 (8.8)	1 (2.9)	0	3 (6.0)	2 (4.0)
	Week 6	Any 18			32			50		
		High 0	0	0	0	0	0	0	0	0
		Normal 0	14 (77.8)	0	0	25 (78.1)	3 (9.4)	0	39 (78.0)	3 (6.0)
		Low 0	3 (16.7)	1 (5.6)	0	3 (9.4)	1 (3.1)	0	6 (12.0)	2 (4.0)
	Week 8	Any 13			24			37		
		High 0	0	0	0	0	0	0	0	0
		Normal 0	12 (92.3)	0	0	21 (87.5)	2 (8.3)	0	33 (89.2)	2 (5.4)
		Low 0	1 (7.7)	0	0	0	1 (4.2)	0	1 (2.7)	1 (2.7)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Bilirubin (umol/L)	Week 10	Any	14		24			38		
		High	0	0	0	0	0	0	0	0
		Normal	0	12 (85.7)	1 (7.1)	1 (4.2)	19 (79.2)	3 (12.5)	1 (2.6)	31 (81.6)
		Low	0	1 (7.1)	0	0	1 (4.2)	0	2 (5.3)	4 (10.5)
	Week 12	Any	12		20			32		
		High	0	0	0	0	0	0	0	0
		Normal	0	11 (91.7)	0	0	17 (85.0)	2 (10.0)	0	28 (87.5)
		Low	0	0	1 (8.3)	0	1 (5.0)	0	1 (3.1)	1 (3.1)
	Week 14	Any	13		22			35		
		High	0	1 (7.7)	0	0	0	0	1 (2.9)	0
		Normal	0	10 (76.9)	0	0	17 (77.3)	2 (9.1)	0	27 (77.1)
		Low	0	1 (7.7)	1 (7.7)	0	3 (13.6)	0	4 (11.4)	1 (2.9)
	Week 16	Any	12		17			29		
		High	0	0	0	0	0	0	0	0
		Normal	0	10 (83.3)	1 (8.3)	0	12 (70.6)	1 (5.9)	0	22 (75.9)
		Low	0	1 (8.3)	0	0	4 (23.5)	0	5 (17.2)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Bilirubin (umol/L)	Week 18	Any 8 0	High 0 0	Normal 5 (62.5) 1 (12.5)	Low 2 (25.0) 0	High 14 0	Normal 11 (78.6) 1 (7.1)	Low 0 0	High 0 0	Normal 16 (72.7) 2 (9.1)	Low 0 0
	Week 20	Any 8 0	High 0 0	Normal 7 (87.5) 0	Low 0 1 (12.5)	High 15 0	Normal 11 (73.3) 2 (13.3)	Low 0 0	High 0 0	Normal 18 (78.3) 2 (8.7)	Low 0 0
	Week 22	Any 8 0	High 0 0	Normal 7 (87.5) 1 (12.5)	Low 0 0	High 15 0	Normal 13 (86.7) 2 (13.3)	Low 0 0	High 0 0	Normal 20 (87.0) 3 (13.0)	Low 0 0
	Week 24	Any 8 0	High 0 0	Normal 5 (62.5) 0	Low 2 (25.0) 1 (12.5)	High 8 0	Normal 7 (87.5) 1 (12.5)	Low 0 0	High 0 0	Normal 12 (75.0) 1 (6.3)	Low 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Bilirubin (umol/L)	Week 26	Any 3	0	0	0	3 (100)	0	0	1 (16.7)	0
	High	0	1 (33.3)	0	0	0	0	0	5 (83.3)	0
	Normal	0	2 (66.7)	0	3 (100)	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0
	Week 28	Any 1	0	0	0	2 (100)	0	0	0	0
	High	0	0	0	0	0	0	0	3 (100)	0
	Normal	0	1 (100)	0	2 (100)	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0
	Week 30	Any 0	0	0	0	1 (100)	0	0	0	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	0	0	0	0	0	0
	Low	0	0	0	1 (100)	0	0	1 (100)	0	0
	Week 32	Any 0	0	0	0	1 (100)	0	0	0	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	0	0	0	0	0	0
	Low	0	0	0	1 (100)	0	0	1 (100)	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Bilirubin (umol/L)	Week 34	Any 0	0	0	1	0	0	0	1	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	1 (100)	0	0	1 (100)	0
	FU W 2	Any 17	0	0	22	0	0	0	39	0
		High 0	0	0	0	0	0	0	0	0
		Normal 1 (5.9)	11 (64.7)	1 (5.9)	1 (4.5)	15 (68.2)	2 (9.1)	2 (5.1)	26 (66.7)	3 (7.7)
		Low 0	3 (17.6)	1 (5.9)	0	3 (13.6)	1 (4.5)	0	6 (15.4)	2 (5.1)
	FU W 4	Any 11	0	0	21	0	0	1 (3.1)	32	0
		High 1 (9.1)	0	0	0	0	0	1 (3.1)	0	0
		Normal 0	8 (72.7)	1 (9.1)	1 (4.8)	15 (71.4)	2 (9.5)	1 (3.1)	23 (71.9)	3 (9.4)
		Low 0	0	1 (9.1)	0	2 (9.5)	1 (4.8)	0	2 (6.3)	2 (6.3)
	FU W 6	Any 10	0	0	16	0	0	1 (3.8)	26	0
		High 1 (10.0)	1 (10.0)	0	0	0	0	1 (3.8)	1 (3.8)	0
		Normal 0	4 (40.0)	1 (10.0)	0	11 (68.8)	2 (12.5)	0	15 (57.7)	3 (11.5)
		Low 0	2 (20.0)	1 (10.0)	0	2 (12.5)	1 (6.3)	0	4 (15.4)	2 (7.7)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Bilirubin (umol/L)	FU W 8	Any 6	0	1 (16.7)	0	9	0	0	15	0
		High 0	0	1 (16.7)	0	0	0	0	1 (6.7)	1 (6.7)
		Normal 0	3 (50.0)	1 (16.7)	0	8 (88.9)	0	0	11 (73.3)	1 (6.7)
		Low 0	1 (16.7)	0	0	1 (11.1)	0	0	2 (13.3)	0
	FU W 10	Any 3	0	0	0	9	0	0	12	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	3 (100)	0	0	7 (77.8)	2 (22.2)	0	10 (83.3)	2 (16.7)
		Low 0	0	0	0	0	0	0	0	0
	FU W 12	Any 4	0	0	0	2	0	0	6	0
		High 0	1 (25.0)	0	0	0	0	0	1 (16.7)	0
		Normal 0	3 (75.0)	0	0	1 (50.0)	0	0	4 (66.7)	0
		Low 0	0	0	0	1 (50.0)	0	0	1 (16.7)	0
	FU M 6	Any 3	0	0	0	3	0	0	6	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	3 (100)	0	0	3 (100)	0	0	6 (100)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Bilirubin (umol/L)	FU M 9	Any 2	0	0	0	1	0	0	3	0
	High 0	0	2 (100)	0	0	1 (100)	0	0	3 (100)	0
	Normal 0	2	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0
	FU M 12	Any 1	0	0	0	1	0	0	2	0
	High 0	0	1 (100)	0	0	1 (100)	0	0	2 (100)	0
	Normal 0	1	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0
	FU M 15	Any 2	0	0	0	0	0	0	2	0
	High 0	0	2 (100)	0	0	0	0	0	2 (100)	0
	Normal 0	2	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0
	FU M 18	Any 1	0	0	0	0	0	0	1	0
	High 0	0	1 (100)	0	0	0	0	0	1 (100)	0
	Normal 0	1	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Creatinine (umol/L)	Week 2	Any 18			36			54		
		High 3 (16.7)	0	0	0	0	0	3 (5.6)	0	0
		Normal 2 (11.1)	13 (72.2)	0	5 (13.9)	25 (69.4)	0	7 (13.0)	38 (70.4)	0
		Low 0	0	0	0	4 (11.1)	2 (5.6)	0	4 (7.4)	2 (3.7)
	Week 4	Any 17			36			53		
		High 0	0	0	3 (8.3)	0	0	3 (5.7)	0	0
		Normal 5 (29.4)	12 (70.6)	0	2 (5.6)	23 (63.9)	2 (5.6)	7 (13.2)	35 (66.0)	2 (3.8)
		Low 0	0	0	0	5 (13.9)	1 (2.8)	0	5 (9.4)	1 (1.9)
	Week 6	Any 18			34			52		
		High 1 (5.6)	0	0	3 (8.8)	1 (2.9)	0	4 (7.7)	1 (1.9)	0
		Normal 4 (22.2)	13 (72.2)	0	1 (2.9)	23 (67.6)	1 (2.9)	5 (9.6)	36 (69.2)	1 (1.9)
		Low 0	0	0	0	3 (8.8)	2 (5.9)	0	3 (5.8)	2 (3.8)
	Week 8	Any 14			25			39		
		High 1 (7.1)	0	0	1 (4.0)	1 (4.0)	0	2 (5.1)	1 (2.6)	0
		Normal 3 (21.4)	10 (71.4)	0	2 (8.0)	16 (64.0)	0	5 (12.8)	26 (66.7)	0
		Low 0	0	0	0	4 (16.0)	1 (4.0)	0	4 (10.3)	1 (2.6)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Creatinine (umol/L)	Week 10	Any 14			24			38		
		High 3 (21.4)	0	0	0	0	0	3 (7.9)	0	0
		Normal 1 (7.1)	10 (71.4)	0	4 (16.7)	15 (62.5)	0	5 (13.2)	25 (65.8)	0
		Low 0	0	0	0	3 (12.5)	2 (8.3)	0	3 (7.9)	2 (5.3)
	Week 12	Any 12			21			33		
		High 2 (16.7)	1 (8.3)	0	1 (4.8)	0	0	3 (9.1)	1 (3.0)	0
		Normal 1 (8.3)	7 (58.3)	0	1 (4.8)	19 (90.5)	0	2 (6.1)	26 (78.8)	0
		Low 0	1 (8.3)	0	0	0	0	0	1 (3.0)	0
	Week 14	Any 13			22			35		
		High 3 (23.1)	0	0	1 (4.5)	0	0	4 (11.4)	0	0
		Normal 1 (7.7)	8 (61.5)	0	1 (4.5)	18 (81.8)	0	2 (5.7)	26 (74.3)	0
		Low 0	1 (7.7)	0	0	2 (9.1)	0	0	3 (8.6)	0
	Week 16	Any 12			17			29		
		High 2 (16.7)	0	0	0	0	0	2 (6.9)	0	0
		Normal 1 (8.3)	8 (66.7)	0	1 (5.9)	15 (88.2)	0	2 (6.9)	23 (79.3)	0
		Low 0	1 (8.3)	0	0	1 (5.9)	0	0	2 (6.9)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Creatinine (umol/L)	Week 18	Any High 0 Normal 0 Low 0	8 0 7 (87.5) 0	0 0 1 (12.5) 0	0 1 (7.1) 0 0	14 0 12 (85.7) 1 (7.1)	0 0 0 0	0 1 (4.5) 19 (86.4) 0	22 0 0 0	0 0 2 (9.1) 0	0
	Week 20	Any High 0 Normal 0 Low 0	8 0 7 (87.5) 1 (12.5)	0 0 0 0	0 2 (13.3) 0 0	15 12 (80.0) 1 (6.7)	0 0 0 0	0 2 (8.7) 19 (82.6) 0	23 0 0 0	0 0 2 (8.7) 0	0
	Week 22	Any High 0 Normal 0 Low 0	8 0 7 (87.5) 1 (12.5)	0 0 0 0	0 2 (13.3) 0 0	15 13 (86.7) 0 0	0 0 0 0	0 2 (8.7) 20 (87.0) 0	23 0 0 0	0 0 1 (4.3) 0	0
	Week 24	Any High 1 (12.5) Normal 0 Low 0	8 0 6 (75.0) 1 (12.5)	0 0 0 0	0 0 7 (87.5) 1 (12.5)	8 0 0 0	0 0 0 0	1 (6.3) 0 13 (81.3) 0	16 0 0 0	0 0 2 (12.5) 0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Creatinine (umol/L)	Week 26	Any 3 High 0 Normal 3 (100) Low 0	0 0 0	0 0 0	0 2 (66.7) 1 (33.3)	0 0 0	0 0 0	0 5 (83.3) 1 (16.7)	0 0 0	0 0 0
	Week 28	Any 1 High 0 Normal 1 (100) Low 0	0 0 0	0 0 0	0 1 (50.0) 1 (50.0)	0 0 0	0 0 0	0 2 (66.7) 1 (33.3)	0 0 0	0 0 0
	Week 30	Any 0 High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	0 0 1 (100)	0 0 0	0 0 0	0 0 1 (100)	0 0 0	0 0 0
	Week 32	Any 0 High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	0 0 1 (100)	0 0 0	0 0 0	0 0 1 (100)	0 0 0	0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Creatinine (umol/L)	Week 34	Any 0	0	0	1	0	0	0	1	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	1 (100)	0	0	1 (100)	0
FU W 2	Any 17	0	0	0	24	0	0	41	0	0
	High 2 (11.8)	1 (5.9)	0	1 (4.2)	1 (4.2)	0	3 (7.3)	2 (4.9)	0	0
	Normal 2 (11.8)	9 (52.9)	1 (5.9)	3 (12.5)	16 (66.7)	0	5 (12.2)	25 (61.0)	1 (2.4)	5 (12.2)
	Low 0	0	2 (11.8)	0	0	3 (12.5)	0	0	0	5 (12.2)
FU W 4	Any 12	0	0	0	21	0	0	33	0	0
	High 1 (8.3)	0	0	3 (14.3)	1 (4.8)	0	4 (12.1)	1 (3.0)	0	0
	Normal 1 (8.3)	7 (58.3)	1 (8.3)	2 (9.5)	11 (52.4)	1 (4.8)	3 (9.1)	18 (54.5)	2 (6.1)	4 (12.1)
	Low 0	0	2 (16.7)	0	1 (4.8)	2 (9.5)	0	1 (3.0)	4 (12.1)	0
FU W 6	Any 10	0	0	0	16	0	0	26	0	0
	High 1 (10.0)	0	0	1 (6.3)	0	0	2 (7.7)	0	0	0
	Normal 1 (10.0)	6 (60.0)	2 (20.0)	1 (6.3)	10 (62.5)	1 (6.3)	2 (7.7)	16 (61.5)	3 (11.5)	0
	Low 0	0	0	0	1 (6.3)	2 (12.5)	0	1 (3.8)	2 (7.7)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Creatinine (umol/L) FU W 8	Any	6			9				15	
	High	1 (16.7)	1 (16.7)	0	1 (11.1)	0	0	2 (13.3)	1 (6.7)	0
	Normal	0	3 (50.0)	1 (16.7)	0	7 (77.8)	0	0	10 (66.7)	1 (6.7)
	Low	0	0	0	0	1 (11.1)	0	0	1 (6.7)	0
FU W 10	Any	3			9				12	
	High	0	0	0	0	0	0	0	0	0
	Normal	0	3 (100)	0	1 (11.1)	8 (88.9)	0	1 (8.3)	11 (91.7)	0
	Low	0	0	0	0	0	0	0	0	0
FU W 12	Any	4			2				6	
	High	0	1 (25.0)	0	0	0	0	0	1 (16.7)	0
	Normal	1 (25.0)	2 (50.0)	0	1 (50.0)	1 (50.0)	0	2 (33.3)	3 (50.0)	0
	Low	0	0	0	0	0	0	0	0	0
FU M 6	Any	3			3				6	
	High	1 (33.3)	0	0	0	0	0	1 (16.7)	0	0
	Normal	0	2 (66.7)	0	0	3 (100)	0	0	5 (83.3)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Creatinine (umol/L) FU M 9	Any	2	0	0	0	1	0	0	3	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	2 (100)	0	1 (100)	0	0	0	3 (100)	0
	Low	0	0	0	0	0	0	0	0	0
FU M 12	Any	1	0	0	0	1	0	0	2	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	0	0	0	0	1 (50.0)	0
	Low	0	0	0	0	1 (100)	0	0	1 (50.0)	0
FU M 15	Any	2	0	0	0	0	0	0	2	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	2 (100)	0	0	0	0	0	2 (100)	0
	Low	0	0	0	0	0	0	0	0	0
FU M 18	Any	1	0	0	0	0	0	0	1	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	0	0	0	0	1 (100)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Sodium (mmol/L)	Week 2	Any 17			36			53		
		High 0	1 (5.9)	0	0	0	0	0	1 (1.9)	0
		Normal 0	13 (76.5)	0	1 (2.8)	28 (77.8)	2 (5.6)	1 (1.9)	41 (77.4)	2 (3.8)
		Low 0	2 (11.8)	1 (5.9)	0	1 (2.8)	4 (11.1)	0	3 (5.7)	5 (9.4)
	Week 4	Any 17			36			53		
		High 0	0	0	0	0	0	0	0	0
		Normal 0	16 (94.1)	0	1 (2.8)	27 (75.0)	4 (11.1)	1 (1.9)	43 (81.1)	4 (7.5)
		Low 0	0	1 (5.9)	0	1 (2.8)	3 (8.3)	0	1 (1.9)	4 (7.5)
	Week 6	Any 18			34			52		
		High 0	0	0	0	0	0	0	0	0
		Normal 0	17 (94.4)	0	1 (2.9)	25 (73.5)	5 (14.7)	1 (1.9)	42 (80.8)	5 (9.6)
		Low 0	0	1 (5.6)	0	1 (2.9)	2 (5.9)	0	1 (1.9)	3 (5.8)
	Week 8	Any 14			26			40		
		High 0	0	0	0	1 (3.8)	0	0	1 (2.5)	0
		Normal 0	13 (92.9)	0	0	19 (73.1)	0	0	32 (80.0)	0
		Low 0	0	1 (7.1)	0	3 (11.5)	3 (11.5)	0	3 (7.5)	4 (10.0)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Sodium (mmol/L)	Week 10	Any 14			23			37		
		High 0	0	0	0	0	0	0	0	0
		Normal 0	14 (100)	0	0	16 (69.6)	3 (13.0)	0	30 (81.1)	3 (8.1)
		Low 0	0	0	0	1 (4.3)	3 (13.0)	0	1 (2.7)	3 (8.1)
	Week 12	Any 12			20			32		
		High 0	0	0	0	0	0	0	0	0
		Normal 0	12 (100)	0	0	15 (75.0)	2 (10.0)	0	27 (84.4)	2 (6.3)
		Low 0	0	0	0	0	3 (15.0)	0	0	3 (9.4)
	Week 14	Any 13			22			35		
		High 0	1 (7.7)	0	0	0	0	0	1 (2.9)	0
		Normal 0	11 (84.6)	0	0	17 (77.3)	2 (9.1)	0	28 (80.0)	2 (5.7)
		Low 0	1 (7.7)	0	0	1 (4.5)	2 (9.1)	0	2 (5.7)	2 (5.7)
	Week 16	Any 12			17			29		
		High 0	0	0	0	0	0	0	0	0
		Normal 0	12 (100)	0	0	14 (82.4)	1 (5.9)	0	26 (89.7)	1 (3.4)
		Low 0	0	0	0	1 (5.9)	1 (5.9)	0	1 (3.4)	1 (3.4)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Sodium (mmol/L)	Week 18	Any 8	0	0	0	14	0	0	22	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	7 (87.5)	0	0	9 (64.3)	3 (21.4)	0	16 (72.7)	3 (13.6)
		Low 0	1 (12.5)	0	0	0	2 (14.3)	0	1 (4.5)	2 (9.1)
	Week 20	Any 8	0	0	0	15	0	0	23	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	8 (100)	0	0	11 (73.3)	2 (13.3)	0	19 (82.6)	2 (8.7)
		Low 0	0	0	0	0	2 (13.3)	0	0	2 (8.7)
	Week 22	Any 8	0	0	0	14	0	0	22	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	6 (75.0)	0	0	8 (57.1)	4 (28.6)	0	14 (63.6)	4 (18.2)
		Low 0	2 (25.0)	0	0	1 (7.1)	1 (7.1)	0	3 (13.6)	1 (4.5)
	Week 24	Any 8	0	0	0	8	0	0	16	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	8 (100)	0	0	5 (62.5)	1 (12.5)	0	13 (81.3)	1 (6.3)
		Low 0	0	0	0	1 (12.5)	1 (12.5)	0	1 (6.3)	1 (6.3)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Sodium (mmol/L)	Week 26	Any	3	0	0	3	0	0	6	0
		High	0	0	0	0	0	0	0	0
		Normal	3 (100)	0	3 (100)	0	0	6 (100)	0	0
		Low	0	0	0	0	0	0	0	0
	Week 28	Any	1	0	0	2	0	0	3	0
		High	0	0	0	0	0	0	0	0
		Normal	1 (100)	0	2 (100)	0	0	3 (100)	0	0
		Low	0	0	0	0	0	0	0	0
	Week 30	Any	0	0	0	1	0	0	1	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	1 (100)	0	0	1 (100)	0	0
		Low	0	0	0	0	0	0	0	0
	Week 32	Any	0	0	0	1	0	0	1	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	1 (100)	0	0	1 (100)	0	0
		Low	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Sodium (mmol/L)	Week 34	Any 0	0	0	1	0	0	0	1 (100)	0
		High 0	0	0	0	1 (100)	0	0	0	0
		Normal 0	0	0	0	0	0	0	1 (100)	0
		Low 0	0	0	0	0	0	0	0	0
FU W 2	Any 17	0	0	0	23	0	0	0	40	0
		High 0	0	0	0	13 (56.5)	3 (13.0)	0	26 (65.0)	4 (10.0)
		Normal 0	13 (76.5)	1 (5.9)	0	13 (56.5)	3 (13.0)	0	26 (65.0)	4 (10.0)
		Low 0	1 (5.9)	2 (11.8)	0	4 (17.4)	3 (13.0)	0	5 (12.5)	5 (12.5)
FU W 4	Any 11	0	0	0	21	0	0	0	32	0
		High 0	0	0	0	15 (71.4)	4 (19.0)	0	24 (75.0)	5 (15.6)
		Normal 0	9 (81.8)	1 (9.1)	0	15 (71.4)	4 (19.0)	0	24 (75.0)	5 (15.6)
		Low 0	0	1 (9.1)	0	0	2 (9.5)	0	0	3 (9.4)
FU W 6	Any 10	0	0	0	16	0	0	0	26	0
		High 0	0	0	0	10 (62.5)	4 (25.0)	0	17 (65.4)	5 (19.2)
		Normal 0	7 (70.0)	1 (10.0)	0	10 (62.5)	4 (25.0)	0	17 (65.4)	5 (19.2)
		Low 0	1 (10.0)	1 (10.0)	0	0	2 (12.5)	0	1 (3.8)	3 (11.5)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Sodium (mmol/L)	FU W 8	Any	6	0	0	8	0	0	14	0
		High	0	0	0	0	0	0	0	0
		Normal	4 (66.7)	0	0	6 (75.0)	1 (12.5)	0	10 (71.4)	1 (7.1)
		Low	2 (33.3)	0	0	0	1 (12.5)	0	2 (14.3)	1 (7.1)
	FU W 10	Any	3	0	0	9	0	0	12	0
		High	0	0	0	0	0	0	0	0
		Normal	3 (100)	0	0	7 (77.8)	1 (11.1)	0	10 (83.3)	1 (8.3)
		Low	0	0	0	0	1 (11.1)	0	0	1 (8.3)
	FU W 12	Any	4	0	0	2	0	0	6	0
		High	0	0	0	0	0	0	0	0
		Normal	2 (50.0)	0	0	2 (100)	0	0	4 (66.7)	0
		Low	1 (25.0)	1 (25.0)	0	0	0	0	1 (16.7)	1 (16.7)
	FU M 6	Any	3	0	0	3	0	0	6	0
		High	0	0	0	0	0	0	0	0
		Normal	2 (66.7)	0	0	1 (33.3)	1 (33.3)	0	3 (50.0)	1 (16.7)
		Low	1 (33.3)	0	0	1 (33.3)	0	0	2 (33.3)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Sodium (mmol/L)	FU M 9	Any 2			1			3		
		High 0	1 (50.0)	0	0	0	0	1 (33.3)	0	
		Normal 0	1 (50.0)	0	0	0	0	1 (33.3)	0	
		Low 0	0	0	0	1 (100)	0	1 (33.3)	0	
	FU M 12	Any 1			1			2		
		High 0	1 (100)	0	0	0	0	1 (50.0)	0	
		Normal 0	0	0	0	0	1 (100)	0	0	
		Low 0	0	0	0	0	0	0	0	0
	FU M 15	Any 2			0			2		
		High 0	0	0	0	0	0	0	0	0
		Normal 0	2 (100)	0	0	0	0	2 (100)	0	
		Low 0	0	0	0	0	0	0	0	0
	FU M 18	Any 1			0			1		
		High 0	1 (100)	0	0	0	0	1 (100)	0	
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Urea Nitrogen (mmol/L)	Week 2	Any 18			34			52		
		High 4 (22.2)	2 (11.1)	0	5 (14.7)	6 (17.6)	0	9 (17.3)	8 (15.4)	0
		Normal 3 (16.7)	9 (50.0)	0	4 (11.8)	19 (55.9)	0	7 (13.5)	28 (53.8)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 4	Any 16			34			50		
		High 5 (31.3)	1 (6.3)	0	6 (17.6)	4 (11.8)	0	11 (22.0)	5 (10.0)	0
		Normal 1 (6.3)	9 (56.3)	0	3 (8.8)	21 (61.8)	0	4 (8.0)	30 (60.0)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 6	Any 17			33			50		
		High 4 (23.5)	0	0	5 (15.2)	6 (18.2)	0	9 (18.0)	6 (12.0)	0
		Normal 3 (17.6)	10 (58.8)	0	3 (9.1)	18 (54.5)	0	6 (12.0)	28 (56.0)	0
		Low 0	0	0	0	1 (3.0)	0	0	1 (2.0)	0
	Week 8	Any 13			25			38		
		High 4 (30.8)	0	0	5 (20.0)	6 (24.0)	0	9 (23.7)	6 (15.8)	0
		Normal 0	9 (69.2)	0	4 (16.0)	10 (40.0)	0	4 (10.5)	19 (50.0)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Urea Nitrogen (mmol/L)	Week 10	Any 13			23			36		
		High 5 (38.5)	0	0	4 (17.4)	4 (17.4)	0	9 (25.0)	4 (11.1)	0
		Normal 1 (7.7)	6 (46.2)	0	2 (8.7)	13 (56.5)	0	3 (8.3)	19 (52.8)	0
		Low 0	1 (7.7)	0	0	0	0	0	1 (2.8)	0
	Week 12	Any 12			19			31		
		High 3 (25.0)	1 (8.3)	0	3 (15.8)	3 (15.8)	0	6 (19.4)	4 (12.9)	0
		Normal 2 (16.7)	6 (50.0)	0	2 (10.5)	11 (57.9)	0	4 (12.9)	17 (54.8)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 14	Any 12			21			33		
		High 4 (33.3)	0	0	3 (14.3)	5 (23.8)	0	7 (21.2)	5 (15.2)	0
		Normal 2 (16.7)	6 (50.0)	0	2 (9.5)	11 (52.4)	0	4 (12.1)	17 (51.5)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 16	Any 11			17			28		
		High 3 (27.3)	0	0	2 (11.8)	4 (23.5)	0	5 (17.9)	4 (14.3)	0
		Normal 1 (9.1)	7 (63.6)	0	1 (5.9)	10 (58.8)	0	2 (7.1)	17 (60.7)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Urea Nitrogen (mmol/L)	Week 18	Any 7			13			20		
		High 2 (28.6)	0	0	1 (7.7)	4 (30.8)	0	3 (15.0)	4 (20.0)	0
		Normal 1 (14.3)	4 (57.1)	0	1 (7.7)	7 (53.8)	0	2 (10.0)	11 (55.0)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 20	Any 8			14			22		
		High 2 (25.0)	1 (12.5)	0	2 (14.3)	5 (35.7)	0	4 (18.2)	6 (27.3)	0
		Normal 2 (25.0)	3 (37.5)	0	2 (14.3)	5 (35.7)	0	4 (18.2)	8 (36.4)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 22	Any 7			14			21		
		High 3 (42.9)	0	0	4 (28.6)	3 (21.4)	0	7 (33.3)	3 (14.3)	0
		Normal 1 (14.3)	3 (42.9)	0	0	7 (50.0)	0	1 (4.8)	10 (47.6)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 24	Any 8			8			16		
		High 3 (37.5)	1 (12.5)	0	2 (25.0)	2 (25.0)	0	5 (31.3)	3 (18.8)	0
		Normal 1 (12.5)	3 (37.5)	0	0	4 (50.0)	0	1 (6.3)	7 (43.8)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Urea Nitrogen (mmol/L)	Week 26	Any High 1 (33.3) Normal 0 Low 0	0 2 (66.7) 0	0 0 0	0 1 (33.3) 0	1 (33.3) 0 0	0 0 0	1 (16.7) 2 (33.3) 0	1 (16.7) 2 (33.3) 0	0 0 0
	Week 28	Any High 0 Normal 1 (100) Low 0	1 0 0	0 0 0	1 (50.0) 0 0	0 1 (50.0) 0	0 0 0	1 (33.3) 1 (33.3) 0	1 (33.3) 1 (33.3) 0	0 0 0
	Week 30	Any High 0 Normal 0 Low 0	0 0 0	0 0 0	1 (100) 0 0	0 0 0	0 0 0	1 (100) 0 0	0 0 0	0 0 0
	Week 32	Any High 0 Normal 0 Low 0	0 0 0	0 0 0	1 (100) 0 0	0 0 0	0 0 0	1 (100) 0 0	0 0 0	0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Urea Nitrogen (mmol/L)	Week 34	Any 0	0	0	1 (100)	0	0	1 (100)	0	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 2	Any 17	17	0	23	23	0	40	40	0
		High 6 (35.3)	3 (17.6)	0	8 (34.8)	1 (4.3)	0	14 (35.0)	4 (10.0)	0
		Normal 1 (5.9)	7 (41.2)	0	1 (4.3)	13 (56.5)	0	2 (5.0)	20 (50.0)	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 4	Any 12	12	0	21	21	0	33	33	0
		High 4 (33.3)	0	0	7 (33.3)	5 (23.8)	0	11 (33.3)	5 (15.2)	0
		Normal 2 (16.7)	6 (50.0)	0	0	9 (42.9)	0	2 (6.1)	15 (45.5)	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 6	Any 10	10	0	15	15	0	25	25	0
		High 4 (40.0)	2 (20.0)	0	1 (6.7)	5 (33.3)	0	5 (20.0)	7 (28.0)	0
		Normal 0	4 (40.0)	0	1 (6.7)	8 (53.3)	0	1 (4.0)	12 (48.0)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Urea Nitrogen (mmol/L)	FU W 8	Any	5			8			13	
		High	2 (40.0)	2 (40.0)	0	1 (12.5)	2 (25.0)	0	3 (23.1)	4 (30.8)
		Normal	0	1 (20.0)	0	0	5 (62.5)	0	0	6 (46.2)
		Low	0	0	0	0	0	0	0	0
	FU W 10	Any	3			8			11	
		High	2 (66.7)	0	0	0	4 (50.0)	0	2 (18.2)	4 (36.4)
		Normal	0	1 (33.3)	0	0	4 (50.0)	0	0	5 (45.5)
		Low	0	0	0	0	0	0	0	0
	FU W 12	Any	4			2			6	
		High	2 (50.0)	0	0	0	2 (100)	0	2 (33.3)	2 (33.3)
		Normal	0	2 (50.0)	0	0	0	0	2 (33.3)	0
		Low	0	0	0	0	0	0	0	0
	FU M 6	Any	3			3			6	
		High	2 (66.7)	0	0	0	1 (33.3)	0	2 (33.3)	1 (16.7)
		Normal	0	1 (33.3)	0	1 (33.3)	1 (33.3)	0	1 (16.7)	2 (33.3)
		Low	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Urea Nitrogen (mmol/L)	FU M 9	Any 1 (50.0)	High 1 (50.0)	0	0	1 (100)	0	1 (33.3)	1 (33.3)	0
		Normal 0	0	0	0	0	0	0	1 (33.3)	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 12	Any 1	High 1 (100)	0	0	0	1 (100)	0	1 (50.0)	2
		Normal 0	0	0	0	1 (100)	0	0	1 (50.0)	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 15	Any 2	High 1 (50.0)	0	0	0	0	1 (50.0)	0	2
		Normal 0	1 (50.0)	0	0	0	0	0	1 (50.0)	0
	FU M 18	Any 1	High 1 (100)	0	0	0	0	1 (100)	0	1
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Chloride (mmol/L)	Week 2	Any 16			36			52		
		High 1 (6.3)	0	0	1 (2.8)	2 (5.6)	0	2 (3.8)	2 (3.8)	0
		Normal 1 (6.3)	11 (68.8)	1 (6.3)	6 (16.7)	21 (58.3)	1 (2.8)	7 (13.5)	32 (61.5)	2 (3.8)
		Low 0	1 (6.3)	1 (6.3)	0	4 (11.1)	1 (2.8)	0	5 (9.6)	2 (3.8)
	Week 4	Any 15			36			51		
		High 1 (6.7)	1 (6.7)	0	2 (5.6)	2 (5.6)	0	3 (5.9)	3 (5.9)	0
		Normal 1 (6.7)	9 (60.0)	1 (6.7)	5 (13.9)	23 (63.9)	1 (2.8)	6 (11.8)	32 (62.7)	2 (3.9)
		Low 0	1 (6.7)	1 (6.7)	0	1 (2.8)	2 (5.6)	0	2 (3.9)	3 (5.9)
	Week 6	Any 16			34			50		
		High 1 (6.3)	2 (12.5)	0	2 (5.9)	4 (11.8)	0	3 (6.0)	6 (12.0)	0
		Normal 2 (12.5)	9 (56.3)	1 (6.3)	4 (11.8)	20 (58.8)	2 (5.9)	6 (12.0)	29 (58.0)	3 (6.0)
		Low 0	0	1 (6.3)	0	1 (2.9)	1 (2.9)	0	1 (2.0)	2 (4.0)
	Week 8	Any 13			26			39		
		High 1 (7.7)	1 (7.7)	0	2 (7.7)	4 (15.4)	0	3 (7.7)	5 (12.8)	0
		Normal 1 (7.7)	8 (61.5)	1 (7.7)	1 (3.8)	16 (61.5)	0	2 (5.1)	24 (61.5)	1 (2.6)
		Low 0	0	1 (7.7)	0	3 (11.5)	0	0	3 (7.7)	1 (2.6)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Chloride (mmol/L)	Week 10	Any	13		23			36			
		High	1 (7.7)	0	2 (8.7)	1 (4.3)	0	3 (8.3)	1 (2.8)	0	
		Normal	2 (15.4)	9 (69.2)	1 (7.7)	2 (10.0)	13 (56.5)	2 (8.7)	4 (11.1)	22 (61.1)	
		Low	0	0	0	3 (13.0)	0	0	3 (8.3)	0	
	Week 12	Any	12		20			32			
		High	2 (16.7)	2 (16.7)	0	3 (15.0)	3 (15.0)	0	5 (15.6)	5 (15.6)	0
		Normal	0	6 (50.0)	0	2 (10.0)	10 (50.0)	2 (10.0)	2 (6.3)	16 (50.0)	2 (6.3)
		Low	0	1 (8.3)	1 (8.3)	0	0	0	1 (3.1)	1 (3.1)	
	Week 14	Any	12		22			34			
		High	3 (25.0)	0	0	3 (13.6)	3 (13.6)	0	6 (17.6)	3 (8.8)	0
		Normal	0	8 (66.7)	1 (8.3)	2 (9.1)	11 (50.0)	2 (9.1)	2 (5.9)	19 (55.9)	3 (8.8)
		Low	0	0	0	0	1 (4.5)	0	0	1 (2.9)	0
	Week 16	Any	11		17			28			
		High	2 (18.2)	1 (9.1)	0	1 (5.9)	2 (11.8)	0	3 (10.7)	3 (10.7)	0
		Normal	0	7 (63.6)	0	2 (11.8)	10 (58.8)	1 (5.9)	2 (7.1)	17 (60.7)	1 (3.6)
		Low	0	1 (9.1)	0	0	1 (5.9)	0	0	2 (7.1)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Chloride (mmol/L)	Week 18	Any	7			14			21		
		High	1 (14.3)	0	1 (7.1)	1 (7.1)	0	2 (9.5)	1 (4.8)	0	
		Normal	1 (14.3)	4 (57.1)	1 (14.3)	0	9 (64.3)	2 (14.3)	1 (4.8)	13 (61.9)	
		Low	0	0	0	1 (7.1)	0	0	1 (4.8)	0	
	Week 20	Any	8			15			23		
		High	1 (12.5)	1 (12.5)	0	2 (13.3)	1 (6.7)	0	3 (13.0)	2 (8.7)	0
		Normal	1 (12.5)	4 (50.0)	1 (12.5)	1 (6.7)	7 (46.7)	2 (13.3)	2 (8.7)	11 (47.8)	3 (13.0)
		Low	0	0	0	0	2 (13.3)	0	0	2 (8.7)	0
	Week 22	Any	7			14			21		
		High	2 (28.6)	1 (14.3)	0	1 (7.1)	2 (14.3)	0	3 (14.3)	3 (14.3)	0
		Normal	0	2 (28.6)	1 (14.3)	1 (7.1)	8 (57.1)	2 (14.3)	1 (4.8)	10 (47.6)	3 (14.3)
		Low	0	1 (14.3)	0	0	0	0	1 (4.8)	0	0
	Week 24	Any	8			8			16		
		High	1 (12.5)	0	0	1 (12.5)	0	1 (6.3)	1 (6.3)	0	
		Normal	1 (12.5)	5 (62.5)	1 (12.5)	0	6 (75.0)	0	1 (6.3)	11 (68.8)	1 (6.3)
		Low	0	0	0	0	1 (12.5)	0	0	1 (6.3)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Chloride (mmol/L)	Week 26	Any 3			3			1 (16.7)	2 (33.3)	6
		High 1 (33.3)	1 (33.3)	0	0	1 (33.3)	0	0	0	0
		Normal 0	1 (33.3)	0	0	2 (66.7)	0	0	3 (50.0)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 28	Any 1			2			0	0	3
		High 0	0	0	0	0	0	0	0	0
		Normal 1 (100)	0	0	0	2 (100)	0	1 (33.3)	2 (66.7)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 30	Any 0			1			0	1 (100)	1
		High 0	0	0	0	1 (100)	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	Week 32	Any 0			1			0	1 (100)	1
		High 0	0	0	0	1 (100)	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Chloride (mmol/L)	Week 34	Any 0	0	0	1 (100)	0	0	1 (100)	0	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 2	Any 16	0	0	23	0	0	39	0	0
		High 0	1 (6.3)	0	0	0	0	2 (5.1)	1 (2.6)	0
		Normal 3 (18.8)	7 (43.8)	1 (6.3)	0	16 (69.6)	0	3 (7.7)	23 (59.0)	1 (2.6)
		Low 0	3 (18.8)	1 (6.3)	0	4 (17.4)	1 (4.3)	0	7 (17.9)	2 (5.1)
	FU W 4	Any 11	0	0	21	0	0	32	0	0
		High 1 (9.1)	0	0	1 (4.8)	0	0	2 (6.3)	0	0
		Normal 1 (9.1)	7 (63.6)	1 (9.1)	1 (4.8)	16 (76.2)	0	2 (6.3)	23 (71.9)	1 (3.1)
		Low 0	0	1 (9.1)	0	2 (9.5)	1 (4.8)	0	2 (6.3)	2 (6.3)
	FU W 6	Any 10	0	0	16	0	0	26	0	0
		High 1 (10.0)	0	0	2 (12.5)	1 (6.3)	0	3 (11.5)	1 (3.8)	0
		Normal 1 (10.0)	5 (50.0)	1 (10.0)	0	10 (62.5)	0	1 (3.8)	15 (57.7)	1 (3.8)
		Low 0	1 (10.0)	1 (10.0)	0	1 (6.3)	2 (12.5)	0	2 (7.7)	3 (11.5)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Chloride (mmol/L)	FU W 8	Any High 0 Normal 4 (66.7) Low 1 (16.7)	6 0 0 0 0	0 0 1 (12.5) 0 0	8 0 7 (87.5) 0 0	1 (7.1) 1 (7.1) 11 (78.6) 0 1 (7.1)	14 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0
	FU W 10	Any High 0 Normal 2 (66.7) Low 0	3 0 2 (33.3) 0 0	0 2 (22.2) 0 0 0	9 0 6 (66.7) 1 (11.1) 0	2 (16.7) 0 8 (66.7) 2 (16.7) 0	12 0 0 0 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0
	FU W 12	Any High 0 Normal 2 (50.0) Low 0	4 0 1 (25.0) 0 0	0 1 (50.0) 0 0 0	2 1 (50.0) 0 0 0	0 0 0 0 0	6 1 (16.7) 2 (33.3) 1 (16.7) 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0
	FU M 6	Any High 0 Normal 2 (66.7) Low 0	3 0 0 1 (33.3) 0	0 0 0 0 0	3 0 2 (66.7) 1 (33.3) 0	0 0 0 0 0	6 0 4 (66.7) 2 (33.3) 0	0 0 0 0 0	0 0 0 0 0	0 0 0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Chloride (mmol/L)	FU M 9	Any 2 (100)	0	0	0	1 (100)	0	0	2 (66.7)	0
	High	0	2 (100)	0	0	0	0	0	1 (33.3)	0
	Normal	0	0	0	1 (100)	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0
	FU M 12	Any 1 (100)	0	0	0	1 (100)	0	0	1 (50.0)	0
	High	0	1 (100)	0	0	0	0	0	1 (50.0)	0
	Normal	0	0	0	1 (100)	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0
	FU M 15	Any 2 (100)	0	0	0	0	0	0	0	0
	High	0	0	0	0	0	0	0	2 (100)	0
	Normal	0	2 (100)	0	0	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0
	FU M 18	Any 1 (100)	0	0	0	0	0	0	0	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	0	0	0	0	1 (100)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Aspartate Aminotransferase (U/L)	Week 2 Any	18			34				52	
	High	2 (11.1)	1 (5.6)	0	3 (8.8)	1 (2.9)	0	5 (9.6)	2 (3.8)	0
	Normal	1 (5.6)	14 (77.8)	0	0	30 (88.2)	0	1 (1.9)	44 (84.6)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 4 Any	16			34				50	
	High	2 (12.5)	0	0	3 (8.8)	2 (5.9)	0	5 (10.0)	2 (4.0)	0
	Normal	0	14 (87.5)	0	1 (2.9)	28 (82.4)	0	1 (2.0)	42 (84.0)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 6 Any	18			34				52	
	High	2 (11.1)	0	0	4 (11.8)	0	0	6 (11.5)	0	0
	Normal	1 (5.6)	15 (83.3)	0	0	30 (88.2)	0	1 (1.9)	45 (86.5)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 8 Any	13			24				37	
	High	1 (7.7)	0	0	1 (4.2)	1 (4.2)	0	2 (5.4)	1 (2.7)	0
	Normal	1 (7.7)	11 (84.6)	0	0	22 (91.7)	0	1 (2.7)	33 (89.2)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Aspartate Aminotransferase (U/L)	Week 10 Any	14			24			38		
	High	0	2 (14.3)	0	1 (4.2)	2 (8.3)	0	1 (2.6)	4 (10.5)	0
	Normal	1 (7.1)	11 (78.6)	0	2 (8.3)	19 (79.2)	0	3 (7.9)	30 (78.9)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 12 Any	12			20			32		
	High	0	0	0	1 (5.0)	0	0	1 (3.1)	0	0
	Normal	0	12 (100)	0	1 (5.0)	18 (90.0)	0	1 (3.1)	30 (93.8)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 14 Any	13			22			35		
	High	0	0	0	1 (4.5)	2 (9.1)	0	1 (2.9)	2 (5.7)	0
	Normal	1 (7.7)	12 (92.3)	0	1 (4.5)	18 (81.8)	0	2 (5.7)	30 (85.7)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 16 Any	12			17			29		
	High	0	0	0	1 (5.9)	0	0	1 (3.4)	0	0
	Normal	1 (8.3)	11 (91.7)	0	1 (5.9)	15 (88.2)	0	2 (6.9)	26 (89.7)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Aspartate Aminotransferase (U/L)	Week 18 Any	8				14			22	
	High	0	0	0	0	0	0	0	0	0
	Normal	1 (12.5)	7 (87.5)	0	1 (7.1)	13 (92.9)	0	2 (9.1)	20 (90.9)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 20 Any	8				15			23	
	High	0	0	0	0	0	0	0	0	0
	Normal	0	8 (100)	0	1 (6.7)	14 (93.3)	0	1 (4.3)	22 (95.7)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 22 Any	8				14			22	
	High	0	0	0	0	1 (7.1)	0	0	1 (4.5)	0
	Normal	1 (12.5)	7 (87.5)	0	1 (7.1)	12 (85.7)	0	2 (9.1)	19 (86.4)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 24 Any	8				8			16	
	High	0	2 (25.0)	0	0	1 (12.5)	0	0	3 (18.8)	0
	Normal	1 (12.5)	5 (62.5)	0	0	7 (87.5)	0	1 (6.3)	12 (75.0)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Aspartate Aminotransferase (U/L)	Any	3			3			6		
	High	0	1 (33.3)	0	0	0	0	0	1 (16.7)	0
	Normal	0	2 (66.7)	0	0	3 (100)	0	0	5 (83.3)	0
	Low	0	0	0	0	0	0	0	0	0
	Any	1			2			3		
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	0	2 (100)	0	0	3 (100)	0
	Low	0	0	0	0	0	0	0	0	0
	Any	0			1			1		
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	0	1 (100)	0	0	1 (100)	0
	Low	0	0	0	0	0	0	0	0	0
	Any	0			1			1		
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	0	1 (100)	0	0	1 (100)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Aspartate Aminotransferase (U/L)	Week 34	Any 0	High 0	Normal 0	Low 0	High 1	Normal 0	Low 0	High 1	Normal 0	Low 0
		High 0	Normal 0	Low 0	High 0	Normal 1 (100)	Low 0	High 0	Normal 1 (100)	Low 0	0
	FU W 2	Any 17	High 2 (11.8)	Normal 1 (5.9)	Low 0	High 3 (13.0)	Normal 1 (4.3)	Low 0	High 5 (12.5)	Normal 2 (5.0)	Low 0
		High 0	Normal 14 (82.4)	Low 0	High 4 (17.4)	Normal 15 (65.2)	Low 0	High 4 (10.0)	Normal 29 (72.5)	Low 0	0
	FU W 4	Any 11	High 2 (18.2)	Normal 0	Low 0	High 4 (19.0)	Normal 0	Low 0	High 6 (18.8)	Normal 0	Low 0
		High 2 (18.2)	Normal 7 (63.6)	Low 0	High 4 (19.0)	Normal 13 (61.9)	Low 0	High 6 (18.8)	Normal 20 (62.5)	Low 0	0
	FU W 6	Any 10	High 1 (10.0)	Normal 0	Low 0	High 2 (12.5)	Normal 1 (6.3)	Low 0	High 3 (11.5)	Normal 1 (3.8)	Low 0
		High 2 (20.0)	Normal 7 (70.0)	Low 0	High 1 (6.3)	Normal 12 (75.0)	Low 0	High 3 (11.5)	Normal 19 (73.1)	Low 0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Aspartate Aminotransferase (U/L)	FU W 8	Any 6			9			15		
		High 0	1 (16.7)	0	1 (11.1)	1 (11.1)	0	1 (6.7)	2 (13.3)	0
		Normal 0	5 (83.3)	0	0	7 (77.8)	0	0	12 (80.0)	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 10	Any 3			9			12		
		High 0	0	0	1 (11.1)	0	0	1 (8.3)	0	0
		Normal 0	3 (100)	0	0	8 (88.9)	0	0	11 (91.7)	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 12	Any 4			2			6		
		High 1 (25.0)	0	0	1 (50.0)	0	0	2 (33.3)	0	0
		Normal 0	3 (75.0)	0	0	1 (50.0)	0	0	4 (66.7)	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 6	Any 3			3			6		
		High 0	0	0	0	1 (33.3)	0	0	1 (16.7)	0
		Normal 0	3 (100)	0	0	2 (66.7)	0	0	5 (83.3)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Aspartate Aminotransferase (U/L)	FU M 9 Any	2	0	0	0	1	0	0	3	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	2 (100)	0	1 (100)	0	0	0	3 (100)	0
	Low	0	0	0	0	0	0	0	0	0
	FU M 12 Any	1	0	0	0	1	0	0	2	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	1 (100)	0	0	0	2 (100)	0
	Low	0	0	0	0	0	0	0	0	0
	FU M 15 Any	2	0	0	0	0	0	0	2	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	2 (100)	0	0	0	0	0	2 (100)	0
	Low	0	0	0	0	0	0	0	0	0
	FU M 18 Any	1	0	0	0	0	0	0	1	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	0	0	0	0	1 (100)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alanine Aminotransferase (U/L)	Week 2	Any 18			34			52		
		High 1 (5.6)	2 (11.1)	0	2 (5.9)	0	0	3 (5.8)	2 (3.8)	0
		Normal 1 (5.6)	14 (77.8)	0	1 (2.9)	31 (91.2)	0	2 (3.8)	45 (86.5)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 4	Any 16			35			51		
		High 1 (6.3)	0	0	4 (11.4)	2 (5.7)	0	5 (9.8)	2 (3.9)	0
		Normal 0	15 (93.8)	0	0	29 (82.9)	0	0	44 (86.3)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 6	Any 18			34			52		
		High 0	1 (5.6)	0	3 (8.8)	2 (5.9)	0	3 (5.8)	3 (5.8)	0
		Normal 2 (11.1)	15 (83.3)	0	1 (2.9)	28 (82.4)	0	3 (5.8)	43 (82.7)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 8	Any 14			24			38		
		High 0	0	0	0	3 (12.5)	0	0	3 (7.9)	0
		Normal 1 (7.1)	13 (92.9)	0	1 (4.2)	20 (83.3)	0	2 (5.3)	33 (86.8)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alanine Aminotransferase (U/L)	Week 10 Any	14			24			38		
	High	0	0	0	1 (4.2)	1 (4.2)	0	1 (2.6)	1 (2.6)	0
	Normal	1 (7.1)	13 (92.9)	0	1 (4.2)	21 (87.5)	0	2 (5.3)	34 (89.5)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 12 Any	12			20			32		
	High	0	1 (8.3)	0	3 (15.0)	0	0	3 (9.4)	1 (3.1)	0
	Normal	0	11 (91.7)	0	0	17 (85.0)	0	0	28 (87.5)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 14 Any	13			22			35		
	High	0	0	0	3 (13.6)	1 (4.5)	0	3 (8.6)	1 (2.9)	0
	Normal	1 (7.7)	12 (92.3)	0	0	18 (81.8)	0	1 (2.9)	30 (85.7)	0
	Low	0	0	0	0	0	0	0	0	0
	Week 16 Any	12			17			29		
	High	0	0	0	2 (11.8)	0	0	2 (6.9)	0	0
	Normal	1 (8.3)	11 (91.7)	0	1 (5.9)	14 (82.4)	0	2 (6.9)	25 (86.2)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alanine Aminotransferase (U/L)	Week 18	Any 8	0	0	1 (7.1)	1 (7.1)	0	1 (4.5)	1 (4.5)	0
		High 0	0	0	1 (7.1)	11 (78.6)	0	2 (9.1)	18 (81.8)	0
		Normal 1 (12.5)	7 (87.5)	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	Week 20	Any 8	0	0	1 (6.7)	0	0	1 (4.3)	0	0
		High 0	0	0	0	14 (93.3)	0	0	22 (95.7)	0
		Normal 0	8 (100)	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	Week 22	Any 8	0	0	1 (7.1)	1 (7.1)	0	1 (4.5)	1 (4.5)	0
		High 0	0	0	1 (7.1)	11 (78.6)	0	2 (9.1)	18 (81.8)	0
		Normal 1 (12.5)	7 (87.5)	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	Week 24	Any 8	1 (12.5)	0	1 (12.5)	0	0	0	2 (12.5)	0
		High 0	1 (12.5)	0	0	7 (87.5)	0	1 (6.3)	13 (81.3)	0
		Normal 1 (12.5)	6 (75.0)	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alanine Aminotransferase (U/L)	Any	3	0	0	0	3	0	0	6	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	3 (100)	0	3 (100)	0	0	6 (100)	0	0
	Low	0	0	0	0	0	0	0	0	0
	Any	1	0	0	2	0	0	3	0	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	2 (100)	0	0	3 (100)	0	0
	Low	0	0	0	0	0	0	0	0	0
	Any	0	0	0	1	0	0	1	0	0
	High	0	0	0	0	0	0	0	1 (100)	0
	Normal	0	0	0	1 (100)	0	0	1 (100)	0	0
	Low	0	0	0	0	0	0	0	0	0
	Any	0	0	0	1	0	0	1	0	0
	High	0	0	0	0	0	0	0	1 (100)	0
	Normal	0	0	0	1 (100)	0	0	1 (100)	0	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Alanine Aminotransferase (U/L)	Week 34	Any 0	High 0	Normal 0	Low 0	High 1 (100)	Normal 0	Low 0	High 1 (100)	Normal 0	Low 0
	FU W 2	Any 17	High 1 (5.9)	Normal 1 (5.9) 15 (88.2)	Low 0	High 1 (4.3) 3 (13.0)	Normal 0	Low 0	High 2 (5.0) 3 (7.5)	Normal 1 (2.5) 34 (85.0)	Low 0
	FU W 4	Any 11	High 1 (9.1)	Normal 0	Low 0	High 2 (9.5) 3 (14.3)	Normal 0	Low 0	High 3 (9.4) 4 (12.5)	Normal 0	Low 0
	FU W 6	Any 10	High 0	Normal 0	Low 0	High 1 (6.3) 1 (6.3)	Normal 0	Low 0	High 1 (3.8) 3 (11.5)	Normal 2 (7.7) 20 (76.9)	Low 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alanine Aminotransferase (U/L)	FU W 8	Any	6	0	9	1 (11.1)	0	0	15	0
		High	0	1 (16.7)	0	1 (11.1)	0	0	2 (13.3)	0
		Normal	0	5 (83.3)	0	8 (88.9)	0	0	13 (86.7)	0
		Low	0	0	0	0	0	0	0	0
	FU W 10	Any	3	0	9	1 (11.1)	0	0	12	0
		High	0	0	0	1 (11.1)	0	1 (8.3)	1 (8.3)	0
		Normal	0	3 (100)	0	7 (77.8)	0	1 (8.3)	10 (83.3)	0
		Low	0	0	0	0	0	0	0	0
	FU W 12	Any	4	0	2	0	0	1 (16.7)	0	0
		High	0	0	1 (50.0)	0	0	1 (16.7)	4 (66.7)	0
		Normal	0	4 (100)	0	1 (50.0)	0	0	0	0
		Low	0	0	0	0	0	0	0	0
	FU M 6	Any	3	0	3	1 (33.3)	0	0	6	0
		High	0	0	0	1 (33.3)	0	1 (16.7)	0	0
		Normal	0	3 (100)	0	2 (66.7)	0	0	5 (83.3)	0
		Low	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alanine Aminotransferase (U/L)	FU M 9 Any	2	0	0	0	1	0	0	3	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	2 (100)	0	1 (100)	0	0	0	3 (100)	0
	Low	0	0	0	0	0	0	0	0	0
	FU M 12 Any	1	0	0	0	1	0	0	2	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	1 (100)	0	0	0	2 (100)	0
	Low	0	0	0	0	0	0	0	0	0
	FU M 15 Any	2	0	0	0	0	0	0	2	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	2 (100)	0	0	0	0	0	2 (100)	0
	Low	0	0	0	0	0	0	0	0	0
	FU M 18 Any	1	0	0	0	0	0	0	1	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	0	0	0	0	1 (100)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alkaline Phosphatase (U/L)	Week 2	Any 18			34			52		
		High 5 (27.8)	0	0	5 (14.7)	0	0	10 (19.2)	0	0
		Normal 1 (5.6)	12 (66.7)	0	0	28 (82.4)	0	1 (1.9)	40 (76.9)	0
		Low 0	0	0	0	1 (2.9)	0	0	1 (1.9)	0
	Week 4	Any 16			35			51		
		High 5 (31.3)	1 (6.3)	0	8 (22.9)	2 (5.7)	0	13 (25.5)	3 (5.9)	0
		Normal 0	10 (62.5)	0	0	25 (71.4)	0	0	35 (68.6)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 6	Any 18			34			52		
		High 5 (27.8)	3 (16.7)	0	7 (20.6)	5 (14.7)	0	12 (23.1)	8 (15.4)	0
		Normal 1 (5.6)	9 (50.0)	0	0	21 (61.8)	0	1 (1.9)	30 (57.7)	0
		Low 0	0	0	0	1 (2.9)	0	0	1 (1.9)	0
	Week 8	Any 13			24			37		
		High 3 (23.1)	2 (15.4)	0	6 (25.0)	2 (8.3)	0	9 (24.3)	4 (10.8)	0
		Normal 2 (15.4)	6 (46.2)	0	0	16 (66.7)	0	2 (5.4)	22 (59.5)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alkaline Phosphatase (U/L)	Week 10	Any 13			24			37		
		High 1 (7.7)	2 (15.4)	0	7 (29.2)	0	0	8 (21.6)	2 (5.4)	0
		Normal 1 (7.7)	9 (69.2)	0	0	16 (66.7)	0	1 (2.7)	25 (67.6)	0
		Low 0	0	0	0	1 (4.2)	0	0	1 (2.7)	0
	Week 12	Any 12			20			32		
		High 1 (8.3)	2 (16.7)	0	3 (15.0)	0	0	4 (12.5)	2 (6.3)	0
		Normal 1 (8.3)	8 (66.7)	0	1 (5.0)	16 (80.0)	0	2 (6.3)	24 (75.0)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 14	Any 12			22			34		
		High 1 (8.3)	3 (25.0)	0	4 (18.2)	0	0	5 (14.7)	3 (8.8)	0
		Normal 1 (8.3)	7 (58.3)	0	0	17 (77.3)	0	1 (2.9)	24 (70.6)	0
		Low 0	0	0	0	1 (4.5)	0	0	1 (2.9)	0
	Week 16	Any 11			17			28		
		High 1 (9.1)	1 (9.1)	0	4 (23.5)	0	0	5 (17.9)	1 (3.6)	0
		Normal 0	9 (81.8)	0	0	13 (76.5)	0	0	22 (78.6)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alkaline Phosphatase (U/L)	Week 18	Any 8			14			22		
	High 0	2 (25.0)	0	2 (14.3)	0	0	2 (9.1)	2 (9.1)	0	
	Normal 2	(25.0)	4 (50.0)	0	0	12 (85.7)	0	2 (9.1)	16 (72.7)	0
	Low 0	0	0	0	0	0	0	0	0	0
	Week 20	Any 8			15			23		
	High 0	1 (12.5)	0	3 (20.0)	0	0	3 (13.0)	1 (4.3)	0	
	Normal 1	(12.5)	6 (75.0)	0	0	11 (73.3)	0	1 (4.3)	17 (73.9)	0
	Low 0	0	0	0	0	1 (6.7)	0	0	1 (4.3)	0
	Week 22	Any 8			15			23		
	High 0	2 (25.0)	0	2 (13.3)	0	0	2 (8.7)	2 (8.7)	0	
	Normal 2	(25.0)	4 (50.0)	0	0	13 (86.7)	0	2 (8.7)	17 (73.9)	0
	Low 0	0	0	0	0	0	0	0	0	0
	Week 24	Any 8			8			16		
	High 0	2 (25.0)	0	2 (25.0)	0	0	2 (12.5)	2 (12.5)	0	
	Normal 2	(25.0)	4 (50.0)	0	0	6 (75.0)	0	2 (12.5)	10 (62.5)	0
	Low 0	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alkaline Phosphatase (U/L)	Any	3	0	0	1 (33.3)	0	0	1 (16.7)	6	0
	High	0	0	0	0	2 (66.7)	0	0	0	0
	Normal	0	3 (100)	0	0	0	0	0	5 (83.3)	0
	Low	0	0	0	0	0	0	0	0	0
Week 26	Any	1	0	0	2	0	0	0	3	0
	High	0	0	0	0	2 (100)	0	0	3 (100)	0
	Normal	0	1 (100)	0	0	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0
Week 28	Any	0	0	0	1	0	0	0	1	0
	High	0	0	0	0	1 (100)	0	0	1 (100)	0
	Normal	0	0	0	0	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0
Week 30	Any	0	0	0	1	0	0	0	1	0
	High	0	0	0	0	1 (100)	0	0	1 (100)	0
	Normal	0	0	0	0	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0
Week 32	Any	0	0	0	1	0	0	0	1	0
	High	0	0	0	0	1 (100)	0	0	1 (100)	0
	Normal	0	0	0	0	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Alkaline Phosphatase (U/L)	Week 34	Any 0	High 0	Normal 0	Low 0	High 1	Normal 0	Low 0	High 1	Normal 0	Low 0
	FU W 2	Any 17	High 8 (47.1)	Normal 1 (5.9)	Low 0	High 5 (21.7)	Normal 2 (8.7)	Low 0	High 13 (32.5)	Normal 3 (7.5)	Low 5 (12.5) 0
	FU W 4	Any 11	High 4 (36.4)	Normal 1 (9.1)	Low 0	High 5 (23.8)	Normal 1 (4.8)	Low 0	High 9 (28.1)	Normal 2 (6.3)	Low 4 (12.5) 0
	FU W 6	Any 10	High 4 (40.0)	Normal 1 (10.0)	Low 0	High 5 (31.3)	Normal 0	Low 1 (6.3)	High 9 (34.6)	Normal 1 (3.8)	Low 3 (11.5) 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alkaline Phosphatase (U/L)	FU W 8	Any High 1 (16.7) Normal 0 Low 0	6 0 0	0 0 0	1 (11.1) 0 0	2 (22.2) 6 (66.7) 0	0 0 0	2 (13.3) 0 0	15 2 (13.3) 11 (73.3) 0	0 0 0
	FU W 10	Any High 0 Normal 1 (33.3) Low 0	3 1 (33.3) 0	0 0 0	2 (22.2) 0 0	0 6 (66.7) 1 (11.1)	0 0 0	2 (16.7) 1 (8.3) 0	12 1 (8.3) 7 (58.3) 1 (8.3)	0 0 0
	FU W 12	Any High 1 (25.0) Normal 1 (25.0) Low 0	4 1 (25.0) 1 (25.0) 0	0 0 0	0 0 0	2 (100) 0 0	0 0 0	1 (16.7) 1 (16.7) 0	6 1 (16.7) 3 (50.0) 0	0 0 0
	FU M 6	Any High 0 Normal 0 Low 0	3 0 0	0 0 0	0 0 0	3 2 (66.7) 0	0 0 0	0 1 (16.7) 0	6 5 (83.3) 0	0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Alkaline Phosphatase (U/L)	Any	2	0	0	0	1	0	0	3	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	2 (100)	0	1 (100)	0	0	0	3 (100)	0
	Low	0	0	0	0	0	0	0	0	0
FU M 12	Any	1	0	0	0	1	0	0	2	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	1 (100)	0	0	0	2 (100)	0
	Low	0	0	0	0	0	0	0	0	0
FU M 15	Any	2	0	0	0	0	0	0	2	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	2 (100)	0	0	0	0	0	2 (100)	0
	Low	0	0	0	0	0	0	0	0	0
FU M 18	Any	1	0	0	0	0	0	0	1	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	0	0	0	0	1 (100)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Prostate Specific Antigen (ug/L)	Week 6	Any 19			33			52		
		High 15 (78.9)	1 (5.3)	0	28 (84.8)	1 (3.0)	0	43 (82.7)	2 (3.8)	0
		Normal 2 (10.5)	1 (5.3)	0	1 (3.0)	3 (9.1)	0	3 (5.8)	4 (7.7)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 12	Any 14			25			39		
		High 11 (78.6)	0	0	21 (84.0)	1 (4.0)	0	32 (82.1)	1 (2.6)	0
		Normal 3 (21.4)	0	0	1 (4.0)	2 (8.0)	0	4 (10.3)	2 (5.1)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 18	Any 11			11			22		
		High 8 (72.7)	1 (9.1)	0	7 (63.6)	0	0	15 (68.2)	1 (4.5)	0
		Normal 2 (18.2)	0	0	2 (18.2)	2 (18.2)	0	4 (18.2)	2 (9.1)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 24	Any 8			11			19		
		High 4 (50.0)	1 (12.5)	0	9 (81.8)	0	0	13 (68.4)	1 (5.3)	0
		Normal 3 (37.5)	0	0	1 (9.1)	1 (9.1)	0	4 (21.1)	1 (5.3)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Prostate Specific Antigen (ug/L)	Week 30	Any 2	0	0	1 (100)	0	0	2 (66.7)	0	0
		High 1 (50.0)	0	0	0	0	0	1 (33.3)	0	0
		Normal 1 (50.0)	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 6	Any 10	0	0	13	0	0	17 (73.9)	0	0
		High 7 (70.0)	0	0	10 (76.9)	0	0	3 (13.0)	3 (13.0)	0
		Normal 2 (20.0)	1 (10.0)	0	1 (7.7)	2 (15.4)	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 3	Any 7	0	0	11	0	0	10 (55.6)	1 (5.6)	0
		High 4 (57.1)	0	0	6 (54.5)	1 (9.1)	0	5 (27.8)	2 (11.1)	0
		Normal 2 (28.6)	1 (14.3)	0	3 (27.3)	1 (9.1)	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 6	Any 3	0	0	3	0	0	1 (16.7)	0	0
		High 0	0	0	1 (33.3)	0	0	4 (66.7)	1 (16.7)	0
		Normal 3 (100)	0	0	1 (33.3)	1 (33.3)	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Prostate Specific Antigen (ug/L)	FU M 9	Any 2	0	0	0	1 (33.3)	0	0	1 (20.0)	0
		High 0	0	0	2 (66.7)	0	0	4 (80.0)	0	0
		Normal 2 (100)	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 12	Any 1	0	0	0	2	0	0	0	0
		High 0	0	0	0	0	0	0	0	0
		Normal 1 (100)	0	0	1 (50.0)	1 (50.0)	0	2 (66.7)	1 (33.3)	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 15	Any 2	0	0	0	1	0	0	0	0
		High 0	0	0	0	0	0	0	0	0
		Normal 2 (100)	0	0	0	1 (100)	0	2 (66.7)	1 (33.3)	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 18	Any 1	0	0	0	0	0	0	0	0
		High 0	0	0	0	0	0	0	0	0
		Normal 1 (100)	0	0	0	0	0	1 (100)	0	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Albumin (g/L)	Week 2	Any	16		28			44		
		High	0	0	0	0	0	0	0	0
		Normal	0	12 (75.0)	1 (6.3)	0	22 (78.6)	1 (3.6)	34 (77.3)	2 (4.5)
		Low	0	1 (6.3)	2 (12.5)	0	2 (7.1)	3 (10.7)	3 (6.8)	5 (11.4)
	Week 4	Any	15		28			43		
		High	0	0	0	0	0	0	0	0
		Normal	0	13 (86.7)	0	0	21 (75.0)	1 (3.6)	34 (79.1)	1 (2.3)
		Low	0	0	2 (13.3)	0	3 (10.7)	3 (10.7)	3 (7.0)	5 (11.6)
	Week 6	Any	17		29			46		
		High	0	0	0	0	0	0	0	0
		Normal	0	13 (76.5)	3 (17.6)	0	24 (82.8)	2 (6.9)	37 (80.4)	5 (10.9)
		Low	0	1 (5.9)	0	0	2 (6.9)	1 (3.4)	3 (6.5)	1 (2.2)
	Week 8	Any	13		20			33		
		High	0	0	0	0	0	0	0	0
		Normal	0	10 (76.9)	3 (23.1)	0	15 (75.0)	1 (5.0)	25 (75.8)	4 (12.1)
		Low	0	0	0	0	2 (10.0)	2 (10.0)	2 (6.1)	2 (6.1)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Albumin (g/L)	Week 10	Any	13		20			33		
		High	0	0	0	0	0	0	0	0
		Normal	0	11 (84.6)	2 (15.4)	0	17 (85.0)	1 (5.0)	28 (84.8)	3 (9.1)
		Low	0	0	0	1 (5.0)	1 (5.0)	0	1 (3.0)	1 (3.0)
	Week 12	Any	11		17			28		
		High	0	0	0	0	0	0	0	0
		Normal	0	10 (90.9)	1 (9.1)	0	13 (76.5)	0	23 (82.1)	1 (3.6)
		Low	0	0	0	2 (11.8)	2 (11.8)	0	2 (7.1)	2 (7.1)
	Week 14	Any	12		19			31		
		High	0	0	0	0	0	0	0	0
		Normal	0	9 (75.0)	2 (16.7)	0	13 (68.4)	1 (5.3)	22 (71.0)	3 (9.7)
		Low	0	1 (8.3)	0	0	4 (21.1)	1 (5.3)	5 (16.1)	1 (3.2)
	Week 16	Any	11		15			26		
		High	0	0	0	0	0	0	0	0
		Normal	0	8 (72.7)	2 (18.2)	0	12 (80.0)	1 (6.7)	20 (76.9)	3 (11.5)
		Low	0	1 (9.1)	0	0	2 (13.3)	0	0	3 (11.5)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Albumin (g/L)	Week 18	Any	7		13			20		
		High	0	0	0	0	0	0	0	0
		Normal	6 (85.7)	1 (14.3)	0	10 (76.9)	1 (7.7)	0	16 (80.0)	2 (10.0)
		Low	0	0	0	2 (15.4)	0	0	2 (10.0)	0
	Week 20	Any	7		13			20		
		High	0	0	0	0	0	0	0	0
		Normal	7 (100)	0	0	11 (84.6)	1 (7.7)	0	18 (90.0)	1 (5.0)
		Low	0	0	0	1 (7.7)	0	0	1 (5.0)	0
	Week 22	Any	7		13			20		
		High	0	0	0	0	0	0	0	0
		Normal	6 (85.7)	1 (14.3)	0	13 (100)	0	0	19 (95.0)	1 (5.0)
		Low	0	0	0	0	0	0	0	0
	Week 24	Any	7		8			15		
		High	0	0	0	0	0	0	0	0
		Normal	5 (71.4)	1 (14.3)	0	7 (87.5)	0	0	12 (80.0)	1 (6.7)
		Low	0	1 (14.3)	0	1 (12.5)	0	0	1 (6.7)	1 (6.7)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Albumin (g/L)	Week 26	Any	3	0	0	3	0	0	6	0
		High	0	0	0	0	0	0	0	0
		Normal	3 (100)	0	0	2 (66.7)	0	0	5 (83.3)	0
		Low	0	0	0	1 (33.3)	0	0	1 (16.7)	0
	Week 28	Any	1	0	0	2	0	0	3	0
		High	0	0	0	0	0	0	0	0
		Normal	1 (100)	0	0	1 (50.0)	0	0	2 (66.7)	0
		Low	0	0	0	1 (50.0)	0	0	1 (33.3)	0
	Week 30	Any	0	0	0	1	0	0	1	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	0	0	1 (100)	0	0	1 (100)	0
	Week 32	Any	0	0	0	1	0	0	1	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	0	0	1 (100)	0	0	1 (100)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Albumin (g/L)	Week 34	Any	0			1			1	
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	0	0	1 (100)	0	0	1 (100)	0
	FU W 2	Any	16			19			35	
		High	0	0	0	0	0	0	0	0
		Normal	0	12 (75.0)	1 (6.3)	13 (68.4)	2 (10.5)	0	25 (71.4)	3 (8.6)
		Low	0	0	3 (18.8)	0	2 (10.5)	2 (10.5)	2 (5.7)	5 (14.3)
	FU W 4	Any	11			20			31	
		High	0	0	0	0	0	0	0	0
		Normal	0	9 (81.8)	0	13 (65.0)	1 (5.0)	0	22 (71.0)	1 (3.2)
		Low	0	0	2 (18.2)	0	4 (20.0)	2 (10.0)	4 (12.9)	4 (12.9)
	FU W 6	Any	9			14			23	
		High	0	0	0	0	0	0	0	0
		Normal	0	6 (66.7)	1 (11.1)	10 (71.4)	0	0	16 (69.6)	1 (4.3)
		Low	0	1 (11.1)	1 (11.1)	0	3 (21.4)	1 (7.1)	0	4 (17.4)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Albumin (g/L)	FU W 8	Any	6	0	8	0	0	0	14	0
		High	0	0	0	0	0	0	0	0
		Normal	3 (50.0)	1 (16.7)	0	5 (62.5)	0	0	8 (57.1)	1 (7.1)
		Low	2 (33.3)	0	0	2 (25.0)	1 (12.5)	0	4 (28.6)	1 (7.1)
	FU W 10	Any	2	0	8	0	0	0	10	0
		High	0	0	0	0	0	0	0	0
		Normal	2 (100)	0	0	8 (100)	0	0	10 (100)	0
		Low	0	0	0	0	0	0	0	0
	FU W 12	Any	3	0	2	0	0	0	5	0
		High	0	0	0	0	0	0	0	0
		Normal	3 (100)	0	0	2 (100)	0	0	5 (100)	0
		Low	0	0	0	0	0	0	0	0
	FU M 6	Any	3	0	3	0	0	0	6	0
		High	0	0	0	0	0	0	0	0
		Normal	2 (66.7)	0	0	3 (100)	0	0	5 (83.3)	0
		Low	0	1 (33.3)	0	0	0	0	0	1 (16.7)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Albumin (g/L)	FU M 9	Any 2	0	0	0	1	0	0	3	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	2 (100)	0	0	0	0	0	2 (66.7)	0
		Low 0	0	0	0	1 (100)	0	0	1 (33.3)	0
	FU M 12	Any 1	0	0	0	1	0	0	2	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	1 (100)	0	0	0	0	0	1 (50.0)	0
		Low 0	0	0	0	1 (100)	0	0	1 (50.0)	0
	FU M 15	Any 2	0	0	0	0	0	0	2	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	2 (100)	0	0	0	0	0	2 (100)	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 18	Any 1	0	0	0	0	0	0	1	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	1 (100)	0	0	0	0	0	1 (100)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Potassium (mmol/L)	Week 2	Any 17			36			53		
		High 0	3 (17.6)	0	1 (2.8)	2 (5.6)	0	1 (1.9)	5 (9.4)	0
		Normal 1	(5.9)	12 (70.6)	1 (5.9)	2 (5.6)	30 (83.3)	1 (2.8)	3 (5.7)	42 (79.2)
		Low 0	0	0	0	0	0	0	0	2 (3.8)
	Week 4	Any 17			36			53		
		High 0	1 (5.9)	0	0	2 (5.6)	0	0	3 (5.7)	0
		Normal 1	(5.9)	14 (82.4)	1 (5.9)	4 (11.1)	28 (77.8)	0	5 (9.4)	42 (79.2)
		Low 0	0	0	0	1 (2.8)	1 (2.8)	0	1 (1.9)	1 (1.9)
	Week 6	Any 18			34			52		
		High 0	2 (11.1)	0	0	0	0	0	2 (3.8)	0
		Normal 1	(5.6)	14 (77.8)	1 (5.6)	4 (11.8)	29 (85.3)	1 (2.9)	5 (9.6)	43 (82.7)
		Low 0	0	0	0	0	0	0	0	2 (3.8)
	Week 8	Any 13			26			39		
		High 0	1 (7.7)	0	2 (7.7)	0	0	2 (5.1)	1 (2.6)	0
		Normal 1	(7.7)	10 (76.9)	1 (7.7)	1 (3.8)	23 (88.5)	0	2 (5.1)	33 (84.6)
		Low 0	0	0	0	0	0	0	0	1 (2.6)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Potassium (mmol/L)	Week 10	Any	14			23			37	
		High	0	3 (21.4)	0	2 (8.7)	0	0	5 (13.5)	0
		Normal	0	10 (71.4)	1 (7.1)	19 (82.6)	0	1 (2.7)	29 (78.4)	1 (2.7)
		Low	0	0	0	0	1 (4.3)	0	0	1 (2.7)
	Week 12	Any	12			20			32	
		High	0	3 (25.0)	0	1 (5.0)	1 (5.0)	0	4 (12.5)	0
		Normal	0	9 (75.0)	0	1 (5.0)	15 (75.0)	1 (5.0)	24 (75.0)	1 (3.1)
		Low	0	0	0	0	1 (5.0)	0	1 (3.1)	0
	Week 14	Any	13			22			35	
		High	0	2 (15.4)	0	1 (4.5)	3 (13.6)	0	5 (14.3)	0
		Normal	0	10 (76.9)	1 (7.7)	2 (9.1)	15 (68.2)	1 (4.5)	25 (71.4)	2 (5.7)
		Low	0	0	0	0	0	0	0	0
	Week 16	Any	12			17			29	
		High	0	2 (16.7)	0	1 (5.9)	0	0	2 (6.9)	0
		Normal	0	9 (75.0)	1 (8.3)	1 (5.9)	14 (82.4)	1 (5.9)	23 (79.3)	2 (6.9)
		Low	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Potassium (mmol/L)	Week 18	Any	8			14			22	
		High	0	0	1 (7.1)	2 (14.3)	0	1 (4.5)	2 (9.1)	0
		Normal	0	7 (87.5)	1 (12.5)	2 (14.3)	8 (57.1)	1 (7.1)	2 (9.1)	15 (68.2)
		Low	0	0	0	0	0	0	0	2 (9.1)
	Week 20	Any	8			15			23	
		High	0	2 (25.0)	0	0	0	0	2 (8.7)	0
		Normal	0	6 (75.0)	0	1 (6.7)	13 (86.7)	1 (6.7)	1 (4.3)	19 (82.6)
		Low	0	0	0	0	0	0	0	1 (4.3)
	Week 22	Any	8			14			22	
		High	0	0	1 (7.1)	2 (14.3)	0	1 (4.5)	2 (9.1)	0
		Normal	0	7 (87.5)	1 (12.5)	1 (7.1)	9 (64.3)	1 (7.1)	1 (4.5)	16 (72.7)
		Low	0	0	0	0	0	0	0	2 (9.1)
	Week 24	Any	8			8			16	
		High	0	1 (12.5)	0	0	1 (12.5)	0	0	2 (12.5)
		Normal	0	6 (75.0)	1 (12.5)	0	6 (75.0)	0	0	12 (75.0)
		Low	0	0	0	0	1 (12.5)	0	0	1 (6.3)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Potassium (mmol/L)	Week 26	Any 3 High 0 Normal 3 (100) Low 0	0 0 0	0 0 0	0 3 (100) 0	0 0 0	0 0 0	0 6 (100) 0	6 0 0	0 0 0
	Week 28	Any 1 High 0 Normal 0 (100) Low 0	0 0 0	0 0 0	0 2 (100) 0	0 0 0	0 0 0	0 3 (100) 0	3 0 0	0 0 0
	Week 30	Any 0 High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0	1 0 0	0 0 0
	Week 32	Any 0 High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	1 0 (100) 0	0 0 0	0 0 0	0 1 (100) 0	1 0 0	0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Potassium (mmol/L)	Week 34	Any 0	High 0	0	0	1 (100)	0	0	1 (100)	0
		High 0	Normal 0	0	0	0	0	0	0	0
		Normal 0	Low 0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
FU W 2	Any 17	High 4 (23.5)	Normal 12 (70.6)	Low 0	2 (8.7)	18 (78.3)	1 (4.3)	3 (7.5)	30 (75.0)	1 (2.5)
		High 0	Normal 1 (5.9)	Low 0	0	0	0	0	6 (15.0)	0
		Normal 0	Low 0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
FU W 4	Any 11	High 3 (27.3)	Normal 7 (63.6)	Low 0	1 (4.8)	3 (14.3)	0	1 (3.1)	6 (18.8)	0
		High 0	Normal 1 (9.1)	Low 0	0	16 (76.2)	1 (4.8)	1 (3.1)	23 (71.9)	1 (3.1)
		Normal 0	Low 0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
FU W 6	Any 10	High 2 (20.0)	Normal 7 (70.0)	Low 0	2 (12.5)	2 (12.5)	0	2 (7.7)	4 (15.4)	0
		High 0	Normal 1 (10.0)	Low 0	1 (6.3)	9 (56.3)	1 (6.3)	2 (7.7)	16 (61.5)	1 (3.8)
		Normal 0	Low 0	0	0	1 (6.3)	0	0	1 (3.8)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Potassium (mmol/L)	FU W 8	Any 6			8			14		
		High 0	1 (16.7)	0	0	2 (25.0)	0	0	3 (21.4)	0
		Normal 0	5 (83.3)	0	0	6 (75.0)	0	0	11 (78.6)	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 10	Any 3			9			12		
		High 0	1 (33.3)	0	0	1 (11.1)	1 (11.1)	0	2 (16.7)	0
		Normal 0	2 (66.7)	0	1 (11.1)	6 (66.7)	1 (11.1)	1 (8.3)	8 (66.7)	1 (8.3)
		Low 0	0	0	0	0	0	0	0	0
	FU W 12	Any 4			2			6		
		High 0	1 (25.0)	0	0	0	0	0	1 (16.7)	0
		Normal 1	(25.0) 2 (50.0)	0	1 (50.0)	0	1 (50.0)	2 (33.3)	2 (33.3)	1 (16.7)
		Low 0	0	0	0	0	0	0	0	0
	FU M 6	Any 3			3			6		
		High 0	0	0	0	0	0	0	0	0
		Normal 0	3 (100)	0	0	3 (100)	0	0	6 (100)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.3
Chemistry Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Potassium (mmol/L)	FU M 9	Any 2	High 0	Normal 1 (50.0)	Low 0	High 0	Normal 1 (100)	Low 0	High 0	Normal 1 (33.3)	Low 0
		High 0	Normal 1 (50.0)	Low 0	High 0	Normal 0	Low 0	High 0	Normal 2 (66.7)	Low 0	
	FU M 12	Any 1	High 0	Normal 0	Low 0	High 0	Normal 1 (100)	Low 0	High 0	Normal 1 (50.0)	Low 0
		High 0	Normal 0	Low 0	High 0	Normal 0	Low 0	High 0	Normal 1 (50.0)	Low 0	
	FU M 15	Any 2	High 0	Normal 2 (100)	Low 0	High 0	Normal 0	Low 0	High 0	Normal 2 (100)	Low 0
		High 0	Normal 0	Low 0	High 0	Normal 0	Low 0	High 0	Normal 0	Low 0	
	FU M 18	Any 1	High 0	Normal 1 (100)	Low 0	High 0	Normal 0	Low 0	High 0	Normal 1 (100)	Low 0
		High 0	Normal 0	Low 0	High 0	Normal 0	Low 0	High 0	Normal 0	Low 0	

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Basophils (10E9/L)	Week 2	Any 13 High 0 Normal 0 Low 0	13 (100) 0 0 0	0 0 0 0	35 0 35 (100) 0	0 0 0 0	0 0 0 0	48 0 48 (100) 0	48 0 0 0	0 0 0 0
	Week 4	Any 15 High 0 Normal 0 Low 0	15 (100) 0 0 0	0 0 0 0	33 0 33 (100) 0	0 0 0 0	0 0 0 0	48 0 48 (100) 0	48 0 0 0	0 0 0 0
	Week 6	Any 15 High 0 Normal 0 Low 0	15 (100) 0 0 0	0 0 0 0	35 0 35 (100) 0	0 0 0 0	0 0 0 0	50 0 50 (100) 0	50 0 0 0	0 0 0 0
	Week 8	Any 11 High 0 Normal 0 Low 0	11 (100) 0 0 0	0 0 0 0	24 0 24 (100) 0	0 0 0 0	0 0 0 0	35 0 35 (100) 0	35 0 0 0	0 0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Basophils (10E9/L)	Week 10	Any 13 High 0 Normal 0 Low 0	13 (100) 0 0 0	0 0 0 0	22 0 22 (100) 0	0 0 0 0	0 0 0 0	35 0 35 (100) 0	0 0 0 0	0 0 0 0
	Week 12	Any 11 High 0 Normal 0 Low 0	11 (100) 0 0 0	0 0 0 0	20 0 20 (100) 0	0 0 0 0	0 0 0 0	31 0 31 (100) 0	0 0 0 0	0 0 0 0
	Week 14	Any 12 High 0 Normal 0 Low 0	12 (100) 0 0 0	0 0 0 0	21 0 21 (100) 0	0 0 0 0	0 0 0 0	33 0 33 (100) 0	0 0 0 0	0 0 0 0
	Week 16	Any 10 High 0 Normal 0 Low 0	10 (100) 0 0 0	0 0 0 0	17 0 17 (100) 0	0 0 0 0	0 0 0 0	27 0 27 (100) 0	0 0 0 0	0 0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Basophils (10E9/L)	Week 18	Any	8	0	14	0	0	0	22	0
		High	0	0	0	0	0	0	0	0
		Normal	8 (100)	0	14 (100)	0	0	22 (100)	0	0
		Low	0	0	0	0	0	0	0	0
	Week 20	Any	9	0	15	0	0	0	24	0
		High	0	0	0	0	0	0	0	0
		Normal	9 (100)	0	15 (100)	0	0	24 (100)	0	0
		Low	0	0	0	0	0	0	0	0
	Week 22	Any	8	0	15	0	0	0	23	0
		High	0	0	0	0	0	0	0	0
		Normal	8 (100)	0	15 (100)	0	0	23 (100)	0	0
		Low	0	0	0	0	0	0	0	0
	Week 24	Any	8	0	6	0	0	0	14	0
		High	0	0	0	0	0	0	0	0
		Normal	8 (100)	0	6 (100)	0	0	14 (100)	0	0
		Low	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Basophils (10E9/L)	Week 26	Any 3 High 0 Normal 3 (100) Low 0	0 0 0	0 0 0	0 3 (100) 0	3 0 0	0 0 0	0 0 0	6 6 (100) 0	0 0 0
	Week 28	Any 1 High 0 Normal 0 (100) Low 0	0 0 0	0 0 0	0 2 (100) 0	2 0 0	0 0 0	0 0 0	3 3 (100) 0	0 0 0
	Week 30	Any 0 High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	0 1 (100) 0	1 0 0	0 0 0	0 0 0	1 1 (100) 0	0 0 0
	Week 32	Any 0 High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	0 1 (100) 0	1 0 0	0 0 0	0 0 0	1 1 (100) 0	0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Basophils (10E9/L)	Week 34	Any 0	High 0	Normal 0	Low 0	High 1 (100)	Normal 0	Low 0	High 1 (100)	Normal 0	Low 0
	FU W 2	Any 14	High 0	Normal 14 (100)	Low 0	High 21 (100)	Normal 0	Low 0	High 35 (100)	Normal 0	Low 0
	FU W 4	Any 10	High 0	Normal 10 (100)	Low 0	High 19 (100)	Normal 0	Low 0	High 29 (100)	Normal 0	Low 0
	FU W 6	Any 9	High 0	Normal 9 (100)	Low 0	High 14 (100)	Normal 0	Low 0	High 23 (100)	Normal 0	Low 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Basophils (10E9/L)	FU W 8	Any	7	0	8	0	0	0	15	0
		High	0	0	0	0	0	0	0	0
		Normal	7 (100)	0	8 (100)	0	0	15 (100)	0	0
		Low	0	0	0	0	0	0	0	0
	FU W 10	Any	4	0	9	0	0	0	13	0
		High	0	1 (25.0)	0	0	0	0	1 (7.7)	0
		Normal	0	3 (75.0)	0	9 (100)	0	0	12 (92.3)	0
		Low	0	0	0	0	0	0	0	0
	FU W 12	Any	4	0	2	0	0	0	6	0
		High	0	0	0	0	0	0	0	0
		Normal	0	4 (100)	0	2 (100)	0	0	6 (100)	0
		Low	0	0	0	0	0	0	0	0
	FU M 6	Any	3	0	3	0	0	0	6	0
		High	0	0	0	0	0	0	0	0
		Normal	0	3 (100)	0	3 (100)	0	0	6 (100)	0
		Low	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Basophils (10E9/L)	FU M 9	Any 2 High 0 Normal 2 (100) Low 0	0 0 0	0 0 0	1 0 1 (100) 0	0 0 0 0	0 0 0 0	3 0 3 (100) 0	0 0 0 0	0 0 0 0
	FU M 12	Any 1 High 0 Normal 1 (100) Low 0	0 1 (100) 0	0 0 0	1 0 1 (100) 0	0 0 0 0	0 0 0 0	2 0 2 (100) 0	0 0 0 0	0 0 0 0
	FU M 15	Any 2 High 0 Normal 2 (100) Low 0	0 2 (100) 0	0 0 0	1 0 1 (100) 0	0 0 0 0	0 0 0 0	3 0 3 (100) 0	0 0 0 0	0 0 0 0
	FU M 18	Any 1 High 0 Normal 1 (100) Low 0	0 1 (100) 0	0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0 0	0 0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

Output ID: t-lb-hemshift-saf 04JUN20 13:08

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Eosinophils (10E9/L)	Week 2	Any 14 High 0 Normal 0 Low 0	14 (100) 0 0 0	0 0 0 0	35 0 35 (100) 0	0 0 0 0	0 0 0 0	49 0 49 (100) 0	49 0 0 0	0 0 0 0
	Week 4	Any 16 High 0 Normal 0 Low 0	16 (100) 0 0 0	0 0 0 0	33 0 33 (100) 0	0 0 0 0	0 0 0 0	49 0 49 (100) 0	49 0 0 0	0 0 0 0
	Week 6	Any 16 High 0 Normal 0 Low 0	16 (100) 0 0 0	0 0 0 0	35 0 35 (100) 0	0 0 0 0	0 0 0 0	51 0 51 (100) 0	51 0 0 0	0 0 0 0
	Week 8	Any 12 High 0 Normal 0 Low 0	12 (100) 0 0 0	0 0 0 0	24 1 (4.2) 23 (95.8) 0	0 0 0 0	0 0 0 0	36 1 (2.8) 35 (97.2) 0	36 1 (2.8) 0 0	0 0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Eosinophils (10E9/L)	Week 10	Any 13 High 0 Normal 0 Low 0	13 (100) 0 0 0	0 0 0 0	22 0 22 (100) 0	0 0 0 0	0 0 0 0	35 0 35 (100) 0	0 0 0 0	0 0 0 0
	Week 12	Any 11 High 0 Normal 0 Low 0	11 (100) 0 0 0	0 0 0 0	20 0 20 (100) 0	0 0 0 0	0 0 0 0	31 0 31 (100) 0	0 0 0 0	0 0 0 0
	Week 14	Any 13 High 0 Normal 0 Low 0	13 (100) 0 0 0	0 0 0 0	21 1 (4.8) 20 (95.2) 0	0 0 0 0	0 0 0 0	34 1 (2.9) 33 (97.1) 0	0 1 (2.9) 0 0	0 0 0 0
	Week 16	Any 11 High 0 Normal 0 Low 0	11 (100) 0 0 0	0 0 0 0	17 0 17 (100) 0	0 0 0 0	0 0 0 0	28 0 28 (100) 0	0 0 0 0	0 0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Eosinophils (10E9/L)	Any	8	0	0	14	0	0	0	22	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	8 (100)	0	14 (100)	0	0	0	22 (100)	0
	Low	0	0	0	0	0	0	0	0	0
Week 18	Any	8	0	0	14	0	0	0	22	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	8 (100)	0	14 (100)	0	0	0	22 (100)	0
	Low	0	0	0	0	0	0	0	0	0
Week 20	Any	9	0	0	15	0	0	0	24	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	9 (100)	0	15 (100)	0	0	0	24 (100)	0
	Low	0	0	0	0	0	0	0	0	0
Week 22	Any	8	0	0	15	0	0	0	23	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	8 (100)	0	15 (100)	0	0	0	23 (100)	0
	Low	0	0	0	0	0	0	0	0	0
Week 24	Any	8	0	0	7	0	0	0	15	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	8 (100)	0	7 (100)	0	0	0	15 (100)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Eosinophils (10E9/L)	Week 26	Any 3 0	High 0 0	Normal 3 (100) 0	Low 0 0	Any 3 0	High 0 0	Normal 3 (100) 0	Low 0 0	Any 6 0	High 0 0
	High	0 0	0 0	3 (100) 0	0 0	Any 3 0	High 0 0	Normal 3 (100) 0	Low 0 0	Any 6 0	High 0 0
	Normal	0 0	3 (100) 0	0 0	0 0	Any 3 0	High 0 0	Normal 3 (100) 0	Low 0 0	Any 6 0	High 0 0
	Low	0 0	0 0	0 0	0 0	Any 3 0	High 0 0	Normal 3 (100) 0	Low 0 0	Any 6 0	High 0 0
	Week 28	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	Any 2 0	High 0 0	Normal 2 (100) 0	Low 0 0	Any 3 0	High 0 0
	High	0 0	0 0	1 (100) 0	0 0	Any 2 0	High 0 0	Normal 2 (100) 0	Low 0 0	Any 3 0	High 0 0
	Normal	0 0	1 (100) 0	0 0	0 0	Any 2 0	High 0 0	Normal 2 (100) 0	Low 0 0	Any 3 0	High 0 0
	Low	0 0	0 0	0 0	0 0	Any 2 0	High 0 0	Normal 2 (100) 0	Low 0 0	Any 3 0	High 0 0
	Week 30	Any 0 0	High 0 0	Normal 0 0	Low 0 0	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	Any 1 0	High 0 0
	High	0 0	0 0	0 0	0 0	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	Any 1 0	High 0 0
	Normal	0 0	0 0	0 0	0 0	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	Any 1 0	High 0 0
	Low	0 0	0 0	0 0	0 0	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	Any 1 0	High 0 0
	Week 32	Any 0 0	High 0 0	Normal 0 0	Low 0 0	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	Any 1 0	High 0 0
	High	0 0	0 0	0 0	0 0	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	Any 1 0	High 0 0
	Normal	0 0	0 0	0 0	0 0	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	Any 1 0	High 0 0
	Low	0 0	0 0	0 0	0 0	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	Any 1 0	High 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Eosinophils (10E9/L) Week 34	Any	0	0	0	1	0	0	0	1	0
	High	0	0	0	0	1 (100)	0	0	0	0
	Normal	0	0	0	1	0	0	1	1 (100)	0
	Low	0	0	0	0	0	0	0	0	0
FU W 2	Any	15	0	0	21	0	0	0	36	0
	High	0	0	0	0	21 (100)	0	0	36	0
	Normal	0	15 (100)	0	0	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0
FU W 4	Any	10	0	0	19	0	0	0	29	0
	High	0	0	0	0	19 (100)	0	0	29	0
	Normal	0	10 (100)	0	0	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0
FU W 6	Any	10	0	0	15	0	0	0	25	0
	High	0	0	0	0	15 (100)	0	0	25	0
	Normal	0	10 (100)	0	0	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Eosinophils (10E9/L)	FU W 8	Any 7 0	0 7 (100)	0 0	0 0	8 8 (100)	0 0	0 0	15 15 (100)	0 0
	High	0 0	7 (100)	0 0	0 0	8 8 (100)	0 0	0 0	15 15 (100)	0 0
	Normal	0 0	7 (100)	0 0	0 0	8 8 (100)	0 0	0 0	15 15 (100)	0 0
	Low	0 0	7 (100)	0 0	0 0	8 8 (100)	0 0	0 0	15 15 (100)	0 0
	FU W 10	Any 4 0	0 4 (100)	0 0	0 0	9 9 (100)	0 0	0 0	13 13 (100)	0 0
	High	0 0	4 (100)	0 0	0 0	9 9 (100)	0 0	0 0	13 13 (100)	0 0
	Normal	0 0	4 (100)	0 0	0 0	9 9 (100)	0 0	0 0	13 13 (100)	0 0
	Low	0 0	4 (100)	0 0	0 0	9 9 (100)	0 0	0 0	13 13 (100)	0 0
	FU W 12	Any 4 0	0 4 (100)	0 0	0 0	2 2 (100)	0 0	0 0	6 6 (100)	0 0
	High	0 0	4 (100)	0 0	0 0	2 2 (100)	0 0	0 0	6 6 (100)	0 0
	Normal	0 0	4 (100)	0 0	0 0	2 2 (100)	0 0	0 0	6 6 (100)	0 0
	Low	0 0	4 (100)	0 0	0 0	2 2 (100)	0 0	0 0	6 6 (100)	0 0
	FU M 6	Any 3 0	0 3 (100)	0 0	0 0	3 3 (100)	0 0	0 0	6 6 (100)	0 0
	High	0 0	3 (100)	0 0	0 0	3 3 (100)	0 0	0 0	6 6 (100)	0 0
	Normal	0 0	3 (100)	0 0	0 0	3 3 (100)	0 0	0 0	6 6 (100)	0 0
	Low	0 0	3 (100)	0 0	0 0	3 3 (100)	0 0	0 0	6 6 (100)	0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Eosinophils (10E9/L)	FU M 9	Any 2	0	0	0	1	0	0	3	0
	High 0	0	2 (100)	0	0	1 (100)	0	0	3 (100)	0
	Normal 0	2	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0
	FU M 12	Any 1	0	0	0	1	0	0	2	0
	High 0	0	1 (100)	0	0	1 (100)	0	0	2 (100)	0
	Normal 0	1	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0
	FU M 15	Any 2	0	0	0	1	0	0	3	0
	High 0	0	2 (100)	0	0	1 (100)	0	0	3 (100)	0
	Normal 0	2	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0
	FU M 18	Any 1	0	0	0	0	0	0	1	0
	High 0	0	1 (100)	0	0	0	0	0	1 (100)	0
	Normal 0	1	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Hemoglobin (pg)	Week 2	Any 17			34			51		
		High 3 (17.6)	1 (5.9)	0	10 (29.4)	0	0	13 (25.5)	1 (2.0)	0
		Normal 0	10 (58.8)	2 (11.8)	0	19 (55.9)	0	0	29 (56.9)	2 (3.9)
		Low 0	1 (5.9)	0	0	0	5 (14.7)	0	1 (2.0)	5 (9.8)
	Week 4	Any 16			32			48		
		High 3 (18.8)	1 (6.3)	0	7 (21.9)	0	0	10 (20.8)	1 (2.1)	0
		Normal 0	10 (62.5)	2 (12.5)	2 (6.3)	17 (53.1)	2 (6.3)	2 (4.2)	27 (56.3)	4 (8.3)
		Low 0	0	0	0	0	4 (12.5)	0	0	4 (8.3)
	Week 6	Any 17			34			51		
		High 2 (11.8)	1 (5.9)	0	7 (20.6)	2 (5.9)	0	9 (17.6)	3 (5.9)	0
		Normal 1 (5.9)	11 (64.7)	2 (11.8)	3 (8.8)	16 (47.1)	1 (2.9)	4 (7.8)	27 (52.9)	3 (5.9)
		Low 0	0	0	0	1 (2.9)	4 (11.8)	0	1 (2.0)	4 (7.8)
	Week 8	Any 14			23			37		
		High 2 (14.3)	1 (7.1)	0	6 (26.1)	1 (4.3)	0	8 (21.6)	2 (5.4)	0
		Normal 0	8 (57.1)	2 (14.3)	0	11 (47.8)	3 (13.0)	0	19 (51.4)	5 (13.5)
		Low 0	1 (7.1)	0	0	0	2 (8.7)	0	1 (2.7)	2 (5.4)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Hemoglobin (pg)	Week 10	Any 14			23			37		
		High 2 (14.3)	1 (7.1)	0	3 (13.0)	2 (8.7)	0	5 (13.5)	3 (8.1)	0
		Normal 0	9 (64.3)	1 (7.1)	4 (17.4)	7 (30.4)	4 (17.4)	4 (10.8)	16 (43.2)	5 (13.5)
		Low 0	1 (7.1)	0	0	1 (4.3)	2 (8.7)	0	2 (5.4)	2 (5.4)
	Week 12	Any 12			20			32		
		High 1 (8.3)	3 (25.0)	0	5 (25.0)	2 (10.0)	0	6 (18.8)	5 (15.6)	0
		Normal 0	6 (50.0)	1 (8.3)	2 (10.0)	6 (30.0)	3 (15.0)	2 (6.3)	12 (37.5)	4 (12.5)
		Low 0	1 (8.3)	0	0	0	2 (10.0)	0	1 (3.1)	2 (6.3)
	Week 14	Any 13			21			34		
		High 2 (15.4)	3 (23.1)	0	5 (23.8)	2 (9.5)	0	7 (20.6)	5 (14.7)	0
		Normal 0	6 (46.2)	1 (7.7)	2 (9.5)	7 (33.3)	4 (19.0)	2 (5.9)	13 (38.2)	5 (14.7)
		Low 0	1 (7.7)	0	0	0	1 (4.8)	0	1 (2.9)	1 (2.9)
	Week 16	Any 12			17			29		
		High 1 (8.3)	4 (33.3)	0	4 (23.5)	2 (11.8)	0	5 (17.2)	6 (20.7)	0
		Normal 0	5 (41.7)	1 (8.3)	1 (5.9)	5 (29.4)	3 (17.6)	1 (3.4)	10 (34.5)	4 (13.8)
		Low 0	1 (8.3)	0	0	0	2 (11.8)	0	1 (3.4)	2 (6.9)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Hemoglobin (pg)	Week 18	Any 8				14			22	
		High 0	4 (50.0)	0	2 (14.3)	3 (21.4)	0	2 (9.1)	7 (31.8)	0
		Normal 0	3 (37.5)	1 (12.5)	2 (14.3)	4 (28.6)	2 (14.3)	2 (9.1)	7 (31.8)	3 (13.6)
		Low 0	0	0	0	0	1 (7.1)	0	0	1 (4.5)
	Week 20	Any 9				15			24	
		High 1 (11.1)	3 (33.3)	0	3 (20.0)	3 (20.0)	0	4 (16.7)	6 (25.0)	0
		Normal 0	4 (44.4)	1 (11.1)	3 (20.0)	2 (13.3)	2 (13.3)	3 (12.5)	6 (25.0)	3 (12.5)
		Low 0	0	0	0	0	2 (13.3)	0	0	2 (8.3)
	Week 22	Any 8				15			23	
		High 1 (12.5)	3 (37.5)	0	2 (13.3)	4 (26.7)	0	3 (13.0)	7 (30.4)	0
		Normal 0	3 (37.5)	1 (12.5)	2 (13.3)	4 (26.7)	1 (6.7)	2 (8.7)	7 (30.4)	2 (8.7)
		Low 0	0	0	0	0	2 (13.3)	0	0	2 (8.7)
	Week 24	Any 8				7			15	
		High 0	3 (37.5)	0	1 (14.3)	1 (14.3)	0	1 (6.7)	4 (26.7)	0
		Normal 0	4 (50.0)	1 (12.5)	0	3 (42.9)	2 (28.6)	0	7 (46.7)	3 (20.0)
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Hemoglobin (pg)	Week 26	Any High 0 Normal 0 Low 0	3 0 1 (33.3) 1 (33.3) 0	0 0 0	3 1 (33.3) 0 0	0 0 1 (33.3)	0 0 0	1 (16.7) 0 2 (33.3) 1 (16.7)	1 (16.7) 2 (33.3) 0 1 (16.7)	0
		Any High Normal Low	1 0 1 (100) 0	0 0 0	2 0 1 (50.0) 0	0 0 0	0 0 0	1 (33.3) 0 2 (66.7) 0	0 2 (66.7) 0 0	0
		Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 0 0 0	0
		Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0
	Week 28	Any High Normal Low	1 0 1 (100) 0	0 0 0	2 0 1 (50.0) 0	0 0 0	0 0 0	1 (33.3) 0 2 (66.7) 0	0 2 (66.7) 0 0	0
		Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0
		Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0
		Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0
	Week 30	Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0
		Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0
		Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0
		Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0
	Week 32	Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0
		Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0
		Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0
		Any High Normal Low	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0	0 0 0	0 1 (100) 0 0	0 1 (100) 0 0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Hemoglobin (pg)	Week 34	Any 0	0	0	1	0	0	0	1	0
		High 0	0	0	0	1 (100)	0	0	1 (100)	0
		Normal 0	0	0	1 (4.8)	9 (42.9)	2 (9.5)	1 (2.7)	15 (40.5)	4 (10.8)
		Low 0	0	0	0	1 (4.8)	2 (9.5)	0	3 (8.1)	2 (5.4)
	FU W 2	Any 16	0	0	21	0	8 (21.6)	4 (10.8)	37	0
		High 3 (18.8)	3 (18.8)	0	5 (23.8)	1 (4.8)	0	8 (21.6)	4 (10.8)	0
		Normal 0 (37.5)	6 (37.5)	2 (12.5)	1 (4.8)	9 (42.9)	2 (9.5)	1 (2.7)	15 (40.5)	4 (10.8)
		Low 0 (12.5)	2 (12.5)	0	0	1 (4.8)	2 (9.5)	0	3 (8.1)	2 (5.4)
	FU W 4	Any 10	0	0	19	0	5 (17.2)	4 (13.8)	29	0
		High 3 (30.0)	1 (10.0)	0	2 (10.5)	3 (15.8)	1 (5.3)	5 (17.2)	4 (13.8)	1 (3.4)
		Normal 0	4 (40.0)	1 (10.0)	2 (10.5)	10 (52.6)	0	2 (6.9)	14 (48.3)	1 (3.4)
		Low 0	1 (10.0)	0	0	1 (5.3)	0	0	2 (6.9)	0
	FU W 6	Any 10	0	0	16	0	6 (23.1)	2 (7.7)	26	0
		High 3 (30.0)	0	0	3 (18.8)	2 (12.5)	0	6 (23.1)	2 (7.7)	0
		Normal 0	6 (60.0)	1 (10.0)	1 (6.3)	9 (56.3)	0	1 (3.8)	15 (57.7)	1 (3.8)
		Low 0	0	0	0	1 (6.3)	0	0	1 (3.8)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Hemoglobin (pg)	FU W 8	Any	7		8			15		
		High	2 (28.6)	1 (14.3)	0	3 (37.5)	2 (25.0)	0	5 (33.3)	3 (20.0)
		Normal	0	2 (28.6)	1 (14.3)	1 (12.5)	2 (25.0)	0	1 (6.7)	4 (26.7)
		Low	0	1 (14.3)	0	0	0	0	1 (6.7)	0
	FU W 10	Any	4		9			13		
		High	2 (50.0)	0	2 (22.2)	2 (22.2)	0	4 (30.8)	2 (15.4)	0
		Normal	0	2 (50.0)	0	1 (11.1)	3 (33.3)	0	1 (7.7)	5 (38.5)
		Low	0	0	0	0	1 (11.1)	0	0	1 (7.7)
	FU W 12	Any	5		2			7		
		High	2 (40.0)	1 (20.0)	0	0	0	2 (28.6)	1 (14.3)	0
		Normal	1 (20.0)	1 (20.0)	0	1 (50.0)	1 (50.0)	0	2 (28.6)	2 (28.6)
		Low	0	0	0	0	0	0	0	0
	FU M 6	Any	3		3			6		
		High	1 (33.3)	0	0	1 (33.3)	0	1 (16.7)	1 (16.7)	0
		Normal	0	2 (66.7)	0	0	1 (33.3)	0	3 (50.0)	1 (16.7)
		Low	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Hemoglobin (pg)	FU M 9	Any High 0	2	0	0	1	0	1 (33.3)	3 0	0
		Normal 0	0	0	0	1 (100)	0	0	1 (33.3)	0
		Low 0	1 (50.0)	0	0	0	0	0	1 (33.3)	0
		Any High 1 (100)	1	0	0	1 (100)	0	1 (50.0)	2 1 (50.0)	0
	FU M 12	Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
		Any High 1 (50.0)	2	0	0	1	0	1 (33.3)	3 1 (33.3)	0
		Normal 0	1 (50.0)	0	0	1 (100)	0	0	1 (33.3)	0
	FU M 15	Low 0	0	0	0	0	0	0	0	0
		Any High 1 (100)	1	0	0	0	0	1 (100)	1 0	0
		Normal 0	0	0	0	0	0	0	1 (33.3)	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 18	Any High 1 (100)	1	0	0	0	0	1 (100)	1 0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Ery. Mean Corpuscular Volume (fL)	Week 2	Any	18			35			53		
		High	2 (11.1)	0	1 (2.9)	2 (5.7)	0	3 (5.7)	2 (3.8)	0	
		Normal	0	16 (88.9)	2 (5.7)	30 (85.7)	0	2 (3.8)	46 (86.8)	0	
		Low	0	0	0	0	0	0	0	0	
	Week 4	Any	17			35			52		
		High	2 (11.8)	1 (5.9)	0	2 (5.7)	1 (2.9)	0	4 (7.7)	2 (3.8)	0
		Normal	0	14 (82.4)	0	0	30 (85.7)	0	44 (84.6)	0	
		Low	0	0	0	1 (2.9)	1 (2.9)	0	1 (1.9)	1 (1.9)	
	Week 6	Any	18			35			53		
		High	2 (11.1)	1 (5.6)	0	1 (2.9)	2 (5.7)	0	3 (5.7)	3 (5.7)	0
		Normal	0	15 (83.3)	0	2 (5.7)	29 (82.9)	1 (2.9)	2 (3.8)	44 (83.0)	1 (1.9)
		Low	0	0	0	0	0	0	0	0	
	Week 8	Any	14			24			38		
		High	0	0	1 (4.2)	0	0	1 (2.6)	0	0	
		Normal	1 (7.1)	13 (92.9)	0	2 (8.3)	19 (79.2)	1 (4.2)	3 (7.9)	32 (84.2)	1 (2.6)
		Low	0	0	0	1 (4.2)	0	0	1 (2.6)	0	

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Volume (fL)	Week 10	Any High 2 (14.3)	14 0	0	23 0	2 (8.7)	0	37 2 (5.4)	2 (5.4)	0
		Normal 0	12 (85.7)	0	3 (13.0)	17 (73.9)	1 (4.3)	3 (8.1)	29 (78.4)	1 (2.7)
		Low 0	0	0	0	0	0	0	0	0
		Any High 0	12 0	0	21 2 (9.5)	1 (4.8)	0	33 2 (6.1)	1 (3.0)	0
	Week 12	Normal 1 (8.3)	11 (91.7)	0	1 (4.8)	16 (76.2)	1 (4.8)	2 (6.1)	27 (81.8)	1 (3.0)
		Low 0	0	0	0	0	0	0	0	0
		Any High 2 (15.4)	13 0	0	22 1 (4.5)	1 (4.5)	0	35 3 (8.6)	1 (2.9)	0
		Normal 0	11 (84.6)	0	2 (9.1)	16 (72.7)	1 (4.5)	2 (5.7)	27 (77.1)	1 (2.9)
	Week 14	Low 0	0	0	0	1 (4.5)	0	0	1 (2.9)	0
		Any High 0	12 1 (8.3)	0	17 1 (5.9)	1 (5.9)	0	29 1 (3.4)	2 (6.9)	0
		Normal 1 (8.3)	10 (83.3)	0	0	13 (76.5)	1 (5.9)	1 (3.4)	23 (79.3)	1 (3.4)
		Low 0	0	0	0	1 (5.9)	0	0	1 (3.4)	0
	Week 16	Any High 0	12 1 (8.3)	0	17 1 (5.9)	1 (5.9)	0	29 1 (3.4)	2 (6.9)	0
		Normal 1 (8.3)	10 (83.3)	0	0	13 (76.5)	1 (5.9)	1 (3.4)	23 (79.3)	1 (3.4)
		Low 0	0	0	0	1 (5.9)	0	0	1 (3.4)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Volume (fL)	Week 18	Any 8			14			22		
		High 0	1 (12.5)	0	1 (7.1)	1 (7.1)	0	1 (4.5)	2 (9.1)	0
		Normal 0	7 (87.5)	0	1 (7.1)	11 (78.6)	0	1 (4.5)	18 (81.8)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 20	Any 9			15			24		
		High 1 (11.1)	1 (11.1)	0	1 (6.7)	2 (13.3)	0	2 (8.3)	3 (12.5)	0
		Normal 0	7 (77.8)	0	2 (13.3)	9 (60.0)	0	2 (8.3)	16 (66.7)	0
		Low 0	0	0	0	1 (6.7)	0	0	1 (4.2)	0
	Week 22	Any 8			15			23		
		High 1 (12.5)	1 (12.5)	0	1 (6.7)	2 (13.3)	0	2 (8.7)	3 (13.0)	0
		Normal 0	6 (75.0)	0	1 (6.7)	10 (66.7)	0	1 (4.3)	16 (69.6)	0
		Low 0	0	0	0	1 (6.7)	0	0	1 (4.3)	0
	Week 24	Any 8			7			15		
		High 0	1 (12.5)	0	0	1 (14.3)	0	0	2 (13.3)	0
		Normal 0	7 (87.5)	0	0	6 (85.7)	0	0	13 (86.7)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Volume (fL)	Week 26	Any High 0	3 (33.3)	0	0	1 (33.3)	0	1 (16.7)	1 (16.7)	0
		Normal 0	2 (66.7)	0	0	2 (66.7)	0	0	4 (66.7)	0
		Low 0	0	0	0	0	0	0	0	0
		Any High 0	1 (0)	0	0	0 (0)	0	0	0 (0)	0
	Week 28	Normal 0	1 (100)	0	0	2 (100)	0	0	3 (100)	0
		Low 0	0	0	0	0	0	0	0	0
		Any High 0	0 (0)	0	0	0 (0)	0	0	0 (0)	0
		Normal 0	0 (0)	0	0	1 (100)	0	0	1 (100)	0
	Week 30	Low 0	0 (0)	0	0	0 (0)	0	0	0 (0)	0
		Any High 0	0 (0)	0	0	0 (0)	0	0	0 (0)	0
		Normal 0	0 (0)	0	0	1 (100)	0	0	1 (100)	0
		Low 0	0 (0)	0	0	0 (0)	0	0	0 (0)	0
	Week 32	Any High 0	0 (0)	0	0	1 (100)	0	0	0 (0)	0
		Normal 0	0 (0)	0	0	0 (0)	0	0	1 (100)	0
		Low 0	0 (0)	0	0	0 (0)	0	0	0 (0)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Volume (fL)	Week 34	Any 0	0	0	1	0	0	0	1	0
		High 0	0	0	0	1 (100)	0	0	1 (100)	0
		Normal 0	0	0	1 (4.5)	17 (77.3)	0	1 (2.6)	31 (79.5)	0
		Low 0	0	0	0	1 (4.5)	0	0	1 (2.6)	0
	FU W 2	Any 17	0	0	22	0	0	2 (5.1)	4 (10.3)	0
		High 1 (5.9)	2 (11.8)	0	1 (4.5)	2 (9.1)	0	1 (2.6)	31 (79.5)	0
		Normal 0	14 (82.4)	0	1 (4.5)	17 (77.3)	0	1 (2.6)	31 (79.5)	0
		Low 0	0	0	0	1 (4.5)	0	0	1 (2.6)	0
	FU W 4	Any 10	0	0	20	0	0	1 (3.3)	3 (10.0)	0
		High 1 (10.0)	2 (20.0)	0	0	1 (5.0)	0	0	26 (86.7)	0
		Normal 0	7 (70.0)	0	0	19 (95.0)	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 6	Any 10	0	0	16	0	0	1 (3.8)	2 (7.7)	0
		High 1 (10.0)	1 (10.0)	0	0	1 (6.3)	0	1 (3.8)	21 (80.8)	0
		Normal 0	8 (80.0)	0	1 (6.3)	13 (81.3)	0	0	0	1 (3.8)
		Low 0	0	0	0	1 (6.3)	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Volume (fL)	FU W 8	Any	7			8			15	
		High	1 (14.3)	1 (14.3)	0	1 (12.5)	2 (25.0)	0	2 (13.3)	3 (20.0)
		Normal	0	5 (71.4)	0	0	5 (62.5)	0	0	10 (66.7)
		Low	0	0	0	0	0	0	0	0
	FU W 10	Any	4			9			13	
		High	1 (25.0)	1 (25.0)	0	0	1 (11.1)	0	1 (7.7)	2 (15.4)
		Normal	0	2 (50.0)	0	1 (11.1)	6 (66.7)	0	1 (7.7)	8 (61.5)
		Low	0	0	0	0	1 (11.1)	0	0	1 (7.7)
	FU W 12	Any	5			2			7	
		High	1 (20.0)	1 (20.0)	0	0	0	0	1 (14.3)	1 (14.3)
		Normal	0	3 (60.0)	0	0	2 (100)	0	0	5 (71.4)
		Low	0	0	0	0	0	0	0	0
	FU M 6	Any	3			3			6	
		High	1 (33.3)	0	0	1 (33.3)	0	1 (16.7)	1 (16.7)	0
		Normal	0	2 (66.7)	0	0	2 (66.7)	0	0	4 (66.7)
		Low	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Ery. Mean Corpuscular Volume (fL)	FU M 9	Any High 1 (50.0)	0	2	0	1	0	1 (33.3)	3	0
		Normal 0	1 (50.0)	0	0	1 (100)	0	0	2 (66.7)	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 12	Any 1	0	0	0	1 (100)	0	1 (50.0)	1 (50.0)	2
		High 1 (100)	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 15	Any 2	0	0	0	1	0	1 (33.3)	3	0
		High 1 (50.0)	0	0	0	0	0	0	2 (66.7)	0
		Normal 0	1 (50.0)	0	0	1 (100)	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	FU M 18	Any 1	0	0	0	0	0	1 (100)	1	0
		High 1 (100)	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes Distribution Width (%)	Week 2	Any 18			35			53		
		High 7 (38.9)	1 (5.6)	0	10 (28.6)	5 (14.3)	0	17 (32.1)	6 (11.3)	0
		Normal 2 (11.1)	8 (44.4)	0	3 (8.6)	17 (48.6)	0	5 (9.4)	25 (47.2)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 4	Any 17			32			49		
		High 8 (47.1)	2 (11.8)	0	9 (28.1)	5 (15.6)	0	17 (34.7)	7 (14.3)	0
		Normal 1 (5.9)	6 (35.3)	0	3 (9.4)	15 (46.9)	0	4 (8.2)	21 (42.9)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 6	Any 18			33			51		
		High 8 (44.4)	2 (11.1)	0	10 (30.3)	6 (18.2)	0	18 (35.3)	8 (15.7)	0
		Normal 1 (5.6)	7 (38.9)	0	3 (9.1)	14 (42.4)	0	4 (7.8)	21 (41.2)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 8	Any 14			23			37		
		High 5 (35.7)	4 (28.6)	0	6 (26.1)	4 (17.4)	0	11 (29.7)	8 (21.6)	0
		Normal 2 (14.3)	3 (21.4)	0	2 (8.7)	11 (47.8)	0	4 (10.8)	14 (37.8)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes Distribution Width (%)	Week 10	Any 14			22			36		
		High 7 (50.0)	4 (28.6)	0	8 (36.4)	4 (18.2)	0	15 (41.7)	8 (22.2)	0
		Normal 0	3 (21.4)	0	1 (4.5)	9 (40.9)	0	1 (2.8)	12 (33.3)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 12	Any 12			19			31		
		High 6 (50.0)	3 (25.0)	0	2 (10.5)	3 (15.8)	0	8 (25.8)	6 (19.4)	0
		Normal 0	3 (25.0)	0	3 (15.8)	11 (57.9)	0	3 (9.7)	14 (45.2)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 14	Any 13			20			33		
		High 5 (38.5)	4 (30.8)	0	3 (15.0)	4 (20.0)	0	8 (24.2)	8 (24.2)	0
		Normal 1 (7.7)	3 (23.1)	0	4 (20.0)	9 (45.0)	0	5 (15.2)	12 (36.4)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 16	Any 12			16			28		
		High 5 (41.7)	2 (16.7)	0	3 (18.8)	3 (18.8)	0	8 (28.6)	5 (17.9)	0
		Normal 2 (16.7)	3 (25.0)	0	4 (25.0)	6 (37.5)	0	6 (21.4)	9 (32.1)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes Distribution Width (%)	Week 18	Any 8			14			22		
		High 2 (25.0)	2 (25.0)	0	1 (7.1)	2 (14.3)	0	3 (13.6)	4 (18.2)	0
		Normal 3 (37.5)	1 (12.5)	0	4 (28.6)	7 (50.0)	0	7 (31.8)	8 (36.4)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 20	Any 8			14			22		
		High 1 (12.5)	2 (25.0)	0	1 (7.1)	3 (21.4)	0	2 (9.1)	5 (22.7)	0
		Normal 3 (37.5)	2 (25.0)	0	3 (21.4)	7 (50.0)	0	6 (27.3)	9 (40.9)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 22	Any 8			14			22		
		High 1 (12.5)	1 (12.5)	0	1 (7.1)	3 (21.4)	0	2 (9.1)	4 (18.2)	0
		Normal 3 (37.5)	3 (37.5)	0	3 (21.4)	7 (50.0)	0	6 (27.3)	10 (45.5)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 24	Any 8			7			15		
		High 3 (37.5)	0	0	2 (28.6)	1 (14.3)	0	5 (33.3)	1 (6.7)	0
		Normal 2 (25.0)	3 (37.5)	0	2 (28.6)	2 (28.6)	0	4 (26.7)	5 (33.3)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes Distribution Width (%)	Week 26	Any	3	0	1 (33.3)	1 (33.3)	0	1 (16.7)	1 (16.7)	0
		High	0	0	1 (33.3)	0	0	3 (50.0)	1 (16.7)	0
		Normal	2 (66.7)	1 (33.3)	0	0	0	0	0	0
		Low	0	0	0	0	0	0	0	0
	Week 28	Any	1	0	2	0	0	1 (33.3)	0	0
		High	0	0	1 (50.0)	0	0	0	2 (66.7)	0
		Normal	0	1 (100)	0	1 (50.0)	0	0	0	0
		Low	0	0	0	0	0	0	0	0
	Week 30	Any	0	0	1 (100)	0	0	1 (100)	0	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	0	0	0	0	0	0	0
	Week 32	Any	0	0	1	0	0	1 (100)	0	0
		High	0	0	1 (100)	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes Distribution Width (%)	Week 34	Any 0	0	0	1 (100)	0	0	1 (100)	0	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 2	Any 17	0	0	22	0	0	39	0	0
		High 5 (29.4)	2 (11.8)	0	6 (27.3)	5 (22.7)	0	11 (28.2)	7 (17.9)	0
		Normal 3 (17.6)	7 (41.2)	0	3 (13.6)	8 (36.4)	0	6 (15.4)	15 (38.5)	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 4	Any 10	0	0	19	0	0	29	0	0
		High 2 (20.0)	1 (10.0)	0	7 (36.8)	2 (10.5)	0	9 (31.0)	3 (10.3)	0
		Normal 2 (20.0)	5 (50.0)	0	2 (10.5)	8 (42.1)	0	4 (13.8)	13 (44.8)	0
		Low 0	0	0	0	0	0	0	0	0
	FU W 6	Any 10	0	0	16	0	0	26	0	0
		High 4 (40.0)	1 (10.0)	0	5 (31.3)	6 (37.5)	0	9 (34.6)	7 (26.9)	0
		Normal 2 (20.0)	3 (30.0)	0	2 (12.5)	3 (18.8)	0	4 (15.4)	6 (23.1)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes Distribution Width (%)	FU W 8	Any	7			8			15	
		High	2 (28.6)	1 (14.3)	0	1 (12.5)	2 (25.0)	0	3 (20.0)	3 (20.0)
		Normal	3 (42.9)	1 (14.3)	0	1 (12.5)	4 (50.0)	0	4 (26.7)	5 (33.3)
		Low	0	0	0	0	0	0	0	0
	FU W 10	Any	4			9			13	
		High	1 (25.0)	1 (25.0)	0	2 (22.2)	2 (22.2)	0	3 (23.1)	3 (23.1)
		Normal	0	2 (50.0)	0	2 (22.2)	3 (33.3)	0	2 (15.4)	5 (38.5)
		Low	0	0	0	0	0	0	0	0
	FU W 12	Any	5			2			7	
		High	1 (20.0)	2 (40.0)	0	0	0	0	1 (14.3)	2 (28.6)
		Normal	0	2 (40.0)	0	1 (50.0)	1 (50.0)	0	1 (14.3)	3 (42.9)
		Low	0	0	0	0	0	0	0	0
	FU M 6	Any	3			3			6	
		High	1 (33.3)	0	0	1 (33.3)	1 (33.3)	0	2 (33.3)	1 (16.7)
		Normal	1 (33.3)	1 (33.3)	0	0	1 (33.3)	0	1 (16.7)	2 (33.3)
		Low	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).
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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes Distribution Width (%)	FU M 9	Any High 0 Normal 0 Low 0	2 0 1 (50.0) 0 0	0 0 0 0	0 0 1 (100) 0	1 0 0 0	0 0 0 0	1 (33.3) 1 (33.3) 1 (33.3) 0	3 0 1 (33.3) 0	0 0 0 0
	FU M 12	Any High 0 Normal 0 Low 0	1 0 1 (100) 0	0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0 0	0 0 0 0	2 0 2 (100) 0	0 0 0 0
	FU M 15	Any High 0 Normal 1 (50.0) Low 0	2 0 1 (50.0) 0	0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0 0	0 1 (33.3) 2 (66.7) 0	3 0 2 (66.7) 0	0 0 0 0
	FU M 18	Any High 0 Normal 0 Low 0	1 0 1 (100) 0	0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	0 0 1 (100) 0	1 0 0 0	0 0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).
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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes (10E12/L)	Week 2	Any	18		36			54		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (5.6)	1 (5.6)	8 (22.2)	2 (5.6)	0	9 (16.7)	3 (5.6)
		Low	0	5 (27.8)	11 (61.1)	2 (5.6)	24 (66.7)	0	7 (13.0)	35 (64.8)
	Week 4	Any	17		35			52		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	1 (5.9)	8 (22.9)	0	0	8 (15.4)	1 (1.9)
		Low	0	6 (35.3)	10 (58.8)	2 (5.7)	25 (71.4)	0	8 (15.4)	35 (67.3)
	Week 6	Any	18		35			53		
		High	0	0	0	0	0	0	0	0
		Normal	0	2 (11.1)	2 (11.1)	8 (22.9)	0	0	10 (18.9)	2 (3.8)
		Low	0	4 (22.2)	10 (55.6)	1 (2.9)	26 (74.3)	0	5 (9.4)	36 (67.9)
	Week 8	Any	14		25			39		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (7.1)	0	4 (16.0)	0	0	5 (12.8)	0
		Low	0	3 (21.4)	10 (71.4)	3 (12.0)	18 (72.0)	0	6 (15.4)	28 (71.8)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes (10E12/L)	Week 10	Any	14		23			37		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (7.1)	1 (7.1)	3 (13.0)	1 (4.3)	0	4 (10.8)	2 (5.4)
		Low	0	5 (35.7)	7 (50.0)	2 (8.7)	17 (73.9)	0	7 (18.9)	24 (64.9)
	Week 12	Any	12		21			33		
		High	0	0	0	0	0	0	0	0
		Normal	0	2 (16.7)	0	3 (14.3)	0	0	5 (15.2)	0
		Low	0	3 (25.0)	7 (58.3)	2 (9.5)	16 (76.2)	0	5 (15.2)	23 (69.7)
	Week 14	Any	13		22			35		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (7.7)	0	5 (22.7)	0	0	6 (17.1)	0
		Low	0	4 (30.8)	8 (61.5)	2 (9.1)	15 (68.2)	0	6 (17.1)	23 (65.7)
	Week 16	Any	12		17			29		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (8.3)	0	4 (23.5)	1 (5.9)	0	5 (17.2)	1 (3.4)
		Low	0	5 (41.7)	6 (50.0)	1 (5.9)	11 (64.7)	0	6 (20.7)	17 (58.6)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes (10E12/L)	Week 18	Any	8			14			22	
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	4 (28.6)	1 (7.1)	0	4 (18.2)	1 (4.5)
		Low	0	3 (37.5) 5 (62.5)	0	0	9 (64.3)	0	3 (13.6) 14 (63.6)	
	Week 20	Any	9			15			24	
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	1 (6.7)	1 (6.7)	0	1 (4.2)	1 (4.2)
		Low	0	4 (44.4) 5 (55.6)	0	1 (6.7)	12 (80.0)	0	5 (20.8) 17 (70.8)	
	Week 22	Any	8			15			23	
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	2 (13.3)	0	0	2 (8.7)	0
		Low	0	3 (37.5) 5 (62.5)	0	2 (13.3)	11 (73.3)	0	5 (21.7) 16 (69.6)	
	Week 24	Any	8			7			15	
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	1 (14.3)	0	0	1 (6.7)	0
		Low	0	3 (37.5) 5 (62.5)	0	1 (14.3)	5 (71.4)	0	4 (26.7) 10 (66.7)	

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes (10E12/L)	Week 26	Any	3		3			6		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	2 (66.7)	1 (33.3)	0	0	3 (100)	0	2 (33.3)	4 (66.7)
	Week 28	Any	1		2			3		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	0	1 (100)	0	2 (100)	0	0	3 (100)
	Week 30	Any	0		1			1		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	0	0	0	1 (100)	0	0	1 (100)
	Week 32	Any	0		1			1		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	0	0	0	1 (100)	0	0	1 (100)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes (10E12/L)	Week 34	Any High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	1 0 0 0	0 0 0 1 (100)	0 0 0 0	1 0 0 0	1 0 0 0	1 (100)
	FU W 2	Any High 0 Normal 0 Low 0	17 0 2 (11.8) 2 (11.8)	0 0 11 (64.7)	22 0 2 (9.1) 2 (9.1)	0 0 18 (81.8)	0 0 0	39 0 4 (10.3) 4 (10.3)	0 0 2 (5.1) 29 (74.4)	0 0 2 (5.1) 29 (74.4)
	FU W 4	Any High 0 Normal 0 Low 0	10 0 1 (10.0) 2 (20.0)	0 0 0 7 (70.0)	20 0 1 (5.0) 4 (20.0)	0 0 0 15 (75.0)	0 0 0 0	30 0 2 (6.7) 6 (20.0)	0 0 0 22 (73.3)	0 0 0 22 (73.3)
	FU W 6	Any High 0 Normal 0 Low 0	10 0 0 1 (10.0) 2 (20.0)	0 0 0 7 (70.0)	16 0 2 (12.5) 3 (18.8)	0 0 0 11 (68.8)	0 0 0 0	26 0 2 (7.7) 5 (19.2)	0 0 1 (3.8) 18 (69.2)	0 0 0 18 (69.2)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes (10E12/L)	FU W 8	Any	7	0	8	0	0	0	15	0
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (14.3)	0	0	1 (12.5)	0	0	2 (13.3)
		Low	4 (57.1)	2 (28.6)	0	2 (25.0)	5 (62.5)	0	6 (40.0)	7 (46.7)
	FU W 10	Any	4	0	9	0	0	0	13	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	3 (33.3)	0	0	0	3 (23.1)	0
		Low	0	1 (25.0)	3 (75.0)	0	1 (11.1)	5 (55.6)	0	2 (15.4)
	FU W 12	Any	5	0	2	0	0	0	7	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	1 (20.0)	4 (80.0)	0	1 (50.0)	1 (50.0)	0	2 (28.6)
	FU M 6	Any	3	0	3	0	0	0	6	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	3 (100)	0	0	1 (33.3)	2 (66.7)	0	4 (66.7)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Erythrocytes (10E12/L)	FU M 9	Any	2	0	0	1	0	0	3	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	1 (100)	0	0	1 (33.3)	0
		Low	0	2 (100)	0	0	0	0	2 (66.7)	0
	FU M 12	Any	1	0	0	1	0	0	2	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	1 (100)	0	0	1 (100)	0	1 (50.0)	1 (50.0)
	FU M 15	Any	2	0	0	1	0	0	3	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	1 (100)	0	0	1 (33.3)	0
		Low	0	2 (100)	0	0	0	0	2 (66.7)	0
	FU M 18	Any	1	0	0	0	0	0	1	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	1 (100)	0	0	0	0	1 (100)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hematocrit (L/L)	Week 2	Any	18		37			55		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (5.6) 1 (5.6)	0	3 (8.1) 2 (5.4)	0	4 (7.3) 3 (5.5)	4 (7.3)	3 (5.5)
		Low	0	3 (16.7) 13 (72.2)	0	1 (2.7) 31 (83.8)	0	4 (7.3) 44 (80.0)	4 (7.3)	44 (80.0)
	Week 4	Any	17		36			53		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (5.9) 1 (5.9)	0	1 (2.8) 2 (5.6)	0	2 (3.8) 3 (5.7)	2 (3.8)	3 (5.7)
		Low	0	3 (17.6) 12 (70.6)	0	3 (8.3) 30 (83.3)	0	6 (11.3) 42 (79.2)	6 (11.3)	42 (79.2)
	Week 6	Any	18		35			53		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (5.6) 1 (5.6)	0	2 (5.7) 0	0	3 (5.7) 1 (1.9)	3 (5.7)	1 (1.9)
		Low	0	3 (16.7) 13 (72.2)	0	2 (5.7) 31 (88.6)	0	5 (9.4) 44 (83.0)	5 (9.4)	44 (83.0)
	Week 8	Any	14		26			40		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	1 (3.8)	0	0	1 (2.5)
		Low	0	3 (21.4) 11 (78.6)	0	2 (7.7) 23 (88.5)	0	5 (12.5) 34 (85.0)	5 (12.5)	34 (85.0)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hematocrit (L/L)	Week 10	Any	14		23			37		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	2 (8.7)	0	0	2 (5.4)
		Low	0	4 (28.6) 10 (71.4)	0	2 (8.7) 19 (82.6)	0	6 (16.2) 29 (78.4)		
	Week 12	Any	12		21			33		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	1 (4.8) 2 (9.5)	0	1 (3.0) 2 (6.1)		
		Low	0	4 (33.3) 8 (66.7)	0	1 (4.8) 17 (81.0)	0	5 (15.2) 25 (75.8)		
	Week 14	Any	13		22			35		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (7.7) 1 (7.7)	0	1 (4.5) 0	0	2 (5.7) 1 (2.9)		
		Low	0	3 (23.1) 8 (61.5)	0	2 (9.1) 19 (86.4)	0	5 (14.3) 27 (77.1)		
	Week 16	Any	12		17			29		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	1 (5.9) 1 (5.9)	0	1 (3.4) 1 (3.4)		
		Low	0	4 (33.3) 8 (66.7)	0	2 (11.8) 13 (76.5)	0	6 (20.7) 21 (72.4)		

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hematocrit (L/L)	Week 18	Any	8		14			22		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	1 (7.1)	1 (7.1)	0	1 (4.5)	1 (4.5)
		Low	0	1 (12.5)	7 (87.5)	0	1 (7.1)	11 (78.6)	2 (9.1)	18 (81.8)
	Week 20	Any	9		15			24		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	3 (33.3)	6 (66.7)	0	1 (6.7)	14 (93.3)	4 (16.7)	20 (83.3)
	Week 22	Any	8		15			23		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	2 (25.0)	6 (75.0)	0	2 (13.3)	13 (86.7)	4 (17.4)	19 (82.6)
	Week 24	Any	8		7			15		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	1 (14.3)	0	0	1 (6.7)
		Low	0	2 (25.0)	6 (75.0)	0	1 (14.3)	5 (71.4)	3 (20.0)	11 (73.3)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hematocrit (L/L)	Week 26 Any	3			3				6	
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	0	0	0	0	0	0
	Low	0	1 (33.3)	2 (66.7)	0	0	3 (100)	0	1 (16.7)	5 (83.3)
	Week 28 Any	1			2				3	
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	0	0	0	0	0	0
	Low	0	0	1 (100)	0	0	2 (100)	0	0	3 (100)
	Week 30 Any	0			1				1	
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	0	0	0	0	0	0
	Low	0	0	0	0	0	1 (100)	0	0	1 (100)
	Week 32 Any	0			1				1	
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	0	0	0	0	0	0
	Low	0	0	0	0	0	1 (100)	0	0	1 (100)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hematocrit (L/L)	Week 34	Any 0	High 0	0	0	1	0	0	1	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	1 (100)	0	0	1 (100)
FU W 2	Any 17	High 0	0	0	0	23	0	0	40	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	1 (5.9)	0	0	0	0	0	1 (2.5)	0
		Low 0	3 (17.6)	13 (76.5)	0	0	23 (100)	0	3 (7.5)	36 (90.0)
FU W 4	Any 10	High 0	0	0	0	20	0	0	30	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	1 (10.0)	0	0	1 (5.0)	0	0	2 (6.7)	0
		Low 0	2 (20.0)	7 (70.0)	0	1 (5.0)	18 (90.0)	0	3 (10.0)	25 (83.3)
FU W 6	Any 10	High 0	0	0	0	17	0	0	27	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	1 (5.9)	0	0	1 (3.7)	0
		Low 0	2 (20.0)	8 (80.0)	0	1 (5.9)	15 (88.2)	0	3 (11.1)	23 (85.2)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hematocrit (L/L)	FU W 8	Any	7		8			15		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	1 (12.5)	0	0	1 (6.7)
		Low	0	3 (42.9) 4 (57.1)	0	1 (12.5)	6 (75.0)	0	4 (26.7) 10 (66.7)	
	FU W 10	Any	4		9			13		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	1 (25.0) 3 (75.0)	0	2 (22.2)	7 (77.8)	0	3 (23.1) 10 (76.9)	
	FU W 12	Any	5		2			7		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	1 (20.0) 4 (80.0)	0	1 (50.0)	1 (50.0)	0	2 (28.6) 5 (71.4)	
	FU M 6	Any	3		3			6		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (33.3)	0	0	0	0	1 (16.7)	0
		Low	0	1 (33.3) 1 (33.3)	0	0	3 (100)	0	1 (16.7) 4 (66.7)	

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hematocrit (L/L)	FU M 9	Any 2	0	0	0	1 (100)	0	0	3 (66.7)	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	1 (50.0)	0	0	0	0	0	2 (33.3)	0
		Low 0	0	1 (50.0)	0	0	0	0	0	1 (33.3)
	FU M 12	Any 1	0	0	0	1 (100)	0	0	2 (50.0)	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	1 (100)	0	0	0	0	0	1 (50.0)	0
		Low 0	0	0	0	0	1 (100)	0	0	1 (50.0)
	FU M 15	Any 2	0	0	0	1 (100)	0	0	3 (33.3)	0
		High 0	0	0	0	0	0	0	1 (33.3)	0
		Normal 0	0	0	0	1 (100)	0	0	1 (33.3)	1 (33.3)
		Low 0	1 (50.0)	1 (50.0)	0	0	0	0	1 (100)	0
	FU M 18	Any 1	0	0	0	0	0	0	1 (100)	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	1 (100)	0	0	0	0	0	1 (100)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hemoglobin (g/L)	Week 2	Any	18		37			55		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (5.6)	0	0	2 (5.4)	0	1 (1.8)	2 (3.6)
		Low	0	1 (5.6)	16 (88.9)	0	1 (2.7)	34 (91.9)	2 (3.6)	50 (90.9)
	Week 4	Any	17		36			53		
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (5.9)	1 (5.9)	0	0	2 (5.6)	0	1 (1.9)
		Low	0	1 (5.9)	14 (82.4)	0	1 (2.8)	33 (91.7)	2 (3.8)	47 (88.7)
	Week 6	Any	18		35			53		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	1 (2.9)	0	0	1 (1.9)
		Low	0	2 (11.1)	16 (88.9)	0	1 (2.9)	33 (94.3)	3 (5.7)	49 (92.5)
	Week 8	Any	14		26			40		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	1 (3.8)	0	0	1 (2.5)
		Low	0	1 (7.1)	13 (92.9)	0	1 (3.8)	24 (92.3)	2 (5.0)	37 (92.5)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hemoglobin (g/L)	Week 10	Any	14		23			37		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	2 (8.7)	0	0	2 (5.4)
		Low	0	2 (14.3) 12 (85.7)	0	0	21 (91.3)	0	2 (5.4) 33 (89.2)	
	Week 12	Any	12		21			33		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	1 (4.8)	1 (4.8)	0	1 (3.0)	1 (3.0)
		Low	0	2 (16.7) 10 (83.3)	0	0	19 (90.5)	0	2 (6.1) 29 (87.9)	
	Week 14	Any	13		22			35		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	1 (7.7)	0	0	0	1 (2.9)	1 (2.9)
		Low	0	2 (15.4) 10 (76.9)	0	0	21 (95.5)	0	2 (5.7) 31 (88.6)	
	Week 16	Any	12		17			29		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	2 (16.7) 10 (83.3)	0	1 (5.9) 16 (94.1)	0	0	3 (10.3) 26 (89.7)	

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hemoglobin (g/L)	Week 18	Any	8		14			22		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	1 (7.1)	0	0	1 (4.5)
		Low	0	1 (12.5)	7 (87.5)	0	1 (7.1)	12 (85.7)	2 (9.1)	19 (86.4)
	Week 20	Any	9		15			24		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	2 (22.2)	7 (77.8)	0	0	15 (100)	0	2 (8.3)
	Week 22	Any	8		15			23		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	2 (25.0)	6 (75.0)	0	1 (6.7)	14 (93.3)	3 (13.0)	20 (87.0)
	Week 24	Any	8		6			14		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	1 (12.5)	7 (87.5)	0	0	6 (100)	0	1 (7.1)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hemoglobin (g/L)	Week 26	Any 3	0	0	0	0	0	0	6	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	1 (33.3)	2 (66.7)	0	0	3 (100)	0	1 (16.7)	5 (83.3)
	Week 28	Any 1	0	0	0	2	0	0	3	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	1 (100)	0	0	2 (100)	0	0	3 (100)
	Week 30	Any 0	0	0	1	0	0	0	1	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	1 (100)	0	0	1 (100)
	Week 32	Any 0	0	0	1	0	0	0	1	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	1 (100)	0	0	1 (100)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Hemoglobin (g/L)	Week 34	Any 0	High 0	Normal 0	Low 0	High 1	Normal 0	Low 0	High 1	Normal 0	Low 0
		High 0	Normal 0	Low 0	High 0	Normal 0	Low 0	High 0	Normal 0	Low 0	
		Normal 0	High 0	Low 0	Normal 0	High 0	Normal 0	Normal 0	High 0	Normal 0	
		Low 0	High 0	Normal 0	Low 0	High 0	Normal 1 (100)	Low 0	High 0	Normal 0	Low 1 (100)
FU W 2	Any 17	High 0	Normal 1 (5.9)	Low 2 (11.8) 14 (82.4)	High 23	Normal 0	Low 0	High 40	Normal 0	Low 0	
	High 0	Normal 0	Low 0	High 0	Normal 0	Low 0	High 0	Normal 1 (2.5)	Low 0	High 0	
	Normal 0	High 1 (5.9)	Normal 0	Low 0	Normal 0	High 0	Normal 0	Normal 2 (5.0)	High 37 (92.5)	Normal 37 (92.5)	
	Low 0	High 2 (11.8)	Normal 14 (82.4)	Low 0	High 0	Normal 23 (100)	Low 0	High 0	Normal 2 (5.0)	Low 37 (92.5)	
FU W 4	Any 10	High 0	Normal 1 (10.0)	Low 2 (20.0) 7 (70.0)	High 20	Normal 0	Low 0	High 30	Normal 0	Low 0	
	High 0	Normal 0	Low 0	High 0	Normal 0	Low 0	High 0	Normal 1 (3.3)	Low 1 (3.3)	High 1 (3.3)	
	Normal 0	High 1 (10.0)	Normal 0	Low 0	Normal 0	High 1 (5.0)	Normal 0	Normal 2 (6.7)	High 26 (86.7)	Normal 26 (86.7)	
	Low 0	High 2 (20.0)	Normal 7 (70.0)	Low 0	High 0	Normal 19 (95.0)	Low 0	High 0	Normal 2 (6.7)	Low 26 (86.7)	
FU W 6	Any 10	High 0	Normal 0	Low 2 (20.0) 8 (80.0)	High 17	Normal 0	Low 0	High 27	Normal 0	Low 0	
	High 0	Normal 0	Low 0	High 0	Normal 0	Low 0	High 0	Normal 0	Low 0	High 0	
	Normal 0	High 0	Normal 0	Low 0	Normal 0	High 0	Normal 0	Normal 0	High 0	Normal 0	
	Low 0	High 2 (20.0)	Normal 8 (80.0)	Low 0	High 1 (5.9)	Normal 16 (94.1)	Low 0	High 0	Normal 3 (11.1)	Low 24 (88.9)	

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hemoglobin (g/L)	FU W 8	Any	7		9			16		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	1 (11.1)	0	0	1 (6.3)
		Low	0	2 (28.6)	5 (71.4)	0	8 (88.9)	0	2 (12.5)	13 (81.3)
	FU W 10	Any	4		9			13		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	1 (25.0)	3 (75.0)	0	9 (100)	0	1 (7.7)	12 (92.3)
	FU W 12	Any	5		2			7		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	1 (20.0)	4 (80.0)	0	1 (50.0)	1 (50.0)	2 (28.6)	5 (71.4)
	FU M 6	Any	3		3			6		
		High	0	0	0	0	0	0	0	0
		Normal	0	0	0	0	0	0	0	0
		Low	0	1 (33.3)	2 (66.7)	0	3 (100)	0	1 (16.7)	5 (83.3)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Hemoglobin (g/L)	FU M 9	Any 2	0	0	0	0	0	0	3	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	1 (100)	0	0	1 (33.3)
		Low 0	1 (50.0)	1 (50.0)	0	0	0	0	1 (33.3)	1 (33.3)
	FU M 12	Any 1	0	0	0	1	0	0	2	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	1 (100)	0	0	0	0	0	1 (50.0)	0
		Low 0	0	0	0	0	1 (100)	0	0	1 (50.0)
	FU M 15	Any 2	0	0	0	1	0	0	3	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	1 (100)	0	0	1 (33.3)	0
		Low 0	1 (50.0)	1 (50.0)	0	0	0	0	1 (33.3)	1 (33.3)
	FU M 18	Any 1	0	0	0	0	0	0	1	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	1 (100)	0	0	0	0	0	1 (100)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Leukocytes (10E9/L)	Week 2	Any	18		37			55			
		High	0	0	1 (2.7)	0	0	1 (1.8)	0	0	
		Normal	0	10 (55.6)	3 (16.7)	20 (54.1)	0	0	30 (54.5)	3 (5.5)	
		Low	0	5 (27.8)	0	4 (10.8)	12 (32.4)	0	4 (7.3)	17 (30.9)	
	Week 4	Any	17		36			53			
		High	0	1 (5.9)	0	0	0	0	1 (1.9)	0	
		Normal	0	6 (35.3)	1 (5.9)	19 (52.8)	1 (2.8)	1 (1.9)	25 (47.2)	2 (3.8)	
		Low	0	3 (17.6)	6 (35.3)	0	4 (11.1)	11 (30.6)	0	7 (13.2)	17 (32.1)
	Week 6	Any	18		35			53			
		High	0	0	0	0	0	0	0	0	
		Normal	0	7 (38.9)	1 (5.6)	18 (51.4)	0	1 (1.9)	25 (47.2)	1 (1.9)	
		Low	0	3 (16.7)	7 (38.9)	0	5 (14.3)	11 (31.4)	0	8 (15.1)	18 (34.0)
	Week 8	Any	14		26			40			
		High	0	0	0	0	0	0	0	0	
		Normal	0	4 (28.6)	2 (14.3)	15 (57.7)	1 (3.8)	0	19 (47.5)	3 (7.5)	
		Low	0	2 (14.3)	6 (42.9)	0	3 (11.5)	7 (26.9)	0	5 (12.5)	13 (32.5)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Leukocytes (10E9/L)	Week 10	Any	14		23			37		
		High	0	0	0	0	0	0	0	0
		Normal	6 (42.9)	2 (14.3)	0	12 (52.2)	2 (8.7)	0	18 (48.6)	4 (10.8)
		Low	2 (14.3)	4 (28.6)	0	2 (8.7)	7 (30.4)	0	4 (10.8)	11 (29.7)
	Week 12	Any	12		21			33		
		High	1 (8.3)	0	0	0	0	0	1 (3.0)	0
		Normal	4 (33.3)	1 (8.3)	0	12 (57.1)	0	0	16 (48.5)	1 (3.0)
		Low	1 (8.3)	5 (41.7)	0	0	9 (42.9)	0	1 (3.0)	14 (42.4)
	Week 14	Any	13		22			35		
		High	0	0	0	0	0	0	0	0
		Normal	6 (46.2)	1 (7.7)	0	11 (50.0)	1 (4.5)	0	17 (48.6)	2 (5.7)
		Low	1 (7.7)	5 (38.5)	0	2 (9.1)	8 (36.4)	0	3 (8.6)	13 (37.1)
	Week 16	Any	12		17			29		
		High	0	0	0	0	0	0	0	0
		Normal	4 (33.3)	0	0	9 (52.9)	0	0	13 (44.8)	0
		Low	2 (16.7)	6 (50.0)	0	3 (17.6)	5 (29.4)	0	5 (17.2)	11 (37.9)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Leukocytes (10E9/L)	Week 18	Any High 0 Normal 0 Low 0	8 0 2 (25.0) 4 (50.0)	0 1 (12.5) 1 (12.5)	0 0 0	14 0 8 (57.1) 0	0 0 6 (42.9)	0 0 0	22 0 10 (45.5) 4 (18.2)	0 1 (4.5) 7 (31.8)
	Week 20	Any High 0 Normal 0 Low 0	9 0 2 (22.2) 3 (33.3)	0 1 (11.1) 3 (33.3)	0 0 0	15 0 6 (40.0) 1 (6.7)	0 0 7 (46.7) 7 (46.7)	0 0 0	24 0 8 (33.3) 4 (16.7)	0 2 (8.3) 10 (41.7)
	Week 22	Any High 0 Normal 0 Low 0	8 0 3 (37.5) 2 (25.0)	0 1 (12.5) 2 (25.0)	0 0 0	15 0 7 (46.7) 1 (6.7)	0 0 6 (40.0)	0 0 0	23 0 10 (43.5) 3 (13.0)	0 2 (8.7) 8 (34.8)
	Week 24	Any High 0 Normal 0 Low 0	8 0 2 (25.0) 3 (37.5)	0 0 0	0 0 0	7 0 2 (28.6) 1 (14.3)	0 0 2 (28.6) 2 (28.6)	0 0 0	15 0 4 (26.7) 4 (26.7)	0 0 2 (13.3) 5 (33.3)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Leukocytes (10E9/L)	Week 26	Any High 0 Normal 0 Low 0	3 0 1 (33.3) 1 (33.3)	0 0 1 (33.3)	0 0 0	3 0 1 (33.3) 0	0 0 2 (66.7)	0 0 0	6 0 2 (33.3) 1 (16.7)	0 0 3 (50.0)
	Week 28	Any High 0 Normal 0 Low 0	1 0 0 0	0 0 1 (100)	0 0 0	2 0 1 (50.0) 0	0 0 1 (50.0)	0 0 0	3 0 1 (33.3) 0	0 0 2 (66.7)
	Week 30	Any High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	0 0 1 (100)	1 0 0 0	0 0 0 0	0 0 0 0	1 0 0 0	0 0 0 0
	Week 32	Any High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	0 0 1 (100)	1 0 0 0	0 0 0 0	0 0 0 0	1 0 0 0	0 0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Leukocytes (10E9/L)	Week 34	Any 0	0	0	1	0	0	0	1	0
		High 0	0	0	0	0	0	0	0	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	1 (100)	0	0	1 (100)	0
FU W 2	Any 17	0	0	0	23	0	0	0	40	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 1 (5.9)	4 (23.5)	3 (17.6)	0	10 (43.5)	0	1 (2.5)	14 (35.0)	3 (7.5)	
	Low 0	5 (29.4)	4 (23.5)	0	6 (26.1)	7 (30.4)	0	11 (27.5)	11 (27.5)	
FU W 4	Any 10	0	0	0	20	0	0	0	30	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 1 (10.0)	0	0	1 (5.0)	12 (60.0)	1 (5.0)	2 (6.7)	12 (40.0)	1 (3.3)	
	Low 0	6 (60.0)	3 (30.0)	0	1 (5.0)	5 (25.0)	0	7 (23.3)	8 (26.7)	
FU W 6	Any 10	0	0	0	16	0	0	0	26	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 0	3 (30.0)	1 (10.0)	1 (6.3)	7 (43.8)	0	1 (3.8)	10 (38.5)	1 (3.8)	
	Low 0	4 (40.0)	2 (20.0)	0	3 (18.8)	5 (31.3)	0	7 (26.9)	7 (26.9)	

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Leukocytes (10E9/L)	FU W 8	Any	7	0	9	0	0	0	16	0
		High	0	0	0	0	0	0	0	0
		Normal	0	3 (42.9)	2 (22.2)	0	0	0	5 (31.3)	0
		Low	0	2 (28.6)	2 (28.6)	0	3 (33.3)	4 (44.4)	5 (31.3)	6 (37.5)
	FU W 10	Any	4	0	9	0	0	0	13	0
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (25.0)	4 (44.4)	0	0	0	5 (38.5)	0
		Low	0	1 (25.0)	2 (50.0)	0	1 (11.1)	4 (44.4)	2 (15.4)	6 (46.2)
	FU W 12	Any	5	0	2	0	0	0	7	0
		High	0	0	0	0	0	0	0	0
		Normal	0	1 (20.0)	2 (40.0)	0	2 (100)	0	3 (42.9)	2 (28.6)
		Low	0	1 (20.0)	1 (20.0)	0	0	0	1 (14.3)	1 (14.3)
	FU M 6	Any	3	0	3	0	0	0	6	0
		High	0	0	0	0	0	0	0	0
		Normal	0	0	1 (33.3)	0	0	1 (16.7)	0	0
		Low	0	1 (33.3)	2 (66.7)	0	2 (66.7)	0	1 (16.7)	4 (66.7)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Leukocytes (10E9/L)	FU M 9	Any High Normal Low	0 0 0 1 (50.0)	2 0 0 1 (50.0)	0 0 1 (100) 0	1 0 0 0	0 0 0 0	0 0 0 0	3 0 1 (33.3) 1 (33.3)	0 0 1 (33.3) 1 (33.3)
	FU M 12	Any High Normal Low	0 0 0 0	1 0 0 1 (100)	0 0 0 0	1 0 1 (100) 0	0 0 0 0	0 0 0 0	2 0 1 (50.0) 1 (50.0)	0 0 0 0
	FU M 15	Any High Normal Low	0 0 0 0	2 0 1 (50.0) 0	0 0 0 1 (50.0)	1 0 1 (100) 0	0 0 0 0	0 0 0 0	3 0 2 (66.7) 0	0 0 0 1 (33.3)
	FU M 18	Any High Normal Low	0 0 0 0	1 0 0 1 (100)	0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0	1 0 0 1 (100)	0 0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Lymphocytes (10E9/L)	Week 2	Any High 0 Normal 0 Low 0	14 0 3 (21.4) 2 (14.3)	0 1 (7.1) 8 (57.1)	0 0 0	35 0 12 (34.3) 7 (20.0)	0 0 16 (45.7)	0 0 0	49 0 15 (30.6) 9 (18.4)	1 (2.0) 24 (49.0)	0 0
	Week 4	Any High 0 Normal 0 Low 0	16 0 5 (31.3) 2 (12.5)	0 0 9 (56.3)	0 0 0	34 0 9 (26.5) 9 (26.5)	0 0 16 (47.1)	0 0 0	50 0 14 (28.0) 11 (22.0)	0 0	0 0
	Week 6	Any High 0 Normal 0 Low 0	17 0 7 (41.2) 0	0 1 (5.9) 9 (52.9)	0 0 0	35 0 11 (31.4) 7 (20.0)	0 0 16 (45.7)	0 0 0	52 0 18 (34.6) 7 (13.5)	0 2 (3.8) 25 (48.1)	0 0
	Week 8	Any High 0 Normal 0 Low 0	12 0 2 (16.7) 1 (8.3)	0 0 8 (66.7)	0 0 0	24 0 7 (29.2) 6 (25.0)	0 0 11 (45.8)	0 0 0	36 0 9 (25.0) 7 (19.4)	0 1 (2.8) 19 (52.8)	0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Lymphocytes (10E9/L)	Week 10	Any High 0 Normal 0 Low 0	13 0 5 (38.5) 1 (7.7) 1 (7.7) 6 (46.2)	0 0 0 0 3 (13.6)	22 0 7 (31.8) 1 (4.5) 11 (50.0)	0 0 0 0 3 (20.0)	0 0 0 0 11 (55.0)	0 0 0 0 0	35 0 12 (34.3) 2 (5.7) 4 (11.4) 17 (48.6)	0 0 0 0 0
	Week 12	Any High 0 Normal 0 Low 0	11 0 4 (36.4) 1 (9.1) 1 (9.1) 5 (45.5)	0 0 0 0 0	20 0 5 (25.0) 0 4 (20.0)	0 0 0 0 11 (55.0)	0 0 0 0 0	31 0 9 (29.0) 1 (3.2) 5 (16.1) 16 (51.6)	0 0 0 0 0	
	Week 14	Any High 0 Normal 0 Low 0	13 0 4 (30.8) 1 (7.7) 3 (23.1) 5 (38.5)	0 0 0 0 0	21 0 9 (42.9) 1 (4.8) 2 (9.5) 9 (42.9)	0 0 0 0 0	0 0 0 0 0	34 0 13 (38.2) 2 (5.9) 5 (14.7) 14 (41.2)	0 0 0 0 0	
	Week 16	Any High 0 Normal 0 Low 0	11 0 2 (18.2) 0 2 (18.2)	0 0 0 0 7 (63.6)	17 0 4 (23.5) 1 (5.9) 5 (29.4)	0 0 0 0 7 (41.2)	0 0 0 0 0	28 0 6 (21.4) 1 (3.6) 7 (25.0) 14 (50.0)	0 0 0 0 0	

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Lymphocytes (10E9/L)	Week 18	Any	8	0	14	0	0	0	22	0
		High	0	0	0	0	0	0	0	0
		Normal	0	3 (37.5)	3 (21.4)	0	0	0	6 (27.3)	0
		Low	0	1 (12.5)	4 (50.0)	0	4 (28.6)	7 (50.0)	5 (22.7)	11 (50.0)
	Week 20	Any	9	0	15	0	0	0	24	0
		High	0	0	0	0	0	0	0	0
		Normal	0	4 (44.4)	2 (13.3)	1 (6.7)	0	0	6 (25.0)	1 (4.2)
		Low	0	1 (11.1)	4 (44.4)	0	3 (20.0)	9 (60.0)	4 (16.7)	13 (54.2)
	Week 22	Any	8	0	15	0	0	0	23	0
		High	0	0	0	0	0	0	0	0
		Normal	0	4 (50.0)	4 (26.7)	0	0	0	8 (34.8)	0
		Low	0	1 (12.5)	3 (37.5)	0	3 (20.0)	8 (53.3)	4 (17.4)	11 (47.8)
	Week 24	Any	8	0	7	0	0	0	15	0
		High	0	0	0	0	0	0	0	0
		Normal	0	3 (37.5)	1 (14.3)	0	0	0	4 (26.7)	0
		Low	0	1 (12.5)	4 (50.0)	0	2 (28.6)	4 (57.1)	3 (20.0)	8 (53.3)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Lymphocytes (10E9/L)	Week 26	Any 3 0	High 0	Normal 2 (66.7)	Low 0	Any 3 0	High 0	Normal 1 (33.3)	Low 0	Any 6 0
		High 0	Normal 0	Low 1 (33.3)	Any 0	High 0	Normal 0	Low 2 (66.7)	High 0	Normal 3 (50.0)
		Normal 0	Low 0		Normal 1	Low 0		Normal 0	Low 0	
	Week 28	Any 1 0	High 0	Normal 0	Low 1 (100)	Any 2 0	High 0	Normal 1 (50.0)	Low 0	Any 3 0
		High 0	Normal 0	Low 0	Any 0	High 0	Normal 0	Low 1 (50.0)	High 0	Normal 1 (33.3)
		Normal 0	Low 0		Normal 0	Low 0		Normal 0	Low 2 (66.7)	
	Week 30	Any 0 0	High 0	Normal 0	Low 0	Any 1 0	High 0	Normal 1 (100)	Low 0	Any 1 0
		High 0	Normal 0	Low 0	Any 0	High 0	Normal 0	Low 0	High 0	Normal 1 (100)
		Normal 0	Low 0		Normal 0	Low 0		Normal 0	Low 0	
	Week 32	Any 0 0	High 0	Normal 0	Low 0	Any 1 0	High 0	Normal 1 (100)	Low 0	Any 1 0
		High 0	Normal 0	Low 0	Any 0	High 0	Normal 0	Low 0	High 0	Normal 1 (100)
		Normal 0	Low 0		Normal 0	Low 0		Normal 0	Low 0	

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Lymphocytes (10E9/L) Week 34	Any	0	0	0	1	0	0	0	1	0
	High	0	0	0	0	1 (100)	0	0	1 (100)	0
	Normal	0	0	0	1	0	0	0	0	0
	Low	0	0	0	0	0	0	0	0	0
FU W 2	Any	16	0	0	22	0	0	0	38	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	5 (31.3)	0	5 (22.7)	0	0	0	10 (26.3)	0
	Low	0	5 (31.3)	6 (37.5)	6 (27.3)	11 (50.0)	0	0	11 (28.9)	17 (44.7)
FU W 4	Any	10	0	0	19	0	0	0	29	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	3 (30.0)	0	5 (26.3)	1 (5.3)	0	0	8 (27.6)	1 (3.4)
	Low	0	3 (30.0)	4 (40.0)	4 (21.1)	9 (47.4)	0	0	7 (24.1)	13 (44.8)
FU W 6	Any	10	0	0	16	0	0	0	26	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	7 (70.0)	0	6 (37.5)	0	0	0	13 (50.0)	0
	Low	0	1 (10.0)	2 (20.0)	3 (18.8)	7 (43.8)	0	0	4 (15.4)	9 (34.6)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Lymphocytes (10E9/L)	FU W 8	Any High Normal Low	7 0 4 (57.1) 1 (14.3)	0 0 0 2 (28.6)	0 0 1 (12.5) 0	8 0 0 5 (62.5)	0 0 0 0	0 0 5 (33.3) 3 (20.0)	15 0 5 (33.3) 7 (46.7)	0 0 0 7 (46.7)
	FU W 10	Any High Normal Low	4 0 3 (75.0) 1 (25.0)	0 0 0 0	0 0 5 (55.6) 1 (11.1)	9 0 0 3 (33.3)	0 0 0 0	0 0 8 (61.5) 2 (15.4)	13 0 8 (61.5) 3 (23.1)	0 0 0 3 (23.1)
	FU W 12	Any High Normal Low	5 0 3 (60.0) 1 (20.0)	0 0 0 1 (20.0)	0 0 0 0	2 0 0 2 (100)	0 0 0 0	0 0 3 (42.9) 3 (42.9)	7 0 3 (42.9) 1 (14.3)	0 0 0 1 (14.3)
	FU M 6	Any High Normal Low	3 0 1 (33.3) 0	0 0 0 2 (66.7)	0 0 1 (33.3) 0	3 0 0 2 (66.7)	0 0 0 0	0 0 2 (33.3) 0	6 0 2 (33.3) 4 (66.7)	0 0 0 4 (66.7)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Lymphocytes (10E9/L)	FU M 9	Any 2	0	0	0	1	0	0	3	0
	High 0	0	1 (50.0)	0	0	0	0	0	1 (33.3)	0
	Normal 0	1 (50.0)	0	0	0	0	0	0	1 (33.3)	1 (33.3)
	Low 0	0	1 (50.0)	0	1 (100)	0	0	0	1 (33.3)	1 (33.3)
FU M 12	Any 1	0	0	0	0	1	0	0	2	0
	High 0	0	1 (100)	0	0	0	0	0	1 (50.0)	0
	Normal 0	1 (100)	0	0	0	0	0	0	0	1 (50.0)
	Low 0	0	0	0	0	0	1 (100)	0	0	1 (50.0)
FU M 15	Any 2	0	0	0	0	1	0	0	3	0
	High 0	0	1 (50.0)	1 (50.0)	0	0	0	0	1 (33.3)	1 (33.3)
	Normal 0	1 (50.0)	1 (50.0)	0	0	0	0	0	1 (33.3)	0
	Low 0	0	0	0	1 (100)	0	0	0	1 (33.3)	0
FU M 18	Any 1	0	0	0	0	0	0	0	1	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 0	0	0	0	0	0	0	0	0	0
	Low 0	1 (100)	0	0	0	0	0	0	1 (100)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Monocytes (10E9/L)	Week 2	Any 14			35			49		
		High 0	0	0	0	0	0	0	0	0
		Normal 1 (7.1)	13 (92.9)	0	1 (2.9)	34 (97.1)	0	2 (4.1)	47 (95.9)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 4	Any 16			34			50		
		High 0	0	0	0	0	0	0	0	0
		Normal 1 (6.3)	15 (93.8)	0	1 (2.9)	33 (97.1)	0	2 (4.0)	48 (96.0)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 6	Any 16			35			51		
		High 0	0	0	0	0	0	0	0	0
		Normal 1 (6.3)	15 (93.8)	0	1 (2.9)	34 (97.1)	0	2 (3.9)	49 (96.1)	0
		Low 0	0	0	0	0	0	0	0	0
	Week 8	Any 12			24			36		
		High 0	0	0	0	0	0	0	0	0
		Normal 1 (8.3)	11 (91.7)	0	0	24 (100)	0	1 (2.8)	35 (97.2)	0
		Low 0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Monocytes (10E9/L)	Week 10	Any 13 High 0 Normal 0 Low 0	13 (100) 0 0 0	0 0 0 0	22 0 21 (95.5) 1 (4.5)	0 0 0 0	0 0 0 0	35 0 34 (97.1) 1 (2.9)	0 0 0 0	0 0 0 0
	Week 12	Any 11 High 0 Normal 0 Low 0	11 (100) 0 0 0	0 0 0 0	20 0 20 (100) 0	0 0 0 0	0 0 0 0	31 0 31 (100) 0	0 0 0 0	0 0 0 0
	Week 14	Any 13 High 0 Normal 1 (7.7) Low 0	12 (92.3) 0 0	0 0 0	21 0 21 (100) 0	0 0 0 0	0 0 0 0	34 0 33 (97.1) 1 (2.9)	0 0 0 0	0 0 0 0
	Week 16	Any 11 High 0 Normal 1 (9.1) Low 0	10 (90.9) 0 0	0 0 0	17 0 17 (100) 0	0 0 0 0	0 0 0 0	28 0 27 (96.4) 1 (3.6)	0 0 0 0	0 0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Monocytes (10E9/L)	Week 18	Any 8 0	High 0 0	Normal 8 (100) 0	Low 0 0	High 0 14	Normal 0 0	Low 0 0	High 0 22	Normal 0 0	Low 0 0
	High										
	Normal										
	Low										
	Week 20	Any 9 0	High 0 0	Normal 9 (100) 0	Low 0 0	High 0 15	Normal 0 0	Low 0 0	High 0 24	Normal 0 0	Low 0 0
	High										
	Normal										
	Low										
	Week 22	Any 8 0	High 0 0	Normal 8 (100) 0	Low 0 0	High 0 15	Normal 0 0	Low 0 0	High 0 23	Normal 0 0	Low 0 0
	High										
	Normal										
	Low										
	Week 24	Any 8 0	High 0 0	Normal 8 (100) 0	Low 0 0	High 0 7	Normal 0 0	Low 0 0	High 0 15	Normal 0 0	Low 0 0
	High										
	Normal										
	Low										

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Monocytes (10E9/L)	Week 26	Any 3 0	High 0 0	Normal 3 (100) 0	Low 0 0	High 0 0	Normal 3 (100) 0	Low 0 0	High 0 0	Normal 6 (100) 0	Low 0 0
	High										
	Normal										
	Low										
	Week 28	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	High 2 0	Normal 2 (100) 0	Low 0 0	High 0 0	Normal 3 (100) 0	Low 0 0
	High										
	Normal										
	Low										
	Week 30	Any 0 0	High 0 0	Normal 0 0	Low 0 0	High 1 0	Normal 1 (100) 0	Low 0 0	High 0 0	Normal 1 (100) 0	Low 0 0
	High										
	Normal										
	Low										
	Week 32	Any 0 0	High 0 0	Normal 0 0	Low 0 0	High 1 0	Normal 1 (100) 0	Low 0 0	High 0 0	Normal 1 (100) 0	Low 0 0
	High										
	Normal										
	Low										

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Monocytes (10E9/L)	Week 34	Any 0	High 0	Normal 0	Low 0	High 1 (100)	Normal 0	Low 0	High 1 (100)	Normal 0	Low 0
	FU W 2	Any 15	High 0	Normal 1 (6.7)	Low 0	High 21 (50.0)	Normal 20 (95.2)	Low 0	High 36 (56.3)	Normal 34 (94.4)	Low 0
	FU W 4	Any 10	High 0	Normal 10 (100)	Low 0	High 19 (5.3)	Normal 17 (89.5)	Low 0	High 29 (45.3)	Normal 27 (93.1)	Low 0
	FU W 6	Any 10	High 0	Normal 9 (90.0)	Low 1 (10.0)	High 16 (6.3)	Normal 14 (87.5)	Low 1 (6.3)	High 26 (40.6)	Normal 23 (88.5)	Low 2 (7.7)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Monocytes (10E9/L)	FU W 8	Any 7 0	High 0 0	Normal 7 (100) 0	Low 0 0	High 0 0	Normal 8 (100) 0	Low 0 0	High 0 0	Normal 15 (100) 0	Low 0 0
	FU W 10	Any 4 0	High 0 0	Normal 3 (75.0) 0	Low 1 (25.0) 0	High 0 0	Normal 9 (100) 0	Low 0 0	High 0 0	Normal 12 (92.3) 1	Low (7.7) 0
	FU W 12	Any 5 0	High 0 0	Normal 4 (80.0) 0	Low 1 (20.0) 0	High 0 0	Normal 2 (100) 0	Low 0 0	High 0 0	Normal 6 (85.7) 1	Low (14.3) 0
	FU M 6	Any 3 0	High 0 0	Normal 3 (100) 0	Low 0 0	High 0 0	Normal 3 (100) 0	Low 0 0	High 0 0	Normal 6 (100) 0	Low 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Monocytes (10E9/L)	FU M 9	Any 2 0	High 0 0	Normal 2 (100) 0	Low 0 0	High 0 1	Normal 0 0	Low 0 0	High 0 3	Normal 0 0	Low 0 0
	FU M 12	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	High 0 1	Normal 0 0	Low 0 0	High 0 2	Normal 0 0	Low 0 0
	FU M 15	Any 2 0	High 0 0	Normal 2 (100) 0	Low 0 0	High 0 1	Normal 0 0	Low 0 0	High 0 3	Normal 0 0	Low 0 0
	FU M 18	Any 1 0	High 0 0	Normal 1 (100) 0	Low 0 0	High 0 0	Normal 0 0	Low 0 0	High 0 1	Normal 0 0	Low 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Neutrophils (10E9/L)	Week 2									
	Any	13			36			49		
	High	0	1 (7.7)	0	1 (2.8)	0	0	1 (2.0)	1 (2.0)	0
	Normal	0	9 (69.2)	1 (7.7)	1 (2.8)	31 (86.1)	0	1 (2.0)	40 (81.6)	1 (2.0)
	Low	0	2 (15.4)	0	0	1 (2.8)	2 (5.6)	0	3 (6.1)	2 (4.1)
	Week 4									
	Any	15			35			50		
	High	0	1 (6.7)	0	0	0	0	0	1 (2.0)	0
	Normal	0	11 (73.3)	1 (6.7)	3 (8.6)	29 (82.9)	1 (2.9)	3 (6.0)	40 (80.0)	2 (4.0)
	Low	0	2 (13.3)	0	0	1 (2.9)	1 (2.9)	0	3 (6.0)	1 (2.0)
	Week 6									
	Any	16			35			51		
	High	0	0	0	0	0	0	0	0	0
	Normal	0	12 (75.0)	1 (6.3)	3 (8.6)	27 (77.1)	1 (2.9)	3 (5.9)	39 (76.5)	2 (3.9)
	Low	0	3 (18.8)	0	0	3 (8.6)	1 (2.9)	0	6 (11.8)	1 (2.0)
	Week 8									
	Any	11			25			36		
	High	0	0	0	0	0	0	0	0	0
	Normal	0	9 (81.8)	1 (9.1)	2 (8.0)	18 (72.0)	2 (8.0)	2 (5.6)	27 (75.0)	3 (8.3)
	Low	0	1 (9.1)	0	0	3 (12.0)	0	0	4 (11.1)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Neutrophils (10E9/L)	Week 10	Any High 0 Normal 0 Low 0	13 0 11 (84.6) 1 (7.7)	0 1 (7.7)	0 1 (4.5)	22 0 18 (81.8)	0 0	0 1 (2.9)	35 0 29 (82.9)	0 1 (2.9)
	Week 12	Any High 0 Normal 0 Low 0	11 0 9 (81.8) 1 (9.1)	0 0	0 1 (5.0)	20 0 15 (75.0)	0 1 (5.0)	0 1 (3.2)	31 0 24 (77.4)	0 2 (6.5)
	Week 14	Any High 0 Normal 0 Low 0	12 0 10 (83.3) 1 (8.3)	0 0	0 1 (4.8)	21 0 18 (85.7)	0 0	0 1 (3.0)	33 0 28 (84.8)	0 1 (3.0)
	Week 16	Any High 0 Normal 0 Low 0	10 0 7 (70.0) 2 (20.0)	0 0	0 1 (5.9)	17 0 15 (88.2) 1 (5.9)	0 0	0 1 (3.7)	27 0 22 (81.5) 3 (11.1)	0 1 (3.7)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Neutrophils (10E9/L)	Week 18	Any High 0 Normal 0 Low 0	8 0 6 (75.0) 2 (25.0)	0 0 0	0 0 13 (92.9)	14 0 0	0 0 1 (7.1)	0 0 0	22 0 19 (86.4)	0 0 2 (9.1)	1 (4.5)
	Week 20	Any High 0 Normal 0 Low 0	9 0 6 (66.7) 2 (22.2)	0 1 (11.1) 0	0 0 0	15 0 12 (80.0)	0 0 0	0 0 1 (6.7)	24 0 18 (75.0)	0 0 4 (16.7)	1 (4.2)
	Week 22	Any High 0 Normal 0 Low 0	8 0 7 (87.5) 1 (12.5)	0 0 0	0 0 0	15 0 13 (86.7)	0 0 0	0 0 1 (6.7)	23 0 20 (87.0)	0 0 2 (8.7)	1 (4.3)
	Week 24	Any High 0 Normal 0 Low 0	8 0 6 (75.0) 1 (12.5)	0 1 (12.5) 0	0 0 0	6 0 5 (83.3)	0 0 0	0 0 0	14 0 11 (78.6)	0 0 2 (14.3)	1 (7.1)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Neutrophils (10E9/L)	Any	3	0	0	3	0	0	0	6	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	2 (66.7)	0	1 (33.3)	0	0	0	3 (50.0)	0
	Low	0	1 (33.3)	0	2 (66.7)	0	0	0	3 (50.0)	0
Week 26	Any	1	0	0	2	0	0	0	3	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	1 (100)	0	2 (100)	0	0	0	3 (100)	0
	Low	0	0	0	0	0	0	0	0	0
Week 28	Any	0	0	0	1	0	0	0	1	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	1 (100)	0	0	0	1 (100)	0
	Low	0	0	0	0	0	0	0	0	0
Week 30	Any	0	0	0	0	0	0	0	0	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	1 (100)	0	0	0	1 (100)	0
	Low	0	0	0	0	0	0	0	0	0
Week 32	Any	0	0	0	1	0	0	0	1	0
	High	0	0	0	0	0	0	0	0	0
	Normal	0	0	0	1 (100)	0	0	0	1 (100)	0
	Low	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Neutrophils (10E9/L)	Week 34	Any 0	0	0	1	0	0	0	1 (100)	0
		High 0	0	0	0	1 (100)	0	0	1 (100)	0
		Normal 0	0	0	0	0	0	0	0	0
		Low 0	0	0	0	0	0	0	0	0
FU W 2	Any 15	0	0	0	22	1 (4.5)	0	0	1 (2.7)	0
	High 0	0	0	0	0	1 (4.5)	0	0	1 (2.7)	0
	Normal 1 (6.7)	12 (80.0)	0	0	15 (68.2)	1 (4.5)	3 (8.1)	27 (73.0)	1 (2.7)	1 (2.7)
	Low 0	2 (13.3)	0	0	2 (9.1)	1 (4.5)	0	4 (10.8)	1 (2.7)	1 (2.7)
FU W 4	Any 10	0	0	0	19	0	0	1 (3.4)	0	0
	High 1 (10.0)	0	0	0	0	1 (5.3)	0	2 (6.9)	21 (72.4)	1 (3.4)
	Normal 0	6 (60.0)	0	0	15 (78.9)	1 (5.3)	0	0	4 (13.8)	1 (0)
	Low 0	3 (30.0)	0	0	1 (5.3)	0	0	0	0	0
FU W 6	Any 10	0	0	0	16	1 (6.3)	0	0	1 (3.8)	0
	High 0	0	0	0	0	1 (6.3)	0	1 (3.8)	17 (65.4)	0
	Normal 0	7 (70.0)	0	0	10 (62.5)	0	1 (3.8)	0	6 (23.1)	1 (3.8)
	Low 0	3 (30.0)	0	0	3 (18.8)	1 (6.3)	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Neutrophils (10E9/L)	FU W 8	Any	7	0	8	0	0	0	15	0
		High	0	0	0	0	0	0	0	0
		Normal	5 (71.4)	1 (14.3)	7 (87.5)	0	0	0	12 (80.0)	1 (6.7)
		Low	1 (14.3)	0	1 (12.5)	0	0	0	2 (13.3)	0
	FU W 10	Any	4	0	9	0	0	0	13	0
		High	0	0	0	0	0	0	0	0
		Normal	1 (25.0)	0	6 (66.7)	0	0	0	7 (53.8)	0
		Low	3 (75.0)	0	2 (22.2)	1 (11.1)	0	0	5 (38.5)	1 (7.7)
	FU W 12	Any	5	0	2	0	0	0	7	0
		High	0	0	0	0	0	0	0	0
		Normal	3 (60.0)	0	2 (100)	0	0	0	5 (71.4)	0
		Low	2 (40.0)	0	0	0	0	0	2 (28.6)	0
	FU M 6	Any	3	0	3	0	0	0	6	0
		High	0	0	0	0	0	0	0	0
		Normal	1 (33.3)	1 (33.3)	2 (66.7)	0	0	0	3 (50.0)	1 (16.7)
		Low	1 (33.3)	0	1 (33.3)	0	0	0	2 (33.3)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Neutrophils (10E9/L)	FU M 9	Any 2	0	0	0	1	0	0	3	0
	High 0	0	2 (100)	0	0	1 (100)	0	0	3 (100)	0
	Normal 0	2	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0
	FU M 12	Any 1	0	0	0	1	0	0	2	0
	High 0	0	0	0	0	1 (100)	0	0	1 (50.0)	0
	Normal 0	0	0	0	0	0	0	0	1 (50.0)	0
	Low 0	1 (100)	0	0	0	0	0	0	0	0
	FU M 15	Any 2	0	0	0	1	0	0	3	0
	High 0	0	2 (100)	0	0	1 (100)	0	0	3 (100)	0
	Normal 0	2	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0
	FU M 18	Any 1	0	0	0	0	0	0	1	0
	High 0	0	1 (100)	0	0	0	0	0	1 (100)	0
	Normal 0	1 (100)	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Platelets (10E9/L)	Week 2	Any 18			37			55		
		High 0	0	0	1 (2.7)	0	0	1 (1.8)	0	0
		Normal 1 (5.6)	13 (72.2)	2 (11.1)	1 (2.7)	31 (83.8)	2 (5.4)	2 (3.6)	44 (80.0)	4 (7.3)
		Low 0	1 (5.6)	1 (5.6)	0	1 (2.7)	1 (2.7)	0	2 (3.6)	2 (3.6)
	Week 4	Any 17			36			53		
		High 0	0	0	0	0	0	0	0	0
		Normal 1 (5.9)	11 (64.7)	0	2 (5.6)	21 (58.3)	1 (2.8)	3 (5.7)	32 (60.4)	1 (1.9)
		Low 0	3 (17.6)	2 (11.8)	0	10 (27.8)	2 (5.6)	0	13 (24.5)	4 (7.5)
	Week 6	Any 18			35			53		
		High 0	0	0	0	0	0	0	0	0
		Normal 1 (5.6)	13 (72.2)	1 (5.6)	2 (5.7)	26 (74.3)	1 (2.9)	3 (5.7)	39 (73.6)	2 (3.8)
		Low 0	1 (5.6)	2 (11.1)	0	4 (11.4)	2 (5.7)	0	5 (9.4)	4 (7.5)
	Week 8	Any 14			26			40		
		High 1 (7.1)	0	0	0	0	0	1 (2.5)	0	0
		Normal 0	10 (71.4)	1 (7.1)	1 (3.8)	21 (80.8)	0	1 (2.5)	31 (77.5)	1 (2.5)
		Low 0	0	2 (14.3)	0	4 (15.4)	0	0	4 (10.0)	2 (5.0)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Platelets (10E9/L)	Week 10	Any High 0 Normal 0 Low 0	14 0 12 (85.7) 0 0	0 0 2 (14.3)	23 0 18 (78.3) 1 (4.3) 0	0 1 (4.3) 2 (8.7)	0 1 (4.3) 1 (4.3)	0 1 (2.7) 0	37 0 30 (81.1) 1 (2.7) 1 (2.7)	0 2 (5.4) 3 (8.1)	0 0 0
	Week 12	Any High 0 Normal 0 Low 0	12 0 7 (58.3) 3 (25.0)	0 1 (8.3) 1 (8.3)	21 0 14 (66.7) 0	0 0 5 (23.8)	0 2 (9.5)	0 0 0	33 0 21 (63.6) 1 (3.0)	0 8 (24.2) 3 (9.1)	0 0 0
	Week 14	Any High 0 Normal 0 Low 0	13 0 9 (69.2) 2 (15.4)	0 1 (7.7) 1 (7.7)	22 0 14 (63.6) 0	0 0 6 (27.3)	0 2 (9.1)	0 0 0	35 0 23 (65.7) 1 (2.9)	0 8 (22.9) 3 (8.6)	0 0 0
	Week 16	Any High 0 Normal 0 Low 0	12 0 9 (75.0) 1 (8.3)	0 0 2 (16.7)	17 0 12 (70.6) 0	0 0 3 (17.6)	0 1 (5.9) 1 (5.9)	0 0 0	29 0 21 (72.4) 1 (3.4)	0 4 (13.8) 3 (10.3)	0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Platelets (10E9/L)	Week 18	Any	8	0	14	0	0	0	22	0
		High	0	0	0	0	0	0	0	0
		Normal	0	7 (87.5)	0	10 (71.4)	1 (7.1)	0	17 (77.3)	1 (4.5)
		Low	0	1 (12.5)	0	2 (14.3)	1 (7.1)	0	2 (9.1)	2 (9.1)
	Week 20	Any	9	0	15	0	0	0	24	0
		High	0	0	0	0	0	0	0	0
		Normal	0	6 (66.7)	1 (11.1)	9 (60.0)	1 (6.7)	0	15 (62.5)	2 (8.3)
		Low	0	1 (11.1)	1 (11.1)	4 (26.7)	1 (6.7)	0	5 (20.8)	2 (8.3)
	Week 22	Any	8	0	15	0	0	0	23	0
		High	0	0	0	0	0	0	0	0
		Normal	0	5 (62.5)	0	10 (66.7)	1 (6.7)	0	15 (65.2)	1 (4.3)
		Low	0	2 (25.0)	1 (12.5)	0	3 (20.0)	1 (6.7)	0	5 (21.7)
	Week 24	Any	8	0	7	0	0	0	15	0
		High	0	0	0	0	0	0	0	0
		Normal	0	5 (62.5)	0	5 (71.4)	1 (14.3)	0	10 (66.7)	1 (6.7)
		Low	0	1 (12.5)	2 (25.0)	0	0	1 (14.3)	0	1 (6.7)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Platelets (10E9/L)	Week 26	Any High 0 Normal 0 Low 0	3 0 2 (66.7) 1 (33.3)	0 0 0	0 2 (66.7) 0	3 0 0	0 0 1 (33.3)	0 0 0	6 0 4 (66.7) 1 (16.7)	0 0 1 (16.7) 1 (16.7)
	Week 28	Any High 0 Normal 0 Low 0	1 0 0 0	0 0 1 (100)	0 1 (50.0) 0	2 0 0	0 0 0	0 0 0	3 0 1 (33.3) 1 (33.3)	0 0 1 (33.3) 1 (33.3)
	Week 30	Any High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	0 0 0 1 (100)	1 0 0 0	0 0 0 0	0 0 0 0	1 0 0 0	0 0 0 0
	Week 32	Any High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	0 1 (100) 0	1 0 0	0 0 0	0 0 0	1 0 1 (100) 0	0 0 0 0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)			
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	
Platelets (10E9/L)	Week 34	Any High 0 Normal 0 Low 0	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0 0	0 0 0 0	1 0 1 (100) 0	0 0 0 0	0 0 0 0	
	FU W 2	Any High 0 Normal 0 Low 0	17 0 11 (64.7) 2 (11.8)	0 1 (5.9) 3 (17.6)	23 0 1 (4.3) 0	0 0 16 (69.6) 5 (21.7)	0 0 0 1 (4.3)	0 0 1 (2.5) 0	40 0 27 (67.5) 7 (17.5)	0 0 1 (2.5) 4 (10.0)	0 0 1 (2.5) 4 (10.0)
	FU W 4	Any High 0 Normal 0 Low 0	10 0 4 (40.0) 3 (30.0)	0 1 (10.0) 2 (20.0)	20 0 2 (10.0) 0	0 0 10 (50.0) 7 (35.0)	0 0 0 1 (5.0)	0 0 2 (6.7) 0	30 0 14 (46.7) 10 (33.3)	0 0 1 (3.3) 3 (10.0)	0 0 1 (3.3) 3 (10.0)
	FU W 6	Any High 0 Normal 0 Low 0	10 0 6 (60.0) 2 (20.0)	0 1 (6.3) 2 (20.0)	16 0 7 (43.8) 6 (37.5)	0 0 0 1 (6.3)	0 0 1 (3.8) 1 (3.8)	0 0 1 (3.8) 8 (30.8)	26 0 13 (50.0) 8 (30.8)	0 0 0 3 (11.5)	0 0 0 3 (11.5)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Visit Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Platelets (10E9/L)	FU W 8	Any High 0 Normal 0 Low 0	7 0 5 (71.4) 0	0 1 (14.3) 1 (14.3)	0 0 0	9 0 4 (44.4) 0	0 0 0	0 0 0	16 0 9 (56.3) 1 (6.3)	0 0 4 (25.0) 2 (12.5)
	FU W 10	Any High 0 Normal 0 Low 0	4 0 1 (25.0) 2 (50.0)	0 0 0	0 0 0	9 0 6 (66.7) 2 (22.2)	0 0 1 (11.1)	0 0 0	13 0 7 (53.8) 4 (30.8)	0 0 2 (15.4)
	FU W 12	Any High 0 Normal 0 Low 0	5 0 2 (40.0) 1 (20.0)	0 0 2 (40.0)	0 0 0	2 0 1 (50.0) 1 (50.0)	0 0 0	0 0 0	7 0 3 (42.9) 2 (28.6)	0 0 0
	FU M 6	Any High 0 Normal 0 Low 0	3 0 2 (66.7) 0	0 1 (33.3) 0	0 0 0	3 0 2 (66.7) 0	0 0 1 (33.3)	0 0 0	6 0 4 (66.7) 0	0 0 1 (16.7)

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.2.4
Hematology Shift Table by Visit
Safety Population

Parameter	Base-line Range	Lu-PSMA-617 6.0 GBq (N=23)			Lu-PSMA-617 7.4 GBq (N=41)			Overall (N=64)		
		High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)	High n (%)	Normal n (%)	Low n (%)
Platelets (10E9/L)	FU M 9	Any 2	0	0	0	1	0	0	3	0
	High 0	0	2 (100)	0	0	1 (100)	0	0	3 (100)	0
	Normal 0	2	0	0	0	0	0	0	0	0
	Low 0	0	0	0	0	0	0	0	0	0
	FU M 12	Any 1	0	0	0	1	0	0	2	0
	High 0	0	0	0	0	1 (100)	0	0	1 (50.0)	0
	Normal 0	0	0	0	0	0	0	0	1 (50.0)	0
	Low 0	1 (100)	0	0	0	0	0	0	1 (50.0)	0
	FU M 15	Any 2	0	0	0	1	0	0	3	0
	High 0	0	1 (50.0)	0	0	1 (100)	0	0	2 (66.7)	0
	Normal 0	1 (50.0)	0	0	0	0	0	0	1 (33.3)	0
	Low 0	0	0	0	0	0	0	0	0	0
	FU M 18	Any 1	0	0	0	0	0	0	1	0
	High 0	0	0	0	0	0	0	0	0	0
	Normal 0	0	0	0	0	0	0	0	0	0
	Low 0	1 (100)	0	0	0	0	0	0	1 (100)	0

FU W x = Follow-up Week x, FU M x = Follow-up Month x.

Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

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Table 14.3.3.1.1
Randomized Treatment Exposure, Summary of Cycles
Safety Population

	Lu-PSMA-617 6.0 GBq (N=23)	Lu-PSMA-617 7.4 GBq (N=41)	Overall (N=64)
Duration of study treatment (months)			
n	23	41	64
Mean (SD)	3.49 (2.366)	3.66 (2.007)	3.60 (2.126)
Median	3.71	3.71	3.71
Q1 ; Q3	1.87 ; 5.75	1.87 ; 5.55	1.87 ; 5.55
Min ; Max	0.0 ; 6.3	0.0 ; 7.7	0.0 ; 7.7
Number of cycles started by patient			
n	23	41	64
Mean (SD)	2.8 (1.23)	3.0 (1.07)	2.9 (1.12)
Median	3.0	3.0	3.0
Q1 ; Q3	2.0 ; 4.0	2.0 ; 4.0	2.0 ; 4.0
Min ; Max	1 ; 4	1 ; 4	1 ; 4
Number of cycles started by patient categories, n (%)			
n	23	41	64
1 cycle	5 (21.7)	3 (7.3)	8 (12.5)
2 cycles	4 (17.4)	15 (36.6)	19 (29.7)
3 cycles	4 (17.4)	4 (9.8)	8 (12.5)
4 cycles	10 (43.5)	19 (46.3)	29 (45.3)

Duration of study treatment (Months) = (Treatment end date - Treatment start date + 1) / 30.4375

Output ID: t-exp-saf 04JUN20 12:59

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Table 14.3.3.1.2
 Randomized Treatment Exposure, Summary of Cycles - by Age Category
 Safety Population

	Lu-PSMA-617		Lu-PSMA-617		Overall	
	6.0 GBq <65 years (N=4)	>=65 years (N=19)	7.4 GBq <65 years (N=12)	>=65 years (N=29)	<65 years (N=16)	>=65 years (N=48)
Duration of study treatment (months)						
n	4	19	12	29	16	48
Mean (SD)	3.76 (1.584)	3.43 (2.531)	2.93 (2.141)	3.96 (1.906)	3.14 (2.001)	3.75 (2.165)
Median	3.71	3.71	1.99	4.86	2.89	4.40
Q1 ; Q3	2.78 ; 4.75	0.03 ; 5.82	1.74 ; 5.42	2.10 ; 5.55	1.84 ; 5.42	1.87 ; 5.55
Min ; Max	1.9 ; 5.7	0.0 ; 6.3	0.0 ; 5.7	0.0 ; 7.7	0.0 ; 5.7	0.0 ; 7.7
Number of cycles started by patient						
n	4	19	12	29	16	48
Mean (SD)	3.0 (0.82)	2.8 (1.32)	2.6 (1.16)	3.1 (1.01)	2.7 (1.08)	3.0 (1.14)
Median	3.0	3.0	2.0	4.0	2.5	3.5
Q1 ; Q3	2.5 ; 3.5	1.0 ; 4.0	2.0 ; 4.0	2.0 ; 4.0	2.0 ; 4.0	2.0 ; 4.0
Min ; Max	2 ; 4	1 ; 4	1 ; 4	1 ; 4	1 ; 4	1 ; 4
Number of cycles started by patient categories, n(%)						
n	4	19	12	29	16	48
1 cycle	0	5 (26.3)	2 (16.7)	1 (3.4)	2 (12.5)	6 (12.5)
2 cycles	1 (25.0)	3 (15.8)	5 (41.7)	10 (34.5)	6 (37.5)	13 (27.1)
3 cycles	2 (50.0)	2 (10.5)	1 (8.3)	3 (10.3)	3 (18.8)	5 (10.4)
4 cycles	1 (25.0)	9 (47.4)	4 (33.3)	15 (51.7)	5 (31.3)	24 (50.0)

Duration of study treatment (Months) = (Treatment end date - Treatment start date + 1) / 30.4375

Output ID: t-expage-saf 04JUN20 12:59

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Table 14.3.3.2.1
Extent of Lu-PSMA-617 Exposure by Cycle and Overall Safety Population

Cycle	Parameter	Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Overall	Cumulative dose (GBq)	n	23	41	64
		Mean (SD)	16.913 (7.6668)	21.404 (8.0335)	19.790 (8.1376)
		Median	18.583	22.287	19.917
		Q1 ; Q3	11.392 ; 24.169	14.711 ; 29.454	14.297 ; 28.394
		Min ; Max	5.07 ; 24.91	6.92 ; 30.59	5.07 ; 30.59
	Dose per cycle (GBq/cycle)	n	23	41	64
		Mean (SD)	5.909 (0.2953)	7.245 (0.5241)	6.765 (0.7891)
		Median	6.031	7.363	7.111
		Q1 ; Q3	5.696 ; 6.142	7.134 ; 7.486	6.048 ; 7.410
		Min ; Max	5.07 ; 6.31	4.91 ; 7.84	4.91 ; 7.84
	Relative dose per cycle (%)	n	23	41	64
		Mean (SD)	98.479 (4.9223)	97.911 (7.0822)	98.115 (6.3547)
		Median	100.511	99.505	99.601
		Q1 ; Q3	94.930 ; 102.362	96.408 ; 101.161	96.090 ; 101.717
		Min ; Max	84.57 ; 105.17	66.41 ; 105.98	66.41 ; 105.98
Cycle 1	Dose (GBq)	n	23	41	64
		Mean (SD)	5.891 (0.3420)	7.398 (0.3255)	6.857 (0.7998)
		Median	5.997	7.428	7.184
		Q1 ; Q3	5.680 ; 6.108	7.225 ; 7.554	6.080 ; 7.471
		Min ; Max	5.07 ; 6.48	6.67 ; 8.14	5.07 ; 8.14
	Relative dose (%)	n	23	41	64
		Mean (SD)	98.178 (5.6996)	99.977 (4.3981)	99.331 (4.9379)
		Median	99.949	100.385	100.262
		Q1 ; Q3	94.658 ; 101.793	97.630 ; 102.075	95.666 ; 101.993
		Min ; Max	84.57 ; 107.92	90.18 ; 110.00	84.57 ; 110.00

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Table 14.3.3.2.1
Extent of Lu-PSMA-617 Exposure by Cycle and Overall Safety Population

Cycle	Parameter	Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Cycle 2	Dose (GBq)	n	18	38	56
		Mean (SD)	6.098 (0.1988)	7.108 (0.9210)	6.783 (0.8996)
		Median	6.120	7.341	7.037
		Q1 ; Q3	5.993 ; 6.209	7.014 ; 7.563	6.192 ; 7.423
		Min ; Max	5.66 ; 6.37	3.52 ; 7.91	3.52 ; 7.91
	Relative dose (%)	n	18	38	56
		Mean (SD)	101.635 (3.3137)	96.049 (12.4464)	97.845 (10.7023)
		Median	101.994	99.200	100.173
		Q1 ; Q3	99.888 ; 103.475	94.780 ; 102.200	95.965 ; 102.915
		Min ; Max	94.38 ; 106.16	47.57 ; 106.85	47.57 ; 106.85
Cycle 3	Dose (GBq)	n	14	23	37
		Mean (SD)	6.029 (0.3072)	7.171 (0.7486)	6.739 (0.8316)
		Median	6.135	7.428	6.987
		Q1 ; Q3	5.908 ; 6.250	7.027 ; 7.541	6.236 ; 7.478
		Min ; Max	5.43 ; 6.35	4.07 ; 7.66	4.07 ; 7.66
	Relative dose (%)	n	14	23	37
		Mean (SD)	100.491 (5.1204)	96.903 (10.1166)	98.260 (8.6675)
		Median	102.256	100.385	101.050
		Q1 ; Q3	98.468 ; 104.174	94.963 ; 101.904	96.740 ; 102.469
		Min ; Max	90.50 ; 105.89	54.94 ; 103.50	54.94 ; 105.89

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Table 14.3.3.2.1
Extent of Lu-PSMA-617 Exposure by Cycle and Overall Safety Population

Cycle	Parameter	Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Cycle 4	Dose (GBq)	n	10	19	29
		Mean (SD)	5.933 (0.3635)	7.328 (0.3173)	6.847 (0.7499)
		Median	5.956	7.430	7.137
		Q1 ; Q3	5.635 ; 6.264	7.137 ; 7.576	6.264 ; 7.434
		Min ; Max	5.41 ; 6.37	6.72 ; 7.82	5.41 ; 7.82
		n	10	19	29
		Mean (SD)	98.887 (6.0582)	99.025 (4.2884)	98.977 (4.8604)
		Median	99.270	100.411	100.356
		Q1 ; Q3	93.918 ; 104.402	96.450 ; 102.373	96.015 ; 102.378
		Min ; Max	90.15 ; 106.20	90.88 ; 105.74	90.15 ; 106.20

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Table 14.3.3.2.2
 Extent of Lu-PSMA-617 Exposure by Cycle and Overall (patients <65 years old)
 Safety Population

Cycle	Parameter	Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16)
			6.0 GBq (N=4)	7.4 GBq (N=12)	
Overall	Cumulative dose (GBq)	n	4	12	16
		Mean (SD)	17.762 (5.1465)	18.251 (8.5674)	18.129 (7.6923)
		Median	17.916	14.857	15.057
		Q1 ; Q3	14.146 ; 21.379	14.232 ; 28.458	14.232 ; 26.060
		Min ; Max	11.39 ; 23.83	6.92 ; 30.27	6.92 ; 30.27
	Dose per cycle (GBq/cycle)	n	4	12	16
		Mean (SD)	5.899 (0.3078)	7.083 (0.7146)	6.787 (0.8209)
		Median	5.826	7.217	7.116
		Q1 ; Q3	5.665 ; 6.133	7.086 ; 7.447	6.133 ; 7.401
		Min ; Max	5.63 ; 6.31	4.91 ; 7.57	4.91 ; 7.57
	Relative dose per cycle (%)	n	4	12	16
		Mean (SD)	98.318 (5.1304)	95.722 (9.6566)	96.371 (8.6600)
		Median	97.101	97.532	97.532
		Q1 ; Q3	94.413 ; 102.224	95.756 ; 100.631	95.261 ; 100.631
		Min ; Max	93.90 ; 105.17	66.41 ; 102.32	66.41 ; 105.17
Cycle 1	Dose (GBq)	n	4	12	16
		Mean (SD)	5.870 (0.4304)	7.295 (0.3708)	6.939 (0.7379)
		Median	5.867	7.337	7.129
		Q1 ; Q3	5.546 ; 6.193	7.056 ; 7.446	6.527 ; 7.410
		Min ; Max	5.36 ; 6.38	6.67 ; 8.14	5.36 ; 8.14
	Relative dose (%)	n	4	12	16
		Mean (SD)	97.826 (7.1738)	98.587 (5.0102)	98.397 (5.3681)
		Median	97.788	99.143	99.143
		Q1 ; Q3	92.436 ; 103.216	95.345 ; 100.620	95.226 ; 100.620
		Min ; Max	89.39 ; 106.34	90.18 ; 110.00	89.39 ; 110.00

Output ID: t-expycagea-saf 04JUN20 13:00

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Table 14.3.3.2.2
 Extent of Lu-PSMA-617 Exposure by Cycle and Overall (patients <65 years old)
 Safety Population

Cycle	Parameter	Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16)
			6.0 GBq (N=4)	7.4 GBq (N=12)	
Cycle 2	Dose (GBq)	n	4	10	14
		Mean (SD)	6.029 (0.2232)	6.886 (1.2284)	6.641 (1.1035)
		Median	6.043	7.187	6.906
		Q1 ; Q3	5.885 ; 6.172	6.808 ; 7.563	6.058 ; 7.507
		Min ; Max	5.74 ; 6.29	3.59 ; 7.87	3.59 ; 7.87
	Relative dose (%)	n	4	10	14
		Mean (SD)	100.479 (3.7203)	93.056 (16.6005)	95.176 (14.3558)
		Median	100.717	97.120	99.162
		Q1 ; Q3	98.088 ; 102.869	91.996 ; 102.200	94.640 ; 102.200
		Min ; Max	95.70 ; 104.78	48.56 ; 106.40	48.56 ; 106.40
Cycle 3	Dose (GBq)	n	3	5	8
		Mean (SD)	5.941 (0.4475)	6.616 (1.4824)	6.363 (1.1980)
		Median	6.128	7.199	6.441
		Q1 ; Q3	5.430 ; 6.264	6.617 ; 7.541	5.779 ; 7.370
		Min ; Max	5.43 ; 6.26	4.07 ; 7.66	4.07 ; 7.66
	Relative dose (%)	n	3	5	8
		Mean (SD)	99.009 (7.4579)	89.410 (20.0325)	93.010 (16.4281)
		Median	102.126	97.287	99.596
		Q1 ; Q3	90.498 ; 104.402	89.425 ; 101.904	89.961 ; 102.813
		Min ; Max	90.50 ; 104.40	54.94 ; 103.50	54.94 ; 104.40

Output ID: t-expycagea-saf 04JUN20 13:00

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Table 14.3.3.2.2

Extent of Lu-PSMA-617 Exposure by Cycle and Overall (patients <65 years old)
Safety Population

Cycle	Parameter	Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=16)
			6.0 GBq (N=4)	7.4 GBq (N=12)	
Cycle 4	Dose (GBq)	n	1	4	5
		Mean (SD)	5.635 (NE)	7.381 (0.4380)	7.032 (0.8682)
		Median	5.635	7.591	7.576
		Q1 ; Q3	5.635 ; 5.635	7.150 ; 7.612	6.725 ; 7.606
		Min ; Max	5.64 ; 5.64	6.72 ; 7.62	5.64 ; 7.62
	Relative dose (%)	n	1	4	5
		Mean (SD)	93.918 (NE)	99.747 (5.9196)	98.581 (5.7511)
		Median	93.918	102.581	102.373
		Q1 ; Q3	93.918 ; 93.918	96.624 ; 102.870	93.918 ; 102.790
		Min ; Max	93.92 ; 93.92	90.88 ; 102.95	90.88 ; 102.95

Output ID: t-expcycagea-saf 04JUN20 13:00

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Table 14.3.3.2.3
 Extent of Lu-PSMA-617 Exposure by Cycle and Overall (patients >=65 years old)
 Safety Population

Cycle	Parameter	Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48)
			6.0 GBq (N=19)	7.4 GBq (N=29)	
Overall	Cumulative dose (GBq)	n	19	29	48
		Mean (SD)	16.734 (8.1996)	22.709 (7.5720)	20.344 (8.2841)
		Median	18.583	26.957	22.582
		Q1 ; Q3	6.054 ; 24.275	14.849 ; 29.510	14.505 ; 28.743
		Min ; Max	5.07 ; 24.91	7.84 ; 30.59	5.07 ; 30.59
	Dose per cycle (GBq/cycle)	n	19	29	48
		Mean (SD)	5.911 (0.3013)	7.312 (0.4194)	6.758 (0.7870)
		Median	6.032	7.378	7.089
		Q1 ; Q3	5.724 ; 6.142	7.248 ; 7.501	6.048 ; 7.418
		Min ; Max	5.07 ; 6.23	5.54 ; 7.84	5.07 ; 7.84
	Relative dose per cycle (%)	n	19	29	48
		Mean (SD)	98.513 (5.0219)	98.817 (5.6671)	98.696 (5.3678)
		Median	100.532	99.696	99.978
		Q1 ; Q3	95.405 ; 102.362	97.950 ; 101.362	96.681 ; 102.080
		Min ; Max	84.57 ; 103.80	74.82 ; 105.98	74.82 ; 105.98
Cycle 1	Dose (GBq)	n	19	29	48
		Mean (SD)	5.895 (0.3346)	7.441 (0.3015)	6.829 (0.8250)
		Median	5.997	7.470	7.209
		Q1 ; Q3	5.680 ; 6.108	7.244 ; 7.618	6.041 ; 7.524
		Min ; Max	5.07 ; 6.48	6.77 ; 8.07	5.07 ; 8.07
	Relative dose (%)	n	19	29	48
		Mean (SD)	98.252 (5.5762)	100.552 (4.0743)	99.642 (4.8052)
		Median	99.949	100.950	100.669
		Q1 ; Q3	94.658 ; 101.793	97.890 ; 102.943	97.425 ; 102.038
		Min ; Max	84.57 ; 107.92	91.46 ; 108.99	84.57 ; 108.99

Output ID: t-expycageb-saf 04JUN20 13:00

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Table 14.3.3.2.3
 Extent of Lu-PSMA-617 Exposure by Cycle and Overall (patients >=65 years old)
 Safety Population

Cycle	Parameter	Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48)
			6.0 GBq (N=19)	7.4 GBq (N=29)	
Cycle 2	Dose (GBq)	n	14	28	42
		Mean (SD)	6.118 (0.1957)	7.187 (0.7967)	6.830 (0.8308)
		Median	6.143	7.356	7.080
		Q1 ; Q3	5.993 ; 6.209	7.080 ; 7.557	6.206 ; 7.420
		Min ; Max	5.66 ; 6.37	3.52 ; 7.91	3.52 ; 7.91
	Relative dose (%)	n	14	28	42
		Mean (SD)	101.966 (3.2613)	97.118 (10.7669)	98.734 (9.2229)
		Median	102.376	99.405	100.173
		Q1 ; Q3	99.888 ; 103.475	95.678 ; 102.126	96.700 ; 102.957
		Min ; Max	94.38 ; 106.16	47.57 ; 106.85	47.57 ; 106.85
Cycle 3	Dose (GBq)	n	11	18	29
		Mean (SD)	6.054 (0.2822)	7.325 (0.3045)	6.843 (0.6919)
		Median	6.143	7.430	7.027
		Q1 ; Q3	5.908 ; 6.250	7.159 ; 7.507	6.246 ; 7.478
		Min ; Max	5.43 ; 6.35	6.55 ; 7.63	5.43 ; 7.63
	Relative dose (%)	n	11	18	29
		Mean (SD)	100.895 (4.7034)	98.984 (4.1143)	99.709 (4.3668)
		Median	102.385	100.407	101.050
		Q1 ; Q3	98.468 ; 104.174	96.740 ; 101.450	98.468 ; 102.469
		Min ; Max	90.58 ; 105.89	88.47 ; 103.08	88.47 ; 105.89

Output ID: t-expycycageb-saf 04JUN20 13:00

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Table 14.3.3.2.3
 Extent of Lu-PSMA-617 Exposure by Cycle and Overall (patients >=65 years old)
 Safety Population

Cycle	Parameter	Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=48)
			6.0 GBq (N=19)	7.4 GBq (N=29)	
Cycle 4	Dose (GBq)	n	9	15	24
		Mean (SD)	5.966 (0.3692)	7.314 (0.2955)	6.808 (0.7379)
		Median	5.957	7.426	7.100
		Q1 ; Q3	5.761 ; 6.264	7.137 ; 7.471	6.244 ; 7.432
		Min ; Max	5.41 ; 6.37	6.73 ; 7.82	5.41 ; 7.82
	Relative dose (%)	n	9	15	24
		Mean (SD)	99.439 (6.1532)	98.832 (3.9934)	99.060 (4.7923)
		Median	99.291	100.356	100.321
		Q1 ; Q3	96.015 ; 104.402	96.450 ; 100.954	96.233 ; 102.099
		Min ; Max	90.15 ; 106.20	90.88 ; 105.74	90.15 ; 106.20

Output ID: t-expycageb-saf 04JUN20 13:00
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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall	
			6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change
Systolic Blood Pressure (mmHg)	Baseline	n	23		41	41	64	64
		Mean	127.48		131.17		129.84	
		SD	15.447		19.952		18.419	
		Median	123.00		129.00		127.50	
		Q1	119.00		115.00		117.50	
		Q3	136.00		142.00		141.50	
		Min	99.0		105.0		99.0	
		Max	164.0		192.0		192.0	
	Treatment Visit 1 injection +30 min	n	23	23	41	41	64	64
		Mean	127.65	0.17	133.80	2.63	131.59	1.75
		SD	20.180	14.828	20.674	10.580	20.553	12.218
		Median	121.00	0.00	133.00	3.00	128.00	1.50
		Q1	114.00	-5.00	117.00	-2.00	116.00	-4.00
		Q3	140.00	8.00	146.00	8.00	146.00	8.00
		Min	90.0	-32.0	92.0	-25.0	90.0	-32.0
		Max	173.0	27.0	186.0	29.0	186.0	29.0
	Treatment Visit 1 injection +60 min	n	23	23	41	41	64	64
		Mean	128.70	1.22	136.54	5.37	133.72	3.88
		SD	14.763	14.712	22.393	11.536	20.221	12.811
		Median	129.00	-1.00	135.00	5.00	133.50	4.00
		Q1	116.00	-6.00	122.00	-3.00	117.00	-5.00
		Q3	141.00	13.00	148.00	13.00	143.00	13.00
		Min	108.0	-35.0	96.0	-15.0	96.0	-35.0
		Max	166.0	26.0	209.0	28.0	209.0	28.0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

Output ID: t-vschg-saf 04JUN20 13:09

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall		
			6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	(N=64)
Systolic Blood Pressure (mmHg)	Treatment Visit 2 injection -20 min	n	18	18	38	38	56	56	
		Mean	130.89	1.39	130.45	-2.16	130.59	-1.02	
		SD	13.451	19.388	15.718	19.510	14.905	19.366	
		Median	136.50	8.00	131.00	-2.50	131.00	-1.00	
		Q1	121.00	-14.00	121.00	-8.00	121.00	-9.50	
		Q3	141.00	17.00	140.00	9.00	141.00	12.00	
		Min	103.0	-37.0	102.0	-63.0	102.0	-63.0	
		Max	149.0	26.0	179.0	33.0	179.0	33.0	
		n	16	16	36	36	52	52	
		Mean	131.13	0.19	136.08	3.25	134.56	2.31	
	Treatment Visit 2 injection +30 min	SD	13.980	16.682	18.185	19.981	17.023	18.917	
		Median	132.00	-0.50	133.00	3.50	133.00	3.00	
		Q1	121.00	-13.00	121.00	-7.50	121.00	-10.00	
		Q3	144.00	10.00	145.50	13.50	144.00	13.00	
		Min	107.0	-24.0	108.0	-54.0	107.0	-54.0	
		Max	152.0	37.0	178.0	40.0	178.0	40.0	
		n	18	18	38	38	56	56	
		Mean	129.06	-0.44	136.55	3.95	134.14	2.54	
		SD	11.445	18.753	18.664	16.077	16.951	16.937	
		Median	128.00	2.50	134.00	3.50	131.00	3.00	
	Treatment Visit 2 injection +60 min	Q1	121.00	-16.00	122.00	-1.00	122.00	-4.00	
		Q3	138.00	12.00	149.00	13.00	144.00	12.50	
		Min	106.0	-43.0	109.0	-54.0	106.0	-54.0	
		Max	145.0	29.0	178.0	30.0	178.0	30.0	

Baseline is the Treatment Visit 1 measurement performed pre-injection.

Output ID: t-vschg-saf 04JUN20 13:09

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall		
			6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	(N=64)
Systolic Blood Pressure (mmHg)	Treatment Visit 3 injection -20 min	n	14	14	23	23	37	37	
		Mean	127.14	-3.21	128.91	-3.52	128.24	-3.41	
		SD	9.355	20.127	16.065	13.863	13.787	16.240	
		Median	126.50	1.50	129.00	-4.00	128.00	-2.00	
		Q1	122.00	-9.00	119.00	-15.00	122.00	-14.00	
	Treatment Visit 3 injection +30 min	Q3	134.00	12.00	135.00	7.00	135.00	10.00	
		Min	107.0	-44.0	94.0	-24.0	94.0	-44.0	
		Max	142.0	19.0	167.0	20.0	167.0	20.0	
		n	14	14	22	22	36	36	
		Mean	127.79	-2.57	133.41	1.36	131.22	-0.17	
Systolic Blood Pressure (mmHg)	Treatment Visit 3 injection +60 min	SD	17.379	22.599	21.731	17.412	20.081	19.375	
		Median	127.00	5.50	130.50	0.50	127.50	2.00	
		Q1	116.00	-12.00	117.00	-10.00	116.50	-11.00	
		Q3	140.00	11.00	146.00	16.00	143.00	11.00	
		Min	96.0	-59.0	99.0	-30.0	96.0	-59.0	
		Max	159.0	26.0	197.0	30.0	197.0	30.0	
		n	14	14	22	22	36	36	
		Mean	125.71	-4.64	133.14	0.55	130.25	-1.47	
		SD	13.820	22.390	21.864	16.868	19.267	19.066	
		Median	127.00	-0.50	129.50	0.00	129.00	-0.50	

Baseline is the Treatment Visit 1 measurement performed pre-injection.

Output ID: t-vschg-saf 04JUN20 13:09

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)	
			6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change
Systolic Blood Pressure (mmHg)	Treatment Visit 4 injection -20 min	n	9	9	19	19	28	28
		Mean	126.22	-8.00	131.16	-2.32	129.57	-4.14
		SD	9.189	22.886	15.917	16.138	14.122	18.334
		Median	126.00	-4.00	132.00	-3.00	130.00	-3.50
		Q1	117.00	+23.00	124.00	-17.00	119.50	-18.00
		Q3	134.00	15.00	141.00	12.00	138.00	13.00
		Min	115.0	-48.0	93.0	-26.0	93.0	-48.0
		Max	139.0	19.0	162.0	31.0	162.0	31.0
		n	9	9	19	19	28	28
		Mean	128.67	-5.78	138.47	5.00	135.32	1.54
	Treatment Visit 4 injection +30 min	SD	9.874	20.204	23.571	17.327	20.519	18.638
		Median	128.00	-2.00	132.00	0.00	132.00	-1.50
		Q1	121.00	-19.00	126.00	-5.00	125.50	-6.00
		Q3	134.00	13.00	143.00	19.00	141.00	15.50
		Min	116.0	-45.0	107.0	-31.0	107.0	-45.0
		Max	145.0	17.0	224.0	36.0	224.0	36.0
		n	10	10	19	19	29	29
		Mean	128.10	-5.00	135.42	1.95	132.90	-0.45
		SD	9.780	21.406	23.284	16.998	19.794	18.556
		Median	128.00	-0.50	131.00	2.00	131.00	0.00

Baseline is the Treatment Visit 1 measurement performed pre-injection.

Output ID: t-vschg-saf 04JUN20 13:09

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall	
			6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change
Systolic Blood Pressure (mmHg)	Follow-up Month 3	n	1	1	0	0	1	1
		Mean	111.00	-10.00			111.00	-10.00
		SD	NE	NE			NE	NE
		Median	111.00	-10.00			111.00	-10.00
		Q1	111.00	-10.00			111.00	-10.00
		Q3	111.00	-10.00			111.00	-10.00
		Min	111.0	-10.0			111.0	-10.0
		Max	111.0	-10.0			111.0	-10.0
		n	0	0	1	1	1	1
		Mean	137.00	137.00	-8.00	137.00	137.00	-8.00
Diastolic Blood Pressure (mmHg)	Follow-up Month 12	SD	NE	NE			NE	NE
		Median	137.00	137.00	-8.00	137.00	137.00	-8.00
		Q1	137.00	137.00	-8.00	137.00	137.00	-8.00
		Q3	137.00	137.00	-8.00	137.00	137.00	-8.00
		Min	137.0	137.0	-8.0	137.0	137.0	-8.0
		Max	137.0	137.0	-8.0	137.0	137.0	-8.0
		n	23	41			64	
		Mean	72.39	75.71			74.52	
		SD	15.162	9.239			11.707	
		Median	71.00	75.00			75.00	

Baseline is the Treatment Visit 1 measurement performed pre-injection.

Output ID: t-vschg-saf 04JUN20 13:09

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)	
			6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change
Diastolic Blood Pressure (mmHg)	Treatment Visit 1 injection +30 min	n	23	23	41	41	64	64
		Mean	70.74	-1.65	76.05	0.34	74.14	-0.38
		SD	9.965	10.709	9.997	6.413	10.234	8.191
		Median	69.00	0.00	75.00	0.00	73.00	0.00
		Q1	64.00	-6.00	71.00	-3.00	67.50	-4.00
		Q3	76.00	6.00	81.00	4.00	80.50	4.50
		Min	55.0	-34.0	57.0	-15.0	55.0	-31.0
		Max	92.0	16.0	101.0	13.0	101.0	16.0
		n	23	23	41	41	64	64
		Mean	69.83	-2.57	74.93	-0.78	73.09	-1.42
	Treatment Visit 1 injection +60 min	SD	10.008	11.377	9.483	9.358	9.907	10.077
		Median	68.00	-1.00	73.00	1.00	71.50	0.00
		Q1	65.00	-6.00	68.00	-5.00	67.00	-6.00
		Q3	75.00	4.00	82.00	4.00	79.00	4.00
		Min	51.0	-36.0	54.0	-26.0	51.0	-36.0
		Max	97.0	18.0	95.0	24.0	97.0	24.0
		n	18	18	38	38	56	56
		Mean	71.83	-2.78	77.18	0.68	75.46	-0.43
		SD	10.280	13.632	10.996	9.456	10.971	10.966
		Median	69.00	1.00	76.00	-1.00	75.00	0.00
	Treatment Visit 2 injection -20 min	Q1	64.00	-6.00	71.00	-6.00	67.50	-6.00
		Q3	79.00	5.00	82.00	5.00	81.00	5.00
		Min	56.0	-46.0	58.0	-17.0	56.0	-46.0
		Max	91.0	13.0	107.0	27.0	107.0	27.0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)	
			6.0 GBq (N=23)	Value	Change	Value	Change	Value
Diastolic Blood Pressure (mmHg)	Treatment Visit 2 injection +30 min	n	16	16	36	36	52	52
		Mean	69.88	-4.31	79.28	2.81	76.38	0.62
		SD	10.072	12.611	11.884	10.698	12.082	11.676
		Median	70.00	-1.00	80.50	2.00	79.50	0.00
		Q1	62.00	-7.00	70.50	-4.00	69.50	-5.00
	Treatment Visit 2 injection +60 min	Q3	80.50	2.50	84.50	7.00	83.00	5.50
		Min	52.0	-42.0	59.0	-12.0	52.0	-42.0
		Max	83.0	14.0	112.0	48.0	112.0	48.0
		n	18	18	38	38	56	56
		Mean	70.50	-4.11	76.76	0.26	74.75	-1.14
Treatment Visit 3 injection -20 min	Treatment Visit 3 injection -20 min	SD	12.277	14.883	11.945	9.742	12.300	11.686
		Median	72.00	-1.50	73.00	-2.00	73.00	-2.00
		Q1	63.00	-8.00	68.00	-6.00	67.00	-6.50
		Q3	82.00	4.00	84.00	5.00	83.50	5.00
		Min	42.0	-50.0	56.0	-15.0	42.0	-50.0
	Treatment Visit 3 injection -20 min	Max	87.0	18.0	115.0	27.0	115.0	27.0
		n	14	14	23	23	37	37
		Mean	73.36	-2.57	75.52	0.91	74.70	-0.41
		SD	10.717	18.993	8.908	8.202	9.545	13.202
		Median	74.00	-1.00	74.00	-1.00	74.00	-1.00

Baseline is the Treatment Visit 1 measurement performed pre-injection.

Output ID: t-vschg-saf 04JUN20 13:09

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)	
			6.0 GBq (N=23)	Value	Change	Value	Change	Value
Diastolic Blood Pressure (mmHg)	Treatment Visit 3 injection +30 min	n	14	14	22	22	36	36
		Mean	72.79	-3.14	73.23	-0.91	73.06	-1.78
		SD	10.047	12.569	10.783	10.258	10.359	11.092
		Median	73.00	-2.00	74.00	-1.50	73.50	-1.50
		Q1	64.00	+10.00	65.00	-7.00	64.50	-8.50
		Q3	80.00	5.00	81.00	4.00	80.00	5.00
		Min	58.0	-29.0	55.0	-21.0	55.0	-29.0
		Max	94.0	20.0	99.0	22.0	99.0	22.0
		n	14	14	22	22	36	36
		Mean	68.86	-7.07	75.95	1.36	73.19	-1.92
Diastolic Blood Pressure (mmHg)	Treatment Visit 3 injection +60 min	SD	10.265	15.420	10.878	11.471	11.066	13.589
		Median	69.50	-3.50	75.50	1.00	73.00	-1.00
		Q1	61.00	-12.00	68.00	-9.00	66.50	-9.50
		Q3	76.00	5.00	84.00	6.00	81.00	6.00
		Min	53.0	-50.0	60.0	-16.0	53.0	-50.0
		Max	84.0	10.0	99.0	35.0	99.0	35.0
		n	9	9	19	19	28	28
		Mean	71.67	-5.56	75.68	1.05	74.39	-1.07
		SD	14.509	18.311	11.672	10.255	12.524	13.391
		Median	76.00	3.00	76.00	1.00	76.00	1.50
Diastolic Blood Pressure (mmHg)	Treatment Visit 4 injection -20 min	Q1	63.00	-12.00	65.00	-11.00	64.00	-11.00
		Q3	81.00	8.00	85.00	8.00	84.50	8.00
		Min	44.0	-47.0	55.0	-12.0	44.0	-47.0
		Max	88.0	9.0	94.0	22.0	94.0	22.0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617 6.0 GBq (N=23)		Lu-PSMA-617 7.4 GBq (N=41)		Overall (N=64)	
			Value	Change	Value	Change	Value	Change
Diastolic Blood Pressure (mmHg)	Treatment Visit 4 injection +30 min	n	9	9	19	19	28	28
		Mean	69.00	-8.00	77.26	2.63	74.61	-0.79
		SD	11.136	18.303	10.697	9.535	11.334	13.617
		Median	74.00	-3.00	81.00	3.00	76.50	2.00
		Q1	62.00	-17.00	67.00	-7.00	66.00	-7.00
		Q3	76.00	4.00	84.00	10.00	83.00	7.50
		Min	50.0	-47.0	56.0	-15.0	50.0	-47.0
		Max	82.0	10.0	98.0	20.0	98.0	20.0
		n	10	10	19	19	29	29
		Mean	70.50	-4.80	77.68	3.05	75.21	0.34
	Treatment Visit 4 injection +60 min	SD	12.376	20.975	10.677	12.791	11.602	16.156
		Median	72.00	-3.00	78.00	1.00	76.00	0.00
		Q1	59.00	-12.00	70.00	-7.00	70.00	-7.00
		Q3	77.00	4.00	82.00	12.00	81.00	5.00
		Min	52.0	-52.0	60.0	-14.0	52.0	-52.0
		Max	91.0	31.0	102.0	38.0	102.0	38.0
		n	1	1	0	0	1	1
		Mean	69.00	9.00			69.00	9.00
		SD	NE	NE			NE	NE
		Median	69.00	9.00			69.00	9.00
	Follow-up Month 3	Q1	69.00	9.00			69.00	9.00
		Q3	69.00	9.00			69.00	9.00
		Min	69.0	9.0			69.0	9.0
		Max	69.0	9.0			69.0	9.0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617 6.0 GBq (N=23)		Lu-PSMA-617 7.4 GBq (N=41)		Overall (N=64)	
			Value	Change	Value	Change	Value	Change
Diastolic Blood Pressure (mmHg)	Follow-up Month 12	n	0	0	1	1	1	1
		Mean	83.00	5.00	83.00	5.00	83.00	5.00
		SD	NE	NE	NE	NE	NE	NE
		Median	83.00	5.00	83.00	5.00	83.00	5.00
		Q1	83.00	5.00	83.00	5.00	83.00	5.00
		Q3	83.00	5.00	83.00	5.00	83.00	5.00
		Min	83.0	5.0	83.0	5.0	83.0	5.0
		Max	83.0	5.0	83.0	5.0	83.0	5.0
Heart Rate (beats/min)	Baseline	n	23	41	41	64	64	64
		Mean	72.17	77.71	77.71	75.72	75.72	75.72
		SD	12.006	14.696	14.696	13.951	13.951	13.951
		Median	72.00	78.00	78.00	74.50	74.50	74.50
		Q1	64.00	64.00	64.00	64.00	64.00	64.00
		Q3	83.00	87.00	87.00	86.50	86.50	86.50
		Min	54.0	56.0	56.0	54.0	54.0	54.0
		Max	96.0	112.0	112.0	112.0	112.0	112.0
Treatment Visit 1 injection +30 min	Treatment Visit 1 injection +30 min	n	23	23	41	41	64	64
		Mean	71.96	-0.22	74.15	-3.56	73.36	-2.36
		SD	16.103	11.677	15.977	9.333	15.930	10.273
		Median	68.00	-2.00	70.00	-5.00	70.00	-4.00
		Q1	61.00	-7.00	63.00	-8.00	62.00	-7.00
		Q3	80.00	4.00	82.00	3.00	81.50	3.00
		Min	51.0	-22.0	52.0	-34.0	51.0	-34.0
		Max	121.0	34.0	115.0	20.0	121.0	34.0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)
			6.0 GBq (N=23)	Value	Change	Value	
Heart Rate (beats/min)	Treatment Visit 1 injection +60 min	n	23	23	41	41	64
		Mean	72.43	0.26	73.93	-3.78	73.39
		SD	11.874	10.498	14.873	9.756	13.792
		Median	74.00	0.00	73.00	-4.00	73.50
		Q1	66.00	-6.00	62.00	-8.00	62.00
		Q3	80.00	4.00	83.00	2.00	81.50
		Min	50.0	-20.0	53.0	-35.0	50.0
		Max	95.0	31.0	110.0	17.0	110.0
		n	18	18	38	38	56
		Mean	75.11	1.06	77.68	1.24	76.86
	Treatment Visit 2 injection -20 min	SD	13.328	14.501	16.277	8.358	15.317
		Median	71.00	3.50	75.50	-0.50	73.00
		Q1	66.00	-9.00	65.00	-4.00	65.50
		Q3	77.00	7.00	90.00	7.00	85.50
		Min	61.0	-26.0	54.0	-13.0	54.0
		Max	105.0	33.0	138.0	26.0	138.0
		n	17	17	36	36	53
		Mean	71.06	-2.24	75.14	-1.44	73.83
		SD	11.750	13.636	17.273	11.619	15.716
		Median	75.00	3.00	72.50	-2.50	73.00
	Treatment Visit 2 injection +30 min	Q1	62.00	-5.00	62.50	-7.00	62.00
		Q3	79.00	6.00	83.50	6.50	81.00
		Min	52.0	-37.0	54.0	-29.0	52.0
		Max	91.0	14.0	135.0	23.0	135.0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)
			6.0 GBq (N=23)	Value	Change	Value	
Heart Rate (beats/min)	Treatment Visit 2 injection +60 min	n	18	18	38	38	56
		Mean	70.22	-3.83	73.68	-2.76	72.57
		SD	11.579	12.477	16.586	11.917	15.138
		Median	74.50	2.00	72.50	-2.00	73.00
		Q1	60.00	-7.00	62.00	-9.00	61.50
		Q3	77.00	4.00	83.00	5.00	80.00
		Min	52.0	-36.0	52.0	-35.0	52.0
		Max	89.0	11.0	129.0	28.0	129.0
		n	14	14	23	23	37
		Mean	73.07	-0.36	76.48	1.74	75.19
	Treatment Visit 3 injection -20 min	SD	10.845	10.051	15.687	10.024	13.988
		Median	72.50	0.50	78.00	2.00	73.00
		Q1	64.00	-4.00	63.00	-4.00	64.00
		Q3	79.00	4.00	88.00	8.00	85.00
		Min	59.0	-24.0	54.0	-16.0	54.0
		Max	94.0	15.0	107.0	24.0	107.0
		n	14	14	22	22	36
		Mean	67.71	-5.71	73.45	-0.32	71.22
		SD	10.291	12.572	16.572	12.996	14.566
		Median	66.50	-2.50	68.00	1.00	68.00
	Treatment Visit 3 injection +30 min	Q1	61.00	-18.00	60.00	-7.00	60.50
		Q3	75.00	5.00	89.00	8.00	80.50
		Min	52.0	-28.0	46.0	-36.0	46.0
		Max	88.0	11.0	108.0	29.0	108.0
		n	14	14	22	22	36
		Mean	67.71	-5.71	73.45	-0.32	71.22
		SD	10.291	12.572	16.572	12.996	14.566
		Median	66.50	-2.50	68.00	1.00	68.00
		Q1	61.00	-18.00	60.00	-7.00	60.50
		Q3	75.00	5.00	89.00	8.00	80.50
		Min	52.0	-28.0	46.0	-36.0	46.0
		Max	88.0	11.0	108.0	29.0	108.0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)
			6.0 GBq (N=23)	Value	Change	Value	
Heart Rate (beats/min)	Treatment Visit 3 injection +60 min	n	14	14	22	22	36
		Mean	67.57	-5.86	70.73	-3.50	69.50
		SD	7.842	11.002	16.539	16.047	13.762
		Median	69.00	-4.50	66.50	-1.00	67.50
		Q1	63.00	+15.00	60.00	-11.00	60.50
		Q3	73.00	2.00	82.00	4.00	75.00
		Min	49.0	-27.0	48.0	-43.0	48.0
		Max	79.0	11.0	99.0	30.0	99.0
		n	9	9	19	19	28
		Mean	69.56	-7.56	73.58	-2.26	72.29
	Treatment Visit 4 injection -20 min	SD	8.762	12.320	15.987	19.980	14.029
		Median	68.00	-12.00	72.00	1.00	70.50
		Q1	65.00	-20.00	60.00	-6.00	61.50
		Q3	76.00	5.00	83.00	7.00	80.00
		Min	58.0	-21.0	50.0	-43.0	50.0
		Max	83.0	6.0	110.0	41.0	110.0
		n	10	10	19	19	29
		Mean	65.80	-9.20	71.05	-4.79	69.24
		SD	10.871	16.798	18.665	22.062	16.383
		Median	64.00	-10.50	66.00	-6.00	65.00
	Treatment Visit 4 injection +30 min	Q1	60.00	-25.00	59.00	-18.00	60.00
		Q3	65.00	8.00	79.00	3.00	76.00
		Min	53.0	-31.0	48.0	-39.0	48.0
		Max	87.0	10.0	114.0	39.0	114.0
		n	10	10	19	19	29
		Mean	65.80	-9.20	71.05	-4.79	69.24
		SD	10.871	16.798	18.665	22.062	16.383
		Median	64.00	-10.50	66.00	-6.00	65.00
		Q1	60.00	-25.00	59.00	-18.00	60.00
		Q3	65.00	8.00	79.00	3.00	76.00

Baseline is the Treatment Visit 1 measurement performed pre-injection.

Output ID: t-vschg-saf 04JUN20 13:09

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall		
			6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change	(N=64)
Heart Rate (beats/min)	Treatment Visit 4 injection +60 min	n	10	10	19	19	29	29	
		Mean	67.10	-7.90	69.95	-5.89	68.97	-6.59	
		SD	13.186	18.138	18.834	23.468	16.906	21.465	
		Median	65.50	-11.00	64.00	-6.00	65.00	-7.00	
		Q1	60.00	-21.00	56.00	-20.00	57.00	-20.00	
		Q3	68.00	11.00	78.00	3.00	78.00	6.00	
		Min	48.0	-33.0	49.0	-53.0	48.0	-53.0	
		Max	90.0	16.0	110.0	35.0	110.0	35.0	
		n	1	1	0	0	1	1	
		Mean	58.00	4.00			58.00	4.00	
Follow-up Month 3	Follow-up Month 3	SD	NE	NE			NE	NE	
		Median	58.00	4.00			58.00	4.00	
		Q1	58.00	4.00			58.00	4.00	
		Q3	58.00	4.00			58.00	4.00	
		Min	58.0	4.0			58.0	4.0	
		Max	58.0	4.0			58.0	4.0	
		n	0	0	1	1	1	1	
		Mean			71.00	-7.00	71.00	-7.00	
		SD			NE	NE	NE	NE	
		Median			71.00	-7.00	71.00	-7.00	
Follow-up Month 12	Follow-up Month 12	Q1			71.00	-7.00	71.00	-7.00	
		Q3			71.00	-7.00	71.00	-7.00	
		Min			71.0	-7.0	71.0	-7.0	
		Max			71.0	-7.0	71.0	-7.0	

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)
			6.0 GBq (N=23)	Value	Change	Value	
Respiratory Rate (breaths/min)	Baseline	n	23			41	64
		Mean	17.30			17.34	17.33
		SD	2.704			3.191	3.003
		Median	16.00			16.00	16.00
		Q1	16.00			16.00	16.00
		Q3	18.00			19.00	18.00
		Min	14.0			11.0	11.0
		Max	28.0			26.0	28.0
Treatment Visit 1 injection +30 min		n	23	23	41	41	64
		Mean	17.17	-0.13	17.37	0.02	17.30
		SD	1.875	2.455	3.072	2.475	2.688
		Median	17.00	0.00	17.00	0.00	17.00
		Q1	16.00	-1.00	16.00	-1.00	16.00
		Q3	18.00	1.00	19.00	1.00	19.00
		Min	14.0	-8.0	10.0	-6.0	10.0
		Max	20.0	4.0	26.0	7.0	26.0
Treatment Visit 1 injection +60 min		n	23	23	41	41	64
		Mean	17.74	0.43	17.34	0.00	17.48
		SD	2.911	2.873	3.504	2.608	3.285
		Median	17.00	0.00	17.00	0.00	17.00
		Q1	16.00	-1.00	16.00	-1.00	16.00
		Q3	21.00	2.00	19.00	2.00	19.50
		Min	12.0	-6.0	12.0	-6.0	12.0
		Max	24.0	6.0	27.0	5.0	27.0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)	
			6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change
Respiratory Rate (breaths/min)	Treatment Visit 2 injection -20 min	n	18	18	38	38	56	56
		Mean	16.28	-1.17	17.00	-0.08	16.77	-0.43
		SD	2.630	4.076	2.885	3.412	2.803	3.637
		Median	16.00	-0.50	16.00	0.00	16.00	0.00
		Q1	15.00	-3.00	16.00	-2.00	15.00	-2.50
		Q3	18.00	1.00	18.00	3.00	18.00	2.00
		Min	11.0	-14.0	10.0	-7.0	10.0	-11.0
		Max	24.0	8.0	27.0	7.0	27.0	8.0
	Treatment Visit 2 injection +30 min	n	17	17	36	36	53	53
		Mean	16.82	-0.59	16.83	-0.33	16.83	-0.42
		SD	3.972	5.269	2.501	2.798	3.011	3.718
		Median	16.00	0.00	16.00	0.00	16.00	0.00
		Q1	14.00	-4.00	16.00	-3.00	16.00	-3.00
		Q3	21.00	4.00	18.00	1.00	18.00	1.00
		Min	9.0	-12.0	12.0	-6.0	9.0	-12.0
		Max	22.0	6.0	23.0	8.0	23.0	8.0
	Treatment Visit 2 injection +60 min	n	18	18	38	38	56	56
		Mean	17.39	-0.06	16.89	-0.18	17.05	-0.14
		SD	3.398	4.721	2.817	3.439	2.993	3.854
		Median	17.50	0.00	16.00	0.00	16.00	0.00
		Q1	15.00	-1.00	16.00	-2.00	15.50	-2.00
		Q3	20.00	4.00	18.00	1.00	18.00	2.00
		Min	11.0	-10.0	12.0	-7.0	11.0	-10.0
		Max	24.0	8.0	28.0	9.0	28.0	9.0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)	
			6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change
Respiratory Rate (breaths/min)	Treatment Visit 3 injection -20 min	n	14	14	23	23	37	37
		Mean	17.21	0.00	17.43	-0.17	17.35	-0.11
		SD	3.534	4.506	2.889	3.576	3.102	3.893
		Median	17.50	1.00	17.00	0.00	17.00	1.00
		Q1	16.00	-2.00	16.00	-2.00	16.00	-2.00
		Q3	18.00	2.00	19.00	3.00	18.00	2.00
		Min	10.0	-8.0	10.0	-8.0	10.0	-8.0
		Max	26.0	10.0	26.0	5.0	26.0	10.0
		n	14	14	23	23	37	37
		Mean	15.79	-1.43	17.30	-0.30	16.73	-0.73
	Treatment Visit 3 injection +30 min	SD	2.778	4.108	2.619	3.759	2.745	3.878
		Median	16.00	-0.50	18.00	0.00	17.00	0.00
		Q1	14.00	-3.00	16.00	-2.00	16.00	-2.00
		Q3	18.00	2.00	19.00	2.00	18.00	2.00
		Min	10.0	-10.0	11.0	-10.0	10.0	-10.0
		Max	19.0	3.0	23.0	7.0	23.0	7.0
		n	14	14	22	22	36	36
		Mean	15.50	-1.71	17.41	-0.27	16.67	-0.83
		SD	2.473	4.714	2.482	4.049	2.619	4.313
		Median	15.50	0.00	17.50	0.00	16.50	0.00
	Treatment Visit 3 injection +60 min	Q1	14.00	-3.00	16.00	-3.00	15.00	-3.00
		Q3	18.00	1.00	19.00	2.00	18.50	1.50
		Min	10.0	-15.0	12.0	-10.0	10.0	-15.0
		Max	19.0	3.0	23.0	8.0	23.0	8.0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617 6.0 GBq (N=23)		Lu-PSMA-617 7.4 GBq (N=41)		Overall (N=64)	
			Value	Change	Value	Change	Value	Change
Respiratory Rate (breaths/min)	Treatment Visit 4 injection -20 min	n	9	9	19	19	28	28
		Mean	15.44	-2.22	17.42	-0.16	16.79	-0.82
		SD	2.068	5.585	3.948	4.879	3.542	5.107
		Median	16.00	0.00	18.00	0.00	16.50	0.00
		Q1	14.00	-3.00	15.00	-6.00	14.50	-4.50
		Q3	16.00	0.00	20.00	3.00	18.50	3.00
		Min	12.0	-15.0	10.0	-10.0	10.0	-15.0
		Max	18.0	4.0	25.0	9.0	25.0	9.0
		n	10	10	19	19	29	29
		Mean	16.80	-0.90	17.11	-0.47	17.00	-0.62
	Treatment Visit 4 injection +30 min	SD	3.120	3.604	3.494	4.195	3.317	3.941
		Median	16.00	0.00	18.00	0.00	18.00	0.00
		Q1	15.00	-3.00	14.00	-4.00	15.00	-3.00
		Q3	18.00	0.00	20.00	3.00	19.00	2.00
		Min	12.0	-6.0	11.0	-10.0	11.0	-10.0
		Max	22.0	6.0	23.0	7.0	23.0	7.0
		n	10	10	19	19	29	29
		Mean	16.60	-1.10	17.84	0.26	17.41	-0.21
		SD	2.914	5.238	3.579	4.344	3.365	4.624
		Median	16.00	-0.50	18.00	2.00	17.00	0.00
	Treatment Visit 4 injection +60 min	Q1	15.00	-3.00	16.00	-3.00	16.00	-3.00
		Q3	17.00	2.00	19.00	3.00	19.00	2.00
		Min	12.0	-12.0	12.0	-9.0	12.0	-12.0
		Max	22.0	6.0	26.0	8.0	26.0	8.0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617 6.0 GBq (N=23)		Lu-PSMA-617 7.4 GBq (N=41)		Overall (N=64)	
			Value	Change	Value	Change	Value	Change
Respiratory Rate (breaths/min)	Follow-up Month 3	n	1	1	0	0	1	1
		Mean	16.00	0.00			16.00	0.00
		SD	NE	NE			NE	NE
		Median	16.00	0.00			16.00	0.00
		Q1	16.00	0.00			16.00	0.00
		Q3	16.00	0.00			16.00	0.00
		Min	16.0	0.0			16.0	0.0
		Max	16.0	0.0			16.0	0.0
	Follow-up Month 12	n	0	0	1	1	1	1
		Mean			16.00	0.00	16.00	0.00
		SD			NE	NE	NE	NE
		Median			16.00	0.00	16.00	0.00
		Q1			16.00	0.00	16.00	0.00
		Q3			16.00	0.00	16.00	0.00
		Min			16.0	0.0	16.0	0.0
		Max			16.0	0.0	16.0	0.0
Temperature (C)	Baseline	n	22		41		63	
		Mean	36.38		36.44		36.42	
		SD	0.440		0.435		0.434	
		Median	36.35		36.40		36.40	
		Q1	36.00		36.10		36.10	
		Q3	36.60		36.70		36.70	
		Min	35.6		35.6		35.6	
		Max	37.1		37.5		37.5	

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)
			6.0 GBq (N=23)	Value	Change	Value	
Temperature (C)	Treatment Visit 1 injection +30 min	n	22	22		40	62
		Mean	36.33	-0.05	36.48	0.05	36.43
		SD	0.511	0.349	0.477	0.406	0.491
		Median	36.30	0.00	36.50	0.00	36.50
		Q1	35.90	-0.20	36.10	-0.10	36.00
		Q3	36.80	0.20	36.85	0.20	36.80
		Min	35.4	-0.7	35.4	-0.9	35.4
		Max	37.1	0.6	37.5	1.1	37.5
		n	22	22		40	62
		Mean	36.41	0.04	36.51	0.07	36.47
Temperature (C)	Treatment Visit 1 injection +60 min	SD	0.461	0.282	0.491	0.436	0.479
		Median	36.30	0.00	36.55	0.00	36.40
		Q1	36.20	-0.10	36.25	-0.15	36.20
		Q3	36.90	0.20	36.85	0.25	36.90
		Min	35.6	-0.5	35.3	-0.9	35.3
		Max	37.1	0.6	37.5	1.1	37.5
		n	17	17		38	55
		Mean	36.45	0.05	36.44	0.03	36.44
		SD	0.453	0.756	0.464	0.530	0.456
		Median	36.40	0.00	36.35	0.00	36.40
Temperature (C)	Treatment Visit 2 injection -20 min	Q1	36.20	-0.60	36.10	-0.40	36.10
		Q3	36.40	0.40	36.70	0.30	36.70
		Min	35.5	-0.9	35.6	-0.7	35.5
		Max	37.4	1.8	37.6	1.6	37.6
		n	17	17		38	55
		Mean	36.45	0.05	36.44	0.03	36.44
		SD	0.453	0.756	0.464	0.530	0.456
		Median	36.40	0.00	36.35	0.00	36.40
		Q1	36.20	-0.60	36.10	-0.40	36.10
		Q3	36.40	0.40	36.70	0.30	36.70

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617 6.0 GBq (N=23)		Lu-PSMA-617 7.4 GBq (N=41)		Overall (N=64)	
			Value	Change	Value	Change	Value	Change
Temperature (C)	Treatment Visit 2 injection +30 min	n	15	15	35	35	50	50
		Mean	36.42	0.03	36.43	0.01	36.42	0.02
		SD	0.492	0.687	0.492	0.565	0.487	0.597
		Median	36.20	0.00	36.40	-0.10	36.30	-0.05
		Q1	36.10	-0.50	36.10	-0.40	36.10	-0.40
		Q3	36.60	0.50	36.90	0.30	36.80	0.30
		Min	36.0	-1.0	35.4	-1.0	35.4	-1.0
		Max	37.5	1.4	37.2	1.4	37.5	1.4
		n	17	17	37	37	54	54
		Mean	36.36	-0.04	36.39	-0.01	36.38	-0.02
	Treatment Visit 2 injection +60 min	SD	0.439	0.649	0.493	0.530	0.473	0.564
		Median	36.30	-0.20	36.40	0.00	36.40	-0.05
		Q1	36.10	-0.50	36.10	-0.40	36.10	-0.50
		Q3	36.40	0.40	36.70	0.20	36.70	0.40
		Min	35.7	-0.9	34.9	-0.9	34.9	-0.9
		Max	37.2	1.2	37.2	1.2	37.2	1.2
		n	13	13	23	23	36	36
		Mean	36.32	-0.03	36.49	-0.01	36.43	-0.02
		SD	0.404	0.731	0.358	0.587	0.379	0.632
		Median	36.40	-0.10	36.50	-0.10	36.40	-0.10
	Treatment Visit 3 injection -20 min	Q1	36.00	-0.60	36.20	-0.50	36.20	-0.50
		Q3	36.50	0.50	36.80	0.40	36.70	0.40
		Min	35.6	-1.2	35.9	-1.1	35.6	-1.2
		Max	37.1	1.1	37.2	1.5	37.2	1.5

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)	
			6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change
Temperature (C)	Treatment Visit 3 injection +30 min	n	13	13	22	22	35	35
		Mean	36.44	0.09	36.55	0.06	36.51	0.07
		SD	0.621	0.930	0.410	0.604	0.493	0.729
		Median	36.60	-0.10	36.45	0.00	36.50	0.00
		Q1	36.00	-0.60	36.30	-0.40	36.30	-0.40
		Q3	36.90	0.90	36.70	0.30	36.90	0.60
		Min	35.2	-1.3	35.8	-1.2	35.2	-1.3
		Max	37.1	1.4	37.5	1.6	37.5	1.6
		n	12	12	22	22	34	34
		Mean	36.29	-0.12	36.52	0.01	36.44	-0.04
	Treatment Visit 3 injection +60 min	SD	0.417	0.699	0.385	0.570	0.405	0.611
		Median	36.35	-0.35	36.45	-0.10	36.40	-0.20
		Q1	36.00	-0.60	36.30	-0.40	36.20	-0.40
		Q3	36.45	0.45	36.80	0.40	36.80	0.40
		Min	35.6	-1.2	35.7	-1.2	35.6	-1.2
		Max	37.1	1.1	37.2	1.4	37.2	1.4
		n	9	9	19	19	28	28
		Mean	36.30	-0.07	36.49	-0.06	36.43	-0.06
		SD	0.394	0.654	0.266	0.510	0.318	0.548
		Median	36.30	-0.30	36.60	0.00	36.50	0.00
	Treatment Visit 4 injection -20 min	Q1	36.00	-0.50	36.30	-0.60	36.30	-0.50
		Q3	36.50	0.10	36.60	0.40	36.60	0.30
		Min	35.7	-0.8	35.9	-0.9	35.7	-0.9
		Max	37.0	1.4	36.9	0.7	37.0	1.4

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617		Lu-PSMA-617		Overall (N=64)	
			6.0 GBq (N=23)	Value	Change	7.4 GBq (N=41)	Value	Change
Temperature (C)	Treatment Visit 4 injection +30 min	n	10	10	18	18	28	28
		Mean	36.40	-0.03	36.46	-0.10	36.44	-0.08
		SD	0.455	0.643	0.355	0.552	0.386	0.575
		Median	36.55	-0.10	36.55	-0.15	36.55	-0.15
		Q1	36.30	-0.40	36.30	-0.60	36.30	-0.50
		Q3	36.70	0.20	36.70	0.20	36.70	0.20
		Min	35.3	-0.9	35.7	-1.0	35.3	-1.0
		Max	36.8	1.2	36.9	0.8	36.9	1.2
		n	10	10	18	18	28	28
		Mean	36.45	0.02	36.59	0.04	36.54	0.03
	Treatment Visit 4 injection +60 min	SD	0.484	0.681	0.353	0.560	0.401	0.593
		Median	36.55	0.00	36.60	0.10	36.60	0.10
		Q1	36.30	-0.50	36.50	-0.50	36.35	-0.50
		Q3	36.80	0.30	36.90	0.40	36.80	0.35
		Min	35.3	-0.9	35.8	-1.0	35.3	-1.0
		Max	36.9	1.3	37.1	0.8	37.1	1.3
		n	1	1	0	0	1	1
		Mean	36.70	0.70			36.70	0.70
		SD	NE	NE			NE	NE
		Median	36.70	0.70			36.70	0.70
	Follow-up Month 3	Q1	36.70	0.70			36.70	0.70
		Q3	36.70	0.70			36.70	0.70
		Min	36.7	0.7			36.7	0.7
		Max	36.7	0.7			36.7	0.7

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.1.1
Change from Baseline Vital Sign Results
Safety Population

Parameter	Analysis Visit Timepoint	Statistics	Lu-PSMA-617 6.0 GBq (N=23)		Lu-PSMA-617 7.4 GBq (N=41)		Overall (N=64)	
			Value	Change	Value	Change	Value	Change
Temperature (C)	Follow-up Month 12	n	0	0	1	1	1	1
		Mean	36.80	0.20	36.80	0.20	36.80	0.20
		SD	NE	NE	NE	NE	NE	NE
		Median	36.80	0.20	36.80	0.20	36.80	0.20
		Q1	36.80	0.20	36.80	0.20	36.80	0.20
		Q3	36.80	0.20	36.80	0.20	36.80	0.20
		Min	36.8	0.2	36.8	0.2	36.8	0.2
		Max	36.8	0.2	36.8	0.2	36.8	0.2

Baseline is the Treatment Visit 1 measurement performed pre-injection.

Output ID: t-vschg-saf 04JUN20 13:09

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Table 14.3.4.2.1
Transition Table from Baseline for Vital Signs
Safety Population

Parameter	Analysis Visit Timepoint	Change from Baseline Category	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Systolic Blood Pressure (mmHg)	Treatment Visit 1 injection +30 min	n	23	41	64
		Decrease >40	0	0	0
		Decrease >20-40	2 (8.7)	2 (4.9)	4 (6.3)
		Difference (+/-) 0-20	18 (78.3)	37 (90.2)	55 (85.9)
		Increase >20-40	3 (13.0)	2 (4.9)	5 (7.8)
	Treatment Visit 1 injection +60 min	n	23	41	64
		Decrease >40	0	0	0
		Decrease >20-40	2 (8.7)	0	2 (3.1)
		Difference (+/-) 0-20	19 (82.6)	35 (85.4)	54 (84.4)
		Increase >20-40	2 (8.7)	6 (14.6)	8 (12.5)
	Treatment Visit 2 injection -20 min	n	18	38	56
		Decrease >40	0	2 (5.3)	2 (3.6)
		Decrease >20-40	3 (16.7)	1 (2.6)	4 (7.1)
		Difference (+/-) 0-20	13 (72.2)	32 (84.2)	45 (80.4)
		Increase >20-40	2 (11.1)	3 (7.9)	5 (8.9)
	Treatment Visit 2 injection +30 min	n	16	36	52
		Decrease >40	0	2 (5.6)	2 (3.8)
		Decrease >20-40	2 (12.5)	1 (2.8)	3 (5.8)
		Difference (+/-) 0-20	12 (75.0)	26 (72.2)	38 (73.1)
		Increase >20-40	2 (12.5)	7 (19.4)	9 (17.3)
		Increase >40	0	0	0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.2.1
Transition Table from Baseline for Vital Signs
Safety Population

Parameter	Analysis Visit Timepoint	Change from Baseline Category	Lu-PSMA-617 6.0 GBq (N=23)	Lu-PSMA-617 7.4 GBq (N=41)	Overall (N=64)
			n (%)	n (%)	n (%)
Systolic Blood Pressure (mmHg)	Treatment Visit 2 injection +60 min	n	18	38	56
		Decrease >40	1 (5.6)	1 (2.6)	2 (3.6)
		Decrease >20-40	1 (5.6)	1 (2.6)	2 (3.6)
		Difference (+/-) 0-20	13 (72.2)	31 (81.6)	44 (78.6)
		Increase >20-40	3 (16.7)	5 (13.2)	8 (14.3)
	Treatment Visit 3 injection -20 min	Increase >40	0	0	0
		n	14	23	37
		Decrease >40	1 (7.1)	0	1 (2.7)
		Decrease >20-40	2 (14.3)	3 (13.0)	5 (13.5)
		Difference (+/-) 0-20	11 (78.6)	20 (87.0)	31 (83.8)
	Treatment Visit 3 injection +30 min	Increase >20-40	0	0	0
		Increase >40	0	0	0
		n	14	22	36
		Decrease >40	1 (7.1)	0	1 (2.8)
		Decrease >20-40	2 (14.3)	3 (13.6)	5 (13.9)
	Treatment Visit 3 injection +60 min	Difference (+/-) 0-20	10 (71.4)	15 (68.2)	25 (69.4)
		Increase >20-40	1 (7.1)	4 (18.2)	5 (13.9)
		Increase >40	0	0	0
		n	14	22	36
		Decrease >40	1 (7.1)	0	1 (2.8)
		Decrease >20-40	1 (7.1)	2 (9.1)	3 (8.3)
		Difference (+/-) 0-20	11 (78.6)	17 (77.3)	28 (77.8)
		Increase >20-40	1 (7.1)	3 (13.6)	4 (11.1)
		Increase >40	0	0	0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.2.1
Transition Table from Baseline for Vital Signs
Safety Population

Parameter	Analysis Visit Timepoint	Change from Baseline Category	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Systolic Blood Pressure (mmHg)	Treatment Visit 4 injection -20 min	n	9	19	28
		Decrease >40	1 (11.1)	0	1 (3.6)
		Decrease >20-40	2 (22.2)	3 (15.8)	5 (17.9)
		Difference (+/-) 0-20	6 (66.7)	14 (73.7)	20 (71.4)
		Increase >20-40	0	2 (10.5)	2 (7.1)
	Treatment Visit 4 injection +30 min	n	9	19	28
		Decrease >40	1 (11.1)	0	1 (3.6)
		Decrease >20-40	1 (11.1)	1 (5.3)	2 (7.1)
		Difference (+/-) 0-20	7 (77.8)	14 (73.7)	21 (75.0)
		Increase >20-40	0	4 (21.1)	4 (14.3)
	Treatment Visit 4 injection +60 min	n	10	19	29
		Decrease >40	1 (10.0)	0	1 (3.4)
		Decrease >20-40	1 (10.0)	2 (10.5)	3 (10.3)
		Difference (+/-) 0-20	7 (70.0)	14 (73.7)	21 (72.4)
		Increase >20-40	1 (10.0)	3 (15.8)	4 (13.8)
	Follow-up Month 3	n	0	0	0
		Decrease >40	1	0	1
		Decrease >20-40	0	0	0
		Difference (+/-) 0-20	0	0	0
		Increase >20-40	0	0	0
		Increase >40	0	0	0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.2.1
Transition Table from Baseline for Vital Signs
Safety Population

Parameter	Analysis Visit Timepoint	Change from Baseline Category	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Systolic Blood Pressure (mmHg)	Follow-up Month 12	n	0	1	1
		Decrease >40	0	0	0
		Decrease >20-40	0	0	0
		Difference (+/-) 0-20	0	1 (100)	1 (100)
		Increase >20-40	0	0	0
		Increase >40	0	0	0
Diastolic Blood Pressure (mmHg)	Treatment Visit 1 injection +30 min	n	23	41	64
		Decrease >30	1 (4.3)	0	1 (1.6)
		Decrease >15-30	2 (8.7)	0	2 (3.1)
		Difference (+/-) 0-15	19 (82.6)	41 (100)	60 (93.8)
		Increase >15-30	1 (4.3)	0	1 (1.6)
		Increase >30	0	0	0
	Treatment Visit 1 injection +60 min	n	23	41	64
		Decrease >30	1 (4.3)	0	1 (1.6)
		Decrease >15-30	1 (4.3)	3 (7.3)	4 (6.3)
		Difference (+/-) 0-15	20 (87.0)	37 (90.2)	57 (89.1)
		Increase >15-30	1 (4.3)	1 (2.4)	2 (3.1)
		Increase >30	0	0	0
	Treatment Visit 2 injection -20 min	n	18	38	56
		Decrease >30	1 (5.6)	0	1 (1.8)
		Decrease >15-30	1 (5.6)	1 (2.6)	2 (3.6)
		Difference (+/-) 0-15	16 (88.9)	33 (86.8)	49 (87.5)
		Increase >15-30	0	4 (10.5)	4 (7.1)
		Increase >30	0	0	0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.2.1
Transition Table from Baseline for Vital Signs
Safety Population

Parameter	Analysis Visit Timepoint	Change from Baseline Category	Lu-PSMA-617 6.0 GBq (N=23)	Lu-PSMA-617 7.4 GBq (N=41)	Overall (N=64)
			n (%)	n (%)	n (%)
Diastolic Blood Pressure (mmHg)	Treatment Visit 2 injection +30 min	n	16	36	52
		Decrease >30	1 (6.3)	0	1 (1.9)
		Decrease >15-30	1 (6.3)	0	1 (1.9)
		Difference (+/-) 0-15	14 (87.5)	34 (94.4)	48 (92.3)
		Increase >15-30	0	1 (2.8)	1 (1.9)
	Treatment Visit 2 injection +60 min	Increase >30	0	1 (2.8)	1 (1.9)
		n	18	38	56
		Decrease >30	1 (5.6)	0	1 (1.8)
		Decrease >15-30	1 (5.6)	0	1 (1.8)
		Difference (+/-) 0-15	15 (83.3)	35 (92.1)	50 (89.3)
	Treatment Visit 3 injection -20 min	Increase >15-30	1 (5.6)	3 (7.9)	4 (7.1)
		Increase >30	0	0	0
		n	14	23	37
		Decrease >30	1 (7.1)	0	1 (2.7)
		Decrease >15-30	1 (7.1)	0	1 (2.7)
	Treatment Visit 3 injection +30 min	Difference (+/-) 0-15	11 (78.6)	22 (95.7)	33 (89.2)
		Increase >15-30	0	1 (4.3)	1 (2.7)
		Increase >30	1 (7.1)	0	1 (2.7)
		n	14	22	36
		Decrease >30	0	0	0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.2.1
Transition Table from Baseline for Vital Signs
Safety Population

Parameter	Analysis Visit Timepoint	Change from Baseline Category	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Diastolic Blood Pressure (mmHg)	Treatment Visit 3 injection +60 min	n	14	22	36
		Decrease >30	1 (7.1)	0	1 (2.8)
		Decrease >15-30	2 (14.3)	1 (4.5)	3 (8.3)
		Difference (+/-) 0-15	11 (78.6)	19 (86.4)	30 (83.3)
		Increase >15-30	0	1 (4.5)	1 (2.8)
	Treatment Visit 4 injection -20 min	Increase >30	0	1 (4.5)	1 (2.8)
		n	9	19	28
		Decrease >30	1 (11.1)	0	1 (3.6)
		Decrease >15-30	0	0	0
		Difference (+/-) 0-15	8 (88.9)	17 (89.5)	25 (89.3)
Treatment Visit 4 injection +30 min	Treatment Visit 4 injection +30 min	Increase >15-30	0	2 (10.5)	2 (7.1)
		Increase >30	0	0	0
		n	9	19	28
		Decrease >30	1 (11.1)	0	1 (3.6)
		Decrease >15-30	2 (22.2)	0	2 (7.1)
	Treatment Visit 4 injection +60 min	Difference (+/-) 0-15	6 (66.7)	17 (89.5)	23 (82.1)
		Increase >15-30	0	2 (10.5)	2 (7.1)
		Increase >30	0	0	0
		n	10	19	29
		Decrease >30	1 (10.0)	0	1 (3.4)

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.2.1
Transition Table from Baseline for Vital Signs
Safety Population

Parameter	Analysis Visit Timepoint	Change from Baseline Category	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Diastolic Blood Pressure (mmHg)	Follow-up Month 3	n	1	0	1 0
		Decrease >30	0	0	0 0
		Decrease >15-30	0	0	0 0
		Difference (+/-) 0-15	1 (100)	0	1 (100)
		Increase >15-30	0	0	0 0
	Follow-up Month 12	Increase >30	0	0	0 0
		Decrease >30	0	1	1 0
		Decrease >15-30	0	0	0 0
		Difference (+/-) 0-15	0	1 (100)	1 (100)
		Increase >15-30	0	0	0 0
Heart Rate (beats/min)	Treatment Visit 1 injection +30 min	n	23	41	64 1 (1.6)
		Decrease >30	0	1 (2.4)	3 (4.7)
		Decrease >15-30	1 (4.3)	2 (4.9)	56 (87.5)
		Difference (+/-) 0-15	20 (87.0)	36 (87.8)	3 (4.7)
		Increase >15-30	1 (4.3)	2 (4.9)	1 (1.6)
	Treatment Visit 1 injection +60 min	Increase >30	1 (4.3)	0	1 (1.6)
		n	23	41	64 1 (1.6)
		Decrease >30	0	1 (2.4)	3 (4.7)
		Decrease >15-30	1 (4.3)	2 (4.9)	58 (90.6)
		Difference (+/-) 0-15	21 (91.3)	37 (90.2)	1 (1.6)
		Increase >15-30	0	1 (2.4)	1 (1.6)
		Increase >30	1 (4.3)	0	1 (1.6)

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.2.1
Transition Table from Baseline for Vital Signs
Safety Population

Parameter	Analysis Visit Timepoint	Change from Baseline Category	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Heart Rate (beats/min)	Treatment Visit 2 injection -20 min	n	18	38	56
		Decrease >30	0	0	0
		Decrease >15-30	3 (16.7)	0	3 (5.4)
		Difference (+/-) 0-15	13 (72.2)	37 (97.4)	50 (89.3)
		Increase >15-30	1 (5.6)	1 (2.6)	2 (3.6)
		Increase >30	1 (5.6)	0	1 (1.8)
	Treatment Visit 2 injection +30 min	n	17	36	53
		Decrease >30	1 (5.9)	0	1 (1.9)
		Decrease >15-30	2 (11.8)	4 (11.1)	6 (11.3)
		Difference (+/-) 0-15	14 (82.4)	30 (83.3)	44 (83.0)
		Increase >15-30	0	2 (5.6)	2 (3.8)
		Increase >30	0	0	0
	Treatment Visit 2 injection +60 min	n	18	38	56
		Decrease >30	1 (5.6)	2 (5.3)	3 (5.4)
		Decrease >15-30	2 (11.1)	1 (2.6)	3 (5.4)
		Difference (+/-) 0-15	15 (83.3)	32 (84.2)	47 (83.9)
		Increase >15-30	0	3 (7.9)	3 (5.4)
		Increase >30	0	0	0
	Treatment Visit 3 injection -20 min	n	14	23	37
		Decrease >30	0	0	0
		Decrease >15-30	1 (7.1)	2 (8.7)	3 (8.1)
		Difference (+/-) 0-15	13 (92.9)	19 (82.6)	32 (86.5)
		Increase >15-30	0	2 (8.7)	2 (5.4)
		Increase >30	0	0	0

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.2.1
Transition Table from Baseline for Vital Signs
Safety Population

Parameter	Analysis Visit Timepoint	Change from Baseline Category	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Heart Rate (beats/min)	Treatment Visit 3 injection +30 min	n	14	22	36
		Decrease >30	0	1 (4.5)	1 (2.8)
		Decrease >15-30	5 (35.7)	0	5 (13.9)
		Difference (+/-) 0-15	9 (64.3)	20 (90.9)	29 (80.6)
		Increase >15-30	0	1 (4.5)	1 (2.8)
	Treatment Visit 3 injection +60 min	n	14	22	36
		Decrease >30	0	2 (9.1)	2 (5.6)
		Decrease >15-30	3 (21.4)	2 (9.1)	5 (13.9)
		Difference (+/-) 0-15	11 (78.6)	16 (72.7)	27 (75.0)
		Increase >15-30	0	2 (9.1)	2 (5.6)
	Treatment Visit 4 injection -20 min	n	9	19	28
		Decrease >30	0	3 (15.8)	3 (10.7)
		Decrease >15-30	3 (33.3)	0	3 (10.7)
		Difference (+/-) 0-15	6 (66.7)	14 (73.7)	20 (71.4)
		Increase >15-30	0	1 (5.3)	1 (3.6)
	Treatment Visit 4 injection +30 min	n	10	19	29
		Decrease >30	1 (10.0)	3 (15.8)	4 (13.8)
		Decrease >15-30	4 (40.0)	2 (10.5)	6 (20.7)
		Difference (+/-) 0-15	5 (50.0)	11 (57.9)	16 (55.2)
		Increase >15-30	0	1 (5.3)	1 (3.4)
		Increase >30	0	2 (10.5)	2 (6.9)

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.4.2.1
Transition Table from Baseline for Vital Signs
Safety Population

Parameter	Analysis Visit Timepoint	Change from Baseline Category	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64) n (%)
			6.0 GBq (N=23) n (%)	7.4 GBq (N=41) n (%)	
Heart Rate (beats/min)	Treatment Visit 4 injection +60 min	n	10	19	29
		Decrease >30	1 (10.0)	3 (15.8)	4 (13.8)
		Decrease >15-30	3 (30.0)	2 (10.5)	5 (17.2)
		Difference (+/-) 0-15	5 (50.0)	11 (57.9)	16 (55.2)
		Increase >15-30	1 (10.0)	0	1 (3.4)
	Follow-up Month 3	Increase >30	0	3 (15.8)	3 (10.3)
		n	1	0	1
		Decrease >30	0	0	0
		Decrease >15-30	0	0	0
		Difference (+/-) 0-15	1 (100)	0	1 (100)
Follow-up Month 12		Increase >15-30	0	0	0
		Increase >30	0	0	0
		n	0	1	1
		Decrease >30	0	0	0
		Decrease >15-30	0	0	0
		Difference (+/-) 0-15	0	1 (100)	1 (100)

Baseline is the Treatment Visit 1 measurement performed pre-injection.

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Table 14.3.5.1
12-Lead Electrocardiography (ECG)
Safety Population

Parameter	Analysis Visit Timepoint	Values/Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Interpretation, n (%)	Treatment Visit 1 n Pre-Dose	Normal	23 14 (60.9)	41 22 (53.7)	64 36 (56.3)
		Abnormal - Clinically Significant	0 0	0 0	0 0
		Abnormal - Not Clinically Significant	9 (39.1)	19 (46.3)	28 (43.8)
	Treatment Visit 1 n Post-Dose	Normal	23 15 (65.2)	41 24 (58.5)	64 39 (60.9)
		Abnormal - Clinically Significant	0 0	0 0	0 0
		Abnormal - Not Clinically Significant	8 (34.8)	17 (41.5)	25 (39.1)
	Treatment Visit 2 n Pre-Dose	Normal	18 12 (66.7)	38 22 (57.9)	56 34 (60.7)
		Abnormal - Clinically Significant	0 0	0 0	0 0
		Abnormal - Not Clinically Significant	6 (33.3)	16 (42.1)	22 (39.3)
	Treatment Visit 2 n Post-Dose	Normal	18 13 (72.2)	38 22 (57.9)	56 35 (62.5)
		Abnormal - Clinically Significant	0 0	0 0	0 0
		Abnormal - Not Clinically Significant	5 (27.8)	16 (42.1)	21 (37.5)
	Treatment Visit 3 n Pre-Dose	Normal	14 10 (71.4)	23 14 (60.9)	37 24 (64.9)
		Abnormal - Clinically Significant	0 0	0 0	0 0
		Abnormal - Not Clinically Significant	4 (28.6)	9 (39.1)	13 (35.1)
	Treatment Visit 3 n Post-Dose	Normal	14 9 (64.3)	22 14 (63.6)	36 23 (63.9)
		Abnormal - Clinically Significant	0 0	0 0	0 0
		Abnormal - Not Clinically Significant	5 (35.7)	8 (36.4)	13 (36.1)

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Table 14.3.5.1
12-Lead Electrocardiography (ECG)
Safety Population

Parameter	Analysis Visit Timepoint	Values/Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
Interpretation, n (%)	Treatment Visit 4 Pre-Dose	n	10	19	29
		Normal	6 (60.0)	9 (47.4)	15 (51.7)
		Abnormal - Clinically Significant	0	0	0
	Treatment Visit 4 Post-Dose	Abnormal - Not Clinically Significant	4 (40.0)	10 (52.6)	14 (48.3)
		n	10	19	29
		Normal	6 (60.0)	12 (63.2)	18 (62.1)
ECG Mean Heart Rate (beats/min)	Treatment Visit 1 Pre-Dose	n	23	41	64
		Mean (SD)	66.83 (11.472)	72.71 (14.049)	70.59 (13.392)
		Median	67.00	72.00	67.50
		Q1 ; Q3	58.00 ; 76.00	62.00 ; 84.00	59.50 ; 80.00
		Min ; Max	50.0 ; 94.0	50.0 ; 100.0	50.0 ; 100.0
	Treatment Visit 1 Post-Dose	n	23	41	64
		Mean (SD)	67.00 (9.606)	70.32 (11.635)	69.13 (10.988)
		Median	66.00	69.00	68.00
		Q1 ; Q3	58.00 ; 72.00	62.00 ; 78.00	61.00 ; 77.00
		Min ; Max	53.0 ; 86.0	48.0 ; 93.0	48.0 ; 93.0
		n	18	38	56
Treatment Visit 2 Pre-Dose	Treatment Visit 2 Pre-Dose	Mean (SD)	69.17 (7.571)	71.79 (12.903)	70.95 (11.457)
		Median	69.00	69.50	69.00
		Q1 ; Q3	62.00 ; 73.00	62.00 ; 80.00	62.00 ; 77.50
		Min ; Max	58.0 ; 88.0	48.0 ; 99.0	48.0 ; 99.0
	Treatment Visit 2 Post-Dose	n	18	38	56
		Mean (SD)	65.11 (8.014)	69.97 (14.866)	68.41 (13.182)
		Median	64.50	69.00	67.00
		Q1 ; Q3	59.00 ; 70.00	60.00 ; 76.00	60.00 ; 75.00
		Min ; Max	51.0 ; 84.0	46.0 ; 108.0	46.0 ; 108.0

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Table 14.3.5.1
12-Lead Electrocardiography (ECG)
Safety Population

Parameter	Analysis Visit Timepoint	Values/Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
ECG Mean Heart Rate (beats/min)	Treatment Visit 3 Pre-Dose	n	14	23	37
		Mean (SD)	64.57 (6.607)	69.09 (13.892)	67.38 (11.774)
		Median	63.50	68.00	65.00
		Q1 ; Q3	60.00 ; 67.00	58.00 ; 79.00	59.00 ; 74.00
	Treatment Visit 3 Post-Dose	Min ; Max	56.0 ; 76.0	49.0 ; 105.0	49.0 ; 105.0
		n	14	22	36
		Mean (SD)	62.57 (8.582)	63.95 (11.898)	63.42 (10.619)
		Median	61.50	62.00	62.00
	Treatment Visit 4 Pre-Dose	Q1 ; Q3	57.00 ; 71.00	56.00 ; 71.00	56.50 ; 71.00
		Min ; Max	51.0 ; 75.0	45.0 ; 102.0	45.0 ; 102.0
		n	10	19	29
		Mean (SD)	65.70 (7.273)	70.21 (16.645)	68.66 (14.138)
	Treatment Visit 4 Post-Dose	Median	67.50	64.00	67.00
		Q1 ; Q3	65.00 ; 70.00	58.00 ; 79.00	60.00 ; 72.00
		Min ; Max	48.0 ; 72.0	50.0 ; 109.0	48.0 ; 109.0
		n	10	19	29
PR Interval, Aggregate (msec)	Treatment Visit 1 Pre-Dose	Mean (SD)	63.80 (10.250)	66.00 (15.850)	65.24 (14.014)
		Median	62.00	61.00	61.00
		Q1 ; Q3	56.00 ; 67.00	54.00 ; 75.00	56.00 ; 74.00
		Min ; Max	51.0 ; 85.0	49.0 ; 106.0	49.0 ; 106.0
	Treatment Visit 1 Post-Dose	n	20	36	56
		Mean (SD)	157.70 (27.419)	160.89 (27.249)	159.75 (27.103)
		Median	156.00	164.00	161.50
		Q1 ; Q3	138.00 ; 182.00	144.50 ; 173.50	140.00 ; 174.00
	Treatment Visit 1 Post-Dose	Min ; Max	110.0 ; 216.0	116.0 ; 238.0	110.0 ; 238.0

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Table 14.3.5.1
12-Lead Electrocardiography (ECG)
Safety Population

Parameter	Analysis Visit Timepoint	Values/Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
PR Interval, Aggregate (msec)	Treatment Visit 1 Post-Dose	n	21	38	59
		Mean (SD)	163.95 (30.044)	165.29 (29.524)	164.81 (29.457)
		Median	162.00	164.00	164.00
		Q1 ; Q3	136.00 ; 185.00	142.00 ; 180.00	140.00 ; 185.00
	Treatment Visit 2 Pre-Dose	Min ; Max	120.0 ; 234.0	103.0 ; 246.0	103.0 ; 246.0
		n	16	35	51
		Mean (SD)	156.44 (28.854)	160.89 (27.978)	159.49 (28.042)
		Median	152.50	164.00	159.00
	Treatment Visit 2 Post-Dose	Q1 ; Q3	135.00 ; 184.00	138.00 ; 182.00	138.00 ; 182.00
		Min ; Max	112.0 ; 200.0	106.0 ; 216.0	106.0 ; 216.0
	Treatment Visit 3 Pre-Dose	n	16	34	50
		Mean (SD)	156.00 (30.683)	169.97 (27.280)	165.50 (28.857)
		Median	158.50	170.50	165.50
		Q1 ; Q3	130.00 ; 170.00	146.00 ; 190.00	144.00 ; 188.00
	Treatment Visit 3 Post-Dose	Min ; Max	109.0 ; 224.0	120.0 ; 234.0	109.0 ; 234.0
		n	13	20	33
		Mean (SD)	158.54 (28.468)	161.45 (24.178)	160.30 (25.556)
		Median	156.00	164.50	160.00
	Treatment Visit 3 Post-Dose	Q1 ; Q3	141.00 ; 178.00	144.50 ; 179.50	141.00 ; 179.00
		Min ; Max	110.0 ; 208.0	118.0 ; 212.0	110.0 ; 212.0
	Treatment Visit 3 Post-Dose	n	13	20	33
		Mean (SD)	163.23 (23.030)	168.95 (25.519)	166.70 (24.364)
		Median	160.00	178.00	171.00
		Q1 ; Q3	151.00 ; 173.00	145.00 ; 189.00	148.00 ; 184.00
		Min ; Max	134.0 ; 220.0	122.0 ; 208.0	122.0 ; 220.0

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Table 14.3.5.1
12-Lead Electrocardiography (ECG)
Safety Population

Parameter	Analysis Visit Timepoint	Values/Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
PR Interval, Aggregate (msec)	Treatment Visit 4 Pre-Dose	n	8	16	24
		Mean (SD)	149.13 (27.074)	164.00 (29.842)	159.04 (29.243)
		Median	152.00	167.50	162.00
		Q1 ; Q3	139.00 ; 164.50	148.00 ; 186.00	142.00 ; 184.00
	Treatment Visit 4 Post-Dose	Min ; Max	96.0 ; 186.0	106.0 ; 206.0	96.0 ; 206.0
		n	9	16	25
		Mean (SD)	176.44 (81.368)	162.44 (32.241)	167.48 (53.886)
		Median	162.00	167.00	162.00
QRS Duration, Aggregate (msec)	Treatment Visit 1 Pre-Dose	n	23	41	64
		Mean (SD)	84.83 (15.532)	88.02 (17.114)	86.88 (16.510)
		Median	80.00	85.00	84.00
		Q1 ; Q3	76.00 ; 88.00	78.00 ; 91.00	78.00 ; 90.00
	Treatment Visit 1 Post-Dose	Min ; Max	66.0 ; 142.0	62.0 ; 148.0	62.0 ; 148.0
		n	23	41	64
		Mean (SD)	85.52 (12.727)	91.49 (20.065)	89.34 (17.903)
		Median	84.00	86.00	86.00
Torsade de Pointes Incidence (%)	Treatment Visit 2 Pre-Dose	n	18	38	56
		Mean (SD)	85.50 (16.271)	91.13 (19.510)	89.32 (18.573)
		Median	81.00	86.00	86.00
		Q1 ; Q3	80.00 ; 86.00	78.00 ; 94.00	78.00 ; 92.00
	Treatment Visit 2 Post-Dose	Min ; Max	70.0 ; 146.0	68.0 ; 150.0	68.0 ; 150.0

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Table 14.3.5.1
12-Lead Electrocardiography (ECG)
Safety Population

Parameter	Analysis Visit Timepoint	Values/Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
QRS Duration, Aggregate (msec)	Treatment Visit 2 Post-Dose	n	18	38	56
		Mean (SD)	88.56 (17.034)	91.55 (20.166)	90.59 (19.112)
		Median	86.00	89.00	87.00
		Q1 ; Q3	82.00 ; 90.00	78.00 ; 94.00	79.00 ; 93.50
	Treatment Visit 3 Pre-Dose	Min ; Max	70.0 ; 150.0	68.0 ; 156.0	68.0 ; 156.0
		n	14	23	37
		Mean (SD)	87.21 (18.440)	87.87 (17.592)	87.62 (17.664)
		Median	82.00	84.00	84.00
	Treatment Visit 3 Post-Dose	Q1 ; Q3	78.00 ; 88.00	74.00 ; 95.00	78.00 ; 91.00
		Min ; Max	72.0 ; 148.0	68.0 ; 136.0	68.0 ; 148.0
	Treatment Visit 4 Pre-Dose	n	14	22	36
		Mean (SD)	89.50 (16.247)	90.82 (19.220)	90.31 (17.891)
		Median	86.00	87.00	86.00
		Q1 ; Q3	80.00 ; 89.00	78.00 ; 94.00	80.00 ; 92.50
	Treatment Visit 4 Post-Dose	Min ; Max	76.0 ; 142.0	66.0 ; 140.0	66.0 ; 142.0
		n	10	19	29
		Mean (SD)	88.50 (20.299)	89.32 (16.757)	89.03 (17.695)
		Median	85.00	86.00	86.00
	Treatment Visit 4 Post-Dose	Q1 ; Q3	76.00 ; 88.00	76.00 ; 96.00	76.00 ; 93.00
		Min ; Max	74.0 ; 144.0	68.0 ; 132.0	68.0 ; 144.0
	Treatment Visit 4 Post-Dose	n	10	19	29
		Mean (SD)	90.60 (19.443)	91.11 (18.120)	90.93 (18.238)
		Median	86.00	88.00	88.00
		Q1 ; Q3	82.00 ; 90.00	78.00 ; 100.00	80.00 ; 92.00
		Min ; Max	76.0 ; 144.0	68.0 ; 136.0	68.0 ; 144.0

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Table 14.3.5.1
12-Lead Electrocardiography (ECG)
Safety Population

Parameter	Analysis Visit Timepoint	Values/Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
QT Interval, Aggregate (msec)	Treatment Visit 1 Pre-Dose	n	23	41	64
		Mean (SD)	410.26 (40.742)	402.05 (42.602)	405.00 (41.806)
		Median	400.00	398.00	400.00
		Q1 ; Q3	386.00 ; 450.00	370.00 ; 436.00	379.50 ; 438.00
	Treatment Visit 1 Post-Dose	Min ; Max	340.0 ; 503.0	320.0 ; 508.0	320.0 ; 508.0
		n	23	41	64
		Mean (SD)	414.35 (34.086)	417.49 (44.453)	416.36 (40.776)
		Median	404.00	418.00	416.00
	Treatment Visit 2 Pre-Dose	Q1 ; Q3	390.00 ; 436.00	392.00 ; 439.00	391.00 ; 438.00
		Min ; Max	364.0 ; 492.0	333.0 ; 556.0	333.0 ; 556.0
		n	18	38	56
		Mean (SD)	406.61 (26.266)	410.13 (32.088)	409.00 (30.144)
	Treatment Visit 2 Post-Dose	Median	404.00	417.00	408.50
		Q1 ; Q3	385.00 ; 436.00	386.00 ; 432.00	385.50 ; 433.50
		Min ; Max	366.0 ; 452.0	348.0 ; 476.0	348.0 ; 476.0
		n	18	38	56
	Treatment Visit 3 Pre-Dose	Mean (SD)	422.89 (35.075)	416.11 (43.101)	418.29 (40.499)
		Median	430.00	414.00	420.00
		Q1 ; Q3	395.00 ; 448.00	383.00 ; 446.00	386.00 ; 447.00
		Min ; Max	346.0 ; 476.0	336.0 ; 546.0	336.0 ; 546.0
	Treatment Visit 3 Post-Dose	n	14	23	37
		Mean (SD)	424.21 (27.016)	407.52 (30.699)	413.84 (30.114)
		Median	435.00	402.00	410.00
		Q1 ; Q3	407.00 ; 440.00	386.00 ; 426.00	392.00 ; 436.00
		Min ; Max	376.0 ; 464.0	358.0 ; 468.0	358.0 ; 468.0

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Table 14.3.5.1
12-Lead Electrocardiography (ECG)
Safety Population

Parameter	Analysis Visit Timepoint	Values/Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
QT Interval, Aggregate (msec)	Treatment Visit 3 Post-Dose	n	14	22	36
		Mean (SD)	439.64 (32.117)	432.36 (34.543)	435.19 (33.347)
		Median	443.00	433.00	435.00
		Q1 ; Q3	409.00 ; 468.00	423.00 ; 444.00	420.00 ; 460.00
	Treatment Visit 4 Pre-Dose	Min ; Max	387.0 ; 494.0	358.0 ; 522.0	358.0 ; 522.0
		n	10	19	29
		Mean (SD)	416.50 (13.377)	412.84 (32.828)	414.10 (27.449)
		Median	415.00	404.00	414.00
	Treatment Visit 4 Post-Dose	Q1 ; Q3	411.00 ; 428.00	394.00 ; 444.00	400.00 ; 434.00
		Min ; Max	394.0 ; 434.0	354.0 ; 468.0	354.0 ; 468.0
		n	10	19	29
		Mean (SD)	429.00 (24.567)	427.53 (34.598)	428.03 (31.049)
	QTcB Interval, Aggregate (msec)	Median	428.50	428.00	428.00
		Q1 ; Q3	412.00 ; 452.00	404.00 ; 452.00	408.00 ; 452.00
		Min ; Max	385.0 ; 466.0	372.0 ; 502.0	372.0 ; 502.0
		n	23	41	64
QTcB Interval, Aggregate (msec)	Treatment Visit 1 Pre-Dose	Mean (SD)	426.65 (26.829)	436.63 (26.368)	433.05 (26.760)
		Median	425.00	434.00	429.50
		Q1 ; Q3	413.00 ; 438.00	420.00 ; 451.00	418.00 ; 449.50
		Min ; Max	387.0 ; 506.0	388.0 ; 524.0	387.0 ; 524.0
	Treatment Visit 1 Post-Dose	n	23	40	63
		Mean (SD)	435.65 (38.357)	447.53 (33.355)	443.19 (35.427)
		Median	427.00	448.50	445.00
		Q1 ; Q3	414.00 ; 455.00	436.50 ; 462.00	421.00 ; 462.00
		Min ; Max	373.0 ; 531.0	360.0 ; 582.0	360.0 ; 582.0

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Table 14.3.5.1
12-Lead Electrocardiography (ECG)
Safety Population

Parameter	Analysis Visit Timepoint	Values/Statistics	Lu-PSMA-617 6.0 GBq (N=23)	Lu-PSMA-617 7.4 GBq (N=41)	Overall (N=64)
QTcB Interval, Aggregate (msec)	Treatment Visit 2 Pre-Dose	n	18	38	56
		Mean (SD)	430.83 (29.462)	443.34 (30.292)	439.32 (30.337)
		Median	431.50	444.50	442.50
		Q1 ; Q3	413.00 ; 450.00	425.00 ; 456.00	420.50 ; 454.50
	Treatment Visit 2 Post-Dose	Min ; Max	384.0 ; 501.0	372.0 ; 536.0	372.0 ; 536.0
		n	18	38	56
		Mean (SD)	437.44 (30.378)	443.08 (31.075)	441.27 (30.691)
		Median	439.50	441.00	440.00
	Treatment Visit 3 Pre-Dose	Q1 ; Q3	416.00 ; 455.00	426.00 ; 457.00	425.00 ; 456.50
		Min ; Max	386.0 ; 509.0	360.0 ; 558.0	360.0 ; 558.0
	Treatment Visit 3 Post-Dose	n	14	23	37
		Mean (SD)	438.29 (22.537)	432.65 (30.158)	434.78 (27.329)
		Median	440.00	428.00	435.00
		Q1 ; Q3	421.00 ; 450.00	410.00 ; 453.00	414.00 ; 450.00
	Treatment Visit 4 Pre-Dose	Min ; Max	407.0 ; 489.0	365.0 ; 512.0	365.0 ; 512.0
		n	14	22	36
		Mean (SD)	446.64 (25.845)	442.14 (24.946)	443.89 (25.029)
		Median	445.00	443.50	444.00
	Treatment Visit 4 Post-Dose	Q1 ; Q3	429.00 ; 466.00	421.00 ; 462.00	425.50 ; 464.00
		Min ; Max	400.0 ; 491.0	405.0 ; 488.0	400.0 ; 491.0
	Treatment Visit 4 Pre-Dose	n	10	19	29
		Mean (SD)	434.60 (21.293)	440.42 (29.641)	438.41 (26.804)
		Median	440.50	439.00	440.00
		Q1 ; Q3	423.00 ; 449.00	425.00 ; 454.00	425.00 ; 452.00
		Min ; Max	387.0 ; 462.0	395.0 ; 525.0	387.0 ; 525.0

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Table 14.3.5.1
12-Lead Electrocardiography (ECG)
Safety Population

Parameter	Analysis Visit Timepoint	Values/Statistics	Lu-PSMA-617	Lu-PSMA-617	Overall (N=64)
			6.0 GBq (N=23)	7.4 GBq (N=41)	
QTcB Interval, Aggregate (msec)	Treatment Post-Dose	n	10	19	29
		Mean (SD)	440.30 (30.266)	442.53 (30.147)	441.76 (29.662)
		Median	432.00	438.00	436.00
		Q1 ; Q3	426.00 ; 457.00	420.00 ; 467.00	426.00 ; 462.00
		Min ; Max	383.0 ; 490.0	390.0 ; 494.0	383.0 ; 494.0

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Table 14.3.6.1.1
Concurrent Radiotherapy
Safety Population

	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Number of patients with at least one radiotherapy	1 (4.3)	1 (2.4)	2 (3.1)
Type of radiotherapy			
BONE TARGETED THERAPY	1 (4.3)	0	1 (1.6)
SALVAGE EBRT	0	1 (2.4)	1 (1.6)
Number of radiotherapies per patient			
n	1	1	2
Mean (SD)	1.0 (NE)	1.0 (NE)	1.0 (0.00)
Median	1.0	1.0	1.0
Q1 ; Q3	1.0 ; 1.0	1.0 ; 1.0	1.0 ; 1.0
Min ; Max	1 ; 1	1 ; 1	1 ; 1

Abbreviations: EBRT = External beam radiation therapy

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Table 14.3.6.1.2
Post-Treatment Radiotherapy
Safety Population

	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Number of patients with at least one radiotherapy	1 (4.3)	1 (2.4)	2 (3.1)
Type of radiotherapy SALVAGE EBRT	1 (4.3)	1 (2.4)	2 (3.1)
Number of radiotherapies per patient			
n	1	1	2
Mean (SD)	1.0 (NE)	2.0 (NE)	1.5 (0.71)
Median	1.0	2.0	1.5
Q1 ; Q3	1.0 ; 1.0	2.0 ; 2.0	1.0 ; 2.0
Min ; Max	1 ; 1	2 ; 2	1 ; 2

Abbreviations: EBRT = External beam radiation therapy

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Table 14.3.6.2.1
Concurrent Other Therapy
Safety Population

	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Patients with at least one other treatment	13 (56.5)	27 (65.9)	40 (62.5)
Type of other treatment			
ABIRATERONE	3 (13.0)	5 (12.2)	8 (12.5)
ENZALUTAMIDE	2 (8.7)	7 (17.1)	9 (14.1)
HORMONAL THERAPY	12 (52.2)	25 (61.0)	37 (57.8)
OTHER	10 (43.5)	16 (39.0)	26 (40.6)
STANDARD ADT	1 (4.3)	2 (4.9)	3 (4.7)
Number of other treatments per patient			
n	13	27	40
Mean (SD)	2.8 (1.42)	2.4 (1.39)	2.5 (1.40)
Median	2.0	2.0	2.0
Q1 ; Q3	2.0 ; 3.0	1.0 ; 3.0	1.5 ; 3.0
Min ; Max	1 ; 6	1 ; 6	1 ; 6

Abbreviations: Turp = Transurethral resection of the prostate, ADT = Androgen deprivation therapy.

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Table 14.3.6.2.2
Post-Treatment Other Therapy
Safety Population

	Lu-PSMA-617 6.0 GBq (N=23) n (%)	Lu-PSMA-617 7.4 GBq (N=41) n (%)	Overall (N=64) n (%)
Patients with at least one other treatment	4 (17.4)	5 (12.2)	9 (14.1)
Type of other treatment			
ABIRATERONE	1 (4.3)	2 (4.9)	3 (4.7)
ENZALUTAMIDE	1 (4.3)	2 (4.9)	3 (4.7)
HORMONAL THERAPY	3 (13.0)	5 (12.2)	8 (12.5)
OTHER	1 (4.3)	2 (4.9)	3 (4.7)
Number of other treatments per patient			
n	4	5	9
Mean (SD)	2.0 (0.82)	2.6 (1.82)	2.3 (1.41)
Median	2.0	2.0	2.0
Q1 ; Q3	1.5 ; 2.5	1.0 ; 4.0	1.0 ; 3.0
Min ; Max	1 ; 3	1 ; 5	1 ; 5

Abbreviations: Turp = Transurethral resection of the prostate, ADT = Androgen deprivation therapy.

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Table 14.3.6.3.1
Concurrent Chemotherapy
Safety Population

No data available.

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Table 14.3.6.3.2
Post-Treatment Chemotherapy
Safety Population

No data available.

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14.3.2 Listings of deaths, other serious and significant adverse events - Not applicable

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¹⁷⁷Lu-PSMA-617

Clinical Protocol No.: PSMA-617-02

PSMA-Directed Endoradiotherapy of Castration-Resistant Prostate Cancer (RESIST-PC). A Phase 2 Clinical Trial.

14.3.3 Narratives of deaths, other serious and certain other significant adverse events

Document type: Clinical Study Report – Section 14.3.3

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Template version 02 dated 24-Jul-2018

Events described in Narratives

The criteria for creation of patient narratives for RESIST, was agreed by the FDA in March 2020 and is as shown below.

9.2.2 Endocyte proposes to write patient narratives for all patients of RESIST-PC and for patients on the ¹⁷⁷Lu-PSMA-617 experimental arm of VISION based on the criteria outlined in the Briefing Document.

- Serious Adverse Events occurring during study treatment or within 30 days of treatment discontinuation
- Death for reasons other than disease progression during study treatment or within 30 days of treatment discontinuation
- Treatment discontinuation due to Adverse Events.

Abbreviations

AE	Adverse event
ADT	Androgen deprivation therapy
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BPH	Benign prostatic hyperplasia
CK	Creatinine kinase
CT	Computed tomography (scan)
DVT	Deep vein thrombosis
ECG	Electrocardiogram
ER	Emergency room
GERD	Gastroesophageal reflux disease
ICU	Intensive care unit
mCRPC	metastatic castration-resistant prostate cancer
MRI	Magnetic resonance imaging
non-STEMI	non-ST-elevation myocardial infarction
PCR	Polymer chain reaction
PSA	Prostate-specific antigen
RBC	Red blood cell
SAE	Serious adverse event
S/P	Status post
SBRT	stereotactic body radiotherapy
WBC	White blood cell

1 Narratives for deaths

1.1 SAE with treatment leading to Death: Treatment PSMA-617-02 Arm 1 [6.0 GBq ^{177}Lu -PSMA-617]

1.1.1 Patient [569283-652 (15-652)] Treatment: PSMA-617-02 Arm 1 [6.0 GBq ^{177}Lu -PSMA-617]

- Brain metastases (leading to death) (SAE)
- Pain (SAE)

MedDRA Preferred Terms (PT): Brain metastases: Pain

Treatment group: 6.0 GBQ ^{177}Lu -PSMA-617 **Patient details:** Aged 76 years, male, [Race].

The patient had the diagnosis of metastatic castration-resistant prostate cancer (mCRPC) diagnosed on [****] and had undergone a [Medical History] on [****]: he was cancer free with no symptoms until [****], when he developed symptoms of infections and infestations that was diagnosed as metastatic adenocarcinoma consistent with prostatic origin. Unsuccessful prior conventional therapies included androgen deprivation therapy (ADT) and cabozantinib ([****]); abiraterone and apulutamide ([****]); and cytotoxin and vincristine ([****]). Other active medical conditions were [Medical History] ([Medical History]); musculoskeletal and connective tissue disorders, [Medical History], and [Medical History]; and [Medical History] (dates unknown for all). The patient received only the first cycle of 6.0 GBq ^{177}Lu -PSMA-617 on 05-Jul-2017 (Day 1).

On 17-Aug-2017 (Day 44), the patient was taken to the Emergency Room (ER) with complaints of bilateral thigh pain that had not been relieved by use of multiple pain medications. He also had extensive bilateral ankle swelling and had a poor appetite for several days. Concomitant medications prior to or during hospitalization included: gabapentin (for [Medical History]), dilaudid (for [Medical History]), tylenol (for [Medical History]), tizanidine (unspecified indication), multivitamin, diethylstilbestrol (unspecified indication), dexamethasone (unspecified indication), fexafenadine hydrochloride (for [Medical History]), loratadine (for [Medical History]), triamcinolone acetonide (for [Medical History]), and enoxaparin sodium (for [Medical History]). Tests showed that he had a low platelet count (unspecified value: laboratory findings not reported), so he was given a blood transfusion. No other information regarding treatment or laboratory test results were available. End stage prostate cancer with brain metastases was established as the final diagnosis.

On 23-Aug-2017 (Day 50), the patient died. The event of brain metastases was noted as the cause of death (no severity listed): the Investigator considered that the brain metastases were probably not related to treatment with ^{177}Lu -PSMA-617. The Investigator considered that the pain (Grade 3 severity) and unlikely related to ^{177}Lu -PSMA-617. There was no information as to whether or not an autopsy was performed.

1.1.2 Patient [756653-263 (76-263)] Treatment: PSMA-617-02 Arm 1 [6.0 GBq ^{177}Lu -PSMA-617]

- Subdural hematoma (leading to death) (SAE)
- Non-STEMI (leading to death) (SAE)

- Pneumonia (leading to death) (SAE)

MedDRA Preferred Terms (PT): Subdural hematoma; Acute myocardial infarction; Pneumonia

Treatment group: 6.0 GBq ^{177}Lu -PSMA-617 **Patient details:** Aged 67 years, male, [Race].

The patient had the diagnosis of mCRPC diagnosed on [****] and had previous unsuccessful treatments with abiraterone ([****] to date unknown); enzalutamide ([****] to date unknown); methotrexate (23-May-2018 to date unknown). Other active medical conditions were listed as prostate cancer metastases to bones, pelvis, ribs, and skull (date unknown); [Medical History] (date unknown), [Medical History] (date unknown), [Medical History] (date unknown), [Medical History] (date unknown), and [Medical History] (date unknown). The patient received the first cycle of 6.0 GBq ^{177}Lu -PSMA-617 on 05-Jul-2017 (Day 1); the second cycle of 6.0 GBq ^{177}Lu -PSMA-617 was received on 30-Aug-2017 (Day 57): the patient discontinued from treatment because of prostate specific antigen (PSA)-level progression above protocol specified limits; however, remained in the study (for the follow-up phase). PSA levels and the exact date of discontinuation from treatment is unknown.

On 30-Nov-2017 (Day 149/92 days after the last date of medication while in the Follow-up phase), the patient was brought to the Emergency Room (ER) with complaints of near-syncope preceded with moderate nausea and vomiting with headache; he had not lost consciousness, but had recently collapsed with no injuries (i.e., did not hit his head). The patient did not report recent chest pain or angina and had no prior known cardiac disease history. At admission, his vital signs were: blood pressure 155/62 mmHg; heart rate 83 bpm; respiratory rate 18/min; body temperature 97.5 degrees F, and oxygen saturation 98%. The patient was alert, oriented to person, place and time, with normal mood/affect, normal cranial nerves and cerebellum, and intact sensory/motor system. Other systems were reviewed and found to be unremarkable. An ECG was done and showed a normal sinus rhythm, wide QRS with intraventricular conduction delay and no other abnormality. He was then admitted to the Intensive Care Unit (ICU) at which time he became somnolent and was unable to follow commands. Laboratory results showed profound hyponatremia, profound anemia, and profound thrombocytopenia; and urinalysis showed positive for bacteria (laboratory values not reported). The patient was taking or prescribed during the hospitalization the following concomitant medications: acetaminophen (unspecified indication); ondansetron HCL, IV (unspecified indication); normal saline, IV (unspecified indication); vancomycin HCL, IV (unspecified indication); acetazolamide (unspecified indication); dutasteride (unspecified indication); estramustine phosphate sodium (unspecified indication); hydrocortisone (unspecified indication); ketoconazole (unspecified indication); levothyroxine sodium (unspecified indication); pregabalin (unspecified indication); metformin (unspecified indication); methylprednisolone (unspecified indication); minocycline HCL (unspecified indication); omeprazole (unspecified indication); tramadol (pain); triamcinolone (unspecified indication); valsartan/hydrochlorothiazide (unspecified indication); abiraterone acetate (unspecified indication); rosuvastatin calcium (unspecified indication); and ondansetron (nausea).

On 01-Dec-2017 (Day 150/Follow-up phase), the patient's cardiac enzymes were as follows: creatine kinase (CK) 355 U/L (high); CK-MB U/L 7.5 (high); myoglobin 108.7 ng/mL (high); and troponin I 1.01 ng/mL (high). A chest x-ray showed patch bilateral airspace disease with multilobar infiltrates suspected: suggesting an atypical pulmonary infection, with multifocal

infiltrates, edema and acute respiratory distress syndrome (ARDS). The cardiologist determined that the patient had also ischemia type II non-ST-elevation myocardial infarction (non-STEMI): it was suspected that the patient had underlying coronary disease. Due to his severe thrombocytopenia, the patient was very limited in the ability to use anticoagulation and antiplatelet therapy: thus, the cardiologist recommended the patient be administered beta blocker and a statin. Additional tests indicated the need for a packed red blood cell transfusion, followed by intubation and mechanical ventilation. A computed brain computed tomography (CT) showed acute subdural hematoma associated with mass effect with right midline shift, downward transtentorial herniation, and intraventricular hemorrhage into the fourth ventricle with resultant mass effect within the posterior fossa compressing the brain stem structures anteriorly.

On 01-Dec-2017 (Day 151/Follow-up phase) the patient died. The Investigator considered the SAE of subdural hematoma as the main cause of death and possibly related to the treatment with ¹⁷⁷Lu-PSMA-617. The Investigator considered that the non-STEMI (Grade 5 severity) was probably not related to the treatment with ¹⁷⁷Lu-PSMA-617; the Investigator considered pneumonia (Grade 5 severity) was probably not related to treatment with ¹⁷⁷Lu-PSMA-617. There was no information as to whether or not an autopsy was performed.

1.1.3 Patient [948318-720 (35-720)] Treatment: PSMA-617-02 Arm 1 [6.0 GBq ¹⁷⁷Lu-PSMA-617]

- Gastrointestinal hemorrhage (leading to death) (SAE)
- Death

MedDRA Preferred Terms: (Gastrointestinal haemorrhage)

Treatment group: 7.4 GBQ ¹⁷⁷Lu-PSMA-617 **Patient details:** Aged [54-95] years, male, [Race].

The patient had the diagnosis of mCRPC (diagnosis [****]). Previous unsuccessful therapies included 6 cycles of [Medical History] (i.e., radium 223 and samarium [[****] to [****]]; abiraterone [unknown [****]], cabazitaxel [unknown [****]], and carboplatin paclitaxel [unknown [****]]). The patient also had an [Medical History] (date unknown). Other active medical conditions were metastases to the lungs, skeleton, urinary bladder, lymph nodes, and right adrenal glands (as diagnosed by [Medical History] from [****] to [****]); [Medical History] ([Medical History]) ([****]); and [Medical History] ([****])). On 05-Jul-2017 the patient received the first cycle of 7.4 GBq ¹⁷⁷Lu-PSMA-617 (Day 1). On 02-Aug-2017, the patient experienced grade 3 hematologic toxicity (i.e., hemoglobin level 7.6 g/dL) that resolved within 12 weeks. On 06-Sep-2017 (Day 64) the patient received the second cycle of ¹⁷⁷Lu-PSMA-617; however, at 50% (i.e., 3.7 GBq) due to hematological toxicity as per posology criteria defined by the protocol. On 27-Sep-2017 (Day 85), the patient was noted to have hematologic toxicity (i.e., hemoglobin level 7.4 g/dL) and platelet count (4800 Tho/uL); therefore, he was discharged from treatment; however, remained in the Follow-up phase.

On 30-Oct-2017 (Day 118/55 days after the last dose of 3.7 GBq ¹⁷⁷Lu-PSMA-617), the patient was hospitalized due to gastrointestinal hemorrhage. The patient was taking or prescribed during the hospitalization the following concomitant medications: tamsulosin hydrochloride

(unspecified indication), dexamethasone (unspecified indication), esomeprazole magnesium (for indigestion), ondansetron (unspecified indication), tramadol (for pain), paracetamol (for pain), and levothyroxine (for [Medical History]).

Laboratory test results from 31-Oct-2017 reported his white blood cell count (WBC) was 1250 Tho/uL, hemoglobin was 7.5 g/dL, and platelet count was 39000 Tho/uL. It was reported that the patient's clinical condition was not stable, and he was given blood and platelet transfusions every 2 days: on 16-Nov-2017 (Day 135/Follow-up phase) the patient died of an unknown event. Although requested by the Investigator, no more details regarding the patient's hospitalization and death were provided: there was no evidence that an autopsy was performed.

The Investigator assessed the unknown event of death as a Grade 5 severity. Because limited information was provided, causality assessment for this SAE was challenging: the Investigator considered that the patient's death could have been due to prostate cancer/disease progression since the patient had mCRPC that metastasized to the bones, lungs, urinary bladder, and right adrenal gland back in [****] as reported at study entry. The Investigator considered the gastrointestinal hemorrhage (Grade 3 severity) was possibly related to treatment with ¹⁷⁷Lu-PSMA-617. However, the patient had also not fully recovered from the hematologic toxicity (no grade severity provided) that was determined related to treatment with ¹⁷⁷Lu-PSMA-617; thus, the Investigator considered that the hematologic toxicity was possibly related to treatment with ¹⁷⁷Lu-PSMA-617.

1.1.4 Patient [487478-890 (23-890)] - Treatment: PSMA-617-02 Arm 1 [6.0 GBq ¹⁷⁷Lu-PSMA-617]

- Metastases to central nervous system (brain) (leading to death) (SAE)

MedDRA Preferred Terms (PT): Metastases to central nervous system

Treatment group: 6.0 GBQ ¹⁷⁷Lu-PSMA-617 **Patient details:** Aged 57 years, male, [Race].

The patient had mCRPC diagnosed [****] and his previous unsuccessful treatments included [Medical History] ([Medical History] (date unknown), docetaxel (date unknown), carboplatin (date unknown), and abiraterone (date unknown)). Active medical conditions were metastases to the osseous structures (date unknown). The first cycle of 6.0 GBq ¹⁷⁷LuPSMA-617 was administered 05-Jul-2017 (Day 1); and the second cycle was administered 30-Aug-2017 (Day 57).

On 21-Sep-2017 (Day 79: 22 days after the second cycle of ¹⁷⁷Lu-PSMA-617), the patient was admitted to the hospital due to 2 newly appearing tumor metastases that the patient had developed on the left side of his brain that were affecting his speech, memory, and proper functioning of the right side of his body. Diagnostic testing regarding the interpretation/findings of the brain tumors were not made available for this report. Concomitant medications prior to or during the hospitalization included: vitamin B6 (unspecified indication), oxycodone hydrochloride (unspecified indication), rivaroxaban (unspecified indication), vitamin D (unspecified indication), atorvastatin (unspecified indication), and pyridoxine hydrochloride (unspecified indication).

The patient was discharged from the hospital on 23-Sep-2017 (Day 81), and was scheduled to have an appointment with his oncologist on 24-Sep-2017 and subsequent radiation for the brain metastases. (Note: records are not available regarding this appointment or procedures.)

On 05-Nov-2017 (Day 124), the patient passed away due to metastases to the brain. Action taken with ¹⁷⁷Lu-PSMA-617 was reported as not applicable.

The Investigator considered that the metastases to the brain (Grade 5 severity) was definitely not related to treatment with ¹⁷⁷Lu-PSMA617.

2 SAEs with Study Discontinuation

2.1 Treatment: PSMA-617-02 Arm 1 [6.0 GBq ¹⁷⁷Lu-PSMA-617]

NA

2.2 Treatment: PSMA-617-02 Arm 2 [7.4 GBq ¹⁷⁷Lu-PSMA-617]

2.2.1 Patient [729943-257 (79-257)] - Treatment: PSMA-617-02 Arm 2 [7.4 GBq ¹⁷⁷Lu-PSMA-617]

- Metastases to meninges (SAE)

MedDRA Preferred Term (PT): Metastases to meninges

Treatment group: 7.4 GBQ ¹⁷⁷Lu-PSMA-617 Patient details: Aged 59 years, male, [Race].

The patient had mCRPC (diagnosed [****]), and had undergone previous unsuccessful treatments with docetaxel ([****] to [****]), carboplatin ([****] to [****]), abiraterone ([****]), and prednisone (unknown start and end dates). Other active medical conditions were prostate-cancer diffuse bone metastases, [Medical History], gastrointestinal disorders, [Medical History], and [Medical History] (unknown start dates for all conditions). The patient was [Circumstances]. The patient received the first dose of 7.4 GBq ¹⁷⁷Lu-PSMA-617 on 05-Jul-2017 (Day 1); the second dose (modified half-dose as per protocol specifications) of 3.7 GBq ¹⁷⁷Lu-PSMA-617 on 31-Aug-2017 (Day 58); and the third dose (modified half-dose as per protocol specifications) of 3.7 GBq ¹⁷⁷Lu-PSMA-617 on 24-Oct-2017 (Day 112).

On 25-Oct-2017 (Day 113), the patient was hospitalized for complaints of headache, chin numbness extending to the right face and scalp, and weakness in the right leg. The patient was taking or prescribed during the hospitalization the following concomitant medications: lidocaine (for [Medical History]), naproxen (for [Medical History]), gabapentin (for [Medical History]), ondansetron (for gastrointestinal disorders), loratadine (for [Medical History]), and acetaminophen/aspirin/caffeine (for [Medical History]). Laboratory tests showed high partial thromboplastin time (PTT) and mildly high prothrombin time (PT). Brain MRI without contrast showed right small 7 mm subdural hematoma and multiple dural metastases. On 26-Oct-2017 (Day 114), a brain MRI with contrast showed enhancing dural based masses bilaterally, concerning for metastatic disease, noting that the plaque meningiomas could also have this appearance: no subdural hematoma was seen. Due to these results, the patient's overall prognosis was assessed as very poor and palliative care was considered

reasonable. The patient received 2 units of packed red blood cells for noted multifactorial unspecified anemia.

On 27-Oct-2017 (Day 115), the patient was discharged from the hospital with the final diagnosis of ongoing bilateral dural metastases. No more information about the hospitalization (i.e., laboratory test results, treatment of the event) was available. On 01-Nov-2017 (Day 120), the patient withdrew from the study at his own request.

The Investigator considered the metastases to meninges (Grade 3 severity) was probably not related to the treatment with ^{177}Lu -PSMA-617.

2.2.2 Patient [808147-323 (20-JR-323)] Treatment: PSMA-617-02 Arm 2 [7.4 GBq ^{177}Lu -PSMA-617]

- Right-sided abdominal pain (SAE)

MedDRA Preferred Term (PT): Abdominal pain

Treatment group: 7.4 GBQ ^{177}Lu -PSMA-617 **Patient details:** Aged 80 years, male, [Race]. The patient had mCRPC diagnosed in [****] and had previous unsuccessful treatments with enzalutamide ([****] to [****]); abiraterone ([****] to [****]); and cabazitaxel ([****] to [****]). Other active medical conditions included: [Medical History] (since [****]); [Medical History] (since [****]); metabolism and nutrition disorders (since [****]); [Medical History] (since [****]); [Medical History] (unknown start date); [Medical History] (since [****]), [Medical History] (unknown start date); and [Medical History] (unknown start date). The patient received one cycle of 7.4 GBq ^{177}Lu -PSMA-617 on 05-Jul-2017 (Day 1).

On 22-Jul-2017 (Day 18), the patient was hospitalized with right-sided abdominal pain. When the patient was admitted to the ER, he was found to be dehydrated; however, he had no fever or chills, and his vital signs were within normal ranges. The patient was taking or prescribed during the hospitalization the following concomitant medications: docusate calcium and lubiprostone (for [Medical History]), losartan potassium (for [Medical History]), omeprazole (for [Medical History]), pembrolizumab and leuprorelin acetate (for prostate cancer), rosuvastatin calcium (for metabolism and nutrition disorders), prednisone (unspecified indication), and dilaudid (unspecified indication). During the hospitalization, the patient underwent an ultrasound of the gallbladder, computerized tomography (CT) scan of the abdomen, a lung ventilation/perfusion scan, and an x-ray of the chest. The scans showed prostate cancer metastases to the liver and bones, and confirmed cancer progression as the cause for pain.

On 02-Sep-2017 (Day 60), the patient was discharged from the hospital. On 06-Sep-2017 (Day 64), the patient discontinued the clinical trial because of cancer progression.

The Investigator considered the right-sided abdominal pain (Grade 3 severity) was unlikely related to the treatment with ^{177}Lu -PSMA-617.

2.2.3 Patient [628540-336 (44-HL-336)] Treatment: PSMA-617-02 Arm 2 [7.4 GBq ^{177}Lu -PSMA-617]

- Acute kidney injury and emesis (SAE)

(MedDRA Preferred Terms: Acute kidney injury; Emesis)

Treatment group: 7.4 GBq ^{177}Lu -PSMA-617 **Patient details:** Aged [54-95] years, male, [Race].

The patient had mCRPC (diagnosis date unknown), and had undergone unspecified treatments prior to study enrollment. Other active medical conditions were [Medical History]; musculoskeletal and connective tissue disorders; [Medical History] (unspecified dates); [Medical History]; [Medical History]; [Medical History]; and [Medical History] (onset date was unknown for all of these conditions). The patient received the first dose of 7.4 GBq ^{177}Lu -PSMA-617 on 05-Jul-2017 (Day 1); and the second dose of 7.4 GBq ^{177}Lu -PSMA-617 on 07-Sep-2017 (Day 56).

On 09-Sep-2017 (Day 58), the patient underwent a CT scan of the abdomen and pelvis, which showed no significant hydronephrosis and diffuse inflammatory-type changes of the mesentery. On 13-Sep-2017 (Day 62), the patient was hospitalized with acute kidney injury and emesis (reported by PI as a secondary cause of the acute kidney injury). The patient was taking or prescribed during the hospitalization to be treated with the following concomitant medications: meloxicam (unspecified indication), acetaminophen (for [Medical History]), aspirin (for blood disorder), vitamin D3 (for supplement), denosumab (for musculoskeletal and connective tissue disorders), leuprolide (for hormone therapy), megestrol (for [Medical History]), metoprolol (for [Medical History]); loratadine (for [Medical History]), and zalepon (for [Medical History]).

During this hospitalization on 14-Sep-2017 (Day 63), the patient underwent a renal ultrasound that showed no hydronephrosis of the right kidney and mild hydronephrosis of the left kidney. Also on 14-Sep-2017 (Day 63), the patient had an x-ray of the abdomen that showed normal bowel gas patterns and extensive bony metastases. The patient was discharged from the hospital on 14-Sep-2017 (Day 63) or 15-Sep-2017 (Day 64) (there are conflicting reports in the source documents), and was then seen by a nephrologist (date unknown). The nephrologist concluded that meloxicam was the suspected cause of the creatinine elevation; however, it could not be excluded that additional renal toxicity was caused by ^{177}Lu -PSMA-617. The Investigator concluded that the prostate-specific antigen (PSA) levels/response for this patient were not very satisfying (on 12-Oct-2017 +86% above baseline at 73 ng/ml). Considering the PSA response and potential kidney damage, the patient was discontinued from the trial on 11-Oct-2017 (Day 90) because of progressive disease.

The Investigator considered the acute kidney injury and emesis (Grade 3 severity) was possibly related to the treatment with ^{177}Lu -PSMA-617.

2.2.4 Patient [778426-403 (61-JR-403)] Treatment: PSMA-617-02 Arm 2 [7.4 GBq ^{177}Lu -PSMA-617]

- Hepatic failure (SAE)
- Thrombocytopenia (SAE)
- Anaemia (SAE)

MedDRA Preferred Terms: Hepatic failure, Thrombocytopenia

Treatment group: 7.4 GBq ^{177}Lu -PSMA-617 **Patient details:** Aged 60 years, male, [Race].

The patient had mCRPC (diagnosis date unknown), liver metastases (diagnosis date unknown), multiple bone metastases (diagnosis date unknown), [Medical History], [Medical History],

[Medical History], [Medical History], and gastrointestinal disorders (onset dates were unknown for all of these conditions). At study entry, the patient had extensive bone marrow tumor invasion. The patient received cycle one of 7.4 GBq ^{177}Lu -PSMA-617 on 05-Jul-2017 (Day 1).

On 18-Aug-2017 (Day 62), the patient was admitted to the hospital due to generalized weakness and jaundice (because he was found to be in hepatic failure and thrombocytopenia [which were determined to be SAEs]: he was also found to be experiencing anemia, deemed to be a Treatment Emergent Adverse Events [TEAEs]). The patient was taking or prescribed during the hospitalization the following concomitant medications: prednisone (unknown indication), pantoprazol ([Medical History]), tamsulosin ([Medical History]), oxycodone ([Medical History]), lactulose ([Medical History]), and ondansetron (gastrointestinal disorders). On the same day, CT scan of the chest, abdomen and pelvis (compared to a positron emission tomography (PET)/CT scan dated [****]) showed infectious/inflammatory infiltrates in the right upper lobe of the liver (not considered an SAE). New small volume right pleural effusion and mild right atelectasis were observed, with markedly increased innumerable lesions seen through both lobes of the liver. Also, new abdominal adenopathy (probably metastatic innumerable lesions) were seen through both lobes of the liver. New abdominal adenopathy was also seen. Diffuse mixed sclerotic and lytic osseous metastases were reported as unchanged. The patient was admitted to the hospital: additionally, a hepatic panel showed liver failure, with elevated liver enzyme functions of AST 867 IU/L and ALT 410. IU/L He had severe thrombocytopenia (10,000/mc) and grade III anemia (6.7 g/dL). Also, on 18-Aug-2017 (Day 62) due to hepatic failure/disease progression, diffuse mixed sclerotic and lytic osseous prostate cancer metastases that were unchanged, the Investigator was contacted and the patient was discontinued from the study (date of discharge from the study 18-Aug-2017 [Day 62]). The patient was discharged to home for hospice care on an unknown date: the patient died on 24-Aug-2017.

The Investigator considered the hepatic failure (Grade 5 severity) was definitely not related to the treatment with ^{177}Lu -PSMA-617: the Investigator considered that the thrombocytopenia (Grade 4 severity) was possibly related to the treatment with ^{177}Lu -PSMA-617.

3 SAEs with Study Delay

3.1 Treatment: PSMA-617-01 Arm 1 [6.0 GBq ^{177}Lu -PSMA-617]

NA

3.2 Treatment: PSMA-617-02 Arm 2 [7.4 GBq ^{177}Lu -PSMA-617]

3.2.1 Patient [603357-815 (86-815)] - Adenocarcinoma of colon: Treatment: PSMA-617-02 Arm 2 [7.4 GBq ^{177}Lu -PSMA-617]

- Adenocarcinoma of colon (SAE)

MedDRA Preferred Term (PT): Adenocarcinoma of colon

Treatment group: 7.4 GBQ ^{177}Lu -PSMA-617 **Patient details:** Aged [54-95] years, male, [Race].

The patient had mCRPC diagnosed in Sep-2017, and had previous unsuccessful treatments with docetaxel ([****] to [****]), cabazitaxel (date unknown), radium-223 (dates unknown), enzalutamide ([****] to [****]), and abiraterone ([****] to Aug-2017). Other concurrent medical conditions included prostate cancer metastases to the mediastinum and osseous structures. Concomitant medications were leuprorelin acetate (prostate cancer), and acetylsalicylic acid ([Medical History]). The patient was administered the first cycle of 7.4 GBq ^{177}Lu -PSMA-617 on 05-Jul-2017 (Day 1), the second cycle on 30-Aug-2017 (Day 57) prior to the SAE onset. (The patient was initially scheduled to receive his third dose of ^{177}Lu -PSMA-617 on 25-Oct-2017; however, the third cycle was postponed until 12-Dec-2017 due to urgent colon surgery.) The patient was administered his third cycle of ^{177}Lu -PSMA-617 on 12-Dec-2017 (Day 161), and his fourth cycle on 22-Feb-2018 (Day 233).

On [****], the patient had a computerized tomography (CT) scan performed that accidentally revealed a mass suspicious for right colon cancer. On 24-Oct-2017 (Day 112), (55 days after the 30-Aug-2017 the second dose of ^{177}Lu -PSMA-617 had been administered), the patient had a colonoscopy performed that revealed a high-grade obstruction of the right colon. An ascending colon mass biopsy confirmed moderately differentiated adenocarcinoma. On 01-Nov-2017 (Day 120), the patient was admitted to the hospital for adenocarcinoma of the colon with elective laparoscopic-assisted right hemicolectomy. The surgical procedures included exploratory laparoscopy, removal of adhesions, and an extended right hemicolectomy. The same day the patient recovered from the event of adenocarcinoma of the colon.

The pathology report described a moderately differentiated colonic adenocarcinoma involving the ascending colon with circumferential growth and obstruction. No other laboratory results during the hospitalization were available. The patient was discharged from the hospital on 08-Nov-2017 (Day 127).

The Investigator considered there was no relationship between the adenocarcinoma of the colon and the treatment with ¹⁷⁷Lu-PSMA-617. The patient resumed participation in the study and continued in the study as noted above.

3.2.2 Patient [708986-468 (21-HT-468)] Treatment: PSMA-617-02 Arm 2 [7.4 GBq ^{177}Lu -PSMA-617]

- [Medical History] (SAE)

MedDRA Preferred Term (PT): [Medical History]

Treatment group: 7.4 GBO ^{177}Lu -PSMA-617 **Patient details:** Aged 75 years, male, [Race].

metabolism and nutrition disorders; [Medical History]; [Medical History]; [Medical History] ([****]); and [Medical History] - [Medical History] (unknown start dates for all indications without dates).

The patient signed the clinical trial informed consent form on [****], and it is unknown as to when he was initially scheduled to receive the first dose of 7.4 GBq ^{177}Lu -PSMA-617.

On [****], the patient went to the [Medical History] and was subsequently [Medical History] with worsening [Medical History]. At that time, the patient was taking the following medications: amlodipine, atorvastatin, carvedilol, cotrimoxazole, dilitiazem, furosemide, gabapentin, hydrochlorothiazide, hydrocortisone, levothyroxine, senna, sodium chloride (IV solution bolus, one treatment), valsartan, zolpidem. Outpatient prescription medications prior to the SAE included: acetaminophen, amlodipine, atrovastatin, carvedilol, cotrimoxazole, dilitiazem, diovan, febuxostat, gabapentin, hydrochlorothiazide, hydrocortisone, levothyroxine, magnesium chloride, melatonin, oxycodone, rabeprazole, senna, tramadol, valsartan, vitamin D/cholecalciferol, zolpidem, and furosemide (indications for medications are unknown). The patient had undergone a [Medical History] on [****] for [Medical History].

Upon presentation to the [Medical History], the patient was found to have [Medical History] and was also likely to be over-medicated with [Medical History], and was likely to be [Medical History]. [Medical History] resolved. During the [****] [Medical History], the patient underwent a [Medical History] that showed findings of [Medical History] (that were confirmed on prior examination of [****]) with an additional [Medical History]. The [Medical History] showed that there was stable [Medical History].

On [****], the patient was [Medical History]. Because of the [Medical History], enrollment in the clinical study PSMA-617-02 was delayed (original planned start date is unknown): the actual study start date (Day 1 of the study) was 05-Jul-2017.

The Investigator considered the [Medical History] (Grade 3 severity) was possibly related to the treatment with ^{177}Lu -PSMA-617. The patient was randomized to treatment; however actually never received treatment so the Sponsor ruled there was no way the SAE could be related to the study treatment.

4 SAEs with Dosage Maintained

4.1 Treatment: PSMA-617-02 Arm 1 [6.0 GBq ^{177}Lu -PSMA-617]

4.1.1 Patient [834112-089 (34-089)] Treatment: PSMA-617-02 Arm 1 [6.0 GBq ^{177}Lu -PSMA-617]

- Fragile bone secondary to cancer (SAE)

MedDRA Preferred Term (PT): (Osteoporosis)

Treatment group: 6.0 GBQ ^{177}Lu -PSMA-617 **Patient details:** Aged [54-95] years, male, [Race].

The patient had mCRPC diagnosed [****], and had previous unsuccessful treatments with docetaxel ([****] to [****]), enzalutamide ([****] to [****]), cabazitaxel ([****] to [****]), cisplatin ([****] to [****]), etoposide ([****] to [****]), and abiraterone ([****] to 16-Dec-2017). Concurrent medical conditions included prostate cancer metastases to bone, prostate cancer metastases to the osseous structures of the axial and appendicular skeleton, prostate cancer metastases to the lymph nodes, and multiple pelvic and perirectal lymph node prostate cancer metastases. The patient received 2 cycles of 6.0 GBq ^{177}Lu -PSMA-617 with administration of cycle one on 05-Jul-2017 (Day 1), and administration of cycle 2 on 07-Sep-2017 (Day 65).

On 14-Sep-2017 (Day 72), the patient had an x-ray of the left hip due to left hip pain that showed generalized osteoporosis and mixed sclerotic/lytic prostate cancer metastases involving the left iliac bone and bilateral proximal femurs. There were no acute pathologic fractures; however, proximal femurs were at risk for impending pathologic fracture: degenerative changes were present in the lower lumbar spine.

On 15-Sep-2017 (Day 73), the patient was admitted to the hospital for an elective surgery to prevent the risk of pathological fracture of the femur due to bony prostate cancer metastatic disease. At the time of hospitalization, the patient presented with a [**] history of [Medical History] that worsened with movement and weight bearing: he denied any right hip or groin pain. The [Medical History] was localized to the groin and did not radiate, he denied any changes in sensation to the left leg, but reported weakness in hip flexion: he used [Circumstances]. Concomitant medications at the time of hospitalization were not available; however naproxen (for pain) is mentioned in the report: concomitant medications at the time of study enrollment were dexamethasone ([Medical History]), atorvastatin ([Medical History]), ondansetron ([Medical History]), senna plus ([Medical History]), pyridoxine (prophylaxis), potassium chloride (prophylaxis), omeprazole ([Medical History]), lisinopril ([Medical History]), coenzyme Q10 (prophylaxis), cholecalciferol (prophylaxis), and aspirin (prophylaxis). Bone scans, x-rays, and MRI of the pelvis and bilateral proximal femurs revealed significant involvement of the left femoral head, neck, and left proximal femur and femoral neck/head. The patient had surgery on 15-Sep-2017 (Day 73) to perform prophylactic intramedullary (cephalo-medullary) nailing of the left femur. After surgery, an x-ray of the left femur showed expected postoperative changes without hardware complications.

The patient reported he was doing well and the SAE of fragile bone secondary to cancer was considered resolved on 15-Sep-2017. He was discharged from the hospital on 18-Sep-2017 (Day 76).

The Investigator considered that fragile bone secondary to cancer (Grade 3 severity) was not related to the treatment with ^{177}Lu -PSMA-617. The patient remained in the study as planned, with no treatment interruption.

4.2 Treatment: PSMA-617-02 Arm 2 [7.4 GBq ^{177}Lu -PSMA-617]

4.2.1 Patient [232914-588 (49-588)] Treatment: PSMA-617-02 Arm 2 [7.4 GBq ^{177}Lu -PSMA-617]

– Pneumonia (SAE)

MedDRA Preferred Term (PT): Pneumonia

Treatment group: 7.4 GBQ ^{177}Lu -PSMA-617 **Patient details:** Aged 59 years, male, [Race].

The patient had mCRPC ([****]), and had unsuccessfully undergone prior conventional mCRPC therapies including docetaxel, leuprolide, enzalutamide, and abiraterone. Other active medical conditions included [Medical History], [Medical History] ([Medical History]), [Medical History], [Medical History], [Medical History], musculoskeletal and connective tissue disorders, [Medical History], and [Medical History] (unknown start dates are left blank). The patient received the first cycle of 7.4 GBq ^{177}Lu -PSMA-617 05-Jul-2017 (Day 1), and the second cycle on 06-Sep-2017 (Day 63).

Concomitant medications were tamsulosine (mCRPC), melatonin (mCRPC), dutasteride (mCRPC), cevimelin (mCRPC), curcumin (mCRPC), zyflamend (mCRPC), ibuprofen ([Medical History]), omeprazole ([Medical History]), oxybutinin ([Medical History]), oxycodone ([Medical History]), cetirizine ([Medical History]), metformin (prophylaxis), polyethylene glycol ([Medical History]), ondansetron([Medical History]), prochlorperazine ([Medical History]), bisacodyl ([Medical History]), cholecalciferol (musculoskeletal and connective tissue disorders), calcium (musculoskeletal and connective tissue disorders), promethazine ([Medical History]), B12 ([Medical History]), cetirizine ([Medical History]), and morphine ([Medical History]).

On 09-Sep-2017 (Day 66), (3 days after the 06-Sep-2017 dose of ^{177}Lu -PSMA-617 had been administered), the patient experienced cough and fever. On 11-Sep-2017 (Day 68), he experienced worsening of these symptoms and went to the Emergency Room, where upon admission he had a body temperature of 103° F. Chest x-ray showed left basilar subsegmental atelectasis with development of opacity in the left posterior costophrenic angle on the lateral view worrisome for pneumonia. Diffuse sclerotic osseous metastases were also noted. Urine was negative for Streptococcus pneumoniae antigen. Respiratory polymerase chain reaction (PCR) panel was also performed, and influenza B was diagnosed; however, it was not considered an SAE. On 11-Sep-2017 the patient was hospitalized for pneumonia and treated with unspecified antibiotics.

The patient recovered from the event of pneumonia and was discharged from the hospital on 13-Sep-2017 (Day 70).

The Investigator considered that the pneumonia (Grade 3 severity) was unlikely related to the treatment with ^{177}Lu -PSMA-617. The patient remained in the study as planned, with no treatment interruption.

14.3.4 Abnormal laboratory values listing (each patient) - Not applicable

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Appendix 16

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Appendix 16.1 Study information

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Appendix 16.1.1 Protocol and protocol amendments

History of changes	
Version	Summary of changes
1.0	Original version

1 Protocols and protocol amendments

Table 1-1 List of protocols, protocol amendments and post text supplements

Document	Effective Date Brany IRB	Effective Date UCLA IRB
<i>Original Protocol 28-Dec-2016</i>	14-Mar-2017	N/A
<i>Amended Protocol Version 01 25-Jan-2017</i> (track change version)	N/A	N/A
<i>Amended Protocol Version 01 24-Feb-2017</i>	14-Mar-2017	N/A
<i>Amended Protocol Version 02 07-Jun-2017</i> (track change version)	N/A	N/A
<i>Amended Protocol Version 02 07-Jun-2017</i>	09-Jun-2017	N/A
<i>Amended Protocol Version 03 29-Jun-2017</i> (track change version)	N/A	N/A
<i>Amended Protocol Version 03 29-Jun-2017</i>	06-Dec-2017	12-Sep-17
<i>Amended Protocol Version 04 18-Sep-2017</i> (track change version)	N/A	N/A
<i>Amended Protocol Version 04 18-Sep-2017</i>	06-Dec-2017	12-Oct-2017
<i>Amended Protocol Version 05 01-Jun-2018</i>	03-Aug-2018	10-Jan-2018

***Czernin site submitted Amended Protocol Version 1 with Amended Protocol 4 and Amended Protocol 2 with Amended Protocol Version 5 to the UCLA IRB, first patient in occurred under Protocol Version 4 on 13-Oct-2017.*

Clinical Trial Protocol: IND # 133661

Study Title: PSMA-directed EndoRadiotherapy of Castration-resISTant prostate cancer (PERCIST). A phase II clinical trial.

Study Number: TBD
IND Number: 133661

Study Phase: Phase II

Product Name: ^{177}Lu - DOTA-PSMA-617

Indication: Metastatic castration resistant prostate cancer

Principle Investigators: Ebrahim S. Delpassand, M.D. F.A.C.N.M.
Johannes Czernin, M.D.

Sponsors: Ebrahim S. Delpassand, M.D. F.A.C.N.M
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Date

Original Protocol Date: 12/28/2016

Confidentiality Statement

This confidential document is the property of sponsors, and is provided for the use of the investigator and other designated site personnel. It may also be distributed to the ethics committee/IRB upon notification from sponsors. No unpublished information contained herein may be disclosed, except as necessary to obtain consent from persons who are considering participating in the study, without the prior written approval of sponsors.

SYNOPSIS

Sponsors:

Ebrahim S. Delpassand, M.D.

Johannes Czernin, M.D.

Name of Finished Product:

^{177}Lu -PSMA-617

Name of Active Ingredient:

2->3-(1-Carboxy-5-{3-naphthalen-2-yl-2->(4-{>2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl`-cyclohexanecarbonyl)-amino]-propionylamino`-pentyl)-ureido]-pentanedioic acid

Study Title:

PSMA-directed EndoRadiotherapy of Castration-resISTant prostate cancer (PERCIST). A phase II clinical trial.

Study Number:

TBD

Study Phase:

Phase II

Primary Objective:

To assess safety and efficacy defined as >50% decline in PSA after ^{177}Lu -PSMA-617 in patients with metastatic castration resistant prostate cancer

Secondary Objectives for each treatment dose:

1. To determine maximum PSA decline.
2. To determine PSA progression-free survival (PFS), measured from start of therapy until death or PSA progression.
3. To determine radiographic PFS, measured from start of therapy until death or radiographic progression using RECIST 1.1/PCWG3 criteria.
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST stable disease (SD), partial response (PR) or complete response (CR).
5. To determine impact on bone pain level
6. To determine impact on quality of life

7. To determine impact on performance status (ECOG)

Study Design:

Open-label, prospective, multicenter clinical trial.

Study Population:

Patients with metastatic castration resistant prostate cancer

Inclusion Criteria:

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2.000/\mu\text{l}$, PLT count $\geq 75.000/\mu\text{l}$, Hb $\geq 8.9 \text{ g/dl}$ and ANC $\geq 1000 \text{ mm}^3$.
8. Signing of the Informed Consent Form

Exclusion Criteria:

1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm) or other radionuclide therapy.
2. Glomerular Filtration Rate (GFR) $< 40 \text{ ml/min}$
3. Grade 3 toxicity serum creatinine using CTCAE v. 4.0
4. AST and ALT $> 5 \times \text{ULN}$
5. Urinary tract obstruction or marked hydronephrosis

Test Product; Dose; and Mode of Administration:

Randomization into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq ($\pm 10\%$, **arm 1**) or 7.4 GBq ($\pm 10\%$, **arm 2**) ^{177}Lu -PSMA-617 every 6 ± 1 weeks; RLT until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy as determined by dosimetry after the first treatment.

Study Duration:

Patients will be followed until either of the following conditions occur:

1. 24 month after the first treatment.
2. Progression by RECIST 1.1/PCWG3 criteria.
3. Death.

Safety Assessments:

Following laboratory tests will be performed one week before each treatment and 4 weeks after the last treatment and every 3 month thereafter:

1. Complete metabolic panel and eGFR
2. CBC

At baseline, 7 (+/- 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 week) until the end of follow up visits (24 months) patients will be called for safety interview.

Efficacy Assessment for each treatment arm:

Primary objective:

12 week PSA response: Proportion of patients with PSA-decline of $\geq 50\%$ at 12-weeks after the first RLT [1]

Secondary objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]
2. Time to PSA progression, for each treatment arm. [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later
 - b. for patients without PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later
3. Radiographic progression free survival (rPFS), for each treatment arm.
4. Change in Pain, Quality of Life and ECOG performance score: Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 month, for each treatment arm

Number of patients enrolled:

As per statistical evaluation, total of 200 patients will be required to have statistical power to achieve the primary endpoints of the study.

Date of Original Protocol: December 28th, 2016

Date of Most Recent Protocol Amendment (if applicable): N/A

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- [**Appendix IV: Consent Form**](#)

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Clinical Trial Protocol: IND #

¹⁷⁷Lu-PSMA-617

LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse event
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
AP	alkaline phosphatase
AST	Aspartate aminotransferase
AUC	Area under the plasma concentration versus time curve
BUN	Blood urea nitrogen
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CI	Confidence interval
CR	Complete response
CRF	Case report form
CT	Computed tomography
DCR	Disease Control Rate
ECOG	Eastern Cooperative Oncology Group
eGFR	estimated Glomerular Filtration Rate
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GGT	Gamma-glutamyl transferase
GH	Growth hormone

Clinical Trial Protocol: IND #

¹⁷⁷Lu-PSMA-617

Hct	Hematocrit
Hgb	Hemoglobin
HIPAA	Health Information Portability and Accountability Act
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intent-to-treat
LDH	Lactic dehydrogenase
MBq	MegaBequerel
mCi	milliCurie
mo	months
GBq	gigabecquerel
MR	Magnetic resonance
MRI	Magnetic resonance imaging
N/A	Not applicable
NDA	New Drug Application
PCa	Prostate cancer
PET/CT	Positron Emission Tomography/Computed Tomography
PFS	Progression-free survival
PSA	Prostate-specific antigen

Clinical Trial Protocol: IND #

¹⁷⁷Lu-PSMA-617

PR	Partial response
RBC	Red blood cell
RECIST	Response Evaluation Criteria In Solid Tumors
RLT	Radioligand therapy
rPFS	Radiographic progression-free survival
SAE	Serious adverse event
SAER	Serious adverse event report
SAP	Statistical analysis plan
SD	Stable disease
SE	Standard error
SPECT	Single-photon emission computerized tomography
PSMA	prostate-specific membrane antigen
US	United States
WBC	White blood cell
WHO-DD	World Health Organization Drug Dictionary

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1. Introduction

1.1 Background

According to the American Cancer Society more than 1 million people in the United States are diagnosed with cancer each year. For American *males*, prostate cancer is the second most common cause of cancer related death [2]. A recent publication [3] estimated the prevalence of prostate cancer as 2,219,280 in the US in 2009 and 3,072,480 in 2020, and incidence of metastatic Castration Resistant Prostate Cancer (mCRPC) as 36,100 and 42,970, respectively. Various therapies have been developed to improve survival of patients with advanced prostate cancer. However, despite such efforts currently all-cause mortality in prostate cancer has been estimated at 168,290 in 2009 and 219,360 in 2020, with 20.5% and 19.5% of these deaths, respectively, occurring in men with mCRPC.

Patients with metastatic castration-resistant prostate cancer (mCRPC) have a poor prognosis, and those patients with metastases are expected to survive ≤ 19 mo [3]. As patient disease progresses, quality of life deteriorates, and until recently, few treatment options were available. Several new therapies have shown an improvement in overall survival for patients with mCRPC who have already received chemotherapy with docetaxel (Fig. 1) [4] [5] [6, 7] [8]. The impact of these new data on clinical practice, treatment sequencing, and best care for individual patients is not yet fully established.

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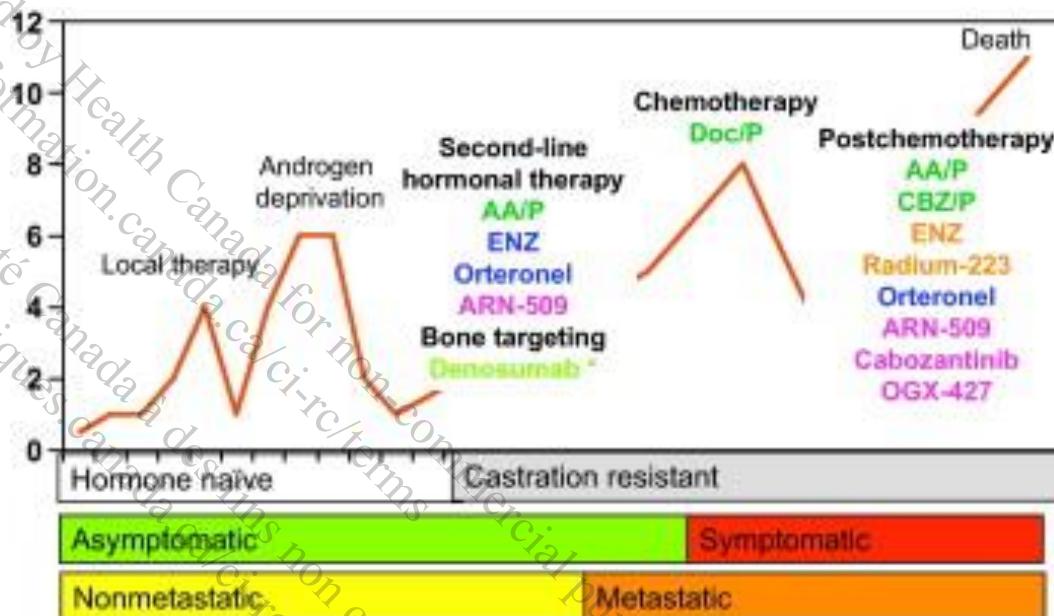


Figure 1: Current, ongoing, and future landscape in the management of castration-resistant prostate cancer. Color key: green = US Food and Drug Administration/European Medicines Agency (FDA/EMA) approved; light green = trial results in high-risk patients positive, but not approved; orange = prospective, randomized, phase 3 clinical trial completed, results positive, FDA/EMA approval awaited; blue = prospective, randomized, phase 3 clinical trial completed, results awaited; purple = promising agent, phase 3 clinical trials ongoing. * Trial results for denosumab in high risk patients positive, but not approved. AA/P = abiraterone acetate with prednisone; ENZ = enzalutamide; Doc/P = docetaxel plus prednisone; CBZ/P = cabazitaxel plus prednisone.

1.1.1. Current treatment options for metastatic castration-resistant prostate cancer: before docetaxel

Sipuleucel-T

Sipuleucel-T is an autologous vaccine consisting of individually collected antigen-presenting cells that are exposed to the fusion protein prostatic acid phosphatase and granulocyte colony-stimulating factor (GCSF), and then reinfused in the patient at weeks 0, 2, and 4. In the Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) study, median survival with sipuleucel-T was 25.8 mo compared with 21.7 mo with placebo [9]. It has to be considered, however, that only patients with a good Eastern Cooperative Oncology Group

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performance status of 0–1, asymptomatic or mildly symptomatic osseous metastases, and absence of visceral metastases were included in the trial.

Abiraterone acetate

The COU-AA-302 (Cougar 302) trial randomized 1088 men with mCRPC to receive abiraterone acetate with prednisone (AA/P) or placebo [4] with the primary end points of overall and radiographic progression-free survival (rPFS) by central review. Median overall survival was 35.3 mo and 27.2 mo in the AA/P group and in the placebo group, respectively ($p = 0.01$) [10]. Also, the co-primary end point of rPFS was significantly improved in the AA/P group, at 16.5 mo, as compared to 8.3 mo in the placebo arm ($p < 0.001$). On all secondary end points, AA/P treatment resulted in significantly improved effects.

Docetaxel/prednisone

In 2004, cytotoxic treatment with docetaxel plus prednisone (Doc/P) was the main option for treatment of mCRPC based on the TAX 327 trial [11]. The median survival was 18.9 mo versus 16.4 mo in the group of patients who received mitoxantrone/prednisone ($p = 0.009$), the 3-yr overall survival rate was 18.6% versus 13.5%, and pain response was 35% versus 22%. It has been shown recently that Doc/P is active in men with symptomatic mCRPC and especially in patients with poorly differentiated prostate cancer (PCa) (Gleason score: 8–10) [12].

Subsequent studies using combinations with docetaxel have not further improved the oncologic outcome [3]. The results of the Randomized Study Comparing Docetaxel Plus Dasatinib to Docetaxel Plus Placebo in Castration-Resistant Prostate Cancer (READY) and the Aflibercept in Combination with Docetaxel in Metastatic Androgen-Independent Prostate Cancer (VENICE) trial were disappointing [13] [11]. The median survival after docetaxel and docetaxel/dasatinib was 21.2 mo versus 21.5 mo, respectively, and the median survival after docetaxel versus docetaxel plus afilbercept was 21.1 mo versus 22.1 mo, respectively.

The differences in the patient cohorts of the Cougar 302, IMPACT, and TAX 327 trials make it evident that AA/P will be used for asymptomatic or mildly symptomatic mCRPC with a

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low metastatic burden, whereas Doc/P might be the treatment of choice in men with symptomatic mCRPC and/or a high metastatic burden as well as an undifferentiated PCA.

1.1.2. After docetaxel treatment

Docetaxel rechallenge

The scientific evidence of this approach results from large, retrospective series that identified patients who might be good candidates for re-exposure [14] [15] [16]. Patients who responded with a ≥30% decrease in prostate-specific antigen (PSA) level, maintained for at least 8 wk after first exposure to docetaxel, demonstrated a positive PSA response in about 55% to 60% of the cases during re-exposure without increasing treatment related toxicity.

Abiraterone acetate plus prednisone

AA/P versus placebo was evaluated in the Cougar 301 trial, which randomized 1195 patients with progressive mCRPC who failed docetaxel-based chemotherapy [5]. The median follow-up in the overall study population was 12.8 mo. Overall survival was significantly improved from 10.9 mo in the placebo arm to 14.8 mo in the AA/P arm ($p < 0.001$). All secondary end points were met and all end points demonstrated a significantly improved benefit for the AA/P group. Adverse events with regard to the CYP 17 blockade were observed significantly more often in the AA/P arm (55% vs 43%; $p < 0.001$).

Recently, Goodman et al. [17] demonstrated that AA/P is effective even in patients with liver or lung metastases, although to a lesser degree. The overall survival times were 12.9 mo versus 8.3 mo in the placebo group ($p = 0.022$). Albiges et al. [18] described an AA withdrawal syndrome that developed in 32% of 66 patients who had been treated for a mean period of 5.7 mo. Clayton et al. [19] presented data from a population-based study that included 187 mCRPC patients with a mean PSA serum concentration of 138 ng/ml who were treated with AA/P. The median overall survival was only 9.3 mo and might reflect the oncologic efficacy of AA/P in a real-world patient population with high metastatic burden.

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Enzalutamide (formerly MDV3100)

Enzalutamide (ENZ) acts as an androgen receptor (AR)-signaling inhibitor, and it was evaluated in the Multinational, Phase 3, Randomized, Double-blind, Placebo-controlled, Efficacy and Safety Study of Oral MDV3100 in Patients with Progressive Castration-Resistant Prostate Cancer Previously Treated with Docetaxel-Based Chemotherapy (AFFIRM) trial, which randomized 1199 mCRPC patients to receive ENZ or placebo [8].

The median follow-up was 14.4 mo and the median overall survival was 18.4 mo and 13.6 mo ($p < 0.0001$) in the ENZ group and in the placebo group, respectively, with a 37% reduction in relative risk for death. All secondary end points were met with a statistically significant benefit in the ENZ arm. With regard to safety, the ENZ group experienced fewer grade 3/4 toxicities than the placebo group (53% vs 45%). The risk of seizures was slightly elevated in the ENZ group, with a frequency of 0.6% versus 0% in the placebo group.

Recently, Scher et al. [20] demonstrated that the use of corticosteroids in parallel to ENZ not only increased grade 3/4 side effects from 34.4% to 63.3%, but it also decreased overall survival to a median 11.5 mo. These data suggest that one of the other second-line therapies, such as AA/P or cabazitaxel plus prednisone (CBZ/P), might be the drug of choice, rather than ENZ, in patients who need corticosteroids for the management of associated comorbidities. Sternberg et al. [21] reported that ENZ is equally effective in patients aged >75 yr, with a median survival time of 18.2 mo as compared to the placebo group with 13.3 mo ($p = 0.0044$). Fleming et al. [22] identified a longer disease history (7.9 yr vs 5.9 yr), a better PSA response (87% vs 52%), and a lower metastatic burden associated with long-term response of 35% and 22% after 12 mo and >18 mo, respectively. These data seem to be important for the decision-making process about the most appropriate therapy for mCRPC patients following docetaxel chemotherapy.

Cabazitaxel plus prednisone

In the XRP6258 Plus Prednisone Compared to Mitoxantrone Plus Prednisone in Hormone-Refractory Metastatic Prostate Cancer (TROPIC) trial, 755 patients with mCRPC who

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progressed during or after docetaxel-based chemotherapy were prospectively randomized to receive CBZ/P or mitoxantrone/prednisone (MP) at 21-d intervals for 10 cycles [5]. The primary end point was achieved and CBZ/P treatment resulted in a median overall survival of 15.1 mo in the CBZ/P compared to 12.7 mo in the mitoxantrone/prednisone group (hazard ratio [HR]: 0.70; 95% confidence interval [CI], 0.59–0.83; $p < 0.0001$). All secondary end points of the trials were reached and they were in favor of CBZ. The most common side effects were neutropenia (CBZ/P group: 82% vs MP group: 58%), leukopenia (CBZ/P group: 68% vs MP group: 42%), and anemia (CBZ/P group: 11% vs MP group: 5%). Diarrhea was the most common non-hematologic side effect and occurred in 6% of the CBZ/P group and <1% of the MP group.

On the other hand, the German compassionate use program (CUP) included 111 patients with mCRPC who met the inclusion criteria of the TROPIC trial; the frequency of neutropenia, leukopenia, and anemia decreased to 7.2%, 9.0%, and 4.5%, respectively [23]. Grade 3/4 gastrointestinal toxicity was observed in only 0.9% of the patients. The most likely reason for the improved toxicity profile is the experience of the investigators, guideline-compliant application of GCSF even at cycle 1, and preventive measures with regard to the treatment of diarrhea.

Recently, Heidenreich et al. [24] analyzed the European CUP, including 746 mCRPC patients, with regard to the frequency and management of adverse events in senior adults. In that study, 325 (43.5%) patients were aged ≥ 70 yr and 145 (19.4%) men were ≥ 75 yr. The type and the frequency of grade 3/4 side effects did not differ significantly between the younger and the older patients except that the frequency of grade 3/4 neutropenia was slightly higher in the group of men aged ≥ 75 yr (19.7% vs 15%). Furthermore, GCSF was used more often at cycle 1 (58.5% vs 47%) and throughout CBZ/P treatment (66.8% vs 58%) in the ≥ 75 age group versus the <70 age group. In their analysis, Heidenreich et al. [24] developed a risk model to predict grade ≥ 3 neutropenia and/or neutropenic complications based on a multivariate analysis. Age ≥ 75 yr, cycle 1, and neutrophil count $<4000/\text{mm}^3$ before CBZ injection were associated with neutropenic complications. It has to be mentioned that even in the presence of these risk factors, prophylactic application of

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GCSF significantly reduced the risk of neutropenic complications by 30% (odds ratio: 0.70; 95% CI, 0.50–0.99; $p = 0.04$).

Bone-targeting agents

More than 90% of patients with CRPC have bone metastases, which are a major cause of death, disability, and decreased quality of life, as well as increased cost of treatment [25]. Zoledronic acid and the receptor activator of nuclear factor κ B (RANK) ligand inhibitor denosumab are the two US Food and Drug Administration-approved bone-targeting agents in the management of CRPC [3].

In a phase 3 study, the median time to first on-study, skeletal-related event was 20.7 mo with denosumab compared with 17.1 mo with zoledronic acid (HR: 0.82; 95% CI, 0.71–0.95; $p = 0.0002$ for noninferiority; $p = 0.008$ for superiority) [26]. In a recent, prospective, randomized, double-blind, placebo-controlled trial, Smith et al. [27] evaluated the therapeutic efficacy of denosumab 120mg every week versus placebo in 1423 men with nonmetastatic CRPC and aggressive PSA kinetics (PSA level >8.0 ng/ml and/or PSA doubling time <10 mo). The median time to first bone metastases was significantly prolonged by 4.3 mo (29.5 mo vs 25.2 mo; $p = 0.028$). Bone metastases-free survival was significantly improved by 16%, 23%, and 29% in patients with a PSA doubling time of <10 mo, <6 mo, and <4 mo, respectively.

Radium-223

Radium-223 is a radiopharmaceutical that acts as a calcium mimic and targets new bone growth in and around bone metastases via heavy alpha particles that have an ultrashort range of <100 μ m. A Phase 3 Study of Radium-223 Dichloride in Patients with Symptomatic Hormone Refractory Prostate Cancer with Skeletal Metastases (ALSYMPCA), which included 921 CRPC patients, the median overall survival was 14.9 mo in patients treated with radium-223 compared with 11.3 mo in the placebo group (HR: 0.695; 95% CI, 0.581–0.8732; $p < 0.0001$) [7].

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1.1.3. New and emerging developments

Agents targeting steroidogenesis

Orteronel (TAK-700) selectively blocks 17,20-lyase, resulting in fewer mineralocorticoid effects than AA [28]. In the phase 2 portion of a dose-finding study, Orteronel (TAK-700) 400mg twice daily with prednisone 5mg twice daily resulted in a reduction in PSA level $\geq 50\%$ in 52% of the 96 chemotherapy-naïve mCRPC patients at 12 wk. There are two ongoing phase 3 clinical trials in the prechemotherapy ($n = 1454$) and postchemotherapy ($n = 1083$) landscape of mCRPC that are evaluating the oncologic activity of orteronel. Both trials have completed recruitment.

Galeterone (TOK-001) has combined activity: It inhibits the human CYP17 enzyme, it has pure antagonistic activity toward the AR, and it inhibits the binding of androgens to both mutant and wild-type AR [29]. In the Androgen Receptor Modulation Optimized for Response (AMORI) trial, 49% of chemotherapy-naïve mCRPC patients experienced a PSA-level reduction of $\geq 30\%$, and a $\geq 50\%$ reduction was achieved by 22% [30]. Despite the absence of steroid co-treatment, no adrenal mineralocorticoid excess was observed and a phase 2 trial is underway.

Androgen-receptor blocking agents

ARN-509 is a full antagonist to AR overexpression: It inhibits androgen-dependent gene description, and it impairs nuclear translocalization and DNA binding of AR [31]. Currently, three prospective randomized phase 3 clinical trials are underway including (1) patients with high-risk and nonmetastatic CRPC, (2) treatment-naïve patients with mCRPC, and (3) patients with progression following AA/P treatment. Preliminary results have been presented for the first two groups and a $\geq 50\%$ decline in PSA level was achieved in 91% of patients with high-risk and nonmetastatic CRPC and in 88% of treatment-naïve patients with mCRPC. The most common side effects were tolerable fatigue and gastrointestinal events.

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Interestingly, PSA changes did not correlate with the antitumor effects in bone metastases and soft-tissue lesions. However, patients with complete resolution (n = 14; 12%) or partial resolution (n = 65; 56%) of bone scans experienced significantly better response rates to soft-tissue metastases as compared to men with stable or progressing bone scans (81% vs 61%), and they also experienced longer progression-free survival rates at 6 mo (56% vs 48%, respectively). Cabozantinib has significant antitumor activity and a well-tolerated toxicity profile, so it might be well integrated into the therapeutic armamentarium to treat mCRPC.

Targeted radionuclide Therapy

Over the past several decades, numerous combined diagnostic and therapeutic radioligands (Theranostics) were designed to target receptors on the cancer cell surface. Antibodies (whole or small fragments), small molecules, peptides with affinities to receptors (agonist or antagonist) have demonstrated in vivo efficacy for targeting cancers based on up-regulated antigens or receptor populations. This approach, also called radioligand therapy (RLT), presents several advantages over conventional chemotherapy. The expression of the antigens or special receptors can be identified by a diagnostic probe before exposing patients to therapeutic doses of these agents allowing identification of suitable subjects for therapeutic procedures and preventing unnecessary exposure of the patients to radiation without significant benefit. This approach allows the physician to select only those patients with high expression of the target prior to treatment. Since the unused radioactive materials are excreted from the body, RLTs are generally well tolerated with no significant or generally reversible or manageable side effects as has been demonstrated for ¹⁷⁷Lu-DOTATATE treatment in patients with neuroendocrine tumor [34].

Prostate cancer demonstrates high expression levels of prostate-specific membrane antigen (PSMA) on its cell surface. Thus PSMA has become a biomarker for prostate cancer [35] [36] and has attracted significant interest as a target for the imaging [37] [38] and therapy [39, 40]. In particular, development of small urea-based PSMA ligands have received significant interest due to their high affinity for PSMA [41] [42]. The urea-based PSMA ligands were modified to deliver a variety of radio-imaging nuclides for both PET and

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SPECT. Gallium (⁶⁸Ga) labeled urea-based PSMA ligands have been developed as diagnostic agents and studied by several groups [43] [44]. More recently a Lutetium (¹⁷⁷Lu) labeled urea based PSMA ligand (DOTA PSMA or PSMA 617) were evaluated in preclinical and clinical phase. Characteristics of ¹⁷⁷Lu labeled PSMA are described below.

1.2 Characteristics of ¹⁷⁷ Lu-DOTA-PSMA (¹⁷⁷Lu-PSMA-617)

Lutetium (¹⁷⁷Lu) -DOTA PSMA has three components: PSMA is the targeting vector , DOTA (1, 4, 7, 10-tetraazacyclododecane-1, 4, 7, 10-tetraacetic acid) is a radiometal chelator and a linking group, and ¹⁷⁷Lu is the beta emitter that upon internalization delivers radiation to the nucleus of tumor cells to cause DNA damage [43] [44, 45]. The targeting vector utilizes glu-urea-lys sequence which is an inhibitor capable of binding to the domain of PSMA. These components have been previously used in human subjects and in medical research.

1.3 Background of Drug Development

There is substantial previous pre-clinical and clinical experience with ¹⁷⁷Lu-PSMA-617 published in peer reviewed medical literature from multiple medical centers throughout the world. Sponsors are relying on studies published in the peer viewed medical journals for preclinical and preliminary clinical information. Summary of such reports is given below.

1.3.1 Preclinical Studies.

Martina Benesova et al. [46] performed a preclinical evaluation of radiolabeled PSMA-617. PSMA-617 was synthesized by solid phase peptide synthesis. PSMA-617 can be labeled with ¹⁷⁷Lu and Ga-68. Both in vivo and vitro studies were performed using LNCaP cell lines expressing PSMA. PSMA-617 showed highest inhibition potency $K_i = 6.91 \pm 1.32$ for Lu

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complex; 6.40 ± 1.02 nM for Ga complex. PSMA-617 showed higher specific internalization in LNCaP cells.

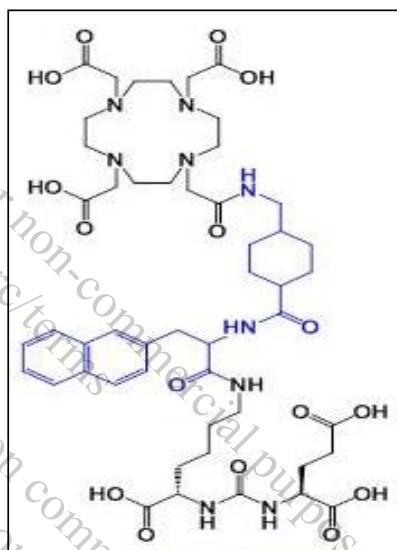


Figure 2: Structure of PSMA 617. Chemical Name 2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-[(2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl]-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid.

The i.v. administered ¹⁷⁷Lu-PSMA-617 effectively cleared the blood by 1 hr. Clearance of radioactivity occurred largely through the renal system. As a result of this, the kidneys exhibited significant uptake $137.2 \pm 77.8\%$ ID/g; this could be effectively blocked ($0.85 \pm 0.22\%$ ID/g) by co-injection of PMPA [2 mg/kg], a high affinity inhibitor of PSMA. At 24 hr ¹⁷⁷Lu-PSMA-617 shows rapid clearance from the kidney $2.13 \pm 1.36\%$ ID/g highlighting its potential use as theranostic agent. At 1 hr time point ¹⁷⁷Lu-PSMA-617 displayed good in vivo tumor targeting with $11.20 \pm 4.17\%$ ID/g. Accumulation in tumor was PSMA specific with reduction to $0.64 \pm 0.07\%$ ID/g by coinjection of 2-PMPA. At 24 h post injection $10.58 \pm 4.50\%$ ID/g uptake was retained in the tumor tissue. For all other non-target tissues, ¹⁷⁷Lu-PSMA-617 demonstrated rapid clearance. The ratio of tumor to blood was 1058; tumor to muscle was 529 at 24 hr post injection. These favorable pharmacokinetics are crucial for

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imaging and therapy. The detailed biodistribution results are summarized in Figure 3. ^{68}Ga -PSMA 617 showed similar uptake in the LnCaP tumors ($11.20 \pm 4.17\text{ %ID/g}$). It also shows similar pharmacokinetic clearance profile compared with ^{177}Lu -PSMA-617.

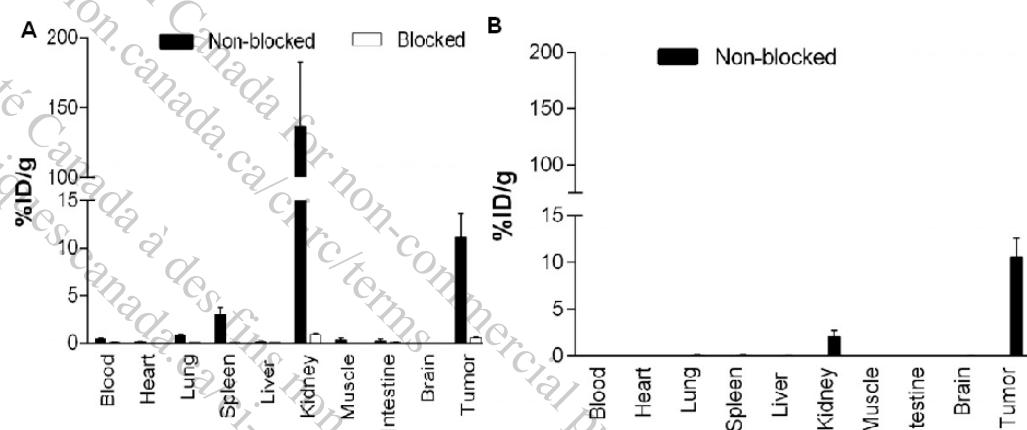


Figure 3: Distribution assay of ^{177}Lu -PSMA-617 in BALB/c mice with LNCap xenografts at 1 h (A) and 24 h (B) post injection.

In summary authors concluded the present radiotracer is suitable for theranostic application in human prostate cancer.

1.3.2 Clinical Studies

Current literature is available to evaluate ^{177}Lu -PSMA-617 therapeutic role in clinical management of patients with prostate cancers. The studies presented in this section were chosen based on novelty of the approach (initial report of application, variables for analyses) and/or the number of patients included.

Clemens Kratochwil et al. [^{177}Lu]Lutetium-labelled PSMA ligand-induced remission in a patient with metastatic prostate cancer. Eur J Nucl Med Mol Imaging 2015; 42:6 ;987-988. [47]

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Study Design: First reported application of ^{177}Lu -PSMA-617 for treatment of a patient with mCRPC. Patient had proven PSMA expression and PSA of 38.0 ng/ml prior to treatment and has received 7.4 GBq of ^{177}Lu -DKFZ-617 in 2 cycles 3 months apart.

Toxicity: No potential side effects were reported in this study.

Results: After the radiotherapy ^{177}Lu -PSMA-617, PSA level of patient decreased to 4.6 ng /ml. PET/CT images showed no signs of metastases lesions either shrunk or were undetectable.

Conclusion: Authors are planning to conduct multicenter a clinical trial as soon as possible to examine clinical potential of ^{177}Lu -PSMA-617.

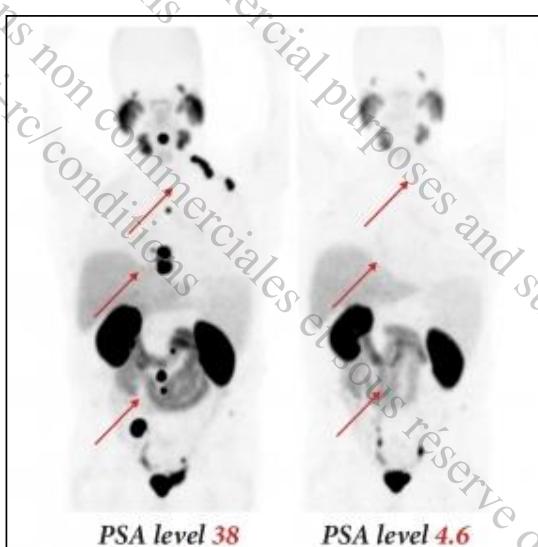


Figure 4: Above Image has recently awarded as image of Year Award and the Berson-Yalow Award at the 2015 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) in Baltimore, USA.

Hojjat Ahmadzadehfar et al. Early side effects and first results of radioligand therapy with ^{177}Lu -DKFZ-617 PSMA of castrate-resistant metastatic prostate cancer: a two-center study. *EJNMMI Research* 2015; 5:36. [48]

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Study Design: A total of 10 consecutive hormone and /or chemo refractory PCa patients with distant metastases and progressive disease with rising PSA levels were recruited in this study.

All patients had prior history or were under therapy with enzalutamide and/or abiraterone.

Four patients had received ²²³Ra-dichloride (1-4 cycles). All 10 patients underwent with ⁶⁸Ga-PSMA HBED-CC (⁶⁸Ga-PSMA) PET /CT prior to therapy to evaluate PSMA expression. Ten patients were treated with range of 4.1-6.1 GBq dose of ¹⁷⁷Lu-DKFZ-617 PSMA. All patients were treated with single dose of ¹⁷⁷Lu-PSMA. The mean and median PSA levels prior to therapy were 339.4 and 298.5 ng/ml. Complete blood chemistry, renal and liver function tests were performed a day before and 2 after the radiotherapy. Patients were followed via telephone every week for safety assessment.

Toxicity: No patient experienced any side effects immediately after injection of ¹⁷⁷Lu-DKFZ-617 PSMA. Relevant hematotoxicity (grade 3 or 4) occurred 7 weeks after the administration in just one patient. The same patient showed a leucopenia grade 2. Two patients showed a disturbance of only 1 hematologic cell line, whereas one patient showed a reduction of grades 1 and 2 in leucocytes and thrombocytes, respectively. Six patients did not show any hematotoxicity during the 8 weeks after therapy. There was no relevant nephrotoxicity (grade 3 or 4).

Results: Eight weeks after the therapy, seven patients (70 %) experienced a PSA decline, of which six experienced more than 30 % and five more than 50 %. Three patients showed a progressive disease according to the PSA increase.

Conclusions: ¹⁷⁷Lu-DKFZ-617 PSMA radiotherapy with single dose for the treatment of metastatic prostate cancer patients without any other therapy option is safe and seems to have a low early side-effect profile with evidence of positive response to the therapy according to PSA decline in 70 % of patients. The authors also stated ¹⁷⁷Lu-DKFZ-617 PSMA has potential to exhibit suitable agent for radionuclide radiotherapy.

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Figure 5: A 74-year-old patient with hormone- and chemo-refractory prostate cancer underwent PSMA PET/CT (a), which showed diffuse abdominal and iliac lymph node metastases. The patient underwent RLT with 5.7 GBq Lu-PSMA. The PSA level was at the time of the therapy 790 ng/ml. (b) A partial response 7 weeks after RLT with 63 % PSA decline; at this time, the PSA level was 293 ng/ml

Clemens Kratochwil, et al. PSMA-targeted radionuclide therapy of metastatic castration-resistant prostate cancer with Lu-177 labeled PSMA-617 J Nucl Med March 16, 2016 [49]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed on 30 patients with PSMA positive tumors were enrolled in this study. 30 patients were treated with 1-3 cycles of ¹⁷⁷Lu-PSMA-617. Pharmacokinetic and radiation dosimetry was also evaluated during the course of the study.

Results: 21 of 30 patients showed response to therapy; for 13/30 the PSA decreased >50%. After 3 cycles 8/11 patients achieved a sustained PSA response (>50%) for over 24 weeks. ¹⁷⁷Lu-PSMA-617 showed fast renal wash out within 48 hours of injection. Patients showed

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mild nausea, fatigue and Xerostomia (<10%) over a period of time. No acute hematotoxicity was observed during the study. Dosimetry results revealed that ¹⁷⁷Lu-PSMA-617 has an exposure of 0.75 Gy/GBq for kidney 0.03 Gy/GBq red-marrow, 1.4 Gy/GBq salivary glands and 6-22 Gy/GBq for tumour lesions.

Conclusion: Based on the results authors concluded that targeted radioligand therapy with ¹⁷⁷Lu-PSMA-617 is safe and promising therapy option for metastasized castrate resistant prostate cancer.

Ahmadvazehfar H, et al. Therapeutic response and side effects of repeated radioligand therapy with ¹⁷⁷Lu-SMA-DKFZ-617 of castrate-resistant metastatic prostate cancer. Oncotarget. 2016 Feb 8. doi: 10.18632/oncotarget.7245. [50]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed in 24 hormone and/or chemo-refractory PC patients. Forty-six cycles of Lu-PSMA were performed. Side effects and response rate was assessed.

Results: Eight weeks after the first cycle of ¹⁷⁷Lu-PSMA-617 therapy 79.1% experienced a decline in PSA-level. Eight weeks after the second cycle of Lu-PSMA therapy 68.2% experienced a decline in PSA relative to the baseline value. Apart from two cases of grade 3 anemia, there was no relevant hemato- or nephrotoxicity (grade 3 or 4).

Conclusion: ¹⁷⁷Lu-PSMA-617 is a safe treatment option for metastatic PC patients and has a low toxicity profile. A positive response to therapy in terms of decline in PSA occurs in about 70% of patients.

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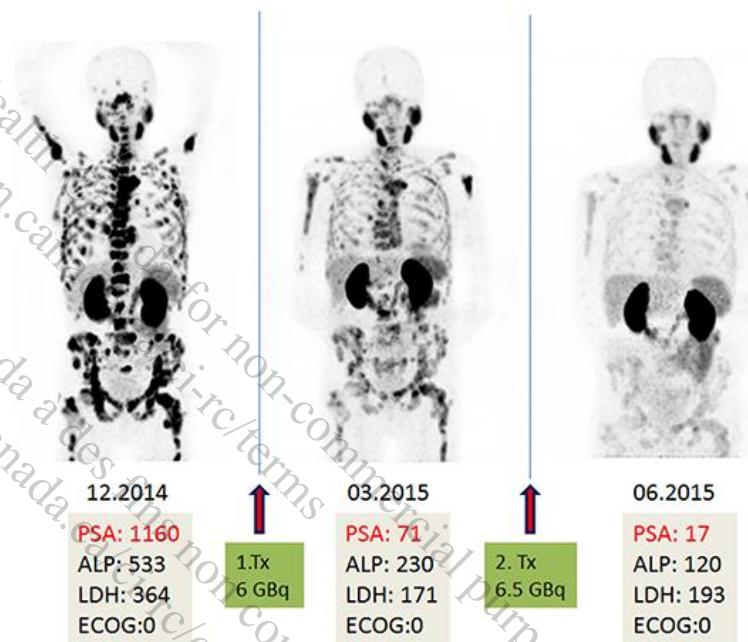


Figure 6: A 75-year-old patient with diffuse bone and lymph node metastases as well as local recurrence (left MIP image). History of chemotherapy and therapy with abiraterone, PSA elevation under enzalutamide. The patient underwent PSMA therapy as the last possible option. Continuing PSA decline and partial response in Ga-PSMA PET images after the first (middle MIP image) and second cycles (right MIP image)

Madhav Prasad Yadav, et al. ¹⁷⁷Lu-DKFZ-PSMA-617 therapy in metastatic castration resistant prostate cancer: safety, efficacy, and quality of life assessment. Eur J Nucl Med Mol Imaging. 2016 Aug 10. [51]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed in 31 patients with progressive disease despite second-line hormonal therapy and/or docetaxel chemotherapy. Patients underwent 1 to 4 cycles after a ⁶⁸Ga-PSMA-HBED-CCP ET/CT for inclusion (mean activity 5069 ± 1845 MBq). Hematological, kidney function, liver function tests, and serum PSA levels were recorded before and after therapy at 2 weeks, 4 weeks, and 3 month intervals. Biochemical response was assessed with trend in serum PSA levels. Metabolic response was assessed by PERCIST 1 criteria. Clinical response was assessed by

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visual analogue score (VASmax) analgesic score (AS), Karanofsky performance status (KPS), and toxicity and response criteria of the Eastern Cooperative Oncology Group (ECOG) criteria.

Results: Biochemical response in terms of complete response (CR), partial response(PR), stable disease (SD), and progressive disease (PD) was observed in 2/31, 20/31, 3/31, and 6/31 had, respectively. Mean VASmax and mean analgesic scores decreased from 7.5 to 3 and 2.5 to 1.8 after therapy, respectively Mean KPS and mean ECOG performance status score improved from 50.32 to 65.42 after therapies, respectively. Two patients experienced grade I and grade II hemoglobin toxicity each. None of the patients experienced nephrotoxicity or hepatotoxicity.

Conclusion: ¹⁷⁷Lu-DKFZ-PSMA-617 radionuclide therapy is a safe and effective approach in the treatment of mCRPC patients.

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1.3.3 Sponsors Experiences

1.3.3.1 Preclinical Toxicity Studies

The aim of study was to evaluate toxicity of PSMA-617. PSMA-617 applied once weekly by intravenous administration to male rats over 22 days. The animals were treated with 40, 160 or 400 µg of PSMA-617/kg b.w. by tail vein intravenous bolus injection on test days 1, 8, 15 and 22. The control group was treated with physiological saline. No deaths were noted. No signs of local or systemic intolerance reactions were observed. Body weight and body weight gain, food intake, and drinking water consumption were not influenced. No test item-related changes were noted for the hematological and biochemical parameters, the urinary status, the eyes and optic region, the auditory acuity, the relative and absolute organ weights, and the myeloid: erythroid ratio. No test item-related abnormalities were noted during macroscopic inspection at necropsy and at histopathological examination.

Under the test conditions of this study, the no-observed-adverse-effect-level (NOAEL) was 400 µg PSMA-617 / kg b.w. administered once weekly by intravenous bolus injection. This dose was the highest dose tested. Detailed description of this study is attached in appendix 1.

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1.3.3.2 Summary of Human Studies - German Multicenter Experience

Rahbar K, et al. German multicenter study investigating ¹⁷⁷Lu-PSMA-617 radioligand therapy in advanced prostate cancer patients. J Nucl Med. 2016 [52]

Study design: Retrospective acquisition and pooling of data for toxicity and PSA response in patients after ¹⁷⁷Lu-PSMA-617 RLT performed in Germany until July 2015 was initiated by the German Society of Nuclear Medicine for research purpose. The following contains a summary of the collected data. 145 patients with metastatic castration-resistant prostate cancer received a median of two cycles (range 1 to 4) of ¹⁷⁷Lu-PSMA RLT at twelve German Nuclear Medicine Clinics. Data on safety and efficacy were reported. Table 1 lists the administered ¹⁷⁷Lu-PSMA-617 activity for this study cohort.

Table 1. Administered ¹⁷⁷ Lu-PSMA-617 activity (n = 248 RLT cycles)				
administered activity (GBq)	Cycle 1	Cycle 2	Cycle 3	Cycle 4
≤ 3.5	9	3	0	1
> 3.5 – 4.5	32	14	2	0
> 4.5 – 5.5	16	12	9	0
> 5.5 – 6.5	71	37	14	2
> 6.5	17	8	1	0

Results:

A. Toxicity: Nuclear medicine physicians responsible for ¹⁷⁷Lu-PSMA RLT and subsequent follow-up reported potentially related or unrelated adverse events based on a standard template. In addition toxicity was determined by baseline and follow-up findings for serum creatinine, AST, ALT, white blood cell count, hemoglobin and platelet count for 121 of 145 (83%) patients. The follow-up period for adverse events was 2 to 30 weeks. Reported toxicity sorted by organ system is given in Table 1. Grade 3-4 anemia occurred in 15 (10%) patients

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and grade 3-4 thrombocytopenia occurred in 5 (4%) patients. The rate of grade 3-4 events was low for all other categories (0 to 3 patients; 0 to 2%).

There were fewer hematologic adverse events when compared to patients with metastatic castration resistant prostate cancer treated with placebo or ²²³Ra within the ALSYMPCA trial [7] (grade ≥ 3 anemia: 14% in the placebo and 13% in the ²²³Ra group; grade ≥ 3 thrombocytopenia: 3% in the placebo and 7% in the ²²³Ra group). Toxicity data thus indicate a favorable safety profile for RLT using 2-7 GBq ¹⁷⁷Lu-PSMA per cycle in patients with metastatic castration resistant prostate cancer.

Majority of patients received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle. Toxicity rates were comparably low: 9 of 71 (13%) patients with 5.5 – 6.5 GBq and 3 of 17 (18%) patients with >6.5 GBq during the first RLT developed grade 3-4 toxicity.

*Clinical Trial Protocol: IND #**¹⁷⁷Lu-PSMA-617***Table 2. Adverse events after ¹⁷⁷Lu-PSMA-617
as determined by blood tests (n=121) or physician reports (n=145)**

Organ system	Category	Evaluated for N	All grades	Grade 3-4
Blood and lymphatic disorders				
	Leukopenia	121	48 (40%)	4 (3%)
	Anemia	145	50 (34%)	15 (10%)
	Thrombocytopenia	121	38 (31%)	5 (4%)
Gastrointestinal disorders				
	AST elevation	121	27 (19%)	0 (0%)
	ALT elevation	121	11 (8%)	0 (0%)
	Xerostomia	145	11 (8%)	0 (0%)
	Nausea	145	9 (6%)	0 (0%)
	Dysgeusia	145	6 (4%)	0 (0%)
	Ascites	145	2 (1%)	0 (0%)
	Biliary obstruction	145	0 (0%)	1 (1%)
General disorders				
	Fatigue	145	19 (13%)	1 (1%)
	Pain	145	5 (3%)	0 (0%)
	Ileus	145	1 (1%)	0 (0%)
Urinary disorders				
	Renal failure	121	14 (12%)	0 (0%)
	Urinary tract infection	145	1 (1%)	0 (0%)
Cardiovascular disorders				
	Edema	145	2 (1%)	0 (0%)
	Lung embolism	145	0 (0%)	3 (2%)

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Respiratory, thoracic and mediastinal disorders

Pleural effusion	145	1 (1%)	0 (0%)
------------------	-----	--------	--------

Dyspnea	145	1 (1%)	0 (0%)
---------	-----	--------	--------

Neurologic disorders

Vertigo	145	1 (1%)	0 (0%)
---------	-----	--------	--------

Stroke	145	0 (0%)	2 (1%)
--------	-----	--------	--------

Musculoskeletal disorders

Bone fracture	145	0 (0%)	3 (2%)
---------------	-----	--------	--------

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Efficacy

Serial PSA levels at baseline and follow-up were recorded for 99 of 145 patients (68%).

Response was expressed as percent change in serum PSA from baseline to the lowest PSA level measured at follow-up (best PSA response).

Over the entire follow-up period 45 of 99 (45%) patients demonstrated a PSA decline $\geq 50\%$ and were considered biochemical responders. Any PSA decline occurred in 59 of 99 (60%) patients (Figure 7). After the first cycle a PSA decline $\geq 50\%$ occurred in 40 of 99 (40%), any PSA decline in 65 of 99 (66%) patients (Figure 8A). After the second therapy cycle of $^{177}\text{Lu-PSMA-617}$ RLT a PSA decline $\geq 50\%$ occurred in 35 of 61 (57%) and any PSA decline in 44 of 61 (72%) patients (Figure 8B). Patients receiving a third or fourth cycle of therapy showed a PSA decline $\geq 50\%$ in 13 of 20 (65%) and 3 of 3 (100%) patients, respectively.

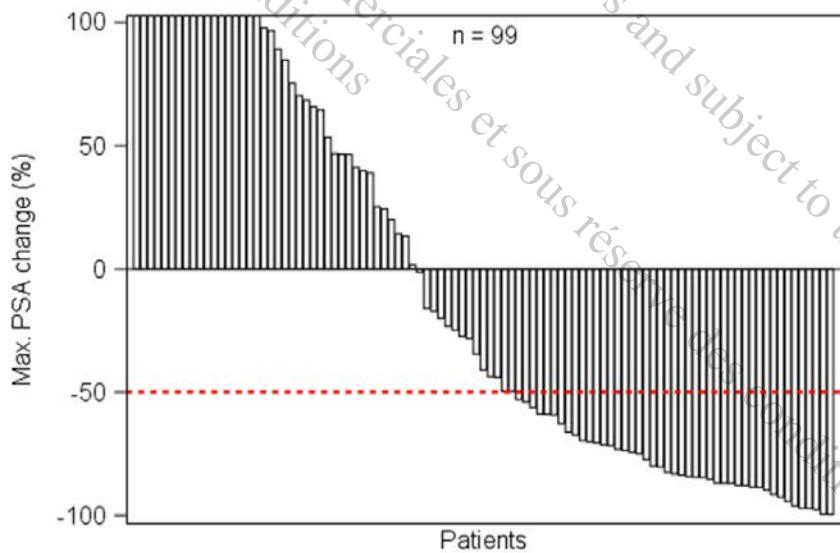


Figure 7. Waterfall plot of maximum PSA change (%) from baseline over total follow-up period. PSA increase of more than 100% was cropped due to simplification.

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^{177}Lu -PSMA-617

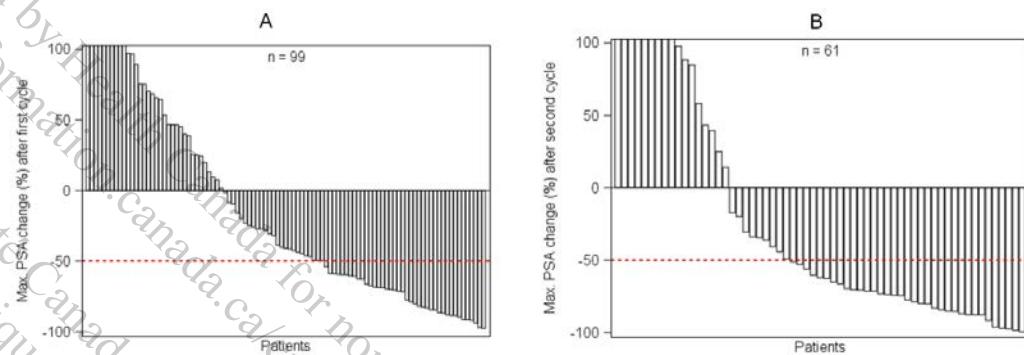


Figure 8. Waterfall plots of maximum PSA change (%) after the first cycle (A) and after the second cycle (B). PSA increase of more than 100% was cropped due to simplification.

Response rate was higher than the rate in patients with metastatic castration resistant prostate cancer treated with abiraterone (best PSA response >50% after abiraterone plus prednisone: 43% (25 of 58) patients) [53]. Data thus indicate good efficacy for ^{177}Lu -PSMA RLT in patients with metastatic castration resistant prostate cancer. Response rates were not significantly associated with mean activity per cycle ($p=0.46$) or cumulative activity after two cycles ($p=0.22$).

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2. Study Objectives

Primary Objectives:

1. To assess the clinical safety of ¹⁷⁷Lu-PSMA-617 by evaluation of adverse events (AE) using the Common Terminology Criteria for Adverse Events (CTCAE)
2. To assess the efficacy as defined by proportion of patients with PSA-response of ≥50% decline at 12-weeks from baseline

Secondary Objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]
2. To determine the time to PSA progression, separate for treatment doses: time from inclusion to date until PSA progression or death (whichever occurs first) [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later
 - b. for patients without PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above baseline
3. To determine radiographic Progression-free Survival (rPFS), for each treatment dose: time from inclusion to date when first site of disease is found to progress or death (whichever occurs first)
 - a. Nodal and visceral disease is evaluated on cross-sectional imaging using RECIST 1.1/PCWG3 criteria
 - b. Bone metastases are evaluated using bone scintigraphy and new lesions have to be confirmed on a second scan (2+2 rule) using PCWG3 criteria
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST 1.1/PCWG3 criteria stable disease (SD), partial response (PR) or complete response (CR).
5. Change in Pain and Quality of Life: Pain and “Epic-26” Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 mo. Pain response will be determined in accordance with PCWG3 [1].
6. Change in ECOG Performance Score

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3. Investigational Plan

3.1 Overall Study Design and Dosing of Targeted PSMA Radioligand Therapy (RLT)

This is a open-label, multicenter, prospective trial. Upon inclusion patients will be randomized into two treatment doses. RLT will be performed by repeated i.v. application of 6.0 GBq ($\pm 10\%$) or 7.4 GBq ($\pm 10\%$) ¹⁷⁷Lu-PSMA-617 every 6±1 weeks until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy. All doses after labeling will be presented in buffered solution for intravenous injection.

In total, 200 subjects with histologically proven prostate cancer and mCRPC will be enrolled. Salivary protection will be accomplished by applying ice pack starting 30 minutes prior to infusion of radiopharmaceutical and will continue for 4 hours. Subjects will be recruited at up to 3 Nuclear Medicine sites selected for this project. Each subject will undergo a screening visit within 14 days prior to receiving study drug.

Dosimetry will be performed according to chapter 8.4.3 by Prof. Dr. [Name], Universitätsklinikum Würzburg Germany - Klinik und Poliklinik für Nuklearmedizin after the first injection to determine dose to the kidneys. Treatment will be continued until either of the following conditions apply:

- PSA/radiographic progression as defined above
- Completion of four RLT cycles
- 23 Gy kidney dose would be exceeded by the next cycle as estimated by dosimetry
- patient withdrawal (e.g. appearance of intolerable adverse events)

Primary objectives of the study is safety and efficacy.

Efficacy is determined by PSA response rate: Patients with baseline to follow-up decline in tumor marker level (PSA) $\geq 50\%$ at 12 weeks will be considered responders.

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For safety assessment, vital signs will be measured within 20 minutes before and for up to an hour after administration of ¹⁷⁷Lu-PSMA-617. A blood sample will be collected within 48 hours before the injection, for assessing clinical chemistries and hematology. Hematologic laboratory testing (CBC) will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until patient is progressed. CBC will be performed every 7 days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery or reaching to their CBC index levels equal to their screening level.

Chemistry will be evaluated 4 weeks after each therapy and within one week prior to the next treatment to evaluate eligibility to receive the next cycle and then every 3 month for 24 months or until the patient is progressed. CTCAE v 4.0 will be used to evaluate renal toxicity. For more information, please refer to the Schedule of Events ([Appendix 2](#)).

3.2 Rationale for Study Design

3.2.1 Rationale for a regimen with multiple therapy cycles

Activity given during targeted radionuclide therapy is limited by radiation dose to healthy organs. Based on dosimetry radiation dose to healthy organs and subsequent maximal cumulative activity can be calculated. To obtain optimal safety margin maximal cumulative activity is not given in one treatment session but approached by application of a defined fraction of this activity in several cycles. The administration of a standard activity over several treatment cycles allows for early and individual estimation of radiation dose and tolerability. The efficacy and safety of a sequential approach was proven in patients with ²²³Ra therapy for metastatic castration-resistant prostate cancer (mCRPC) [7] and in patients with ¹⁷⁷Lu-DOTATATE therapy for midgut neuroendocrine tumor (NET) [54] each in prospective, double-blind, randomized, international, and multicenter phase III trials. Based on this evidence targeted PSMA Radioligand Therapy (RLT) will be performed by sequential applications of ¹⁷⁷Lu-PSMA-617 with treatment-free intervals.

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3.2.2 Rationale for a six weeks interval

Highest level of evidence for subacute adverse events after radionuclide therapy was published for patients with non-Hodgkin's lymphoma. Witzig et al analyzed safety and efficacy of ^{90}Y -Ibritumomab Tiuxetan in 73 patients in a prospective Phase III randomized trial. This study reports neutrophil, platelet and hemoglobin nadir approximately six weeks after application of the beta emitter [55]. Based on this study ^{177}Lu -PSMA-617 RLT will be performed by sequential applications with a treatment-free interval of six weeks to minimize risk of repeated ^{177}Lu -PSMA-617 therapy before reaching blood level nadir. This scheme is also supported by safety data from the phase III NETTER-1 trial on safety and efficacy of ^{177}Lu -DOTATATE in patients with midgut NET. Here ^{177}Lu -DOTATATE was administered at seven to nine week intervals and rate of severe adverse events was below 10% for 115 patients in the treatment arm [54].

3.2.3 Rationale for dose regimen

Ahmazadehfar et al reports safety and efficacy after application of a mean activity of 6.0 GBq ^{177}Lu -PSMA-617 in 24 patients with mCRPC [50]. Patients were treated with up to two cycles of ^{177}Lu -PSMA-617 RLT at eight week intervals. Grade 3 hematotoxicity occurred in two patients. No nephrotoxicity or hepatotoxicity grade ≥ 3 was documented. Kratochwil et al reports safety and efficacy after repeated application of ^{177}Lu -PSMA-617 in 30 mCRPC patients [49]. 19 of 30 patients (63%) received 6.0 GBq ^{177}Lu -PSMA-617 every two mo. One patient developed grade 3 anemia, one patient grade 3 thrombocytopenia. Both patients had diffuse pattern of bone marrow infiltration at baseline. The German Society of Nuclear Medicine (DGN) performed a questionnaire based survey on the use of ^{177}Lu -PSMA-617 RLT in December 2015. Nuclear Medicine Clinics in Germany reported compassionate use of ^{177}Lu -PSMA-617 RLT in 145 mCRPC patients until June 30th 2015 [52]. Majority of

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patients received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle (Table 1) and rate of serious adverse events was below 20% for both subgroups. Phase III data for ¹⁷⁷Lu-DOTATATE, a similar RLT for midgut NET patients, demonstrates a rate of severe adverse events below 10% after application of four cycles of 7.4 GBq in 115 patients [54]. Thus, present evidence indicates that repeated applications of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 RLT are well tolerated with low to very low rates of serious adverse events.

Standard activities of 6.0 and 7.4 GBq are also supported by dosimetry data available in more than ten patients [56] [57]. Maximal cumulative activity is limited by the absorbed dose in critical organs. Dosimetry identifies kidney and salivary glands as organs with highest absorbed dose [56] [57]. Thus maximum cumulative activity is determined by absorbed kidney dose. Based on earlier evidence obtained from external beam radiotherapy the maximum tolerable per kidney dose is generally accepted 23 Gy [58]. Dosimetry after ¹⁷⁷Lu-PSMA-617 application revealed absorbed doses of 0.6 Gy/GBq per kidney [56] [57]. Therefore maximum cumulative activity for ¹⁷⁷Lu-PSMA-617 RLT is considered 38.3 GBq (38.3 GBq x 0.6 Gy/GBq = 23.0 Gy radiation dose per kidney). Both the application of four cycles of 6.0 GBq (total 24.0 GBq) or 7.4 GBq (total 29.6 GBq) ¹⁷⁷Lu-PSMA-617 results in lower cumulative activities with acceptable safety margin. Whether either activity regimen is associated with longer rPFS is unknown and will be evaluated as secondary endpoint of this trial.

Salivary glands receive highest off-target radiation dose according to dosimetry [56] [57]. Absorbed dose after four cycles of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 (34.0 Gy or 41.6 Gy respectively) falls within the range of maximum tolerable dose reported for salivary glands in the literature [58] [59] [60]. Maximum tolerable dose to the bone marrow is generally accepted 2 Gy [61]. Bone marrow dose will not exceed this limit after four cycles of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 [57].

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3.2.4 Determination of Sample Size

Sample size calculation was based on the primary endpoint of this protocol, i.e. baseline to 12-week decline in tumor marker level (PSA) $\geq 50\%$ [53]. Based on a recent publication [52], we estimate that the proportion of patients who meet the primary end point will range between 38% and 65% for both treatment doses. We thus define the following null hypothesis: Less than 40% of patients will reach the endpoint after ^{177}Lu -PSMA RLT. ^{177}Lu -PSMA RLT would therefore be considered worthy of further study if 50% or more patients met the end point and not worthy of further study if 40% and less achieved the end point. This rationale was adapted from a single-arm study on mCRPC patients with same end point definition, published 2010 in the Journal of Clinical Oncology [53]. We have performed power analysis for the two sided binomial test (beta 0.2, alpha 0.05) to measure the efficacy of ^{177}Lu -PSMA RLT. A sample size of 200 achieves 78% power (beta 0.2) at a given alpha of 0.05 to distinguish between 40% versus 50% response rates. The power analysis was performed by a trained Biostatistician from the Department of Biostatistics, University of California at Los Angeles using Power Analysis and Sample Size (PASS) 14 software (NCSS LLC).

3.3 Study Duration and Dates

The duration of subject participation will be from the time of signing informed consent through the 24 months post-injection visit or progression. Subjects will be deemed enrolled in the study once the subject signs informed consent.

3.4 Randomization protocol

Randomization will be performed in accordance with Vickers et al. [62]. In order to obtain adequate “allocation concealment” a list of random allocations was created for patients 1

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through 200. This list will be stored at investigator's sites and will not be modified. The list will only be accessible for researchers or study personnel not actively involved in the recruitment process.

3.5 Dose modification

In some circumstances, it might be necessary to suspend treatment with ¹⁷⁷Lu-PSMA-617, adapt the posology (i.e. administer a half activity), or even definitively stop administration, as described in the following tables.

Table 3: When to definitely stop treatment with ¹⁷⁷Lu-PSMA-617

Definitively stop further administrations in patients who have experienced or are at risk of any of the following conditions during treatment:
Severe heart failure (defined as grade III or IV of the NYHA classification)
Hypersensitivity to the active substance or to any of the components of this radiopharmaceutical
In case some specific adverse reactions to ¹⁷⁷ Lu-PSMA-617 persist or reoccur, see Table 5

Table 4: When to suspend treatment with ¹⁷⁷Lu-PSMA-617?

Suspend treatment with ¹⁷⁷ Lu-PSMA-617 in patients who have experienced or are at risk of any of the following conditions during treatment:	
Criterion	Action
Occurrence of an intercurrent disease (e.g. urinary tract obstruction, ...) which according to the physician opinion could increase the risks linked to ¹⁷⁷ Lu-PSMA-617 administration.	Suspend administration until resolution or stabilization. Treatment can be resumed after resolution or stabilization.
In case of some specific adverse reactions to ¹⁷⁷ Lu-PSMA-617, see Table 5	see Table 5

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Table 5: When to adapt ¹⁷⁷Lu-PSMA-617 posology?

Adapt ¹⁷⁷Lu-PSMA-617 posology according to the following actions in patients who have presented any of the following severe adverse reactions:	
Severe adverse reactions / Dose-modifying toxicity (DMT) criteria	Action
Anemia, thrombocytopenia or neutropenia of grade 3 or superior (CTCAE 4.0)	1. suspend treatment with ¹⁷⁷ Lu-PSMA-617 2. monitor biological parameters every 2 weeks, and eventually treat appropriately if needed; in case of renal failure, good hydration is recommended if not otherwise contraindicated.
Renal toxicity as defined by grade 3 toxicity by serum creatinine (CTCAE 4.0)	a. If he observed toxicity continues beyond 16 weeks after the last infusion, treatment with ¹⁷⁷ Lu-PSMA-617 must be definitively stopped. b. If he observed toxicity resolves within 16 weeks after the last infusion, it is possible to continue treatment with ¹⁷⁷ Lu-PSMA-617 by infusing a half activity. 3. If he half activity is well tolerated (i.e. no DMT re-occurrence), the next remaining treatment administration should continue with full activity; but, if DMT recurs after treatment with a half dose, treatment with ¹⁷⁷ Lu-PSMA-617 must be definitively stopped.
Liver toxicity as defined as AST and ALT >5xULN	
Any other serious or intolerable adverse event that in the opinion of the investigator, requires the subject's discontinuation.	

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4. Study Population Selection

4.1 Study Population

It is anticipated that a total of 200 subjects will be recruited. Such a number is considered appropriate to achieve statistical power for the endpoints of this clinical trial. The patients will be recruited at up to 3 clinical sites. The dose being administered will be prepared at RadioMedix Inc. in Houston and shipped to the trial sites.

4.2 Inclusion Criteria

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ⁶⁸Ga-PSMA-11 PET/CT or diagnostic ¹⁷⁷Lu-PSMA-617 scintigraphy
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2.000/\mu\text{l}$, platelet count $\geq 75.000/\mu\text{l}$, Hb $> 8.9 \text{ g/dl}$, and ANC $> 1000 \text{ mm}^3$
8. Signing Informed Consent Form.

4.3 Exclusion Criteria

1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ²²³Ra, ¹⁵³Sm)
2. Glomerular Filtration Rate (GFR) $< 40 \text{ ml/min}$
3. Grade 3 toxicity serum creatinine using CTCAE v. 4.0
4. AST and ALT $> 5 \times \text{ULN}$
5. Urinary tract obstruction or marked hydronephrosis

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5. Study Treatment(s)

5.1 Description of Treatments(s)

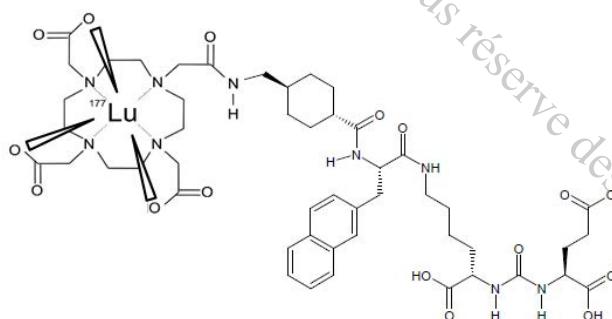
5.1.1 Study drug

The agent to be evaluated in the present study is ¹⁷⁷Lu-PSMA-617. Its chemical name is lutetium-177-N_α-2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{{[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid.

¹⁷⁷Lu-PSMA-617 is radiolabelled with carrier-free lutetium-177 (¹⁷⁷Lu), a synthetic, low-energy beta and gamma emitting isotope of lutetium, the last element in the lanthanide series of metallic elements. Carrier-free ¹⁷⁷Lu is generated by neutron irradiation of the isotope ytterbium-176 (¹⁷⁶Yb) and subsequent fractionation of ¹⁷⁷Lu and ¹⁷⁶Yb with caution chromatography. Key physical characteristics of ¹⁷⁷Lu are summarised below:

Physical half-life T _{1/2}	Decay product	Main β ⁻ emission	Maximum range (β ⁻)	Main γ emission
6.6 d	¹⁷⁷ Hf	498 keV	1.7 mm	208 keV 113 keV

The structural formula of ¹⁷⁷Lu-PSMA-617 is shown below



The chemical formula of ¹⁷⁷Lu-PSMA-617 is Lu₁C₄₉H₆₈N₉O₁₆. The molar weight is 1214.1 g/mol.

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5.1.2 Pharmaceutical Properties of ¹⁷⁷Lu-PSMA-617

¹⁷⁷Lu-PSMA-617 is administered intravenously.

A description of ¹⁷⁷Lu-PSMA-617 solution for infusion is shown in below table

Composition of ¹⁷⁷Lu-PSMA-617 solution

Pharmaceutically active component	¹⁷⁷ Lu-PSMA-617
Physical dose	≤ 7.4 GBq / cycle
Substance dose	130 - 170 µg PSMA-617
Primary unit dose container	20 mL glass vial containing 5 - 15 mL of stabilised aqueous solution
Appearance	Clear, colourless or slightly yellowish solution, without visible particles
pH	4.0 - 7.5
Bacterial Endotoxin	≤ 100 EU/Dose
Radionuclidic purity	≥ 99.99 %
Sterility	Sterile

The components include ¹⁷⁷Lu-PSMA-617, sodium acetate, sodium ascorbate, gentisic acid, and water for injection. The labelled drug product is produced, tested and released under GMP conditions by RadioMedix, Inc. as a sterile solution for injection infusion, ready for use. The labelled drug product will be manufactured upon individual order and delivered directly to the study sites.

Patients will be randomized into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq (±10%, arm 1) or 7.4 GBq (±10%, arm 2) ¹⁷⁷Lu-PSMA-617 every 6±1 weeks; RLT will be performed until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy as determined by dosimetry, after the first treatment.

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5.2. Treatment(s) administered

Cold ice pack in the region of salivary glands will start 30 minutes prior to administration of the investigational drug and will continue for 4 hours. Intravenous access will be inserted in either arm. Assurance will be made to have reliable IV line with no evidence of extravasation or infiltration. Investigational drug will be infused over approximately 30 minutes using infusion pump. Patients will be monitored for any evidence of pain, or burning sensation during the infusion.

Imaging and blood and urine samples for dosimetry after the first treatment will be accomplished as per dosimetry protocol by Prof. Dr. [Name], Universitätsklinikum Würzburg - Klinik und Poliklinik für Nuklearmedizin. For subsequent therapies only 24 hour whole body images will be performed to assure satisfactory distribution of the investigational radiopharmaceutical.

5.3 Restrictions

5.3.1 Fluid and Food Intake

Subjects should follow their normal diet before and after the administration of the study drug. Subjects should be encouraged to increase fluid intake at baseline and after each image acquisition to maintain proper hydration throughout the study period and decrease radiation exposure to the urinary bladder. There are no dietary or food restrictions for this study.

5.3.2 Subject Activity Restriction

There are no activity restrictions.

5.4 Dosing Compliance

All study drug administration will be administered under the supervision of the investigator. Details of study drug injection will be captured in each subject's source documents.

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5.5 Packaging and Labeling

¹⁷⁷Lu-PSMA-617 will be supplied in vials for injection in appropriate packaging.

The outer packaging of ¹⁷⁷Lu-PSMA-617 will contain label(s) which will include the following minimum information:

- Name and address of Manufacturer Study number
- Investigator identification
- Name of study drug and formulation
- Dosage strength
- Batch number
- Patient number
- Expiry date (or retest date)
- Storage instructions
- “For Clinical Trial Use only”

A system of medication numbering in accordance with all requirements of Good Manufacturing Practice (GMP) and any other applicable regulatory requirement will be used for all study drugs. This will ensure that for each patient, any dose of study drug can be identified and traced back to the original bulk ware of the active ingredients. Lists linking all numbering levels will be maintained by the institutions in charge of study drug packaging.

5.6 Storage and Accountability

5.6.1 Storage

The drug product contains radioactive material and should only be handled by personnel trained in the use of radioactive isotopes with proper shielding and monitoring. Receipt and use is limited to a facility licensed by applicable government regulations and/or local/state laws. Unused or residual waste should be disposed of as radioactive waste following the institution's standard operating procedures (SOPs) and/or applicable regulations or guidance.

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5.6.2 Accountability

In accordance with International Conference on Harmonization (ICH) and US Food and Drug Administration (FDA) requirements, the investigator and/or drug dispenser must at all times be able to account for all study drugs furnished to the institution. The appropriate site personnel must sign, date and immediately forward to the sponsor or sponsor's designee the packing slip for clinical shipment included with each shipment.

No study drug is to be used outside of this study. The investigator or designee will record the use of the study drug on the appropriate Drug Accountability record. All study radiopharmaceuticals must be accounted for, whether used or unused, during the course of and at the conclusion of the study. The shipment of drugs from the sponsor or designee to the investigator or other designated persons cooperating with the investigator will be accompanied by a receipt form that indicates the lot number(s) and the amount of drug provided for the study. This form will be signed, dated and returned to the sponsor or designee.

The investigator is responsible for ensuring that study drug is recorded, handled and stored safely and properly in accordance with ICH and applicable government regulations, local/state laws, and used in accordance with this protocol.

5.7 Investigational Product Retention at Study Site

Unused product will be disposed of according to institutional regulations. Record the use and/or disposal of the study drug on the Drug Accountability record. This Drug Accountability record should account for the receipt and disposition of all clinical supplies shipped to the investigator and must be available for review by the study monitor.

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6. Study Procedures

6.1 Informed Consent

All subjects must sign and personally date an IRB/IEC approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug prior to the initiation of any study-related procedures. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for Good Clinical Practice (GCP) and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27.

The subject must be made aware and agree that personal information may be reviewed during an audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. A copy of the Informed Consent Form is attached as Exhibit.

6.2 Medical History

A relevant medical history and subject demographics will be obtained at the screening visit. Cancer medical history includes review of disease history, cancer staging, biopsy results, any past/present cancer therapies (e.g., hormone, drug, biologic, radiologic, or surgical treatment). Demographic information to be collected includes date of birth, race, ethnicity, height, and weight.

6.3 Vital Signs

Vital signs will include measurement of blood pressure, temperature, respiratory rate, and heart rate.

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6.4 Dispensing Study Drug

The estimated radioactive dose will be determined by measuring the amount of radioactivity in the syringe pre- and post-injection, using an appropriately calibrated radioisotope dose calibrator in accordance with the nuclear medicine department's SOPs.

Any complication related to administration of the drug (e.g., overdose, observable extravasation, medication error) is a protocol-related event and will be reported to the pharmacovigilance designee. Refer to Section 7 for contact information.

6.5 Clinical Laboratory Tests

Clinical laboratory tests will include hematology and clinical chemistry. Clinical laboratory analytes to be assessed in the study are shown in Table 6. Timing of collection of clinical laboratory tests are presented in Section 8.

Table 6: Laboratory Analytes Assessed

Hematology	Clinical Chemistry
Hematocrit	eGFR
Hemoglobin	Bilirubin
RBC count	Creatinine
WBC count	Glucose
WBC differential	Urea nitrogen
Platelets	BUN/Creatinine
ANC	AST/SGOT
MCV/MCH/MCHC	ALT/SGPT
Eosinophils	Alkaline Phosphatase
Basophils	PSA*
Lymphocytes	
RDW	

*PSA will be done only at the time intervals called by the protocol.

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6.6 Sample Collection, Storage and Shipping

Blood samples will be collected using accepted phlebotomy techniques by trained site personnel. All samples for clinical laboratory testing will be processed and analyzed at an accredited laboratory

6.7 Electrocardiogram

Continuous ECG recording at least 15 minutes prior to administration of the study drug and at least 1 hour after administration will be performed. Also a 12 lead ECG will be performed in two time points: before injection of Lu-177 PSMA and after completion of the 4 hr scan.

6.8 Adverse Events

Immediate adverse drug reactions will be collected from the time of ¹⁷⁷Lu-PSMA-617 injection until 24 hours post-injection visit. Data will be collected for any adverse events (AEs) as defined in Section 7.

All study monitoring will be performed at the primary clinical study sites in accordance with Good Clinical Practice (GCP). All records related to this study will be retained at each clinical site. Serious adverse reactions will be collected and reported to FDA and IRB according to 21 CFR 312.32. **Sponsors at each individual site will be responsible for obligations of a sponsor enumerated in 21 CFR 312.50-59. FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the investigational drug.** Annual reports on the progress of the investigation and any adverse events related to the investigational drug will be prepared and reported to FDA according to 21 CFR 312.33.

6.9 Removal of Subjects from the Trial or Study Drug

The investigator may withdraw a subject from the trial for any of the following reasons:

1. Protocol violation

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2. Serious or intolerable adverse event (that in the opinion of the investigator, requires the subject's discontinuation),
3. Investigator withdraws the subject (at the investigator's discretion for reasons other than an adverse event),
4. Sponsor terminates the study,
5. Subject requests to be discontinued from the study, or
6. Subject is lost to follow-up

During course of the study patients have the right to withdraw their consents any time without need for explaining the reason of consent withdrawal to the investigator or sponsor. Principal investigator will closely monitor patients during the course of the study and will consider terminating investigational product administration or any other trial related procedures in order to maintain the safety of subjects. In cases of withdrawal either in patient's favor or principal investigator decision due to the safety issues or technical issues, withdrawn subjects will be replaced in order to maintain data integrity but follow up visits will be continued to maintain safety of patients based on the visits predicted in the protocol.

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7. Reporting Safety Information

Any untoward medical event that occurs from the time that the subject is administered ¹⁷⁷Lu-PSMA-617 until the subject completes the study will be reported. Serious adverse events and non-serious adverse events will be collected and reported as required under 21 CFR 312.32 until the final study visit. Toxicity will be evaluated according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

7.1 Adverse Events

7.1.1 Definitions

An **adverse event (AE)** is any untoward medical occurrence in a study subject that is administered a pharmaceutical product, at any dose, which does not necessarily have a causal relationship with the treatment.

An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a study drug, whether or not considered related to the study drug.

A **serious adverse event (SAE)** is any untoward medical occurrence that falls into one or more of the following categories:

1. Results in death
2. Is life-threatening: An event which, in the view of the investigator, places the subject at immediate risk of death from the event as it occurred and does not include an event which hypothetically might have caused death if it were more severe.
3. Requires subject hospitalization or prolongation of existing hospitalization: For the seriousness criterion of subject hospitalization to apply, an overnight stay in the hospital is required. Admission to an emergency room and release without an overnight stay would not satisfy the subject hospitalization seriousness criterion.
4. Results in persistent or significant disability/incapacity: Persistent or significant disability/incapacity is defined as a substantial disruption of a person's ability to conduct normal life functions, either reported or defined as per clinical judgment.

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5. A congenital anomaly/birth defect: A congenital anomaly/birth defect is defined as a condition believed to have been the result of exposure to study drug just before conception or during pregnancy.
6. Any other important medical event: An important medical event may not result in death, be life-threatening, or require hospitalization, but based upon appropriate medical judgment, the event may significantly jeopardize the subject's health or may require medical or surgical intervention to prevent one of the outcomes listed in the serious definitions above. An important medical event may include development of drug dependency or drug abuse.

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

7.1.2 Reporting Serious Adverse Events

Seriousness is based on subject, event outcome, or action criteria that are usually associated with events that pose a threat to a subject's life or functioning. Seriousness (not severity) serves as the guide for defining the sponsor's regulatory reporting obligations to the applicable regulatory authorities. Adverse event severity and seriousness should be assessed independently by investigators. If the investigator is unsure if the event is serious it should be classified as serious.

Sponsors of the study, and the investigators are responsible for reporting relevant SAEs as safety reports to the FDA and other applicable regulatory authorities, and participating investigators, in accordance with ICH guidelines, the US Code of Federal Regulations Title 21 CFR 312.32 for Good Clinical Practice, and/or local regulatory requirements. The investigators must report all SAEs to project pharmacovigilance designee within 24 hours, by telephone, email or fax, and confirm that the information was received. A Serious Adverse Event Report (SAER) must be completed by the investigator or designee and faxed or emailed to project pharmacovigilance designee within 24 hours after the investigator first

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becomes aware of the serious event. A separate SAER will be needed for each reported SAE so that the onset, resolution date, causality and outcome can be assessed for each event. Any source documents relevant to the event should be forwarded to sponsor's pharmacovigilance designee with the SAER form. The SAER form must be signed and dated by the investigator. The Original copy of the SAER form should remain at the investigational site. All SAEs are also to be entered into the CRF.

In case of death, a comprehensive narrative report of the case should be prepared by the investigator and sent to project pharmacovigilance designee with the SAER. If an autopsy is performed, a copy of the autopsy report should be actively sought by the investigator and sent to the sponsor or designee as soon as available. A copy of the autopsy report should remain at the investigational site with the subject's source documents.

A new follow-up SAER form will be completed by the investigator if important follow-up information (i.e., diagnosis, outcome, causality assessment, results of specific investigations) are made available after submission of the initial form. The follow-up SAER must be signed and dated by the investigator. The follow-up form and any additional source documentation regarding the event will be sent to project pharmacovigilance designee.

If a serious medical occurrence or death is reported to the investigator outside the follow up window which is believed to be related to the administration of the study drug, it is the investigator's responsibility to report this occurrence to project pharmacovigilance designee. Such occurrences will be reported using a SAER form or other form of communication deemed appropriate by the investigator and pharmacovigilance designee.

Sites must contact project pharmacovigilance designee to report all SAEs within 24 hours, by telephone, e-mail, or fax. Contact information for SAE reporting is presented in Table 7.

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Table 7: Pharmacovigilance Designee

[Name].MD
[Contact]
Excel Diagnostics and Nuclear Oncology Center
9701 Richmond Avenue, Suite 122
Houston, TX 77042
PHONE: 713.781.6200 [Contact]
FAX: 713.781.6206
Email: [Contact]

Sites must also report all overdoses, extravasations and medication errors to the project pharmacovigilance designee.

7.2 Adverse Event Data Collection

The investigator will elicit information through non-leading questioning and examination of the subject about the occurrence of adverse events from the time that the subject is administered ¹⁷⁷ Lu-PSMA-617 until study completion. AEs can be reported any time after study enrollment until the end of the subject's study participation. For each event, the following information will be recorded in the subject's source documents and entered into the Adverse Event CRF according to the instructions below:

Classification of the Event as serious or non-serious: Classify the event as serious or non-serious (see definitions in Section 7).

Description of Signs or Symptoms: Whenever possible, record a specific diagnosis for the event. If a diagnosis cannot be made, then record each sign or symptom representing a

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distinct medical concept separately, (e.g. nausea and vomiting should be recorded as separate events).

Onset Date and Time: Record the date and time the event starts. If a laboratory result is reported as an AE, record the start date as the date of collection of the first lab sample that shows the change.

Stop Date and Time: Record the date and time the event resolves, returns to baseline, or resolves with sequelae.

Grade: Refer to the common terminology criteria for adverse events (CTCAE) Version 4.

Relationship to the Study Drug:

We make every effort to evaluate the relationship between the study drug and the AE as determined by the investigator per the definitions below:

1. **Related:** The event is reasonably suspected of a causal relationship to the study drug. Suspected adverse reaction means any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of IND safety reporting, ‘reasonable possibility’ means there is evidence to suggest a causal relationship between the drug and the adverse event. A suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by a drug.

ASSESSING RELATIONSHIP TO STUDY TREATMENT

Items to be considered when assessing the relationship of an AE to the study treatment are:

- Temporal relationship of the onset of the event to the initiation of the study treatment;

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- The course of the event, considering especially the effect of discontinuation of study treatment or reintroduction of study treatment, as applicable;
 - Whether the event is known to be associated with the study treatment or with other similar treatments;
 - The presence of risk factors in the study subject known to increase the occurrence of the event;
 - The presence of non-study treatment-related factors which are known to be associated with the occurrence of the event.
2. Not Related: The event is definitely due to causes separate from study drug administration such as:
- documented pre-existing condition
 - technical and manual procedural problem
 - concomitant medication
 - subject's clinical state
3. Adverse Event Outcome:
- Recovered/Resolved without sequelae
 - Recovered/Resolved with sequelae
 - Not Recovered/Not Resolved: event is ongoing at the end of the AE collection period.
 - Death (Fatal): the event description must be the primary cause of death.

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7.3 Clinical Significance

7.3.1 Reporting and Evaluation of Clinical Laboratory Test Results

The investigator should assess all clinical laboratory results for clinical significance and record the assessment in source documents.

The investigator should evaluate any laboratory result change from pre- and post-study drug administration to determine if the change meets the definition of an AE or SAE. **Record any clinically significant lab results determined to meet the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

7.3.2 Repeat Testing

Additional laboratory testing may be performed at the discretion of the investigator.

7.3.3 Vital Signs

The investigator should evaluate any vital sign changes pre- and post-study drug administration to determine if the change meets the definition of AE or SAE. Vital sign measurements may be repeated at the discretion of the investigator. **Record any clinically significant vital sign measurement that meets the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

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8. Study Activities

Visit-specific schedule for efficacy and safety variables is presented in Appendix II.

8.1 Screening Visit

- Written informed consent
- Demographic information
- Relevant medical history
- Prior therapy for Prostate cancer
- Medication assessment
- Histology
- Vital signs
- Questionnaires
- Morphological and PSMA-ligand imaging studies if no comparable available within 4 weeks of treatment.

8.2 Within 2 Weeks of Screening

- Clinical laboratory testing (see Section 6)

8.3 Injection Visit

Once all screening/baseline procedures are performed, the following procedures will be completed on the day of injection:

8.3.1 Pre-dose and Dosing Procedures

- Pre-dose vital signs – within 20 minutes before dose
- Apply Ice pack to the salivary glands 30 minutes prior to investigational drug injection and continue for 4 hours.

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- Adequate hydration of the patient (IV or oral).
- Inject study drug ¹⁷⁷Lu-PSMA-617
- Post-dose vital signs
- Adverse events

8.3.2 Post-Dose Procedures

Adverse events during the entire stay. At first treatment blood sampling and scintigraphy 1-4h, 24h, 48h, 72h and 7d after injection for dosimetry.

8.3.3 ECG Procedures

Continues ECG recording starts at least 15 minutes prior to the administration of study drug and ends at least 1 hour after administration. A 12 lead ECG also will be performed at two time points: before administration of LU-177 PSMA and after completion of 4 hour WB scan.

8.4 Follow-up

8.4.1 PSA Measurements

Every 6 weeks during the treatment and every 3 months after the last treatment until reaching endpoint or 24 month after the first treatment.

8.4.2 Imaging Studies

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Baseline imaging within 12 weeks of start of therapy including (a) CT of the chest preferably with contrast and CT or MRI of the Abdomen and pelvis preferably with contrast and (b) bone scintigraphy or (c) equivalent to above [1].

Relevant imaging studies will be repeated approximately every 12 weeks until reaching the endpoint or 24 month after the first treatment.

8.4.3 Dosimetry

Prof. Dr. [Name], Universitätsklinikum Würzburg, Germany - Klinik und Poliklinik für Nuklearmedizin will perform the dosimetry for this protocol.

Radiation dosimetry will be acquired for each patient after the first cycle of treatment. Data acquisition plan is summarized in Table 8. Dosimetry will be considered appropriate, if at least three time points for scintigraphy and blood sampling more than 48 hours apart were acquired.

Time p.i.	Blood sampling	Urine collection	Scintigraphy (whole body planar)	Quantitative SPECT/CT head/thorax/abdomen
5 min	X	X (from injection until 4h in one container)		
30 min	X			
1 h	X			
4 h	X	X (from 4h until discharge in one container)	X	
18 – 30 h	X		X	X
42-54h	X		X	
66-78h	X		X	
7-9d*	X		X	

Table 8: Acquisition plan for individual dosimetry during the first cycle of RLT.

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Dosimetry data will be sent to experts in the field for centralized analysis. Radiation dose will be calculated for all relevant organs. Maximum number of RLT cycles for reaching threshold maximum dose to the kidneys of 23 Gy will be determined.

*7-9d is optional.

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8.4.4 Follow-up Labs for Hematological and Kidney Toxicities

Hematologic laboratory testing (CBC) will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until patient is progressed. CBC will be performed every 7 days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery or reaching to their CBC index levels equal to their screening level.

Chemistry will be evaluated 4 weeks after each therapy and within one week prior to the next treatment to evaluate eligibility to receive the next cycle and then every 3 month for 24 months or until the patient is progressed.

8.4.5 Telephone Follow ups

7 (+/- 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 week) until the end of follow up visits (24 months).

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9. Quality Control and Assurance

The study sites are chosen with regard to the capability and expertise of the principal investigators and the site staff. Prior to initiation of the study, the investigator and the sponsor's representative will meet to discuss the study design and conduct of the study. The investigator will sign the protocol acknowledging that he understands the design and all procedures and intends to conduct the study and all procedures according to protocol.

During the study, a representative of the sponsors will make periodic visits to the investigational site while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government regulations and guidelines. The investigator will permit authorized representatives and the respective local and national health authorities to inspect facilities and records relevant to this study, if needed.

Subject data will be collected on source documents and entered in the CRF. Data will be reviewed and validated. The investigator will sign and date a declaration on the CRF attesting to his/her responsibility for the quality of all data recorded and that the data represents a complete and accurate record of each subject in the study.

Records of subjects, source documents, monitoring visit logs, inventory of study product, regulatory documents (e.g., protocol and amendments, IRB/IEC correspondence and approvals, approved and signed informed consent forms, Investigator's Agreement, clinical supplies receipts, and distribution and return records), and other sponsor correspondence pertaining to the study will be kept in the appropriate study files at the site. Source documents include all recordings and observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical study. At the end of the study, CRF data will be provided to the sponsor.

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10. Planned statistical methods

10.1 Primary endpoints

1. **Safety** of ¹⁷⁷Lu-PSMA-617 RLT will be assessed by analysis of toxicity. Descriptive statistics (number and percentage) will be reported separately for AE in total and SAE based on CTC. These descriptive statistics will be presented for the whole treatment as well as separate for each cycle. In addition, the relationship of AE to the study drug (related, not related) will be reported. Both results from laboratory test, physical examinations and patients surveys will be included.
2. **Efficacy** of ¹⁷⁷Lu-PSMA-617 will be reported using descriptive statistics by means of number and percentage of patients with $\geq 50\%$ decline at 12-weeks from baseline.

10.2. Secondary endpoints

1. Descriptive analyses (median, standard deviation) will be used to determine the **progression-free survival (PFS)**, measured from start of therapy until death or PSA progression. PSA progression is defined a) for patients with PSA decline after start of treatment as time from baseline to time the PSA increases to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later or b) for patients without PSA decline as time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq ¹⁷⁷Lu-PSMA-617) and a statistical significant difference will be tested.
2. Each clinical site will perform image analysis on their own patients. Descriptive analyses (median, standard deviation) will be used to determine the **radiographic progression-free survival (rPFS)**, measured from start of therapy until death or radiographic progression. Radiographic progression is defined as a) for extraskeletal

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disease progressive disease (PD) following Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 [63] and/or b) skeletal disease the development of ≥ 2 new lesions on first post-treatment bone scan, with at least two additional lesions on the next scan (2+2 rule). The date of progression is the date of the first post-treatment scan, when the first two new lesions were documented. This approach is applied in accordance to PCWG3 criteria to exclude pseudoprogression in the absence of symptoms or other signs of progression [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq 177 Lu-PSMA-617) and a statistical significant difference will be tested.

3. Descriptive analysis will be used to determine the **disease control rate (DCR)** at the end of each cycle defined as the number and percentage of patients achieving a) RECIST stable disease (SD), partial response (PR) or complete response (CR) for extraskeletal tumor manifestation and b) PCWG3 non-progressive disease for skeletal manifestations.
4. Descriptive analysis will be used to evaluate the impact on **bone pain level** by determining the proportion of patients with pain response defined by improvement from baseline (all patients with $\geq 4/10$) of at least 2-point absolute improvement without an overall increase in opiate use.
5. Change in **Quality of Life** over time will be documented by comparing the summary scores investigated by the Quality of life questionnaire "EPIC-26" at baseline and at 3, 6, 9, 12, 18 and 24 months after start of 177 Lu-PSMA-617 RLT [64].
6. Changes in **performance status (ECOG)** from baseline will be evaluated over time at 3, 6, 9, 12, 18 and 24 months after start of 177 Lu-PSMA-617 RLT.

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11. Administrative Considerations

11.1 Investigators and Study Administrative Structure

This study will be conducted in accordance with the Declaration of Helsinki, ICH E6 Guideline and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 312.50 through 312.70, directive 2001/20/EC of 4 April 2001 and implementing directives and regulations. To ensure compliance the investigator agrees, by written consent to this protocol, to fully cooperate with compliance checks by allowing access to all documentation by authorized individuals. The investigator must conduct the trial as outlined in the protocol and in accordance with the Declaration of Helsinki and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 56 – Institutional Review Boards. The administrative structure of the study (e.g., monitoring and vendor personnel, statistician, and laboratory facilities) and a complete and controlled list of the investigators participating in this study can be found in the study file maintained by the sponsor or its agent.

11.2 Institutional Review Board (IRB) or Independent Ethics Committee (IEC) Approval

The protocol, informed consent form, and any advertisement for the recruitment of subjects must be reviewed and approved by an appropriately constituted IRB or IEC, as required in Chapter 3 of the ICH E6 Guideline and government regulations, including (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 56.107 through 56.115 of Good Clinical Practice. Written IRB approval must be provided to sponsor or designee prior to shipment of study drug or subject enrollment. The investigator is committed in accordance with local requirements to provide the IRB with updates, and to inform the IRB of any emergent problem, SAEs, and/or protocol amendments.

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11.3 Ethical Conduct of the Study

It is mandatory that all considerations regarding the protection of human subjects be carried out in accordance with the Declaration of Helsinki.

11.4 Subject Information and Consent

It is the responsibility of the investigator to obtain written informed consent from subjects. All subjects must sign and personally date an approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for GCP, and the requirements of (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27 of Good Clinical Practice.

The subject must be made aware and agree that personal information may be scrutinized during audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. Prior to IRB/IEC submission, the investigator must send a copy of the informed consent form to be used at their institution to sponsor or designee for review to assure compliance with the ICH E6 and government regulations of the region.

11.5 Subject Confidentiality

Data collected during this study may be used to support the development, registration or marketing of ¹⁷⁷Lu-PSMA-617. All data collected during the study will be controlled by sponsor or designee and sponsor will abide by all relevant data protection laws. In order to maintain subject privacy, all CRFs, study drug accountability records, study reports and communications will identify the subject by initials and the assigned subject number. The

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investigator will grant monitor(s) and auditor(s) from sponsor or its designee and regulatory authority (ies) access to the subject's original medical records for verification of data entered into the CRF and to audit the data collection process. The subject's confidentiality will be maintained and will not be made publicly available to the extent permitted by the applicable laws and regulations.

Written authorization is to be obtained from each subject prior to enrollment into the study in accordance with the applicable privacy requirements [e.g., the Health Insurance Portability and Accountability Act of 1996 Standards for Privacy of Individually Identifiable Health Information ("HIPAA

11.6 Study Monitoring

11.6.1 Monitoring Procedures

An appropriate representative of the sponsors (Study Monitor) will oversee the progress of the study, and ensuring it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and applicable regulatory requirements.

An initiation visit will be made by the study monitor at each site to discuss the protocol and the obligations of both the Sponsor and the investigator. The investigator must allow the study monitor to perform periodic, interim monitoring visits. The actual frequency of monitoring visits will be dependent on the enrollment rate and performance at each site. The purposes of these visits are to verify that written informed consent was obtained prior to each subject's participation in the trial, and to:

- assess the progress of the study
- review the compliance with the study protocol
- determine whether all AEs and SAEs were appropriately reported
- determine whether the investigator is maintaining the essential documents
- discuss any emergent problem

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- check the CRF for accuracy and completeness
- validate the contents of the CRF against source
- assess the status of drug storage, dispensing and retrieval
- retrieve study data

All data required by the protocol must be reported accurately on the CRF and must be consistent with the source documents. Source documents are original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays or other diagnostic images, subject files, pharmacy records and laboratory records). The investigator will make available the source documents for inspection. This information will be considered as confidential.

During scheduled monitoring visits, the investigator and the investigational site staff should be available to meet with the study monitor in order to discuss the progress of the study, make necessary corrections to CRF entries, respond to data clarification requests and respond to any other study-related inquiries of the monitor. The investigational site staff in addition to the study coordinator should also include nuclear medicine staff, radiopharmacist, and radiology staff.

The study monitor will perform a closeout visit at the conclusion of the investigator's involvement in the study.

11.6.2 Auditing

The investigator will make all pertinent records available including source documentation for inspection by regulatory authorities and for auditing by the sponsor. This information will be considered as confidential.

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Representatives of local or foreign health authorities may review the conduct or results of the study at the investigational site. The investigator must promptly inform the sponsor of any audit requests by health authorities, and will provide sponsor with the results of any such audits and with copies of any regulatory documents related to such audits.

11.7 Case Report Forms and Study Records

Sponsor will provide a CRF and CRF instructions for the entry of study data. CRFs must be completed for each subject. All study data will be entered on CRFs from original source data. Entries should be made on the case report forms directly and promptly onscreen. The CRF will be reviewed, signed and dated by the investigator.

11.8 Protocol Violations/Deviations

Protocol violations/deviations will be documented by investigator and submitted to the IRB/IEC, as required by IRB/IEC requirements.

11.9 Access to Source Documentation

During the study, a representative of the sponsor will make periodic visits to the investigational sites while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government regulations and guidelines. The investigator will permit authorized representatives of the sponsor and the respective local and national health authorities to inspect facilities and records relevant to this study, if needed.

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11.10 Data Generation and Analysis

Sponsor(s) or its designee will be responsible for data collection, data management, generation of data outputs and statistical analysis of all data.

11.11 Retention of Data

As described in the ICH GCP Guidelines, ‘essential documents’, including copies of the protocol, subject identification codes, CRF, source data, informed consent form(s) and other documents pertaining to the study conduction must be kept for the maximum period of time as required by the study site. This time period must be at least two years after the last follow up of the patients enrolled.

No study document should be destroyed without prior written agreement between sponsors and the investigators. Originals of all documentation generated by sponsor and copies of outgoing sponsor correspondence concerning the study will be stored and retained in a safe area under the control of sponsor for the lifetime of the product. In particular, the final report must be retained by sponsor, or the subsequent owner, for 5 years beyond the lifetime of the study drug.

11.12 Financial Disclosure

All investigators must provide financial disclosure information in accordance with the US Code of Federal Regulations Title 21 CFR 54.2 through 54.6.

11.13 Publication and Disclosure Policy

All unpublished documentation (including the protocol, CRF and Investigator Brochure (IB) given to the investigator is strictly confidential. All recipients must agree not to disclose the

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information herein contained to any person without the prior written authorization of sponsor. The submission of these documents to the IRB is expressly permitted. The investigator agrees that sponsor maintains the right to use the results of this study in their original form and/or in a global report for submission to governmental and regulatory authorities of any country.

The results of the study may be presented during scientific symposia or published in a scientific journal only after review by sponsor in accordance with the guidelines set forth in the applicable publication or financial agreement.

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Appendices

Appendix 1- Preclinical Toxicity studies

This exhibit is 303 pages. Therefore we are providing it in the attached CD.

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Appendix II: Visit Specific Schedule

	Month	Screening			Therapy												F/U																					
		Week	1	0	3	5	6	9	11	12	15	17	18	21	23	24	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24			
	Therapy			1			2			3			4																									
1	Signing informed consent form	*																																				
2	Randomization		*																																			
1	Evaluation of blood tests (*CBC, CMP)	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	
2	Evaluation of Imaging studies (CT , MRI)	*																																				
3	Ga-68 or Lu-177 PSMA PET/CT	*																																				
4	Medication & Hypersensitivity assessment	*																																				
5	Current Disease(somatic or psychiatric)	*																																				
6	Histopathology evaluation	*																																				
7	Relevant medical history & demographics	*																																				
8	Vital Signs(BP, HR, T, RR)	*			*		*		*		*		*		*																							
9	Evaluation of life expectancy	*																																				
10	Prior therapy for Prostate cancer	*																																				
11	ECG and continues ECG Monitoring	*			*		*		*		*		*		*																							
12	Quality of life assessment (EPIC-26)	*																																				
13	PSA determination		*			*		*		*		*		*		*		*		*		*		*		*		*		*		*		*		*		*
14	Whole body (Anterior And Posterior) scan			*			*		*		*		*		*		*								*		*		*		*		*		*		*	
15	Follow up calls for AE Monitoring			+7 days		+7 days		+7 days		+7 days		+7 days		+7 days		+7 days									*		*		*		*		*		*			

- 1 A blood sample will be collected within 48 hours (preferably 30 minutes) before the injection to evaluate CMP and CBC for safety purposes.
- 1 Only at first treatment several blood samples will be required for dosimetry purposes at 5 minutes ,30 minutes, 1, 4,24, 48, and 72 hours. 7 to 9 days sample is optional.
- 1 Laboratory test will be acceptable only if they performed within one week of each scheduled visit. Screening visit and week -1 can be combined if screening visit performed within 2 weeks of the first cycle
- 1 *CBC will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until disease progression
- 1 CMP will be checked 4 weeks after each cycle, one week prior to the subsequent cycle, and every three months up to 24 months after the last treatment.
- 2 Baseline imaging within 12 weeks of start of therapy including (a) Chest CT preferably with contrast & CT or MRI of the Abdomen- pelvis preferably with contrast, (b) bone imaging, (c) or equivalent
- 2 Relevant imaging studies will be repeated every 12 to 16 weeks until reaching the endpoint or 24 months after the first treatment.
- 2 For patients whom are eligible for 7th cycle of RLT "Imaging study" will be performed only either in cycle number 7 of follow up number 1.
- 8 For safety assessment, vital signs will be measured within 20 minutes before and for up to an hour after administration of ¹⁷⁷Lu-PSMA 617

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- 11 Continues ECG recording starts at least 15 minutes prior to administration of the study drug and lasts at least 1 hour after administration. Also two 12 lead ECGs :one before injection and one after 4 hr scan
- 12 Quality of life questionnaire (EPIC-26) will be completed at baseline and in 3, 6,9, 12,18 and 24 months (+/- 1 month for each) after the start of treatment
- 13 PSA will be measured every 6 weeks during the treatment and every 3 months after the last treatment until reaching endpoint or 24 months after the first treatment.
- 14 Only at first treatment Scintigraphy will be performed several times (4, 24, 48 , and 72 hours)after injection for dosimetry purposes. Please refer to dosimetry schedule of events.
- 15 Telephone follow up: 7 (+/- 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 week) until the end of follow up visits (24 months).
In each time point that the therapy stops follow up visits will be started.

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Appendix III: Chemistry, Manufacturing, and Control (CMC) of Lu-177 PSMA

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Appendix IV: Informed Consent Form

Not provided with original protocol

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Sponsor Signatures

Study Title: PSMA-directed EndoRadiotherapy of Castration-resISTant prostate cancer (PERCIST). A phase II clinical trial.
Study Number: TBD
IND Number: TBD
Final Date: TBD

This clinical study protocol was subject to critical review and has been approved by the sponsor.

Signed: _____ Date: _____

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Investigator's Signature

Study Title: PSMA-directed EndoRadiotherapy of Castration-resistant prostate cancer (PERCIST). A phase II clinical trial.
Study Number: TBD
IND Number: TBD
Final Date: TBD

I acknowledge that I have read the attached protocol as amended and I agree that it contains all information necessary to conduct the study. I also agree to and will comply with all provisions set forth therein and herein, and certify as follows:

I will comply with all Health Authority regulations/guidelines relevant to the conduct of human clinical trials, as set forth in 21 CFR Parts 50, 54, 56, and 312 part D as they may be amended or supplemented from time to time. I will not initiate the study until I have obtained written approval from the appropriate Institutional Review Board/Independent Ethics Committee and have complied with all financial and administrative requirements of the governing body of my clinical institution. I will obtain written informed consent from all study participants prior to performing any screening procedures.

I understand that my signature (or that of a Sub-Investigator) on a case report form indicates that the data therein have been reviewed and are deemed to be complete, accurate, and acceptable to me.

I have not been disqualified by any regulatory authority or otherwise disqualified from serving as a Principal Investigator, or debarred by the U.S. FDA or any other regulatory authority. In the event that during the term of the study, I become debarred, or receive notice of an action by a health authority or threat of an action with respect to my conduct of clinical research, I shall immediately notify sponsor. In the event I become debarred, I shall immediately cease all activities relating to the study.

I understand and acknowledge that confidential information related to this study includes, but is not limited to, (1) this document, (2) the Protocol for the study, (3) the data derived from the study and (4) my impressions of the progress or results of the study ("Confidential Information") all of which is the proprietary and sole property of sponsor. I will comply with the terms of the Confidentiality and Non-Disclosure Agreement and Clinical Trial Agreement, which stipulate that no Confidential Information will be disclosed or generally described to anyone other than sponsor, personnel or designees, participating study staff, regulatory authorities with appropriate jurisdiction, or members of the responsible Institutional Review Board/Independent Ethics Committee. I will not use such Confidential Information for any purpose other than the evaluation or conduct of the clinical investigation. I am not presently, nor will I be during the term of the study, a consultant or advisor to any division of any financial or securities firm.

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Investigator Signature

Site Name

Investigator Printed Name (with degree)

Date (DD/MM/YYYY)

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Clinical Trial Protocol: IND #

¹⁷⁷Lu-PSMA-617

Baseline and follow-Up Questionnaire for Pain and Adverse Events

PATIENT INFORMATION

Last name: _____ First Name: _____

Date of Birth: _____ Medical Record Number: _____

Change of pain medication since last ¹⁷⁷Lu-PSMA-617 cycle

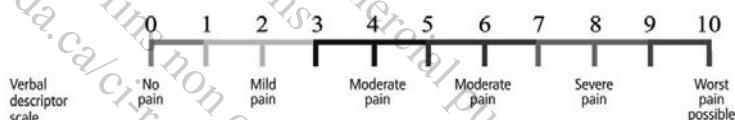
- No change
 Change in dosage/administration: medication _____ increase or decrease
 Addition/removal of medication: medication _____ addition or removal

Pain

- No or Yes:

Locations: _____

Overall level:



Change since last cycle:

- increase, no change, decrease

Nausea

- No nausea
 Nausea with loss of appetite only
 Nausea with eating/drinking less than usual
 Had to go to hospital for nausea

Vomiting

- No vomiting
 1 - 2 episodes per day
 3 - 5 episodes per day
 more than 5 episodes per day

Dry mouth

- No dry mouth
 Dry or thick saliva
 Normal eating only with water/lubricants possible
 Tube feeding or total i.v. nutrition

Taste

- Normal taste
 Altered taste but no change in diet
 Altered taste with change in diet

Fatigue

- No fatigue
 Fatigue relieved by rest
 Fatigue not relieved by rest, limiting work
 Fatigue not relieved by rest, limiting self-care

Hematoma

- No Hematoma
 Occurrence of hematoma without known event

Fever

- No fever
 38.0 - 39.0 °C (100.4 - 102.2 °F)
 >39.0 - 40.0 degrees °C (102.3 - 104.0 °F)
 >40.0 °C (>104.0 °F)

Urinary retention

- Able to void normally
 Able to void with some pressure
 Unable to void or voiding only after catheter/intervention/treatment

Diarrhea

- Normal bowel movements
 Increase by <4 stools per day

Other (symptom, grade: mild/moderate/severe):

Clinical Trial Protocol: IND #

¹⁷⁷Lu-PSMA-617

- Increase by 4-6 stools per day
- Increase by more than 6 stools per day
- Had to go to hospital for diarrhea

Date: _____ Name: _____ Signature: _____

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¹⁷⁷Lu-PSMA-617

EPIC-26
The Expanded Prostate Cancer Index Composite
Short Form

This questionnaire is designed to measure Quality of Life issues in patients with Prostate cancer. To help us get the most accurate measurement, it is important that you answer all questions honestly and completely.

Remember, as with all medical records, information contained within this survey will remain strictly confidential.

Today's Date (please enter date when survey completed): Month _____ Day _____ Year _____

Name (optional): _____

Date of Birth (optional): Month _____ Day _____ Year _____

Clinical Trial Protocol: IND #

¹⁷⁷Lu-PSMA-617

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Space

1. Over the **past 4 weeks**, how often have you leaked urine?

- | | | | |
|----------------------------|---|---------------------|-----|
| More than once a day..... | 1 | (Circle one number) | 23/ |
| About once a day..... | 2 | | |
| More than once a week..... | 3 | | |
| About once a week..... | 4 | | |
| Rarely or never..... | 5 | | |

2. Which of the following best describes your urinary control **during the last 4 weeks**?

- | | | | |
|------------------------------------|---|---------------------|-----|
| No urinary control whatsoever..... | 1 | (Circle one number) | 26/ |
| Frequent dribbling..... | 2 | | |
| Occasional dribbling..... | 3 | | |
| Total control..... | 4 | | |

3. How many pads or adult diapers per day did you usually use to control leakage
during the last 4 weeks?

- | | | | |
|-----------------------------|---|---------------------|-----|
| None | 0 | (Circle one number) | 27/ |
| 1 pad per day..... | 1 | | |
| 2 pads per day..... | 2 | | |
| 3 or more pads per day..... | 3 | | |

4. How big a problem, if any, has each of the following been for you **during the last 4 weeks?**

(Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem	
a. Dripping or leaking urine	0	1	2	3	4	28/
b. Pain or burning on urination.....	0	1	2	3	4	29/
c. Bleeding with urination.....	0	1	2	3	4	30/
d. Weak urine stream or incomplete emptying.....	0	1	2	3	4	31/
e. Need to urinate frequently during the day.....	0	1	2	3	4	33/

Clinical Trial Protocol: IND #

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5. Overall, how big a problem has your urinary function been for you **during the last 4 weeks?**

No problem.....	1					
Very small problem.....	2					
Small problem.....	3					
Moderate problem.....	4					
Big problem.....	5					

(Circle one number)

34/

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6. How big a problem, if any, has each of the following been for you? (Circle one number on each line)

	<u>No Problem</u>	<u>Very Small Problem</u>	<u>Small Problem</u>	<u>Moderate Problem</u>	<u>Big Problem</u>	
a. Urgency to have a bowel movement	0	1	2	3	4	49/
b. Increased frequency of bowel movements.....	0	1	2	3	4	50/
c. Losing control of your stools.....	0	1	2	3	4	52/
d. Bloody stools	0	1	2	3	4	53/
e. Abdominal/ Pelvic/Rectal pain...	0	1	2	3	4	54/

7. Overall, how big a problem have your bowel habits been for you **during the last 4 weeks?**

No problem.....	1					
Very small problem.....	2					
Small problem.....	3					
Moderate problem.....	4					
Big problem.....	5					

(Circle one number)

55/

8. How would you rate each of the following **during the last 4 weeks?** (Circle one number on each line)

	<u>Very Poor to None</u>	<u>Poor</u>	<u>Fair</u>	<u>Good</u>	<u>Very Good</u>	
a. Your ability to have an erection?.....	1	2	3	4	5	57/
b. Your ability to reach orgasm (climax)?.....	1	2	3	4	5	58/

Clinical Trial Protocol: IND #

¹⁷⁷Lu-PSMA-617

9. How would you describe the usual QUALITY of your erections **during the last 4 weeks?**

- | | | | |
|---|---|---------------------|-----|
| None at all..... | 1 | | |
| Not firm enough for any sexual activity..... | 2 | | |
| Firm enough for masturbation and foreplay only..... | 3 | (Circle one number) | 59/ |
| Firm enough for intercourse..... | 4 | | |

10. How would you describe the FREQUENCY of your erections **during the last 4 weeks?**

- | | | | |
|---|---|---------------------|-----|
| I NEVER had an erection when I wanted one..... | 1 | | |
| I had an erection LESS THAN HALF the time I wanted one..... | 2 | | |
| I had an erection ABOUT HALF the time I wanted one | 3 | (Circle one number) | 60/ |
| I had an erection MORE THAN HALF the time I wanted one..... | 4 | | |
| I had an erection WHENEVER I wanted one..... | 5 | | |

Do Not
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Space

11. Overall, how would you rate your ability to function sexually **during the last 4 weeks?**

- | | | | |
|----------------|---|---------------------|-----|
| Very poor..... | 1 | | |
| Poor..... | 2 | | |
| Fair..... | 3 | (Circle one number) | 64/ |
| Good..... | 4 | | |
| Very good..... | 5 | | |

12. Overall, how big a problem has your sexual function or lack of sexual function been for you
during the last 4 weeks?

- | | | | |
|-------------------------|---|---------------------|-----|
| No problem..... | 1 | | |
| Very small problem..... | 2 | | |
| Small problem..... | 3 | (Circle one number) | 68/ |
| Moderate problem..... | 4 | | |
| Big problem..... | 5 | | |

13. How big a problem **during the last 4 weeks**, if any, has each of the following been for you?
(Circle one number on each line)

No Very Small Small Moderate Big

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¹⁷⁷Lu-PSMA-617

	<u>Problem</u>	<u>Problem</u>	<u>Problem</u>	<u>Problem</u>	<u>Problem</u>	
a. Hot flashes.....	0	1	2	3	4	74/
b. Breast tenderness/enlargement..	0	1	2	3	4	75/
c. Feeling depressed.....	0	1	2	3	4	77/
d. Lack of energy.....	0	1	2	3	4	78/
e. Change in body weight.....	0	1	2	3	4	79/

THANK YOU VERY MUCH!!

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¹⁷⁷Lu-PSMA-617

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Clinical Trial Protocol: IND # 133661

Study Title: PSMA-directed EndoRadiotherapy of Castration-resISTant prostate cancer (PERCIST). A phase II clinical trial.

Study Number: TBD
IND Number: 133661

Study Phase: Phase II

Product Name: ¹⁷⁷Lu- DOTA-PSMA-617

Indication: Metastatic castration resistant prostate cancer

Principle Investigators: Ebrahim S. Delpassand, M.D. F.A.C.N.M.
Johannes Czernin, M.D.

Sponsors: Ebrahim S. Delpassand, M.D. F.A.C.N.M
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	Date
Original Protocol Date:	12/28/2016

Amendment 1 Date: 2/24/2017

Confidentiality Statement

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SYNOPSIS

Sponsors:

Ebrahim S. Delpassand, M.D.

Johannes Czernin, M.D.

Name of Finished Product:

¹⁷⁷Lu-PSMA-617

Name of Active Ingredient:

2-[3-(1-Carboxy-5-{3-naphthalen-2-yl}-2-[(4-{[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid

Study Title:

PSMA-directed EndoRadiotherapy of Castration-resISTant prostate cancer (PERCIST). A phase II clinical trial.

Study Number:

TBD

Study Phase:

Phase II

Primary Objective:

To assess safety and efficacy defined as >50% decline in PSA after ¹⁷⁷Lu-PSMA-617 in patients with metastatic castration resistant prostate cancer

Secondary Objectives for each treatment dose:

1. To determine maximum PSA decline.
2. To determine PSA progression-free survival (PFS), measured from start of therapy until death or PSA progression.
3. To determine radiographic PFS, measured from start of therapy until death or radiographic progression using RECIST 1.1/PCWG3 criteria.
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST stable disease (SD), partial response (PR) or complete response (CR).
5. To determine impact on bone pain level
6. To determine impact on quality of life

7. To determine impact on performance status (ECOG)

Study Design:

Open-label, prospective, multicenter clinical trial.

Study Population:

Patients with metastatic castration resistant prostate cancer

Inclusion Criteria:

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel naive and docetaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2500/\mu\text{l}$, PLT count $\geq 100,000/\mu\text{l}$, Hb ≥ 9.9 g/dl and ANC $\geq 1500 \text{ mm}^3$ for the first cycle and WBC $\geq 2,000/\mu\text{l}$, PLT count $\geq 75,000/\mu\text{l}$, Hb ≥ 8.9 g/dl and ANC $\geq 1000 \text{ mm}^3$ for the subsequent cycles
8. Signing of the Informed Consent Form
9. Patients enrolling in this trial should have received either enzalutamide or abiraterone

Exclusion Criteria:

1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm) or other radionuclide therapy.
2. Glomerular Filtration Rate (GFR) <40 ml/min
3. serum creatinine $>1.5 \times \text{ULN}$
4. AST and ALT $>5 \times \text{ULN}$
5. Urinary tract obstruction or marked hydronephrosis
6. Patients who had received both docetaxel and cabazitaxel will be excluded from this study. Enrolment will be limited to patients who had received prior docetaxel only.
7. Diffuse bone marrow involvement confirmed by super-scans

Test Product; Dose; and Mode of Administration:

Randomization into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq ($\pm 10\%$, **arm 1**) or 7.4 GBq ($\pm 10\%$, **arm 2**) ^{177}Lu -PSMA-617 every 8 ± 1 weeks; RLT until reaching four cycles or threshold maximum dose to the kidneys of 23

Gy as determined by dosimetry after the first treatment.

Study Duration:

Patients will be followed until either of the following conditions occur:

1. 24 month after the first treatment.
2. Progression by RECIST 1.1/PCWG3 criteria.
3. Death.

Safety Assessments:

Following laboratory tests will be performed one week before each treatment and 4 weeks after the last treatment and every 3 month thereafter:

1. Complete metabolic panel and eGFR
2. CBC

At baseline, 7 (+/- 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 week) until the end of follow up visits (24 months) patients will be called for safety interview.

Following conditions if in view point of investigators deemed study related, will result in permanent discontinuation:

- i. Grade 3-4 non-hematologic toxicities with select exceptions for:
 1. Grade 3 fatigue < 10 days
 2. Grade 3 nausea, vomiting, and diarrhea and grade 4 vomiting and diarrhea that persist for < 72 hours in the absence of maximum medical therapy.
 3. Asymptomatic grade 3 non-hematological laboratory abnormalities that resolve in 72 hours.
 4. Grade 3 infections that resolve under medical treatment within 10 days
- ii. AST/ALT > 3x ULN and bilirubin > 2x ULN
- iii. Grade 4 Hematological toxicities persisting >3 weeks.
- iv. Grade 3 Hematological abnormalities that do not return to baseline for > 12 weeks.

Data Safety Monitoring Board

A Data Safety Monitoring Board (DSMB) has established and will evaluate safety throughout the study. The DSMB will advise the Sponsor, Investigators and investigational sites regarding the continuing safety of study patients and the patients yet to be recruited to the study as well as maintaining validity and scientific merit of the study. The DSMB will review ongoing examinations of safety data and promptly give recommendations to continue, continue with modification, or terminate the study.

Interim safety analyses: 4 interim safety analyses will be conducted by DSMB that will be initiated at the time when 25%, 50%, 75% and 100% of the total 177Lu-PSMA treatments in the trial have been completed. The DSMB will meet and assess up-to-date safety information within two weeks of a treatment exposure rate being achieved (i.e., the point when 25%, 50%, 75% and 100% of treatments have occurred). Further patients may only be randomized two weeks after the treatment exposure rate has been reached and after a positive opinion from the DSMB.

Efficacy Assessment for each treatment arm:

Primary objective:

12 week PSA response: Proportion of patients with PSA-decline of $\geq 50\%$ at 12-weeks after the first RLT [1]

Secondary objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]
2. Time to PSA progression, for each treatment arm. [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later
 - b. for patients without PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later
3. Radiographic progression free survival (rPFS), for each treatment arm.
4. Change in Pain, Quality of Life and ECOG performance score: Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 month, for each treatment arm

Number of patients enrolled:

As per statistical evaluation, total of 200 patients will be required to have statistical power to achieve the primary endpoints of the study.

Date of Original Protocol: December 28th, 2016

Date of Most Recent Protocol Amendment (if applicable): N/A

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LIST OF APPENDICES

Appendix I: Preclinical Toxicity Studies

Appendix II: Visit Specific Schedule

Appendix III: Chemistry, Manufacturing, and Control (CMC) of ¹⁷⁷Lu- PSMA

Appendix IV: Consent Form

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse event
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
AP	alkaline phosphatase
AST	Aspartate aminotransferase
AUC	Area under the plasma concentration versus time curve
BUN	Blood urea nitrogen
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CI	Confidence interval
CR	Complete response
CRF	Case report form
CT	Computed tomography
DCR	Disease Control Rate
ECOG	Eastern Cooperative Oncology Group
eGFR	estimated Glomerular Filtration Rate
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GGT	Gamma-glutamyl transferase
GH	Growth hormone

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Hct	Hematocrit
Hgb	Hemoglobin
HIPAA	Health Information Portability and Accountability Act
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intent-to-treat
LDH	Lactic dehydrogenase
MBq	MegaBequerel
mCi	milliCurie
mo	months
GBq	gigabecquerel
MR	Magnetic resonance
MRI	Magnetic resonance imaging
N/A	Not applicable
NDA	New Drug Application
PCa	Prostate cancer
PET/CT	Positron Emission Tomography/Computed Tomography
PFS	Progression-free survival
PSA	Prostate-specific antigen

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PR	Partial response
RBC	Red blood cell
RECIST	Response Evaluation Criteria In Solid Tumors
RLT	Radioligand therapy
RPFS	Radiographic progression-free survival
SAE	Serious adverse event
SAER	Serious adverse event report
SAP	Statistical analysis plan
SD	Stable disease
SE	Standard error
SPECT	Single-photon emission computerized tomography
PSMA	prostate-specific membrane antigen
US	United States
WBC	White blood cell
WHO-DD	World Health Organization Drug Dictionary

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1. Introduction

1.1 Background

According to the American Cancer Society more than 1 million people in the United States are diagnosed with cancer each year. For American *males*, prostate cancer is the second most common cause of cancer related death [2]. A recent publication [3] estimated the prevalence of prostate cancer as 2,219,280 in the US in 2009 and 3,072,480 in 2020, and incidence of metastatic Castration Resistant Prostate Cancer (mCRPC) as 36,100 and 42,970, respectively. Various therapies have been developed to improve survival of patients with advanced prostate cancer. However, despite such efforts currently all-cause mortality in prostate cancer has been estimated at 168,290 in 2009 and 219,360 in 2020, with 20.5% and 19.5% of these deaths, respectively, occurring in men with mCRPC.

Patients with metastatic castration-resistant prostate cancer (mCRPC) have a poor prognosis, and those patients with metastases are expected to survive ≤ 19 mo [3]. As patient disease progresses, quality of life deteriorates, and until recently, few treatment options were available. Several new therapies have shown an improvement in overall survival for patients with mCRPC who have already received chemotherapy with docetaxel (Fig. 1) [4] [5] [6, 7] [8]. The impact of these new data on clinical practice, treatment sequencing, and best care for individual patients is not yet fully established.

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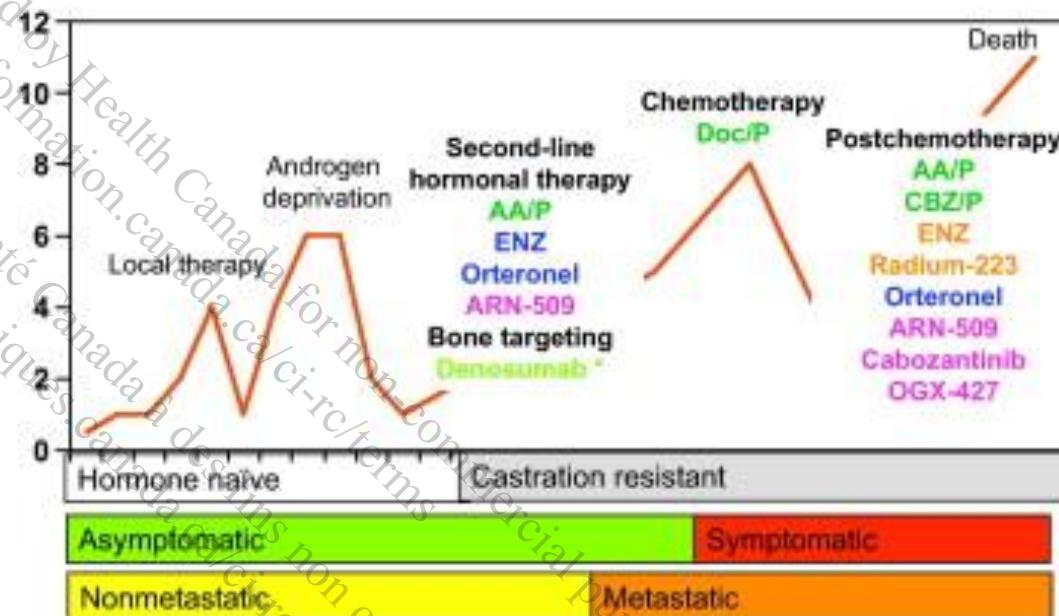


Figure 1: Current, ongoing, and future landscape in the management of castration-resistant prostate cancer. Color key: green = US Food and Drug Administration/European Medicines Agency (FDA/EMA) approved; light green = trial results in high-risk patients positive, but not approved; orange = prospective, randomized, phase 3 clinical trial completed, results positive, FDA/EMA approval awaited; blue = prospective, randomized, phase 3 clinical trial completed, results awaited; purple = promising agent, phase 3 clinical trials ongoing. * Trial results for denosumab in high risk patients positive, but not approved. AA/P = abiraterone acetate with prednisone; ENZ = enzalutamide; Doc/P = docetaxel plus prednisone; CBZ/P = cabazitaxel plus prednisone.

1.1.1. Current treatment options for metastatic castration-resistant prostate cancer: before docetaxel

Sipuleucel-T

Sipuleucel-T is an autologous vaccine consisting of individually collected antigen-presenting cells that are exposed to the fusion protein prostatic acid phosphatase and granulocyte colony-stimulating factor (GCSF), and then reinfused in the patient at weeks 0, 2, and 4. In the Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) study, median survival with sipuleucel-T was 25.8 mo compared with 21.7 mo with placebo [9]. It has to be considered, however, that only patients with a good Eastern Cooperative Oncology Group

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performance status of 0–1, asymptomatic or mildly symptomatic osseous metastases, and absence of visceral metastases were included in the trial.

Abiraterone acetate

The COU-AA-302 (Cougar 302) trial randomized 1088 men with mCRPC to receive abiraterone acetate with prednisone (AA/P) or placebo [4] with the primary end points of overall and radiographic progression-free survival (rPFS) by central review. Median overall survival was 35.3 mo and 27.2 mo in the AA/P group and in the placebo group, respectively ($p = 0.01$) [10]. Also, the co-primary end point of rPFS was significantly improved in the AA/P group, at 16.5 mo, as compared to 8.3 mo in the placebo arm ($p < 0.001$). On all secondary end points, AA/P treatment resulted in significantly improved effects.

Docetaxel/prednisone

In 2004, cytotoxic treatment with docetaxel plus prednisone (Doc/P) was the main option for treatment of mCRPC based on the TAX 327 trial [11]. The median survival was 18.9 mo versus 16.4 mo in the group of patients who received mitoxantrone/prednisone ($p = 0.009$), the 3-yr overall survival rate was 18.6% versus 13.5%, and pain response was 35% versus 22%. It has been shown recently that Doc/P is active in men with symptomatic mCRPC and especially in patients with poorly differentiated prostate cancer (PCa) (Gleason score: 8–10) [12].

Subsequent studies using combinations with docetaxel have not further improved the oncologic outcome [3]. The results of the Randomized Study Comparing Docetaxel Plus Dasatinib to Docetaxel Plus Placebo in Castration-Resistant Prostate Cancer (READY) and the Aflibercept in Combination with Docetaxel in Metastatic Androgen-Independent Prostate Cancer (VENICE) trial were disappointing [13] [11]. The median survival after docetaxel and docetaxel/dasatinib was 21.2 mo versus 21.5 mo, respectively, and the median survival after docetaxel versus docetaxel plus afilbercept was 21.1 mo versus 22.1 mo, respectively. The differences in the patient cohorts of the Cougar 302, IMPACT, and TAX 327 trials make it evident that AA/P will be used for asymptomatic or mildly symptomatic mCRPC with a

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low metastatic burden, whereas Doc/P might be the treatment of choice in men with symptomatic mCRPC and/or a high metastatic burden as well as an undifferentiated PCA.

1.1.2. After docetaxel treatment

Docetaxel rechallenge

The scientific evidence of this approach results from large, retrospective series that identified patients who might be good candidates for re-exposure [14] [15] [16]. Patients who responded with a ≥30% decrease in prostate-specific antigen (PSA) level, maintained for at least 8 wk after first exposure to docetaxel, demonstrated a positive PSA response in about 55% to 60% of the cases during re-exposure without increasing treatment related toxicity.

Abiraterone acetate plus prednisone

AA/P versus placebo was evaluated in the Cougar 301 trial, which randomized 1195 patients with progressive mCRPC who failed docetaxel-based chemotherapy [5]. The median follow-up in the overall study population was 12.8 mo. Overall survival was significantly improved from 10.9 mo in the placebo arm to 14.8 mo in the AA/P arm ($p < 0.001$). All secondary end points were met and all end points demonstrated a significantly improved benefit for the AA/P group. Adverse events with regard to the CYP 17 blockade were observed significantly more often in the AA/P arm (55% vs 43%; $p < 0.001$).

Recently, Goodman et al. [17] demonstrated that AA/P is effective even in patients with liver or lung metastases, although to a lesser degree. The overall survival times were 12.9 mo versus 8.3 mo in the placebo group ($p = 0.022$). Albiges et al. [18] described an AA withdrawal syndrome that developed in 32% of 66 patients who had been treated for a mean period of 5.7 mo. Clayton et al. [19] presented data from a population-based study that included 187 mCRPC patients with a mean PSA serum concentration of 138 ng/ml who were treated with AA/P. The median overall survival was only 9.3 mo and might reflect the oncologic efficacy of AA/P in a real-world patient population with high metastatic burden.

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Enzalutamide (formerly MDV3100)

Enzalutamide (ENZ) acts as an androgen receptor (AR)-signaling inhibitor, and it was evaluated in the Multinational, Phase 3, Randomized, Double-blind, Placebo-controlled, Efficacy and Safety Study of Oral MDV3100 in Patients with Progressive Castration-Resistant Prostate Cancer Previously Treated with Docetaxel-Based Chemotherapy (AFFIRM) trial, which randomized 1199 mCRPC patients to receive ENZ or placebo [8].

The median follow-up was 14.4 mo and the median overall survival was 18.4 mo and 13.6 mo ($p < 0.0001$) in the ENZ group and in the placebo group, respectively, with a 37% reduction in relative risk for death. All secondary end points were met with a statistically significant benefit in the ENZ arm. With regard to safety, the ENZ group experienced fewer grade 3/4 toxicities than the placebo group (53% vs 45%). The risk of seizures was slightly elevated in the ENZ group, with a frequency of 0.6% versus 0% in the placebo group.

Recently, Scher et al. [20] demonstrated that the use of corticosteroids in parallel to ENZ not only increased grade 3/4 side effects from 34.4% to 63.3%, but it also decreased overall survival to a median 11.5 mo. These data suggest that one of the other second-line therapies, such as AA/P or cabazitaxel plus prednisone (CBZ/P), might be the drug of choice, rather than ENZ, in patients who need corticosteroids for the management of associated comorbidities. Sternberg et al. [21] reported that ENZ is equally effective in patients aged >75 yr, with a median survival time of 18.2 mo as compared to the placebo group with 13.3 mo ($p = 0.0044$). Fleming et al. [22] identified a longer disease history (7.9 yr vs 5.9 yr), a better PSA response (87% vs 52%), and a lower metastatic burden associated with long-term response of 35% and 22% after 12 mo and >18 mo, respectively. These data seem to be important for the decision-making process about the most appropriate therapy for mCRPC patients following docetaxel chemotherapy.

Cabazitaxel plus prednisone

In the XRP6258 Plus Prednisone Compared to Mitoxantrone Plus Prednisone in Hormone-Refractory Metastatic Prostate Cancer (TROPIC) trial, 755 patients with mCRPC who

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progressed during or after docetaxel-based chemotherapy were prospectively randomized to receive CBZ/P or mitoxantrone/prednisone (MP) at 21-d intervals for 10 cycles [5]. The primary end point was achieved and CBZ/P treatment resulted in a median overall survival of 15.1 mo in the CBZ/P compared to 12.7 mo in the mitoxantrone/prednisone group (hazard ratio [HR]: 0.70; 95% confidence interval [CI], 0.59–0.83; $p < 0.0001$). All secondary end points of the trials were reached and they were in favor of CBZ. The most common side effects were neutropenia (CBZ/P group: 82% vs MP group: 58%), leukopenia (CBZ/P group: 68% vs MP group: 42%), and anemia (CBZ/P group: 11% vs MP group: 5%). Diarrhea was the most common non-hematologic side effect and occurred in 6% of the CBZ/P group and <1% of the MP group.

On the other hand, the German compassionate use program (CUP) included 111 patients with mCRPC who met the inclusion criteria of the TROPIC trial; the frequency of neutropenia, leukopenia, and anemia decreased to 7.2%, 9.0%, and 4.5%, respectively [23]. Grade 3/4 gastrointestinal toxicity was observed in only 0.9% of the patients. The most likely reason for the improved toxicity profile is the experience of the investigators, guideline-compliant application of GCSF even at cycle 1, and preventive measures with regard to the treatment of diarrhea.

Recently, Heidenreich et al. [24] analyzed the European CUP, including 746 mCRPC patients, with regard to the frequency and management of adverse events in senior adults. In that study, 325 (43.5%) patients were aged ≥ 70 yr and 145 (19.4%) men were ≥ 75 yr. The type and the frequency of grade 3/4 side effects did not differ significantly between the younger and the older patients except that the frequency of grade 3/4 neutropenia was slightly higher in the group of men aged ≥ 75 yr (19.7% vs 15%). Furthermore, GCSF was used more often at cycle 1 (58.5% vs 47%) and throughout CBZ/P treatment (66.8% vs 58%) in the ≥ 75 age group versus the <70 age group. In their analysis, Heidenreich et al. [24] developed a risk model to predict grade ≥ 3 neutropenia and/or neutropenic complications based on a multivariate analysis. Age ≥ 75 yr, cycle 1, and neutrophil count $<4000/\text{mm}^3$ before CBZ injection were associated with neutropenic complications. It has to be mentioned that even in the presence of these risk factors, prophylactic application of

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GCSF significantly reduced the risk of neutropenic complications by 30% (odds ratio: 0.70; 95% CI, 0.50–0.99; $p = 0.04$).

Bone-targeting agents

More than 90% of patients with CRPC have bone metastases, which are a major cause of death, disability, and decreased quality of life, as well as increased cost of treatment [25]. Zoledronic acid and the receptor activator of nuclear factor κ B (RANK) ligand inhibitor denosumab are the two US Food and Drug Administration-approved bone-targeting agents in the management of CRPC [3].

In a phase 3 study, the median time to first on-study, skeletal-related event was 20.7 mo with denosumab compared with 17.1 mo with zoledronic acid (HR: 0.82; 95% CI, 0.71–0.95; $p = 0.0002$ for noninferiority; $p = 0.008$ for superiority) [26]. In a recent, prospective, randomized, double-blind, placebo-controlled trial, Smith et al. [27] evaluated the therapeutic efficacy of denosumab 120mg every week versus placebo in 1423 men with nonmetastatic CRPC and aggressive PSA kinetics (PSA level >8.0 ng/ml and/or PSA doubling time <10 mo). The median time to first bone metastases was significantly prolonged by 4.3 mo (29.5 mo vs 25.2 mo; $p = 0.028$). Bone metastases-free survival was significantly improved by 16%, 23%, and 29% in patients with a PSA doubling time of <10 mo, <6 mo, and <4 mo, respectively.

Radium-223

Radium-223 is a radiopharmaceutical that acts as a calcium mimic and targets new bone growth in and around bone metastases via heavy alpha particles that have an ultrashort range of <100 μ m. A Phase 3 Study of Radium-223 Dichloride in Patients with Symptomatic Hormone Refractory Prostate Cancer with Skeletal Metastases (ALSYMPCA), which included 921 CRPC patients, the median overall survival was 14.9 mo in patients treated with radium-223 compared with 11.3 mo in the placebo group (HR: 0.695; 95% CI, 0.581–0.8732; $p < 0.0001$) [7].

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1.1.3. New and emerging developments

Agents targeting steroidogenesis

Orteronel (TAK-700) selectively blocks 17,20-lyase, resulting in fewer mineralocorticoid effects than AA [28]. In the phase 2 portion of a dose-finding study, Orteronel (TAK-700) 400mg twice daily with prednisone 5mg twice daily resulted in a reduction in PSA level $\geq 50\%$ in 52% of the 96 chemotherapy-naïve mCRPC patients at 12 wk. There are two ongoing phase 3 clinical trials in the prechemotherapy ($n = 1454$) and postchemotherapy ($n = 1083$) landscape of mCRPC that are evaluating the oncologic activity of orteronel. Both trials have completed recruitment.

Galeterone (TOK-001) has combined activity: It inhibits the human CYP17 enzyme, it has pure antagonistic activity toward the AR, and it inhibits the binding of androgens to both mutant and wild-type AR [29]. In the Androgen Receptor Modulation Optimized for Response (AMORI) trial, 49% of chemotherapy-naïve mCRPC patients experienced a PSA-level reduction of $\geq 30\%$, and a $\geq 50\%$ reduction was achieved by 22% [30]. Despite the absence of steroid co-treatment, no adrenal mineralocorticoid excess was observed and a phase 2 trial is underway.

Androgen-receptor blocking agents

ARN-509 is a full antagonist to AR overexpression: It inhibits androgen-dependent gene description, and it impairs nuclear translocalization and DNA binding of AR [31]. Currently, three prospective randomized phase 3 clinical trials are underway including (1) patients with high-risk and nonmetastatic CRPC, (2) treatment-naïve patients with mCRPC, and (3) patients with progression following AA/P treatment. Preliminary results have been presented for the first two groups and a $\geq 50\%$ decline in PSA level was achieved in 91% of patients with high-risk and nonmetastatic CRPC and in 88% of treatment-naïve patients with mCRPC. The most common side effects were tolerable fatigue and gastrointestinal events.

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ODM-201 is another antiandrogen with similar mechanisms of actions as described for ENZ and ARN-509 [31]. The potential advantage of ODM-201 is that it does not cross the blood-brain barrier and so might prevent the development of seizures. ENZ-4176 is a novel, nucleic acid-based antisense oligonucleotide against AR, which results in selective and specific downregulation of AR mRNA and protein.

Heat shock proteins

Heat shock proteins (HSPs) have been identified as AR coactivators and chaperone proteins that are increased in PCa cell lines after castration [32]. Quite recently, antisense oligonucleotides targeting HSP27 were evaluated in a phase 2 clinical trial including 72 patients chemotherapy-naïve mCRPC patients who received OGX-427 plus prednisone versus prednisone alone. At 12 wk, 71% and 40% of the patients were progression-free after OGX-427 or prednisone, respectively. A decline of $\geq 50\%$ in PSA level was observed in 50% and 20% in the OGX-427 group and in the prednisone group, respectively. Furthermore, measurable disease response occurred in 44% and 0% of the OGX-427 group and the prednisone group, respectively.

1.1.4 Targeted therapies

Cabozantinib

Cabozantinib is another promising bone-targeting agent that inhibits both vascular endothelial growth factor and met proto-oncogene (hepatocyte growth factor receptor; MET). In a prospective, randomized, placebo-controlled, phase 2 clinical trial, 171 mCRPC patients were enrolled to receive cabozantinib (100mg daily) or placebo [33]. Random assignment was halted early based on the observed activity of cabozantinib. Respectively 5% and 75% of patients treated with cabozantinib had a confirmed partial response and stable disease. The median progression-free survival was 29.7 wk, 23.9 wk, and 5.9 wk for patients who were docetaxel naïve, docetaxel pretreated, and on placebo treatment ($p < 0.001$), respectively.

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Interestingly, PSA changes did not correlate with the antitumor effects in bone metastases and soft-tissue lesions. However, patients with complete resolution (n = 14; 12%) or partial resolution (n = 65; 56%) of bone scans experienced significantly better response rates to soft-tissue metastases as compared to men with stable or progressing bone scans (81% vs 61%), and they also experienced longer progression-free survival rates at 6 mo (56% vs 48%, respectively). Cabozantinib has significant antitumor activity and a well-tolerated toxicity profile, so it might be well integrated into the therapeutic armamentarium to treat mCRPC.

Targeted radionuclide Therapy

Over the past several decades, numerous combined diagnostic and therapeutic radioligands (Theranostics) were designed to target receptors on the cancer cell surface. Antibodies (whole or small fragments), small molecules, peptides with affinities to receptors (agonist or antagonist) have demonstrated *in vivo* efficacy for targeting cancers based on up-regulated antigens or receptor populations. This approach, also called radioligand therapy (RLT), presents several advantages over conventional chemotherapy. The expression of the antigens or special receptors can be identified by a diagnostic probe before exposing patients to therapeutic doses of these agents allowing identification of suitable subjects for therapeutic procedures and preventing unnecessary exposure of the patients to radiation without significant benefit. This approach allows the physician to select only those patients with high expression of the target prior to treatment. Since the unused radioactive materials are excreted from the body, RLTs are generally well tolerated with no significant or generally reversible or manageable side effects as has been demonstrated for ¹⁷⁷Lu-DOTATATE treatment in patients with neuroendocrine tumor [34].

Prostate cancer demonstrates high expression levels of prostate-specific membrane antigen (PSMA) on its cell surface. Thus PSMA has become a biomarker for prostate cancer [35] [36] and has attracted significant interest as a target for the imaging [37] [38] and therapy [39, 40]. In particular, development of small urea-based PSMA ligands have received significant interest due to their high affinity for PSMA [41] [42]. The urea-based PSMA ligands were modified to deliver a variety of radio-imaging nuclides for both PET and

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SPECT. Gallium (⁶⁸Ga) labeled urea-based PSMA ligands have been developed as diagnostic agents and studied by several groups [43] [44]. More recently a Lutetium (¹⁷⁷Lu) labeled urea based PSMA ligand (DOTA PSMA or PSMA 617) were evaluated in preclinical and clinical phase. Characteristics of ¹⁷⁷Lu labeled PSMA are described below.

1.2 Characteristics of ¹⁷⁷ Lu-DOTA-PSMA (¹⁷⁷Lu-PSMA-617)

Lutetium (¹⁷⁷Lu) -DOTA PSMA has three components: PSMA is the targeting vector , DOTA(1, 4, 7, 10-tetraazacyclododecane-1, 4, 7, 10-tetraacetic acid) is a radiometal chelator and a linking group, and ¹⁷⁷Lu is the beta emitter that upon internalization delivers radiation to the nucleus of tumor cells to cause DNA damage [43] [44, 45]. The targeting vector utilizes glu-urea-lys sequence which is an inhibitor capable of binding to the domain of PSMA. These components have been previously used in human subjects and in medical research.

1.3 Background of Drug Development

There is substantial previous pre-clinical and clinical experience with ¹⁷⁷Lu-PSMA-617 published in peer reviewed medical literature from multiple medical centers throughout the world. Sponsors are relying on studies published in the peer viewed medical journals for preclinical and preliminary clinical information. Summary of such reports is given below.

1.3.1 Preclinical Studies.

Martina Benesova et al. [46] performed a preclinical evaluation of radiolabeled PSMA-617. PSMA-617 was synthesized by solid phase peptide synthesis. PSMA-617 can be labeled with ¹⁷⁷Lu and Ga-68. Both in vivo and vitro studies were performed using LNCaP cell lines expressing PSMA. PSMA-617 showed highest inhibition potency $K_i = 6.91 \pm 1.32$ for Lu

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complex; 6.40 ± 1.02 nM for Ga complex. PSMA-617 showed higher specific internalization in LNCaP cells.

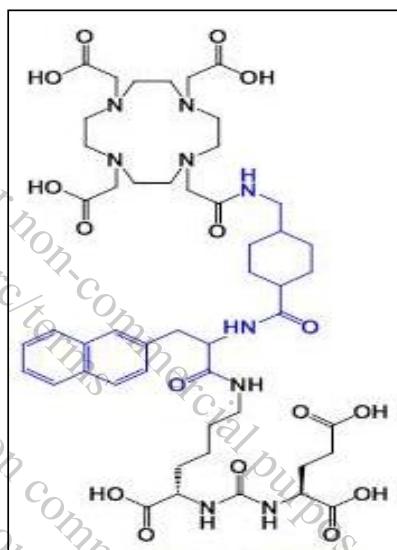


Figure 2: Structure of PSMA 617. Chemical Name 2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-[(2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl]-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid.

The i.v. administered ¹⁷⁷Lu-PSMA-617 effectively cleared the blood by 1 hr. Clearance of radioactivity occurred largely through the renal system. As a result of this, the kidneys exhibited significant uptake $137.2 \pm 77.8\%$ ID/g; this could be effectively blocked ($0.85 \pm 0.22\%$ ID/g) by co-injection of PMPA [2 mg/kg], a high affinity inhibitor of PSMA. At 24 hr ¹⁷⁷Lu-PSMA-617 shows rapid clearance from the kidney $2.13 \pm 1.36\%$ ID/g highlighting its potential use as theranostic agent. At 1 hr time point ¹⁷⁷Lu-PSMA-617 displayed good in vivo tumor targeting with $11.20 \pm 4.17\%$ ID/g. Accumulation in tumor was PSMA specific with reduction to $0.64 \pm 0.07\%$ ID/g by coinjection of 2-PMPA. At 24 h post injection $10.58 \pm 4.50\%$ ID/ uptake was retained in the tumor tissue. For all other non-target tissues, ¹⁷⁷Lu-PSMA-617 demonstrated rapid clearance. The ratio of tumor to blood was 1058; tumor to muscle was 529 at 24 hr post injection. These favorable pharmacokinetics are crucial for

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imaging and therapy. The detailed biodistribution results are summarized in Figure 3. ^{68}Ga -PSMA 617 showed similar uptake in the LnCaP tumors ($11.20 \pm 4.17\text{ %ID/g}$). It also shows similar pharmacokinetic clearance profile compared with ^{177}Lu -PSMA-617.

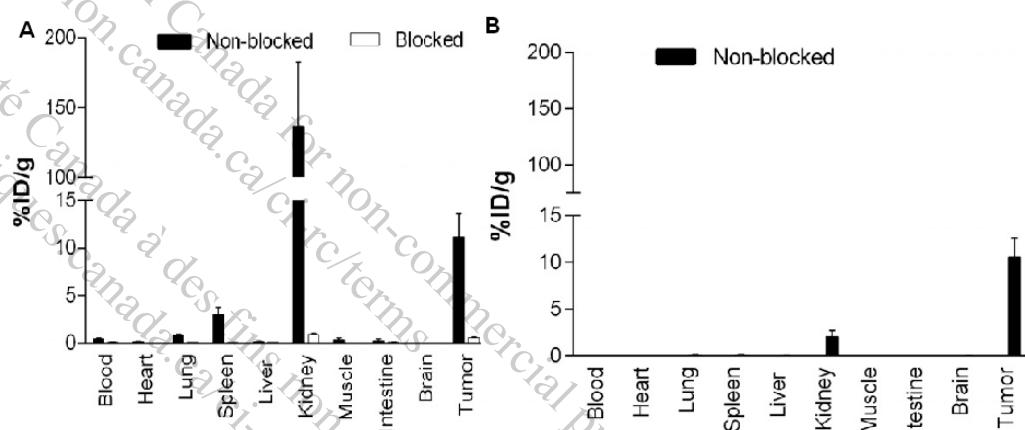


Figure 3: Distribution assay of ^{177}Lu -PSMA-617 in BALB/c mice with LNCap xenografts at 1 h (a) and 24 h (B) post injection.

In summary authors concluded the present radiotracer is suitable for theranostic application in human prostate cancer.

1.3.2 Clinical Studies

Current literature is available to evaluate ^{177}Lu -PSMA-617 therapeutic role in clinical management of patients with prostate cancers. The studies presented in this section were chosen based on novelty of the approach (initial report of application, variables for analyses) and/or the number of patients included.

Clemens Kratochwil et al. [^{177}Lu]Lutetium-labelled PSMA ligand-induced remission in a patient with metastatic prostate cancer. Eur J Nucl Med Mol Imaging 2015; 42:6 :987-988. [47]

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Study Design: First reported application of ^{177}Lu -PSMA-617 for treatment of a patient with mCRPC. Patient had proven PSMA expression and PSA of 38.0 ng/ml prior to treatment and has received 7.4 GBq of ^{177}Lu -DKFZ-617 in 2 cycles 3 months apart.

Toxicity: No potential side effects were reported in this study.

Results: After the radiotherapy ^{177}Lu -PSMA-617, PSA level of patient decreased to 4.6 ng /ml. PET/CT images showed no signs of metastases lesions either shrunk or were undetectable.

Conclusion: Authors are planning to conduct multicenter a clinical trial as soon as possible to examine clinical potential of ^{177}Lu -PSMA-617.

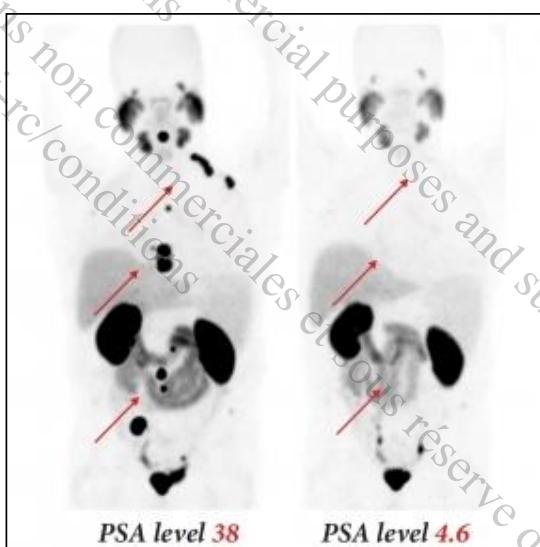


Figure 4: Above Image has recently awarded as image of Year Award and the Berson-Yalow Award at the 2015 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) in Baltimore, USA.

Hojjat Ahmadzadehfar et al. Early side effects and first results of radioligand therapy with ^{177}Lu -DKFZ-617 PSMA of castrate-resistant metastatic prostate cancer: a two-center study. *EJNMMI Research* 2015; 5:36. [48]

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Study Design: A total of 10 consecutive hormone and /or chemo refractory PCa patients with distant metastases and progressive disease with rising PSA levels were recruited in this study.

All patients had prior history or were under therapy with enzalutamide and/or abiraterone.

Four patients had received ²²³Ra-dichloride (1-4 cycles). All 10 patients underwent with ⁶⁸Ga-PSMA HBED-CC (⁶⁸Ga-PSMA) PET /CT prior to therapy to evaluate PSMA expression. Ten patients were treated with range of 4.1-6.1 GBq dose of ¹⁷⁷Lu-DKFZ-617 PSMA. All patients were treated with single dose of ¹⁷⁷Lu-PSMA. The mean and median PSA levels prior to therapy were 339.4 and 298.5 ng/ml. Complete blood chemistry, renal and liver function tests were performed a day before and 2 after the radiotherapy. Patients were followed via telephone every week for safety assessment.

Toxicity: No patient experienced any side effects immediately after injection of ¹⁷⁷Lu-DKFZ-617 PSMA. Relevant hematotoxicity (grade 3 or 4) occurred 7 weeks after the administration in just one patient. The same patient showed a leucopenia grade 2. Two patients showed a disturbance of only 1 hematologic cell line, whereas one patient showed a reduction of grades 1 and 2 in leucocytes and thrombocytes, respectively. Six patients did not show any hematotoxicity during the 8 weeks after therapy. There was no relevant nephrotoxicity (grade 3 or 4).

Results: Eight weeks after the therapy, seven patients (70 %) experienced a PSA decline, of which six experienced more than 30 % and five more than 50 %. Three patients showed a progressive disease according to the PSA increase.

Conclusions: ¹⁷⁷Lu-DKFZ-617 PSMA radiotherapy with single dose for the treatment of metastatic prostate cancer patients without any other therapy option is safe and seems to have a low early side-effect profile with evidence of positive response to the therapy according to PSA decline in 70 % of patients. The authors also stated ¹⁷⁷Lu-DKFZ-617 PSMA has potential to exhibit suitable agent for radionuclide radiotherapy.

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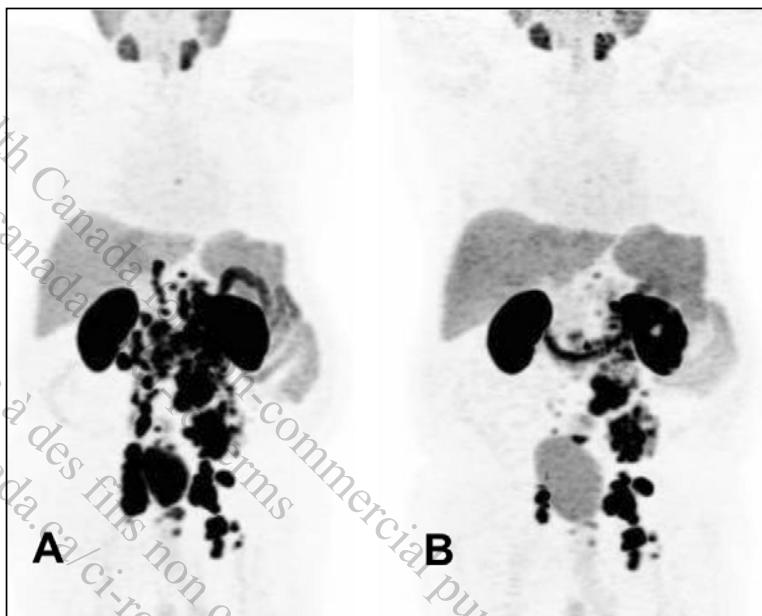


Figure 5: A 74-year-old patient with hormone- and chemo-refractory prostate cancer underwent PSMA PET/CT (a), which showed diffuse abdominal and iliac lymph node metastases. The patient underwent RLT with 5.7 GBq Lu-PSMA. The PSA level was at the time of the therapy 790 ng/ml. (b) A partial response 7 weeks after RLT with 63 % PSA decline; at this time, the PSA level was 293 ng/ml

Clemens Kratochwil, et al. PSMA-targeted radionuclide therapy of metastatic castration-resistant prostate cancer with Lu-177 labeled PSMA-617 J Nucl Med March 16, 2016 [49]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed on 30 patients with PSMA positive tumors were enrolled in this study. 30 patients were treated with 1-3 cycles of ¹⁷⁷Lu-PSMA-617. Pharmacokinetic and radiation dosimetry was also evaluated during the course of the study.

Results: 21 of 30 patients showed response to therapy; for 13/30 the PSA decreased >50%. After 3 cycles 8/11 patients achieved a sustained PSA response (>50%) for over 24 weeks. ¹⁷⁷Lu-PSMA-617 showed fast renal wash out within 48 hours of injection. Patients showed

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mild nausea, fatigue and Xerostomia (<10%) over a period of time. No acute hematotoxicity was observed during the study. Dosimetry results revealed that ¹⁷⁷Lu-PSMA-617 has an exposure of 0.75 Gy/GBq for kidney 0.03 Gy/GBq red-marrow, 1.4 Gy/GBq salivary glands and 6-22 Gy/GBq for tumour lesions.

Conclusion: Based on the results authors concluded that targeted radioligand therapy with ¹⁷⁷Lu-PSMA-617 is safe and promising therapy option for metastasized castrate resistant prostate cancer.

Ahmadvazehfar H, et al. Therapeutic response and side effects of repeated radioligand therapy with ¹⁷⁷Lu-SMA-DKFZ-617 of castrate-resistant metastatic prostate cancer. Oncotarget. 2016 Feb 8. doi: 10.18632/oncotarget.7245. [50]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed in 24 hormone and/or chemo-refractory PC patients. Forty-six cycles of Lu-PSMA were performed. Side effects and response rate was assessed.

Results: Eight weeks after the first cycle of ¹⁷⁷Lu-PSMA-617 therapy 79.1% experienced a decline in PSA-level. Eight weeks after the second cycle of Lu-PSMA therapy 68.2% experienced a decline in PSA relative to the baseline value. Apart from two cases of grade 3 anemia, there was no relevant hemato- or nephrotoxicity (grade 3 or 4).

Conclusion: ¹⁷⁷Lu-PSMA-617 is a safe treatment option for metastatic PC patients and has a low toxicity profile. A positive response to therapy in terms of decline in PSA occurs in about 70% of patients.

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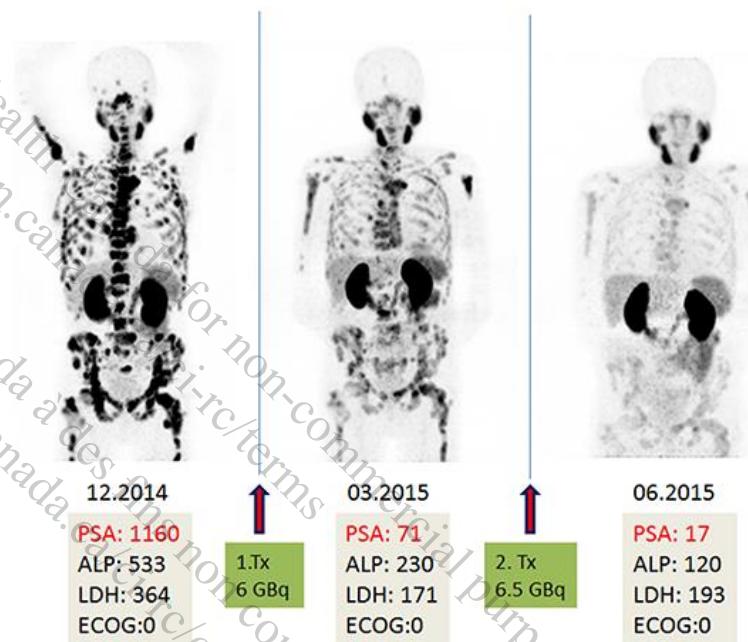


Figure 6: A 75-year-old patient with diffuse bone and lymph node metastases as well as local recurrence (left MIP image). History of chemotherapy and therapy with abiraterone, PSA elevation under enzalutamide. The patient underwent PSMA therapy as the last possible option. Continuing PSA decline and partial response in Ga-PSMA PET images after the first (middle MIP image) and second cycles (right MIP image)

Madhav Prasad Yadav, et al. ¹⁷⁷Lu-DKFZ-PSMA-617 therapy in metastatic castration resistant prostate cancer: safety, efficacy, and quality of life assessment. Eur J Nucl Med Mol Imaging. 2016 Aug 10. [51]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed in 31 patients with progressive disease despite second-line hormonal therapy and/or docetaxel chemotherapy. Patients underwent 1 to 4 cycles after a ⁶⁸Ga-PSMA-HBED-CCP ET/CT for inclusion (mean activity 5069 ± 1845 MBq). Hematological, kidney function, liver function tests, and serum PSA levels were recorded before and after therapy at 2 weeks, 4 weeks, and 3 month intervals. Biochemical response was assessed with trend in serum PSA levels. Metabolic response was assessed by PERCIST 1 criteria. Clinical response was assessed by

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visual analogue score (VASmax) analgesic score (AS), Karanofsky performance status (KPS), and toxicity and response criteria of the Eastern Cooperative Oncology Group (ECOG) criteria.

Results: Biochemical response in terms of complete response (CR), partial response(PR), stable disease (SD), and progressive disease (PD) was observed in 2/31, 20/31, 3/31, and 6/31 had, respectively. Mean VASmax and mean analgesic scores decreased from 7.5 to 3 and 2.5 to 1.8 after therapy, respectively. Mean KPS and mean ECOG performance status score improved from 50.32 to 65.42 after therapies, respectively. Two patients experienced grade I and grade II hemoglobin toxicity each. None of the patients experienced nephrotoxicity or hepatotoxicity.

Conclusion: ¹⁷⁷Lu-DKFZ-PSMA-617 radionuclide therapy is a safe and effective approach in the treatment of mCRPC patients.

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1.3.3 Sponsors Experiences

1.3.3.1 Preclinical Toxicity Studies

The aim of study was to evaluate toxicity of PSMA-617. PSMA-617 applied once weekly by intravenous administration to male rats over 22 days. The animals were treated with 40, 160 or 400 µg of PSMA-617/kg b.w. by tail vein intravenous bolus injection on test days 1, 8, 15 and 22. The control group was treated with physiological saline. No deaths were noted. No signs of local or systemic intolerance reactions were observed. Body weight and body weight gain, food intake, and drinking water consumption were not influenced. No test item-related changes were noted for the hematological and biochemical parameters, the urinary status, the eyes and optic region, the auditory acuity, the relative and absolute organ weights, and the myeloid: erythroid ratio. No test item-related abnormalities were noted during macroscopic inspection at necropsy and at histopathological examination.

Under the test conditions of this study, the no-observed-adverse-effect-level (NOAEL) was 400 µg PSMA-617 / kg b.w. administered once weekly by intravenous bolus injection. This dose was the highest dose tested. Detailed description of this study is attached in appendix 1.

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1.3.3.2 Summary of Human Studies - German Multicenter Experience

Rahbar K, et al. German multicenter study investigating ¹⁷⁷Lu-PSMA-617 radioligand therapy in advanced prostate cancer patients. J Nucl Med. 2016 [52]

Study design: Retrospective acquisition and pooling of data for toxicity and PSA response in patients after ¹⁷⁷Lu-PSMA-617 RLT performed in Germany until July 2015 was initiated by the German Society of Nuclear Medicine for research purpose. The following contains a summary of the collected data. 145 patients with metastatic castration-resistant prostate cancer received a median of two cycles (range 1 to 4) of ¹⁷⁷Lu-PSMA RLT at twelve German Nuclear Medicine Clinics. Data on safety and efficacy were reported. Table 1 lists the administered ¹⁷⁷Lu-PSMA-617 activity for this study cohort.

Table 1. Administered ¹⁷⁷Lu-PSMA-617 activity (n = 248 RLT cycles)

administered activity (GBq)	Cycle 1	Cycle 2	Cycle 3	Cycle 4
≤ 3.5	9	3	0	1
> 3.5 – 4.5	32	14	2	0
> 4.5 – 5.5	16	12	9	0
> 5.5 – 6.5	71	37	14	2
> 6.5	17	8	1	0

Results:

A. Toxicity: Nuclear medicine physicians responsible for ¹⁷⁷Lu-PSMA RLT and subsequent follow-up reported potentially related or unrelated adverse events based on a standard template. In addition toxicity was determined by baseline and follow-up findings for serum creatinine, AST, ALT, white blood cell count, hemoglobin and platelet count for 121 of 145 (83%) patients. The follow-up period for adverse events was 2 to 30 weeks. Reported toxicity sorted by organ system is given in Table 1. Grade 3-4 anemia occurred in 15 (10%) patients

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and grade 3-4 thrombocytopenia occurred in 5 (4%) patients. The rate of grade 3-4 events was low for all other categories (0 to 3 patients; 0 to 2%).

There were fewer hematologic adverse events when compared to patients with metastatic castration resistant prostate cancer treated with placebo or ²²³Ra within the ALSYMPCA trial [7] (grade ≥ 3 anemia: 14% in the placebo and 13% in the ²²³Ra group; grade ≥ 3 thrombocytopenia: 3% in the placebo and 7% in the ²²³Ra group). Toxicity data thus indicate a favorable safety profile for RLT using 2-7 GBq ¹⁷⁷Lu-PSMA per cycle in patients with metastatic castration resistant prostate cancer.

Majority of patients received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle. Toxicity rates were comparably low: 9 of 71 (13%) patients with 5.5 – 6.5 GBq and 3 of 17 (18%) patients with >6.5 GBq during the first RLT developed grade 3-4 toxicity.

*Clinical Trial Protocol: IND #**¹⁷⁷Lu-PSMA-617***Table 2. Adverse events after ¹⁷⁷Lu-PSMA-617
as determined by blood tests (n=121) or physician reports (n=145)**

Organ system	Category	Evaluated for N	All grades	Grade 3-4
Blood and lymphatic disorders				
	Leukopenia	121	48 (40%)	4 (3%)
	Anemia	145	50 (34%)	15 (10%)
	Thrombocytopenia	121	38 (31%)	5 (4%)
Gastrointestinal disorders				
	AST elevation	121	27 (19%)	0 (0%)
	ALT elevation	121	11 (8%)	0 (0%)
	Xerostomia	145	11 (8%)	0 (0%)
	Nausea	145	9 (6%)	0 (0%)
	Dysgeusia	145	6 (4%)	0 (0%)
	Ascites	145	2 (1%)	0 (0%)
	Biliary obstruction	145	0 (0%)	1 (1%)
General disorders				
	Fatigue	145	19 (13%)	1 (1%)
	Pain	145	5 (3%)	0 (0%)
	Ileus	145	1 (1%)	0 (0%)
Urinary disorders				
	Renal failure	121	14 (12%)	0 (0%)
	Urinary tract infection	145	1 (1%)	0 (0%)
Cardiovascular disorders				
	Edema	145	2 (1%)	0 (0%)
	Lung embolism	145	0 (0%)	3 (2%)

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Respiratory, thoracic and mediastinal disorders

Pleural effusion	145	1 (1%)	0 (0%)
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Dyspnea	145	1 (1%)	0 (0%)
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Neurologic disorders

Vertigo	145	1 (1%)	0 (0%)
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Stroke	145	0 (0%)	2 (1%)
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Musculoskeletal disorders

Bone fracture	145	0 (0%)	3 (2%)
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Efficacy

Serial PSA levels at baseline and follow-up were recorded for 99 of 145 patients (68%).

Response was expressed as percent change in serum PSA from baseline to the lowest PSA level measured at follow-up (best PSA response).

Over the entire follow-up period 45 of 99 (45%) patients demonstrated a PSA decline $\geq 50\%$ and were considered biochemical responders. Any PSA decline occurred in 59 of 99 (60%) patients (Figure 7). After the first cycle a PSA decline $\geq 50\%$ occurred in 40 of 99 (40%), any PSA decline in 65 of 99 (66%) patients (Figure 8A). After the second therapy cycle of $^{177}\text{Lu-PSMA-617}$ RLT a PSA decline $\geq 50\%$ occurred in 35 of 61 (57%) and any PSA decline in 44 of 61 (72%) patients (Figure 8B). Patients receiving a third or fourth cycle of therapy showed a PSA decline $\geq 50\%$ in 13 of 20 (65%) and 3 of 3 (100%) patients, respectively.

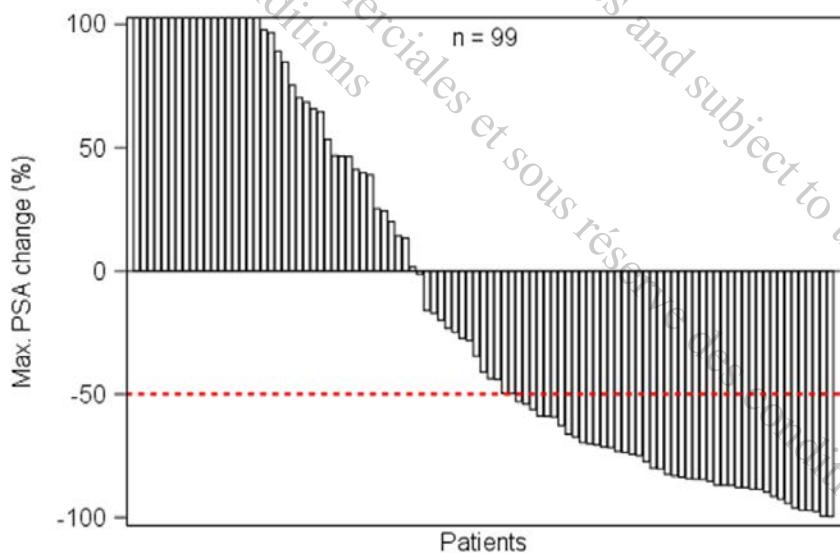


Figure 7. Waterfall plot of maximum PSA change (%) from baseline over total follow-up period. PSA increase of more than 100% was cropped due to simplification.

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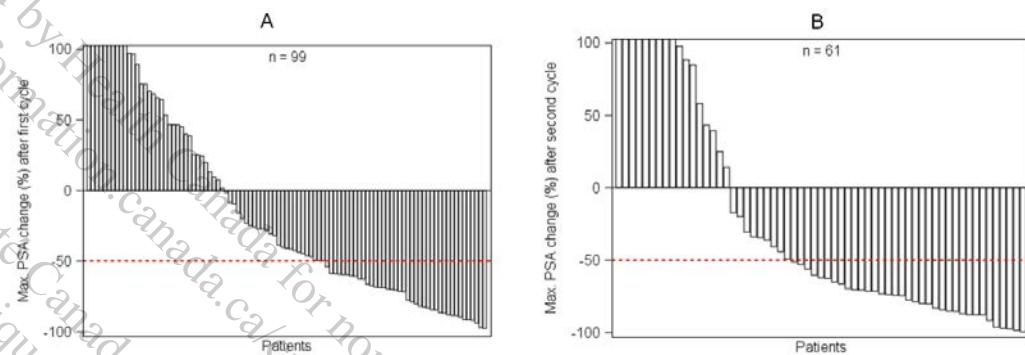


Figure 8. Waterfall plots of maximum PSA change (%) after the first cycle (A) and after the second cycle (B). PSA increase of more than 100% was cropped due to simplification.

Response rate was higher than the rate in patients with metastatic castration resistant prostate cancer treated with abiraterone (best PSA response >50% after abiraterone plus prednisone: 43% (25 of 58) patients) [53]. Data thus indicate good efficacy for ^{177}Lu -PSMA RLT in patients with metastatic castration resistant prostate cancer. Response rates were not significantly associated with mean activity per cycle ($p=0.46$) or cumulative activity after two cycles ($p=0.22$).

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2. Study Objectives

Primary Objectives:

1. To assess the clinical safety of ¹⁷⁷Lu-PSMA-617 by evaluation of adverse events (AE) using the Common Terminology Criteria for Adverse Events (CTCAE)
2. To assess the efficacy as defined by proportion of patients with PSA-response of ≥50% decline at 12-weeks from baseline

Secondary Objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]
2. To determine the time to PSA progression, separate for treatment doses: time from inclusion to date until PSA progression or death (whichever occurs first) [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later
 - b. for patients without PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above baseline
3. To determine radiographic Progression-free Survival (rPFS), for each treatment dose: time from inclusion to date when first site of disease is found to progress or death (whichever occurs first)
 - a. Nodal and visceral disease is evaluated on cross-sectional imaging using RECIST 1.1/PCWG3 criteria
 - b. Bone metastases are evaluated using bone scintigraphy and new lesions have to be confirmed on a second scan (2+2 rule) using PCWG3 criteria
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST 1.1/PCWG3 criteria stable disease (SD), partial response (PR) or complete response (CR).
5. Change in Pain and Quality of Life: Pain and “Epic-26” Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 mo. Pain response will be determined in accordance with PCWG3 [1].
6. Change in ECOG Performance Score

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3. Investigational Plan

3.1 Overall Study Design and Dosing of Targeted PSMA Radioligand Therapy (RLT)

This is an open-label, multicenter, prospective trial. Upon inclusion patients will be randomized into two treatment doses. RLT will be performed by repeated i.v. application of 6.0 GBq ($\pm 10\%$) or 7.4 GBq ($\pm 10\%$) ¹⁷⁷Lu-PSMA-617 every 8±1 weeks until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy. All doses after labeling will be presented in buffered solution for intravenous injection.

In total, 200 subjects with histologically proven prostate cancer and mCRPC will be enrolled. Salivary protection will be accomplished by applying ice pack starting 30 minutes prior to infusion of radiopharmaceutical and will continue for 4 hours. Subjects will be recruited at up to 3 Nuclear Medicine sites selected for this project. Each subject will undergo a screening visit within 14 days prior to receiving study drug.

Dosimetry will be performed according to chapter 8.4.3 by Prof. Dr. [Name], Universitätsklinikum Würzburg Germany - Klinik und Poliklinik für Nuklearmedizin after the first injection to determine dose to the kidneys. Treatment will be continued until either of the following conditions apply:

- PSA/radiographic progression as defined above
- Completion of four RLT cycles
- 23 Gy kidney dose would be exceeded by the next cycle as estimated by dosimetry
- patient withdrawal (e.g. appearance of intolerable adverse events)

Primary objectives of the study is safety and efficacy.

Efficacy is determined by PSA response rate: Patients with baseline to follow-up decline in tumor marker level (PSA) $\geq 50\%$ at 12 weeks will be considered responders.

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For safety assessment, vital signs will be measured within 20 minutes before and for up to an hour after administration of ¹⁷⁷Lu-PSMA-617. A blood sample will be collected within 48 hours before the injection, for assessing clinical chemistries and hematology. Hematologic laboratory testing (CBC) will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until patient is progressed. CBC will be performed every 7 days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery which is defined as grade 2 toxicity or lower. Chemistry will be evaluated 4 weeks after each therapy and within one week prior to the next treatment to evaluate eligibility to receive the next cycle and then every 3 month for 24 months or until the patient is progressed. CTCAE v 4.0 will be used to evaluate renal toxicity. For more information, please refer to the Schedule of Events ([Appendix 2](#)).

3.2 Rationale for Study Design

3.2.1 Rationale for a regimen with multiple therapy cycles

Activity given during targeted radionuclide therapy is limited by radiation dose to healthy organs. Based on dosimetry radiation dose to healthy organs and subsequent maximal cumulative activity can be calculated. To obtain optimal safety margin maximal cumulative activity is not given in one treatment session but approached by application of a defined fraction of this activity in several cycles. The administration of a standard activity over several treatment cycles allows for early and individual estimation of radiation dose and tolerability. The efficacy and safety of a sequential approach was proven in patients with ²²³Ra therapy for metastatic castration-resistant prostate cancer (mCRPC) [7] and in patients with ¹⁷⁷Lu-DOTATATE therapy for midgut neuroendocrine tumor (NET) [54] each in prospective, double-blind, randomized, international, and multicenter phase III trials. Based on this evidence targeted PSMA Radioligand Therapy (RLT) will be performed by sequential applications of ¹⁷⁷Lu-PSMA-617 with treatment-free intervals.

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3.2.2 Rationale for eight weeks interval

Highest level of evidence for subacute adverse events after radionuclide therapy was published for patients with non-Hodgkin's lymphoma. Witzig et al analyzed safety and efficacy of ⁹⁰Y-Ibritumomab Tiuxetan in 73 patients in a prospective Phase III randomized trial. This study reports neutrophil, platelet and hemoglobin nadir approximately six weeks after application of the beta emitter [55]. Based on this study ¹⁷⁷Lu-PSMA-617 RLT will be performed by sequential applications with a treatment-free interval of eight weeks to minimize risk of repeated ¹⁷⁷Lu-PSMA-617 therapy before reaching blood level nadir. This scheme is also supported by safety data from the phase III NETTER-1 trial on safety and efficacy of ¹⁷⁷Lu-DOTATATE in patients with midgut NET. Here ¹⁷⁷Lu-DOTATATE was administered at seven to nine week intervals and rate of severe adverse events was below 10% for 115 patients in the treatment arm [54].

3.2.3 Rationale for dose regimen

Ahmazadehfar et al reports safety and efficacy after application of a mean activity of 6.0 GBq ¹⁷⁷Lu-PSMA-617 in 24 patients with mCRPC [50]. Patients were treated with up to two cycles of ¹⁷⁷Lu-PSMA-617 RLT at eight week intervals. Grade 3 hematotoxicity occurred in two patients. No nephrotoxicity or hepatotoxicity grade ≥ 3 was documented. Kratochwil et al reports safety and efficacy after repeated application of ¹⁷⁷Lu-PSMA-617 in 30 mCRPC patients [49]. 19 of 30 patients (63%) received 6.0 GBq ¹⁷⁷Lu-PSMA-617 every two mo. One patient developed grade 3 anemia, one patient grade 3 thrombocytopenia. Both patients had diffuse pattern of bone marrow infiltration at baseline. The German Society of Nuclear Medicine (DGN) performed a questionnaire based survey on the use of ¹⁷⁷Lu-PSMA-617 RLT in December 2015. Nuclear Medicine Clinics in Germany reported compassionate use of ¹⁷⁷Lu-PSMA-617 RLT in 145 mCRPC patients until June 30th 2015 [52]. Majority of

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patients received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle (Table 1) and rate of serious adverse events was below 20% for both subgroups. Phase III data for ¹⁷⁷Lu-DOTATATE, a similar RLT for midgut NET patients, demonstrates a rate of severe adverse events below 10% after application of four cycles of 7.4 GBq in 115 patients [54]. Thus, present evidence indicates that repeated applications of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 RLT are well tolerated with low to very low rates of serious adverse events.

Standard activities of 6.0 and 7.4 GBq are also supported by dosimetry data available in more than ten patients [56] [57]. Maximal cumulative activity is limited by the absorbed dose in critical organs. Dosimetry identifies kidney and salivary glands as organs with highest absorbed dose [56] [57]. Thus maximum cumulative activity is determined by absorbed kidney dose. Based on earlier evidence obtained from external beam radiotherapy the maximum tolerable per kidney dose is generally accepted 23 Gy [58]. Dosimetry after ¹⁷⁷Lu-PSMA-617 application revealed absorbed doses of 0.6 Gy/GBq per kidney [56] [57]. Therefore maximum cumulative activity for ¹⁷⁷Lu-PSMA-617 RLT is considered 38.3 GBq (38.3 GBq x 0.6 Gy/GBq = 23.0 Gy radiation dose per kidney). Both the application of four cycles of 6.0 GBq (total 24.0 GBq) or 7.4 GBq (total 29.6 GBq) ¹⁷⁷Lu-PSMA-617 results in lower cumulative activities with acceptable safety margin. Whether either activity regimen is associated with longer rPFS is unknown and will be evaluated as secondary endpoint of this trial.

Salivary glands receive highest off-target radiation dose according to dosimetry [56] [57]. Absorbed dose after four cycles of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 (34.0 Gy or 41.6 Gy respectively) falls within the range of maximum tolerable dose reported for salivary glands in the literature [58] [59] [60]. Maximum tolerable dose to the bone marrow is generally accepted 2 Gy [61]. Bone marrow dose will not exceed this limit after four cycles of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 [57].

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3.2.4 Determination of Sample Size

Sample size calculation was based on the primary endpoint of this protocol, i.e. baseline to 12-week decline in tumor marker level (PSA) $\geq 50\%$ [53]. Based on a recent publication [52], we estimate that the proportion of patients who meet the primary end point will range between 38% and 65% for both treatment doses. We thus define the following null hypothesis: Less than 40% of patients will reach the endpoint after ^{177}Lu -PSMA RLT. ^{177}Lu -PSMA RLT would therefore be considered worthy of further study if 50% or more patients met the end point and not worthy of further study if 40% and less achieved the end point. This rationale was adapted from a single-arm study on mCRPC patients with same end point definition, published 2010 in the Journal of Clinical Oncology [53]. We have performed power analysis for the two sided binomial test (beta 0.2, alpha 0.05) to measure the efficacy of ^{177}Lu -PSMA RLT. A sample size of 200 achieves 78% power (beta 0.2) at a given alpha of 0.05 to distinguish between 40% versus 50% response rates. The power analysis was performed by a trained Biostatistician from the Department of Biostatistics, University of California at Los Angeles using Power Analysis and Sample Size (PASS) 14 software (NCSS LLC).

3.3 Study Duration and Dates

The duration of subject participation will be from the time of signing informed consent through the 24 months post-injection visit or progression. Subjects will be deemed enrolled in the study once the subject signs informed consent.

3.4 Randomization protocol

Randomization will be performed in accordance with Vickers et al. [62]. In order to obtain adequate “allocation concealment” a list of random allocations was created for patients 1

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through 200. This list will be stored at investigator's sites and will not be modified. The list will only be accessible for researchers or study personnel not actively involved in the recruitment process.

3.5 Dose modification

In some circumstances, it might be necessary to suspend treatment with ¹⁷⁷Lu-PSMA-617, adapt the posology (i.e. administer a half activity), or even definitively stop administration, as described in the following tables.

Table 3: Criteria for permanent discontinuation of treatment with ¹⁷⁷Lu-PSMA-617

Definitively stop further administrations in patients who have experienced or are at risk of any of the following conditions during treatment:

a) Severe heart failure (defined as grade III or IV of the NYHA classification)
b) Hypersensitivity to the active substance or to any of the components of this radiopharmaceutical
c) Grade 3 hematologic toxicities that persist > 12 weeks and Grade 4 that persist > 3 weeks.
d) Grade 3 renal toxicity as determined by serum creatinine measurements
e) AST/ALT > 3x ULN and bilirubin > 2x ULN
f) Grade 3-4 non-hematologic toxicities with select exceptions for <ul style="list-style-type: none">- Grade 3 fatigue < 10 days- Grade 3 nausea, vomiting, and diarrhoea and grade 4 vomiting and diarrhoea that persist for < 72 hours in the absence of maximum medical therapy- Asymptomatic grade 3 non-hematological laboratory abnormalities that resolve in 72 hours- Grade 3 infections which do not improve under i.v. medication within 10 days

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In case some specific adverse reactions to ¹⁷⁷Lu-PSMA-617 persist or reoccur, see Table 5

Table 4: When to suspend treatment with ¹⁷⁷Lu-PSMA-617?

Suspend treatment with ¹⁷⁷Lu-PSMA-617 in patients who have experienced or are at risk of any of the following conditions during treatment:	
Criterion	Action
Occurrence of an intercurrent disease (e.g. urinary tract obstruction, ...) which according to the physician opinion could increase the risks linked to ¹⁷⁷ Lu-PSMA-617 administration.	Suspend administration until resolution or stabilization. Treatment can be resumed after resolution or stabilization. Resolution is defined as grade II toxicity or lower. (by CTCAE) at the time of the next treatment. Treatment can be suspended up to 12 weeks after the last infusion. After that treatment with ¹⁷⁷ Lu-PSMA-617 must be definitively stopped.
In case of some specific adverse reactions to ¹⁷⁷ Lu-PSMA-617, see Table 5	see Table 5

Table 5: When to adapt ¹⁷⁷Lu-PSMA-617 posology?

Adapt ¹⁷⁷Lu-PSMA-617 posology according to the following actions in patients who have presented any of the following severe adverse reactions:	
Severe adverse reactions / Dose-modifying toxicity (DMT) criteria	Action
Anemia, thrombocytopenia or neutropenia of grade 3 or superior (CTCAE 4.0)	1. Suspend treatment with ¹⁷⁷ Lu-PSMA-617
Renal toxicity as defined by grade 3 toxicity by serum creatinine (CTCAE 4.0)	2. Monitor biological parameters every 2 weeks, and eventually treat appropriately if needed; in case of renal function impairment, good hydration is recommended if not otherwise contraindicated.
Liver toxicity as defined as AST and ALT >3xULN	a. If the observed toxicity continues beyond 12 weeks after the last infusion, treatment
Any serious or intolerable adverse event not listed in Table 2 that in the opinion of the investigator, requires the subject's	

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discontinuation.	with ¹⁷⁷ Lu-PSMA-617 must be definitively stopped. b. If the observed toxicity resolves within 12 weeks after the last infusion, it is possible to continue treatment with ¹⁷⁷ Lu-PSMA-617 by infusing a half activity. 3. Even if the half activity is well tolerated (i.e. no DMT re-occurrence), the next remaining treatment administration should be continued with the reduced (half) activity but, if DMT recurs after treatment with a half dose, treatment with ¹⁷⁷ Lu-PSMA-617 must be permanently stopped.
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4. Study Population Selection

4.1 Study Population

It is anticipated that a total of 200 subjects will be recruited. Such a number is considered appropriate to achieve statistical power for the endpoints of this clinical trial. The patients will be recruited at up to 3 clinical sites. The dose being administered will be prepared at RadioMedix Inc. in Houston and shipped to the trial sites.

4.2 Inclusion Criteria

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ⁶⁸Ga-PSMA-11 PET/CT or diagnostic ¹⁷⁷Lu-PSMA-617 scintigraphy
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2500/\mu\text{l}$, PLT count $\geq 100.000/\mu\text{l}$, Hb ≥ 9.9 g/dl and ANC $\geq 1500 \text{ mm}^3$ for the first cycle and WBC $\geq 2.000/\mu\text{l}$, PLT count $\geq 75.000/\mu\text{l}$, Hb ≥ 8.9 g/dl and ANC $\geq 1000 \text{ mm}^3$ for the subsequent cycles
8. Signing of the Informed Consent Form
9. Patients enrolling in this trial should have received either enzalutamide or abiraterone

4.3 Exclusion Criteria

1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ²²³Ra, ¹⁵³Sm)
2. Glomerular Filtration Rate (GFR) $< 40 \text{ ml/min}$
3. serum creatinine $> 1.5 \times \text{ULN}$ AST and ALT $> 5 \times \text{ULN}$
4. Urinary tract obstruction or marked hydronephrosis
5. Patients who had received both docetaxel and cabazitaxel will be excluded from this study. Enrolment will be limited to patients who had received prior docetaxel only.
6. Diffuse bone marrow involvement confirmed by super-scans

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5. Study Treatment(s)

5.1 Description of Treatments(s)

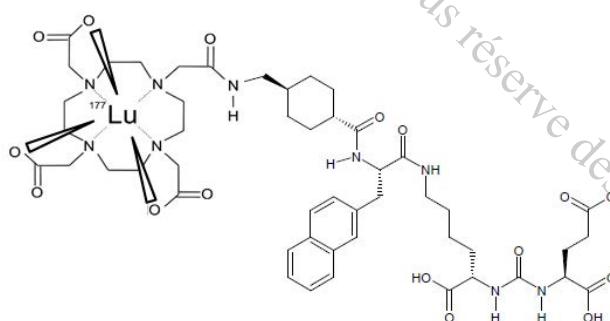
5.1.1 Study drug

The agent to be evaluated in the present study is ¹⁷⁷Lu-PSMA-617. Its chemical name is lutetium-177-N_α-2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid.

¹⁷⁷Lu-PSMA-617 is radiolabelled with carrier-free lutetium-177 (¹⁷⁷Lu), a synthetic, low-energy beta and gamma emitting isotope of lutetium, the last element in the lanthanide series of metallic elements. Carrier-free ¹⁷⁷Lu is generated by neutron irradiation of the isotope ytterbium-176 (¹⁷⁶Yb) and subsequent fractionation of ¹⁷⁷Lu and ¹⁷⁶Yb with caution chromatography. Key physical characteristics of ¹⁷⁷Lu are summarised below:

Physical half-life T _{1/2}	Decay product	Main β ⁻ emission	Maximum range (β ⁻)	Main γ emission
6.6 d	¹⁷⁷ Hf	498 keV	1.7 mm	208 keV 113 keV

The structural formula of ¹⁷⁷Lu-PSMA-617 is shown below



The chemical formula of ¹⁷⁷Lu-PSMA-617 is Lu₁C₄₉H₆₈N₉O₁₆. The molar weight is 1214.1 g/mol.

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5.1.2 Pharmaceutical Properties of ¹⁷⁷Lu-PSMA-617

¹⁷⁷Lu-PSMA-617 is administered intravenously.

A description of ¹⁷⁷Lu-PSMA-617 solution for infusion is shown in below table

Composition of ¹⁷⁷Lu-PSMA-617 solution

Pharmaceutically active component	¹⁷⁷ Lu-PSMA-617
Physical dose	≤ 7.4 GBq / cycle
Substance dose	130 - 170 µg PSMA-617
Primary unit dose container	20 mL glass vial containing 5 - 15 mL of stabilised aqueous solution
Appearance	Clear, colourless or slightly yellowish solution, without visible particles
pH	4.0 - 7.5
Bacterial Endotoxin	≤ 100 EU/Dose
Radionuclidic purity	≥ 99.99 %
Sterility	Sterile

The components include ¹⁷⁷Lu-PSMA-617, sodium acetate, sodium ascorbate, gentisic acid, and water for injection. The labelled drug product is produced, tested and released under GMP conditions by RadioMedix, Inc. as a sterile solution for injection infusion, ready for use. The labelled drug product will be manufactured upon individual order and delivered directly to the study sites.

Patients will be randomized into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq (±10%, arm 1) or 7.4 GBq (±10%, arm 2) ¹⁷⁷Lu-PSMA-617 every 8±1 weeks; RLT will be performed until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy as determined by dosimetry, after the first treatment.

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5.2. Treatment(s) administered

Cold ice pack in the region of salivary glands will start 30 minutes prior to administration of the investigational drug and will continue for 4 hours. Intravenous access will be inserted in either arm. Assurance will be made to have reliable IV line with no evidence of extravasation or infiltration. Investigational drug will be infused over approximately 30 minutes using infusion pump. Patients will be monitored for any evidence of pain, or burning sensation during the infusion.

Imaging and blood and urine samples for dosimetry after the first treatment will be accomplished as per dosimetry protocol by Prof. Dr. [Name], Universitätsklinikum Würzburg - Klinik und Poliklinik für Nuklearmedizin. For subsequent therapies only 24 hour whole body images will be performed to assure satisfactory distribution of the investigational radiopharmaceutical.

5.3 Restrictions

5.3.1 Fluid and Food Intake

Subjects should follow their normal diet before and after the administration of the study drug. Subjects should be encouraged to increase fluid intake at baseline and after each image acquisition to maintain proper hydration throughout the study period and decrease radiation exposure to the urinary bladder. There are no dietary or food restrictions for this study.

5.3.2 Subject Activity Restriction

There are no activity restrictions.

5.4 Dosing Compliance

All study drug administration will be administered under the supervision of the investigator. Details of study drug injection will be captured in each subject's source documents.

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5.5 Packaging and Labeling

¹⁷⁷Lu-PSMA-617 will be supplied in vials for injection in appropriate packaging.

The outer packaging of ¹⁷⁷Lu-PSMA-617 will contain label(s) which will include the following minimum information:

- Name and address of Manufacturer Study number
- Investigator identification
- Name of study drug and formulation
- Dosage strength
- Batch number
- Patient number
- Expiry date (or retest date)
- Storage instructions
- “For Clinical Trial Use only”

A system of medication numbering in accordance with all requirements of Good Manufacturing Practice (GMP) and any other applicable regulatory requirement will be used for all study drugs. This will ensure that for each patient, any dose of study drug can be identified and traced back to the original bulk ware of the active ingredients. Lists linking all numbering levels will be maintained by the institutions in charge of study drug packaging.

5.6 Storage and Accountability

5.6.1 Storage

The drug product contains radioactive material and should only be handled by personnel trained in the use of radioactive isotopes with proper shielding and monitoring. Receipt and use is limited to a facility licensed by applicable government regulations and/or local/state laws. Unused or residual waste should be disposed of as radioactive waste following the institution's standard operating procedures (SOPs) and/or applicable regulations or guidance.

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5.6.2 Accountability

In accordance with International Conference on Harmonization (ICH) and US Food and Drug Administration (FDA) requirements, the investigator and/or drug dispenser must at all times be able to account for all study drugs furnished to the institution. The appropriate site personnel must sign, date and immediately forward to the sponsor or sponsor's designee the packing slip for clinical shipment included with each shipment.

No study drug is to be used outside of this study. The investigator or designee will record the use of the study drug on the appropriate Drug Accountability record. All study radiopharmaceuticals must be accounted for, whether used or unused, during the course of and at the conclusion of the study. The shipment of drugs from the sponsor or designee to the investigator or other designated persons cooperating with the investigator will be accompanied by a receipt form that indicates the lot number(s) and the amount of drug provided for the study. This form will be signed, dated and returned to the sponsor or designee.

The investigator is responsible for ensuring that study drug is recorded, handled and stored safely and properly in accordance with ICH and applicable government regulations, local/state laws, and used in accordance with this protocol.

5.7 Investigational Product Retention at Study Site

Unused product will be disposed of according to institutional regulations. Record the use and/or disposal of the study drug on the Drug Accountability record. This Drug Accountability record should account for the receipt and disposition of all clinical supplies shipped to the investigator and must be available for review by the study monitor.

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6. Study Procedures

6.1 Informed Consent

All subjects must sign and personally date an IRB/IEC approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug prior to the initiation of any study-related procedures. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for Good Clinical Practice (GCP) and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27.

The subject must be made aware and agree that personal information may be reviewed during an audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. A copy of the Informed Consent Form is attached as Exhibit.

6.2 Medical History

A relevant medical history and subject demographics will be obtained at the screening visit. Cancer medical history includes review of disease history, cancer staging, biopsy results, any past/present cancer therapies (e.g., hormone, drug, biologic, radiologic, or surgical treatment). Demographic information to be collected includes date of birth, race, ethnicity, height, and weight.

6.3 Vital Signs

Vital signs will include measurement of blood pressure, temperature, respiratory rate, pulse oximetry and heart rate.

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6.4 Dispensing Study Drug

The estimated radioactive dose will be determined by measuring the amount of radioactivity in the syringe pre- and post-injection, using an appropriately calibrated radioisotope dose calibrator in accordance with the nuclear medicine department's SOPs.

Any complication related to administration of the drug (e.g., overdose, observable extravasation, medication error) is a protocol-related event and will be reported to the pharmacovigilance designee. Refer to Section 7 for contact information.

6.5 Clinical Laboratory Tests

Clinical laboratory tests will include hematology and clinical chemistry. Clinical laboratory analytes to be assessed in the study are shown in Table 6. Timing of collection of clinical laboratory tests are presented in Section 8.

Table 6: Laboratory Analytes Assessed

Hematology	Clinical Chemistry
Hematocrit	eGFR
Hemoglobin	Bilirubin
RBC count	Creatinine
WBC count	Glucose
WBC differential	Urea nitrogen
Platelets	BUN/Creatinine
ANC	AST/SGOT
MCV/MCH/MCHC	ALT/SGPT
Eosinophils	Alkaline Phosphatase
Basophils	PSA*
Lymphocytes	
RDW	

*PSA will be done only at the time intervals called by the protocol.

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6.6 Sample Collection, Storage and Shipping

Blood samples will be collected using accepted phlebotomy techniques by trained site personnel. All samples for clinical laboratory testing will be processed and analyzed at an accredited laboratory

6.7 Electrocardiogram

Continuous ECG recording at least 15 minutes prior to administration of the study drug and at least 1 hour after administration will be performed. Also a 12 lead ECG will be performed in two time points: before injection of Lu-177 PSMA and after completion of the 4 hr scan.

6.8 Adverse Events

Immediate adverse drug reactions will be collected from the time of ¹⁷⁷Lu-PSMA-617 injection until 24 hours post-injection visit. Data will be collected for any adverse events (AEs) as defined in Section 7.

All study monitoring will be performed at the primary clinical study sites in accordance with Good Clinical Practice (GCP). All records related to this study will be retained at each clinical site. Serious adverse reactions will be collected and reported to FDA and IRB according to 21 CFR 312.32. **Sponsors at each individual site will be responsible for obligations of a sponsor enumerated in 21 CFR 312.50-59. FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the investigational drug.** Annual reports on the progress of the investigation and any adverse events related to the investigational drug will be prepared and reported to FDA according to 21 CFR 312.33.

6.9 Removal of Subjects from the Trial or Study Drug

The investigator may withdraw a subject from the trial for any of the following reasons:

1. Protocol violation

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2. Serious or intolerable adverse event (that in the opinion of the investigator, requires the subject's discontinuation),
3. Investigator withdraws the subject (at the investigator's discretion for reasons other than an adverse event),
4. Sponsor terminates the study,
5. Subject requests to be discontinued from the study, or
6. Subject is lost to follow-up

During course of the study patients have the right to withdraw their consents any time without need for explaining the reason of consent withdrawal to the investigator or sponsor. Principal investigator will closely monitor patients during the course of the study and will consider terminating investigational product administration or any other trial related procedures in order to maintain the safety of subjects. In cases of withdrawal either in patient's favor or principal investigator decision due to the safety issues or technical issues, withdrawn subjects will be replaced in order to maintain data integrity but follow up visits will be continued to maintain safety of patients based on the visits predicted in the protocol.

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7. Reporting Safety Information

Any untoward medical event that occurs from the time that the subject is administered ¹⁷⁷Lu-PSMA-617 until the subject completes the study will be reported. Serious adverse events and non-serious adverse events will be collected and reported as required under 21 CFR 312.32 until the final study visit. Toxicity will be evaluated according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

7.1 Adverse Events

7.1.1 Definitions

An **adverse event (AE)** is any untoward medical occurrence in a study subject that is administered a pharmaceutical product, at any dose, which does not necessarily have a causal relationship with the treatment.

An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a study drug, whether or not considered related to the study drug.

A **serious adverse event (SAE)** is any untoward medical occurrence that falls into one or more of the following categories:

1. Results in death
2. Is life-threatening: An event which, in the view of the investigator, places the subject at immediate risk of death from the event as it occurred and does not include an event which hypothetically might have caused death if it were more severe.
3. Requires subject hospitalization or prolongation of existing hospitalization: For the seriousness criterion of subject hospitalization to apply, an overnight stay in the hospital is required. Admission to an emergency room and release without an overnight stay would not satisfy the subject hospitalization seriousness criterion.
4. Results in persistent or significant disability/incapacity: Persistent or significant disability/incapacity is defined as a substantial disruption of a person's ability to conduct normal life functions, either reported or defined as per clinical judgment.

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5. A congenital anomaly/birth defect: A congenital anomaly/birth defect is defined as a condition believed to have been the result of exposure to study drug just before conception or during pregnancy.
6. Any other important medical event: An important medical event may not result in death, be life-threatening, or require hospitalization, but based upon appropriate medical judgment, the event may significantly jeopardize the subject's health or may require medical or surgical intervention to prevent one of the outcomes listed in the serious definitions above. An important medical event may include development of drug dependency or drug abuse.

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

7.1.2 Reporting Serious Adverse Events

Seriousness is based on subject, event outcome, or action criteria that are usually associated with events that pose a threat to a subject's life or functioning. Seriousness (not severity) serves as the guide for defining the sponsor's regulatory reporting obligations to the applicable regulatory authorities. Adverse event severity and seriousness should be assessed independently by investigators. If the investigator is unsure if the event is serious it should be classified as serious.

Sponsors of the study, and the investigators are responsible for reporting relevant SAEs as safety reports to the FDA and other applicable regulatory authorities, and participating investigators, in accordance with ICH guidelines, the US Code of Federal Regulations Title 21 CFR 312.32 for Good Clinical Practice, and/or local regulatory requirements. The investigators must report all SAEs to project pharmacovigilance designee within 24 hours, by telephone, email or fax, and confirm that the information was received. A Serious Adverse Event Report (SAER) must be completed by the investigator or designee and faxed or emailed to project pharmacovigilance designee within 24 hours after the investigator first

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becomes aware of the serious event. A separate SAER will be needed for each reported SAE so that the onset, resolution date, causality and outcome can be assessed for each event. Any source documents relevant to the event should be forwarded to sponsor's pharmacovigilance designee with the SAER form. The SAER form must be signed and dated by the investigator. The Original copy of the SAER form should remain at the investigational site. All SAEs are also to be entered into the CRF.

In case of death, a comprehensive narrative report of the case should be prepared by the investigator and sent to project pharmacovigilance designee with the SAER. If an autopsy is performed, a copy of the autopsy report should be actively sought by the investigator and sent to the sponsor or designee as soon as available. A copy of the autopsy report should remain at the investigational site with the subject's source documents.

A new follow-up SAER form will be completed by the investigator if important follow-up information (i.e., diagnosis, outcome, causality assessment, results of specific investigations) are made available after submission of the initial form. The follow-up SAER must be signed and dated by the investigator. The follow-up form and any additional source documentation regarding the event will be sent to project pharmacovigilance designee.

If a serious medical occurrence or death is reported to the investigator outside the follow up window which is believed to be related to the administration of the study drug, it is the investigator's responsibility to report this occurrence to project pharmacovigilance designee. Such occurrences will be reported using a SAER form or other form of communication deemed appropriate by the investigator and pharmacovigilance designee.

Sites must contact project pharmacovigilance designee to report all SAEs within 24 hours, by telephone, e-mail, or fax. Contact information for SAE reporting is presented in Table 7.

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Table 7: Pharmacovigilance Designee

[Name].MD
[Contact]
Excel Diagnostics and Nuclear Oncology Center
9701 Richmond Avenue, Suite 122
Houston, TX 77042
PHONE: 713.781.6200 [Contact]
FAX: 713.781.6206
Email: [Contact]

Sites must also report all overdoses, extravasations and medication errors to the project pharmacovigilance designee.

7.2 Adverse Event Data Collection

The investigator will elicit information through non-leading questioning and examination of the subject about the occurrence of adverse events from the time that the subject is administered ¹⁷⁷ Lu-PSMA-617 until study completion. AEs can be reported any time after study enrollment until the end of the subject's study participation. For each event, the following information will be recorded in the subject's source documents and entered into the Adverse Event CRF according to the instructions below:

Classification of the Event as serious or non-serious: Classify the event as serious or non-serious (see definitions in Section 7).

Description of Signs or Symptoms: Whenever possible, record a specific diagnosis for the event. If a diagnosis cannot be made, then record each sign or symptom representing a

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distinct medical concept separately, (e.g. nausea and vomiting should be recorded as separate events).

Onset Date and Time: Record the date and time the event starts. If a laboratory result is reported as an AE, record the start date as the date of collection of the first lab sample that shows the change.

Stop Date and Time: Record the date and time the event resolves, returns to baseline, or resolves with sequelae.

Grade: Refer to the common terminology criteria for adverse events (CTCAE) Version 4.

Relationship to the Study Drug:

We make every effort to evaluate the relationship between the study drug and the AE as determined by the investigator per the definitions below:

1. **Related:** The event is reasonably suspected of a causal relationship to the study drug. Suspected adverse reaction means any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of IND safety reporting, ‘reasonable possibility’ means there is evidence to suggest a causal relationship between the drug and the adverse event. A suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by a drug.

ASSESSING RELATIONSHIP TO STUDY TREATMENT

Items to be considered when assessing the relationship of an AE to the study treatment are:

- Temporal relationship of the onset of the event to the initiation of the study treatment;

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- The course of the event, considering especially the effect of discontinuation of study treatment or reintroduction of study treatment, as applicable;
 - Whether the event is known to be associated with the study treatment or with other similar treatments;
 - The presence of risk factors in the study subject known to increase the occurrence of the event;
 - The presence of non-study treatment-related factors which are known to be associated with the occurrence of the event.
2. Not Related: The event is definitely due to causes separate from study drug administration such as:
- documented pre-existing condition
 - technical and manual procedural problem
 - concomitant medication
 - subject's clinical state
3. Adverse Event Outcome:
- Recovered/Resolved without sequelae
 - Recovered/Resolved with sequelae
 - Not Recovered/Not Resolved: event is ongoing at the end of the AE collection period.
 - Death (Fatal): the event description must be the primary cause of death.

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7.3 Clinical Significance

7.3.1 Reporting and Evaluation of Clinical Laboratory Test Results

The investigator should assess all clinical laboratory results for clinical significance and record the assessment in source documents.

The investigator should evaluate any laboratory result change from pre- and post-study drug administration to determine if the change meets the definition of an AE or SAE. **Record any clinically significant lab results determined to meet the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

7.3.2 Repeat Testing

Additional laboratory testing may be performed at the discretion of the investigator.

7.3.3 Vital Signs

The investigator should evaluate any vital sign changes pre- and post-study drug administration to determine if the change meets the definition of AE or SAE. Vital sign measurements may be repeated at the discretion of the investigator. **Record any clinically significant vital sign measurement that meets the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

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8. Study Activities

Visit-specific schedule for efficacy and safety variables is presented in Appendix II.

8.1 Screening Visit

- Written informed consent
- Demographic information
- Relevant medical history
- Prior therapy for Prostate cancer
- Medication assessment
- Histology
- Vital signs
- Questionnaires
- Morphological and PSMA-ligand imaging studies if no comparable available within 4 weeks of treatment.

8.2 Within 2 Weeks of Screening

- Clinical laboratory testing (see Section 6)

8.3 Injection Visit

Once all screening/baseline procedures are performed, the following procedures will be completed on the day of injection:

8.3.1 Pre-dose and Dosing Procedures

- Pre-dose vital signs – within 20 minutes before dose
- Apply Ice pack to the salivary glands 30 minutes prior to investigational drug injection and continue for 4 hours.

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- Adequate hydration of the patient (IV or oral).
- Inject study drug ¹⁷⁷Lu-PSMA-617
- Post-dose vital signs
- Adverse events

8.3.2 Post-Dose Procedures

Adverse events during the entire stay. At first treatment blood sampling and scintigraphy 1-4h, 24h, 48h, 72h and 7d after injection for dosimetry.

8.3.3 ECG Procedures

Continues ECG recording starts at least 15 minutes prior to the administration of study drug and ends at least 1 hour after administration. A 12 lead ECG also will be performed at two time points: before administration of LU-177 PSMA and after completion of 4 hour WB scan.

8.4 Follow-up

8.4.1 PSA Measurements

Every 6 weeks during the treatment and every 3 months after the last treatment until reaching endpoint or 24 month after the first treatment.

8.4.2 Imaging Studies

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Baseline imaging within 12 weeks of start of therapy including (a) CT of the chest preferably with contrast and CT or MRI of the Abdomen and pelvis preferably with contrast and (b) bone scintigraphy or (c) equivalent to above [1].

Relevant imaging studies will be repeated approximately every 12 weeks until reaching the endpoint or 24 month after the first treatment.

8.4.3 Dosimetry

Prof. Dr. [Name], Universitätsklinikum Würzburg, Germany - Klinik und

Poliklinik für Nuklearmedizin will perform the dosimetry for this protocol.

Radiation dosimetry will be acquired for each patient after the first cycle of treatment. Data acquisition plan is summarized in Table 8. Dosimetry will be considered appropriate, if at least three time points for scintigraphy and blood sampling more than 48 hours apart were acquired.

Time p.i.	Blood sampling	Urine collection	Scintigraphy (whole body planar)	Quantitative SPECT/CT head/thorax/abdomen
5 min	X	X (from injection until 4h in one container)		
30 min	X			
1 h	X			
4 h	X	X (from 4h until discharge in one container)	X	
18 - 30 h	X		X	X
42-54h	X		X	
66-78h	X		X	
7-9d*	X		X	

Table 8: Acquisition plan for individual dosimetry during the first cycle of RLT.

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Dosimetry data will be sent to experts in the field for centralized analysis. Radiation dose will be calculated for all relevant organs. Maximum number of RLT cycles for reaching threshold maximum dose to the kidneys of 23 Gy will be determined.

*7-9d is optional.

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8.4.4 Follow-up Labs for Hematological and Kidney Toxicities

All enrolled patients will follow the scheduled follow up visits.

Hematologic laboratory testing (CBC) will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until patient is progressed. CBC will be performed every 7 days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery which is defined as grade 2 toxicity or lower..

In order to detect myelodysplasia, patients who withdrawn by the investigator for safety reasons will only perform CBC test until the end of their follow up visits as long as they do not start other cytotoxic therapies.

Chemistry will be evaluated every 4 weeks during therapy cycles to evaluate safety and also eligibility to receive the next cycle and then every 3 months for 24 months or until the patient is progressed. Patients on protocol should also have a physical exam and in-person physician evaluation periodically while on study and until recovery from last dose. During dosing period patients will be evaluated by the investigator or under his / her direct supervision. During follow up period local patients can come back to the facility for physical exam and for non-local patients they need to see their physician each 3 months for in-person physical exam assessment and send the results of exam to the investigator.

8.4.5 Telephone Follow ups

7 (+/- 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 week) until the end of follow up visits (24 months).

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9. Quality Control and Assurance

The study sites are chosen with regard to the capability and expertise of the principal investigators and the site staff. Prior to initiation of the study, the investigator and the sponsor's representative will meet to discuss the study design and conduct of the study. The investigator will sign the protocol acknowledging that he understands the design and all procedures and intends to conduct the study and all procedures according to protocol.

During the study, a representative of the sponsors will make periodic visits to the investigational site while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government regulations and guidelines. The investigator will permit authorized representatives and the respective local and national health authorities to inspect facilities and records relevant to this study, if needed.

Subject data will be collected on source documents and entered in the CRF. Data will be reviewed and validated. The investigator will sign and date a declaration on the CRF attesting to his her responsibility for the quality of all data recorded and that the data represents a complete and accurate record of each subject in the study.

Records of subjects, source documents, monitoring visit logs, inventory of study product, regulatory documents (e.g., protocol and amendments, IRB/IEC correspondence and approvals, approved and signed informed consent forms, Investigator's Agreement, clinical supplies receipts, and distribution and return records), and other sponsor correspondence pertaining to the study will be kept in the appropriate study files at the site. Source documents include all recordings and observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical study. At the end of the study, CRF data will be provided to the sponsor.

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10. Planned statistical methods

10.1 Primary endpoints

1. **Safety** of ¹⁷⁷Lu-PSMA-617 RLT will be assessed by analysis of toxicity. Descriptive statistics (number and percentage) will be reported separately for AE in total and SAE based on CTC. These descriptive statistics will be presented for the whole treatment as well as separate for each cycle. In addition, the relationship of AE to the study drug (related, not related) will be reported. Both results from laboratory test, physical examinations and patients surveys will be included.
2. **Efficacy** of ¹⁷⁷Lu-PSMA-617 will be reported using descriptive statistics by means of number and percentage of patients with $\geq 50\%$ decline at 12-weeks from baseline.

10.2. Secondary endpoints

1. Descriptive analyses (median, standard deviation) will be used to determine the **progression-free survival (PFS)**, measured from start of therapy until death or PSA progression. PSA progression is defined a) for patients with PSA decline after start of treatment as time from baseline to time the PSA increases to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later or b) for patients without PSA decline as time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq ¹⁷⁷Lu-PSMA-617) and a statistical significant difference will be tested.
2. Each clinical site will perform image analysis on their own patients. Descriptive analyses (median, standard deviation) will be used to determine the **radiographic progression-free survival (rPFS)**, measured from start of therapy until death or radiographic progression. Radiographic progression is defined as a) for extraskeletal

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disease progressive disease (PD) following Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 [63] and/or b) skeletal disease the development of ≥ 2 new lesions on first post-treatment bone scan, with at least two additional lesions on the next scan (2+2 rule). The date of progression is the date of the first post-treatment scan, when the first two new lesions were documented. This approach is applied in accordance to PCWG3 criteria to exclude pseudoprogression in the absence of symptoms or other signs of progression [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq ¹⁷⁷Lu-PSMA-617) and a statistical significant difference will be tested.

3. Descriptive analysis will be used to determine the **disease control rate (DCR)** at the end of each cycle defined as the number and percentage of patients achieving a) RECIST stable disease (SD), partial response (PR) or complete response (CR) for extraskeletal tumor manifestation and b) PCWG3 non-progressive disease for skeletal manifestations.
4. Descriptive analysis will be used to evaluate the impact on **bone pain level** by determining the proportion of patients with pain response defined by improvement from baseline (all patients with $\geq 4/10$) of at least 2-point absolute improvement without an overall increase in opiate use.
5. Change in **Quality of Life** over time will be documented by comparing the summary scores investigated by the Quality of life questionnaire "EPIC-26" at baseline and at 3, 6, 9, 12, 18 and 24 months after start of ¹⁷⁷Lu-PSMA-617 RLT [64].
6. Changes in **performance status (ECOG)** from baseline will be evaluated over time at 3, 6, 9, 12, 18 and 24 months after start of ¹⁷⁷Lu-PSMA-617 RLT.

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11. Administrative Considerations

This study will be conducted in accordance with the Declaration of Helsinki, ICH E6 Guideline and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 312.50 through 312.70, directive 2001/20/EC of 4 April 2001 and implementing directives and regulations. To ensure compliance the investigator agrees, by written consent to this protocol, to fully cooperate with compliance checks by allowing access to all documentation by authorized individuals. The investigator must conduct the trial as outlined in the protocol and in accordance with the Declaration of Helsinki and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 56 – Institutional Review Boards. The administrative structure of the study (e.g., monitoring and vendor personnel, statistician, and laboratory facilities) and a complete and controlled list of the investigators participating in this study can be found in the study file maintained by the sponsor or its agent.

11.2 Institutional Review Board (IRB) or Independent Ethics Committee (IEC) Approval

The protocol, informed consent form, and any advertisement for the recruitment of subjects must be reviewed and approved by an appropriately constituted IRB or IEC, as required in Chapter 3 of the ICH E6 Guideline and government regulations, including (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 56.107 through 56.115 of Good Clinical Practice. Written IRB approval must be provided to sponsor or designee prior to shipment of study drug or subject enrollment. The investigator is committed in accordance with local requirements to provide the IRB with updates, and to inform the IRB of any emergent problem, SAEs, and/or protocol amendments.

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11.3 Ethical Conduct of the Study

It is mandatory that all considerations regarding the protection of human subjects be carried out in accordance with the Declaration of Helsinki.

11.4 Subject Information and Consent

It is the responsibility of the investigator to obtain written informed consent from subjects. All subjects must sign and personally date an approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for GCP, and the requirements of (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27 of Good Clinical Practice.

The subject must be made aware and agree that personal information may be scrutinized during audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. Prior to IRB/IEC submission, the investigator must send a copy of the informed consent form to be used at their institution to sponsor or designee for review to assure compliance with the ICH E6 and government regulations of the region.

11.5 Subject Confidentiality

Data collected during this study may be used to support the development, registration or marketing of ¹⁷⁷Lu-PSMA-617. All data collected during the study will be controlled by sponsor or designee and sponsor will abide by all relevant data protection laws. In order to maintain subject privacy, all CRFs, study drug accountability records, study reports and communications will identify the subject by initials and the assigned subject number. The

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investigator will grant monitor(s) and auditor(s) from sponsor or its designee and regulatory authority (ies) access to the subject's original medical records for verification of data entered into the CRF and to audit the data collection process. The subject's confidentiality will be maintained and will not be made publicly available to the extent permitted by the applicable laws and regulations.

Written authorization is to be obtained from each subject prior to enrollment into the study in accordance with the applicable privacy requirements [e.g., the Health Insurance Portability and Accountability Act of 1996 Standards for Privacy of Individually Identifiable Health Information ("HIPAA

11.6 Study Monitoring

11.6.1 Monitoring Procedures

An appropriate representative of the sponsors (Study Monitor) will oversee the progress of the study, and ensuring it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and applicable regulatory requirements.

An initiation visit will be made by the study monitor at each site to discuss the protocol and the obligations of both the Sponsor and the investigator. The investigator must allow the study monitor to perform periodic, interim monitoring visits. The actual frequency of monitoring visits will be dependent on the enrollment rate and performance at each site. The purposes of these visits are to verify that written informed consent was obtained prior to each subject's participation in the trial, and to:

- assess the progress of the study
- review the compliance with the study protocol
- determine whether all AEs and SAEs were appropriately reported
- determine whether the investigator is maintaining the essential documents
- discuss any emergent problem

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- check the CRF for accuracy and completeness
- validate the contents of the CRF against source
- assess the status of drug storage, dispensing and retrieval
- retrieve study data

All data required by the protocol must be reported accurately on the CRF and must be consistent with the source documents. Source documents are original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays or other diagnostic images, subject files, pharmacy records and laboratory records). The investigator will make available the source documents for inspection. This information will be considered as confidential.

During scheduled monitoring visits, the investigator and the investigational site staff should be available to meet with the study monitor in order to discuss the progress of the study, make necessary corrections to CRF entries, respond to data clarification requests and respond to any other study-related inquiries of the monitor. The investigational site staff in addition to the study coordinator should also include nuclear medicine staff, radiopharmacist, and radiology staff.

The study monitor will perform a closeout visit at the conclusion of the investigator's involvement in the study.

11.6.2 Auditing

The investigator will make all pertinent records available including source documentation for inspection by regulatory authorities and for auditing by the sponsor. This information will be considered as confidential.

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Representatives of local or foreign health authorities may review the conduct or results of the study at the investigational site. The investigator must promptly inform the sponsor of any audit requests by health authorities, and will provide sponsor with the results of any such audits and with copies of any regulatory documents related to such audits.

11.7 Case Report Forms and Study Records

Sponsor will provide a CRF and CRF instructions for the entry of study data. CRFs must be completed for each subject. All study data will be entered on CRFs from original source data. Entries should be made on the case report forms directly and promptly onscreen. The CRF will be reviewed, signed and dated by the investigator.

11.8 Protocol Violations/Deviations

Protocol violations/deviations will be documented by investigator and submitted to the IRB/IEC, as required by IRB/IEC requirements.

11.9 Access to Source Documentation

During the study, a representative of the sponsor will make periodic visits to the investigational sites while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government regulations and guidelines. The investigator will permit authorized representatives of the sponsor and the respective local and national health authorities to inspect facilities and records relevant to this study, if needed.

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11.10 Data Generation and Analysis

Sponsor(s) or its designee will be responsible for data collection, data management, generation of data outputs and statistical analysis of all data.

11.11 Retention of Data

As described in the ICH GCP Guidelines, ‘essential documents’, including copies of the protocol, subject identification codes, CRF, source data, informed consent form(s) and other documents pertaining to the study conduction must be kept for the maximum period of time as required by the study site. This time period must be at least two years after the last follow up of the patients enrolled.

No study document should be destroyed without prior written agreement between sponsors and the investigators. Originals of all documentation generated by sponsor and copies of outgoing sponsor correspondence concerning the study will be stored and retained in a safe area under the control of sponsor for the lifetime of the product. In particular, the final report must be retained by sponsor, or the subsequent owner, for 5 years beyond the lifetime of the study drug.

11.12 Financial Disclosure

All investigators must provide financial disclosure information in accordance with the US Code of Federal Regulations Title 21 CFR 54.2 through 54.6.

11.13 Publication and Disclosure Policy

All unpublished documentation (including the protocol, CRF and Investigator Brochure (IB) given to the investigator is strictly confidential. All recipients must agree not to disclose the

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information herein contained to any person without the prior written authorization of sponsor. The submission of these documents to the IRB is expressly permitted. The investigator agrees that sponsor maintains the right to use the results of this study in their original form and/or in a global report for submission to governmental and regulatory authorities of any country.

The results of the study may be presented during scientific symposia or published in a scientific journal only after review by sponsor in accordance with the guidelines set forth in the applicable publication or financial agreement.

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Appendices

Appendix 1- Preclinical Toxicity studies

This exhibit is 303 pages. Therefore we are providing it in the attached CD.

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Appendix II: Visit Specific Schedule

- 1 A blood sample will be collected within 48 hours(preferably 30 minutes) before the injection to document CMP and CBC for safety purposes .
 - 1 Only at first treatment several blood samples will be required for dosimetry purposes at 5 minutes ,30 minutes, 1, 4,24, 48, and 72 hours. 7 to 9 days sample is optional.
 - 1 Laboratory test will be acceptable only if they performed within one week of each scheduled visit. Screening visit and week -1 can be combined if screening visit performed within 2 weeks of the first cycle
 - 1 *CBC will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until disease progression
 - 1 CMP will be checked every 4 weeks during therapy cycles and then every three months up to 24 months after the last treatment.
 - 2 Baseline imaging within 12 weeks of start of therapy including (a) Chest CT preferably with contrast & CT or MRI of the Abdomen- pelvis preferably with contrast, (b) bone imaging, (c) or equivalent
 - 2 Relevant imaging studies will be repeated every 12 to 16 weeks until reaching the endpoint or 24 months after the first treatment.
 - 2 For patients whom are eligible for 7th cycle of RLT "Imaging study" will be performed only either in cycle number 7 or follow up number 1.
 - 8 For safety assessment, vital signs will be measured within 20 minutes before and for up to an hour after administration of 177Lu-PSMA 617
 - 11 Continues ECG recording starts at least 15 minutes prior to administration of the study drug and lasts at least 1 hour after administration.Also two 12 lead ECGs :one before injection and one after 4 hr scan
 - 12 Quality of life questionnaire (EPIC-26) and ECOG will be completed at baseline and in 3, 6,9, 12,18 and 24 months (+/- 1 month for each) after the start of treatment
 - 13 PSA will be measured every 6 weeks during the treatment and every 3 months after the last treatment until reaching endpoint or 24 months after the first treatment.
 - 14 Only at first treatment Scintigraphy will be performed several times (4, 24, 48 , and 72 hours)after injection for dosimetry purposes. Please refer to dosimetry schedule of events.
 - 15 Telephone follow up: 7(+/- 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 week) until the end of follow up visits (24 months).

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Appendix III: Chemistry, Manufacturing, and Control (CMC) of Lu-177 PSMA

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Appendix IV: Informed Consent Form

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Sponsor Signatures

Study Title: PSMA-directed EndoRadiotherapy of Castration-resISTant prostate cancer (PERCIST). A phase II clinical trial.
Study Number:
IND Number: 133661
Final Date: 01/31/2017

This clinical study protocol was subject to critical review and has been approved by the sponsor.

Signed: _____ Date: _____

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Investigator's Signature

Study Title: PSMA-directed EndoRadiotherapy of Castration-resISTant prostate cancer (PERCIST). A phase II clinical trial.

Study Number:

IND Number:

133661

Final Date:

01/31/2017

I acknowledge that I have read the attached protocol as amended and I agree that it contains all information necessary to conduct the study. I also agree to and will comply with all provisions set forth therein and herein, and certify as follows:

I will comply with all Health Authority regulations/guidelines relevant to the conduct of human clinical trials, as set forth in 21 CFR Parts 50, 54, 56, and 312 part D as they may be amended or supplemented from time to time. I will not initiate the study until I have obtained written approval from the appropriate Institutional Review Board/Independent Ethics Committee and have complied with all financial and administrative requirements of the governing body of my clinical institution. I will obtain written informed consent from all study participants prior to performing any screening procedures.

I understand that my signature (or that of a Sub-Investigator) on a case report form indicates that the data therein have been reviewed and are deemed to be complete, accurate, and acceptable to me.

I have not been disqualified by any regulatory authority or otherwise disqualified from serving as a Principal Investigator, or debarred by the U.S. FDA or any other regulatory authority. In the event that during the term of the study, I become debarred, or receive notice of an action by a health authority or threat of an action with respect to my conduct of clinical research, I shall immediately notify sponsor. In the event I become debarred, I shall immediately cease all activities relating to the study.

I understand and acknowledge that confidential information related to this study includes, but is not limited to, (1) this document, (2) the Protocol for the study, (3) the data derived from the study and (4) my impressions of the progress or results of the study ("Confidential Information") all of which is the proprietary and sole property of sponsor. I will comply with the terms of the Confidentiality and Non-Disclosure Agreement and Clinical Trial Agreement, which stipulate that no Confidential Information will be disclosed or generally described to anyone other than sponsor, personnel or designees, participating study staff, regulatory authorities with appropriate jurisdiction, or members of the responsible Institutional Review Board/Independent Ethics Committee. I will not use such Confidential Information for any purpose other than the evaluation or conduct of the clinical investigation. I am not presently, nor will I be during the term of the study, a consultant or advisor to any division of any financial or securities firm.

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Investigator Signature

Site Name

Investigator Printed Name (with degree)

Date (DD/MM/YYYY)

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Baseline and follow-Up Questionnaire for Pain and Adverse Events

PATIENT INFORMATION

Last name: _____ First Name: _____

Date of Birth: _____ Medical Record Number: _____

Change of pain medication since last ¹⁷⁷Lu-PSMA-617 cycle

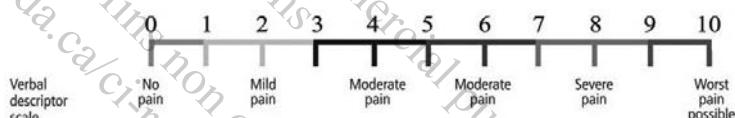
- No change
 Change in dosage/administration: medication _____ increase or decrease
 Addition/removal of medication: medication _____ addition or removal

Pain

- No or Yes:

Locations: _____

Overall level: _____



Change since last cycle: _____

- increase, no change, decrease

Nausea

- No nausea
 Nausea with loss of appetite only
 Nausea with eating/drinking less than usual
 Had to go to hospital for nausea

Vomiting

- No vomiting
 1 - 2 episodes per day
 3 - 5 episodes per day
 more than 5 episodes per day

Dry mouth

- No dry mouth
 Dry or thick saliva
 Normal eating only with water/lubricants possible
 Tube feeding or total i.v. nutrition

Taste

- Normal taste
 Altered taste but no change in diet
 Altered taste with change in diet

Fatigue

- No fatigue
 Fatigue relieved by rest
 Fatigue not relieved by rest, limiting work
 Fatigue not relieved by rest, limiting self-care

Hematoma

- No Hematoma
 Occurrence of hematoma without known event

Fever

- No fever
 38.0 - 39.0 °C (100.4 - 102.2 °F)
 >39.0 - 40.0 degrees °C (102.3 - 104.0 °F)
 >40.0 °C (>104.0 °F)

Urinary retention

- Able to void normally
 Able to void with some pressure
 Unable to void or voiding only after catheter/intervention/treatment

Diarrhea

- Normal bowel movements
 Increase by <4 stools per day

Other (symptom, grade: mild/moderate/severe):

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- Increase by 4-6 stools per day
- Increase by more than 6 stools per day
- Had to go to hospital for diarrhea

Date: _____ Name: _____ Signature: _____

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EPIC-26
The Expanded Prostate Cancer Index Composite
Short Form

This questionnaire is designed to measure Quality of Life issues in patients with Prostate cancer. To help us get the most accurate measurement, it is important that you answer all questions honestly and completely.

Remember, as with all medical records, information contained within this survey will remain strictly confidential.

Today's Date (please enter date when survey completed): Month _____ Day _____ Year _____

Name (optional): _____

Date of Birth (optional): Month _____ Day _____ Year _____

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Do Not
Mark in
This
Space

1. Over the **past 4 weeks**, how often have you leaked urine?

- | | | | |
|----------------------------|---|---------------------|-----|
| More than once a day..... | 1 | (Circle one number) | 23/ |
| About once a day..... | 2 | | |
| More than once a week..... | 3 | | |
| About once a week..... | 4 | | |
| Rarely or never..... | 5 | | |

2. Which of the following best describes your urinary control **during the last 4 weeks**?

- | | | | |
|------------------------------------|---|---------------------|-----|
| No urinary control whatsoever..... | 1 | (Circle one number) | 26/ |
| Frequent dribbling..... | 2 | | |
| Occasional dribbling..... | 3 | | |
| Total control..... | 4 | | |

3. How many pads or adult diapers per day did you usually use to control leakage
during the last 4 weeks?

- | | | | |
|-----------------------------|---|---------------------|-----|
| None | 0 | (Circle one number) | 27/ |
| 1 pad per day..... | 1 | | |
| 2 pads per day..... | 2 | | |
| 3 or more pads per day..... | 3 | | |

4. How big a problem, if any, has each of the following been for you **during the last 4 weeks?**

(Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem	
a. Dripping or leaking urine	0	1	2	3	4	28/
b. Pain or burning on urination.....	0	1	2	3	4	29/
c. Bleeding with urination.....	0	1	2	3	4	30/
d. Weak urine stream or incomplete emptying.....	0	1	2	3	4	31/
e. Need to urinate frequently during the day.....	0	1	2	3	4	33/

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5. Overall, how big a problem has your urinary function been for you **during the last 4 weeks?**

- No problem..... 1
Very small problem..... 2
Small problem..... 3
Moderate problem..... 4
Big problem..... 5

(Circle one number)

34/

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6. How big a problem, if any, has each of the following been for you? (Circle one number on each line)

	<u>No Problem</u>	<u>Very Small Problem</u>	<u>Small Problem</u>	<u>Moderate Problem</u>	<u>Big Problem</u>	
a. Urgency to have a bowel movement	0	1	2	3	4	49/
b. Increased frequency of bowel movements.....	0	1	2	3	4	50/
c. Losing control of your stools.....	0	1	2	3	4	52/
d. Bloody stools	0	1	2	3	4	53/
e. Abdominal/ Pelvic/Rectal pain...	0	1	2	3	4	54/

7. Overall, how big a problem have your bowel habits been for you **during the last 4 weeks?**

- No problem..... 1
Very small problem..... 2
Small problem..... 3
Moderate problem..... 4
Big problem..... 5

(Circle one number)

55/

8. How would you rate each of the following **during the last 4 weeks?** (Circle one number on each line)

	<u>Very Poor to None</u>	<u>Poor</u>	<u>Fair</u>	<u>Good</u>	<u>Very Good</u>	
a. Your ability to have an erection?.....	1	2	3	4	5	57/
b. Your ability to reach orgasm (climax)?.....	1	2	3	4	5	58/

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9. How would you describe the usual QUALITY of your erections **during the last 4 weeks?**

- | | |
|---|---|
| None at all..... | 1 |
| Not firm enough for any sexual activity..... | 2 |
| Firm enough for masturbation and foreplay only..... | 3 |
| Firm enough for intercourse..... | 4 |

(Circle one number) 59/

10. How would you describe the FREQUENCY of your erections **during the last 4 weeks?**

- | | |
|---|---|
| I NEVER had an erection when I wanted one..... | 1 |
| I had an erection LESS THAN HALF the time I wanted one..... | 2 |
| I had an erection ABOUT HALF the time I wanted one | 3 |
| I had an erection MORE THAN HALF the time I wanted one..... | 4 |
| I had an erection WHENEVER I wanted one..... | 5 |

(Circle one number) 60/

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11. Overall, how would you rate your ability to function sexually **during the last 4 weeks?**

- | | |
|----------------|---|
| Very poor..... | 1 |
| Poor..... | 2 |
| Fair..... | 3 |
| Good..... | 4 |
| Very good..... | 5 |

(Circle one number) 64/

12. Overall, how big a problem has your sexual function or lack of sexual function been for you
during the last 4 weeks?

- | | |
|-------------------------|---|
| No problem..... | 1 |
| Very small problem..... | 2 |
| Small problem..... | 3 |
| Moderate problem..... | 4 |
| Big problem..... | 5 |

(Circle one number) 68/

13. How big a problem **during the last 4 weeks**, if any, has each of the following been for you?
(Circle one number on each line)

No Very Small Small Moderate Big

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	<u>Problem</u>	<u>Problem</u>	<u>Problem</u>	<u>Problem</u>	<u>Problem</u>	
a. Hot flashes.....	0	1	2	3	4	74/
b. Breast tenderness/enlargement..	0	1	2	3	4	75/
c. Feeling depressed.....	0	1	2	3	4	77/
d. Lack of energy.....	0	1	2	3	4	78/
e. Change in body weight.....	0	1	2	3	4	79/

THANK YOU VERY MUCH!!

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Clinical Trial Protocol: IND # 133661

Study Title: PSMA-directed EndoRadiotherapy of Castration-resISTant prostate cancer (PERCIST). A phase II clinical trial.

Study Number: TBD
IND Number: 133661

Study Phase: Phase II

Product Name: ¹⁷⁷Lu- DOTA-PSMA-617

Indication: Metastatic castration resistant prostate cancer

Principle Investigators: Ebrahim S. Delpassand, M.D. F.A.C.N.M.
Johannes Czernin, M.D.

Sponsors: Ebrahim S. Delpassand, M.D. F.A.C.N.M
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	Date
Original Protocol Date:	12/28/2016

Amendment 2 Date: 6/7/2017

Confidentiality Statement

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SYNOPSIS

Sponsors:

Ebrahim S. Delpassand, M.D.

Johannes Czernin, M.D.

Name of Finished Product:

^{177}Lu -PSMA-617

Name of Active Ingredient:

2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-[[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid

Study Title:

PSMA-directed EndoRadiotherapy of Castration-resISTant prostate cancer (PERCIST). A phase II clinical trial.

Study Number:

TBD

Study Phase:

Phase II

Primary Objective:

To assess safety and efficacy defined as >50% decline in PSA after ^{177}Lu -PSMA-617 in patients with metastatic castration resistant prostate cancer

Secondary Objectives for each treatment dose:

1. To determine maximum PSA decline.
2. To determine PSA progression-free survival (PFS), measured from start of therapy until death or PSA progression.
3. To determine radiographic PFS, measured from start of therapy until death or radiographic progression using RECIST 1.1/PCWG3 criteria.
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST stable disease (SD), partial response (PR) or complete response (CR).
5. To determine impact on bone pain level
6. To determine impact on quality of life

7. To determine impact on performance status (ECOG)

Study Design:

Open-label, prospective, multicenter clinical trial.

Study Population:

Patients with metastatic castration resistant prostate cancer

Inclusion Criteria:

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel naive and docetaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2500/\mu\text{l}$, PLT count $\geq 100.000/\mu\text{l}$, Hb ≥ 9.9 g/dl and ANC $\geq 1500 \text{ mm}^3$ for the first cycle and WBC $\geq 2.000/\mu\text{l}$, PLT count $\geq 75.000/\mu\text{l}$, Hb ≥ 8.9 g/dl and ANC $\geq 1000 \text{ mm}^3$ for the subsequent cycles
8. Signing of the Informed Consent Form
9. Patients enrolling in this trial should have received either Enzalutamide or Abiraterone

Exclusion Criteria:

1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm) or other radionuclide therapy.
2. Glomerular Filtration Rate (GFR) $< 40 \text{ ml/min}$
3. serum creatinine $> 1.5 \times \text{ULN}$
4. AST and ALT $> 5 \times \text{ULN}$
5. Urinary tract obstruction or marked hydronephrosis
6. Diffuse bone marrow involvement confirmed by super-scans

Test Product; Dose; and Mode of Administration:

Randomization into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq ($\pm 10\%$, arm 1) or 7.4 GBq ($\pm 10\%$, arm 2) ^{177}Lu -PSMA-617 every 8 ± 1 weeks; RLT until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy as determined by dosimetry after the first treatment.

Study Duration:

Patients will be followed until either of the following conditions occur:

1. 24 month after the first treatment.
2. Progression by RECIST 1.1/PCWG3 criteria.
3. Death.

Safety Assessments:

Following laboratory tests will be performed one week before each treatment and 4 weeks after the last treatment and every 3 month thereafter:

1. Complete metabolic panel and eGFR
2. CBC

At baseline, 7 (+/- 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 week) until the end of follow up visits (24 months) patients will be called for safety interview.

Following conditions if in view point of investigators deemed study related, will result in permanent discontinuation:

- i. Grade 3-4 non-hematologic toxicities with select exceptions for:
 1. Grade 3 fatigue < 10 days
 2. Grade 3 nausea, vomiting, and diarrhea and grade 4 vomiting and diarrhea that persist for < 72 hours in the absence of maximum medical therapy.
 3. Asymptomatic grade 3 non-hematological laboratory abnormalities that resolve in 72 hours.
 4. Grade 3 infections that resolve under medical treatment within 10 days
- ii. AST/ALT > 3x ULN and bilirubin > 2x ULN
- iii. Grade 4 Hematological toxicities persisting >3 weeks.
- iv. Grade 3 Hematological abnormalities that do not return to baseline for > 12 weeks.

Data Safety Monitoring Board

A Data Safety Monitoring Board (DSMB) has established and will evaluate safety throughout the study. The DSMB will advise the Sponsor, Investigators and investigational sites regarding the continuing safety of study patients and the patients yet to be recruited to the study as well as maintaining validity and scientific merit of the study. The DSMB will review ongoing examinations of safety data and promptly give recommendations to continue, continue with modification, or terminate the study.

Interim safety analyses: 4 interim safety analyses will be conducted by DSMB that will be initiated at the time when 25%, 50%, 75% and 100% of the total ¹⁷⁷Lu-PSMA treatments in the trial have been completed. The DSMB will meet and assess up-to-date safety information within two weeks of a treatment exposure rate being achieved (i.e., the point when 25%, 50%, 75% and 100% of treatments have occurred). Further patients may only be randomized two weeks after the treatment exposure rate has been reached and after a positive opinion from the DSMB.

Efficacy Assessment for each treatment arm:

Primary objective:

12 week PSA response: Proportion of patients with PSA-decline of $\geq 50\%$ at

12-weeks after the first RLT [1]

Secondary objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]
2. Time to PSA progression, for each treatment arm. [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later
 - b. for patients without PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later
3. Radiographic progression free survival (rPFS), for each treatment arm.
4. Change in Pain, Quality of Life and ECOG performance score: Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 month, for each treatment arm

Number of patients enrolled:

As per statistical evaluation, total of 200 patients will be required to have statistical power to achieve the primary endpoints of the study.

Date of Original Protocol: December 28th, 2016

Date of Most Recent Protocol Amendment (if applicable): N/A

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse event
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
AP	alkaline phosphatase
AST	Aspartate aminotransferase
AUC	Area under the plasma concentration versus time curve
BUN	Blood urea nitrogen
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CI	Confidence interval
CR	Complete response
CRF	Case report form
CT	Computed tomography
DCR	Disease Control Rate
ECOG	Eastern Cooperative Oncology Group
eGFR	estimated Glomerular Filtration Rate
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GGT	Gamma-glutamyl transferase
GH	Growth hormone

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Hct	Hematocrit
Hgb	Hemoglobin
HIPAA	Health Information Portability and Accountability Act
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intent-to-treat
LDH	Lactic dehydrogenase
MBq	MegaBequerel
mCi	milliCurie
mo	months
GBq	gigabecquerel
MR	Magnetic resonance
MRI	Magnetic resonance imaging
N/A	Not applicable
NDA	New Drug Application
PCa	Prostate cancer
PET/CT	Positron Emission Tomography/Computed Tomography
PFS	Progression-free survival
PSA	Prostate-specific antigen

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PR	Partial response
RBC	Red blood cell
RECIST	Response Evaluation Criteria In Solid Tumors
RLT	Radioligand therapy
RPFS	Radiographic progression-free survival
SAE	Serious adverse event
SAER	Serious adverse event report
SAP	Statistical analysis plan
SD	Stable disease
SE	Standard error
SPECT	Single-photon emission computerized tomography
PSMA	prostate-specific membrane antigen
US	United States
WBC	White blood cell
WHO-DD	World Health Organization Drug Dictionary

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1. Introduction

1.1 Background

According to the American Cancer Society more than 1 million people in the United States are diagnosed with cancer each year. For American *males*, prostate cancer is the second most common cause of cancer related death [2]. A recent publication [3] estimated the prevalence of prostate cancer as 2,219,280 in the US in 2009 and 3,072,480 in 2020, and incidence of metastatic Castration Resistant Prostate Cancer (mCRPC) as 36,100 and 42,970, respectively. Various therapies have been developed to improve survival of patients with advanced prostate cancer. However, despite such efforts currently all-cause mortality in prostate cancer has been estimated at 168,290 in 2009 and 219,360 in 2020, with 20.5% and 19.5% of these deaths, respectively, occurring in men with mCRPC.

Patients with metastatic castration-resistant prostate cancer (mCRPC) have a poor prognosis, and those patients with metastases are expected to survive ≤ 19 mo [3]. As patient disease progresses, quality of life deteriorates, and until recently, few treatment options were available. Several new therapies have shown an improvement in overall survival for patients with mCRPC who have already received chemotherapy with docetaxel (Fig. 1) [4] [5] [6, 7] [8]. The impact of these new data on clinical practice, treatment sequencing, and best care for individual patients is not yet fully established.

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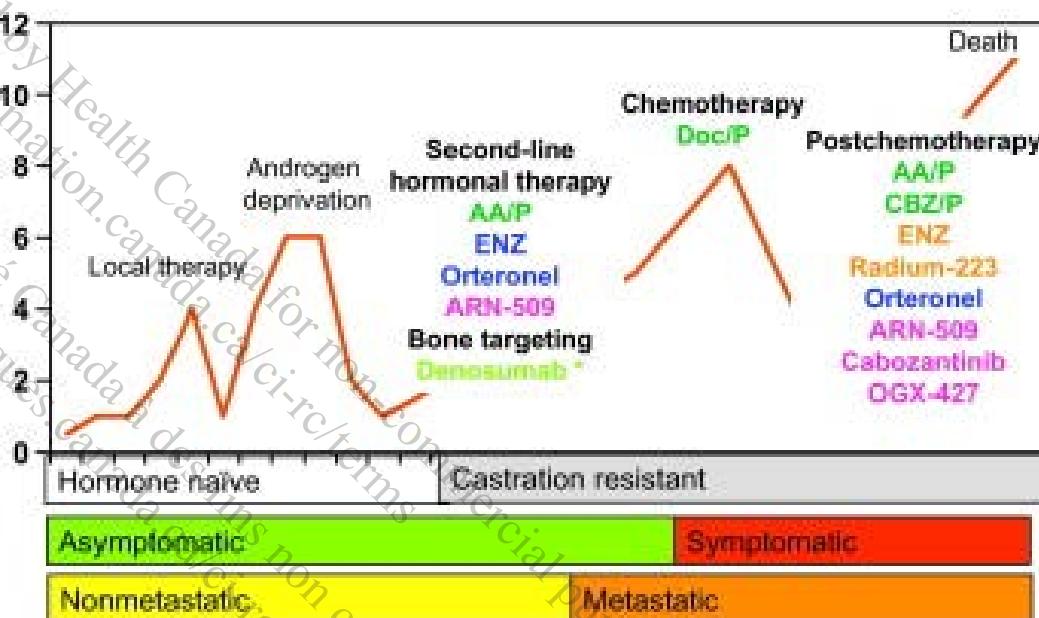


Figure 1: Current, ongoing, and future landscape in the management of castration-resistant prostate cancer. Color key: green = US Food and Drug Administration/European Medicines Agency (FDA/EMA) approved; light green = trial results in high-risk patients positive, but not approved; orange = prospective, randomized, phase 3 clinical trial completed, results positive, FDA/EMA approval awaited; blue = prospective, randomized, phase 3 clinical trial completed, results awaited; purple = promising agent, phase 3 clinical trials ongoing. * Trial results for denosumab in high risk patients positive, but not approved. AA/P = abiraterone acetate with prednisone; ENZ = enzalutamide; Doc/P = docetaxel plus prednisone; CBZ/P = cabazitaxel plus prednisone.

1.1.1. Current treatment options for metastatic castration-resistant prostate cancer: before docetaxel

Sipuleucel-T

Sipuleucel-T is an autologous vaccine consisting of individually collected antigen-presenting cells that are exposed to the fusion protein prostatic acid phosphatase and granulocyte colony-stimulating factor (GCSF), and then reinfused in the patient at weeks 0, 2, and 4. In the Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) study, median survival with sipuleucel-T was 25.8 mo compared with 21.7 mo with placebo [9]. It has to be considered, however, that only patients with a good Eastern Cooperative Oncology Group

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performance status of 0–1, asymptomatic or mildly symptomatic osseous metastases, and absence of visceral metastases were included in the trial.

Abiraterone acetate

The COU-AA-302 (Cougar 302) trial randomized 1088 men with mCRPC to receive abiraterone acetate with prednisone (AA/P) or placebo [4] with the primary end points of overall and radiographic progression-free survival (rPFS) by central review. Median overall survival was 35.3 mo and 27.2 mo in the AA/P group and in the placebo group, respectively ($p = 0.01$) [10]. Also, the co-primary end point of rPFS was significantly improved in the AA/P group, at 16.5 mo, as compared to 8.3 mo in the placebo arm ($p < 0.001$). On all secondary end points, AA/P treatment resulted in significantly improved effects.

Docetaxel/prednisone

In 2004, cytotoxic treatment with docetaxel plus prednisone (Doc/P) was the main option for treatment of mCRPC based on the TAX 327 trial [11]. The median survival was 18.9 mo versus 16.4 mo in the group of patients who received mitoxantrone/prednisone ($p = 0.009$), the 3-yr overall survival rate was 18.6% versus 13.5%, and pain response was 35% versus 22%. It has been shown recently that Doc/P is active in men with symptomatic mCRPC and especially in patients with poorly differentiated prostate cancer (PCa) (Gleason score: 8–10) [12].

Subsequent studies using combinations with docetaxel have not further improved the oncologic outcome [3]. The results of the Randomized Study Comparing Docetaxel Plus Dasatinib to Docetaxel Plus Placebo in Castration-Resistant Prostate Cancer (READY) and the Aflibercept in Combination with Docetaxel in Metastatic Androgen-Independent Prostate Cancer (VENICE) trial were disappointing [13] [11]. The median survival after docetaxel and docetaxel/dasatinib was 21.2 mo versus 21.5 mo, respectively, and the median survival after docetaxel versus docetaxel plus afilbercept was 21.1 mo versus 22.1 mo, respectively. The differences in the patient cohorts of the Cougar 302, IMPACT, and TAX 327 trials make it evident that AA/P will be used for asymptomatic or mildly symptomatic mCRPC with a

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low metastatic burden, whereas Doc/P might be the treatment of choice in men with symptomatic mCRPC and/or a high metastatic burden as well as an undifferentiated PCA.

1.1.2. After docetaxel treatment

Docetaxel rechallenge

The scientific evidence of this approach results from large, retrospective series that identified patients who might be good candidates for re-exposure [14] [15] [16]. Patients who responded with a ≥30% decrease in prostate-specific antigen (PSA) level, maintained for at least 8 wk after first exposure to docetaxel, demonstrated a positive PSA response in about 55% to 60% of the cases during re-exposure without increasing treatment related toxicity.

Abiraterone acetate plus prednisone

AA/P versus placebo was evaluated in the Cougar 301 trial, which randomized 1195 patients with progressive mCRPC who failed docetaxel-based chemotherapy [5]. The median follow-up in the overall study population was 12.8 mo. Overall survival was significantly improved from 10.9 mo in the placebo arm to 14.8 mo in the AA/P arm ($p < 0.001$). All secondary end points were met and all end points demonstrated a significantly improved benefit for the AA/P group. Adverse events with regard to the CYP 17 blockade were observed significantly more often in the AA/P arm (55% vs 43%; $p < 0.001$).

Recently, Goodman et al. [17] demonstrated that AA/P is effective even in patients with liver or lung metastases, although to a lesser degree. The overall survival times were 12.9 mo versus 8.3 mo in the placebo group ($p = 0.022$). Albiges et al. [18] described an AA withdrawal syndrome that developed in 32% of 66 patients who had been treated for a mean period of 5.7 mo. Clayton et al. [19] presented data from a population-based study that included 187 mCRPC patients with a mean PSA serum concentration of 138 ng/ml who were treated with AA/P. The median overall survival was only 9.3 mo and might reflect the oncologic efficacy of AA/P in a real-world patient population with high metastatic burden.

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Enzalutamide (formerly MDV3100)

Enzalutamide (ENZ) acts as an androgen receptor (AR)-signaling inhibitor, and it was evaluated in the Multinational, Phase 3, Randomized, Double-blind, Placebo-controlled, Efficacy and Safety Study of Oral MDV3100 in Patients with Progressive Castration-Resistant Prostate Cancer Previously Treated with Docetaxel-Based Chemotherapy (AFFIRM) trial, which randomized 1199 mCRPC patients to receive ENZ or placebo [8].

The median follow-up was 14.4 mo and the median overall survival was 18.4 mo and 13.6 mo ($p < 0.0001$) in the ENZ group and in the placebo group, respectively, with a 37% reduction in relative risk for death. All secondary end points were met with a statistically significant benefit in the ENZ arm. With regard to safety, the ENZ group experienced fewer grade 3/4 toxicities than the placebo group (53% vs 45%). The risk of seizures was slightly elevated in the ENZ group, with a frequency of 0.6% versus 0% in the placebo group.

Recently, Scher et al. [20] demonstrated that the use of corticosteroids in parallel to ENZ not only increased grade 3/4 side effects from 34.4% to 63.3%, but it also decreased overall survival to a median 11.5 mo. These data suggest that one of the other second-line therapies, such as AA/P or cabazitaxel plus prednisone (CBZ/P), might be the drug of choice, rather than ENZ, in patients who need corticosteroids for the management of associated comorbidities. Sternberg et al. [21] reported that ENZ is equally effective in patients aged >75 yr, with a median survival time of 18.2 mo as compared to the placebo group with 13.3 mo ($p = 0.0044$). Fleming et al. [22] identified a longer disease history (7.9 yr vs 5.9 yr), a better PSA response (87% vs 52%), and a lower metastatic burden associated with long-term response of 35% and 22% after 12 mo and >18 mo, respectively. These data seem to be important for the decision-making process about the most appropriate therapy for mCRPC patients following docetaxel chemotherapy.

Cabazitaxel plus prednisone

In the XRP6258 Plus Prednisone Compared to Mitoxantrone Plus Prednisone in Hormone-Refractory Metastatic Prostate Cancer (TROPIC) trial, 755 patients with mCRPC who

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progressed during or after docetaxel-based chemotherapy were prospectively randomized to receive CBZ/P or mitoxantrone/prednisone (MP) at 21-d intervals for 10 cycles [5]. The primary end point was achieved and CBZ/P treatment resulted in a median overall survival of 15.1 mo in the CBZ/P compared to 12.7 mo in the mitoxantrone/prednisone group (hazard ratio [HR]: 0.70; 95% confidence interval [CI], 0.59–0.83; $p < 0.0001$). All secondary end points of the trials were reached and they were in favor of CBZ. The most common side effects were neutropenia (CBZ/P group: 82% vs MP group: 58%), leukopenia (CBZ/P group: 68% vs MP group: 42%), and anemia (CBZ/P group: 11% vs MP group: 5%). Diarrhea was the most common non-hematologic side effect and occurred in 6% of the CBZ/P group and <1% of the MP group.

On the other hand, the German compassionate use program (CUP) included 111 patients with mCRPC who met the inclusion criteria of the TROPIC trial; the frequency of neutropenia, leukopenia, and anemia decreased to 7.2%, 9.0%, and 4.5%, respectively [23]. Grade 3/4 gastrointestinal toxicity was observed in only 0.9% of the patients. The most likely reason for the improved toxicity profile is the experience of the investigators, guideline-compliant application of GCSF even at cycle 1, and preventive measures with regard to the treatment of diarrhea.

Recently, Heidenreich et al. [24] analyzed the European CUP, including 746 mCRPC patients, with regard to the frequency and management of adverse events in senior adults. In that study, 325 (43.5%) patients were aged ≥ 70 yr and 145 (19.4%) men were ≥ 75 yr. The type and the frequency of grade 3/4 side effects did not differ significantly between the younger and the older patients except that the frequency of grade 3/4 neutropenia was slightly higher in the group of men aged ≥ 75 yr (19.7% vs 15%). Furthermore, GCSF was used more often at cycle 1 (58.5% vs 47%) and throughout CBZ/P treatment (66.8% vs 58%) in the ≥ 75 age group versus the < 70 age group. In their analysis, Heidenreich et al. [24] developed a risk model to predict grade ≥ 3 neutropenia and/or neutropenic complications based on a multivariate analysis. Age ≥ 75 yr, cycle 1, and neutrophil count $< 4000/\text{mm}^3$ before CBZ injection were associated with neutropenic complications. It has to be mentioned that even in the presence of these risk factors, prophylactic application of

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GCSF significantly reduced the risk of neutropenic complications by 30% (odds ratio: 0.70; 95% CI, 0.50–0.99; $p = 0.04$).

Bone-targeting agents

More than 90% of patients with CRPC have bone metastases, which are a major cause of death, disability, and decreased quality of life, as well as increased cost of treatment [25]. Zoledronic acid and the receptor activator of nuclear factor κ B (RANK) ligand inhibitor denosumab are the two US Food and Drug Administration-approved bone-targeting agents in the management of CRPC [3].

In a phase 3 study, the median time to first on-study, skeletal-related event was 20.7 mo with denosumab compared with 17.1 mo with zoledronic acid (HR: 0.82; 95% CI, 0.71–0.95; $p = 0.0002$ for noninferiority; $p = 0.008$ for superiority) [26]. In a recent, prospective, randomized, double-blind, placebo-controlled trial, Smith et al. [27] evaluated the therapeutic efficacy of denosumab 120mg every week versus placebo in 1423 men with nonmetastatic CRPC and aggressive PSA kinetics (PSA level >8.0 ng/ml and/or PSA doubling time <10 mo). The median time to first bone metastases was significantly prolonged by 4.3 mo (29.5 mo vs 25.2 mo; $p = 0.028$). Bone metastases-free survival was significantly improved by 16%, 23%, and 29% in patients with a PSA doubling time of <10 mo, <6 mo, and <4 mo, respectively.

Radium-223

Radium-223 is a radiopharmaceutical that acts as a calcium mimic and targets new bone growth in and around bone metastases via heavy alpha particles that have an ultrashort range of <100 μ m. A Phase 3 Study of Radium-223 Dichloride in Patients with Symptomatic Hormone Refractory Prostate Cancer with Skeletal Metastases (ALSYMPCA), which included 921 CRPC patients, the median overall survival was 14.9 mo in patients treated with radium-223 compared with 11.3 mo in the placebo group (HR: 0.695; 95% CI, 0.581–0.8732; $p < 0.0001$) [7].

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1.1.3. New and emerging developments

Agents targeting steroidogenesis

Orteronel (TAK-700) selectively blocks 17,20-lyase, resulting in fewer mineralocorticoid effects than AA [28]. In the phase 2 portion of a dose-finding study, Orteronel (TAK-700) 400mg twice daily with prednisone 5mg twice daily resulted in a reduction in PSA level $\geq 50\%$ in 52% of the 96 chemotherapy-naïve mCRPC patients at 12 wk. There are two ongoing phase 3 clinical trials in the prechemotherapy ($n = 1454$) and postchemotherapy ($n = 1083$) landscape of mCRPC that are evaluating the oncologic activity of orteronel. Both trials have completed recruitment.

Galeterone (TOK-001) has combined activity: It inhibits the human CYP17 enzyme, it has pure antagonistic activity toward the AR, and it inhibits the binding of androgens to both mutant and wild-type AR [29]. In the Androgen Receptor Modulation Optimized for Response (AMORI) trial, 49% of chemotherapy-naïve mCRPC patients experienced a PSA-level reduction of $\geq 30\%$, and a $\geq 50\%$ reduction was achieved by 22% [30]. Despite the absence of steroid co-treatment, no adrenal mineralocorticoid excess was observed and a phase 2 trial is underway.

Androgen-receptor blocking agents

ARN-509 is a full antagonist to AR overexpression: It inhibits androgen-dependent gene description, and it impairs nuclear translocalization and DNA binding of AR [31]. Currently, three prospective randomized phase 3 clinical trials are underway including (1) patients with high-risk and nonmetastatic CRPC, (2) treatment-naïve patients with mCRPC, and (3) patients with progression following AA/P treatment. Preliminary results have been presented for the first two groups and a $\geq 50\%$ decline in PSA level was achieved in 91% of patients with high-risk and nonmetastatic CRPC and in 88% of treatment-naïve patients with mCRPC. The most common side effects were tolerable fatigue and gastrointestinal events.

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ODM-201 is another antiandrogen with similar mechanisms of actions as described for ENZ and ARN-509 [31]. The potential advantage of ODM-201 is that it does not cross the blood-brain barrier and so might prevent the development of seizures. ENZ-4176 is a novel, nucleic acid-based antisense oligonucleotide against AR, which results in selective and specific downregulation of AR mRNA and protein.

Heat shock proteins

Heat shock proteins (HSPs) have been identified as AR coactivators and chaperone proteins that are increased in PCa cell lines after castration [32]. Quite recently, antisense oligonucleotides targeting HSP27 were evaluated in a phase 2 clinical trial including 72 patients chemotherapy-naïve mCRPC patients who received OGX-427 plus prednisone versus prednisone alone. At 12 wk, 71% and 40% of the patients were progression-free after OGX-427 or prednisone, respectively. A decline of $\geq 50\%$ in PSA level was observed in 50% and 20% in the OGX-427 group and in the prednisone group, respectively. Furthermore, measurable disease response occurred in 44% and 0% of the OGX-427 group and the prednisone group, respectively.

1.1.4 Targeted therapies

Cabozantinib

Cabozantinib is another promising bone-targeting agent that inhibits both vascular endothelial growth factor and met proto-oncogene (hepatocyte growth factor receptor; MET). In a prospective, randomized, placebo-controlled, phase 2 clinical trial, 171 mCRPC patients were enrolled to receive cabozantinib (100mg daily) or placebo [33]. Random assignment was halted early based on the observed activity of cabozantinib. Respectively 5% and 75% of patients treated with cabozantinib had a confirmed partial response and stable disease. The median progression-free survival was 29.7 wk, 23.9 wk, and 5.9 wk for patients who were docetaxel naïve, docetaxel pretreated, and on placebo treatment ($p < 0.001$), respectively.

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Interestingly, PSA changes did not correlate with the antitumor effects in bone metastases and soft-tissue lesions. However, patients with complete resolution (n = 14; 12%) or partial resolution (n = 65; 56%) of bone scans experienced significantly better response rates to soft-tissue metastases as compared to men with stable or progressing bone scans (81% vs 61%), and they also experienced longer progression-free survival rates at 6 mo (56% vs 48%, respectively). Cabozantinib has significant antitumor activity and a well-tolerated toxicity profile, so it might be well integrated into the therapeutic armamentarium to treat mCRPC.

Targeted radionuclide Therapy

Over the past several decades, numerous combined diagnostic and therapeutic radioligands (Theranostics) were designed to target receptors on the cancer cell surface. Antibodies (whole or small fragments), small molecules, peptides with affinities to receptors (agonist or antagonist) have demonstrated in vivo efficacy for targeting cancers based on up-regulated antigens or receptor populations. This approach, also called radioligand therapy (RLT), presents several advantages over conventional chemotherapy. The expression of the antigens or special receptors can be identified by a diagnostic probe before exposing patients to therapeutic doses of these agents allowing identification of suitable subjects for therapeutic procedures and preventing unnecessary exposure of the patients to radiation without significant benefit. This approach allows the physician to select only those patients with high expression of the target prior to treatment. Since the unused radioactive materials are excreted from the body, RLTs are generally well tolerated with no significant or generally reversible or manageable side effects as has been demonstrated for ¹⁷⁷Lu-DOTATATE treatment in patients with neuroendocrine tumor [34].

Prostate cancer demonstrates high expression levels of prostate-specific membrane antigen (PSMA) on its cell surface. Thus PSMA has become a biomarker for prostate cancer [35] [36] and has attracted significant interest as a target for the imaging [37] [38] and therapy [39, 40]. In particular, development of small urea-based PSMA ligands have received significant interest due to their high affinity for PSMA [41] [42]. The urea-based PSMA ligands were modified to deliver a variety of radio-imaging nuclides for both PET and

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SPECT. Gallium (^{68}Ga) labeled urea-based PSMA ligands have been developed as diagnostic agents and studied by several groups [43] [44]. More recently a Lutetium (^{177}Lu) labeled urea based PSMA ligand (DOTA PSMA or PSMA 617) were evaluated in preclinical and clinical phase. Characteristics of ^{177}Lu labeled PSMA are described below.

1.2 Characteristics of ^{177}Lu -DOTA-PSMA (^{177}Lu -PSMA-617)

Lutetium (^{177}Lu) -DOTA PSMA has three components: PSMA is the targeting vector , DOTA(1, 4, 7, 10-tetraazacyclododecane-1, 4, 7, 10-tetraacetic acid) is a radiometal chelator and a linking group, and ^{177}Lu is the beta emitter that upon internalization delivers radiation to the nucleus of tumor cells to cause DNA damage [43] [44, 45]. The targeting vector utilizes glu-urea-lys sequence which is an inhibitor capable of binding to the domain of PSMA. These components have been previously used in human subjects and in medical research.

1.3 Background of Drug Development

There is substantial previous pre-clinical and clinical experience with ^{177}Lu -PSMA-617 published in peer reviewed medical literature from multiple medical centers throughout the world. Sponsors are relying on studies published in the peer viewed medical journals for preclinical and preliminary clinical information. Summary of such reports is given below.

1.3.1 Preclinical Studies.

Martina Benesova et al. [46] performed a preclinical evaluation of radiolabeled PSMA-617. PSMA-617 was synthesized by solid phase peptide synthesis. PSMA-617 can be labeled with ^{177}Lu and Ga-68. Both in vivo and vitro studies were performed using LNCaP cell lines expressing PSMA. PSMA-617 showed highest inhibition potency $K_i = 6.91 \pm 1.32$ for Lu

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complex; $6.40 \pm 1.02\text{nM}$ for Ga complex. PSMA-617 showed higher specific internalization in LNCaP cells.

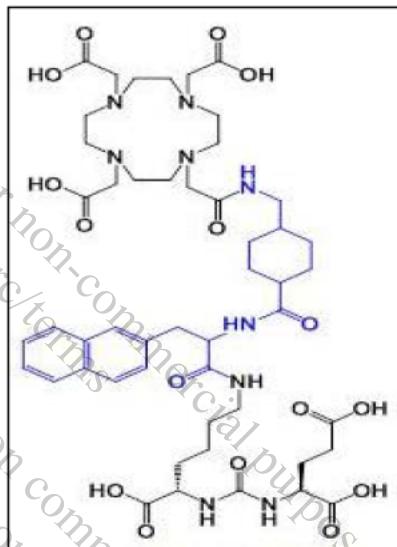


Figure 2: Structure of PSMA 617. Chemical Name 2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-[(2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylaminomethyl]-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid.

The i.v. administered ^{177}Lu -PSMA-617 effectively cleared the blood by 1 hr. Clearance of radioactivity occurred largely through the renal system. As a result of this, the kidneys exhibited significant uptake $137.2 \pm 77.8\%\text{ID/g}$; this could be effectively blocked ($0.85 \pm 0.22\%\text{ID/g}$) by co-injection of PMPA [2 mg/kg], a high affinity inhibitor of PSMA. At 24 hr ^{177}Lu -PSMA-617 shows rapid clearance from the kidney $2.13 \pm 1.36\%\text{ID/g}$ highlighting its potential use as theranostic agent. At 1 hr time point ^{177}Lu -PSMA-617 displayed good in vivo tumor targeting with $11.20 \pm 4.17\%\text{ID/g}$. Accumulation in tumor was PSMA specific with reduction to $0.64 \pm 0.07\%\text{ID/g}$ by coinjection of 2-PMPA. At 24 h post injection $10.58 \pm 4.50\%\text{ID/g}$ uptake was retained in the tumor tissue. For all other non-target tissues, ^{177}Lu -PSMA-617 demonstrated rapid clearance. The ratio of tumor to blood was 1058; tumor to muscle was 529 at 24 hr post injection. These favorable pharmacokinetics are crucial for

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imaging and therapy. The detailed biodistribution results are summarized in Figure 3. ^{68}Ga -PSMA 617 showed similar uptake in the LnCaP tumors ($11.20 \pm 4.17\text{ %ID/g}$). It also shows similar pharmacokinetic clearance profile compared with ^{177}Lu -PSMA-617.

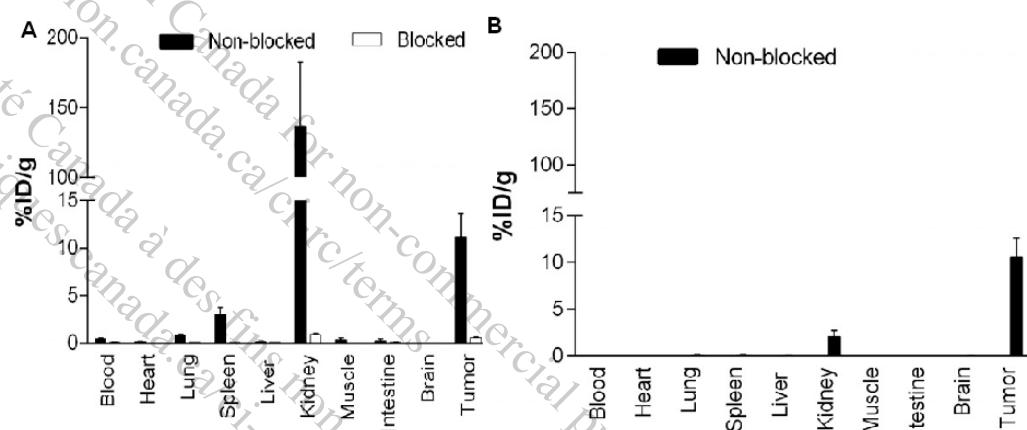


Figure 3: Distribution assay of ^{177}Lu -PSMA-617 in BALB/c mice with LNCap xenografts at 1 h (a) and 24 h (B) post injection.

In summary authors concluded the present radiotracer is suitable for theranostic application in human prostate cancer.

1.3.2 Clinical Studies

Current literature is available to evaluate ^{177}Lu -PSMA-617 therapeutic role in clinical management of patients with prostate cancers. The studies presented in this section were chosen based on novelty of the approach (initial report of application, variables for analyses) and/or the number of patients included.

Clemens Kratochwil et al. [^{177}Lu]Lutetium-labelled PSMA ligand-induced remission in a patient with metastatic prostate cancer. Eur J Nucl Med Mol Imaging 2015; 42:6 ;987-988. [47]

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Study Design: First reported application of ^{177}Lu -PSMA-617 for treatment of a patient with mCRPC. Patient had proven PSMA expression and PSA of 38.0 ng/ml prior to treatment and has received 7.4 GBq of ^{177}Lu -DKFZ-617 in 2 cycles 3 months apart.

Toxicity: No potential side effects were reported in this study.

Results: After the radiotherapy ^{177}Lu -PSMA-617, PSA level of patient decreased to 4.6 ng /ml. PET/CT images showed no signs of metastases lesions either shrunk or were undetectable.

Conclusion: Authors are planning to conduct multicenter a clinical trial as soon as possible to examine clinical potential of ^{177}Lu -PSMA-617.

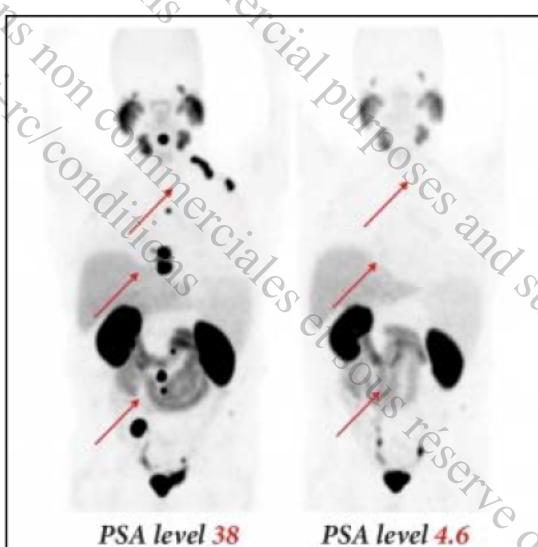


Figure 4: Above Image has recently awarded as image of Year Award and the Berson-Yalow Award at the 2015 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) in Baltimore, USA.

Hojjat Ahmadzadehfar et al. Early side effects and first results of radioligand therapy with ^{177}Lu -DKFZ-617 PSMA of castrate-resistant metastatic prostate cancer: a two-center study. *EJNMMI Research* 2015; 5:36. [48]

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Study Design: A total of 10 consecutive hormone and /or chemo refractory PCa patients with distant metastases and progressive disease with rising PSA levels were recruited in this study.

All patients had prior history or were under therapy with enzalutamide and/or abiraterone.

Four patients had received ²²³Ra-dichloride (1-4 cycles). All 10 patients underwent with ⁶⁸Ga-PSMA HBED-CC (⁶⁸Ga-PSMA) PET /CT prior to therapy to evaluate PSMA expression. Ten patients were treated with range of 4.1-6.1 GBq dose of ¹⁷⁷Lu-DKFZ-617 PSMA. All patients were treated with single dose of ¹⁷⁷Lu-PSMA. The mean and median PSA levels prior to therapy were 339.4 and 298.5 ng/ml. Complete blood chemistry, renal and liver function tests were performed a day before and 2 after the radiotherapy. Patients were followed via telephone every week for safety assessment.

Toxicity: No patient experienced any side effects immediately after injection of ¹⁷⁷Lu-DKFZ-617 PSMA. Relevant hematotoxicity (grade 3 or 4) occurred 7 weeks after the administration in just one patient. The same patient showed a leucopenia grade 2. Two patients showed a disturbance of only 1 hematologic cell line, whereas one patient showed a reduction of grades 1 and 2 in leucocytes and thrombocytes, respectively. Six patients did not show any hematotoxicity during the 8 weeks after therapy. There was no relevant nephrotoxicity (grade 3 or 4).

Results: Eight weeks after the therapy, seven patients (70 %) experienced a PSA decline, of which six experienced more than 30 % and five more than 50 %. Three patients showed a progressive disease according to the PSA increase.

Conclusions: ¹⁷⁷Lu-DKFZ-617 PSMA radiotherapy with single dose for the treatment of metastatic prostate cancer patients without any other therapy option is safe and seems to have a low early side-effect profile with evidence of positive response to the therapy according to PSA decline in 70 % of patients. The authors also stated ¹⁷⁷Lu-DKFZ-617 PSMA has potential to exhibit suitable agent for radionuclide radiotherapy.

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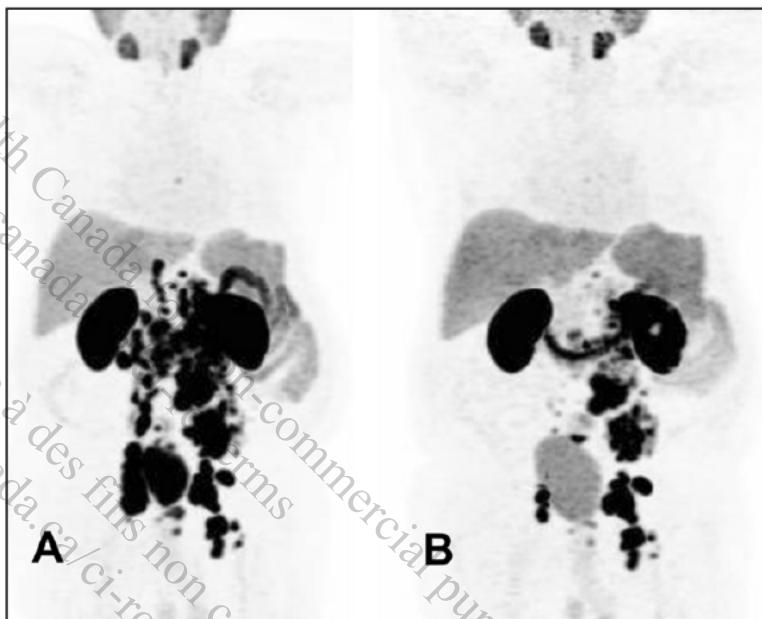


Figure 5: A 74-year-old patient with hormone- and chemo-refractory prostate cancer underwent PSMA PET/CT (a), which showed diffuse abdominal and iliac lymph node metastases. The patient underwent RLT with 5.7 GBq Lu-PSMA. The PSA level was at the time of the therapy 790 ng/ml. (b) A partial response 7 weeks after RLT with 63 % PSA decline; at this time, the PSA level was 293 ng/ml

Clemens Kratochwil, et al. PSMA-targeted radionuclide therapy of metastatic castration-resistant prostate cancer with Lu-177 labeled PSMA-617 J Nucl Med March 16, 2016 [49]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed on 30 patients with PSMA positive tumors were enrolled in this study. 30 patients were treated with 1-3 cycles of ¹⁷⁷Lu-PSMA-617. Pharmacokinetic and radiation dosimetry was also evaluated during the course of the study.

Results: 21 of 30 patients showed response to therapy; for 13/30 the PSA decreased >50%. After 3 cycles 8/11 patients achieved a sustained PSA response (>50%) for over 24 weeks. ¹⁷⁷Lu-PSMA-617 showed fast renal wash out within 48 hours of injection. Patients showed

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mild nausea, fatigue and Xerostomia (<10%) over a period of time. No acute hematotoxicity was observed during the study. Dosimetry results revealed that ¹⁷⁷Lu-PSMA-617 has an exposure of 0.75 Gy/GBq for kidney 0.03 Gy/GBq red-marrow, 1.4 Gy/GBq salivary glands and 6-22 Gy/GBq for tumour lesions.

Conclusion: Based on the results authors concluded that targeted radioligand therapy with ¹⁷⁷Lu-PSMA-617 is safe and promising therapy option for metastasized castrate resistant prostate cancer.

Ahmadvazehfar H, et al. Therapeutic response and side effects of repeated radioligand therapy with ¹⁷⁷Lu-SMA-DKFZ-617 of castrate-resistant metastatic prostate cancer. Oncotarget. 2016 Feb 8. doi: 10.18632/oncotarget.7245. [50]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed in 24 hormone and/or chemo-refractory PC patients. Forty-six cycles of Lu-PSMA were performed. Side effects and response rate was assessed.

Results: Eight weeks after the first cycle of ¹⁷⁷Lu-PSMA-617 therapy 79.1% experienced a decline in PSA-level. Eight weeks after the second cycle of Lu-PSMA therapy 68.2% experienced a decline in PSA relative to the baseline value. Apart from two cases of grade 3 anemia, there was no relevant hemato- or nephrotoxicity (grade 3 or 4).

Conclusion: ¹⁷⁷Lu-PSMA-617 is a safe treatment option for metastatic PC patients and has a low toxicity profile. A positive response to therapy in terms of decline in PSA occurs in about 70% of patients.

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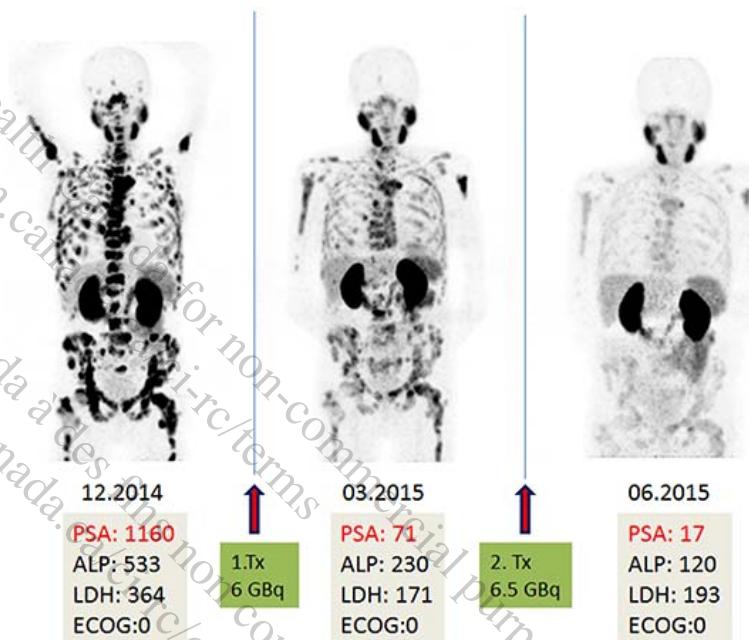


Figure 6: A 75-year-old patient with diffuse bone and lymph node metastases as well as local recurrence (left MIP image). History of chemotherapy and therapy with abiraterone, PSA elevation under enzalutamide. The patient underwent PSMA therapy as the last possible option. Continuing PSA decline and partial response in Ga-PSMA PET images after the first (middle MIP image) and second cycles (right MIP image)

Madhav Prasad Yadav, et al. ¹⁷⁷Lu-DKFZ-PSMA-617 therapy in metastatic castration resistant prostate cancer: safety, efficacy, and quality of life assessment. Eur J Nucl Med Mol Imaging. 2016 Aug 10. [51]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed in 31 patients with progressive disease despite second-line hormonal therapy and/or docetaxel chemotherapy. Patients underwent 1 to 4 cycles after a ⁶⁸Ga-PSMA-HBED-CCP ET/CT for inclusion (mean activity 5069 ± 1845 MBq). Hematological, kidney function, liver function tests, and serum PSA levels were recorded before and after therapy at 2 weeks, 4 weeks, and 3 month intervals. Biochemical response was assessed with trend in serum PSA levels. Metabolic response was assessed by PERCIST 1 criteria. Clinical response was assessed by

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visual analogue score (VASmax) analgesic score (AS), Karanofsky performance status (KPS), and toxicity and response criteria of the Eastern Cooperative Oncology Group (ECOG) criteria.

Results: Biochemical response in terms of complete response (CR), partial response(PR), stable disease (SD), and progressive disease (PD) was observed in 2/31, 20/31, 3/31, and 6/31 had, respectively. Mean VASmax and mean analgesic scores decreased from 7.5 to 3 and 2.5 to 1.8 after therapy, respectively. Mean KPS and mean ECOG performance status score improved from 50.32 to 65.42 after therapies, respectively. Two patients experienced grade I and grade II hemoglobin toxicity each. None of the patients experienced nephrotoxicity or hepatotoxicity.

Conclusion: ¹⁷⁷Lu-DKFZ-PSMA-617 radionuclide therapy is a safe and effective approach in the treatment of mCRPC patients.

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1.3.3 Sponsors Experiences

1.3.3.1 Preclinical Toxicity Studies

The aim of study was to evaluate toxicity of PSMA-617. PSMA-617 applied once weekly by intravenous administration to male rats over 22 days. The animals were treated with 40, 160 or 400 µg of PSMA-617/kg b.w. by tail vein intravenous bolus injection on test days 1, 8, 15 and 22. The control group was treated with physiological saline. No deaths were noted. No signs of local or systemic intolerance reactions were observed. Body weight and body weight gain, food intake, and drinking water consumption were not influenced. No test item-related changes were noted for the hematological and biochemical parameters, the urinary status, the eyes and optic region, the auditory acuity, the relative and absolute organ weights, and the myeloid: erythroid ratio. No test item-related abnormalities were noted during macroscopic inspection at necropsy and at histopathological examination.

Under the test conditions of this study, the no-observed-adverse-effect-level (NOAEL) was 400 µg PSMA-617 / kg b.w. administered once weekly by intravenous bolus injection. This dose was the highest dose tested. Detailed description of this study is attached in appendix 1.

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1.3.3.2 Summary of Human Studies - German Multicenter Experience

Rahbar K, et al. German multicenter study investigating ¹⁷⁷Lu-PSMA-617 radioligand therapy in advanced prostate cancer patients. J Nucl Med. 2016 [52]

Study design: Retrospective acquisition and pooling of data for toxicity and PSA response in patients after ¹⁷⁷Lu-PSMA-617 RLT performed in Germany until July 2015 was initiated by the German Society of Nuclear Medicine for research purpose. The following contains a summary of the collected data. 145 patients with metastatic castration-resistant prostate cancer received a median of two cycles (range 1 to 4) of ¹⁷⁷Lu-PSMA RLT at twelve German Nuclear Medicine Clinics. Data on safety and efficacy were reported. Table 1 lists the administered ¹⁷⁷Lu-PSMA-617 activity for this study cohort.

Table 1. Administered ¹⁷⁷ Lu-PSMA-617 activity (n = 248 RLT cycles)				
administered activity (GBq)	Cycle 1	Cycle 2	Cycle 3	Cycle 4
≤ 3.5	9	3	0	1
> 3.5 – 4.5	32	14	2	0
> 4.5 – 5.5	16	12	9	0
> 5.5 – 6.5	71	37	14	2
> 6.5	17	8	1	0

Results:

A. Toxicity: Nuclear medicine physicians responsible for ¹⁷⁷Lu-PSMA RLT and subsequent follow-up reported potentially related or unrelated adverse events based on a standard template. In addition toxicity was determined by baseline and follow-up findings for serum creatinine, AST, ALT, white blood cell count, hemoglobin and platelet count for 121 of 145 (83%) patients. The follow-up period for adverse events was 2 to 30 weeks. Reported toxicity sorted by organ system is given in Table 1. Grade 3-4 anemia occurred in 15 (10%) patients

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and grade 3-4 thrombocytopenia occurred in 5 (4%) patients. The rate of grade 3-4 events was low for all other categories (0 to 3 patients; 0 to 2%).

There were fewer hematologic adverse events when compared to patients with metastatic castration resistant prostate cancer treated with placebo or ²²³Ra within the ALSYMPCA trial [7] (grade ≥ 3 anemia: 14% in the placebo and 13% in the ²²³Ra group; grade ≥ 3 thrombocytopenia: 3% in the placebo and 7% in the ²²³Ra group). Toxicity data thus indicate a favorable safety profile for RLT using 2-7 GBq ¹⁷⁷Lu-PSMA per cycle in patients with metastatic castration resistant prostate cancer.

Majority of patients received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle. Toxicity rates were comparably low: 9 of 71 (13%) patients with 5.5 – 6.5 GBq and 3 of 17 (18%) patients with >6.5 GBq during the first RLT developed grade 3-4 toxicity.

*Clinical Trial Protocol: IND #**¹⁷⁷Lu-PSMA-617***Table 2. Adverse events after ¹⁷⁷Lu-PSMA-617 as determined by blood tests (n=121) or physician reports (n=145)**

Organ system	Category	Evaluated for N	All grades	Grade 3-4
Blood and lymphatic disorders				
	Leukopenia	121	48 (40%)	4 (3%)
	Anemia	145	50 (34%)	15 (10%)
	Thrombocytopenia	121	38 (31%)	5 (4%)
Gastrointestinal disorders				
	AST elevation	121	27 (19%)	0 (0%)
	ALT elevation	121	11 (8%)	0 (0%)
	Xerostomia	145	11 (8%)	0 (0%)
	Nausea	145	9 (6%)	0 (0%)
	Dysgeusia	145	6 (4%)	0 (0%)
	Ascites	145	2 (1%)	0 (0%)
	Biliary obstruction	145	0 (0%)	1 (1%)
General disorders				
	Fatigue	145	19 (13%)	1 (1%)
	Pain	145	5 (3%)	0 (0%)
	Ileus	145	1 (1%)	0 (0%)
Urinary disorders				
	Renal failure	121	14 (12%)	0 (0%)
	Urinary tract infection	145	1 (1%)	0 (0%)
Cardiovascular disorders				
	Edema	145	2 (1%)	0 (0%)
	Lung embolism	145	0 (0%)	3 (2%)

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Respiratory, thoracic and mediastinal disorders				
	Pleural effusion	145	1 (1%)	0 (0%)
	Dyspnea	145	1 (1%)	0 (0%)
Neurologic disorders				
	Vertigo	145	1 (1%)	0 (0%)
	Stroke	145	0 (0%)	2 (1%)
Musculoskeletal disorders				
	Bone fracture	145	0 (0%)	3 (2%)

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Efficacy

Serial PSA levels at baseline and follow-up were recorded for 99 of 145 patients (68%).

Response was expressed as percent change in serum PSA from baseline to the lowest PSA level measured at follow-up (best PSA response).

Over the entire follow-up period 45 of 99 (45%) patients demonstrated a PSA decline $\geq 50\%$ and were considered biochemical responders. Any PSA decline occurred in 59 of 99 (60%) patients (Figure 7). After the first cycle a PSA decline $\geq 50\%$ occurred in 40 of 99 (40%), any PSA decline in 65 of 99 (66%) patients (Figure 8A). After the second therapy cycle of $^{177}\text{Lu-PSMA-617}$ RLT a PSA decline $\geq 50\%$ occurred in 35 of 61 (57%) and any PSA decline in 44 of 61 (72%) patients (Figure 8B). Patients receiving a third or fourth cycle of therapy showed a PSA decline $\geq 50\%$ in 13 of 20 (65%) and 3 of 3 (100%) patients, respectively.

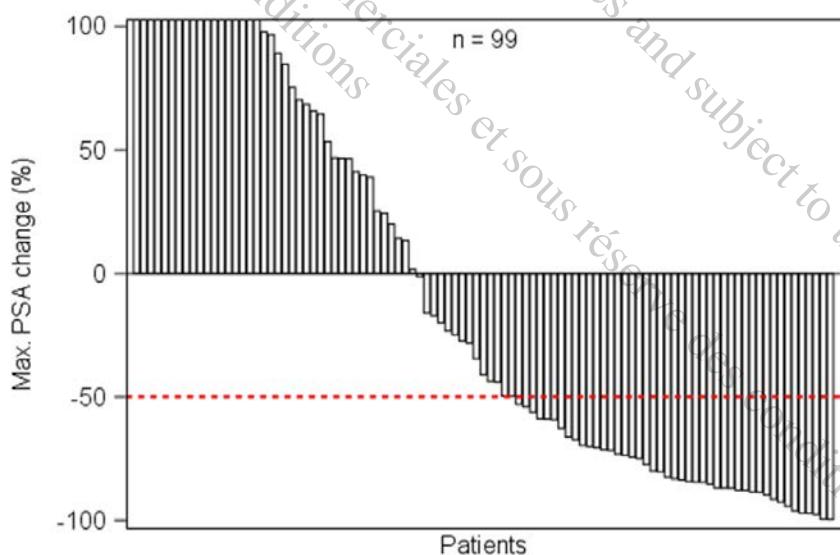


Figure 7. Waterfall plot of maximum PSA change (%) from baseline over total follow-up period. PSA increase of more than 100% was cropped due to simplification.

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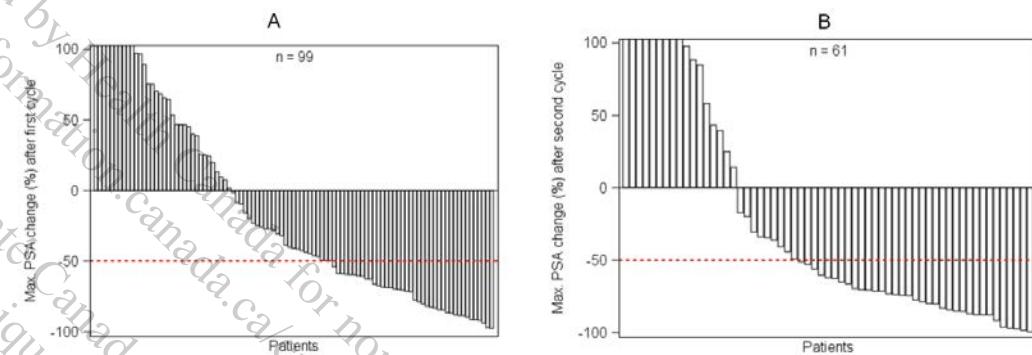


Figure 8. Waterfall plots of maximum PSA change (%) after the first cycle (A) and after the second cycle (B). PSA increase of more than 100% was cropped due to simplification.

Response rate was higher than the rate in patients with metastatic castration resistant prostate cancer treated with abiraterone (best PSA response >50% after abiraterone plus prednisone: 43% (25 of 58) patients) [53]. Data thus indicate good efficacy for $^{177}\text{Lu-PSMA RLT}$ in patients with metastatic castration resistant prostate cancer. Response rates were not significantly associated with mean activity per cycle ($p=0.46$) or cumulative activity after two cycles ($p=0.22$).

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2. Study Objectives

Primary Objectives:

1. To assess the clinical safety of ¹⁷⁷Lu-PSMA-617 by evaluation of adverse events (AE) using the Common Terminology Criteria for Adverse Events (CTCAE)
2. To assess the efficacy as defined by proportion of patients with PSA-response of ≥50% decline at 12-weeks from baseline

Secondary Objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]
2. To determine the time to PSA progression, separate for treatment doses: time from inclusion to date until PSA progression or death (whichever occurs first) [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later
 - b. for patients without PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above baseline
3. To determine radiographic Progression-free Survival (rPFS), for each treatment dose: time from inclusion to date when first site of disease is found to progress or death (whichever occurs first)
 - a. Nodal and visceral disease is evaluated on cross-sectional imaging using RECIST 1.1/PCWG3 criteria
 - b. Bone metastases are evaluated using bone scintigraphy and new lesions have to be confirmed on a second scan (2+2 rule) using PCWG3 criteria
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST 1.1/PCWG3 criteria stable disease (SD), partial response (PR) or complete response (CR).
5. Change in Pain and Quality of Life: Pain and "Epic-26" Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 mo. Pain response will be determined in accordance with PCWG3 [1].
6. Change in ECOG Performance Score

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3. Investigational Plan

3.1 Overall Study Design and Dosing of Targeted PSMA Radioligand Therapy (RLT)

This is a open-label, multicenter, prospective trial. Upon inclusion patients will be randomized into two treatment doses. RLT will be performed by repeated i.v. application of 6.0 GBq ($\pm 10\%$) or 7.4 GBq ($\pm 10\%$) ^{177}Lu -PSMA-617 every 8 ± 1 weeks until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy. All doses after labeling will be presented in buffered solution for intravenous injection.

In total, 200 subjects with histologically proven prostate cancer and mCRPC will be enrolled. Salivary protection will be accomplished by applying ice pack starting 30 minutes prior to infusion of radiopharmaceutical and will continue for 4 hours. Subjects will be recruited at up to 3 Nuclear Medicine sites selected for this project. Each subject will undergo a screening visit within 14 days prior to receiving study drug.

Dosimetry will be performed according to chapter 8.4.3 by Prof. Dr. [Name], Universitätsklinikum Tübingen Germany - Klinik und Poliklinik für Nuklearmedizin after the first injection to determine dose to the kidneys. Treatment will be continued until either of the following conditions apply:

- PSA/radiographic progression as defined above
- Completion of four RLT cycles
- 23 Gy kidney dose would be exceeded by the next cycle as estimated by dosimetry
- patient withdrawal (e.g. appearance of intolerable adverse events)

Primary objectives of the study is safety and efficacy.

Efficacy is determined by PSA response rate: Patients with baseline to follow-up decline in tumor marker level (PSA) $\geq 50\%$ at 12 weeks will be considered responders.

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For safety assessment, vital signs will be measured within 20 minutes before and for up to an hour after administration of ^{177}Lu -PSMA-617. A blood sample will be collected within 48 hours before the injection, for assessing clinical chemistries and hematology. Hematologic laboratory testing (CBC) will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until patient is progressed. CBC will be performed every 7 days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery which is defined as grade 2 toxicity or lower. Chemistry will be evaluated 4 weeks after each therapy and within one week prior to the next treatment to evaluate eligibility to receive the next cycle and then every 3 month for 24 months or until the patient is progressed. CTCAE v 4.0 will be used to evaluate renal toxicity. For more information, please refer to the Schedule of Events ([Appendix 2](#)).

3.2 Rationale for Study Design

3.2.1 Rationale for a regimen with multiple therapy cycles

Activity given during targeted radionuclide therapy is limited by radiation dose to healthy organs. Based on dosimetry radiation dose to healthy organs and subsequent maximal cumulative activity can be calculated. To obtain optimal safety margin maximal cumulative activity is not given in one treatment session but approached by application of a defined fraction of this activity in several cycles. The administration of a standard activity over several treatment cycles allows for early and individual estimation of radiation dose and tolerability. The efficacy and safety of a sequential approach was proven in patients with ^{223}Ra therapy for metastatic castration-resistant prostate cancer (mCRPC) [7] and in patients with ^{177}Lu -DOTATATE therapy for midgut neuroendocrine tumor (NET) [54] each in prospective, double-blind, randomized, international, and multicenter phase III trials. Based on this evidence targeted PSMA Radioligand Therapy (RLT) will be performed by sequential applications of ^{177}Lu -PSMA-617 with treatment-free intervals.

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3.2.2 Rationale for eight weeks interval

Highest level of evidence for subacute adverse events after radionuclide therapy was published for patients with non-Hodgkin's lymphoma. Witzig et al analyzed safety and efficacy of ^{90}Y -Ibritumomab Tiuxetan in 73 patients in a prospective Phase III randomized trial. This study reports neutrophil, platelet and hemoglobin nadir approximately six weeks after application of the beta emitter [55]. Based on this study ^{177}Lu -PSMA-617 RLT will be performed by sequential applications with a treatment-free interval of eight weeks to minimize risk of repeated ^{177}Lu -PSMA-617 therapy before reaching blood level nadir. This scheme is also supported by safety data from the phase III NETTER-1 trial on safety and efficacy of ^{177}Lu -DOTATATE in patients with midgut NET. Here ^{177}Lu -DOTATATE was administered at seven to nine week intervals and rate of severe adverse events was below 10% for 115 patients in the treatment arm [54].

3.2.3 Rationale for dose regimen

Ahmazadehfar et al reports safety and efficacy after application of a mean activity of 6.0 GBq ^{177}Lu -PSMA-617 in 24 patients with mCRPC [50]. Patients were treated with up to two cycles of ^{177}Lu -PSMA-617 RLT at eight week intervals. Grade 3 hematotoxicity occurred in two patients. No nephrotoxicity or hepatotoxicity grade ≥ 3 was documented. Kratochwil et al reports safety and efficacy after repeated application of ^{177}Lu -PSMA-617 in 30 mCRPC patients [49]. 19 of 30 patients (63%) received 6.0 GBq ^{177}Lu -PSMA-617 every two mo. One patient developed grade 3 anemia, one patient grade 3 thrombocytopenia. Both patients had diffuse pattern of bone marrow infiltration at baseline. The German Society of Nuclear Medicine (DGN) performed a questionnaire based survey on the use of ^{177}Lu -PSMA-617 RLT in December 2015. Nuclear Medicine Clinics in Germany reported compassionate use of ^{177}Lu -PSMA-617 RLT in 145 mCRPC patients until June 30th 2015 [52]. Majority of

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patients received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle (Table 1) and rate of serious adverse events was below 20% for both subgroups. Phase III data for ¹⁷⁷Lu-DOTATATE, a similar RLT for midgut NET patients, demonstrates a rate of severe adverse events below 10% after application of four cycles of 7.4 GBq in 115 patients [54]. Thus, present evidence indicates that repeated applications of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 RLT are well tolerated with low to very low rates of serious adverse events.

Standard activities of 6.0 and 7.4 GBq are also supported by dosimetry data available in more than ten patients [56] [57]. Maximal cumulative activity is limited by the absorbed dose in critical organs. Dosimetry identifies kidney and salivary glands as organs with highest absorbed dose [56] [57]. Thus maximum cumulative activity is determined by absorbed kidney dose. Based on earlier evidence obtained from external beam radiotherapy the maximum tolerable per kidney dose is generally accepted 23 Gy [58]. Dosimetry after ¹⁷⁷Lu-PSMA-617 application revealed absorbed doses of 0.6 Gy/GBq per kidney [56] [57]. Therefore maximum cumulative activity for ¹⁷⁷Lu-PSMA-617 RLT is considered 38.3 GBq (38.3 GBq x 0.6 Gy/GBq = 23.0 Gy radiation dose per kidney). Both the application of four cycles of 6.0 GBq (total 24.0 GBq) or 7.4 GBq (total 29.6 GBq) ¹⁷⁷Lu-PSMA-617 results in lower cumulative activities with acceptable safety margin. Whether either activity regimen is associated with longer rPFS is unknown and will be evaluated as secondary endpoint of this trial.

Salivary glands receive highest off-target radiation dose according to dosimetry [56] [57]. Absorbed dose after four cycles of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 (34.0 Gy or 41.6 Gy respectively) falls within the range of maximum tolerable dose reported for salivary glands in the literature [58] [59] [60]. Maximum tolerable dose to the bone marrow is generally accepted 2 Gy [61]. Bone marrow dose will not exceed this limit after four cycles of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 [57].

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3.2.4 Determination of Sample Size

Sample size calculation was based on the primary endpoint of this protocol, i.e. baseline to 12-week decline in tumor marker level (PSA) $\geq 50\%$ [53]. Based on a recent publication [52], we estimate that the proportion of patients who meet the primary end point will range between 38% and 65% for both treatment doses. We thus define the following null hypothesis: Less than 40% of patients will reach the endpoint after ^{177}Lu -PSMA RLT. ^{177}Lu -PSMA RLT would therefore be considered worthy of further study if 50% or more patients met the end point and not worthy of further study if 40% and less achieved the end point. This rationale was adapted from a single-arm study on mCRPC patients with same end point definition, published 2010 in the Journal of Clinical Oncology [53]. We have performed power analysis for the two sided binomial test (beta 0.2, alpha 0.05) to measure the efficacy of ^{177}Lu -PSMA RLT. A sample size of 200 achieves 78% power (beta 0.2) at a given alpha of 0.05 to distinguish between 40% versus 50% response rates. The power analysis was performed by a trained Biostatistician from the Department of Biostatistics, University of California at Los Angeles using Power Analysis and Sample Size (PASS) 14 software (NCSS LLC).

3.3 Study Duration and Dates

The duration of subject participation will be from the time of signing informed consent through the 24 months post-injection visit or progression. Subjects will be deemed enrolled in the study once the subject signs informed consent.

3.4 Randomization protocol

Randomization will be performed in accordance with Vickers et al. [62]. In order to obtain adequate “allocation concealment” a list of random allocations was created for patients 1

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through 200. This list will be stored at investigator's sites and will not be modified. The list will only be accessible for researchers or study personnel not actively involved in the recruitment process.

3.5 Dose modification

In some circumstances, it might be necessary to suspend treatment with ¹⁷⁷Lu-PSMA-617, adapt the posology (i.e. administer a half activity), or even definitively stop administration, as described in the following tables.

Table 3: Criteria for permanent discontinuation of treatment with ¹⁷⁷Lu-PSMA-617

Definitively stop further administrations in patients who have experienced or are at risk of any of the following conditions during treatment:

a) Severe heart failure (defined as grade III or IV of the NYHA classification)
b) Hypersensitivity to the active substance or to any of the components of this radiopharmaceutical
c) Grade 3 hematologic toxicities that persist > 12 weeks and Grade 4 that persist > 3 weeks.
d) Grade 3 renal toxicity as determined by serum creatinine measurements
e) AST/ALT > 3x ULN and bilirubin > 2x ULN
f) Grade 3-4 non-hematologic toxicities with select exceptions for <ul style="list-style-type: none">- Grade 3 fatigue < 10 days- Grade 3 nausea, vomiting, and diarrhoea and grade 4 vomiting and diarrhoea that persist for < 72 hours in the absence of maximum medical therapy- Asymptomatic grade 3 non-hematological laboratory abnormalities that resolve in 72 hours- Grade 3 infections which do not improve under i.v. medication within 10 days

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In case some specific adverse reactions to $^{177}\text{Lu-PSMA-617}$ persist or reoccur, see Table 5

Table 4: When to suspend treatment with $^{177}\text{Lu-PSMA-617}$?

Suspend treatment with $^{177}\text{Lu-PSMA-617}$ in patients who have experienced or are at risk of any of the following conditions during treatment:	
Criterion	Action
Occurrence of an intercurrent disease (e.g. urinary tract obstruction, ...) which according to the physician opinion could increase the risks linked to $^{177}\text{Lu-PSMA-617}$ administration.	Suspend administration until resolution or stabilization. Treatment can be resumed after resolution or stabilization. Resolution is defined as grade II toxicity or lower. (by CTCAE) at the time of the next treatment. Treatment can be suspended up to 12 weeks after the last infusion. After that treatment with $^{177}\text{Lu-PSMA-617}$ must be definitively stopped.
In case of some specific adverse reactions to $^{177}\text{Lu-PSMA-617}$, see Table 5	see Table 5

Table 5: When to adapt $^{177}\text{Lu-PSMA-617}$ posology?

Adapt $^{177}\text{Lu-PSMA-617}$ posology according to the following actions in patients who have presented any of the following severe adverse reactions:	
Severe adverse reactions / Dose-modifying toxicity (DMT) criteria	Action
Anemia, thrombocytopenia or neutropenia of grade 3 or superior (CTCAE 4.0)	1. Suspend treatment with $^{177}\text{Lu-PSMA-617}$
Renal toxicity as defined by grade 3 toxicity by serum creatinine (CTCAE 4.0)	2. Monitor biological parameters every 2 weeks, and eventually treat appropriately if needed; in case of renal function impairment, good hydration is recommended if not otherwise contraindicated.
Liver toxicity as defined as AST and ALT >3xULN	a. If the observed toxicity continues beyond 12 weeks after the last infusion, treatment
Any serious or intolerable adverse event not listed in Table 2 that in the opinion of the investigator, requires the subject's	

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discontinuation.	with ^{177}Lu -PSMA-617 must be definitively stopped. b. If the observed toxicity resolves within 12 weeks after the last infusion, it is possible to continue treatment with ^{177}Lu -PSMA-617 by infusing a half activity. 3. Even if the half activity is well tolerated (i.e. no DMT re-occurrence), the next remaining treatment administration should be continued with the reduced (half) activity but, if DMT recurs after treatment with a half dose, treatment with ^{177}Lu -PSMA-617 must be permanently stopped.
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4. Study Population Selection

4.1 Study Population

It is anticipated that a total of 200 subjects will be recruited. Such a number is considered appropriate to achieve statistical power for the endpoints of this clinical trial. The patients will be recruited at up to 3 clinical sites. The dose being administered will be prepared at RadioMedix Inc. in Houston and shipped to the trial sites.

4.2 Inclusion Criteria

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2500/\mu\text{l}$, PLT count $\geq 100.000/\mu\text{l}$, Hb ≥ 9.9 g/dl and ANC $\geq 1500 \text{ mm}^3$ for the first cycle and WBC $\geq 2.000/\mu\text{l}$, PLT count $\geq 75.000/\mu\text{l}$, Hb ≥ 8.9 g/dl and ANC $\geq 1000 \text{ mm}^3$ for the subsequent cycles
8. Signing of the Informed Consent Form
9. Patients enrolling in this trial should have received either enzalutamide or abiraterone

4.3 Exclusion Criteria

1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm)
2. Glomerular Filtration Rate (GFR) $< 40 \text{ ml/min}$
3. serum creatinine $> 1.5 \times \text{ULN}$ AST and ALT $> 5 \times \text{ULN}$
4. Urinary tract obstruction or marked hydronephrosis
5. Diffuse bone marrow involvement confirmed by super-scans

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5. Study Treatment(s)

5.1 Description of Treatments(s)

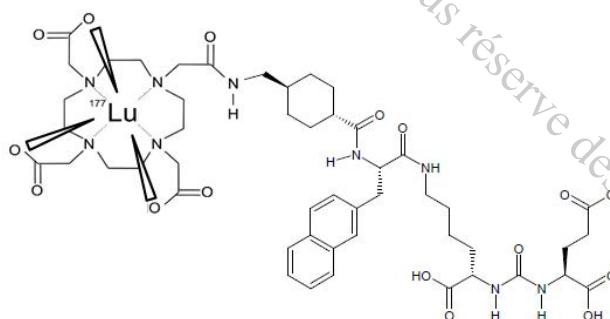
5.1.1 Study drug

The agent to be evaluated in the present study is ¹⁷⁷Lu-PSMA-617. Its chemical name is lutetium-177-N_α-2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid.

¹⁷⁷Lu-PSMA-617 is radiolabelled with carrier-free lutetium-177 (¹⁷⁷Lu), a synthetic, low-energy beta and gamma emitting isotope of lutetium, the last element in the lanthanide series of metallic elements. Carrier-free ¹⁷⁷Lu is generated by neutron irradiation of the isotope ytterbium-176 (¹⁷⁶Yb) and subsequent fractionation of ¹⁷⁷Lu and ¹⁷⁶Yb with caution chromatography. Key physical characteristics of ¹⁷⁷Lu are summarised below:

Physical half-life T _{1/2}	Decay product	Main β ⁻ emission	Maximum range (β ⁻)	Main γ emission
6.6 d	¹⁷⁷ Hf	498 keV	1.7 mm	208 keV 113 keV

The structural formula of ¹⁷⁷Lu-PSMA-617 is shown below



The chemical formula of ¹⁷⁷Lu-PSMA-617 is Lu₁C₄₉H₆₈N₉O₁₆. The molar weight is 1214.1 g/mol.

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5.1.2 Pharmaceutical Properties of ^{177}Lu -PSMA-617

^{177}Lu -PSMA-617 is administered intravenously.

A description of ^{177}Lu -PSMA-617 solution for infusion is shown in below table

Composition of ^{177}Lu -PSMA-617 solution

Pharmaceutically active component	^{177}Lu -PSMA-617
Physical dose	$\leq 7.4 \text{ GBq} / \text{cycle}$
Substance dose	130 - 170 μg PSMA-617
Primary unit dose container	20 mL glass vial containing 5 - 15 mL of stabilised aqueous solution
Appearance	Clear, colourless or slightly yellowish solution, without visible particles
pH	4.0 - 7.5
Bacterial Endotoxin	$\leq 100 \text{ EU/Dose}$
Radionuclidic purity	$\geq 99.99 \%$
Sterility	Sterile

The components include ^{177}Lu -PSMA-617, sodium acetate, sodium ascorbate, gentisic acid, and water for injection. The labelled drug product is produced, tested and released under GMP conditions by RadioMedix, Inc. as a sterile solution for injection infusion, ready for use. The labelled drug product will be manufactured upon individual order and delivered directly to the study sites.

Patients will be randomized into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq ($\pm 10\%$, arm 1) or 7.4 GBq ($\pm 10\%$, arm 2) ^{177}Lu -PSMA-617 every 8±1 weeks; RLT will be performed until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy as determined by dosimetry, after the first treatment.

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5.2. Treatment(s) administered

Cold ice pack in the region of salivary glands will start 30 minutes prior to administration of the investigational drug and will continue for 4 hours. Intravenous access will be inserted in either arm. Assurance will be made to have reliable IV line with no evidence of extravasation or infiltration. Investigational drug will be infused over approximately 30 minutes using infusion pump. Patients will be monitored for any evidence of pain, or burning sensation during the infusion.

Imaging and blood and urine samples for dosimetry after the first treatment will be accomplished as per dosimetry protocol by Prof. Dr. [Name], Universitätsklinikum Würzburg - Klinik und Poliklinik für Nuklearmedizin. For subsequent therapies only 24 hour whole body images will be performed to assure satisfactory distribution of the investigational radiopharmaceutical.

5.3 Restrictions

5.3.1 Fluid and Food Intake

Subjects should follow their normal diet before and after the administration of the study drug. Subjects should be encouraged to increase fluid intake at baseline and after each image acquisition to maintain proper hydration throughout the study period and decrease radiation exposure to the urinary bladder. There are no dietary or food restrictions for this study.

5.3.2 Subject Activity Restriction

There are no activity restrictions.

5.4 Dosing Compliance

All study drug administration will be administered under the supervision of the investigator. Details of study drug injection will be captured in each subject's source documents.

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5.5 Packaging and Labeling

¹⁷⁷Lu-PSMA-617 will be supplied in vials for injection in appropriate packaging.

The outer packaging of ¹⁷⁷Lu-PSMA-617 will contain label(s) which will include the following minimum information:

- Name and address of Manufacturer Study number
- Investigator identification
- Name of study drug and formulation
- Dosage strength
- Batch number
- Patient number
- Expiry date (or retest date)
- Storage instructions
- “For Clinical Trial Use only”

A system of medication numbering in accordance with all requirements of Good Manufacturing Practice (GMP) and any other applicable regulatory requirement will be used for all study drugs. This will ensure that for each patient, any dose of study drug can be identified and traced back to the original bulk ware of the active ingredients. Lists linking all numbering levels will be maintained by the institutions in charge of study drug packaging.

5.6 Storage and Accountability

5.6.1 Storage

The drug product contains radioactive material and should only be handled by personnel trained in the use of radioactive isotopes with proper shielding and monitoring. Receipt and use is limited to a facility licensed by applicable government regulations and/or local/state laws. Unused or residual waste should be disposed of as radioactive waste following the institution's standard operating procedures (SOPs) and/or applicable regulations or guidance.

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5.6.2 Accountability

In accordance with International Conference on Harmonization (ICH) and US Food and Drug Administration (FDA) requirements, the investigator and/or drug dispenser must at all times be able to account for all study drugs furnished to the institution. The appropriate site personnel must sign, date and immediately forward to the sponsor or sponsor's designee the packing slip for clinical shipment included with each shipment.

No study drug is to be used outside of this study. The investigator or designee will record the use of the study drug on the appropriate Drug Accountability record. All study radiopharmaceuticals must be accounted for, whether used or unused, during the course of and at the conclusion of the study. The shipment of drugs from the sponsor or designee to the investigator or other designated persons cooperating with the investigator will be accompanied by a receipt form that indicates the lot number(s) and the amount of drug provided for the study. This form will be signed, dated and returned to the sponsor or designee.

The investigator is responsible for ensuring that study drug is recorded, handled and stored safely and properly in accordance with ICH and applicable government regulations, local/state laws, and used in accordance with this protocol.

5.7 Investigational Product Retention at Study Site

Unused product will be disposed of according to institutional regulations. Record the use and/or disposal of the study drug on the Drug Accountability record. This Drug Accountability record should account for the receipt and disposition of all clinical supplies shipped to the investigator and must be available for review by the study monitor.

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6. Study Procedures

6.1 Informed Consent

All subjects must sign and personally date an IRB/IEC approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug prior to the initiation of any study-related procedures. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for Good Clinical Practice (GCP) and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27.

The subject must be made aware and agree that personal information may be reviewed during an audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. A copy of the Informed Consent Form is attached as Exhibit.

6.2 Medical History

A relevant medical history and subject demographics will be obtained at the screening visit. Cancer medical history includes review of disease history, cancer staging, biopsy results, any past/present cancer therapies (e.g., hormone, drug, biologic, radiologic, or surgical treatment). Demographic information to be collected includes date of birth, race, ethnicity, height, and weight.

6.3 Vital Signs

Vital signs will include measurement of blood pressure, temperature, respiratory rate, pulse oximetry and heart rate.

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6.4 Dispensing Study Drug

The estimated radioactive dose will be determined by measuring the amount of radioactivity in the syringe pre- and post-injection, using an appropriately calibrated radioisotope dose calibrator in accordance with the nuclear medicine department's SOPs.

Any complication related to administration of the drug (e.g., overdose, observable extravasation, medication error) is a protocol-related event and will be reported to the pharmacovigilance designee. Refer to Section 7 for contact information.

6.5 Clinical Laboratory Tests

Clinical laboratory tests will include hematology and clinical chemistry. Clinical laboratory analytes to be assessed in the study are shown in Table 6. Timing of collection of clinical laboratory tests are presented in Section 8.

Table 6: Laboratory Analytes Assessed

Hematology	Clinical Chemistry
Hematocrit	eGFR
Hemoglobin	Bilirubin
RBC count	Creatinine
WBC count	Glucose
WBC differential	Urea nitrogen
Platelets	BUN/Creatinine
ANC	AST/SGOT
MCV/MCH/MCHC	ALT/SGPT
Eosinophils	Alkaline Phosphatase
Basophils	PSA*
Lymphocytes	
RDW	

*PSA will be done only at the time intervals called by the protocol.

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6.6 Sample Collection, Storage and Shipping

Blood samples will be collected using accepted phlebotomy techniques by trained site personnel. All samples for clinical laboratory testing will be processed and analyzed at an accredited laboratory

6.7 Electrocardiogram

Continuous ECG recording at least 15 minutes prior to administration of the study drug and at least 1 hour after administration will be performed. Also a 12 lead ECG will be performed in two time points: before injection of Lu-177 PSMA and after completion of the 4 hr scan.

6.8 Adverse Events

Immediate adverse drug reactions will be collected from the time of ¹⁷⁷Lu-PSMA-617 injection until 24 hours post-injection visit. Data will be collected for any adverse events (AEs) as defined in Section 7.

All study monitoring will be performed at the primary clinical study sites in accordance with Good Clinical Practice (GCP). All records related to this study will be retained at each clinical site. Serious adverse reactions will be collected and reported to FDA and IRB according to 21 CFR 312.32. **Sponsors at each individual site will be responsible for obligations of a sponsor enumerated in 21 CFR 312.50-59. FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the investigational drug.** Annual reports on the progress of the investigation and any adverse events related to the investigational drug will be prepared and reported to FDA according to 21 CFR 312.33.

6.9 Removal of Subjects from the Trial or Study Drug

The investigator may withdraw a subject from the trial for any of the following reasons:

1. Protocol violation

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2. Serious or intolerable adverse event (that in the opinion of the investigator, requires the subject's discontinuation),
3. Investigator withdraws the subject (at the investigator's discretion for reasons other than an adverse event),
4. Sponsor terminates the study,
5. Subject requests to be discontinued from the study, or
6. Subject is lost to follow-up

During course of the study patients have the right to withdraw their consents any time without need for explaining the reason of consent withdrawal to the investigator or sponsor. Principal investigator will closely monitor patients during the course of the study and will consider terminating investigational product administration or any other trial related procedures in order to maintain the safety of subjects. In cases of withdrawal either in patient's favor or principal investigator decision due to the safety issues or technical issues, withdrawn subjects will be replaced in order to maintain data integrity but follow up visits will be continued to maintain safety of patients based on the visits predicted in the protocol.

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7. Reporting Safety Information

Any untoward medical event that occurs from the time that the subject is administered ¹⁷⁷Lu-PSMA-617 until the subject completes the study will be reported. Serious adverse events and non-serious adverse events will be collected and reported as required under 21 CFR 312.32 until the final study visit. Toxicity will be evaluated according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

7.1 Adverse Events

7.1.1 Definitions

An **adverse event (AE)** is any untoward medical occurrence in a study subject that is administered a pharmaceutical product, at any dose, which does not necessarily have a causal relationship with the treatment.

An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a study drug, whether or not considered related to the study drug.

A **serious adverse event (SAE)** is any untoward medical occurrence that falls into one or more of the following categories:

1. Results in death
2. Is life-threatening: An event which, in the view of the investigator, places the subject at immediate risk of death from the event as it occurred and does not include an event which hypothetically might have caused death if it were more severe.
3. Requires subject hospitalization or prolongation of existing hospitalization: For the seriousness criterion of subject hospitalization to apply, an overnight stay in the hospital is required. Admission to an emergency room and release without an overnight stay would not satisfy the subject hospitalization seriousness criterion.
4. Results in persistent or significant disability/incapacity: Persistent or significant disability/incapacity is defined as a substantial disruption of a person's ability to conduct normal life functions, either reported or defined as per clinical judgment.

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5. A congenital anomaly/birth defect: A congenital anomaly/birth defect is defined as a condition believed to have been the result of exposure to study drug just before conception or during pregnancy.
6. Any other important medical event: An important medical event may not result in death, be life-threatening, or require hospitalization, but based upon appropriate medical judgment, the event may significantly jeopardize the subject's health or may require medical or surgical intervention to prevent one of the outcomes listed in the serious definitions above. An important medical event may include development of drug dependency or drug abuse.

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

7.1.2 Reporting Serious Adverse Events

Seriousness is based on subject, event outcome, or action criteria that are usually associated with events that pose a threat to a subject's life or functioning. Seriousness (not severity) serves as the guide for defining the sponsor's regulatory reporting obligations to the applicable regulatory authorities. Adverse event severity and seriousness should be assessed independently by investigators. If the investigator is unsure if the event is serious it should be classified as serious.

Sponsors of the study, and the investigators are responsible for reporting relevant SAEs as safety reports to the FDA and other applicable regulatory authorities, and participating investigators, in accordance with ICH guidelines, the US Code of Federal Regulations Title 21 CFR 312.32 for Good Clinical Practice, and/or local regulatory requirements. The investigators must report all SAEs to project pharmacovigilance designee within 24 hours, by telephone, email or fax, and confirm that the information was received. A Serious Adverse Event Report (SAER) must be completed by the investigator or designee and faxed or emailed to project pharmacovigilance designee within 24 hours after the investigator first

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becomes aware of the serious event. A separate SAER will be needed for each reported SAE so that the onset, resolution date, causality and outcome can be assessed for each event. Any source documents relevant to the event should be forwarded to sponsor's pharmacovigilance designee with the SAER form. The SAER form must be signed and dated by the investigator. The Original copy of the SAER form should remain at the investigational site. All SAEs are also to be entered into the CRF.

In case of death, a comprehensive narrative report of the case should be prepared by the investigator and sent to project pharmacovigilance designee with the SAER. If an autopsy is performed, a copy of the autopsy report should be actively sought by the investigator and sent to the sponsor or designee as soon as available. A copy of the autopsy report should remain at the investigational site with the subject's source documents.

A new follow-up SAER form will be completed by the investigator if important follow-up information (i.e., diagnosis, outcome, causality assessment, results of specific investigations) are made available after submission of the initial form. The follow-up SAER must be signed and dated by the investigator. The follow-up form and any additional source documentation regarding the event will be sent to project pharmacovigilance designee.

If a serious medical occurrence or death is reported to the investigator outside the follow up window which is believed to be related to the administration of the study drug, it is the investigator's responsibility to report this occurrence to project pharmacovigilance designee. Such occurrences will be reported using a SAER form or other form of communication deemed appropriate by the investigator and pharmacovigilance designee.

Sites must contact project pharmacovigilance designee to report all SAEs within 24 hours, by telephone, e-mail, or fax. Contact information for SAE reporting is presented in Table 7.

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Table 7: Pharmacovigilance Designee

[Name], MD
[Contact]
Excel Diagnostics and Nuclear Oncology Center
9701 Richmond Avenue, Suite 122
Houston, TX 77042
PHONE: 713.781.6200 [Contact]
FAX: 713.781.6206
Email: [Contact]

Sites must also report all overdoses, extravasations and medication errors to the project pharmacovigilance designee.

7.2 Adverse Event Data Collection

The investigator will elicit information through non-leading questioning and examination of the subject about the occurrence of adverse events from the time that the subject is administered ¹⁷⁷Lu-PSMA-617 until study completion. AEs can be reported any time after study enrollment until the end of the subject's study participation. For each event, the following information will be recorded in the subject's source documents and entered into the Adverse Event CRF according to the instructions below:

Classification of the Event as serious or non-serious: Classify the event as serious or non-serious (see definitions in Section 7).

Description of Signs or Symptoms: Whenever possible, record a specific diagnosis for the event. If a diagnosis cannot be made, then record each sign or symptom representing a

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distinct medical concept separately, (e.g. nausea and vomiting should be recorded as separate events).

Onset Date and Time: Record the date and time the event starts. If a laboratory result is reported as an AE, record the start date as the date of collection of the first lab sample that shows the change.

Stop Date and Time: Record the date and time the event resolves, returns to baseline, or resolves with sequelae.

Grade: Refer to the common terminology criteria for adverse events (CTCAE) Version 4.

Relationship to the Study Drug:

We make every effort to evaluate the relationship between the study drug and the AE as determined by the investigator per the definitions below:

1. **Related:** The event is reasonably suspected of a causal relationship to the study drug. Suspected adverse reaction means any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of IND safety reporting, ‘reasonable possibility’ means there is evidence to suggest a causal relationship between the drug and the adverse event. A suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by a drug.

ASSESSING RELATIONSHIP TO STUDY TREATMENT

Items to be considered when assessing the relationship of an AE to the study treatment are:

- Temporal relationship of the onset of the event to the initiation of the study treatment;

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- The course of the event, considering especially the effect of discontinuation of study treatment or reintroduction of study treatment, as applicable;
 - Whether the event is known to be associated with the study treatment or with other similar treatments;
 - The presence of risk factors in the study subject known to increase the occurrence of the event;
 - The presence of non-study treatment-related factors which are known to be associated with the occurrence of the event.
2. Not Related: The event is definitely due to causes separate from study drug administration such as:
- documented pre-existing condition
 - technical and manual procedural problem
 - concomitant medication
 - subject's clinical state
3. Adverse Event Outcome:
- Recovered/Resolved without sequelae
 - Recovered/Resolved with sequelae
 - Not Recovered/Not Resolved: event is ongoing at the end of the AE collection period.
 - Death (Fatal): the event description must be the primary cause of death.

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7.3 Clinical Significance

7.3.1 Reporting and Evaluation of Clinical Laboratory Test Results

The investigator should assess all clinical laboratory results for clinical significance and record the assessment in source documents.

The investigator should evaluate any laboratory result change from pre- and post-study drug administration to determine if the change meets the definition of an AE or SAE. **Record any clinically significant lab results determined to meet the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

7.3.2 Repeat Testing

Additional laboratory testing may be performed at the discretion of the investigator.

7.3.3 Vital Signs

The investigator should evaluate any vital sign changes pre- and post-study drug administration to determine if the change meets the definition of AE or SAE. Vital sign measurements may be repeated at the discretion of the investigator. **Record any clinically significant vital sign measurement that meets the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

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8. Study Activities

Visit-specific schedule for efficacy and safety variables is presented in Appendix II.

8.1 Screening Visit

- Written informed consent
- Demographic information
- Relevant medical history
- Prior therapy for Prostate cancer
- Medication assessment
- Histology
- Vital signs
- Questionnaires
- Morphological and PSMA-ligand imaging studies if no comparable available within 4 weeks of treatment.

8.2 Within 2 Weeks of Screening

- Clinical laboratory testing (see Section 6)

8.3 Injection Visit

Once all screening/baseline procedures are performed, the following procedures will be completed on the day of injection:

8.3.1 Pre-dose and Dosing Procedures

- Pre-dose vital signs – within 20 minutes before dose
- Apply Ice pack to the salivary glands 30 minutes prior to investigational drug injection and continue for 4 hours.

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- Adequate hydration of the patient (IV or oral).
- Inject study drug ¹⁷⁷Lu-PSMA-617
- Post-dose vital signs
- Adverse events

8.3.2 Post-Dose Procedures

Adverse events during the entire stay. At first treatment blood sampling and scintigraphy 1-4h, 24h, 48h, 72h and 7d after injection for dosimetry.

8.3.3 ECG Procedures

Continues ECG recording starts at least 15 minutes prior to the administration of study drug and ends at least 1 hour after administration. A 12 lead ECG also will be performed at two time points: before administration of LU-177 PSMA and after completion of 4 hour WB scan.

8.4 Follow-up

8.4.1 PSA Measurements

Every 6 weeks during the treatment and every 3 months after the last treatment until reaching endpoint or 24 month after the first treatment.

8.4.2 Imaging Studies

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Baseline imaging within 12 weeks of start of therapy including (a) CT of the chest preferably with contrast and CT or MRI of the Abdomen and pelvis preferably with contrast and (b) bone scintigraphy or (c) equivalent to above [1].

Relevant imaging studies will be repeated approximately every 12 weeks until reaching the endpoint or 24 month after the first treatment.

8.4.3 Dosimetry

Prof. Dr. [Name], Universitätsklinikum Würzburg, Germany - Klinik und

Poliklinik für Nuklearmedizin will perform the dosimetry for this protocol.

Radiation dosimetry will be acquired for each patient after the first cycle of treatment. Data acquisition plan is summarized in Table 8. Dosimetry will be considered appropriate, if at least three time points for scintigraphy and blood sampling more than 48 hours apart were acquired.

Time p.i.	Blood sampling	Urine collection	Scintigraphy (whole body planar)	Quantitative SPECT/CT head/thorax/abdomen
5 min	X	X (from injection until 4h in one container)		
30 min	X			
1 h	X			
4 h	X	X (from 4h until discharge in one container)	X	
18 - 30 h	X		X	X
42-54h	X		X	
66-78h	X		X	
7-9d*	X		X	

Table 8: Acquisition plan for individual dosimetry during the first cycle of RLT.

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Dosimetry data will be sent to experts in the field for centralized analysis. Radiation dose will be calculated for all relevant organs. Maximum number of RLT cycles for reaching threshold maximum dose to the kidneys of 23 Gy will be determined.

*7-9d is optional.

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8.4.4 Follow-up Labs for Hematological and Kidney Toxicities

All enrolled patients will follow the scheduled follow up visits.

Hematologic laboratory testing (CBC) will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until patient is progressed. CBC will be performed every 7 days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery which is defined as grade 2 toxicity or lower..

In order to detect myelodysplasia, patients who withdrawn by the investigator for safety reasons will only perform CBC test until the end of their follow up visits as long as they do not start other cytotoxic therapies.

Chemistry will be evaluated every 4 weeks during therapy cycles to evaluate safety and also eligibility to receive the next cycle and then every 3 months for 24 months or until the patient is progressed. Patients on protocol should also have a physical exam and in-person physician evaluation periodically while on study and until recovery from last dose. During dosing period patients will be evaluated by the investigator or under his / her direct supervision. During follow up period local patients can come back to the facility for physical exam and for non-local patients they need to see their physician each 3 months for in-person physical exam assessment and send the results of exam to the investigator.

8.4.5 Telephone Follow ups

7 (+/- 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 week) until the end of follow up visits (24 months).

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9. Quality Control and Assurance

The study sites are chosen with regard to the capability and expertise of the principal investigators and the site staff. Prior to initiation of the study, the investigator and the sponsor's representative will meet to discuss the study design and conduct of the study. The investigator will sign the protocol acknowledging that he understands the design and all procedures and intends to conduct the study and all procedures according to protocol.

During the study, a representative of the sponsors will make periodic visits to the investigational site while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government regulations and guidelines. The investigator will permit authorized representatives and the respective local and national health authorities to inspect facilities and records relevant to this study, if needed.

Subject data will be collected on source documents and entered in the CRF. Data will be reviewed and validated. The investigator will sign and date a declaration on the CRF attesting to his/her responsibility for the quality of all data recorded and that the data represents a complete and accurate record of each subject in the study.

Records of subjects, source documents, monitoring visit logs, inventory of study product, regulatory documents (e.g., protocol and amendments, IRB/IEC correspondence and approvals, approved and signed informed consent forms, Investigator's Agreement, clinical supplies receipts, and distribution and return records), and other sponsor correspondence pertaining to the study will be kept in the appropriate study files at the site. Source documents include all recordings and observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical study. At the end of the study, CRF data will be provided to the sponsor.

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10. Planned statistical methods

10.1 Primary endpoints

1. **Safety** of ^{177}Lu -PSMA-617 RLT will be assessed by analysis of toxicity. Descriptive statistics (number and percentage) will be reported separately for AE in total and SAE based on CTC. These descriptive statistics will be presented for the whole treatment as well as separate for each cycle. In addition, the relationship of AE to the study drug (related, not related) will be reported. Both results from laboratory test, physical examinations and patients surveys will be included.
2. **Efficacy** of ^{177}Lu -PSMA-617 will be reported using descriptive statistics by means of number and percentage of patients with $\geq 50\%$ decline at 12-weeks from baseline.

10.2. Secondary endpoints

1. Descriptive analyses (median, standard deviation) will be used to determine the **progression-free survival (PFS)**, measured from start of therapy until death or PSA progression. PSA progression is defined a) for patients with PSA decline after start of treatment as time from baseline to time the PSA increases to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later or b) for patients without PSA decline as time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq ^{177}Lu -PSMA-617) and a statistical significant difference will be tested.
2. Each clinical site will perform image analysis on their own patients. Descriptive analyses (median, standard deviation) will be used to determine the **radiographic progression-free survival (rPFS)**, measured from start of therapy until death or radiographic progression. Radiographic progression is defined as a) for extraskeletal

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disease progressive disease (PD) following Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 [63] and/or b) skeletal disease the development of ≥ 2 new lesions on first post-treatment bone scan, with at least two additional lesions on the next scan (2+2 rule). The date of progression is the date of the first post-treatment scan, when the first two new lesions were documented. This approach is applied in accordance to PCWG3 criteria to exclude pseudoprogression in the absence of symptoms or other signs of progression [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq 177 Lu-PSMA-617) and a statistical significant difference will be tested.

3. Descriptive analysis will be used to determine the **disease control rate (DCR)** at the end of each cycle defined as the number and percentage of patients achieving a RECIST stable disease (SD), partial response (PR) or complete response (CR) for extraskeletal tumor manifestation and b) PCWG3 non-progressive disease for skeletal manifestations.
4. Descriptive analysis will be used to evaluate the impact on **bone pain level** by determining the proportion of patients with pain response defined by improvement from baseline (all patients with $\geq 4/10$) of at least 2-point absolute improvement without an overall increase in opiate use.
5. Change in **Quality of Life** over time will be documented by comparing the summary scores investigated by the Quality of life questionnaire "EPIC-26" at baseline and at 3, 6, 9, 12, 18 and 24 months after start of 177 Lu-PSMA-617 RLT [64].
6. Changes in **performance status (ECOG)** from baseline will be evaluated over time at 3, 6, 9, 12, 18 and 24 months after start of 177 Lu-PSMA-617 RLT.

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11. Administrative Considerations

11.1 Investigators and Study Administrative Structure

This study will be conducted in accordance with the Declaration of Helsinki, ICH E6 Guideline and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 312.50 through 312.70, directive 2001/20/EC of 4 April 2001 and implementing directives and regulations. To ensure compliance the investigator agrees, by written consent to this protocol, to fully cooperate with compliance checks by allowing access to all documentation by authorized individuals. The investigator must conduct the trial as outlined in the protocol and in accordance with the Declaration of Helsinki and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 56 – Institutional Review Boards. The administrative structure of the study (e.g., monitoring and vendor personnel, statistician, and laboratory facilities) and a complete and controlled list of the investigators participating in this study can be found in the study file maintained by the sponsor or its agent.

11.2 Institutional Review Board (IRB) or Independent Ethics Committee (IEC) Approval

The protocol, informed consent form, and any advertisement for the recruitment of subjects must be reviewed and approved by an appropriately constituted IRB or IEC, as required in Chapter 3 of the ICH E6 Guideline and government regulations, including (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 56.107 through 56.115 of Good Clinical Practice. Written IRB approval must be provided to sponsor or designee prior to shipment of study drug or subject enrollment. The investigator is committed in accordance with local requirements to provide the IRB with updates, and to inform the IRB of any emergent problem, SAEs, and/or protocol amendments.

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11.3 Ethical Conduct of the Study

It is mandatory that all considerations regarding the protection of human subjects be carried out in accordance with the Declaration of Helsinki.

11.4 Subject Information and Consent

It is the responsibility of the investigator to obtain written informed consent from subjects. All subjects must sign and personally date an approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for GCP, and the requirements of (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27 of Good Clinical Practice.

The subject must be made aware and agree that personal information may be scrutinized during audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. Prior to IRB/IEC submission, the investigator must send a copy of the informed consent form to be used at their institution to sponsor or designee for review to assure compliance with the ICH E6 and government regulations of the region.

11.5 Subject Confidentiality

Data collected during this study may be used to support the development, registration or marketing of ¹⁷⁷Lu-PSMA-617. All data collected during the study will be controlled by sponsor or designee and sponsor will abide by all relevant data protection laws. In order to maintain subject privacy, all CRFs, study drug accountability records, study reports and communications will identify the subject by initials and the assigned subject number. The

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investigator will grant monitor(s) and auditor(s) from sponsor or its designee and regulatory authority (ies) access to the subject's original medical records for verification of data entered into the CRF and to audit the data collection process. The subject's confidentiality will be maintained and will not be made publicly available to the extent permitted by the applicable laws and regulations.

Written authorization is to be obtained from each subject prior to enrollment into the study in accordance with the applicable privacy requirements [e.g., the Health Insurance Portability and Accountability Act of 1996 Standards for Privacy of Individually Identifiable Health Information ("HIPAA

11.6 Study Monitoring

11.6.1 Monitoring Procedures

An appropriate representative of the sponsors (Study Monitor) will oversee the progress of the study, and ensuring it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and applicable regulatory requirements.

An initiation visit will be made by the study monitor at each site to discuss the protocol and the obligations of both the Sponsor and the investigator. The investigator must allow the study monitor to perform periodic, interim monitoring visits. The actual frequency of monitoring visits will be dependent on the enrollment rate and performance at each site. The purposes of these visits are to verify that written informed consent was obtained prior to each subject's participation in the trial, and to:

- assess the progress of the study
- review the compliance with the study protocol
- determine whether all AEs and SAEs were appropriately reported
- determine whether the investigator is maintaining the essential documents
- discuss any emergent problem

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- check the CRF for accuracy and completeness
- validate the contents of the CRF against source
- assess the status of drug storage, dispensing and retrieval
- retrieve study data

All data required by the protocol must be reported accurately on the CRF and must be consistent with the source documents. Source documents are original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays or other diagnostic images, subject files, pharmacy records and laboratory records). The investigator will make available the source documents for inspection. This information will be considered as confidential.

During scheduled monitoring visits, the investigator and the investigational site staff should be available to meet with the study monitor in order to discuss the progress of the study, make necessary corrections to CRF entries, respond to data clarification requests and respond to any other study-related inquiries of the monitor. The investigational site staff in addition to the study coordinator should also include nuclear medicine staff, radiopharmacist, and radiology staff.

The study monitor will perform a closeout visit at the conclusion of the investigator's involvement in the study.

11.6.2 Auditing

The investigator will make all pertinent records available including source documentation for inspection by regulatory authorities and for auditing by the sponsor. This information will be considered as confidential.

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Representatives of local or foreign health authorities may review the conduct or results of the study at the investigational site. The investigator must promptly inform the sponsor of any audit requests by health authorities, and will provide sponsor with the results of any such audits and with copies of any regulatory documents related to such audits.

11.7 Case Report Forms and Study Records

Sponsor will provide a CRF and CRF instructions for the entry of study data. CRFs must be completed for each subject. All study data will be entered on CRFs from original source data. Entries should be made on the case report forms directly and promptly onscreen. The CRF will be reviewed, signed and dated by the investigator.

11.8 Protocol Violations/Deviations

Protocol violations/deviations will be documented by investigator and submitted to the IRB/IEC, as required by IRB/IEC requirements.

11.9 Access to Source Documentation

During the study, a representative of the sponsor will make periodic visits to the investigational sites while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government regulations and guidelines. The investigator will permit authorized representatives of the sponsor and the respective local and national health authorities to inspect facilities and records relevant to this study, if needed.

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11.10 Data Generation and Analysis

Sponsor(s) or its designee will be responsible for data collection, data management, generation of data outputs and statistical analysis of all data.

11.11 Retention of Data

As described in the ICH GCP Guidelines, ‘essential documents’, including copies of the protocol, subject identification codes, CRF, source data, informed consent form(s) and other documents pertaining to the study conduction must be kept for the maximum period of time as required by the study site. This time period must be at least two years after the last follow up of the patients enrolled.

No study document should be destroyed without prior written agreement between sponsors and the investigators. Originals of all documentation generated by sponsor and copies of outgoing sponsor correspondence concerning the study will be stored and retained in a safe area under the control of sponsor for the lifetime of the product. In particular, the final report must be retained by sponsor, or the subsequent owner, for 5 years beyond the lifetime of the study drug.

11.12 Financial Disclosure

All investigators must provide financial disclosure information in accordance with the US Code of Federal Regulations Title 21 CFR 54.2 through 54.6.

11.13 Publication and Disclosure Policy

All unpublished documentation (including the protocol, CRF and Investigator Brochure (IB) given to the investigator is strictly confidential. All recipients must agree not to disclose the

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information herein contained to any person without the prior written authorization of sponsor. The submission of these documents to the IRB is expressly permitted. The investigator agrees that sponsor maintains the right to use the results of this study in their original form and/or in a global report for submission to governmental and regulatory authorities of any country.

The results of the study may be presented during scientific symposia or published in a scientific journal only after review by sponsor in accordance with the guidelines set forth in the applicable publication or financial agreement.

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Appendices

Appendix 1- Preclinical Toxicity studies

This exhibit is 303 pages. Therefore we are providing it in the attached CD.

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Appendix II: Visit Specific Schedule

	Month	Screening												Therapy												F/U											
		Week		-1	0	2	4	6	8	10	12	14	16	18	20	22	24	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	
		Therapy		1																																	
Signing informed consent form	*																																				
Randomization	*																																				
1 Evaluation of blood tests (*CBC, CMP)	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
2 Evaluation of Imaging studies (CT, MRI)	*																																				
3 Ga-68 or Lu-177 PSMA PET/CT	*																																				
4 Medication & Hypersensitivity assessment	*																																				
5 Current Disease(somatic or psychiatric)	*																																				
6 Histopathology evaluation	*																																				
7 Relevant medical history & demographics	*																																				
8 Vital Signs(BP, HR, T, RR)	*								*											*																	
9 Evaluation of life expectancy	*																																				
10 Prior therapy for Prostate cancer	*																																				
11 ECG and continues ECG Monitoring	*			*					*										*																		
12 Quality of life assessment (EPIC-26)&ECOG	*																	*																			
13 PSA determination	*								*									*																			
14 Whole body (Anterior And Posterior) scan				*					*									*																			
15 Follow up calls for AE Monitoring						+7 days			+7 days									+7 days					+7 days	*		*		*		*			*		*		

1 A blood sample will be collected within 48 hours(preferably 30 minutes) before the injection to document CMP and CBC for safety purposes .

1 Only at first treatment several blood samples will be required for dosimetry purposes at 5 minutes ,30 minutes, 1, 4,24, 48, and 72 hours. 7 to 9 days sample is optional.

1 Laboratory test will be acceptable only if they performed within one week of each scheduled visit. Screening visit and week -1 can be combined if screening visit performed within 2 weeks of the first cycle

1 *CBC will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until disease progression

1 CMP will be checked every 4 weeks during therapy cycles and then every three months up to 24 months after the last treatment.

2 Baseline imaging within 12 weeks of start of therapy including (a) Chest CT preferably with contrast & CT or MRI of the Abdomen-pelvis preferably with contrast, (b) bone imaging, (c) or equivalent

2 Relevant imaging studies will be repeated every 12 to 16 weeks until reaching the endpoint or 24 months after the first treatment.

2 For patients whom are eligible for 7th cycle of RLT "Imaging study" will be performed only either in cycle number 7 of follow up number 1.8 For safety assessment, vital signs will be measured within 20 minutes before and for up to an hour after administration of ¹⁷⁷Lu-PSMA 617

11 Continues ECG recording starts at least 15 minutes prior to administration of the study drug and lasts at least 1 hour after administration.Also two 12 lead ECGs :one before injection and one after 4 hr scan

12 Quality of life questionnaire (EPIC-26) and ECOG will be completed at baseline and in 3, 6,9, 12,18 and 24 months (+/- 1 month for each) after the start of treatment

13 PSA will be measured every 6 weeks during the treatment and every 3 months after the last treatment until reaching endpoint or 24 months after the first treatment.

14 Only at first treatment Scintigraphy will be performed several times (4, 24, 48, and 72 hours)after injection for dosimetry purposes. Please refer to dosimetry schedule of events.

15 Telephone follow up: 7 (+/- 3) days after each treatment cycles and for follow up phase , every 3 months (+/- 1 week) until the end of follow up visits (24 months).

In each time point that the therapy stops follow up visits will be started.

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Appendix III: Chemistry, Manufacturing, and Control (CMC) of Lu-177 PSMA

Not provided with original protocol

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Appendix IV: Informed Consent Form

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Sponsor Signatures

Study Title: PSMA-directed EndoRadiotherapy of Castration-resISTant prostate cancer (PERCIST). A phase II clinical trial.
Study Number:
IND Number: 133661
Final Date: 01/31/2017

This clinical study protocol was subject to critical review and has been approved by the sponsor.

Signed: _____ Date: _____

*Clinical Trial Protocol: IND #
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Investigator's Signature

Study Title: PSMA-directed EndoRadiotherapy of Castration-resISTant prostate cancer (PERCIST). A phase II clinical trial.

Study Number:

IND Number:

133661

Final Date: 01/31/2017

I acknowledge that I have read the attached protocol as amended and I agree that it contains all information necessary to conduct the study. I also agree to and will comply with all provisions set forth therein and herein, and certify as follows:

I will comply with all Health Authority regulations/guidelines relevant to the conduct of human clinical trials, as set forth in 21 CFR Parts 50, 54, 56, and 312 part D as they may be amended or supplemented from time to time. I will not initiate the study until I have obtained written approval from the appropriate Institutional Review Board/Independent Ethics Committee and have complied with all financial and administrative requirements of the governing body of my clinical institution. I will obtain written informed consent from all study participants prior to performing any screening procedures.

I understand that my signature (or that of a Sub-Investigator) on a case report form indicates that the data therein have been reviewed and are deemed to be complete, accurate, and acceptable to me.

I have not been disqualified by any regulatory authority or otherwise disqualified from serving as a Principal Investigator, or debarred by the U.S. FDA or any other regulatory authority. In the event that during the term of the study, I become debarred, or receive notice of an action by a health authority or threat of an action with respect to my conduct of clinical research, I shall immediately notify sponsor. In the event I become debarred, I shall immediately cease all activities relating to the study.

I understand and acknowledge that confidential information related to this study includes, but is not limited to, (1) this document, (2) the Protocol for the study, (3) the data derived from the study and (4) my impressions of the progress or results of the study ("Confidential Information") all of which is the proprietary and sole property of sponsor. I will comply with the terms of the Confidentiality and Non-Disclosure Agreement and Clinical Trial Agreement, which stipulate that no Confidential Information will be disclosed or generally described to anyone other than sponsor, personnel or designees, participating study staff, regulatory authorities with appropriate jurisdiction, or members of the responsible Institutional Review Board/Independent Ethics Committee. I will not use such Confidential Information for any purpose other than the evaluation or conduct of the clinical investigation. I am not presently, nor will I be during the term of the study, a consultant or advisor to any division of any financial or securities firm.

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Investigator Signature

Site Name

Investigator Printed Name (with degree)

Date (DD/MM/YYYY)

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Baseline and follow-Up Questionnaire for Pain and Adverse Events

PATIENT INFORMATION

Last name: _____ First Name: _____

Date of Birth: _____ Medical Record Number: _____

Change of pain medication since last ¹⁷⁷Lu-PSMA-617 cycle

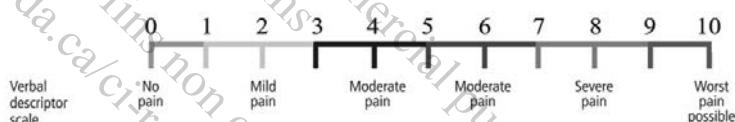
- No change
 Change in dosage/administration: medication _____ increase or decrease
 Addition/removal of medication: medication _____ addition or removal

Pain

- No or Yes:

Locations: _____

Overall level: _____



Change since last cycle: _____

- increase, no change, decrease

Nausea

- No nausea
 Nausea with loss of appetite only
 Nausea with eating/drinking less than usual
 Had to go to hospital for nausea

Vomiting

- No vomiting
 1 - 2 episodes per day
 3 - 5 episodes per day
 more than 5 episodes per day

Dry mouth

- No dry mouth
 Dry or thick saliva
 Normal eating only with water/lubricants possible
 Tube feeding or total i.v. nutrition

Taste

- Normal taste
 Altered taste but no change in diet
 Altered taste with change in diet

Fatigue

- No fatigue
 Fatigue relieved by rest
 Fatigue not relieved by rest, limiting work
 Fatigue not relieved by rest, limiting self-care

Hematoma

- No Hematoma
 Occurrence of hematoma without known event

Fever

- No fever
 38.0 - 39.0 °C (100.4 - 102.2 °F)
 >39.0 - 40.0 degrees °C (102.3 - 104.0 °F)
 >40.0 °C (>104.0 °F)

Urinary retention

- Able to void normally
 Able to void with some pressure
 Unable to void or voiding only after catheter/intervention/treatment

Diarrhea

- Normal bowel movements
 Increase by <4 stools per day

Other (symptom, grade: mild/moderate/severe):

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- Increase by 4-6 stools per day
- Increase by more than 6 stools per day
- Had to go to hospital for diarrhea

Date: _____ Name: _____ Signature: _____

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EPIC-26
The Expanded Prostate Cancer Index Composite
Short Form

This questionnaire is designed to measure Quality of Life issues in patients with Prostate cancer. To help us get the most accurate measurement, it is important that you answer all questions honestly and completely.

Remember, as with all medical records, information contained within this survey will remain strictly confidential.

Today's Date (please enter date when survey completed): Month _____ Day _____ Year _____

Name (optional): _____

Date of Birth (optional): Month _____ Day _____ Year _____

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Do Not
Mark in
This
Space

1. Over the **past 4 weeks**, how often have you leaked urine?

- | | | | |
|----------------------------|---|---------------------|-----|
| More than once a day..... | 1 | (Circle one number) | 23/ |
| About once a day..... | 2 | | |
| More than once a week..... | 3 | | |
| About once a week..... | 4 | | |
| Rarely or never..... | 5 | | |

2. Which of the following best describes your urinary control **during the last 4 weeks**?

- | | | | |
|------------------------------------|---|---------------------|-----|
| No urinary control whatsoever..... | 1 | (Circle one number) | 26/ |
| Frequent dribbling..... | 2 | | |
| Occasional dribbling..... | 3 | | |
| Total control..... | 4 | | |

3. How many pads or adult diapers per day did you usually use to control leakage
during the last 4 weeks?

- | | | | |
|-----------------------------|---|---------------------|-----|
| None | 0 | (Circle one number) | 27/ |
| 1 pad per day..... | 1 | | |
| 2 pads per day..... | 2 | | |
| 3 or more pads per day..... | 3 | | |

4. How big a problem, if any, has each of the following been for you **during the last 4 weeks?**

(Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem	
a. Dripping or leaking urine	0	1	2	3	4	28/
b. Pain or burning on urination.....	0	1	2	3	4	29/
c. Bleeding with urination.....	0	1	2	3	4	30/
d. Weak urine stream or incomplete emptying.....	0	1	2	3	4	31/
e. Need to urinate frequently during the day.....	0	1	2	3	4	33/

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5. Overall, how big a problem has your urinary function been for you **during the last 4 weeks?**

No problem.....	1
Very small problem.....	2
Small problem.....	3
Moderate problem.....	4
Big problem.....	5

(Circle one number)

34/

Do Not
Mark in
This
Space

6. How big a problem, if any, has each of the following been for you? (Circle one number on each line)

	<u>No Problem</u>	<u>Very Small Problem</u>	<u>Small Problem</u>	<u>Moderate Problem</u>	<u>Big Problem</u>	
a. Urgency to have a bowel movement	0	1	2	3	4	49/
b. Increased frequency of bowel movements.....	0	1	2	3	4	50/
c. Losing control of your stools.....	0	1	2	3	4	52/
d. Bloody stools	0	1	2	3	4	53/
e. Abdominal/ Pelvic/Rectal pain...	0	1	2	3	4	54/

7. Overall, how big a problem have your bowel habits been for you **during the last 4 weeks?**

No problem.....	1
Very small problem.....	2
Small problem.....	3
Moderate problem.....	4
Big problem.....	5

(Circle one number)

55/

8. How would you rate each of the following **during the last 4 weeks?** (Circle one number on each line)

	<u>Very Poor to None</u>	<u>Poor</u>	<u>Fair</u>	<u>Good</u>	<u>Very Good</u>	
a. Your ability to have an erection?.....	1	2	3	4	5	57/
b. Your ability to reach orgasm (climax)?.....	1	2	3	4	5	58/

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9. How would you describe the usual QUALITY of your erections **during the last 4 weeks?**

- | | |
|---|---------------------------|
| None at all..... | 1 |
| Not firm enough for any sexual activity..... | 2 |
| Firm enough for masturbation and foreplay only..... | 3 (Circle one number) 59/ |
| Firm enough for intercourse..... | 4 |

10. How would you describe the FREQUENCY of your erections **during the last 4 weeks?**

- | | |
|---|---------------------------|
| I NEVER had an erection when I wanted one..... | 1 |
| I had an erection LESS THAN HALF the time I wanted one..... | 2 |
| I had an erection ABOUT HALF the time I wanted one | 3 (Circle one number) 60/ |
| I had an erection MORE THAN HALF the time I wanted one..... | 4 |
| I had an erection WHENEVER I wanted one..... | 5 |

Do Not
Mark in
This
Space

11. Overall, how would you rate your ability to function sexually **during the last 4 weeks?**

- | | |
|----------------|---------------------------|
| Very poor..... | 1 |
| Poor..... | 2 |
| Fair..... | 3 (Circle one number) 64/ |
| Good..... | 4 |
| Very good..... | 5 |

12. Overall, how big a problem has your sexual function or lack of sexual function been for you
during the last 4 weeks?

- | | |
|-------------------------|---------------------------|
| No problem..... | 1 |
| Very small problem..... | 2 |
| Small problem..... | 3 (Circle one number) 68/ |
| Moderate problem..... | 4 |
| Big problem..... | 5 |

13. How big a problem **during the last 4 weeks**, if any, has each of the following been for you?
(Circle one number on each line)

No Very Small Small Moderate Big

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	<u>Problem</u>	<u>Problem</u>	<u>Problem</u>	<u>Problem</u>	<u>Problem</u>	
a. Hot flashes.....	0	1	2	3	4	74/
b. Breast tenderness/enlargement..	0	1	2	3	4	75/
c. Feeling depressed.....	0	1	2	3	4	77/
d. Lack of energy.....	0	1	2	3	4	78/
e. Change in body weight.....	0	1	2	3	4	79/

THANK YOU VERY MUCH!!

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Clinical Trial Protocol: IND # 133661

Study Title: PSMA-directed endoRadioThErApy of castration-reSISTAnt Prostate Cancer (RESISTA-PC). A phase II clinical trial.

Study Number: NCT03042312

IND Number: 133661

Study Phase: Phase II

Product Name: ¹⁷⁷Lu- DOTA-PSMA-617

Indication: Metastatic castration resistant prostate cancer

Principle Investigators: Ebrahim S. Delpassand, M.D. F.A.C.N.M.
Johannes Czernin, M.D.

Sponsors: Ebrahim S. Delpassand, M.D. F.A.C.N.M
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	Date
Original Protocol Date:	12/28/2016

Amendment 2 Date: 6/7/2017

Amendment 3 Date: 6/29/2017

Confidentiality Statement

This confidential document is the property of sponsors, and is provided for the use of the investigator and other designated site personnel. It may also be distributed to the ethics committee/IRB upon notification from sponsors. No unpublished information contained herein may be disclosed, except as necessary to obtain consent from persons who are considering participating in the study, without the prior written approval of sponsors.

Study Design:

Open-label, prospective, multicenter clinical trial.

Study Population:

Patients with metastatic castration resistant prostate cancer

Inclusion Criteria:

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel naive and docetaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2500/\mu\text{l}$, PLT count $\geq 100.000/\mu\text{l}$, Hb $\geq 9.9 \text{ g/dl}$ and ANC $\geq 1500 \text{ mm}^3$ for the first cycle and WBC $\geq 2.000/\mu\text{l}$, PLT count $\geq 75.000/\mu\text{l}$, Hb $\geq 8.9 \text{ g/dl}$ and ANC $\geq 1000 \text{ mm}^3$ for the subsequent cycles
8. Signing of the Informed Consent Form
9. Patients enrolling in this trial should have received either Enzalutamide or Abiraterone

Exclusion Criteria:

1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm) or other radionuclide therapy.
2. Glomerular Filtration Rate (GFR) $< 40 \text{ ml/min}$
3. serum creatinine $> 1.5 \times \text{ULN}$
4. AST and ALT $> 5 \times \text{ULN}$
5. Urinary tract obstruction or marked hydronephrosis
6. Diffuse bone marrow involvement confirmed by super-scans

Test Product; Dose; and Mode of Administration:

Randomization into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq ($\pm 10\%$, **arm 1**) or 7.4 GBq ($\pm 10\%$, **arm 2**) ^{177}Lu -PSMA-617 every 8 ± 1 weeks; RLT until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy as determined by dosimetry.

SYNOPSIS

Sponsors:

Ebrahim S. Delpassand, M.D.

Johannes Czernin, M.D.

Name of Finished Product:

^{177}Lu -PSMA-617

Name of Active Ingredient:

2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid

Study Title:

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESISTA-PC). A phase II clinical trial.

Study Number:

TBD

Study Phase:

Phase II

Primary Objective:

To assess safety and efficacy defined as >50% decline in PSA after ^{177}Lu -PSMA-617 in patients with metastatic castration resistant prostate cancer

Secondary Objectives for each treatment dose:

1. To determine maximum PSA decline.
2. To determine PSA progression-free survival (PFS), measured from start of therapy until death or PSA progression.
3. To determine radiographic PFS, measured from start of therapy until death or radiographic progression using RECIST 1.1/PCWG criteria.
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST stable disease (SD), partial response (PR) or complete response (CR).
5. To determine impact on bone pain level
6. To determine impact on quality of life
7. To determine impact on performance status (ECOG)

Study Duration:

Patients will be followed until either of the following conditions occur:

1. 24 month after the first treatment.
2. Progression by RECIST 1.1/PCWG criteria.
3. Death.

Safety Assessments:

Following laboratory tests will be performed one week before each treatment and 4 weeks after the last treatment and every 3 month thereafter:

1. Complete metabolic panel and eGFR
2. CBC

At baseline, 7 (+/- 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 week) until the end of follow up visits (24 months) patients will be called for safety interview.

Following conditions if in view point of investigators deemed study related, will result in permanent discontinuation:

i. Grade 3-4 non-hematologic toxicities with select exceptions for:

1. Grade 3 fatigue < 10 days
 2. Grade 3 nausea, vomiting, and diarrhea and grade 4 vomiting and diarrhea that persist for < 72 hours in the absence of maximum medical therapy.
 3. Asymptomatic grade 3 non-hematological laboratory abnormalities that resolve in 72 hours.
 4. Grade 3 infections that resolve under medical treatment within 10 days
- ii. AST/ALT > 3x ULN and bilirubin > 2x ULN
- iii. Grade 4 Hematological toxicities persisting >3 weeks.
- iv. Grade 3 Hematological abnormalities that do not return to baseline for > 12 weeks.

Data Safety Monitoring Board

A Data Safety Monitoring Board (DSMB) has established and will evaluate safety throughout the study. The DSMB will advise the Sponsor, Investigators and investigational sites regarding the continuing safety of study patients and the patients yet to be recruited to the study as well as maintaining validity and scientific merit of the study. The DSMB will review ongoing examinations of safety data and promptly give recommendations to continue, continue with modification, or terminate the study.

Interim safety analyses: 4 interim safety analyses will be conducted by DSMB that will be initiated at the time when 25%, 50%, 75% and 100% of the total 177Lu-PSMA treatments in the trial have been completed. The DSMB will meet and assess up-to-date safety information within two weeks of a treatment exposure rate being achieved (i.e., the point when 25%, 50%, 75% and 100% of treatments have occurred). Further patients may only be randomized two weeks after the treatment exposure rate has been reached and after a positive opinion from the DSMB.

Efficacy Assessment for each treatment arm:

Primary objective:

12 week PSA response: Proportion of patients with PSA-decline of $\geq 50\%$ at 12-weeks after the first RLT [1]

Secondary objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]
2. Time to PSA progression, for each treatment arm. [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later
 - b. for patients without PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later
3. Radiographic progression free survival (rPFS), for each treatment arm.
4. Change in Pain, Quality of Life and ECOG performance score: Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 month, for each treatment arm

Number of patients enrolled:

As per statistical evaluation, total of 200 patients will be required to have statistical power to achieve the primary endpoints of the study.

Date of Original Protocol: December 28th, 2016

Date of Most Recent Protocol Amendment (if applicable): N/A

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse event
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
AP	alkaline phosphatase
AST	Aspartate aminotransferase
AUC	Area under the plasma concentration versus time curve
BUN	Blood urea nitrogen
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CI	Confidence interval
CR	Complete response
CRF	Case report form
CT	Computed tomography
DCR	Disease Control Rate
ECOG	Eastern Cooperative Oncology Group
eGFR	estimated Glomerular Filtration Rate
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GGT	Gamma-glutamyl transferase
GH	Growth hormone

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Hct	Hematocrit
Hgb	Hemoglobin
HIPAA	Health Information Portability and Accountability Act
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intent-to-treat
LDH	Lactic dehydrogenase
MBq	MegaBequerel
mCi	milliCurie
mo	months
GBq	gigabecquerel
MR	Magnetic resonance
MRI	Magnetic resonance imaging
N/A	Not applicable
NDA	New Drug Application
PCa	Prostate cancer
PET/CT	Positron Emission Tomography/Computed Tomography
PFS	Progression-free survival
PSA	Prostate-specific antigen

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PR	Partial response
RBC	Red blood cell
RECIST	Response Evaluation Criteria In Solid Tumors
RLT	Radioligand therapy
rPFS	Radiographic progression-free survival
SAE	Serious adverse event
SAER	Serious adverse event report
SAP	Statistical analysis plan
SD	Stable disease
SE	Standard error
SPECT	Single-photon emission computerized tomography
PSMA	prostate-specific membrane antigen
US	United States
WBC	White blood cell
WHO-DD	World Health Organization Drug Dictionary

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1. Introduction

1.1 Background

According to the American Cancer Society more than 1 million people in the United States are diagnosed with cancer each year. For American males, prostate cancer is the second most common cause of cancer related death [2]. A recent publication [3] estimated the prevalence of prostate cancer as 2,219,280 in the US in 2009 and 3,072,480 in 2020, and incidence of metastatic Castration Resistant Prostate Cancer (mCRPC) as 36,100 and 42,970, respectively. Various therapies have been developed to improve survival of patients with advanced prostate cancer. However, despite such efforts currently all-cause mortality in prostate cancer has been estimated at 168,290 in 2009 and 219,360 in 2020, with 20.5% and 19.5% of these deaths, respectively, occurring in men with mCRPC.

Patients with metastatic castration-resistant prostate cancer (mCRPC) have a poor prognosis, and those patients with metastases are expected to survive ≤ 19 mo [3]. As patient disease progresses, quality of life deteriorates, and until recently, few treatment options were available. Several new therapies have shown an improvement in overall survival for patients with mCRPC who have already received chemotherapy with docetaxel (Fig. 1) [4] [5] [6, 7] [8]. The impact of these new data on clinical practice, treatment sequencing, and best care for individual patients is not yet fully established.

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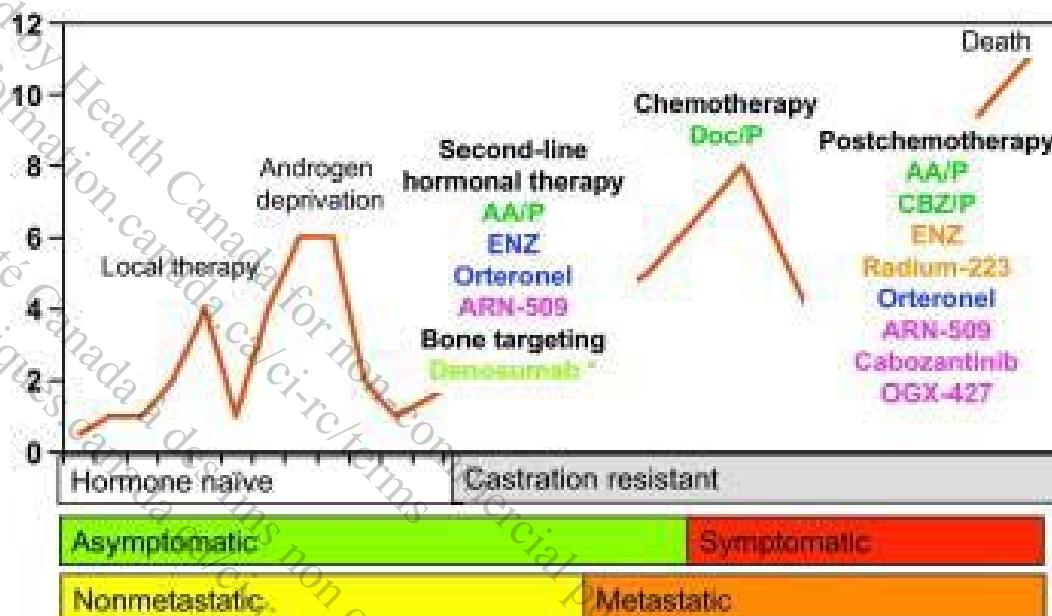


Figure 1: Current, ongoing, and future landscape in the management of castration-resistant prostate cancer. Color key: green = US Food and Drug Administration/European Medicines Agency (FDA/EMA) approved; light green = trial results in high-risk patients positive, but not approved; orange = prospective, randomized, phase 3 clinical trial completed, results positive, FDA/EMA approval awaited; blue = prospective, randomized, phase 3 clinical trial completed, results awaited; purple = promising agent, phase 3 clinical trials ongoing.* Trial results for denusomab in high risk patients positive, but not approved. AA/P = abiraterone acetate with prednisone; ENZ = enzalutamide; Doc/P = docetaxel plus prednisone; CBZ/P = cabazitaxel plus prednisone.

1.1.1. Current treatment options for metastatic castration-resistant prostate cancer: before docetaxel

Sipuleucel-T

Sipuleucel-T is an autologous vaccine consisting of individually collected antigen-presenting cells that are exposed to the fusion protein prostatic acid phosphatase and granulocyte colony-stimulating factor (GCSF), and then reinfused in the patient at weeks 0, 2, and 4. In the Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) study, median survival with sipuleucel-T was 25.8 mo compared with 21.7 mo with placebo [9]. It has to be considered, however, that only patients with a good Eastern Cooperative Oncology Group

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performance status of 0–1, asymptomatic or mildly symptomatic osseous metastases, and absence of visceral metastases were included in the trial.

Abiraterone acetate

The COU-AA-302 (Cougar 302) trial randomized 1088 men with mCRPC to receive abiraterone acetate with prednisone (AA/P) or placebo [4] with the primary end points of overall and radiographic progression-free survival (rPFS) by central review. Median overall survival was 35.3 mo and 27.2 mo in the AA/P group and in the placebo group, respectively ($p = 0.01$) [10]. Also, the co-primary end point of rPFS was significantly improved in the AA/P group, at 16.5 mo, as compared to 8.3 mo in the placebo arm ($p < 0.001$). On all secondary end points, AA/P treatment resulted in significantly improved effects.

Docetaxel/prednisone

In 2004, cytotoxic treatment with docetaxel plus prednisone (Doc/P) was the main option for treatment of mCRPC based on the TAX 327 trial [11]. The median survival was 18.9 mo versus 16.4 mo in the group of patients who received mitoxantrone/prednisone ($p = 0.009$), the 3-yr overall survival rate was 18.6% versus 13.5%, and pain response was 35% versus 22%. It has been shown recently that Doc/P is active in men with symptomatic mCRPC and especially in patients with poorly differentiated prostate cancer (PCa) (Gleason score: 8–10) [12].

Subsequent studies using combinations with docetaxel have not further improved the oncologic outcome [3]. The results of the Randomized Study Comparing Docetaxel Plus Dasatinib to Docetaxel Plus Placebo in Castration-Resistant Prostate Cancer (READY) and the Aflibercept in Combination with Docetaxel in Metastatic Androgen-Independent Prostate Cancer (VENICE) trial were disappointing [13] [11]. The median survival after docetaxel and docetaxel/dasatinib was 21.2 mo versus 21.5 mo, respectively, and the median survival after docetaxel versus docetaxel plus afilbercept was 21.1 mo versus 22.1 mo, respectively.

The differences in the patient cohorts of the Cougar 302, IMPACT, and TAX 327 trials make it evident that AA/P will be used for asymptomatic or mildly symptomatic mCRPC with a low

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metastatic burden, whereas Doc/P might be the treatment of choice in men with symptomatic mCRPC and/or a high metastatic burden as well as an undifferentiated PCa.

1.1.2. After docetaxel treatment

Docetaxel rechallenge

The scientific evidence of this approach results from large, retrospective series that identified patients who might be good candidates for re-exposure [14] [15] [16]. Patients who responded with a ≥30% decrease in prostate-specific antigen (PSA) level, maintained for at least 8 wk after first exposure to docetaxel, demonstrated a positive PSA response in about 55% to 60% of the cases during re-exposure without increasing treatment related toxicity.

Abiraterone acetate plus prednisone

AA/P versus placebo was evaluated in the Cougar 301 trial, which randomized 1195 patients with progressive mCRPC who failed docetaxel-based chemotherapy [5]. The median follow-up in the overall study population was 12.8 mo. Overall survival was significantly improved from 10.9 mo in the placebo arm to 14.8 mo in the AA/P arm ($p < 0.001$). All secondary end points were met and all end points demonstrated a significantly improved benefit for the AA/P group. Adverse events with regard to the CYP 17 blockade were observed significantly more often in the AA/P arm (55% vs 43%; $p < 0.001$).

Recently, Goodman et al. [17] demonstrated that AA/P is effective even in patients with liver or lung metastases, although to a lesser degree. The overall survival times were 12.9 mo versus 8.3 mo in the placebo group ($p = 0.022$). Albiges et al. [18] described an AA withdrawal syndrome that developed in 32% of 66 patients who had been treated for a mean period of 5.7 mo. Clayton et al. [19] presented data from a population-based study that included 187 mCRPC patients with a mean PSA serum concentration of 138 ng/ml who were treated with AA/P. The median overall survival was only 9.3 mo and might reflect the oncologic efficacy of AA/P in a real-world patient population with high metastatic burden.

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Enzalutamide (formerly MDV3100)

Enzalutamide (ENZ) acts as an androgen receptor (AR)-signaling inhibitor, and it was evaluated in the Multinational, Phase 3, Randomized, Double-blind, Placebo-controlled, Efficacy and Safety Study of Oral MDV3100 in Patients with Progressive Castration-Resistant Prostate Cancer Previously Treated with Docetaxel-Based Chemotherapy (AFFIRM) trial, which randomized 1199 mCRPC patients to receive ENZ or placebo [8]. The median follow-up was 14.4 mo and the median overall survival was 18.4 mo and 13.6 mo ($p < 0.0001$) in the ENZ group and in the placebo group, respectively, with a 37% reduction in relative risk for death. All secondary end points were met with a statistically significant benefit in the ENZ arm. With regard to safety, the ENZ group experienced fewer grade 3/4 toxicities than the placebo group (53% vs 45%). The risk of seizures was slightly elevated in the ENZ group, with a frequency of 0.6% versus 0% in the placebo group.

Recently, Scher et al. [20] demonstrated that the use of corticosteroids in parallel to ENZ not only increased grade 3/4 side effects from 34.4% to 63.3%, but it also decreased overall survival to a median 11.5 mo. These data suggest that one of the other second-line therapies, such as AA/P or cabazitaxel plus prednisone (CBZ/P), might be the drug of choice, rather than ENZ, in patients who need corticosteroids for the management of associated comorbidities. Sternberg et al. [21] reported that ENZ is equally effective in patients aged >75 yr, with a median survival time of 18.2 mo as compared to the placebo group with 13.3 mo ($p = 0.0044$). Fleming et al. [22] identified a longer disease history (7.9 yr vs 5.9 yr), a better PSA response (87% vs 52%), and a lower metastatic burden associated with long-term response of 35% and 22% after 12 mo and >18 mo, respectively. These data seem to be important for the decision-making process about the most appropriate therapy for mCRPC patients following docetaxel chemotherapy.

Cabazitaxel plus prednisone

In the XRP6258 Plus Prednisone Compared to Mitoxantrone Plus Prednisone in Hormone-Refractory Metastatic Prostate Cancer (TROPIC) trial, 755 patients with mCRPC who

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progressed during or after docetaxel-based chemotherapy were prospectively randomized to receive CBZ/P or mitoxantrone/prednisone (MP) at 21-d intervals for 10 cycles [5]. The primary end point was achieved and CBZ/P treatment resulted in a median overall survival of 15.1 mo in the CBZ/P compared to 12.7 mo in the mitoxantrone/prednisone group (hazard ratio [HR]: 0.70; 95% confidence interval [CI], 0.59–0.83; $p < 0.0001$). All secondary end points of the trials were reached and they were in favor of CBZ. The most common side effects were neutropenia (CBZ/P group: 82% vs MP group: 58%), leukopenia (CBZ/P group: 68% vs MP group: 42%), and anemia (CBZ/P group: 11% vs MP group: 5%). Diarrhea was the most common non-hematologic side effect and occurred in 6% of the CBZ/P group and <1% of the MP group.

On the other hand, the German compassionate use program (CUP) included 111 patients with mCRPC who met the inclusion criteria of the TROPIC trial; the frequency of neutropenia, leukopenia, and anemia decreased to 7.2%, 9.0%, and 4.5%, respectively [23]. Grade 3/4 gastrointestinal toxicity was observed in only 0.9% of the patients. The most likely reason for the improved toxicity profile is the experience of the investigators, guideline-compliant application of GCSF even at cycle 1, and preventive measures with regard to the treatment of diarrhea.

Recently, Heidenreich et al. [24] analyzed the European CUP, including 746 mCRPC patients, with regard to the frequency and management of adverse events in senior adults. In that study, 325 (43.5%) patients were aged ≥ 70 yr and 145 (19.4%) men were ≥ 75 yr. The type and the frequency of grade 3/4 side effects did not differ significantly between the younger and the older patients except that the frequency of grade 3/4 neutropenia was slightly higher in the group of men aged ≥ 75 yr (19.7% vs 15%). Furthermore, GCSF was used more often at cycle 1 (58.5% vs 47%) and throughout CBZ/P treatment (66.8% vs 58%) in the ≥ 75 age group versus the <70 age group. In their analysis, Heidenreich et al. [24] developed a risk model to predict grade ≥ 3 neutropenia and/or neutropenic complications based on a multivariate analysis. Age ≥ 75 yr, cycle 1, and neutrophil count $<4000/\text{mm}^3$ before CBZ injection were associated with neutropenic complications. It has to be mentioned that even in the presence of

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these risk factors, prophylactic application of GCSF significantly reduced the risk of neutropenic complications by 30% (odds ratio: 0.70; 95% CI, 0.50–0.99; $p = 0.04$).

Bone-targeting agents

More than 90% of patients with CRPC have bone metastases, which are a major cause of death, disability, and decreased quality of life, as well as increased cost of treatment [25]. Zoledronic acid and the receptor activator of nuclear factor κ B (RANK) ligand inhibitor denosumab are the two US Food and Drug Administration–approved bone-targeting agents in the management of CRPC [3].

In a phase 3 study, the median time to first on-study, skeletal-related event was 20.7 mo with denosumab compared with 17.1 mo with zoledronic acid (HR: 0.82; 95% CI, 0.71–0.95; $p = 0.0002$ for noninferiority; $p = 0.008$ for superiority) [26]. In a recent, prospective, randomized, double-blind, placebo-controlled trial, Smith et al. [27] evaluated the therapeutic efficacy of denosumab 120mg every week versus placebo in 1423 men with nonmetastatic CRPC and aggressive PSA kinetics (PSA level >8.0 ng/ml and/or PSA doubling time <10 mo). The median time to first bone metastases was significantly prolonged by 4.3 mo (29.5 mo vs 25.2 mo; $p = 0.028$). Bone metastases-free survival was significantly improved by 16%, 23%, and 29% in patients with a PSA doubling time of <10 mo, <6 mo, and <4 mo, respectively.

Radium-223

Radium-223 is a radiopharmaceutical that acts as a calcium mimic and targets new bone growth in and around bone metastases via heavy alpha particles that have an ultrashort range of $<100\mu\text{m}$. A Phase 3 Study of Radium-223 Dichloride in Patients with Symptomatic Hormone Refractory Prostate Cancer with Skeletal Metastases (ALSYMPCA), which included 921 CRPC patients, the median overall survival was 14.9 mo in patients treated with radium-223 compared with 11.3 mo in the placebo group (HR: 0.695; 95% CI, 0.581–0.8732; $p < 0.0001$) [7].

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1.1.3. New and emerging developments

Agents targeting steroidogenesis

Orteronel (TAK-700) selectively blocks 17,20-lyase, resulting in fewer mineralocorticoid effects than AA [28]. In the phase 2 portion of a dose-finding study, Orteronel (TAK-700) 400mg twice daily with prednisone 5mg twice daily resulted in a reduction in PSA level $\geq 50\%$ in 52% of the 96 chemotherapy-naïve mCRPC patients at 12 wk. There are two ongoing phase 3 clinical trials in the prechemotherapy ($n = 1454$) and postchemotherapy ($n = 1083$) landscape of mCRPC that are evaluating the oncologic activity of orteronel. Both trials have completed recruitment.

Galeterone (TOK-001) has combined activity: It inhibits the human CYP17 enzyme, it has pure antagonistic activity toward the AR, and it inhibits the binding of androgens to both mutant and wild-type AR [29]. In the Androgen Receptor Modulation Optimized for Response (AMORI) trial, 49% of chemotherapy-naïve mCRPC patients experienced a PSA-level reduction of $\geq 30\%$, and a $\geq 50\%$ reduction was achieved by 22% [30]. Despite the absence of steroid co-treatment, no adrenal mineralocorticoid excess was observed and a phase 2 trial is underway.

Androgen-receptor blocking agents

ARN-509 is a full antagonist to AR overexpression: It inhibits androgen-dependent gene description, and it impairs nuclear translocalization and DNA binding of AR [31]. Currently, three prospective randomized phase 3 clinical trials are underway including (1) patients with high-risk and nonmetastatic CRPC, (2) treatment-naïve patients with mCRPC, and (3) patients with progression following AA/P treatment. Preliminary results have been presented for the first two groups and a $\geq 50\%$ decline in PSA level was achieved in 91% of patients with high-risk and nonmetastatic CRPC and in 88% of treatment-naïve patients with mCRPC. The most common side effects were tolerable fatigue and gastrointestinal events.

ODM-201 is another antiandrogen with similar mechanisms of actions as described for ENZ and ARN-509 [31]. The potential advantage of ODM-201 is that it does not cross the blood–

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brain barrier and so might prevent the development of seizures. ENZ-4176 is a novel, nucleic acid-based antisense oligonucleotide against AR, which results in selective and specific downregulation of AR mRNA and protein.

Heat shock proteins

Heat shock proteins (HSPs) have been identified as AR coactivators and chaperone proteins that are increased in PCa cell lines after castration [32]. Quite recently, antisense oligonucleotides targeting HSP27 were evaluated in a phase 2 clinical trial including 72 patients chemotherapy-naïve mCRPC patients who received OGX-427 plus prednisone versus prednisone alone. At 12 wk, 71% and 40% of the patients were progression-free after OGX-427 or prednisone, respectively. A decline of $\geq 50\%$ in PSA level was observed in 50% and 20% in the OGX-427 group and in the prednisone group, respectively. Furthermore, measurable disease response occurred in 44% and 0% of the OGX-427 group and the prednisone group, respectively.

1.1.4 Targeted therapies

Cabozantinib

Cabozantinib is another promising bone-targeting agent that inhibits both vascular endothelial growth factor and met proto-oncogene (hepatocyte growth factor receptor; MET). In a prospective, randomized, placebo-controlled, phase 2 clinical trial, 171 mCRPC patients were enrolled to receive cabozantinib (100mg daily) or placebo [33]. Random assignment was halted early based on the observed activity of cabozantinib. Respectively 5% and 75% of patients treated with cabozantinib had a confirmed partial response and stable disease. The median progression-free survival was 29.7 wk, 23.9 wk, and 5.9 wk for patients who were docetaxel naïve, docetaxel pretreated, and on placebo treatment ($p < 0.001$), respectively. Interestingly, PSA changes did not correlate with the antitumor effects in bone metastases and soft-tissue lesions. However, patients with complete resolution ($n = 14$; 12%) or partial resolution ($n =$

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65; 56%) of bone scans experienced significantly better response rates to soft-tissue metastases as compared to men with stable or progressing bone scans (81% vs 61%), and they also experienced longer progression-free survival rates at 6 mo (56% vs 48%, respectively). Cabozantinib has significant antitumor activity and a well-tolerated toxicity profile, so it might be well integrated into the therapeutic armamentarium to treat mCRPC.

Targeted radionuclide Therapy

Over the past several decades, numerous combined diagnostic and therapeutic radioligands (Theranostics) were designed to target receptors on the cancer cell surface. Antibodies (whole or small fragments), small molecules, peptides with affinities to receptors (agonist or antagonist) have demonstrated in vivo efficacy for targeting cancers based on up-regulated antigens or receptor populations. This approach, also called radioligand therapy (RLT), presents several advantages over conventional chemotherapy. The expression of the antigens or special receptors can be identified by a diagnostic probe before exposing patients to therapeutic doses of these agents allowing identification of suitable subjects for therapeutic procedures and preventing unnecessary exposure of the patients to radiation without significant benefit. This approach allows the physician to select only those patients with high expression of the target prior to treatment. Since the unused radioactive materials are excreted from the body, RLTs are generally well tolerated with no significant or generally reversible or manageable side effects as has been demonstrated for ¹⁷⁷Lu-DOTATATE treatment in patients with neuroendocrine tumor [34].

Prostate cancer demonstrates high expression levels of prostate-specific membrane antigen (PSMA) on its cell surface. Thus PSMA has become a biomarker for prostate cancer [35] [36] and has attracted significant interest as a target for the imaging [37] [38] and therapy [39, 40]. In particular, development of small urea-based PSMA ligands have received significant interest due to their high affinity for PSMA [41] [42]. The urea-based PSMA ligands were modified to deliver a variety of radio-imaging nuclides for both PET and SPECT. Gallium (⁶⁸Ga) labeled urea-based PSMA ligands have been developed as diagnostic agents and studied by several groups [43] [44]. More recently a Lutetium (¹⁷⁷Lu) labeled urea based PSMA ligand

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(DOTA PSMA or PSMA 617) were evaluated in preclinical and clinical phase. Characteristics of ^{177}Lu labeled PSMA are described below.

1.2 Characteristics of ^{177}Lu -DOTA-PSMA (^{177}Lu -PSMA-617)

Lutetium (^{177}Lu)-DOTA PSMA has three components: PSMA is the targeting vector, DOTA (1, 4, 7, 10-tetraazacyclododecane-1, 4, 7, 10-tetraacetic acid) is a radiometal chelator and a linking group, and ^{177}Lu is the beta emitter that upon internalization delivers radiation to the nucleus of tumor cells to cause DNA damage [43] [44, 45]. The targeting vector utilizes glutamyl-lys sequence which is an inhibitor capable of binding to the domain of PSMA. These components have been previously used in human subjects and in medical research.

1.3 Background of Drug Development

There is substantial previous pre-clinical and clinical experience with ^{177}Lu -PSMA-617 published in peer reviewed medical literature from multiple medical centers throughout the world. Sponsors are relying on studies published in the peer reviewed medical journals for preclinical and preliminary clinical information. Summary of such reports is given below.

1.3.1 Preclinical Studies.

Martina Benesova et al. [46] performed a preclinical evaluation of radiolabeled PSMA-617. PSMA-617 was synthesized by solid phase peptide synthesis. PSMA-617 can be labeled with ^{177}Lu and Ga-68. Both in vivo and vitro studies were performed using LNCaP cell lines expressing PSMA. PSMA-617 showed highest inhibition potency $K_i = 6.91 \pm 1.32$ for Lu complex; $6.40 \pm 1.02\text{nM}$ for Ga complex. PSMA-617 showed higher specific internalization in LNCaP cells.

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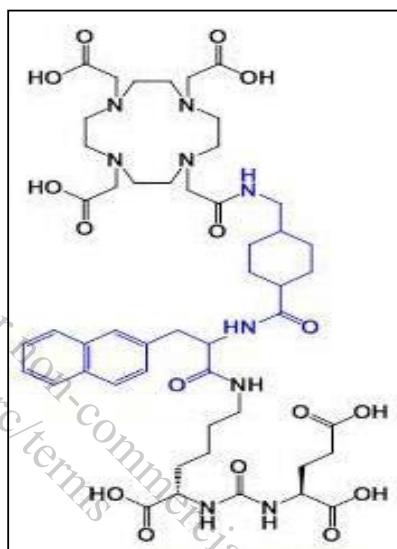


Figure 2: Structure of PSMA 617. Chemical Name 2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-[(2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid.

The i.v. administered ¹⁷⁷Lu-PSMA-617 effectively cleared the blood by 1 hr. Clearance of radioactivity occurred largely through the renal system. As a result of this, the kidneys exhibited significant uptake $137.2 \pm 77.8\%$ ID/g; this could be effectively blocked ($0.85 \pm 0.22\%$ ID/g) by co-injection of PMPA [2 mg/kg], a high affinity inhibitor of PSMA. At 24 hr ¹⁷⁷Lu-PSMA-617 shows rapid clearance from the kidney $2.13 \pm 1.36\%$ ID/g highlighting its potential use as a theranostic agent. At 1 hr time point ¹⁷⁷Lu-PSMA-617 displayed good in vivo tumor targeting with $11.20 \pm 4.17\%$ ID/g. Accumulation in tumor was PSMA specific with reduction to $0.64 \pm 0.07\%$ ID/g by coinjection of 2-PMPA. At 24 h post injection $10.58 \pm 4.50\%$ ID/g uptake was retained in the tumor tissue. For all other non-target tissues, ¹⁷⁷Lu-PSMA-617 demonstrated rapid clearance. The ratio of tumor to blood was 1058; tumor to muscle was 529 at 24 hr post injection. These favorable pharmacokinetics are crucial for imaging and therapy. The detailed biodistribution results are summarized in Figure 3. ⁶⁸Ga-PSMA 617 showed similar uptake in the LnCaP tumors ($11.20 \pm 4.17\%$ ID/g). It also shows similar pharmacokinetic clearance profile compared with ¹⁷⁷Lu-PSMA-617.

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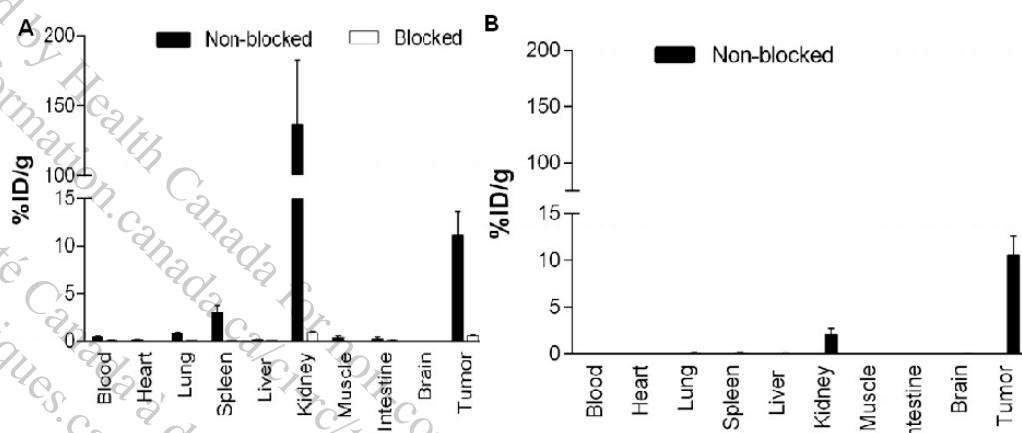


Figure 3: Distribution assay of ^{177}Lu -PSMA-617 in BALB/c mice with LNCap xenografts at 1 h (a) and 24 h (B) post injection.

In summary authors concluded the present radiotracer is suitable for theranostic application in human prostate cancer.

1.3.2 Clinical Studies

Current literature is available to evaluate ^{177}Lu -PSMA-617 therapeutic role in clinical management of patients with prostate cancers. The studies presented in this section were chosen based on novelty of the approach (initial report of application, variables for analyses) and/or the number of patients included.

Clemens Kratochwil et al. [^{177}Lu]Lutetium-labelled PSMA ligand-induced remission in a patient with metastatic prostate cancer. Eur J Nucl Med Mol Imaging 2015; 42:6 ;987-988. [47]

Study Design: First reported application of ^{177}Lu -PSMA-617 for treatment of a patient with mCRPC. Patient had proven PSMA expression and PSA of 38.0 ng/ml prior to treatment and has received 7.4 GBq of ^{177}Lu -DKFZ-617 in 2 cycles 3 months apart.

Toxicity: No potential side effects were reported in this study.

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Results: After the radiotherapy ^{177}Lu -PSMA-617, PSA level of patient decreased to 4.6 ng /ml. PET/CT images showed no signs of metastases lesions either shrunk or were undetectable.

Conclusion: Authors are planning to conduct multicenter a clinical trial as soon as possible to examine clinical potential of ^{177}Lu -PSMA-617.

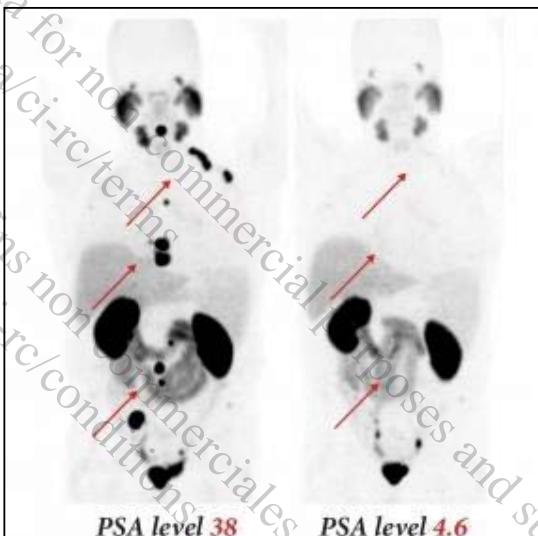


Figure 4: Above Image has recently awarded as image of Year Award and the Berson-Yalow Award at the 2015 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) in Baltimore, USA.

Hojjat Ahmadzadehfar et al. Early side effects and first results of radioligand therapy with ^{177}Lu -DKFZ-617 PSMA of castrate-resistant metastatic prostate cancer: a two-center study. EJNMMI Research 2015; 5:36. [48]

Study Design: A total of 10 consecutive hormone and /or chemo refractory PCa patients with distant metastases and progressive disease with rising PSA levels were recruited in this study. All patients had prior history or were under therapy with enzalutamide and/or abiraterone. Four patients had received ^{223}Ra -dichloride (1-4 cycles). All 10 patients underwent with ^{68}Ga -PSMA HBED-CC (^{68}Ga -PSMA) PET /CT prior to therapy to evaluate PSMA expression. Ten patients were treated with range of 4.1-6.1 GBq dose of ^{177}Lu -DKFZ-617 PSMA. All patients

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were treated with single dose of ¹⁷⁷Lu-PSMA. The mean and median PSA levels prior to therapy were 339.4 and 298.5 ng/ml. Complete blood chemistry, renal and liver function tests were performed a day before and 2 after the radiotherapy. Patients were followed via telephone every week for safety assessment.

Toxicity: No patient experienced any side effects immediately after injection of ¹⁷⁷Lu-DKFZ-617 PSMA. Relevant hematotoxicity (grade 3 or 4) occurred 7 weeks after the administration in just one patient. The same patient showed a leucopenia grade 2. Two patients showed a disturbance of only 1 hematologic cell line, whereas one patient showed a reduction of grades 1 and 2 in leucocytes and thrombocytes, respectively. Six patients did not show any hematotoxicity during the 8 weeks after therapy. There was no relevant nephrotoxicity (grade 3 or 4).

Results: Eight weeks after the therapy, seven patients (70 %) experienced a PSA decline, of which six experienced more than 30 % and five more than 50 %. Three patients showed a progressive disease according to the PSA increase.

Conclusions: ¹⁷⁷Lu-DKFZ-617 PSMA radiotherapy with single dose for the treatment of metastatic prostate cancer patients without any other therapy option is safe and seems to have a low early side-effect profile with evidence of positive response to the therapy according to PSA decline in 70 % of patients. The authors also stated ¹⁷⁷Lu-DKFZ-617 PSMA has potential to exhibit suitable agent for radionuclide radiotherapy.

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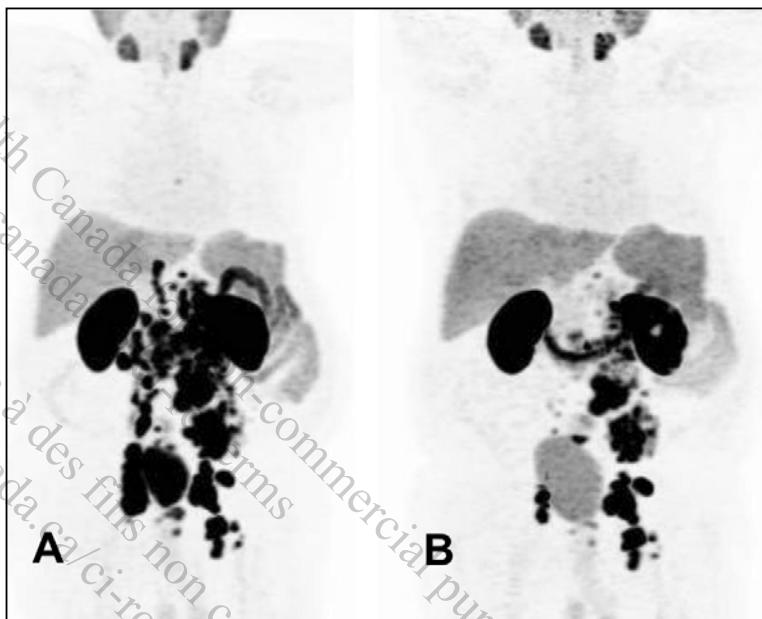


Figure 5: A 74-year-old patient with hormone- and chemo-refractory prostate cancer underwent PSMA PET/CT (a), which showed diffuse abdominal and iliac lymph node metastases. The patient underwent RLT with 5.7 GBq Lu-PSMA. The PSA level was at the time of the therapy 790 ng/ml. (b) A partial response 7 weeks after RLT with 63 % PSA decline; at this time, the PSA level was 293 ng/ml

Clemens Kratochwil, et al. PSMA-targeted radionuclide therapy of metastatic castration-resistant prostate cancer with Lu-177 labeled PSMA-617 J Nucl Med March 16, 2016 [49]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed on 30 patients with PSMA positive tumors were enrolled in this study. 30 patients were treated with 1-3 cycles of ¹⁷⁷Lu-PSMA-617. Pharmacokinetic and radiation dosimetry was also evaluated during the course of the study.

Results: 21 of 30 patients showed response to therapy; for 13/30 the PSA decreased >50%. After 3 cycles 8/11 patients achieved a sustained PSA response (>50%) for over 24 weeks. ¹⁷⁷Lu-PSMA-617 showed fast renal wash out within 48 hours of injection. Patients showed

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mild nausea, fatigue and Xerostomia (<10%) over a period of time. No acute hematotoxicity was observed during the study. Dosimetry results revealed that ¹⁷⁷Lu-PSMA-617 has an exposure of 0.75 Gy/GBq for kidney 0.03 Gy/GBq red-marrow, 1.4 Gy/GBq salivary glands and 6-22 Gy/GBq for tumour lesions.

Conclusion: Based on the results authors concluded that targeted radioligand therapy with ¹⁷⁷Lu-PSMA-617 is safe and promising therapy option for metastasized castrate resistant prostate cancer.

Ahmadvazehfar H, et al. Therapeutic response and side effects of repeated radioligand therapy with ¹⁷⁷Lu-SMA-DKFZ-617 of castrate-resistant metastatic prostate cancer. Oncotarget. 2016 Feb 8. doi: 10.18632/oncotarget.7245. [50]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed in 24 hormone and/or chemo-refractory PC patients. Forty-six cycles of Lu-PSMA were performed. Side effects and response rate was assessed.

Results: Eight weeks after the first cycle of ¹⁷⁷Lu-PSMA-617 therapy 79.1% experienced a decline in PSA-level. Eight weeks after the second cycle of Lu-PSMA therapy 68.2% experienced a decline in PSA relative to the baseline value. Apart from two cases of grade 3 anemia, there was no relevant hemato- or nephrotoxicity (grade 3 or 4).

Conclusion: ¹⁷⁷Lu-PSMA-617 is a safe treatment option for metastatic PC patients and has a low toxicity profile. A positive response to therapy in terms of decline in PSA occurs in about 70% of patients.

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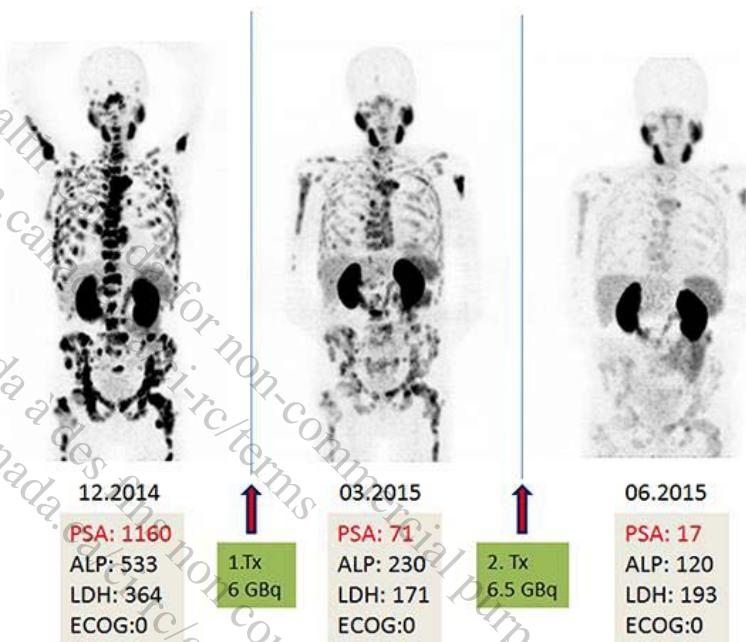


Figure 6: A 75-year-old patient with diffuse bone and lymph node metastases as well as local recurrence (left MIP image). History of chemotherapy and therapy with abiraterone, PSA elevation under enzalutamide. The patient underwent PSMA therapy as the last possible option. Continuing PSA decline and partial response in Ga-PSMA PET images after the first (middle MIP image) and second cycles (right MIP image)

Madhav Prasad Yadav, et al. ¹⁷⁷Lu-DKFZ-PSMA-617 therapy in metastatic castration-resistant prostate cancer: safety, efficacy, and quality of life assessment. Eur J Nucl Med Mol Imaging. 2016 Aug 10. [51]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed in 31 patients with progressive disease despite second-line hormonal therapy and/or docetaxel chemotherapy. Patients underwent 1 to 4 cycles after a ⁶⁸Ga-PSMA-HBED-CCP ET/CT for inclusion (mean activity 5069 ± 1845 MBq). Hematological, kidney function, liver function tests, and serum PSA levels were recorded before and after therapy at 2 weeks, 4 weeks, and 3 month intervals. Biochemical response was assessed with trend in serum PSA levels. Metabolic response was assessed by PERCIST 1 criteria. Clinical response was assessed by visual analogue score

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(VASmax) analgesic score (AS), Karanofsky performance status (KPS), and toxicity and response criteria of the Eastern Cooperative Oncology Group (ECOG) criteria.

Results: Biochemical response in terms of complete response (CR), partial response(PR), stable disease (SD), and progressive disease (PD) was observed in 2/31, 20/31, 3/31, and 6/31 had, respectively. Mean VASmax and mean analgesic scores decreased from 7.5 to 3 and 2.5 to 1.8 after therapy, respectively Mean KPS and mean ECOG performance status score improved from 50.32 to 65.42 after therapies, respectively. Two patients experienced grade I and grade II hemoglobin toxicity each. None of the patients experienced nephrotoxicity or hepatotoxicity.

Conclusion: ¹⁷⁷Lu-DKFZ-PSMA-617 radionuclide therapy is a safe and effective approach in the treatment of mCRPC patients.

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1.3.3 Sponsors Experiences

1.3.3.1 Preclinical Toxicity Studies

The aim of study was to evaluate toxicity of PSMA-617. PSMA-617 applied once weekly by intravenous administration to male rats over 22 days. The animals were treated with 40, 160 or 400 µg of PSMA-617/kg b.w. by tail vein intravenous bolus injection on test days 1, 8, 15 and 22. The control group was treated with physiological saline. No deaths were noted. No signs of local or systemic intolerance reactions were observed. Body weight and body weight gain, food intake, and drinking water consumption were not influenced. No test item-related changes were noted for the hematological and biochemical parameters, the urinary status, the eyes and optic region, the auditory acuity, the relative and absolute organ weights, and the myeloid: erythroid ratio. No test item-related abnormalities were noted during macroscopic inspection at necropsy and at histopathological examination.

Under the test conditions of this study, the no-observed-adverse-effect-level (NOAEL) was 400 µg PSMA-617 / kg b.w. administered once weekly by intravenous bolus injection. This dose was the highest dose tested. Detailed description of this study is attached in appendix 1.

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1.3.3.2 Summary of Human Studies - German Multicenter Experience

Rahbar K, et al. German multicenter study investigating ¹⁷⁷Lu-PSMA-617 radioligand therapy in advanced prostate cancer patients. J Nucl Med. 2016 [52]

Study design: Retrospective acquisition and pooling of data for toxicity and PSA response in patients after ¹⁷⁷Lu-PSMA-617 RLT performed in Germany until July 2015 was initiated by the German Society of Nuclear Medicine for research purpose. The following contains a summary of the collected data. 145 patients with metastatic castration-resistant prostate cancer received a median of two cycles (range 1 to 4) of ¹⁷⁷Lu-PSMA RLT at twelve German Nuclear Medicine Clinics. Data on safety and efficacy were reported. Table 1 lists the **administered ¹⁷⁷Lu-PSMA-617 activity** for this study cohort.

Table 1. Administered ¹⁷⁷Lu-PSMA-617 activity (n = 248 RLT cycles)

administered activity (GBq)	Cycle 1	Cycle 2	Cycle 3	Cycle 4
≤ 3.5	9	3	0	1
> 3.5 – 4.5	32	14	2	0
> 4.5 – 5.5	16	12	9	0
> 5.5 – 6.5	71	37	14	2
> 6.5	17	8	1	0

Results:

A. Toxicity: Nuclear medicine physicians responsible for ¹⁷⁷Lu-PSMA RLT and subsequent follow-up reported potentially related or unrelated adverse events based on a standard template. In addition toxicity was determined by baseline and follow-up findings for serum creatinine, AST, ALT, white blood cell count, hemoglobin and platelet count for 121 of 145 (83%) patients. The follow-up period for adverse events was 2 to 30 weeks. Reported toxicity sorted by organ system is given in Table 1. Grade 3-4 anemia occurred in 15 (10%) patients and grade

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3-4 thrombocytopenia occurred in 5 (4%) patients. The rate of grade 3-4 events was low for all other categories (0 to 3 patients; 0 to 2%).

There were fewer hematologic adverse events when compared to patients with metastatic castration resistant prostate cancer treated with placebo or ²²³Ra within the ALSYMPCA trial [7] (grade ≥ 3 anemia: 14% in the placebo and 13% in the ²²³Ra group; grade ≥ 3 thrombocytopenia: 3% in the placebo and 7% in the ²²³Ra group). Toxicity data thus indicate a favorable safety profile for RLT using 2-7 GBq ¹⁷⁷Lu-PSMA per cycle in patients with metastatic castration resistant prostate cancer.

Majority of patients received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle. Toxicity rates were comparably low: 9 of 71 (13%) patients with 5.5 – 6.5 GBq and 3 of 17 (18%) patients with >6.5 GBq during the first RLT developed grade 3-4 toxicity.

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Table 2. Adverse events after ¹⁷⁷Lu-PSMA-617
as determined by blood tests (n=121) or physician reports (n=145)

Organ system	Category	Evaluated for N	All grades	Grade 3-4
Blood and lymphatic disorders				
	Leukopenia	121	48 (40%)	4 (3%)
	Anemia	145	50 (34%)	15 (10%)
	Thrombocytopenia	121	38 (31%)	5 (4%)
Gastrointestinal disorders				
	AST elevation	121	27 (19%)	0 (0%)
	ALT elevation	121	11 (8%)	0 (0%)
	Xerostomia	145	11 (8%)	0 (0%)
	Nausea	145	9 (6%)	0 (0%)
	Dysgeusia	145	6 (4%)	0 (0%)
	Ascites	145	2 (1%)	0 (0%)
	Biliary obstruction	145	0 (0%)	1 (1%)
General disorders				
	Fatigue	145	19 (13%)	1 (1%)
	Pain	145	5 (3%)	0 (0%)
	Ileus	145	1 (1%)	0 (0%)
Urinary disorders				
	Renal failure	121	14 (12%)	0 (0%)
	Urinary tract infection	145	1 (1%)	0 (0%)
Cardiovascular disorders				
	Edema	145	2 (1%)	0 (0%)
	Lung embolism	145	0 (0%)	3 (2%)

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Respiratory, thoracic and mediastinal disorders				
	Pleural effusion	145	1 (1%)	0 (0%)
	Dyspnea	145	1 (1%)	0 (0%)
Neurologic disorders				
	Vertigo	145	1 (1%)	0 (0%)
	Stroke	145	0 (0%)	2 (1%)
Musculoskeletal disorders				
	Bone fracture	145	0 (0%)	3 (2%)

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Efficacy

Serial PSA levels at baseline and follow-up were recorded for 99 of 145 patients (68%).

Response was expressed as percent change in serum PSA from baseline to the lowest PSA level measured at follow-up (best PSA response).

Over the entire follow-up period 45 of 99 (45%) patients demonstrated a PSA decline $\geq 50\%$ and were considered biochemical responders. Any PSA decline occurred in 59 of 99 (60%) patients (Figure 7). After the first cycle a PSA decline $\geq 50\%$ occurred in 40 of 99 (40%), any PSA decline in 65 of 99 (66%) patients (Figure 8A). After the second therapy cycle of ^{177}Lu -PSMA-617 RLT a PSA decline $\geq 50\%$ occurred in 35 of 61 (57%) and any PSA decline in 44 of 61 (72%) patients (Figure 8B). Patients receiving a third or fourth cycle of therapy showed a PSA decline $\geq 50\%$ in 13 of 20 (65%) and 3 of 3 (100%) patients, respectively.

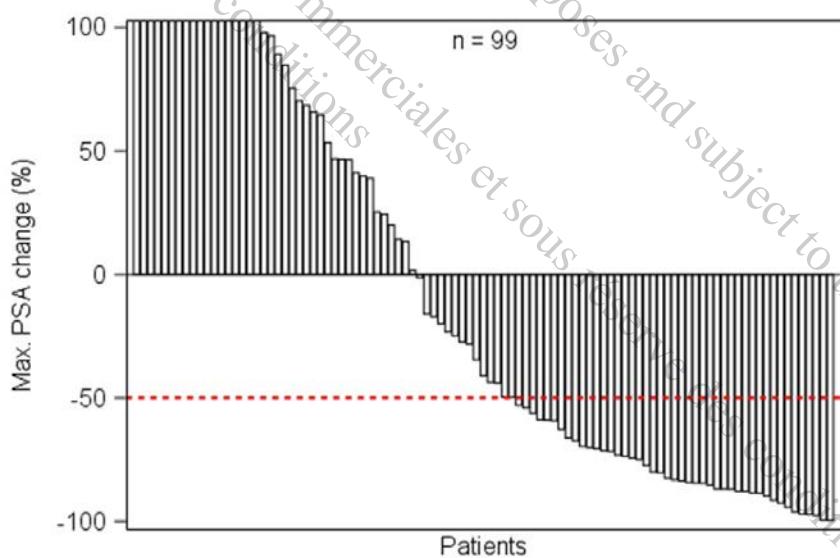


Figure 7. Waterfall plot of maximum PSA change (%) from baseline over total follow-up period. PSA increase of more than 100% was cropped due to simplification.

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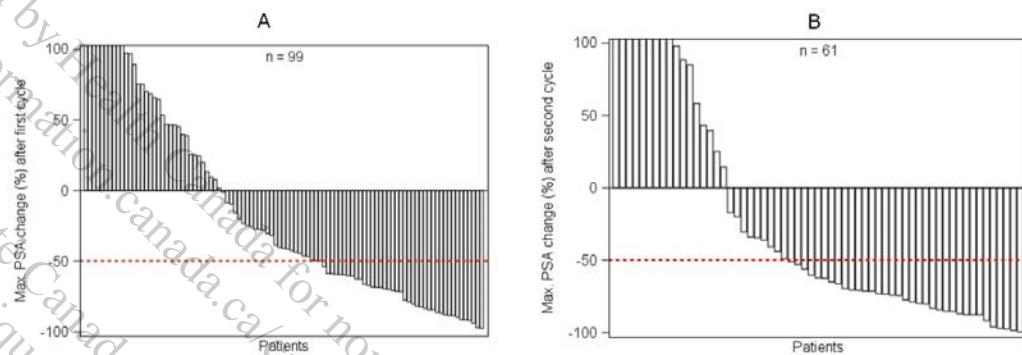


Figure 8. Waterfall plots of maximum PSA change (%) after the first cycle (A) and after the second cycle (B). PSA increase of more than 100% was cropped due to simplification.

Response rate was higher than the rate in patients with metastatic castration resistant prostate cancer treated with abiraterone (best PSA response >50% after abiraterone plus prednisone: 43% (25 of 58) patients) [53]. Data thus indicate good efficacy for ¹⁷⁷Lu-PSMA RLT in patients with metastatic castration resistant prostate cancer. Response rates were not significantly associated with mean activity per cycle ($p=0.46$) or cumulative activity after two cycles ($p=0.22$).

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2. Study Objectives

Primary Objectives:

1. To assess the clinical safety of ¹⁷⁷Lu-PSMA-617 by evaluation of adverse events (AE) using the Common Terminology Criteria for Adverse Events (CTCAE)
2. To assess the efficacy as defined by proportion of patients with PSA-response of ≥50% decline at 12-weeks from baseline

Secondary Objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]
2. To determine the time to PSA progression, separate for treatment doses: time from inclusion to date until PSA progression or death (whichever occurs first) [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later
 - b. for patients without PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above baseline
3. To determine radiographic Progression-free Survival (rPFS), for each treatment dose: time from inclusion to date when first site of disease is found to progress or death (whichever occurs first)
 - a. Nodal and visceral disease is evaluated on cross-sectional imaging using RECIST 1.1/PCWG criteria
 - b. Bone metastases are evaluated using bone scintigraphy and new lesions have to be confirmed on a second scan (2+2 rule) using PCWG criteria
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST 1.1/PCWG criteria stable disease (SD), partial response (PR) or complete response (CR).
5. Change in Pain and Quality of Life: Pain and “Epic-26” Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 mo. Pain response will be determined in accordance with PCWG [1].
6. Change in ECOG Performance Score

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3. Investigational Plan

3.1 Overall Study Design and Dosing of Targeted PSMA Radioligand Therapy (RLT)

This is a open-label, multicenter, prospective trial. Upon inclusion patients will be randomized into two treatment doses. RLT will be performed by repeated i.v. application of 6.0 GBq ($\pm 10\%$) or 7.4 GBq ($\pm 10\%$) ^{177}Lu -PSMA-617 every 8±1 weeks until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy. All doses after labeling will be presented in buffered solution for intravenous injection.

In total, 200 subjects with histologically proven prostate cancer and mCRPC will be enrolled. Salivary protection will be accomplished by applying ice pack starting 30 minutes prior to infusion of radiopharmaceutical and will continue for 4 hours. Subjects will be recruited at up to 3 Nuclear Medicine sites selected for this project. Each subject will undergo a screening visit within 14 days prior to receiving study drug.

Dosimetry will be performed according to chapter 8.4.3 by Prof. Dr. [Name],

Universitätsklinikum Würzburg Germany - Klinik und Poliklinik für Nuklearmedizin to determine dose to the kidneys. Treatment will be continued until either of the following conditions apply:

- PSA/radiographic progression as defined above
- Completion of four RLT cycles
- 23 Gy kidney dose would be exceeded by the next cycle as estimated by dosimetry
- patient withdrawal (e.g. appearance of intolerable adverse events)

Primary objectives of the study is safety and efficacy.

Efficacy is determined by PSA response rate: Patients with baseline to follow-up decline in tumor marker level (PSA) $\geq 50\%$ at 12 weeks will be considered responders.

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For safety assessment, vital signs will be measured within 20 minutes before and for up to an hour after administration of ¹⁷⁷Lu-PSMA-617. A blood sample will be collected within 48 hours before the injection, for assessing clinical chemistries and hematology. Hematologic laboratory testing (CBC) will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until patient is progressed. CBC will be performed every 7 days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery which is defined as grade 2 toxicity or lower. Chemistry will be evaluated 4 weeks after each therapy and within one week prior to the next treatment to evaluate eligibility to receive the next cycle and then every 3 month for 24 months or until the patient is progressed. CTCAE v 4.0 will be used to evaluate renal toxicity. For more information, please refer to the Schedule of Events ([Appendix 2](#)).

3.2 Rationale for Study Design

3.2.1 Rationale for a regimen with multiple therapy cycles

Activity given during targeted radionuclide therapy is limited by radiation dose to healthy organs. Based on dosimetry radiation dose to healthy organs and subsequent maximal cumulative activity can be calculated. To obtain optimal safety margin maximal cumulative activity is not given in one treatment session but approached by application of a defined fraction of this activity in several cycles. The administration of a standard activity over several treatment cycles allows for early and individual estimation of radiation dose and tolerability. The efficacy and safety of a sequential approach was proven in patients with ²²³Ra therapy for metastatic castration-resistant prostate cancer (mCRPC) [7] and in patients with ¹⁷⁷Lu-DOTATATE therapy for midgut neuroendocrine tumor (NET) [54] each in prospective, double-blind, randomized, international, and multicenter phase III trials. Based on this evidence targeted PSMA Radioligand Therapy (RLT) will be performed by sequential applications of ¹⁷⁷Lu-PSMA-617 with treatment-free intervals.

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3.2.2 Rationale for eight weeks interval

Highest level of evidence for subacute adverse events after radionuclide therapy was published for patients with non-Hodgkin's lymphoma. Witzig et al analyzed safety and efficacy of ^{90}Y -Ibritumomab Tiuxetan in 73 patients in a prospective Phase III randomized trial. This study reports neutrophil, platelet and hemoglobin nadir approximately six weeks after application of the beta emitter [55]. Based on this study ^{177}Lu -PSMA-617 RLT will be performed by sequential applications with a treatment-free interval of eight weeks to minimize risk of repeated ^{177}Lu -PSMA-617 therapy before reaching blood level nadir. This scheme is also supported by safety data from the phase III NETTER-1 trial on safety and efficacy of ^{177}Lu -DOTATATE in patients with midgut NET. Here ^{177}Lu -DOTATATE was administered at seven to nine week intervals and rate of severe adverse events was below 10% for 115 patients in the treatment arm [54].

3.2.3 Rationale for dose regimen

Ahmazadehfar et al reports safety and efficacy after application of a mean activity of 6.0 GBq ^{177}Lu -PSMA-617 in 24 patients with mCRPC [50]. Patients were treated with up to two cycles of ^{177}Lu -PSMA-617 RLT at eight week intervals. Grade 3 hematotoxicity occurred in two patients. No nephrotoxicity or hepatotoxicity grade ≥ 3 was documented. Kratochwil et al reports safety and efficacy after repeated application of ^{177}Lu -PSMA-617 in 30 mCRPC patients [49]. 19 of 30 patients (63%) received 6.0 GBq ^{177}Lu -PSMA-617 every two mo. One patient developed grade 3 anemia, one patient grade 3 thrombocytopenia. Both patients had diffuse pattern of bone marrow infiltration at baseline. The German Society of Nuclear Medicine (DGN) performed a questionnaire based survey on the use of ^{177}Lu -PSMA-617 RLT in December 2015. Nuclear Medicine Clinics in Germany reported compassionate use of ^{177}Lu -PSMA-617 RLT in 145 mCRPC patients until June 30th 2015 [52]. Majority of patients

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received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle (Table 1) and rate of serious adverse events was below 20% for both subgroups. Phase III data for ¹⁷⁷Lu-DOTATATE, a similar RLT for midgut NET patients, demonstrates a rate of severe adverse events below 10% after application of four cycles of 7.4 GBq in 115 patients [54]. Thus, present evidence indicates that repeated applications of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 RLT are well tolerated with low to very low rates of serious adverse events.

Standard activities of 6.0 and 7.4 GBq are also supported by dosimetry data available in more than ten patients [56] [57]. Maximal cumulative activity is limited by the absorbed dose in critical organs. Dosimetry identifies kidney and salivary glands as organs with highest absorbed dose [56] [57]. Thus maximum cumulative activity is determined by absorbed kidney dose. Based on earlier evidence obtained from external beam radiotherapy the maximum tolerable per kidney dose is generally accepted 23 Gy [58]. Dosimetry after ¹⁷⁷Lu-PSMA-617 application revealed absorbed doses of 0.6 Gy/GBq per kidney [56] [57]. Therefore maximum cumulative activity for ¹⁷⁷Lu-PSMA-617 RLT is considered 38.3 GBq (38.3 GBq x 0.6 Gy/GBq = 23.0 Gy radiation dose per kidney). Both the application of four cycles of 6.0 GBq (total 24.0 GBq) or 7.4 GBq (total 29.6 GBq) ¹⁷⁷Lu-PSMA-617 results in lower cumulative activities with acceptable safety margin. Whether either activity regimen is associated with longer rPFS is unknown and will be evaluated as secondary endpoint of this trial.

Salivary glands receive highest off-target radiation dose according to dosimetry [56] [57]. Absorbed dose after four cycles of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 (34.0 Gy or 41.6 Gy respectively) falls within the range of maximum tolerable dose reported for salivary glands in the literature [58] [59] [60]. Maximum tolerable dose to the bone marrow is generally accepted 2 Gy [61]. Bone marrow dose will not exceed this limit after four cycles of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 [57].

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3.2.4 Determination of Sample Size

Sample size calculation was based on the primary endpoint of this protocol, i.e. baseline to 12-week decline in tumor marker level (PSA) $\geq 50\%$ [53]. Based on a recent publication [52], we estimate that the proportion of patients who meet the primary end point will range between 38% and 65% for both treatment doses. We thus define the following null hypothesis: Less than 40% of patients will reach the endpoint after ^{177}Lu -PSMA RLT. ^{177}Lu -PSMA RLT would therefore be considered worthy of further study if 50% or more patients met the end point and not worthy of further study if 40% and less achieved the end point. This rationale was adapted from a single-arm study on mCRPC patients with same end point definition, published 2010 in the Journal of Clinical Oncology [53]. We have performed power analysis for the two sided binomial test (beta 0.2, alpha 0.05) to measure the efficacy of ^{177}Lu -PSMA RLT. A sample size of 200 achieves 78% power (beta 0.2) at a given alpha of 0.05 to distinguish between 40% versus 50% response rates. The power analysis was performed by a trained Biostatistician from the Department of Biostatistics, University of California at Los Angeles using Power Analysis and Sample Size (PASS) 14 software (NCSS LLC).

3.3 Study Duration and Dates

The duration of subject participation will be from the time of signing informed consent through the 24 months post-injection visit or progression. Subjects will be deemed enrolled in the study once the subject signs informed consent.

3.4 Randomization protocol

Randomization will be performed in accordance with Vickers et al. [62]. In order to obtain adequate “allocation concealment” a list of random allocations was created for patients 1 through 200. This list will be stored at investigator’s sites and will not be modified. The list

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will only be accessible for researchers or study personnel not actively involved in the recruitment process.

3.5 Dose modification

In some circumstances, it might be necessary to suspend treatment with ¹⁷⁷Lu-PSMA-617, adapt the posology (i.e. administer a half activity), or even definitively stop administration, as described in the following tables.

Table 3: Criteria for permanent discontinuation of treatment with ¹⁷⁷Lu-PSMA-617

Definitively stop further administrations in patients who have experienced or are at risk of any of the following conditions during treatment:

a) Severe heart failure (defined as grade III or IV of the NYHA classification)
b) Hypersensitivity to the active substance or to any of the components of this radiopharmaceutical
c) Grade 3 hematologic toxicities that persist > 12 weeks and Grade 4 that persist > 3 weeks.
d) Grade 3 renal toxicity as determined by serum creatinine measurements
e) AST/ALT > 3x ULN and bilirubin > 2x ULN
f) Grade 3-4 non-hematologic toxicities with select exceptions for <ul style="list-style-type: none">- Grade 3 fatigue < 10 days- Grade 3 nausea, vomiting, and diarrhoea and grade 4 vomiting and diarrhoea that persist for < 72 hours in the absence of maximum medical therapy- Asymptomatic grade 3 non-hematological laboratory abnormalities that resolve in 72 hours- Grade 3 infections which do not improve under i.v. medication within 10 days

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In case some specific adverse reactions to ¹⁷⁷Lu-PSMA-617 persist or reoccur, see Table 5

Table 4: When to suspend treatment with ¹⁷⁷Lu-PSMA-617?

Suspend treatment with ¹⁷⁷Lu-PSMA-617 in patients who have experienced or are at risk of any of the following conditions during treatment:

Criterion	Action
Occurrence of an intercurrent disease (e.g. urinary tract obstruction, ...) which according to the physician opinion could increase the risks linked to ¹⁷⁷ Lu-PSMA-617 administration.	Suspend administration until resolution or stabilization. Treatment can be resumed after resolution or stabilization. Resolution is defined as grade II toxicity or lower. (by CTCAE) at the time of the next treatment. Treatment can be suspended up to 12 weeks after the last infusion. After that treatment with ¹⁷⁷ Lu-PSMA-617 must be definitively stopped.
In case of some specific adverse reactions to ¹⁷⁷ Lu-PSMA-617, see Table 5	see Table 5

Table 5: When to adapt ¹⁷⁷Lu-PSMA-617 posology?

Adapt ¹⁷⁷Lu-PSMA-617 posology according to the following actions in patients who have presented any of the following severe adverse reactions:

Severe adverse reactions / Dose-modifying toxicity (DMT) criteria	Action
Anemia, thrombocytopenia or neutropenia of grade 3 or superior (CTCAE 4.0)	1. Suspend treatment with ¹⁷⁷ Lu-PSMA-617
Renal toxicity as defined by grade 3 toxicity by serum creatinine (CTCAE 4.0)	2. Monitor biological parameters every 2 weeks, and eventually treat appropriately if needed; in case of renal function impairment, good hydration is recommended if not otherwise contraindicated.
Liver toxicity as defined as AST and ALT >3xULN	a. If the observed toxicity continues beyond 12 weeks after the last infusion,
Any serious or intolerable adverse event not listed in Table 2 that in the opinion of	

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the investigator, requires the subject's discontinuation.	treatment with ¹⁷⁷ Lu-PSMA-617 must be definitively stopped. b. If the observed toxicity resolves within 12 weeks after the last infusion, it is possible to continue treatment with ¹⁷⁷ Lu-PSMA-617 by infusing a half activity. 3. Even if the half activity is well tolerated (i.e. no DMT re-occurrence), the next remaining treatment administration should be continued with the reduced (half) activity but, if DMT recurs after treatment with a half dose, treatment with ¹⁷⁷ Lu-PSMA-617 must be permanently stopped.
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4. Study Population Selection

4.1 Study Population

It is anticipated that a total of 200 subjects will be recruited. Such a number is considered appropriate to achieve statistical power for the endpoints of this clinical trial. The patients will be recruited at up to 3 clinical sites. The dose being administered will be prepared at RadioMedix Inc. in Houston and shipped to the trial sites.

4.2 Inclusion Criteria

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ⁶⁸Ga-PSMA-11 PET/CT or diagnostic ¹⁷⁷Lu-PSMA-617 scintigraphy
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2500/\mu\text{l}$, PLT count $\geq 100.000/\mu\text{l}$, Hb ≥ 9.9 g/dl and ANC $\geq 1500 \text{ mm}^3$ for the first cycle and WBC $\geq 2.000/\mu\text{l}$, PLT count $\geq 75.000/\mu\text{l}$, Hb ≥ 8.9 g/dl and ANC $\geq 1000 \text{ mm}^3$ for the subsequent cycles
8. Signing of the Informed Consent Form
9. Patients enrolling in this trial should have received either enzalutamide or abiraterone

4.3 Exclusion Criteria

1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ²²³Ra, ¹⁵³Sm)
2. Glomerular Filtration Rate (GFR) $< 40 \text{ ml/min}$
3. serum creatinine $> 1.5 \times \text{ULN}$ AST and ALT $> 5 \times \text{ULN}$
4. Urinary tract obstruction or marked hydronephrosis
5. Diffuse bone marrow involvement confirmed by super-scans

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5. Study Treatment(s)

5.1 Description of Treatments(s)

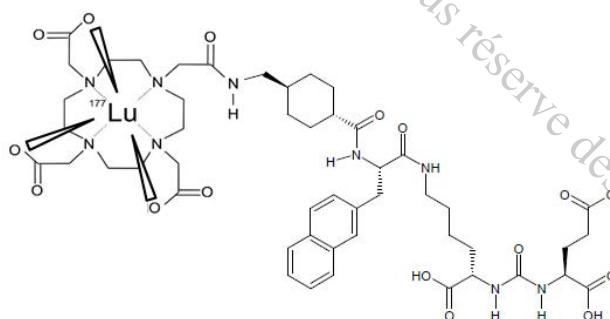
5.1.1 Study drug

The agent to be evaluated in the present study is ¹⁷⁷Lu-PSMA-617. Its chemical name is lutetium-177-Na-2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid.

¹⁷⁷Lu-PSMA-617 is radiolabelled with carrier-free lutetium-177 (¹⁷⁷Lu), a synthetic, low-energy beta and gamma emitting isotope of lutetium, the last element in the lanthanide series of metallic elements. Carrier-free ¹⁷⁷Lu is generated by neutron irradiation of the isotope ytterbium-176 (¹⁷⁶Yb) and subsequent fractionation of ¹⁷⁷Lu and ¹⁷⁶Yb with caution chromatography. Key physical characteristics of ¹⁷⁷Lu are summarised below:

Physical half-life T _{1/2}	Decay product	Main β ⁻ emission	Maximum range (β ⁻)	Main γ emission
6.6 d	¹⁷⁷ Hf	498 keV	1.7 mm	208 keV 113 keV

The structural formula of ¹⁷⁷Lu-PSMA-617 is shown below



The chemical formula of ¹⁷⁷Lu-PSMA-617 is Lu₁C₄₉H₆₈N₉O₁₆. The molar weight is 1214.1 g/mol.

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5.1.2 Pharmaceutical Properties of ^{177}Lu -PSMA-617

^{177}Lu -PSMA-617 is administered intravenously.

A description of ^{177}Lu -PSMA-617 solution for infusion is shown in below table

Composition of ^{177}Lu -PSMA-617 solution

Pharmaceutically active component	^{177}Lu -PSMA-617
Physical dose	$\leq 7.4 \text{ GBq} / \text{cycle}$
Substance dose	130 - 170 μg PSMA-617
Primary unit dose container	20 mL glass vial containing 5 - 15 mL of stabilised aqueous solution
Appearance	Clear, colourless or slightly yellowish solution, without visible particles
pH	4.0 - 7.5
Bacterial Endotoxin	$\leq 100 \text{ EU/Dose}$
Radionuclidic purity	$\geq 99.99 \%$
Sterility	Sterile

The components include ^{177}Lu -PSMA-617, sodium acetate, sodium ascorbate, gentisic acid, and water for injection. The labelled drug product is produced, tested and released under GMP conditions by RadioMedix, Inc. as a sterile solution for injection infusion, ready for use. The labelled drug product will be manufactured upon individual order and delivered directly to the study sites.

Patients will be randomized into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq ($\pm 10\%$, arm 1) or 7.4 GBq ($\pm 10\%$, arm 2) ^{177}Lu -PSMA-617 every 8±1 weeks; RLT will be performed until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy as determined by dosimetry, after the first treatment.

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5.2. Treatment(s) administered

Cold ice pack in the region of salivary glands will start 30 minutes prior to administration of the investigational drug and will continue for 4 hours. Intravenous access will be inserted in either arm. Assurance will be made to have reliable IV line with no evidence of extravasation or infiltration. Investigational drug will be infused over approximately 30 minutes using infusion pump. Patients will be monitored for any evidence of pain, or burning sensation during the infusion.

Imaging and blood and urine samples for dosimetry will be accomplished as per dosimetry protocol by Prof. Dr. [Name], Universitätsklinikum Würzburg - Klinik und Poliklinik für Nuklearmedizin. For subsequent therapies only whole body images will be performed to assure satisfactory distribution of the investigational radiopharmaceutical.

5.3 Restrictions

5.3.1 Fluid and Food Intake

Subjects should follow their normal diet before and after the administration of the study drug. Subjects should be encouraged to increase fluid intake at baseline and after each image acquisition to maintain proper hydration throughout the study period and decrease radiation exposure to the urinary bladder. There are no dietary or food restrictions for this study.

5.3.2 Subject Activity Restriction

There are no activity restrictions.

5.4 Dosing Compliance

All study drug administration will be administered under the supervision of the investigator. Details of study drug injection will be captured in each subject's source documents.

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5.5 Packaging and Labeling

¹⁷⁷Lu-PSMA-617 will be supplied in vials for injection in appropriate packaging.

The outer packaging of ¹⁷⁷Lu-PSMA-617 will contain label(s) which will include the following minimum information:

- Name and address of Manufacturer Study number
- Investigator identification
- Name of study drug and formulation
- Dosage strength
- Batch number
- Patient number
- Expiry date (or retest date)
- Storage instructions
- “For Clinical Trial Use only”

A system of medication numbering in accordance with all requirements of Good Manufacturing Practice (GMP) and any other applicable regulatory requirement will be used for all study drugs. This will ensure that for each patient, any dose of study drug can be identified and traced back to the original bulk ware of the active ingredients. Lists linking all numbering levels will be maintained by the institutions in charge of study drug packaging.

5.6 Storage and Accountability

5.6.1 Storage

The drug product contains radioactive material and should only be handled by personnel trained in the use of radioactive isotopes with proper shielding and monitoring. Receipt and use is limited to a facility licensed by applicable government regulations and/or local/state laws. Unused or residual waste should be disposed of as radioactive waste following the institution's standard operating procedures (SOPs) and/or applicable regulations or guidance.

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5.6.2 Accountability

In accordance with International Conference on Harmonization (ICH) and US Food and Drug Administration (FDA) requirements, the investigator and/or drug dispenser must at all times be able to account for all study drugs furnished to the institution. The appropriate site personnel must sign, date and immediately forward to the sponsor or sponsor's designee the packing slip for clinical shipment included with each shipment.

No study drug is to be used outside of this study. The investigator or designee will record the use of the study drug on the appropriate Drug Accountability record. All study radiopharmaceuticals must be accounted for, whether used or unused, during the course of and at the conclusion of the study. The shipment of drugs from the sponsor or designee to the investigator or other designated persons cooperating with the investigator will be accompanied by a receipt form that indicates the lot number(s) and the amount of drug provided for the study. This form will be signed, dated and returned to the sponsor or designee.

The investigator is responsible for ensuring that study drug is recorded, handled and stored safely and properly in accordance with ICH and applicable government regulations, local/state laws, and used in accordance with this protocol.

5.7 Investigational Product Retention at Study Site

Unused product will be disposed of according to institutional regulations. Record the use and/or disposal of the study drug on the Drug Accountability record. This Drug Accountability record should account for the receipt and disposition of all clinical supplies shipped to the investigator and must be available for review by the study monitor.

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6. Study Procedures

6.1 Informed Consent

All subjects must sign and personally date an IRB/IEC approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug prior to the initiation of any study-related procedures. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for Good Clinical Practice (GCP) and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27.

The subject must be made aware and agree that personal information may be reviewed during an audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. A copy of the Informed Consent Form is attached as Exhibit.

6.2 Medical History

A relevant medical history and subject demographics will be obtained at the screening visit. Cancer medical history includes review of disease history, cancer staging, biopsy results, any past/present cancer therapies (e.g., hormone, drug, biologic, radiologic, or surgical treatment). Demographic information to be collected includes date of birth, race, ethnicity, height, and weight.

6.3 Vital Signs

Vital signs will include measurement of blood pressure, temperature, respiratory rate, pulse oximetry and heart rate.

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6.4 Dispensing Study Drug

The estimated radioactive dose will be determined by measuring the amount of radioactivity in the syringe pre- and post-injection, using an appropriately calibrated radioisotope dose calibrator in accordance with the nuclear medicine department's SOPs.

Any complication related to administration of the drug (e.g., overdose, observable extravasation, medication error) is a protocol-related event and will be reported to the pharmacovigilance designee. Refer to Section 7 for contact information.

6.5 Clinical Laboratory Tests

Clinical laboratory tests will include hematology and clinical chemistry. Clinical laboratory analytes to be assessed in the study are shown in Table 6. Timing of collection of clinical laboratory tests are presented in Section 8.

Table 6: Laboratory Analytes Assessed

Hematology	Clinical Chemistry
Hematocrit	eGFR
Hemoglobin	Bilirubin
RBC count	Creatinine
WBC count	Glucose
WBC differential	Urea nitrogen
Platelets	BUN/Creatinine
ANC	AST/SGOT
MCV/MCH/MCHC	ALT/SGPT
Eosinophils	Alkaline Phosphatase
Basophils	PSA*
Lymphocytes	
RDW	

*PSA will be done only at the time intervals called by the protocol.

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6.6 Sample Collection, Storage and Shipping

Blood samples will be collected using accepted phlebotomy techniques by trained site personnel. All samples for clinical laboratory testing will be processed and analyzed at an accredited laboratory

6.7 Electrocardiogram

Continuous ECG monitoring at least 15 minutes prior to administration of the study drug and at least 1 hour after administration will be performed. Also a 12 lead ECG will be performed in two time points: before injection of Lu-177 PSMA and after completion of the 4 hr scan.

6.8 Adverse Events

Immediate adverse drug reactions will be collected from the time of ¹⁷⁷Lu-PSMA-617 injection until 24 hours post-injection visit. Data will be collected for any adverse events (AEs) as defined in Section 7.

All study monitoring will be performed at the primary clinical study sites in accordance with Good Clinical Practice (GCP). All records related to this study will be retained at each clinical site. Serious adverse reactions will be collected and reported to FDA and IRB according to 21 CFR 312.32. **Sponsors at each individual site will be responsible for obligations of a sponsor enumerated in 21 CFR 312.50-59. FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the investigational drug.** Annual reports on the progress of the investigation and any adverse events related to the investigational drug will be prepared and reported to FDA according to 21 CFR 312.33.

6.9 Removal of Subjects from the Trial or Study Drug

The investigator may withdraw a subject from the trial for any of the following reasons:

1. Protocol violation

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2. Serious or intolerable adverse event (that in the opinion of the investigator, requires the subject's discontinuation),
3. Investigator withdraws the subject (at the investigator's discretion for reasons other than an adverse event),
4. Sponsor terminates the study,
5. Subject requests to be discontinued from the study, or
6. Subject is lost to follow-up

During course of the study patients have the right to withdraw their consents any time without need for explaining the reason of consent withdrawal to the investigator or sponsor. Principal investigator will closely monitor patients during the course of the study and will consider terminating investigational product administration or any other trial related procedures in order to maintain the safety of subjects. In cases of withdrawal either in patient's favor or principal investigator decision due to the safety issues or technical issues, withdrawn subjects will be replaced in order to maintain data integrity but follow up visits will be continued to maintain safety of patients based on the visits predicted in the protocol.

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7. Reporting Safety Information

Any untoward medical event that occurs from the time that the subject is administered ¹⁷⁷Lu-PSMA-617 until the subject completes the study will be reported. Serious adverse events and non-serious adverse events will be collected and reported as required under 21 CFR 312.32 until the final study visit. Toxicity will be evaluated according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

7.1 Adverse Events

7.1.1 Definitions

An **adverse event (AE)** is any untoward medical occurrence in a study subject that is administered a pharmaceutical product, at any dose, which does not necessarily have a causal relationship with the treatment.

An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a study drug, whether or not considered related to the study drug.

A **serious adverse event (SAE)** is any untoward medical occurrence that falls into one or more of the following categories:

1. Results in death
2. Is life-threatening: An event which, in the view of the investigator, places the subject at immediate risk of death from the event as it occurred and does not include an event which hypothetically might have caused death if it were more severe.
3. Requires subject hospitalization or prolongation of existing hospitalization: For the seriousness criterion of subject hospitalization to apply, an overnight stay in the hospital is required. Admission to an emergency room and release without an overnight stay would not satisfy the subject hospitalization seriousness criterion.
4. Results in persistent or significant disability/incapacity: Persistent or significant disability/incapacity is defined as a substantial disruption of a person's ability to conduct normal life functions, either reported or defined as per clinical judgment.

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5. A congenital anomaly/birth defect: A congenital anomaly/birth defect is defined as a condition believed to have been the result of exposure to study drug just before conception or during pregnancy.
6. Any other important medical event: An important medical event may not result in death, be life-threatening, or require hospitalization, but based upon appropriate medical judgment, the event may significantly jeopardize the subject's health or may require medical or surgical intervention to prevent one of the outcomes listed in the serious definitions above. An important medical event may include development of drug dependency or drug abuse.

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

7.1.2 Reporting Serious Adverse Events

Seriousness is based on subject, event outcome, or action criteria that are usually associated with events that pose a threat to a subject's life or functioning. Seriousness (not severity) serves as the guide for defining the sponsor's regulatory reporting obligations to the applicable regulatory authorities. Adverse event severity and seriousness should be assessed independently by investigators. If the investigator is unsure if the event is serious it should be classified as serious.

Sponsors of the study, and the investigators are responsible for reporting relevant SAEs as safety reports to the FDA and other applicable regulatory authorities, and participating investigators, in accordance with ICH guidelines, the US Code of Federal Regulations Title 21 CFR 312.32 for Good Clinical Practice, and/or local regulatory requirements. The investigators must report all SAEs to project pharmacovigilance designee within 24 hours, by telephone, email or fax, and confirm that the information was received. A Serious Adverse Event Report (SAER) must be completed by the investigator or designee and faxed or emailed to project pharmacovigilance designee within 24 hours after the investigator first becomes aware of the

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serious event. A separate SAER will be needed for each reported SAE so that the onset, resolution date, causality and outcome can be assessed for each event. Any source documents relevant to the event should be forwarded to sponsor's pharmacovigilance designee with the SAER form. The SAER form must be signed and dated by the investigator. The Original copy of the SAER form should remain at the investigational site. All SAEs are also to be entered into the CRF.

In case of death, a comprehensive narrative report of the case should be prepared by the investigator and sent to project pharmacovigilance designee with the SAER. If an autopsy is performed, a copy of the autopsy report should be actively sought by the investigator and sent to the sponsor or designee as soon as available. A copy of the autopsy report should remain at the investigational site with the subject's source documents.

A new follow-up SAER form will be completed by the investigator if important follow-up information (i.e., diagnosis, outcome, causality assessment, results of specific investigations) are made available after submission of the initial form. The follow-up SAER must be signed and dated by the investigator. The follow-up form and any additional source documentation regarding the event will be sent to project pharmacovigilance designee.

If a serious medical occurrence or death is reported to the investigator outside the follow up window which is believed to be related to the administration of the study drug, it is the investigator's responsibility to report this occurrence to project pharmacovigilance designee. Such occurrences will be reported using a SAER form or other form of communication deemed appropriate by the investigator and pharmacovigilance designee.

Sites must contact project pharmacovigilance designee to report all SAEs within 24 hours, by telephone, e-mail, or fax. Contact information for SAE reporting is presented in Table 7.

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Table 7: Pharmacovigilance Designee

[Name], MD
[Contact]
Excel Diagnostics and Nuclear Oncology Center
9701 Richmond Avenue, Suite 122
Houston, TX 77042
PHONE: 713.781.6200 [Contact]
FAX: 713.781.6206
Email: [Contact]

Sites must also report all overdoses, extravasations and medication errors to the project pharmacovigilance designee.

7.2 Adverse Event Data Collection

The investigator will elicit information through non-leading questioning and examination of the subject about the occurrence of adverse events from the time that the subject is administered ¹⁷⁷ Lu-PSMA-617 until study completion. AEs can be reported any time after study enrollment until the end of the subject's study participation. For each event, the following information will be recorded in the subject's source documents and entered into the Adverse Event CRF according to the instructions below:

Classification of the Event as serious or non-serious: Classify the event as serious or non-serious (see definitions in Section 7).

Description of Signs or Symptoms: Whenever possible, record a specific diagnosis for the event. If a diagnosis cannot be made, then record each sign or symptom representing a distinct medical concept separately, (e.g. nausea and vomiting should be recorded as separate events).

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Onset Date and Time: Record the date and time the event starts. If a laboratory result is reported as an AE, record the start date as the date of collection of the first lab sample that shows the change.

Stop Date and Time: Record the date and time the event resolves, returns to baseline, or resolves with sequelae.

Grade: Refer to the common terminology criteria for adverse events (CTCAE) Version 4.

Relationship to the Study Drug:

We make every effort to evaluate the relationship between the study drug and the AE as determined by the investigator per the definitions below:

1. **Related:** The event is reasonably suspected of a causal relationship to the study drug. Suspected adverse reaction means any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of IND safety reporting, ‘reasonable possibility’ means there is evidence to suggest a causal relationship between the drug and the adverse event. A suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by a drug.

ASSESSING RELATIONSHIP TO STUDY TREATMENT

Items to be considered when assessing the relationship of an AE to the study treatment are:

- Temporal relationship of the onset of the event to the initiation of the study treatment;
- The course of the event, considering especially the effect of discontinuation of study treatment or reintroduction of study treatment, as applicable;
- Whether the event is known to be associated with the study treatment or with other similar treatments;

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- The presence of risk factors in the study subject known to increase the occurrence of the event;
- The presence of non-study treatment-related factors which are known to be associated with the occurrence of the event.

2. Not Related: The event is definitely due to causes separate from study drug administration such as:

- documented pre-existing condition
- technical and manual procedural problem
- concomitant medication
- subject's clinical state

3. Adverse Event Outcome:

- Recovered/Resolved without sequelae
- Recovered/Resolved with sequelae
- Not Recovered/Not Resolved: event is ongoing at the end of the AE collection period.
- Death (Fatal): the event description must be the primary cause of death.

7.3 Clinical Significance

7.3.1 Reporting and Evaluation of Clinical Laboratory Test Results

The investigator should assess all clinical laboratory results for clinical significance and record the assessment in source documents.

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The investigator should evaluate any laboratory result change from pre- and post-study drug administration to determine if the change meets the definition of an AE or SAE. **Record any clinically significant lab results determined to meet the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

7.3.2 Repeat Testing

Additional laboratory testing may be performed at the discretion of the investigator.

7.3.3 Vital Signs

The investigator should evaluate any vital sign changes pre- and post-study drug administration to determine if the change meets the definition of AE or SAE. Vital sign measurements may be repeated at the discretion of the investigator. **Record any clinically significant vital sign measurement that meets the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

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8. Study Activities

Visit-specific schedule for efficacy and safety variables is presented in Appendix II.

8.1 Screening Visit

- Written informed consent
- Demographic information
- Relevant medical history
- Prior therapy for Prostate cancer
- Medication assessment
- Histology
- Vital signs
- Questionnaires
- Morphological and PSMA-ligand imaging studies if no comparable available within 12 weeks of treatment.

8.2 Within 2 Weeks of Screening

- Clinical laboratory testing (see Section 6)

8.3 Injection Visit

Once all screening/baseline procedures are performed, the following procedures will be completed on the day of injection:

8.3.1 Pre-dose and Dosing Procedures

- Pre-dose vital signs – within 20 minutes before dose
- Apply Ice pack to the salivary glands 30 minutes prior to investigational drug injection and continue for 4 hours.

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- Adequate hydration of the patient (IV or oral).
- Inject study drug ¹⁷⁷Lu-PSMA-617
- Post-dose vital signs
- Adverse events

8.3.2 Post-Dose Procedures

Adverse events during the entire stay. At first or second treatment blood sampling and scintigraphy 1-4h, 24h, 48h, 72h and 7d after injection for dosimetry.

8.3.3 ECG Procedures

Continues ECG monitoring starts at least 15 minutes prior to the administration of study drug and ends at least 1 hour after administration. A 12 lead ECG also will be performed at two time points: before administration of LU-177 PSMA and after completion of 4 hour WB scan.

8.4 Follow-up

8.4.1 PSA Measurements

Every 6 weeks during the treatment and every 3 months after the last treatment until reaching endpoint or 24 month after the first treatment.

8.4.2 Imaging Studies

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Baseline imaging within 12 weeks of start of therapy including (a) CT of the chest preferably with contrast and CT or MRI of the Abdomen and pelvis preferably with contrast and (b) bone scintigraphy or (c) equivalent to above [1].

Relevant imaging studies will be repeated approximately every 12 weeks until reaching the endpoint or 24 month after the first treatment.

8.4.3 Dosimetry

Prof. Dr. [Name], Universitätsklinikum Würzburg, Germany - Klinik und Poliklinik für Nuklearmedizin will perform the dosimetry for this protocol.

Radiation dosimetry will be acquired for each patient after the first or second cycle of treatment. Data acquisition plan is summarized in Table 8. Dosimetry will be considered appropriate, if at least three time points for scintigraphy and blood sampling more than 48 hours apart were acquired.

Time p.i.	Blood sampling	Urine collection	Scintigraphy (whole body planar)	Quantitative SPECT/CT head/thorax/abdomen
5 min	X	X (from injection until 4h in one container)		
30 min	X			
1 h	X			
4 h	X	X (from 4h until discharge in one container)	X	
18 - 30 h	X		X	X
42-54h	X		X	
66-78h	X		X	
7-9d*	X		X	

Table 8: Acquisition plan for individual dosimetry.

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Dosimetry data will be sent to experts in the field for centralized analysis. Radiation dose will be calculated for all relevant organs. Maximum number of RLT cycles for reaching threshold maximum dose to the kidneys of 23 Gy will be determined.

*7-9d is optional.

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8.4.4 Follow-up Labs for Hematological and Kidney Toxicities

All enrolled patients will follow the scheduled follow up visits.

Hematologic laboratory testing (CBC) will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until patient is progressed. CBC will be performed every 7 days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery which is defined as grade 2 toxicity or lower..

In order to detect myelodysplasia, patients who withdrawn by the investigator for safety reasons will only perform CBC test until the end of their follow up visits as long as they do not start other cytotoxic therapies.

Chemistry will be evaluated every 4 weeks during therapy cycles to evaluate safety and also eligibility to receive the next cycle and then every 3 months for 24 months or until the patient is progressed. Patients on protocol should also have a physical exam and in-person physician evaluation periodically while on study and until recovery from last dose. During dosing period patients will be evaluated by the investigator or under his / her direct supervision. During follow up period local patients can come back to the facility for physical exam and for non-local patients they need to see their physician each 3 months for in-person physical exam assessment and send the results of exam to the investigator.

8.4.5 Telephone Follow ups

7 (+/- 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 week) until the end of follow up visits (24 months).

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9. Quality Control and Assurance

The study sites are chosen with regard to the capability and expertise of the principal investigators and the site staff. Prior to initiation of the study, the investigator and the sponsor's representative will meet to discuss the study design and conduct of the study. The investigator will sign the protocol acknowledging that he understands the design and all procedures and intends to conduct the study and all procedures according to protocol.

During the study, a representative of the sponsors will make periodic visits to the investigational site while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government regulations and guidelines. The investigator will permit authorized representatives and the respective local and national health authorities to inspect facilities and records relevant to this study, if needed.

Subject data will be collected on source documents and entered in the CRF. Data will be reviewed and validated. The investigator will sign and date a declaration on the CRF attesting to his/her responsibility for the quality of all data recorded and that the data represents a complete and accurate record of each subject in the study.

Records of subjects, source documents, monitoring visit logs, inventory of study product, regulatory documents (e.g., protocol and amendments, IRB/IEC correspondence and approvals, approved and signed informed consent forms, Investigator's Agreement, clinical supplies receipts, and distribution and return records), and other sponsor correspondence pertaining to the study will be kept in the appropriate study files at the site. Source documents include all recordings and observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical study. At the end of the study, CRF data will be provided to the sponsor.

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10. Planned statistical methods

10.1 Primary endpoints

1. **Safety** of ¹⁷⁷Lu-PSMA-617 RLT will be assessed by analysis of toxicity. Descriptive statistics (number and percentage) will be reported separately for AE in total and SAE based on CTC. These descriptive statistics will be presented for the whole treatment as well as separate for each cycle. In addition, the relationship of AE to the study drug (related, not related) will be reported. Both results from laboratory test, physical examinations and patients surveys will be included.
2. **Efficacy** of ¹⁷⁷Lu-PSMA-617 will be reported using descriptive statistics by means of number and percentage of patients with $\geq 50\%$ decline at 12-weeks from baseline.

10.2. Secondary endpoints

1. Descriptive analyses (median, standard deviation) will be used to determine the **progression-free survival (PFS)**, measured from start of therapy until death or PSA progression. PSA progression is defined a) for patients with PSA decline after start of treatment as time from baseline to time the PSA increases to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later or b) for patients without PSA decline as time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq ¹⁷⁷Lu-PSMA-617) and a statistical significant difference will be tested.
2. Each clinical site will perform image analysis on their own patients. Descriptive analyses (median, standard deviation) will be used to determine the **radiographic progression-free survival (rPFS)**, measured from start of therapy until death or radiographic progression. Radiographic progression is defined as a) for extraskeletal

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disease progressive disease (PD) following Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 [63] and/or b) skeletal disease the development of ≥ 2 new lesions on first post-treatment bone scan, with at least two additional lesions on the next scan (2+2 rule). The date of progression is the date of the first post-treatment scan, when the first two new lesions were documented. This approach is applied in accordance to PCWG criteria to exclude pseudoprogression in the absence of symptoms or other signs of progression [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq ¹⁷⁷Lu-PSMA-617) and a statistical significant difference will be tested.

3. Descriptive analysis will be used to determine the **disease control rate (DCR)** at the end of each cycle defined as the number and percentage of patients achieving a RECIST stable disease (SD), partial response (PR) or complete response (CR) for extraskeletal tumor manifestation and b) PCWG non-progressive disease for skeletal manifestations.
4. Descriptive analysis will be used to evaluate the impact on **bone pain level** by determining the proportion of patients with pain response defined by improvement from baseline (all patients with $\geq 4/10$) of at least 2-point absolute improvement without an overall increase in opiate use.
5. Change in **Quality of Life** over time will be documented by comparing the summary scores investigated by the Quality of life questionnaire “EPIC-26” at baseline and at 3, 6, 9, 12, 18 and 24 months after start of ¹⁷⁷Lu-PSMA-617 RLT [64].
6. Changes in **performance status (ECOG)** from baseline will be evaluated over time at 3, 6, 9, 12, 18 and 24 months after start of ¹⁷⁷Lu-PSMA-617 RLT.

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11. Administrative Considerations

11.1 Investigators and Study Administrative Structure

This study will be conducted in accordance with the Declaration of Helsinki, ICH E6 Guideline and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 312.50 through 312.70, directive 2001/20/EC of 4 April 2001 and implementing directives and regulations. To ensure compliance the investigator agrees, by written consent to this protocol, to fully cooperate with compliance checks by allowing access to all documentation by authorized individuals. The investigator must conduct the trial as outlined in the protocol and in accordance with the Declaration of Helsinki and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 56 – Institutional Review Boards. The administrative structure of the study (e.g., monitoring and vendor personnel, statistician, and laboratory facilities) and a complete and controlled list of the investigators participating in this study can be found in the study file maintained by the sponsor or its agent.

11.2 Institutional Review Board (IRB) or Independent Ethics Committee (IEC) Approval

The protocol, informed consent form, and any advertisement for the recruitment of subjects must be reviewed and approved by an appropriately constituted IRB or IEC, as required in Chapter 3 of the ICH E6 Guideline and government regulations, including (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 56.107 through 56.115 of Good Clinical Practice. Written IRB approval must be provided to sponsor or designee prior to shipment of study drug or subject enrollment. The investigator is committed in accordance with local requirements to provide the IRB with updates, and to inform the IRB of any emergent problem, SAEs, and/or protocol amendments.

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11.3 Ethical Conduct of the Study

It is mandatory that all considerations regarding the protection of human subjects be carried out in accordance with the Declaration of Helsinki.

11.4 Subject Information and Consent

It is the responsibility of the investigator to obtain written informed consent from subjects. All subjects must sign and personally date an approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for GCP, and the requirements of (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27 of Good Clinical Practice.

The subject must be made aware and agree that personal information may be scrutinized during audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. Prior to IRB/IEC submission, the investigator must send a copy of the informed consent form to be used at their institution to sponsor or designee for review to assure compliance with the ICH E6 and government regulations of the region.

11.5 Subject Confidentiality

Data collected during this study may be used to support the development, registration or marketing of ¹⁷⁷Lu-PSMA-617. All data collected during the study will be controlled by sponsor or designee and sponsor will abide by all relevant data protection laws. In order to maintain subject privacy, all CRFs, study drug accountability records, study reports and communications will identify the subject by initials and the assigned subject number. The

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investigator will grant monitor(s) and auditor(s) from sponsor or its designee and regulatory authority (ies) access to the subject's original medical records for verification of data entered into the CRF and to audit the data collection process. The subject's confidentiality will be maintained and will not be made publicly available to the extent permitted by the applicable laws and regulations.

Written authorization is to be obtained from each subject prior to enrollment into the study in accordance with the applicable privacy requirements [e.g., the Health Insurance Portability and Accountability Act of 1996 Standards for Privacy of Individually Identifiable Health Information ("HIPAA

11.6 Study Monitoring

11.6.1 Monitoring Procedures

An appropriate representative of the sponsors (Study Monitor) will oversee the progress of the study, and ensuring it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and applicable regulatory requirements.

An initiation visit will be made by the study monitor at each site to discuss the protocol and the obligations of both the Sponsor and the investigator. The investigator must allow the study monitor to perform periodic, interim monitoring visits. The actual frequency of monitoring visits will be dependent on the enrollment rate and performance at each site. The purposes of these visits are to verify that written informed consent was obtained prior to each subject's participation in the trial, and to:

- assess the progress of the study
- review the compliance with the study protocol
- determine whether all AEs and SAEs were appropriately reported
- determine whether the investigator is maintaining the essential documents
- discuss any emergent problem

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- check the CRF for accuracy and completeness
- validate the contents of the CRF against source
- assess the status of drug storage, dispensing and retrieval
- retrieve study data

All data required by the protocol must be reported accurately on the CRF and must be consistent with the source documents. Source documents are original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays or other diagnostic images, subject files, pharmacy records and laboratory records). The investigator will make available the source documents for inspection. This information will be considered as confidential.

During scheduled monitoring visits, the investigator and the investigational site staff should be available to meet with the study monitor in order to discuss the progress of the study, make necessary corrections to CRF entries, respond to data clarification requests and respond to any other study-related inquiries of the monitor. The investigational site staff in addition to the study coordinator should also include nuclear medicine staff, radiopharmacist, and radiology staff.

The study monitor will perform a closeout visit at the conclusion of the investigator's involvement in the study.

11.6.2 Auditing

The investigator will make all pertinent records available including source documentation for inspection by regulatory authorities and for auditing by the sponsor. This information will be considered as confidential.

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Representatives of local or foreign health authorities may review the conduct or results of the study at the investigational site. The investigator must promptly inform the sponsor of any audit requests by health authorities, and will provide sponsor with the results of any such audits and with copies of any regulatory documents related to such audits.

11.7 Case Report Forms and Study Records

Sponsor will provide a CRF and CRF instructions for the entry of study data. CRFs must be completed for each subject. All study data will be entered on CRFs from original source data. Entries should be made on the case report forms directly and promptly onscreen. The CRF will be reviewed, signed and dated by the investigator.

11.8 Protocol Violations/Deviations

Protocol violations/deviations will be documented by investigator and submitted to the IRB/IEC, as required by IRB/IEC requirements.

11.9 Access to Source Documentation

During the study, a representative of the sponsor will make periodic visits to the investigational sites while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government regulations and guidelines. The investigator will permit authorized representatives of the sponsor and the respective local and national health authorities to inspect facilities and records relevant to this study, if needed.

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11.10 Data Generation and Analysis

Sponsor(s) or its designee will be responsible for data collection, data management, generation of data outputs and statistical analysis of all data.

11.11 Retention of Data

As described in the ICH GCP Guidelines, ‘essential documents’, including copies of the protocol, subject identification codes, CRF, source data, informed consent form(s) and other documents pertaining to the study conduction must be kept for the maximum period of time as required by the study site. This time period must be at least two years after the last follow up of the patients enrolled.

No study document should be destroyed without prior written agreement between sponsors and the investigators. Originals of all documentation generated by sponsor and copies of outgoing sponsor correspondence concerning the study will be stored and retained in a safe area under the control of sponsor for the lifetime of the product. In particular, the final report must be retained by sponsor, or the subsequent owner, for 5 years beyond the lifetime of the study drug.

11.12 Financial Disclosure

All investigators must provide financial disclosure information in accordance with the US Code of Federal Regulations Title 21 CFR 54.2 through 54.6.

11.13 Publication and Disclosure Policy

All unpublished documentation (including the protocol, CRF and Investigator Brochure (IB) given to the investigator is strictly confidential. All recipients must agree not to disclose the

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information herein contained to any person without the prior written authorization of sponsor.

The submission of these documents to the IRB is expressly permitted. The investigator agrees that sponsor maintains the right to use the results of this study in their original form and/or in a global report for submission to governmental and regulatory authorities of any country.

The results of the study may be presented during scientific symposia or published in a scientific journal only after review by sponsor in accordance with the guidelines set forth in the applicable publication or financial agreement.

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Appendices

Appendix 1- Preclinical Toxicity studies

This exhibit is 303 pages. Therefore we are providing it in the attached CD.

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Appendix II: Visit Specific Schedule

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7	Screening						Therapy						F/II												30																														
	Month		Week		Day		1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23		24		
	Week		Day		1		2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		22		23		24				
Signing informed consent form	*																																																						
Randomization	*																																																						
1 Evaluation of blood tests (CBC)	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*																
1 Evaluation of blood tests (CMP)	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*																	
2 Evaluation of imaging studies (CT, MRI, bone imaging)	*																				*			*		*		*		*		*		*		*		*																	
3 Ga-68 or Lu-177 PSMA PET/CT	*																																																						
4 Medication & Hypersensitivity assessment	*																																																						
5 Current Disease(somatic or psychiatric)	*																																																						
6 Histopathology evaluation	*																																																						
7 Relevant medical history & demographics	*																																																						
8 Vital Signs(BP, HR, T, RR)	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*																
9 Evaluation of life expectancy	*																																																						
10 Prior therapy for Prostate cancer	*																																																						
11 ECG and continues ECG monitoring	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*																
12 Quality of life assessment (EPIC-26) & FQOL	*																																																						
13 PSA determination	*		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*																
14 Whole body(Anterior And Posterior) scan	*		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*																
15 Followup calls for AEM Monitoring		+7 days			+7 days			+7 days			+7 days			+7 days			+7 days	*																																					
days	-10	-7	0	14	28	42	56	70	84	98	112	126	140	154	168	182	196	210	224	238	252	266	280	294	308	322	336	350	364	378	392	406	420	434	448	462	476	490	504	518	532	546	560	574	588	602	616	630	644	658	672	686	698		

- 1 A blood sample will be collected within 48 hours (preferably 30 minutes) before the injection to document CMP and CBC for safety purposes.

1 Only at first treatment several blood samples will be required for dosimetry purposes 5 minutes, 30 minutes, 1, 4, 24, 48, and 72 hours, 7 to 10 days sample (optional).

1 Laboratory test will be acceptable only if they performed within 1 week of each scheduled visit. Screening visit and week -1 can be combined if screening visit performed within 2 weeks of the first cycle. 1 °CBE will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 months for 24 month or until disease progression.

1 CMP will be checked every 4 weeks during therapy cycles and then every three months up to 24 months after the last treatment.

2 Baseline imaging within 12 weeks of start of therapy including (a) Chest CT, preferably with contrast & CT or MRI of the abdomen- pelvic preferably with contrast, (b) bone imaging, (c) or equivalent

2 Relevant imaging studies will be repeated every 1.2 to 1.6 weeks until reaching the endpoint or 24 months after the first treatment.

8 For safety assessment, vital signs will be measured with in 20 minutes before and/or up to 1 hour after adm initiation of 177Lu-PSMA 617.

11 Continuous ECG monitoring at least 15 minutes prior to administration of the study drug and lasts at least 1 hour after administration. Also two 12 lead ECGs: one before injection and one after 4 hr scan.

12 Quality of life questionnaire (EPIC-36 and ECOG will be completed at baseline and in 3, 6, 9, 12, 18 and 24 months (+/- 1 month for each) after the start of treatment.

13 PSA will be measured every 6 weeks during the treatment and every 3 months after the last treatment until reaching endpoint or 24 months after the first treatment.

14 Only at first treatment Scintigraphy will be performed several times [4, 24, 48, and 72 hours] after injection for dosimetry purposes. Please refer to dosimetry schedule of events.

15 Telephone follow up: 7 (+/- 5) days after each treatment cycles until completion of 4 cycles and for follow up phase, every 3 months (+/- 1 week) until the end of follow up visits (24 months).

In each time point that the above shows follow up will be started.

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Appendix III: Chemistry, Manufacturing, and Control (CMC) of Lu-177 PSMA

Not provided with original protocol

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Appendix IV: Informed Consent Form

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Sponsor Signatures

Study Title: PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESISTA-PC). A phase II clinical trial.
Study Number: 133661
IND Number:
Final Date: 01/31/2017

This clinical study protocol was subject to critical review and has been approved by the sponsor.

Signed: _____ Date: _____

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Investigator's Signature

Study Title: PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESISTA-PC). A phase II clinical trial.

Study Number:

IND Number:

133661

Final Date: 01/31/2017

I acknowledge that I have read the attached protocol as amended and I agree that it contains all information necessary to conduct the study. I also agree to and will comply with all provisions set forth therein and herein, and certify as follows:

I will comply with all Health Authority regulations/guidelines relevant to the conduct of human clinical trials, as set forth in 21 CFR Parts 50, 54, 56, and 312 part D as they may be amended or supplemented from time to time. I will not initiate the study until I have obtained written approval from the appropriate Institutional Review Board/Independent Ethics Committee and have complied with all financial and administrative requirements of the governing body of my clinical institution. I will obtain written informed consent from all study participants prior to performing any screening procedures.

I understand that my signature (or that of a Sub-Investigator) on a case report form indicates that the data therein have been reviewed and are deemed to be complete, accurate, and acceptable to me.

I have not been disqualified by any regulatory authority or otherwise disqualified from serving as a Principal Investigator, or debarred by the U.S. FDA or any other regulatory authority. In the event that during the term of the study, I become debarred, or receive notice of an action by a health authority or threat of an action with respect to my conduct of clinical research, I shall immediately notify sponsor. In the event I become debarred, I shall immediately cease all activities relating to the study.

I understand and acknowledge that confidential information related to this study includes, but is not limited to, (1) this document, (2) the Protocol for the study, (3) the data derived from the study and (4) my impressions of the progress or results of the study ("Confidential Information") all of which is the proprietary and sole property of sponsor. I will comply with the terms of the Confidentiality and Non-Disclosure Agreement and Clinical Trial Agreement, which stipulate that no Confidential Information will be disclosed or generally described to anyone other than sponsor, personnel or designees, participating study staff, regulatory authorities with appropriate jurisdiction, or members of the responsible Institutional Review Board/Independent Ethics Committee. I will not use such Confidential Information for any purpose other than the evaluation or conduct of the clinical investigation. I am not presently, nor will I be during the term of the study, a consultant or advisor to any division of any financial or securities firm.

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Investigator Signature

Site Name

Investigator Printed Name (with degree)

Date (DD/MM/YYYY)

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Baseline and follow-Up Questionnaire for Pain and Adverse Events

PATIENT INFORMATION

Last name: _____ First Name: _____

Date of Birth: _____ Medical Record Number: _____

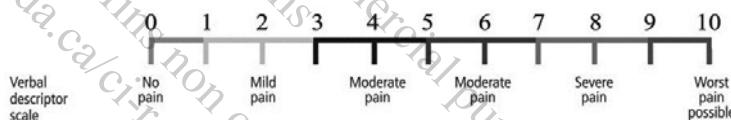
Change of pain medication since last ¹⁷⁷Lu-PSMA-617 cycle

- No change
 Change in dosage/administration: medication _____ increase or decrease
 Addition/removal of medication: medication _____ addition or removal

Pain

- No or Yes:

Locations: _____
Overall level: _____



Change since last cycle: _____

- increase, no change, decrease

Nausea

- No nausea
 Nausea with loss of appetite only
 Nausea with eating/drinking less than usual
 Had to go to hospital for nausea

Vomiting

- No vomiting
 1 - 2 episodes per day
 3 - 5 episodes per day
 more than 5 episodes per day

Dry mouth

- No dry mouth
 Dry or thick saliva
 Normal eating only with water/lubricants possible
 Tube feeding or total i.v. nutrition

Taste

- Normal taste
 Altered taste but no change in diet
 Altered taste with change in diet

Fatigue

- No fatigue
 Fatigue relieved by rest
 Fatigue not relieved by rest, limiting work
 Fatigue not relieved by rest, limiting self-care

Hematoma

- No Hematoma
 Occurrence of hematoma without known event

Fever

- No fever
 38.0 - 39.0 °C (100.4 - 102.2 °F)
 >39.0 - 40.0 degrees °C (102.3 - 104.0 °F)
 >40.0 °C (>104.0 °F)

Urinary retention

- Able to void normally
 Able to void with some pressure
 Unable to void or voiding only after catheter/intervention/treatment

Diarrhea

- Normal bowel movements
 Increase by <4 stools per day

Other (symptom, grade: mild/moderate/severe):

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- Increase by 4-6 stools per day
- Increase by more than 6 stools per day
- Had to go to hospital for diarrhea

Date: _____ Name: _____ Signature: _____

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EPIC-26
The Expanded Prostate Cancer Index Composite
Short Form

This questionnaire is designed to measure Quality of Life issues in patients with Prostate cancer. To help us get the most accurate measurement, it is important that you answer all questions honestly and completely.

Remember, as with all medical records, information contained within this survey will remain strictly confidential.

Today's Date (please enter date when survey completed): Month _____ Day _____ Year _____

Name (optional): _____

Date of Birth (optional): Month _____ Day _____ Year _____

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Do Not
Mark in
This
Space

1. Over the **past 4 weeks**, how often have you leaked urine?

- | | |
|----------------------------|---|
| More than once a day..... | 1 |
| About once a day..... | 2 |
| More than once a week..... | 3 |
| About once a week..... | 4 |
| Rarely or never..... | 5 |

(Circle one number)

23/

2. Which of the following best describes your urinary control **during the last 4 weeks**?

- | | |
|------------------------------------|---|
| No urinary control whatsoever..... | 1 |
| Frequent dribbling..... | 2 |
| Occasional dribbling..... | 3 |
| Total control..... | 4 |

(Circle one number)

26/

3. How many pads or adult diapers per day did you usually use to control leakage
during the last 4 weeks?

- | | |
|-----------------------------|---|
| None | 0 |
| 1 pad per day..... | 1 |
| 2 pads per day..... | 2 |
| 3 or more pads per day..... | 3 |

(Circle one number)

27/

4. How big a problem, if any, has each of the following been for you **during the last 4 weeks?**

(Circle one number on each line)

	<u>No Problem</u>	<u>Very Small Problem</u>	<u>Small Problem</u>	<u>Moderate Problem</u>	<u>Big Problem</u>	
a. Dripping or leaking urine	0	1	2	3	4	28/
b. Pain or burning on urination.....	0	1	2	3	4	29/
c. Bleeding with urination.....	0	1	2	3	4	30/
d. Weak urine stream or incomplete emptying.....	0	1	2	3	4	31/
e. Need to urinate frequently during the day.....	0	1	2	3	4	33/

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5. Overall, how big a problem has your urinary function been for you **during the last 4 weeks?**

No problem.....	1				
Very small problem.....	2				
Small problem.....	3				
Moderate problem.....	4				
Big problem.....	5				

(Circle one number)

34/

Do Not
Mark in
This
Space

6. How big a problem, if any, has each of the following been for you? (Circle one number on each line)

	<u>No Problem</u>	<u>Very Small Problem</u>	<u>Small Problem</u>	<u>Moderate Problem</u>	<u>Big Problem</u>	
a. Urgency to have a bowel movement	0	1	2	3	4	49/
b. Increased frequency of bowel movements.....	0	1	2	3	4	50/
c. Losing control of your stools.....	0	1	2	3	4	52/
d. Bloody stools	0	1	2	3	4	53/
e. Abdominal/ Pelvic/Rectal pain...	0	1	2	3	4	54/

7. Overall, how big a problem have your bowel habits been for you **during the last 4 weeks?**

No problem.....	1					
Very small problem.....	2					
Small problem.....	3					
Moderate problem.....	4					
Big problem.....	5					

(Circle one number)

55/

8. How would you rate each of the following **during the last 4 weeks?** (Circle one number on each line)

	<u>Very Poor to None</u>	<u>Poor</u>	<u>Fair</u>	<u>Good</u>	<u>Very Good</u>	
a. Your ability to have an erection?.....	1	2	3	4	5	57/
b. Your ability to reach orgasm (climax)?.....	1	2	3	4	5	58/

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9. How would you describe the usual QUALITY of your erections **during the last 4 weeks?**

- | | |
|---|---|
| None at all..... | 1 |
| Not firm enough for any sexual activity..... | 2 |
| Firm enough for masturbation and foreplay only..... | 3 |
| Firm enough for intercourse..... | 4 |
- (Circle one number) 59/

10. How would you describe the FREQUENCY of your erections **during the last 4 weeks?**

- | | |
|---|---|
| I NEVER had an erection when I wanted one..... | 1 |
| I had an erection LESS THAN HALF the time I wanted one..... | 2 |
| I had an erection ABOUT HALF the time I wanted one | 3 |
| I had an erection MORE THAN HALF the time I wanted one..... | 4 |
| I had an erection WHENEVER I wanted one..... | 5 |
- (Circle one number) 60/

Do Not
Mark in
This
Space

11. Overall, how would you rate your ability to function sexually **during the last 4 weeks?**

- | | |
|----------------|---|
| Very poor..... | 1 |
| Poor..... | 2 |
| Fair..... | 3 |
| Good..... | 4 |
| Very good..... | 5 |
- (Circle one number) 64/

12. Overall, how big a problem has your sexual function or lack of sexual function been for you
during the last 4 weeks?

- | | |
|-------------------------|---|
| No problem..... | 1 |
| Very small problem..... | 2 |
| Small problem..... | 3 |
| Moderate problem..... | 4 |
| Big problem..... | 5 |
- (Circle one number) 68/

13. How big a problem **during the last 4 weeks**, if any, has each of the following been for you?
(Circle one number on each line)

No Very Small Small Moderate Big

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	Problem	Problem	Problem	Problem	Problem	
a. Hot flashes.....	0	1	2	3	4	74/
b. Breast tenderness/enlargement..	0	1	2	3	4	75/
c. Feeling depressed.....	0	1	2	3	4	77/
d. Lack of energy.....	0	1	2	3	4	78/
e. Change in body weight.....	0	1	2	3	4	79/

THANK YOU VERY MUCH!!

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Clinical Trial Protocol: IND # 133661

Study Title: PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC). A phase II clinical trial

Study Number: NCT03042312

IND Number: 133661

Study Phase: Phase II

Product Name: ^{177}Lu -DOTA-PSMA-617

Indication: Metastatic castration resistant prostate cancer

Principal Investigators: Ebrahim S. Delpassand, M.D. F.A.C.N.M.

Investigators: Johannes Czernin, M.D.

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Original Protocol Date: 12/28/2016

Amendment 2 Date: 06/07/2017

Amendment 3 Date: 06/29/2017

Amendment 4 Date: 09/18/2017

Confidentiality Statement

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Clinical Trial Protocol: IND #133661
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SYNOPSIS

Sponsors:

Ebrahim S. Delpassand, M.D.

Johannes Czernin, M.D.

Name of Finished Product:

¹⁷⁷Lu-PSMA-617

Name of Active Ingredient:

2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid

Study Title:

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC). A phase II clinical trial.

Study Number:

NCT03042312

Study Phase:

Phase II

Primary Objective:

To assess safety and efficacy defined as >50% decline in PSA after ¹⁷⁷Lu-PSMA-617 in patients with metastatic castration resistant prostate cancer

Secondary Objectives for each Treatment Dose:

1. To determine maximum PSA decline.

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2. To determine PSA progression-free survival (PFS), measured from start of therapy until death or PSA progression.
3. To determine radiographic PFS, measured from start of therapy until death or radiographic progression using RECIST 1.1/PCWG criteria.
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST stable disease (SD), partial response (PR) or complete response (CR).
5. To determine impact on bone pain level
6. To determine impact on quality of life
7. To determine impact on performance status (ECOG)

Study Design:

Open-label, prospective, multicenter clinical trial.

Study Population:

Patients with metastatic castration resistant prostate cancer

Inclusion Criteria:

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel naive and docetaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ⁶⁸Ga-PSMA-11 PET/CT or diagnostic ¹⁷⁷Lu-PSMA-617 scintigraphy or any equivalent PSMA-directed imaging
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2500/\mu\text{l}$, PLT count $\geq 100,000/\mu\text{l}$, Hb ≥ 9.9 g/dl and ANC $\geq 1500 \text{ mm}^3$ for the first cycle and WBC $\geq 2,000/\mu\text{l}$, PLT count $\geq 75,000/\mu\text{l}$, Hb ≥ 8.9 g/dl and ANC $\geq 1000 \text{ mm}^3$ for the subsequent cycles
8. Signing of the Informed Consent Form
9. Patients enrolling in this trial should have received either Enzalutamide or Abiraterone

Exclusion Criteria:

1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ²²³Ra, ¹⁵³Sm) or other radionuclide therapy.
2. Glomerular Filtration Rate (GFR) < 40 ml/min
3. Serum creatinine $> 1.5 \times \text{ULN}$
4. AST and ALT $> 5 \times \text{ULN}$
5. Urinary tract obstruction or marked hydronephrosis

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6. Diffuse bone marrow involvement confirmed by super-scans

*super-scan is defined by kidney uptake equal or below background due to diffuse bone involvement on staging PET/CT or scintigraphy

Test Product; Dose; and Mode of Administration:

Randomization into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq ($\pm 10\%$, **arm 1**) or 7.4 GBq ($\pm 10\%$, **arm 2**) ¹⁷⁷Lu-PSMA-617 every 8 \pm 1 weeks; RLT until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy as determined by dosimetry.

Study Duration:

Patients will be followed until either of the following conditions occur:

1. 24 month after the first treatment.
2. Progression by RECIST 1.1/PCWG criteria.
3. Death.

Safety Assessments:

AE and safety assessments will be performed through the following mechanisms, also listed in Appendix II:

a. Following laboratory tests will be performed at baseline (within 72 hours of first treatment dose) and then every 2 weeks (+/- 3 days) after first dose, continued until 12 weeks after the last dose and then every 3 months (+/- 1 week) thereafter until the end of follow-up visits (24 months from 1st therapy date) or upon disease progression. The CBC and CMP within 2 weeks of each subsequent treatment cycle will be used to assess eligibility of the corresponding treatment cycle.

1. Complete metabolic panel and eGFR
2. CBC

b. Telephone Follow-up: 7(± 3) days after each treatment cycle and for follow-up phase every 3 (± 1 month) until the end of follow-up visits (24 months).

Following conditions if in view point of investigators deemed study related, will result in permanent discontinuation:

i. Grade 3-4 non-hematologic toxicities with select exceptions for:

1. Grade 3 fatigue < 10 days
2. Grade 3 nausea, vomiting, and diarrhea and grade 4 vomiting and diarrhea that persist

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for < 72 hours in the absence of maximum medical therapy.

3. Asymptomatic grade 3 non-hematological laboratory abnormalities that resolve in 72 hours.
4. Grade 3 infections that resolve under medical treatment within 10 days
 - ii. AST/ALT > 3x ULN and bilirubin > 2x ULN
 - iii. Grade 4 Hematological toxicities persisting >3 weeks.
 - iv. Grade 3 Hematological abnormalities that do not return to baseline for > 12 weeks.

Data Safety Monitoring Board (DSMB) and Data Safety Monitoring Plan (DSMP):

A Data Safety Monitoring Board (DSMB) has established and will evaluate safety throughout the study. The DSMB will advise the Sponsor, Investigators and investigational sites regarding the continuing safety of study patients and the patients yet to be recruited to the study as well as maintaining validity and scientific merit of the study. The DSMB will review ongoing examinations of safety data and promptly give recommendations to continue, continue with modification, or terminate the study.

The Excel Diagnostics DSMB will serve as the lead site DSMB. At UCLA, DSMB oversight will be provided by JCCC Data Safety Monitoring Board (DSMB). The monitoring board will meet quarterly to review safety records including compliance with follow up visits.

Interim safety analyses: 4 interim safety analyses will be conducted by DSMB that will be initiated at the time when 25%, 50%, 75% and 100% of the total ¹⁷⁷Lu-PSMA treatments in the trial have been completed. The DSMB will meet and assess up-to-date safety information within two weeks of a treatment exposure rate being achieved (i.e., the point when 25%, 50%, 75% and 100% of treatments have occurred). Further patients may only be randomized two weeks after the treatment exposure rate has been reached and after a positive opinion from the DSMB.

Efficacy Assessment for each treatment arm:

Primary objective:

12 week PSA response: Proportion of patients with PSA-decline of $\geq 50\%$ at 12 (± 1) week after the first RLT [1].

Secondary objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]
2. Time to PSA progression, for each treatment arm. [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later

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- b. for patients without PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later
- 3. Radiographic progression free survival (rPFS), for each treatment arm.
- 4. Change in Pain, Quality of Life and ECOG performance score: Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 month, for each treatment arm

Number of patients enrolled:

As per statistical evaluation, total of 200 patients will be required to have statistical power to achieve the primary endpoints of the study.

Date of Original Protocol: December 28th, 2016

Date of Most Recent Protocol Amendment (if applicable): 09/18/2017

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LIST OF APPENDICES

Appendix I: Preclinical Toxicity Studies

Appendix II: Visit Specific Schedule

Appendix III: Chemistry, Manufacturing, and Control (CMC) of ¹⁷⁷Lu- PSMA

Appendix IV: Consent Form

Appendix V: Dosimetry Protocol

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse event
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
AP	Alkaline phosphatase
AST	Aspartate aminotransferase
AUC	Area under the plasma concentration versus time curve
BUN	Blood urea nitrogen
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CI	Confidence interval
CR	Complete response
CRF	Case report form
CT	Computed tomography
DCR	Disease Control Rate
ECOG	Eastern Cooperative Oncology Group
eGFR	estimated Glomerular Filtration Rate
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GGT	Gamma-glutamyl transferase
GH	Growth hormone
Hct	Hematocrit
Hgb	Hemoglobin

HIPAA	Health Information Portability and Accountability Act
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intent-to-treat
LDH	Lactic dehydrogenase
MBq	MegaBequerel
mCi	milliCurie
mo	months
GBq	gigabecquerel
MR	Magnetic resonance
MRI	Magnetic resonance imaging
N/A	Not applicable
NDA	New Drug Application
PCa	Prostate cancer
PET/CT	Positron Emission Tomography/Computed Tomography
PFS	Progression-free survival
PSA	Prostate-specific antigen
PR	Partial response
RBC	Red blood cell
RECIST	Response Evaluation Criteria In Solid Tumors
RLT	Radioligand therapy

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rPFS	Radiographic progression-free survival
SAE	Serious adverse event
SAER	Serious adverse event report
SAP	Statistical analysis plan
SD	Stable disease
SE	Standard error
SPECT	Single-photon emission computerized tomography
PSMA	Prostate-specific membrane antigen
US	United States
WBC	White blood cell
WHO-DD	World Health Organization Drug Dictionary

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1. Introduction

1.1 Background

According to the American Cancer Society more than 1 million people in the United States are diagnosed with cancer each year. For American *males*, prostate cancer is the second most common cause of cancer related death [2]. A recent publication [3] estimated the prevalence of prostate cancer as 2,219,280 in the US in 2009 and 3,072,480 in 2020, and incidence of metastatic Castration Resistant Prostate Cancer (mCRPC) as 36,100 and 42,970, respectively. Various therapies have been developed to improve survival of patients with advanced prostate cancer. However, despite such efforts currently all-cause mortality in prostate cancer has been estimated at 168,290 in 2009 and 219,360 in 2020, with 20.5% and 19.5% of these deaths, respectively, occurring in men with mCRPC.

Patients with metastatic castration-resistant prostate cancer (mCRPC) have a poor prognosis, and those patients with metastases are expected to survive ≤ 19 mo [3]. As patient disease progresses, quality of life deteriorates, and until recently, few treatment options were available. Several new therapies have shown an improvement in overall survival for patients with mCRPC who have already received chemotherapy with docetaxel (Fig. 1) [4] [5] [6, 7] [8]. The impact of these new data on clinical practice, treatment sequencing, and best care for individual patients is not yet fully established.

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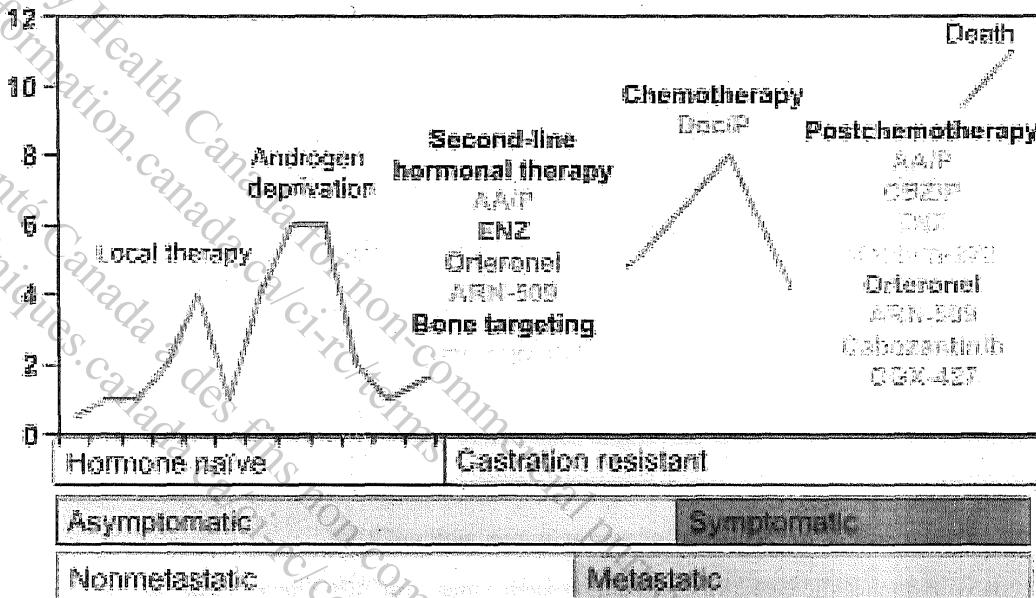


Figure 1: Current, ongoing, and future landscape in the management of castration-resistant prostate cancer.

Color key: green = US Food and Drug Administration/European Medicines Agency (FDA/EMA) approved; light green = trial results in high-risk patients positive, but not approved; orange = prospective, randomized, phase 3 clinical trial completed, results positive, FDA/EMA approval awaited; blue = prospective, randomized, phase 3 clinical trial completed, results awaited; purple = promising agent, phase 3 clinical trials ongoing. * Trial results for denusomab in high risk patients positive, but not approved. AA/P = abiraterone acetate with prednisone; ENZ = enzalutamide; Doc/P = docetaxel plus prednisone; CBZ/P = cabazitaxel plus prednisone.

1.1.1. Current treatment options for metastatic castration-resistant prostate cancer: before docetaxel

Sipuleucel-T

Sipuleucel-T is an autologous vaccine consisting of individually collected antigen-presenting cells that are exposed to the fusion protein prostatic acid phosphatase and granulocyte colony-stimulating factor (GCSF), and then reinfused in the patient at weeks 0, 2, and 4. In the Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) study, median survival with sipuleucel-T was 25.8 mo compared with 21.7 mo with placebo [9]. It has to be

considered, however, that only patients with a good Eastern Cooperative Oncology Group performance status of 0–1, asymptomatic or mildly symptomatic osseous metastases, and absence of visceral metastases were included in the trial.

Abiraterone acetate

The COU-AA-302 (Cougar 302) trial randomized 1088 men with mCRPC to receive abiraterone acetate with prednisone (AA/P) or placebo [4] with the primary end points of overall and radiographic progression-free survival (rPFS) by central review. Median overall survival was 35.3 mo and 27.2 mo in the AA/P group and in the placebo group, respectively ($p = 0.01$) [10]. Also, the co-primary end point of rPFS was significantly improved in the AA/P group, at 16.5 mo, as compared to 8.3 mo in the placebo arm ($p < 0.001$). On all secondary end points, AA/P treatment resulted in significantly improved effects.

Docetaxel/prednisone

In 2004, cytotoxic treatment with docetaxel plus prednisone (Doc/P) was the main option for treatment of mCRPC based on the TAX 327 trial [11]. The median survival was 18.9 mo versus 16.4 mo in the group of patients who received mitoxantrone/prednisone ($p = 0.009$), the 3-yr overall survival rate was 18.6% versus 13.5%, and pain response was 35% versus 22%. It has been shown recently that Doc/P is active in men with symptomatic mCRPC and especially in patients with poorly differentiated prostate cancer (PCa) (Gleason score: 8–10) [12].

Subsequent studies using combinations with docetaxel have not further improved the oncologic outcome [3]. The results of the Randomized Study Comparing Docetaxel Plus Dasatinib to Docetaxel Plus Placebo in Castration-Resistant Prostate Cancer (READY) and the Aflibercept in Combination with Docetaxel in Metastatic Androgen-Independent Prostate Cancer (VENICE) trial were disappointing [13] [11]. The median survival after docetaxel and docetaxel/dasatinib was 21.2 mo versus 21.5 mo, respectively, and the median survival after

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docetaxel versus docetaxel plus afilbercept was 21.1 mo versus 22.1 mo, respectively.

The differences in the patient cohorts of the Cougar 302, IMPACT, and TAX 327 trials make it evident that AA/P will be used for asymptomatic or mildly symptomatic mCRPC with a low metastatic burden, whereas Doc/P might be the treatment of choice in men with symptomatic mCRPC and/or a high metastatic burden as well as an undifferentiated PCa.

1.1.2. After docetaxel treatment

Docetaxel rechallenge

The scientific evidence of this approach results from large, retrospective series that identified patients who might be good candidates for re-exposure [14] [15] [16]. Patients who responded with a $\geq 30\%$ decrease in prostate-specific antigen (PSA) level, maintained for at least 8 wk after first exposure to docetaxel, demonstrated a positive PSA response in about 55% to 60% of the cases during re-exposure without increasing treatment related toxicity.

Abiraterone acetate plus prednisone

AA/P versus placebo was evaluated in the Cougar 301 trial, which randomized 1195 patients with progressive mCRPC who failed docetaxel-based chemotherapy [5]. The median follow-up in the overall study population was 12.8 mo. Overall survival was significantly improved from 10.9 mo in the placebo arm to 14.8 mo in the AA/P arm ($p < 0.001$). All secondary end points were met and all end points demonstrated a significantly improved benefit for the AA/P group. Adverse events with regard to the CYP 17 blockade were observed significantly more often in the AA/P arm (55% vs 43%; $p < 0.001$).

Recently, Goodman et al. [17] demonstrated that AA/P is effective even in patients with liver or lung metastases, although to a lesser degree. The overall survival times were 12.9 mo versus 8.3 mo in the placebo group ($p = 0.022$). Albiges et al. [18] described an AA withdrawal syndrome that developed in 32% of 66 patients who had been treated for a mean period of 5.7

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mo. Clayton et al. [19] presented data from a population-based study that included 187 mCRPC patients with a mean PSA serum concentration of 138 ng/ml who were treated with AA/P. The median overall survival was only 9.3 mo and might reflect the oncologic efficacy of AA/P in a real-world patient population with high metastatic burden.

Enzalutamide (formerly MDV3100)

Enzalutamide (ENZ) acts as an androgen receptor (AR)-signaling inhibitor, and it was evaluated in the Multinational, Phase 3, Randomized, Double-blind, Placebo-controlled, Efficacy and Safety Study of Oral MDV3100 in Patients with Progressive Castration-Resistant Prostate Cancer Previously Treated with Docetaxel-Based Chemotherapy (AFFIRM) trial, which randomized 1199 mCRPC patients to receive ENZ or placebo [8]. The median follow-up was 14.4 mo and the median overall survival was 18.4 mo and 13.6 mo ($p < 0.0001$) in the ENZ group and in the placebo group, respectively, with a 37% reduction in relative risk for death. All secondary end points were met with a statistically significant benefit in the ENZ arm. With regard to safety, the ENZ group experienced fewer grade 3/4 toxicities than the placebo group (53% vs 45%). The risk of seizures was slightly elevated in the ENZ group, with a frequency of 0.6% versus 0% in the placebo group.

Recently, Scher et al. [20] demonstrated that the use of corticosteroids in parallel to ENZ not only increased grade 3/4 side effects from 34.4% to 63.3%, but it also decreased overall survival to a median 11.5 mo. These data suggest that one of the other second-line therapies, such as AA/P or cabazitaxel plus prednisone (CBZ/P), might be the drug of choice, rather than ENZ, in patients who need corticosteroids for the management of associated comorbidities.

Sternberg et al. [21] reported that ENZ is equally effective in patients aged >75 yr, with a median survival time of 18.2 mo as compared to the placebo group with 13.3 mo ($p = 0.0044$). Fleming et al. [22] identified a longer disease history (7.9 yr vs 5.9 yr), a better PSA response (87% vs 52%), and a lower metastatic burden associated with long-term response of 35% and 22% after 12 mo and >18 mo, respectively. These data seem to be important for the decision-making process about the most appropriate therapy for mCRPC patients following docetaxel

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chemotherapy.

Cabazitaxel plus prednisone

In the XRP6258 Plus Prednisone Compared to Mitoxantrone Plus Prednisone in Hormone-Refractory Metastatic Prostate Cancer (TROPIC) trial, 755 patients with mCRPC who progressed during or after docetaxel-based chemotherapy were prospectively randomized to receive CBZ/P or mitoxantrone/prednisone (MP) at 21-d intervals for 10 cycles [5]. The primary end point was achieved and CBZ/P treatment resulted in a median overall survival of 15.1 mo in the CBZ/P compared to 12.7 mo in the mitoxantrone/prednisone group (hazard ratio [HR]: 0.70; 95% confidence interval [CI], 0.59–0.83; $p < 0.0001$). All secondary end points of the trials were reached and they were in favor of CBZ. The most common side effects were neutropenia (CBZ/P group: 82% vs MP group: 58%), leukopenia (CBZ/P group: 68% vs MP group: 42%), and anemia (CBZ/P group: 11% vs MP group: 5%). Diarrhea was the most common non-hematologic side effect and occurred in 6% of the CBZ/P group and <1% of the MP group.

On the other hand, the German compassionate use program (CUP) included 111 patients with mCRPC who met the inclusion criteria of the TROPIC trial; the frequency of neutropenia, leukopenia, and anemia decreased to 7.2%, 9.0%, and 4.5%, respectively [23]. Grade 3/4 gastrointestinal toxicity was observed in only 0.9% of the patients. The most likely reason for the improved toxicity profile is the experience of the investigators, guideline-compliant application of GCSF even at cycle 1, and preventive measures with regard to the treatment of diarrhea.

Recently, Heidenreich et al. [24] analyzed the European CUP, including 746 mCRPC patients, with regard to the frequency and management of adverse events in senior adults. In that study, 325 (43.5%) patients were aged ≥ 70 yr and 145 (19.4%) men were ≥ 75 yr. The type and the frequency of grade 3/4 side effects did not differ significantly between the younger and the older patients except that the frequency of grade 3/4 neutropenia was slightly higher in the

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group of men aged ≥ 75 yr (19.7% vs 15%). Furthermore, GCSF was used more often at cycle 1 (58.5% vs 47%) and throughout CBZ/P treatment (66.8% vs 58%) in the ≥ 75 age group versus the <70 age group. In their analysis, Heidenreich et al. [24] developed a risk model to predict grade ≥ 3 neutropenia and/or neutropenic complications based on a multivariate analysis. Age ≥ 75 yr, cycle 1, and neutrophil count $<4000/\text{mm}^3$ before CBZ injection were associated with neutropenic complications. It has to be mentioned that even in the presence of these risk factors, prophylactic application of GCSF significantly reduced neutropenic complications by 30% (odds ratio: 0.70; 95% CI, 0.50–0.99; $p = 0.04$).

Bone-targeting agents

More than 90% of patients with CRPC have bone metastases, which are a major cause of death, disability, and decreased quality of life, as well as increased cost of treatment [25]. Zoledronic acid and the receptor activator of nuclear factor κ B (RANK) ligand inhibitor denosumab are the two US Food and Drug Administration-approved bone-targeting agents in the management of CRPC [3].

In a phase 3 study, the median time to first on-study, skeletal-related event was 20.7 mo with denosumab compared with 17.1 mo with zoledronic acid (HR: 0.82; 95% CI, 0.71–0.95; $p = 0.0002$ for noninferiority; $p = 0.008$ for superiority) [26]. In a recent, prospective, randomized, double-blind, placebo-controlled trial, Smith et al. [27] evaluated the therapeutic efficacy of denosumab 120mg every week versus placebo in 1423 men with nonmetastatic CRPC and aggressive PSA kinetics (PSA level $>8.0 \text{ ng/ml}$ and/or PSA doubling time $<10 \text{ mo}$). The median time to first bone metastases was significantly prolonged by 4.3 mo (29.5 mo vs 25.2 mo; $p = 0.028$). Bone metastases-free survival was significantly improved by 16%, 23%, and 29% in patients with a PSA doubling time of $<10 \text{ mo}$, $<6 \text{ mo}$, and $<4 \text{ mo}$, respectively.

Radium-223

Radium-223 is a radiopharmaceutical that acts as a calcium mimic and targets new bone

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growth in and around bone metastases via heavy alpha particles that have an ultrashort range of <100 μ m. A Phase 3 Study of Radium-223 Dichloride in Patients with Symptomatic Hormone Refractory Prostate Cancer with Skeletal Metastases (ALSYMPCA), which included 921 CRPC patients, the median overall survival was 14.9 mo in patients treated with radium-223 compared with 11.3 mo in the placebo group (HR: 0.695; 95% CI, 0.581–0.8732; $p < 0.0001$) [7].

1.1.3. New and emerging developments

Agents targeting steroidogenesis

Orteronel (TAK-700) selectively blocks 17,20-lyase, resulting in fewer mineralocorticoid effects than AA [28]. In the phase 2 portion of a dose-finding study, Orteronel (TAK-700) 400mg twice daily with prednisone 5mg twice daily resulted in a reduction in PSA level $\geq 50\%$ in 52% of the 96 chemotherapy-naïve mCRPC patients at 12 wk. There are two ongoing phase 3 clinical trials in the prechemotherapy ($n = 1454$) and postchemotherapy ($n = 1083$) landscape of mCRPC that are evaluating the oncologic activity of orteronel. Both trials have completed recruitment.

Galeterone (TOK-001) has combined activity: It inhibits the human CYP17 enzyme, it has pure antagonistic activity toward the AR, and it inhibits the binding of androgens to both mutant and wild-type AR [29]. In the Androgen Receptor Modulation Optimized for Response (AMORI) trial, 49% of chemotherapy-naïve mCRPC patients experienced a PSA-level reduction of $\geq 30\%$, and a $\geq 50\%$ reduction was achieved by 22% [30]. Despite the absence of steroid co-treatment, no adrenal mineralocorticoid excess was observed and a phase 2 trial is underway.

Androgen-receptor blocking agents

ARN-509 is a full antagonist to AR overexpression: It inhibits androgen-dependent gene

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description, and it impairs nuclear translocalization and DNA binding of AR [31]. Currently, three prospective randomized phase 3 clinical trials are underway including (1) patients with high-risk and nonmetastatic CRPC, (2) treatment-naïve patients with mCRPC, and (3) patients with progression following AA/P treatment. Preliminary results have been presented for the first two groups and a ≥50% decline in PSA level was achieved in 91% of patients with high-risk and nonmetastatic CRPC and in 88% of treatment-naïve patients with mCRPC. The most common side effects were tolerable fatigue and gastrointestinal events.

ODM-201 is another antiandrogen with similar mechanisms of actions as described for ENZ and ARN-509 [31]. The potential advantage of ODM-201 is that it does not cross the blood–brain barrier and so might prevent the development of seizures. ENZ-4176 is a novel, nucleic acid–based antisense oligonucleotide against AR, which results in selective and specific downregulation of AR mRNA and protein.

Heat shock proteins

Heat shock proteins (HSPs) have been identified as AR coactivators and chaperone proteins that are increased in PCa cell lines after castration [32]. Quite recently, antisense oligonucleotides targeting HSP27 were evaluated in a phase 2 clinical trial including 72 patients chemotherapy-naïve mCRPC patients who received OGX-427 plus prednisone versus prednisone alone. At 12 wk, 71% and 40% of the patients were progression-free after OGX-427 or prednisone, respectively. A decline of ≥50% in PSA level was observed in 50% and 20% in the OGX-427 group and in the prednisone group, respectively. Furthermore, measurable disease response occurred in 44% and 0% of the OGX-427 group and the prednisone group, respectively.

1.1.4 Targeted therapies

Cabozantinib

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Cabozantinib is another promising bone-targeting agent that inhibits both vascular endothelial growth factor and met proto-oncogene (hepatocyte growth factor receptor; MET). In a prospective, randomized, placebo-controlled, phase 2 clinical trial, 171 mCRPC patients were enrolled to receive cabozantinib (100mg daily) or placebo [33]. Random assignment was halted early based on the observed activity of cabozantinib. Respectively 5% and 75% of patients treated with cabozantinib had a confirmed partial response and stable disease. The median progression-free survival was 29.7 wk, 23.9 wk, and 5.9 wk for patients who were docetaxel naïve, docetaxel pretreated, and on placebo treatment ($p < 0.001$), respectively. Interestingly, PSA changes did not correlate with the antitumor effects in bone metastases and soft-tissue lesions. However, patients with complete resolution ($n = 14$; 12%) or partial resolution ($n = 65$; 56%) of bone scans experienced significantly better response rates to soft-tissue metastases as compared to men with stable or progressing bone scans (81% vs 61%), and they also experienced longer progression-free survival rates at 6 mo (56% vs 48%, respectively). Cabozantinib has significant antitumor activity and a well-tolerated toxicity profile, so it might be well integrated into the therapeutic armamentarium to treat mCRPC.

Targeted radionuclide Therapy

Over the past several decades, numerous combined diagnostic and therapeutic radioligands (Theranostics) were designed to target receptors on the cancer cell surface. Antibodies (whole or small fragments), small molecules, peptides with affinities to receptors (agonist or antagonist) have demonstrated *in vivo* efficacy for targeting cancers based on up-regulated antigens or receptor populations. This approach, also called radioligand therapy (RLT), presents several advantages over conventional chemotherapy. The expression of the antigens or special receptors can be identified by a diagnostic probe before exposing patients to therapeutic doses of these agents allowing identification of suitable subjects for therapeutic procedures and preventing unnecessary exposure of the patients to radiation without significant benefit. This approach allows the physician to select only those patients with high expression

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of the target prior to treatment. Since the unused radioactive materials are excreted from the body, RLTs are generally well tolerated with no significant or generally reversible or manageable side effects as has been demonstrated for ¹⁷⁷Lu-DOTATATE treatment in patients with neuroendocrine tumor [34].

Prostate cancer demonstrates high expression levels of prostate-specific membrane antigen (PSMA) on its cell surface. Thus PSMA has become a biomarker for prostate cancer [35] [36] and has attracted significant interest as a target for the imaging [37] [38] and therapy [39, 40]. In particular, development of small urea-based PSMA ligands have received significant interest due to their high affinity for PSMA [41] [42]. The urea-based PSMA ligands were modified to deliver a variety of radio-imaging nuclides for both PET and SPECT. Gallium (⁶⁸Ga) labeled urea-based PSMA ligands have been developed as diagnostic agents and studied by several groups [43] [44]. More recently a Lutetium (¹⁷⁷Lu) labeled urea based PSMA ligand (DOTA PSMA or PSMA 617) were evaluated in preclinical and clinical phase. Characteristics of ¹⁷⁷Lu labeled PSMA are described below.

1.2 Characteristics of ¹⁷⁷ Lu-DOTA-PSMA (¹⁷⁷Lu-PSMA-617)

Lutetium (¹⁷⁷Lu) -DOTA PSMA has three components: PSMA is the targeting vector, DOTA (1, 4, 7, 10-tetraazacyclododecane-1, 4, 7, 10-tetraacetic acid) is a radiometal chelator and a linking group, and ¹⁷⁷Lu is the beta emitter that upon internalization delivers radiation to the nucleus of tumor cells to cause DNA damage [43] [44, 45]. The targeting vector utilizes glu-urea-lys sequence which is an inhibitor capable of binding to the domain of PSMA. These components have been previously used in human subjects and in medical research.

1.3 Background of Drug Development

There is substantial previous pre-clinical and clinical experience with ¹⁷⁷Lu-PSMA-617

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published in peer reviewed medical literature from multiple medical centers throughout the world. Sponsors are relying on studies published in the peer viewed medical journals for preclinical and preliminary clinical information. Summary of such reports is given below.

1.3.1 Preclinical Studies.

Martina Benesova et al. [46] performed a preclinical evaluation of radiolabeled PSMA-617. PSMA-617 was synthesized by solid phase peptide synthesis. PSMA-617 can be labeled with ¹⁷⁷Lu and Ga-68. Both in vivo and vitro studies were performed using LNCaP cell lines expressing PSMA. PSMA-617 showed highest inhibition potency $K_i = 6.91 \pm 1.32$ for Lu complex; 6.40 ± 1.02 nM for Ga complex. PSMA-617 showed higher specific internalization in LNCaP cells.

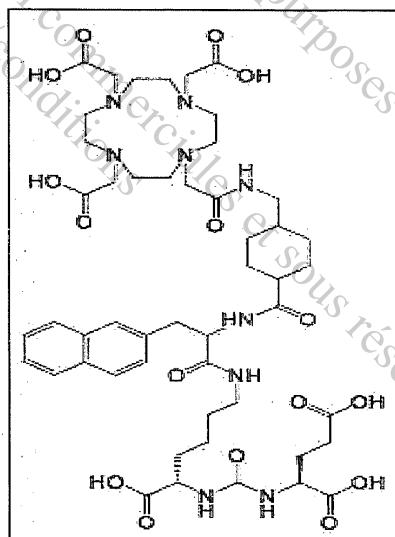


Figure 2: Structure of PSMA 617. Chemical Name 2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl]-ureido]-pentanedioic acid.

The i.v. administered Lu-PSMA-617 effectively cleared the blood by 1 hr. Clearance of

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radioactivity occurred largely through the renal system. As a result of this, the kidneys exhibited significant uptake $137.2 \pm 77.8\% \text{ID/g}$; this could be effectively blocked ($0.85 \pm 0.22\% \text{ID/g}$) by co-injection of PMPA [2 mg/kg], a high affinity inhibitor of PSMA. At 24 hr ^{177}Lu -PSMA-617 shows rapid clearance from the kidney $2.13 \pm 1.36\% \text{ID/g}$ highlighting its potential use as theranostic agent. At 1 hr time point ^{177}Lu -PSMA-617 displayed good in vivo tumor targeting with $11.20 \pm 4.17\% \text{ID/g}$. Accumulation in tumor was PSMA specific with reduction to $0.64 \pm 0.07\% \text{ID/g}$ by coinjection of 2-PMPA. At 24 h post injection $10.58 \pm 4.50\% \text{ID/g}$ uptake was retained in the tumor tissue. For all other non-target tissues, ^{177}Lu -PSMA-617 demonstrated rapid clearance. The ratio of tumor to blood was 1058; tumor to muscle was 529 at 24 hr post injection. These favorable pharmacokinetics are crucial for imaging and therapy. The detailed biodistribution results are summarized in Figure 3. ^{68}Ga -PSMA-617 showed similar uptake in the LnCaP tumors ($11.20 \pm 4.17\% \text{ID/g}$). It also shows similar pharmacokinetic clearance profile compared with ^{177}Lu -PSMA-617.

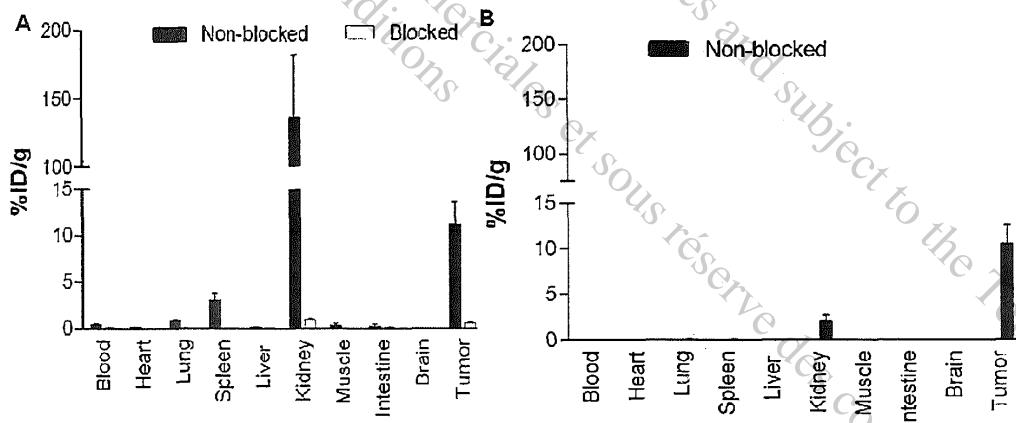


Figure 3: Distribution assay of ^{177}Lu -PSMA-617 in BALB/c mice with LNCap xenografts at 1 h (A) and 24 h (B) post injection.

In summary authors concluded the present radiotracer is suitable for theranostic application in

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human prostate cancer.

1.3.2 Clinical Studies

Current literature is available to evaluate management of patients with prostate cancers. The studies presented in this section were chosen based on novelty of the approach (initial report of application, variables for analyses) and/or the number of patients included.

Clemens Kratochwil et al. [¹⁷⁷Lu]Lutetium-labelled PSMA ligand-induced remission in a patient with metastatic prostate cancer. Eur J Nucl Med Mol Imaging 2015; 42:6 ;987-988. [47]

Study Design: First reported application of ¹⁷⁷Lu-PSMA-617 for treatment of a patient with mCRPC. Patient had proven PSMA expression and PSA of 38.0 ng/ml prior to treatment and has received 7.4 GBq of ¹⁷⁷Lu-DKFZ-617 in 2 cycles 3 months apart.

Toxicity: No potential side effects were reported in this study.

Results: After the radiotherapy ¹⁷⁷Lu-PSMA-617, PSA level of patient decreased to 4.6 ng /ml. PET/CT images showed no signs of metastases lesions either shrunk or were undetectable.

Conclusion: Authors are planning to conduct multicenter a clinical trial as soon as possible to examine clinical potential of ¹⁷⁷Lu-PSMA-617.

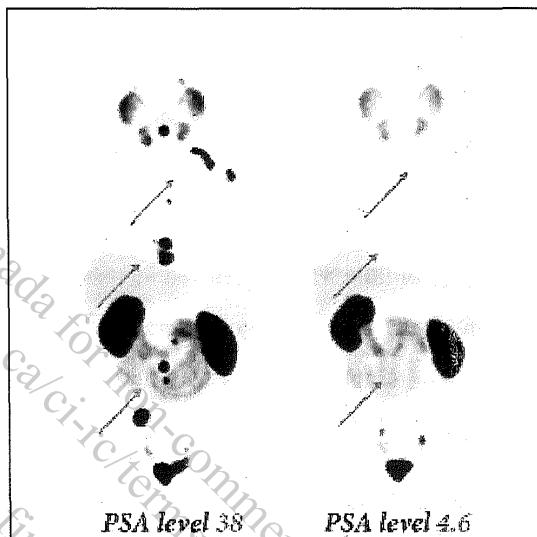


Figure 4: Above Image has recently awarded as image of Year Award and the Berson-Yalow Award at the 2015 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) in Baltimore, USA.

Hojjat Ahmadzadehfar et al. Early side effects and first results of radioligand therapy with ¹⁷⁷Lu-DKFZ-617 PSMA of castrate-resistant metastatic prostate cancer: a two-center study. *EJNMMI Research* 2015; 5:36. [48]

Study Design: A total of 10 consecutive hormone and /or chemo refractory PCa patients with distant metastases and progressive disease with rising PSA levels were recruited in this study. All patients had prior history or were under therapy with enzalutamide and/or abiraterone. Four patients had received ²²³Ra-dichloride (1-4 cycles). All 10 patients underwent with ⁶⁸Ga-PSMA HBED-CC (⁶⁸Ga-PSMA) PET /CT prior to therapy to evaluate PSMA expression. Ten patients were treated with range of 4.1-6.1 GBq dose of ¹⁷⁷Lu-DKFZ-617 PSMA. All patients were treated with single dose of Lu-PSMA. The mean and median PSA levels prior to therapy were 339.4 and 298.5 ng/ml. Complete blood chemistry, renal and liver function tests were performed a day before and 2 after the radiotherapy. Patients were followed via telephone

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every week for safety assessment.

Toxicity: No patient experienced any side effects immediately after injection of ¹⁷⁷Lu-DKFZ-617 PSMA. Relevant hematotoxicity (grade 3 or 4) occurred 7 weeks after the administration in just one patient. The same patient showed a leucopenia grade 2. Two patients showed a disturbance of only 1 hematologic cell line, whereas one patient showed a reduction of grades 1 and 2 in leucocytes and thrombocytes, respectively. Six patients did not show any hematotoxicity during the 8 weeks after therapy. There was no relevant nephrotoxicity (grade 3 or 4).

Results: Eight weeks after the therapy, seven patients (70 %) experienced a PSA decline, of which six experienced more than 30 % and five more than 50 %. Three patients showed a progressive disease according to the PSA increase.

Conclusions: ¹⁷⁷Lu-DKFZ-617 PSMA radiotherapy with single dose for the treatment of metastatic prostate cancer patients without any other therapy option is safe and seems to have a low early side-effect profile with evidence of positive response to the therapy according to PSA decline in 70 % of patients. The authors also stated ¹⁷⁷Lu-DKFZ-617 PSMA has potential to exhibit suitable agent for radionuclide radiotherapy.

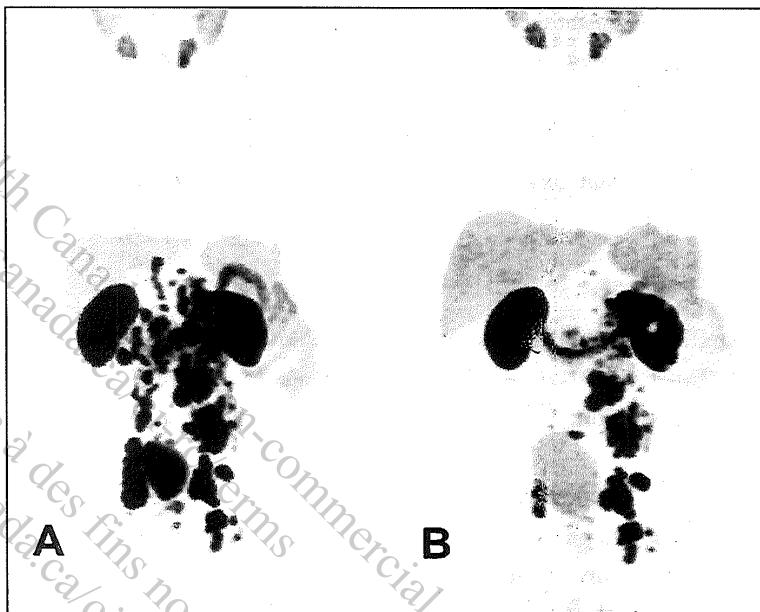


Figure 5: A 74-year-old patient with hormone- and chemo-refractory prostate cancer underwent PSMA PET/CT (a), which showed diffuse abdominal and iliac lymph node metastases. The patient underwent RLT with 5.7 GBq Lu-PSMA. The PSA level was at the time of the therapy 790 ng/ml. (b) A partial response 7 weeks after RLT with 63 % PSA decline; at this time, the PSA level was 293 ng/ml

Clemens Kratochwil, et al. PSMA-targeted radionuclide therapy of metastatic castration-resistant prostate cancer with Lu-177 labeled PSMA-617 J Nucl Med March 16, 2016 [49]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed on 30 patients with PSMA positive tumors were enrolled in this study. 30 patients were treated with 1-3 cycles of ¹⁷⁷Lu-PSMA-617. Pharmacokinetic and radiation dosimetry was also evaluated during course of the study.

Results: 21 of 30 patients showed response to therapy; for 13/30 the PSA decreased >50%. After 3 cycles 8/11 patients achieved a sustained PSA response (>50%) for over 24 weeks. ¹⁷⁷Lu-PSMA-617 showed fast renal wash out within 48 hours of injection. Patients showed mild nausea, fatigue and Xerostomia (<10%) over a period of time. No

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acute hematotoxicity was observed during the study. Dosimetry results revealed that ¹⁷⁷Lu-PSMA-617 has an exposure of 0.75 Gy/GBq for kidney 0.03 Gy/GBq red-marrow, 1.4 Gy/GBq salivary glands and 6-22 Gy/GBq for tumour lesions.

Conclusion: Based on the results authors concluded that targeted radioligand therapy with ¹⁷⁷Lu- PSMA-617 is safe and promising therapy option for metastasized castrate resistant prostate cancer.

Ahmadzadehfar H, et al. Therapeutic response and side effects of repeated radioligand therapy with ¹⁷⁷Lu-SMA-DKFZ-617 of castrate-resistant metastatic prostate cancer. Oncotarget. 2016 Feb 8. doi: 10.18632/oncotarget.7245. [50]

Study Design: Radionuclide therapy with Lu-PSMA-617 was performed in 24 hormone and/or chemo-refractory PC patients. Forty-six cycles of Lu-PSMA were performed. Side effects and response rate was assessed.

Results: Eight weeks after the first cycle of ¹⁷⁷Lu-PSMA-617 therapy 79.1% experienced A decline in PSA-level. Eight weeks after the second cycle of Lu-PSMA therapy 68.2% experienced a decline in PSA relative to the baseline value. Apart from two cases of grade 3 anemia, there was no relevant hemato- or nephrotoxicity (grade 3 or 4).

Conclusion: ¹⁷⁷Lu-PSMA-617 is a safe treatment option for metastatic PC patients and has a low toxicity profile. A positive response to therapy in terms of decline in PSA occurs in about 70% of patients..

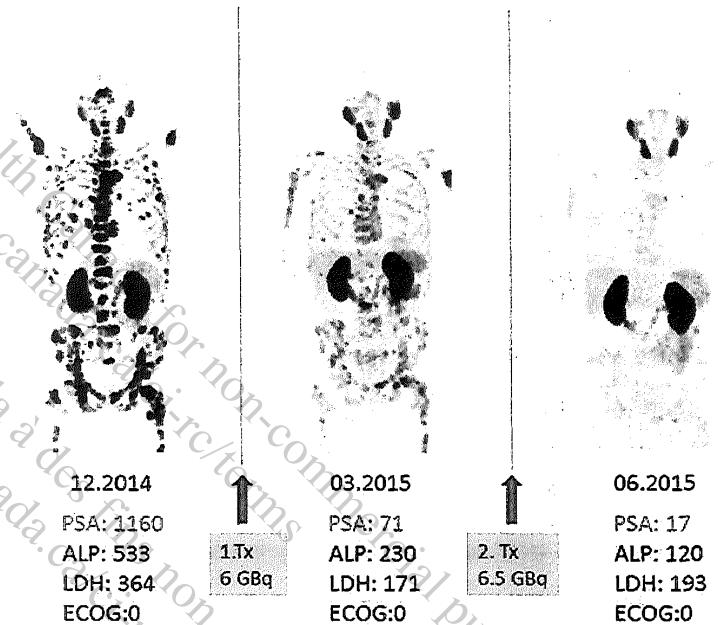


Figure 6: A 75-year-old patient with diffuse bone and lymph node metastases as well as local recurrence (left MIP image). History of chemotherapy and therapy with abiraterone, PSA elevation under enzalutamide. The patient underwent PSMA therapy as the last possible option. Continuing PSA decline and partial response in Ga-PSMA PET images after the first (middle MIP image) and second cycles (right MIP image)

Madhav Prasad Yadav, et al. ¹⁷⁷Lu-DKFZ-PSMA-617 therapy in metastatic castration resistant prostate cancer: safety, efficacy, and quality of life assessment. Eur J Nucl Med Mol Imaging. 2016 Aug 10. [51]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed in 31 patients with progressive disease despite second-line hormonal therapy and/or docetaxel chemotherapy. Patients underwent 1 to 4 cycles after a ⁶⁸Ga-PSMA-HBED-CCP ET/CT for inclusion (mean activity 5069 ± 1845 MBq). Hematological, kidney function, liver function tests, and serum PSA levels were recorded before and after therapy at 2 weeks, 4 weeks, and 3 month intervals. Biochemical response was assessed with trend in serum PSA levels. Metabolic response was assessed by PERCIST 1 criteria. Clinical response was assessed by visual analogue score

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(VASmax) analgesic score (AS), Karanofsky performance status (KPS), and toxicity and response criteria of the Eastern Cooperative Oncology Group (ECOG) criteria.

Results: Biochemical response in terms of complete response (CR), partial response(PR), stable disease (SD), and progressive disease (PD) was observed in 2/31, 20/31, 3/31, and 6/31 had, respectively. Mean VASmax and mean analgesic scores decreased from 7.5 to 3 and 2.5 to 1.8 after therapy, respectively Mean KPS and mean ECOG performance status score improved from 50.32 to 65.42 after therapies, respectively. Two patients experienced grade I and grade II hemoglobin toxicity each. None of the patients experienced nephrotoxicity or hepatotoxicity.

Conclusion: ¹⁷⁷Lu-DKFZ-PSMA-617 radionuclide therapy is a safe and effective approach in the treatment of mCRPC patients.

1.3.3 Sponsors Experiences

1.3.3.1 Preclinical Toxicity Studies

The aim of study was to evaluate toxicity of PSMA-617. PSMA-617 applied once weekly by intravenous administration to male rats over 22 days. The animals were treated with 40, 160 or 400 µg of PSMA-617/kg b.w. by tail vein intravenous bolus injection on test days 1, 8, 15 and 22. The control group was treated with physiological saline. No deaths were noted. No signs of local or systemic intolerance reactions were observed. Body weight and body weight gain, food intake, and drinking water consumption were not influenced. No test item-related changes were noted for the hematological and biochemical parameters, the urinary status, the eyes and optic region, the auditory acuity, the relative and absolute organ weights, and the myeloid: erythroid ratio. No test item-related abnormalities were noted during macroscopic inspection at necropsy and at histopathological examination.

Under the test conditions of this study, the no-observed-adverse-effect-level (NOAEL) was 400 µg PSMA-617 / kg b.w. administered once weekly by intravenous bolus injection. This dose was the highest dose tested. Detailed description of this study is attached in appendix I.

1.3.3.2 Summary of Human Studies - German Multicenter Experience

Rahbar K, et al. German multicenter study investigating ¹⁷⁷Lu-PSMA-617 radioligand therapy in advanced prostate cancer patients. J Nucl Med. 2016 [52]

Study design: Retrospective acquisition and pooling of data for toxicity and PSA response in patients after ¹⁷⁷Lu-PSMA-617 RLT performed in Germany until July 2015 was initiated by the German Society of Nuclear Medicine for research purpose. The following contains a summary of the collected data. 145 patients with metastatic castration-resistant prostate cancer received a median of two cycles (range 1 to 4) of ¹⁷⁷Lu-PSMA RLT at twelve German Nuclear

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Medicine Clinics. Data on safety and efficacy were reported. Table 1 lists the **administered ¹⁷⁷Lu-PSMA-617 activity** for this study cohort.

Table 1. Administered ¹⁷⁷Lu-PSMA-617 activity (n = 248 RLT cycles)

Administered activity (GBq)	Cycle 1	Cycle 2	Cycle 3	Cycle 4
≤ 3.5	9	3	0	1
> 3.5 – 4.5	32	14	2	0
> 4.5 – 5.5	16	12	9	0
> 5.5 – 6.5	71	37	14	2
> 6.5	17	8	1	0

Results:

A. Toxicity: Nuclear medicine physicians responsible for ¹⁷⁷Lu-PSMA RLT and subsequent follow-up reported potentially related or unrelated adverse events based on a standard template. In addition toxicity was determined by baseline and follow-up findings for serum creatinine, AST, ALT, white blood cell count, hemoglobin and platelet count for 121 of 145 (83%) patients. The follow-up period for adverse events was 2 to 30 weeks. Reported toxicity sorted by organ system is given in Table 1. Grade 3-4 anemia occurred in 15 (10%) patients and grade 3-4 thrombocytopenia occurred in 5 (4%) patients. The rate of grade 3-4 events was low for all other categories (0 to 3 patients; 0 to 2%).

There were fewer hematologic adverse events when compared to patients with metastatic castration resistant prostate cancer treated with placebo or ²²³Ra within the ALSYMPCA trial [7] (grade ≥3 anemia: 14% in the placebo and 13% in the ²²³Ra group; grade ≥ thrombocytopenia: 3% in the placebo and 7% in the ²²³Ra group). Toxicity data thus indicate a favorable safety profile for RLT using 2-7 GBq Lu-PSMA per cycle in patients with metastatic castration resistant prostate cancer.

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Majority of patients received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle. Toxicity rates were comparably low: 9 of 71 (13%) patients with 5.5 – 6.5 GBq and 3 of 17 (18%) patients with >6.5 GBq during the first RLT developed grade 3-4 toxicity.

Table 2. Adverse events after ¹⁷⁷Lu-PSMA-617 as determined by blood tests (n=121) or physician reports (n=145)

Organ system	Category	Evaluated for N	All grades	Grade 3-4
Blood and Lymphatic disorders				
	Leukopenia	121	48 (40%)	4 (3%)
	Anemia	145	50 (34%)	15 (10%)
	Thrombocytopenia	121	38 (31%)	5 (4%)
Gastrointestinal disorders				
	AST elevation	121	27 (19%)	0 (0%)
	ALT elevation	121	11 (8%)	0 (0%)
	Xerostomia	145	11 (8%)	0 (0%)
	Nausea	145	9 (6%)	0 (0%)
	Dysgeusia	145	6 (4%)	0 (0%)
	Ascites	145	2 (1%)	0 (0%)
	Biliary obstruction	145	0 (0%)	1 (1%)
General disorders				
	Fatigue	145	19 (13%)	1 (1%)
	Pain	145	5 (3%)	0 (0%)
	Ileus	145	1 (1%)	0 (0%)
Urinary disorders				
	Renal failure	121	14 (12%)	0 (0%)
	Urinary tract inf.	145	1 (1%)	0 (0%)
Cardiovascular disorders				
	Edema	145	2 (1%)	0 (0%)
	Lung embolism	145	0 (0%)	3 (2%)
Respiratory, thoracic and mediastinal disorders				
	Pleural effusion	145	1 (1%)	0 (0%)
	Dyspnea	145	1 (1%)	0 (0%)
Neurologic disorders				
	Vertigo	145	1 (1%)	0 (0%)
	Stroke	145	0 (0%)	2 (1%)

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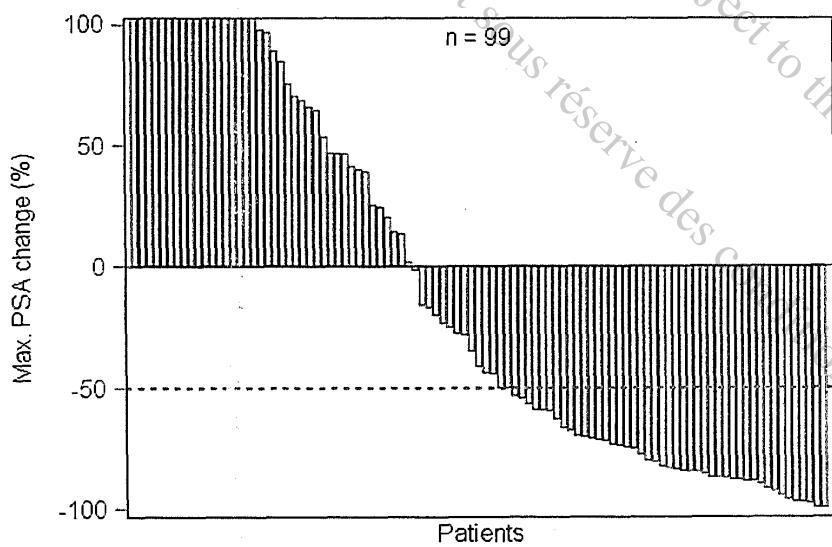
Musculoskeletal disorders	Bone fracture	145	0 (0%)	3 (2%)

Efficacy

Serial PSA levels at baseline and follow-up were recorded for 99 of 145 patients (68%).

Response was expressed as percent change in serum PSA from baseline to the lowest PSA level measured at follow-up (best PSA response).

Over the entire follow-up period 45 of 99 (45%) patients demonstrated a PSA decline $\geq 50\%$ and were considered biochemical responders. Any PSA decline occurred in 59 of 99 (60%) patients (Figure 7). After the first cycle a PSA decline $\geq 50\%$ occurred in 40 of 99 (40%), any PSA decline in 65 of 99 (66%) patients (Figure 8A). After the second therapy cycle of ¹⁷⁷Lu-PSMA-617 RLT a PSA decline $\geq 50\%$ occurred in 35 of 61 (57%) and any PSA decline in 44 of 61 (72%) patients (Figure 8B). Patients receiving a third or fourth cycle of therapy showed a PSA decline $\geq 50\%$ in 13 of 20 (65%) and 3 of 3 (100%) patients, respectively.



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Figure 7. Waterfall plot of maximum PSA change (%) from baseline over total follow-up period. PSA increase of more than 100% was cropped due to simplification.

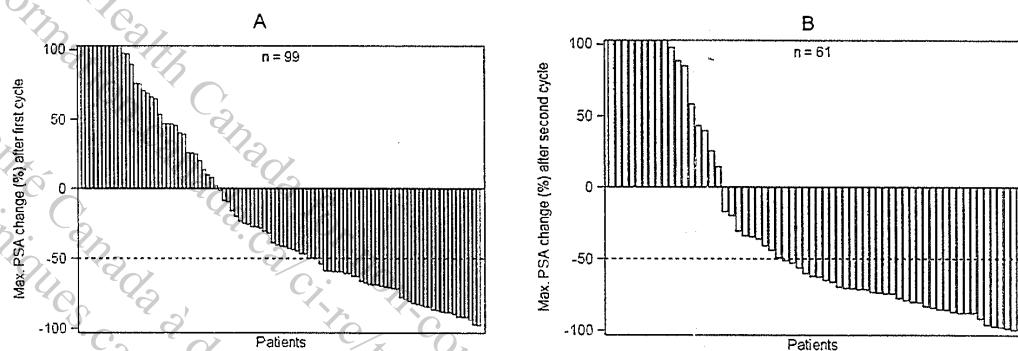


Figure 8. Waterfall plots of maximum PSA change (%) after the first cycle (A) and after the second cycle (B). PSA increase of more than 100% was cropped due to simplification.

Response rate was higher than the rate in patients with metastatic castration resistant prostate cancer treated with abiraterone (best PSA response >50% after abiraterone plus prednisone: 43% (25 of 58) patients) [53]. Data thus indicate good efficacy for ¹⁷⁷Lu-PSMA RLT in patients with metastatic castration resistant prostate cancer. Response rates were not significantly associated with mean activity per cycle ($p=0.46$) or cumulative activity after two cycles ($p=0.22$).

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2. Study Objectives

Primary Objectives:

1. To assess the clinical safety of ¹⁷⁷Lu-PSMA-617 by evaluation of adverse events (AE) using the Common Terminology Criteria for Adverse Events (CTCAE)
2. To assess the efficacy as defined by proportion of patients with PSA-response of $\geq 50\%$ decline at 12-weeks from baseline

Secondary Objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]
2. To determine the time to PSA progression, separate for treatment doses: time from inclusion to date until PSA progression or death (whichever occurs first) [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later
 - b. for patients without PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above baseline
3. To determine radiographic Progression-free Survival (rPFS), for each treatment dose: time from inclusion to date when first site of disease is found to progress or death (whichever occurs first)
 - a. Nodal and visceral disease is evaluated on cross-sectional imaging using RECIST 1.1/PCWG criteria
 - b. Bone metastases are evaluated using bone scintigraphy and new lesions have to be confirmed on a second scan (2+2 rule) using PCWG criteria
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST 1.1/PCWG criteria stable disease (SD), partial response (PR) or complete response (CR).
5. Change in Pain and Quality of Life: Pain and "Epic-26" Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 mo. Pain response will be determined in accordance with PCWG [1].

6. Change in ECOG Performance Score.

3. Investigational Plan

3.1 Overall Study Design and Dosing of Targeted PSMA Radioligand Therapy (RLT)

This is an open-label, multicenter, prospective trial. Upon inclusion patients will be randomized into two treatment doses. RLT will be performed by repeated i.v. application of 6.0 GBq ($\pm 10\%$) or 7.4 GBq ($\pm 10\%$) ¹⁷⁷Lu-PSMA-617 every 8±1 weeks until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy. All doses after labeling will be presented in buffered solution for intravenous injection.

In total, 200 subjects with histologically proven prostate cancer and mCRPC will be enrolled. Salivary protection will be accomplished by applying ice pack starting 30 minutes prior to infusion of radiopharmaceutical and will continue for 4 hours. Subjects will be recruited at up to 3 Nuclear Medicine sites selected for this project. Each subject will undergo a screening visit within 14 days prior to receiving study drug.

Dosimetry will be performed according to dosimetry protocol (Appendix V) provided by Prof. Dr. PI [REDACTED] Universitätsklinikum Würzburg Germany - Klinik und Poliklinik für Nuklearmedizin) to determine dose to the kidneys. Treatment will be continued until either of The following conditions apply:

- PSA/radiographic progression at ≥ 12 weeks as defined above
- Completion of four RLT cycles
- 23 Gy kidney dose would be exceeded by the next cycle as estimated by dosimetry
- Patient withdrawal (e.g. appearance of intolerable adverse events)

Primary objectives of the study is efficacy and safety.

Efficacy is determined by PSA response rate: Patients with baseline to follow-up decline in tumor marker level (PSA) $\geq 50\%$ at 12 (± 1) week will be considered responders.

For safety assessment, vital signs will be measured within 20 minutes before and for up to an

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hour after administration of ¹⁷⁷Lu-PSMA-617. Blood samples will be collected for CBC and CMP with eGFR at baseline (within 72 hours of first treatment dose) and then every 2 weeks (+/- 3 days) after first dose continued until 12 weeks after the last dose and then every 3 months (+/- 1 week) thereafter until the end of follow-up visits (24 months from 1st therapy date). The CBC and CMP within 2 weeks of each subsequent treatment cycle will be used to assess eligibility of the corresponding treatment cycle. CBC will be performed every 7 days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery which is defined as grade 2 toxicity or lower. CTCAE v 4.0 will be used to evaluate renal toxicity. For more information, please refer to the Schedule of Events (Appendix II).

3.2 Rationale for Study Design

3.2.1 Rationale for a regimen with multiple therapy cycles

Activity given during targeted radionuclide therapy is limited by radiation dose to healthy organs. Based on dosimetry radiation dose to healthy organs and subsequent maximal cumulative activity can be calculated. To obtain optimal safety margin maximal cumulative activity is not given in one treatment session but approached by application of a defined fraction of this activity in several cycles. The administration of a standard activity over several treatment cycles allows for early and individual estimation of radiation dose and tolerability. The efficacy and safety of a sequential approach was proven in patients with ²²³Ra therapy for metastatic castration-resistant prostate cancer (mCRPC) [7] and in patients with ¹⁷⁷Lu-DOTATATE therapy for midgut neuroendocrine tumor (NET) [54] each in prospective, double-blind, randomized, international, and multicenter phase III trials. Based on this evidence targeted PSMA Radioligand Therapy (RLT) will be performed by sequential applications of ¹⁷⁷Lu-PSMA-617 with treatment-free intervals.

3.2.2 Rationale for eight weeks interval

Highest level of evidence for subacute adverse events after radionuclide therapy was published for patients with non-Hodgkin's lymphoma. Witzig et al analyzed safety and efficacy of ⁹⁰Y-Ibritumomab Tiuxetan in 73 patients in a prospective Phase III randomized trial. This study reports neutrophil, platelet and hemoglobin nadir approximately six weeks after application of the beta emitter [55]. Based on this study ¹⁷⁷Lu-PSMA-617 RLT will be performed by sequential applications with a treatment-free interval of eight weeks to minimize risk of repeated ¹⁷⁷Lu-PSMA-617 therapy before reaching blood level nadir. This scheme is also supported by safety data from the phase III NETTER-1 trial on safety and efficacy of ¹⁷⁷Lu-DOTATATE in patients with midgut NET. Here ¹⁷⁷Lu-DOTATATE was administered at seven to nine week intervals and rate of severe adverse events was below 10% for 115 patients in the treatment arm [54].

3.2.3 Rationale for dose regimen

Ahmadzadehfar et al reports safety and efficacy after application of a mean activity of 6.0 GBq ¹⁷⁷Lu-PSMA-617 in 24 patients with mCRPC [50]. Patients were treated with up to two cycles of Lu-PSMA-617 RLT at eight week intervals. Grade 3 hematotoxicity occurred in two patients. No nephrotoxicity or hepatotoxicity grade ≥ 3 was documented. Kratochwil et al reports safety and efficacy after repeated application of Lu-PSMA-617 in 30 mCRPC patients [49]. 19 of 30 patients (63%) received 6.0 GBq ¹⁷⁷Lu-PSMA-617 every two mo. One patient developed grade 3 anemia, one patient grade 3 thrombocytopenia. Both patients had diffuse pattern of bone marrow infiltration at baseline. The German Society of Nuclear Medicine (DGN) performed a questionnaire based survey on the use of ¹⁷⁷Lu-PSMA-617 RLT in December 2015. Nuclear Medicine Clinics in Germany reported compassionate use of ¹⁷⁷Lu-PSMA-617 RLT in 145 mCRPC patients until June 30th 2015 [52]. Majority of patients received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle (Table 1) and rate of serious adverse events was below 20% for both subgroups. Phase III data for ¹⁷⁷Lu-

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DOTATATE, a similar RLT for midgut NET patients, demonstrates a rate of severe adverse events below 10% after application of four cycles of 7.4 GBq in 115 patients [54]. Thus, present evidence indicates that repeated applications of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 RLT are well tolerated with low to very low rates of serious adverse events.

Standard activities of 6.0 and 7.4 GBq are also supported by dosimetry data available in more than ten patients [56] [57]. Maximal cumulative activity is limited by the absorbed dose in critical organs. Dosimetry identifies kidney and salivary glands as organs with highest absorbed dose [56] [57]. Thus maximum cumulative activity is determined by absorbed kidney dose. Based on earlier evidence obtained from external beam radiotherapy the maximum tolerable per kidney dose is generally accepted 23 Gy [58]. Dosimetry after ¹⁷⁷Lu-PSMA-617 application revealed absorbed doses of 0.6 Gy/GBq per kidney [56] [57]. Therefore maximum cumulative activity for ¹⁷⁷Lu-PSMA-617 RLT is considered 38.3 GBq (38.3 GBq x 0.6 Gy/GBq = 23.0 Gy radiation dose per kidney). Both the application of four cycles of 6.0 GBq (total 24.0 GBq) or 7.4 GBq (total 29.6 GBq) ¹⁷⁷Lu-PSMA-617 results in lower cumulative activities with acceptable safety margin. Whether either activity regimen is associated with longer rPFS is unknown and will be evaluated as secondary endpoint of this trial.

Salivary glands receive highest off-target radiation dose according to dosimetry [56] [57]. Absorbed dose after four cycles of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 (34.0 Gy or 41.6 Gy respectively) falls within the range of maximum tolerable dose reported for salivary glands in the literature [58] [59] [60]. Maximum tolerable dose to the bone marrow is generally accepted 2 Gy [61]. Bone marrow dose will not exceed this limit after four cycles of 6.0 or 7.4 GBq ¹⁷⁷Lu-PSMA-617 [57]

3.2.4 Determination of Sample Size

Sample size calculation was based on the primary endpoint of this protocol, i.e. baseline to 12-

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week decline in tumor marker level (PSA) $\geq 50\%$ [53]. Based on a recent publication [52], we estimate that the proportion of patients who meet the primary end point will range between 38% and 65% for both treatment doses. We thus define the following null hypothesis: Less than 40% of patients will reach the endpoint after ^{177}Lu -PSMA RLT. ^{177}Lu -PSMA RLT would therefore be considered worthy of further study if 50% or more patients met the end point and not worthy of further study if 40% and less achieved the end point. This rationale was adapted from a single-arm study on mCRPC patients with same end point definition, published 2010 in the Journal of Clinical Oncology [53]. We have performed power analysis for the two sided binomial test (beta 0.2, alpha 0.05) to measure the efficacy of ^{177}Lu -PSMA RLT. A sample size of 200 achieves 78% power (beta 0.2) at a given alpha of 0.05 to distinguish between 40% versus 50% response rates. The power analysis was performed by a trained Biostatistician from the Department of Biostatistics, University of California at Los Angeles using Power Analysis and Sample Size (PASS) 14 software (NCSS LLC).

3.3 Study Duration and Dates

The duration of subject participation will be from the time of signing informed consent through the 24 months post-injection visit or progression. Subjects will be deemed enrolled in the study once the subject signs informed consent.

3.4 Randomization protocol

Randomization will be performed in accordance with Vickers et al. [62]. In order to obtain adequate “allocation concealment” a list of random allocations was created for patients 1 through 200. This list will be stored at investigator’s sites and will not be modified. The list will only be accessible for researchers or study personnel not actively involved in the recruitment process.

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3.5 Dose modification

In some circumstances, it might be necessary to suspend treatment with ¹⁷⁷Lu-PSMA-617, adapt the posology (i.e. administer a half activity), or even definitively stop administration, as described in the following tables. Table 3 lists conditions, if deemed study related by the DSMB, will result in permanent discontinuation.

Table 3: Criteria for permanent discontinuation of treatment with ¹⁷⁷Lu-PSMA-617

Definitively stop further administrations in patients who have experienced or are at risk of any of the following conditions during treatment:
a) Severe heart failure (defined as grade III or IV of the NYHA classification)
b) Hypersensitivity to the active substance or to any of the components of this radiopharmaceutical
c) Grade 3 hematologic toxicities that persist > 12 weeks and Grade 4 that persist > 3 weeks.
d) Grade 3 renal toxicity as determined by serum creatinine measurements
e) AST/ALT > 3x ULN and bilirubin > 2x ULN
f) Grade 3-4 non-hematologic toxicities with select exceptions for <ul style="list-style-type: none">- Grade 3 fatigue < 10 days- Grade 3 nausea, vomiting, and diarrhea and grade 4 vomiting and diarrhoea that persist for < 72 hours in the absence of maximum medical therapy- Asymptomatic grade 3 non-hematological laboratory abnormalities that resolve in 72 hours- Grade 3 infections which do not improve under i.v. medication within 10 days
In case some specific adverse reactions to ¹⁷⁷ Lu-PSMA-617 persist or reoccur, see Table 5

Table 4: When to suspend treatment with ¹⁷⁷Lu-PSMA-617?

Suspend treatment with ¹⁷⁷Lu-PSMA-617 in patients who have experienced or are at risk of any of the following conditions during treatment:	
Criterion	Action
Occurrence of an intercurrent disease (e.g. urinary tract obstruction, ...) which according to the physician opinion could increase the risks linked to ¹⁷⁷ Lu-PSMA-617 administration.	<p>Suspend administration until resolution or stabilization. Treatment can be resumed after resolution or stabilization.</p> <p>Resolution is defined as grade II toxicity or lower. (by CTCAE) at the time of the next treatment.</p> <p>Treatment can be suspended up to 12 weeks after the last infusion. After that treatment with ¹⁷⁷Lu-PSMA-617 must be definitively stopped.</p>
In case of some specific adverse reactions to ¹⁷⁷ Lu-PSMA-617, see Table 5	See Table 5

Table 5: When to adapt ¹⁷⁷Lu-PSMA-617 posology?

Adapt ¹⁷⁷Lu-PSMA-617 posology according to the following actions in patients who have presented any of the following severe adverse reactions:	
Severe adverse reactions / Dose-modifying toxicity (DMT) criteria	Action
Anemia, thrombocytopenia or neutropenia of grade 3 or superior (CTCAE 4.0)	1. Suspend treatment with ¹⁷⁷ Lu-PSMA-617
Renal toxicity as defined by grade 3 toxicity by serum creatinine (CTCAE 4.0)	2. Monitor biological parameters every 2 weeks, and eventually treat appropriately if needed; in case of renal function impairment, good hydration is recommended if not otherwise contraindicated.
Liver toxicity as defined as AST and ALT >3xULN	a. If the observed toxicity continues beyond 12 weeks after the last infusion, treatment with ¹⁷⁷ Lu-PSMA-617 must be definitively stopped. b. If the observed toxicity resolves within 12 weeks after the last infusion, it is possible to continue treatment with ¹⁷⁷ Lu-PSMA-617 by infusing a half activity. 3. Even if the half activity is well tolerated (i.e. no DMT re-occurrence), the next
Any serious or intolerable adverse event not listed in Table 2 that in the opinion of the investigator, requires the subject's discontinuation	

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	remaining treatment administration should be continued with the reduced (half) activity but, if DMT recurs after treatment with a half dose, treatment with ¹⁷⁷ Lu-PSMA-617 must be permanently stopped.
--	---

4. Study Population Selection

4.1 Study Population

It is anticipated that a total of 200 subjects will be recruited. Such a number is considered appropriate to achieve statistical power for the endpoints of this clinical trial. The patients will be recruited at up to 3 clinical sites. The dose being administered will be prepared at RadioMedix Inc. in Houston and shipped to the trial sites.

4.2 Inclusion Criteria

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ⁶⁸Ga-PSMA-11 PET/CT or diagnostic ¹⁷⁷Lu-PSMA-617 scintigraphy or any equivalent PSMA-directed imaging
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2500/\mu\text{l}$, PLT count $\geq 100.000/\mu\text{l}$, Hb ≥ 9.9 g/dl and ANC $\geq 1500 \text{ mm}^3$ for the first cycle and WBC $\geq 2.000/\mu\text{l}$, PLT count $\geq 75.000/\mu\text{l}$, Hb ≥ 8.9 g/dl and ANC $\geq 1000 \text{ mm}^3$ for the subsequent cycles
8. Signing of the Informed Consent Form
9. Patients enrolling in this trial should have received either enzalutamide or abiraterone.

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4.3 Exclusion Criteria

1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ²²³Ra, ¹⁵³Sm)
2. Glomerular Filtration Rate (GFR) <40 ml/min
3. Serum creatinine >1.5xULN; AST and ALT >5xULN
4. Urinary tract obstruction or marked hydronephrosis
5. Diffuse bone marrow involvement confirmed by super-scans

5. Study Treatment(s)

5.1 Description of Treatments(s)

5.1.1 Study drug

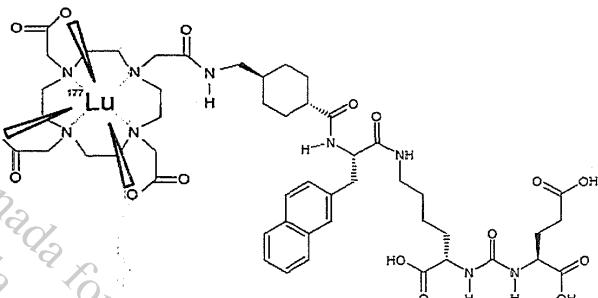
The agent to be evaluated in the present study is ¹⁷⁷Lu-PSMA-617. Its chemical name is lutetium-177-Na-2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid.

¹⁷⁷Lu-PSMA-617 is radiolabelled with carrier-free lutetium-177 (¹⁷⁷Lu), a synthetic, low-energy beta and gamma emitting isotope of lutetium, the last element in the lanthanide series of metallic elements. Carrier-free ¹⁷⁷Lu is generated by neutron irradiation of the isotope ytterbium-176 (¹⁷⁶Yb) and subsequent fractionation of ¹⁷⁷Lu and ¹⁷⁶Yb with caution chromatography. Key physical characteristics of ¹⁷⁷Lu are summarised below:

Physical Half-life T _{1/2}	Decay Product	Main Emission (β ⁻)	Maximum Range (β ⁻)	Main Emission (γ)
6.6 d	¹⁷⁷ Hf	498 keV	1.7mm	208 keV 113 keV

The structural formula of ¹⁷⁷Lu-PSMA-617 is shown below:

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The chemical formula of ¹⁷⁷Lu-PSMA-617 is Lu₁C₄₉H₆₈N₉O₁₆. The molar weight is 1214.1 g/mol.

5.1.2 Pharmaceutical Properties of ¹⁷⁷Lu-PSMA-617

Lu-PSMA-617 is administered intravenously.

A description of ¹⁷⁷Lu-PSMA-617 solution for infusion is shown in below table:

Composition of ¹⁷⁷Lu-PSMA-617 solution

Pharmaceutically active component	177Lu-PSMA-617
Physical dose	≤ 7.4 GBq / cycle
Substance dose	130 - 170 µg PSMA-617
Primary unit dose container	20 mL glass vial containing 5 - 15 mL of stabilised aqueous solution
Appearance	Clear, colourless or slightly yellowish solution, without visible particles
pH	4.0 - 7.5
Bacterial endotoxin	≤ 100 EU/Dose

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Radionuclidic purity	≥ 99.99%
Sterility	Sterile

The components include ¹⁷⁷Lu-PSMA-617, sodium acetate, sodium ascorbate, gentisic acid, and water for injection. The labelled drug product is produced, tested and released under GMP conditions by RadioMedix, Inc. as a sterile solution for injection infusion, ready for use. The labelled drug product will be manufactured upon individual order and delivered directly to the study sites.

Patients will be randomized into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq ($\pm 10\%$, arm 1) or 7.4 GBq ($\pm 10\%$, arm 2) ¹⁷⁷Lu-PSMA-617 every 8±1 weeks; RLT will be performed until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy as determined by dosimetry, after the first treatment.

5.2. Treatment(s) administered

Cold ice pack in the region of salivary glands will start 30 minutes prior to administration of the investigational drug and will continue for 4 hours. Intravenous access will be inserted in either arm. Assurance will be made to have reliable IV line with no evidence of extravasation or infiltration. Investigational drug will be infused over approximately 15-30 minutes using infusion pump. Patients will be monitored for any evidence of pain, or burning sensation during the infusion.

Imaging and blood and urine samples for dosimetry will be accomplished as per dosimetry protocol (Appendix V) provided by Prof. Dr. PI [REDACTED], Universitätsklinikum Würzburg - Klinik und Poliklinik für Nuklearmedizin. For subsequent therapies, only one (optional) post-therapy whole body image will be performed to assure satisfactory distribution of the investigational radiopharmaceutical.

5.3 Restrictions

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5.3.1 Fluid and Food Intake

Subjects should follow their normal diet before and after the administration of the study drug.

Subjects should be encouraged to increase fluid intake at baseline and after each image acquisition to maintain proper hydration throughout the study period and decrease radiation exposure to the urinary bladder. There are no dietary or food restrictions for this study.

5.3.2 Subject Activity Restriction

There are no activity restrictions.

5.4 Dosing Compliance

All study drug administration will be administered under the supervision of the investigator.

Details of study drug injection will be captured in each subject's source documents.

5.5 Packaging and Labeling

¹⁷⁷Lu-PSMA-617 will be supplied in vials for injection in appropriate packaging.

The outer packaging of ¹⁷⁷Lu-PSMA-617 will contain label(s) which will include the following minimum information:

- Name and address of Manufacturer Study number
- Investigator identification
- Name of study drug and formulation
- Dosage strength
- Batch number
- Patient number
- Expiry date (or retest date)
- Storage instructions
- “For Clinical Trial Use only”

A system of medication numbering in accordance with all requirements of Good Manufacturing

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Practice (GMP) and any other applicable regulatory requirement will be used for all study drugs.

This will ensure that for each patient, any dose of study drug can be identified and traced back to the original bulk ware of the active ingredients. Lists linking all numbering levels will be maintained by the institutions in charge of study drug packaging.

5.6 Storage and Accountability

5.6.1 Storage

The drug product contains radioactive material and should only be handled by personnel trained in the use of radioactive isotopes with proper shielding and monitoring. Receipt and use is limited to a facility licensed by applicable government regulations and/or local/state laws. Unused or residual waste should be disposed of as radioactive waste following the institution's standard operating procedures (SOPs) and/or applicable regulations or guidance.

5.6.2 Accountability

In accordance with International Conference on Harmonization (ICH) and US Food and Drug Administration (FDA) requirements, the investigator and/or drug dispenser must at all times be able to account for all study drugs furnished to the institution. The appropriate site personnel must sign, date and immediately forward to the sponsor or sponsor's designee the packing slip for clinical shipment included with each shipment.

No study drug is to be used outside of this study. The investigator or designee will record the use of the study drug on the appropriate Drug Accountability record. All study radiopharmaceuticals must be accounted for, whether used or unused, during the course of and at the conclusion of the study. The shipment of drugs from the sponsor or designee to the investigator or other designated persons cooperating with the investigator will be accompanied by a receipt form that indicates the lot number(s) and the amount of drug provided for the

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study. This form will be signed, dated and returned to the sponsor or designee.

The investigator is responsible for ensuring that study drug is recorded, handled and stored safely and properly in accordance with ICH and applicable government regulations, local/state laws, and used in accordance with this protocol.

5.7 Investigational Product Retention at Study Site

Unused product will be disposed of according to institutional regulations. Record the use and/or disposal of the study drug on the Drug Accountability record. This Drug Accountability record should account for the receipt and disposition of all clinical supplies shipped to the investigator and must be available for review by the study monitor.

6. Study Procedures

6.1 Informed Consent

All subjects must sign and personally date an IRB/IEC approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug prior to the initiation of any study-related procedures. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for Good Clinical Practice (GCP) and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27.

The subject must be made aware and agree that personal information may be reviewed during an audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. A copy of the Informed Consent Form is attached as Exhibit.

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6.2 Medical History

A relevant medical history and subject demographics will be obtained at the screening visit.

Cancer medical history includes review of disease history, cancer staging, biopsy results, any past/present cancer therapies (e.g., hormone, drug, biologic, radiologic, or surgical treatment).

Demographic information to be collected includes date of birth, race, ethnicity, height, and weight.

6.3 Vital Signs

Vital signs will include measurement of blood pressure, temperature, respiratory rate, pulse Oximetry (only at baseline) and heart rate.

6.4 Dispensing Study Drug

The estimated radioactive dose will be determined by measuring the amount of radioactivity in the syringe pre- and post-injection, using an appropriately calibrated radioisotope dose calibrator in accordance with the nuclear medicine department's SOPs.

Any complication related to administration of the drug (e.g., overdose, observable extravasation, medication error) is a protocol-related event and will be reported to the pharmacovigilance designee. Refer to Section 7 for contact information.

6.5 Clinical Laboratory Tests

Clinical laboratory tests will include hematology and clinical chemistry. Clinical laboratory analytes to be assessed in the study are shown in Table 6. Timing of collection of clinical laboratory tests are presented in Section 8.

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Table 6: Laboratory Analytes Assessed

Hematology	Clinical Chemistry
Hematocrit	eGFR
Hemoglobin	Bilirubin
RBC count	Creatinine
WBC count	Glucose
WBC differential	Urea nitrogen
Platelets	BUN/creatinine
ANC	AST/SGOT
MCV/MCH/MCHC	ALT/SGPT
Eosinophils	Alkaline phosphatase
Basophils	PSA*
Lymphocytes	
RDW	

*PSA will be done only at the time intervals called by the protocol.

6.6 Sample Collection, Storage and Shipping

Blood samples will be collected using accepted phlebotomy techniques by trained site personnel. All samples for clinical laboratory testing will be processed and analyzed at an accredited laboratory

6.7 Electrocardiogram

Continuous ECG monitoring at least 15 minutes prior to administration of the study drug and up to at least 1 hour after administration will be performed during treatment cycle 1 and 2. Also a 12 lead ECG will be performed at two time points: before injection of Lu-177 PSMA for all treatment cycles and after completion of the 4 hr scan for dosimetry cycle and after the salivary protection is completed for non-dosimetry cycles.

6.8 Adverse Events

Immediate adverse drug reactions will be collected from the time of ¹⁷⁷Lu-PSMA-617 injection until 24 hours post-injection visit. Data will be collected for any adverse events (AEs) as

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defined in Section 7.

All study monitoring will be performed at the primary clinical study sites in accordance with Good Clinical Practice (GCP). All records related to this study will be retained at each clinical site. Serious adverse reactions will be collected and reported to FDA and IRB according to 21 CFR 312.32. **Sponsors at each individual site will be responsible for obligations of a sponsor enumerated in 21 CFR 312.50-59. FDA and all participating investigators are promptly informed of significant new adverse effects or risks with respect to the investigational drug.** Annual reports on the progress of the investigation and any adverse events related to the investigational drug will be prepared and reported to FDA according to 21 CFR 312.33.

6.9 Removal of Subjects from the Trial or Study Drug

The investigator may withdraw a subject from the trial for any of the following reasons:

1. Protocol violation
2. Serious or intolerable adverse event (that in the opinion of the investigator, requires the subject's discontinuation),
3. Investigator withdraws the subject (at the investigator's discretion for reasons other than an adverse event),
4. Sponsor terminates the study,
5. Subject requests to be discontinued from the study, or
6. Subject is lost to follow-up

During course of the study patients have the right to withdraw their consents any time without need for explaining the reason of consent withdrawal to the investigator or sponsor. Principal investigator will closely monitor patients during the course of the study and will consider terminating investigational product administration or any other trial related procedures in order to maintain the safety of subjects. In cases of withdrawal either in patient's favor or principal investigator decision due to the safety issues or technical issues, withdrawn subjects will be

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replaced in order to maintain data integrity but follow up visits will be continued to maintain safety of patients based on the visits predicted in the protocol.

7. Reporting Safety Information

Any untoward medical event that occurs from the time that the subject is administered ¹⁷⁷Lu-PSMA-617 until the subject completes the study will be reported. Serious adverse events and non-serious adverse events will be collected and reported as required under 21 CFR 312.32 until the final study visit. Toxicity will be evaluated according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

7.1 Adverse Events

7.1.1 Definitions

An **adverse event (AE)** is any untoward medical occurrence in a study subject that is administered a pharmaceutical product, at any dose, which does not necessarily have a causal relationship with the treatment.

An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a study drug, whether or not considered related to the study drug.

A **serious adverse event (SAE)** is any untoward medical occurrence that falls into one or more of the following categories:

1. Results in death
2. Is life-threatening: An event which, in the view of the investigator, places the subject at immediate risk of death from the event as it occurred and does not include an event which hypothetically might have caused death if it were more severe.
3. Requires subject hospitalization or prolongation of existing hospitalization: For the seriousness criterion of subject hospitalization to apply, an overnight stay in the

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hospital is required. Admission to an emergency room and release without an overnight stay would not satisfy the subject hospitalization seriousness criterion.

4. Results in persistent or significant disability/incapacity: Persistent or significant disability/incapacity is defined as a substantial disruption of a person's ability to conduct normal life functions, either reported or defined as per clinical judgment.
5. A congenital anomaly/birth defect: A congenital anomaly/birth defect is defined as a condition believed to have been the result of exposure to study drug just before conception or during pregnancy.
6. Any other important medical event: An important medical event may not result in death, be life-threatening, or require hospitalization, but based upon appropriate medical judgment, the event may significantly jeopardize the subject's health or may require medical or surgical intervention to prevent one of the outcomes listed in the serious definitions above. An important medical event may include development of drug dependency or drug abuse.

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

7.1.2 Reporting Serious Adverse Events

Seriousness is based on subject, event outcome, or action criteria that are usually associated with events that pose a threat to a subject's life or functioning. Seriousness (not severity) serves as the guide for defining the sponsor's regulatory reporting obligations to the applicable regulatory authorities. Adverse event severity and seriousness should be assessed independently by investigators. If the investigator is unsure if the event is serious it should be classified as serious.

Sponsors of the study, and the investigators are responsible for reporting relevant SAEs as safety reports to the FDA and other applicable regulatory authorities, and participating

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investigators, in accordance with ICH guidelines, the US Code of Federal Regulations Title 21 CFR 312.32 for Good Clinical Practice, and/or local regulatory requirements. The investigators must report all SAEs to project pharmacovigilance designee within 24 hours, by telephone, email or fax, and confirm that the information was received.

A Serious Adverse Event Report (SAER) must be completed by the investigator or designee and faxed or emailed to project pharmacovigilance designee within 24 hours after the investigator first becomes aware of the serious event. A separate SAER will be needed for each reported SAE so that the onset, resolution date, causality and outcome can be assessed for each event. A copy of the source documents relevant to the event should be forwarded to sponsor's pharmacovigilance designee with the SAER form. The SAER form must be signed and dated by the investigator. If paper SAE forms are used, the original copy of the SAER form should remain at the investigational site. All SAEs are also to be entered into the CRF.

In case of death, a comprehensive narrative report of the case should be prepared by the investigator and sent to project pharmacovigilance designee with the SAER. If an autopsy is performed, a copy of the autopsy report should be actively sought by the investigator and sent to the sponsor or designee as soon as available. A copy of the autopsy report should remain at the investigational site with the subject's source documents.

A new follow-up SAER form will be completed by the investigator if important follow-up information (i.e., diagnosis, outcome, causality assessment, results of specific investigations) are made available after submission of the initial form. The follow-up SAER must be signed and dated by the investigator. The follow-up form and any additional source documentation regarding the event will be sent to project pharmacovigilance designee.

If a serious medical occurrence or death is reported to the investigator outside the follow up window which is believed to be related to the administration of the study drug, it is the investigator's responsibility to report this occurrence to project pharmacovigilance designee. Such occurrences will be reported using a SAER form or other form of communication deemed appropriate by the investigator and pharmacovigilance designee.

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Sites must contact project pharmacovigilance designee to report all SAEs within 24 hours, by telephone, e-mail, or fax. Contact information for SAE reporting is presented in Table 7.

Table 7: Pharmacovigilance Designee

PI	MD
PI	
Excel Diagnostics and Nuclear Oncology Center	
9701 Richmond Avenue, Suite 122	
Houston, TX 77042	
PHONE: 713.781.6200	PI
FAX: 713.781.6206	
Email	PI

Sites must also report all overdoses, extravasations and medication errors to the project pharmacovigilance designee.

7.2 Adverse Event Data Collection

The investigator will elicit information through non-leading questioning and examination of the subject about the occurrence of adverse events from the time that the subject is administered ¹⁷⁷Lu-PSMA-617 until study completion.

AE monitoring will be performed through following mechanisms, also listed in Appendix II:

- a. Safety lab tests: CBC and CMP with eGFR will be performed at baseline (within 72 hours of first treatment dose) and then every 2 weeks (+/- 3 days) after first dose, continued until 12 weeks after the last dose and then every 3 months (+/- 1 week) thereafter until the end of follow-up visits (24 months from 1st therapy date) or upon disease progression. The CBC and CMP within 2 weeks of each subsequent treatment

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cycle will be used to assess eligibility of the corresponding treatment cycle.

- b. Telephone follow up: 7 (± 3) days after each treatment cycle and for follow-up phase, every 3 (± 1) month until the end of follow up visits (24 months).

AEs can be reported any time after study enrollment until the end of the subject's study participation. For each event, the following information will be recorded in the subject's source documents and entered into the Adverse Event CRF according to the instructions below:

Classification of the Event as serious or non-serious: Classify the event as serious or non-serious (see definitions in Section 7).

Description of Signs or Symptoms: Whenever possible, record a specific diagnosis for the event. If a diagnosis cannot be made, then record each sign or symptom representing a distinct medical concept separately, (e.g. nausea and vomiting should be recorded as separate events).

Onset Date and Time: Record the date and time the event starts. If a laboratory result is reported as an AE, record the start date as the date of collection of the first lab sample that shows the change.

Stop Date and Time: Record the date and time the event resolves, returns to baseline, or resolves with sequelae.

Grade: Refer to the common terminology criteria for adverse events (CTCAE) Version 4.

Relationship to the Study Drug:

We make every effort to evaluate the relationship between the study drug and the AE as

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determined by the investigator per the definitions below:

1. Related: The event is reasonably suspected of a causal relationship to the study drug. Suspected adverse reaction means any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of IND safety reporting, ‘reasonable possibility’ means there is evidence to suggest a causal relationship between the drug and the adverse event. A suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by a drug.

ASSESSING RELATIONSHIP TO STUDY TREATMENT

Items to be considered when assessing the relationship of an AE to the study treatment are:

- Temporal relationship of the onset of the event to the initiation of the study treatment;
- The course of the event, considering especially the effect of discontinuation of study treatment or reintroduction of study treatment, as applicable;
- Whether the event is known to be associated with the study treatment or with other similar treatments;
- The presence of risk factors in the study subject known to increase the occurrence of the event;
- The presence of non-study treatment-related factors which are known to be associated with the occurrence of the event.

2. Not Related: The event is definitely due to causes separate from study drug administration such as:

- documented pre-existing condition

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- technical and manual procedural problem
- concomitant medication
- subject's clinical state

3. Adverse Event Outcome:

- Recovered/Resolved without sequelae
- Recovered/Resolved with sequelae
- Not Recovered/Not Resolved: event is ongoing at the end of the AE collection period.
- Death (Fatal): the event description must be the primary cause of death.

7.3 Clinical Significance

7.3.1 Reporting and Evaluation of Clinical Laboratory Test Results

The investigator should assess all clinical laboratory results for clinical significance and record the assessment in source documents.

The investigator should evaluate any laboratory result change from pre- and post-study drug administration to determine if the change meets the definition of an AE or SAE. **Record any clinically significant lab results determined to meet the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

7.3.2 Repeat Testing

Additional laboratory testing may be performed at the discretion of the investigator.

7.3.3 Vital Signs

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The investigator should evaluate any vital sign changes pre- and post-study drug administration to determine if the change meets the definition of AE or SAE. Vital sign measurements may be repeated at the discretion of the investigator. **Record any clinically significant vital sign measurement that meets the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

8. Study Activities

Visit-specific schedule for efficacy and safety variables is presented in Appendix II.

8.1 Screening Visit

- Written informed consent
- Demographic information
- Relevant medical history
- Prior therapy for Prostate cancer
- Medication assessment
- Histology
- Vital signs
- Questionnaires
- Morphological and PSMA-ligand imaging studies if no comparable available within 12 weeks of treatment.

8.2 Within 2 Weeks of Screening

- Clinical laboratory testing (see Section 6)

8.3.1 Pre-dose and Dosing Procedures

- Pre-dose vital signs – within 20 minutes before dose
- Blood tests (CBC, CMP and PSA) within 72 hours of first treatment cycle

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- Apply Ice pack to the salivary glands approximately 30 minutes prior to investigational drug injection and continue for 4 hours.
- Adequate hydration of the patient (IV or oral).
- Inject study drug ¹⁷⁷Lu-PSMA-617
- Post-dose vital signs
- Adverse events

8.3.2 Post-Dose Procedures

Adverse events during the entire stay.

For dosimetry cycle (performed at first or second treatment cycle), whole body scintigraphy will be performed at 4h (± 10 min), 18-30h, 42-54h, 66-78h and 7-9d (optional) intervals after injection. One SPECT/CT scan (Head/thorax/abdomen) will also be performed at 18-24 hour post injection time. For dosimetry cycle, urine collections from dose injection until 4 hours and from 4 hours until discharge on the day of treatment on dosing day, will be collected. Blood collection will be done for dosimetry cycle at following time points: Before injection, 5 min (± 1 min) post injection (p.i), 30 min (± 3 min) p.i, 60 min (± 5 min) p.i, 4 hrs (± 10 min) p.i, 18-30 hr p.i, 42-54 hr p.i and 66-78 hr p.i. In the event multiple tasks need to be performed at the same time or within a short time frame, every effort will be made to complete all tasks back to back in the most efficient way. For non-dosimetry cycles, only one post-therapy whole body scintigraphy will be performed (optional).

8.3.3 ECG Procedures

Continuous ECG monitoring at least 15 minutes prior to administration of the study drug and up to at least 1 hour after administration will be performed during treatment cycle 1 and 2. Also a 12 lead ECG will be performed at two time points: before injection of Lu-177 PSMA for all treatment cycles and after completion of the 4 hr scan for dosimetry cycle and after the salivary protection is completed for non-dosimetry cycles.

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8.4 Follow-up

8.4.1 PSA Measurements

At baseline, then every 6 weeks during the treatment period and every 3 (± 1) months after the last treatment until reaching endpoint or 24 month after the first treatment.

8.4.2 Imaging Studies

Baseline imaging within 12 weeks of start of therapy including (a) CT of the chest Preferably with contrast and CT or MRI of the Abdomen and pelvis preferably with contrast and (b) bone scintigraphy or (c) equivalent to above [1].

Relevant imaging studies will be performed before third RLT cycle, 3 (± 1) months after the last RLT, then every 3 (± 1) months in follow-up period until reaching the endpoint or 24 month after the first treatment.

At each subsequent RLT cycle visit and with every long term follow-up visit, any concomitant cancer-related therapy since last visit will be documented.

8.4.3 Dosimetry

Prof. Dr. PI Universitätsklinikum Würzburg, Germany – Klinik und Poliklinik für Nuklearmedizin will perform the dosimetry for this protocol. Radiation dosimetry will be acquired for each patient after the first or second cycle of treatment. Data acquisition plan is summarized in Table 8. Dosimetry will be

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considered appropriate, if at least three time points for scintigraphy and blood sampling more than 48 hours apart were acquired.

Table 8: Acquisition plan for individual dosimetry.

Time (p.i)	Blood samples	Urine Collection	Scintigraphy (Whole body planar)	Quantitative SPECT/CT Head/thorax/abd
Before injection	X			
5 min (± 1 min)	X			
30 min (± 3 min)	X			
60 min (± 5 min)	X			
4 hours (± 10 min)	X	X (0-4 hours) X (4 h-discharge)	X	
18-30 hours	X		X	X
42-54 hours	X		X	
66-78 hours	X		X	
7-9 days (optional)	X		X	

Radiation dose will be calculated for all relevant organs. Maximum number of RLT cycles for reaching threshold maximum dose to the kidneys of 23 Gy will be determined.

8.4.4 Follow-up Labs for Hematological and Kidney Toxicities

All enrolled patients will follow the scheduled follow up visits.

Hematologic laboratory testing (CBC and CMP with eGFR) will be performed every 2 weeks (+/- 3 days) after first dose, continued until 12 weeks after the last dose and then every 3 months (+/- 1 month) thereafter until the end of follow-up visits (24 months from 1st therapy date) or upon disease progression. The CBC and

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CMP within 2 weeks of each subsequent treatment cycle will be used to assess eligibility of the corresponding treatment cycle. CBC will be performed every 7 days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery which is defined as grade 2 toxicity or lower.

In order to detect myelodysplasia, patients who withdrawn by the investigator for safety reasons will only perform CBC test until the end of their follow up visits as long as they do not start other cytotoxic therapies.

Patients on protocol should also have a physical exam and in-person physician evaluation periodically while on study and until recovery from last dose. During dosing period and longterm follow up period local physical exam will be done as per clinical routine.

8.4.5 Telephone Follow ups

7 (\pm 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 month) until the end of follow up visits (24 months).

8.4.6 Longterm Follow ups

At each follow-up visit (every 3 (\pm 1) months) following tasks will be performed:

1. Physical exam, vital signs
2. Documentation of concomitant cancer related therapies since last visit

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3. Laboratory tests (CBC, CMP with eGFR and PSA)
4. Relevant imaging studies
5. Quality of life questionnaire and ECOG performance score (baseline, 3, 6, 9, 12, 18, 24 months from first RLT cycle)

9. Quality Control and Assurance

The study sites are chosen with regard to the capability and expertise of the principal investigators and the site staff. Prior to initiation of the study, the investigator and the sponsor's representative will meet to discuss the study design and conduct of the study. The investigator will sign the protocol acknowledging that he understands the design and all procedures and intends to conduct the study and all procedures according to protocol.

During the study, a representative of the sponsors will make periodic visits to the investigational site while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government regulations and guidelines. The investigator will permit authorized representatives and the respective local and national health authorities to inspect facilities and records relevant to this study, if needed.

Subject data will be collected on source documents and entered in the CRF. Data will be reviewed and validated. The investigator will sign and date a declaration on the CRF attesting to his/her responsibility for the quality of all data recorded and that the data represents a complete and accurate record of each subject in the study.

Records of subjects, source documents, monitoring visit logs, inventory of study product, regulatory documents (e.g., protocol and amendments, IRB/IEC correspondence and approvals, approved and signed informed consent forms, Investigator's Agreement, clinical

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supplies receipts, and distribution and return records), and other sponsor correspondence pertaining to the study will be kept in the appropriate study files at the site. Source documents include all recordings and observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical study. At the end of the study, CRF data will be provided to the sponsor.

10. Planned statistical methods

10.1 Primary endpoints

1. Safety of ¹⁷⁷Lu-PSMA-617 RLT will be assessed by analysis of toxicity. Descriptive statistics (number and percentage) will be reported separately for AE in total and SAE based on CTC. These descriptive statistics will be presented for the whole treatment as well as separate for each cycle. In addition, the relationship of AE to the study drug (related, not related) will be reported. Both results from laboratory test, physical examinations and patients surveys will be included.
2. Efficacy of ¹⁷⁷Lu-PSMA-617 will be reported using descriptive statistics by means of number and percentage of patients with $\geq 50\%$ decline at 12-weeks from baseline.

10.2. Secondary endpoints

1. Descriptive analyses (median, standard deviation) will be used to determine the **progression-free survival (PFS)**, measured from start of therapy until death or PSA progression. PSA progression is defined a) for patients with PSA decline after start of treatment as time from baseline to time the PSA increases to 25% and 2 ng/ml above

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nadir which is confirmed by a second value ≥ 3 weeks later or b) for patients without PSA decline as time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq 177 Lu-PSMA-617) and a statistical significant difference will be tested.

2. Each clinical site will perform image analysis on their own patients. Descriptive analyses (median, standard deviation) will be used to determine the **radiographic progression-free survival (rPFS)**, measured from start of therapy until death or radiographic progression. Radiographic progression is defined as a) for extraskeletal disease progressive disease (PD) following Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 [63] and/or b) skeletal disease the development of ≥ 2 new lesions on first post-treatment bone scan, with at least two additional lesions on the next scan (2+2 rule). The date of progression is the date of the first post-treatment scan, when the first two new lesions were documented. This approach is applied in accordance to PCWG criteria to exclude pseudoprogression in the absence of symptoms or other signs of progression [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq 177 Lu-PSMA-617) and a statistical significant difference will be tested.
3. Descriptive analysis will be used to determine the **disease control rate (DCR)** at the end of each cycle defined as the number and percentage of patients achieving a) RECIST stable disease (SD), partial response (PR) or complete response (CR) for extraskeletal tumor manifestation and b) PCWG non-progressive disease for skeletal manifestations.
4. Descriptive analysis will be used to evaluate the impact on **bone pain level** by determining the proportion of patients with pain response defined by improvement from baseline (all patients with $\geq 4/10$) of at least 2-point absolute improvement without an overall increase in opiate use.

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5. Change in **Quality of Life** over time will be documented by comparing the summary scores investigated by the Quality of life questionnaire "EPIC-26" at baseline and at 3, 6, 9, 12, 18 and 24 months after start of ¹⁷⁷Lu-PSMA-617 RLT [64].
6. Changes in **performance status (ECOG)** from baseline will be evaluated over time at 3, 6, 9, 12, 18 and 24 months after start of ¹⁷⁷Lu-PSMA-617 RLT.

11. Administrative Considerations

11.1 Investigators and Study Administrative Structure

This study will be conducted in accordance with the Declaration of Helsinki, ICH E6 Guideline and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 312.50 through 312.70, directive 2001/20/EC of 4 April 2001 and implementing directives and regulations. To ensure compliance the investigator agrees, by written consent to this protocol, to fully cooperate with compliance checks by allowing access to all documentation by authorized individuals. The investigator must conduct the trial as outlined in the protocol and in accordance with the Declaration of Helsinki and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 56 – Institutional Review Boards. The administrative structure of the study (e.g., monitoring and vendor personnel, statistician, and laboratory facilities) and a complete and controlled list of the investigators participating in this study can be found in the study file maintained by the sponsor or its agent.

11.2 Institutional Review Board (IRB) or Independent Ethics Committee (IEC) Approval

The protocol, informed consent form, and any advertisement for the recruitment of subjects

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must be reviewed and approved by an appropriately constituted IRB or IEC, as required in Chapter 3 of the ICH E6 Guideline and government regulations, including (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 56.107 through 56.115 of Good Clinical Practice. Written IRB approval must be provided to sponsor or designee prior to shipment of study drug or subject enrollment. The investigator is committed in accordance with local requirements to provide the IRB with updates, and to inform the IRB of any emergent problem, SAEs, and/or protocol amendments.

11.3 Ethical Conduct of the Study

It is mandatory that all considerations regarding the protection of human subjects be carried out in accordance with the Declaration of Helsinki.

11.4 Subject Information and Consent

It is the responsibility of the investigator to obtain written informed consent from subjects. All subjects must sign and personally date an approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for GCP, and the requirements of (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27 of Good Clinical Practice.

The subject must be made aware and agree that personal information may be scrutinized during audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. Prior to IRB/IEC submission, the investigator must send a copy of the informed consent form to be used at their institution to sponsor or designee for review to assure compliance with the ICH E6 and government regulations of the region.

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11.5 Subject Confidentiality

Data collected during this study may be used to support the development, registration or marketing of ¹⁷⁷Lu-PSMA-617. All data collected during the study will be controlled by sponsor or designee and sponsor will abide by all relevant data protection laws. In order to maintain subject privacy, all CRFs, study drug accountability records, study reports and communications will identify the subject by initials and the assigned subject number. The investigator will grant monitor(s) and auditor(s) from sponsor or its designee and regulatory authority (ies) access to the subject's original medical records for verification of data entered into the CRF and to audit the data collection process. The subject's confidentiality will be maintained and will not be made publicly available to the extent permitted by the applicable laws and regulations.

Written authorization is to be obtained from each subject prior to enrollment into the study in accordance with the applicable privacy requirements [e.g., the Health Insurance Portability and Accountability Act (HIPAA) of 1996 Standards for Privacy of Individually Identifiable Health Information.

11.6 Study Monitoring

11.6.1 Data and Safety Monitoring Plan (DSMP)

Excel Diagnostics is the lead site; the Excel Diagnostics Data Safety Monitoring Board (DSMB) will serve as overall DSMB for both sites. At UCLA, DSMB oversight will be provided by JCCC Data Safety Monitoring Board (DSMB). The monitoring board will meet quarterly to review safety records including compliance with follow up visits.

The Excel Diagnostics DSMB consists of:

- PI [REDACTED] MDPI [REDACTED] Green Imaging
- PI [REDACTED] MDPI [REDACTED] Green Imaging

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PI [REDACTED] MD PI
PI [REDACTED] MD PI

Westchase Oncology Institute
Westchase Clinical Associates

The Data Safety Monitoring Boards will evaluate safety throughout the study. The DSMB will advise the Sponsor, Investigators and investigational sites regarding the continuing safety of study patients and the patients yet to be recruited to the study as well as maintaining validity and scientific merit of the study. The DSMB will review ongoing examinations of safety data and promptly give recommendations to continue, continue with modification, or terminate the study. Each DSMB will evaluate and advise locally throughout the trial at the pre-specified milestones of 25%, 50%, 75% and 100% completion. UCLA JCCC DSMB will send their reports to the lead site DSMB for overall analysis.

Copies of all monitoring and audit reports must be submitted by the UCLA PI to the lead site DSMB (via the lead site PI) within 10 working days of receipt by the UCLA Investigator. UCLA investigator will be responsible for ensuring that all reportable adverse events are submitted to the appropriate regulatory body.(FDA, NIH, etc.).Adverse events will be recorded and reported to the FDA as well as the UCLA IRB and the JCCC DSMB per the regulatory body and institutional committee requirements (refer to UCLA IRB and JCCC DSMB) websites.

The UCLA investigators will also be required to report to the lead Principal Investigator (who is then responsible for reporting to the lead site DSMB) all serious or unexpected and related adverse events within 10 days, and all deaths within 2 working days. Lead site will be expected to report this event to their respective IRB according to their IRB's reporting requirements. The lead investigator will be responsible for providing all participating sites with copies of any adverse event reports submitted to the lead site DSMB.

Specific interim safety analyses will be done as follows:

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Interim safety analyses: 4 interim safety analyses will be conducted by both DSMBs Analyses will be initiated at the time when 25%, 50%, 75% and 100% of the total ¹⁷⁷Lu-PSMA treatments in the trial have been completed. The DSMBs will meet and assess up-to-date safety information within two weeks of a treatment exposure rate being achieved (i.e., the point when 25%, 50%, 75% and 100% of subjects have completed their treatments). Further patients may only be randomized two weeks after the treatment exposure rate has been reached and after a positive opinion from the DSMBs. An interim analysis for overall survival will be performed at the time of the final PFS analysis. UCLA JCCC DSMB will send its summary reports based on a predetermined frequency to the lead site DSMB for overall safety analysis as the Excel Diagnostics DSMB will be serving as the overall DSMB for both sites.

11.6.2 Monitoring Procedures

An appropriate representative of the sponsors (Study Monitor) will oversee the progress of the study, and ensuring it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and applicable regulatory requirements.

An initiation visit will be made by the study monitor at each site to discuss the protocol and the obligations of both the Sponsor and the investigator. The investigator must allow the study monitor to perform periodic, interim monitoring visits. The actual frequency of monitoring visits will be dependent on the enrollment rate and performance at each site. The purposes of these visits are to verify that written informed consent was obtained prior to each subject's participation in the trial, and to:

- assess the progress of the study
- review the compliance with the study protocol
- determine whether all AEs and SAEs were appropriately reported
- determine whether the investigator is maintaining the essential documents
- discuss any emergent problem

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- check the CRF for accuracy and completeness
- validate the contents of the CRF against source
- assess the status of drug storage, dispensing and retrieval
- retrieve study data

All data required by the protocol must be reported accurately on the CRF and must be consistent with the source documents. Source documents are original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays or other diagnostic images, subject files, pharmacy records and laboratory records). The investigator will make available the source documents for inspection. This information will be considered as confidential.

During scheduled monitoring visits, the investigator and the investigational site staff should be available to meet with the study monitor in order to discuss the progress of the study, make necessary corrections to CRF entries, respond to data clarification requests and respond to any other study-related inquiries of the monitor. The investigational site staff in addition to the study coordinator should also include nuclear medicine staff, radiopharmacist, and radiology staff.

The study monitor will perform a closeout visit at the conclusion of the investigator's involvement in the study.

11.6.3 Auditing

The investigator will make all pertinent records available including source documentation for inspection by regulatory authorities and for auditing by the sponsor. This information will be considered as confidential. Clinical Research Compliance Officers from the UCLA JCCC Office

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of Regulatory Compliance will be conducting the auditing for the UCLA site.

Representatives of local or foreign health authorities may review the conduct or results of the study at the investigational site. The investigator must promptly inform the sponsor of any audit requests by health authorities, and will provide sponsor with the results of any such audits and with copies of any regulatory documents related to such audits.

11.7 Case Report Forms and Study Records

Sponsor will provide a CRF and CRF instructions for the entry of study data. CRFs must be completed for each subject. All study data will be entered on CRFs from original source data. Entries should be made on the case report forms directly and promptly onscreen. The CRF will be reviewed, signed and dated by the investigator.

11.8 Protocol Violations/Deviations

Protocol violations/deviations will be documented by investigator and submitted to the IRB/IEC, as required by IRB/IEC requirements.

11.9 Access to Source Documentation

During the study, a representative of the sponsor will make periodic visits to the investigational sites while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government

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regulations and guidelines.

The investigator will permit authorized representatives of the sponsor and the respective local
And national health authorities to inspect facilities and records relevant to this study, if needed.

11.10 Data Generation and Analysis

Sponsor(s) or its designee will be responsible for data collection, data management, generation
of data outputs and statistical analysis of all data.

11.11 Retention of Data

As described in the ICH GCP Guidelines, 'essential documents', including copies of the
protocol, subject identification codes, CRF, source data, informed consent form(s) and other
documents pertaining to the study conduction must be kept for the maximum period of time as
required by the study site. This time period must be at least two years after the last follow up
of the patients enrolled.

No study document should be destroyed without prior written agreement between sponsors
and the investigators. Originals of all documentation generated by sponsor and copies of
outgoing sponsor correspondence concerning the study will be stored and retained in a safe
area under the control of sponsor for the lifetime of the product. In particular, the final report
must be retained by sponsor, or the subsequent owner, for 5 years beyond the lifetime of the
study drug.

11.12 Financial Disclosure

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All investigators must provide financial disclosure information in accordance with the US Code of Federal Regulations Title 21 CFR 54.2 through 54.6.

11.13 Publication and Disclosure Policy

All unpublished documentation (including the protocol, CRF and Investigator Brochure (IB) given to the investigator is strictly confidential. All recipients must agree not to disclose the information herein contained to any person without the prior written authorization of sponsor. The submission of these documents to the IRB is expressly permitted. The investigator agrees that sponsor maintains the right to use the results of this study in their original form and/or in a global report for submission to governmental and regulatory authorities of any country. The results of the study may be presented during scientific symposia or published in a scientific journal only after review by sponsor in accordance with the guidelines set forth in the applicable publication or financial agreement.

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Appendices

Appendix 1- Preclinical Toxicity studies

This exhibit is 303 pages. Therefore we are providing it in the attached CD.

Appendix II: Visit Specific Schedule

	7	Screening	Therapy												FU												30						
	Month	Week	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Month						
	Week	-2	0	2	4	6	8	10	12	14	16	18	20	22	24												Weeks						
Therapy		1				2				3					4																		
Signing informed consent form		*																															
Randomization		*																															
Evaluation of blood tests (CBC, CMP with eGFR)	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*		Every 2 weeks		*	*	*	*	*	*	*	*	*	*					
PSA determination	*	*																	*	*	*	*	*	*	*	*	*	*					
Evaluation of Imaging studies (CT, MRI, bone imaging)	*																		*	*	*	*	*	*	*	*	*	*					
Ga-68 or Lu-177 PSMA imaging	*																		*	*	*	*	*	*	*	*	*	*					
Medication & Hyperactivity assessment	*																		*	*	*	*	*	*	*	*	*	*					
Current Disease (somatic or psychiatric)	*																		*	*	*	*	*	*	*	*	*	*					
Histopathology evaluation	*																		*	*	*	*	*	*	*	*	*	*					
Relevant medical history & demographics	*																		*	*	*	*	*	*	*	*	*	*					
Physical exam	*	*																*	*	*	*	*	*	*	*	*	*	*					
Concomitant cancer related therapies since last visit																			*	*	*	*	*	*	*	*	*	*					
Vital signs (BP, HR, T, RR)	*	*																	*	*	*	*	*	*	*	*	*	*					
Evaluation of life expectancy	*																		*	*	*	*	*	*	*	*	*	*					
Prior therapy for Prostate cancer	*																																
Continuous ECG monitoring	*		*		*		*		*		*		*		*		*		*		*		*		*								
12 lead static ECG	*	*			*		*		*		*		*		*		*		*		*		*		*								
Quality of life assessment (EPIC-26) & ECOG	*																																
Whole body (Anterior And Posterior) scan	*		*																														
Followup calls for AE Monitoring		+7 days		+7 days		+7 days		+7 days		+7 days		+7 days		+7 days		+7 days		+7 days		+7 days		+7 days		+7 days		+7 days		+7 days					
days	-10	-7	0	14	28	42	56	70	84	98	112	126	140	154	168	192	228	258	288	318	348	378	408	438	468	498	528	558	588	618	648	678	703

A blood sample will be collected within 48 hours before the injection to document CrP and CBC for safety purposes and PSA as baseline determination.

Only at first or second treatment, several blood and urine samples will be required for dosing by purpose: Blood: before injection, 5 (\pm) min, 30 (\pm 5) min, 60 (\pm 5) min, 4 (\pm 10) min, 18-30, 42-54, and 66-78 hours post injection. Urine collection will include 0-4 hrs and 4 hrs until discharge.

Laboratory tests will be acceptable only if performed within two weeks of each scheduled visit. Screening visit and week -2 can be combined if screening visit performed within 2 weeks of the first cycle.

CBC/CMP with eGFR will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 (\pm 1) months during follow-up for 24 months or until disease progression as per clinical routine.

PSA will be measured every 6 weeks during the treatment and every 3 (\pm 1) months after the last treatment until reaching endpoint or 24 months after the first treatment.

Baseline imaging within 12 weeks of start of therapy including [a] Chest CT preferably with contrast, & CT or MRI of the Abdomen-pelvis preferably with contrast, [b] bone imaging, [c] or equivalent as per clinical routine.

Relevant imaging studies will be done at baseline, before 3rd RLT cycle, 3 (\pm 1) months after last RLT cycle, and then every 3 (\pm 1) months during follow-up until reaching the endpoint or 24 months after the first treatment as per clinical routine.

For safety assessment, vital signs will be measured within 20 minutes before and up to an hour after administration of 177Lu-PSMA 617.

Continuous ECG monitoring (only in first 2 RLT cycles) starts at least 15 minutes prior to administration of the study drug and lasts at least 1 hour after administration.

Two 12 lead ECGs: one before injection and one after 4 hrs in non-dosimetry RLT and after completion of salivary gland protection in non-dosimetry RLT.

Quality of life questionnaire (EPIC-26) and ECOG will be completed at baseline, and at 3, 6, 9, 12, 18 and 24 months from first RLT cycle.

Only at first or second treatment, whole body scintigraphy will be performed several times (4 hrs \pm 10 min, 18-30, 42-54, and 66-78 hours) after injection for dosimetry purposes. For non-dosimetry RLTs, only one (optional) post therapy WB scan will be performed. Please refer to dosimetry schedule of events.

Telephone follow up: 7 (\pm 3) days after each treatment cycle until completion of 4 cycles and for follow up phase, every 3 months (\pm 1 month) until the end of follow up visits (24 months).

At each time point that the therapy stops follow up visits will be started.

Appendix III: Chemistry, Manufacturing, and Control (CMC) of Lu-177

PSMA

Not provided with original protocol

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Appendix IV: Informed Consent Form

Not provided with original protocol

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Sponsor Signatures

Study Title: PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC). A Phase II clinical trial.

Study Number: NCT03042312

IND Number: 133661

Final Date: 01/31/2017

This clinical study protocol was subject to critical review and has been approved by the sponsor.

Signed: _____ Date: _____

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Investigator's Signature

Study Title: PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC). A Phase II clinical trial.

Study Number: NCT03042312

IND Number: 133661

Final Date: 01/31/2017

I acknowledge that I have read the attached protocol as amended and I agree that it contains all information necessary to conduct the study. I also agree to and will comply with all provisions set forth therein and herein, and certify as follows:

I will comply with all Health Authority regulations/guidelines relevant to the conduct of human clinical trials, as set forth in 21 CFR Parts 50, 54, 56, and 312 part D as they may be amended or supplemented from time to time. I will not initiate the study until I have obtained written approval from the appropriate Institutional Review Board/Independent Ethics Committee and have complied with all financial and administrative requirements of the governing body of my clinical institution. I will obtain written informed consent from all study participants prior to performing any screening procedures.

I understand that my signature (or that of a Sub-Investigator) on a case report form indicates that the data therein have been reviewed and are deemed to be complete, accurate, and acceptable to me.

I have not been disqualified by any regulatory authority or otherwise disqualified from serving as a Principal Investigator, or debarred by the U.S. FDA or any other regulatory authority. In the event that during the term of the study, I become debarred, or receive notice of an action by a health authority or threat of an action with respect to my conduct of clinical research, I shall immediately notify sponsor. In the event I become debarred, I shall immediately cease all activities relating to the study.

I understand and acknowledge that confidential information related to this study includes, but is not limited to, (1) this document, (2) the Protocol for the study, (3) the data derived from the study and (4) my impressions of the progress or results of the study ("Confidential Information") all of which is the proprietary and sole property of sponsor. I will comply with the terms of the Confidentiality and Non-Disclosure Agreement and Clinical Trial Agreement, which stipulate that no Confidential Information will be disclosed or generally described to anyone other than sponsor, personnel or designees, participating study staff, regulatory authorities with appropriate jurisdiction, or members of the responsible Institutional Review Board/Independent

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Ethics Committee. I will not use such Confidential Information for any purpose other than the evaluation or conduct of the clinical investigation. I am not presently, nor will I be during the term of the study, a consultant or advisor to any division of any financial or securities firm.

Investigator Signature

Site Name

Investigator Printed Name (with degree)

Date (DD/MM/YYYY)

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Baseline and follow-Up Questionnaire for Pain and Adverse Events

PATIENT INFORMATION

Last name: _____ First Name: _____

Date of Birth: _____ Medical Record Number: _____

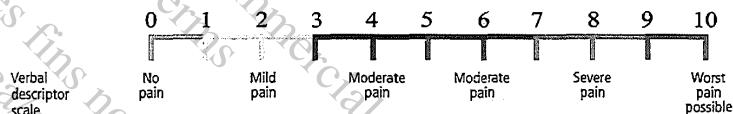
Change of pain medication since last ¹⁷⁷Lu-PSMA-617 cycle

- No change
 Change in dosage/administration: medication _____ increase or decrease
 Addition/removal of medication: medication _____ addition or removal

Pain No or Yes:

Locations: _____

Overall level:



Change since last cycle: increase, no change, decrease

Nausea

- No nausea
 Nausea with loss of appetite only
 Nausea with eating/drinking less than usual
 Had to go to hospital for nausea

Vomiting

- No vomiting
 1 - 2 episodes per day
 3 - 5 episodes per day
 more than 5 episodes per day

Dry mouth

- No dry mouth
 Dry or thick saliva
 Normal eating only with water/lubricants possible
 Tube feeding or total i.v. nutrition

Taste

- Normal taste.
 Altered taste but no change in diet
 Altered taste with change in diet

Fatigue

- No fatigue
 Fatigue relieved by rest
 Fatigue not relieved by rest, limiting work
 Fatigue not relieved by rest, limiting self-care

Hematoma

- No Hematoma
 Occurrence of hematoma without known event

Fever

- No fever
 38.0 - 39.0 °C (100.4 - 101.2 °F)
 >39.0 - 40.0 degrees °C (101.3 - 104.0 °F)
 >40.0 °C (>104.0 °F)

Urinary retention

- Able to void normally
 Able to void with some pressure
 Unable to void or voiding only after catheter/intervention/treatment

Diarrhea

- Normal bowel movements
 Increase by <4 stools per day

Other (symptom, grade: mild/moderate/severe):

*Clinical Trial Protocol: IND #13366I
¹⁷⁷Lu-PSMA-617*

- Increase by 4-6 stools per day
- Increase by more than 6 stools per day
- Had to go to hospital for diarrhea

Date: _____ Name: _____ Signature: _____

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EPIC-26

The Expanded Prostate Cancer Index Composite

Short Form

This questionnaire is designed to measure Quality of Life issues in patients with Prostate cancer. To help us get the most accurate measurement, it is important that you answer all questions honestly and completely.

Remember, as with all medical records, information contained within this survey will remain strictly confidential.

Today's Date (please enter date when survey completed): Month _____ Day _____ Year _____

Name (optional): _____

Date of Birth (optional): Month _____ Day _____ Year _____

Do Not Mark in This Space

1. Over the **past 4 weeks**, how often have you leaked urine?

- More than once a day 1
About once a day 2
More than once a week 3 (Circle one number)
About once a week 4
Rarely or never 5

23/

2. Which of the following best describes your urinary control **during the last 4 weeks**?

- No urinary control whatsoever 1
Frequent dribbling 2 (Circle one number)
Occasional dribbling 3
Total control 4

26/

3. How many pads or adult diapers per day did you usually use to control leakage
during the last 4 weeks?

- None 0
1 pad per day 1
2 pads per day 2 (Circle one number)
3 or more pads per day 3

27/

4. How big a problem, if any, has each of the following been for you **during the last 4 weeks?**

(Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem	
a. Dripping or leaking urine	0	1	2	3	4	28/
b. Pain or burning on urination.....	0	1	2	3	4	29/
c. Bleeding with urination.....	0	1	2	3	4	30/
d. Weak urine stream or incomplete emptying.....	0	1	2	3	4	31/
e. Need to urinate frequently during the day	0	1	2	3	4	33/

Clinical Trial Protocol IND #133661
¹⁷⁷Lu-PSMA-617

5. Overall, how big a problem has your urinary function been for you **during the last 4 weeks?**

No problem.....	1	(Circle one number)
Very small problem.....	2	
Small problem.....	3	
Moderate problem.....	4	
Big problem.....	5	

34/

Do Not
Mark in
This
Space

6. How big a problem, if any, has each of the following been for you? (Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem	
a. Urgency to have a bowel movement	0	1	2	3	4	49/
b. Increased frequency of bowel movements.....	0	1	2	3	4	50/
c. Losing control of your stools.....	0	1	2	3	4	52/
d. Bloody stools	0	1	2	3	4	53/
e. Abdominal/ Pelvic/Rectal pain...	0	1	2	3	4	54/

7. Overall, how big a problem have your bowel habits been for you **during the last 4 weeks?**

No problem.....	1	(Circle one number)
Very small problem.....	2	
Small problem.....	3	
Moderate problem.....	4	
Big problem.....	5	

55/

8. How would you rate each of the following **during the last 4 weeks?** (Circle one number on each line)

	Very Poor to None	Poor	Fair	Good	Very Good	
a. Your ability to have an erection?.....	1	2	3	4	5	57/
b. Your ability to reach orgasm (climax)?.....	1	2	3	4	5	58/

Clinical Trial Protocol IND #133661
¹⁷⁷Lu-PSMA-617

9. How would you describe the usual QUALITY of your erections **during the last 4 weeks?**

None at all.....	1	
Not firm enough for any sexual activity.....	2	
Firm enough for masturbation and foreplay only.....	3	(Circle one number) 59/
Firm enough for intercourse.....	4	

10. How would you describe the FREQUENCY of your erections **during the last 4 weeks?**

I NEVER had an erection when I wanted one.....	1	
I had an erection LESS THAN HALF the time I wanted one.....	2	
I had an erection ABOUT HALF the time I wanted one	3	(Circle one number) 60/
I had an erection MORE THAN HALF the time I wanted one.....	4	
I had an erection WHENEVER I wanted one.....	5	

Do Not
Mark in
This
Space

11. Overall, how would you rate your ability to function sexually **during the last 4 weeks?**

Very poor.....	1	
Poor.....	2	
Fair.....	3	(Circle one number) 64/
Good.....	4	
Very good.....	5	

12. Overall, how big a problem has your sexual function or lack of sexual function been for you
during the last 4 weeks?

No problem.....	1	
Very small problem.....	2	
Small problem.....	3	(Circle one number) 68/
Moderate problem.....	4	
Big problem.....	5	

13. How big a problem **during the last 4 weeks**, if any, has each of the following been for you?

Clinical Trial Protocol IND #133661
¹⁷⁷Lu-PSMA-617

(Circle one number on each line)

No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem
a. Hot flashes.....	0	1	2	3
b. Breast tenderness/enlargement..	0	1	2	3
c. Feeling depressed.....	0	1	2	3
d. Lack of energy.....	0	1	2	3
e. Change in body weight.....	0	1	2	3

THANK YOU VERY MUCH!!

EPIC-SF 6.2002

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*Clinical Trial Protocol: IND #133661
¹⁷⁷Lu-PSMA-617*

Appendix V: Dosimetry protocol attached as pdf copy

Not provided with original protocol

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ENDOCYTE

PROTOCOL NO. PSMA-617-02:

PSMA-DIRECTED ENDORADIOTHERAPY OF CASTRATION-RESISTANT PROSTATE
CANCER (RESIST-PC). A PHASE II CLINICAL TRIAL

Clinical Protocol No.: PSMA-617-02

CT.gov Study Number NCT03042312

IND No.: 133661

Phase of Study: Phase II

Investigational Products: ¹⁷⁷Lu- PSMA-617

Sponsor: Endocyte, Inc.
3000 Kent Avenue - Suite A1-100
West Lafayette, Indiana 47906-1075
(765) 463-7175

Medical Monitor: Richard Messmann, M.D., M.H.S., M.Sc.
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Version 1.0 28 December 2016
Version 2.0 07 June 2017
Version 3.0 29 June 2017
Version 4.0 18 September 2017
Version 5.0 01 June 2018

Approval:

[signed electronically in MasterControl]

Medical Monitor Signature

Date

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PSMA-617-02

SYNOPSIS

Sponsor:

Endocyte, Inc.

3000 Kent Avenue - Suite A1-100

West Lafayette, Indiana 47906-10758

(765) 463-7175

Name of Finished Product:

¹⁷⁷Lu-PSMA-617

Name of Active Ingredient:

2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{{[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid

Study Title:

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC). A phase II clinical trial.

Study Number:

NCT03042312

Study Phase:

Phase II

Primary Objective:

To assess safety and efficacy defined as >50% decline in PSA after ¹⁷⁷Lu-PSMA-617 in patients with metastatic castration resistant prostate cancer

PSMA-617-02

Secondary Objectives for each Treatment Dose:

1. To determine maximum PSA decline.
2. To determine PSA progression-free survival (PFS), measured from start of therapy until death or PSA progression.
3. To determine radiographic PFS, measured from start of therapy until death or radiographic progression using RECIST 1.1/PCWG criteria.
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST stable disease (SD), partial response (PR) or complete response (CR).
5. To determine impact on bone pain level
6. To determine impact on quality of life
7. To determine impact on performance status (ECOG)

Study Design:

Open-label, prospective, multicenter clinical trial.

Study Population:

Patients with metastatic castration resistant prostate cancer

Inclusion Criteria:

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel naive and docetaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy or any equivalent PSMA-directed imaging
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2500/\mu\text{l}$, PLT count $\geq 100.000/\mu\text{l}$, Hb $\geq 9.9 \text{ g/dl}$ and ANC $\geq 1500 \text{ mm}^3$ for the first cycle and WBC $\geq 2.000/\mu\text{l}$, PLT count $\geq 75.000/\mu\text{l}$, Hb $\geq 8.9 \text{ g/dl}$ and ANC $\geq 1000 \text{ mm}^3$ for the subsequent cycles
8. Signing of the Informed Consent Form
9. Patients enrolling in this trial should have received either Enzalutamide or Abiraterone

Exclusion Criteria:

1. Less than 6 weeks since last myelosuppressive therapy (including

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- Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm) or other radionuclide therapy.
2. Glomerular Filtration Rate (GFR) <40 ml/min
 3. Serum creatinine > 1.5xULN
 4. AST and ALT > 5xULN
 5. Urinary tract obstruction or marked hydronephrosis
 6. Diffuse bone marrow involvement confirmed by super-scans

*super-scan is defined by kidney uptake equal or below background due to diffuse bone involvement on staging PET/CT or scintigraphy

Test Product; Dose; and Mode of Administration:

Randomization into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq ($\pm 10\%$, **arm 1**) or 7.4 GBq ($\pm 10\%$, **arm 2**) ^{177}Lu -PSMA-617 every 8 \pm 1 weeks; RLT until reaching four cycles.

Study Duration:

Patients will be followed until either of the following conditions occur:

1. 24 month after the first treatment.
2. Progression by RECIST 1.1/PCWG criteria.
3. Death.

Safety Assessments:

AE and safety assessments will be performed through the following mechanisms, also listed in Appendix II:

a. Following laboratory tests will be performed at baseline (within 72 hours of first treatment dose) and then every 2 weeks (+/- 3 days) after first dose, continued until 12 weeks after the last dose and then every 3 months (+/- 1 week) thereafter until the end of follow-up visits (24 months from 1st therapy date) or upon disease progression. The CBC and CMP within 2 weeks of each subsequent treatment cycle will be used to assess eligibility of the corresponding treatment cycle.

1. Complete metabolic panel and eGFR
2. CBC

b. Telephone Follow-up: 7(± 3) days after each treatment cycle and for follow-up phase every 3 (± 1 month) until the end of follow-up visits (24 months).

Following conditions if in view point of investigators deemed study related, will result in permanent discontinuation:

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- i. Grade 3-4 non-hematologic toxicities with select exceptions for:
 - 1. Grade 3 fatigue < 10 days
 - 2. Grade 3 nausea, vomiting, and diarrhea and grade 4 vomiting and diarrhea that persist for < 72 hours in the absence of maximum medical therapy.
 - 3. Asymptomatic grade 3 non-hematological laboratory abnormalities that resolve in 72 hours.
 - 4. Grade 3 infections that resolve under medical treatment within 10 days
- ii. AST/ALT > 3x ULN and bilirubin > 2x ULN
 - iii. Grade 4 Hematological toxicities persisting >3 weeks.
 - iv. Grade 3 Hematological abnormalities that do not return to baseline for > 12 weeks.

Data Safety Monitoring Board (DSMB) and Data Safety Monitoring Plan (DSMP):

A Data Safety Monitoring Board (DSMB) has established and will evaluate safety throughout the study. The DSMB will advise the Sponsor, Investigators and investigational sites regarding the continuing safety of study patients and the patients yet to be recruited to the study as well as maintaining validity and scientific merit of the study. The DSMB will review ongoing examinations of safety data and promptly give recommendations to continue, continue with modification, or terminate the study.

The Excel Diagnostics DSMB will serve as the lead site DSMB. At UCLA, DSMB oversight will be provided by JCCC Data Safety Monitoring Board (DSMB). The monitoring board will meet quarterly to review safety records including compliance with follow up visits.

Interim safety analyses: 4 interim safety analyses will be conducted by DSMB that will be initiated at the time when 25%, 50%, 75% and 100% of the total ¹⁷⁷Lu-PSMA-617 treatments in the trial have been completed. The DSMB will meet and assess up-to-date safety information within two weeks of a treatment exposure rate being achieved (i.e., the point when 25%, 50%, 75% and 100% of treatments have occurred). Further patients may only be randomized two weeks after the treatment exposure rate has been reached and after a positive opinion from the DSMB.

Efficacy Assessment for each treatment arm:

Primary objective:

12 week PSA response: Proportion of patients with PSA-decline of $\geq 50\%$ at 12 (± 1) week after the first RLT [1].

Secondary objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]

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2. Time to PSA progression, for each treatment arm. [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later
 - b. for patients without PSA decline: Time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later
3. Radiographic progression free survival (rPFS), for each treatment arm.
4. Change in Pain, Quality of Life and ECOG performance score: Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 month, for each treatment arm

Number of patients enrolled:

As per statistical evaluation, total of 200 patients will be required to have statistical power to achieve the primary endpoints of the study.

Date of Original Protocol: December 28th, 2016

Date of Most Recent Protocol Amendment (if applicable): 09/18/2017

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Appendix I: Preclinical Toxicity Studies

Appendix II: Visit Specific Schedule

Appendix III: Principal Investigator Signature

Appendix VI: Dosimetry Protocol *Not applicable to previous versions

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

AE	Adverse event
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
AP	Alkaline phosphatase
AST	Aspartate aminotransferase
AUC	Area under the plasma concentration versus time curve
BUN	Blood urea nitrogen
CBC	Complete Blood Count
CFR	Code of Federal Regulations
CI	Confidence interval
CR	Complete response
CRF	Case report form
CT	Computed tomography
DCR	Disease Control Rate
ECOG	Eastern Cooperative Oncology Group
eGFR	estimated Glomerular Filtration Rate
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GGT	Gamma-glutamyl transferase
GH	Growth hormone

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Hct	Hematocrit
Hgb	Hemoglobin
HIPAA	Health Information Portability and Accountability Act
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intent-to-treat
LDH	Lactic dehydrogenase
MBq	MegaBequerel
mCi	milliCurie
mo	months
GBq	gigabecquerel
MR	Magnetic resonance
MRI	Magnetic resonance imaging
N/A	Not applicable
NDA	New Drug Application
PCa	Prostate cancer
PET/CT	Positron Emission Tomography/Computed Tomography
PFS	Progression-free survival
PSA	Prostate-specific antigen
PR	Partial response
RBC	Red blood cell

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RECIST	Response Evaluation Criteria In Solid Tumors
RLT	Radioligand therapy
rPFS	Radiographic progression-free survival
SAE	Serious adverse event
SAER	Serious adverse event report
SAP	Statistical analysis plan
SD	Stable disease
SE	Standard error
SPECT	Single-photon emission computerized tomography
PSMA	Prostate-specific membrane antigen
US	United States
WBC	White blood cell
WHO-DD	World Health Organization Drug Dictionary

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1. Introduction

1.1 Background

According to the American Cancer Society more than 1 million people in the United States are diagnosed with cancer each year. For American *males*, prostate cancer is the second most common cause of cancer related death [2]. A recent publication [3] estimated the prevalence of prostate cancer as 2,219,280 in the US in 2009 and 3,072,480 in 2020, and incidence of metastatic Castration Resistant Prostate Cancer (mCRPC) as 36,100 and 42,970, respectively. Various therapies have been developed to improve survival of patients with advanced prostate cancer. However, despite such efforts currently all-cause mortality in prostate cancer has been estimated at 168,290 in 2009 and 219,360 in 2020, with 20.5% and 19.5% of these deaths, respectively, occurring in men with mCRPC.

Patients with metastatic castration-resistant prostate cancer (mCRPC) have a poor prognosis, and those patients with metastases are expected to survive ≤ 19 mo [3]. As patient disease progresses, quality of life deteriorates, and until recently, few treatment options were available. Several new therapies have shown an improvement in overall survival for patients with mCRPC who have already received chemotherapy with docetaxel (Fig. 1) [4] [5] [6, 7] [8]. The impact of these new data on clinical practice, treatment sequencing, and best care for individual patients is not yet fully established.

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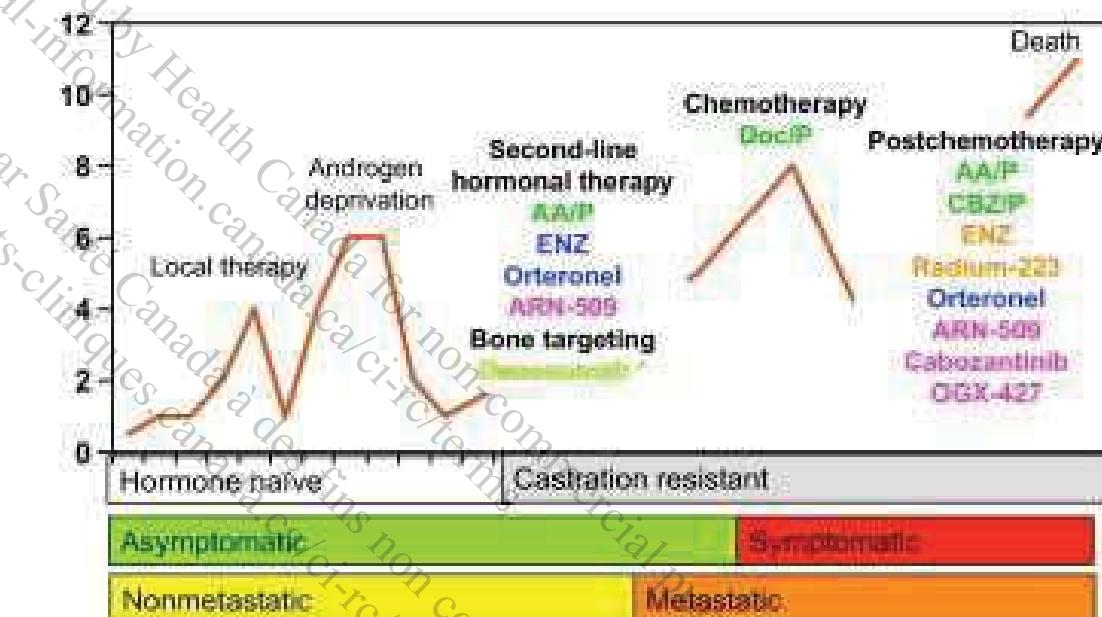


Figure 1: Current, ongoing, and future landscape in the management of castration-resistant prostate cancer.

Color key: green = US Food and Drug Administration/European Medicines Agency (FDA/EMA) approved; light green = trial results in high-risk patients positive, but not approved; orange = prospective, randomized, phase 3 clinical trial completed, results positive, FDA/EMA approval awaited; blue = prospective, randomized, phase 3 clinical trial completed, results awaited; purple = promising agent, phase 3 clinical trials ongoing. * Trial results for denusomab in high risk patients positive, but not approved. AA/P = abiraterone acetate with prednisone; ENZ = enzalutamide; Doc/P = docetaxel plus prednisone; CBZ/P = cabazitaxel plus prednisone.

1.1.1. Current treatment options for metastatic castration-resistant prostate cancer: before docetaxel

Sipuleucel-T

Sipuleucel-T is an autologous vaccine consisting of individually collected antigen-presenting cells that are exposed to the fusion protein prostatic acid phosphatase and granulocyte colony-stimulating factor (GCSF), and then reinfused in the patient at weeks 0, 2, and 4. In the Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT) study, median survival with sipuleucel-T was 25.8 mo compared with 21.7 mo with placebo [9]. It has to be considered, however, that only patients with a good Eastern Cooperative Oncology Group performance status of 0–1, asymptomatic or mildly symptomatic osseous metastases, and

PSMA-617-02

absence of visceral metastases were included in the trial.

Abiraterone acetate

The COU-AA-302 (Cougard 302) trial randomized 1088 men with mCRPC to receive abiraterone acetate with prednisone (AA/P) or placebo [4] with the primary end points of overall and radiographic progression-free survival (rPFS) by central review. Median overall survival was 35.3 mo and 27.2 mo in the AA/P group and in the placebo group, respectively ($p = 0.01$) [10]. Also, the co-primary end point of rPFS was significantly improved in the AA/P group, at 16.5 mo, as compared to 8.3 mo in the placebo arm ($p < 0.001$). On all secondary end points, AA/P treatment resulted in significantly improved effects.

Docetaxel/prednisone

In 2004, cytotoxic treatment with docetaxel plus prednisone (Doc/P) was the main option for treatment of mCRPC based on the TAX 327 trial [11]. The median survival was 18.9 mo versus 16.4 mo in the group of patients who received mitoxantrone/prednisone ($p = 0.009$), the 3-yr overall survival rate was 18.6% versus 13.5%, and pain response was 35% versus 22%. It has been shown recently that Doc/P is active in men with symptomatic mCRPC and especially in patients with poorly differentiated prostate cancer (PCa) (Gleason score: 8–10) [12].

Subsequent studies using combinations with docetaxel have not further improved the oncologic outcome [3]. The results of the Randomized Study Comparing Docetaxel Plus Dasatinib to Docetaxel Plus Placebo in Castration-Resistant Prostate Cancer (READY) and the Aflibercept in Combination with Docetaxel in Metastatic Androgen-Independent Prostate Cancer (VENICE) trial were disappointing [13] [11]. The median survival after docetaxel and docetaxel/dasatinib was 21.2 mo versus 21.5 mo, respectively, and the median survival after docetaxel versus docetaxel plus afilbercept was 21.1 mo versus 22.1 mo, respectively.

The differences in the patient cohorts of the Cougar 302, IMPACT, and TAX 327 trials make

PSMA-617-02

it evident that AA/P will be used for asymptomatic or mildly symptomatic mCRPC with a low metastatic burden, whereas Doc/P might be the treatment of choice in men with symptomatic mCRPC and/or a high metastatic burden as well as an undifferentiated PCa.

1.1.2. After docetaxel treatment

Docetaxel rechallenge

The scientific evidence of this approach results from large, retrospective series that identified patients who might be good candidates for re-exposure [14] [15] [16]. Patients who responded with a ≥30% decrease in prostate-specific antigen (PSA) level, maintained for at least 8 wk after first exposure to docetaxel, demonstrated a positive PSA response in about 55% to 60% of the cases during re-exposure without increasing treatment related toxicity.

Abiraterone acetate plus prednisone

AA/P versus placebo was evaluated in the Cougar 301 trial, which randomized 1195 patients with progressive mCRPC who failed docetaxel-based chemotherapy [5]. The median follow-up in the overall study population was 12.8 mo. Overall survival was significantly improved from 10.9 mo in the placebo arm to 14.8 mo in the AA/P arm ($p < 0.001$). All secondary end points were met and all end points demonstrated a significantly improved benefit for the AA/P group. Adverse events with regard to the CYP 17 blockade were observed significantly more often in the AA/P arm (55% vs 43%; $p < 0.001$).

Recently, Goodman et al. [17] demonstrated that AA/P is effective even in patients with liver or lung metastases, although to a lesser degree. The overall survival times were 12.9 mo versus 8.3 mo in the placebo group ($p = 0.022$). Albiges et al. [18] described an AA withdrawal syndrome that developed in 32% of 66 patients who had been treated for a mean period of 5.7 mo. Clayton et al. [19] presented data from a population-based study that included 187 mCRPC patients with a mean PSA serum concentration of 138 ng/ml who were treated with AA/P. The

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median overall survival was only 9.3 mo and might reflect the oncologic efficacy of AA/P in a real-world patient population with high metastatic burden.

Enzalutamide (formerly MDV3100)

Enzalutamide (ENZ) acts as an androgen receptor (AR)-signaling inhibitor, and it was evaluated in the Multinational, Phase 3, Randomized, Double-blind, Placebo-controlled, Efficacy and Safety Study of Oral MDV3100 in Patients with Progressive Castration-Resistant Prostate Cancer Previously Treated with Docetaxel-Based Chemotherapy (AFFIRM) trial, which randomized 1199 mCRPC patients to receive ENZ or placebo [8]. The median follow-up was 14.4 mo and the median overall survival was 18.4 mo and 13.6 mo ($p < 0.0001$) in the ENZ group and in the placebo group, respectively, with a 37% reduction in relative risk for death. All secondary end points were met with a statistically significant benefit in the ENZ arm. With regard to safety, the ENZ group experienced fewer grade 3/4 toxicities than the placebo group (53% vs 45%). The risk of seizures was slightly elevated in the ENZ group, with a frequency of 0.6% versus 0% in the placebo group.

Recently, Scher et al. [20] demonstrated that the use of corticosteroids in parallel to ENZ not only increased grade 3/4 side effects from 34.4% to 63.3%, but it also decreased overall survival to a median 11.5 mo. These data suggest that one of the other second-line therapies, such as AA/P or cabazitaxel plus prednisone (CBZ/P), might be the drug of choice, rather than ENZ, in patients who need corticosteroids for the management of associated comorbidities. Sternberg et al. [21] reported that ENZ is equally effective in patients aged >75 yr, with a median survival time of 18.2 mo as compared to the placebo group with 13.3 mo ($p = 0.0044$). Fleming et al. [22] identified a longer disease history (7.9 yr vs 5.9 yr), a better PSA response (87% vs 52%), and a lower metastatic burden associated with long-term response of 35% and 22% after 12 mo and >18 mo, respectively. These data seem to be important for the decision-making process about the most appropriate therapy for mCRPC patients following docetaxel chemotherapy.

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Cabazitaxel plus prednisone

In the XRP6258 Plus Prednisone Compared to Mitoxantrone Plus Prednisone in Hormone-Refractory Metastatic Prostate Cancer (TROPIC) trial, 755 patients with mCRPC who progressed during or after docetaxel-based chemotherapy were prospectively randomized to receive CBZ/P or mitoxantrone/prednisone (MP) at 21-d intervals for 10 cycles [5]. The primary end point was achieved and CBZ/P treatment resulted in a median overall survival of 15.1 mo in the CBZ/P compared to 12.7 mo in the mitoxantrone/prednisone group (hazard ratio [HR]: 0.70; 95% confidence interval [CI], 0.59–0.83; $p < 0.0001$). All secondary end points of the trials were reached and they were in favor of CBZ. The most common side effects were neutropenia (CBZ/P group: 82% vs MP group: 58%), leukopenia (CBZ/P group: 68% vs MP group: 42%), and anemia (CBZ/P group: 11% vs MP group: 5%). Diarrhea was the most common non-hematologic side effect and occurred in 6% of the CBZ/P group and <1% of the MP group.

On the other hand, the German compassionate use program (CUP) included 111 patients with mCRPC who met the inclusion criteria of the TROPIC trial; the frequency of neutropenia, leukopenia, and anemia decreased to 7.2%, 9.0%, and 4.5%, respectively [23]. Grade 3/4 gastrointestinal toxicity was observed in only 0.9% of the patients. The most likely reason for the improved toxicity profile is the experience of the investigators, guideline-compliant application of GCSF even at cycle 1, and preventive measures with regard to the treatment of diarrhea.

Recently, Heidenreich et al. [24] analyzed the European CUP, including 746 mCRPC patients, with regard to the frequency and management of adverse events in senior adults. In that study, 325 (43.5%) patients were aged ≥ 70 yr and 145 (19.4%) men were ≥ 75 yr. The type and the frequency of grade 3/4 side effects did not differ significantly between the younger and the older patients except that the frequency of grade 3/4 neutropenia was slightly higher in the group of men aged ≥ 75 yr (19.7% vs 15%). Furthermore, GCSF was used more often at cycle 1 (58.5% vs 47%) and throughout CBZ/P treatment (66.8% vs 58%) in the ≥ 75 age group.

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versus the <70 age group. In their analysis, Heidenreich et al. [24] developed a risk model to predict grade ≥ 3 neutropenia and/or neutropenic complications based on a multivariate analysis. Age ≥ 75 yr, cycle 1, and neutrophil count $<4000/\text{mm}^3$ before CBZ injection were associated with neutropenic complications. It has to be mentioned that even in the presence of these risk factors, prophylactic application of GCSF significantly reduced neutropenic complications by 30% (odds ratio: 0.70; 95% CI, 0.50–0.99; $p = 0.04$).

Bone-targeting agents

More than 90% of patients with CRPC have bone metastases, which are a major cause of death, disability, and decreased quality of life, as well as increased cost of treatment [25]. Zoledronic acid and the receptor activator of nuclear factor κ B (RANK) ligand inhibitor denosumab are the two US Food and Drug Administration-approved bone-targeting agents in the management of CRPC [3].

In a phase 3 study, the median time to first on-study, skeletal-related event was 20.7 mo with denosumab compared with 17.1 mo with zoledronic acid (HR: 0.82; 95% CI, 0.71–0.95; $p = 0.0002$ for noninferiority; $p = 0.008$ for superiority) [26]. In a recent, prospective, randomized, double-blind, placebo-controlled trial, Smith et al. [27] evaluated the therapeutic efficacy of denosumab 120mg every week versus placebo in 1423 men with nonmetastatic CRPC and aggressive PSA kinetics (PSA level $>8.0 \text{ ng/ml}$ and/or PSA doubling time $<10 \text{ mo}$). The median time to first bone metastases was significantly prolonged by 4.3 mo (29.5 mo vs 25.2 mo; $p = 0.028$). Bone metastases-free survival was significantly improved by 16%, 23%, and 29% in patients with a PSA doubling time of $<10 \text{ mo}$, $<6 \text{ mo}$, and $<4 \text{ mo}$, respectively.

Radium-223

Radium-223 is a radiopharmaceutical that acts as a calcium mimic and targets new bone growth in and around bone metastases via heavy alpha particles that have an ultrashort range of $<100\mu\text{m}$. A Phase 3 Study of Radium-223 Dichloride in Patients with Symptomatic

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Hormone Refractory Prostate Cancer with Skeletal Metastases (ALSYMPCA), which included 921 CRPC patients, the median overall survival was 14.9 mo in patients treated with radium-223 compared with 11.3 mo in the placebo group (HR: 0.695; 95% CI, 0.581–0.8732; $p < 0.0001$) [7].

1.1.3. New and emerging developments

Agents targeting steroidogenesis

Orteronel (TAK-700) selectively blocks 17,20-lyase, resulting in fewer mineralocorticoid effects than AA [28]. In the phase 2 portion of a dose-finding study, Orteronel (TAK-700) 400mg twice daily with prednisone 5mg twice daily resulted in a reduction in PSA level $\geq 50\%$ in 52% of the 96 chemotherapy-naïve mCRPC patients at 12 wk. There are two ongoing phase 3 clinical trials in the prechemotherapy ($n = 1454$) and postchemotherapy ($n = 1083$) landscape of mCRPC that are evaluating the oncologic activity of orteronel. Both trials have completed recruitment.

Galeterone (TOK-001) has combined activity: It inhibits the human CYP17 enzyme, it has pure antagonistic activity toward the AR, and it inhibits the binding of androgens to both mutant and wild-type AR [29]. In the Androgen Receptor Modulation Optimized for Response (AMORI) trial, 49% of chemotherapy-naïve mCRPC patients experienced a PSA-level reduction of $\geq 30\%$, and a $\geq 50\%$ reduction was achieved by 22% [30]. Despite the absence of steroid co-treatment, no adrenal mineralocorticoid excess was observed and a phase 2 trial is underway.

Androgen-receptor blocking agents

ARN-509 is a full antagonist to AR overexpression: It inhibits androgen-dependent gene description, and it impairs nuclear translocalization and DNA binding of AR [31]. Currently, three prospective randomized phase 3 clinical trials are underway including (1) patients with

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high-risk and nonmetastatic CRPC, (2) treatment-naïve patients with mCRPC, and (3) patients with progression following AA/P treatment. Preliminary results have been presented for the first two groups and a ≥50% decline in PSA level was achieved in 91% of patients with high-risk and nonmetastatic CRPC and in 88% of treatment-naïve patients with mCRPC. The most common side effects were tolerable fatigue and gastrointestinal events.

ODM-201 is another antiandrogen with similar mechanisms of actions as described for ENZ and ARN-509 [31]. The potential advantage of ODM-201 is that it does not cross the blood– brain barrier and so might prevent the development of seizures. ENZ-4176 is a novel, nucleic acid–based antisense oligonucleotide against AR, which results in selective and specific downregulation of AR mRNA and protein.

Heat shock proteins

Heat shock proteins (HSPs) have been identified as AR coactivators and chaperone proteins that are increased in PCa cell lines after castration [32]. Quite recently, antisense oligonucleotides targeting HSP27 were evaluated in a phase 2 clinical trial including 72 patients chemotherapy-naïve mCRPC patients who received OGX-427 plus prednisone versus prednisone alone. At 12 wk, 71% and 40% of the patients were progression-free after OGX-427 or prednisone, respectively. A decline of ≥50% in PSA level was observed in 50% and 20% in the OGX-427 group and in the prednisone group, respectively. Furthermore, measurable disease response occurred in 44% and 0% of the OGX-427 group and the prednisone group, respectively.

1.1.4 Targeted therapies

Cabozantinib

Cabozantinib is another promising bone-targeting agent that inhibits both vascular endothelial growth factor and met proto-oncogene (hepatocyte growth factor receptor; MET). In a

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prospective, randomized, placebo-controlled, phase 2 clinical trial, 171 mCRPC patients were enrolled to receive cabozantinib (100mg daily) or placebo [33]. Random assignment was halted early based on the observed activity of cabozantinib. Respectively 5% and 75% of patients treated with cabozantinib had a confirmed partial response and stable disease. The median progression-free survival was 29.7 wk, 23.9 wk, and 5.9 wk for patients who were docetaxel naïve, docetaxel pretreated, and on placebo treatment ($p < 0.001$), respectively. Interestingly, PSA changes did not correlate with the antitumor effects in bone metastases and soft-tissue lesions. However, patients with complete resolution ($n = 14$; 12%) or partial resolution ($n = 65$; 56%) of bone scans experienced significantly better response rates to soft-tissue metastases as compared to men with stable or progressing bone scans (81% vs 61%), and they also experienced longer progression-free survival rates at 6 mo (56% vs 48%, respectively). Cabozantinib has significant antitumor activity and a well-tolerated toxicity profile, so it might be well integrated into the therapeutic armamentarium to treat mCRPC.

Targeted radionuclide Therapy

Over the past several decades, numerous combined diagnostic and therapeutic radioligands (Theranostics) were designed to target receptors on the cancer cell surface. Antibodies (whole or small fragments), small molecules, peptides with affinities to receptors (agonist or antagonist) have demonstrated in vivo efficacy for targeting cancers based on up-regulated antigens or receptor populations. This approach, also called radioligand therapy (RLT), presents several advantages over conventional chemotherapy. The expression of the antigens or special receptors can be identified by a diagnostic probe before exposing patients to therapeutic doses of these agents allowing identification of suitable subjects for therapeutic procedures and preventing unnecessary exposure of the patients to radiation without significant benefit. This approach allows the physician to select only those patients with high expression of the target prior to treatment. Since the unused radioactive materials are excreted from the body, RLTs are generally well tolerated with no significant or generally reversible or

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manageable side effects as has been demonstrated for ¹⁷⁷Lu-DOTATATE treatment in patients with neuroendocrine tumor [34].

Prostate cancer demonstrates high expression levels of prostate-specific membrane antigen (PSMA) on its cell surface. Thus PSMA has become a biomarker for prostate cancer [35] [36] and has attracted significant interest as a target for the imaging [37] [38] and therapy [39, 40].

In particular, development of small urea-based PSMA ligands have received significant interest due to their high affinity for PSMA [41] [42]. The urea-based PSMA ligands were modified to deliver a variety of radio-imaging nuclides for both PET and SPECT. Gallium (⁶⁸Ga) labeled urea-based PSMA ligands have been developed as diagnostic agents and studied by several groups [43] [44]. More recently a Lutetium (¹⁷⁷Lu) labeled urea based PSMA ligand (DOTA PSMA or PSMA 617) were evaluated in preclinical and clinical phase. Characteristics of ¹⁷⁷Lu labeled PSMA are described below.

1.2 Characteristics of 177 Lu-DOTA-PSMA (177Lu-PSMA-617)

Lutetium (¹⁷⁷Lu) –DOTA PSMA has three components: PSMA is the targeting vector , DOTA (1, 4, 7, 10-tetraazacyclododecane-1, 4, 7, 10-tetraacetic acid) is a radiometal chelator and a linking group, and ¹⁷⁷Lu is the beta emitter that upon internalization delivers radiation to the nucleus of tumor cells to cause DNA damage [43] [44, 45]. The targeting vector utilizes glutamyl-urea–lys sequence which is an inhibitor capable of binding to the domain of PSMA. These components have been previously used in human subjects and in medical research.

1.3 Background of Drug Development

There is substantial previous pre-clinical and clinical experience with ¹⁷⁷Lu-PSMA-617 published in peer reviewed medical literature from multiple medical centers throughout the world. Sponsors are relying on studies published in the peer viewed medical journals for

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preclinical and preliminary clinical information. Summary of such reports is given below.

1.3.1 Preclinical Studies.

Martina Benesova et al. [46] performed a preclinical evaluation of radiolabeled PSMA-617.

PSMA-617 was synthesized by solid phase peptide synthesis. PSMA-617 can be labeled with ^{177}Lu and Ga-68. Both in vivo and vitro studies were performed using LNCaP cell lines expressing PSMA. PSMA-617 showed highest inhibition potency $K_i = 6.91 \pm 1.32$ for Lu complex, $6.40 \pm 1.02\text{nM}$ for Ga complex. PSMA-617 showed higher specific internalization in LNCaP cells.

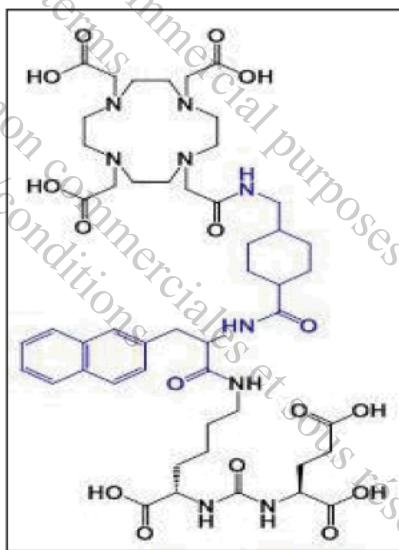


Figure 2: Structure of PSMA 617. Chemical Name 2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{[2-(4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid.

The i.v. administered Lu-PSMA-617 effectively cleared the blood by 1 hr. Clearance of radioactivity occurred largely through the renal system. As a result of this, the kidneys exhibited significant uptake $137.2 \pm 77.8\% \text{ID/g}$; this could be effectively blocked ($0.85 \pm 0.22 \% \text{ID/g}$)

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by co-injection of PMPA [2 mg/kg], a high affinity inhibitor of PSMA. At 24 hr ^{177}Lu -PSMA-617 shows rapid clearance from the kidney $2.13 \pm 1.36\text{ %ID/g}$ highlighting its potential use as theranostic agent. At 1 hr time point ^{177}Lu -PSMA-617 displayed good in vivo tumor targeting with $11.20 \pm 4.17\text{ %ID/g}$. Accumulation in tumor was PSMA specific with reduction to $0.64 \pm 0.07\text{ %ID/g}$ by coinjection of 2-PMPA. At 24 h post injection $10.58 \pm 4.50\text{ %ID/g}$ uptake was retained in the tumor tissue. For all other non-target tissues, ^{177}Lu -PSMA-617 demonstrated rapid clearance. The ratio of tumor to blood was 1058; tumor to muscle was 529 at 24 hr post injection. These favorable pharmacokinetics are crucial for imaging and therapy. The detailed biodistribution results are summarized in Figure 3. ^{68}Ga -PSMA 617 showed similar uptake in the LnCaP tumors ($11.20 \pm 4.17\text{ %ID/g}$). It also shows similar pharmacokinetic clearance profile compared with ^{177}Lu -PSMA-617.

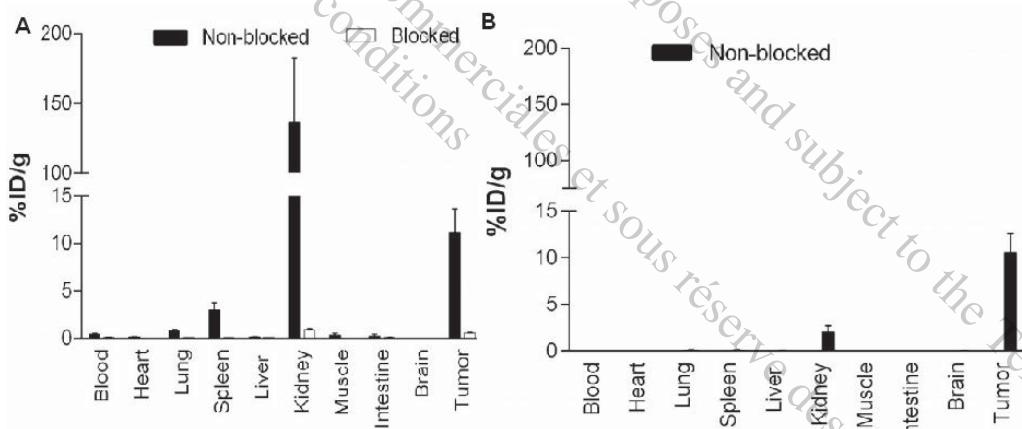


Figure 3: Distribution assay of ^{177}Lu -PSMA-617 in BALB/c mice with LNCap xenografts at 1 h (A) and 24 h (B) post injection.

In summary authors concluded the present radiotracer is suitable for theranostic application in human prostate cancer.

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1.3.2 Clinical Studies

Current literature is available to evaluate

management of patients with prostate cancers. The studies presented in this section were chosen based on novelty of the approach (initial report of application, variables for analyses) and/or the number of patients included.

Clemens Kratochwil et al. [¹⁷⁷Lu]Lutetium-labelled PSMA ligand-induced remission in a patient with metastatic prostate cancer. Eur J Nucl Med Mol Imaging 2015; 42:6 ;987-988. [47]

Study Design: First reported application of ¹⁷⁷Lu-PSMA-617 for treatment of a patient with mCRPC. Patient had proven PSMA expression and PSA of 38.0 ng/ml prior to treatment and has received 7.4 GBq of ¹⁷⁷Lu-DKFZ-617 in 2 cycles 3 months apart.

Toxicity: No potential side effects were reported in this study.

Results: After the radiotherapy ¹⁷⁷Lu-PSMA-617, PSA level of patient decreased to 4.6 ng /ml. PET/CT images showed no signs of metastases lesions either shrunk or were undetectable.

Conclusion: Authors are planning to conduct multicenter a clinical trial as soon as possible to examine clinical potential of ¹⁷⁷Lu-PSMA-617.

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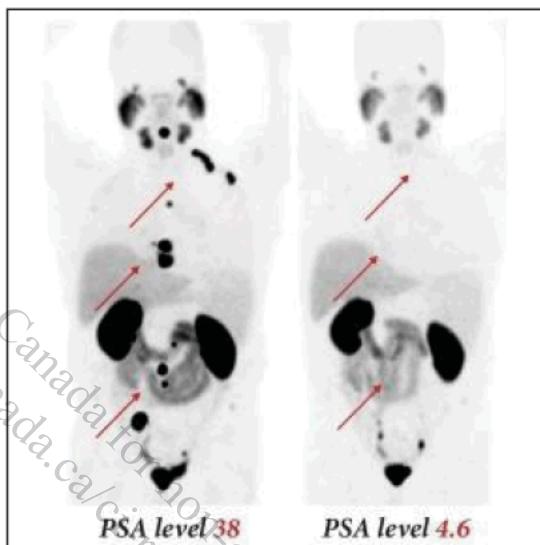


Figure 4: Above Image has recently awarded as image of Year Award and the Berson-YalowAward at the 2015 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI) in Baltimore, USA.

Hojjat Ahmadzadehfari et al. Early side effects and first results of radioligand therapy with ^{177}Lu -DKFZ-617 PSMA of castrate-resistant metastatic prostate cancer: a two-center study. *EJNMMI Research* 2015; 5:36. [48]

Study Design: A total of 10 consecutive hormone and/or chemo refractory PCa patients with distant metastases and progressive disease with rising PSA levels were recruited in this study. All patients had prior history or were under therapy with enzalutamide and/or abiraterone. Four patients had received ^{223}Ra -dichloride (1-4 cycles). All 10 patients underwent with ^{68}Ga -PSMA HBED-CC (^{68}Ga -PSMA) PET /CT prior to therapy to evaluate PSMA expression. Ten patients were treated with range of 4.1-6.1 GBq dose of ^{177}Lu -DKFZ-617 PSMA. All patients were treated with single dose of ^{177}Lu -PSMA-617. The mean and median PSA levels prior to therapy were 339.4 and 298.5 ng/ml. Complete blood chemistry, renal and liver function tests were performed a day before and 2 after the radiotherapy. Patients were followed via telephone every week for safety assessment.

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Toxicity: No patient experienced any side effects immediately after injection of ¹⁷⁷Lu-DKFZ-617 PSMA. Relevant hematotoxicity (grade 3 or 4) occurred 7 weeks after the administration in just one patient. The same patient showed a leucopenia grade 2. Two patients showed a disturbance of only 1 hematologic cell line, whereas one patient showed a reduction of grades 1 and 2 in leucocytes and thrombocytes, respectively. Six patients did not show any hematotoxicity during the 8 weeks after therapy. There was no relevant nephrotoxicity (grade 3 or 4).

Results: Eight weeks after the therapy, seven patients (70 %) experienced a PSA decline, of which six experienced more than 30 % and five more than 50 %. Three patients showed a progressive disease according to the PSA increase.

Conclusions: ¹⁷⁷Lu-DKFZ-617 PSMA radiotherapy with single dose for the treatment of metastatic prostate cancer patients without any other therapy option is safe and seems to have a low early side-effect profile with evidence of positive response to the therapy according to PSA decline in 70 % of patients. The authors also stated ¹⁷⁷Lu-DKFZ-617 PSMA has potential to exhibit suitable agent for radionuclide radiotherapy.

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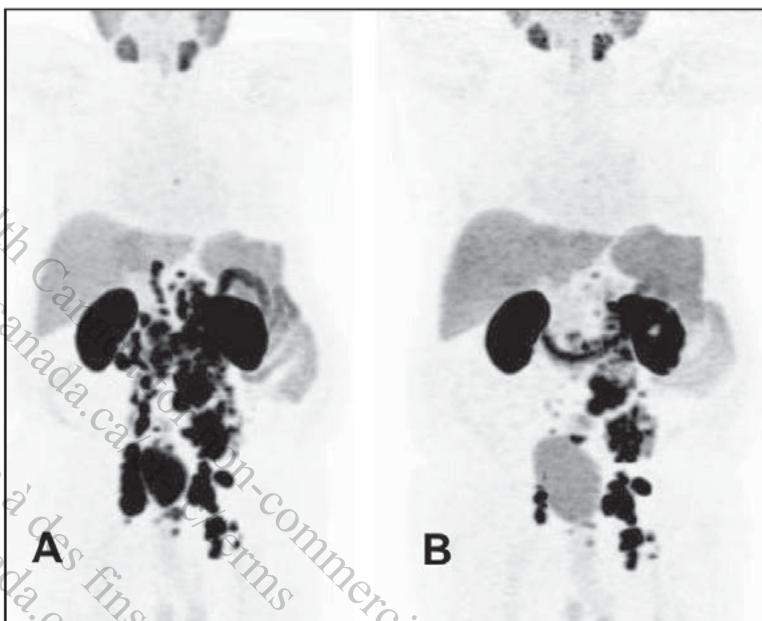


Figure 5: A 74-year-old patient with hormone- and chemo-refractory prostate cancer underwent PSMA PET/CT (a), which showed diffuse abdominal and iliac lymph node metastases. The patient underwent RLT with 5.7 GBq ^{177}Lu -PSMA-617. The PSA level was at the time of the therapy 790 ng/ml. (b) A partial response 7 weeks after RLT with 63 % PSA decline; at this time, the PSA level was 293 ng/ml

Clemens Kratochwil, et al. PSMA-targeted radionuclide therapy of metastatic castration-resistant prostate cancer with Lu-177 labeled PSMA-617 J Nucl Med March 16, 2016 [49]

Study Design: Radionuclide therapy with ^{177}Lu -PSMA-617 was performed on 30 patients with PSMA positive tumors were enrolled in this study. 30 patients were treated with 1-3 cycles of ^{177}Lu -PSMA-617. Pharmacokinetic and radiation dosimetry was also evaluated during course of the study.

Results: 21 of 30 patients showed response to therapy; for 13/30 the PSA decreased >50%. After 3 cycles 8/11 patients achieved a sustained PSA response (>50%) for over 24 weeks. ^{177}Lu -PSMA-617 showed fast renal wash out within 48 hours of injection. Patients showed mild nausea, fatigue and Xerostomia (<10%) over a period of time. No acute hematotoxicity was observed during the study. Dosimetry results revealed that ^{177}Lu -PSMA-617 has an exposure of 0.75 Gy/GBq for kidney 0.03 Gy/GBq red-marrow, 1.4 Gy/GBq salivary glands and 6-22 Gy/GBq for tumour lesions.

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Conclusion: Based on the results authors concluded that targeted radioligand therapy with ¹⁷⁷Lu- PSMA-617 is safe and promising therapy option for metastasized castrate resistant prostate cancer.

Ahmadzadehfar H, et al. Therapeutic response and side effects of repeated radioligand therapy with ¹⁷⁷Lu-SMA-DKFZ-617 of castrate-resistant metastatic prostate cancer. Oncotarget. 2016 Feb 8. doi: 10.18632/oncotarget.7245. [50]

Study Design: Radionuclide therapy with ¹⁷⁷Lu-PSMA-617 was performed in 24 hormone and/or chemo-refractory PC patients. Forty-six cycles of ¹⁷⁷Lu-PSMA-617 were performed. Side effects and response rate was assessed.

Results: Eight weeks after the first cycle of ¹⁷⁷Lu-PSMA-617 therapy 79.1% experienced A decline in PSA-level. Eight weeks after the second cycle of Lu-PSMA therapy 68.2% experienced a decline in PSA relative to the baseline value. Apart from two cases of grade 3 anemia, there was no relevant hemato- or nephrotoxicity (grade 3 or 4).

Conclusion: ¹⁷⁷Lu-PSMA-617 is a safe treatment option for metastatic PC patients and has a low toxicity profile. A positive response to therapy in terms of decline in PSA occurs in about 70% of patients.

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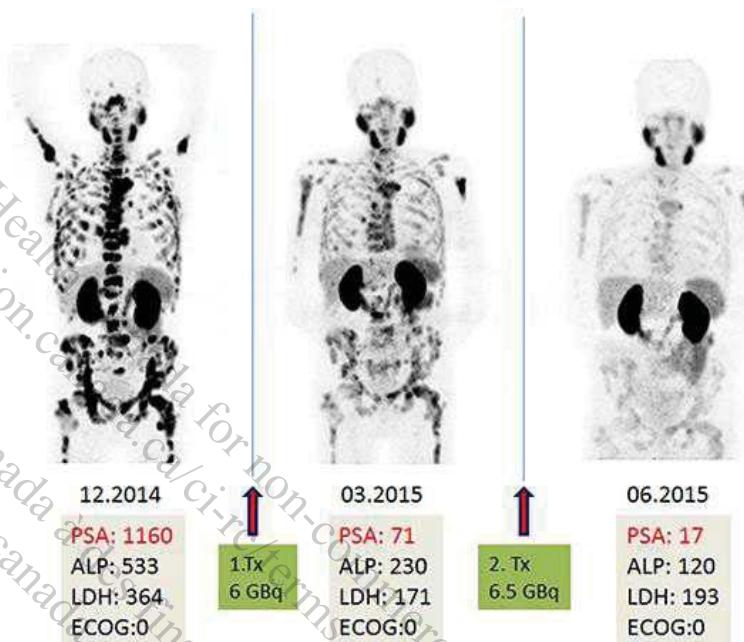


Figure 6: A 75-year-old patient with diffuse bone and lymph node metastases as well as local recurrence (left MIP image). History of chemotherapy and therapy with abiraterone, PSA elevation under enzalutamide. The patient underwent PSMA therapy as the last possible option. Continuing PSA decline and partial response in Ga-PSMA PET images after the first (middle MIP image) and second cycles (right MIP image)

Madhav Prasad Yadav, et al. ^{177}Lu -DKFZ-PSMA-617 therapy in metastatic castration resistant prostate cancer: safety, efficacy, and quality of life assessment. Eur J Nucl Med Mol Imaging. 2016 Aug 10. [51]

Study Design: Radionuclide therapy with ^{177}Lu -PSMA-617 was performed in 31 patients with progressive disease despite second-line hormonal therapy and/or docetaxel chemotherapy. Patients underwent 1 to 4 cycles after a ^{68}Ga -PSMA-HBED-CCP ET/CT for inclusion (mean activity 5069 ± 1845 MBq). Hematological, kidney function, liver function tests, and serum PSA levels were recorded before and after therapy at 2 weeks, 4 weeks, and 3 month intervals. Biochemical response was assessed with trend in serum PSA levels. Metabolic response was assessed by PERCIST 1 criteria. Clinical response was assessed by visual analogue score (VASmax) analgesic score (AS), Karanofsky performance status (KPS), and toxicity and response criteria of the Eastern Cooperative Oncology Group (ECOG) criteria.

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Results: Biochemical response in terms of complete response (CR), partial response(PR), stable disease (SD), and progressive disease (PD) was observed in 2/31, 20/31, 3/31, and 6/31 had, respectively. Mean VASmax and mean analgesic scores decreased from 7.5 to 3 and 2.5 to 1.8 after therapy, respectively. Mean KPS and mean ECOG performance status score improved from 50.32 to 65.42 after therapies, respectively. Two patients experienced grade I and grade II hemoglobin toxicity each. None of the patients experienced nephrotoxicity or hepatotoxicity.

Conclusion: ¹⁷⁷Lu-DKFZ-PSMA-617 radionuclide therapy is a safe and effective approach in the treatment of mCRPC patients.

1.3.3 Sponsors Experiences

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1.3.3.1 Preclinical Toxicity Studies

The aim of study was to evaluate toxicity of PSMA-617. PSMA-617 applied once weekly by intravenous administration to male rats over 22 days. The animals were treated with 40, 160 or 400 µg of PSMA-617/kg b.w. by tail vein intravenous bolus injection on test days 1, 8, 15 and 22. The control group was treated with physiological saline. No deaths were noted. No signs of local or systemic intolerance reactions were observed. Body weight and body weight gain, food intake, and drinking water consumption were not influenced. No test item-related changes were noted for the hematological and biochemical parameters, the urinary status, the eyes and optic region, the auditory acuity, the relative and absolute organ weights, and the myeloid: erythroid ratio. No test item-related abnormalities were noted during macroscopic inspection at necropsy and at histopathological examination.

Under the test conditions of this study, the no-observed-adverse-effect-level (NOAEL) was 400 µg PSMA-617 / kg b.w. administered once weekly by intravenous bolus injection. This dose was the highest dose tested. Detailed description of this study is attached in appendix I.

1.3.3.2 Summary of Human Studies - German Multicenter Experience

Rahbar K, et al. German multicenter study investigating ^{177}Lu -PSMA-617 radioligand therapy in advanced prostate cancer patients. J Nucl Med. 2016 [52]

Study design: Retrospective acquisition and pooling of data for toxicity and PSA response in patients after ^{177}Lu -PSMA-617 RLT performed in Germany until July 2015 was initiated by the German Society of Nuclear Medicine for research purpose. The following contains a summary of the collected data. 145 patients with metastatic castration-resistant prostate cancer received a median of two cycles (range 1 to 4) of ^{177}Lu -PSMA RLT at twelve German Nuclear Medicine Clinics. Data on safety and efficacy were reported. Table 1 lists the **administered ^{177}Lu -PSMA-617 activity** for this study cohort.

Table 1. Administered ^{177}Lu -PSMA-617 activity (n = 248 RLT cycles)

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Administered activity (GBq)	Cycle 1	Cycle 2	Cycle 3	Cycle 4
≤ 3.5	9	3	0	1
> 3.5 – 4.5	32	14	2	0
> 4.5 – 5.5	16	12	9	0
> 5.5 – 6.5	71	37	14	2
> 6.5	17	8	1	0

Results:

A. Toxicity: Nuclear medicine physicians responsible for ¹⁷⁷Lu-PSMA RLT and subsequent follow-up reported potentially related or unrelated adverse events based on a standard template. In addition toxicity was determined by baseline and follow-up findings for serum creatinine, AST, ALT, white blood cell count, hemoglobin and platelet count for 121 of 145 (83%) patients. The follow-up period for adverse events was 2 to 30 weeks. Reported toxicity sorted by organ system is given in Table 1. Grade 3-4 anemia occurred in 15 (10%) patients and grade 3-4 thrombocytopenia occurred in 5 (4%) patients. The rate of grade 3-4 events was low for all other categories (0 to 3 patients; 0 to 2%).

There were fewer hematologic adverse events when compared to patients with metastatic castration resistant prostate cancer treated with placebo or ²²³Ra within the ALSYMPCA trial [7] (grade ≥3 anemia: 14% in the placebo and 13% in the ²²³Ra group; grade ≥ thrombocytopenia: 3% in the placebo and 7% in the ²²³Ra group). Toxicity data thus indicate a favorable safety profile for RLT using 2-7 GBq ¹⁷⁷Lu-PSMA-617 per cycle in patients with metastatic castration resistant prostate cancer.

Majority of patients received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle. Toxicity rates were comparably low: 9 of 71 (13%) patients with 5.5 – 6.5 GBq and 3 of 17 (18%) patients with >6.5 GBq during the first RLT developed grade 3-4 toxicity.

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Table 2. Adverse events after ¹⁷⁷Lu-PSMA-617 as determined by blood tests (n=121) or physician reports (n=145)

Organ system	Category	Evaluated for N	All grades	Grade 3-4
Blood and Lymphatic disorders	Leukopenia	121	48 (40%)	4 (3%)
	Anemia	145	50 (34%)	15 (10%)
	Thrombocytopenia	121	38 (31%)	5 (4%)
Gastrointestinal disorders	AST elevation	121	27 (19%)	0 (0%)
	ALT elevation	121	11 (8%)	0 (0%)
	Xerostomia	145	11 (8%)	0 (0%)
	Nausea	145	9 (6%)	0 (0%)
	Dysgeusia	145	6 (4%)	0 (0%)
	Ascites	145	2 (1%)	0 (0%)
General disorders	Biliary obstruction	145	0 (0%)	1 (1%)
	Fatigue	145	19 (13%)	1 (1%)
	Pain	145	5 (3%)	0 (0%)
	Ileus	145	1 (1%)	0 (0%)
Urinary disorders	Renal failure	121	14 (12%)	0 (0%)
	Urinary tract inf.	145	1 (1%)	0 (0%)
Cardiovascular disorders	Edema	145	2 (1%)	0 (0%)
	Lung embolism	145	0 (0%)	3 (2%)
Respiratory, thoracic and mediastinal disorders	Pleural effusion	145	1 (1%)	0 (0%)
	Dyspnea	145	1 (1%)	0 (0%)
Neurologic disorders	Vertigo	145	1 (1%)	0 (0%)
	Stroke	145	0 (0%)	2 (1%)
Musculoskeletal disorders	Bone fracture	145	0 (0%)	3 (2%)

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Efficacy

Serial PSA levels at baseline and follow-up were recorded for 99 of 145 patients (68%).

Response was expressed as percent change in serum PSA from baseline to the lowest PSA level measured at follow-up (best PSA response).

Over the entire follow-up period 45 of 99 (45%) patients demonstrated a PSA decline $\geq 50\%$ and were considered biochemical responders. Any PSA decline occurred in 59 of 99 (60%) patients (Figure 7). After the first cycle a PSA decline $\geq 50\%$ occurred in 40 of 99 (40%), any PSA decline in 65 of 99 (66%) patients (Figure 8A). After the second therapy cycle of ^{177}Lu -PSMA-617 RLT a PSA decline $\geq 50\%$ occurred in 35 of 61 (57%) and any PSA decline in 44 of 61 (72%) patients (Figure 8B). Patients receiving a third or fourth cycle of therapy showed a PSA decline $\geq 50\%$ in 13 of 20 (65%) and 3 of 3 (100%) patients, respectively.

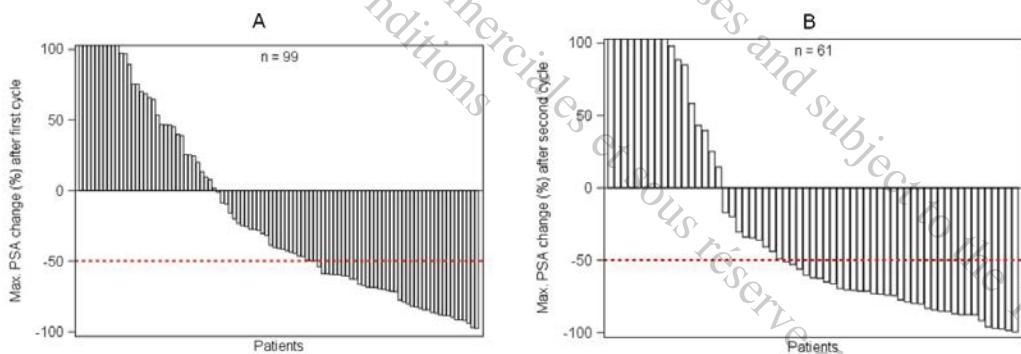


Figure 7. Waterfall plot of maximum PSA change (%) from baseline over total follow-up period. PSA increase of more than 100% was cropped due to simplification.

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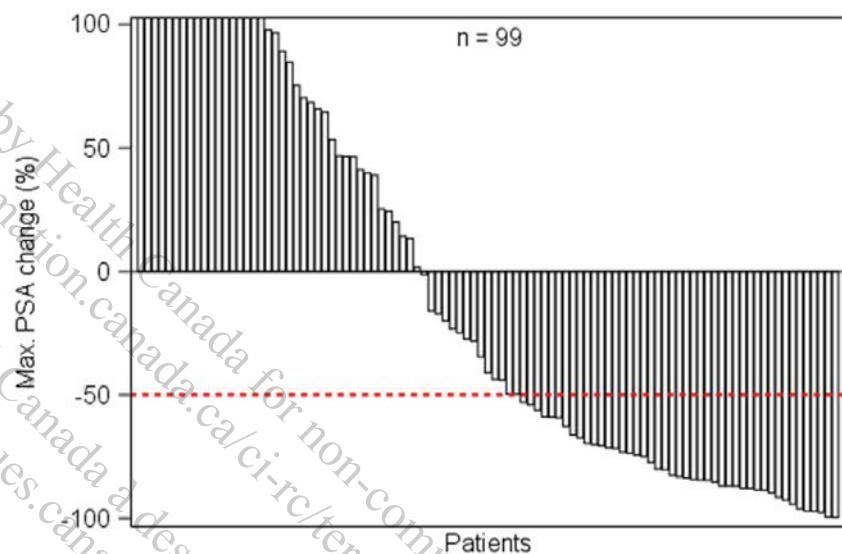


Figure 8. Waterfall plots of maximum PSA change (%) after the first cycle (A) and after the second cycle (B). PSA increase of more than 100% was cropped due to simplification.

Response rate was higher than the rate in patients with metastatic castration resistant prostate cancer treated with abiraterone (best PSA response >50% after abiraterone plus prednisone: 43% (25 of 58) patients) [53]. Data thus indicate good efficacy for ^{177}Lu -PSMA RLT in patients with metastatic castration resistant prostate cancer. Response rates were not significantly associated with mean activity per cycle ($p=0.46$) or cumulative activity after two cycles ($p=0.22$).

2. Study Objectives

Primary Objectives:

1. To assess the clinical safety of ^{177}Lu -PSMA-617 by evaluation of adverse events (AE) using the Common Terminology Criteria for Adverse Events (CTCAE)
2. To assess the efficacy as defined by proportion of patients with PSA-response of $\geq 50\%$ decline at 12-weeks from baseline

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Secondary Objectives:

1. Maximum PSA response: Maximal baseline to follow-up PSA decline at any time during or after therapy [1]
2. To determine the time to PSA progression, separate for treatment doses: time from inclusion to date until PSA progression or death (whichever occurs first) [1]
 - a. for patients with PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later
 - b. for patients without PSA decline: Time from baseline to time the PSA increase to 25% and 2 ng/ml above baseline
3. To determine radiographic Progression-free Survival (rPFS), for each treatment dose: time from inclusion to date when first site of disease is found to progress or death (whichever occurs first)
 - a. Nodal and visceral disease is evaluated on cross-sectional imaging using RECIST 1.1/PCWG criteria
 - b. Bone metastases are evaluated using bone scintigraphy and new lesions have to be confirmed on a second scan (2+2 rule) using PCWG criteria
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST 1.1/PCWG criteria stable disease (SD), partial response (PR) or complete response (CR).
5. Change in Pain and Quality of Life: Pain and "Epic-26" Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 mo. Pain response will be determined in accordance with PCWG [1].
6. Change in ECOG Performance Score.

3. Investigational Plan

3.1 Overall Study Design and Dosing of Targeted PSMA Radioligand Therapy (RLT)

This is an open-label, multicenter, prospective trial. Upon inclusion patients will be randomized into two treatment doses. RLT will be performed by repeated i.v. application of 6.0 GBq ($\pm 10\%$) or 7.4 GBq ($\pm 10\%$) ^{177}Lu -PSMA-617 every 8±1 weeks until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy. All doses after labeling will be presented in

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buffered solution for intravenous injection.

In total, 200 subjects with histologically proven prostate cancer and mCRPC will be enrolled.

Salivary protection will be accomplished by applying ice pack starting 30 minutes prior to infusion of radiopharmaceutical and will continue for 4 hours. Subjects will be recruited at up to 3 Nuclear Medicine sites selected for this project. Each subject will undergo a screening visit within 14 days prior to receiving study drug.

Dosimetry was required to be performed in the initial versions of the study according to dosimetry protocol (Appendix V) provided by Prof.r. [Name] (Universitätsklinikum Würzburg Germany - Klinik und Poliklinik für Nuklearmedizin) to determine dose to the kidneys. Treatment was continued until either of the following conditions applied:

- PSA/radiographic progression at ≥ 12 weeks as defined above
- Completion of four RLT cycles
- 23 Gy kidney dose would be exceeded by the next cycle as estimated by dosimetry
- Patient withdrawal (e.g. appearance of intolerable adverse events)

Dosimetry data for 20 patients on study (16 from UCLA and 4 from Excel Diagnostics) was analyzed and it was found that the permitted renal dose of 23 Gy was not exceeded in any patient after 4 cycles demonstrating overall favorable renal dosimetry and dosimetry is no longer required per protocol. (see Section 8.4.3 for additional details)

Primary objectives of the study is efficacy and safety.

Efficacy is determined by PSA response rate: Patients with baseline to follow-up decline in tumor marker level (PSA) $\geq 50\%$ at 12 (± 1) week will be considered responders.

For safety assessment, vital signs will be measured within 20 minutes before and for up to an hour after administration of ^{177}Lu -PSMA-617. Blood samples will be collected for CBC and CMP with eGFR at baseline (within 72 hours of first treatment dose) and then every 2 weeks (± 3 days) after first dose continued until 12 weeks after the last dose and then every 3 months (± 1 week) thereafter until the end of follow-up visits (24 months from 1st therapy date). The CBC and CMP within 2 weeks of each subsequent treatment cycle will be used to assess

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eligibility of the corresponding treatment cycle. CBC will be performed every 7 days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery which is defined as grade 2 toxicity or lower. CTCAE v 4.0 will be used to evaluate renal toxicity. For more information, please refer to the Schedule of Events (Appendix II).

3.2 Rationale for Study Design

3.2.1 Rationale for a regimen with multiple therapy cycles

Activity given during targeted radionuclide therapy is limited by radiation dose to healthy organs. Based on dosimetry radiation dose to healthy organs and subsequent maximal cumulative activity can be calculated. To obtain optimal safety margin maximal cumulative activity is not given in one treatment session but approached by application of a defined fraction of this activity in several cycles. The administration of a standard activity over several treatment cycles allows for early and individual estimation of radiation dose and tolerability. The efficacy and safety of a sequential approach was proven in patients with ²²³Ra therapy for metastatic castration-resistant prostate cancer (mCRPC) [7] and in patients with ¹⁷⁷Lu-DOTATATE therapy for midgut neuroendocrine tumor (NET) [54] each in prospective, double-blind, randomized, international, and multicenter phase III trials. Based on this evidence targeted PSMA Radioligand Therapy (RLT) will be performed by sequential applications of ¹⁷⁷Lu-PSMA-617 with treatment-free intervals.

3.2.2 Rationale for eight weeks interval

Highest level of evidence for subacute adverse events after radionuclide therapy was published for patients with non-Hodgkin's lymphoma. Witzig et al analyzed safety and efficacy of ⁹⁰Y-Ibritumomab Tiuxetan in 73 patients in a prospective Phase III randomized trial. This study reports neutrophil, platelet and hemoglobin nadir approximately six weeks after application of the beta emitter [55]. Based on this study ¹⁷⁷Lu-PSMA-617 RLT will be performed by

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sequential applications with a treatment-free interval of eight weeks to minimize risk of repeated ^{177}Lu -PSMA-617 therapy before reaching blood level nadir. This scheme is also supported by safety data from the phase III NETTER-1 trial on safety and efficacy of ^{177}Lu -DOTATATE in patients with midgut NET. Here ^{177}Lu -DOTATATE was administered at seven to nine week intervals and rate of severe adverse events was below 10% for 115 patients in the treatment arm [54].

3.2.3 Rationale for dose regimen

Ahmazadehfar et al reports safety and efficacy after application of a mean activity of 6.0 GBq ^{177}Lu -PSMA-617 in 24 patients with mCRPC [50]. Patients were treated with up to two cycles of ^{177}Lu -PSMA-617 RLT at eight week intervals. Grade 3 hematotoxicity occurred in two patients. No nephrotoxicity or hepatotoxicity grade ≥ 3 was documented. Kratochwil et al reports safety and efficacy after repeated application of ^{177}Lu -PSMA-617 in 30 mCRPC patients [49]. 19 of 30 patients (63%) received 6.0 GBq ^{177}Lu -PSMA-617 every two mo. One patient developed grade 3 anemia, one patient grade 3 thrombocytopenia. Both patients had diffuse pattern of bone marrow infiltration at baseline. The German Society of Nuclear Medicine (DGN) performed a questionnaire based survey on the use of ^{177}Lu -PSMA-617 RLT in December 2015. Nuclear Medicine Clinics in Germany reported compassionate use of ^{177}Lu -PSMA-617 RLT in 145 mCRPC patients until June 30th 2015 [52]. Majority of patients received 5.5 – 6.5 GBq (median 6.0 GBq) or >6.5 GBq (median 7.4 GBq) per cycle (Table 1) and rate of serious adverse events was below 20% for both subgroups. Phase III data for ^{177}Lu -DOTATATE, a similar RLT for midgut NET patients, demonstrates a rate of severe adverse events below 10% after application of four cycles of 7.4 GBq in 115 patients [54]. Thus, present evidence indicates that repeated applications of 6.0 or 7.4 GBq ^{177}Lu -PSMA-617 RLT are well tolerated with low to very low rates of serious adverse events.

Standard activities of 6.0 and 7.4 GBq are also supported by dosimetry data available in more

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than ten patients [56] [57]. Maximal cumulative activity is limited by the absorbed dose in critical organs. Dosimetry identifies kidney and salivary glands as organs with highest absorbed dose [56] [57]. Thus maximum cumulative activity is determined by absorbed kidney dose. Based on earlier evidence obtained from external beam radiotherapy the maximum tolerable per kidney dose is generally accepted 23 Gy [58]. Dosimetry after ^{177}Lu -PSMA-617 application revealed absorbed doses of 0.6 Gy/GBq per kidney [56] [57]. Therefore maximum cumulative activity for ^{177}Lu -PSMA-617 RLT is considered 38.3 GBq (38.3 GBq \times 0.6 Gy/GBq = 23.0 Gy radiation dose per kidney). Both the application of four cycles of 6.0 GBq (total 24.0 GBq) or 7.4 GBq (total 29.6 GBq) ^{177}Lu -PSMA-617 results in lower cumulative activities with acceptable safety margin. Whether either activity regimen is associated with longer rPFS is unknown and will be evaluated as secondary endpoint of this trial.

Salivary glands receive highest off-target radiation dose according to dosimetry [56] [57]. Absorbed dose after four cycles of 6.0 or 7.4 GBq ^{177}Lu -PSMA-617 (34.0 Gy or 41.6 Gy respectively) falls within the range of maximum tolerable dose reported for salivary glands in the literature [58] [59] [60]. Maximum tolerable dose to the bone marrow is generally accepted 2 Gy [61]. Bone marrow dose will not exceed this limit after four cycles of 6.0 or 7.4 GBq ^{177}Lu -PSMA-617 [57]

3.2.4 Determination of Sample Size

Sample size calculation was based on the primary endpoint of this protocol, i.e. baseline to 12-week decline in tumor marker level (PSA) $\geq 50\%$ [53]. Based on a recent publication [52], we estimate that the proportion of patients who meet the primary end point will range between 38% and 65% for both treatment doses. We thus define the following null hypothesis: Less than 40% of patients will reach the endpoint after ^{177}Lu -PSMA RLT. ^{177}Lu -PSMA RLT would therefore be considered worthy of further study if 50% or more patients met the end point and not worthy of further study if 40% and less achieved the end point. This rationale was adapted

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from a single-arm study on mCRPC patients with same end point definition, published 2010 in the Journal of Clinical Oncology [53]. We have performed power analysis for the two sided binomial test (beta 0.2, alpha 0.05) to measure the efficacy of ^{177}Lu -PSMA RLT. A sample size of 200 achieves 78% power (beta 0.2) at a given alpha of 0.05 to distinguish between 40% versus 50% response rates. The power analysis was performed by a trained Biostatistician from the Department of Biostatistics, University of California at Los Angeles using Power Analysis and Sample Size (PASS) 14 software (NCSS LLC).

3.3 Study Duration and Dates

The duration of subject participation will be from the time of signing informed consent through the 24 months post-injection visit or progression. Subjects will be deemed enrolled in the study once the subject signs informed consent.

3.4 Randomization protocol

Randomization will be performed in accordance with Vickers et al. [62]. In order to obtain adequate “allocation concealment” a list of random allocations was created for patients 1 through 200. This list will be stored at investigator’s sites and will not be modified. The list will only be accessible for researchers or study personnel not actively involved in the recruitment process.

3.5 Dose modification

In some circumstances, it might be necessary to suspend treatment with ^{177}Lu -PSMA-617, adapt the posology (i.e. administer a half activity), or even definitively stop administration, as described in the following tables. Table 3 lists conditions, if deemed study related by the DSMB, will result in permanent discontinuation.

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Table 3: Criteria for permanent discontinuation of treatment with ^{177}Lu -PSMA-617

Definitively stop further administrations in patients who have experienced or are at risk of any of the following conditions during treatment:
a) Severe heart failure (defined as grade III or IV of the NYHA classification)
b) Hypersensitivity to the active substance or to any of the components of this radiopharmaceutical
c) Grade 3 hematologic toxicities that persist > 12 weeks and Grade 4 that persist > 3 weeks.
d) Grade 3 renal toxicity as determined by serum creatinine measurements
e) AST/ALT > 3x ULN and bilirubin > 2x ULN
f) Grade 3-4 non-hematologic toxicities with select exceptions for <ul style="list-style-type: none">- Grade 3 fatigue < 10 days- Grade 3 nausea, vomiting, and diarrhea and grade 4 vomiting and diarrhoea that persist for < 72 hours in the absence of maximum medical therapy- Asymptomatic grade 3 non-hematological laboratory abnormalities that resolve in 72 hours- Grade 3 infections which do not improve under i.v. medication within 10 days
In case some specific adverse reactions to ^{177}Lu -PSMA-617 persist or reoccur, see Table 5

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Table 4: When to suspend treatment with ^{177}Lu -PSMA-617?

Suspend treatment with ^{177}Lu-PSMA-617 in patients who have experienced or are at risk of any of the following conditions during treatment:	
Criterion	Action
Occurrence of an intercurrent disease (e.g. urinary tract obstruction, ...) which according to the physician opinion could increase the risks linked to ^{177}Lu -PSMA-617 administration.	Suspend administration until resolution or stabilization. Treatment can be resumed after resolution or stabilization. Resolution is defined as grade II toxicity or lower. (by CTCAE) at the time of the next treatment. Treatment can be suspended up to 12 weeks after the last infusion. After that treatment with ^{177}Lu -PSMA-617 must be definitively stopped.
In case of some specific adverse reactions to ^{177}Lu -PSMA-617, see Table 5	See Table 5

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Table 5: When to adapt ^{177}Lu -PSMA-617 posology?

Adapt ^{177}Lu-PSMA-617 posology according to the following actions in patients who have presented any of the following severe adverse reactions:	
Severe adverse reactions / Dose-modifying toxicity (DMT) criteria	Action
Anemia, thrombocytopenia or neutropenia of grade 3 or superior (CTCAE 4.0)	1. Suspend treatment with ^{177}Lu -PSMA-617 2. Monitor biological parameters every 2 weeks, and eventually treat appropriately if needed; in case of renal function impairment, good hydration is recommended if not otherwise contraindicated.
Renal toxicity as defined by grade 3 toxicity by serum creatinine (CTCAE 4.0)	a. If the observed toxicity continues beyond 12weeks after the last infusion, treatment with ^{177}Lu -PSMA-617 must be definitively stopped. b. If the observed toxicity resolves within 12weeks after the last infusion, it is possible to continue treatment with ^{177}Lu -PSMA-617 by infusing a half activity.
Liver toxicity as defined as AST and ALT $>3\times\text{ULN}$	3. Even if the half activity is well tolerated (i.e. no DMT re-occurrence), the next remaining treatment administration should be continued with the reduced (half) activity but, if DMT recurs after treatment with a half dose, treatment with ^{177}Lu -PSMA-617 must be permanently stopped.
Any serious or intolerable adverse event not listed in Table 2 that in the opinion of the investigator, requires the subject's discontinuation	

4. Study Population Selection

4.1 Study Population

It is anticipated that a total of 200 subjects will be recruited. Such a number is considered appropriate to achieve statistical power for the endpoints of this clinical trial. The patients will be recruited at up to 3 clinical sites. The dose being administered will be prepared at RadioMedix Inc. in Houston and shipped to the trial sites.

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4.2 Inclusion Criteria

1. Prostate cancer proven by histopathology
2. Unresectable metastases
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated.
4. Castration resistant disease with confirmed testosterone level ≤ 50 ng/ml under prior androgen deprivation therapy (ADT)
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy or any equivalent PSMA-directed imaging
6. ECOG 0-2
7. Sufficient bone marrow capacity as defined by WBC $\geq 2500/\mu\text{l}$, PLT count $\geq 100.000/\mu\text{l}$, Hb $\geq 9.9 \text{ g/dl}$ and ANC $\geq 1500 \text{ mm}^3$ for the first cycle and WBC $\geq 2.000/\mu\text{l}$, PLT count $\geq 75.000/\mu\text{l}$, Hb $\geq 8.9 \text{ g/dl}$ and ANC $\geq 1000 \text{ mm}^3$ for the subsequent cycles
8. Signing of the Informed Consent Form
9. Patients enrolling in this trial should have received either enzalutamide or abiraterone.

4.3 Exclusion Criteria

1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm)
2. Glomerular Filtration Rate (GFR) $< 40 \text{ ml/min}$
3. Serum creatinine $> 1.5 \times \text{ULN}$; AST and ALT $> 5 \times \text{ULN}$
4. Urinary tract obstruction or marked hydronephrosis
5. Diffuse bone marrow involvement confirmed by super-scans

5. Study Treatment(s)

5.1 Description of Treatments(s)

5.1.1 Study drug

The agent to be evaluated in the present study is ^{177}Lu -PSMA-617. Its chemical name is lutetium-177-Na-2-[3-(1-Carboxy-5-{3-naphthalen-2-yl-2-[(4-{[2-(4,7,10-tris-carboxymethyl-

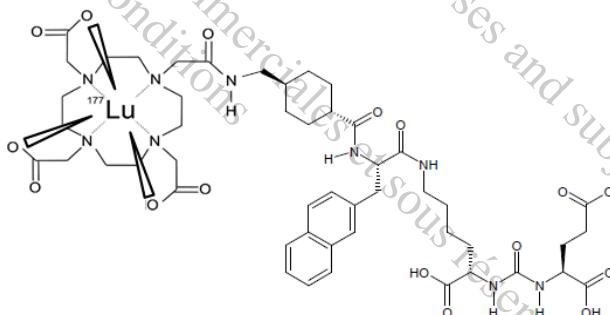
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1,4,7,10-tetraaza-cyclododec-1-yl)-acetylamino]-methyl}-cyclohexanecarbonyl)-amino]-propionylamino}-pentyl)-ureido]-pentanedioic acid.

¹⁷⁷Lu-PSMA-617 is radilabelled with carrier-free lutetium-177 (¹⁷⁷Lu), a synthetic, low-energy beta and gamma emitting isotope of lutetium, the last element in the lanthanide series of metallic elements. Carrier-free ¹⁷⁷Lu is generated by neutron irradiation of the isotope ytterbium-176 (¹⁷⁶Yb) and subsequent fractionation of ¹⁷⁷Lu and ¹⁷⁶Yb with caution chromatography. Key physical characteristics of ¹⁷⁷Lu are summarised below:

Physical Half-life T _½	Decay Product	Main Emission (β^-)	Maximum Range (β^-)	Main Emission (γ)
6.6 d	¹⁷⁷ Hf	498 keV	1.7mm	208 keV 113 keV

The structural formula of ^{177}Lu -PSMA-617 is shown below:



The chemical formula of ¹⁷⁷Lu-PSMA-617 is Lu₁C₄₉H₆₈N₉O₁₆. The molar weight is 1214.1 g/mol.

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5.1.2 Pharmaceutical Properties of ^{177}Lu -PSMA-617

^{177}Lu -PSMA-617 is administered intravenously.

A description of ^{177}Lu -PSMA-617 solution for infusion is shown in below table:

Composition of ^{177}Lu -PSMA-617 solution

Pharmaceutically active component	^{177}Lu -PSMA-617
Physical dose	$\leq 7.4 \text{ GBq / cycle}$
Substance dose	130 - 170 μg PSMA-617
Primary unit dose container	20 mL glass vial containing 5 - 15 mL of stabilised aqueous solution
Appearance	Clear, colourless or slightly yellowish solution, without visible particles
pH	4.0 - 7.5
Bacterial endotoxin	$\leq 100 \text{ EU/Dose}$
Radionuclidic purity	$\geq 99.99\%$
Sterility	Sterile

The components include ^{177}Lu -PSMA-617, sodium acetate, sodium ascorbate, gentisic acid, and water for injection. The labelled drug product is produced, tested and released under GMP conditions by RadioMedix, Inc. as a sterile solution for injection infusion, ready for use. The labelled drug product will be manufactured upon individual order and delivered directly to the study sites.

Patients will be randomized into two treatment doses; radioligand therapy (RLT) by repeated i.v. application of 6.0 GBq ($\pm 10\%$, arm 1) or 7.4 GBq ($\pm 10\%$, arm 2) ^{177}Lu -PSMA-617 every 8 \pm 1 weeks; RLT will be performed until reaching four cycles or threshold maximum dose to the kidneys of 23 Gy as determined by dosimetry, after the first treatment.

5.2. Treatment(s) administered

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Cold ice pack in the region of salivary glands will start 30 minutes prior to administration of the investigational drug and will continue for 4 hours. Intravenous access will be inserted in either arm. Assurance will be made to have reliable IV line with no evidence of extravasation or infiltration. Investigational drug will be infused over approximately 15-30 minutes using infusion pump. Patients will be monitored for any evidence of pain, or burning sensation during the infusion.

5.3 Restrictions

5.3.1 Fluid and Food Intake

Subjects should follow their normal diet before and after the administration of the study drug. Subjects should be encouraged to increase fluid intake at baseline and after each image acquisition to maintain proper hydration throughout the study period and decrease radiation exposure to the urinary bladder. There are no dietary or food restrictions for this study.

5.3.2 Subject Activity Restriction

There are no activity restrictions.

5.4 Dosing Compliance

All study drug administration will be administered under the supervision of the investigator.

Details of study drug injection will be captured in each subject's source documents.

5.5 Packaging and Labeling

¹⁷⁷Lu-PSMA-617 will be supplied in vials for injection in appropriate packaging.

The outer packaging of ¹⁷⁷Lu-PSMA-617 will contain label(s) which will include the following minimum information:

- Name and address of Manufacturer Study number
- Investigator identification
- Name of study drug and formulation
- Dosage strength

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- Batch number
- Patient number
- Expiry date (or retest date)
- Storage instructions
- “For Clinical Trial Use only”

A system of medication numbering in accordance with all requirements of Good Manufacturing Practice (GMP) and any other applicable regulatory requirement will be used for all study drugs.

This will ensure that for each patient, any dose of study drug can be identified and traced back to the original bulk ware of the active ingredients. Lists linking all numbering levels will be maintained by the institutions in charge of study drug packaging.

5.6 Storage and Accountability

5.6.1 Storage

The drug product contains radioactive material and should only be handled by personnel trained in the use of radioactive isotopes with proper shielding and monitoring. Receipt and use is limited to a facility licensed by applicable government regulations and/or local/state laws. Unused or residual waste should be disposed of as radioactive waste following the institution’s standard operating procedures (SOPs) and/or applicable regulations or guidance.

5.6.2 Accountability

In accordance with International Conference on Harmonization (ICH) and US Food and Drug Administration (FDA) requirements, the investigator and/or drug dispenser must at all times be able to account for all study drugs furnished to the institution. The appropriate site personnel must sign, date and immediately forward to the sponsor or sponsor’s designee the packing slip for clinical shipment included with each shipment.

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No study drug is to be used outside of this study. The investigator or designee will record the use of the study drug on the appropriate Drug Accountability record. All study radiopharmaceuticals must be accounted for, whether used or unused, during the course of and at the conclusion of the study. The shipment of drugs from the sponsor or designee to the investigator or other designated persons cooperating with the investigator will be accompanied by a receipt form that indicates the lot number(s) and the amount of drug provided for the study. This form will be signed, dated and returned to the sponsor or designee.

The investigator is responsible for ensuring that study drug is recorded, handled and stored safely and properly in accordance with ICH and applicable government regulations, local/state laws, and used in accordance with this protocol.

5.7 Investigational Product Retention at Study Site

Unused product will be disposed of according to institutional regulations. Record the use and/or disposal of the study drug on the Drug Accountability record. This Drug Accountability record should account for the receipt and disposition of all clinical supplies shipped to the investigator and must be available for review by the study monitor.

6. Study Procedures

6.1 Informed Consent

All subjects must sign and personally date an IRB/IEC approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug prior to the initiation of any study-related procedures. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for Good Clinical Practice (GCP) and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27.

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The subject must be made aware and agree that personal information may be reviewed during an audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. A copy of the Informed Consent Form is attached as Exhibit.

6.2 Medical History

A relevant medical history and subject demographics will be obtained at the screening visit. Cancer medical history includes review of disease history, cancer staging, biopsy results, any past/present cancer therapies (e.g., hormone, drug, biologic, radiologic, or surgical treatment). Demographic information to be collected includes date of birth, race, ethnicity, height, and weight.

6.3 Vital Signs

Vital signs will include measurement of blood pressure, temperature, respiratory rate, pulse Oximetry (only at baseline) and heart rate.

6.4 Dispensing Study Drug

The estimated radioactive dose will be determined by measuring the amount of radioactivity in the syringe pre- and post-injection, using an appropriately calibrated radioisotope dose calibrator in accordance with the nuclear medicine department's SOPs.

Any complication related to administration of the drug (e.g., overdose, observable extravasation, medication error) is a protocol-related event and will be reported to the pharmacovigilance designee. Refer to Section 7 for contact information.

6.5 Clinical Laboratory Tests

Clinical laboratory tests will include hematology and clinical chemistry. Clinical laboratory analytes to be assessed in the study are shown in Table 6. Timing of collection of clinical

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laboratory tests are presented in Section 8.

Table 6: Laboratory Analytes Assessed

Hematology	Clinical Chemistry
Hematocrit	eGFR
Hemoglobin	Bilirubin
RBC count	Creatinine
WBC count	Glucose
WBC differential	Urea nitrogen
Platelets	BUN/creatinine
ANC	AST/SGOT
MCV/MCH/MCHC	ALT/SGPT
Eosinophils	Alkaline phosphatase
Basophils	PSA*
Lymphocytes	
RDW	

*PSA will be done only at the time intervals called by the protocol.

6.6 Sample Collection, Storage and Shipping

Blood samples will be collected using accepted phlebotomy techniques by trained site personnel.

All samples for clinical laboratory testing will be processed and analyzed at an accredited laboratory

6.7 Electrocardiogram

Continuous ECG monitoring at least 15 minutes prior to administration of the study drug and up to at least 1 hour after administration will be performed during treatment cycle 1 and 2. Also a 12 lead ECG will be performed at two time points: before injection of Lu-177 PSMA-617 for all treatment cycles and after the salivary protection is completed.

6.8 Adverse Events

Immediate adverse drug reactions will be collected from the time of ¹⁷⁷Lu-PSMA-617 injection

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until 24 hours post-injection visit. Data will be collected for any adverse events (AEs) as defined in Section 7.

All study monitoring will be performed at the primary clinical study sites in accordance with Good Clinical Practice (GCP). All records related to this study will be retained at each clinical site. Serious adverse reactions will be collected and reported to FDA and IRB according to 21 CFR 312.32. Annual reports on the progress of the investigation and any adverse events related to the investigational drug will be prepared and reported to FDA according to 21 CFR 312.33.

6.9 Removal of Subjects from the Trial or Study Drug

The investigator may withdraw a subject from the trial for any of the following reasons:

1. Protocol violation,
2. Serious or intolerable adverse event (that in the opinion of the investigator, requires the subject's discontinuation),
3. Investigator withdraws the subject (at the investigator's discretion for reasons other than an adverse event),
4. Sponsor terminates the study,
5. Subject requests to be discontinued from the study, or
6. Subject is lost to follow-up

During course of the study patients have the right to withdraw their consents any time without need for explaining the reason of consent withdrawal to the investigator or sponsor. Principal investigator will closely monitor patients during the course of the study and will consider terminating investigational product administration or any other trial related procedures in order to maintain the safety of subjects. In cases of withdrawal either in patient's favor or principal investigator decision due to the safety issues or technical issues, withdrawn subjects will be replaced in order to maintain data integrity but follow up visits will be continued to maintain safety of patients based on the visits predicted in the protocol.

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7. Reporting Safety Information

Any untoward medical event that occurs from the time that the subject is administered¹⁷⁷ Lu-PSMA-617 until the subject completes the study will be reported. Serious adverse events and non-serious adverse events will be collected and reported as required under 21 CFR 312.32 until the final study visit. Toxicity will be evaluated according to Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.

7.1 Adverse Events

7.1.1 Definitions

An **adverse event (AE)** is any untoward medical occurrence in a study subject that is administered a pharmaceutical product, at any dose, which does not necessarily have a causal relationship with the treatment.

An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a study drug, whether or not considered related to the study drug.

A **serious adverse event (SAE)** is any untoward medical occurrence that falls into one or more of the following categories:

1. Results in death
2. Is life-threatening: An event which, in the view of the investigator, places the subject at immediate risk of death from the event as it occurred and does not include an event which hypothetically might have caused death if it were more severe.
3. Requires subject hospitalization or prolongation of existing hospitalization: For the seriousness criterion of subject hospitalization to apply, an overnight stay in the hospital is required. Admission to an emergency room and release without an overnight stay would not satisfy the subject hospitalization seriousness criterion.
4. Results in persistent or significant disability/incapacity: Persistent or significant

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disability/incapacity is defined as a substantial disruption of a person's ability to conduct normal life functions, either reported or defined as per clinical judgment.

5. A congenital anomaly/birth defect: A congenital anomaly/birth defect is defined as a condition believed to have been the result of exposure to study drug just before conception or during pregnancy.
6. Any other important medical event: An important medical event may not result in death, be life-threatening, or require hospitalization, but based upon appropriate medical judgment, the event may significantly jeopardize the subject's health or may require medical or surgical intervention to prevent one of the outcomes listed in the serious definitions above. An important medical event may include development of drug dependency or drug abuse.

All adverse events that do not meet any of the criteria for serious should be regarded as ***non-serious adverse events***.

7.1.2 Reporting Serious Adverse Events

Seriousness is based on subject, event outcome, or action criteria that are usually associated with events that pose a threat to a subject's life or functioning. Seriousness (not severity) serves as the guide for defining the sponsor's regulatory reporting obligations to the applicable regulatory authorities. Adverse event severity and seriousness should be assessed independently by investigators. If the investigator is unsure if the event is serious it should be classified as serious.

Sponsors of the study, and the investigators are responsible for reporting relevant SAEs as safety reports to the FDA and other applicable regulatory authorities, and participating investigators, in accordance with ICH guidelines, the US Code of Federal Regulations Title 21 CFR 312.32 for Good Clinical Practice, and/or local regulatory requirements. The investigators must report all SAEs to project pharmacovigilance designee within 24 hours, by telephone,

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email or fax, and confirm that the information was received.

A Serious Adverse Event Report (SAER) must be completed by the investigator or designee and faxed or emailed to project pharmacovigilance designee within 24 hours after the investigator first becomes aware of the serious event. A separate SAER will be needed for each reported SAE so that the onset, resolution date, causality and outcome can be assessed for each event. A copy of the source documents relevant to the event should be forwarded to sponsor's pharmacovigilance designee with the SAER form. The SAER form must be signed and dated by the investigator. If paper SAE forms are used, the original copy of the SAER form should remain at the investigational site. All SAEs are also to be entered into the CRF.

In case of death, a comprehensive narrative report of the case should be prepared by the investigator and sent to project pharmacovigilance designee with the SAER. If an autopsy is performed, a copy of the autopsy report should be actively sought by the investigator and sent to the sponsor or designee as soon as available. A copy of the autopsy report should remain at the investigational site with the subject's source documents.

A new follow-up SAER form will be completed by the investigator if important follow-up information (i.e., diagnosis, outcome, causality assessment, results of specific investigations) are made available after submission of the initial form. The follow-up SAER must be signed and dated by the investigator. The follow-up form and any additional source documentation regarding the event will be sent to project pharmacovigilance designee.

If a serious medical occurrence or death is reported to the investigator outside the follow up window which is believed to be related to the administration of the study drug, it is the investigator's responsibility to report this occurrence to project pharmacovigilance designee.

Such occurrences will be reported using a SAER form or other form of communication deemed appropriate by the investigator and pharmacovigilance designee.

Sites must contact project pharmacovigilance designee to report all SAEs within 24 hours, by telephone, e-mail, or fax. Contact information for SAE reporting is presented in Table 7.

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Table 7: Pharmacovigilance Designee

PrimeVigilance
The Surrey Research Park
26-28 Frederick Sanger Road
Guildford, Surrey GU2 7YD
PHONE: +44(0) 1483.566.462
FAX: 1.800.886.0743
Email: endocyte@primevigilance.com

Sites must also report all overdoses, extravasations and medication errors to the project pharmacovigilance designee.

7.2 Adverse Event Data Collection

The investigator will elicit information through non-leading questioning and examination of the subject about the occurrence of adverse events from the time that the subject is administered ¹⁷⁷Lu-PSMA-617 until study completion.

AE monitoring will be performed through following mechanisms, also listed in Appendix II:

- a. Safety lab tests: CBC and CMP with eGFR will be performed at baseline (within 72 hours of first treatment dose) and then every 2 weeks (+/- 3 days) after first dose, continued until 12 weeks after the last dose and then every 3 months (+/- 1 week) thereafter until the end of follow-up visits (24 months from 1st therapy date) or upon disease progression. The CBC and CMP within 2 weeks of each subsequent treatment cycle will be used to assess eligibility of the corresponding treatment cycle.
- b. Telephone follow up: 7 (± 3) days after each treatment cycle and for follow-up phase, every 3 (± 1) month until the end of follow up visits (24 months).

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AEs can be reported any time after study enrollment until the end of the subject's study participation. For each event, the following information will be recorded in the subject's source documents and entered into the Adverse Event CRF according to the instructions below:

Classification of the Event as serious or non-serious: Classify the event as serious or non-serious (see definitions in Section 7).

Description of Signs or Symptoms: Whenever possible, record a specific diagnosis for the event. If a diagnosis cannot be made, then record each sign or symptom representing a distinct medical concept separately, (e.g. nausea and vomiting should be recorded as separate events).

Onset Date and Time: Record the date and time the event starts. If a laboratory result is reported as an AE, record the start date as the date of collection of the first lab sample that shows the change.

Stop Date and Time: Record the date and time the event resolves, returns to baseline, or resolves with sequelae.

Grade: Refer to the common terminology criteria for adverse events (CTCAE) Version 4.

Relationship to the Study Drug:

We make every effort to evaluate the relationship between the study drug and the AE as determined by the investigator per the definitions below:

1. Related: The event is reasonably suspected of a causal relationship to the study drug. Suspected adverse reaction means any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of IND safety reporting, 'reasonable possibility' means there is evidence to

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suggest a causal relationship between the drug and the adverse event. A suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by a drug.

ASSESSING RELATIONSHIP TO STUDY TREATMENT

Items to be considered when assessing the relationship of an AE to the study treatment are:

- Temporal relationship of the onset of the event to the initiation of the study treatment;
- The course of the event, considering especially the effect of discontinuation of study treatment or reintroduction of study treatment, as applicable;
- Whether the event is known to be associated with the study treatment or with other similar treatments;
- The presence of risk factors in the study subject known to increase the occurrence of the event;
- The presence of non-study treatment-related factors which are known to be associated with the occurrence of the event.

2. Not Related: The event is definitely due to causes separate from study drug administration such as:

- documented pre-existing condition
- technical and manual procedural problem
- concomitant medication
- subject's clinical state

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3. Adverse Event Outcome:

- Recovered/Resolved without sequelae
- Recovered/Resolved with sequelae
- Not Recovered/Not Resolved: event is ongoing at the end of the AE collection period.
- Death (Fatal): the event description must be the primary cause of death.

7.3 Clinical Significance

7.3.1 Reporting and Evaluation of Clinical Laboratory Test Results

The investigator should assess all clinical laboratory results for clinical significance and record the assessment in source documents.

The investigator should evaluate any laboratory result change from pre- and post-study drug administration to determine if the change meets the definition of an AE or SAE. **Record any clinically significant lab results determined to meet the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

7.3.2 Repeat Testing

Additional laboratory testing may be performed at the discretion of the investigator.

7.3.3 Vital Signs

The investigator should evaluate any vital sign changes pre- and post-study drug administration to determine if the change meets the definition of AE or SAE. Vital sign measurements may be repeated at the discretion of the investigator. **Record any clinically significant vital sign measurement that meets the definition of an AE and SAE on the AE CRF and SAER form, respectively.**

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8. Study Activities

Visit-specific schedule for efficacy and safety variables is presented in Appendix II.

8.1 Screening Visit

- Written informed consent
- Demographic information
- Relevant medical history
- Prior therapy for Prostate cancer
- Medication assessment
- Histology
- Vital signs
- Questionnaires
- Morphological and PSMA-ligand imaging studies if no comparable available within 12 weeks of treatment.

8.2 Within 2 Weeks of Screening

- Clinical laboratory testing (see Section 6)

8.3.1 Pre-dose and Dosing Procedures

- Pre-dose vital signs – within 20 minutes before dose
- Blood tests (CBC, CMP and PSA) within 72 hours of first treatment cycle
- Apply Ice pack to the salivary glands approximately 30 minutes prior to investigational drug injection and continue for 4 hours.
- Adequate hydration of the patient (IV or oral).
- Inject study drug ¹⁷⁷Lu-PSMA-617
- Post-dose vital signs
- Adverse events

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8.3.2 Post-Dose Procedures

Adverse events during the entire stay.

One post-therapy whole body scintigraphy will be performed (optional).

8.3.3 ECG Procedures

Continuous ECG monitoring at least 15 minutes prior to administration of the study drug and up to at least 1 hour after administration will be performed during treatment cycle 1 and 2. Also a 12 lead ECG will be performed at two time points: before injection of Lu-177 PSMA-617 for all treatment cycles and after the salivary protection is completed.

8.4 Follow-up

8.4.1 PSA Measurements

At baseline, then every 6 weeks during the treatment period and every 3 (± 1) months after the last treatment until reaching endpoint or 24 month after the first treatment.

8.4.2 Imaging Studies

Baseline imaging within 12 weeks of start of therapy including (a) CT of the chest Preferably with contrast and CT or MRI of the Abdomen and pelvis preferably with contrast and (b) bone scintigraphy or (c) equivalent to above >1].

Relevant imaging studies will be performed before third RLT cycle, 3 (± 1) months after the last RLT, then every 3 (± 1) months in follow-up period until reaching the endpoint or 24 month after the first treatment.

At each subsequent RLT cycle visit and with every long term follow-up visit, any concomitant cancer-related therapy since last visit will be documented.

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8.4.3 Dosimetry

Prior versions of the protocol mandated dosimetry studies aimed at assessing kidney dosimetry associated with the intravenous application of ¹⁷⁷Lu-PSMA-617.

Dosimetry data of 20 patients (16 from UCLA and 4 from Excel Houston) was analyzed and it was found that the renal dose limit of 23 Gy was not exceeded in any patient after 4 cycles and no additional on study dosimetry is required.

Below are the individual dosimetry measurements for each patient performed during cycle #1.

Table 8: Individual Dosimetry Measurements for Patients Performed During Cycle 1.

PC #	Activity (GBq)	Dosimetry Right Kidney (Gy/GBq)	Dosimetry Right Kidney (Gy)	Dosimetry Left Kidney (Gy/GBq)	Dosimetry Left Kidney (Gy)
ORLO-563	7.84	pending	pending	pending	pending
GZJC-639	5.07	0.36	1.80	0.34	1.70
ZDUK-630	7.23	0.48	3.40	0.53	3.80
ZAYH-600	5.88	0.72	4.30	0.56	3.30
YLSV-927	5.92	0.45	2.7	0.45	2.7
HIQI-599	6.03	0.27	1.63	0.35	2.12
JMVM-985	7.31	0.29	2.15	0.28	2.02
YQEH-947	7.03	0.37	2.59	0.43	2.99
DBZO-666	6.77	0.33	2.25	0.27	1.85
UIIT-921	5.68	0.39	2.22	0.35	1.98
BHIG-534	7.68	0.27	2.07	0.27	2.07
RBST-884	7.46	0.47	3.52	0.49	3.66
HGPY-826	7.84	0.54	4.22	0.51	4.00
NXLR-884	6.30	0.50	3.15	0.55	3.48
BPVT-824	NO	NO	NO	NO	NO
LHUB-942	NO	NO	NO	NO	NO
ERZA-557	7.43	pending	pending	pending	pending
GIQU-474	6.38	pending	pending	0.84	5.41
ZTHD-641	6.23	0.81	5.07	0.9	5.61
ISXP-277	7.53	pending	pending	pending	pending
LEVS-705	8.07	0.36	2.89	0.38	3.06
KGSHIFY-728	NA	pending	pending	pending	pending
SNCHCSQ-850	NA	NA	NA	NA	NA
CZOMFLX-564	NA	NA	NA	NA	NA
VTKMMEF-764	NA	NA	NA	NA	NA
CRXTBQA-596	NA	NA	NA	NA	NA
TLEWETA-426	NA	NA	NA	NA	NA
LYPBMVV-788	7.01	0.4	2.81	0.45	3.16
MKSIJCZ-721	NA	NA	NA	NA	NA
VWFOMP-822	NA	pending	pending	pending	pending

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XESEGHX-817	5.73	0.25	1.43	0.24	1 37
IIJQJWB-731	6.86	0.23	1.61	0.22	1 51
XOKQGXF-818	7.07	0.22	1.57	0.21	1 5
WRHXZUP-531	NO	NO	NO	NO	NO

After an average injected activity of 6.75 ± 0.81 GBq (range 5.1-8.1) the mean absorbed kidney dose was 0.42 ± 0.17 Gy/GBq (range 0.21-0.9) corresponding to a cumulated absorbed dose of 2.79 ± 1.12 Gy (range 1.37-5.61).

These results are consistent with prior studies as shown in the following table.

Table 9: Prior Completed Study Dosimetry Measurements

Author	Journal	year	n=	Activity GBq	Activity range	mean kidney dose Gy/GBq
Scarpa et al.	Eur J Nucl Med Mol Imaging	2017	10	6.1	5.4-6.5	0.60 ± 0.36
Yadav et al.	Nucl Med Comp	2017	26	2.52	1.1-5.5	0.99 ± 0.31
Kabasakal et al.	Mol Imaging Radionucl Ther	2017	7	5.2	3.6-7.4	0.82 ± 0.25
Fendler et al.	Oncotarget	2017	15	5.23	3.7-6.0	0.6 ± 0.3
Baum et al.	J Nucl Med	2016	30	5.76	3.6-8.7	0.8 ± 0.4
Delker et al.	Eur J Nucl Med Mol Imaging	2016	5	3.6	3.4-3.9	0.6 ± 0.2

Furthermore the absorbed kidney dose limit of 23 Gy is an assumption derived from external beam radiation therapy (63) which probably does not predict renal toxicity from radionuclides. Correction of these data for radionuclide therapy suggested a renal absorbed biologic effective dose (BED) limit of 37 Gy (64).

8.4.4 Follow-up Labs for Hematological and Kidney Toxicities

All enrolled patients will follow the scheduled follow up visits.

Hematologic laboratory testing (CBC and CMP with eGFR) will be performed every 2 weeks (+/- 3 days) after first dose, continued until 12 weeks after the last dose and then every 3 months (+/- 1 month) thereafter until the end of follow-up visits (24 months from 1st therapy date) or upon disease progression. The CBC and CMP within 2 weeks of each subsequent treatment cycle will be used to assess eligibility of the corresponding treatment cycle. CBC will be performed every 7

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days for patients who experienced toxicity more than grade II due to this study (based on NCI CTCAE Ver.4) until recovery which is defined as grade 2 toxicity or lower.

In order to detect myelodysplasia, patients who withdrawn by the investigator for safety reasons will only perform CBC test until the end of their follow up visits as long as they do not start other cytotoxic therapies.

Patients on protocol should also have a physical exam and in-person physician evaluation periodically while on study and until recovery from last dose. During dosing period and longterm follow up period local physical exam will be done as per clinical routine.

8.4.5 Telephone Follow ups

7 (\pm 3) days after each treatment cycles until completion of 4 cycles and for follow up phase , every 3 months (+/- 1 month) until the end of follow up visits (24 months).

8.4.6 Longterm Follow ups

At each follow-up visit (every 3 (\pm 1) months) following tasks will be performed:

1. Physical exam, vital signs
2. Documentation of concomitant cancer related therapies since last visit
3. Laboratory tests (CBC, CMP with eGFR and PSA)
4. Relevant imaging studies
5. Quality of life questionnaire and ECOG performance score (baseline, 3, 6, 9, 12, 18, 24 months from first RLT cycle)

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9. Quality Control and Assurance

The study sites are chosen with regard to the capability and expertise of the principal investigators and the site staff. Prior to initiation of the study, the investigator and the sponsor's representative will meet to discuss the study design and conduct of the study. The investigator will sign the protocol acknowledging that he understands the design and all procedures and intends to conduct the study and all procedures according to protocol.

During the study, a representative of the sponsors will make periodic visits to the investigational site while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government regulations and guidelines. The investigator will permit authorized representatives and the respective local and national health authorities to inspect facilities and records relevant to this study, if needed.

Subject data will be collected on source documents and entered in the CRF. Data will be reviewed and validated. The investigator will sign and date a declaration on the CRF attesting to his/her responsibility for the quality of all data recorded and that the data represents a complete and accurate record of each subject in the study.

Records of subjects, source documents, monitoring visit logs, inventory of study product, regulatory documents (e.g., protocol and amendments, IRB/IEC correspondence and approvals, approved and signed informed consent forms, Investigator's Agreement, clinical supplies receipts, and distribution and return records), and other sponsor correspondence pertaining to the study will be kept in the appropriate study files at the site. Source documents include all recordings and observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical study. At the end of the study, CRF data will be provided to the sponsor.

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10. Planned statistical methods

10.1 Primary endpoints

1. **Safety** of ^{177}Lu -PSMA-617 RLT will be assessed by analysis of toxicity. Descriptive statistics (number and percentage) will be reported separately for AE in total and SAE based on CTC. These descriptive statistics will be presented for the whole treatment as well as separate for each cycle. In addition, the relationship of AE to the study drug (related, not related) will be reported. Both results from laboratory test, physical examinations and patients surveys will be included.
2. **Efficacy** of ^{177}Lu -PSMA-617 will be reported using descriptive statistics by means of number and percentage of patients with $\geq 50\%$ decline at 12-weeks from baseline.

10.2. Secondary endpoints

1. Descriptive analyses (median, standard deviation) will be used to determine the **progression-free survival (PFS)**, measured from start of therapy until death or PSA progression. PSA progression is defined a) for patients with PSA decline after start of treatment as time from baseline to time the PSA increases to 25% and 2 ng/ml above nadir which is confirmed by a second value ≥ 3 weeks later or b) for patients without PSA decline as time from baseline to time the PSA increases to 25% and 2 ng/ml above baseline which is confirmed by a second value ≥ 3 weeks later [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq ^{177}Lu -PSMA-617) and a statistical significant difference will be tested.
2. Each clinical site will perform image analysis on their own patients. Descriptive analyses (median, standard deviation) will be used to determine the **radiographic**

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progression-free survival (rPFS), measured from start of therapy until death or radiographic progression. Radiographic progression is defined as a) for extraskeletal disease progressive disease (PD) following Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 [65] and/or b) skeletal disease the development of ≥ 2 new lesions on first post-treatment bone scan, with at least two additional lesions on the next scan (2+2 rule). The date of progression is the date of the first post-treatment scan, when the first two new lesions were documented. This approach is applied in accordance to PCWG criteria to exclude pseudoprogression in the absence of symptoms or other signs of progression [1]. Data will be given separately for the both treatment groups (6.0 vs. 7.4 GBq ^{177}Lu -PSMA-617) and a statistical significant difference will be tested.

3. Descriptive analysis will be used to determine the **disease control rate (DCR)** at the end of each cycle defined as the number and percentage of patients achieving a) RECIST stable disease (SD), partial response (PR) or complete response (CR) for extraskeletal tumor manifestation and b) PCWG non-progressive disease for skeletal manifestations.
4. Descriptive analysis will be used to evaluate the impact on **bone pain level** by determining the proportion of patients with pain response defined by improvement from baseline (all patients with $\geq 4/10$) of at least 2-point absolute improvement without an overall increase in opiate use.
5. Change in **Quality of Life** over time will be documented by comparing the summary scores investigated by the Quality of life questionnaire "EPIC-26" at baseline and at 3, 6, 9, 12, 18 and 24 months after start of ^{177}Lu -PSMA-617 RLT [66].
6. Changes in **performance status (ECOG)** from baseline will be evaluated over time at 3, 6, 9, 12, 18 and 24 months after start of ^{177}Lu -PSMA-617 RLT.

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11. Administrative Considerations

11.1 Investigators and Study Administrative Structure

This study will be conducted in accordance with the Declaration of Helsinki, ICH E6 Guideline and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 312.50 through 312.70, directive 2001/20/EC of 4 April 2001 and implementing directives and regulations. To ensure compliance the investigator agrees, by written consent to this protocol, to fully cooperate with compliance checks by allowing access to all documentation by authorized individuals. The investigator must conduct the trial as outlined in the protocol and in accordance with the Declaration of Helsinki and government regulations, including (as applicable) the US Code of Federal Regulations Title 21 CFR 56 – Institutional Review Boards. The administrative structure of the study (e.g., monitoring and vendor personnel, statistician, and laboratory facilities) and a complete and controlled list of the investigators participating in this study can be found in the study file maintained by the sponsor or its agent.

11.2 Institutional Review Board (IRB) or Independent Ethics Committee (IEC) Approval

The protocol, informed consent form, and any advertisement for the recruitment of subjects must be reviewed and approved by an appropriately constituted IRB or IEC, as required in Chapter 3 of the ICH E6 Guideline and government regulations, including (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 56.107 through 56.115 of Good Clinical Practice. Written IRB approval must be provided to sponsor or designee prior to shipment of study drug or subject enrollment. The investigator is committed in accordance with local requirements to provide the IRB with updates, and to inform the IRB of any emergent problem, SAEs, and/or protocol amendments.

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11.3 Ethical Conduct of the Study

It is mandatory that all considerations regarding the protection of human subjects be carried out in accordance with the Declaration of Helsinki.

11.4 Subject Information and Consent

It is the responsibility of the investigator to obtain written informed consent from subjects. All subjects must sign and personally date an approved informed consent form after receiving detailed written and verbal information about the reason, the nature and the possible risks associated with the administration of the study drug. This must be done according to the guidelines provided in the Declaration of Helsinki, ICH E6 Guideline for GCP, and the requirements of (as applicable in the region) the US Code of Federal Regulations Title 21 CFR 50.20 through 50.27 of Good Clinical Practice.

The subject must be made aware and agree that personal information may be scrutinized during audit by competent authorities and properly authorized persons. However, personal information will be treated as strictly confidential and will not be publicly available. Prior to IRB/IEC submission, the investigator must send a copy of the informed consent form to be used at their institution to sponsor or designee for review to assure compliance with the ICH E6 and government regulations of the region.

11.5 Subject Confidentiality

Data collected during this study may be used to support the development, registration or marketing of ¹⁷⁷Lu-PSMA-617. All data collected during the study will be controlled by sponsor or designee and sponsor will abide by all relevant data protection laws. In order to maintain subject privacy, all CRFs, study drug accountability records, study reports and communications will identify the subject by initials and the assigned subject number. The investigator will grant monitor(s) and auditor(s) from sponsor or its designee and regulatory

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authority (ies) access to the subject's original medical records for verification of data entered into the CRF and to audit the data collection process. The subject's confidentiality will be maintained and will not be made publicly available to the extent permitted by the applicable laws and regulations.

Written authorization is to be obtained from each subject prior to enrollment into the study in accordance with the applicable privacy requirements >e.g., the Health Insurance Portability and Accountability Act (HIPAA) of 1996 Standards for Privacy of Individually Identifiable Health Information.

11.6 Study Monitoring

11.6.1 Data and Safety Monitoring Plan (DSMP)

Excel Diagnostics is the lead site; the Excel Diagnostics Data Safety Monitoring Board (DSMB) will serve as overall DSMB for both sites. At UCLA, DSMB oversight will be provided by JCCC Data Safety Monitoring Board (DSMB). The monitoring board will meet quarterly to review safety records including compliance with follow up visits.

The Excel Diagnostics DSMB consists of:

- [Name], MD [Contact], Green Imaging
- [Name], MD [Contact], Green Imaging
- [Name], MD [Contact], Westchase Oncology Institute
- [Name], MD [Contact], Westchase Clinical Associates

The Data Safety Monitoring Boards will evaluate safety throughout the study. The DSMB will advise the Sponsor, Investigators and investigational sites regarding the continuing safety of study patients and the patients yet to be recruited to the study as well as maintaining validity and scientific merit of the study. The DSMB will review ongoing examinations of safety data and promptly give recommendations to continue, continue with modification, or terminate the study. Each DSMB will evaluate and advise locally throughout the trial at the pre-specified milestones

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of 25%, 50%, 75% and 100% completion. UCLA JCCC DSMB will send their reports to the lead site DSMB for overall analysis.

Copies of all monitoring and audit reports must be submitted by Endocyte to the lead site DSMB within 10 working days of receipt by Endocyte.

Endocyte will be responsible for ensuring that all reportable adverse events are submitted to the appropriate regulatory body.(FDA, NIH, etc.).Adverse events will be recorded and reported to the FDA as well as applicable IRBs and the JCCC DSMB per the regulatory body and institutional committee requirements (refer to JCCC DSMB) website.

Specific interim safety analyses will be done as follows:

Interim safety analyses: 4 interim safety analyses will be conducted by both DSMBs Analyses will be initiated at the time when 25%, 50%, 75% and 100% of the total ¹⁷⁷Lu-PSMA-617 treatments in the trial have been completed. The DSMBs will meet and assess up-to-date safety information within two weeks of a treatment exposure rate being achieved (i.e., the point when 25%, 50%, 75% and 100% of subjects have completed their treatments). Further patients may only be randomized two weeks after the treatment exposure rate has been reached and after a positive opinion from the DSMBs. An interim analysis for overall survival will be performed at the time of the final PFS analysis. UCLA JCCC DSMB will send its summary reports based on a predetermined frequency to the lead site DSMB for overall safety analysis as the Excel Diagnostics DSMB will be serving as the overall DSMB for both sites.

11.6.2 Monitoring Procedures

An appropriate representative of the sponsors (Study Monitor) will oversee the progress of the study, and ensuring it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and applicable regulatory requirements.

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An initiation visit will be made by the study monitor at each site to discuss the protocol and the obligations of both the Sponsor and the investigator. The investigator must allow the study monitor to perform periodic, interim monitoring visits. The actual frequency of monitoring visits will be dependent on the enrollment rate and performance at each site. The purposes of these visits are to verify that written informed consent was obtained prior to each subject's participation in the trial, and to:

- assess the progress of the study
- review the compliance with the study protocol
- determine whether all AEs and SAEs were appropriately reported
- determine whether the investigator is maintaining the essential documents
- discuss any emergent problem
- check the CRF for accuracy and completeness
- validate the contents of the CRF against source
- assess the status of drug storage, dispensing and retrieval
- retrieve study data

All data required by the protocol must be reported accurately on the CRF and must be consistent with the source documents. Source documents are original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays or other diagnostic images, subject files, pharmacy records and laboratory records). The investigator will make available the source documents for inspection. This information will be considered as confidential.

During scheduled monitoring visits, the investigator and the investigational site staff should be available to meet with the study monitor in order to discuss the progress of the study, make necessary corrections to CRF entries, respond to data clarification requests and respond to any

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other study-related inquiries of the monitor. The investigational site staff in addition to the study coordinator should also include nuclear medicine staff, radiopharmacist, and radiology staff.

The study monitor will perform a closeout visit at the conclusion of the investigator's involvement in the study.

11.6.3 Auditing

The investigator will make all pertinent records available including source documentation for inspection by regulatory authorities and for auditing by the sponsor. This information will be considered as confidential. Clinical Research Compliance Officers from the UCLA JCCC Office of Regulatory Compliance will be conducting the auditing for the UCLA site.

Representatives of local or foreign health authorities may review the conduct or results of the study at the investigational site. The investigator must promptly inform the sponsor of any audit requests by health authorities, and will provide sponsor with the results of any such audits and with copies of any regulatory documents related to such audits.

11.7 Case Report Forms and Study Records

Sponsor will provide a CRF and CRF instructions for the entry of study data. CRFs must be completed for each subject. All study data will be entered on CRFs from original source data. Entries should be made on the case report forms directly and promptly onscreen. The CRF will be reviewed, signed and dated by the investigator.

11.8 Protocol Violations/Deviations

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Protocol violations/deviations will be documented by investigator and submitted to the IRB/IEC, as required by IRB/IEC requirements.

11.9 Access to Source Documentation

During the study, a representative of the sponsor will make periodic visits to the investigational sites while the study is in progress to check the accuracy and completeness of the data being entered. Site visits will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ICH guidelines, GCPs, and the respective local and national government regulations and guidelines.

The investigator will permit authorized representatives of the sponsor and the respective local And national health authorities to inspect facilities and records relevant to this study, if needed.

11.10 Data Generation and Analysis

Sponsor(s) or its designee will be responsible for data collection, data management, generation of data outputs and statistical analysis of all data.

11.11 Retention of Data

As described in the ICH GCP Guidelines, 'essential documents', including copies of the protocol, subject identification codes, CRF, source data, informed consent form(s) and other documents pertaining to the study conduction must be kept for the maximum period of time as required by the study site. This time period must be at least two years after the last follow up of the patients enrolled.

No study document should be destroyed without prior written agreement between sponsors and the investigators. Originals of all documentation generated by sponsor and copies of

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outgoing sponsor correspondence concerning the study will be stored and retained in a safe area under the control of sponsor for the lifetime of the product. In particular, the final report must be retained by sponsor, or the subsequent owner, for 5 years beyond the lifetime of the study drug.

11.12 Financial Disclosure

All investigators must provide financial disclosure information in accordance with the US Code of Federal Regulations Title 21 CFR 54.2 through 54.6.

11.13 Publication and Disclosure Policy

All unpublished documentation (including the protocol, CRF and Investigator Brochure (IB) given to the investigator is strictly confidential. All recipients must agree not to disclose the information herein contained to any person without the prior written authorization of sponsor. The submission of these documents to the IRB is expressly permitted. The investigator agrees that sponsor maintains the right to use the results of this study in their original form and/or in a global report for submission to governmental and regulatory authorities of any country.

The results of the study may be presented during scientific symposia or published in a scientific journal only after review by sponsor in accordance with the guidelines set forth in the applicable publication or financial agreement.

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Appendices

Appendix 1- Preclinical Toxicity studies

This exhibit is 303 pages. Therefore we are providing it in the attached CD.

Appendix II: Visit Specific Schedule

7	Screening		Therapy												FIU												30						
	Month	Week	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23								
	Therapy		1		2		3		4																								
1 Signing informed consent form																																	
2 Randomization																																	
3 Evaluation of blood tests (CBC, CMP with eGFR)																																	
4 PSA determination																																	
5 Medication & Hypersensitivity assessment																																	
6 Current Disease (somatic or psychiatric)																																	
7 Histopathology evaluation																																	
8 Relevant medical history & demographics																																	
9 Physical exam																																	
10 Concomitant cancer-related therapies since last visit																																	
11 Vital Signs (BP, HR, T, RR)																																	
12 Evaluation of life expectancy																																	
13 Prior therapy for Prostate cancer																																	
14 Continuous ECG monitoring																																	
15 12 lead static ECG																																	
16 Quality of life assessment (EPIC-26) & ECOG																																	
17 Whole body (Anterior And Posterior) scan																																	
18 Follow up calls for AE Monitoring		-7 days																															
days	-40	-7	-6	-14	-28	-42	-56	-70	-84	-98	-112	-126	-140	-154	-168	-188	-228	-258	-288	-318	-348	-378	-408	-438	-468	-498	-528	-558	-588	-618	-648	-678	-708

1 Only at first or second treatment, several blood and urine samples will be required for dosimetry purposes. Blood: before injection, 5 (\pm) min, 30 (\pm) min, 60 (\pm) min, 18-30, 42-54, and 66-78 hours post injection. 7 to 9 days sample is optional. Urine collection will include 0-4 hrs and 4 hrs until discharge.

1 Laboratory tests will be acceptable only if performed within two weeks of each scheduled visit. Screening visit and week -2 can be combined if screening visit performed within 2 weeks of the first cycle.

1 CBC/CMP with eGFR will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 (\pm) months during follow-up for 24 months or until disease progression as per clinical routine.

2 PSA will be measured every 8 weeks during the treatment and every 3 (\pm) months after the last treatment until reaching endpoint or 24 months after the first treatment.

3 Baseline imaging within 12 weeks of start of therapy including (a) Chest CT preferably with contrast & MRI of the Abdomen- pelvis preferably with contrast, (b) bone imaging, (c) or equivalent as per clinical routine

3 Relevant Imaging studies will be done at baseline, before 3rd PLT cycle, 3 (\pm) months after last PLT cycle, and then every 3 (\pm) months during follow-up until reaching the endpoint or 24 months after the first treatment as per clinical routine

11 For safety assessment, vital signs will be measured within 20 minutes before and for up to an hour after administration of 177Lu-PSMA-837.

14 Continuous ECG monitoring (only in first 2 PLT cycles) starts at least 15 minutes prior to administration of the study drug and lasts at least 1 hour after administration.

15 Two 12 lead ECGs: one before injection and one after 4 hr scan in dosimetry PLT and after completion of salivary gland protection in non-dosimetry PLT

16 Quality of life questionnaire (EPIC-26) and ECOG will be completed at baseline, and at 3, 6, 9, 12, 18 and 24 months from first PLT cycle

17 Only at first or second treatment, whole body scintigraphy will be performed several times (4 hrs \pm 10 min), 18-30, 42-54, and 66-78 hours) after injection for dosimetry purposes. For non-dosimetry PLTs, only one (optional) post therapy WB scan will be performed. Please refer to dosimetry schedule of events.

18 Telephone follow up: 7 (\pm 3) days after each treatment cycle until completion of 4 cycles and for follow up phase , every 3 months (\pm 1 month) until the end of follow up visits (24 months).

In each time point that the therapy stops follow up visits will be started.

Appendix III: Principal Investigator Signature

I have read this clinical protocol, no. ¹⁷⁷Lu-PSMA-617-02, in its entirety and:

- I agree to implement and conduct this clinical study diligently and in strict compliance with the protocol, good clinical practices, and all applicable national, federal, and local laws and/or regulations.
- I agree that this clinical protocol will not be modified by me or any member of my staff without the written consent of Endocyte, Inc. and, if required, I will receive approval of these modifications by my institution's IRB/REB/Independent Ethics Committee (IEC).
- I certify that neither I nor any member of my staff has been disqualified or debarred by the Food and Drug Administration (FDA), European or any other regulatory bodies for clinical investigations or any other purpose.
- I understand that this clinical protocol and the accompanying clinical Investigator's Brochure contains trade secrets and/or commercial information that are privileged and/or confidential and may not be disclosed unless such disclosure is required by national, federal, or local laws and/or regulations.

Pursuant to 21 CFR § 312.53(c), each US investigator will complete and sign FDA Form 1572, Statement of Investigator, prior to participating in the study. The completed form, along with a curriculum vitae, will be returned to Endocyte and maintained on record.

Form FDA 1572, Statement of Investigator, which must be completed, is available at:
<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM074728.pdf>

Principal Investigator Signature

Date

Name (Printed)

Title (Printed)

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Baseline and follow-Up Questionnaire for Pain and Adverse Events

PATIENT INFORMATION

Last name: _____ First Name: _____

Date of Birth: _____ Medical Record Number: _____

Change of pain medication since last ¹⁷⁷Lu-PSMA-617 cycle

- No change
 Change in dosage/administration: medication _____ increase or decrease
 Addition/removal of medication: medication _____ addition or removal

Pain No or Yes:

Locations: _____

Overall level:



Change since last cycle: increase, no change, decrease

Nausea

- No nausea
 Nausea with loss of appetite only
 Nausea with eating/drinking less than usual
 Had to go to hospital for nausea

Vomiting

- No vomiting
 1 - 2 episodes per day
 3 - 5 episodes per day
 more than 5 episodes per day

Dry mouth

- No dry mouth
 Dry or thick saliva
 Normal eating only with water/lubricants possible
 Tube feeding or total i.v. nutrition

Taste

- Normal taste
 Altered taste but no change in diet
 Altered taste with change in diet

Fatigue

- No fatigue
 Fatigue relieved by rest
 Fatigue not relieved by rest, limiting work
 Fatigue not relieved by rest, limiting self-care

Hematoma

- No Hematoma
 Occurrence of hematoma without known event

Fever

- No fever
 38.0 - 39.0 °C (100.4 - 101.2 °F)
 >39.0 - 40.0 degrees °C (101.3 - 104.0 °F)
 >40.0 °C (>104.0 °F)

Urinary retention

- Able to void normally
 Able to void with some pressure
 Unable to void or voiding only after catheter/intervention/treatment

Diarrhea

- Normal bowel movements
 Increase by <4 stools per day

Other (symptom, grade: mild/moderate/severe):

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- Increase by 4-6 stools per day
- Increase by more than 6 stools per day
- Had to go to hospital for diarrhea

Date: _____ Name: _____ Signature: _____

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PSMA-617-02

EPIC-26

The Expanded Prostate Cancer Index Composite

Short Form

This questionnaire is designed to measure Quality of Life issues in patients with Prostate cancer. To help us get the most accurate measurement, it is important that you answer all questions honestly and completely.

Remember, as with all medical records, information contained within this survey will remain strictly confidential.

Today's Date (please enter date when survey completed): Month _____ Day _____ Year _____

Name (optional): _____

Date of Birth (optional): Month _____ Day _____ Year _____

PSMA-617-02

Do Not Mark in This Space

1. Over the **past 4 weeks**, how often have you leaked urine?

- | | | |
|----------------------------|---|---------------------|
| More than once a day..... | 1 | (Circle one number) |
| About once a day..... | 2 | |
| More than once a week..... | 3 | |
| About once a week..... | 4 | |
| Rarely or never..... | 5 | |

23/

2. Which of the following best describes your urinary control **during the last 4 weeks**?

- | | | |
|------------------------------------|---|---------------------|
| No urinary control whatsoever..... | 1 | (Circle one number) |
| Frequent dribbling..... | 2 | |
| Occasional dribbling..... | 3 | |
| Total control..... | 4 | |

26/

3. How many pads or adult diapers per day did you usually use to control leakage
during the last 4 weeks?

- | | | |
|-----------------------------|---|---------------------|
| None | 0 | (Circle one number) |
| 1 pad per day..... | 1 | |
| 2 pads per day..... | 2 | |
| 3 or more pads per day..... | 3 | |

27/

4. How big a problem, if any, has each of the following been for you **during the last 4 weeks?**

(Circle one number on each line)

	No Problem	Very Small Problem	Small Problem	Moderate Problem	Big Problem	
a. Dripping or leaking urine	0	1	2	3	4	28/
b. Pain or burning on urination.....	0	1	2	3	4	29/
c. Bleeding with urination.....	0	1	2	3	4	30/
d. Weak urine stream or incomplete emptying	0	1	2	3	4	31/
e. Need to urinate frequently during the day.....	0	1	2	3	4	33/

PSMA-617-02

5. Overall, how big a problem has your urinary function been for you **during the last 4 weeks?**

No problem..... 1
Very small problem..... 2
Small problem..... 3
Moderate problem..... 4
Big problem..... 5

(Circle one number)

34/

Do Not
Mark in
This
Space

6. How big a problem, if any, has each of the following been for you? (Circle one number on each line)

	<u>No Problem</u>	<u>Very Small Problem</u>	<u>Small Problem</u>	<u>Moderate Problem</u>	<u>Big Problem</u>	
a. Urgency to have a bowel movement	0	1	2	3	4	49/
b. Increased frequency of bowel movements.....	0	1	2	3	4	50/
c. Losing control of your stools.....	0	1	2	3	4	52/
d. Bloody stools	0	1	2	3	4	53/
e. Abdominal/ Pelvic/Rectal pain...	0	1	2	3	4	54/

7. Overall, how big a problem have your bowel habits been for you **during the last 4 weeks?**

No problem..... 1
Very small problem..... 2
Small problem..... 3
Moderate problem..... 4
Big problem..... 5

(Circle one number)

55/

8. How would you rate each of the following **during the last 4 weeks?** (Circle one number on each line)

	<u>Very Poor to None</u>	<u>Poor</u>	<u>Fair</u>	<u>Good</u>	<u>Very Good</u>	
a. Your ability to have an erection?.....	1	2	3	4	5	57/
b. Your ability to reach orgasm (climax)?.....	1	2	3	4	5	58/

PSMA-617-02

9. How would you describe the usual QUALITY of your erections **during the last 4 weeks?**

- | | |
|---|---|
| None at all..... | 1 |
| Not firm enough for any sexual activity..... | 2 |
| Firm enough for masturbation and foreplay only..... | 3 |
| Firm enough for intercourse..... | 4 |
- (Circle one number)

59/

10. How would you describe the FREQUENCY of your erections **during the last 4 weeks?**

- | | |
|---|---|
| I NEVER had an erection when I wanted one..... | 1 |
| I had an erection LESS THAN HALF the time I wanted one..... | 2 |
| I had an erection ABOUT HALF the time I wanted one | 3 |
| I had an erection MORE THAN HALF the time I wanted one..... | 4 |
| I had an erection WHENEVER I wanted one..... | 5 |
- (Circle one number)

60/

Do Not
Mark in
This
Space

11. Overall, how would you rate your ability to function sexually **during the last 4 weeks?**

- | | |
|----------------|---|
| Very poor..... | 1 |
| Poor..... | 2 |
| Fair..... | 3 |
| Good..... | 4 |
| Very good..... | 5 |
- (Circle one number)

64/

12. Overall, how big a problem has your sexual function or lack of sexual function been for you
during the last 4 weeks?

- | | |
|-------------------------|---|
| No problem..... | 1 |
| Very small problem..... | 2 |
| Small problem..... | 3 |
| Moderate problem..... | 4 |
| Big problem..... | 5 |
- (Circle one number)

68/

13. How big a problem **during the last 4 weeks**, if any, has each of the following been for you?

PSMA-617-02

(Circle one number on each line)

No	Very Small	Small	Moderate	Big
Problem	Problem	Problem	Problem	Problem
a. Hot flashes.....	0	1	2	3
b. Breast tenderness/enlargement..	0	1	2	3
c. Feeling depressed.....	0	1	2	3
d. Lack of energy.....	0	1	2	3
e. Change in body weight.....	0	1	2	3

THANK YOU VERY MUCH!!

EPIC-SF 6.2002

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PSMA-617-02

Appendix VI: Dosimetry protocol attached as pdf copy
***Not applicable to previous versions of protocol**

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Appendix 16.1.2 Sample case report form(s)

History of changes	
Version	Summary of changes
1.0	Original version

1 Sample case report form

The [blank sample case report form Version 1.0](#) provided includes updates from Protocol Amendment 1, Protocol Amendment 2, and Protocol Amendment 3.

The [blank sample case report form Version 1.1](#) provided includes updates from Protocol Amendment 3 and Protocol Amendment 4.

The [blank sample case report form Version 1.2](#) provided includes updates from [Amendment 4](#).

The [blank sample case report form Version 1.3](#) provided includes updates from Protocol Amendment 4.

The [blank sample case report form Version 1.4](#) provided includes updates from Protocol Amendment 4 and Protocol Amendment 5 (Final Version).

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Case Report Form

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC). A phase II clinical trial.

Phase II

Version 1.0

Sponsor

Ebrahim S. Delpassand, M.D. F.A.C.N.M
Johannes Czernin, M.D.

PSMA-directed endoRadioThErApy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline				
Study short title RESIST-PC	Patient identifier [] - [] - []	Site	Initials	
• Informed consent				
The patient has been informed about the aims, rationale and procedures of the RECIST-PC trial and he/she has voluntarily agreed to participate and given				
<input type="checkbox"/> written informed consent.				
A copy of the patient information has been handed out to the patient.				
Date of informed consent:				
Day	/	Month	/	Year

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Inclusion / Exclusion criteria		
Study short title	Patient identifier	
RESIST-PC	[REDACTED] - [REDACTED] - [REDACTED]	
• Inclusion criteria		
1. Prostate cancer proven by histopathology	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Unresectable metastases	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Castration resistant disease with confirmed testosterone level \leq 50 ng/ml under prior androgen deprivation therapy (ADT)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{113}Lu -PSMA-617 scintigraphy	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. ECOG 0-2	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Sufficient bone marrow capacity as defined by WBC \geq 2.500/ μl , PLT count \geq 100.000/ μl , Hb \geq 9.9 g/dl and ANC \geq 1500 mm 3 for the first cycle and WBC \geq 2.000/ μl , PLT count \geq 75.000/ μl , Hb \geq 8.9 g/dl and ANC \geq 1000 mm 3 for the subsequent cycles	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Signing Informed Consent Form	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Patients enrolling in this trial should have received either Enzalutamide or Abiraterone	<input type="checkbox"/> Yes	<input type="checkbox"/> No
NOTE: If any inclusion criterion is answered "No", the patient is NOT eligible to enter the study!		
• Exclusion criteria		
1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm) or other radionuclide therapy	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Glomerular Filtration Rate (GFR) $<$ 40 ml/min	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Grade 3 toxicity serum creatinine using CTCAE v4.0	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. AST and ALT $>$ 5xULN	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Urinary tract obstruction or marked hydronephrosis	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Diffuse bone marrow involvement confirmed by super-scans	<input type="checkbox"/> Yes	<input type="checkbox"/> No
NOTE: If any exclusion criterion is answered "Yes", the patient is NOT eligible to enter the study!		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier [] - [] - []
• Demographic Data	
Date of Assessment:	[] / [] / [] day month year
Date of Birth	[] / [] / [] day month year
Do you consider yourself Hispanic/Latino or not Hispanic/Latino?	<input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> Not Hispanic or Latino <input type="checkbox"/> Unknown <input type="checkbox"/> Not reported
Which of the following five racial designations best describes you? More than one choice is acceptable. (If mixed race, please check race of each parent)	<input type="checkbox"/> American Indian or Alaska Native <input type="checkbox"/> Asian <input type="checkbox"/> Black or African American <input type="checkbox"/> Native Hawaiian or Other Pacific Islander <input type="checkbox"/> White <input type="checkbox"/> other:

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier [REDACTED] - [REDACTED] - [REDACTED]	
• Anthropometric Measurements – Vital Signs		
Height	[REDACTED].[REDACTED]	Unit: <input type="checkbox"/> inch <input checked="" type="checkbox"/> cm
Weight	[REDACTED].[REDACTED]	Unit: <input type="checkbox"/> lbs <input checked="" type="checkbox"/> kg
Temperature	[REDACTED].[REDACTED]	°C
Heart Rate	[REDACTED]	1/min
Respiratory Rate	[REDACTED]	1/min
Blood Pressure Systolic	[REDACTED]	mmHg
Blood Pressure Diastolic	[REDACTED]	mm Hg
Pulse Oximetry	[REDACTED]	%

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• Physical Examination		
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done, if not done provide comment _____	
Date Physical Examination	_____/_____/_____	day month year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal	
Comments: General Appearance	_____	
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____	
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Cardiovascular	_____	
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Respiratory	_____	
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Gastrointestinal	_____	
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Musculoskeletal	_____	
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Genitourinary	_____	
Skin	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
Comments: Skin	_____	
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
Comments Neurological	_____	
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
	<input type="checkbox"/> not done	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
• Prostate Cancer History	
Histopathology reports available	<input type="checkbox"/> yes <input type="checkbox"/> no, please comment: _____
N.B.: Histopathologically confirmed prostate cancer is an inclusion criterion	
Date of histopathology report/biopsy	_____/_____/_____ day month year
Type of prostate cancer tumor	<input type="checkbox"/> adenocarcinoma <input type="checkbox"/> other: _____
PSA at initial diagnosis:	date of determination _____/_____/_____ day month year result _____._____ <u>unit:</u> <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Gleason Score (preferred format X+Y=Z; Biopsy or Prostatectomy)	____ + ____ = ____ <input type="checkbox"/> biopsy <input type="checkbox"/> prostatectomy
TNM at initial diagnosis (tick one per category)	<input type="checkbox"/> pT2 <input type="checkbox"/> pT2a <input type="checkbox"/> pT2b <input type="checkbox"/> pT2c <input type="checkbox"/> pT3 <input type="checkbox"/> pT3a <input type="checkbox"/> pT3b <input type="checkbox"/> pT4 <input type="checkbox"/> pNX <input type="checkbox"/> pN0 <input type="checkbox"/> pN1 <input type="checkbox"/> cN0 <input type="checkbox"/> cN1 <input type="checkbox"/> M0 <input type="checkbox"/> M1

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
Last three PSA values:	
Date 1: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Date 2: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Date 3: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Change of therapy between date #1 to #3	<input type="checkbox"/> Yes, please document all therapies on prostate cancer treatment history section <input type="checkbox"/> No
Documented PSA value doubling time:	_____ days
Current TNM (at study inclusion) (tick one per category)	<input type="checkbox"/> pT2 <input type="checkbox"/> pT2a <input type="checkbox"/> pT2b <input type="checkbox"/> pT2c <input type="checkbox"/> pT3 <input type="checkbox"/> pT3a <input type="checkbox"/> pT3b <input type="checkbox"/> pT4

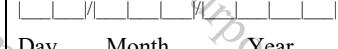
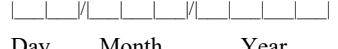
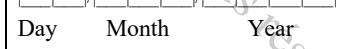
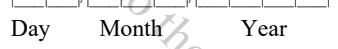
PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title	Patient identifier
RESIST-PC	_____ - _____ - _____
(tick one per category)	<input type="checkbox"/> pNX <input type="checkbox"/> pN0 <input type="checkbox"/> pN1 <input type="checkbox"/> cN0 <input type="checkbox"/> cN1
(tick one per category)	<input type="checkbox"/> M0 <input type="checkbox"/> M1

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title RESIST-PC		Patient identifier [] - [] - []				
• Prostate Cancer Treatment History: Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
2	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
3

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
• Prostate Cancer Treatment History: Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> standard ADT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	<input type="text"/> . OR <input type="text"/> . 	Gy OR GBq	<input type="checkbox"/> Unknown 	<input type="checkbox"/> Unknown 	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
2	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> standard ADT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	<input type="text"/> . OR <input type="text"/> . 	Gy OR GBq	<input type="checkbox"/> Unknown 	<input type="checkbox"/> Unknown 	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
3

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline					
Study short title RESIST-PC		Patient identifier [] - [] - []			
• Prostate Cancer Treatment History: Other Treatment					
Any other treatment?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below	
#	Therapy	Comments	started	ended	best response
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> primary lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing
2	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> primary lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing
3

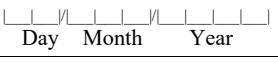
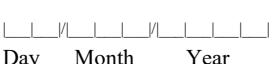
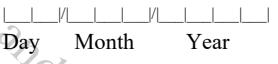
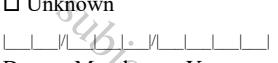
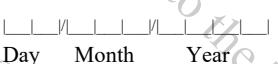
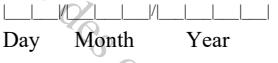
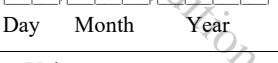
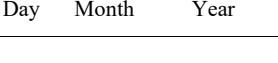
PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
Imaging within the past three months	Date of imaging	
CT (repeatable event)	_____ / _____ / _____ day month year	
MRI (repeatable event)	_____ / _____ / _____ day month year	
PET/CT (repeatable event)	_____ / _____ / _____ day month year	
Scintigraphy (repeatable event)	_____ / _____ / _____ day month year	
other, specify:	_____ / _____ / _____ day month year	

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier [] - [] - []	
• Medical History		
Date of Assessment:	[] / [] / [] day month year	
Any relevant medical history?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify below:	
Condition / Illness	Started <input type="checkbox"/> Unknown [] / [] / [] Day Month Year	Ended <input type="checkbox"/> Unknown [] / [] / [] Day Month Year
1.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	
2.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	
3.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	
4.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	
5.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	
6.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	
7.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	
8.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier [REDACTED]
• Baseline findings	
<p>Note: Please list below all conditions which started before the patient signed the informed consent form and for which symptoms or treatment were recorded during the time between signature of informed consent and first administration of the study drug, including conditions which were stabilized by treatment</p> <p>Conditions present before study drug administration are to be documented as Baseline Findings; conditions which started or deteriorated after administration of the study drug will be documented as Adverse Events on a specific AE page of the CRF</p>	
Hypersensitivity assessment	
Known allergies:	<input type="checkbox"/> no <input type="checkbox"/> yes, specify _____
Abnormal findings / symptoms / diseases	Started
1.	<input type="checkbox"/> Unknown  Day Month Year
2.	<input type="checkbox"/> Unknown  Day Month Year
3.	<input type="checkbox"/> Unknown  Day Month Year
4.	<input type="checkbox"/> Unknown  Day Month Year
5.	<input type="checkbox"/> Unknown  Day Month Year
6.	<input type="checkbox"/> Unknown  Day Month Year
7.	<input type="checkbox"/> Unknown  Day Month Year
8.	<input type="checkbox"/> Unknown  Day Month Year

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• ECOG		
Date of Assessment:	_____ / _____ / _____ day month year	
ECOG performance status	<input type="checkbox"/> 0 Fully active, able to carry on all pre-disease performance without restriction 1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work 2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours 3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours 4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title		Patient identifier				
RESIST-PC						_____ - _____ - _____
Laboratory						
Date of Assessment:		_____ / _____ / _____ day month year				
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC		Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC		Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets		Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin		mmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit				<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV				<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH				<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW				<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
CRP				<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST		μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT		μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase		μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin		μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin		g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN		mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine		μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

eGFR	_____	mL/min		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title	Patient identifier	
RESIST-PC	[] - [] - []	
• PSA measurement		
Date of Assessment:	[] / [] / [] day month year	
[] . []		
<u>unit:</u>		
<input type="checkbox"/> ng/mL		
<input type="checkbox"/> if other unit, specify:		

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline			
Study short title RESIST-PC	Patient identifier _____ - _____ - _____		
•ECG			
date and time of ECG	_____	_____	_____
Day	Month	Year	hrs : min
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below		
Comment	_____		
heart rate	_____	1/min	
QT interval	_____	msec	
QTc interval (corrected QT interval)	_____	msec	

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline			
Study short title RESIST-PC	Patient No.+ Initials [] - [] - []		
• Imaging			
Date and time of imaging Ga-68 PSMA PET/CT or Lu-177 PSMA scintigraphy result	[] ____/____/____ ____ : ____ Day Month Year hrs : min <input type="checkbox"/> positive (tumor lesions visible) <input type="checkbox"/> negative (no tumor lesion visible)		
Mean PSMA expression of lesions by visual assessment:	Score	Reported PSMA expression	Uptake
<input type="checkbox"/> 0	no	Below bloodpool	
<input type="checkbox"/> +	low	Equal to or above bloodpool and lower than liver	
<input type="checkbox"/> ++	intermediate	Equal to or above liver and lower than salivary glands	
<input type="checkbox"/> +++	high	Equal to or above salivary glands	

Please make sure all additional questionnaires are completed by the patient as applicable

- EPIC-26 (see page 94-99 in the protocol version amendment 2 from 7 Jun 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see page 92-93 in the protocol version amendment 2 from 7 Jun 2017)
- Patient diary
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Concomitant Medication							
Study short title RESIST-PC			Patient No.+ Initials _____ - _____ - _____				
Any medication taken between 28 days before inclusion and "end of study"?					<input type="checkbox"/> No	<input type="checkbox"/> Yes, please specify details below	
Generic name (Brand name for combination drugs)	Indication	Total daily dose	Dose unit	Regimen 1 = PRN, 2 daily, 3 = once, 4 = QD, 5 = BID, 6 = TID, 7 = Q6H, 8 = Q8H, 9 = Q12H, 10 QHS, 11 infusion, 12 continuous infusion, 13 other, specify	Route 1 = oral, 2 = s c , 3 = i m , 4 = IV, 5 = inhalation, 6 = topical, 7 = transdermal, 8 rectal, 9 = other, specify	Date of first administration Day Month Year <input type="checkbox"/> unknown	Date of last administration Day Month Year <input type="checkbox"/> Continuing at end of study
1.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study
2.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study
3.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study
4.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Randomization	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
Date of Randomization:	_____/_____/_____ day month year
Patient is randomized to	<input type="checkbox"/> arm 1 (6.0 GBq per Radioligand therapy) <input type="checkbox"/> arm 2 (7.4 GBq per Radioligand therapy)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
Date of 1. RLT:	_____ / _____ / _____ day month year
• 12 lead ECG Before Injection	
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
Heart rate	_____ b/min
RR interval	_____ msec
QT interval	_____ msec
QTc interval (corrected QT interval)	_____ msec

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• Salivary protection (30 min before injection and continued for 4 hours)	
Applying ice pack	<input type="checkbox"/> done <input type="checkbox"/> not done, provide comment _____
• Vital Signs Before Injection (within 20 min before injection)	
Temperature	_____ . ____ °C
Heart Rate	_____ 1/min
Respiratory Rate	_____ 1/min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg
Pulse Oximetry	_____ %
• 1. RLT	
Activity in syringe before injection	_____ .____ GBq
Date and time of start of measurement	_____ /_____ /_____ - _____ :_____ day month year hr min
Injected activity	_____ .____ GBq
Date and time of RLT	_____ /_____ /_____ - _____ :_____ day month year hr min
Activity in syringe after injection	_____ .____ GBq
Date and time of end of measurement	_____ /_____ /_____ - _____ :_____ day month year hr min
Completed as planned	<input type="checkbox"/> yes <input type="checkbox"/> no, specify _____
Any adverse event	<input type="checkbox"/> yes, complete AE page <input type="checkbox"/> no

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• Vital Signs After Injection	
Time	_____ : _____ hh min
Temperature	_____ . _____ °C
Heart Rate	_____ 1/min
Respiratory Rate	_____ 1/min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg
Pulse Oximetry	_____ %

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• ECG after injection	
Date and time of ECG	____/____/____ ____:____ Day Month Year hrs : min
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below _____
Comment	_____
Heart rate	____/____ 1/min
QT interval	____ msec
QTc interval (corrected QT interval) = QT interval / (RR interval)	____ msec

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• 12 lead ECG 4 hours after Injection	
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below _____
Comment	_____
Heart rate	_____ 1/min
QT interval	_____ msec
QTc interval (corrected QT interval) = QT interval / (RR interval)	_____ msec

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit						
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____					
• Dosimetry: Blood Samples						
With regard to injection site, was the blood draw performed			<input type="checkbox"/> X contralateral <input type="checkbox"/> X ipsilateral, different i.v. access <input type="checkbox"/> X ipsilateral, same i.v. access			
5 min	<input type="checkbox"/> sample obtained, specify exact time post $^{177}\text{LuPSMA}$ injection _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not obtained
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not measured
	Volume measured: _____ mL					
	Activity measured: _____ kBq					
30 min	<input type="checkbox"/> sample obtained specify exact time (post inj) _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not obtained
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not measured
	Volume measured: _____ mL					
	Activity measured: _____ kBq					
1 h	<input type="checkbox"/> sample obtained specify exact time (post inj) _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not obtained
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not measured
	Volume measured: _____ mL					
	Activity measured: _____ kBq					

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PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
4 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____/_____/_____ Day Month Year hrs : min <input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____/_____/_____ Day Month Year hrs : min Volume measured: _____ mL Activity measured: _____ kBq
18-30 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____/_____/_____ Day Month Year hrs : min <input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____/_____/_____ Day Month Year hrs : min Volume measured: _____ mL Activity measured: _____ kBq
42-54 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____/_____/_____ Day Month Year hrs : min <input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____/_____/_____ Day Month Year hrs : min Volume measured: _____ mL Activity measured: _____ kBq
66-78 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____/_____/_____ Day Month Year hrs : min

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit					
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____				
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured ____/____/____ ____:____ Day Month Year hrs : min				
	Volume measured: _____ mL				
	Activity measured: _____ kBq				
7-9 d	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained ____/____/____ ____:____ Day Month Year hrs : min				
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured ____/____/____ ____:____ Day Month Year hrs : min				
	Volume measured: _____ mL				
	Activity measured: _____ kBq				

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____		
• Dosimetry: Scintigraphy			
4 h	<input type="checkbox"/> whole body planar obtained, specify exact time <input type="checkbox"/> not obtained _____ : _____ hh min Scan duration _____ min		
18-30 h	date: ____ / ____ / ____ hrs : min Day Month Year		
	whole body planar: <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____ : _____ hrs : min Scan duration _____ min		
	SPECT/CT head <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____ : _____ hrs : min Duration per angle _____ min		
	SPECT/CT thorax <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____ : _____ hrs : min Duration per angle _____ min		
	SPECT/CT abd. <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____ : _____ hrs : min Duration per angle _____ min		
42-54 h	<input type="checkbox"/> whole body planar obtained, specify date/time <input type="checkbox"/> not obtained _____ / _____ / _____ hrs : min Day Month Year Scan duration _____ min		

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit			
Study short title RESIST-PC	Patient No.+ Initials - -		
66-78 h	<input type="checkbox"/> whole body planar obtained, specify date/time <input type="checkbox"/> not obtained / / : Day Month Year hrs : min Scan duration min		
7-9 d	<input type="checkbox"/> whole body planar obtained, specify date/time <input type="checkbox"/> not obtained / / : Day Month Year hrs : min Scan duration min		

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• Dosimetry: Urine Collection	
collected from injection until 4 h p.i.	<input type="checkbox"/> done <input type="checkbox"/> not done, specify Volume measured: _____ mL Activity measured: _____ . _____ MBq
collected from 4 h until discharge	<input type="checkbox"/> done <input type="checkbox"/> not done, specify date and time of discharge: _____/_____/_____ Day Month Year hrs : min Volume measured: _____ mL Activity measured: _____ . _____ MBq

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)						
Study short title	Patient No.+ Initials					
RESIST-PC	_____ - _____ - _____					
• Laboratory						
Date of Assessment:	_____/_____/_____ day month year					
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	_____	Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	_____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	_____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
CRP	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	_____	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	_____	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	_____	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	_____	µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	_____	g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)							
Study short title	Patient No.+ Initials						
RESIST-PC	[REDACTED] - [REDACTED] - [REDACTED]						
creatinine	[REDACTED]	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
eGFR	[REDACTED]	mL/min		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
sodium	[REDACTED]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
potassium	[REDACTED]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
chloride	[REDACTED]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)		
Study short title	Patient identifier	
RESIST-PC	[] - [] - []	
• PSA measurement		
Date of Assessment:	[] / [] / []	[] day month year
[] . []		
<u>unit:</u>		
<input type="checkbox"/> ng/mL		
<input type="checkbox"/> if other unit, specify:		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit	
Study short title	Patient No.+ Initials
RESIST-PC	_____ - _____ - _____
• Study drug administration complications	
Has any complication related to administration of the drug occurred (e.g., overdose, observable extravasation, medication error)?	<input type="checkbox"/> no <input type="checkbox"/> yes, please specify <input type="checkbox"/> Report was sent to the pharmacovigilance designee.

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see page 94-99 in the protocol version amendment 2 from 7 Jun 2017)
- Baseline and follow –Up Questionnaire for Pain and Adverse Events (see page 92-93 in the protocol version amendment 2 from 7 Jun 2017)
- Patient diary
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

12 weeks PSA measurement		
Study short title	Patient identifier	
RESIST-PC	- -	
• PSA measurement		
Date of Assessment:	/ /	
day month year		
.		
<u>unit:</u>		
<input type="checkbox"/> ng/mL		
<input type="checkbox"/> if other unit, specify:		

• ECOG		
Date of Assessment:	/ /	
day month year		
ECOG performance status		
	0	Fully active, able to carry on all pre-disease performance without restriction
	1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
	2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
	3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
	4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair

At week 12 also to be completed:

- Lab values (CBC, CMP)
- Imaging questionnaires
- EPIC-26

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Additional evaluation of blood tests every 2 weeks (not cycle 1-4 and not Follow-up)						
Study short title		Patient No.+ Initials				
RESIST-PC						
• Laboratory						
Date of Assessment:		day	month	year		
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	██████ ████	Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	███████ █████	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	███████ █████	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	███████ █████	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	███████ █████	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	███████ █████	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	███████ █████	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	███████ █████	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	███████ █████	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	███████ █████			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	███████ █████			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	███████ █████			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	███████ █████			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
CRP	███████ █████			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	███████ █████	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	███████ █████	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	███████ █████	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	███████ █████	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	███████ █████	g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	███████ █████	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Additional evaluation of blood tests every 2 weeks (not cycle 1-4 and not Follow-up)						
Study short title	Patient No.+ Initials					
RESIST-PC	<u> </u> - <u> </u> - <u> </u>					
creatinine	<u> </u> <u> </u> <u> </u>	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eGFR	<u> </u> <u> </u> <u> </u>	mL/min		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	<u> </u> <u> </u> <u> </u>	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	<u> </u> <u> </u> <u> </u>	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	<u> </u> <u> </u> <u> </u>	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

Additional PSA measurements								
Study short title	Patient identifier							
RESIST-PC	<u> </u> - <u> </u> - <u> </u>							
• PSA measurement								
Date of Assessment:	<u> </u> / <u> </u> / <u> </u>	day	month	year				
<u> </u> . <u> </u>								
unit:								
<input type="checkbox"/> ng/mL								
<input type="checkbox"/> if other unit, specify:								

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)			
Study short title	Patient No.+ Initials		
RESIST-PC	_____ - _____ - _____		
• Physical Examination			
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done		
Date Physical Examination:	day	month	year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal		
Comments: General Appearance	_____		
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____		
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Cardiovascular	_____		
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Respiratory	_____		
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Gastrointestinal	_____		
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Musculoskeletal	_____		
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Genitourinary	_____		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)			
Study short title	Patient No.+ Initials		
RESIST-PC	- -		
Skin	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments: Skin	_____		
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments Neurological	_____		
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments	_____		

• ECOG			
Date of Assessment:	/ / day month year		
ECOG performance status		<ul style="list-style-type: none">0 Fully active, able to carry on all pre-disease performance without restriction1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)	
Study short title	Patient No.+ Initials
RESIST-PC	____ - ____ - ____
Date of RLT:	____ / ____ / ____ day month year
• 12 lead ECG Before Injection	
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
heart rate	______ 1/min
QT interval	______ msec
QTc interval (corrected QT interval) = QT interval / (RR interval)	______ msec

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)				
Study short title	Patient No.+ Initials			
RESIST-PC	- -			
• ECG before injection				
date and time of ECG	 Day Month Year hrs : min			
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below			
Comment				
heart rate	1/min			
QT interval	msec			
QTc interval (corrected QT interval) = QT interval / (RR interval)	msec			

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• Salivary protection (30 min before injection and continued for 4 hours)	
Applying ice pack	<input type="checkbox"/> done <input type="checkbox"/> not done, provide comment _____
• Vital Signs Before Injection (within 20 min before injection)	
Temperature	_____ . ____ °C
Heart Rate	_____ 1/min
Respiratory Rate	_____ 1/min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg
Pulse Oximetry	_____ %
• RLT	
activity in syringe before injection	_____ . _____ GBq
Date and time of measurement	_____ / _____ / _____ - _____ : _____ day month year hrs min
injected activity	_____ . _____ GBq
date and time of RLT	_____ / _____ / _____ - _____ : _____ day month year hrs min
activity in syringe after injection	_____ . _____ GBq
Date and time of measurement	_____ / _____ / _____ - _____ : _____ day month year hrs min
completed as planned	<input type="checkbox"/> yes <input type="checkbox"/> no, specify _____
any adverse event	<input type="checkbox"/> yes, complete AE page <input type="checkbox"/> no

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

•Vital Signs After Injection	
time	____:____ hh min
Temperature	____.____ °C
Heart Rate	____ 1/min
Respiratory Rate	____ 1/min
Blood Pressure Systolic	____ mmHg
Blood Pressure Diastolic	____ mm Hg
Pulse Oximetry	____ %

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)				
Study short title	Patient No.+ Initials			
RESIST-PC	- -			
• ECG after injection				
date and time of ECG	 Day Month Year hrs : min			
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below			
Comment				
heart rate	1/min			
QT interval	msec			
QTc interval (corrected QT interval) = QT interval / (RR interval)	msec			

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• 12 lead ECG 4 hours after Injection	
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below _____
Comment	_____
heart rate	_____ /min
QT interval	_____ msec
QTc interval (corrected QT interval) = QT interval / (RR interval)	_____ msec

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see page 94-99 in the protocol version amendment 2 from 7 Jun 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see page 92-93 in the protocol version amendment 2 from 7 Jun 2017)
- Patient diary
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up		
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____	
• Physical Examination		
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done	
Date Physical Examination:	_____/_____/_____	day month year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal	
Comments: General Appearance	_____	
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____	
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Cardiovascular	_____	
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Respiratory	_____	
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Gastrointestinal	_____	
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Musculoskeletal	_____	
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Genitourinary	_____	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up		
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____	
Skin	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
Comments: Skin	_____	
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
Comments Neurological	_____	
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
Comments	_____	

• Vital Signs Before Injection (within 20 min before injection)		
Temperature	____ .____ °C	
Heart Rate	____ 1/min	
Respiratory Rate	____ 1/min	
Blood Pressure Systolic	_____ mmHg	
Blood Pressure Diastolic	_____ mm Hg	
Pulse Oximetry	____ %	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up											
Study short title RESIST-PC	Patient No.+ Initials ____ - ____ - ____										
• ECOG											
Date of Assessment:	____/____/____ day month year										
ECOG performance status	<table><tr><td>0</td><td>Fully active, able to carry on all pre-disease performance without restriction</td></tr><tr><td>1</td><td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work</td></tr><tr><td>2</td><td>Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours</td></tr><tr><td>3</td><td>Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours</td></tr><tr><td>4</td><td>Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair</td></tr></table>	0	Fully active, able to carry on all pre-disease performance without restriction	1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours	3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours	4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
0	Fully active, able to carry on all pre-disease performance without restriction										
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work										
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours										
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours										
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair										

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

•Follow up						
Study short title RESIST-PC		Patient No.+ Initials. _____ - _____ - _____				
•Laboratory						
Date of Assessment: _____ /_____ /_____ day month year						
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	_____	Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	_____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	_____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
CRP	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	_____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	_____	g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

creatinine	_____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eGFR	_____	mL/min		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow up			
Study short title RESIST-PC	Patient identifier _____ - _____ - _____		
• PSA measurement			
Date of Assessment: _____._____._____	day	month	year
<u>unit:</u> <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____			

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

•Follow up		
Study short title RESIST-PC	Patient No.+ Initials. - -	
Imaging		
CT (repeatable event) Tumor location Location of metastases	/ / day month year	
MRI (repeatable event)	/ / day month year	
PET/CT (repeatable event)	/ / day month year	
Scintigraphy (repeatable event)	/ / day month year	
Imaging result:	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD	

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see page 94-99 in the protocol version amendment 2 from 7 Jun 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see page 92-93 in the protocol version amendment 2 from 7 Jun 2017)
- Patient diary
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

End of study	
Study short title RESIST-PC	Patient No.+ Initials. [] - [] - []
Study course	<input type="checkbox"/> Patient completed study if study course completed, last day on study: []/[]/[] Day Month Year reason : <input type="checkbox"/> Progression <input type="checkbox"/> Follow-up completed <input type="checkbox"/> Death <input type="checkbox"/> Patient withdrew from study
If withdrawn, give date and time of withdrawal (24 h clock):	[]/[]/[] []:[] Day Month Year hr min
Specify main reason	<input type="checkbox"/> Withdrawal of consent <input type="checkbox"/> Lost to Follow-up <input type="checkbox"/> Any occurrence of conditions which prevented the patient's participation in the study? Please specify: <input type="checkbox"/> Protocol deviations? Please specify: <input type="checkbox"/> (Serious) AE? Please specify: <input type="checkbox"/> Administrative reasons? Please, specify: <input type="checkbox"/> Other? Please specify:
Who decided the withdrawal?	<input type="checkbox"/> Patient <input type="checkbox"/> Investigator <input type="checkbox"/> Other, please specify:

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Adverse Events						
Study short title RESIST-PC	Patient No.+ Initials. _____ - _____ - _____					
• Adverse Events <small>(Note: Adverse Event is any untoward medical occurrence in a volunteer or clinical investigation subject administered a pharmaceutical product and which does Not necessarily have a causal relationship with this treatment An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medical product)</small>						
Any AE experienced?	<input type="checkbox"/> No <input type="checkbox"/> If yes, please specify details on this form					
Adverse event description						
Onset date and time if available	Day	Month	Year	-	hrs	min
Serious AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please complete also the SAE form					
Maximum intensity:	<input type="checkbox"/> mild (easily tolerated) <input type="checkbox"/> moderate (interferes with usual functions) <input type="checkbox"/> severe (incapacitating)					
Specific drug treatment of AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify on "concomitant medication" page					
Specific Non-drug treatment of AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify.					
Relationship to study drug / study conduct	Study drug relationship: <input type="checkbox"/> None <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite	Study conduct: <input type="checkbox"/> None <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite				
Outcome / status	<input type="checkbox"/> Recovered / resolved without sequelae <input type="checkbox"/> Recovered / resolved with sequelae, specify <input type="checkbox"/> Not recovered / Not resolved <input type="checkbox"/> Death / Fatal <input type="checkbox"/> Unknown					
Study drug action	<input type="checkbox"/> Drug withdrawn <input type="checkbox"/> Dose reduced <input type="checkbox"/> Dose not changed <input type="checkbox"/> Other action: _____					
Date and time if available (24 h clock) AE ended (only if recovered / resolved)	<input type="checkbox"/> ongoing at end of study _____ / _____ / _____ - _____ : _____ Day Month Year hr min					
<input type="checkbox"/> Tick box if this page is the last adverse event						

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Case Report Form

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC). A phase II clinical trial.

Phase II

Version 1.1

Sponsor

Ebrahim S. Delpassand, M.D. F.A.C.N.M
Johannes Czernin, M.D.

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline				
Study short title RESIST-PC	Patient identifier [] - [] - []	Site	Initials	
• Informed consent				
The patient has been informed about the aims, rationale and procedures of the RECIST-PC trial and he/she has voluntarily agreed to participate and given				
<input type="checkbox"/> written informed consent.				
A copy of the patient information has been handed out to the patient.				
Date of informed consent:				
Day	/	Month	/	Year

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Inclusion / Exclusion criteria		
Study short title	Patient identifier	
RESIST-PC	[REDACTED] - [REDACTED] - [REDACTED]	
• Inclusion criteria		
1. Prostate cancer proven by histopathology	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Unresectable metastases	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Castration resistant disease with confirmed testosterone level \leq 50 ng/ml under prior androgen deprivation therapy (ADT)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. ECOG 0-2	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Sufficient bone marrow capacity as defined by WBC \geq 2.500/ μl , PLT count \geq 100.000/ μl , Hb \geq 9.9 g/dl and ANC \geq 1500 mm 3 for the first cycle and WBC \geq 2.000/ μl , PLT count \geq 75.000/ μl , Hb \geq 8.9 g/dl and ANC \geq 1000 mm 3 for the subsequent cycles	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Signing Informed Consent Form	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Patients enrolling in this trial should have received either Enzalutamide or Abiraterone	<input type="checkbox"/> Yes	<input type="checkbox"/> No
NOTE: If any inclusion criterion is answered "No", the patient is NOT eligible to enter the study!		
• Exclusion criteria		
1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm) or other radionuclide therapy	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Glomerular Filtration Rate (GFR) $<$ 40 ml/min	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Grade 3 toxicity serum creatinine using CTCAE v4.0	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. AST and ALT $>$ 5xULN	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Urinary tract obstruction or marked hydronephrosis	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Diffuse bone marrow involvement confirmed by super-scans	<input type="checkbox"/> Yes	<input type="checkbox"/> No
NOTE: If any exclusion criterion is answered "Yes", the patient is NOT eligible to enter the study!		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
• Demographic Data	
Date of Assessment:	_____/_____/_____ day month year
Date of Birth	_____/_____/_____ day month year
Do you consider yourself Hispanic/Latino or not Hispanic/Latino?	<input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> Not Hispanic or Latino <input type="checkbox"/> Unknown <input type="checkbox"/> Not reported
Which of the following five racial designations best describes you? More than one choice is acceptable. (If mixed race, please check race of each parent)	<input type="checkbox"/> American Indian or Alaska Native <input type="checkbox"/> Asian <input type="checkbox"/> Black or African American <input type="checkbox"/> Native Hawaiian or Other Pacific Islander <input type="checkbox"/> White <input type="checkbox"/> other:

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier [REDACTED] - [REDACTED] - [REDACTED]	
• Anthropometric Measurements – Vital Signs		
Height	[REDACTED].[REDACTED]	Unit: <input type="checkbox"/> inch <input checked="" type="checkbox"/> cm
Weight	[REDACTED].[REDACTED]	Unit: <input type="checkbox"/> lbs <input checked="" type="checkbox"/> kg
Temperature	[REDACTED].[REDACTED]	°C
Heart Rate	[REDACTED]	1/min
Respiratory Rate	[REDACTED]	1/min
Blood Pressure Systolic	[REDACTED]	mmHg
Blood Pressure Diastolic	[REDACTED]	mm Hg
Pulse Oximetry	[REDACTED]	%

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• Physical Examination		
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done, if not done provide comment _____	
Date Physical Examination	_____/_____/_____	day month year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal	
Comments: General Appearance	_____	
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____	
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Cardiovascular	_____	
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Respiratory	_____	
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Gastrointestinal	_____	
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Musculoskeletal	_____	
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Genitourinary	_____	
Skin	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
Comments: Skin	_____	
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
Comments Neurological	_____	
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
	<input type="checkbox"/> not done	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
• Prostate Cancer History	
Histopathology reports available	<input type="checkbox"/> yes <input type="checkbox"/> no, please comment: _____
N.B.: Histopathologically confirmed prostate cancer is an inclusion criterion	
Date of histopathology report/biopsy	_____/_____/_____ day month year
Type of prostate cancer tumor	<input type="checkbox"/> adenocarcinoma <input type="checkbox"/> other: _____
PSA at initial diagnosis:	date of determination _____/_____/_____ day month year result _____._____ <u>unit:</u> <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Gleason Score (preferred format X+Y=Z; Biopsy or Prostatectomy)	____ + ____ = ____ <input type="checkbox"/> biopsy <input type="checkbox"/> prostatectomy
TNM at initial diagnosis (tick one per category)	<input type="checkbox"/> pT2 <input type="checkbox"/> pT2a <input type="checkbox"/> pT2b <input type="checkbox"/> pT2c <input type="checkbox"/> pT3 <input type="checkbox"/> pT3a <input type="checkbox"/> pT3b <input type="checkbox"/> pT4 <input type="checkbox"/> pNX <input type="checkbox"/> pN0 <input type="checkbox"/> pN1 <input type="checkbox"/> cN0 <input type="checkbox"/> cN1 <input type="checkbox"/> M0 <input type="checkbox"/> M1

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
Last three PSA values:	
Date 1: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Date 2: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Date 3: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Change of therapy between date #1 to #3	<input type="checkbox"/> Yes, please document all therapies on prostate cancer treatment history section <input type="checkbox"/> No
Documented PSA value doubling time:	_____ days
Current TNM (at study inclusion) (tick one per category)	<input type="checkbox"/> pT2 <input type="checkbox"/> pT2a <input type="checkbox"/> pT2b <input type="checkbox"/> pT2c <input type="checkbox"/> pT3 <input type="checkbox"/> pT3a <input type="checkbox"/> pT3b <input type="checkbox"/> pT4

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
(tick one per category)	<input type="checkbox"/> pNX <input type="checkbox"/> pN0 <input type="checkbox"/> pN1 <input type="checkbox"/> cN0 <input type="checkbox"/> cN1
(tick one per category)	<input type="checkbox"/> M0 <input type="checkbox"/> M1

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title RESIST-PC		Patient identifier [] - [] - []				
• Prostate Cancer Treatment History: Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
2	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
3

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
• Prostate Cancer Treatment History: Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> standard ADT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	<input type="text"/> . <input type="text"/> OR <input type="text"/> <input type="text"/> . <input type="text"/> . <input type="text"/>	Gy OR GBq	<input type="checkbox"/> Unknown Day Month Year	<input type="checkbox"/> Unknown Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
2	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> standard ADT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	<input type="text"/> OR <input type="text"/> <input type="text"/> . <input type="text"/> . <input type="text"/>	Gy OR GBq	<input type="checkbox"/> Unknown Day Month Year	<input type="checkbox"/> Unknown Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
3

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline					
Study short title RESIST-PC		Patient identifier [] - [] - []			
• Prostate Cancer Treatment History: Other Treatment					
Any other treatment?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below	
#	Therapy	Comments	started	ended	best response
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> primary lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing
2	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> primary lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing
3

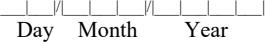
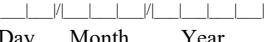
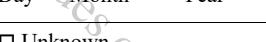
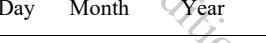
PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier ____ - ____ - ____	
Imaging within the past three months CT (repeatable event)	Date of imaging ____/____/____ day month year	
MRI (repeatable event)	____/____/____ day month year	
PET/CT (repeatable event)	____/____/____ day month year	
Scintigraphy (repeatable event)	____/____/____ day month year	
other, specify: _____	____/____/____ day month year	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier [] - [] - []	
• Medical History		
Date of Assessment:	[] / [] / [] day month year	
Any relevant medical history?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify below:	
Condition / Illness	Started	Ended
1.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year
2.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year
3.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year
4.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year
5.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year
6.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year
7.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year
8.	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• Baseline findings		
Note: Please list below all conditions which started before the patient signed the informed consent form and for which symptoms or treatment were recorded during the time between signature of informed consent and first administration of the study drug, including conditions which were stabilized by treatment		
Conditions present before study drug administration are to be documented as Baseline Findings ; conditions which started or deteriorated after administration of the study drug will be documented as Adverse Events on a specific AE page of the CRF		
Hypersensitivity assessment		
Known allergies:	<input type="checkbox"/> no <input type="checkbox"/> yes, specify	
Abnormal findings / symptoms / diseases	Started	
1.	<input type="checkbox"/> Unknown  Day Month Year	
2.	<input type="checkbox"/> Unknown  Day Month Year	
3.	<input type="checkbox"/> Unknown  Day Month Year	
4.	<input type="checkbox"/> Unknown  Day Month Year	
5.	<input type="checkbox"/> Unknown  Day Month Year	
6.	<input type="checkbox"/> Unknown  Day Month Year	
7.	<input type="checkbox"/> Unknown  Day Month Year	
8.	<input type="checkbox"/> Unknown  Day Month Year	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier ____ - ____ - ____	
• ECOG		
Date of Assessment:	____ / ____ / ____ day month year	
ECOG performance status	<input type="checkbox"/> 0 Fully active, able to carry on all pre-disease performance without restriction 1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work 2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours 3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours 4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
• Laboratory						
Date of Assessment:		[] / [] / [] day month year				
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	[]	Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	[]	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	[]	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	[]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	[]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	[]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	[]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	[]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	[]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	[]			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	[]			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	[]			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	[]			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
CRP	[]			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	[]	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	[]	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	[]	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	[]	µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	[]	g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	[]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine	[]	µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eGFR	[]	mL/min		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

sodium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline			
Study short title RESIST-PC	Patient identifier ____ - ____ - ____		
• PSA measurement			
Date of Assessment: _____._____._____ <small>unit:</small> <input type="checkbox"/> ng/mL	day	month	year
<input type="checkbox"/> if other unit, specify:			

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier ____ - ____ - ____
• ECG	
date and time of ECG	____/____/____ ____ ____ ____ : ____ Day Month Year hrs : min
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
heart rate	____ ____ 1/min
RR interval	____ ____ msec
QT interval	____ ____ msec

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FINAL 1.1 (22 August 2017)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline				
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____			
• Imaging				
Date and time of imaging	 ____/____/____ ____/____/____ ____ : ____ Day Month Year hrs : min			
Ga-68 PSMA PET/CT or Lu-177 PSMA scintigraphy result	<input type="checkbox"/> positive (tumor lesions visible) <input type="checkbox"/> negative (no tumor lesion visible)			
Mean PSMA expression of lesions by visual assessment:	Score	Reported PSMA expression	Uptake	
	<input type="checkbox"/>	0	no	Below bloodpool
	<input type="checkbox"/>	+	low	Equal to or above bloodpool and lower than liver
	<input type="checkbox"/>	++	intermediate	Equal to or above liver and lower than salivary glands
	<input type="checkbox"/>	+++	high	Equal to or above salivary glands

Please make sure all additional questionnaires are completed by the patient as applicable

- EPIC-26 (see page 94-99 in the protocol version amendment 2 from 7 Jun 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see page 92-93 in the protocol version amendment 2 from 7 Jun 2017)
- Patient diary
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Concomitant Medication							
Study short title RESIST-PC			Patient No.+ Initials _____ - _____ - _____				
Any medication taken between 28 days before inclusion and "end of study"?					<input type="checkbox"/> No	<input type="checkbox"/> Yes, please specify details below	
Generic name (Brand name for combination drugs)	Indication	Total daily dose	Dose unit	Regimen 1 = PRN, 2 daily, 3 = once, 4 = QD, 5 = BID, 6 = TID, 7 = Q6H, 8 = Q8H, 9 = Q12H, 10 QHS, 11 infusion, 12 continuous infusion, 13 other, specify	Route 1 = oral, 2 = s c , 3 = i m , 4 = IV, 5 = inhalation, 6 = topical, 7 = transdermal, 8 rectal, 9 = other, specify	Date of first administration Day Month Year <input type="checkbox"/> unknown	Date of last administration Day Month Year <input type="checkbox"/> Continuing at end of study
1.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study
2.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study
3.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study
4.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Randomization	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
Date of Randomization:	_____/_____/_____ day month year
Patient is randomized to	<input type="checkbox"/> arm 1 (6.0 GBq per Radioligand therapy) <input type="checkbox"/> arm 2 (7.4 GBq per Radioligand therapy)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
Date of 1. RLT:	_____ / _____ / _____ day month year
• 12 lead ECG Before Injection	
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
Heart rate	_____ b/min
RR interval	_____ msec
QT interval	_____ msec

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• Salivary protection (30 min before injection and continued for 4 hours)	
Applying ice pack	<input type="checkbox"/> done <input type="checkbox"/> not done, provide comment _____
• Vital Signs Before Injection (within 20 min before injection)	
Temperature	_____ . ____ °C
Heart Rate	_____ 1/min
Respiratory Rate	_____ 1/min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg
Pulse Oximetry	_____ %
• 1. RLT	
Activity in syringe before injection	_____ .____ GBq
Date and time of start of measurement	_____ /_____ /_____ - _____ :_____ day month year hr min
Injected activity	_____ .____ GBq
Date and time of RLT	_____ /_____ /_____ - _____ :_____ day month year hr min
Activity in syringe after injection	_____ .____ GBq
Date and time of end of measurement	_____ /_____ /_____ - _____ :_____ day month year hr min
Completed as planned	<input type="checkbox"/> yes <input type="checkbox"/> no, specify _____
Any adverse event	<input type="checkbox"/> yes, complete AE page <input type="checkbox"/> no

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• Vital Signs After Injection	
Time	_____ : _____ hh min
Temperature	_____ . _____ °C
Heart Rate	_____ 1/min
Respiratory Rate	_____ 1/min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg
Pulse Oximetry	_____ %

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• ECG after injection	
Date and time of ECG	____/____/____ ____:____ Day Month Year hrs : min
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below _____
Comment	_____
Heart rate	____/____/____ 1/min
RR interval	____/____/____ msec
QT interval	____/____/____ msec

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• 12 lead ECG 4 hours after Injection	
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below _____
Comment	_____
Heart rate	_____ 1/min
RR interval	_____ msec
QT interval	_____ msec

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit						
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____					
• Dosimetry: Blood Samples						
With regard to injection site, was the blood draw performed			<input type="checkbox"/> X contralateral <input type="checkbox"/> X ipsilateral, different i.v. access <input type="checkbox"/> X ipsilateral, same i.v. access			
5 min	<input type="checkbox"/> sample obtained, specify exact time post $^{177}\text{LuPSMA}$ injection _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not obtained
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not measured
	Volume measured: _____ mL					
	Activity measured: _____ kBq					
30 min	<input type="checkbox"/> sample obtained specify exact time (post inj) _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not obtained
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not measured
	Volume measured: _____ mL					
	Activity measured: _____ kBq					
1 h	<input type="checkbox"/> sample obtained specify exact time (post inj) _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not obtained
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) _____ _____ _____ : _____ Day Month Year hrs : min					<input type="checkbox"/> not measured
	Volume measured: _____ mL					
	Activity measured: _____ kBq					

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
4 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____/_____/_____ Day Month Year hrs : min <input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____/_____/_____ Day Month Year hrs : min Volume measured: _____ mL Activity measured: _____ kBq
18-30 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____/_____/_____ Day Month Year hrs : min <input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____/_____/_____ Day Month Year hrs : min Volume measured: _____ mL Activity measured: _____ kBq
42-54 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____/_____/_____ Day Month Year hrs : min <input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____/_____/_____ Day Month Year hrs : min Volume measured: _____ mL Activity measured: _____ kBq
66-78 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____/_____/_____ Day Month Year hrs : min

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit					
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____				
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured ____/____/____ ____:____ Day Month Year hrs : min				
	Volume measured: _____ mL Activity measured: _____ kBq				
7-9 d	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained ____/____/____ ____:____ Day Month Year hrs : min				
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured ____/____/____ ____:____ Day Month Year hrs : min				
Volume measured: _____ mL Activity measured: _____ kBq					

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• Dosimetry: Scintigraphy	
4 h	<p><input type="checkbox"/> whole body planar obtained, specify exact time <input type="checkbox"/> not obtained</p> <p>_____ : _____ hh min</p> <p>Scan duration _____ min</p>
18-30 h	<p>date: ____ / ____ / ____ Day Month Year hrs : min</p> <p>whole body planar: <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____ : _____ hrs : min Scan duration _____ min</p> <p>SPECT/CT head <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____ : _____ hrs : min Duration per angle _____ min</p> <p>SPECT/CT thorax <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____ : _____ hrs : min Duration per angle _____ min</p> <p>SPECT/CT abd. <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____ : _____ hrs : min Duration per angle _____ min</p>
42-54 h	<p><input checked="" type="checkbox"/> whole body planar obtained, specify date/time <input type="checkbox"/> not obtained</p> <p>____ / ____ / ____ Day Month Year hrs : min</p> <p>Scan duration _____ min</p>

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit			
Study short title RESIST-PC	Patient No.+ Initials - -		
66-78 h	<input type="checkbox"/> whole body planar obtained, specify date/time <input type="checkbox"/> not obtained / / : Day Month Year hrs : min Scan duration min		
7-9 d	<input type="checkbox"/> whole body planar obtained, specify date/time <input type="checkbox"/> not obtained / / : Day Month Year hrs : min Scan duration min		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

1. Radioligand Therapy (RLT) – Injection Visit	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• Dosimetry: Urine Collection	
collected from injection until 4 h p.i.	<input type="checkbox"/> done <input type="checkbox"/> not done, specify Volume measured: _____ mL Activity measured: _____ . _____ MBq
collected from 4 h until discharge	<input type="checkbox"/> done <input type="checkbox"/> not done, specify date and time of discharge: _____/_____/_____ Day Month Year ____:_____ hrs : min Volume measured: _____ mL Activity measured: _____ . _____ MBq

PSMA-directed endoRadiotherEapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)						
Study short title	Patient No.+ Initials					
RESIST-PC	[REDACTED] - [REDACTED] - [REDACTED]					
• Laboratory						
Date of Assessment:	[REDACTED]	[REDACTED]	[REDACTED]	day	month	year
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	[REDACTED]	Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	[REDACTED]	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	[REDACTED]	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	[REDACTED]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	[REDACTED]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	[REDACTED]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	[REDACTED]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	[REDACTED]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	[REDACTED]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	[REDACTED]			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	[REDACTED]			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	[REDACTED]			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	[REDACTED]			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
CRP	[REDACTED]			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	[REDACTED]	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	[REDACTED]	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	[REDACTED]	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	[REDACTED]	µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	[REDACTED]	g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	[REDACTED]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)							
Study short title	Patient No.+ Initials						
RESIST-PC	[REDACTED] - [REDACTED] - [REDACTED]						
creatinine	[REDACTED]	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
eGFR	[REDACTED]	mL/min		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
sodium	[REDACTED]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
potassium	[REDACTED]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
chloride	[REDACTED]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)		
Study short title	Patient identifier	
RESIST-PC	_____ - _____ - _____	
• PSA measurement		
Date of Assessment:	_____/_____/_____	
	day	month
	year	
_____.	_____	_____
<u>unit:</u>		
<input type="checkbox"/> ng/mL		
<input type="checkbox"/> if other unit, specify:		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit	
Study short title	Patient No.+ Initials
RESIST-PC	_____ - _____ - _____
• Study drug administration complications	
Has any complication related to administration of the drug occurred (e.g., overdose, observable extravasation, medication error)?	<input type="checkbox"/> no <input type="checkbox"/> yes, please specify: _____
<input type="checkbox"/> Report was sent to the pharmacovigilance designee.	

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see page 94-99 in the protocol version amendment 2 from 7 Jun 2017)
- Baseline and follow –Up Questionnaire for Pain and Adverse Events (see page 92-93 in the protocol version amendment 2 from 7 Jun 2017)
- Patient diary
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

12 weeks PSA measurement		
Study short title	Patient identifier	
RESIST-PC	- -	
• PSA measurement		
Date of Assessment:	/ /	day month year
.		
<u>unit:</u> <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____		

• ECOG													
Date of Assessment:	/ / day month year												
ECOG performance status	<table><tr><td> </td><td></td></tr><tr><td>0</td><td>Fully active, able to carry on all pre-disease performance without restriction</td></tr><tr><td>1</td><td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work</td></tr><tr><td>2</td><td>Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours</td></tr><tr><td>3</td><td>Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours</td></tr><tr><td>4</td><td>Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair</td></tr></table>			0	Fully active, able to carry on all pre-disease performance without restriction	1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours	3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours	4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
0	Fully active, able to carry on all pre-disease performance without restriction												
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work												
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours												
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours												
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair												

At week 12 also to be completed:

- Lab values (CBC, CMP)
- Imaging questionnaires
- EPIC-26

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Additional evaluation of blood tests every 2 weeks (not cycle 1-4 and not Follow-up)						
Study short title		Patient No.+ Initials				
RESIST-PC		- -				
• Laboratory						
Date of Assessment:		/ / day month year				
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC		Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC		Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets		Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin		mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit				<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV				<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH				<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW				<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
CRP				<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST		μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT		μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase		μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin		μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin		g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN		mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Additional evaluation of blood tests every 2 weeks (not cycle 1-4 and not Follow-up)						
Study short title	Patient No.+ Initials					
RESIST-PC	_____ - _____ - _____					
creatinine	_____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eGFR	_____	mL/min		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

Additional PSA measurements						
Study short title	Patient identifier					
RESIST-PC	_____ - _____ - _____					
• PSA measurement						
Date of Assessment:	_____	/	_____	/	_____	
	day	month		year		
_____ . _____						
unit:						
<input type="checkbox"/> ng/mL						
<input type="checkbox"/> if other unit, specify:						

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)			
Study short title	Patient No.+ Initials		
RESIST-PC	_____ - _____ - _____		
• Physical Examination			
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done		
Date Physical Examination:	day	month	year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal		
Comments: General Appearance	_____		
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____		
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Cardiovascular	_____		
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Respiratory	_____		
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Gastrointestinal	_____		
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Musculoskeletal	_____		
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Genitourinary	_____		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)			
Study short title	Patient No.+ Initials		
RESIST-PC	- -		
Skin	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments: Skin	_____		
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments Neurological	_____		
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments	_____		

• ECOG			
Date of Assessment:	/ / day month year		
ECOG performance status		<ul style="list-style-type: none">0 Fully active, able to carry on all pre-disease performance without restriction1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)	
Study short title	Patient No.+ Initials
RESIST-PC	____ - ____ - ____
Date of RLT:	____ / ____ / ____ day month year
• 12 lead ECG Before Injection	
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
heart rate	____ 1/min
RR interval	____ msec
QT interval	____ msec

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)				
Study short title	Patient No.+ Initials			
RESIST-PC	- -			
• ECG before injection				
date and time of ECG	 Day Month Year hrs : min			
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below			
Comment				
heart rate	1/min			
RR interval	msec			
QT interval	msec			

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• Salivary protection (30 min before injection and continued for 4 hours)	
Applying ice pack	<input type="checkbox"/> done <input type="checkbox"/> not done, provide comment _____
• Vital Signs Before Injection (within 20 min before injection)	
Temperature	_____ . ____ °C
Heart Rate	_____ 1/min
Respiratory Rate	_____ 1/min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg
Pulse Oximetry	_____ %
• RLT	
activity in syringe before injection	_____ . _____ GBq
Date and time of measurement	_____ / _____ / _____ - _____ : _____ day month year hrs min
injected activity	_____ . _____ GBq
date and time of RLT	_____ / _____ / _____ - _____ : _____ day month year hrs min
activity in syringe after injection	_____ . _____ GBq
Date and time of measurement	_____ / _____ / _____ - _____ : _____ day month year hrs min
completed as planned	<input type="checkbox"/> yes <input type="checkbox"/> no, specify _____
any adverse event	<input type="checkbox"/> yes, complete AE page <input type="checkbox"/> no

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

• Vital Signs After Injection	
time	____:____ hh min
Temperature	_____.____ °C
Heart Rate	____ 1/min
Respiratory Rate	____ 1/min
Blood Pressure Systolic	____ mmHg
Blood Pressure Diastolic	____ mm Hg
Pulse Oximetry	____ %

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)				
Study short title	Patient No.+ Initials			
RESIST-PC	- -			
• ECG after injection				
date and time of ECG	 Day Month Year hrs : min			
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below			
Comment				
heart rate	1/min			
RR interval	msec			
QT interval	msec			

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (2-4)	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• 12 lead ECG 4 hours after Injection	
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below _____
Comment	_____
heart rate	_____ /min
RR interval	_____ msec
QT interval	_____ msec

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see page 94-99 in the protocol version amendment 2 from 7 Jun 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see page 92-93 in the protocol version amendment 2 from 7 Jun 2017)
- Patient diary
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up		
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____	
• Physical Examination		
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done	
Date Physical Examination:	_____/_____/_____	day month year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal	
Comments: General Appearance	_____	
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____	
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Cardiovascular	_____	
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Respiratory	_____	
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Gastrointestinal	_____	
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Musculoskeletal	_____	
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Genitourinary	_____	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up		
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____	
Skin	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
Comments: Skin	_____	
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
Comments Neurological	_____	
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
Comments	_____	

• Vital Signs		
Temperature	____ .____ °C	
Heart Rate	____ 1/min	
Respiratory Rate	____ 1/min	
Blood Pressure Systolic	_____ mmHg	
Blood Pressure Diastolic	_____ mm Hg	
Pulse Oximetry	____ %	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up		
Study short title RESIST-PC	Patient No.+ Initials [] - [] - []	
• ECOG		
Date of Assessment:	[] / [] / [] day month year	
ECOG performance status	[] 0 Fully active, able to carry on all pre-disease performance without restriction 1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work 2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours 3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours 4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

•Follow up						
Study short title RESIST-PC		Patient No.+ Initials. _____ - _____ - _____				
•Laboratory						
Date of Assessment: _____ /_____ /_____ day month year						
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	_____	Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	_____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	_____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
CRP	_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	_____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	_____	g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

creatinine	_____	µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eGFR	_____	mL/min		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow up			
Study short title RESIST-PC	Patient identifier _____ - _____ - _____		
• PSA measurement			
Date of Assessment: _____._____._____	day	month	year
<u>unit:</u> <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____			

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FINAL 1.1 (22 August 2017)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

•Follow up		
Study short title RESIST-PC	Patient No.+ Initials. ____ - ____ - ____	
Imaging		
CT (repeatable event) Tumor location Location of metastases	____ / ____ / ____ day month year	
MRI (repeatable event)	____ / ____ / ____ day month year	
PET/CT (repeatable event)	____ / ____ / ____ day month year	
Scintigraphy (repeatable event)	____ / ____ / ____ day month year	
other, specify: _____	____ / ____ / ____ day month year	
Imaging result:	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD	

Please make sure all additional questionnaires are completed by the patient as applicable:

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- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see page 92-93 in the protocol version amendment 2 from 7 Jun 2017)
- Patient diary
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

End of study	
Study short title RESIST-PC	Patient No.+ Initials. [] - [] - []
Study course	<input type="checkbox"/> Patient completed study if study course completed, last day on study: [] / [] / [] Day Month Year reason : <input type="checkbox"/> Progression <input type="checkbox"/> Follow-up completed <input type="checkbox"/> Death <input type="checkbox"/> Patient withdrew from study
If withdrawn, give date and time of withdrawal (24 h clock):	[] / [] / [] [] : [] Day Month Year hr min
Specify main reason	<input type="checkbox"/> Withdrawal of consent <input type="checkbox"/> Lost to Follow-up <input type="checkbox"/> Any occurrence of conditions which prevented the patient's participation in the study? Please specify: <input type="checkbox"/> Protocol deviations? Please specify: <input type="checkbox"/> (Serious) AE? Please specify: <input type="checkbox"/> Administrative reasons? Please, specify: <input type="checkbox"/> Other? Please specify:
Who decided the withdrawal?	<input type="checkbox"/> Patient <input type="checkbox"/> Investigator <input type="checkbox"/> Other, please specify:

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Adverse Events		
Study short title RESIST-PC	Patient No.+ Initials. _____ - _____ - _____	
• Adverse Events (Note: Adverse Event is any untoward medical occurrence in a volunteer or clinical investigation subject administered a pharmaceutical product and which does Not necessarily have a causal relationship with this treatment An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medical product)		
Any AE experienced?	<input type="checkbox"/> No	<input type="checkbox"/> If yes, please specify details on this form
Adverse event description		
Onset date and time if available	_____ _____ _____ / _____ _____ _____ - _____ : ____ Day Month Year hrs min	
Serious AE?	<input type="checkbox"/> No	<input type="checkbox"/> Yes, please complete also the SAE form
Maximum intensity:	<input type="checkbox"/> mild (easily tolerated) <input type="checkbox"/> moderate (interferes with usual functions) <input type="checkbox"/> severe (incapacitating)	
Specific drug treatment of AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify on "concomitant medication" page	
Specific Non-drug treatment of AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify.	
Relationship to study drug / study conduct	<u>Study drug relationship:</u> <input type="checkbox"/> None <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite	<u>Study conduct:</u> <input type="checkbox"/> None <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite
Outcome / status	<input type="checkbox"/> Recovered / resolved without sequelae <input type="checkbox"/> Recovered / resolved with sequelae, specify <input type="checkbox"/> Not recovered / Not resolved <input type="checkbox"/> Death / Fatal <input type="checkbox"/> Unknown	
Study drug action	<input type="checkbox"/> Drug withdrawn <input type="checkbox"/> Dose not changed	<input type="checkbox"/> Dose reduced <input type="checkbox"/> Other action: _____
Date and time if available (24 h clock) AE ended (only if recovered / resolved)	<input type="checkbox"/> ongoing at end of study _____ _____ _____ / _____ _____ _____ - _____ : ____ Day Month Year hr min	
<input type="checkbox"/> Tick box if this page is the last adverse event		

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Case Report Form

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC). A phase II clinical trial.

Phase II

Version 1.2

Sponsor

Ebrahim S. Delpassand, M.D. F.A.C.N.M
Johannes Czernin, M.D.

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier Site _____ - Initials _____ - Subject no. _____	
• Informed consent		
The patient has been informed about the aims, rationale and procedures of the RESIST-PC trial and he/she has voluntarily agreed to participate and given		
<input type="checkbox"/> written informed consent.		
A copy of the patient information has been handed out to the patient.		
Date of informed consent:		
_____ Day	_____ Month	_____ Year

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Inclusion / Exclusion criteria		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• Inclusion criteria		
1. Prostate cancer proven by histopathology	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Unresectable metastases	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Castration resistant disease with confirmed testosterone level \leq 50 ng/ml under prior androgen deprivation therapy (ADT)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy or any equivalent PSMA-directed imaging	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. ECOG 0-2	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Sufficient bone marrow capacity as defined by WBC \geq 2.500/ μl , PLT count \geq 100.000/ μl , Hb \geq 9.9 g/dl and ANC \geq 1500 mm 3 for the first cycle and WBC \geq 2.000/ μl , PLT count \geq 75.000/ μl , Hb \geq 8.9 g/dl and ANC \geq 1000 mm 3 for the subsequent cycles	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Signing Informed Consent Form	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Patients enrolling in this trial should have received either Enzalutamide or Abiraterone	<input type="checkbox"/> Yes	<input type="checkbox"/> No
NOTE: If any inclusion criterion is answered "No", the patient is NOT eligible to enter the study!		
• Exclusion criteria		
1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm) or other radionuclide therapy	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Glomerular Filtration Rate (GFR) $<$ 40 ml/min	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Serum creatinine $>$ 1.5xULN	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. AST and ALT $>$ 5xULN	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Urinary tract obstruction or marked hydronephrosis	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Diffuse bone marrow involvement confirmed by super-scans	<input type="checkbox"/> Yes	<input type="checkbox"/> No
NOTE: If any exclusion criterion is answered "Yes", the patient is NOT eligible to enter the study!		

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
• Demographic Data	
Date of Assessment:	_____ / _____ / _____ day month year
Date of Birth	_____ / _____ / _____ day month year
Do you consider yourself Hispanic/Latino or not Hispanic/Latino?	<input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> Not Hispanic or Latino <input type="checkbox"/> Unknown <input type="checkbox"/> Not reported
Which of the following five racial designations best describes you? More than one choice is acceptable. (If mixed race, please check race of each parent)	<input type="checkbox"/> American Indian or Alaska Native <input type="checkbox"/> Asian <input type="checkbox"/> Black or African American <input type="checkbox"/> Native Hawaiian or Other Pacific Islander <input type="checkbox"/> White <input type="checkbox"/> other:

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier	_____ - _____ - _____
• Anthropometric Measurements – Vital Signs		
Height	____ .____	Unit: <input type="checkbox"/> inch <input type="checkbox"/> cm
Weight	____ .____	Unit: <input type="checkbox"/> lbs <input type="checkbox"/> kg
Temperature	____ .____ °C	
Heart Rate	____ /min	
Respiratory Rate	____ /min	
Blood Pressure Systolic	____ mmHg	
Blood Pressure Diastolic	____ mm Hg	
Pulse Oximetry	____ %	

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline			
Study short title RESIST-PC	Patient identifier _____ - _____ - _____		
• Physical Examination			
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done, if not done provide comment _____		
Date Physical Examination	_____ / _____ / _____	day	month year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal		
Comments: General Appearance	_____		
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____		
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Cardiovascular	_____		
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Respiratory	_____		
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Gastrointestinal	_____		
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Musculoskeletal	_____		
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Genitourinary	_____		
Skin	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		

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PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
Comments: Skin	_____	
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
Comments Neurological	_____	
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal

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FINAL 1.2 (25 September 2017)

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
• Prostate Cancer History	
Histopathology reports available	<input type="checkbox"/> yes <input type="checkbox"/> no, please comment: _____
N.B.: Histopathologically confirmed prostate cancer is an inclusion criterion	
Date of histopathology report / biopsy	_____ / _____ / _____ day month year
Type of prostate cancer tumor	<input type="checkbox"/> adenocarcinoma <input type="checkbox"/> other: _____
PSA at initial diagnosis:	date of determination _____ / _____ / _____ day month year result _____ . _____ <input type="checkbox"/> not done unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Gleason Score (preferred format X+Y=Z; Biopsy or Prostatectomy)	_____ + _____ = _____ <input type="checkbox"/> biopsy <input type="checkbox"/> prostatectomy
TNM at initial diagnosis	T _____ N _____ M ____

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
Last three PSA values:	
Date 1: _____ / _____ / _____ day month year	PSA: _____ . unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Date 2: _____ / _____ / _____ day month year	PSA: _____ . unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Date 3: _____ / _____ / _____ day month year	PSA: _____ . unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Change of therapy between date #1 to #3	<input type="checkbox"/> Yes, please document all therapies on prostate cancer treatment history section <input type="checkbox"/> No
Documented PSA value doubling time:	_____ days
Current TNM (at study inclusion)	T ____ N ____ M ____

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
• Prostate Cancer Treatment History: Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section			<input type="checkbox"/> yes, please complete below	
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> CR (Complete response) <input type="checkbox"/> PR partial response <input type="checkbox"/> SD stable disease <input type="checkbox"/> PD progressive disease <input type="checkbox"/> missing
2	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title		Patient identifier				
RESIST-PC		[REDACTED]				
• Prostate Cancer Treatment History: Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	[REDACTED] OR [REDACTED]. [REDACTED]	Gy mCi	<input type="checkbox"/> Unknown [REDACTED] Day Month Year	<input type="checkbox"/> Unknown [REDACTED] Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
2	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	[REDACTED] OR [REDACTED]. [REDACTED]	Gy mCi	<input type="checkbox"/> Unknown [REDACTED] Day Month Year	<input type="checkbox"/> Unknown [REDACTED] Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
3

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline					
Study short title		Patient identifier			
RESIST-PC		- -			
• Prostate Cancer Treatment History: Other Treatment					
Any other treatment?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below	
#	Therapy	Comments	started	ended	best response
1	<input type="checkbox"/> prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing
2	<input type="checkbox"/> prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> standard ADT		<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing

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 FINAL 1.2 (25 September 2017)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline					
Study short title	Patient identifier				
RESIST-PC	- -				
	<input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: _____				
3

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
Imaging within the past three months CT (repeatable event)	Date of imaging _____ / _____ / _____ day month year	
MRI (repeatable event)	_____ / _____ / _____ day month year	
PET/CT ⁶⁸ Ga-PSMA (repeatable event)	_____ / _____ / _____ day month year	
SPECT/CT ¹¹³ Lu-PSMA	_____ / _____ / _____ day month year	
BONE SCAN (repeatable event)	_____ / _____ / _____ day month year tracer: _____	
other, specify: _____	_____ / _____ / _____ day month year	
RENAL SCAN (OPTIONAL) ADD IN	_____ / _____ / _____ day month year Result: _____	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• Medical History		
Date of Assessment:	_____ / _____ / _____ day month year	
Any relevant medical history?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify below:	
Condition / Illness	Started	Ended
1.	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year
2.	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year
3.	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year
4.	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year
5.	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year
6.	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year
7.	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year
8.	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year	<input type="checkbox"/> Unknown _____ / _____ / _____ Day Month Year

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier ____ - ____ - ____	
• Baseline findings		
Note: Please list below all conditions which started before the patient signed the informed consent form and for which symptoms or treatment were recorded during the time between signature of informed consent and first administration of the study drug, including conditions which were stabilized by treatment.		
Conditions present before study drug administration are to be documented as Baseline Findings ; conditions which started or deteriorated after administration of the study drug will be documented as Adverse Events on a specific AE page of the CRF.		
Date of Assessment:	____/____/____	day month year
Any relevant baseline findings?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify below:	
Hypersensitivity assessment		
Known allergies:	<input type="checkbox"/> no <input type="checkbox"/> yes, specify below_____	
Abnormal findings / symptoms / diseases		Started
1.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
2.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
3.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
4.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
5.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
6.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
7.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title	Patient identifier	____ - ____ - ____
RESIST-PC		
• ECOG		
Date of Assessment:	____ / ____ / ____ day month year	
ECOG performance status	____ 0 Fully active, able to carry on all pre-disease performance without restriction 1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work 2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours 3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours 4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline							
Study short title		Patient identifier					
RESIST-PC		_____ - _____ - _____					
Laboratory							
	Date of Assessment:		_____ / _____ / _____	day month year			
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant	
RBC	_____.	Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
WBC	_____.	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
platelets	_____.	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
neutrophils	_____.	absolute #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
lymphocytes	_____.	absolute #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
monocytes	_____.	absolute #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
eosinophils	_____.	absolute #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
basophils	_____.	absolute #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
hemoglobin	_____.	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
hematocrit	_____.			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
MCV	_____.			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
MCH	_____.			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
RDW	_____.			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
SGOT / AST	_____.	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
SGPT / ALT	_____.	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
alk. phosphatase	_____.	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
total bilirubin	_____.	µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
total albumin	_____.	g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
BUN	_____.	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

creatinine	_____	µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR	_____	mL/min/1, 73m ²		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier [] - [] - []	
• PSA measurement		
Date of Assessment: [] . [] unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____	[]	[] / [] / [] day month year

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline			
Study short title RESIST-PC	Patient No.+ Initials ____ - ____ - ____		
• Imaging			
Date and time of imaging	____/____/____/____/____ : ____ Day Month Year hrs : min		
Ga-68 PSMA PET/CT or Lu-177 PSMA scintigraphy or equivalent result	<input type="checkbox"/> positive (tumor lesions visible) <input type="checkbox"/> negative (no tumor lesion visible)		
Mean PSMA expression of lesions by visual assessment:	Score	Reported PSMA expression	Uptake
	<input type="checkbox"/> 0	no	Below bloodpool
	<input type="checkbox"/> +	low	Equal to or above bloodpool and lower than liver
	<input type="checkbox"/> ++	intermediate	Equal to or above liver and lower than salivary glands
	<input type="checkbox"/> +++	high	Equal to or above salivary glands

Please make sure all additional questionnaires are completed by the patient as applicable

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Concomitant Medication							
Study short title RESIST-PC		Patient No.+ Initials [] - [] - []					
Any medication taken between 28 days before inclusion and "end of study"?					<input type="checkbox"/> No	<input type="checkbox"/> Yes, please specify details below	
Generic name (Brand name for combination drugs)	Indication	Total daily dose	Dose unit	Regimen 1 = PRN, 2 daily, 3 = once, 4 = QD, 5 = BID, 6 = TID, 7 = Q6H, 8 = Q8H, 9 = Q12H, 10 QHS, 11 infusion, 12 continuous infusion, 13 other, specify	Route 1 = oral, 2 = s.c., 3 = i.m., 4 = IV, 5 = inhalation, 6 = topical, 7 = transdermal, 8 rectal, 9 = other, specify	Date of first administration [] Day [] Month [] Year <input type="checkbox"/> unknown	Date of last administration [] Day [] Month [] Year <input type="checkbox"/> Continuing at end of study
1.				[]	[]	[] Day [] Month [] Year <input type="checkbox"/> unknown	[] Day [] Month [] Year <input type="checkbox"/> Continuing at end of study
2.				[]	[]	[] Day [] Month [] Year <input type="checkbox"/> unknown	[] Day [] Month [] Year <input type="checkbox"/> Continuing at end of study
3.				[]	[]	[] Day [] Month [] Year <input type="checkbox"/> unknown	[] Day [] Month [] Year <input type="checkbox"/> Continuing at end of study
4.				[]	[]	[] Day [] Month [] Year <input type="checkbox"/> unknown	[] Day [] Month [] Year <input type="checkbox"/> Continuing at end of study

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Randomization		
Study short title	Patient No.+ Initials	
RESIST-PC	_____ - _____ - _____	
Date of Randomization:	_____ / _____ / _____ day month year	
Patient is randomized to	<input type="checkbox"/> arm 1 (6.0 GBq per Radioligand therapy) corresponds to 162 mCi <input type="checkbox"/> arm 2 (7.4 GBq per Radioligand therapy)) corresponds to 200 mCi	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry	
Study short title	Patient No.+ Initials
RESIST-PC	____ - ____ - ____
Date of RLT:	____ / ____ / ____ day month year
Cycle for dosimetry	<input type="checkbox"/> Cycle 1 <input type="checkbox"/> Cycle 2
• 12 lead ECG Before Injection	
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
Heart rate	____ /min
QRS interval	____ msec
QT interval	____ msec
QTc interval	____ msec

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry						
Study short title	Patient No.+ Initials					
RESIST-PC	_____ - _____ - _____					
• Laboratory						
Date of Assessment:		day	month	year		
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	_____ .____	Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	_____ .____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	_____ .____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	_____ .____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	_____ .____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	_____ .____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	_____ .____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	_____ .____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	_____ .____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	_____ .____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	_____ .____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	_____ .____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	_____ .____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	_____ .____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	_____ .____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	_____ .____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	_____ .____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	_____ .____	g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry						
Study short title	Patient No.+ Initials					
RESIST-PC	_____ - _____ - _____					
BUN	_____ .____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine	_____ .____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR <input type="checkbox"/> eGFR <input type="checkbox"/> estimated from renal scan	_____ .____	mL/min/1, 73m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	_____ .____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____ .____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____ .____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

Radioligand Therapy (RLT) – Injection Visit including dosimetry						
Study short title	Patient No.+ Initials					
RESIST-PC	_____ - _____ - _____					
• Salivary protection (30 min before injection and continued for 4 hours)						
Applying ice pack	<input type="checkbox"/> done <input type="checkbox"/> not done, provide comment _____					
• Vital Signs Before Injection (within 20 min before injection)						
Temperature	_____ .____	°C	<input type="checkbox"/>	F		
Heart Rate	_____ /min					
Respiratory Rate	_____ /min					
Blood Pressure Systolic	_____ mmHg					
Blood Pressure Diastolic	_____ mm Hg					

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

• RLT					
Activity in syringe before injection	____ ._____ _____ mCi ____ / ____ / ____ - ____ : ____ day month year hr min				
Date and time of start of measurement					
Injected activity	____ ._____ _____ mCi ____ / ____ / ____ - ____ : ____ day month year hr min				
Date and time of RLT					
Activity in syringe after injection	____ ._____ _____ mCi ____ / ____ / ____ - ____ : ____ day month year hr min				
Date and time of end of measurement					
Completed as planned	<input type="checkbox"/> yes <input type="checkbox"/> no, specify _____				
Any adverse event	<input type="checkbox"/> yes, complete AE page <input type="checkbox"/> no				
• Vital Signs After Injection - 30 minutes post-infusion					
Time	____ . _____ hh min				
Temperature	____ ._____ °C <input type="checkbox"/> F				
Heart Rate	____ _____ /min				
Respiratory Rate	____ _____ /min				
Blood Pressure Systolic	____ _____ mmHg				
Blood Pressure Diastolic	____ _____ mm Hg				
• Vital Signs After Injection - 60 minutes post-infusion					
Time	____ . _____ hh min				
Temperature	____ ._____ °C <input type="checkbox"/> F				
Heart Rate	____ _____ /min				

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PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Respiratory Rate	_____ /min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____		
• Holter ECG monitor results for the period 20 prior to and 1 hour post-infusion			
Date and time of ECG	_____ / _____ / _____ _____ : _____ Day Month Year hrs : min		
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below		
Comment	_____		
Heart rate	_____ / min		
RR interval	_____ msec		
PR interval	_____ msec		
QRS interval	_____ msec		
QT interval	_____ msec		
QTc interval	_____ msec		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry	
Study short title	Patient No.+ Initials
RESIST-PC	____ - ____ - ____
• 12 lead ECG 4 hours after Injection	
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
Heart rate	____ /min
RR interval	____ msec
PR interval	____ msec
QRS interval	____ msec
QT interval	____ msec
QTc interval	____ msec

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry							
Study short title RESIST-PC		Patient No.+ Initials ____ - ____ - ____					
• Dosimetry: Blood Samples							
With regard to injection site, was the blood draw performed				<input type="checkbox"/> contralateral <input type="checkbox"/> ipsilateral, different i.v. access <input type="checkbox"/> (ipsilateral, same i.v. access)			
0 min	<input type="checkbox"/> sample obtained, specify exact time post ¹⁷⁷ LuPSMA injection <input type="checkbox"/> not obtained ____/____/____/____/____/____ ____:____ Day Month Year hrs : min						
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured ____/____/____/____/____/____ ____:____ Day Month Year hrs : min						
	Volume measured: ____/____/____/____/____ mL						
	Activity measured: ____/____/____ . ____/____/____ μCi/mL						
5 min	<input type="checkbox"/> sample obtained, specify exact time post ¹⁷⁷ LuPSMA injection <input type="checkbox"/> not obtained ____/____/____/____/____/____ ____:____ Day Month Year hrs : min						
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured ____/____/____/____/____/____ ____:____ Day Month Year hrs : min						
	Volume measured: ____/____/____/____/____ mL						
	Activity measured: ____/____/____ . ____/____/____ μCi/mL						
30 min	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained ____/____/____/____/____/____ ____:____ Day Month Year hrs : min						
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured ____/____/____/____/____/____ ____:____ Day Month Year hrs : min						

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry					
Study short title RESIST-PC		Patient No.+ Initials _____ - _____ - _____			
1 h	Volume measured: _____ mL				
	Activity measured: _____ . _____ μ Ci/mL				
	Measurement duration time: _____ min				
	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min				
<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min					
Volume measured: _____ mL					
Activity measured: _____ . _____ μ Ci/mL					
Measurement duration time: _____ min					
4 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min				
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min				
	Volume measured: _____ mL				
	Activity measured: _____ . _____ μ Ci/mL				
Measurement duration time: _____ min					
18-30 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min				
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min				
	Volume measured: _____ mL				

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry							
Study short title RESIST-PC		Patient No.+ Initials _____ - _____ - _____					
		Activity measured: _____ . _____ $\mu\text{Ci}/\text{mL}$					
		Measurement duration time: _____ min (10 min needed)					
42-54 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min						
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min						
	Volume measured: _____ mL Activity measured: _____ . _____ $\mu\text{Ci}/\text{mL}$ Measurement duration time: _____ min (10 min needed)						
66-78 h	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min						
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min						
	Volume measured: _____ mL Activity measured: _____ . _____ $\mu\text{Ci}/\text{mL}$ Measurement duration time: _____ min (10 min needed)						
7-9 d (optional)	<input type="checkbox"/> sample obtained specify exact time (post inj) <input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min						
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min						
	Volume measured: _____ mL						

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry	
Study short title	Patient No.+ Initials
RESIST-PC	_____ - _____ - _____
Activity measured:	_____ . _____ μ Ci/mL
Measurement duration time:	_____ min (10 min needed)

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry					
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____				
66-78 h	<input type="checkbox"/> whole body planar obtained, specify date/time <input type="checkbox"/> not obtained _____ / _____ / _____ / _____ _____ : _____ Day Month Year hrs : min Scan duration _____ min				
7-9 d (optional)	<input type="checkbox"/> whole body planar obtained, specify date/time <input type="checkbox"/> not obtained _____ / _____ / _____ / _____ _____ : _____ Day Month Year hrs : min Scan duration _____ min				

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry			
Study short title RESIST-PC	Patient Identifier _____ - _____ - _____		
• Dosimetry: Urine Collection			
collected from injection until 4 h p.i.	<input type="checkbox"/> done <input type="checkbox"/> not done, specify Urine net weight: _____ g date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min Volume measured: _____ mL Activity measured: _____ . _____ <input type="checkbox"/> μ Ci/mL <input type="checkbox"/> μ Ci/g Measurement duration time: _____ min		
collected from 4h-until discharge from hospital	<input type="checkbox"/> done <input type="checkbox"/> not done, specify date and time of discharge: _____ / _____ / _____ _____ : _____ Day Month Year hrs : min Urine net weight: _____ g Activity measured: _____ . _____ <input type="checkbox"/> μ Ci/mL <input type="checkbox"/> μ Ci/g Measurement duration time: _____ min		

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry		
Study short title	Patient identifier	
RESIST-PC	_____ - _____ - _____	
• PSA measurement (PSA is measured every 6 weeks during treatment+after treatment period every 3 months)		
Date of Assessment:	_____ / _____ / _____ day month year	
_____ . _____		
unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry - Concomitant cancer-related therapy since last visit						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown [] / [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] / [] Day Month Year	<input type="checkbox"/> CR (Complete response) <input type="checkbox"/> PR partial response <input type="checkbox"/> SD stable disease <input type="checkbox"/> PD progressive disease <input type="checkbox"/> missing
Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT	[]		<input type="checkbox"/> Unknown [] / [] / [] / []	<input type="checkbox"/> Unknown [] / [] / [] / []	<input type="checkbox"/> CR

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry - Concomitant cancer-related therapy since last visit											
Study short title		Patient identifier									
RESIST-PC		[] - [] - []									
	<input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	OR [.] [.] [.] [.] mCi	Gy	Day	Month	Year	Day	Month	Year	<input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing	
Other Treatment											
Any other treatment?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below							
#	Therapy	Comments	started	ended			best response				
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <hr/> <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown <hr/>	Day	Month	Year	<input type="checkbox"/> Unknown <hr/>	Day	Month	Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title	Patient No.+ Initials
RESIST-PC	____ - ____ - ____
• Study drug administration complications	
Has any complication related to administration of the drug occurred (e.g., overdose, observable extravasation, medication error)?	<input type="checkbox"/> no <input type="checkbox"/> yes, please specify: _____
<input type="checkbox"/> Report was sent to the pharmacovigilance designee.	

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

12 weeks PSA measurement		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• PSA measurement		
Date of Assessment: _____ . _____ . <small>unit:</small> <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____	_____ / _____ / _____ <small>day month year</small>	

• ECOG												
Date of Assessment: _____ / _____ / _____ <small>day month year</small>												
ECOG performance status _____	<table><tr><td>0</td><td>Fully active, able to carry on all pre-disease performance without restriction</td></tr><tr><td>1</td><td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work</td></tr><tr><td>2</td><td>Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours</td></tr><tr><td>3</td><td>Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours</td></tr><tr><td>4</td><td>Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair</td></tr></table>		0	Fully active, able to carry on all pre-disease performance without restriction	1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours	3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours	4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
0	Fully active, able to carry on all pre-disease performance without restriction											
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work											
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours											
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours											
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair											

At week 12 also to be completed:

- Lab values (CBC, CMP)
- Imaging questionnaires
- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Additional evaluation of blood tests every 2 weeks (not cycle 1-4 and not Follow-up)						
Study short title	Patient No.+ Initials					
RESIST-PC	_____ - _____ - _____					
• Laboratory						
Date of Assessment:			day	month	year	
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	_____ , ____	Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	_____ , ____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	_____ , ____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	_____ , ____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	_____ , ____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	_____ , ____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	_____ , ____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	_____ , ____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	_____ , ____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	_____ , ____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	_____ , ____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	_____ , ____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	_____ , ____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	_____ , ____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	_____ , ____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	_____ , ____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	_____ , ____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	_____ , ____	g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Additional evaluation of blood tests every 2 weeks (not cycle 1-4 and not Follow-up)						
Study short title	Patient No.+ Initials					
RESIST-PC	_____ - _____ - _____					
BUN	_____ .____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine	_____ .____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR <input type="checkbox"/> eGFR <input type="checkbox"/> estimated from renal scan	_____ .____	mL/min/1, 73m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	_____ .____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____ .____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____ .____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

Additional PSA measurements						
Study short title	Patient identifier					
RESIST-PC	_____ - _____ - _____					
• PSA measurement						
Date of Assessment:	_____ / _____ / _____ day month year					
_____ .____						
unit:						
<input type="checkbox"/> ng/mL						
<input type="checkbox"/> if other unit, specify: _____						

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____		
• Physical Examination			
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done		
Date Physical Examination:	_____ / _____ / _____ day month year		
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal		
Comments: General Appearance	_____		
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____		
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Cardiovascular	_____		
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Respiratory	_____		
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Gastrointestinal	_____		
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Musculoskeletal	_____		
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Genitourinary	_____		

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____		
Skin	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments: Skin	_____		
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments Neurological	_____		
Other, specify	_____		
	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments	_____		

• ECOG			
Date of Assessment:	_____ / _____ / _____ day month year		
ECOG performance status	_____	<ul style="list-style-type: none">0 Fully active, able to carry on all pre-disease performance without restriction1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Relevant imaging before new cycle		
Study short title RESIST-PC	Patient No.+ Initials. _____ - _____ - _____	
Imaging		
CT (repeatable event) Tumor location Location of metastases	_____ / _____ / _____ day month year	
MRI (repeatable event)	_____ / _____ / _____ day month year	
PET/CT (repeatable event)	_____ / _____ / _____ day month year	tracer: _____
Scintigraphy (repeatable event)	_____ / _____ / _____ day month year	tracer: _____
other, specify: _____	_____ / _____ / _____ day month year	
Imaging result:	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ _____ - _____ _____
Date of RLT: _____ / _____ / _____ day month year	
• 12 lead ECG Before Injection	
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
heart rate	_____ min
RR interval	_____ msec
PR interval	_____ msec
QRS interval	_____ msec
QT interval	_____ msec
QTc interval	_____ msec

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ _____ - _____ _____		
• ECG before injection			
date and time of ECG	_____ _____ _____ _____ _____ _____ Day Month Year hrs : min		
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below		
Comment	_____		
heart rate	_____ _____ _____ /min		
RR interval	_____ _____ msec		
PR interval	_____ _____ msec		
QRS interval	_____ _____ msec		
QT interval	_____ _____ msec		
QTc interval	_____ _____ msec		

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)								
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____							
• Salivary protection (30 min before injection and continued for 4 hours)								
Applying ice pack	<input type="checkbox"/> done <input type="checkbox"/> not done, provide comment _____							
• Vital Signs Before Injection (within 20 min before injection)								
Temperature	____ .____ °C		<input type="checkbox"/> F					
Heart Rate	____ /min							
Respiratory Rate	____ /min							
Blood Pressure Systolic	____ mmHg							
Blood Pressure Diastolic	____ mm Hg							
• RLT								
activity in syringe before injection	____ .. ____ mCi							
Date and time of measurement	____ / ____ / ____	-	____ : ____	day	month	year	hrs	min
injected activity	____ .. ____ mCi							
date and time of RLT	____ / ____ / ____	-	____ : ____	day	month	year	hrs	min
activity in syringe after injection	____ .. ____ mCi							
Date and time of measurement	____ / ____ / ____	-	____ : ____	day	month	year	hrs	min
completed as planned	<input type="checkbox"/> yes <input type="checkbox"/> no, specify _____							
any adverse event	<input type="checkbox"/> yes, complete AE page <input type="checkbox"/> no							

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

• Vital Signs After Injection - 30 minutes post-infusion	
time	1:11 hh : mm
Temperature	37.1 °C <input type="checkbox"/> F
Heart Rate	65/min
Respiratory Rate	16/min
Blood Pressure Systolic	120 mmHg
Blood Pressure Diastolic	70 mm Hg
• Vital Signs After Injection - 60 minutes post-infusion	
time	1:11 hh : mm
Temperature	37.1 °C <input type="checkbox"/> F
Heart Rate	65/min
Respiratory Rate	16/min
Blood Pressure Systolic	120 mmHg
Blood Pressure Diastolic	70 mm Hg

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ _____ - _____ _____		
• Holter ECG monitor results for the period 20 prior to and 1 hour post-infusion			
date and time of ECG	_____ _____ _____ _____ _____ _____ Day Month Year hrs : min		
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below		
Comment	_____		
heart rate	_____ _____ _____ /min		
RR interval	_____ _____ msec		
PR interval	_____ _____ msec		
QRS interval	_____ _____ msec		
QT interval	_____ _____ msec		
QTc interval	_____ _____ msec		

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit 1-4						
Study short title		Patient No.+ Initials				
RESIST-PC		_____ - _____ - _____				
• Laboratory						
Date of Assessment:		_____ / _____ / _____ day month year				
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	_____ , ____	Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	_____ , ____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	_____ , ____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	_____ , ____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	_____ , ____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	_____ , ____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	_____ , ____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	_____ , ____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	_____ , ____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	_____ , ____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	_____ , ____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	_____ , ____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	_____ , ____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	_____ , ____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	_____ , ____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	_____ , ____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	_____ , ____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	_____ , ____	g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit 1-4						
Study short title	Patient No.+ Initials					
RESIST-PC	_____ - _____ - _____					
BUN	_____ . ____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine	_____ . ____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR <input type="checkbox"/> eGFR <input type="checkbox"/> estimated from renal scan	_____ . ____	mL/min/1, 73m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	_____ . ____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____ . ____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____ . ____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

PSA measurements						
Study short title	Patient identifier					
RESIST-PC	_____ - _____ - _____					
• PSA measurement						
Date of Assessment:	_____ / _____ / _____	day	month	year		
_____ . _____						
unit: <input type="checkbox"/> ng/mL						
<input type="checkbox"/> if other unit, specify: _____						

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• 12 lead ECG 4 hours after Injection (after salivary protection is completed)	
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	
heart rate	_____ /min
RR interval	_____ msec
PR interval	_____ msec
QRS interval	_____ msec
QT interval	_____ msec
QTc interval	_____ msec

Scintigraphy	
optional	<input type="checkbox"/> whole body planar obtained, specify date/time <input type="checkbox"/> not obtained _____ / _____ / _____ / _____ _____ : _____ Day Month Year hrs : min Scan duration _____ min

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title	Patient No.+ Initials
RESIST-PC	_____ - _____ - _____
• Study drug administration complications	
Has any complication related to administration of the drug occurred (e.g., overdose, observable extravasation, medication error)?	<input type="checkbox"/> no <input type="checkbox"/> yes, please specify: _____
<input type="checkbox"/> Report was sent to the pharmacovigilance designee.	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit 1-4 - Concomitant cancer-related therapy since last visit						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown [] / [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] / [] Day Month Year	<input type="checkbox"/> CR (Complete response) <input type="checkbox"/> PR partial response <input type="checkbox"/> SD stable disease <input type="checkbox"/> PD progressive disease <input type="checkbox"/> missing
Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT	[]		<input type="checkbox"/> Unknown [] / [] / [] / []	<input type="checkbox"/> Unknown [] / [] / [] / []	<input type="checkbox"/> CR

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit 1-4 - Concomitant cancer-related therapy since last visit										
Study short title		Patient identifier								
RESIST-PC		[] - [] - []								
	<input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	OR [] . [] mCi	Gy	Day	Month	Year	Day	Month	Year	
				<input type="checkbox"/> PR	<input type="checkbox"/> SD	<input type="checkbox"/> PD	<input type="checkbox"/> missing			
Other Treatment										
Any other treatment?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below						
#	Therapy	Comments	started	ended			best response			
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <hr/> <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown <hr/>	Day	Month	Year	<input type="checkbox"/> Unknown <hr/>	Day	Month	Year

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow –Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ _____ - _____ _____		
• Physical Examination			
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done		
Date Physical Examination:	_____ _____ / _____ _____ / _____ _____ day month year		
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal		
Comments: General Appearance	_____		
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____		
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Cardiovascular	_____		
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Respiratory	_____		
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Gastrointestinal	_____		
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Musculoskeletal	_____		
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Genitourinary	_____		

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PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____		
Skin	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments: Skin	_____		
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments Neurological	_____		
Other, specify	_____		
	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments	_____		

• Vital Signs			
Temperature	____ .____ °C	<input type="checkbox"/> F	
Heart Rate	____ /min		
Respiratory Rate	____ /min		
Blood Pressure Systolic	____ mmHg		
Blood Pressure Diastolic	____ mm Hg		

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up		
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ _____ - _____ _____	
• ECOG		
Date of Assessment:	_____ / _____ / _____ day month year	
ECOG performance status	_____ 0 Fully active, able to carry on all pre-disease performance without restriction 1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work 2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours 3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours 4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

•Follow up						
Study short title RESIST-PC	Patient No.+ Initials. _____ - _____ - _____					
•Laboratory						
Date of Assessment: _____ / _____ / _____ day month year						
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	_____ ,_____	Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	_____ ,_____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	_____ ,_____	Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	_____ ,_____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	_____ ,_____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	_____ ,_____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	_____ ,_____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	_____ ,_____	absolut e #		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	_____ ,_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	_____ ,_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	_____ ,_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	_____ ,_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	_____ ,_____			<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	_____ ,_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	_____ ,_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	_____ ,_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	_____ ,_____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	_____ ,_____	g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

BUN	_____ . ____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine	_____ . ____	μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR <input type="checkbox"/> eGFR <input type="checkbox"/> estimated from renal scan	_____ . ____	mL/min/1, 73m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	_____ . ____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____ . ____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____ . ____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

End of treatment

Treatment was discontinued after 1 cycle due to the following conditions:

- PSA/radiographic progression at ≥12 weeks
- Completion of four RLT cycles
- 23 Gy kidney dose would be exceeded by the next cycle as estimated by dosimetry
- patient withdrawal (e.g. appearance of intolerable adverse events)

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow up		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• PSA measurement		
Date of Assessment: unit: <input type="checkbox"/> ng/mL	_____ / _____ / _____ day month year	
_____ . _____ <input type="checkbox"/> if other unit, specify: _____		

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PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

•Follow up		
Study short title RESIST-PC	Patient No.+ Initials. _____ - _____ - _____	
Imaging		
CT (repeatable event)	_____ / _____ / _____ day month year	
Tumor location Location of metastases		
MRI (repeatable event)	_____ / _____ / _____ day month year	
PET/CT (repeatable event)	_____ / _____ / _____ day month year tracer: _____	
Scintigraphy (repeatable event)	_____ / _____ / _____ day month year tracer: _____	
other, specify: _____	_____ / _____ / _____ day month year	
Imaging result:	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD	

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-up - Concomitant cancer-related therapy since last visit						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown [] / [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] / [] Day Month Year	<input type="checkbox"/> CR (Complete response) <input type="checkbox"/> PR partial response <input type="checkbox"/> SD stable disease <input type="checkbox"/> PD progressive disease <input type="checkbox"/> missing
Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT	[]		<input type="checkbox"/> Unknown [] / [] / [] / []	<input type="checkbox"/> Unknown [] / [] / [] / []	<input type="checkbox"/> CR

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-up - Concomitant cancer-related therapy since last visit											
Study short title		Patient identifier									
RESIST-PC		[] - [] - []									
	<input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	OR [] . [] mCi	Gy	Day	Month	Year	Day	Month	Year		
									<input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing		
Other Treatment											
Any other treatment?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below							
#	Therapy	Comments	started	ended			best response				
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <hr/> <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown <hr/>	Day	Month	Year	<input type="checkbox"/> Unknown <hr/>	Day	Month	Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow –Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

End of study	
Study short title RESIST-PC	Patient No.+ Initials. [] - [] - []
Study course	<input type="checkbox"/> Patient completed study if study course completed, last day on study: [] / [] / [] Day Month Year reason : <input type="checkbox"/> Progression <input type="checkbox"/> Follow-up completed <input type="checkbox"/> Death <input type="checkbox"/> Patient withdrew from study
If withdrawn, give date and time of withdrawal (24 h clock):	[] / [] / [] : [] : [] Day Month Year hr min
Specify main reason	<input type="checkbox"/> Withdrawal of consent <input type="checkbox"/> Lost to Follow-up <input type="checkbox"/> Any occurrence of conditions which prevented the patient's participation in the study? Please specify: <input type="checkbox"/> Protocol deviations? Please specify: <input type="checkbox"/> (Serious) AE? Please specify: <input type="checkbox"/> Administrative reasons? Please, specify: <input type="checkbox"/> Other? Please specify:
Who decided the withdrawal?	<input type="checkbox"/> Patient <input type="checkbox"/> Investigator <input type="checkbox"/> Other, please specify:

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Adverse Events		
Study short title RESIST-PC	Patient No.+ Initials. ____ - ____ - ____	
• Adverse Events <small>(Note: Adverse Event is any untoward medical occurrence in a volunteer or clinical investigation subject administered a pharmaceutical product and which does Not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medical product.)</small>		
Any AE experienced?	<input type="checkbox"/> No <input type="checkbox"/> If yes, please specify details on this form	
Adverse event description		
Onset date and time if available	____/____/____ - ____:____ Day Month Year hrs min	
Serious AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please complete also the SAE form	
Maximum intensity:	<input type="checkbox"/> mild (easily tolerated) <input type="checkbox"/> moderate (interferes with usual functions) <input type="checkbox"/> severe (incapacitating)	
Specific drug treatment of AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify on "concomitant medication" page	
Specific Non-drug treatment of AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify.	
Relationship to study drug / study conduct	Study drug relationship: <input type="checkbox"/> None <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite	Study conduct: <input type="checkbox"/> None <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite
Outcome / status	<input type="checkbox"/> Recovered / resolved without sequelae <input type="checkbox"/> Recovered / resolved with sequelae, specify <input type="checkbox"/> Not recovered / Not resolved <input type="checkbox"/> Death / Fatal <input type="checkbox"/> Unknown	
Study drug action	<input type="checkbox"/> Drug withdrawn <input type="checkbox"/> Dose reduced <input type="checkbox"/> Dose not changed <input type="checkbox"/> Other action: _____	
Date and time if available (24 h clock) AE ended (only if recovered / resolved)	<input type="checkbox"/> ongoing at end of study ____/____/____ - ____:____ Day Month Year hr min	
<input type="checkbox"/> Tick box if this page is the last adverse event		

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Serious Adverse Events	
Study short title RESIST-PC	Patient No.+ Initials. ____ - ____ - ____
This view opens when AE serious: "yes" is ticked Also an automatic email is sent to resist-pc@pharmtrace.com AND mali@excdiagnostics.com	
Seriousness criterion	
<input type="checkbox"/> Results in death (Date ____/____/____/ ____/____/____) <input type="checkbox"/> Life threatening <input type="checkbox"/> Hospitalization – initial or prolonged <input type="checkbox"/> Required intervention to prevent permanent impairment	<input type="checkbox"/> Congenital anomaly / birth defect <input type="checkbox"/> Persistent or significant disability/incapacity <input type="checkbox"/> Other serious (Important Medical Events)
Diagnosis	
Description / Symptoms including course of SAE and comments (continue description on additional pages, if required)	
Date of onset	____/____/____ day month year
Date ended (check ongoing box if not ended yet)	____/____/____ day month year <input type="checkbox"/> ongoing
Maximum intensity (CTCAE)	<input type="checkbox"/> 1 <input type="checkbox"/> 4 <input type="checkbox"/> 2 <input type="checkbox"/> 5 <input type="checkbox"/> 3 <input type="checkbox"/> unclassifiable
Study drug relationship ¹⁷⁷ Lu-PSMA-617	<input type="checkbox"/> none <input type="checkbox"/> unlikely <input type="checkbox"/> possible <input type="checkbox"/> probable <input type="checkbox"/> definite <input type="checkbox"/> unclassifiable
Study conduct relationship	<input type="checkbox"/> none <input type="checkbox"/> unlikely <input type="checkbox"/> possible <input type="checkbox"/> probable <input type="checkbox"/> definite <input type="checkbox"/> unclassifiable
Comment on assessment of study drug relationship	

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PSMA-directed endoRadioThErApy of castration-reSISTant Prostate Cancer (RESIST-PC)

Outcome of SAE								
<input type="checkbox"/> Recovered without sequelae <input type="checkbox"/> Recovered with sequelae <input type="checkbox"/> Recovering / resolving			<input type="checkbox"/> Not recovered / not resolved <input type="checkbox"/> Recovered / resolved with residual effects <input type="checkbox"/> Fatal					
Other possible causes of the event								
Check all that apply			Please specify					
<input type="checkbox"/> pre-existing / underlying disease								
<input type="checkbox"/> other treatment (concomitant or previous)								
<input type="checkbox"/> other (e.g. accident, new or intercurrent illness)								
Diagnostic tests and relevant lab values								
Test performed	Result			Normal Range		Date		
SAE Treatment								
Drug to treat SAE (brand name)	Active agent	Indication	total daily dose	dose unit	route	first admin date	last admin date	ongoing
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
Non-drug treatment: yes <input type="checkbox"/> no <input type="checkbox"/>								
If yes, please specify:								

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Study drug administration		
Study drug	<input type="checkbox"/> ¹⁷⁷ Lu-PSMA-617	<input type="checkbox"/> not injected
Administration date and time	____/____/____ - ____:____	day month year hr min
Injected activity MBq mCi		
Most relevant study drug action due to SAE (please check one box only)	<input type="checkbox"/> drug withdrawn <input type="checkbox"/> administration stopped early	<input type="checkbox"/> dose not changed <input type="checkbox"/> dose reduced <input type="checkbox"/> not applicable
Event abated after use/stopped or dose reduced	<input type="checkbox"/> Yes <input type="checkbox"/> Doesn't apply	<input type="checkbox"/> No
Event reappeared after reintroduction	<input type="checkbox"/> Yes <input type="checkbox"/> Doesn't apply	<input type="checkbox"/> No

PSMA-directed endoRadiotherapy of castration-resistant Prostate Cancer (RESIST-PC)

Concomitant medication at onset of SAE								
Medication (brand name)	Active agent	Indication	total daily dose	dose unit	route	first admin. date	last admin. date	ongoing
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
Medical history, including preexisting medical conditions								
Disease / symptoms (e.g. allergies, smoking and alcohol use, liver/kidney problems, etc.)						started	ended	ongoing
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>

Please fax additional pages to this report, if needed. Number of pages faxed: 1 none

Reporting Person	
Name	
Address	
Fax no.	
Phone no.	
E-Mail	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Case Report Form

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC). A phase II clinical trial.

Phase II

Version 1.3 (01 October 2017)

Sponsor

Ebrahim S. Delpassand, M.D. F.A.C.N.M
Johannes Czernin, M.D.

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FINAL 1.3 (01 October 2017)

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline				
Study short title RESIST-PC	Patient identifier [] - [] - []	Site	Initials	
• Informed consent				
The patient has been informed about the aims, rationale and procedures of the RESIST-PC trial and he/she has voluntarily agreed to participate and given				
<input type="checkbox"/> written informed consent.				
A copy of the patient information has been handed out to the patient.				
Date of informed consent:				
Day	/	Month	/	Year

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Inclusion / Exclusion criteria		
Study short title RESIST-PC	Patient identifier [] - [] - []	
• Inclusion criteria		
1. Prostate cancer proven by histopathology	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Unresectable metastases	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Castration resistant disease with confirmed testosterone level \leq 50 ng/ml under prior androgen deprivation therapy (ADT)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy or any equivalent PSMA-directed imaging	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. ECOG 0-2	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Sufficient bone marrow capacity as defined by WBC \geq 2.500/ μl , PLT count \geq 100.000/ μl , Hb \geq 9.9 g/dl and ANC \geq 1500 mm^3 for the first cycle and WBC \geq 2.000/ μl , PLT count \geq 75.000/ μl , Hb \geq 8.9 g/dl and ANC \geq 1000 mm^3 for the subsequent cycles	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Signing Informed Consent Form	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Patients enrolling in this trial should have received either Enzalutamide or Abiraterone	<input type="checkbox"/> Yes	<input type="checkbox"/> No
NOTE: If any inclusion criterion is answered "No", the patient is NOT eligible to enter the study!		
• Exclusion criteria		
1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm) or other radionuclide therapy	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Glomerular Filtration Rate (GFR) $<$ 40 ml/min	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Serum creatinine $>$ 1.5xULN	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. AST and ALT $>$ 5xULN	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Urinary tract obstruction or marked hydronephrosis	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Diffuse bone marrow involvement confirmed by super-scans	<input type="checkbox"/> Yes	<input type="checkbox"/> No
NOTE: If any exclusion criterion is answered "Yes", the patient is NOT eligible to enter the study!		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
• Demographic Data	
Date of Assessment:	_____/_____/_____ day month year
Date of Birth	_____/_____/_____ day month year
Do you consider yourself Hispanic/Latino or not Hispanic/Latino?	<input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> Not Hispanic or Latino <input type="checkbox"/> Unknown <input type="checkbox"/> Not reported
Which of the following five racial designations best describes you? More than one choice is acceptable. (If mixed race, please check race of each parent)	<input type="checkbox"/> American Indian or Alaska Native <input type="checkbox"/> Asian <input type="checkbox"/> Black or African American <input type="checkbox"/> Native Hawaiian or Other Pacific Islander <input type="checkbox"/> White <input type="checkbox"/> other:

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier [REDACTED] - [REDACTED] - [REDACTED]	
• Anthropometric Measurements – Vital Signs		
Height	[REDACTED].[REDACTED]	Unit: <input type="checkbox"/> inch <input checked="" type="checkbox"/> cm
Weight	[REDACTED].[REDACTED]	Unit: <input type="checkbox"/> lbs <input checked="" type="checkbox"/> kg
Temperature	[REDACTED].[REDACTED]	<input checked="" type="checkbox"/> °C <input type="checkbox"/> F
Heart Rate	[REDACTED]/min	
Respiratory Rate	[REDACTED]/min	
Blood Pressure Systolic	[REDACTED] mmHg	
Blood Pressure Diastolic	[REDACTED] mm Hg	
Pulse Oximetry	[REDACTED]%	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• Physical Examination		
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done, if not done provide comment _____	
Date Physical Examination	_____/_____/_____	day month year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal	
Comments: General Appearance	_____	
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____	
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Cardiovascular	_____	
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Respiratory	_____	
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Gastrointestinal	_____	
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Musculoskeletal	_____	
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Genitourinary	_____	
Skin	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier [] - [] - []	
Comments: Skin		
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
Comments Neurological		
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
	<input type="checkbox"/> not done	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

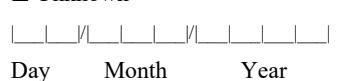
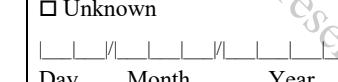
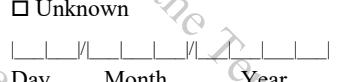
Baseline	
Study short title RESIST-PC	Patient identifier ____ - ____ - ____
• Prostate Cancer History	
Histopathology reports available	<input type="checkbox"/> yes <input type="checkbox"/> no, please comment: _____
N.B.: Histopathologically confirmed prostate cancer is an inclusion criterion	
Date of histopathology report/biopsy	____/____/____ day month year
Type of prostate cancer tumor	<input type="checkbox"/> adenocarcinoma <input type="checkbox"/> other: _____
PSA at initial diagnosis:	date of determination ____/____/____ day month year result _____._____ <u>unit:</u> <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____ <input type="checkbox"/> not done
Gleason Score (preferred format X+Y=Z; Biopsy or Prostatectomy)	____ + ____ = ____ <input type="checkbox"/> biopsy <input type="checkbox"/> prostatectomy
TNM at initial diagnosis	T ____ N ____ M ____

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

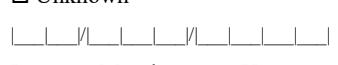
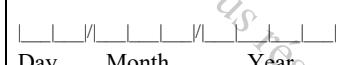
Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
Last three PSA values:	
Date 1: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Date 2: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Date 3: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Change of therapy between date #1 to #3	<input type="checkbox"/> Yes, please document all therapies on prostate cancer treatment history section <input type="checkbox"/> No
Documented PSA value doubling time:*	_____ days
Current TNM (at study inclusion)	T ____ N ____ M ____

*Please use the calculator system: <http://www.doubling-time.com/compute-PSA-doubling-time.php>

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title RESIST-PC		Patient identifier [] - [] - []				
• Prostate Cancer Treatment History: Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR Complete response <input type="checkbox"/> PR partial response <input type="checkbox"/> SD stable disease <input type="checkbox"/> PD progressive disease <input type="checkbox"/> missing
2	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
3

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title		Patient identifier				
RESIST-PC		[] - [] - [] - [] - []				
• Prostate Cancer Treatment History: Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	<input type="text"/> . OR <input type="text"/> . <input type="text"/>	Gy mCi	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
2	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	<input type="text"/> . OR <input type="text"/> . <input type="text"/>	Gy mCi	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
3

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline					
Study short title		Patient identifier			
RESIST-PC		[] - [] - []			
• Prostate Cancer Treatment History: Other Treatment					
Any other treatment?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below			
#	Therapy	Comments	started	ended	best response
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing
2	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> standard ADT		<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline					
Study short title RESIST-PC		Patient identifier [] - [] - []			
	<input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: _____				
3

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
Imaging within the past three months CT (repeatable event)	Date of imaging _____/_____/_____	day month year
MRI (repeatable event)	_____/_____/_____	day month year
PET/CT ⁶⁸ Ga-PSMA (repeatable event)	_____/_____/_____	day month year
SPECT/CT ¹⁷⁷ Lu-PSMA	_____/_____/_____	day month year
BONE SCAN (repeatable event)	_____/_____/_____	day month year
tracer:		
RENAL SCAN (OPTIONAL) ADD IN	_____/_____/_____	day month year
Result:		
other, specify: _____	_____/_____/_____	day month year

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier [] - [] - []	
• Medical History		
Date of Assessment:	[]/[]/[] day month year	
Any relevant medical history?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify below:	
Condition / Illness	Started	Ended
1.	<input type="checkbox"/> Unknown []/[]/[] Day Month Year	<input type="checkbox"/> Unknown []/[]/[] Day Month Year
2.	<input type="checkbox"/> Unknown []/[]/[] Day Month Year	<input type="checkbox"/> Unknown []/[]/[] Day Month Year
3.	<input type="checkbox"/> Unknown []/[]/[] Day Month Year	<input type="checkbox"/> Unknown []/[]/[] Day Month Year
4.	<input type="checkbox"/> Unknown []/[]/[] Day Month Year	<input type="checkbox"/> Unknown []/[]/[] Day Month Year
5.	<input type="checkbox"/> Unknown []/[]/[] Day Month Year	<input type="checkbox"/> Unknown []/[]/[] Day Month Year
6.	<input type="checkbox"/> Unknown []/[]/[] Day Month Year	<input type="checkbox"/> Unknown []/[]/[] Day Month Year
7.	<input type="checkbox"/> Unknown []/[]/[] Day Month Year	<input type="checkbox"/> Unknown []/[]/[] Day Month Year
8.	<input type="checkbox"/> Unknown []/[]/[] Day Month Year	<input type="checkbox"/> Unknown []/[]/[] Day Month Year

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• Baseline findings		
<p>Note: Please list below all conditions which started before the patient signed the informed consent form and for which symptoms or treatment were recorded during the time between signature of informed consent and first administration of the study drug, including conditions which were stabilized by treatment</p> <p>Conditions present before study drug administration are to be documented as Baseline Findings; conditions which started or deteriorated after administration of the study drug will be documented as Adverse Events on a specific AE page of the CRF</p>		
Date of Assessment:	_____/_____/_____ day month year	
Any relevant baseline findings?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify below:	
Hypersensitivity assessment		
Known allergies:	<input type="checkbox"/> no <input type="checkbox"/> yes, specify below	
Abnormal findings / symptoms / diseases		Started
1.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
2.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
3.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
4.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
5.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
6.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
7.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title	Patient identifier	
RESIST-PC		
• ECOG		
Date of Assessment:	_____ / _____ / _____ day month year	
ECOG performance status		

	0 Fully active, able to carry on all pre-disease performance without restriction	
	1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	
	2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
Laboratory						
Date of Assessment:		[] / [] / [] day month year				
Test	Result	Unit	Unit, if differ- ent	mark if abnormal	clarification of abnormal	clinically significant
RBC	[] [] [] [] [] [] []	□ 10E6/ μ L □ Million/ μ L □ Tpt/L		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	[] [] [] [] [] [] []	□ 10E3/ μ L □ Thousand/ μ L □ Gpt/L		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	[] [] [] [] [] [] []	□ 10E3/ μ L □ Thousand/ μ L □ Gpt/L		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	[] [] [] [] [] [] []	absolute # □ cells/ μ L □ 10E3/ μ L		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	[] [] [] [] [] [] []	absolute # □ cells/ μ L □ 10E3/ μ L		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	[] [] [] [] [] [] []	absolute # □ cells/ μ L □ 10E3/ μ L		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	[] [] [] [] [] [] []	absolute # □ cells/ μ L □ 10E3/ μ L		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	[] [] [] [] [] [] []	absolute # □ cells/ μ L □ 10E3/ μ L		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	[] [] [] [] [] [] []	□ g/dL □ mmol/L		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	[] [] [] [] [] [] []	%		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	[] [] [] [] [] [] []	fL		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	[] [] [] [] [] [] []	pg		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	[] [] [] [] [] [] []	%		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	[] [] [] [] [] [] []	μ mol/sL		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	[] [] [] [] [] [] []	μ mol/sL		<input type="checkbox"/>	□ high □ low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

alk. phosphatase	□□□□□	<input type="checkbox"/> IU/L <input type="checkbox"/> U/L <input type="checkbox"/> µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	□□□□□	<input type="checkbox"/> mg/L <input type="checkbox"/> mg/dL <input type="checkbox"/> µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	□□□□□	<input type="checkbox"/> g/dL <input type="checkbox"/> g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	□□□□□	<input type="checkbox"/> mg/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine	□□□□□	<input type="checkbox"/> mg/dL <input type="checkbox"/> µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR*	□□□□□	mL/min/1,73 m ²		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	□□□□□	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	□□□□□	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	□□□□□	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

*eGFR calculation formula (<https://www.kidney.org/content/ckd-epi-creatinine-equation-2009>)

CKD-EPI Creatinine Equation (2009)	Abbreviations / Units
Expressed as a single equation: eGFR = 141 x min (SCr/κ, 1) ^α x max(SCr/κ, 1) ^{-1.209} x 0.993 ^{Age} x 1.018 [if female] x 1.159 [if Black]	eGFR (estimated glomerular filtration rate) = mL/min/1.73 m ² SCr (standardized serum creatinine) = mg/dL κ = 0.7 (females) or 0.9 (males) α = -0.329 (females) or -0.411 (males) min = indicates the minimum of SCr/κ or 1 max = indicates the maximum of SCr/κ or 1 age = years

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline			
Study short title RESIST-PC	Patient identifier _____ - _____ - _____		
• PSA measurement			
Date of Assessment: _____._____._____	day	month	year
unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____			

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____		
• Imaging			
Date and time of imaging	 ____/____/____ ____ ____ : ____ Day Month Year hrs : min		
Ga-68 PSMA PET/CT or Lu-177 PSMA scintigraphy or equivalent result	<input type="checkbox"/> positive (tumor lesions visible) <input type="checkbox"/> negative (no tumor lesion visible)		
Mean PSMA expression of lesions by visual assessment:	Score	Reported PSMA expression	Uptake
	<input type="checkbox"/> 0	no	Below bloodpool
	<input type="checkbox"/> +	low	Equal to or above bloodpool and lower than liver
	<input type="checkbox"/> ++	intermediate	Equal to or above liver and lower than salivary glands
	<input type="checkbox"/> +++	high	Equal to or above salivary glands

Please make sure all additional questionnaires are completed by the patient as applicable

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Concomitant Medication							
Study short title RESIST-PC			Patient No.+ Initials _____ - _____ - _____				
Any medication taken between 28 days before inclusion and "end of study"?					<input type="checkbox"/> No	<input type="checkbox"/> Yes, please specify details below	
Generic name (Brand name for combination drugs)	Indication	Total daily dose	Dose unit	Regimen 1 = PRN, 2 daily, 3 = once, 4 = QD, 5 = BID, 6 = TID, 7 = Q6H, 8 = Q8H, 9 = Q12H, 10 QHS, 11 infusion, 12 continuous infusion, 13 other, specify	Route 1 = oral, 2 = s c , 3 = i m , 4 = IV, 5 = inhalation, 6 = topical, 7 = transdermal, 8 rectal, 9 = other, specify	Date of first administration Day Month Year <input type="checkbox"/> unknown	Date of last administration Day Month Year <input type="checkbox"/> Continuing at end of study
1.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study
2.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study
3.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study
4.				_____	_____	Day Month Year <input type="checkbox"/> unknown	Day Month Year <input type="checkbox"/> Continuing at end of study

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Randomization	
Study short title RESIST-PC	Patient No.+ Initials [] - [] - []
Date of Randomization:	[] / [] / [] day month year
Patient is randomized to	<input type="checkbox"/> arm 1 (6.0 GBq per Radioligand therapy) corresponds to 162 mCi <input type="checkbox"/> arm 2 (7.4 GBq per Radioligand therapy)) corresponds to 200 mCi

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry	
Study short title RESIST-PC	Patient No.+ Initials ____ - ____ - ____
Date of RLT:	____ / ____ / ____ day month year
Cycle for dosimetry	<input type="checkbox"/> Cycle 1 <input type="checkbox"/> Cycle 2
• 12 lead ECG Before Injection	
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
Heart rate	____ /min
PR interval	____ msec
QRS interval	____ msec
QT interval	____ msec
QTc interval	____ msec

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry						
Study short title		Patient No.+ Initials				
RESIST-PC		- -				
• Laboratory						
Date of Assessment:		/ / day month year				
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC		<input type="checkbox"/> 10E6/ μ L <input type="checkbox"/> Million/ μ L <input type="checkbox"/> Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin		<input type="checkbox"/> g/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV		fL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH		pg		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry						
Study short title	Patient No.+ Initials					
RESIST-PC	_____ - _____ - _____					
RDW	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	_____	□ IU/L □ U/L □ μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	_____	□ mg/L □ mg/dL □ μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	_____	□ g/dL □ g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	_____	□ mg/dL □ mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine	_____	□ mg/dL □ μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR*	_____	mL/min/1,73m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no
<input type="checkbox"/> eGFR <input type="checkbox"/> estimated from renal scan						
sodium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

*eGFR calculation formula (<https://www.kidney.org/content/ckd-epi-creatinine-equation-2009>):

CKD-EPI Creatinine Equation (2009)	Abbreviations / Units
Expressed as a single equation: eGFR = 141 x min(SCr/k, 1)α x max(SCr /k, 1)-1 209 x 0 993Age x 1 018 [if female] x1 159 [if Black]	eGFR (estimated glomerular filtration rate) = mL/min/1.73 m ² SCr (standardized serum creatinine) = mg/dL k = 0.7 (females) or 0.9 (males) α = -0.329 (females) or -0.411 (males) min = indicates the minimum of SCr/k or 1 max = indicates the maximum of SCr/k or 1 age = years

Radioligand Therapy (RLT) – Injection Visit including dosimetry

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Study short title RESIST-PC	Patient No.+ Initials ____ - ____ - ____
• Salivary protection (30 min before injection and continued for 4 hours)	
Applying ice pack	<input type="checkbox"/> done <input type="checkbox"/> not done, provide comment _____
• Vital Signs Before Injection (within 20 min before injection)	
Temperature	_____.____ °C <input type="checkbox"/> F
Heart Rate	_____/min
Respiratory Rate	_____/min
Blood Pressure Systolic	____ mmHg
Blood Pressure Diastolic	____ mm Hg

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC)

• RLT					
Activity in syringe before injection	_____._____ mCi				
Date and time of start of measurement	day	month	year	hr	min
Injected activity	_____._____ mCi				
Date and time of RLT	day	month	year	hr	min
Activity in syringe after injection	_____._____ mCi				
Date and time of end of measurement	day	month	year	hr	min
Completed as planned	<input type="checkbox"/> yes <input type="checkbox"/> no, specify _____				
Any adverse event	<input type="checkbox"/> yes, complete AE page <input type="checkbox"/> no				
• Vital Signs After Injection - 30 minutes post-infusion					
Time	_____._____ hh min				
Temperature	_____.____ <input type="checkbox"/> °C <input type="checkbox"/> F				
Heart Rate	_____ /min				
Respiratory Rate	_____ /min				
Blood Pressure Systolic	_____ mmHg				
Blood Pressure Diastolic	_____ mm Hg				
• Vital Signs After Injection - 60 minutes post-infusion					
Time	_____._____ hh min				
Temperature	_____.____ <input type="checkbox"/> °C <input type="checkbox"/> F				
Heart Rate	_____ /min				

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Respiratory Rate	_____ /min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____		
• (Holter) ECG monitoring results for the period 20 min prior to and 1 hour post-infusion			
<input type="checkbox"/> done, please fill out the below <input type="checkbox"/> not done, provide comment _____			
Date and time of ECG monitoring	_____ _____ _____ _____ _____ Day Month Year	_____ _____ hrs : min	
Overall evaluation of ECG monitoring	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below _____		
Comment	_____		
Heart rate	_____ _____ /min		
PR interval	_____ _____ _____ msec		
QRS interval	_____ _____ _____ msec		
QT interval	_____ _____ _____ msec		
QTc interval	_____ _____ _____ msec		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• 12 lead ECG 4 hours after Injection	
<input type="checkbox"/> done, please fill out the below <input type="checkbox"/> not done, provide comment _____	
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
Heart rate	_____ /min
PR interval	_____ msec
QRS interval	_____ msec
QT interval	_____ msec
QTc interval	_____ msec

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry					
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____				
• Dosimetry: Blood Samples					
With regard to injection site, was the blood draw performed			<input type="checkbox"/> contralateral <input type="checkbox"/> ipsilateral, different i.v. access <input type="checkbox"/> (ipsilateral, same i.v. access)		
0 min	<input type="checkbox"/> sample obtained, specify exact time post ¹⁷⁷ LuPSMA injection _____/_____/_____ :_____ Day Month Year hrs : min			<input type="checkbox"/> not obtained	
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) _____/_____/_____ :_____ Day Month Year hrs : min			<input type="checkbox"/> not measured	
	Volume measured: _____,_____ mL				
	Activity measured: _____ . _____ μCi/mL				
	Measurement duration time: _____ min				
5 min	<input type="checkbox"/> sample obtained, specify exact time post ¹⁷⁷ LuPSMA injection _____/_____/_____ :_____ Day Month Year hrs : min			<input type="checkbox"/> not obtained	
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) _____/_____/_____ :_____ Day Month Year hrs : min			<input type="checkbox"/> not measured	
	Volume measured: _____,_____ mL				
	Activity measured: _____ . _____ μCi/mL				
	Measurement duration time: _____ min				
30 min	<input type="checkbox"/> sample obtained specify exact time (post inj) _____/_____/_____ :_____ Day Month Year hrs : min			<input type="checkbox"/> not obtained	
	<input type="checkbox"/> date and time of measurement,, specify exact time (post inj) _____/_____/_____ :_____ Day Month Year hrs : min			<input type="checkbox"/> not measured	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry						
Study short title RESIST-PC		Patient No.+ Initials _____ - _____ - _____				
1 h	Volume measured: _____ mL					
	Activity measured: _____ . _____ μCi/mL					
	Measurement duration time: ____ min					
<input type="checkbox"/> sample obtained specify exact time (post inj) ____ / ____ / ____ ____ : Day Month Year hrs : min		<input type="checkbox"/> not obtained ____ / ____ / ____ ____ : Day Month Year hrs : min		<input type="checkbox"/> not measured ____ / ____ / ____ ____ : Day Month Year hrs : min		
Volume measured: _____ mL		Activity measured: _____ . _____ μCi/mL		Measurement duration time: ____ min		
4 h	<input type="checkbox"/> sample obtained specify exact time (post inj) ____ / ____ / ____ ____ : Day Month Year hrs : min		<input type="checkbox"/> not obtained ____ / ____ / ____ ____ : Day Month Year hrs : min		<input type="checkbox"/> not measured ____ / ____ / ____ ____ : Day Month Year hrs : min	
	Volume measured: _____ mL		Activity measured: _____ . _____ μCi/mL		Measurement duration time: ____ min	
	<input type="checkbox"/> sample obtained specify exact time (post inj) ____ / ____ / ____ ____ : Day Month Year hrs : min		<input type="checkbox"/> not obtained ____ / ____ / ____ ____ : Day Month Year hrs : min		<input type="checkbox"/> not measured ____ / ____ / ____ ____ : Day Month Year hrs : min	
18-30 h	Volume measured: _____ mL					
	<input type="checkbox"/> sample obtained specify exact time (post inj) ____ / ____ / ____ ____ : Day Month Year hrs : min		<input type="checkbox"/> not obtained ____ / ____ / ____ ____ : Day Month Year hrs : min		<input type="checkbox"/> not measured ____ / ____ / ____ ____ : Day Month Year hrs : min	

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry					
Study short title RESIST-PC		Patient No.+ Initials _____ - _____ - _____			
		Activity measured: _____ . _____ $\mu\text{Ci}/\text{mL}$			
		Measurement duration time: _____ min (10 min needed)			
42-54 h	<input type="checkbox"/> sample obtained specify exact time (post inj)				<input type="checkbox"/> not obtained
	____/____/_____		____:____		
	Day	Month	Year	hrs	: min
<input type="checkbox"/> date and time of measurement,, specify exact time (post inj)				<input type="checkbox"/> not measured	
____/____/_____		____:____			
Day	Month	Year	hrs	: min	
Volume measured: _____ mL					
Activity measured: _____ . _____ $\mu\text{Ci}/\text{mL}$					
Measurement duration time: _____ min (10 min needed)					
66-78 h	<input type="checkbox"/> sample obtained specify exact time (post inj)				<input type="checkbox"/> not obtained
	____/____/_____		____:____		
	Day	Month	Year	hrs	: min
<input type="checkbox"/> date and time of measurement,, specify exact time (post inj)				<input type="checkbox"/> not measured	
____/____/_____		____:____			
Day	Month	Year	hrs	: min	
Volume measured: _____ mL					
Activity measured: _____ . _____ $\mu\text{Ci}/\text{mL}$					
Measurement duration time: _____ min (10 min needed)					
7-9 d (optional)	<input type="checkbox"/> sample obtained specify exact time (post inj)				<input type="checkbox"/> not obtained
	____/____/_____		____:____		
	Day	Month	Year	hrs	: min
<input type="checkbox"/> date and time of measurement,, specify exact time (post inj)				<input type="checkbox"/> not measured	
____/____/_____		____:____			
Day	Month	Year	hrs	: min	
Volume measured: _____ mL					

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
Activity measured: _____ . _____	µCi/mL
Measurement duration time: _____ min (10 min needed)	

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PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry			
Study short title	Patient No.+ Initials		
RESIST-PC	_____ - _____ - _____		
• Dosimetry: Scintigraphy			
4 h	<input type="checkbox"/> whole body planar obtained, specify exact time <input type="checkbox"/> not obtained _____:_____ hh min Scan duration _____ min		
18-30 h	date: _____ / _____ / _____ Day Month Year hrs : min whole body planar: <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____:_____ hrs : min Scan duration _____ min		
	SPECT/CT head <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____:_____ hrs : min Duration per angle _____ min		
	SPECT/CT thorax <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____:_____ hrs : min Duration per angle _____ min		
	SPECT/CT abd. <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____:_____ hrs : min Duration per angle _____ min		
42-54 h	<input checked="" type="checkbox"/> whole body planar obtained, specify date/time <input type="checkbox"/> not obtained _____ / _____ / _____ Day Month Year hrs : min Scan duration _____ min		

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC)

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry			
Study short title RESIST-PC	Patient Identifier _____ - _____ - _____		
• Dosimetry: Urine Collection			
collected from injection until 4 h p.i.	<input type="checkbox"/> done <input type="checkbox"/> not done, specify Urine net weight: _____ g date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured ____/____/____ ____:____ Day Month Year hrs : min Volume measured: _____ mL Activity measured: _____ . _____ <input type="checkbox"/> μCi/mL <input type="checkbox"/> μCi/g Measurement duration time: _____ min		
collected from 4h-until discharge from hospital	<input type="checkbox"/> done <input type="checkbox"/> not done, specify date and time of discharge: ____/____/____ ____:____ Day Month Year hrs : min Urine net weight: _____ g Activity measured: _____ . _____ <input type="checkbox"/> μCi/mL <input type="checkbox"/> μCi/g Measurement duration time: _____ min		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry		
Study short title	Patient identifier	
RESIST-PC	[REDACTED] - [REDACTED] - [REDACTED]	
• PSA measurement (PSA is measured every 6 weeks during treatment+after treatment period every 3 months)		
Date of Assessment:	[REDACTED]	[REDACTED] / [REDACTED] / [REDACTED] day month year
unit:	[REDACTED]	
<input type="checkbox"/> ng/mL		
<input type="checkbox"/> if other unit, specify:		

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) - Injection Visit including dosimetry - Concomitant cancer-related therapy since last visit						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown <div style="text-align: center;">[] [] [] [] [] []</div> Day Month Year	<input type="checkbox"/> Unknown <div style="text-align: center;">[] [] [] [] [] []</div> Day Month Year	<input type="checkbox"/> CR (Complete response) <input type="checkbox"/> PR partial response <input type="checkbox"/> SD stable disease <input type="checkbox"/> PD progressive disease <input type="checkbox"/> missing
Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT	[] []		<input type="checkbox"/> Unknown <div style="text-align: center;">[] [] [] [] [] []</div>	<input type="checkbox"/> Unknown <div style="text-align: center;">[] [] [] [] [] []</div>	<input type="checkbox"/> CR

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) - Injection Visit including dosimetry - Concomitant cancer-related therapy since last visit									
Study short title		Patient identifier							
RESIST-PC		[] - [] - []							
<input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	Gy OR [] . [] mCi		Day	Month	Year	Day	Month	Year	<input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
Other Treatment									
Any other treatment?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below							
#	Therapy	Comments	started			ended			best response
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown	[]	/	[]	/	[]	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing
			Day	Month	Year	Day	Month	Year	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title	Patient No.+ Initials
RESIST-PC	_____ - _____ - _____
• Study drug administration complications	
Has any complication related to administration of the drug occurred (e.g., overdose, observable extravasation, medication error)?	<input type="checkbox"/> no <input type="checkbox"/> yes, please specify: _____
<input type="checkbox"/> Report was sent to the pharmacovigilance designee.	

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow –Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

12 weeks PSA measurement		
Study short title	Patient identifier	
RESIST-PC	____ - ____ - ____	
• PSA measurement		
Date of Assessment:	____ / ____ / ____	day month year
____ . ____		
<u>unit:</u>		
<input type="checkbox"/> ng/mL		
<input type="checkbox"/> if other unit, specify:		

• ECOG		
Date of Assessment:	____ / ____ / ____	
ECOG performance status	____	
	0	Fully active, able to carry on all pre-disease performance without restriction
	1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
	2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
	3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
	4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair

At week 12 also to be completed:

- Lab values (CBC, CMP)
- Imaging questionnaires
- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Additional evaluation of blood tests every 2 weeks (not cycle 1-4 and not Follow-up)						
Study short title		Patient No.+ Initials				
RESIST-PC		_____ - _____ - _____				
• Laboratory						
Date of Assessment:		_____ / _____ / _____ day month year				
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	 	<input type="checkbox"/> 10E6/ μ L <input type="checkbox"/> Million/ μ L <input type="checkbox"/> Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	 	<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	 	<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	 	absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	 	absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	 	absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	 	absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	 	absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	 	<input type="checkbox"/> g/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	 	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Additional evaluation of blood tests every 2 weeks (not cycle 1-4 and not Follow-up)						
Study short title	Patient No.+ Initials					
RESIST-PC	[] - [] - []					
MCV	[]	fL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	[]	pg		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	[]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	[]	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	[]	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	[]	<input type="checkbox"/> IU/L <input type="checkbox"/> U/L <input type="checkbox"/> µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	[]	<input type="checkbox"/> mg/L <input type="checkbox"/> mg/dL <input type="checkbox"/> µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	[]	<input type="checkbox"/> g/dL <input type="checkbox"/> g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	[]	<input type="checkbox"/> mg/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatininine	[]	<input type="checkbox"/> mg/dL <input type="checkbox"/> µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR <input type="checkbox"/> eGFR <input type="checkbox"/> estimated from renal scan	[]	mL/min/1,73 m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	[]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	[]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	[]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

*eGFR calculation formula (<https://www.kidney.org/content/ckd-epi-creatinine-equation-2009>):

CKD-EPI Creatinine Equation (2009)	Abbreviations / Units
Expressed as a single equation: eGFR = 141 x min (S _{Cr} /κ, 1) ^a x	eGFR (estimated glomerular filtration rate) = mL/min/1.73 m ² SCr (standardized serum creatinine) = mg/dL κ = 0.7 (females) or 0.9 (males)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

max(SCr /κ, 1) ^{-1.209} x 0.993 ^{Age} x 1.018 [if female] x 1.159 [if Black]	$\alpha = -0.329$ (females) or -0.411 (males) min = indicates the minimum of SCr/κ or 1 max = indicates the maximum of SCr/κ or 1 age = years
---	--

Additional PSA measurements	
Study short title	Patient identifier
RESIST-PC	_____ - _____ - _____
• PSA measurement	
Date of Assessment:	_____/_____/_____ day month year
_____ · _____	
<u>unit:</u> <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title	Patient No.+ Initials		
RESIST-PC	_____ - _____ - _____		
• Physical Examination			
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done		
Date Physical Examination:	day	month	year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal		
Comments: General Appearance	_____		
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____		
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Cardiovascular	_____		
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Respiratory	_____		
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Gastrointestinal	_____		
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Musculoskeletal	_____		
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Genitourinary	_____		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title	Patient No.+ Initials		
RESIST-PC	- -		
Skin	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments: Skin	_____		
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments Neurological	_____		
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments	_____		

• ECOG			
Date of Assessment:	/ / day month year		
ECOG performance status		<ul style="list-style-type: none">0 Fully active, able to carry on all pre-disease performance without restriction1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	

PSMA-directed endoRadioThErApy of castration-reSISTant Prostate Cancer (RESIST-PC)

Relevant imaging before new cycle		
Study short title RESIST-PC	Patient No.+ Initials. ____ - ____ - ____	
Imaging		
CT (repeatable event)	____ / ____ / ____	day month year
Tumor location Location of metastases		
MRI (repeatable event)	____ / ____ / ____	day month year
PET/CT (repeatable event)	____ / ____ / ____	day month year
Scintigraphy (repeatable event)	____ / ____ / ____	day month year
other, specify: _____	____ / ____ / ____	day month year
Imaging result:	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title	Patient No.+ Initials
RESIST-PC	____ - ____ - ____
Date of RLT:	____ / ____ / ____ day month year
• 12 lead ECG Before Injection	
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
heart rate	____ /min
PR interval	____ msec
QRS interval	____ msec
QT interval	____ msec
QTc interval	____ msec

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title	Patient No.+ Initials		
RESIST-PC	_____	-	_____ - _____
• ECG before injection			
date and time of ECG	_____	_____	_____
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below _____		
Comment	_____		
heart rate	_____	/min	
PR interval	_____	msec	
QRS interval	_____	msec	
QT interval	_____	msec	
QTc interval	_____	msec	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• Salivary protection (30 min before injection and continued for 4 hours)	
Applying ice pack	<input type="checkbox"/> done, please fill out the below <input type="checkbox"/> not done, provide comment _____
• Vital Signs Before Injection (within 20 min before injection)	
Temperature	_____ . ____ °C <input type="checkbox"/> F
Heart Rate	_____ /min
Respiratory Rate	_____ /min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg
• RLT	
activity in syringe before injection	_____ mCi
Date and time of measurement	_____ /_____ /_____ - _____ : _____ day month year hrs min
injected activity date and time of RLT	_____ mCi _____ /_____ /_____ - _____ : _____ day month year hrs min
activity in syringe after injection Date and time of measurement	_____ mCi _____ /_____ /_____ - _____ : _____ day month year hrs min
completed as planned	<input type="checkbox"/> yes <input type="checkbox"/> no, specify _____
any adverse event	<input type="checkbox"/> yes, complete AE page <input type="checkbox"/> no

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

• Vital Signs After Injection - 30 minutes post-infusion	
time	_____ hh : mm
Temperature	_____ . ____ °C <input type="checkbox"/> F
Heart Rate	_____ /min
Respiratory Rate	_____ /min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg
• Vital Signs After Injection - 60 minutes post-infusion	
time	_____ hh : mm
Temperature	_____ . ____ °C <input type="checkbox"/> F
Heart Rate	_____ /min
Respiratory Rate	_____ /min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg

PSMA-directed endoRadiotherEapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title	Patient No.+ Initials		
RESIST-PC	_____	-	_____ - _____
• Holter ECG monitor results for the period 20 prior to and 1 hour post-infusion			
date and time of ECG	_____	_____	_____
	Day	Month	Year
	hrs	:	min
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below		
Comment	_____		
heart rate	_____ /min		
PR interval	_____ msec		
QRS interval	_____ msec		
QT interval	_____ msec		
QTc interval	_____ msec		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit 1-4						
Study short title		Patient No.+ Initials				
RESIST-PC		_____ - _____ - _____				
• Laboratory						
Date of Assessment:		_____ / _____ / _____ day month year				
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC		<input type="checkbox"/> 10E6/ μ L <input type="checkbox"/> Million/ μ L <input type="checkbox"/> Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin		<input type="checkbox"/> g/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV		fL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit 1-4						
Study short title	Patient No.+ Initials					
RESIST-PC	[REDACTED] - [REDACTED] - [REDACTED]					
MCH	[REDACTED]	pg		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	[REDACTED]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	[REDACTED]	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	[REDACTED]	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	[REDACTED]	<input type="checkbox"/> IU/L <input type="checkbox"/> U/L <input type="checkbox"/> μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	[REDACTED]	<input type="checkbox"/> mg/L <input type="checkbox"/> mg/dL <input type="checkbox"/> μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	[REDACTED]	<input type="checkbox"/> g/dL <input type="checkbox"/> g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	[REDACTED]	<input type="checkbox"/> mg/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine	[REDACTED]	<input type="checkbox"/> mg/dL <input type="checkbox"/> μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR*	[REDACTED]	mL/min/1,73 m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	[REDACTED]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	[REDACTED]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	[REDACTED]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

*eGFR calculation formula (<https://www.kidney.org/content/ckd-epi-creatinine-equation-2009>):

CKD-EPI Creatinine Equation (2009)	Abbreviations / Units
Expressed as a single equation: eGFR = 141 x min (S _{Cr} /κ, 1) ^a x max(S _{Cr} /κ, 1) ^{-1.209} x 0.993 ^{Age} x 1.018 [if female] x 1.159 [if Black]	eGFR (estimated glomerular filtration rate) = mL/min/1.73 m ² SCr (standardized serum creatinine) = mg/dL κ = 0.7 (females) or 0.9 (males) a = -0.329 (females) or -0.411 (males) min = indicates the minimum of SCr/κ or 1 max = indicates the maximum of SCr/κ or 1 age = years

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

PSA measurements		
Study short title	Patient identifier	
RESIST-PC	_____ - _____ - _____	
• PSA measurement		
Date of Assessment:	_____ / _____ / _____	day month year
_____ . _____		
<u>unit:</u>		
<input type="checkbox"/> ng/mL		
<input type="checkbox"/> if other unit, specify:		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title RESIST-PC	Patient No.+ Initials <u> </u> - <u> </u> - <u> </u>
• 12 lead ECG 4 hours after Injection (after salivary protection is completed)	
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below <hr/>
Comment	<hr/>
heart rate	<u> </u> /min
PR interval	<u> </u> msec
QRS interval	<u> </u> msec
QT interval	<u> </u> msec
QTc interval	<u> </u> msec

Scintigraphy	
optional	<input type="checkbox"/> whole body planar obtained, specify date/time obtained <u> </u> / <u> </u> / <u> </u> : <u> </u> Day Month Year hrs : min Scan duration <u> </u> min

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title	Patient No.+ Initials
RESIST-PC	_____ - _____ - _____
• Study drug administration complications	
Has any complication related to administration of the drug occurred (e.g., overdose, observable extravasation, medication error)?	<input type="checkbox"/> no <input type="checkbox"/> yes, please specify: _____
<input type="checkbox"/> Report was sent to the pharmacovigilance designee.	

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) - Injection Visit 1-4 - Concomitant cancer-related therapy since last visit						
Study short title RESIST-PC		Patient identifier [] - [] - []				
Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR (Complete response) <input type="checkbox"/> PR partial response <input type="checkbox"/> SD stable disease <input type="checkbox"/> PD progressive disease <input type="checkbox"/> missing
Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) - Injection Visit 1-4 - Concomitant cancer-related therapy since last visit													
Study short title RESIST-PC		Patient identifier [] - [] - []											
<input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	Gy OR [] . [] mCi		Day	Month	Year	Day	Month	Year					
			<input type="checkbox"/> PR	<input type="checkbox"/> SD	<input type="checkbox"/> PD	<input type="checkbox"/> missing							
Other Treatment													
Any other treatment?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below											
#	Therapy	Comments	started			ended			best response				
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <hr/> <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown	[]	/ []	/ []	<input type="checkbox"/> Unknown	[]	/ []	/ []	Day Month Year	Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up		
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____	
• Physical Examination		
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done	
Date Physical Examination:	_____/_____/_____	day month year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal	
Comments: General Appearance	_____	
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____	
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Cardiovascular	_____	
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Respiratory	_____	
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Gastrointestinal	_____	
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Musculoskeletal	_____	
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Genitourinary	_____	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up			
Study short title	Patient No.+ Initials		
RESIST-PC	- -		
Skin	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments: Skin	_____		
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments Neurological	_____		
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments	_____		

• Vital Signs			
Temperature	.	<input type="checkbox"/> °C	<input type="checkbox"/> F
Heart Rate		/min	
Respiratory Rate		/min	
Blood Pressure Systolic		mmHg	
Blood Pressure Diastolic		mm Hg	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up		
Study short title RESIST-PC	Patient No.+ Initials ____ - ____ - ____	
• ECOG		
Date of Assessment:	____/____/____	day month year
ECOG performance status	____ 0 Fully active, able to carry on all pre-disease performance without restriction 1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work 2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours 3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours 4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

•Follow up						
Study short title RESIST-PC		Patient No.+ Initials. _____ - _____ - _____				
•Laboratory						
Date of Assessment: _____ _____ _____ _____ _____ _____ _____		day	month	year		
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC		<input type="checkbox"/> 10E6/ μ L <input type="checkbox"/> Million/ μ L <input type="checkbox"/> Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin		<input type="checkbox"/> g/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV		fL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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MCH		pg		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST		μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT		μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase		<input type="checkbox"/> IU/L <input type="checkbox"/> U/L <input type="checkbox"/> μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin		<input type="checkbox"/> mg/L <input type="checkbox"/> mg/dL <input type="checkbox"/> μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin		<input type="checkbox"/> g/dL <input type="checkbox"/> g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN		<input type="checkbox"/> mg/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine		<input type="checkbox"/> mg/dL <input type="checkbox"/> μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR*		mL/min/1,73 m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium		mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium		mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride		mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

*eGFR calculation formula (<https://www.kidney.org/content/ckd-epi-creatinine-equation-2009>):

CKD-EPI Creatinine Equation (2009)	Abbreviations / Units
Expressed as a single equation: eGFR = 141 x min (S _{Cr} /κ, 1) ^α x max(S _{Cr} /κ, 1) ^{-1.209} x 0.993 ^{Age} x 1.018 [if female] x 1.159 [if Black]	eGFR (estimated glomerular filtration rate) = mL/min/1.73 m ² SCr (standardized serum creatinine) = mg/dL κ = 0.7 (females) or 0.9 (males) α = -0.329 (females) or -0.411 (males) min = indicates the minimum of SCr/κ or 1 max = indicates the maximum of SCr/κ or 1 age = years

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

End of treatment

Treatment was discontinued after cycle due to the following conditions:

- PSA/radiographic progression at ≥ 12 weeks
- Completion of four RLT cycles
- 23 Gy kidney dose would be exceeded by the next cycle as estimated by dosimetry
- patient withdrawal (e.g. appearance of intolerable adverse events)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow up			
Study short title	Patient identifier		
RESIST-PC	- -		
• PSA measurement			
Date of Assessment:	/ /		
	day	month	year
unit:			
<input type="checkbox"/> ng/mL			
<input type="checkbox"/> if other unit, specify:			

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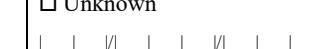
PSMA-directed endoRadioThErApy of castration-reSISTant Prostate Cancer (RESIST-PC)

•Follow up		
Study short title RESIST-PC	Patient No.+ Initials. _____ - _____ - _____	
Imaging		
CT (repeatable event) Tumor location Location of metastases	_____ / _____ / _____ day month year	
MRI (repeatable event)	_____ / _____ / _____ day month year	
PET/CT (repeatable event)	_____ / _____ / _____ day month year tracer:	
Scintigraphy (repeatable event)	_____ / _____ / _____ day month year tracer:	
other, specify: _____	_____ / _____ / _____ day month year	
Imaging result:	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD	

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-up - Concomitant cancer-related therapy since last visit						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR (Complete response) <input type="checkbox"/> PR partial response <input type="checkbox"/> SD stable disease <input type="checkbox"/> PD progressive disease <input type="checkbox"/> missing
Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT			<input type="checkbox"/> Unknown 	<input type="checkbox"/> Unknown 	<input type="checkbox"/> CR

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-up - Concomitant cancer-related therapy since last visit								
Study short title		Patient identifier						
RESIST-PC		[] - [] - []						
<input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	Gy OR [] . [] mCi	Day	Month	Year	Day	Month	Year	<input type="checkbox"/> PR
								<input type="checkbox"/> SD
<input type="checkbox"/> PD								
<input type="checkbox"/> missing								
Other Treatment								
Any other treatment?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below						
#	Therapy	Comments	started	ended			best response	
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <hr/> <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown [] / [] / [] Day Month Year	<input type="checkbox"/> Unknown [] / [] / [] Day Month Year			<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

End of study	
Study short title RESIST-PC	Patient No.+ Initials. [] - [] - []
Study course	<input type="checkbox"/> Patient completed study if study course completed, last day on study: []/[]/[] Day Month Year reason : <input type="checkbox"/> Progression <input type="checkbox"/> Follow-up completed <input type="checkbox"/> Death <input type="checkbox"/> Patient withdrew from study
If withdrawn, give date and time of withdrawal (24 h clock):	[]/[]/[] []:[] Day Month Year hr min
Specify main reason	<input type="checkbox"/> Withdrawal of consent <input type="checkbox"/> Lost to Follow-up <input type="checkbox"/> Any occurrence of conditions which prevented the patient's participation in the study? Please specify: <input type="checkbox"/> Protocol deviations? Please specify: <input type="checkbox"/> (Serious) AE? Please specify: <input type="checkbox"/> Administrative reasons? Please, specify: <input type="checkbox"/> Other? Please specify:
Who decided the withdrawal?	<input type="checkbox"/> Patient <input type="checkbox"/> Investigator <input type="checkbox"/> Other, please specify:

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Adverse Events		
Study short title RESIST-PC	Patient No.+ Initials. _____ - _____ - _____	
• Adverse Events <small>(Note: Adverse Event is any untoward medical occurrence in a volunteer or clinical investigation subject administered a pharmaceutical product and which does Not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medical product.)</small>		
Any AE experienced?	<input type="checkbox"/> No <input type="checkbox"/> If yes, please specify details on this form	
Adverse event description		
Onset date and time if available	_____ _____ _____ / _____ _____ _____ - _____ : ____	Day Month Year hrs min
Serious AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please complete also the SAE form	
Maximum intensity:	<input type="checkbox"/> mild (easily tolerated) <input type="checkbox"/> moderate (interferes with usual functions) <input type="checkbox"/> severe (incapacitating)	
Specific drug treatment of AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify on "concomitant medication" page	
Specific Non-drug treatment of AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify.	
Relationship to study drug / study conduct	Study drug relationship: <input type="checkbox"/> None <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite	Study conduct: <input type="checkbox"/> None <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite
Outcome / status	<input type="checkbox"/> Recovered / resolved without sequelae <input type="checkbox"/> Recovered / resolved with sequelae, specify <input type="checkbox"/> Not recovered / Not resolved <input type="checkbox"/> Death / Fatal <input type="checkbox"/> Unknown	
Study drug action	<input type="checkbox"/> Drug withdrawn <input type="checkbox"/> Dose reduced <input type="checkbox"/> Dose not changed <input type="checkbox"/> Other action: _____	
Date and time if available (24 h clock) AE ended (only if recovered / resolved)	<input type="checkbox"/> ongoing at end of study _____ _____ _____ / _____ _____ _____ - _____ : _____ Day Month Year hr min	
<input type="checkbox"/> Tick box if this page is the last adverse event		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Serious Adverse Events	
Study short title RESIST-PC	Patient No. + Initials. [] - [] - []
This view opens when AE serious: "yes" is ticked Also an automatic email is sent to resist-pc@phamtrace.com AND mali@excelediagnostics.com	
Seriousness criterion	
<input type="checkbox"/> Results in death (Date []/[]/[]) <input type="checkbox"/> Life threatening <input type="checkbox"/> Hospitalization – initial or prolonged <input type="checkbox"/> Required intervention to prevent permanent impairment	<input type="checkbox"/> Congenital anomaly / birth defect <input type="checkbox"/> Persistent or significant disability/incapacity <input type="checkbox"/> Other serious (Important Medical Events)
Diagnosis	
Description / Symptoms including course of SAE and comments (continue description on additional pages, if required)	
Date of onset	[]/[]/[] day month year
Date ended (check ongoing box if not ended yet)	[]/[]/[] day month year <input type="checkbox"/> ongoing
Maximum intensity (CTCAE)	<input type="checkbox"/> 1 <input type="checkbox"/> 4 <input type="checkbox"/> 2 <input type="checkbox"/> 5 <input type="checkbox"/> 3 <input type="checkbox"/> unclassifiable
Study drug relationship ¹⁷⁷ Lu-PSMA-617	<input type="checkbox"/> none <input type="checkbox"/> unlikely <input type="checkbox"/> possible <input type="checkbox"/> probable <input type="checkbox"/> definite <input type="checkbox"/> unclassifiable
Study conduct relationship	<input type="checkbox"/> none <input type="checkbox"/> unlikely <input type="checkbox"/> possible <input type="checkbox"/> probable <input type="checkbox"/> definite <input type="checkbox"/> unclassifiable
Comment on assessment of study drug relationship	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Outcome of SAE									
<input type="checkbox"/> Recovered without sequelae <input type="checkbox"/> Recovered with sequelae <input type="checkbox"/> Recovering / resolving					<input type="checkbox"/> Not recovered / not resolved <input type="checkbox"/> Recovered / resolved with residual effects <input type="checkbox"/> Fatal				
Other possible causes of the event									
Check all that apply					Please specify				
<input type="checkbox"/> pre-existing / underlying disease									
<input type="checkbox"/> other treatment (concomitant or previous)									
<input type="checkbox"/> other (e.g. accident, new or intercurrent illness)									
Diagnostic tests and relevant lab values									
Test performed		Result			Normal Range		Date		
SAE Treatment									
Drug to treat SAE (brand name)	Active agent	Indication	total daily dose	dose unit	route	first admin date	last admin date	ongoing	
								<input type="checkbox"/>	
								<input type="checkbox"/>	
								<input type="checkbox"/>	
								<input type="checkbox"/>	
								<input type="checkbox"/>	
Non-drug treatment: yes <input type="checkbox"/> no <input type="checkbox"/>									
If yes, please specify:									

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Study drug administration		
Study drug	<input checked="" type="checkbox"/> ¹⁷⁷ Lu-PSMA-617	<input type="checkbox"/> not injected
Administration date and time	11/11/2017 - 11:11 day month year	hr : min
Injected activity MBq mCi		
Most relevant study drug action due to SAE (please check one box only)	<input type="checkbox"/> drug withdrawn <input type="checkbox"/> administration stopped early	<input type="checkbox"/> dose not changed <input type="checkbox"/> dose reduced <input type="checkbox"/> not applicable
Event abated after use/stopped or dose reduced	<input type="checkbox"/> Yes <input type="checkbox"/> Doesn't apply	<input type="checkbox"/> No
Event reappeared after reintroduction	<input type="checkbox"/> Yes <input type="checkbox"/> Doesn't apply	<input type="checkbox"/> No

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Concomitant medication at onset of SAE									
Medication (brand name)	Active agent	Indication	total daily dose	dose unit	route	first admin. date	last admin. date	ongoing	
								<input type="checkbox"/>	
								<input type="checkbox"/>	
								<input type="checkbox"/>	
								<input type="checkbox"/>	
								<input type="checkbox"/>	
								<input type="checkbox"/>	

Medical history, including preexisting medical conditions

Disease / symptoms (e.g. allergies, smoking and alcohol use, liver/kidney problems, etc.)	started	ended	ongoing
			<input type="checkbox"/>

Please fax additional pages to this report, if needed. Number of pages faxed: 1 | none

Reporting Person	
Name	
Address	
Fax no.	
Phone no.	
E-Mail	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Case Report Form

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC). A phase II clinical trial.

Phase II

Version 1.4 (03 November 2017)

Sponsor

Ebrahim S. Delpassand, M.D. F.A.C.N.M
Johannes Czernin, M.D.

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline				
Study short title RESIST-PC	Patient identifier [] - [] - []	Site	Initials	
• Informed consent				
The patient has been informed about the aims, rationale and procedures of the RESIST-PC trial and he/she has voluntarily agreed to participate and given				
<input type="checkbox"/> written informed consent.				
A copy of the patient information has been handed out to the patient.				
Date of informed consent:				
Day	/	Month	/	Year

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Inclusion / Exclusion criteria		
Study short title	Patient identifier	
RESIST-PC		_____ - _____ - _____
• Inclusion criteria		
1. Prostate cancer proven by histopathology	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Unresectable metastases	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Progressive disease, both docetaxel/cabazitaxel naive and docetaxel/cabazitaxel treated	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Castration resistant disease with confirmed testosterone level \leq 50 ng/ml under prior androgen deprivation therapy (ADT)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Positive ^{68}Ga -PSMA-11 PET/CT or diagnostic ^{177}Lu -PSMA-617 scintigraphy or any equivalent PSMA-directed imaging	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. ECOG 0-2	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Sufficient bone marrow capacity as defined by WBC \geq 2.500/ μl , PLT count \geq 100.000/ μl , Hb \geq 9.9 g/dl and ANC \geq 1500 mm^3 for the first cycle and WBC \geq 2.000/ μl , PLT count \geq 75.000/ μl , Hb \geq 8.9 g/dl and ANC \geq 1000 mm^3 for the subsequent cycles	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Signing Informed Consent Form	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Patients enrolling in this trial should have received either Enzalutamide or Abiraterone	<input type="checkbox"/> Yes	<input type="checkbox"/> No
NOTE: If any inclusion criterion is answered "No", the patient is NOT eligible to enter the study!		
• Exclusion criteria		
1. Less than 6 weeks since last myelosuppressive therapy (including Docetaxel, Cabazitaxel, ^{223}Ra , ^{153}Sm) or other radionuclide therapy	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Glomerular Filtration Rate (GFR) $<$ 40 ml/min	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Serum creatinine $>$ 1.5xULN	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. AST and ALT $>$ 5xULN	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Urinary tract obstruction or marked hydronephrosis	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Diffuse bone marrow involvement confirmed by super-scans	<input type="checkbox"/> Yes	<input type="checkbox"/> No
NOTE: If any exclusion criterion is answered "Yes", the patient is NOT eligible to enter the study!		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
• Demographic Data	
Date of Assessment:	_____/_____/_____ day month year
Date of Birth	_____/_____/_____ day month year
Do you consider yourself Hispanic/Latino or not Hispanic/Latino?	<input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> Not Hispanic or Latino <input type="checkbox"/> Unknown <input type="checkbox"/> Not reported
Which of the following five racial designations best describes you? More than one choice is acceptable. (If mixed race, please check race of each parent)	<input type="checkbox"/> American Indian or Alaska Native <input type="checkbox"/> Asian <input type="checkbox"/> Black or African American <input type="checkbox"/> Native Hawaiian or Other Pacific Islander <input type="checkbox"/> White <input type="checkbox"/> other:

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier [REDACTED] - [REDACTED] - [REDACTED]	
• Anthropometric Measurements – Vital Signs		
Height	[REDACTED].[REDACTED]	Unit: <input type="checkbox"/> inch <input checked="" type="checkbox"/> cm
Weight	[REDACTED].[REDACTED]	Unit: <input type="checkbox"/> lbs <input checked="" type="checkbox"/> kg
Temperature	[REDACTED].[REDACTED]	<input checked="" type="checkbox"/> °C <input type="checkbox"/> F
Heart Rate	[REDACTED]/min	
Respiratory Rate	[REDACTED]/min	
Blood Pressure Systolic	[REDACTED] mmHg	
Blood Pressure Diastolic	[REDACTED] mm Hg	
Pulse Oximetry	[REDACTED]%	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• Physical Examination		
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done, if not done provide comment _____	
Date Physical Examination	_____/_____/_____	day month year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal	
Comments: General Appearance	_____	
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____	
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Cardiovascular	_____	
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Respiratory	_____	
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Gastrointestinal	_____	
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Musculoskeletal	_____	
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Genitourinary	_____	
Skin	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
Comments: Skin	_____	
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
Comments Neurological	_____	
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal
	<input type="checkbox"/> not done	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

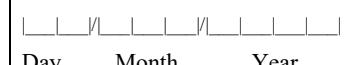
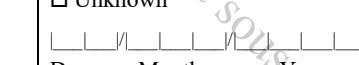
Baseline	
Study short title RESIST-PC	Patient identifier ____ - ____ - ____
• Prostate Cancer History	
Histopathology reports available	<input type="checkbox"/> yes <input type="checkbox"/> no, please comment: _____
N.B.: Histopathologically confirmed prostate cancer is an inclusion criterion	
Date of histopathology report/biopsy	____/____/____ day month year
Type of prostate cancer tumor	<input type="checkbox"/> adenocarcinoma <input type="checkbox"/> other: _____
PSA at initial diagnosis:	date of determination ____/____/____ day month year result _____._____ <u>unit:</u> <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____ <input type="checkbox"/> not done
Gleason Score (preferred format X+Y=Z; Biopsy or Prostatectomy)	____ + ____ = ____ <input type="checkbox"/> biopsy <input type="checkbox"/> prostatectomy
TNM at initial diagnosis	T ____ N ____ M ____

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline	
Study short title RESIST-PC	Patient identifier _____ - _____ - _____
Last three PSA values:	
Date 1: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Date 2: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Date 3: _____/_____/_____ day month year	PSA: _____ . ____ unit: <input type="checkbox"/> ng/mL <input type="checkbox"/> if other unit, specify: _____
Change of therapy between date #1 to #3	<input type="checkbox"/> Yes, please document all therapies on prostate cancer treatment history section <input type="checkbox"/> No
Documented PSA value doubling time:*	_____ days
Current TNM (at study inclusion)	T ____ N ____ M ____

*Please use the calculator system: <http://www.doubling-time.com/compute-PSA-doubling-time.php>

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title RESIST-PC		Patient identifier [] - [] - []				
• Prostate Cancer Treatment History: Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
2	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
3

Baseline

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Study short title RESIST-PC		Patient identifier [] - [] - []				
• Prostate Cancer Treatment History: Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	<input type="checkbox"/> [] Gy OR <input type="checkbox"/> []. [] mCi		<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
2	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy <input type="checkbox"/> other, specify: <hr/>	<input type="checkbox"/> [] Gy OR <input type="checkbox"/> []. [] mCi		<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> Unknown <hr/> Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
3
• Prostate Cancer Treatment History: Other Treatment						
Any other treatment?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below		

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title		Patient identifier				
#	Therapy	Comments	started	ended		best response
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year		<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing
2	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: <hr/>		<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year		<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title	Patient identifier					
RESIST-PC	[REDACTED] - [REDACTED] - [REDACTED]					
3

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier ____ - ____ - ____	
Imaging within the past three months CT (repeatable event)	Date of imaging ____/____/____ day month year	
MRI (repeatable event)	____/____/____ day month year	
PET/CT ⁶⁸ Ga-PSMA (repeatable event)	____/____/____ day month year	
SPECT/CT ¹⁷⁷ Lu-PSMA	____/____/____ day month year	
BONE SCAN (repeatable event)	____/____/____ day month year	tracer: _____
RENAL SCAN (OPTIONAL) ADD IN	____/____/____ day month year	Result: _____
other, specify: _____	____/____/____ day month year	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline			
Study short title RESIST-PC	Patient identifier ____ - ____ - ____		
• Medical History			
Date of Assessment:	____/____/____		
	day	month	year
Any relevant medical history?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify below:		
Condition / Illness	Started	Ended	
1.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
2.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
3.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
4.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
5.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
6.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
7.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	
8.	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	<input type="checkbox"/> Unknown ____/____/____ Day Month Year	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title RESIST-PC	Patient identifier _____ - _____ - _____	
• Baseline findings		
<p>Note: Please list below all conditions which started before the patient signed the informed consent form and for which symptoms or treatment were recorded during the time between signature of informed consent and first administration of the study drug, including conditions which were stabilized by treatment</p> <p>Conditions present before study drug administration are to be documented as Baseline Findings; conditions which started or deteriorated after administration of the study drug will be documented as Adverse Events on a specific AE page of the CRF</p>		
Date of Assessment:	_____/_____/_____ day month year	
Any relevant baseline findings?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify below:	
Hypersensitivity assessment		
Known allergies:	<input type="checkbox"/> no <input type="checkbox"/> yes, specify below	
Abnormal findings / symptoms / diseases	Started	
1.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
2.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
3.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
4.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
5.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
6.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	
7.	<input type="checkbox"/> Unknown ____/____/_____ Day Month Year	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline		
Study short title	Patient identifier	_____ - _____ - _____
RESIST-PC		
• ECOG		
Date of Assessment:	_____ / _____ / _____ day month year	
ECOG performance status	_____	<p>0 Fully active, able to carry on all pre-disease performance without restriction</p> <p>1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work</p> <p>2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours</p>

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
• Laboratory						
Date of Assessment:		[] / [] / [] day month year				
Test	Result	Unit	Unit, if differ- ent	mark if abnormal	clarification of abnormal	clinically significant
RBC	[] [] [] [] [] [] []	[] 10E6/ μ L [] Million/ μ L [] Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	[] [] [] [] [] [] []	[] 10E3/ μ L [] Thousand/ μ L [] Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	[] [] [] [] [] [] []	[] 10E3/ μ L [] Thousand/ μ L [] Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	[] [] [] [] [] [] []	absolute # [] cells/ μ L [] 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	[] [] [] [] [] [] []	absolute # [] cells/ μ L [] 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	[] [] [] [] [] [] []	absolute # [] cells/ μ L [] 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	[] [] [] [] [] [] []	absolute # [] cells/ μ L [] 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	[] [] [] [] [] [] []	absolute # [] cells/ μ L [] 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	[] [] [] [] [] [] []	[] g/dL [] mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	[] [] [] [] [] [] []	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV	[] [] [] [] [] [] []	fL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	[] [] [] [] [] [] []	pg		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	[] [] [] [] [] [] []	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	[] [] [] [] [] [] []	μ mol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	[] [] [] [] [] [] []	μ mol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

alk. phosphatase	□□□□□	<input type="checkbox"/> IU/L <input type="checkbox"/> U/L <input type="checkbox"/> μ mol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	□□□□□	<input type="checkbox"/> mg/L <input type="checkbox"/> mg/dL <input type="checkbox"/> μ mol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	□□□□□	<input type="checkbox"/> g/dL <input type="checkbox"/> g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	□□□□□	<input type="checkbox"/> mg/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine	□□□□□	<input type="checkbox"/> mg/dL <input type="checkbox"/> μ mol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR*	□□□□□	mL/min/1,73 m^2		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	□□□□□	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	□□□□□	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	□□□□□	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

*eGFR calculation formula (<https://www.kidney.org/content/ckd-epi-creatinine-equation-2009>)

CKD-EPI Creatinine Equation (2009)	Abbreviations / Units
Expressed as a single equation: eGFR = 141 x min (SCr/ κ , 1) $^\alpha$ x max(SCr/ κ , 1) $^{1-2.09}$ x 0.993 Age x 1.018 [if female] x 1.159 [if Black]	eGFR (estimated glomerular filtration rate) = mL/min/1.73 m ² SCr (standardized serum creatinine) = mg/dL κ = 0.7 (females) or 0.9 (males) α = -0.329 (females) or -0.411 (males) min = indicates the minimum of SCr/ κ or 1 max = indicates the maximum of SCr/ κ or 1 age = years

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline			
Study short title RESIST-PC	Patient identifier ____ - ____ - ____		
• PSA measurement			
Date of Assessment: _____._____._____ <small>unit:</small> <input type="checkbox"/> ng/mL	_____ <small>day</small>	_____ <small>month</small>	_____ <small>year</small>
<input type="checkbox"/> if other unit, specify:			

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FINAL 1.4 (03 November 2017)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Baseline			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____		
• Imaging			
Date and time of imaging	_____	_____	_____ Day Month Year hrs : min
Ga-68 PSMA PET/CT or Lu-177 PSMA scintigraphy or equivalent result	<input type="checkbox"/> positive (tumor lesions visible) <input type="checkbox"/> negative (no tumor lesion visible)		
Mean PSMA expression of lesions by visual assessment:	Score	Reported PSMA expression	Uptake
	<input type="checkbox"/> 0	no	Below bloodpool
	<input type="checkbox"/> +	low	Equal to or above bloodpool and lower than liver
	<input type="checkbox"/> ++	intermediate	Equal to or above liver and lower than salivary glands
	<input type="checkbox"/> +++	high	Equal to or above salivary glands

Please make sure all additional questionnaires are completed by the patient as applicable

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Concomitant Medication								
Study short title RESIST-PC			Patient No.+ Initials _____ - _____ - _____					
Any medication taken between 28 days before inclusion and "end of study"?					<input type="checkbox"/> No		<input type="checkbox"/> Yes, please specify details below	
Generic name (Brand name for combination drugs)	Indication	Total daily dose	Dose unit	Regimen 1 = PRN, 2 daily, 3 = once, 4 = QD, 5 = BID, 6 = TID, 7 = Q6H, 8 = Q8H, 9 = Q12H, 10 QHS, 11 infusion, 12 continuous infusion, 13 other, specify	Route 1 = oral, 2 = s c , 3 = i m , 4 = IV, 5 = inhalation, 6 = topical, 7 = transdermal, 8 rectal, 9 = other, specify	Date of first administration	Date of last administration	
1.				_____	_____	_____/_____/_____ <input type="checkbox"/> Day <input type="checkbox"/> Month <input type="checkbox"/> Year <input type="checkbox"/> unknown	_____/_____/_____ <input type="checkbox"/> Day <input type="checkbox"/> Month <input type="checkbox"/> Year <input type="checkbox"/> Continuing at end of study	
2.				_____	_____	_____/_____/_____ <input type="checkbox"/> Day <input type="checkbox"/> Month <input type="checkbox"/> Year <input type="checkbox"/> unknown	_____/_____/_____ <input type="checkbox"/> Day <input type="checkbox"/> Month <input type="checkbox"/> Year <input type="checkbox"/> Continuing at end of study	
3.				_____	_____	_____/_____/_____ <input type="checkbox"/> Day <input type="checkbox"/> Month <input type="checkbox"/> Year <input type="checkbox"/> unknown	_____/_____/_____ <input type="checkbox"/> Day <input type="checkbox"/> Month <input type="checkbox"/> Year <input type="checkbox"/> Continuing at end of study	
4.				_____	_____	_____/_____/_____ <input type="checkbox"/> Day <input type="checkbox"/> Month <input type="checkbox"/> Year <input type="checkbox"/> unknown	_____/_____/_____ <input type="checkbox"/> Day <input type="checkbox"/> Month <input type="checkbox"/> Year <input type="checkbox"/> Continuing at end of study	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Randomization	
Study short title RESIST-PC	Patient No.+ Initials [] - [] - []
Date of Randomization:	[] / [] / [] day month year
Patient is randomized to	<input type="checkbox"/> arm 1 (6.0 GBq per Radioligand therapy) corresponds to 162 mCi <input type="checkbox"/> arm 2 (7.4 GBq per Radioligand therapy)) corresponds to 200 mCi

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry	
Study short title RESIST-PC	Patient No.+ Initials ____ - ____ - ____
Date of RLT:	____ / ____ / ____ day month year
Cycle for dosimetry	<input type="checkbox"/> Cycle 1 <input type="checkbox"/> Cycle 2
• 12 lead ECG Before Injection	
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
Heart rate	____ /min
PR interval	____ msec
QRS interval	____ msec
QT interval	____ msec
QTc interval	____ msec

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry						
Study short title		Patient No.+ Initials				
RESIST-PC		- -				
• Laboratory						
Date of Assessment:		/ /	day	month	year	
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC		<input type="checkbox"/> 10E6/ μ L <input type="checkbox"/> Million/ μ L <input type="checkbox"/> Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin		<input type="checkbox"/> g/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV		fL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH		pg		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry						
Study short title	Patient No.+ Initials					
RESIST-PC	_____ - _____ - _____					
RDW	_____	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	_____	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	_____	□ IU/L □ U/L □ μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	_____	□ mg/L □ mg/dL □ μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	_____	□ g/dL □ g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	_____	□ mg/dL □ mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine	_____	□ mg/dL □ μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR*	_____	mL/min/1,73m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no
<input type="checkbox"/> eGFR <input type="checkbox"/> estimated from renal scan						
sodium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	_____	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

*eGFR calculation formula (<https://www.kidney.org/content/ckd-epi-creatinine-equation-2009>):

CKD-EPI Creatinine Equation (2009)	Abbreviations / Units
Expressed as a single equation: eGFR = 141 x min(SCr/k, 1)α x max(SCr /k, 1)-1 209 x 0 993Age x 1 018 [if female] x1 159 [if Black]	eGFR (estimated glomerular filtration rate) = mL/min/1.73 m ² SCr (standardized serum creatinine) = mg/dL k = 0.7 (females) or 0.9 (males) α = -0.329 (females) or -0.411 (males) min = indicates the minimum of SCr/k or 1 max = indicates the maximum of SCr/k or 1 age = years

Radioligand Therapy (RLT) – Injection Visit including dosimetry

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Study short title RESIST-PC	Patient No.+ Initials ____ - ____ - ____
• Salivary protection (30 min before injection and continued for 4 hours)	
Applying ice pack	<input type="checkbox"/> done <input type="checkbox"/> not done, provide comment _____
• Vital Signs Before Injection (within 20 min before injection)	
Temperature	____.____ °C <input type="checkbox"/> F
Heart Rate	____ /min
Respiratory Rate	____ /min
Blood Pressure Systolic	____ mmHg
Blood Pressure Diastolic	____ mm Hg

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

• RLT					
Activity in syringe before injection	_____._____ mCi				
Date and time of start of measurement	day	month	year	hr	min
Injected activity	_____._____ mCi				
Date and time of RLT	day	month	year	hr	min
Activity in syringe after injection	_____._____ mCi				
Date and time of end of measurement	day	month	year	hr	min
Completed as planned	<input type="checkbox"/> yes <input type="checkbox"/> no, specify _____				
Any adverse event	<input type="checkbox"/> yes, complete AE page <input type="checkbox"/> no				
• Vital Signs After Injection - 30 minutes post-infusion					
Time	_____._____ hh min				
Temperature	_____.____ <input type="checkbox"/> °C <input type="checkbox"/> F				
Heart Rate	_____ /min				
Respiratory Rate	_____ /min				
Blood Pressure Systolic	_____ mmHg				
Blood Pressure Diastolic	_____ mm Hg				
• Vital Signs After Injection - 60 minutes post-infusion					
Time	_____._____ hh min				
Temperature	_____.____ <input type="checkbox"/> °C <input type="checkbox"/> F				
Heart Rate	_____ /min				

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Respiratory Rate	_____ /min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____		
• (Holter) ECG monitoring results for the period 20 min prior to and 1 hour post-infusion			
<input type="checkbox"/> done, please fill out the below <input type="checkbox"/> not done, provide comment _____			
Date and time of ECG monitoring	____/____/____	____	____:____ Day Month Year hrs : min
Overall evaluation of ECG monitoring	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below _____		
Comment	_____		
Heart rate	_____/min		
PR interval	____ msec		
QRS interval	____ msec		
QT interval	____ msec		
QTc interval	____ msec		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• 12 lead ECG 4 hours after Injection	
<input type="checkbox"/> done, please fill out the below <input type="checkbox"/> not done, provide comment _____	
Overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
Heart rate	_____ /min
PR interval	_____ msec
QRS interval	_____ msec
QT interval	_____ msec
QTc interval	_____ msec

PSMA-directed endoRadiotherEapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry							
Study short title RESIST-PC		Patient No.+ Initials _____ - _____ - _____					
• Dosimetry: Blood Samples							
With regard to injection site, was the blood draw performed				<input type="checkbox"/> contralateral <input type="checkbox"/> ipsilateral, different i.v. access <input type="checkbox"/> (ipsilateral, same i.v. access)			
0 min	<input type="checkbox"/> sample obtained, specify exact time post ¹⁷⁷ LuPSMA injection			<input type="checkbox"/> not obtained			
	____/____/____ ____ : ____			Day	Month	Year	hrs : min
	<input type="checkbox"/> date and time of measurement, specify exact time			<input type="checkbox"/> not measured			
	____/____/____ ____ : ____			Day	Month	Year	hrs : min
Volume measured: ____ , ____ mL							
Activity measured: ____ . ____ µCi/mL							
Measurement duration time: ____ min							
5 min	<input type="checkbox"/> sample obtained, specify exact time			<input type="checkbox"/> not obtained			
	____/____/____ ____ : ____			Day	Month	Year	hrs : min
	<input type="checkbox"/> date and time of measurement, specify exact time			<input type="checkbox"/> not measured			
	____/____/____ ____ : ____			Day	Month	Year	hrs : min
Volume measured: ____ , ____ mL							
Activity measured: ____ . ____ µCi/mL							
Measurement duration time: ____ min							
30 min	<input type="checkbox"/> sample obtained specify exact time			<input type="checkbox"/> not obtained			
	____/____/____ ____ : ____			Day	Month	Year	hrs : min
	<input type="checkbox"/> date and time of measurement, specify exact time			<input type="checkbox"/> not measured			
	____/____/____ ____ : ____			Day	Month	Year	hrs : min

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry							
Study short title RESIST-PC		Patient No.+ Initials _____ - _____ - _____					
		Volume measured: _____ mL					
		Activity measured: _____ . _____ μ Ci/mL					
		Measurement duration time: _____ min					
1 h	<input type="checkbox"/> sample obtained specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min				
	<input type="checkbox"/> date and time of measurement, specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min				
4 h	<input type="checkbox"/> sample obtained specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min				
	<input type="checkbox"/> date and time of measurement, specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min				
18-30 h	<input type="checkbox"/> sample obtained specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min				
	<input type="checkbox"/> date and time of measurement, specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min				
Volume measured: _____ mL							
Activity measured: _____ . _____ μ Ci/mL							
Measurement duration time: _____ min							

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry					
Study short title RESIST-PC		Patient No.+ Initials _____ - _____ - _____			
		Activity measured: _____ . _____ $\mu\text{Ci}/\text{mL}$ Measurement duration time: _____ min (10 min needed)			
42-54 h	<input type="checkbox"/> sample obtained specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		
	<input type="checkbox"/> date and time of measurement, specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		
	Volume measured: _____ mL		Activity measured: _____ . _____ $\mu\text{Ci}/\text{mL}$		
		Measurement duration time: _____ min (10 min needed)			
66-78 h	<input type="checkbox"/> sample obtained specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		
	<input type="checkbox"/> date and time of measurement, specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		
	Volume measured: _____ mL		Activity measured: _____ . _____ $\mu\text{Ci}/\text{mL}$		
		Measurement duration time: _____ min (10 min needed)			
7-9 d (optional)	<input type="checkbox"/> sample obtained specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not obtained _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		
	<input type="checkbox"/> date and time of measurement, specify exact time _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		<input type="checkbox"/> not measured _____ / _____ / _____ _____ : _____ Day Month Year hrs : min		
	Volume measured: _____ mL				

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
Activity measured: _____ . _____	µCi/mL
Measurement duration time: _____ min (10 min needed)	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____		
• Dosimetry: Scintigraphy			
4 h	<input type="checkbox"/> whole body planar obtained, specify exact time <input type="checkbox"/> not obtained ____:____ hh min Scan duration _____ min		
18-30 h	date: ____/____/____ Day Month Year hrs : min whole body planar: <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____:_____ hrs : min Scan duration _____ min SPECT/CT head <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____:_____ hrs : min Duration per angle _____ min SPECT/CT thorax <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____:_____ hrs : min Duration per angle _____ min SPECT/CT abd. <input type="checkbox"/> not obtained <input type="checkbox"/> obtained, start time: _____:_____ hrs : min Duration per angle _____ min		
42-54 h	<input type="checkbox"/> whole body planar obtained, specify date/time <input type="checkbox"/> not obtained ____/____/____ Day Month Year hrs : min Scan duration _____ min		

PSMA-directed endoRadioThErapy of castration-reSISTant Prostate Cancer (RESIST-PC)

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FINAL 1.4 (03 November 2017)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry			
Study short title RESIST-PC	Patient Identifier _____ - _____ - _____		
• Dosimetry: Urine Collection			
collected from injection until 4 h p.i.	<input type="checkbox"/> done <input type="checkbox"/> not done, specify Urine net weight: _____ g date and time of measurement,, specify exact time (post inj) <input type="checkbox"/> not measured ____/____/____ ____:____ Day Month Year hrs : min Volume measured: _____ mL Activity measured: _____ . _____ <input type="checkbox"/> μCi/mL <input type="checkbox"/> μCi/g Measurement duration time: _____ min		
collected from 4h-until discharge from hospital	<input type="checkbox"/> done <input type="checkbox"/> not done, specify date and time of discharge: ____/____/____ ____:____ Day Month Year hrs : min Urine net weight: _____ g Activity measured: _____ . _____ <input type="checkbox"/> μCi/mL <input type="checkbox"/> μCi/g Measurement duration time: _____ min		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit including dosimetry		
Study short title	Patient identifier	
RESIST-PC	[REDACTED] - [REDACTED] - [REDACTED]	
• PSA measurement (PSA is measured every 6 weeks during treatment+after treatment period every 3 months)		
Date of Assessment:	[REDACTED]	[REDACTED] / [REDACTED] / [REDACTED] day month year
unit:	[REDACTED]. [REDACTED]	
<input type="checkbox"/> ng/mL		
<input type="checkbox"/> if other unit, specify: _____		

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) - Injection Visit including dosimetry - Concomitant cancer-related therapy since last visit						
Study short title RESIST-PC		Patient identifier - -				
Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify _____			<input type="checkbox"/> Unknown Day Month Year	<input type="checkbox"/> Unknown Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy	 OR	Gy	<input type="checkbox"/> Unknown Day Month Year	<input type="checkbox"/> Unknown Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD

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FINAL 1.4 (03 November 2017)

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) - Injection Visit including dosimetry - Concomitant cancer-related therapy since last visit					
Study short title RESIST-PC		Patient identifier _____ - _____ - _____			
<input type="checkbox"/> other, specify: _____	<input type="checkbox"/> _____ mCi				<input type="checkbox"/> missing
Other Treatment					
Any other treatment?		<input type="checkbox"/> no, please skip this section		<input type="checkbox"/> yes, please complete below	
#	Therapy	Comments	started	ended	best response
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: _____		<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title	Patient No.+ Initials
RESIST-PC	_____ - _____ - _____
• Study drug administration complications	
Has any complication related to administration of the drug occurred (e.g., overdose, observable extravasation, medication error)?	<input type="checkbox"/> no <input type="checkbox"/> yes, please specify: _____
<input type="checkbox"/> Report was sent to the pharmacovigilance designee.	

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow –Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

12 weeks PSA measurement		
Study short title	Patient identifier	
RESIST-PC	____ - ____ - ____	
• PSA measurement		
Date of Assessment:	____ / ____ / ____	day month year
____ . ____		
<u>unit:</u>		
<input type="checkbox"/> ng/mL		
<input type="checkbox"/> if other unit, specify:		

• ECOG		
Date of Assessment:	____ / ____ / ____	
ECOG performance status	____	
	0	Fully active, able to carry on all pre-disease performance without restriction
	1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
	2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
	3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
	4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair

At week 12 also to be completed:

- Lab values (CBC, CMP)
- Imaging questionnaires
- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Additional evaluation of blood tests every 2 weeks (not cycle 1-4 and not Follow-up)						
Study short title		Patient No.+ Initials				
RESIST-PC		_____ - _____ - _____				
• Laboratory						
Date of Assessment:		_____ / _____ / _____ day month year				
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC	 	<input type="checkbox"/> 10E6/ μ L <input type="checkbox"/> Million/ μ L <input type="checkbox"/> Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC	 	<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets	 	<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils	 	absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes	 	absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes	 	absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils	 	absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils	 	absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin	 	<input type="checkbox"/> g/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit	 	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Additional evaluation of blood tests every 2 weeks (not cycle 1-4 and not Follow-up)						
Study short title	Patient No.+ Initials					
RESIST-PC	[] - [] - []					
MCV	[]	fL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCH	[]	pg		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	[]	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	[]	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	[]	µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	[]	<input type="checkbox"/> IU/L <input type="checkbox"/> U/L <input type="checkbox"/> µmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	[]	<input type="checkbox"/> mg/L <input type="checkbox"/> mg/dL <input type="checkbox"/> µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	[]	<input type="checkbox"/> g/dL <input type="checkbox"/> g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	[]	<input type="checkbox"/> mg/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatininine	[]	<input type="checkbox"/> mg/dL <input type="checkbox"/> µmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR <input type="checkbox"/> eGFR <input type="checkbox"/> estimated from renal scan	[]	mL/min/1,73 m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	[]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	[]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	[]	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

*eGFR calculation formula (<https://www.kidney.org/content/ckd-epi-creatinine-equation-2009>):

CKD-EPI Creatinine Equation (2009)	Abbreviations / Units
Expressed as a single equation: eGFR = 141 x min (S _{Cr} /κ, 1) ^a x	eGFR (estimated glomerular filtration rate) = mL/min/1.73 m ² SCr (standardized serum creatinine) = mg/dL κ = 0.7 (females) or 0.9 (males)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

max(SCr /κ, 1) ^{-1.209} x 0.993 ^{Age} x 1.018 [if female] x 1.159 [if Black]	$\alpha = -0.329$ (females) or -0.411 (males) min = indicates the minimum of SCr/κ or 1 max = indicates the maximum of SCr/κ or 1 age = years
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Additional PSA measurements	
Study short title	Patient identifier
RESIST-PC	_____ - _____ - _____
• PSA measurement	
Date of Assessment:	_____/_____/_____ day month year
_____ · _____	
<u>unit:</u>	
<input type="checkbox"/> ng/mL	
<input type="checkbox"/> if other unit, specify: _____	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title	Patient No.+ Initials		
RESIST-PC	_____ - _____ - _____		
• Physical Examination			
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done		
Date Physical Examination:	day	month	year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal		
Comments: General Appearance	_____		
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____		
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Cardiovascular	_____		
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Respiratory	_____		
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Gastrointestinal	_____		
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Musculoskeletal	_____		
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done		
Comments: Genitourinary	_____		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title	Patient No.+ Initials		
RESIST-PC	- -		
Skin	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments: Skin	_____		
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments Neurological	_____		
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments	_____		

• ECOG			
Date of Assessment:	/ / day month year		
ECOG performance status		<p>0 Fully active, able to carry on all pre-disease performance without restriction 1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work 2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours 3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours 4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair</p>	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Relevant imaging before new cycle		
Study short title RESIST-PC	Patient No.+ Initials. ____ - ____ - ____	
Imaging		
<input type="checkbox"/> CT <input type="checkbox"/> MRI <input type="checkbox"/> PET/CT <input type="checkbox"/> Scintigraphy <input type="checkbox"/> Other <input type="checkbox"/> Not done		
CT (repeatable event)	____ / ____ / ____	day month year
Tumor location Location of metastases		
MRI (repeatable event)	____ / ____ / ____	day month year
PET/CT (repeatable event)	____ / ____ / ____	day month year
tracer:		
Scintigraphy (repeatable event)	____ / ____ / ____	day month year
tracer:		
other, specify: _____	____ / ____ / ____	day month year
Imaging result:	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title	Patient No.+ Initials
RESIST-PC	____ - ____ - ____
Date of RLT:	____ / ____ / ____ day month year
• 12 lead ECG Before Injection	
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below
Comment	_____
heart rate	____ /min
PR interval	____ msec
QRS interval	____ msec
QT interval	____ msec
QTc interval	____ msec

PSMA-directed endoRadiotherEapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____		
• ECG before injection			
date and time of ECG	_____	_____	_____ Day Month Year hrs : min
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below _____		
Comment	_____		
heart rate	_____ /min		
PR interval	_____ msec		
QRS interval	_____ msec		
QT interval	_____ msec		
QTc interval	_____ msec		

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____
• Salivary protection (30 min before injection and continued for 4 hours)	
Applying ice pack	<input type="checkbox"/> done, please fill out the below <input type="checkbox"/> not done, provide comment _____
• Vital Signs Before Injection (within 20 min before injection)	
Temperature	_____ . ____ °C <input type="checkbox"/> F
Heart Rate	_____ /min
Respiratory Rate	_____ /min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg
• RLT	
activity in syringe before injection	_____ mCi
Date and time of measurement	_____ /_____ /_____ - _____ : _____ day month year hrs min
injected activity date and time of RLT	_____ mCi _____ /_____ /_____ - _____ : _____ day month year hrs min
activity in syringe after injection Date and time of measurement	_____ mCi _____ /_____ /_____ - _____ : _____ day month year hrs min
completed as planned	<input type="checkbox"/> yes <input type="checkbox"/> no, specify _____
any adverse event	<input type="checkbox"/> yes, complete AE page <input type="checkbox"/> no

PSMA-directed endoRadiotherapY of castration-reSISTant Prostate Cancer (RESIST-PC)

• Vital Signs After Injection - 30 minutes post-infusion	
time	_____ hh : mm
Temperature	_____ . ____ °C <input type="checkbox"/> F
Heart Rate	_____ /min
Respiratory Rate	_____ /min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg
• Vital Signs After Injection - 60 minutes post-infusion	
time	_____ hh : mm
Temperature	_____ . ____ °C <input type="checkbox"/> F
Heart Rate	_____ /min
Respiratory Rate	_____ /min
Blood Pressure Systolic	_____ mmHg
Blood Pressure Diastolic	_____ mm Hg

PSMA-directed endoRadiotherEapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)			
Study short title	Patient No.+ Initials		
RESIST-PC	_____	-	_____ - _____
• Holter ECG monitor results for the period 20 prior to and 1 hour post-infusion			
date and time of ECG	_____	_____	_____
Day	Month	Year	hrs : min
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below		
Comment	_____		
heart rate	_____ /min		
PR interval	_____ msec		
QRS interval	_____ msec		
QT interval	_____ msec		
QTc interval	_____ msec		

PSMA-directed endoRadiotherEapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit 1-4						
Study short title		Patient No.+ Initials				
RESIST-PC		_____ - _____ - _____				
• Laboratory						
Date of Assessment:		_____ / _____ / _____ day month year				
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC		<input type="checkbox"/> 10E6/ μ L <input type="checkbox"/> Million/ μ L <input type="checkbox"/> Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin		<input type="checkbox"/> g/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV		fL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherEapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit 1-4						
Study short title	Patient No.+ Initials					
RESIST-PC	[REDACTED] - [REDACTED] - [REDACTED]					
MCH	[REDACTED] pg		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
RDW	[REDACTED] %		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
SGOT / AST	[REDACTED] $\mu\text{mol/L}$		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
SGPT / ALT	[REDACTED] $\mu\text{mol/L}$		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
alk. phosphatase	[REDACTED] IU/L U/L $\mu\text{mol/L}$		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
total bilirubin	[REDACTED] mg/L mg/dL $\mu\text{mol/L}$		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
total albumin	[REDACTED] g/dL g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
BUN	[REDACTED] mg/dL mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
creatinine	[REDACTED] mg/dL $\mu\text{mol/L}$		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
GFR*	[REDACTED] mL/min/1.73 m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no	
eGFR estimated from renal scan						
sodium	[REDACTED] mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
potassium	[REDACTED] mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	
chloride	[REDACTED] mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no	

*eGFR calculation formula (<https://www.kidney.org/content/ckd-epi-creatinine-equation-2009>):

CKD-EPI Creatinine Equation (2009)	Abbreviations / Units
Expressed as a single equation: eGFR = 141 x min (S _{Cr} /κ, 1) ^a x max(S _{Cr} / κ, 1) ^{-1.209} x 0.993 ^{Age} x 1.018 [if female] x 1.159 [if Black]	eGFR (estimated glomerular filtration rate) = mL/min/1.73 m ² SCr (standardized serum creatinine) = mg/dL κ = 0.7 (females) or 0.9 (males) a = -0.329 (females) or -0.411 (males) min = indicates the minimum of SCr/κ or 1 max = indicates the maximum of SCr/κ or 1 age = years

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

PSA measurements		
Study short title	Patient identifier	
RESIST-PC	[] - [] - []	
• PSA measurement		
Date of Assessment:	[] / [] / []	[] day [] month [] year
[] . []		
<u>unit:</u>		
<input type="checkbox"/> ng/mL		
<input type="checkbox"/> if other unit, specify:		

PSMA-directed endoRadiotherEapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title RESIST-PC	Patient No.+ Initials <u> </u> - <u> </u> - <u> </u>
• 12 lead ECG 4 hours after Injection (after salivary protection is completed)	
overall evaluation of ECG	<input type="checkbox"/> normal <input type="checkbox"/> abnormal not clinically significant <input type="checkbox"/> abnormal, clinically significant, please provide comment below <hr/>
Comment	<hr/>
heart rate	<u> </u> /min
PR interval	<u> </u> msec
QRS interval	<u> </u> msec
QT interval	<u> </u> msec
QTc interval	<u> </u> msec

Scintigraphy	
optional	<input type="checkbox"/> whole body planar obtained, specify date/time obtained <u> </u> / <u> </u> / <u> </u> : <u> </u> Day Month Year hrs : min Scan duration <u> </u> min

PSMA-directed endoRadioThErapY of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) – Injection Visit (1-4)	
Study short title	Patient No.+ Initials
RESIST-PC	_____ - _____ - _____
• Study drug administration complications	
Has any complication related to administration of the drug occurred (e.g., overdose, observable extravasation, medication error)?	<input type="checkbox"/> no <input type="checkbox"/> yes, please specify: _____
<input type="checkbox"/> Report was sent to the pharmacovigilance designee.	

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) - Injection Visit 1-4 - Concomitant cancer-related therapy since last visit						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify _____			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy	 OR Gy		<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD

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PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Radioligand Therapy (RLT) - Injection Visit 1-4 - Concomitant cancer-related therapy since last visit					
Study short title		Patient identifier			
RESIST-PC		_____ - _____ - _____			
<input type="checkbox"/> other, specify: _____	_____ mCi	_____	_____	_____	<input type="checkbox"/> missing
Other Treatment					
Any other treatment?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below			
#	Therapy	Comments	started <input type="checkbox"/> Unknown _____ Day Month Year	ended <input type="checkbox"/> Unknown _____ Day Month Year	best response
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: _____				<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up		
Study short title RESIST-PC	Patient No.+ Initials _____ - _____ - _____	
• Physical Examination		
Physical Examination:	<input type="checkbox"/> done <input type="checkbox"/> not done	
Date Physical Examination:	_____/_____/_____	day month year
General Appearance	<input type="checkbox"/> normal <input type="checkbox"/> abnormal	
Comments: General Appearance	_____	
Head/Ears/Eyes/Nose/Mouth/Throat	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Head/Ears/Eyes/Nose/Mouth/Throat	_____	
Cardiovascular	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Cardiovascular	_____	
Respiratory	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Respiratory	_____	
Gastrointestinal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Gastrointestinal	_____	
Musculoskeletal	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Musculoskeletal	_____	
Genitourinary	<input type="checkbox"/> normal <input type="checkbox"/> abnormal <input type="checkbox"/> not done	
Comments: Genitourinary	_____	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up			
Study short title	Patient No.+ Initials		
RESIST-PC	- -		
Skin	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments: Skin	_____		
Neurological / Development	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments Neurological	_____		
Other, specify	<input type="checkbox"/> normal	<input type="checkbox"/> abnormal	<input type="checkbox"/> not done
Comments	_____		

• Vital Signs			
Temperature	.	<input type="checkbox"/> °C	<input type="checkbox"/> F
Heart Rate		/min	
Respiratory Rate		/min	
Blood Pressure Systolic		mmHg	
Blood Pressure Diastolic		mm Hg	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-Up		
Study short title RESIST-PC	Patient No.+ Initials ____ - ____ - ____	
• ECOG		
Date of Assessment:	____/____/____	day month year
ECOG performance status	____ 0 Fully active, able to carry on all pre-disease performance without restriction 1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work 2 Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours 3 Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours 4 Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

•Follow up						
Study short title RESIST-PC		Patient No.+ Initials. _____ - _____ - _____				
•Laboratory						
Date of Assessment:		_____ / _____ / _____ day month year				
Test	Result	Unit	Unit, if different	mark if abnormal	clarification of abnormal	clinically significant
RBC		<input type="checkbox"/> 10E6/ μ L <input type="checkbox"/> Million/ μ L <input type="checkbox"/> Tpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
WBC		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
platelets		<input type="checkbox"/> 10E3/ μ L <input type="checkbox"/> Thousand/ μ L <input type="checkbox"/> Gpt/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
neutrophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
lymphocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
monocytes		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
eosinophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
basophils		absolute # <input type="checkbox"/> cells/ μ L <input type="checkbox"/> 10E3/ μ L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hemoglobin		<input type="checkbox"/> g/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
hematocrit		%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
MCV		fL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

MCH	□□□□□ □□	pg		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
RDW	□□□□□ □□	%		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGOT / AST	□□□□□ □□	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
SGPT / ALT	□□□□□ □□	μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
alk. phosphatase	□□□□□ □□	<input type="checkbox"/> IU/L <input type="checkbox"/> U/L <input type="checkbox"/> μmol/sL		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total bilirubin	□□□□□ □□	<input type="checkbox"/> mg/L <input type="checkbox"/> mg/dL <input type="checkbox"/> μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
total albumin	□□□□□ □□	<input type="checkbox"/> g/dL <input type="checkbox"/> g/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
BUN	□□□□□ □□	<input type="checkbox"/> mg/dL <input type="checkbox"/> mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
creatinine	□□□□□ □□	<input type="checkbox"/> mg/dL <input type="checkbox"/> μmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
GFR*	□□□□□ □□	mL/min/1,73 m ²		<input type="checkbox"/>	<input type="checkbox"/> yes <input type="checkbox"/> no	<input type="checkbox"/> yes <input type="checkbox"/> no
sodium	□□□□□ □□	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
potassium	□□□□□ □□	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no
chloride	□□□□□ □□	mmol/L		<input type="checkbox"/>	<input type="checkbox"/> high <input type="checkbox"/> low	<input type="checkbox"/> yes <input type="checkbox"/> no

*eGFR calculation formula (<https://www.kidney.org/content/ckd-epi-creatinine-equation-2009>):

CKD-EPI Creatinine Equation (2009)	Abbreviations / Units
Expressed as a single equation: eGFR = 141 x min (S _{Cr} /κ, 1) ^α x max(SCr /κ, 1) ^{-1.209} x 0.993 ^{Age} x 1.018 [if female] x 1.159 [if Black]	eGFR (estimated glomerular filtration rate) = mL/min/1.73 m ² SCr (standardized serum creatinine) = mg/dL κ = 0.7 (females) or 0.9 (males) α = -0.329 (females) or -0.411 (males) min = indicates the minimum of SCr/κ or 1 max = indicates the maximum of SCr/κ or 1 age = years

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

End of treatment

Treatment was discontinued after cycle due to the following conditions:

- PSA/radiographic progression at ≥ 12 weeks
- Completion of four RLT cycles
- 23 Gy kidney dose would be exceeded by the next cycle as estimated by dosimetry
- patient withdrawal (e.g. appearance of intolerable adverse events)

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow up			
Study short title	Patient identifier		
RESIST-PC	- -		
• PSA measurement			
Date of Assessment:	/ /		
	day	month	year
unit:			
<input type="checkbox"/> ng/mL			
<input type="checkbox"/> if other unit, specify:			

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

•Follow up		
Study short title RESIST-PC	Patient No.+ Initials. _____ - _____ - _____	
Imaging		
<input type="checkbox"/> CT <input type="checkbox"/> MRI <input type="checkbox"/> PET/CT <input type="checkbox"/> Scintigraphy <input type="checkbox"/> Other <input type="checkbox"/> Not done		
CT (repeatable event)	_____ / _____ / _____ day month year	
Tumor location Location of metastases		
MRI (repeatable event)	_____ / _____ / _____ day month year	
PET/CT (repeatable event)	_____ / _____ / _____ day month year tracer:	
Scintigraphy (repeatable event)	_____ / _____ / _____ day month year tracer:	
other, specify: _____	_____ / _____ / _____ day month year	
Imaging result:	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD	

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-up - Concomitant cancer-related therapy since last visit						
Study short title		Patient identifier				
RESIST-PC		[] - [] - []				
Chemotherapy						
Any chemotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	no. of cycles	total dose	started	ended	best response
1	<input type="checkbox"/> Abiraterone <input type="checkbox"/> Enzalutamide <input type="checkbox"/> chemotherapy (docetaxel) <input type="checkbox"/> chemotherapy (cabazitaxel) <input type="checkbox"/> chemotherapy (other), specify <hr/>			<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> missing
Radiotherapy						
Any radiotherapy?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below				
#	Therapy	total dose	irradiated body region	started	ended	best response
1	<input type="checkbox"/> primary EBRT <input type="checkbox"/> salvage EBRT <input type="checkbox"/> bone targeted therapy <input type="checkbox"/> Radium223 <input type="checkbox"/> PSMA-directed radioligand therapy	 OR Gy		<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> Unknown  Day Month Year	<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Follow-up - Concomitant cancer-related therapy since last visit					
Study short title		Patient identifier			
RESIST-PC		[] - [] - []			
<input type="checkbox"/> other, specify: _____	[] mCi				<input type="checkbox"/> missing
Other Treatment					
Any other treatment?		<input type="checkbox"/> no, please skip this section <input type="checkbox"/> yes, please complete below			
#	Therapy	Comments	started <input type="checkbox"/> Unknown [] Day Month Year	ended <input type="checkbox"/> Unknown [] Day Month Year	best response
1	<input type="checkbox"/> Prostatectomy <input type="checkbox"/> TURP <input type="checkbox"/> salvage prostatectomy <input type="checkbox"/> cryotherapy <input type="checkbox"/> high-intensity focused ultrasound <input type="checkbox"/> pelvic lymph node resection <input type="checkbox"/> salvage lymph node resection <input type="checkbox"/> immunotherapy, specify <input type="checkbox"/> standard ADT <input type="checkbox"/> hormonal therapy <input type="checkbox"/> other, specify: _____				<input type="checkbox"/> CR <input type="checkbox"/> PR <input type="checkbox"/> SD <input type="checkbox"/> PD <input type="checkbox"/> NA <input type="checkbox"/> missing

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Please make sure all additional questionnaires are completed by the patient as applicable:

- EPIC-26 (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Baseline and follow -Up Questionnaire for Pain and Adverse Events (see appendix of protocol version amendment 4 from 18 Sep 2017)
- Imaging questionnaires (RECIST and Bone scan assessment)

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PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

End of study	
Study short title RESIST-PC	Patient No.+ Initials. [] - [] - []
Study course	<input type="checkbox"/> Patient completed study if study course completed, last day on study: []/[]/[] Day Month Year reason : <input type="checkbox"/> Progression <input type="checkbox"/> Follow-up completed <input type="checkbox"/> Death <input type="checkbox"/> Patient withdrew from study
If withdrawn, give date and time of withdrawal (24 h clock):	[]/[]/[] []:[] Day Month Year hr min
Specify main reason	<input type="checkbox"/> Withdrawal of consent <input type="checkbox"/> Lost to Follow-up <input type="checkbox"/> Any occurrence of conditions which prevented the patient's participation in the study? Please specify: <input type="checkbox"/> Protocol deviations? Please specify: <input type="checkbox"/> (Serious) AE? Please specify: <input type="checkbox"/> Administrative reasons? Please, specify: <input type="checkbox"/> Other? Please specify:
Who decided the withdrawal?	<input type="checkbox"/> Patient <input type="checkbox"/> Investigator <input type="checkbox"/> Other, please specify:

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Adverse Events						
Study short title RESIST-PC	Patient No.+ Initials. _____ - _____ - _____					
• Adverse Events <small>(Note: Adverse Event is any untoward medical occurrence in a volunteer or clinical investigation subject administered a pharmaceutical product and which does Not necessarily have a causal relationship with this treatment An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medical product)</small>						
Any AE experienced?	<input type="checkbox"/> No <input type="checkbox"/> If yes, please specify details on this form					
Adverse event description						
Onset date and time if available	Day	Month	Year	-	hrs	min
Serious AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please complete also the SAE form					
Maximum intensity:	<input type="checkbox"/> mild (easily tolerated) <input type="checkbox"/> moderate (interferes with usual functions) <input type="checkbox"/> severe (incapacitating)					
Specific drug treatment of AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify on "concomitant medication" page					
Specific Non-drug treatment of AE?	<input type="checkbox"/> No <input type="checkbox"/> Yes, please specify. _____					
Relationship to study drug / study conduct	Study drug relationship: <input type="checkbox"/> None <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite	Study conduct: <input type="checkbox"/> None <input type="checkbox"/> Unlikely <input type="checkbox"/> Possible <input type="checkbox"/> Probable <input type="checkbox"/> Definite				
Outcome / status	<input type="checkbox"/> Recovered / resolved without sequelae <input type="checkbox"/> Recovered / resolved with sequelae, specify <input type="checkbox"/> Not recovered / Not resolved <input type="checkbox"/> Death / Fatal <input type="checkbox"/> Unknown					
Study drug action	<input type="checkbox"/> Drug withdrawn <input type="checkbox"/> Dose not changed	<input type="checkbox"/> Dose reduced <input type="checkbox"/> Other action: _____				
Date and time if available (24 h clock) AE ended (only if recovered / resolved)	Day	Month	Year	-	hr	min
<input type="checkbox"/> Tick box if this page is the last adverse event						

PSMA-directed endoRadiotherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Serious Adverse Events	
Study short title RESIST-PC	Patient No.+ Initials. [] - [] - []
This view opens when AE serious: "yes" is ticked Also an automatic email is sent to resist-pc@phamtrace.com AND mali@excelediagnostics.com	
Seriousness criterion	
<input type="checkbox"/> Results in death (Date []/[]/[]) / <input type="checkbox"/> Life threatening <input type="checkbox"/> Hospitalization – initial or prolonged <input type="checkbox"/> Required intervention to prevent permanent impairment	<input type="checkbox"/> Congenital anomaly / birth defect <input type="checkbox"/> Persistent or significant disability/incapacity <input type="checkbox"/> Other serious (Important Medical Events)
Diagnosis	
Description / Symptoms including course of SAE and comments (continue description on additional pages, if required)	
Date of onset	[]/[]/[] day month year
Date ended (check ongoing box if not ended yet)	[]/[]/[] [] day month year <input type="checkbox"/> ongoing
Maximum intensity (CTCAE)	<input type="checkbox"/> 1 <input type="checkbox"/> 4 <input type="checkbox"/> 2 <input type="checkbox"/> 5 <input type="checkbox"/> 3 <input type="checkbox"/> unclassifiable
Study drug relationship ¹⁷⁷ Lu-PSMA-617	<input type="checkbox"/> none <input type="checkbox"/> unlikely <input type="checkbox"/> possible <input type="checkbox"/> probable <input type="checkbox"/> definite <input type="checkbox"/> unclassifiable
Study conduct relationship	<input type="checkbox"/> none <input type="checkbox"/> unlikely <input type="checkbox"/> possible <input type="checkbox"/> probable <input type="checkbox"/> definite <input type="checkbox"/> unclassifiable
Comment on assessment of study drug relationship	

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Outcome of SAE								
<input type="checkbox"/> Recovered without sequelae <input type="checkbox"/> Recovered with sequelae <input type="checkbox"/> Recovering / resolving			<input type="checkbox"/> Not recovered / not resolved <input type="checkbox"/> Fatal <input type="checkbox"/> Unknown					
Other possible causes of the event								
Check all that apply			Please specify					
<input type="checkbox"/> pre-existing / underlying disease								
<input type="checkbox"/> other treatment (concomitant or previous)								
<input type="checkbox"/> other (e.g. accident, new or intercurrent illness)								
Diagnostic tests and relevant lab values								
Diagnostic tests and relevant lab values		<input type="checkbox"/> Yes <input type="checkbox"/> No						
Test performed	Result			Normal Range		Date		
SAE Treatment								
SAE treatment	<input type="checkbox"/> Yes <input type="checkbox"/> No							
Drug to treat SAE (brand name)	Active agent	Indication	total daily dose	dose unit	route	first admin date	last admin date	ongoing
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>

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FINAL 1.4 (03 November 2017)

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Non-drug treatment: yes <input type="checkbox"/> no <input type="checkbox"/> If yes, please specify:						
Study drug administration						
Study drug	<input type="checkbox"/> ¹⁷⁷ Lu-PSMA-617 <input type="checkbox"/> not injected					
Administration date and time	day	month	year	hr	:	min
Injected activity	<input type="checkbox"/> MBq <input type="checkbox"/> mCi					
Most relevant study drug action due to SAE (please check one box only)	<input type="checkbox"/> drug withdrawn <input type="checkbox"/> administration stopped early	<input type="checkbox"/> dose not changed <input type="checkbox"/> dose reduced <input type="checkbox"/> not applicable				
Event abated after use/stopped or dose reduced	<input type="checkbox"/> Yes <input type="checkbox"/> Doesn't apply	<input type="checkbox"/> No				
Event reappeared after reintroduction	<input type="checkbox"/> Yes <input type="checkbox"/> Doesn't apply	<input type="checkbox"/> No				

PSMA-directed endoRadioTherapy of castration-reSISTant Prostate Cancer (RESIST-PC)

Concomitant medication at onset of SAE								
Concomitant medication at onset of SAE		<input type="checkbox"/> Yes <input type="checkbox"/> No						
Medication (brand name)	Active agent	Indication	total daily dose	dose unit	route	first admin. date	last admin. date	ongoing
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
								<input type="checkbox"/>
Medical history, including preexisting medical conditions								
Medical history, including preexisting medical conditions				<input type="checkbox"/> Yes <input type="checkbox"/> No				
Disease / symptoms (e.g. allergies, smoking and alcohol use, liver/kidney problems, etc.)				started	ended	ongoing		
						<input type="checkbox"/>		
						<input type="checkbox"/>		
						<input type="checkbox"/>		
						<input type="checkbox"/>		
						<input type="checkbox"/>		

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**Pages 1679 to 1768 of CSR Appendix
16.1.3 were removed due to being Out of
Scope as per Health Canada Guidance on
Public Release of Clinical Information -
List of IECs or IRBs (plus the name of the
committee Chair if required by the
regulatory authority) - Representative
written information for patient and
sample consent forms.**

**Pages 1769 to 1776 of CSR Appendix
16.1.4 were removed due to being Out of
Scope as per Health Canada Guidance on
Public Release of Clinical Information -
List and description of investigators and
other important participants in the study,
including brief (1 page) CVs or equivalent
summaries of training and experience
relevant to the performance of the clinical
study.**

**Pages 1777 to 1782 of CSR Appendix 16.1.5
were removed due to being Out of Scope as
per Health Canada Guidance on Public
Release of Clinical Information - Signatures
of principal or coordinating investigator(s)
or sponsor's responsible medical officer,
depending on the regulatory authority's
requirement.**

**Pages 1783 to 1788 of CSR Appendix 16.1.6
were removed due to being Out of Scope as
per Health Canada Guidance on Public
Release of Clinical Information - Listing of
patients receiving test drug(s)/investigational
product(s) from specific batches, where more
than one batch was used.**

Page 1789 of CSR Appendix 16.1.7 was removed due to being Out of Scope as per Health Canada Guidance on Public Release of Clinical Information - Randomisation scheme and codes (patient identification and treatment assigned).

Page 1790 of CSR Appendix 16.1.8 was removed due to being Out of Scope as per Health Canada Guidance on Public Release of Clinical Information - Audit certificates (if available) (see Annex IVa and IVb of the guideline).

Appendix 16.1.9 Documentation of statistical methods

History of changes	
Version	Summary of changes
1.0	Original version

1 Statistical methods

PSMA-617-02
Statistical Analysis Plan

Final

STATISTICAL ANALYSIS PLAN

Study PSMA-617-02

Title: (as per protocol/amendment)	PSMA-Directed Endoradiotherapy Of Castration-Resistant Prostate Cancer (RESIST-PC). A Phase II Clinical Trial
Version:	Final, Version 2.0
Date:	15-May-2020

CONFIDENTIAL

PSMA-617-02
Statistical Analysis Plan

DOCUMENT HISTORY

1 VERSION HISTORY

Version #	Version Date
Final v1.0	24Sep2019
Final v2.0	15May2020

2 REVISION HISTORY

Version #	Chapter	Revision Summary	Reason(s) for Revision
Final v1.0	N/A	Initial release	N/A
Final v.2.0	2.3.2	Definition of secondary objectives updated PSA progression is defined as the date that a $\geq 25\%$ increase in PSA and an absolute increase of 2 ng/mL or more from the nadir is documented and confirmed by a second value obtained 3 or more weeks later. Rises in PSA within the first 12 weeks will be ignored in the absence of other evidence of disease progression (PCWG3 Guidance). and PSA progression is defined as a 25% increase from the baseline value along with an increase in absolute value of 2 ng/mL or more after 12 weeks of treatment.	To be in line with the Prostate Cancer Clinical Trials Work Group 3 (Scher et al 2016) and to have comparable data for the two main studies in this indication, VISION and RESIST-PC.
	2.5	MedDRA version changed from 22.0 to 22.1	The clinical database was updated to the most current version of MedDRA; to correctly reflect the MedDRA version used in the study.
	3.4.1	Rules for imputation of missing dates clarified	To be consistent with the SAP sections 3.11.8-9.
	3.4.2	Rules for visit assignment for laboratory tests, PSA, Epic-26, ECG, vital signs, ECOG and AE questionnaire were added.	To account for the CRF structure, where data collected at different timepoints is presented under the same visit name,
	3.4.2	Baseline definition: If there is no time, only date of assessment is collected, then the last non-missing assessment prior or on date of first administration of Lu-PSMA-617 is used.	To clarify how baseline for assessments for which only date is collected is derived.
	3.5	Selection of the first result for the same assessment collected during a visit extended to all assessments.	To account for the changes in section 3.4.2, visit assignment.
	3.9	Clarification on data analyzed as Prior Cancer Related Therapy added.	To clarify based on the CRF structure.

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	3.9	Best overall response categories removed from the summaries for Other Treatment and Radiotherapy,	Patients could have multiple therapies recorded; therefore, a summary of best overall response would not be informative.
	3.10.2	<p>PSA progression-free survival (PFS): PSA PFS is measured from date of randomization until death or PSA progression.</p> <p>date that a $\geq 25\%$ increase in PSA and an absolute increase of 2 ng/mL or more from the nadir (from all visits prior to the current visit being evaluated) is documented and confirmed by a second value obtained 3 or more weeks later. Rises in PSA within the first 12 weeks of date of first dose will be ignored and</p> <p>PSA progression is defined as a $\geq 25\%$ increase from the baseline value along with an increase in absolute value of 2 ng/mL or more after 12 weeks from the date of first dose of treatment (without confirmation) as specified in PCWG3 guidelines.</p> <p>PSA PFS is calculated as the time from randomization to the date of first documentation of PSA progression or date of death due to any cause, whichever occurs first:</p> <p>PSA PFS = Date of PSA progression or death - date of randomization + 1</p> <p>Additional analysis for PSA PFS was added: Median follow-up (months) with 95% CI, censoring for deaths or PSA Progression, and range will be provided.</p>	To be in line with the Prostate Cancer Clinical Trials Work Group 3 (Scher et al 2016) and to have comparable data for the two main studies in this indication, VISION and RESIST-PC.
	3.10.2	Change in ECOG-PS	Data for ECOG was captured in CRF with each ^{177}Lu -PSMA-617 treatment visit and during follow-up
	3.11.3	MedDRA version changed from 22.0 to 22.1	The clinical database was updated to the most current version of MedDRA; to correctly reflect the MedDRA version used in the study.
	3.11.8-11	Best overall Response removed from the summaries for Concurrent and Post-Treatment Radiotherapy and Other Treatments, and for the Post-Treatment Chemotherapy	Patients could have multiple therapies recorded; therefore, a summary of best overall response would not be informative.
	2.1	The PSA related efficacy will not be analyzed. Only listing will be presented	The PSA related efficacy will not be analyzed due to the significantly smaller sample size and investigator's inconsistent timing of PSA data collection. PSA data will only be able to be listed

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	2.4.1-2.4.2, 3.10	Efficacy endpoints associated with efficacy objectives will not be analyzed.	The PSA related efficacy will not be analyzed due to the significantly smaller sample size and investigator's inconsistent timing of PSA data collection. PSA data will only be able to be listed
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3 APPROVAL SIGNATURES

STUDY TITLE: PSMA-Directed Endoradiotherapy Of Castration-Resistant Prostate Cancer (RESIST-PC). A Phase II Clinical Trial
PROTOCOL NUMBER: PSMA-617-02
SAP Final version 2.0, 15May2020

PSI:

Author: PI [REDACTED]

PI [REDACTED]

Date: 20-May-20 | 7:01:31 PM IST

Signature: [REDACTED]

Peer-reviewer Statistician: PI [REDACTED]

PI [REDACTED]

Date: 20-май-20 | 7:10:50 PM IST

Signature: [REDACTED]

Endocyte, Inc.

Reviewed/Approved By: PI [REDACTED]

PI [REDACTED]

PI [REDACTED]

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PI [REDACTED]

PI [REDACTED]

Signature: [REDACTED]

Date: [REDACTED]

Reviewed/Approved By: PI [REDACTED]

PI [REDACTED]

Date: 20-May-20 | 7:39:37 PM IST

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Reviewed/Approved By: PI [REDACTED]

M.H.S., M.Sc., Vice President, Medical Affairs

Signature: [REDACTED]

Date: 05-19-2020

Signature: [REDACTED]

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Abbreviations

Abbreviation	Description
AE	Adverse event
ALT/SGPT	Alanine aminotransferase/Serum glutamic-pyruvic transaminase
ANC	Absolute neutrophil count
AST/SGOT	Aspartate aminotransferase/Serum glutamic-oxaloacetic transaminase
ATC	Anatomic Therapeutic Chemical Classification
BUN	Blood urea nitrogen
CBC	Complete Blood Count
CI	Confidence interval
CMP	Comprehensive metabolic panel
CR	Complete response
CRF	Case report form
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
DCR	Disease control rate
ECG	Electrocardiogram
ECOG	Eastern cooperative oncology group
eGFR	estimated Glomerular Filtration Rate
EPIC	Expanded prostate cancer index composite
FT	Frequency table (prototype)
GBq	Gigabecquerel
Gy	Gray
IND	Investigational New Drug (application)
ITT	Intent-to-treat
i.v.	Intravenous
¹⁷⁷ Lu	Lutetium 177
mCRPC	Metastatic castration-resistant prostate cancer
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
MCV	Mean corpuscular volume

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Abbreviation	Description
MedDRA	Medical Dictionary for Regulatory Activities
ND/UNK/NA	Not determined / unknown / not applicable
PASS	Power Analysis and Sample Size (PASS)
PCWG3	Prostate Cancer Working Group 3
PD	Progressive disease
PFS	Progression-free survival
PR	Partial response
PSA	Prostate-specific antigen
PSMA	Prostate-specific membrane antigen
PT	Preferred term
RBC	Red blood cell
RDW	Red cell distribution width
RECIST	Response evaluation criteria in solid tumors
RLT	Radioligand therapy
rPFS	(radiographic) Progression-free survival
SAE	Serious adverse event
SD	Stable disease
SOC	System organ class
TEAE	Treatment emergent adverse event
UCLA	University of California at Los Angeles
WBC	White blood cell

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1 Relevant Documents and Standards

1.1 Protocol Version and Amendments

The statistical analysis plan is based on version 5.0 of the study protocol of study PSMA-617-02 dated 01 June 2018.

1.2 Changes from Protocol

The protocol does not include any planned interim analyses. Enrollment was ceased when Endocyte acquired the Investigational New Drug (IND) application in order to do a phase 3 study of ¹⁷⁷Lu-PSMA-617, now currently under way. The RESIST-PC study (NCT03042312), now identified as PSMA-617-02, was ongoing when Endocyte acquired global development rights to the clinical development of PSMA-617 and to the PSMA-617 IND. It was agreed with the two principal investigators that the study was to stay open until the start of the Phase 3 VISION study (NCT03511664) in the USA. On 23 May 2018, the first site for the Phase 3 VISION study was opened to enrollment; therefore, the investigators were notified that enrollment to PSMA-617-02 would end on 22 June 2018, prior to full enrollment of the study. All enrolled patients were to continue to follow the protocol visit schedule.

To support the phase 3 study, a database lock of the RESIST phase 2 study is to occur after randomized patients have completed the treatment phase and 2 years follow-up period of the study.

Using the locked database, protocol analyses will be performed to summarize only safety. Most of the objectives will not be able to be met due to the early stopping of enrollment into the study; the modeling approaches stated in the protocol cannot be carried out as there is insufficient data to perform the analyses. Limited imaging data is available, and thus the endpoints associated with it will not be analyzed nor described with summary statistics (i.e., radiographic Progression-free survival [rPFS] and disease control rate [DCR]). The PSA related efficacy will not be analyzed due to the significantly smaller sample size than the planned 200 and investigator's inconsistent timing of PSA data collection. PSA data will only be able to be listed. Statistical testing will also not be applied to EPIC 26 Quality of life (QoL) questionnaire results and ECOG performance status, but summary statistics will be presented for these endpoints. Bone level pain data will only be able to be listed due to the nature of the data (i.e., free text pain levels).

For the laboratory parameters listed in Table 6 in the protocol, there is no data for white blood cell (WBC) differential (percentage), mean corpuscular hemoglobin concentration (MCHC), BUN/creatinine, and glucose; however, there is additional data for white blood cell (WBC) differential (absolute), sodium, chloride, potassium and albumin. All laboratory parameters for which most patients have data will be included in the summary tables. All laboratory parameters for which there is any data will be listed.

Section 2.3.2 and 3.10.2 - Definition and algorithm of PSA Progression Free Survival was updated to be in line with the Prostate Cancer Clinical Trials Work Group 3 (Scher et al 2016) and to have comparable data for the two main studies in this indication, VISION and RESIST-PC.

Section 3.10.2 – Timepoints for Changes in performance status (ECOG) from baseline was to be evaluated over time at 3, 6, 9, 12, 18 and 24 months after start of ¹⁷⁷Lu-PSMA-617 RLT; however, the eCRFs only captured ECOG with each ¹⁷⁷Lu-PSMA-617 treatment visit and during follow-up.

2 Study Design and Objectives

2.1 Study Design

This is an open-label, multicenter, prospective trial. Upon inclusion patients will be randomized in a 1:1 ratio into two treatment doses. Radioligand therapy (RLT) will be performed by repeated intravenous (i.v.) injection of 6.0 gigabecquerel (GBq) ($\pm 10\%$) or 7.4 GBq ($\pm 10\%$) ^{177}Lu -PSMA-617 every 8 \pm 1 weeks until reaching four cycles or threshold maximum dose to the kidneys of 23 Gray (Gy). All doses after labeling will be presented in buffered solution for i.v. injection.

In the initial plan for the study design a total of 200 patients with histologically proven prostate cancer and metastatic castration-resistant prostate cancer (mCRPC) were to be enrolled, however due to early stopping of enrollment only 71 patients were enrolled at time of data base lock. Salivary protection will be accomplished by applying ice pack starting 30 minutes prior to infusion of radiopharmaceutical and will continue for 4 hours. Patients will be recruited at up to 3 Nuclear Medicine sites selected for this project. Each patient will undergo a screening visit within 14 days prior to receiving study drug.

Dosimetry was required to be performed in the initial versions of the study according to dosimetry protocol (Appendix VI of the protocol) provided by Prof. [Name] (Universitätsklinikum Würzburg Germany - Klinik und Poliklinik für Nuklearmedizin) to determine dose to the kidneys. Dosimetry data for 20 patients on study (16 from University of California at Los Angeles (UCLA) and 4 from Excel Diagnostics) was analyzed and it was found that the permitted renal dose of 23 Gy was not exceeded in any patient after 4 cycles demonstrating overall favorable renal dosimetry and dosimetry is no longer required per protocol.

Treatment was continued until either of the following conditions applied:

- Prostate-specific antigen (PSA)/radiographic progression at ≥ 12 weeks
- Completion of four RLT cycles
- 23 Gy kidney dose would be exceeded by the next cycle as estimated by dosimetry
- Patient withdrawal (e.g. appearance of intolerable adverse events)

2.2 Sample Size Determination

Per the protocol, sample size calculation was based on the primary endpoint of this protocol, i.e. baseline to 12-week decline in tumor marker level (prostate-specific antigen; PSA) $\geq 50\%$ [3]. Based on a recent publication [2], we estimate that the proportion of patients who meet the primary endpoint will range between 38% and 65% for both treatment doses combined. We thus define the following null hypothesis: Less than 40% of patients will reach the endpoint after ^{177}Lu -PSMA RLT. ^{177}Lu -PSMA RLT would therefore be considered worthy of further study if 50% or more patients met the endpoint and not worthy of further study if 40% or less achieved the endpoint. This rationale was adapted from a single-arm study on mCRPC patients with same endpoint definition, published in 2010 in the Journal of Clinical Oncology [53]. We have performed power analysis for the two-sided binomial test (beta 0.2, alpha 0.05) to measure the efficacy of ^{177}Lu -PSMA RLT. A sample size of 200 achieves 78% power (beta 0.2) at a given alpha of 0.05 to distinguish between 40% versus 50% response rates. The power analysis was performed by a trained Biostatistician from the Department of Biostatistics, UCLA using Power Analysis and Sample Size (PASS) 14 software (NCSS LLC).

At the time of study enrollment stoppage only approximately 71 of the planned 200 patients were enrolled. The exact number of patients at the time of study enrollment stoppage will be reported in the tables and all analyses will be performed on this number of patients, and not the 200 patients originally planned.

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2.3 Study Objectives

2.3.1 Primary objectives

1. To assess the clinical safety of ^{177}Lu -PSMA-617 by evaluation of adverse events (AE) using severity (mild moderate and severe). SAE will be assessed by Common Terminology Criteria for Adverse Events (Common Terminology Criteria for Adverse Events (CTCAE))
2. To assess the efficacy as defined by proportion of patients with PSA-response of $\geq 50\%$ decline at 12-weeks from baseline

2.3.2 Secondary objectives

1. Maximum PSA response: Maximal baseline to follow-up PSA decline, at any time during or after therapy [1].
2. PSA Progression Free Survival (PFS): To determine the time to PSA progression, separate for treatment doses: time from inclusion (date of randomization) to date of PSA progression or death (whichever occurs first) [1].
 - a. For patients with PSA decline from baseline at any time during or after therapy: PSA progression is defined as the date that a $\geq 25\%$ increase in PSA and an absolute increase of 2 ng/mL or more from the nadir is documented and confirmed by a second value obtained 3 or more weeks later. Rises in PSA within the first 12 weeks will be ignored in the absence of other evidence of disease progression (PCWG3 Guidance).
 - b. For patients without PSA decline from baseline: PSA progression is defined as a $\geq 25\%$ increase from the baseline value along with an increase in absolute value of 2 ng/mL or more after 12 weeks of treatment.
3. rPFS: To determine the radiographic progression free survival (rPFS), for each treatment dose: time from randomization to date when first site of disease is found to progress or death (whichever occurs first).
 - a. Nodal and visceral disease is evaluated on cross-sectional imaging using Response Evaluation Criteria in Solid Tumors (RECIST) 1.1/ Prostate Cancer Working Group (PCWG3) criteria.
 - b. Bone metastases are evaluated using bone scintigraphy and new lesions have to be confirmed on a second scan (2+2 rule) using PCWG3 criteria.
4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST 1.1/PCWG3 criteria stable disease (SD), partial response (PR) or complete response (CR).
5. Change in Bone Pain Level and Quality of Life: Pain and Expanded prostate cancer index composite ("Epic-26") Questionnaires will be completed at baseline and at 3, 6, 9, 12, 18 and 24 months. Pain response will be determined in accordance with PCWG3 [1].
6. Change in Eastern cooperative oncology group (ECOG) performance score.

2.4 Primary and secondary endpoints

2.4.1 Primary endpoints

1. Safety of ^{177}Lu -PSMA-617RLT will be assessed by analysis of toxicity through adverse events. Both results from laboratory tests, physical examination and patient surveys will be included.
2. Efficacy of ^{177}Lu -PSMA-617 will be assessed at week 12 by means of number and percentage of patients with $\geq 50\%$ decline in PSA at 12 weeks from baseline. Due to not enough patients to ensure the statistical power, and investigator's inconsistent timing of PSA data collection. PSA data will only be able to be listed.

2.4.2 Secondary endpoints

1. Maximum PSA response, time to PSA nadir, PSA PFS (Due to not enough patients to ensure the statistical power, and investigator's inconsistent timing of PSA data collection. PSA data will only be able to be listed).

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-
2. Radiographic progression-free survival (rPFS) (only limited imaging data is available for this endpoint)
 3. Disease control rate (DCR) (only limited imaging data is available for this endpoint)
 4. Bone pain level (as measured in the Baseline and Follow-Up Questionnaire for Pain and Adverse Events CRF)
 5. Quality of Life by the Quality of life questionnaire "EPIC-26"
 6. Performance status (ECOG)

Due to the early stopping of enrollment into the study an abbreviated CSR will be written primarily concentrating on the primary endpoints.

2.5 Coding dictionaries

- Adverse events: Medical Dictionary for Regulatory Activities (MedDRA) version 22.1, CTCAE version 4.0

3 Statistical Evaluation

The analysis cut-off date for the final analysis of study data will be established after all randomized patients have completed last follow-up visit or have discontinued study. All statistical analyses will be performed using all data collected in the database up to the data cutoff date. All data with an assessment date or event start date (e.g. vital sign assessment date or start date of an adverse event) prior to or on the cut-off date will be included in the analysis. Any data collected beyond the cut-off date will not be included in the analysis and will not be used for any derivations. The cutoff date for the final analysis is database lock date.

All events with start date before or on the cut-off date and end date after the cut-off date will be reported as 'ongoing'. The same rule will be applied to events starting before or on the cut-off date and not having documented end date. This approach applies, in particular, to adverse event and concomitant medication reports. For these events, the end date will not be imputed and therefore will not appear in the listings.

3.1 Populations for Analysis

Population	Description
Intention-to-Treat (ITT) Population	All randomized patients. Patients will be included in the treatment arm to which they were randomized regardless of actual treatment received.
Safety Population (SAF)	The subset of patients in the ITT population who received at least one dose of randomized therapy. Patients will be included in the treatment arm corresponding to the actual treatment received.

Baseline summaries will be presented for the Safety and ITT populations.

All efficacy analyses will be performed on the ITT population.

Safety analyses will be presented for the Safety population.

3.2 Interim analyses

None are planned in the protocol, however due to the early stopping of the study enrollment a database lock is to occur at some time after randomized patients have completed the treatment phase of the study. Using the locked database, the analyses described in this SAP will be performed to summarize

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efficacy and safety (see section 1.2 for more details). At end of study, the safety summary will be updated to include all data collected during follow-up.

3.3 Subgroup analyses

All Safety endpoints will have summary statistics provided by the following subgroup:

1. Age (<65 years old, >= 65 years old)

3.4 Derived Data and Data Sets

3.4.1 Rules for incomplete data

Missing data will not be replaced. Only partial dates as described below will be imputed for purposes of assignment of adverse events to treatment emergent. The imputed dates will not be listed.

For the calculation of the time since initial cancer diagnosis, the following imputation rules will be applied when the date of initial diagnosis is incomplete:

- If the day is missing: first day of the month.
- If the day and month are missing: first day of January.

For the assignment of AEs to treatment emergent, the following rules will be applied in case of incomplete dates:

- If start date is incomplete:

Missing Element	Rule
day, month, and year	<ul style="list-style-type: none">• No imputation will be done for completely missing dates
day, month	<ul style="list-style-type: none">• If available year = year of study treatment start date then<ul style="list-style-type: none">◦ If stop date contains a full date and stop date is earlier than study treatment start date then set start date = 01JanYYYY◦ Else set start date = study treatment start date.• If available year > year of study treatment start date then 01JanYYYY• If available year < year of study treatment start date then 01JulYYYY
day	<ul style="list-style-type: none">• If available month and year = month and year of study treatment start date then<ul style="list-style-type: none">◦ If stop date contains a full date and stop date is earlier than study treatment start date then set start date= 01MONYYYY.◦ Else set start date = study treatment start date.• If available month and year > month and year of study treatment start date then 01MONYYYY• If available month and year < month year of study treatment start date then 15MONYYYY

Any adverse events and concomitant medications with partial/missing dates will be displayed as such in the data listings.

Also, any adverse events and concomitant medications which are continuing as per data cut-off will be shown as 'ongoing' rather than the end date provided.

3.4.2 General Analysis Definitions

Study day

The study day describes the day of the event or assessment date, relative to the reference date.

The study day is defined as:

- Study Day = Assessment date – Reference date +1 if assessment date is after or on the reference date
- Study Day = Assessment date – Reference date if assessment date is before the reference date

For visit's assignment during treatment phase for the laboratory tests and PSA, and for Epic-26, for both treatment and follow-up phase, the reference date is defined as specified below in the table.

For visit's assignment during follow-up phase for the laboratory tests and PSA the reference date is defined the reference date for FU should be date of last dose + 1, as specified below in the table.

Data collected for the following procedures according to the visit windows as specified below in the table:

Parameters	Analysis visit	Reference day	Target day of assessment compare to the reference day	Time interval start (>=) end (<)
Lab test	Baseline	First dose Day 1	The last assessment on or before first injection	Day 7 to day 21
	Week 2			14
	Week 4			28
	Week 6			42
	Week 2k (till week 36)			D=7*2k
	FU week 2	Day 1 is the day after treatment end date, treatment end date is defined as the date of last injection	Day D-7 to day D+7	Day 7 to day 21
	FU week 4			Day 21 to day 35
	FU week 6			Day 35 to day 49
	FU week 2k (till FU week 12)			D=7*2k
	FU Month 6			Day 140 to day 196
	FU Month 9			Day 224 to day 280

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Parameters	Analysis visit	Reference day	Target day of assessment compare to the reference day	Time interval start end (\geq) ($<$)
	FU Month 12		336	Day 308 to day 364
	FU Month 3k (till FU MONTH 24)		D=28*3k	Day D-28 to day D+28
PSA	Baseline	SAF:First dose Day 1 Day 1 is the day after treatment end date	Safety analysis with SAF: the last assessment on or before treatment start date (PSA baseline disease characteristic uses last assessment on or before randomization for both ITT and SAF)	
	Week 6		42	Day 35 to day 49
	Week 12		84	Day 77 to day 91
	Week 18		126	Day 119 to day 133
	Week 6k (till end of the last dose)		D=7*3k	Day D-7 to day D+7
	FU Week 6		42	Day 35 to day 49
	FU month 3		84	Day 56 to day 112
	FU month 6		168	Day 140 to day 196
	FU month 9		252	Day 224 to day 280
	FU month 3k (Till early termination of study or 24 month after the first treatment)		D=28*3k	Day D-28 to day D+28
ECOG	Baseline			the last assessment before treatment start date

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Parameters	Analysis visit	Reference day	Target day of assessment compare to the reference day	Time interval
				start (>=) end (<)
Epic-26	Treatment visit 1			Treatment visit +-7days
	Treatment visit 2			
	Treatment visit 3			
	Treatment visit 4			
	FU month 3	Day 1 is the day after treatment end date	84	Day 56 to day 112
	FU month 6		168	Day 140 to day 196
	FU month 9		252	Day 224 to day 280
	FU month 3k (Till early termination of study or 24 month after the first treatment)		D=28*3k	Day D-28 to day D+28
	Baseline			the last assessment before or on treatment start date
Epic-26	Month 3	First dose Day 1	84	Day 56 to day 112
	Month 6		168	Day 140 to day 196
	Month 9		252	Day 224 to day 280
	Month 3k		D=28*3k	Day D-28 to day D+28
	FU month 3	Day 1 is the day after treatment end date	84	Day 56 to day 112
	FU month 6		168	Day 140 to day 196
	FU month 9		252	Day 224 to day 280
	FU month 3k (Till early termination of study or 24 month after the first treatment)		D=28*3k	Day D-28 to day D+28

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Parameters	Analysis visit	Reference day	Target day of assessment compare to the reference day	Time interval start end (>=) (<)
Pain and AE questionnaire	Baseline	Injection 1	Day of the first injection	Cycle 1 pre-dose
	Cycle 1 Post Dose	Injection 1	Day of the first injection +1	For pre dose, a window of 10 days before will be applied and the last assessment within this window will be used for the table,
	Cycle 2 Pre Dose	Injection 2	Day of the second injection	
	Cycle 2 Post Dose	Injection 2	Day of the second injection +1	
	Cycle 3 Pre Dose	Injection 3	Day of the third injection	
	Cycle 3 Post Dose	Injection 3	Day of the third injection +1	For post dose, a window of 10 days after will be applied and the earliest assessment within this window will be used for the table
	Cycle 4 Pre Dose	Injection 4	Day of the fourth injection	
	Cycle 4 Post Dose	Injection 4	Day of the fourth injection +1	
	FU month 3	Day 1 is the day after treatment end date	84	
	FU month 6		168	Day 56 to day 112
	FU month 9		252	Day 140 to day 196
	FU month 3k (Till early termination of study or 24 month after the first treatment)		D=28*3k	Day 224 to day 280
Vital sign	Baseline			Treatment visit 1, pre-dose,
	Treatment visit 1, 30 mins post dose, 60 mins post dose	Injection 1		Treatment visit x is from injection x to the day before injection

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Parameters	Analysis visit	Reference day	Target day of assessment compare to the reference day	Time interval start end (>=) (<)
	Treatment visit 2, pre-dose, 30 mins post dose, 60 mins post dose	Injection 2		x+1. For the last injection Treatment visit y is from the last injection to last injection + 28 days.
	Treatment visit 3, pre-dose, 30 mins post dose, 60 mins post dose	Injection 3		
	Treatment visit 4, pre-dose, 30 mins post dose, 60 mins post dose	Injection 4		
	FU month 3	Day 1 is the day after treatment end date	84	Day 56 to day 112
	FU month 6		168	Day 140 to day 196
	FU month 9		252	Day 224 to day 280
	FU month 3k (Till early termination of study or 24 month after the first treatment)		D=28*3k	Day D-28 to day D+28
12 lead ECG	Baseline			Treatment visit 1, pre-dose
	Treatment visit 1, post-dose	Injection 1		Treatment visit x is from injection x to the day before injection x+1. For the last injection Treatment visit y is from the last injection to last injection + 28 days.
	Treatment visit 2, pre-dose, post-dose	Injection 2		
	Treatment visit 3, pre-dose, post-dose	Injection 3		
	Treatment visit 4, pre-dose, post-dose	Injection 4		

If more than one assessment is done within the same time window, the assessment performed closest to the target date will be used. If two assessments within a time window are equidistant from the target date, then the earlier of the two assessments will be used. If multiple assessments on the same date

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then the worst case will be used. Data from all assessments (scheduled and unscheduled), including multiple assessments, will be listed. For those parameter analysis at timepoints should be analyzed separately at timepoints, not be considered as multiple test within one window.

Time unit

A year length is defined as 365.25 days. A month length is 30.4375 days (365.25/12). If duration is reported in months, duration in days will be divided by 30.4375; if duration is provided in days, duration in months will be multiplied by 30.4375. If duration is reported in years, duration in days will be divided by 365.25.

Baseline

For safety evaluations, the last available assessment on or before the date of start of study treatment is taken as "baseline" assessment. Evaluation of EPIC-26 will use safety definition for baseline.

For PSA relevant safety analysis, baseline for safety evaluation definition will be used with SAF population. PSA data will only be able to be listed.

ECOG Baseline is defined as last assessment before treatment start date

3.4.3 Rules for adverse events

Intensity

AE is collected in eCRF based on severity (mild, moderate and severe), SAE is based on CTCAE Grading.

Body System

Adverse events will be categorized by MedDRA preferred term (PT) and system organ class (SOC).

Attribution of the AE to Study Drug

A frequency table will be presented showing the information on attribution of the AE to study drug using the categorization given on the case report forms (CRFs):

1 ≈ 'none', 2 ≈ 'unlikely', 3 ≈ 'possible', 4 ≈ 'probable', 5 ≈ 'definite'.

Moreover, this categorization will be used in data listings.

3.4.4 Rules for vital signs

Systolic blood pressure

Following categories will be used for analysis of changes:

- | | |
|----------------------------|------------------------------------|
| 1 ≈ 'Decrease (Dec) >40 | (i.e. Difference (D) < -40 mm Hg)' |
| 2 ≈ 'Dec >20-40 | (i.e. -40 mm Hg ≤ D < -20 mm Hg)' |
| 3 ≈ 'Difference (+/-) 0-20 | (i.e. -20 mm Hg ≤ D ≤ 20 mm Hg)' |
| 4 ≈ 'Increase (Inc) >20-40 | (i.e. 20 mm Hg < D ≤ 40 mm Hg)' |
| 5 ≈ 'Inc >40 | (i.e. D > 40 mm Hg)'. |

Diastolic Blood Pressure

Following categories will be used for analysis of changes:

- | | |
|-----------------|-----------------------------------|
| 1 ≈ 'Dec >30 | (i.e. D < -30 mm Hg)' |
| 2 ≈ 'Dec >15-30 | (i.e. -30 mm Hg ≤ D < -15 mm Hg)' |
| 3 ≈ '+/- 0-15 | (i.e. -15 mm Hg ≤ D ≤ 15 mm Hg)' |
| 4 ≈ 'Inc >15-30 | (i.e. 15 mm Hg < D ≤ 30 mm Hg)' |
| 5 ≈ 'Inc >30 | (i.e. D > 30 mm Hg)'. |

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Heart Rate

Following categories will be used for analysis of changes:

- 1 ≈ 'Dec >30 (i.e. D < -30 beats/min)'
- 2 ≈ 'Dec >15-30 (i.e. -30 beats/min ≤ D < -15 beats/min)'
- 3 ≈ '+/- 0-15 (i.e. -15 beats/min ≤ D ≤ 15 beats/min)'
- 4 ≈ 'Inc >15-30 (i.e. 15 beats/min < D ≤ 30 beats/min)'
- 5 ≈ 'Inc >30 (i.e. D > 30 beats/min)'.

3.5 General Variable Definitions

Data will be analyzed using SAS version 9.4 or higher.

Descriptive statistics will be presented in tables as follows:

- Categorical data will be summarized in contingency tables presenting frequencies and percentages.
- Continuous data will be summarized using number of non-missing values (n), mean, standard deviation, median, minimum, and maximum values.

Unless otherwise indicated, for frequency tables, patients with missing data will be excluded from the denominator of percentage calculations.

Individual patient listings will include all study-related data. The sort order of the listings will be by treatment, patient ID, and date of assessment (if available).

If multiple results for the same assessment are collected during a visit time window, the first result will be utilized unless indicated otherwise.

The following definitions will be used:

- Age (years): year of informed consent - year of birth
- Time since initial cancer diagnosis (years): (Date of randomization - Date of initial cancer diagnosis)/(365.25)
- Weight (kg) = weight (lb) * 0.45359237
- Height (cm) = height (in) * 2.54

3.6 Patient Disposition, Deviations, Demography

The following patient data will be summarized in tables for all patients:

- Number (%) of patients who signed informed consent
- Number (%) of patients in each analysis population

The following patient data will be summarized in tables for the ITT population:

- Number (%) of patients discontinued from study treatment
- Number (%) of patients discontinued from the study
- Number (%) for the primary reason for discontinuation for each of the above

For the ITT population, protocol deviations will be listed by treatment and patient ID.

Demographic data (age (years), age categorical (< 65 years, ≥ 65 years), ethnicity, race, weight (kg), height (cm), and pulse oximetry (%)) will be summarized using descriptive statistics (n, mean, standard deviation, median, minimum and maximum for quantitative variables; frequency counts by category will

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be given for qualitative variables). All demographic summary tables will be based on the ITT and Safety populations. An individual listing will be provided for demographic data for the ITT population.

For demographic and baseline characteristics, the last available assessment on or before the date of start of study treatment is taken as "baseline" assessment for both ITT and safety population analyses.

3.7 Baseline Disease Characteristics

Descriptive statistics of patient disease characteristics at baseline will be presented for the following variables for the ITT and Safety population:

- Time since initial cancer diagnosis (years)
- Initial Histopathological Classification (type of prostate cancer tumor)
- Initial Gleason score
 - Categorical: 2-3,4-7,8-10, unknown
- Baseline PSA doubling time (months): continuous and categorical (\leq 6 months vs. $>$ 6 months)

Baseline PSA doubling time (months): PSA doubling time will be calculated as natural log of 2 (0.693) divided by the sum of the fixed slope (common to all patients) and the random slope (specific for the patient) of the random coefficient linear model between the natural log of PSA and time of PSA measurement (Svatek et al., 2006). If the PSA doubling time is less than zero (i.e. stable, nonincreasing, or decreasing PSA levels as defined by a negative slope from the random coefficient linear model), the PSA doubling time is set to 0. PSA is collected at screening visit and for the most recent 2 PSA measurements available prior to screening. Calculations will be performed only for subjects with (1) all 3 PSA values with each value \geq 0.2 ng/mL and (2) for which the interval between the first and last PSA values are \geq 8 weeks but \leq 12 months as stated in PCWG3 guidelines (Scher et al., 2016; Pound et al., 1999).

For interpretation of PSA doubling time it should be noted that PCWG3 guidelines state the calculation should be based on the most recent PSA values during androgen deprivation therapy, and that 3 PSA values \geq 0.2 ng/mL should be consecutive. These additional criteria will not be applied since the information is not available.

- Baseline PSA

For Baseline PSA as baseline disease characteristic, the last available assessment on or before the date of randomization is taken as "baseline" assessment for both ITT and safety population analyses.

Listings of baseline disease characteristics will be provided for the ITT population.

3.8 Medical History

A medical history listing will be provided for the ITT population.

3.9 Prior Cancer Related Therapy

Descriptive statistics with respect to prior therapy collected on the Prostate Cancer Treatment History CRF pages (Chemotherapy, Other Treatment, and Radiotherapy) will be displayed for the ITT population. A listing of data recorded on the Prostate Cancer Treatment History CRF pages (Chemotherapy, Other Treatment, and Radiotherapy) will also be provided for the ITT population.

The variables to be summarized in tables are:

- Prostate Cancer Treatment History: Chemotherapy

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-
- Prior number of therapies
 - Prior number of taxane-containing regimens
 - Number of unique agents
 - Prostate Cancer Treatment History: Chemotherapy - Last Taxane Therapy
 - Number of cycles
 - Duration of therapy (months)
 - Best overall response (BOR) to last taxane-therapy (Complete response (CR), Partial response (PR), Stable disease (SD), Progressive Disease (PD), Missing)
 - Prostate Cancer Treatment History: Chemotherapy - Last Therapy
 - Type of last prior therapy
 - Number of cycles
 - Duration of therapy (months)
 - Best Response (CR, PR, SD, PD, Missing)
 - Prostate Cancer Treatment History: Other Treatment
 - Number of patients with at least one prostate cancer-related other treatment
 - Type of other treatment
 - Prior number of other treatments
 - Prostate Cancer Treatment History: Radiotherapy
 - Number of patients with at least one prostate cancer-related radiotherapy
 - Type of prior radiotherapy
 - Prior number of radiotherapies

3.10 Efficacy Analysis

All efficacy analyses will be based on the ITT population.

Due to not enough patients to ensure the statistical power, and investigator's inconsistent timing of PSA data collection. PSA efficacy endpoints will not be analyzed and therefore are not described in this SAP. PSA results will be listed by visit for all patients in the SAF population

Due to only limited imaging data being available, the relevant endpoints (i.e., rPFS and DCR) will not be analyzed and therefore are not described in this SAP.

Bone pain level

Bone pain level will be listed by visit for all patients in the ITT population.

QoL: EPIC-26

Quality of Life questionnaire "EPIC-26" item value will be transformed into score as below. HRQOL domain score will be calculated as below. If >20% of the items that comprise a domain summary score or subscale score are missing a response, the corresponding domain summary or subscale score cannot be calculated. Domain scores at each time point, along with the change from baseline, will be summarized as continuous variable at baseline and at treatment visits and follow-up 3, 6, 9, 12, 18 and 24 months after start of ¹⁷⁷Lu-PSMA-617 RLT. Results will be presented separately for both treatment groups (6.0 vs. 7.4 GBq ¹⁷⁷Lu-PSMA-617) and overall. Item value with standardized score will also be listed.

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There are 2 steps involved in scoring EPIC-26:
Step 1. The response for each item is standardized to a 0 to 100 scale according to the table below.

Item Number	Item Response Value	Standardized Value
23,57,58,60,64	1 2 3 4 5	0 25 50 75 100
26,59	1 2 3 4	0 33 67 100
27	0 1 2 3	100 67 33 0
28,29,30,31,33,49,50,52,53, 54,74,75,77,78,79	0 1 2 3 4	100 75 50 25 0
34,55,68	1 2 3 4 5	100 75 50 25 0

Step 2. Using the item groupings listed below for each HRQOL Domain Score, average the standardized values (see Step 1, above) for all items within a group to create the summary or subscale score. (If ≥20% of the items that comprise a domain summary score or subscale score are missing a response, the corresponding domain summary or subscale score can not be calculated).

To calculate the following HRQOL domain Summary Score or Subscale Score:	Determine the average of the Standardized Values (see Step 1, above) for the following items:	Number of non-missing items needed to compute score (otherwise, set score to missing)
HRQOL Domain Summary Scores		
Urinary Incontinence	23, 26-28	4
Urinary Irritative/Obstructive	29-31, 33	4
Bowel	49, 50, 52-55	5
Sexual	57-60, 64, 68	5
Hormonal	74, 75, 77-79	4

Item numbers are indicated along the right border of the questionnaire (question numbers on left of questionnaire pages are not used for scoring because some questions contain multiple items).

Change in ECOG-PS

The changes in ECOG from baseline will be evaluated over time at treatment visit 1, 2, 3 and 4 administration, and at follow-up visits. Shift tables will be provided for each post administration time point and FU visits compared to baseline. Results will be presented separately for both treatment groups (6.0 vs. 7.4 GBq ¹⁷⁷Lu-PSMA-617) and overall. Results will also be listed for the ITT population.

Exploratory efficacy analysis not planned.

3.11 Safety Analysis

The safety analysis will be based on the safety population. Tables will show results by treatment arm and for all patients combined. Listings will be created by treatment arm.

For all safety summary tables, the tables will also be provided by age (<65 years old, ≥ 65 years old).

Reference date is the date of first dose of Lu-PSMA-617 unless otherwise noted.

3.11.1 Safety Variable Definitions

- **¹⁷⁷Lu-PSMA-617 exposure variables:**
Duration of exposure/study treatment (months) = (Date of last study drug administration – Reference date + 1)/30.4375

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Dose per cycle

Dose for each cycle/overall (GBq/cycle) = (actual total dose during the cycle/study) / (1 or actual # of cycles)

Planned dose for each cycle/overall (GBq/cycle) = (planned total dose during the cycle) / (1 or planned # of cycles)

Note: Planned number of cycles = received number of cycles unless there was a missed dose

Relative dose per cycle/overall (%) = (dose by cycle/overall) / (planned dose by cycle/overall)

3.11.2 Extent of Exposure

A listing of study drug administration will be provided.

Randomized Treatment Exposure, Summary of Cycles

For the Safety population, summary of treatment cycle variables to be included are:

- Duration of study treatment (months)
- Number of cycles started per patient (both as categorical and continuous variable)
- Average duration of treatment cycles (months)

Randomized Treatment Exposure, By Cycle and Across Cycles Combined

For the Safety population, ¹⁷⁷Lu-PSMA-167 exposure variables to be summarized for the entire study and for each cycle are:

- Cumulative dose (GBq) of patient
- Dose per cycle/overall (GBq/cycle)
- Relative dose per cycle/overall (%)

To convert from mCi units to GBq units the conversion 1 mCi = 0.037 GBq will be used.

3.11.3 Adverse Events

Safety of ¹⁷⁷Lu-PSMA-617 RLT will be assessed by analysis of toxicity.

Adverse events (AE) will be coded using MedDRA version 22.1, by SOC and PT. Serious AEs will be graded according to the NCI CTCAE criteria version 4.0 while AEs will be described by severity (i.e., Mild, Moderate, Severe).

In case a patient experienced the same event more than once, the maximum toxicity grade will be presented.

In all AE tables, multiple occurrences of the same adverse events occurring in one individual are counted only once.

Definition of Treatment Emergent Adverse Event (TEAE)

A randomized treatment TEAE is defined as an AE that was not present prior to initiation of randomized treatment, defined as first dose of ¹⁷⁷Lu-PSMA-617, but appeared following treatment, or was present at treatment initiation but worsened during treatment. An AE that was present at treatment initiation but resolved and then reappeared while the patient was on treatment is a TEAE (regardless of the intensity of the AE when the treatment was initiated).

Any event that is considered study drug-related (stated as possible, probably, definite relationship, or missing assessment of relatedness), regardless of the start date of the event, or any event that worsens in toxicity grade while on treatment or is subsequently considered study drug-related by the investigator is also defined as a treatment-emergent adverse event.

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The treatment-emergent period will be defined as the period from the date of initiation of randomized treatment up to 30 days after date of last administration of study treatment or the day prior to the initiation of subsequent anticancer treatment, whichever occurs first.

Randomized Treatment Adverse Events

A summary table including the number of patients with at least one event, will be presented for the AE variables below.

- TEAE^{1, 3}
- Serious TEAE^{1, 2, 3}
- Drug-related TEAE¹
- Serious drug-related TEAE¹
- TEAE leading to reduction of ¹⁷⁷Lu-PSMA-617 dose¹
- TEAE leading to permanent discontinuation of ¹⁷⁷Lu-PSMA-617 treatment¹
- Fatal TEAE¹

¹AE variables to be tabulated by SOC and PT.

²Serious AE variables to be tabulated by SOC and PT by CTCAE grade.

³AE variables are to be tabulated by SOC and PT, CTCAE grade (serious AEs) or severity grade (TEAEs), and cycle.

A listing for each patient will include the same variables as mentioned above and will also include action taken regarding ¹⁷⁷Lu-PSMA-617.

Deaths

All deaths will be summarized by treatment groups (6.0 vs. 7.4 GBq ¹⁷⁷Lu-PSMA-617) and overall with the End of Treatment status table; deaths will also be listed.

Specific Adverse Events Questionnaire

Adverse events as captured on the pain and adverse events questionnaire form will be summarized and listed by treatment arm. A listing will also be created.

3.11.4 Laboratory Data

Laboratory parameters will be analyzed descriptively by summary tables.

Hematology	Clinical Chemistry
Hematocrit	eGFR
Hemoglobin	Bilirubin
Red blood cell (RBC) count (Erythrocytes)	Creatinine
WBC count (Leukocytes)	Sodium
Absolute Monocyte count	Urea nitrogen (BUN)
Platelets	Chloride
Absolute neutrophil count (ANC)	AST/SGOT
Mean corpuscular volume (MCV) / Mean corpuscular hemoglobin (MCH)	ALT/SGPT
Absolute Eosinophil count	Alkaline phosphatase
Absolute Basophil count	PSA*
Absolute Lymphocyte count	Albumin
RDW (Erythrocytes Distribution Width)	Potassium

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*PSA will be done only at the time intervals called by the protocol (see Schedule of Events in Section 3.13).

Laboratory values and, for assessments measured over time, change from baseline will be summarized by visit. Frequency statistics for qualitative laboratory parameters will also be presented by visit.

Shift tables of high-normal-low laboratory values from baseline to each measurement time point will be provided for each parameter that has a reference range. The abnormal flag be derived based on the upper and lower limits of normal range. Reference ranges are taken from the Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood Count for all parameters except estimated Glomerular Filtration Rate (eGFR; reference range from National Kidney Foundation).

The mean (\pm standard error) values over time will be plotted for PSA by treatment arm.

Patient listings of all lab values will be provided, values outside of the laboratory's reference range will be flagged for all parameters with ranges. The patient listings will indicate the CTCAE grade if one is provided in the data.

3.11.5 Vital Signs

Systolic blood pressure (mmHg), diastolic blood pressure (mmHg), heart rate (bpm), temperature (C), and respiratory rate (breaths per min) will be analyzed descriptively by summary tables noting observed values and change from baseline. Transition tables will be provided for the transitions from baseline to each follow-up time point.

3.11.6 12-Lead ECG Data

Overall ECG interpretation will be summarized. Heart rate (bpm), PR (msec), QRS (msec), QT (msec) and QTc (msec; measured by both sites as QTcB using Bazett's formula) intervals will be summarized as continuous variables. All ECG variables will also be listed.

3.11.7 Physical Exam

Physical examination results will be listed for the Safety population

3.11.8 Concomitant Medications

Medications as recorded on the Concomitant Medications CRF will be listed.

Medications will be classified as prior and/or concomitant. Prior medications are all medications taken or occurring prior to first dose of ^{177}Lu -PSMA-617. Concomitant medications are all medications continued or started on or after the date of the first randomized study drug administration

3.11.9 Concurrent and Post Chemotherapy

Descriptive statistics for Concurrent Chemotherapy and Post-Treatment Chemotherapy will be displayed using the data collected on the Treatment Visit Concomitant Cancer-related Therapy Chemotherapy CRF and Follow-up Concomitant Cancer-related Therapy Chemotherapy CRF, respectively. Separate listings of Concurrent Chemotherapy and Post-Treatment Chemotherapy will be provided.

The variables to be summarized in the table are:

- Number of patients with at least one chemotherapies
- Number of chemotherapies
- Type of chemotherapies

3.11.10 Concurrent and Post Radiotherapy

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Descriptive statistics for Concurrent Radiotherapy and Post-Treatment Radiotherapy will be displayed using the data collected on the Treatment Visit Concomitant Cancer-related Therapy Radiotherapy CRF and Follow-up Concomitant Cancer-related Therapy Radiotherapy CRF, respectively. Separate listings of Concurrent Radiotherapy and Post-Treatment Radiotherapy will be provided.

The variables to be summarized in the table are:

- Number of patients with at least one radiotherapy
- Number of radiotherapies
- Type of radiotherapies

3.11.11 Concurrent and Post Other Treatments

Descriptive statistics for Concurrent Other Therapy and Post-Treatment Other Therapy will be displayed using the data collected on the Treatment Visit Concomitant Cancer-related Therapy Other Therapy CRF and Follow-up Concomitant Cancer-related Therapy Other Therapy CRF, respectively. Separate listings of Concurrent Other Therapy and Post-Treatment Other Therapy will be provided.

The variables to be summarized in the table are:

- Number of patients with at least one other treatments
- Number of other treatments
- Type of other treatments

3.12 Other Analyses

None.

3.13 Schedule of Events

	1	Screening			Therapy			FDU																30			
	Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	Month	
	Week	-2	0	2	4	6	8	10	12	14	16	18	20	22	24										Week		
	Therapy	1		2		3		4		5		6		7		8		9		10		11		12		13	
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days	-10	-7	0	14	28	42	56	70	84	98	112	126	140	154	168	182	200	216	230	248	262	276	290	304	318	332	

PSMA-617-02
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1 Only at first or second treatment, several blood and urine samples will be required for dosimetry purposes. Blood before injection, 5 (\pm 1) min, 30 (\pm 3) min, 60 (\pm 5) min, 4 (\pm 10 min), 10-30, 42-54, and 66-78 hours post injection. 7 to 9 days sample is optional. Urine collection will include 0-4 hrs and 4 hrs until discharge
2 Laboratory tests will be acceptable only if performed within two weeks of each scheduled visit. Screening visit and week 2 can be combined if screening visit performed within 2 weeks of the first visit.
3 CBG/MP with eGFR will be performed at least once every other week continued for 12 weeks after the last treatment and then continued every 3 (\pm 1) months during follow-up for 24 months or until disease progression as per clinical routine
4 PSMA will be measured every 6 weeks during the treatment and every 3 (\pm 1) months after the last treatment until reaching endpoint or 24 months after the first treatment
5 Baseline imaging within 12 weeks of start of therapy including (a) Chest CT, preferably with contrast, (b) bone imaging, (c) or equivalent as per clinical routine
6 Relevant imaging studies will be done at baseline, before 3rd PLT cycle, 3 (\pm 1) months after last PLT cycle, and then every 3 (\pm 1) months during follow-up until reaching the endpoint or 24 months after the first treatment as per clinical routine
7 If F or safety assessment, vital signs will be measured within 20 minutes before and/or up to 1 hour after administration of 177Lu-PSMA-617
8 Continuous ECG monitoring (only 1st 2 PLT cycles) starts at least 15 minutes prior to administration of the study drug and lasts at least 1 hour after administration.
9 Two 2D/3D ECGs, one before injection and one after 4 hr scan in dosimetry PLT and after completion of salivary gland protection in non-dosimetry PLT
10 Quality of life questionnaire (EPIC-29) and ECOG will be completed at baseline, and at 3, 6, 9, 12, 18 and 24 months from first PLT cycle
11 Only at first or second treatment, whole body scans may be performed several times (4 hrs off min), 10-30, 42-54, and 66-78 hours) after injection for dosimetry purposes. For non-dosimetry PLTs, only one (optional) post therapy VB scan will be performed. Please refer to dosimetry schedule of events.
12 Telephone follow-up 7 (\pm 1) days after each treatment cycle and completion of 4 cycles and for follow up up, every 3 months (\pm 1 month) until the end of follow up visits (24 months).
13 At each time point that the therapy stops, follow up visits will be started.

Note: ECOG was done at every treatment visit then every three month FU visits

3.14 References

1. Scher, H.I., et al., Trial Design and Objectives for Castration-Resistant Prostate Cancer: Updated Recommendations From the Prostate Cancer Clinical Trials Working Group 3. J Clin Oncol, 2016. 34(12): p. 1402-18.
2. Rahbar, K., et al., German multicenter study investigating 177Lu-PSMA-617 radioligand therapy in advanced prostate cancer patients. J Nucl Med, 2016.
3. Danila, D.C., et al., Phase II multicenter study of abiraterone acetate plus prednisone therapy in patients with docetaxel-treated castration-resistant prostate cancer. J Clin Oncol, 2010. 28(9): p. 1496-501.

Appendix I Generalized Reference Ranges

Laboratory Test	Units	Merck Low	Merck High	National Kidney Foundation Low	National Kidney Foundation High
Albumin	g/dL	3.5	5.4		
Alkaline Phosphatase	U/L	36	150		
Alanine Aminotransferase	U/L	0	35		
Aspartate Aminotransferase	U/L	0	35		
Bilirubin	mg/dL	0.3	1.2		
Chloride	mEq/L	98	106		
Creatininine	mg/dL	0.7	1.3		
Glomerular Filtration Rate, Estimated*	mL/min/1.73 m ²			>90	
Potassium	mEq/L	3.5	5		
Sodium	mEq/L	136	145		
Urea Nitrogen	mg/dL	8	20		
Basophils	x10 ³ /mcL	0	0.3		
Basophils/Leukocytes	%	0	3		
Eosinophils	x10 ³ /mcL	0	0.9		

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Eosinophils/Leukocytes	%	0	8
Hematocrit	%	41	51
Hemoglobin	g/dL	14	17
Lymphocytes	$\times 10^3/\text{mCL}$	1.0	4.8
Lymphocytes/Leukocytes	%	22	44
Ery. Mean Corpuscular Hemoglobin	pg	28	32
Ery. Mean Corpuscular Volume	fL	80	100
Monocytes	$\times 10^3/\text{mCL}$	0.2	1.2
Monocytes/Leukocytes	%	4	11
Neutrophils	$\times 10^3/\text{mCL}$	1.8	7.7
Neutrophils/Leukocytes	%	40	70
Platelets	$\times 10^3/\text{mCL}$	150	450
Erythrocytes	$\times 10^6/\text{mCL}$	4.2	5.9
Erythrocytes Distribution Width	%	11.5	14.5
Leukocytes	$\times 10^3/\text{mCL}$	4.5	11
Prostate Specific Antigen	ng/mL	0	4
Prostate Specific Antigen	ng/mL	0	4

Ranges taken from Merck Manual Professional Version, 2018 and the Merck Manual Consumer Version for Complete Blood

*estimated Glomerular Filtration Rate (eGFR) taken from the National Kidney Foundation

Final

STATISTICAL ANALYSIS PLAN ADDENDUM 1

Study PSMA-617-02

Title: (as per protocol/amendment)
PSMA-Directed Endoradiotherapy Of
Castration-Resistant Prostate Cancer
(RESIST-PC). A Phase II Clinical Trial

Version:

Final Addendum 1

Date:

15-Dec-2020

CONFIDENTIAL

DocuSign Envelope D: PI [REDACTED]

1 APPROVAL SIGNATURES

STUDY TITLE: PSMA-Directed Endoradiotherapy Of Castration-Resistant Prostate Cancer (RESIST-PC). A Phase II Clinical Trial

PROTOCOL NUMBER: PSMA-617-02
SAP Addendum 1 Final, 15-Dec-2020

Endocyte, Inc.:

Reviewed/Approved By: PI [REDACTED] PI [REDACTED]

Signature: [REDACTED]

Reviewed/Approved By: PI [REDACTED]

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Date: 12-Jan-21 | 6:45:27 PM GMT

Reviewed/Approved By: Richard Messmann, M.D., M.H.S., M.Sc., Vice President, Medical Affairs

Messmann Richard [REDACTED]

Signature: [REDACTED]

Date: [REDACTED]

2 Abbreviations

Abbreviation	Description
CR	Complete response
DCR	Disease control rate
ITT	Intent-to-treat
PCWG3	Prostate Cancer Working Group 3
PD	Progressive disease
PFS	Progression-free survival
PR	Partial response
PSA	Prostate-specific antigen
RECIST	Response evaluation criteria in solid tumors
rPFS	(radiographic) Progression-free survival
SD	Stable disease

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4 Reason for addendum

The original statistical analysis plan (SAP), Version 2.0, dated 15-May-2020, describes the analyses planned for the abbreviated clinical study report (aCSR) that summarized the safety data and listed the efficacy data. The efficacy data was not summarized for the aCSR due to the significantly smaller sample size than the planned 200 patients since enrollment into the study was stopped early. The modeling approaches stated in the protocol could not be carried out as there was insufficient data to perform the analyses that would allow for appropriate evaluation of effectiveness.

Clinicaltrials.gov requires all available data for primary and secondary endpoints to be disclosed. The purpose of this SAP addendum is to describe the analyses planned for clinicaltrials.gov using the limited data available. Due to only limited imaging and PSA data being available, some secondary endpoints could not be analyzed as planned in the protocol and the changes to the analyses are described in this SAP addendum. The source of the data is the clinical database.

5 Objectives and Endpoints for SAP Addendum

5.1 Study Objectives

5.1.1 Primary objectives

1. To assess the efficacy as defined by proportion of patients with PSA-response of $\geq 50\%$ decline at 12-weeks from baseline

5.1.2 Secondary objectives

1. Maximum PSA response: Maximum baseline to follow-up PSA decline, at any time during or after therapy.
2. PSA Progression Free Survival (PFS): To determine the time to PSA progression, separate for treatment doses: time from inclusion (date of randomization) to date of PSA progression or death (whichever occurs first). SAP Addendum Note: Time to PSA progression will not be analyzed; only number of PSA progression or death events can be summarized for this objective.
 - a. For patients with PSA decline from baseline at any time during or after therapy: PSA progression is defined as the date that a $\geq 25\%$ increase in PSA and an absolute increase of 2 ng/mL or more from the nadir is documented and confirmed by a second value obtained 3 or more weeks later. Rises in PSA within the first 12 weeks will be ignored in the absence of other evidence of disease progression (PCWG3 Guidance).
 - b. For patients without PSA decline from baseline: PSA progression is defined as a $\geq 25\%$ increase from the baseline value along with an increase in absolute value of 2 ng/mL or more after 12 weeks of treatment.
3. rPFS: To determine the radiographic progression free survival (rPFS), for each treatment dose: time from randomization to date when first site of disease is found to progress or death (whichever occurs first). SAP Addendum Note: rPFS cannot be analyzed; only investigator assessment of RECIST 1.1 overall response by each follow-up assessment and investigator assessment of PCWG3 bone scan clinical impression by visit can be summarized for this objective.
 - a. Nodal and visceral disease is evaluated on cross-sectional imaging using Response Evaluation Criteria in Solid Tumors (RECIST) 1.1/ Prostate Cancer Working Group (PCWG3) criteria.
 - b. Bone metastases are evaluated using bone scintigraphy and new lesions have to be confirmed on a second scan (2+2 rule) using PCWG3 criteria.

4. To determine disease control rate (DCR) defined as the proportion of patients achieving RECIST 1.1/PCWG3 criteria stable disease (SD), partial response (PR) or complete response (CR). SAP Addendum Note: Only RECIST 1.1 disease control rate by each follow-up assessment can be summarized for this objective.

5.2 Primary and secondary endpoints

5.2.1 Primary endpoints

1. Efficacy of ¹⁷⁷Lu-PSMA-617 will be assessed at week 12 by means of number and percentage of patients with $\geq 50\%$ decline in PSA at 12 weeks from baseline.

5.2.2 Secondary endpoints

1. Maximum PSA response
2. PSA-PFS
3. Radiographic progression-free survival (rPFS)
4. Disease control rate (DCR)

6 Analyses

Tables will show results by treatment arm and for all patients combined. The following patient data will be summarized in tables for the ITT population:

- PSA Response at Week 12
- Percent change in PSA from baseline to Week 12
- Maximum PSA response
- PSA Progression and Death Events
- RECIST 1.1 Overall Response by Follow-up Assessment Visit
- RECIST 1.1 Disease Control Rate by Follow-up Assessment visit
- PCWG3 Bone Scan Clinical Impression by Visit

7 Statistical Methods and Definitions for Addendum

The same statistical methods as described the original SAP will be followed, with any exceptions noted below. Table shells are created along with this document.

- Baseline PSA is defined as the last available assessment prior to or on first dose date of ¹⁷⁷Lu-PSMA-617.
- PSA response at Week 12: PSA response is defined as the proportion of patients who have a $\geq 50\%$ decrease in PSA from baseline at Week 12.
- Maximum PSA response includes all available PSA results, including unscheduled, up to and including the last assessment visit.
- PSA progression is defined as:
 - (a) For patients with PSA decline: PSA progression is defined as the date that a $\geq 25\%$ increase in PSA and an absolute increase of 2 ng/mL or more from the nadir is documented and confirmed by a second consecutive value obtained 3 or more weeks later. Rises in PSA within the first 12 weeks will be ignored (PCWG3 Guidance).
 - (b) For patients without PSA decline: PSA progression is defined as a $\geq 25\%$ increase from the baseline value along with an increase in absolute value of 2 ng/mL or more after 12 weeks of treatment.
- RECIST 1.1 Overall Response = Number of patients with an overall response of Complete Response (CR), Partial Response (PR), Stable Disease (SD), or Progressive Disease (PD) according to RECIST v1.1 using investigators assessments.

- There is no minimum time after first dose of ^{177}Lu -PSMA-617 to when first assessment is included in analysis.
- Data is summarized by assessment visit; therefore, the data presented is unconfirmed response.

- RECIST 1.1 Disease Control Rate = Proportion of patients with Overall Response of CR, PR, or SD according to RECIST v1.1 using investigators assessments.
- PCWG3 Bone Scan Clinical Impression = Number of patients with a clinical impression of Improved, Stable or Progression according to PCWG3 using investigators assessments.

As stated in the original SAP, the investigator's had inconsistent timing of PSA data collection; therefore PSA-PFS will not be derived because censoring rules are not applicable given this inconsistent timing of PSA data collection. Instead, number and percentage of patients with a PSA progression event or death event will be summarized.

As stated in the original SAP, limited imaging data is available. The date of radiographic tumor assessment for the RECIST 1.1 follow-up assessments is not available; therefore, the rPFS analysis cannot be performed. Instead, the available RECIST v1.1 overall response and disease control rate will be summarized by number and percentage of patients at each follow-up assessment and the available PCWG3 bone scan clinical impression will be summarized by number and percentage of patients at each visit.

Page 1828 of CSR Appendix 16.1.10 was removed due to being Out of Scope as per Health Canada Guidance on Public Release of Clinical Information - Documentation of inter-laboratory standardisation methods and quality assurance procedures if used.

Page 1829 of CSR Appendix 16.1.11 was removed due to being Out of Scope as per Health Canada Guidance on Public Release of Clinical Information - Publications based on the study.

Page 1830 of CSR Appendix 16.1.12 was removed due to being Out of Scope as per Health Canada Guidance on Public Release of Clinical Information - Important publications referenced in the report.

**Pages 1831 to 4249 of CSR Appendix 16.2
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