



Clinical Development

gallium (⁶⁸Ga) gozetotide

AAA517 ([⁶⁸Ga]Ga-PSMA-11)

Imaging Study Report: Quantitative Analysis

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Title page information

Study title: Imaging study report: [⁶⁸Ga]Ga-PSMA-11 PET quantitative analysis

Name of investigational product: [⁶⁸Ga]Ga-PSMA-11, gallium (⁶⁸Ga) gozetotide

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

Study aim: To assess association between quantitative PSMA imaging parameters extracted from pre-treatment [⁶⁸Ga]Ga-PSMA-11 PET/CT scans and treatment outcomes of [¹⁷⁷Lu]Lu-PSMA-617 therapy in the VISION study

Sponsor(s): Endocyte, Inc., a Novartis Company; Novartis acquired Advanced Accelerator Applications (AAA) in Jan-2018 and then Endocyte, Inc. in Dec-2018. Endocyte, Inc. operations functionally report into AAA.

Name and address of CRO: Invicro: A Konica Minolta Company, located at 27 Drydock Ave, Boston, MA 02210 USA

Images types used: PET/CT and CT/MRI scans

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| BSC | Best Supportive Care |
| BSoC | Best Standard of Care |
| CT | Computerized Tomography |
| DTA | Data Transfer Agreement |
| iPACS | Imaging Picture Archiving and Communication System |
| IPS | Image Processing Specialist |
| IRC | Imaging Review Charter |
| PSA | Prostate-Specific Antigen |
| PSMA | Prostate-Specific Membrane Antigen |
| PSMA+ | Prostate-Specific Membrane Antigen Positive |
| mCRPC | Metastatic Castration-Resistant Prostate Cancer |
| MINT | Mint Lesion™ software application |
| MRI | Magnetic Resonance Imaging |
| QC | Quality Control |
| rPFS | Radiographic Progression-Free Survival |
| SUVmax | Maximum Standardized Uptake Value |
| SUVmean | Mean Standardized Uptake Value |

Synopsis

[⁶⁸Ga]Ga-PSMA-11 is a radioligand imaging agent used in the identification of Prostate-Specific Membrane Antigen (PSMA)-positive lesions on PET/CT scan. In the VISION study (Study PSMA-617-01, NCT03511664, EudraCT No 2018-000459-41), [⁶⁸Ga]Ga-PSMA-11 was used to determine patient eligibility for [¹⁷⁷Lu]Lu-PSMA-617 therapy based on PET imaging patterns defined by the central read criteria. Only metastatic castration-resistant prostate cancer (mCRPC) patients with at least one PSMA-positive lesion identified on PSMA-PET and no PSMA-negative lesion fulfilling the exclusion criteria were enrolled in the study, provided all other inclusion criteria were met.

[¹⁷⁷Lu]Lu-PSMA-617 specifically targets PSMA protein on cell surface. Thus, the level and pattern of tumor PSMA expression in patients measured by [⁶⁸Ga]Ga-PSMA-11 PET/CT scan prior to treatment may associate with clinical benefits of [¹⁷⁷Lu]Lu-PSMA-617 therapy. In the VISION study, a total of 551 patients were randomized to the investigational arm and received [¹⁷⁷Lu]Lu-PSMA-617 treatment in combination with standard of care, of which 548 patients had imaging data that met the quality requirements to be included in this quantitative analysis study. Tumor PSMA expression from the [⁶⁸Ga]Ga-PSMA-11 PET/CT scan acquired during screening from each of these 548 patients was quantified by five PSMA PET parameters, including the presence or absence of PSMA-positive (PSMA+) lesions in different anatomical regions, mean standardized uptake value (SUVmean), maximum standardized uptake value (SUVmax), volume of tumor with positive [⁶⁸Ga]Ga-PSMA-11 uptake in the lesion (PSMA+ tumor volume), and tumor load, a composite measurement defined as the product of PSMA+ tumor volume and SUVmean. Each PSMA PET imaging parameter was extracted from each of the following five anatomical regions, including bone, liver, lymph node and non-liver parenchymal organs (soft tissue), as well as the whole body represented by the combination of all PSMA+ lesions present in the individual segmented anatomical regions.

The association between these extracted PSMA PET parameters from each anatomical region and four clinical outcome parameters were subsequently assessed. The outcome parameters evaluated in this study include radiographic progression-free survival (rPFS) as the primary objective, and overall survival (OS), objective response rate (ORR) and prostate specific antigen (PSA) response as secondary objectives. The association with rPFS and OS was assessed using univariate and multivariate Cox proportional hazards models, whereas the association with ORR and PSA response was assessed using univariate and multiple logistic regression models. The subset of patients included in each analysis was consistent with the patient populations used in the corresponding efficacy analysis in the VISION study.

Statistically significant association was observed between a subset of PSMA PET parameters extracted from pre-treatment [⁶⁸Ga]Ga-PSMA-11 PET/CT scans and clinical outcomes in the VISION study patients who received [¹⁷⁷Lu]Lu-PSMA-617 plus standard of care treatment. In particular, both increased whole body SUVmean and the absence of PSMA+ lesions in liver associated with the strongest clinical benefits in all clinical outcome parameters analyzed, including rPFS, OS, ORR and PSA response. Specifically, a 1-unit increase of whole body SUVmean was associated with 14% lower risk of rPFS event, whereas the absence of PSMA+ lesions in liver was associated with 52% lower risk of rPFS event.

Notably, patients in the highest quartile of whole body SUVmean (≥ 10.2 among the patients included in the rPFS analysis and ≥ 9.9 among the patients included in the OS analysis) had a

median rPFS of 14.1 and median OS of 21.4 months, compared to rPFS of 5.8 months and OS of 14.5 months in patients in the lowest whole body SUVmean quartile (<6.0 among the patients in the rPFS analysis and <5.7 among the patients included in the OS analysis).

The association between increased whole body SUVmean with both prolonged rPFS and prolonged OS demonstrated in this study is well aligned with the mechanism of action of [¹⁷⁷Lu]Lu-PSMA-617, which targets cancer cells by binding to the PSMA molecules on the cell surface. Thus, increased expression of PSMA molecules on the cancer cells indicated by high SUVmean should lead to proportionally increased binding of [¹⁷⁷Lu]Lu-PSMA-617 to the tumor and thus enhanced efficacy. When compared to mCRPC patients who received standard of care only in the control arm of the VISION study, patients in the lowest quartile of whole body SUVmean in the treatment arm who received [¹⁷⁷Lu]Lu-PSMA-617 therapy still demonstrated improved median rPFS (5.8 months vs 3.4 months) and median OS (14.5 months vs 11.3 months) ([\[Study PSMA-617-01\]](#)). In conclusion, [¹⁷⁷Lu]Lu-PSMA-617 treatment in combination with standard of care is effective in mCRPC patients who have PSMA positive tumor confirmed by [⁶⁸Ga]Ga-PSMA-11 PET/CT scans using the read criteria defined in the VISION study. Among the patients treated with [¹⁷⁷Lu]Lu-PSMA-617, those with higher [⁶⁸Ga]Ga-PSMA-11 uptake on the PET/CT scan were associated with improved clinical benefits. These quantitative analysis results also provide evidence to support the indication of using [⁶⁸Ga]Ga-PSMA-11 PET/CT scan for patient selection for a PSMA-targeted radioligand therapy such as [¹⁷⁷Lu]Lu-PSMA-617.

Signatures

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Clinical Development

gallium (68Ga) gozetotide

AAA517 ([⁶⁸Ga]Ga-PSMA-11)

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1 Overview

The VISION study (Study PSMA-617-01, NCT03511664, EudraCT No 2018-000459-41) sponsored by Endocyte is a global, randomized, open-label phase 3 study of [¹⁷⁷Lu]Lu-PSMA-617 in addition to best supportive/best standard of care in the treatment of patients with progressive PSMA-positive mCRPC. [⁶⁸Ga]Ga-PSMA-11 is the radioligand imaging agent used in the VISION study to select eligible patients for treatment with [¹⁷⁷Lu]Lu-PSMA-617 based on pre-defined central read criteria.

Given that [¹⁷⁷Lu]Lu-PSMA-617 specifically targets PSMA protein expressed on cancer cell surface, it is possible that PSMA expression and pattern may associate with treatment response. This study aimed to evaluate the association between quantitative PSMA imaging parameters extracted from pre-treatment [⁶⁸Ga]Ga-PSMA-11 PET/CT scans and [¹⁷⁷Lu]Lu-PSMA-617 treatment outcomes in the VISION study, including rPFS (primary objective of the quantitative analysis), OS, ORR and PSA response (secondary objectives of the quantitative analysis). To enable the analysis, Endocyte designated Invicro, a Konica Minolta Company, to extract quantitative PSMA imaging parameters from the [⁶⁸Ga]Ga-PSMA-11 PET/CT scans of 548 patients acquired during screening as described in the [\[Independent Review Charter Quantitative Analysis \(IRC-QA\)\]](#) and [\[Statistical Analysis Plan \(SAP\) Quantitative Analysis addendum version 1.0\]](#). Invicro then transferred the quantitative imaging data to Endocyte/AAA, who performed all subsequent statistical analysis to assess the association between PSMA PET parameters and clinical outcomes.

2 Methods

The [⁶⁸Ga]Ga-PSMA-11 PET/CT scans acquired during screening from all 831 patients enrolled in the VISION study were transferred to Invicro during the study, with the final scan transferred on April 13, 2021. On April 7, 2021, Endocyte provided Invicro with the screening identification numbers of the 551 patients randomized to the [¹⁷⁷Lu]Lu-PSMA-617 treatment arm of the study to be included in this quantitative image analysis. During quality assessment of the transferred images, Invicro identified 3 patients whose scans were not analyzable. Invicro completed the extraction of quantitative imaging parameters from the remaining 548 scans and transferred the data to Endocyte/AAA on 19 July, 2021. Subsequently, statistical analysis was performed by Endocyte/AAA.

2.1 Study population

In the VISION study, a total of 831 patients were randomized in a 2:1 ratio to receive either [¹⁷⁷Lu]Lu-PSMA-617 plus best supportive care (BSC)/best standard of care (BSOC) or BSC/BSOC only. [⁶⁸Ga]Ga-PSMA-11 was used to determine patient eligibility for [¹⁷⁷Lu]Lu-PSMA-617 therapy based on PET imaging patterns defined by the central read criteria. Only mCRPC patients with at least one PSMA-positive lesion identified on PSMA-PET and no PSMA-negative lesion fulfilling the exclusion criteria were enrolled in the study, provided all other inclusion criteria were met. Of the 551 patients who were randomized to the [¹⁷⁷Lu]Lu-PSMA-617 treatment arm, 548 had PET/CT images that met the rigorous quality requirements to be included in this quantitative imaging analysis. All [⁶⁸Ga]Ga-PSMA-11 PET/CT scan images used in this study were collected during patient screening in the VISION study, after all other eligibility criteria were confirmed and within 4 weeks (+ 2 weeks) of the start of treatment,

but not within the 6 days prior to the start of treatment. Additional information on specific patient populations included in different statistical analyses in this study is provided in [Section 2.6.](#)

2.2 Transfer of the VISION study imaging data to Invicro

The 831 sets of baseline [⁶⁸Ga]Ga-PSMA-11 PET/CT scans with matching diagnostic CT/MRI images from all patients enrolled in the VISION study were transferred to Invicro following instructions in the Image Transfer Agreement and Data Transfer Agreement (DTA) agreed upon between Endocyte and Invicro. All details related to the transfer were pre-specified, including a list of image and associated image metadata (e.g. injected dose, patient weight and scan acquisition date), data format, frequency of data transfer and structure of the database.

All images and associated image metadata were received, archived and tracked by Invicro following their standard operating procedures. All imaging data were backed-up in the original file format. A copy of each image was transferred to a 21CFR §11 compliant workstation for initial review and reconciliation within the iPACS system.

2.3 Initial checks and reconciliation of imaging data

Upon receipt of the imaging data, Invicro cross-checked the digital file identifiers and associated data against the list of included data provided by Endocyte. The following parameters were included and documented in the initial review:

- Name of file(s) received
- Confirmation of patient identity between images and submission form
- Clerical accuracy in the submission form
- Missing images
- Completeness of required series/sequences

Discrepancies identified, such as missing images or conflicts in submission, were submitted to Endocyte for verification.

2.4 Extraction of quantitative imaging parameters from [⁶⁸Ga]Ga-PSMA-11 PET/CT scans

2.4.1 Personnel and software

All image processing and analysis was performed by an Image Processing Specialist (IPS) using the imaging quantification software VivoQuant™. The software generated audit trails that included date-, time-, and user-stamps for any images accessed and any analysis performed on the imaging data. No imaging file was erased or overwritten during the process since each new step in the analysis procedure generated a new unique file tracked electronically for change, date, time, and image processor.

2.4.2 Imaging data blinding

All institution-specific site and patient identifiers, patient demographics, clinical outcomes, and other clinical information not deemed essential for the quantitative analysis were masked.

However, the IPS was not blinded to essential clinical information (e.g. injected dose and patient weight) needed for the imaging analysis.

2.4.3 Audit trail of assessments

In compliance with Good Clinical Practice guidelines and 21CFR §11, all assessments performed by the IPS were captured in an audit trail. The iPACS database maintained a log of all application trigger events to produce a complete audit trail that could re-create the events within any assessment. Events and data captured by the audit trail included annotations and measurements generated during the quantitative analysis, as well as date- and time-stamps, and user identity.

2.4.4 Extraction of quantitative PSMA imaging parameters from [⁶⁸Ga]Ga-PSMA-11 PET/CT scans

A validated, semi-automated segmentation and calculation workflow was used to extract PSMA PET parameters from the baseline [⁶⁸Ga]Ga-PSMA-11 PET/CT scans of the 548 [¹⁷⁷Lu]Lu-PSMA-617 treated patients included in this analysis. The workflow consisted of three primary steps, including the segmentation of the PET/CT scan image into different tumor anatomical regions, review and revision as necessary by expert nuclear radiologist, and quantitation of multiple PSMA PET parameters for each anatomical region. Segmentation and quantitation steps were performed by trained image processing specialists using the VivoQuant™ software, and review of segmentations was performed in MIM Premier™ software.

Each PET/CT scan was segmented into five anatomical regions, including:

- bone
- liver
- lymph node
- non-liver parenchymal organs (soft tissue)
- whole body (combination of all individual segmented anatomical regions)

A multi-step validated, 21-CFR Part 11-compliant workflow was executed for segmentation and metrics calculation. Due to the high presence of bone disease in this patient population, a multi-modal PET/CT deep learning model, developed within the AntsRNet architecture, was utilized to automatically segment bone disease (Tustison et al 2021, Tustison et al 2019). Individual bone lesions were assigned a bone label. Soft tissue disease was segmented in VivoQuant, using a semi-automated approach. A 41% threshold was applied around the local maximum of each lesion, followed by manual editing, if needed. Soft tissue disease lesions were labeled as lymph node, liver, and non-liver soft tissue. Bone lesion and soft tissue lesion segmentations were merged and reviewed by a radiologist who directly edited lesions, as needed. Following radiologist review and approval, lesion metrics were computed, including SUVmean, SUVmax, PSMA+ tumor volume and tumor load (Schmuck et al 2017). These metrics were computed for each of the four regions (bone, lymph node, liver, non-liver soft tissue) and whole body, which included all segmented lesions.

All PSMA PET parameters are based on the number of counts (i.e. standardized [⁶⁸Ga]Ga-PSMA-11 uptake) within the voxels in a segmented region. Each voxel has a defined volume measured in cc. The five PSMA PET parameters used in this study included (Table 2-1):

- Presence of PSMA+ lesion (No/Yes): positive [⁶⁸Ga]Ga-PSMA-11 uptake within a segmented anatomical region
- SUV_{mean}: the mean number of counts from all voxels within a segmented anatomical region, including all lesions pooled together in that region
- SUV_{max}: the uptake of the voxel with the highest number of counts among all voxels within a segmented anatomical region, including all lesions pooled together in that region
- PSMA+ tumor volume: the volume of PSMA+ lesions within a segmented anatomical region calculated from the total volume of voxels with positive uptake. Note that PSMA+ tumor volume might be different from the actual tumor volume measured by conventional imaging because some of the lesions might not have positive PSMA PET uptake or the uptake is very high in a small lesion
- Tumor load: a composite measurement defined as the product of PSMA+ tumor volume and SUV_{mean} of the segmented anatomical region

Among the PSMA PET parameters, SUV_{mean} and SUV_{max} express the [⁶⁸Ga]Ga-PSMA-11 uptake in the lesions, whereas PSMA+ tumor volume express the volume included in the segmented voxels, and tumor load was derived from the uptake and the volume of the segmented voxels.

While SUV_{mean} and SUV_{max} values were provided with a unit of g/ml in this analysis, SUV is typically presented as a unitless parameter in clinical practice. Therefore, a generic unit instead of g/ml was used throughout this report in describing SUVs, as appropriate. Since tumor load is a composite measurement derived from SUV_{mean}, a generic unit was used as well. PSMA+ tumor volume was based on the volume of voxels, so the unit was represented in cc.

Table 2-1 PSMA PET imaging parameters extracted from each anatomical region in pre-treatment [⁶⁸Ga]Ga-PSMA-11 PET/CT scans from mCRPC patients treated with [¹⁷⁷Lu]Lu-PSMA-617 in the VISION study

| Parameter | Definition | Unit |
|--------------------------------|---|------|
| Presence of PSMA+ lesion (Y/N) | Positive PSMA uptake in tumor | N/A |
| SUV _{mean} | Mean SUV | g/ml |
| SUV _{max} | Maximum SUV | g/ml |
| PSMA+ tumor volume | Volume of segmented PSMA-positive tumor | cc |
| Tumor load | Product of PSMA+ tumor volume and SUV _{mean} | g |

Source: [\[IRC-QA\]](#)

2.5 Transfer of PSMA PET imaging data to Endocyte

2.5.1 Database entry

Extracted quantitative PSMA imaging data were uploaded into the validated Invicro database iPACS. The uploaded data were subsequently combined with relevant source data and extracted for final quality control (QC) prior to the data transfer.

2.5.2 Database QC

After outbound data were extracted for delivery, Invicro conducted a final QC check to ensure the extracted data match with the original data sources. This step verified that the file transfer format, required fields, and structure were complete and aligned with the approved DTA.

2.5.3 Transfer of data to Endocyte

Data transfer to Endocyte was performed in accordance with the approved DTA, following pre-defined requirements on data encryption, data security, data structure, specified data variables transfer type and frequency, as well as delivery method.

2.5.4 Database lock

Once all data requested by Endocyte were transferred and the final study report completed, Invicro performed the database closure process and locked the database to read-only access in order to prevent any changes to the final database. A copy of the final database was permanently saved and could not be further altered.

2.6 Study objectives and statistical analysis

All statistical analyses were pre-defined in the [\[Statistical Analysis Plan \(SAP\) Quantitative Analysis addendum version 1.0\]](#).

2.6.1 Study objectives

2.6.1.1 Primary objective

The primary objective of this study was to examine the association between PSMA PET parameters extracted from screening [⁶⁸Ga]Ga-PSMA-11 PET/CT scans from [¹⁷⁷Lu]Lu-PSMA-617 treated patients in the VISION study and rPFS as determined by RECIST v1.1 and PCWG3 criteria. rPFS was one of the alternate primary endpoints of the Phase 3 VISION study. Analysis was performed for each pre-specified anatomical region, including the whole body.

2.6.1.2 Secondary objectives

Multiple secondary objectives were included in this study:

- Evaluate the association between OS and PSMA PET parameters assessed by [⁶⁸Ga]Ga-PSMA-11 PET/CT scans at the time of enrollment. OS was one of the alternate primary endpoints of the Phase 3 VISION study.
- Evaluate the association between ORR and PSMA PET parameters assessed by [⁶⁸Ga]Ga-PSMA-11 PET/CT scans at the time of enrollment.
- Evaluate the association between PSA response and PSMA PET parameters assessed by [⁶⁸Ga]Ga-PSMA-11 scans at the time of enrollment.
- Identify an optimal cutpoint based on the linear predictor of the model identified from the primary analysis of rPFS. This optimal cutpoint will be the linear predictor value that best separates rPFS.

- Identify an optimal cutpoint based on the linear predictor of the model identified from the secondary analysis of OS. This optimal cutpoint will be the linear predictor value that best separates OS.

Each objective was evaluated for every anatomical region, including the whole body.

2.6.2 Sample size

The VISION study was originally designed to randomize 750 patients, targeting the primary analysis of rPFS with 457 events, an interim analysis of OS (to be conducted contemporaneously with the primary analysis of rPFS), and a final analysis of OS with 489 deaths. However, shortly after commencement of the trial, a high, early dropout rate amongst those randomized to BSC/BSoC only arm became evident with the majority of these dropouts withdrawing consent to follow-up. This meant that rPFS data could not be collected for these patients that consequently could result in bias in the analysis of rPFS. Remedial measures to curtail this phenomenon were implemented and made effective on March 5th, 2019. As part of the plan to address the early withdrawal of consent in the BSC/BSoC only arm, the primary analysis of rPFS was altered to focus on patients prospectively randomized on or after March 5th, 2019. These changes in study conduct and statistical analysis were discussed and agreed with the Division of Oncology 1 review team of the FDA as well as with BfArM (German Health Authority) and the Scientific Advice Working Party of the EMA.

Thus, in this analysis, association of PSMA PET parameters with rPFS included only patients prospectively randomized to the [¹⁷⁷Lu]Lu-PSMA-617 treatment arm on or after March 5, 2019 based on the January 27, 2021 data cut-off. The same data cut-off was used for the primary analysis of rPFS in the VISION study.

Association with OS was analyzed based on the intent to treat (ITT) population, thus including all patients randomized to the [¹⁷⁷Lu]Lu-PSMA-617 treatment arm (i.e. including patients randomized before March 5, 2019) based on the January 27, 2021 data cut-off. The same data cut-off was used for the primary analysis of OS in the VISION study.

Association of PSMA PET parameters with ORR and PSA response was analyzed using the patients randomized to the investigational arm and included in the primary ORR and PSA response analysis in the VISION study respectively based on the January 27, 2021 data cut-off.

2.6.3 Analysis sets

Each analysis set included the subset of patients used in the corresponding efficacy analysis in the VISION study, who had at least one PSMA+ lesion in the anatomical region being analyzed, as well as good quality images available for the quantitative analysis. The number of patients in each analysis set is summarized in [Table 2-2](#). As expected, the number of patients in the whole body analysis set was the highest, as all enrolled patients had at least one PSMA+ lesion per the eligibility criteria of the VISION study. The sample size in the liver analysis set was the smallest due to the low prevalence of liver metastasis in this study.

Body-Full Analysis Set (Body-FAS) included all patients randomized to [¹⁷⁷Lu]Lu-PSMA-617+BSC/BSoC arm who had good quality images available for the quantitative analysis.

Body-PFS Full Analysis Set (Body-PFS-FAS) included all patients randomized to [¹⁷⁷Lu]Lu-PSMA-617+BSC/BSoC arm on or after March 5, 2019 who had good quality images available for the quantitative analysis.

Body-Response Evaluable Analysis Set (Body-REAS) included the subset of patients in the Body-PFS-FAS with evaluable disease by RECIST at baseline (i.e. at least one target and/or non-target lesion per central review).

Bone-Full Analysis Set (Bone-FAS) included all patients randomized to [¹⁷⁷Lu]Lu-PSMA-617+BSC/BSoC arm who had good quality images available for the quantitative analysis, and with at least one PSMA+ lesion in the bone.

Bone-PFS Full Analysis Set (Bone-PFS-FAS) included all patients randomized to [¹⁷⁷Lu]Lu-PSMA-617+BSC/BSoC arm on or after March 5, 2019 who had good quality images available for the quantitative analysis, and with at least one PSMA+ lesion in the bone.

Bone-Response Evaluable Analysis Set (Bone-REAS) included the subset of patients in the Bone-PFS-FAS with evaluable disease by RECIST at baseline (i.e. at least one target and/or non-target lesion per central review) with at least one PSMA+ lesion in the bone.

Liver-Full Analysis Set (Liver-FAS) included all patients randomized to [¹⁷⁷Lu]Lu-PSMA-617+BSC/BSoC arm who had good quality images available for the quantitative analysis, and with at least one PSMA+ lesion in the liver.

Liver-PFS Full Analysis Set (Liver-PFS-FAS) included all patients randomized to [¹⁷⁷Lu]Lu-PSMA-617+BSC/BSoC arm on or after March 5, 2019 who had good quality images available for the quantitative analysis, and with at least one PSMA+ lesion in the liver.

Liver-Response Evaluable Analysis Set (Liver-REAS) included the subset of patients in the Liver-PFS-FAS with evaluable disease by RECIST at baseline (i.e. at least one target and/or non-target lesion per central review) with at least one PSMA+ lesion in the liver.

Lymph Node-Full Analysis Set (Lymph Node-FAS) included all patients randomized to [¹⁷⁷Lu]Lu-PSMA-617+BSC/BSoC arm who had good quality images available for the quantitative analysis, and with at least one PSMA+ lesion in the lymph node.

Lymph Node-PFS Full Analysis Set (Lymph Node-PFS-FAS) included all patients randomized to [¹⁷⁷Lu]Lu-PSMA-617+BSC/BSoC arm on or after March 5, 2019 who had good quality images available for the quantitative analysis, and with at least one PSMA+ lesion in the lymph node.

Lymph Node-Response Evaluable Analysis Set (Lymph Node-REAS) included the subset of patients in the Lymph Node-PFS-FAS with evaluable disease by RECIST at baseline (i.e. at least one target and/or non-target lesion per central review) with at least one PSMA+ lesion in the lymph node.

Soft Tissue-Full Analysis Set (Soft Tissue-FAS) included all patients randomized to [¹⁷⁷Lu]Lu-PSMA-617+BSC/BSoC arm who had good quality images available for the quantitative analysis, and with at least one PSMA+ lesion in the soft tissue.

Soft Tissue-PFS Full Analysis Set (Soft Tissue-PFS-FAS) included all patients randomized to [¹⁷⁷Lu]Lu-PSMA-617+BSC/BSoC arm on or after March 5, 2019 who had good quality images available for the quantitative analysis, and with at least one PSMA+ lesion in the soft tissue.

Soft Tissue-Response Evaluable Analysis Set (Soft Tissue-REAS) included the subset of patients in the Soft Tissue-PFS-FAS with evaluable disease by RECIST at baseline (i.e. at least one target and/or non-target lesion per central review) with at least one PSMA+ lesion in the soft tissue.

Table 2-2 Number of patients in each analysis set

| Analysis set | Lu-PSMA-617+BSC/BSoC (N=551) n (%) |
|--|--|
| Body-Full Analysis Set (Body-FAS) | 548 (99.5) |
| Body-PFS Full Analysis Set (Body-PFS-FAS) | 382 (69.3) |
| Body-Response Evaluable Analysis Set (Body-REAS) | 317 (57.5) |
| Bone-Full Analysis Set (Bone-FAS) | 508 (92.2) |
| Bone-PFS Full Analysis Set (Bone-PFS-FAS) | 353 (64.1) |
| Bone-Response Evaluable Analysis Set (Bone-REAS) | 291 (52.8) |
| Liver-Full Analysis Set (Liver-FAS) | 72 (13.1) |
| Liver-PFS Full Analysis Set (Liver-PFS-FAS) | 51 (9.3) |
| Liver-Response Evaluable Analysis Set (Liver-REAS) | 44 (8.0) |
| Lymph Node-Full Analysis Set (Lymph Node-FAS) | 369 (67.0) |
| Lymph Node-PFS Full Analysis Set (Lymph Node-PFS-FAS) | 258 (46.8) |
| Lymph Node-Response Evaluable Analysis Set (Lymph Node-REAS) | 220 (39.9) |
| Soft Tissue-Full Analysis Set (Soft Tissue-FAS) | 233 (42.3) |
| Soft Tissue-PFS Full Analysis Set (Soft Tissue-PFS-FAS) | 173 (31.4) |
| Soft Tissue-Response Evaluable Analysis Set (Soft Tissue-REAS) | 148 (26.9) |

Source: [Post-text Table 1.1](#)

2.6.4 Quantitative PSMA PET covariates used for primary and secondary objective analysis

For the whole body anatomical region, the following covariates were included in the analysis of association between PSMA PET parameters and treatment outcome (rPFS, OS, ORR and PSA response):

- Whole body SUVmean
- Whole body SUVmax
- Whole body PSMA+ tumor volume
- Whole body tumor load
- PSMA+ lesion in the liver (No/Yes with “Yes” as the reference value)
- PSMA+ lesion in the bones (No/Yes with “Yes” as the reference value)
- PSMA+ lesion in the lymph nodes (No/Yes with “Yes” as the reference value)
- PSMA+ lesion in the soft tissue (No/Yes with “Yes” as the reference value)

PSMA+ lesions in the whole body (No/Yes) was not included as a covariate for the whole body analysis because the answer was a ‘YES’ for all patients based on the VISION study eligibility criteria.

For the bone region, the following covariates were included in the analysis:

- Bone SUVmean
- Bone SUVmax
- Bone PSMA+ tumor volume
- Bone Tumor load

For the liver region, the following covariates were included in the analysis:

- Liver SUVmean
- Liver SUVmax
- Liver PSMA+ tumor volume
- Liver tumor load

For the lymph node region, the following covariates were included in the analysis:

- Lymph node SUVmean
- Lymph node SUVmax
- Lymph node PSMA+ tumor volume
- Lymph node tumor load

For the soft tissue region, the following covariates were included in the analysis:

- Soft tissue SUVmean
- Soft tissue SUVmax
- Soft tissue PSMA+ tumor volume
- Soft tissue tumor load

The analysis for each individual anatomical region included only patients with at least one PSMA+ lesion in that specific anatomical region.

2.6.5 Statistical analysis

For the time-to-event outcomes (rPFS/OS), we constructed a univariate Cox proportional hazard model (Cox 1972), and Kaplan–Meier curves for different patient groups based on either the quartiles of the continuous covariates or the binary ones. Both these methods are examples of univariate analysis; they describe the outcomes with respect to the covariate under investigation, but necessarily ignore the impact of any others. However, multiple covariates may potentially affect patient outcome. For example, suppose two groups of patients are compared: those with the presence of PSMA+ lesions in the bone and those without. If one of the groups also contains individuals with higher SUVmean, any difference in outcome may be attributable to presence/absence of PSMA+ lesions in the bone or SUVmean or indeed both. Hence, when investigating rPFS/OS in relation to any one covariate, it is often desirable to adjust for the impact of others. The use of a multivariate Cox proportional hazard model improves on these methods by allowing the outcomes to be assessed with respect to several covariates simultaneously, and in addition, offers estimates of the strength of effect for each covariate.

Similarly, for the binary covariates (ORR/PSA response), a univariate logistic regression was applied by taking just one covariate at a time and a multiple logistic regression was then constructed to assess these outcomes with respect to several covariates simultaneously.

Univariate Cox proportional hazards models was used to assess the individual predictive value of each baseline [⁶⁸Ga]⁶⁸Ga-PSMA-11 PET/CT scan quantitative PSMA PET covariate for each anatomical region (including whole body) on rPFS. Hazard ratios (increase in hazard ratio for a unit increase for the continuous variables) and corresponding 95% confidence intervals were estimated. Statistical significance was assessed for each covariate based on a 2-sided alpha = 0.05 significance level. Imaging covariates found to be individually related to outcome were included in a Cox proportional hazards multivariable model, and backwards elimination was utilized to identify imaging covariates that are independently predictor variables for rPFS (elimination threshold will be based on a 2-sided alpha = 0.05 significance level). Subsequently, forward selection was utilized on all covariates not included from the univariate models or eliminated from the backwards elimination analysis (inclusion threshold will be based on a 2-sided alpha = 0.05 significance level).

The final model was subsequently estimated. Statistical significance for each imaging covariate was assessed. After a final model identifying independently important imaging covariates is established, a threshold analysis was conducted to identify an optimal cutpoint that best separates subjects with the longest rPFS interval versus subjects with the shortest rPFS interval. This was accomplished utilizing the linear predictor from the final model.

The optimal cutpoint was defined as the value that maximizes the rPFS/OS hazard ratio among the cutpoints associated with a statistically significant difference in rPFS in subjects above versus below the cutpoint. The [Contal and O'Quigley \(1999\)](#) technique was used to identify the optimal cutpoint separately for each covariate that remained in the final model.

The analyses described for rPFS was conducted on secondary endpoints including OS. Association of quantitative imaging parameters with objective response and PSA response were analyzed using logistic regression ([Wright 1995](#)).

The continuous variables were re-scaled based on the range of values for both the Cox and logistic regression models. For each of the tables involving continuous variables in the Cox and logistic regression models, a footnote was added, for example, HR/OR is computed for a 10 units increase in the covariate.

[⁶⁸Ga]Ga-PSMA-11 PET/CT scan covariates that were considered in the modeling are shown in [Table 2-1](#).

3 Results

3.1 Summary descriptive statistics of PSMA PET parameters in different anatomical regions

All PSMA PET parameters, including the presence of PSMA+ lesions, SUVmean, SUVmax, PSMA+ tumor volume, and tumor load, were successfully extracted from the pre-treatment [⁶⁸Ga]Ga-PSMA-11 PET/CT scans from patients in each analysis set ([Table 2-2](#)) and for each anatomical region. Among the patients included in the Full Analysis Set (FAS), patients most frequently had positive PSMA uptake in bone (92.7%) and least frequently in liver (13.1%)

(Table 3-1). The mean SUVmean ranged from 7.3 in bone to 8.9 in soft tissue. The mean SUVmax ranged from 19.6 in liver to 35.2 in bone. Both mean PSMA+ tumor volume and mean tumor load were lowest in soft tissue (74.7 cc and 865.8 respectively) and highest in bone (684.3 cc and 5296.8 respectively).

Among the patients included in the PFS Full Analysis Set (PFS-FAS), patients most frequently had positive PSMA uptake in bone (92.4%) and least frequently in liver (13.4%) (Table 3-1). The mean SUVmean ranged from 7.6 in bone to 9.4 in lymph node. The mean SUVmax ranged from 20.4 in liver to 38.0 in bone. Both mean PSMA+ tumor volume and mean tumor load were lowest in soft tissue (84.1 cc and 975.4 respectively) and highest in bone (738.2 cc and 5675.7 respectively).

Among the patients included in the Response Evaluable Analysis Set (REAS), patients most frequently had positive PSMA uptake in bone (91.8%) and least frequently in liver (13.9%) (Table 3-1). The mean SUVmean ranged from 7.7 in bone to 9.5 in lymph node. The mean SUVmax ranged from 21.3 in liver to 38.1 in bone. Both mean PSMA+ tumor volume and mean tumor load were lowest in soft tissue (88.7 cc and 1056.5 respectively) and highest in bone (668.7 cc and 5240.8 respectively).

Overall, the pattern of PSMA PET parameters in the different anatomical regions were highly comparable between the three analysis sets, which consisted of slightly different subsets of patients based on the corresponding efficacy analysis in the VISION study.

Table 3-1 Summary statistics of PSMA PET parameters in different anatomical regions and different analysis sets

| Analysis set | Anatomical Region | n (%) of subjects with PSMA+ tumor | Mean (Q1-Q3) SUVmean | Mean (Q1-Q3) SUVmax | Mean (Q1-Q3) PSMA+ tumor volume (cc) | Mean (Q1-Q3) tumor load |
|-----------------|-------------------|------------------------------------|----------------------|---------------------|--------------------------------------|-------------------------|
| FAS (N=548) | Whole body | 548 (100) | 8.4 (5.7-9.9) | 41.5 (20.2-53.0) | 805.0 (140.6-1160.3) | 6925.1 (1017.9-9835.8) |
| | Bone | 508 (92.7) | 7.3 (5.0-8.6) | 35.2 (15.9-45.7) | 684.3 (67.8-986.4) | 5296.8 (415.6-7653.4) |
| | Liver | 72 (13.1) | 8.6 (6.2-10.4) | 19.6 (9.7-26.0) | 280.0 (6.9-180.0) | 3021.2 (37.7-1746.3) |
| | Lymph node | 369 (67.3) | 8.8 (5.0-11.5) | 32.4 (11.2-44.3) | 151.7 (10.0-159.6) | 1856.2 (51.9-1688.1) |
| | Soft tissue | 233 (42.5) | 8.9 (5.1-10.6) | 22.7 (8.6-32.1) | 74.7 (3.3-35.1) | 865.8 (22.4-369.6) |
| PFS-FAS (N=382) | Whole body | 382 (100) | 8.8 (6.0-10.2) | 44.2 (22.5-55.1) | 869.3 (191.6-1271.0) | 7471.5 (1582.9-10279.2) |
| | Bone | 353 (92.4) | 7.6 (5.3-8.7) | 38.0 (17.7-48.2) | 738.2 (88.1-1076.7) | 5675.7 (620.5-7921.3) |
| | Liver | 51 (13.4) | 8.6 (6.2-10.3) | 20.4 (9.8-28.2) | 343.2 (8.2-270.8) | 3588.7 (46.6-2322.3) |
| | Lymph node | 258 (67.5) | 9.4 (5.3-11.7) | 34.3 (13.6-46.0) | 152.9 (10.4-157.8) | 1933.4 (76.4-1764.3) |
| | Soft tissue | 173 (45.3) | 9.2 (5.4-10.9) | 23.9 (10.1-33.2) | 84.1 (3.3-35.5) | 975.4 (23.7-391.6) |
| REAS (N=317) | Whole body | 317 (100) | 8.9 (6.1-10.4) | 45.0 (22.7-57.6) | 812.4 (183.4-1177.5) | 7245.5 (1406.9-9550.7) |
| | Bone | 291 (91.8) | 7.7 (5.3-8.8) | 38.1 (17.1-50.9) | 668.7 (77.2-984.9) | 5240.8 (503.8-7625.5) |
| | Liver | 44 (13.9) | 8.9 (6.2-10.4) | 21.3 (9.8-28.7) | 308.8 (9.7-212.1) | 3391.5 (71.9-1746.3) |
| | Lymph node | 220 (69.4) | 9.5 (5.5-12.1) | 35.6 (14.4-46.7) | 164.6 (11.8-168.9) | 2114.7 (84.1-1878.1) |
| | Soft tissue | 148 (46.7) | 9.2 (5.5-11.0) | 24.1 (10.0-33.2) | 88.7 (3.3-35.3) | 1056.5 (24.0-363.0) |

Source: Post-text Table 1.2, Table 1.3, Table 1.4, Table 1.5

3.2 Results of rPFS analysis (primary objective)

3.2.1 Cox proportional hazards model

Univariate and multivariate Cox proportional hazards models were utilized to assess the association between PSMA PET parameters and rPFS. The hazard ratio (HR), its 95% confidence interval (CI) and p-value for each of the covariates in the univariate and initial multivariate analyses are provided in the appendix. In the final multivariate model for the whole body analysis, the PSMA PET parameters that demonstrated statistically significant association with rPFS are listed in [Table 3-2](#) and summarized below:

- Whole body SUVmean
- Whole body tumor load
- Absence of PSMA+ lesion in bone
- Absence of PSMA+ lesion in liver

Specifically, a 1-unit increase of whole body SUVmean was associated with a 14% decrease in the risk of rPFS event (radiographic progression or death), a 1000-unit increase in tumor load was associated with a 2% increase in the risk of rPFS event, and the absence of PSMA+ lesions in bone and liver were associated with 55% and 52% decrease in the risk of rPFS event.

In the final multivariate model for individual anatomical regions, PSMA PET parameters that demonstrated statistically significant association with rPFS included ([Table 3-2](#)):

- Bone SUVmean
- Bone tumor load
- Liver PSMA+ tumor volume
- Lymph node SUVmax
- Soft tissue SUVmax

A 1-unit increase of bone SUVmean was associated with a 13% decrease in the risk of rPFS event. A 1-unit increase of lymph node and soft tissue SUVmax was associated with a 2% and 2% decrease in the risk of rPFS event respectively. A 1000-unit increase in bone tumor load was associated with a 3% increase in the risk of rPFS event, and 1000 cc increase in liver PSMA+ tumor volume was associated with a 44% increase in the risk of rPFS event.

Table 3-2 Hazard ratios and statistical significance of quantitative PSMA imaging parameters in final multivariate rPFS analysis

| Analysis set | Anatomical region | Parameter | HR | 95% CI | p-value |
|----------------|-------------------|-------------------------|------|--------------|---------|
| Whole body FAS | Whole body | SUVmean | 0.86 | [0.82, 0.90] | <0.001 |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | 1.02 | [1.01, 1.04] | 0.001 |
| | | Absence of PSMA+ lesion | 0.45 | [0.26, 0.78] | 0.004 |
| | Liver | Absence of PSMA+ lesion | 0.48 | [0.34, 0.67] | <0.001 |
| | | Absence of PSMA+ lesion | n.s. | | |
| | Lymph node | Absence of PSMA+ lesion | n.s. | | |
| | | Absence of PSMA+ lesion | n.s. | | |

| Analysis set | Anatomical region | Parameter | HR | 95% CI | p-value |
|------------------------|-------------------|--------------------|------|--------------|---------|
| Bone FAS | Bone | SUVmean | 0.87 | [0.82, 0.91] | <0.001 |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | 1.03 | [1.01, 1.05] | 0.001 |
| Liver FAS | Liver | SUVmean | n.s. | | |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | 1.44 | [1.00, 2.08] | 0.05 |
| | | Tumor load | n.s. | | |
| Lymph node FAS | Lymph node | SUVmean | n.s. | | |
| | | SUVmax | 0.98 | [0.98, 0.99] | <0.001 |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | n.s. | | |
| Soft tissue FAS | Soft tissue | SUVmean | n.s. | | |
| | | SUVmax | 0.98 | [0.97, 0.99] | 0.004 |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | n.s. | | |

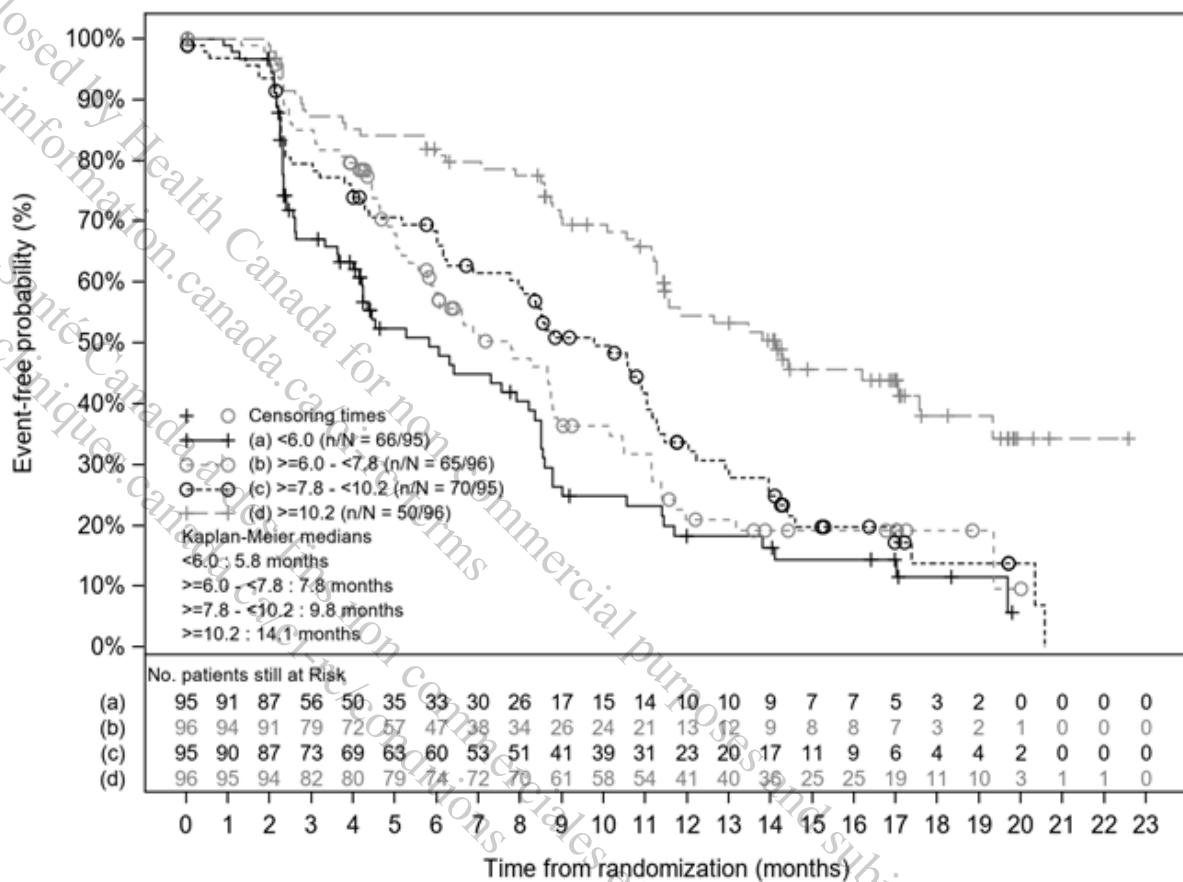
n.s. = not statistically significant

Source: [Post-text Table 3.1, Table 3.2, Table 3.3, Table 3.4, Table 3.5](#)

3.2.2 rPFS Kaplan-Meier analysis

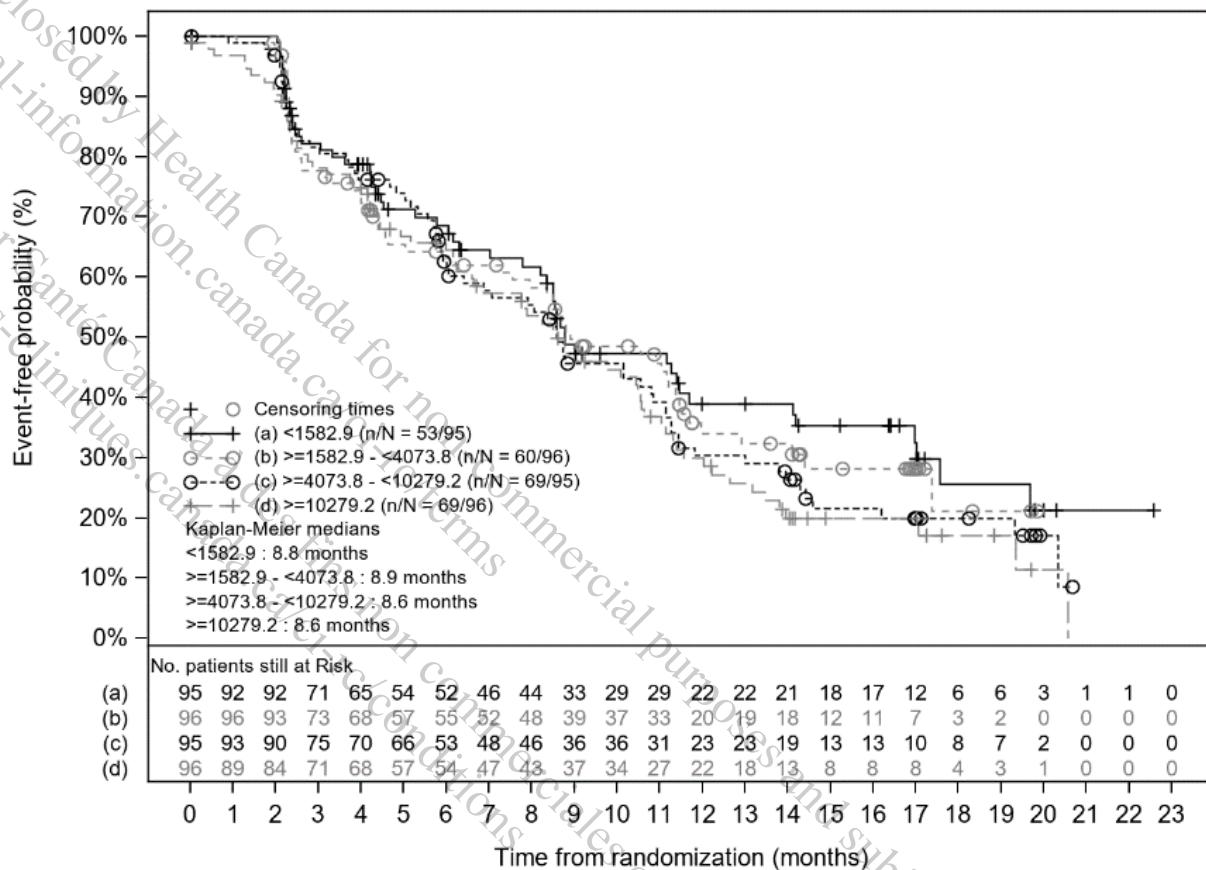
In order to have visual representation, Kaplan-Meier (KM) curves of rPFS were plotted for different patient groups based on either the quartiles of the continuous PSMA PET parameter or the levels of the binary ones. The KM curves corresponding to the PSMA PET parameter that demonstrated a statistically significant association with rPFS in the whole body PFS-FAS analysis set are shown in [Figure 3-1](#) to [Figure 3-4](#).

In the whole body SUVmean analysis, patients in the highest quartile (≥ 10.2) had a median rPFS of 14.1 months, compared with 9.8 months in the second highest quartile ($\geq 7.8 - < 10.2$), 7.8 months in the third highest quartile ($\geq 6.0 - < 7.8$), and 5.8 months in the lowest quartile (< 6.0) ([Figure 3-1](#)).

Figure 3-1 Kaplan-Meier plot for rPFS by whole body SUVmean quartiles in the PFS-FAS analysis set

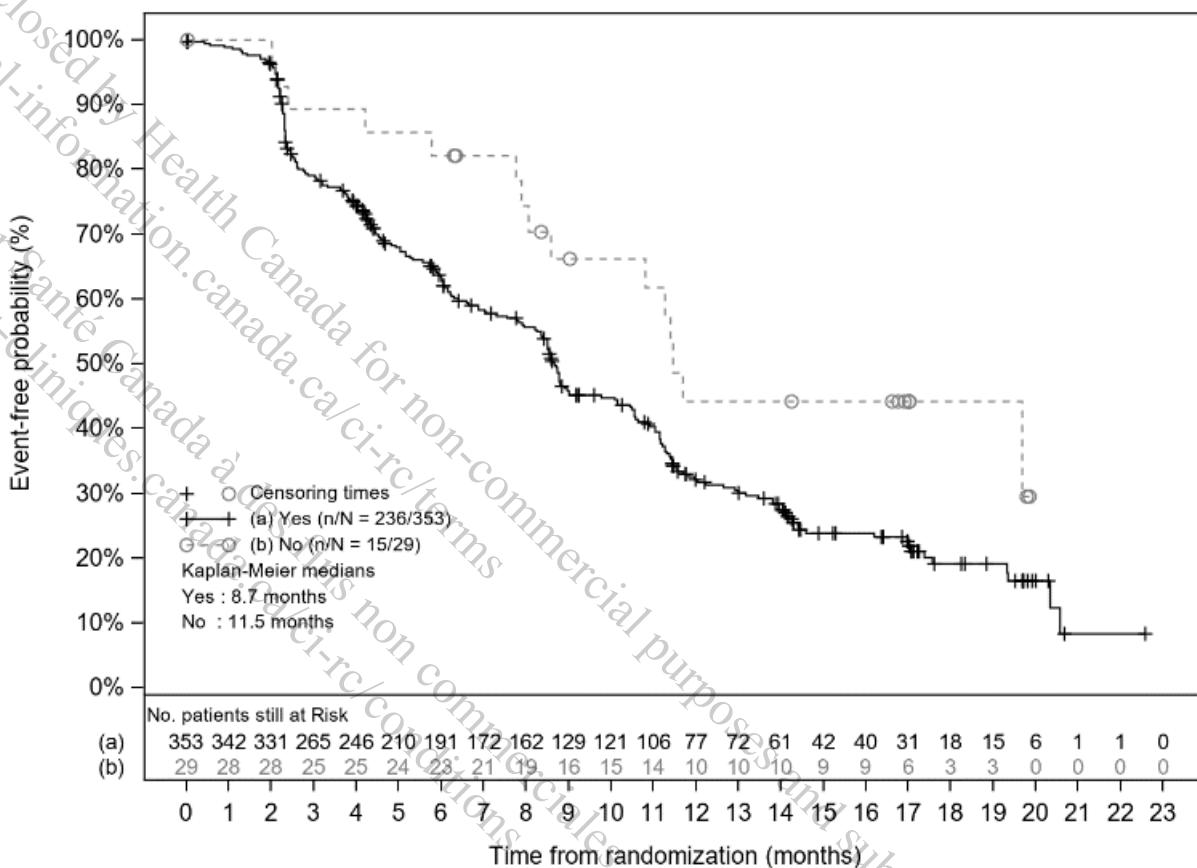
Source: Post-text Figure 2-1-1

In the whole body tumor load analysis, patients in the highest quartile (≥ 10279.2) had a median rPFS of 8.6 months, compared with 8.6 months in the second highest quartile ($\geq 4073.8 - < 10279.2$), 8.9 months in the third highest quartile ($\geq 1582.9 - < 4073.8$), and 8.8 months in the lowest quartile (< 1582.9) (Figure 3-2).

Figure 3-2 Kaplan-Meier plot for rPFS by whole body tumor load quartiles in the PFS-FAS analysis set

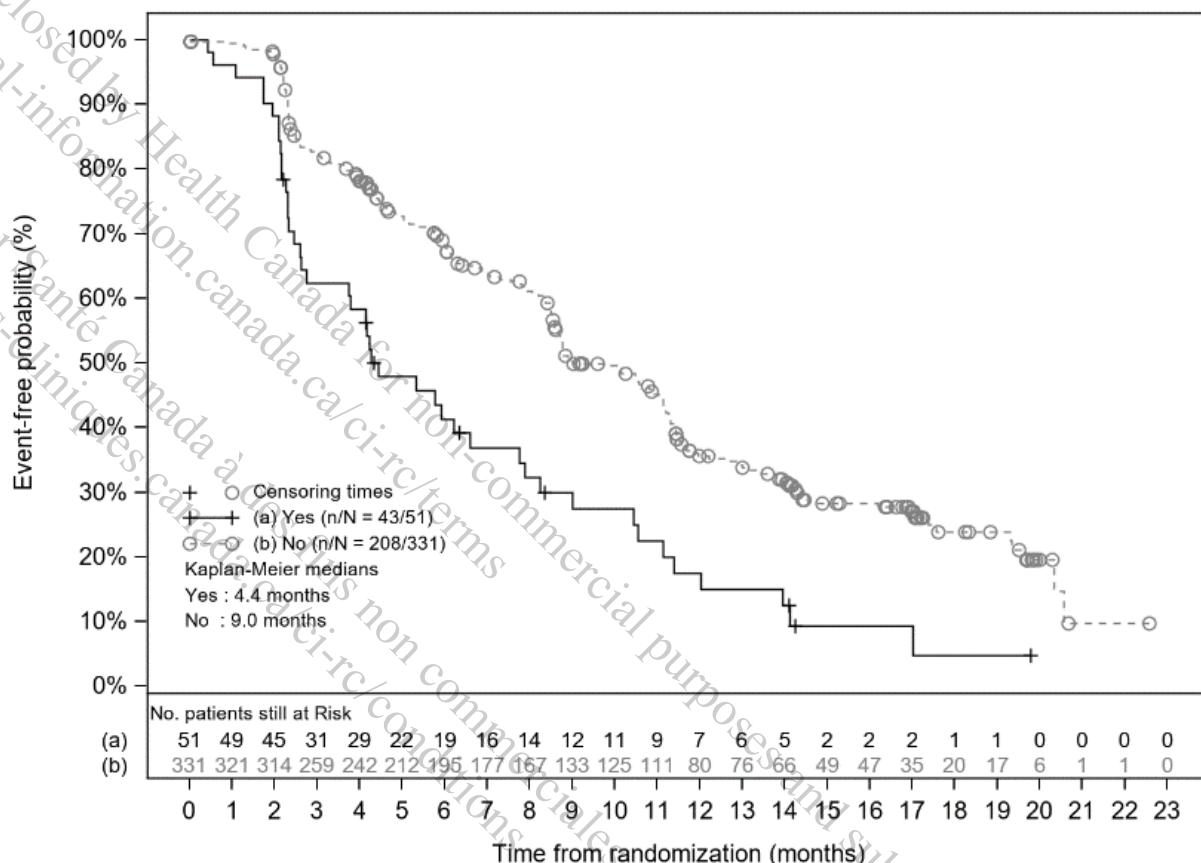
Source: Post-text Figure 2-1-4

In the presence of PSMA+ lesion in bone analysis, patients with PSMA+ bone lesions had a median rPFS of 8.7 months, compared with 11.5 months in patients without (Figure 3-3).

Figure 3-3 Kaplan-Meier plot for rPFS by presence of PSMA+ bone lesions in the PFS-FAS analysis set

Source: Post-text Figure 2-1-5

In the presence of PSMA+ lesion in liver analysis, patients with PSMA+ liver lesions had a median rPFS of 4.4 months, compared with 9.0 months in patients without (Figure 3-4).

Figure 3-4 Kaplan-Meier plot for rPFS by presence of PSMA+ liver lesions in the PFS-FAS analysis set

Source: Post-text Figure 2-1-6

3.2.3 Optimal cutpoint analysis for rPFS

An optimal cutpoint, a value that maximized the rPFS hazard ratio, was identified for each of the continuous imaging covariates that demonstrated statistically significant association with rPFS in the final multivariate analysis. The HR, its 95% CI and p-value for each covariate in the multivariate model were re-calculated using the optimal cutpoint (Table 3-3). Kaplan-Meier analysis was also performed to compare rPFS between patients above and below the optimal cutpoint for each covariate.

Table 3-3 Hazard ratios and statistical significance of PSMA PET parameters in multivariate rPFS analysis using optimal cutpoints for each imaging covariate

| Parameter | Anatomical region | Parameter | Optimal cutpoint ^b | HR | 95% CI | p-value |
|----------------|-------------------|----------------------------------|-------------------------------|------|--------------|---------|
| Whole body FAS | Whole body | SUVmean | <19 vs ≥19 | 0.05 | [0.01, 0.34] | 0.003 |
| | | Tumor load | <26000 vs ≥26000 | 2.24 | [1.30, 3.87] | 0.004 |
| | Bone | PSMA+ lesion No/Yes ^a | Yes vs No | 0.44 | [0.26, 0.76] | 0.003 |

| Parameter | Anatomical region | Parameter | Optimal cutpoint ^b | HR | 95% CI | p-value |
|-----------------|-------------------|----------------------------------|-------------------------------|------|--------------|---------|
| Bone FAS | Liver | PSMA+ lesion No/Yes ^a | Yes vs No | 0.44 | [0.31, 0.61] | <0.001 |
| | Bone | SUVmean | <16 vs ≥16 | 0.13 | [0.03, 0.52] | 0.004 |
| Liver FAS | Liver | Tumor load | <25500 vs ≥25500 | 2.44 | [1.25, 4.77] | 0.009 |
| Lymph node FAS | Lymph node | PSMA+ tumor volume (cc) | <200 vs ≥200 | 2.58 | [1.34, 4.99] | 0.005 |
| Soft tissue FAS | Soft tissue | SUVmax | <86 vs ≥86 | 0.12 | [0.03, 0.50] | 0.003 |
| | | SUVmax | <51 vs ≥51 | 0.35 | [0.14, 0.86] | 0.022 |

^aReference is 'Yes'^bReference is '<'

Source: Post-text Table 4.1, Table 4.2, Table 4.3, Table 4.4, Table 4.5

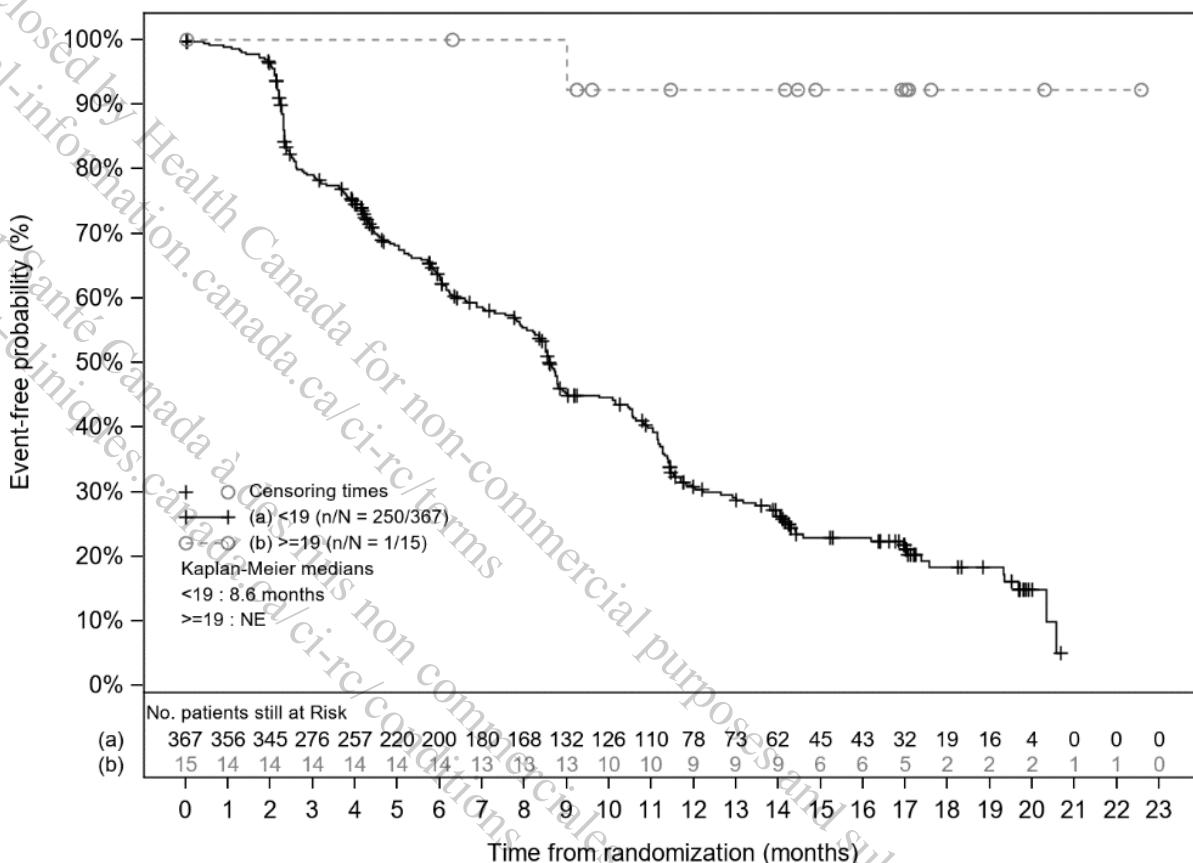
Notably, in the whole body SUVmean analysis, while 19 was identified as the cutpoint associated with the lowest hazard ratio of 0.05, all the other cutpoints tested at <19 resulted in a statistically significant association with rPFS (Table 3-4). In addition, patients above the optimal cutpoint (≥19) had not yet reached median rPFS at the time of this analysis, compared with 8.6 months rPFS in patients below the cutpoint (<19) (Figure 3-5). Nonetheless, it should be noted only 1 rPFS event was observed among the 15 patients above the optimal cutpoint.

Table 3-4 Whole body SUVmean rPFS cutpoint analysis

| Predictor variables | Cut point ^b | p-value | Hazard ratio | No. of events / No. of patients (%) | |
|--|------------------------|--------------------|--------------|-------------------------------------|-------------------------------|
| | | | | <cut point | ≥cut point |
| SUVmean -Optimal cutpoint | <19 | 0.003 ^a | 0.05 | [0.01, 0.37] | 250/367 (68.1) 1/15 (6.7) |
| SUVmean - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <5 | <.001 ^a | 0.47 | [0.32, 0.68] | 34/50 (68.0) 217/332 (65.4) |
| | <6 | <.001 ^a | 0.54 | [0.41, 0.72] | 65/94 (69.1) 186/288 (64.6) |
| | <7 | <.001 ^a | 0.57 | [0.44, 0.73] | 102/151 (67.5) 149/231 (64.5) |
| | <8 | <.001 ^a | 0.54 | [0.42, 0.70] | 136/199 (68.3) 115/183 (62.8) |
| | <9 | <.001 ^a | 0.46 | [0.35, 0.60] | 173/247 (70.0) 78/135 (57.8) |
| | <10 | <.001 ^a | 0.45 | [0.33, 0.61] | 198/283 (70.0) 53/99 (53.5) |
| | <11 | <.001 ^a | 0.45 | [0.32, 0.64] | 214/310 (69.0) 37/72 (51.4) |
| | <12 | <.001 ^a | 0.37 | [0.25, 0.55] | 224/324 (69.1) 27/58 (46.6) |
| | <13 | <.001 ^a | 0.29 | [0.17, 0.48] | 235/339 (69.3) 16/43 (37.2) |
| | <14 | <.001 ^a | 0.17 | [0.08, 0.36] | 244/352 (69.3) 7/30 (23.3) |
| | <15 | <.001 ^a | 0.16 | [0.07, 0.39] | 246/357 (68.9) 5/25 (20.0) |
| | <16 | <.001 ^a | 0.14 | [0.05, 0.38] | 247/360 (68.6) 4/22 (18.2) |
| | <17 | <.001 ^a | 0.11 | [0.04, 0.36] | 248/362 (68.5) 3/20 (15.0) |
| | <18 | <.001 ^a | 0.09 | [0.02, 0.36] | 249/365 (68.2) 2/17 (11.8) |
| | <19 | 0.003 ^a | 0.05 | [0.01, 0.37] | 250/367 (68.1) 1/15 (6.7) |
| | <20 | 0.012 ^a | 0.08 | [0.01, 0.58] | 250/371 (67.4) 1/11 (9.1) |

^aIndicates statistical significance (2-sided) at the 0.05 level.^bReference is '<'

Source: Post-text Table 4.1-s

Figure 3-5 Kaplan-Meier plot for rPFS above and below the optimal cutpoint in whole body SUVmean in the PFS-FAS analysis set

Source: Post-text Figure 4-1-1

3.3 Results of OS analysis (secondary objective)

3.3.1 Cox proportional hazards model

Univariate and multivariate Cox proportional hazards model were utilized to assess the association between PSMA PET parameters and OS. The HR, its 95% CI and p-value for each of the covariates in the univariate and initial multivariate analyses are provided in the appendix. In the final multivariate model for the whole body analysis, PSMA PET parameters that demonstrated statistically significant association with OS were listed in Table 3-5 and summarized below:

- Whole body SUVmean
- Whole body tumor load
- Absence of PSMA+ lesion in bone
- Absence of PSMA+ lesion in liver
- Absence of PSMA+ lesion in lymph node

Specifically, a 1-unit increase of whole body SUVmean was associated with a 12% decrease in the risk of OS event, a 1000-unit increase in tumor load was associated with a 4% increase in risk of death, and the absence of PSMA+ lesions in bone, liver and lymph node were associated with 62%, 51% and 26% decrease in the risk of death.

In the final multivariate model for individual anatomical regions, PSMA PET parameters that demonstrated statistically significant association with OS included ([Table 3-5](#)):

- Bone SUVmean
- Bone PSMA+ tumor volume
- Liver PSMA+ tumor volume
- Lymph node SUVmean
- Lymph node PSMA+ tumor volume
- Soft tissue SUVmax
- Soft tissue PSMA+ tumor volume

Notably, PSMA+ tumor volume in each individual anatomical region associated with OS in a statistically significant manner.

A 1-unit increase of bone and lymph node SUVmean was associated with a 11% and 7% decrease in risk of death respectively. A 1-unit increase of soft tissue SUVmax was associated with 1% decrease in risk of death. A 1000-cc increase in PSMA+ tumor volume in bone, liver, lymph node and soft tissue was associated with a 36%, 82%, 77% and 77% increase in the risk of death respectively.

Table 3-5 Hazard ratios and statistical significance of quantitative PSMA imaging parameters in final multivariate OS analysis

| Analysis set | Anatomical region | Parameter | HR | 95% CI | p-value |
|----------------|-------------------|-------------------------|------|--------------|---------|
| Whole body FAS | Whole body | SUVmean | 0.88 | [0.84, 0.91] | <0.001 |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | 1.04 | [1.03, 1.05] | <0.001 |
| | Bone | Absence of PSMA+ lesion | 0.38 | [0.22, 0.67] | <0.001 |
| | Liver | Absence of PSMA+ lesion | 0.49 | [0.37, 0.66] | <0.001 |
| | Lymph node | Absence of PSMA+ lesion | 0.74 | [0.58, 0.94] | 0.014 |
| | Soft tissue | Absence of PSMA+ lesion | n.s. | | |
| Bone FAS | Bone | SUVmean | 0.89 | [0.85, 0.93] | <0.001 |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | 1.36 | [1.23, 1.50] | <0.001 |
| | | Tumor load | n.s. | | |
| Liver FAS | Liver | SUVmean | n.s. | | |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | 1.82 | [1.24, 2.67] | 0.002 |
| | | Tumor load | n.s. | | |
| Lymph node FAS | Lymph node | SUVmean | 0.93 | [0.90, 0.96] | <0.001 |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | 1.77 | [1.20, 2.62] | 0.004 |

| Analysis set | Anatomical region | Parameter | HR | 95% CI | p-value |
|-----------------|-------------------|--------------------|------|--------------|---------|
| Soft tissue FAS | Soft tissue | Tumor load | n.s. | | |
| | | SUVmean | n.s. | | |
| | | SUVmax | 0.99 | [0.98, 1.00] | 0.008 |
| | | PSMA+ tumor volume | 1.77 | [1.19, 2.65] | 0.005 |
| | | Tumor load | n.s. | | |

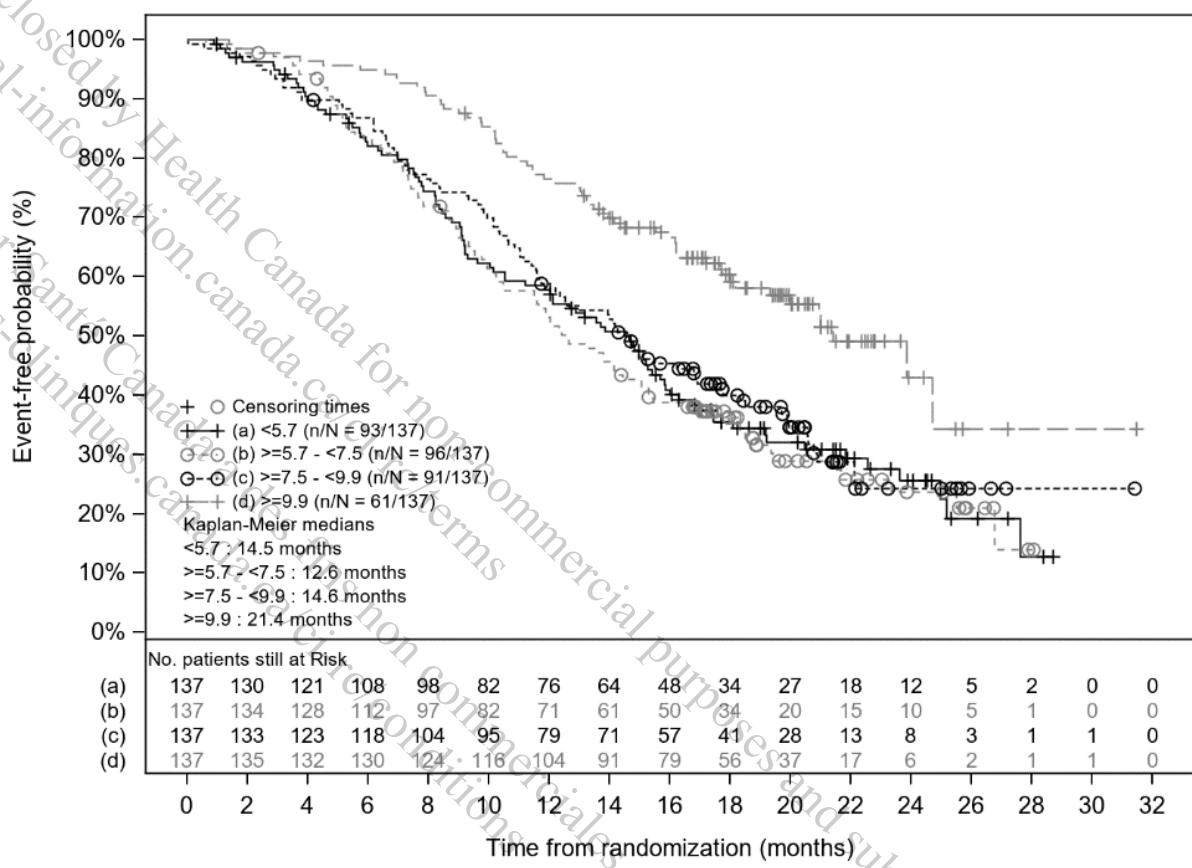
n.s. = not statistically significant

Source: [Post-text Table 6.1, Table 6.2, Table 6.3, Table 6.4, Table 6.5](#)

3.3.2 OS Kaplan-Meier analysis

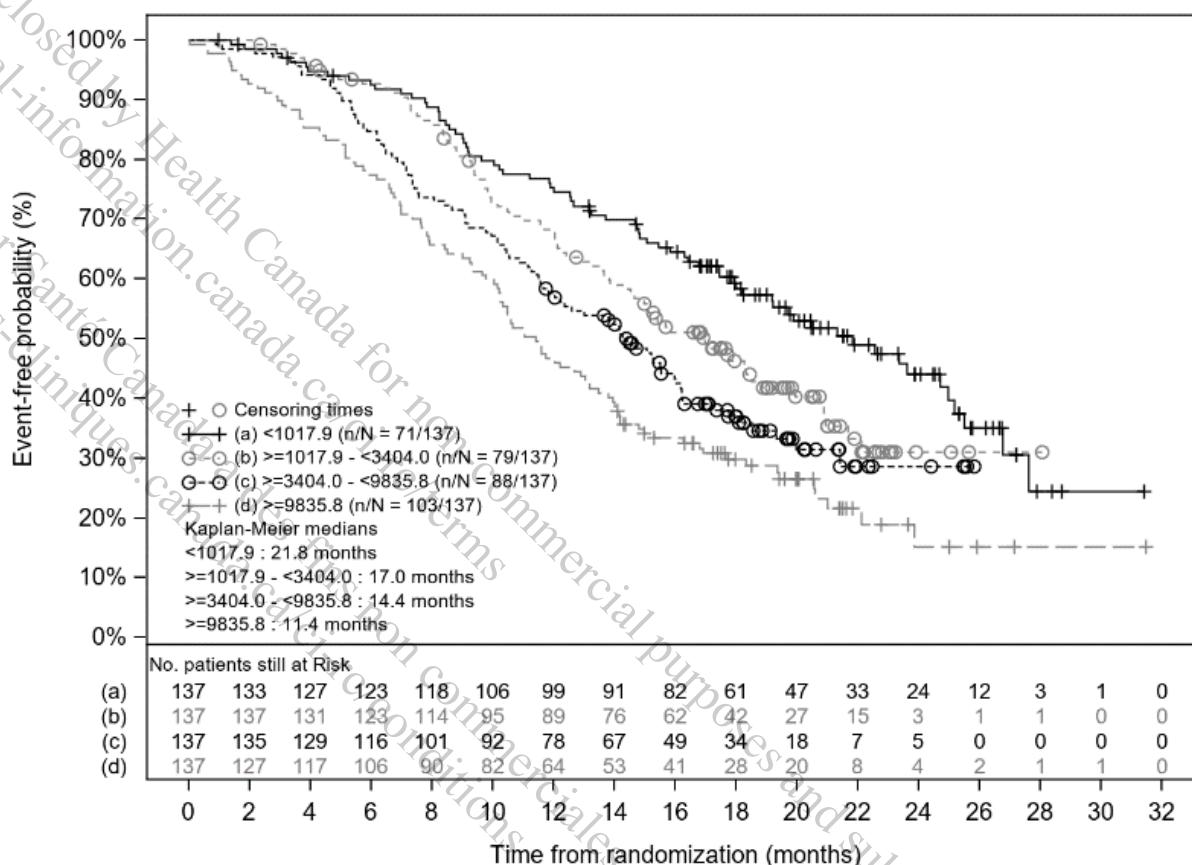
In order to have visual representation, KM curves of OS were plotted for different patient groups based on either the quartiles of the continuous PSMA PET parameter or the levels of the binary ones. The KM curves corresponding to the PSMA PET parameter that demonstrated a statistically significant association with OS in the whole body FAS analysis set are shown in [Figure 3-6](#) to [Figure 3-10](#).

In the whole body SUVmean analysis, patients in the highest quartile (≥ 9.9) had a median OS of 21.4 months, compared with 14.6 months in the second highest quartile ($\geq 7.5 - < 9.9$), 12.6 months in the third highest quartile ($\geq 5.7 - < 7.5$), and 14.5 months in the lowest quartile (< 5.7) ([Figure 3-6](#)).

Figure 3-6 Kaplan-Meier plot for OS by whole body SUVmean quartiles in the FAS analysis set

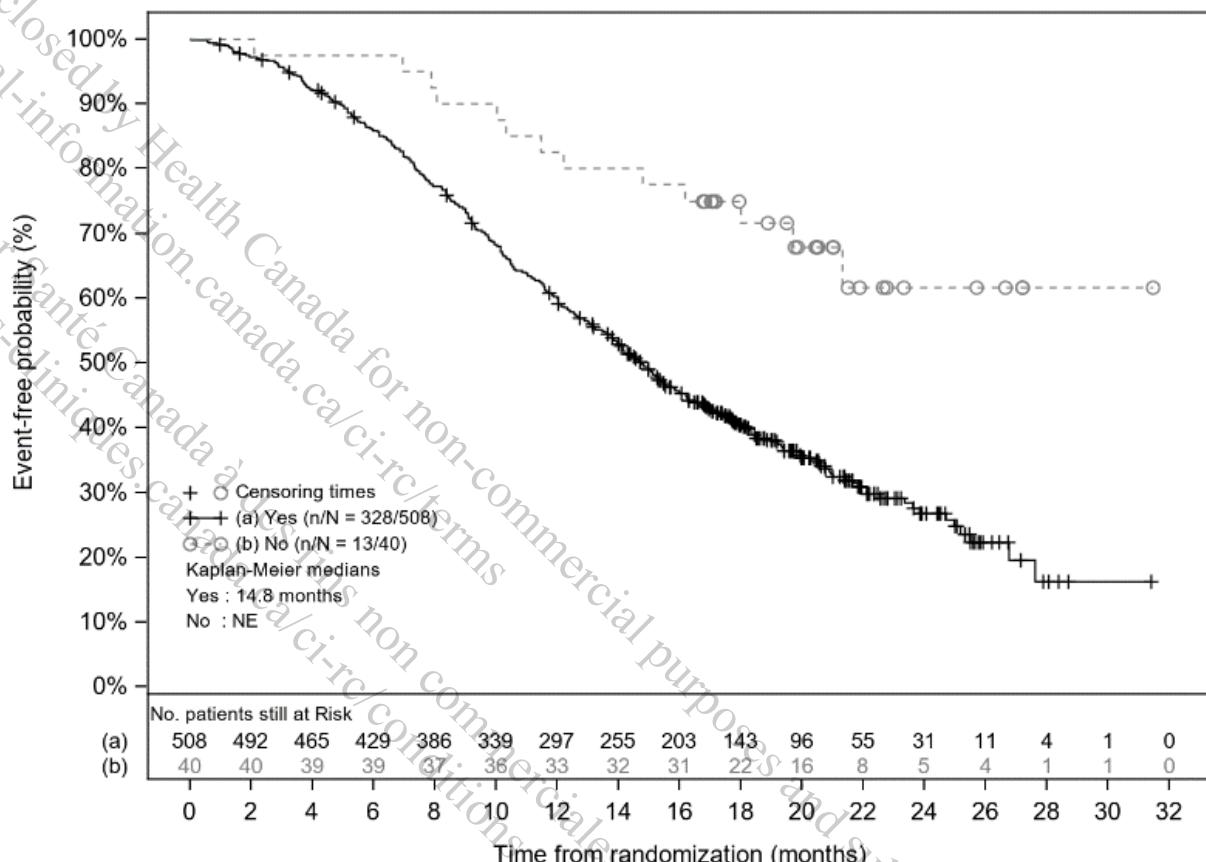
Source: Post-text Figure 5-1-1

In the whole body tumor load analysis, patients in the highest quartile (≥ 9835.8) had a median OS of 11.4 months, compared with 14.4 months in the second highest quartile ($\geq 3404.0 - < 9835.8$), 17.0 months in the third highest quartile ($\geq 1017.9 - < 3404.0$), and 21.8 months in the lowest quartile (< 1017.9) (Figure 3-7).

Figure 3-7 Kaplan-Meier plot for OS by whole body tumor load quartiles in the FAS analysis set

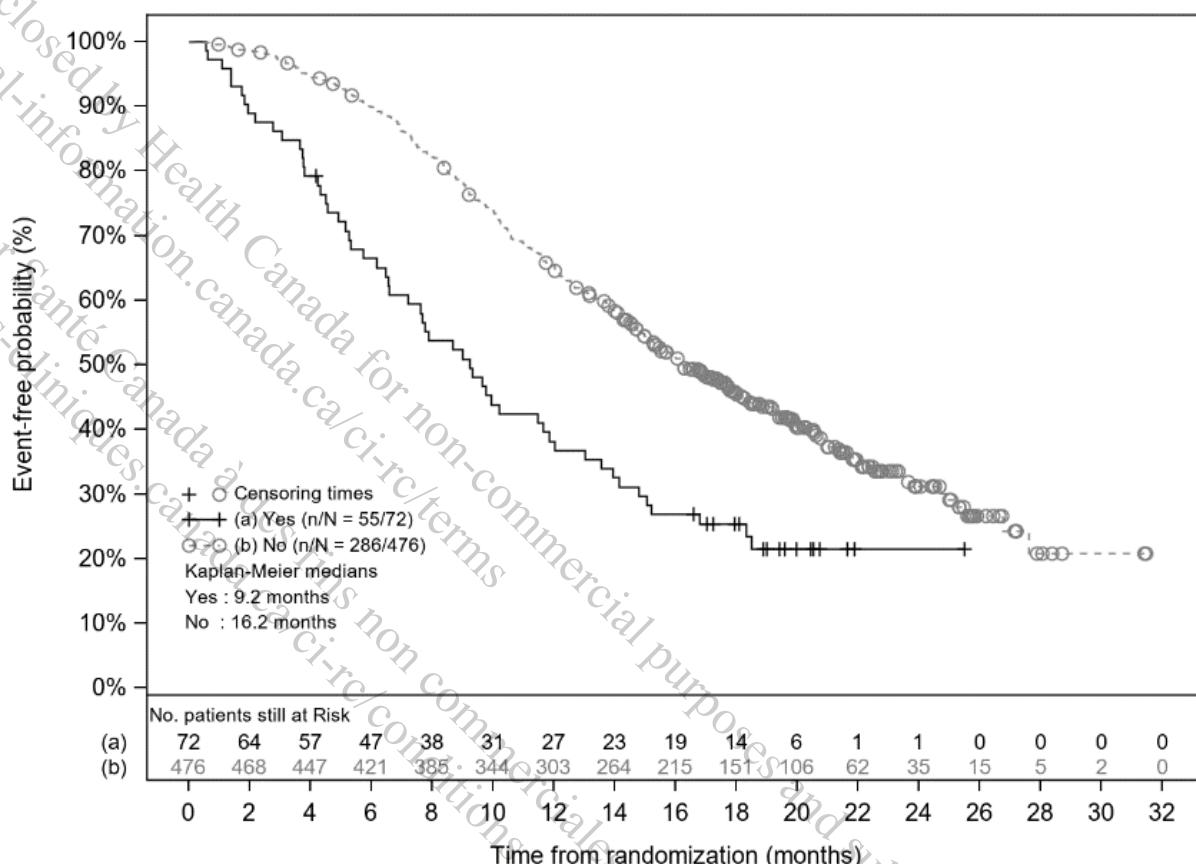
Source: Post-text Figure 5-1-4

In the presence of PSMA+ lesion in bone analysis, patients with PSMA+ bone lesions had a median OS of 14.8 months, whereas OS had not been reached in patients without PSMA+ bone lesions (Figure 3-8).

Figure 3-8 Kaplan-Meier plot for OS by presence of PSMA+ bone lesions in the FAS analysis set

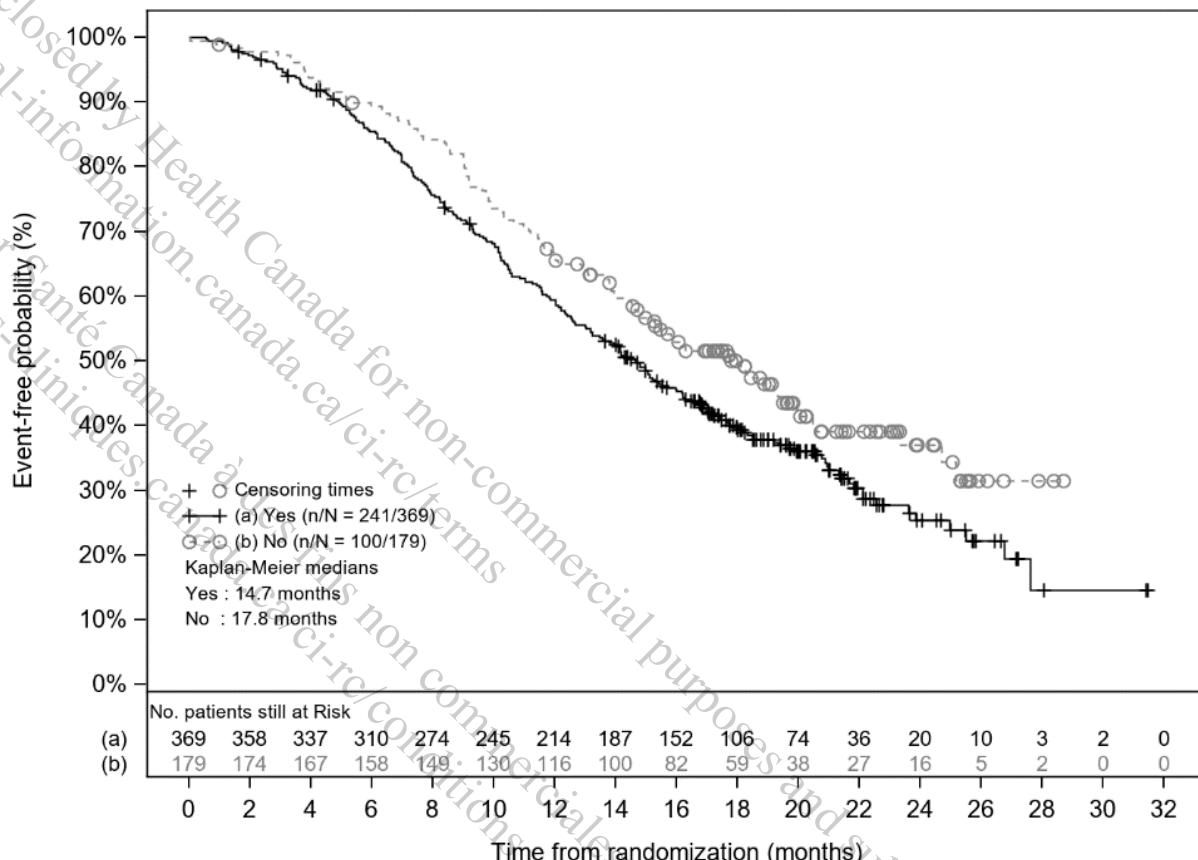
Source: Post-text Figure 5-1-5

In the presence of PSMA+ lesion in liver analysis, patients with PSMA+ liver lesions had a median OS of 9.2 months, compared with 16.2 months in patients without ([Figure 3-9](#)).

Figure 3-9 Kaplan-Meier plot for OS by presence of PSMA+ liver lesions in the FAS analysis set

Source: Post-text Figure 5-1-6

In the presence of PSMA+ lesion in lymph node analysis, patients with PSMA+ lymph node lesions had a median OS of 14.7 months, compared with 17.8 months in patients without (Figure 3-10).

Figure 3-10 Kaplan-Meier plot for OS by presence of PSMA+ lymph node lesions in the FAS analysis set

Source: Post-text Figure 5-1-7

3.3.3 Optimal cutpoint analysis for OS

An optimal cutpoint, a value that maximized the OS hazard ratio, was identified for each of the continuous imaging covariates that demonstrated statistically significant association with OS in the final multivariate Cox proportional hazard model, except for the PSMA+ tumor volume in lymph node and soft tissue because none of the candidate cutpoints were statistically significant. The HR, its 95% CI and p-value for each covariate in the multivariate model were re-calculated using the optimal cutpoint (Table 3-6). Kaplan-Meier analysis was also performed to compare OS between patients above and below the optimal cutpoint for each covariate.

Table 3-6 Hazard ratios and statistical significance of PSMA PET parameters in multivariate OS analysis using optimal cutpoints for each imaging covariate

| Analysis set | Anatomic region | Parameter | Optimized cutpoint | HR | 95% CI | p-value |
|----------------|-----------------|---------------------------------|--------------------|------|--------------|---------|
| Whole body FAS | Whole body | SUVmean | <18 vs ≥18 | 0.06 | [0.01, 0.43] | 0.005 |
| | | Tumor load | <200 vs ≥200 | 1.75 | [1.07, 2.84] | 0.025 |
| | Bone | PSMA+ tumor No/Yes ^a | Yes vs No | 0.36 | [0.20, 0.63] | <0.001 |
| | Liver | PSMA+ tumor No/Yes ^a | Yes vs No | 0.48 | [0.36, 0.64] | <0.001 |

| Analysis set | Anatomic region | Parameter | Optimized cutpoint | HR | 95% CI | p-value |
|-----------------|-----------------|---------------------------------|--------------------|------|---------------------|---------|
| Bone FAS | Lymph node | PSMA+ tumor No/Yes ^a | Yes vs No | 0.75 | [0.59, 0.95] | 0.018 |
| | | SUVmean | <18 vs ≥18 | 0.11 | [0.02, 0.77] | 0.027 |
| Liver FAS | Liver | PSMA+ tumor volume (cc) | <3000 vs ≥3000 | 2.01 | [1.18, 3.44] | 0.011 |
| | | PSMA+ tumor volume (cc) | <200 vs ≥200 | 2.13 | [1.17, 3.88] | 0.013 |
| Lymph node FAS | Lymph node | SUVmean | <20 vs ≥20 | 0.08 | [0.01, 0.59] | 0.013 |
| | | PSMA+ tumor volume (cc) | | | No optimal cutpoint | |
| Soft tissue FAS | Soft tissue | SUVmax | <59 vs ≥59 | 0.27 | [0.09, 0.85] | 0.026 |
| | | PSMA+ tumor volume (cc) | | | No optimal cutpoint | |

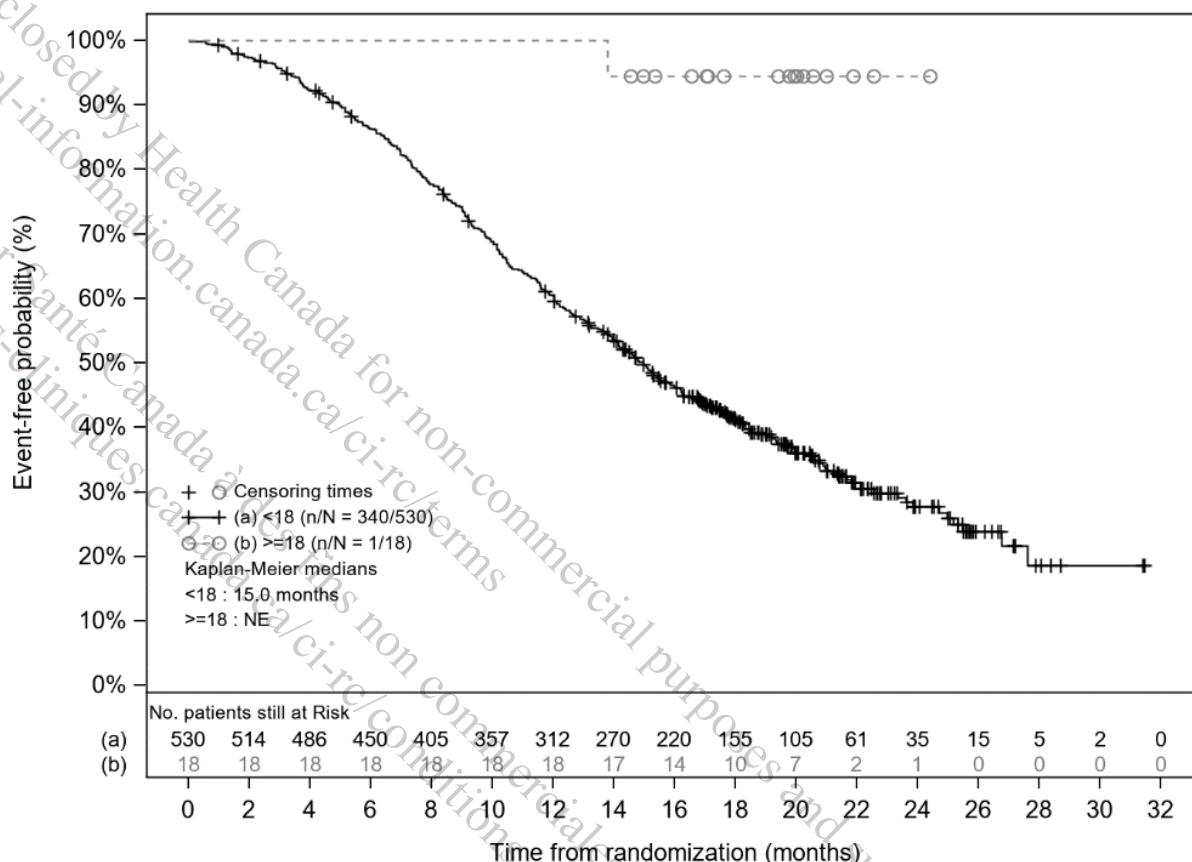
^aReference is 'Yes'^bReference is '<'Source: [Post-text Table 7.1, Table 7.2, Table 7.3, Table 7.4, Table 7.5](#)

Notably, in the whole body SUVmean analysis, while 18 was identified as the cutpoint associated with the lowest hazard ratio of 0.06, all the other cutpoints tested at <18 resulted in a statistically significant association with OS ([Table 3-7](#)). In addition, patients above the optimal cutpoint (≥18) had not yet reached median OS at the time of this analysis, compared with 15.0 months OS in patients below the cutpoint (<18) ([Figure 3-11](#)). Nonetheless, it should be noted only 1 OS event was observed among the 18 patients above the optimal cutpoint.

Table 3-7 Whole body SUVmean OS cutpoint analysis

| Predictor variables | Cut point ^b | p-value | Hazard ratio | # of events / # of patients (%) | | |
|--|------------------------|---------------------|--------------|---------------------------------|----------------|----------------|
| | | | | <cut point | ≥cut point | |
| SUVmean -Optimal cutpoint | <18 | 0.005 ^a | 0.06 | [0.01, 0.42] | 340/530 (64.2) | 1/18 (5.6) |
| SUVmean - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <7 | 0.002 ^a | 0.71 | [0.57, 0.88] | 167/241 (69.3) | 174/307 (56.7) |
| | <8 | <0.001 ^a | 0.65 | [0.52, 0.81] | 212/308 (68.8) | 129/240 (53.8) |
| | <9 | <0.001 ^a | 0.56 | [0.44, 0.71] | 253/367 (68.9) | 88/181 (48.6) |
| | <10 | <0.001 ^a | 0.50 | [0.38, 0.66] | 282/413 (68.3) | 59/135 (43.7) |
| | <11 | <0.001 ^a | 0.48 | [0.35, 0.67] | 300/447 (67.1) | 41/101 (40.6) |
| | <12 | <0.001 ^a | 0.42 | [0.29, 0.61] | 312/468 (66.7) | 29/80 (36.3) |
| | <13 | <0.001 ^a | 0.33 | [0.20, 0.54] | 324/490 (66.1) | 17/58 (29.3) |
| | <14 | <0.001 ^a | 0.21 | [0.10, 0.44] | 334/509 (65.6) | 7/39 (17.9) |
| | <15 | <0.001 ^a | 0.26 | [0.12, 0.55] | 334/515 (64.9) | 7/33 (21.2) |
| | <16 | <0.001 ^a | 0.13 | [0.04, 0.40] | 338/522 (64.8) | 3/26 (11.5) |
| | <17 | <0.001 ^a | 0.10 | [0.02, 0.39] | 339/526 (64.4) | 2/22 (9.1) |
| | <18 | 0.005 ^a | 0.06 | [0.01, 0.42] | 340/530 (64.2) | 1/18 (5.6) |

^aIndicates statistical significance (2-sided) at the 0.05 level.^bReference is '<'Source: [Post-text Table 7.1-s](#)

Figure 3-11 Kaplan-Meier plot for OS above and below the optimal cutpoint in whole body SUVmean in the FAS analysis set

Source: Post-text Figure 7-1-1

3.4 Results of ORR analysis (secondary objective analysis)

3.4.1 Logistic regression model

Univariate and multiple logistic regression models were utilized to assess the association between quantitative PSMA imaging parameters and ORR. The Odds Ratio (OR), its 95% CI and p-value of all univariate and initial multivariate analyses are provided in the appendix.

In the final multivariate model for the whole body analysis, imaging parameters that demonstrated statistically significant association with ORR were listed in Table 3-8 and summarized below:

- Whole body SUVmean
- Whole body SUVmax
- Absence of PSMA+ lesion in bone
- Absence of PSMA+ lesion in liver
- Absence of PSMA+ lesion in lymph node

A 1-unit increase of whole body SUVmean and SUVmax was associated with a 43% increase and 2% decrease in the odds of objective response respectively, and the absence of PSMA+

lesions in bone, liver and lymph node were associated with a 206% increase, 155% increase and 90% decrease of the odds of objective response respectively.

In the final multivariate model for individual anatomical regions, imaging parameters that demonstrated statistically significant association with ORR included ([Table 3-8](#)):

- Lymph node SUVmean
- Lymph node PSMA+ tumor volume
- Soft tissue SUVmax

A 1-unit increase of lymph node SUVmean and soft tissue SUVmax was associated with a 21% and 2% increase in the odds of objective response respectively, and 1000 cc increase in lymph node PSMA+ tumor volume was associated with a 626% increase of the odds of objective response.

Table 3-8 Odds ratios and statistical significance of quantitative PSMA imaging parameters in final multivariate ORR analysis

| Analysis set | Anatomical region | Parameter | OR | 95% CI | p-value |
|-----------------|-------------------|-------------------------|------|---------------|---------|
| Whole body FAS | Whole body | SUVmean | 1.43 | [1.24, 1.65] | <0.001 |
| | | SUVmax | 0.98 | [0.96, 0.99] | 0.009 |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | n.s. | | |
| | Bone | Absence of PSMA+ lesion | 3.06 | [1.12, 8.38] | 0.03 |
| | Liver | Absence of PSMA+ lesion | 2.55 | [1.02, 6.34] | 0.045 |
| | Lymph node | Absence of PSMA+ lesion | 0.1 | [0.04, 0.25] | <0.001 |
| | Soft tissue | Absence of PSMA+ lesion | n.s. | | |
| Bone FAS | Bone | SUVmean | n.s. | | |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | n.s. | | |
| Liver FAS | Liver | SUVmean | n.s. | | |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | n.s. | | |
| Lymph node FAS | Lymph node | SUVmean | 1.21 | [1.12, 1.31] | <0.001 |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | 7.26 | [1.45, 36.46] | 0.016 |
| | | Tumor load | n.s. | | |
| Soft tissue FAS | Soft tissue | SUVmean | n.s. | | |
| | | SUVmax | 1.02 | [1.00, 1.04] | 0.029 |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | n.s. | | |

n.s. = not statistically significant

Source: [Post-text Table 9.1](#), [Table 9.2](#), [Table 9.3](#), [Table 9.4](#), [Table 9.5](#)

3.5 Results of PSA response analysis (secondary objective)

3.5.1 Logistic regression model

Univariate and multiple logistic regression models were utilized to assess the association between quantitative PSMA imaging parameters and PSA response. The OR, its 95% CI and p-value of all univariate and initial multivariate analyses are provided in the appendix.

In the final multivariate model for the whole body analysis, imaging parameters that demonstrated statistically significant association with PSA response were listed in [Table 3-9](#) and summarized below:

- Whole body SUVmean
- Absence of PSMA+ lesion in liver

A 1-unit increase of whole body SUVmean was associated with a 34% increase in the odds of PSA response, and the absence of PSMA+ lesions in liver was associated with a 142% increase in the odds of PSA response.

In the final multivariate model for individual anatomical regions, imaging parameters that demonstrated statistically significant association with PSA response included ([Table 3-9](#)):

- Bone SUVmean
- Lymph node SUVmean
- Soft tissue SUVmax

A 1-unit increase of bone SUVmean, lymph node SUVmean and soft tissue SUVmax was associated with a 32%, 17% and 2% increase in the odds of PSA response respectively.

Table 3-9 Hazard ratios and statistical significance of quantitative PSMA imaging parameters in final multivariate PSA response analysis

| Analysis set | Anatomical region | Parameter | HR | 95% CI | p-value |
|----------------|-------------------|-------------------------|------|--------------|---------|
| Whole body FAS | Whole body | SUVmean | 1.34 | [1.23, 1.45] | <0.001 |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | n.s. | | |
| | Bone | Absence of PSMA+ lesion | n.s. | | |
| | | Absence of PSMA+ lesion | 2.42 | [1.21, 4.86] | 0.013 |
| | Lymph node | Absence of PSMA+ lesion | n.s. | | |
| | Soft tissue | Absence of PSMA+ lesion | n.s. | | |
| Bone FAS | Bone | SUVmean | 1.32 | [1.21, 1.45] | <0.001 |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | n.s. | | |
| Liver FAS | Liver | SUVmean | n.s. | | |
| | | SUVmax | n.s. | | |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | n.s. | | |
| Lymph node FAS | Lymph node | SUVmean | 1.17 | [1.09, 1.24] | <0.001 |
| | | SUVmax | n.s. | | |

| Analysis set | Anatomical region | Parameter | HR | 95% CI | p-value |
|-----------------|-------------------|--------------------|------|--------------|---------|
| Soft tissue FAS | Soft tissue | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | n.s. | | |
| Soft tissue FAS | Soft tissue | SUVmean | n.s. | | |
| | | SUVmax | 1.02 | [1.00, 1.04] | 0.043 |
| | | PSMA+ tumor volume | n.s. | | |
| | | Tumor load | n.s. | | |

n.s. = not statistically significant

Source: Post-text Table 11.1, Table 11.2, Table 11.3, Table 11.4, Table 11.5

4 Discussion and Conclusion

In this study, we demonstrated an association between a subset of PSMA PET parameters extracted from pre-treatment [⁶⁸Ga]Ga-PSMA-11 PET/CT scans and clinical outcomes in the VISION study patients who received [¹⁷⁷Lu]Lu-PSMA-617 treatment in combination with standard of care.

The PSMA PET parameters assessed in this study included the presence or absence of PSMA+ lesion, SUVmean, SUVmax, PSMA+ tumor volume, and tumor load defined as the product of PSMA+ tumor volume and SUVmean. The pre-specified anatomical regions from which PSMA PET parameters were extracted included bone, liver, lymph node, soft tissue, and the whole body defined as the combination of all anatomical regions assessed. The clinical outcome parameters assessed included rPFS in the primary objective, as well as OS, ORR and PSA response in the secondary objective.

Consistent with the fact that prostate cancer metastasizes with avidity to bone (Logothetis et al 2018, La Manna et al 2019), among all the anatomical regions assessed, the presence of PSMA+ lesion was most frequently observed in bone. More than 90% of the mCRPC patients in this quantitative analysis demonstrated positive PSMA uptake in bone. In contrast, PSMA+ lesions were least frequently observed in liver and found in only ~13% of patients. The SUVmean values observed were consistent across all anatomical regions in all three analysis sets, indicating similar level of PSMA expression independent of the location of the lesion. The mean SUVmean values ranged from 7.3-7.7 in bone to 8.8-9.5 in lymph node. The mean SUVmax values ranged from 19.6-21.3 in liver to 35.2-38.1 in bone. Both PSMA+ tumor volume and tumor load values ranged from ~80 cc and ~1000 respectively in soft tissue to ~700 cc and ~5000 respectively in bone.

The association between each quantitative imaging parameter in each anatomical region and each clinical outcome parameter was assessed. The imaging parameters that demonstrated statistically significant association with clinical outcome are summarized in Table 4-1. Notably, increased baseline SUVmean and SUVmax were strongly associated with decreased risks in rPFS and OS, as well as increased odds of ORR and PSA response. While SUVmean and SUVmax both measure the level of [⁶⁸Ga]Ga-PSMA-11 uptake in the lesions, SUVmean appears to be a better predictor of clinical response than SUVmax, as the former demonstrated statistically significant associations with more clinical outcome parameters. This observation is consistent with the mechanism of action of [¹⁷⁷Lu]Lu-PSMA-617. Increased SUVmean indicates on average an increased expression of PSMA molecules on the cancer cells, which may lead to increased binding of [¹⁷⁷Lu]Lu-PSMA-617 to the tumor and thus enhanced efficacy.

In contrast, SUVmax measures the highest uptake found in one single voxel within an anatomical region, which is more susceptible to higher variability and influence by outlier measurements, thus making it a less reliable predictor of outcome.

Increased baseline PSMA+ tumor volume and tumor load seem to associate with worse clinical outcomes. Interestingly, while an increase in these parameters demonstrated statistically significant associations with increased risks of rPFS and OS, they associated with ORR minimally and not at all with PSA response. Between these two parameters, PSMA+ tumor volume appears to be a better predictor of outcome as it demonstrated statistically significant associations with more clinical parameters than tumor load. In particular, increased PSMA+ tumor volume in all individual anatomical regions, including bone, liver, lymph node and soft tissue, demonstrated statistically significant association with worse OS. This is consistent with the notion that patients with more severe disease tend to achieve less desirable clinical responses. Moreover, absence of PSMA+ lesions in liver, bone and lymph node was associated with improved outcome. This is also consistent with the known prognostic impact of metastatic occurrence in prostate cancer ([La Manna et al 2019](#)).

Table 4-1 Summary table of association between quantitative imaging parameters and clinical outcome

| Anatomic region | Parameter | rPFS | OS | ORR | PSA |
|-----------------|--|------|----|-----|-----|
| Whole body | SUVmean | S+ | S+ | S+ | S+ |
| | SUVmax | | S- | | |
| | Total PSMA+ tumor volume | | | | |
| | Tumor load | S- | S- | | |
| | Absence of PSMA+ lesion in bone | S+ | S+ | S+ | |
| | Absence of PSMA+ lesion in liver | S+ | S+ | S+ | S+ |
| | Absence of PSMA+ lesion in lymph node | S+ | S- | | |
| Bone | Absence of PSMA+ lesion in soft tissue | S+ | | | |
| | SUVmean | S+ | S+ | | S+ |
| | SUVmax | | | | |
| | PSMA+ tumor volume | | S- | | |
| Liver | Tumor load | S- | | | |
| | SUVmean | | | | |
| | SUVmax | | | | |
| | PSMA+ tumor volume | S- | S- | | |
| Lymph node | Tumor load | | | | |
| | SUVmean | | S+ | S+ | S+ |
| | SUVmax | S+ | | | |
| | PSMA+ tumor volume | | S- | S+ | |
| Soft tissue | Tumor load | | | | |
| | SUVmean | | | | |
| | SUVmax | S+ | S+ | S+ | S+ |
| | PSMA+ tumor volume | | S- | | |
| | Tumor load | | | | |

S+ = statistically significant association with improved clinical outcome

S- = statistically significant association with worse clinical outcome

Blank = no statistical significant association observed

Source: Post-text Table 3.1, Table 3.2, Table 3.3, Table 3.4, Table 3.5, Table 6.1, Table 6.2, Table 6.3, Table 6.4, Table 6.5, Table 9.1, Table 9.2, Table 9.3, Table 9.4, Table 9.5, Table 11.1, Table 11.2, Table 11.3, Table 11.4, Table 11.5

Among all the PSMA PET parameters, three of the parameters were found to be consistently associated with all clinical outcome parameters assessed in this study, including whole body SUVmean, lack of PSMA+ lesion in liver, and soft tissue SUVmax. In addition, lack of PSMA+ lesion in bone was associated with rPFS, OS and ORR, though not PSA response. Increased whole body SUVmean consistently associated with improved clinical outcome, whereby a 1-unit increase was associated with a 14% and 12% decrease in the risk of rPFS event and OS event respectively, as well as a 1.43 and 1.34 times higher odds of objective response and PSA response respectively. Patients in the highest quartile of whole body SUVmean had a median rPFS of 14.1 and median OS of 21.4 months, compared to rPFS of 5.8 months and OS of 14.5 months in patients in the lowest quartile. Nonetheless, patients in the lowest quartile of whole body SUVmean still demonstrated improved median rPFS (5.8 months vs 3.4 months) and median OS (14.5 months vs 11.3 months) compared to patients who received standard of care only in the control arm of the VISION study ([Study PSMA-617-01], Sartor et al 2021), though additional analysis is required to understand whether SUVmean is associated with rPFS and OS in the control arm (Table 4-2). In addition, increased SUVmean in bone was associated with improved rPFS, OS and PSA response, whereas increased SUVmean in lymph node was associated with improved OS, ORR and PSA response.

Table 4-2 Comparison of median rPFS and OS in patients with different PSMA PET parameters and VISION control arm

| Patient population ^{a,b} | Median rPFS (months) | Median OS (months) |
|---|----------------------|--------------------|
| Highest quartile of SUVmean in treatment arm | 14.1 | 21.4 |
| Lowest quartile of SUVmean in treatment arm | 5.8 | 14.5 |
| Absence of PSMA+ lesions in liver in treatment arm | 9.0 | 16.2 |
| Presence of PSMA+ lesions in liver in treatment arm | 4.4 | 9.2 |
| Absence of PSMA+ lesions in bone in treatment arm | 11.5 | Not reached |
| Presence of PSMA+ lesions in bone in treatment arm | 8.7 | 14.8 |
| VISION control arm (BSC/BSoC only) | 3.4 | 11.3 |

^aTreatment arm = [¹⁷⁷Lu]Lu-PSMA-61 +BSC/BSoC

^bControl arm = BSC/BSoC only

Source: Post-text Figure 2-1-1, Figure 2-1-5, Figure 2-1-6, Figure 5-1-1, Figure 5-1-5, Figure 5-1-6, [Study PSMA-617-01]

For PSMA+ liver, the absence of PSMA+ lesions in liver was associated with a 52% and 51% decrease in the risk of rPFS event and death (OS event), as well as a 2.55 and 2.42 times higher odds of objective response and PSA response. The median rPFS and OS for patients without PSMA+ lesions in liver was 9.0 months and 16.2 months, compared to 4.4 months and 9.2 months for patients with PSMA+ lesions in liver. Patients with PSMA+ lesions in liver demonstrated improved median rPFS compared to patients in control arm of the VISION study (4.4 months vs 3.4 months) but not median OS (9.2 months vs 11.3 months) (Table 4-2, [Study PSMA-617-01], Sartor et al 2021). Nonetheless, it should be noted that due to the low prevalence of PSMA+ lesions in liver, the number of patients included in the rPFS and OS analysis in this study was only 51 and 72 respectively.

For PSMA+ bone, the absence of PSMA+ lesions in bone was associated with a 55% and 62% decrease in the risk of rPFS event and OS event, as well as a 3.06 times higher odds of objective response. The median rPFS for patients without PSMA+ lesion in bone was 11.5 months and OS had not been reached, compared to 8.7 months and 14.8 months for patients with PSMA+ lesions in bone. Despite being associated with less pronounced clinical benefits, patients with PSMA+ lesions in bone still demonstrated improved median rPFS (8.7 months vs 3.4 months) and median OS (14.8 months vs 11.3 months) compared to patients who received standard of care only in control arm of the VISION study ([Table 4-2, \[Study PSMA-617-01\], Sartor et al 2021](#)).

For soft tissue SUVmax, a 1-unit increase was associated with a 2% and 1% decrease in the risk of rPFS event and OS event respectively, as well as a 1.02 and 1.02 times higher odds of objective response and PSA response respectively. Given its small impact on clinical benefits, the predictive biomarker utility of soft tissue SUVmax was not further explored.

Taken together, these results indicated that among mCRPC patients who have confirmed tumor PSMA expression by [⁶⁸Ga]Ga-PSMA-11 PET/CT scan using VISION read criteria, those with increased SUVmean, absence of PSMA+ lesions in liver and bone, and smaller PSMA+ tumor volume were most likely to be associated with maximized clinical benefits in [¹⁷⁷Lu]Lu-PSMA-617 plus standard of care treatment. In particular, increased SUVmean appears to be the best predictor of improved clinical treatment outcomes in a manner that is consistent with the mechanism of action of [¹⁷⁷Lu]Lu-PSMA-617. Nonetheless, among these patients, even those in the less desirable categories of PSMA PET parameters still demonstrated improved clinical outcomes compared to patients who received standard of care alone in VISION. This demonstrates the importance of selecting for patients with positive PSMA expression based on [⁶⁸Ga]Ga-PSMA-11 PET/CT scan using the VISION read criteria in increasing the likelihood of beneficial therapeutic effects of [¹⁷⁷Lu]Lu-PSMA-617 plus standard of care treatment. While we did not assess how these PSMA PET parameters associated with clinical outcome in the control arm of the VISION study, high radiographic PSMA expression on SPECT or PET/CT had been associated with poor prognosis in mCRPC patients treated with standard systemic therapies ([Vlachostergios et al 2021](#)). Thus, it is possible that the association between high SUVmean and maximized treatment benefits is specific to [¹⁷⁷Lu]Lu-PSMA-617 treatment. These quantitative analysis results provide evidence to support the indication of the [⁶⁸Ga]Ga-PSMA-11 PET/CT scan for patient selection to a PSMA-targeted radioligand therapy such as [¹⁷⁷Lu]Lu-PSMA-617.

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6 Post-text tables and figures

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Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.1: Analysis sets (All subjects)

| | Lu-PSMA-617 +BSC/BSoC (N=551) n (%) |
|--|--|
| Body-Full Analysis Set (Body-FAS) | 548 (99.5) |
| Body-PFS Full Analysis Set (Body-PFS-FAS) | 382 (69.3) |
| Body-Response Evaluable Analysis Set (Body-REAS) | 317 (57.5) |
| Bone-Full Analysis Set (Bone-FAS) | 508 (92.2) |
| Bone-PFS Full Analysis Set (Bone-PFS-FAS) | 353 (64.1) |
| Bone-Response Evaluable Analysis Set (Bone-REAS) | 291 (52.8) |
| Liver-Full Analysis Set (Liver-FAS) | 72 (13.1) |
| Liver-PFS Full Analysis Set (Liver-PFS-FAS) | 51 (9.3) |
| Liver-Response Evaluable Analysis Set (Liver-REAS) | 44 (8.0) |
| Lymph Node-Full Analysis Set (Lymph Node-FAS) | 369 (67.0) |
| Lymph Node-PFS Full Analysis Set (Lymph Node-PFS-FAS) | 258 (46.8) |
| Lymph Node-Response Evaluable Analysis Set (Lymph Node-REAS) | 220 (39.9) |
| Soft Tissue-Full Analysis Set (Soft Tissue-FAS) | 233 (42.3) |
| Soft Tissue-PFS Full Analysis Set (Soft Tissue-PFS-FAS) | 173 (31.4) |
| Soft Tissue-Response Evaluable Analysis Set (Soft Tissue-REAS) | 148 (26.9) |

N is the number of patients who have good quality images available for the quantitative analysis in Lu-PSMA-617+BSC/BSoC arm of VISION

For each anatomical region,

- FAS includes all patients randomized to Lu-PSMA-617+BSC/BSoC arm who have good quality images available for the quantitative analysis, and with PSMA+ lesion in the respective anatomical region.
- PFS-FAS includes all patients randomized to Lu-PSMA-617+BSC/BSoC arm on or after 5 March 2019 who have good quality images available for the quantitative analysis, and with PSMA+ lesion in the respective anatomical region.
- REAS includes the subset of patients in the PFS-FAS (for that anatomical region) with evaluable disease by RECIST at baseline (i.e. at least one target and/or non-target lesion per central review) with PSMA+ lesion in the respective anatomical region.

Output ID: T-1-1 2021-08-30 10:25

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Source data: adsl.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.2: Descriptive statistics for each covariate in each anatomical region by rPFS event (Body-PFS Full Analysis Set)

| | Subjects with rPFS event (N=251) | Subjects without rPFS event (N=131) | All subjects (N=382) |
|---|-------------------------------------|--|-------------------------|
| Whole Body | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 251 (100) 0 | 131 (100) 0 | 382 (100) 0 |
| No | | | |
| SUVmean (g/ml) | | | |
| n | 251 | 131 | 382 |
| Mean | 8.1 | 10.1 | 8.8 |
| SD | 3.00 | 6.05 | 4.40 |
| Median | 7.7 | 8.1 | 7.8 |
| Min-Max | 3-25 | 4-38 | 3-38 |
| Q1-Q3 | 5.9-9.7 | 6.2-11.7 | 6.0-10.2 |
| SUVmax (g/ml) | | | |
| n | 251 | 131 | 382 |
| Mean | 40.4 | 51.6 | 44.2 |
| SD | 24.48 | 45.46 | 33.57 |
| Median | 34.3 | 39.7 | 37.2 |
| Min-Max | 7-155 | 6-317 | 6-317 |
| Q1-Q3 | 22.3-53.3 | 23.2-58.3 | 22.5-55.1 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 251 | 131 | 382 |
| Mean | 970.1 | 676.3 | 869.3 |
| SD | 991.14 | 873.41 | 961.44 |
| Median | 630.7 | 325.5 | 496.8 |
| Min-Max | 14-4884 | 2-4105 | 2-4884 |
| Q1-Q3 | 257.6-1379.3 | 97.1-692.0 | 191.6-1271.0 |
| Tumor Load (g) | | | |
| n | 251 | 131 | 382 |
| Mean | 8138.6 | 6193.2 | 7471.5 |
| SD | 8932.38 | 8507.57 | 8826.39 |
| Median | 5149.2 | 3165.4 | 4073.8 |
| Min-Max | 42-54176 | 8-47780 | 8-54176 |
| Q1-Q3 | 1698.3-11620.9 | 1031.7-6775.9 | 1582.9-10279.2 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-2 2021-08-30 10:26

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.2: Descriptive statistics for each covariate in each anatomical region by rPFS event (Body-PFS Full Analysis Set)

| | Subjects with rPFS event (N=251) | Subjects without rPFS event (N=131) | All subjects (N=382) |
|---|-------------------------------------|--|-------------------------|
| Bone | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 236 (94.0) | 117 (89.3) | 353 (92.4) |
| No | 15 (6.0) | 14 (10.7) | 29 (7.6) |
| SUVmean (g/ml) | | | |
| n | 236 | 117 | 353 |
| Mean | 7.1 | 8.5 | 7.6 |
| SD | 2.71 | 5.95 | 4.12 |
| Median | 6.7 | 7.1 | 6.8 |
| Min-Max | 2-18 | 3-53 | 2-53 |
| Q1-Q3 | 5.3-8.5 | 5.3-9.5 | 5.3-8.7 |
| SUVmax (g/ml) | | | |
| n | 236 | 117 | 353 |
| Mean | 35.3 | 43.5 | 38.0 |
| SD | 24.77 | 43.09 | 32.20 |
| Median | 29.1 | 33.3 | 30.1 |
| Min-Max | 2-155 | 4-317 | 2-317 |
| Q1-Q3 | 17.3-47.4 | 18.9-51.0 | 17.7-48.2 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 236 | 117 | 353 |
| Mean | 800.7 | 612.1 | 738.2 |
| SD | 916.33 | 858.98 | 900.90 |
| Median | 447.2 | 248.2 | 379.7 |
| Min-Max | 0-4440 | 1-4096 | 0-4440 |
| Q1-Q3 | 99.5-1181.4 | 68.5-692.0 | 88.1-1076.7 |
| Tumor Load (g) | | | |
| n | 236 | 117 | 353 |
| Mean | 6177.4 | 4663.6 | 5675.7 |
| SD | 7515.81 | 6258.17 | 7150.35 |
| Median | 3037.8 | 2238.9 | 2812.5 |
| Min-Max | 0-35032 | 4-32412 | 0-35032 |
| Q1-Q3 | 694.7-8461.2 | 480.7-6328.7 | 620.5-7921.3 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-2 2021-08-30 10:26

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.2: Descriptive statistics for each covariate in each anatomical region by rPFS event (Body-PFS Full Analysis Set)

| | Subjects with rPFS event (N=251) | Subjects without rPFS event (N=131) | All subjects (N=382) |
|---|-------------------------------------|--|-------------------------|
| Liver | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 43 (17.1) | 8 (6.1) | 51 (13.4) |
| No | 208 (82.9) | 123 (93.9) | 331 (86.6) |
| SUVmean (g/ml) | | | |
| n | 43 | 8 | 51 |
| Mean | 8.9 | 7.2 | 8.6 |
| SD | 4.57 | 2.37 | 4.33 |
| Median | 8.6 | 7.3 | 8.3 |
| Min-Max | 2-33 | 3-11 | 2-33 |
| Q1-Q3 | 6.3-10.4 | 5.7-8.8 | 6.2-10.3 |
| SUVmax (g/ml) | | | |
| n | 43 | 8 | 51 |
| Mean | 22.1 | 10.9 | 20.4 |
| SD | 14.94 | 4.27 | 14.38 |
| Median | 19.8 | 10.1 | 18.3 |
| Min-Max | 2-73 | 5-18 | 2-73 |
| Q1-Q3 | 9.9-28.8 | 8.6-13.2 | 9.8-28.2 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 43 | 8 | 51 |
| Mean | 404.5 | 13.3 | 343.2 |
| SD | 755.96 | 12.86 | 707.61 |
| Median | 74.2 | 9.7 | 45.2 |
| Min-Max | 1-3761 | 1-40 | 1-3761 |
| Q1-Q3 | 11.1-432.6 | 3.7-19.4 | 8.2-270.8 |
| Tumor Load (g) | | | |
| n | 43 | 8 | 51 |
| Mean | 4238.0 | 98.8 | 3588.7 |
| SD | 8087.84 | 98.75 | 7567.01 |
| Median | 759.4 | 65.7 | 460.4 |
| Min-Max | 2-42787 | 4-294 | 2-42787 |
| Q1-Q3 | 75.6-4637.4 | 30.0-150.2 | 46.6-2322.3 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-2 2021-08-30 10:26

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.2: Descriptive statistics for each covariate in each anatomical region by rPFS event (Body-PFS Full Analysis Set)

| | Subjects with rPFS event (N=251) | Subjects without rPFS event (N=131) | All subjects (N=382) |
|---|-------------------------------------|--|-------------------------|
| Lymph Node | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 178 (70.9) | 80 (61.1) | 258 (67.5) |
| No | 73 (29.1) | 51 (38.9) | 124 (32.5) |
| SUVmean (g/ml) | | | |
| n | 178 | 80 | 258 |
| Mean | 8.4 | 11.5 | 9.4 |
| SD | 4.03 | 8.21 | 5.82 |
| Median | 7.7 | 9.4 | 8.2 |
| Min-Max | 2-24 | 2-53 | 2-53 |
| Q1-Q3 | 5.1-10.8 | 6.3-13.9 | 5.3-11.7 |
| SUVmax (g/ml) | | | |
| n | 178 | 80 | 258 |
| Mean | 29.3 | 45.6 | 34.3 |
| SD | 22.07 | 41.32 | 30.29 |
| Median | 23.2 | 37.2 | 25.5 |
| Min-Max | 3-119 | 3-208 | 3-208 |
| Q1-Q3 | 12.8-39.4 | 16.7-56.4 | 13.6-46.0 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 178 | 80 | 258 |
| Mean | 138.2 | 185.6 | 152.9 |
| SD | 235.07 | 432.43 | 309.87 |
| Median | 45.4 | 64.7 | 52.4 |
| Min-Max | 0-1379 | 1-3104 | 0-3104 |
| Q1-Q3 | 11.0-151.3 | 10.2-174.6 | 10.4-157.8 |
| Tumor Load (g) | | | |
| n | 178 | 80 | 258 |
| Mean | 1507.5 | 2881.0 | 1933.4 |
| SD | 2758.47 | 7662.33 | 4867.56 |
| Median | 353.7 | 776.7 | 410.6 |
| Min-Max | 1-16390 | 2-47771 | 1-47771 |
| Q1-Q3 | 62.6-1522.8 | 81.9-1984.2 | 76.4-1764.3 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-2 2021-08-30 10:26

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.2: Descriptive statistics for each covariate in each anatomical region by rPFS event (Body-PFS Full Analysis Set)

| | Subjects with rPFS event (N=251) | Subjects without rPFS event (N=131) | All subjects (N=382) |
|---|-------------------------------------|--|-------------------------|
| Soft Tissue | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 122 (48.6) | 51 (38.9) | 173 (45.3) |
| No | 129 (51.4) | 80 (61.1) | 209 (54.7) |
| SUVmean (g/ml) | | | |
| n | 122 | 51 | 173 |
| Mean | 8.6 | 10.7 | 9.2 |
| SD | 5.14 | 6.59 | 5.67 |
| Median | 7.4 | 8.9 | 7.8 |
| Min-Max | 1-35 | 3-36 | 1-36 |
| Q1-Q3 | 5.1-10.6 | 6.6-13.1 | 5.4-10.9 |
| SUVmax (g/ml) | | | |
| n | 122 | 51 | 173 |
| Mean | 21.6 | 29.4 | 23.9 |
| SD | 16.85 | 26.96 | 20.58 |
| Median | 16.4 | 23.1 | 19.2 |
| Min-Max | 2-108 | 4-167 | 2-167 |
| Q1-Q3 | 9.1-29.5 | 13.1-35.6 | 10.1-33.2 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 122 | 51 | 173 |
| Mean | 102.7 | 39.8 | 84.1 |
| SD | 400.58 | 98.33 | 341.35 |
| Median | 12.2 | 15.0 | 14.7 |
| Min-Max | 0-3886 | 1-641 | 0-3886 |
| Q1-Q3 | 2.9-38.2 | 3.6-31.0 | 3.3-35.5 |
| Tumor Load (g) | | | |
| n | 122 | 51 | 173 |
| Mean | 1101.2 | 674.4 | 975.4 |
| SD | 5167.15 | 2054.17 | 4477.44 |
| Median | 89.4 | 146.0 | 99.7 |
| Min-Max | 1-52318 | 4-13399 | 1-52318 |
| Q1-Q3 | 22.9-480.3 | 27.8-324.1 | 23.7-391.6 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-2 2021-08-30 10:26

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Source data: adsl.xpt, adtte.xpt

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Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.3: Descriptive statistics for each covariate in each anatomical region by OS event (Body-Full Analysis Set)

| | Death (N=341) | Alive (N=207) | All subjects (N=548) |
|---|------------------|------------------|-------------------------|
| Whole Body | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 341 (100) | 207 (100) | 548 (100) |
| No | 0 | 0 | 0 |
| SUVmean (g/ml) | | | |
| n | 341 | 207 | 548 |
| Mean | 7.6 | 9.8 | 8.4 |
| SD | 2.81 | 5.48 | 4.16 |
| Median | 7.1 | 8.7 | 7.5 |
| Min-Max | 2-18 | 2-38 | 2-38 |
| Q1-Q3 | 5.5-9.3 | 6.1-12.0 | 5.7-9.9 |
| SUVmax (g/ml) | | | |
| n | 341 | 207 | 548 |
| Mean | 36.5 | 49.9 | 41.5 |
| SD | 22.80 | 41.82 | 32.01 |
| Median | 32.9 | 39.7 | 34.2 |
| Min-Max | 4-155 | 2-317 | 2-317 |
| Q1-Q3 | 19.7-47.9 | 22.2-66.6 | 20.2-53.0 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 341 | 207 | 548 |
| Mean | 965.6 | 540.6 | 805.0 |
| SD | 995.74 | 805.91 | 950.47 |
| Median | 589.9 | 228.7 | 398.1 |
| Min-Max | 2-4884 | 2-5370 | 2-5370 |
| Q1-Q3 | 217.9-1451.1 | 79.4-581.4 | 140.6-1160.3 |
| Tumor Load (g) | | | |
| n | 341 | 207 | 548 |
| Mean | 7959.7 | 5220.7 | 6925.1 |
| SD | 9042.92 | 7734.67 | 8667.49 |
| Median | 4330.9 | 2255.2 | 3404.0 |
| Min-Max | 6-54176 | 3-47780 | 3-54176 |
| Q1-Q3 | 1287.6-12220.2 | 639.3-5610.7 | 1017.9-9835.8 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-3 2021-08-30 10:26

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.3: Descriptive statistics for each covariate in each anatomical region by OS event (Body-Full Analysis Set)

| | Death (N=341) | Alive (N=207) | All subjects (N=548) |
|---|------------------|------------------|-------------------------|
| Bone | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 328 (96.2) | 180 (87.0) | 508 (92.7) |
| No | 13 (3.8) | 27 (13.0) | 40 (7.3) |
| SUVmean (g/ml) | | | |
| n | 328 | 180 | 508 |
| Mean | 6.7 | 8.4 | 7.3 |
| SD | 2.50 | 5.23 | 3.79 |
| Median | 6.3 | 7.3 | 6.6 |
| Min-Max | 2-18 | 2-53 | 2-53 |
| Q1-Q3 | 4.9-8.0 | 5.5-10.2 | 5.0-8.6 |
| SUVmax (g/ml) | | | |
| n | 328 | 180 | 508 |
| Mean | 31.0 | 42.9 | 35.2 |
| SD | 21.51 | 39.54 | 29.72 |
| Median | 27.1 | 34.1 | 28.2 |
| Min-Max | 2-155 | 4-317 | 2-317 |
| Q1-Q3 | 15.6-41.5 | 16.5-54.2 | 15.9-45.7 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 328 | 180 | 508 |
| Mean | 789.9 | 492.0 | 684.3 |
| SD | 935.20 | 802.47 | 900.99 |
| Median | 401.2 | 193.2 | 289.0 |
| Min-Max | 0-4440 | 1-4919 | 0-4919 |
| Q1-Q3 | 90.7-1209.3 | 42.3-483.3 | 67.8-986.4 |
| Tumor Load (g) | | | |
| n | 328 | 180 | 508 |
| Mean | 5967.2 | 4075.1 | 5296.8 |
| SD | 7673.44 | 6381.83 | 7292.24 |
| Median | 2535.4 | 1396.3 | 2221.7 |
| Min-Max | 0-39673 | 2-35554 | 0-39673 |
| Q1-Q3 | 570.6-8781.9 | 324.2-5022.6 | 415.6-7653.4 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-3 2021-08-30 10:26

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.3: Descriptive statistics for each covariate in each anatomical region by OS event (Body-Full Analysis Set)

| | Death (N=341) | Alive (N=207) | All subjects (N=548) |
|---|------------------|------------------|-------------------------|
| Liver | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 55 (16.1) | 17 (8.2) | 72 (13.1) |
| No | 286 (83.9) | 190 (91.8) | 476 (86.9) |
| SUVmean (g/ml) | | | |
| n | 55 | 17 | 72 |
| Mean | 8.3 | 9.5 | 8.6 |
| SD | 2.94 | 6.71 | 4.13 |
| Median | 8.2 | 7.4 | 8.2 |
| Min-Max | 2-18 | 3-33 | 2-33 |
| Q1-Q3 | 6.3-10.4 | 5.9-10.3 | 6.2-10.4 |
| SUVmax (g/ml) | | | |
| n | 55 | 17 | 72 |
| Mean | 19.2 | 21.1 | 19.6 |
| SD | 12.92 | 19.21 | 14.52 |
| Median | 18.2 | 11.7 | 16.1 |
| Min-Max | 2-66 | 5-73 | 2-73 |
| Q1-Q3 | 9.8-26.0 | 9.1-30.6 | 9.7-26.0 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 55 | 17 | 72 |
| Mean | 336.9 | 95.8 | 280.0 |
| SD | 692.28 | 194.30 | 619.40 |
| Median | 67.0 | 15.9 | 42.6 |
| Min-Max | 1-3761 | 1-728 | 1-3761 |
| Q1-Q3 | 6.0-270.8 | 7.6-49.2 | 6.9-180.0 |
| Tumor Load (g) | | | |
| n | 55 | 17 | 72 |
| Mean | 3490.0 | 1504.5 | 3021.2 |
| SD | 7556.16 | 3686.93 | 6870.89 |
| Median | 504.6 | 109.9 | 416.0 |
| Min-Max | 2-42787 | 4-14148 | 2-42787 |
| Q1-Q3 | 28.0-2322.3 | 46.3-759.8 | 37.7-1746.3 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-3 2021-08-30 10:26

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.3: Descriptive statistics for each covariate in each anatomical region by OS event (Body-Full Analysis Set)

| | Death (N=341) | Alive (N=207) | All subjects (N=548) |
|---|------------------|------------------|-------------------------|
| Lymph Node | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 241 (70.7) | 128 (61.8) | 369 (67.3) |
| No | 100 (29.3) | 79 (38.2) | 179 (32.7) |
| SUVmean (g/ml) | | | |
| n | 241 | 128 | 369 |
| Mean | 7.8 | 10.7 | 8.8 |
| SD | 3.90 | 7.19 | 5.45 |
| Median | 6.8 | 9.1 | 7.7 |
| Min-Max | 2-24 | 2-53 | 2-53 |
| Q1-Q3 | 4.8-9.9 | 5.9-13.5 | 5.0-11.5 |
| SUVmax (g/ml) | | | |
| n | 241 | 128 | 369 |
| Mean | 26.6 | 43.3 | 32.4 |
| SD | 22.12 | 38.47 | 29.88 |
| Median | 20.6 | 34.7 | 22.7 |
| Min-Max | 3-155 | 2-208 | 2-208 |
| Q1-Q3 | 10.0-38.0 | 16.3-56.5 | 11.2-44.3 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 241 | 128 | 369 |
| Mean | 155.1 | 145.3 | 151.7 |
| SD | 302.89 | 258.65 | 287.99 |
| Median | 43.6 | 52.4 | 45.8 |
| Min-Max | 0-3104 | 0-1932 | 0-3104 |
| Q1-Q3 | 9.3-157.7 | 10.9-175.6 | 10.0-159.6 |
| Tumor Load (g) | | | |
| n | 241 | 128 | 369 |
| Mean | 1711.1 | 2129.3 | 1856.2 |
| SD | 3862.61 | 5368.10 | 4440.14 |
| Median | 294.9 | 457.7 | 357.4 |
| Min-Max | 1-41125 | 1-47771 | 1-47771 |
| Q1-Q3 | 43.9-1528.9 | 88.5-1956.1 | 51.9-1688.1 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-3 2021-08-30 10:26

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.3: Descriptive statistics for each covariate in each anatomical region by OS event (Body-Full Analysis Set)

| | Death (N=341) | Alive (N=207) | All subjects (N=548) |
|---|------------------|------------------|-------------------------|
| Soft Tissue | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 154 (45.2) | 79 (38.2) | 233 (42.5) |
| No | 187 (54.8) | 128 (61.8) | 315 (57.5) |
| SUVmean (g/ml) | | | |
| n | 154 | 79 | 233 |
| Mean | 8.4 | 9.9 | 8.9 |
| SD | 4.86 | 6.52 | 5.51 |
| Median | 7.5 | 7.9 | 7.6 |
| Min-Max | 1-35 | 2-36 | 1-36 |
| Q1-Q3 | 5.3-9.9 | 4.5-13.7 | 5.1-10.6 |
| SUVmax (g/ml) | | | |
| n | 154 | 79 | 233 |
| Mean | 20.2 | 27.4 | 22.7 |
| SD | 14.24 | 26.86 | 19.69 |
| Median | 16.0 | 20.0 | 16.5 |
| Min-Max | 2-81 | 2-167 | 2-167 |
| Q1-Q3 | 8.8-28.1 | 8.0-35.6 | 8.6-32.1 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 154 | 79 | 233 |
| Mean | 92.7 | 39.6 | 74.7 |
| SD | 359.93 | 88.12 | 297.79 |
| Median | 11.8 | 14.9 | 13.6 |
| Min-Max | 0-3886 | 1-641 | 0-3886 |
| Q1-Q3 | 3.3-37.1 | 2.9-33.4 | 3.3-35.1 |
| Tumor Load (g) | | | |
| n | 154 | 79 | 233 |
| Mean | 991.4 | 620.8 | 865.8 |
| SD | 4627.23 | 1779.64 | 3900.78 |
| Median | 91.3 | 103.4 | 93.4 |
| Min-Max | 1-52318 | 3-13399 | 1-52318 |
| Q1-Q3 | 22.9-428.5 | 20.1-354.8 | 22.4-369.6 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-3 2021-08-30 10:26

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 1.4: Descriptive statistics for each covariate in each anatomical region by objective response
(Body-Response Evaluable Analysis Set)

| | Subjects with response (N=95) | Subjects without response (N=222) | All subjects (N=317) |
|---|----------------------------------|--------------------------------------|-------------------------|
| Whole Body | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 95 (100) 0 | 222 (100) 0 | 317 (100) 0 |
| No | | | |
| SUVmean (g/ml) | | | |
| n | 95 | 222 | 317 |
| Mean | 11.6 | 7.8 | 8.9 |
| SD | 5.40 | 3.58 | 4.54 |
| Median | 10.2 | 7.1 | 8.1 |
| Min-Max | 5-38 | 3-34 | 3-38 |
| Q1-Q3 | 8.2-13.2 | 5.5-9.5 | 6.1-10.4 |
| SUVmax (g/ml) | | | |
| n | 95 | 222 | 317 |
| Mean | 56.3 | 40.1 | 45.0 |
| SD | 35.60 | 32.19 | 34.01 |
| Median | 48.3 | 33.6 | 39.0 |
| Min-Max | 10-208 | 6-317 | 6-317 |
| Q1-Q3 | 31.4-73.1 | 19.8-51.0 | 22.7-57.6 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 95 | 222 | 317 |
| Mean | 801.5 | 817.0 | 812.4 |
| SD | 909.07 | 921.30 | 916.24 |
| Median | 478.6 | 449.0 | 452.4 |
| Min-Max | 18-4884 | 2-4440 | 2-4884 |
| Q1-Q3 | 215.9-1162.5 | 153.2-1193.9 | 183.4-1177.5 |
| Tumor Load (g) | | | |
| n | 95 | 222 | 317 |
| Mean | 8800.0 | 6576.1 | 7242.5 |
| SD | 9849.08 | 8242.89 | 8798.61 |
| Median | 5312.5 | 3740.7 | 4108.8 |
| Min-Max | 114-47780 | 8-54176 | 8-54176 |
| Q1-Q3 | 2036.7-12384.8 | 1136.6-8635.2 | 1406.9-9550.7 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-4 2021-08-30 10:26

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Source data: adsl.xpt, adtte.xpt, adrs.xpt

Data Cutoff Date: 27JAN2021

Table 1.4: Descriptive statistics for each covariate in each anatomical region by objective response
(Body-Response Evaluable Analysis Set)

| | Subjects with response (N=95) | Subjects without response (N=222) | All subjects (N=317) |
|---|----------------------------------|--------------------------------------|-------------------------|
| Bone | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 80 (84.2) | 211 (95.0) | 291 (91.8) |
| No | 15 (15.8) | 11 (5.0) | 26 (8.2) |
| SUVmean (g/ml) | | | |
| n | 80 | 211 | 291 |
| Mean | 8.5 | 7.4 | 7.7 |
| SD | 4.07 | 4.43 | 4.35 |
| Median | 7.8 | 6.6 | 6.9 |
| Min-Max | 3-23 | 2-53 | 2-53 |
| Q1-Q3 | 5.9-10.0 | 5.0-8.5 | 5.3-8.8 |
| SUVmax (g/ml) | | | |
| n | 80 | 211 | 291 |
| Mean | 41.0 | 36.9 | 38.1 |
| SD | 30.49 | 33.30 | 32.55 |
| Median | 33.5 | 28.1 | 29.6 |
| Min-Max | 3-141 | 2-317 | 2-317 |
| Q1-Q3 | 18.6-54.5 | 16.0-48.8 | 17.1-50.9 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 80 | 211 | 291 |
| Mean | 572.7 | 705.1 | 668.7 |
| SD | 817.15 | 848.82 | 840.92 |
| Median | 188.9 | 380.0 | 335.5 |
| Min-Max | 0-4412 | 1-4440 | 0-4440 |
| Q1-Q3 | 20.9-832.0 | 97.3-1030.8 | 77.2-984.9 |
| Tumor Load (g) | | | |
| n | 80 | 211 | 291 |
| Mean | 5059.6 | 5309.5 | 5240.8 |
| SD | 6840.82 | 6749.28 | 6763.66 |
| Median | 2072.4 | 2652.4 | 2472.8 |
| Min-Max | 0-35032 | 1-34893 | 0-35032 |
| Q1-Q3 | 162.4-7903.4 | 687.8-6964.2 | 503.8-7625.5 |

N is the number of patients with the presence PSMA positive tumors in the body

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Table 1.4: Descriptive statistics for each covariate in each anatomical region by objective response
(Body-Response Evaluable Analysis Set)

| | Subjects with response (N=95) | Subjects without response (N=222) | All subjects (N=317) |
|---|----------------------------------|--------------------------------------|-------------------------|
| Liver | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 9 (9.5) | 35 (15.8) | 44 (13.9) |
| No | 86 (90.5) | 187 (84.2) | 273 (86.1) |
| SUVmean (g/ml) | | | |
| n | 9 | 35 | 44 |
| Mean | 11.7 | 8.2 | 8.9 |
| SD | 8.02 | 2.88 | 4.54 |
| Median | 9.3 | 8.0 | 8.5 |
| Min-Max | 6-33 | 2-15 | 2-33 |
| Q1-Q3 | 9.0-10.6 | 6.1-10.4 | 6.2-10.4 |
| SUVmax (g/ml) | | | |
| n | 9 | 35 | 44 |
| Mean | 27.3 | 19.7 | 21.3 |
| SD | 19.68 | 13.36 | 14.93 |
| Median | 19.8 | 18.2 | 18.9 |
| Min-Max | 10-73 | 2-54 | 2-73 |
| Q1-Q3 | 15.7-28.8 | 9.1-28.6 | 9.8-28.7 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 9 | 35 | 44 |
| Mean | 99.4 | 362.7 | 308.8 |
| SD | 137.55 | 752.47 | 680.27 |
| Median | 69.6 | 45.2 | 47.2 |
| Min-Max | 2-433 | 1-3761 | 1-3761 |
| Q1-Q3 | 11.8-114.3 | 8.4-270.8 | 9.7-212.1 |
| Tumor Load (g) | | | |
| n | 9 | 35 | 44 |
| Mean | 2068.3 | 3731.8 | 3391.5 |
| SD | 4564.47 | 8256.97 | 7631.82 |
| Median | 678.7 | 460.4 | 467.2 |
| Min-Max | 20-14148 | 2-42787 | 2-42787 |
| Q1-Q3 | 75.6-1179.7 | 68.2-2322.3 | 71.9-1746.3 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-4 2021-08-30 10:26

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Table 1.4: Descriptive statistics for each covariate in each anatomical region by objective response
(Body-Response Evaluable Analysis Set)

| | Subjects with response (N=95) | Subjects without response (N=222) | All subjects (N=317) |
|---|----------------------------------|--------------------------------------|-------------------------|
| Lymph Node | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 89 (93.7) | 131 (59.0) | 220 (69.4) |
| No | 6 (6.3) | 91 (41.0) | 97 (30.6) |
| SUVmean (g/ml) | | | |
| n | 89 | 131 | 220 |
| Mean | 12.3 | 7.6 | 9.5 |
| SD | 5.54 | 4.16 | 5.30 |
| Median | 11.5 | 6.5 | 8.6 |
| Min-Max | 5-38 | 2-25 | 2-38 |
| Q1-Q3 | 8.8-14.3 | 4.7-9.2 | 5.5-12.1 |
| SUVmax (g/ml) | | | |
| n | 89 | 131 | 220 |
| Mean | 50.3 | 25.7 | 35.6 |
| SD | 34.65 | 22.75 | 30.59 |
| Median | 43.3 | 18.0 | 26.3 |
| Min-Max | 6-208 | 3-161 | 3-208 |
| Q1-Q3 | 24.6-66.6 | 10.2-37.6 | 14.4-46.7 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 89 | 131 | 220 |
| Mean | 280.9 | 85.6 | 164.6 |
| SD | 432.05 | 194.83 | 326.76 |
| Median | 149.0 | 28.1 | 55.6 |
| Min-Max | 0-3104 | 0-1379 | 0-3104 |
| Q1-Q3 | 54.3-325.5 | 6.9-81.9 | 11.8-168.9 |
| Tumor Load (g) | | | |
| n | 89 | 131 | 220 |
| Mean | 3972.7 | 852.4 | 2114.7 |
| SD | 7350.58 | 2185.40 | 5186.74 |
| Median | 1753.4 | 165.8 | 505.1 |
| Min-Max | 2-47771 | 1-16390 | 1-47771 |
| Q1-Q3 | 509.9-4325.4 | 40.9-723.5 | 84.1-1878.1 |

N is the number of patients with the presence PSMA positive tumors in the body

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Table 1.4: Descriptive statistics for each covariate in each anatomical region by objective response
(Body-Response Evaluable Analysis Set)

| | Subjects with response (N=95) | Subjects without response (N=222) | All subjects (N=317) |
|---|----------------------------------|--------------------------------------|-------------------------|
| Soft Tissue | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 55 (57.9) | 93 (41.9) | 148 (46.7) |
| No | 40 (42.1) | 129 (58.1) | 169 (53.3) |
| SUVmean (g/ml) | | | |
| n | 55 | 93 | 148 |
| Mean | 10.5 | 8.5 | 9.2 |
| SD | 6.27 | 4.87 | 5.50 |
| Median | 8.9 | 7.4 | 7.9 |
| Min-Max | 3-36 | 1-35 | 1-36 |
| Q1-Q3 | 6.1-13.0 | 5.3-10.4 | 5.5-11.0 |
| SUVmax (g/ml) | | | |
| n | 55 | 93 | 148 |
| Mean | 29.5 | 20.9 | 24.1 |
| SD | 26.41 | 17.09 | 21.36 |
| Median | 22.8 | 14.8 | 18.7 |
| Min-Max | 4-167 | 2-108 | 2-167 |
| Q1-Q3 | 13.3-36.4 | 8.0-28.2 | 10.0-33.2 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 55 | 93 | 148 |
| Mean | 80.5 | 93.5 | 88.7 |
| SD | 173.88 | 443.28 | 366.23 |
| Median | 18.9 | 10.0 | 14.0 |
| Min-Max | 1-801 | 0-3886 | 0-3886 |
| Q1-Q3 | 6.2-49.5 | 2.9-25.7 | 3.3-35.3 |
| Tumor Load (g) | | | |
| n | 55 | 93 | 148 |
| Mean | 1073.5 | 1046.4 | 1056.5 |
| SD | 2454.90 | 5801.60 | 4824.86 |
| Median | 221.0 | 67.4 | 94.3 |
| Min-Max | 4-13399 | 1-52318 | 1-52318 |
| Q1-Q3 | 31.5-585.4 | 18.8-276.2 | 24.0-363.0 |

N is the number of patients with the presence PSMA positive tumors in the body

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Table 1.5: Descriptive statistics for each covariate in each anatomical region by PSA response (Body-PFS Full Analysis Set)

| | Subjects with response (N=176) | Subjects without response (N=206) | All subjects (N=382) |
|---|--------------------------------|-----------------------------------|----------------------|
| Whole Body | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 176 (100) 0 | 206 (100) 0 | 382 (100) 0 |
| No | | | |
| SUVmean (g/ml) | | | |
| n | 176 | 206 | 382 |
| Mean | 10.6 | 7.2 | 8.8 |
| SD | 5.27 | 2.61 | 4.40 |
| Median | 9.5 | 6.8 | 7.8 |
| Min-Max | 4-38 | 3-20 | 3-38 |
| Q1-Q3 | 7.3-12.4 | 5.4-8.6 | 6.0-10.2 |
| SUVmax (g/ml) | | | |
| n | 176 | 206 | 382 |
| Mean | 56.2 | 34.0 | 44.2 |
| SD | 41.30 | 20.23 | 33.57 |
| Median | 45.4 | 29.0 | 37.2 |
| Min-Max | 8-317 | 6-113 | 6-317 |
| Q1-Q3 | 31.5-69.8 | 18.9-44.6 | 22.5-55.1 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 176 | 206 | 382 |
| Mean | 815.8 | 915.1 | 869.3 |
| SD | 912.69 | 1001.15 | 961.44 |
| Median | 438.2 | 555.6 | 496.8 |
| Min-Max | 2-4884 | 6-4440 | 2-4884 |
| Q1-Q3 | 178.0-1258.9 | 195.0-1272.8 | 191.6-1271.0 |
| Tumor Load (g) | | | |
| n | 176 | 206 | 382 |
| Mean | 7940.2 | 7071.0 | 7471.5 |
| SD | 8935.48 | 8733.91 | 8826.39 |
| Median | 4852.6 | 3585.7 | 4073.8 |
| Min-Max | 8-47780 | 31-54176 | 8-54176 |
| Q1-Q3 | 1706.9-10830.9 | 1230.8-9928.1 | 1582.9-10279.2 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-5 2021-08-30 10:27

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
68Ga-PSMA-11 Quantitative analysis

Final Version

Table 1.5: Descriptive statistics for each covariate in each anatomical region by PSA response (Body-PFS Full Analysis Set)

| | Subjects with response (N=176) | Subjects without response (N=206) | All subjects (N=382) |
|---|--------------------------------|-----------------------------------|----------------------|
| Bone | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 161 (91.5) | 192 (93.2) | 353 (92.4) |
| No | 15 (8.5) | 14 (6.8) | 29 (7.6) |
| SUVmean (g/ml) | | | |
| n | 161 | 192 | 353 |
| Mean | 9.0 | 6.4 | 7.6 |
| SD | 5.32 | 2.09 | 4.12 |
| Median | 7.9 | 6.0 | 6.8 |
| Min-Max | 3-53 | 2-13 | 2-53 |
| Q1-Q3 | 6.0-10.7 | 4.8-7.7 | 5.3-8.7 |
| SUVmax (g/ml) | | | |
| n | 161 | 192 | 353 |
| Mean | 47.6 | 30.0 | 38.0 |
| SD | 40.41 | 20.01 | 32.20 |
| Median | 37.7 | 26.1 | 30.1 |
| Min-Max | 3-317 | 2-113 | 2-317 |
| Q1-Q3 | 21.5-60.0 | 14.9-40.7 | 17.7-48.2 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 161 | 192 | 353 |
| Mean | 690.9 | 777.8 | 738.2 |
| SD | 871.39 | 925.33 | 900.90 |
| Median | 328.5 | 439.9 | 379.7 |
| Min-Max | 0-4412 | 1-4440 | 0-4440 |
| Q1-Q3 | 73.8-988.0 | 115.5-1151.9 | 88.1-1076.7 |
| Tumor Load (g) | | | |
| n | 161 | 192 | 353 |
| Mean | 5891.5 | 5494.7 | 5675.7 |
| SD | 7220.66 | 7104.69 | 7150.35 |
| Median | 3144.8 | 2765.3 | 2812.5 |
| Min-Max | 0-35032 | 1-34893 | 0-35032 |
| Q1-Q3 | 613.8-7980.3 | 658.4-7770.1 | 620.5-7921.3 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-5 2021-08-30 10:27

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 1.5: Descriptive statistics for each covariate in each anatomical region by PSA response (Body-PFS Full Analysis Set)

| | Subjects with response (N=176) | Subjects without response (N=206) | All subjects (N=382) |
|---|--------------------------------|-----------------------------------|----------------------|
| Liver | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 15 (8.5) | 36 (17.5) | 51 (13.4) |
| No | 161 (91.5) | 170 (82.5) | 331 (86.6) |
| SUVmean (g/ml) | | | |
| n | 15 | 36 | 51 |
| Mean | 9.8 | 8.1 | 8.6 |
| SD | 6.63 | 2.89 | 4.33 |
| Median | 9.0 | 8.3 | 8.3 |
| Min-Max | 6-33 | 2-15 | 2-33 |
| Q1-Q3 | 6.1-10.3 | 6.3-10.2 | 6.2-10.3 |
| SUVmax (g/ml) | | | |
| n | 15 | 36 | 51 |
| Mean | 21.5 | 19.9 | 20.4 |
| SD | 17.24 | 13.26 | 14.38 |
| Median | 18.3 | 18.5 | 18.3 |
| Min-Max | 6-73 | 2-54 | 2-73 |
| Q1-Q3 | 9.9-28.8 | 9.7-28.0 | 9.8-28.2 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 15 | 36 | 51 |
| Mean | 99.9 | 444.5 | 343.2 |
| SD | 205.74 | 813.90 | 707.61 |
| Median | 11.8 | 73.7 | 45.2 |
| Min-Max | 1-728 | 1-3761 | 1-3761 |
| Q1-Q3 | 6.0-75.7 | 16.4-425.3 | 8.2-270.8 |
| Tumor Load (g) | | | |
| n | 15 | 36 | 51 |
| Mean | 1638.4 | 4401.3 | 3588.7 |
| SD | 3916.62 | 8564.71 | 7567.01 |
| Median | 83.4 | 632.8 | 460.4 |
| Min-Max | 8-14148 | 2-42787 | 2-42787 |
| Q1-Q3 | 35.6-772.1 | 85.0-4136.7 | 46.6-2322.3 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-5 2021-08-30 10:27

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Table 1.5: Descriptive statistics for each covariate in each anatomical region by PSA response (Body-PFS Full Analysis Set)

| | Subjects with response (N=176) | Subjects without response (N=206) | All subjects (N=382) |
|---|--------------------------------|-----------------------------------|----------------------|
| Lymph Node | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 128 (72.7) | 130 (63.1) | 258 (67.5) |
| No | 48 (27.3) | 76 (36.9) | 124 (32.5) |
| SUVmean (g/ml) | | | |
| n | 128 | 130 | 258 |
| Mean | 11.2 | 7.6 | 9.4 |
| SD | 6.81 | 3.93 | 5.82 |
| Median | 10.3 | 6.5 | 8.2 |
| Min-Max | 2-53 | 2-24 | 2-53 |
| Q1-Q3 | 6.4-13.6 | 4.8-8.9 | 5.3-11.7 |
| SUVmax (g/ml) | | | |
| n | 128 | 130 | 258 |
| Mean | 43.9 | 24.9 | 34.3 |
| SD | 36.10 | 19.05 | 30.29 |
| Median | 36.7 | 19.2 | 25.5 |
| Min-Max | 3-208 | 3-100 | 3-208 |
| Q1-Q3 | 17.0-56.7 | 10.4-37.4 | 13.6-46.0 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 128 | 130 | 258 |
| Mean | 202.1 | 104.5 | 152.9 |
| SD | 386.59 | 198.48 | 309.87 |
| Median | 66.0 | 40.3 | 52.4 |
| Min-Max | 0-3104 | 0-1379 | 0-3104 |
| Q1-Q3 | 14.6-230.8 | 9.3-111.1 | 10.4-157.8 |
| Tumor Load (g) | | | |
| n | 128 | 130 | 258 |
| Mean | 2824.8 | 1055.7 | 1933.4 |
| SD | 6406.94 | 2285.91 | 4867.56 |
| Median | 665.0 | 282.2 | 410.6 |
| Min-Max | 2-47771 | 1-16390 | 1-47771 |
| Q1-Q3 | 140.9-3046.0 | 41.0-960.1 | 76.4-1764.3 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-5 2021-08-30 10:27

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
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Table 1.5: Descriptive statistics for each covariate in each anatomical region by PSA response (Body-PFS Full Analysis Set)

| | Subjects with response (N=176) | Subjects without response (N=206) | All subjects (N=382) |
|---|--------------------------------|-----------------------------------|----------------------|
| Soft Tissue | | | |
| Presence of PSMA positive tumors, (n (%)) | | | |
| Yes | 82 (46.6) | 91 (44.2) | 173 (45.3) |
| No | 94 (53.4) | 115 (55.8) | 209 (54.7) |
| SUVmean (g/ml) | | | |
| n | 82 | 91 | 173 |
| Mean | 9.9 | 8.6 | 9.2 |
| SD | 5.99 | 5.32 | 5.67 |
| Median | 8.9 | 7.3 | 7.8 |
| Min-Max | 1-36 | 2-35 | 1-36 |
| Q1-Q3 | 6.1-12.1 | 5.3-9.6 | 5.4-10.9 |
| SUVmax (g/ml) | | | |
| n | 82 | 91 | 173 |
| Mean | 27.4 | 20.8 | 23.9 |
| SD | 25.22 | 14.70 | 20.58 |
| Median | 20.6 | 16.0 | 19.2 |
| Min-Max | 2-167 | 2-81 | 2-167 |
| Q1-Q3 | 12.0-35.6 | 9.9-29.5 | 10.1-33.2 |
| Volume of segmented PSMA positive tumors (cc) | | | |
| n | 82 | 91 | 173 |
| Mean | 60.6 | 105.3 | 84.1 |
| SD | 145.94 | 450.07 | 341.35 |
| Median | 16.2 | 11.0 | 14.7 |
| Min-Max | 0-801 | 0-3886 | 0-3886 |
| Q1-Q3 | 4.1-35.6 | 2.9-35.5 | 3.3-35.5 |
| Tumor Load (g) | | | |
| n | 82 | 91 | 173 |
| Mean | 765.8 | 1164.3 | 975.4 |
| SD | 1988.45 | 5888.83 | 4477.44 |
| Median | 157.8 | 86.4 | 99.7 |
| Min-Max | 3-13399 | 1-52318 | 1-52318 |
| Q1-Q3 | 26.7-451.7 | 21.4-371.2 | 23.7-391.6 |

N is the number of patients with the presence PSMA positive tumors in the body

Output ID: T-1-5 2021-08-30 10:27

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 2.1: rPFS univariate Cox proportional hazards model - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|---|--------------|--------------|--------------------|
| Whole Body | | | |
| SUVmean | 0.88 | [0.84, 0.91] | <.001 ^a |
| SUVmax | 0.99 | [0.98, 0.99] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 1.28 | [1.13, 1.44] | <.001 ^a |
| Tumor load | 1.01 | [1.00, 1.03] | 0.050 ^a |
| Bone | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.56 | [0.33, 0.95] | 0.032 ^a |
| Liver | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.48 | [0.35, 0.67] | <.001 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.95 | [0.73, 1.25] | 0.729 |
| Soft Tissue | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.85 | [0.66, 1.09] | 0.199 |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-2-1 2021-08-30 17:29

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Data Cutoff Date: 27JAN2021

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Table 2.2: rPFS univariate Cox proportional hazards model - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Bone | | | |
| SUVmean | 0.88 | [0.84, 0.92] | <.001 ^a |
| SUVmax | 0.99 | [0.98, 0.99] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 1.22 | [1.06, 1.39] | 0.005 ^a |
| Tumor load | 1.02 | [1.00, 1.04] | 0.047 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-2-2 2021-08-30 17:29

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-univ-hr-log.sas

Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 2.3: rPFS univariate Cox proportional hazards model - Liver (Liver-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Liver | | | |
| SUVmean | 1.01 | [0.95, 1.07] | 0.797 |
| SUVmax | 1.01 | [0.99, 1.03] | 0.354 |
| Volume of segmented PSMA positive tumors | 1.44 | [1.00, 2.08] | 0.050 ^a |
| Tumor load | 1.03 | [0.99, 1.06] | 0.123 |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-2-3 2021-08-30 17:29

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

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Table 2.4: rPFS univariate Cox proportional hazards model - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Lymph node | | | |
| SUVmean | 0.92 | [0.89, 0.95] | <.001 ^a |
| SUVmax | 0.98 | [0.98, 0.99] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 0.69 | [0.37, 1.27] | 0.228 |
| Tumor load | 0.95 | [0.90, 1.00] | 0.047 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-2-4 2021-08-30 17:30

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-univ-hr-log.sas

Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 2.5: rPFS univariate Cox proportional hazards model - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Soft tissue | | | |
| SUVmean | 0.95 | [0.92, 0.99] | 0.012 ^a |
| SUVmax | 0.98 | [0.97, 0.99] | 0.004 ^a |
| Volume of segmented PSMA positive tumors | 1.23 | [0.80, 1.87] | 0.343 |
| Tumor load | 1.01 | [0.97, 1.05] | 0.736 |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-2-5 2021-08-30 17:30

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Table 3.1: rPFS multivariate Cox proportional hazards model - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Whole body | | | |
| SUVmean | 0.84 | [0.78, 0.91] | <.001 ^a |
| SUVmax | 1.00 | [0.99, 1.01] | 0.585 |
| Volume of segmented PSMA positive tumors | 0.67 | [0.43, 1.04] | 0.077 |
| Tumor load | 1.07 | [1.02, 1.13] | 0.007 ^a |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.40 | [0.23, 0.70] | 0.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.49 | [0.35, 0.69] | <.001 ^a |
| Final multivariate model from the backward/forward selection | | | |
| Whole body | | | |
| SUVmean | 0.86 | [0.82, 0.90] | <.001 ^a |
| Tumor load | 1.02 | [1.01, 1.04] | 0.001 ^a |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.45 | [0.26, 0.78] | 0.004 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.48 | [0.34, 0.67] | <.001 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-3-1 2021-08-30 19:07

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Table 3-1-b-s: rPFS multivariate Cox proportional hazards model - backward selection - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Whole body | | | |
| SUVmean | 0.84 | [0.78, 0.91] | <.001 ^a |
| SUVmax | 1.00 | [0.99, 1.01] | 0.585 |
| Volume of segmented PSMA positive tumors | 0.67 | [0.43, 1.04] | 0.077 |
| Tumor load | 1.07 | [1.02, 1.13] | 0.007 ^a |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.40 | [0.23, 0.70] | 0.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.49 | [0.35, 0.69] | <.001 ^a |
| Step 1 | | | |
| Whole body | | | |
| SUVmean | 0.83 | [0.79, 0.88] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 0.66 | [0.43, 1.03] | 0.069 |
| Tumor load | 1.07 | [1.02, 1.13] | 0.007 ^a |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.41 | [0.24, 0.72] | 0.002 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.49 | [0.35, 0.69] | <.001 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-3-1-B-S 2021-08-30 19:07

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Table 3-1-b-s: rPFS multivariate Cox proportional hazards model - backward selection - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Whole body | 0.86 | [0.82, 0.90] | <.001 ^a |
| SUVmean | 1.02 | [1.01, 1.04] | 0.001 ^a |
| Tumor load | | | |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.45 | [0.26, 0.78] | 0.004 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.48 | [0.34, 0.67] | <.001 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-3-1-B-S 2021-08-30 19:07

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Table 3-1-f-s: rPFS multivariate Cox proportional hazards model - forward selection - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Whole body | | | |
| SUVmean | 0.86 | [0.82, 0.90] | <.001 ^a |
| Tumor load | 1.02 | [1.01, 1.04] | 0.001 ^a |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.45 | [0.26, 0.78] | 0.004 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.48 | [0.34, 0.67] | <.001 ^a |
| Step 1 - Candidate | | | |
| Whole body | | | |
| SUVmax | | | 0.488 |
| Volume of segmented PSMA positive tumors | | | 0.068 |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | | | 0.371 |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | | | 0.348 |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-3-1-F-S 2021-08-30 19:07

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Source data: adsl.xpt, adtte.xpt

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Table 3-1-f-s: rPFS multivariate Cox proportional hazards model - forward selection - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward/forward selection | | | |
| Whole body | 0.86 | [0.82, 0.90] | <.001 ^a |
| SUVmean | 1.02 | [1.01, 1.04] | 0.001 ^a |
| Tumor load | | | |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.45 | [0.26, 0.78] | 0.004 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.48 | [0.34, 0.67] | <.001 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

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Table 3.2: rPFS multivariate Cox proportional hazards model - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Bone | | | |
| SUVmean | 0.83 | [0.76, 0.91] | <.001 ^a |
| SUVmax | 1.00 | [0.99, 1.01] | 0.667 |
| Volume of segmented PSMA positive tumors | 0.65 | [0.36, 1.16] | 0.143 |
| Tumor load | 1.09 | [1.01, 1.18] | 0.030 ^a |
| Final multivariate model from the backward/forward selection | | | |
| Bone | | | |
| SUVmean | 0.87 | [0.82, 0.91] | <.001 ^a |
| Tumor load | 1.03 | [1.01, 1.05] | 0.001 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-2 2021-08-30 19:07

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Source data: adsl.xpt, adtte.xpt

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Table 3-2-b-s: rPFS multivariate Cox proportional hazards model - backward selection - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Bone | | | |
| SUVmean | 0.83 | [0.76, 0.91] | <.001 ^a |
| SUVmax | 1.00 | [0.99, 1.01] | 0.667 |
| Volume of segmented PSMA positive tumors | 0.65 | [0.36, 1.16] | 0.143 |
| Tumor load | 1.09 | [1.01, 1.18] | 0.030 ^a |
| Step 1 | | | |
| Bone | | | |
| SUVmean | 0.84 | [0.80, 0.90] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 0.65 | [0.36, 1.16] | 0.143 |
| Tumor load | 1.09 | [1.01, 1.18] | 0.028 ^a |
| Final multivariate model from the backward selection | | | |
| Bone | | | |
| SUVmean | 0.87 | [0.82, 0.91] | <.001 ^a |
| Tumor load | 1.03 | [1.01, 1.05] | 0.001 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-2-B-S 2021-08-30 19:08

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Source data: adsl.xpt, adtte.xpt

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Table 3-2-f-s: rPFS multivariate Cox proportional hazards model - forward selection - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Bone | | | |
| SUVmean | 0.87 | [0.82, 0.91] | <.001 ^a |
| Tumor load | 1.03 | [1.01, 1.05] | 0.001 ^a |
| Step 1 - Candidate | | | |
| Bone | | | |
| SUVmax | | | 0.668 |
| Volume of segmented PSMA positive tumors | | | 0.144 |
| Final multivariate model from the backward/forward selection | | | |
| Bone | | | |
| SUVmean | 0.87 | [0.82, 0.91] | <.001 ^a |
| Tumor load | 1.03 | [1.01, 1.05] | 0.001 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-2-F-S 2021-08-30 19:08

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Table 3.3: rPFS multivariate Cox proportional hazards model - backward/forward selection - Liver (Liver-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 1.44 | [1.00, 2.08] | 0.050 ^a |
| Final multivariate model from the backward/forward selection | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 1.44 | [1.00, 2.08] | 0.050 ^a |

Note: The hazard ratios for tumor volume are computed for a 1000cc increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-3 2021-08-30 19:08

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Source data: adsl.xpt, adtte.xpt

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Table 3-3-b-s: rPFS multivariate Cox proportional hazards model - backward selection - Liver (Liver-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 1.44 | [1.00, 2.08] | 0.050 ^a |
| Final multivariate model from the backward selection | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 1.44 | [1.00, 2.08] | 0.050 ^a |

Note: The hazard ratios for tumor volume are computed for a 1000cc increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-3-B-S 2021-08-30 19:09

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Table 3-3-f-s: rPFS multivariate Cox proportional hazards model - forward selection - Liver (Liver-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 1.44 | [1.00, 2.08] | 0.050 ^a |
| Step 1 - Candidate | | | |
| Liver | | | |
| SUVmean | 0.905 | | |
| SUVmax | 0.594 | | |
| Tumor load | 0.164 | | |
| Final multivariate model from the backward/forward selection | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 1.44 | [1.00, 2.08] | 0.050 ^a |

Note: The hazard ratios for tumor volume are computed for a 1000cc increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-3-F-S 2021-08-30 19:09

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Source data: adsl.xpt, adtte.xpt

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Table 3.4: rPFS multivariate Cox proportional hazards model - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Lymph Node | 0.95 | [0.90, 1.02] | 0.143 |
| SUVmean | 0.99 | [0.98, 1.00] | 0.140 |
| SUVmax | 1.01 | [0.97, 1.06] | 0.665 |
| Tumor load | | | |
| Final multivariate model from the backward/forward selection | | | |
| Lymph Node | 0.98 | [0.98, 0.99] | <.001 ^a |
| SUVmax | | | |

Note: The hazard ratios for tumor load are computed for a 1000g increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-4 2021-08-30 19:09

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Table 3-4-b-s: rPFS multivariate Cox proportional hazards model - backward selection - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Lymph Node | 0.95 | [0.90, 1.02] | 0.143 |
| SUVmean | 0.99 | [0.98, 1.00] | 0.140 |
| SUVmax | 1.01 | [0.97, 1.06] | 0.665 |
| Tumor load | | | |
| Step 1 | | | |
| Lymph Node | 0.96 | [0.90, 1.02] | 0.156 |
| SUVmean | 0.99 | [0.98, 1.00] | 0.153 |
| SUVmax | | | |
| Final multivariate model from the backward selection | | | |
| Lymph Node | 0.98 | [0.98, 0.99] | <.001 ^a |
| SUVmax | | | |

Note: The hazard ratios for tumor load are computed for a 1000g increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-4-B-S 2021-08-30 19:09

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 3-4-f-s: rPFS multivariate Cox proportional hazards model - forward selection - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Lymph Node | 0.98 | [0.98, 0.99] | <.001 ^a |
| SUVmax | | | |
| Step 1 - Candidate | | | |
| Lymph Node | 0.157 | | |
| SUVmean | 0.359 | | |
| Volume of segmented PSMA positive tumors | 0.837 | | |
| Tumor load | | | |
| Final multivariate model from the backward/forward selection | | | |
| Lymph Node | 0.98 | [0.98, 0.99] | <.001 ^a |
| SUVmax | | | |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-4-F-S 2021-08-30 19:10

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Source data: adsl.xpt, adtte.xpt

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Table 3.5: rPFS multivariate Cox proportional hazards model - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Soft Tissue | 1.03 | [0.94, 1.13] | 0.543 |
| SUVmean | 0.98 | [0.95, 1.00] | 0.080 |
| Final multivariate model from the backward/forward selection | | | |
| Soft Tissue | 0.98 | [0.97, 0.99] | 0.004 ^a |
| SUVmax | | | |

Note: The hazard ratios of SUVmean and SUVmax are computed for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-5 2021-08-30 19:10

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Source data: adsl.xpt, adtte.xpt

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Table 3-5-b-s: rPFS multivariate Cox proportional hazards model - backward selection - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Soft Tissue | | | |
| SUVmean | 1.03 | [0.94, 1.13] | 0.543 |
| SUVmax | 0.98 | [0.95, 1.00] | 0.080 |
| Final multivariate model from the backward selection | | | |
| Soft Tissue | | | |
| SUVmax | 0.98 | [0.97, 0.99] | 0.004 ^a |

Note: The hazard ratios of SUVmean and SUVmax are computed for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-5-B-S 2021-08-30 19:10

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Source data: adsl.xpt, adtte.xpt

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Table 3-5-f-s: rPFS multivariate Cox proportional hazards model - forward selection - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Soft Tissue SUVmax | 0.98 | [0.97, 0.99] | 0.004 ^a |
| Step 1 - Candidate | | | |
| Soft Tissue SUVmean | 0.543 | | |
| Volume of segmented PSMA positive tumors | 0.062 | | |
| Tumor load | 0.165 | | |
| Final multivariate model from the backward/forward selection | | | |
| Soft Tissue SUVmax | 0.98 | [0.97, 0.99] | 0.004 ^a |

Note: The hazard ratios for tumor load are computed for a 1000g increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-3-5-F-S 2021-08-30 19:11

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Table 4.1: rPFS multivariate Cox proportional hazards model - with optimal cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|---|--------------|--------------|--------------------|
| Whole body | | | |
| SUVmean (g/ml) <19 vs. >=19 ^c | 0.05 | [0.01, 0.34] | 0.003 ^a |
| Tumor load (g) <26000 vs. >=26000 ^c | 2.24 | [1.30, 3.87] | 0.004 ^a |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.44 | [0.26, 0.76] | 0.003 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.44 | [0.31, 0.61] | <.001 ^a |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

^c Reference is '<'

Output ID: T-4-1 2021-08-30 19:44

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Source data: adsl.xpt, adtte.xpt

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Table 4.1-s: rPFS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmean (g/ml) - Optimal cut | <19 | 0.003 ^a | 0.05 | [0.01, 0.37] | 250/367 (68.1) | 1/15 (6.7) |
| SUVmean (g/ml) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <5 | <.001 ^a | 0.47 | [0.32, 0.68] | 34/50 (68.0) | 217/332 (65.4) |
| | <6 | <.001 ^a | 0.54 | [0.41, 0.72] | 65/94 (69.1) | 186/288 (64.6) |
| | <7 | <.001 ^a | 0.57 | [0.44, 0.73] | 102/151 (67.5) | 149/231 (64.5) |
| | <8 | <.001 ^a | 0.54 | [0.42, 0.70] | 136/199 (68.3) | 115/183 (62.8) |
| | <9 | <.001 ^a | 0.46 | [0.35, 0.60] | 173/247 (70.0) | 78/135 (57.8) |
| | <10 | <.001 ^a | 0.45 | [0.33, 0.61] | 198/283 (70.0) | 53/99 (53.5) |
| | <11 | <.001 ^a | 0.45 | [0.32, 0.64] | 214/310 (69.0) | 37/72 (51.4) |
| | <12 | <.001 ^a | 0.37 | [0.25, 0.55] | 224/324 (69.1) | 27/58 (46.6) |
| | <13 | <.001 ^a | 0.29 | [0.17, 0.48] | 235/339 (69.3) | 16/43 (37.2) |
| | <14 | <.001 ^a | 0.17 | [0.08, 0.36] | 244/352 (69.3) | 7/30 (23.3) |
| | <15 | <.001 ^a | 0.16 | [0.07, 0.39] | 246/357 (68.9) | 5/25 (20.0) |
| | <16 | <.001 ^a | 0.14 | [0.05, 0.38] | 247/360 (68.6) | 4/22 (18.2) |
| | <17 | <.001 ^a | 0.11 | [0.04, 0.36] | 248/362 (68.5) | 3/20 (15.0) |
| | <18 | <.001 ^a | 0.09 | [0.02, 0.36] | 249/365 (68.2) | 2/17 (11.8) |
| | <19 | 0.003 ^a | 0.05 | [0.01, 0.37] | 250/367 (68.1) | 1/15 (6.7) |
| | <20 | 0.012 ^a | 0.08 | [0.01, 0.58] | 250/371 (67.4) | 1/11 (9.1) |
| SUVmean (g/ml) - All cuts | <3 | 0.003 ^a | 0.12 | [0.03, 0.50] | 2/2 (100.0) | 249/380 (65.5) |
| | <4 | 0.168 | 0.61 | [0.30, 1.23] | 8/13 (61.5) | 243/369 (65.9) |
| | <5 | <.001 ^a | 0.47 | [0.32, 0.68] | 34/50 (68.0) | 217/332 (65.4) |
| | <6 | <.001 ^a | 0.54 | [0.41, 0.72] | 65/94 (69.1) | 186/288 (64.6) |
| | <7 | <.001 ^a | 0.57 | [0.44, 0.73] | 102/151 (67.5) | 149/231 (64.5) |
| | <8 | <.001 ^a | 0.54 | [0.42, 0.70] | 136/199 (68.3) | 115/183 (62.8) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.1-s: rPFS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|------------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmean (g/ml) - All cuts | <9 | <.001 ^a | 0.46 | [0.35, 0.60] | 173/247 (70.0) | 78/135 (57.8) |
| | <10 | <.001 ^a | 0.45 | [0.33, 0.61] | 198/283 (70.0) | 53/99 (53.5) |
| | <11 | <.001 ^a | 0.45 | [0.32, 0.64] | 214/310 (69.0) | 37/72 (51.4) |
| | <12 | <.001 ^a | 0.37 | [0.25, 0.55] | 224/324 (69.1) | 27/58 (46.6) |
| | <13 | <.001 ^a | 0.29 | [0.17, 0.48] | 235/339 (69.3) | 16/43 (37.2) |
| | <14 | <.001 ^a | 0.17 | [0.08, 0.36] | 244/352 (69.3) | 7/30 (23.3) |
| | <15 | <.001 ^a | 0.16 | [0.07, 0.39] | 246/357 (68.9) | 5/25 (20.0) |
| | <16 | <.001 ^a | 0.14 | [0.05, 0.38] | 247/360 (68.6) | 4/22 (18.2) |
| | <17 | <.001 ^a | 0.11 | [0.04, 0.36] | 248/362 (68.5) | 3/20 (15.0) |
| | <18 | <.001 ^a | 0.09 | [0.02, 0.36] | 249/365 (68.2) | 2/17 (11.8) |
| | <19 | 0.003 ^a | 0.05 | [0.01, 0.37] | 250/367 (68.1) | 1/15 (6.7) |
| | <20 | 0.012 ^a | 0.08 | [0.01, 0.58] | 250/371 (67.4) | 1/11 (9.1) |
| | <22 | 0.018 ^a | 0.09 | [0.01, 0.67] | 250/373 (67.0) | 1/9 (11.1) |
| | <23 | 0.022 ^a | 0.10 | [0.01, 0.72] | 250/374 (66.8) | 1/8 (12.5) |
| | <24 | 0.034 ^a | 0.12 | [0.02, 0.85] | 250/376 (66.5) | 1/6 (16.7) |
| | <25 | 0.976 | 0.00 | [0.00,] | 251/378 (66.4) | 0/4 (0.0) |
| | <26 | 0.968 | 0.00 | [0.00, 1.47E268] | 251/379 (66.2) | 0/3 (0.0) |
| | <33 | 0.973 | 0.00 | [0.00,] | 251/380 (66.1) | 0/2 (0.0) |
| | <38 | 0.973 | 0.00 | [0.00, 2.21E292] | 251/381 (65.9) | 0/1 (0.0) |
| Tumor load (g) - Optimal cut | <26000 | 0.037 ^a | 1.78 | [1.04, 3.05] | 237/362 (65.5) | 14/20 (70.0) |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <4300 | 0.034 ^a | 1.31 | [1.02, 1.68] | 116/200 (58.0) | 135/182 (74.2) |
| | <5100 | 0.020 ^a | 1.34 | [1.05, 1.72] | 124/213 (58.2) | 127/169 (75.1) |
| | <5200 | 0.041 ^a | 1.30 | [1.01, 1.66] | 128/218 (58.7) | 123/164 (75.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Data Cutoff Date: 27JAN2021

Table 4.1-s: rPFS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <5400 | 0.047 ^a | 1.29 | [1.00, 1.65] | 133/224 (59.4) | 118/158 (74.7) |
| | <5700 | 0.022 ^a | 1.34 | [1.04, 1.71] | 136/229 (59.4) | 115/153 (75.2) |
| | <5800 | 0.028 ^a | 1.32 | [1.03, 1.69] | 138/231 (59.7) | 113/151 (74.8) |
| | <5900 | 0.041 ^a | 1.30 | [1.01, 1.66] | 140/233 (60.1) | 111/149 (74.5) |
| | <6800 | 0.031 ^a | 1.32 | [1.03, 1.71] | 153/252 (60.7) | 98/130 (75.4) |
| | <6900 | 0.031 ^a | 1.32 | [1.03, 1.71] | 154/253 (60.9) | 97/129 (75.2) |
| | <7100 | 0.024 ^a | 1.34 | [1.04, 1.73] | 155/255 (60.8) | 96/127 (75.6) |
| | <7200 | 0.014 ^a | 1.38 | [1.07, 1.78] | 155/256 (60.5) | 96/126 (76.2) |
| | <7300 | 0.013 ^a | 1.38 | [1.07, 1.78] | 156/257 (60.7) | 95/125 (76.0) |
| | <7600 | 0.017 ^a | 1.37 | [1.06, 1.77] | 158/259 (61.0) | 93/123 (75.6) |
| | <7700 | 0.023 ^a | 1.35 | [1.04, 1.74] | 159/260 (61.2) | 92/122 (75.4) |
| | <7800 | 0.011 ^a | 1.39 | [1.08, 1.80] | 159/261 (60.9) | 92/121 (76.0) |
| | <7900 | 0.017 ^a | 1.37 | [1.06, 1.77] | 161/263 (61.2) | 90/119 (75.6) |
| | <8100 | 0.014 ^a | 1.39 | [1.07, 1.80] | 163/266 (61.3) | 88/116 (75.9) |
| | <8300 | 0.012 ^a | 1.40 | [1.08, 1.82] | 165/268 (61.6) | 86/114 (75.4) |
| | <8400 | 0.016 ^a | 1.38 | [1.06, 1.79] | 166/269 (61.7) | 85/113 (75.2) |
| | <8600 | 0.018 ^a | 1.37 | [1.06, 1.79] | 167/270 (61.9) | 84/112 (75.0) |
| | <8700 | 0.016 ^a | 1.38 | [1.06, 1.80] | 168/271 (62.0) | 83/111 (74.8) |
| | <9000 | 0.020 ^a | 1.37 | [1.05, 1.78] | 169/272 (62.1) | 82/110 (74.5) |
| | <9100 | 0.035 ^a | 1.33 | [1.02, 1.74] | 171/274 (62.4) | 80/108 (74.1) |
| | <9200 | 0.043 ^a | 1.32 | [1.01, 1.72] | 172/275 (62.5) | 79/107 (73.8) |
| | <9400 | 0.048 ^a | 1.31 | [1.00, 1.71] | 173/276 (62.7) | 78/106 (73.6) |
| | <13700 | 0.047 ^a | 1.36 | [1.00, 1.83] | 196/310 (63.2) | 55/72 (76.4) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Final Version

Table 4.1-s: rPFS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <16100 | 0.025 ^a | 1.49 | [1.05, 2.10] | 213/332 (64.2) | 38/50 (76.0) |
| | <16200 | 0.026 ^a | 1.49 | [1.05, 2.12] | 214/333 (64.3) | 37/49 (75.5) |
| | <16400 | 0.026 ^a | 1.49 | [1.05, 2.12] | 214/334 (64.1) | 37/48 (77.1) |
| | <16600 | 0.042 ^a | 1.45 | [1.01, 2.06] | 215/335 (64.2) | 36/47 (76.6) |
| | <16800 | 0.031 ^a | 1.48 | [1.04, 2.11] | 215/336 (64.0) | 36/46 (78.3) |
| | <17100 | 0.048 ^a | 1.44 | [1.00, 2.05] | 216/337 (64.1) | 35/45 (77.8) |
| | <22600 | 0.027 ^a | 1.61 | [1.06, 2.46] | 227/351 (64.7) | 24/31 (77.4) |
| | <22900 | 0.020 ^a | 1.67 | [1.08, 2.56] | 228/352 (64.8) | 23/30 (76.7) |
| | <23000 | 0.016 ^a | 1.71 | [1.10, 2.66] | 229/353 (64.9) | 22/29 (75.9) |
| | <23200 | 0.026 ^a | 1.67 | [1.06, 2.61] | 230/354 (65.0) | 21/28 (75.0) |
| | <23400 | 0.039 ^a | 1.62 | [1.02, 2.56] | 231/355 (65.1) | 20/27 (74.1) |
| | <23800 | 0.040 ^a | 1.64 | [1.02, 2.62] | 232/356 (65.2) | 19/26 (73.1) |
| | <25100 | 0.031 ^a | 1.75 | [1.05, 2.91] | 235/360 (65.3) | 16/22 (72.7) |
| | <25800 | 0.042 ^a | 1.72 | [1.02, 2.90] | 236/361 (65.4) | 15/21 (71.4) |
| | <26000 | 0.037 ^a | 1.78 | [1.04, 3.05] | 237/362 (65.5) | 14/20 (70.0) |
| Tumor load (g) - All cuts | <100 | 0.252 | 1.95 | [0.62, 6.08] | 3/8 (37.5) | 248/374 (66.3) |
| | <200 | 0.234 | 1.58 | [0.74, 3.35] | 7/16 (43.8) | 244/366 (66.7) |
| | <300 | 0.704 | 1.10 | [0.66, 1.83] | 16/30 (53.3) | 235/352 (66.8) |
| | <400 | 0.590 | 1.13 | [0.72, 1.77] | 21/40 (52.5) | 230/342 (67.3) |
| | <500 | 0.529 | 1.14 | [0.75, 1.74] | 24/46 (52.2) | 227/336 (67.6) |
| | <600 | 0.970 | 0.99 | [0.67, 1.46] | 29/51 (56.9) | 222/331 (67.1) |
| | <700 | 0.961 | 1.01 | [0.71, 1.44] | 35/59 (59.3) | 216/323 (66.9) |
| | <800 | 0.831 | 0.96 | [0.68, 1.37] | 37/61 (60.7) | 214/321 (66.7) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Table 4.1-s: rPFS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|---------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <900 | 0.825 | 1.04 | [0.74, 1.46] | 39/68 (57.4) | 212/314 (67.5) |
| | <1000 | 0.783 | 1.05 | [0.75, 1.47] | 41/72 (56.9) | 210/310 (67.7) |
| | <1100 | 0.290 | 1.20 | [0.86, 1.67] | 42/77 (54.5) | 209/305 (68.5) |
| | <1200 | 0.209 | 1.23 | [0.89, 1.69] | 46/84 (54.8) | 205/298 (68.8) |
| | <1300 | 0.209 | 1.22 | [0.89, 1.67] | 49/89 (55.1) | 202/293 (68.9) |
| | <1400 | 0.239 | 1.20 | [0.89, 1.63] | 52/93 (55.9) | 199/289 (68.9) |
| | <1500 | 0.199 | 1.22 | [0.90, 1.66] | 52/94 (55.3) | 199/288 (69.1) |
| | <1600 | 0.177 | 1.23 | [0.91, 1.66] | 54/96 (56.3) | 197/286 (68.9) |
| | <1700 | 0.337 | 1.15 | [0.86, 1.53] | 63/107 (58.9) | 188/275 (68.4) |
| | <1800 | 0.567 | 1.08 | [0.82, 1.43] | 69/114 (60.5) | 182/268 (67.9) |
| | <1900 | 0.396 | 1.13 | [0.86, 1.48] | 72/120 (60.0) | 179/262 (68.3) |
| | <2000 | 0.347 | 1.14 | [0.87, 1.50] | 73/122 (59.8) | 178/260 (68.5) |
| | <2100 | 0.326 | 1.15 | [0.87, 1.50] | 74/124 (59.7) | 177/258 (68.6) |
| | <2200 | 0.274 | 1.16 | [0.89, 1.53] | 74/125 (59.2) | 177/257 (68.9) |
| | <2300 | 0.227 | 1.18 | [0.90, 1.55] | 75/129 (58.1) | 176/253 (69.6) |
| | <2400 | 0.177 | 1.20 | [0.92, 1.57] | 77/133 (57.9) | 174/249 (69.9) |
| | <2500 | 0.168 | 1.21 | [0.92, 1.57] | 80/139 (57.6) | 171/243 (70.4) |
| | <2600 | 0.119 | 1.23 | [0.95, 1.60] | 83/144 (57.6) | 168/238 (70.6) |
| | <2700 | 0.104 | 1.24 | [0.96, 1.61] | 85/148 (57.4) | 166/234 (70.9) |
| | <2800 | 0.127 | 1.23 | [0.94, 1.59] | 86/149 (57.7) | 165/233 (70.8) |
| | <2900 | 0.173 | 1.20 | [0.92, 1.55] | 88/151 (58.3) | 163/231 (70.6) |
| | <3000 | 0.270 | 1.16 | [0.89, 1.49] | 92/157 (58.6) | 159/225 (70.7) |
| | <3100 | 0.320 | 1.14 | [0.88, 1.47] | 94/159 (59.1) | 157/223 (70.4) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company

68Ga-PSMA-11 Quantitative analysis

Final Version

Table 4.1-s: rPFS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <3200 | 0.402 | 1.11 | [0.86, 1.44] | 97/163 (59.5) | 154/219 (70.3) |
| | <3300 | 0.486 | 1.09 | [0.85, 1.41] | 102/169 (60.4) | 149/213 (70.0) |
| | <3400 | 0.390 | 1.12 | [0.87, 1.44] | 102/170 (60.0) | 149/212 (70.3) |
| | <3500 | 0.446 | 1.10 | [0.86, 1.42] | 104/172 (60.5) | 147/210 (70.0) |
| | <3600 | 0.525 | 1.08 | [0.84, 1.39] | 105/173 (60.7) | 146/209 (69.9) |
| | <3700 | 0.524 | 1.08 | [0.84, 1.39] | 106/175 (60.6) | 145/207 (70.0) |
| | <3800 | 0.353 | 1.13 | [0.88, 1.44] | 110/182 (60.4) | 141/200 (70.5) |
| | <3900 | 0.241 | 1.16 | [0.90, 1.49] | 111/185 (60.0) | 140/197 (71.1) |
| | <4000 | 0.136 | 1.21 | [0.94, 1.55] | 112/188 (59.6) | 139/194 (71.6) |
| | <4100 | 0.103 | 1.23 | [0.96, 1.58] | 113/191 (59.2) | 138/191 (72.3) |
| | <4200 | 0.070 | 1.26 | [0.98, 1.61] | 115/196 (58.7) | 136/186 (73.1) |
| | <4300 | 0.034 ^a | 1.31 | [1.02, 1.68] | 116/200 (58.0) | 135/182 (74.2) |
| | <4500 | 0.063 | 1.27 | [0.99, 1.62] | 119/203 (58.6) | 132/179 (73.7) |
| | <4600 | 0.074 | 1.25 | [0.98, 1.61] | 120/204 (58.8) | 131/178 (73.6) |
| | <4700 | 0.060 | 1.27 | [0.99, 1.63] | 121/206 (58.7) | 130/176 (73.9) |
| | <4900 | 0.059 | 1.27 | [0.99, 1.63] | 123/208 (59.1) | 128/174 (73.6) |
| | <5000 | 0.071 | 1.26 | [0.98, 1.61] | 124/209 (59.3) | 127/173 (73.4) |
| | <5100 | 0.020 ^a | 1.34 | [1.05, 1.72] | 124/213 (58.2) | 127/169 (75.1) |
| | <5200 | 0.041 ^a | 1.30 | [1.01, 1.66] | 128/218 (58.7) | 123/164 (75.0) |
| | <5300 | 0.063 | 1.26 | [0.99, 1.62] | 132/222 (59.5) | 119/160 (74.4) |
| | <5400 | 0.047 ^a | 1.29 | [1.00, 1.65] | 133/224 (59.4) | 118/158 (74.7) |
| | <5500 | 0.058 | 1.27 | [0.99, 1.63] | 134/225 (59.6) | 117/157 (74.5) |
| | <5600 | 0.064 | 1.26 | [0.99, 1.62] | 135/226 (59.7) | 116/156 (74.4) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.1-s: rPFS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <5700 | 0.022 ^a | 1.34 | [1.04, 1.71] | 136/229 (59.4) | 115/153 (75.2) |
| | <5800 | 0.028 ^a | 1.32 | [1.03, 1.69] | 138/231 (59.7) | 113/151 (74.8) |
| | <5900 | 0.041 ^a | 1.30 | [1.01, 1.66] | 140/233 (60.1) | 111/149 (74.5) |
| | <6000 | 0.061 | 1.27 | [0.99, 1.63] | 142/235 (60.4) | 109/147 (74.1) |
| | <6100 | 0.079 | 1.25 | [0.97, 1.61] | 143/236 (60.6) | 108/146 (74.0) |
| | <6300 | 0.060 | 1.27 | [0.99, 1.63] | 144/239 (60.3) | 107/143 (74.8) |
| | <6400 | 0.064 | 1.27 | [0.99, 1.63] | 145/241 (60.2) | 106/141 (75.2) |
| | <6500 | 0.084 | 1.25 | [0.97, 1.60] | 146/242 (60.3) | 105/140 (75.0) |
| | <6600 | 0.125 | 1.22 | [0.95, 1.57] | 149/245 (60.8) | 102/137 (74.5) |
| | <6700 | 0.070 | 1.26 | [0.98, 1.63] | 151/249 (60.6) | 100/133 (75.2) |
| | <6800 | 0.031 ^a | 1.32 | [1.03, 1.71] | 153/252 (60.7) | 98/130 (75.4) |
| | <6900 | 0.031 ^a | 1.32 | [1.03, 1.71] | 154/253 (60.9) | 97/129 (75.2) |
| | <7100 | 0.024 ^a | 1.34 | [1.04, 1.73] | 155/255 (60.8) | 96/127 (75.6) |
| | <7200 | 0.014 ^a | 1.38 | [1.07, 1.78] | 155/256 (60.5) | 96/126 (76.2) |
| | <7300 | 0.013 ^a | 1.38 | [1.07, 1.78] | 156/257 (60.7) | 95/125 (76.0) |
| | <7600 | 0.017 ^a | 1.37 | [1.06, 1.77] | 158/259 (61.0) | 93/123 (75.6) |
| | <7700 | 0.023 ^a | 1.35 | [1.04, 1.74] | 159/260 (61.2) | 92/122 (75.4) |
| | <7800 | 0.011 ^a | 1.39 | [1.08, 1.80] | 159/261 (60.9) | 92/121 (76.0) |
| | <7900 | 0.017 ^a | 1.37 | [1.06, 1.77] | 161/263 (61.2) | 90/119 (75.6) |
| | <8100 | 0.014 ^a | 1.39 | [1.07, 1.80] | 163/266 (61.3) | 88/116 (75.9) |
| | <8300 | 0.012 ^a | 1.40 | [1.08, 1.82] | 165/268 (61.6) | 86/114 (75.4) |
| | <8400 | 0.016 ^a | 1.38 | [1.06, 1.79] | 166/269 (61.7) | 85/113 (75.2) |
| | <8600 | 0.018 ^a | 1.37 | [1.06, 1.79] | 167/270 (61.9) | 84/112 (75.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company

68Ga-PSMA-11 Quantitative analysis

Final Version

Table 4.1-s: rPFS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|---------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <8700 | 0.016 ^a | 1.38 | [1.06, 1.80] | 168/271 (62.0) | 83/111 (74.8) |
| | <9000 | 0.020 ^a | 1.37 | [1.05, 1.78] | 169/272 (62.1) | 82/110 (74.5) |
| | <9100 | 0.035 ^a | 1.33 | [1.02, 1.74] | 171/274 (62.4) | 80/108 (74.1) |
| | <9200 | 0.043 ^a | 1.32 | [1.01, 1.72] | 172/275 (62.5) | 79/107 (73.8) |
| | <9400 | 0.048 ^a | 1.31 | [1.00, 1.71] | 173/276 (62.7) | 78/106 (73.6) |
| | <9500 | 0.062 | 1.29 | [0.99, 1.69] | 174/277 (62.8) | 77/105 (73.3) |
| | <9700 | 0.099 | 1.26 | [0.96, 1.65] | 177/280 (63.2) | 74/102 (72.5) |
| | <9900 | 0.064 | 1.29 | [0.98, 1.70] | 177/281 (63.0) | 74/101 (73.3) |
| | <10000 | 0.107 | 1.25 | [0.95, 1.65] | 180/284 (63.4) | 71/98 (72.4) |
| | <10200 | 0.168 | 1.22 | [0.92, 1.60] | 182/286 (63.6) | 69/96 (71.9) |
| | <10400 | 0.175 | 1.21 | [0.92, 1.60] | 183/287 (63.8) | 68/95 (71.6) |
| | <10600 | 0.121 | 1.25 | [0.94, 1.65] | 183/288 (63.5) | 68/94 (72.3) |
| | <10900 | 0.126 | 1.24 | [0.94, 1.65] | 184/289 (63.7) | 67/93 (72.0) |
| | <11100 | 0.114 | 1.25 | [0.95, 1.66] | 184/290 (63.4) | 67/92 (72.8) |
| | <11200 | 0.079 | 1.29 | [0.97, 1.70] | 184/291 (63.2) | 67/91 (73.6) |
| | <11300 | 0.096 | 1.27 | [0.96, 1.69] | 186/294 (63.3) | 65/88 (73.9) |
| | <11500 | 0.090 | 1.28 | [0.96, 1.70] | 187/295 (63.4) | 64/87 (73.6) |
| | <11600 | 0.086 | 1.28 | [0.97, 1.71] | 188/296 (63.5) | 63/86 (73.3) |
| | <12200 | 0.136 | 1.25 | [0.93, 1.66] | 190/298 (63.8) | 61/84 (72.6) |
| | <12300 | 0.136 | 1.25 | [0.93, 1.66] | 190/299 (63.5) | 61/83 (73.5) |
| | <12500 | 0.128 | 1.25 | [0.94, 1.68] | 191/300 (63.7) | 60/82 (73.2) |
| | <12700 | 0.144 | 1.24 | [0.93, 1.67] | 193/303 (63.7) | 58/79 (73.4) |
| | <12900 | 0.171 | 1.23 | [0.91, 1.65] | 194/305 (63.6) | 57/77 (74.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.1-s: rPFS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <13100 | 0.195 | 1.22 | [0.90, 1.64] | 195/306 (63.7) | 56/76 (73.7) |
| | <13400 | 0.156 | 1.24 | [0.92, 1.68] | 196/307 (63.8) | 55/75 (73.3) |
| | <13500 | 0.054 | 1.34 | [0.99, 1.81] | 196/309 (63.4) | 55/73 (75.3) |
| | <13700 | 0.047 ^a | 1.36 | [1.00, 1.83] | 196/310 (63.2) | 55/72 (76.4) |
| | <13800 | 0.063 | 1.33 | [0.99, 1.80] | 197/311 (63.3) | 54/71 (76.1) |
| | <13900 | 0.121 | 1.28 | [0.94, 1.74] | 200/314 (63.7) | 51/68 (75.0) |
| | <14100 | 0.139 | 1.26 | [0.93, 1.72] | 201/315 (63.8) | 50/67 (74.6) |
| | <14400 | 0.159 | 1.25 | [0.92, 1.71] | 202/316 (63.9) | 49/66 (74.2) |
| | <14700 | 0.206 | 1.23 | [0.89, 1.68] | 203/317 (64.0) | 48/65 (73.8) |
| | <14800 | 0.231 | 1.21 | [0.88, 1.67] | 204/318 (64.2) | 47/64 (73.4) |
| | <15000 | 0.202 | 1.23 | [0.89, 1.70] | 206/321 (64.2) | 45/61 (73.8) |
| | <15100 | 0.213 | 1.23 | [0.89, 1.71] | 208/323 (64.4) | 43/59 (72.9) |
| | <15400 | 0.263 | 1.21 | [0.87, 1.69] | 210/325 (64.6) | 41/57 (71.9) |
| | <15500 | 0.076 | 1.35 | [0.97, 1.89] | 210/327 (64.2) | 41/55 (74.5) |
| | <15600 | 0.076 | 1.35 | [0.97, 1.89] | 210/328 (64.0) | 41/54 (75.9) |
| | <15900 | 0.081 | 1.35 | [0.96, 1.90] | 211/329 (64.1) | 40/53 (75.5) |
| | <16000 | 0.057 | 1.39 | [0.99, 1.96] | 212/331 (64.0) | 39/51 (76.5) |
| | <16100 | 0.025 ^a | 1.49 | [1.05, 2.10] | 213/332 (64.2) | 38/50 (76.0) |
| | <16200 | 0.026 ^a | 1.49 | [1.05, 2.12] | 214/333 (64.3) | 37/49 (75.5) |
| | <16400 | 0.026 ^a | 1.49 | [1.05, 2.12] | 214/334 (64.1) | 37/48 (77.1) |
| | <16600 | 0.042 ^a | 1.45 | [1.01, 2.06] | 215/335 (64.2) | 36/47 (76.6) |
| | <16800 | 0.031 ^a | 1.48 | [1.04, 2.11] | 215/336 (64.0) | 36/46 (78.3) |
| | <17100 | 0.048 ^a | 1.44 | [1.00, 2.05] | 216/337 (64.1) | 35/45 (77.8) |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is '<'

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Data Cutoff Date: 27JAN2021

Table 4.1-s: rPFS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <17200 | 0.061 | 1.41 | [0.98, 2.03] | 217/338 (64.2) | 34/44 (77.3) |
| | <18000 | 0.083 | 1.38 | [0.96, 2.00] | 218/339 (64.3) | 33/43 (76.7) |
| | <18500 | 0.053 | 1.44 | [1.00, 2.08] | 218/340 (64.1) | 33/42 (78.6) |
| | <18900 | 0.065 | 1.42 | [0.98, 2.06] | 219/341 (64.2) | 32/41 (78.0) |
| | <19800 | 0.079 | 1.41 | [0.96, 2.07] | 221/343 (64.4) | 30/39 (76.9) |
| | <19900 | 0.105 | 1.38 | [0.93, 2.03] | 222/344 (64.5) | 29/38 (76.3) |
| | <20100 | 0.161 | 1.33 | [0.89, 1.97] | 223/345 (64.6) | 28/37 (75.7) |
| | <20700 | 0.154 | 1.34 | [0.90, 2.00] | 224/346 (64.7) | 27/36 (75.0) |
| | <21400 | 0.131 | 1.37 | [0.91, 2.06] | 225/347 (64.8) | 26/35 (74.3) |
| | <21600 | 0.107 | 1.41 | [0.93, 2.13] | 226/348 (64.9) | 25/34 (73.5) |
| | <22500 | 0.072 | 1.47 | [0.97, 2.25] | 227/350 (64.9) | 24/32 (75.0) |
| | <22600 | 0.027 ^a | 1.61 | [1.06, 2.46] | 227/351 (64.7) | 24/31 (77.4) |
| | <22900 | 0.020 ^a | 1.67 | [1.08, 2.56] | 228/352 (64.8) | 23/30 (76.7) |
| | <23000 | 0.016 ^a | 1.71 | [1.10, 2.66] | 229/353 (64.9) | 22/29 (75.9) |
| | <23200 | 0.026 ^a | 1.67 | [1.06, 2.61] | 230/354 (65.0) | 21/28 (75.0) |
| | <23400 | 0.039 ^a | 1.62 | [1.02, 2.56] | 231/355 (65.1) | 20/27 (74.1) |
| | <23800 | 0.040 ^a | 1.64 | [1.02, 2.62] | 232/356 (65.2) | 19/26 (73.1) |
| | <23900 | 0.052 | 1.61 | [1.00, 2.61] | 233/357 (65.3) | 18/25 (72.0) |
| | <24000 | 0.060 | 1.60 | [0.98, 2.63] | 234/358 (65.4) | 17/24 (70.8) |
| | <24900 | 0.114 | 1.51 | [0.91, 2.50] | 235/359 (65.5) | 16/23 (69.6) |
| | <25100 | 0.031 ^a | 1.75 | [1.05, 2.91] | 235/360 (65.3) | 16/22 (72.7) |
| | <25800 | 0.042 ^a | 1.72 | [1.02, 2.90] | 236/361 (65.4) | 15/21 (71.4) |
| | <26000 | 0.037 ^a | 1.78 | [1.04, 3.05] | 237/362 (65.5) | 14/20 (70.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.1-s: rPFS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|---------|--------------|---------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <26200 | 0.081 | 1.65 | [0.94, 2.88] | 238/363 (65.6) | 13/19 (68.4) |
| | <26600 | 0.168 | 1.53 | [0.84, 2.81] | 240/365 (65.8) | 11/17 (64.7) |
| | <27500 | 0.268 | 1.43 | [0.76, 2.70] | 241/366 (65.8) | 10/16 (62.5) |
| | <28700 | 0.456 | 1.29 | [0.66, 2.51] | 242/367 (65.9) | 9/15 (60.0) |
| | <29800 | 0.708 | 1.14 | [0.57, 2.32] | 243/368 (66.0) | 8/14 (57.1) |
| | <30900 | 0.932 | 1.03 | [0.49, 2.19] | 244/369 (66.1) | 7/13 (53.8) |
| | <31000 | 0.688 | 1.17 | [0.55, 2.48] | 244/370 (65.9) | 7/12 (58.3) |
| | <31700 | 0.992 | 1.00 | [0.44, 2.24] | 245/371 (66.0) | 6/11 (54.5) |
| | <32200 | 0.993 | 1.00 | [0.44, 2.24] | 245/372 (65.9) | 6/10 (60.0) |
| | <32400 | 0.568 | 1.27 | [0.56, 2.85] | 245/373 (65.7) | 6/9 (66.7) |
| | <32700 | 0.470 | 1.35 | [0.60, 3.03] | 245/374 (65.5) | 6/8 (75.0) |
| | <34800 | 0.527 | 1.33 | [0.55, 3.23] | 246/375 (65.6) | 5/7 (71.4) |
| | <37100 | 0.862 | 1.09 | [0.41, 2.94] | 247/376 (65.7) | 4/6 (66.7) |
| | <39600 | 0.995 | 1.00 | [0.32, 3.11] | 248/377 (65.8) | 3/5 (60.0) |
| | <41100 | 0.731 | 0.78 | [0.19, 3.15] | 249/378 (65.9) | 2/4 (50.0) |
| | <43600 | 0.924 | 0.93 | [0.23, 3.75] | 249/379 (65.7) | 2/3 (66.7) |
| | <47700 | 0.524 | 0.53 | [0.07, 3.77] | 250/380 (65.8) | 1/2 (50.0) |
| | <54100 | 0.546 | 1.83 | [0.26, 13.09] | 250/381 (65.6) | 1/1 (100.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is '<'

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Source data: adsl.xpt, adtte.xpt

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68Ga-PSMA-11 Quantitative analysis

Final Version

Table 4.2: rPFS multivariate Cox proportional hazards model - with optimal cut points - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|---|--------------|--------------|--------------------|
| Bone SUVmean (g/ml) <16 vs. >=16 ^c | 0.13 | [0.03, 0.52] | 0.004 ^a |
| Tumor load (g) <25500 vs. >=25500 ^c | 2.44 | [1.25, 4.77] | 0.009 ^a |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is '<'.

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ut-hr.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.2-s: rPFS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmean (g/ml) - Optimal cut | <16 | 0.004 ^a | 0.13 | [0.03, 0.52] | 234/343 (68.2) | 2/10 (20.0) |
| SUVmean (g/ml) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <5 | 0.002 ^a | 0.60 | [0.44, 0.82] | 50/75 (66.7) | 186/278 (66.9) |
| | <6 | <.001 ^a | 0.54 | [0.41, 0.70] | 95/135 (70.4) | 141/218 (64.7) |
| | <7 | <.001 ^a | 0.53 | [0.40, 0.69] | 130/187 (69.5) | 106/166 (63.9) |
| | <8 | <.001 ^a | 0.56 | [0.43, 0.75] | 161/236 (68.2) | 75/117 (64.1) |
| | <9 | <.001 ^a | 0.44 | [0.32, 0.62] | 192/277 (69.3) | 44/76 (57.9) |
| | <10 | <.001 ^a | 0.43 | [0.29, 0.63] | 205/295 (69.5) | 31/58 (53.4) |
| | <11 | <.001 ^a | 0.42 | [0.27, 0.67] | 216/313 (69.0) | 20/40 (50.0) |
| | <12 | <.001 ^a | 0.40 | [0.24, 0.66] | 220/321 (68.5) | 16/32 (50.0) |
| | <13 | <.001 ^a | 0.24 | [0.12, 0.48] | 228/331 (68.9) | 8/22 (36.4) |
| | <14 | <.001 ^a | 0.17 | [0.06, 0.47] | 232/338 (68.6) | 4/15 (26.7) |
| | <15 | <.001 ^a | 0.14 | [0.04, 0.44] | 233/339 (68.7) | 3/14 (21.4) |
| | <16 | 0.004 ^a | 0.13 | [0.03, 0.52] | 234/343 (68.2) | 2/10 (20.0) |
| SUVmean (g/ml) - All cuts | <2 | 0.001 ^a | 0.04 | [0.00, 0.27] | 1/1 (100.0) | 235/352 (66.8) |
| | <3 | <.001 ^a | 0.05 | [0.01, 0.22] | 2/2 (100.0) | 234/351 (66.7) |
| | <4 | 0.477 | 0.84 | [0.53, 1.35] | 19/29 (65.5) | 217/324 (67.0) |
| | <5 | 0.002 ^a | 0.60 | [0.44, 0.82] | 50/75 (66.7) | 186/278 (66.9) |
| | <6 | <.001 ^a | 0.54 | [0.41, 0.70] | 95/135 (70.4) | 141/218 (64.7) |
| | <7 | <.001 ^a | 0.53 | [0.40, 0.69] | 130/187 (69.5) | 106/166 (63.9) |
| | <8 | <.001 ^a | 0.56 | [0.43, 0.75] | 161/236 (68.2) | 75/117 (64.1) |
| | <9 | <.001 ^a | 0.44 | [0.32, 0.62] | 192/277 (69.3) | 44/76 (57.9) |
| | <10 | <.001 ^a | 0.43 | [0.29, 0.63] | 205/295 (69.5) | 31/58 (53.4) |
| | <11 | <.001 ^a | 0.42 | [0.27, 0.67] | 216/313 (69.0) | 20/40 (50.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.2-s: rPFS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|------------------------------|---|--------------------|--------------------|------------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmean (g/ml) - All cuts | <12 | <.001 ^a | 0.40 | [0.24, 0.66] | 220/321 (68.5) | 16/32 (50.0) |
| | <13 | <.001 ^a | 0.24 | [0.12, 0.48] | 228/331 (68.9) | 8/22 (36.4) |
| | <14 | <.001 ^a | 0.17 | [0.06, 0.47] | 232/338 (68.6) | 4/15 (26.7) |
| | <15 | <.001 ^a | 0.14 | [0.04, 0.44] | 233/339 (68.7) | 3/14 (21.4) |
| | <16 | 0.004 ^a | 0.13 | [0.03, 0.52] | 234/343 (68.2) | 2/10 (20.0) |
| | <18 | 0.007 ^a | 0.07 | [0.01, 0.47] | 235/344 (68.3) | 1/9 (11.1) |
| | <19 | 0.969 | 0.00 | [0.00, 2.19E299] | 236/347 (68.0) | 0/6 (0.0) |
| | <22 | 0.976 | 0.00 | [0.00,] | 236/349 (67.6) | 0/4 (0.0) |
| | <23 | 0.966 | 0.00 | [0.00, 2.54E256] | 236/350 (67.4) | 0/3 (0.0) |
| | <26 | 0.973 | 0.00 | [0.00,] | 236/351 (67.2) | 0/2 (0.0) |
| Tumor load (g) - Optimal cut | <25500 | 0.006 ^a | 2.54 | [1.30, 4.97] | 227/342 (66.4) | 9/11 (81.8) |
| | Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <4200 | 0.046 ^a | 1.30 | [1.01, 1.68] | 131/212 (61.8) |
| | | <15900 | 0.034 ^a | 1.53 | [1.03, 2.26] | 207/318 (65.1) |
| | | <17100 | 0.032 ^a | 1.57 | [1.04, 2.36] | 210/322 (65.2) |
| | | <17500 | 0.047 ^a | 1.53 | [1.01, 2.32] | 211/323 (65.3) |
| | | <18500 | 0.030 ^a | 1.60 | [1.05, 2.44] | 212/325 (65.2) |
| | | <18600 | 0.021 ^a | 1.67 | [1.08, 2.57] | 213/326 (65.3) |
| | | <19100 | 0.034 ^a | 1.61 | [1.04, 2.50] | 214/327 (65.4) |
| | | <19400 | 0.050 ^a | 1.57 | [1.00, 2.46] | 215/328 (65.5) |
| | | <21400 | 0.040 ^a | 1.68 | [1.02, 2.76] | 219/332 (66.0) |
| | | <22900 | 0.018 ^a | 1.89 | [1.12, 3.19] | 221/335 (66.0) |
| | | <23100 | 0.011 ^a | 2.02 | [1.17, 3.48] | 222/336 (66.1) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.2-s: rPFS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <23200 | 0.014 ^a | 2.02 | [1.15, 3.54] | 223/337 (66.2) | 13/16 (81.3) |
| | <23700 | 0.024 ^a | 1.95 | [1.09, 3.50] | 224/338 (66.3) | 12/15 (80.0) |
| | <23900 | 0.033 ^a | 1.94 | [1.06, 3.55] | 225/339 (66.4) | 11/14 (78.6) |
| | <24000 | 0.036 ^a | 1.97 | [1.05, 3.72] | 226/340 (66.5) | 10/13 (76.9) |
| | <25500 | 0.006 ^a | 2.54 | [1.30, 4.97] | 227/342 (66.4) | 9/11 (81.8) |
| | <25800 | 0.024 ^a | 2.26 | [1.11, 4.59] | 228/343 (66.5) | 8/10 (80.0) |
| Tumor load (g) - All cuts | <100 | 0.953 | 0.99 | [0.66, 1.48] | 27/40 (67.5) | 209/313 (66.8) |
| | <200 | 0.945 | 1.01 | [0.70, 1.46] | 34/50 (68.0) | 202/303 (66.7) |
| | <300 | 0.948 | 0.99 | [0.70, 1.39] | 40/62 (64.5) | 196/291 (67.4) |
| | <400 | 0.835 | 0.97 | [0.70, 1.34] | 45/72 (62.5) | 191/281 (68.0) |
| | <500 | 0.814 | 0.96 | [0.70, 1.32] | 50/80 (62.5) | 186/273 (68.1) |
| | <600 | 0.578 | 0.92 | [0.68, 1.24] | 55/85 (64.7) | 181/268 (67.5) |
| | <700 | 0.807 | 0.96 | [0.72, 1.29] | 59/92 (64.1) | 177/261 (67.8) |
| | <800 | 0.462 | 0.90 | [0.67, 1.20] | 63/96 (65.6) | 173/257 (67.3) |
| | <900 | 0.628 | 0.93 | [0.70, 1.24] | 67/104 (64.4) | 169/249 (67.9) |
| | <1000 | 0.847 | 0.97 | [0.73, 1.29] | 68/108 (63.0) | 168/245 (68.6) |
| | <1100 | 0.720 | 1.05 | [0.80, 1.39] | 70/114 (61.4) | 166/239 (69.5) |
| | <1200 | 0.486 | 1.10 | [0.84, 1.45] | 76/122 (62.3) | 160/231 (69.3) |
| | <1300 | 0.407 | 1.12 | [0.86, 1.47] | 80/128 (62.5) | 156/225 (69.3) |
| | <1400 | 0.549 | 1.09 | [0.83, 1.42] | 83/131 (63.4) | 153/222 (68.9) |
| | <1500 | 0.506 | 1.09 | [0.84, 1.43] | 84/133 (63.2) | 152/220 (69.1) |
| | <1600 | 0.481 | 1.10 | [0.84, 1.44] | 85/134 (63.4) | 151/219 (68.9) |
| | <1700 | 0.462 | 1.10 | [0.85, 1.44] | 90/141 (63.8) | 146/212 (68.9) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.2-s: rPFS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <1800 | 0.364 | 1.13 | [0.87, 1.46] | 94/150 (62.7) | 142/203 (70.0) |
| | <1900 | 0.381 | 1.12 | [0.87, 1.46] | 95/151 (62.9) | 141/202 (69.8) |
| | <2000 | 0.369 | 1.13 | [0.87, 1.46] | 97/153 (63.4) | 139/200 (69.5) |
| | <2200 | 0.416 | 1.11 | [0.86, 1.44] | 99/155 (63.9) | 137/198 (69.2) |
| | <2300 | 0.121 | 1.23 | [0.95, 1.59] | 101/163 (62.0) | 135/190 (71.1) |
| | <2400 | 0.184 | 1.19 | [0.92, 1.54] | 103/165 (62.4) | 133/188 (70.7) |
| | <2500 | 0.298 | 1.15 | [0.89, 1.48] | 107/170 (62.9) | 129/183 (70.5) |
| | <2600 | 0.278 | 1.15 | [0.89, 1.49] | 108/171 (63.2) | 128/182 (70.3) |
| | <2700 | 0.388 | 1.12 | [0.87, 1.45] | 110/173 (63.6) | 126/180 (70.0) |
| | <2800 | 0.538 | 1.08 | [0.84, 1.40] | 113/176 (64.2) | 123/177 (69.5) |
| | <2900 | 0.728 | 1.05 | [0.81, 1.35] | 116/179 (64.8) | 120/174 (69.0) |
| | <3000 | 0.714 | 1.05 | [0.81, 1.35] | 117/181 (64.6) | 119/172 (69.2) |
| | <3100 | 0.693 | 1.05 | [0.82, 1.36] | 120/186 (64.5) | 116/167 (69.5) |
| | <3200 | 0.549 | 1.08 | [0.84, 1.40] | 123/191 (64.4) | 113/162 (69.8) |
| | <3300 | 0.683 | 1.05 | [0.82, 1.36] | 127/196 (64.8) | 109/157 (69.4) |
| | <3600 | 0.651 | 1.06 | [0.82, 1.37] | 127/197 (64.5) | 109/156 (69.9) |
| | <3700 | 0.473 | 1.10 | [0.85, 1.42] | 128/201 (63.7) | 108/152 (71.1) |
| | <3800 | 0.220 | 1.17 | [0.91, 1.52] | 130/206 (63.1) | 106/147 (72.1) |
| | <3900 | 0.107 | 1.23 | [0.96, 1.60] | 130/208 (62.5) | 106/145 (73.1) |
| | <4000 | 0.115 | 1.23 | [0.95, 1.59] | 131/209 (62.7) | 105/144 (72.9) |
| | <4100 | 0.080 | 1.26 | [0.97, 1.63] | 131/210 (62.4) | 105/143 (73.4) |
| | <4200 | 0.046 ^a | 1.30 | [1.01, 1.68] | 131/212 (61.8) | 105/141 (74.5) |
| | <4300 | 0.054 | 1.29 | [1.00, 1.67] | 132/213 (62.0) | 104/140 (74.3) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.2-s: rPFS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|---------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <4500 | 0.085 | 1.25 | [0.97, 1.62] | 134/215 (62.3) | 102/138 (73.9) |
| | <4600 | 0.099 | 1.24 | [0.96, 1.61] | 135/216 (62.5) | 101/137 (73.7) |
| | <4700 | 0.076 | 1.26 | [0.98, 1.64] | 137/219 (62.6) | 99/134 (73.9) |
| | <4900 | 0.079 | 1.26 | [0.97, 1.63] | 138/220 (62.7) | 98/133 (73.7) |
| | <5000 | 0.094 | 1.25 | [0.96, 1.62] | 139/221 (62.9) | 97/132 (73.5) |
| | <5100 | 0.116 | 1.23 | [0.95, 1.60] | 141/224 (62.9) | 95/129 (73.6) |
| | <5200 | 0.168 | 1.20 | [0.93, 1.56] | 145/228 (63.6) | 91/125 (72.8) |
| | <5300 | 0.203 | 1.19 | [0.91, 1.54] | 146/229 (63.8) | 90/124 (72.6) |
| | <5400 | 0.155 | 1.21 | [0.93, 1.57] | 146/230 (63.5) | 90/123 (73.2) |
| | <5500 | 0.131 | 1.23 | [0.94, 1.60] | 148/232 (63.8) | 88/121 (72.7) |
| | <5600 | 0.125 | 1.23 | [0.94, 1.60] | 149/234 (63.7) | 87/119 (73.1) |
| | <5900 | 0.166 | 1.21 | [0.93, 1.57] | 151/237 (63.7) | 85/116 (73.3) |
| | <6100 | 0.209 | 1.19 | [0.91, 1.55] | 152/238 (63.9) | 84/115 (73.0) |
| | <6300 | 0.141 | 1.22 | [0.94, 1.59] | 152/239 (63.6) | 84/114 (73.7) |
| | <6500 | 0.077 | 1.27 | [0.97, 1.67] | 154/244 (63.1) | 82/109 (75.2) |
| | <6600 | 0.127 | 1.23 | [0.94, 1.62] | 157/247 (63.6) | 79/106 (74.5) |
| | <6700 | 0.065 | 1.29 | [0.98, 1.70] | 158/250 (63.2) | 78/103 (75.7) |
| | <6800 | 0.077 | 1.28 | [0.97, 1.68] | 160/252 (63.5) | 76/101 (75.2) |
| | <6900 | 0.077 | 1.28 | [0.97, 1.69] | 161/253 (63.6) | 75/100 (75.0) |
| | <7300 | 0.071 | 1.29 | [0.98, 1.70] | 163/255 (63.9) | 73/98 (74.5) |
| | <7400 | 0.081 | 1.28 | [0.97, 1.69] | 164/256 (64.1) | 72/97 (74.2) |
| | <7600 | 0.105 | 1.26 | [0.95, 1.66] | 165/257 (64.2) | 71/96 (74.0) |
| | <7800 | 0.093 | 1.27 | [0.96, 1.69] | 167/261 (64.0) | 69/92 (75.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.2-s: rPFS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|---------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <7900 | 0.122 | 1.25 | [0.94, 1.66] | 170/264 (64.4) | 66/89 (74.2) |
| | <8000 | 0.096 | 1.27 | [0.96, 1.70] | 171/266 (64.3) | 65/87 (74.7) |
| | <8100 | 0.100 | 1.27 | [0.95, 1.70] | 172/267 (64.4) | 64/86 (74.4) |
| | <8300 | 0.084 | 1.29 | [0.97, 1.72] | 173/268 (64.6) | 63/85 (74.1) |
| | <8400 | 0.116 | 1.26 | [0.94, 1.69] | 175/270 (64.8) | 61/83 (73.5) |
| | <8500 | 0.191 | 1.22 | [0.91, 1.64] | 177/272 (65.1) | 59/81 (72.8) |
| | <8600 | 0.222 | 1.20 | [0.89, 1.62] | 178/273 (65.2) | 58/80 (72.5) |
| | <8800 | 0.190 | 1.22 | [0.91, 1.65] | 180/275 (65.5) | 56/78 (71.8) |
| | <8900 | 0.236 | 1.20 | [0.89, 1.62] | 181/276 (65.6) | 55/77 (71.4) |
| | <9000 | 0.280 | 1.18 | [0.87, 1.60] | 182/277 (65.7) | 54/76 (71.1) |
| | <9100 | 0.348 | 1.16 | [0.85, 1.58] | 184/279 (65.9) | 52/74 (70.3) |
| | <9600 | 0.383 | 1.15 | [0.84, 1.57] | 185/281 (65.8) | 51/72 (70.8) |
| | <9700 | 0.402 | 1.14 | [0.84, 1.56] | 186/282 (66.0) | 50/71 (70.4) |
| | <9800 | 0.285 | 1.19 | [0.87, 1.62] | 186/283 (65.7) | 50/70 (71.4) |
| | <9900 | 0.365 | 1.16 | [0.84, 1.59] | 187/284 (65.8) | 49/69 (71.0) |
| | <10300 | 0.551 | 1.10 | [0.80, 1.52] | 190/287 (66.2) | 46/66 (69.7) |
| | <10400 | 0.516 | 1.11 | [0.81, 1.54] | 190/288 (66.0) | 46/65 (70.8) |
| | <10600 | 0.379 | 1.16 | [0.84, 1.60] | 190/289 (65.7) | 46/64 (71.9) |
| | <10700 | 0.477 | 1.13 | [0.81, 1.56] | 191/290 (65.9) | 45/63 (71.4) |
| | <10900 | 0.479 | 1.13 | [0.81, 1.56] | 192/291 (66.0) | 44/62 (71.0) |
| | <11100 | 0.390 | 1.16 | [0.83, 1.61] | 193/292 (66.1) | 43/61 (70.5) |
| | <11200 | 0.237 | 1.22 | [0.88, 1.70] | 193/294 (65.6) | 43/59 (72.9) |
| | <11500 | 0.189 | 1.25 | [0.90, 1.74] | 193/295 (65.4) | 43/58 (74.1) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.2-s: rPFS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <11600 | 0.133 | 1.29 | [0.93, 1.80] | 194/297 (65.3) | 42/56 (75.0) |
| | <12000 | 0.176 | 1.26 | [0.90, 1.77] | 195/299 (65.2) | 41/54 (75.9) |
| | <12100 | 0.157 | 1.28 | [0.91, 1.80] | 196/300 (65.3) | 40/53 (75.5) |
| | <12500 | 0.153 | 1.28 | [0.91, 1.80] | 196/301 (65.1) | 40/52 (76.9) |
| | <13400 | 0.205 | 1.25 | [0.89, 1.76] | 197/302 (65.2) | 39/51 (76.5) |
| | <13500 | 0.178 | 1.27 | [0.90, 1.79] | 197/303 (65.0) | 39/50 (78.0) |
| | <13600 | 0.114 | 1.32 | [0.93, 1.87] | 198/305 (64.9) | 38/48 (79.2) |
| | <13800 | 0.118 | 1.32 | [0.93, 1.88] | 199/306 (65.0) | 37/47 (78.7) |
| | <14000 | 0.173 | 1.28 | [0.90, 1.84] | 201/308 (65.3) | 35/45 (77.8) |
| | <14700 | 0.197 | 1.27 | [0.88, 1.83] | 202/309 (65.4) | 34/44 (77.3) |
| | <14800 | 0.223 | 1.26 | [0.87, 1.82] | 203/310 (65.5) | 33/43 (76.7) |
| | <15000 | 0.115 | 1.35 | [0.93, 1.95] | 203/311 (65.3) | 33/42 (78.6) |
| | <15100 | 0.089 | 1.38 | [0.95, 1.99] | 203/312 (65.1) | 33/41 (80.5) |
| | <15200 | 0.112 | 1.36 | [0.93, 1.98] | 205/314 (65.3) | 31/39 (79.5) |
| | <15500 | 0.093 | 1.39 | [0.95, 2.04] | 206/315 (65.4) | 30/38 (78.9) |
| | <15800 | 0.093 | 1.39 | [0.95, 2.04] | 206/316 (65.2) | 30/37 (81.1) |
| | <15900 | 0.034 ^a | 1.53 | [1.03, 2.26] | 207/318 (65.1) | 29/35 (82.9) |
| | <16000 | 0.088 | 1.42 | [0.95, 2.12] | 209/320 (65.3) | 27/33 (81.8) |
| | <17100 | 0.032 ^a | 1.57 | [1.04, 2.36] | 210/322 (65.2) | 26/31 (83.9) |
| | <17500 | 0.047 ^a | 1.53 | [1.01, 2.32] | 211/323 (65.3) | 25/30 (83.3) |
| | <17800 | 0.058 | 1.51 | [0.99, 2.30] | 212/324 (65.4) | 24/29 (82.8) |
| | <18500 | 0.030 ^a | 1.60 | [1.05, 2.44] | 212/325 (65.2) | 24/28 (85.7) |
| | <18600 | 0.021 ^a | 1.67 | [1.08, 2.57] | 213/326 (65.3) | 23/27 (85.2) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

Output ID: T-4-2-S 2021-08-30 20:13

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-cut-hr.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.2-s: rPFS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|---------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <19100 | 0.034 ^a | 1.61 | [1.04, 2.50] | 214/327 (65.4) | 22/26 (84.6) |
| | <19400 | 0.050 ^a | 1.57 | [1.00, 2.46] | 215/328 (65.5) | 21/25 (84.0) |
| | <20000 | 0.073 | 1.52 | [0.96, 2.41] | 216/329 (65.7) | 20/24 (83.3) |
| | <21200 | 0.062 | 1.58 | [0.98, 2.56] | 218/331 (65.9) | 18/22 (81.8) |
| | <21400 | 0.040 ^a | 1.68 | [1.02, 2.76] | 219/332 (66.0) | 17/21 (81.0) |
| | <21500 | 0.063 | 1.62 | [0.97, 2.70] | 220/333 (66.1) | 16/20 (80.0) |
| | <21600 | 0.069 | 1.63 | [0.96, 2.75] | 221/334 (66.2) | 15/19 (78.9) |
| | <22900 | 0.018 ^a | 1.89 | [1.12, 3.19] | 221/335 (66.0) | 15/18 (83.3) |
| | <23100 | 0.011 ^a | 2.02 | [1.17, 3.48] | 222/336 (66.1) | 14/17 (82.4) |
| | <23200 | 0.014 ^a | 2.02 | [1.15, 3.54] | 223/337 (66.2) | 13/16 (81.3) |
| | <23700 | 0.024 ^a | 1.95 | [1.09, 3.50] | 224/338 (66.3) | 12/15 (80.0) |
| | <23900 | 0.033 ^a | 1.94 | [1.06, 3.55] | 225/339 (66.4) | 11/14 (78.6) |
| | <24000 | 0.036 ^a | 1.97 | [1.05, 3.72] | 226/340 (66.5) | 10/13 (76.9) |
| | <24900 | 0.092 | 1.77 | [0.91, 3.46] | 227/341 (66.6) | 9/12 (75.0) |
| | <25500 | 0.006 ^a | 2.54 | [1.30, 4.97] | 227/342 (66.4) | 9/11 (81.8) |
| | <25800 | 0.024 ^a | 2.26 | [1.11, 4.59] | 228/343 (66.5) | 8/10 (80.0) |
| | <26200 | 0.012 ^a | 2.65 | [1.24, 5.65] | 229/344 (66.6) | 7/9 (77.8) |
| | <26300 | 0.005 ^a | 3.23 | [1.43, 7.31] | 230/345 (66.7) | 6/8 (75.0) |
| | <26500 | 0.028 ^a | 2.72 | [1.12, 6.64] | 231/346 (66.8) | 5/7 (71.4) |
| | <27500 | 0.074 | 2.47 | [0.92, 6.68] | 232/347 (66.9) | 4/6 (66.7) |
| | <30600 | 0.038 ^a | 3.37 | [1.07, 10.61] | 233/348 (67.0) | 3/5 (60.0) |
| | <31500 | 0.259 | 2.24 | [0.55, 9.05] | 234/349 (67.0) | 2/4 (50.0) |
| | <32400 | 0.257 | 2.24 | [0.55, 9.08] | 234/350 (66.9) | 2/3 (66.7) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

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68Ga-PSMA-11 Quantitative analysis

Final Version

Table 4.2-s: rPFS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | # of events / # of patients (%) | |
|---------------------------|------------------------|---------|--------------|---------------------------------|----------------|
| | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <34800 | 0.090 | 3.35 | [0.83, 13.57] | 234/351 (66.7) |
| | <35000 | 0.473 | 2.05 | [0.29, 14.69] | 235/352 (66.8) |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is '<'

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Table 4.3: rPFS multivariate Cox proportional hazards model - with optimal cut points - Liver (Liver-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|---|--------------|--------------|--------------------|
| Liver Volume of segmented PSMA positive tumors (cc) <200 vs. >=200 ^c | 2.58 | [1.34, 4.99] | 0.005 ^a |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^c Reference is '<

Output ID: T-4-3 2021-08-30 20:14

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 4.3-s: rPFS univariate Cox proportional hazards model - candidate cut points - Liver (Liver-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|---------------|---------------------------------|---------------|
| | | | | | <cut point | >=cut point |
| Volume of segmented PSMA positive tumors (cc) - Optimal cut | <200 | 0.005 ^a | 2.58 | [1.34, 4.99] | 29/37 (78.4) | 14/14 (100.0) |
| Volume of segmented PSMA positive tumors (cc) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <100 | 0.022 ^a | 2.08 | [1.11, 3.89] | 24/32 (75.0) | 19/19 (100.0) |
| | <200 | 0.005 ^a | 2.58 | [1.34, 4.99] | 29/37 (78.4) | 14/14 (100.0) |
| | <400 | 0.020 ^a | 2.25 | [1.14, 4.44] | 31/39 (79.5) | 12/12 (100.0) |
| Volume of segmented PSMA positive tumors (cc) - All cuts | <100 | 0.022 ^a | 2.08 | [1.11, 3.89] | 24/32 (75.0) | 19/19 (100.0) |
| | <200 | 0.005 ^a | 2.58 | [1.34, 4.99] | 29/37 (78.4) | 14/14 (100.0) |
| | <400 | 0.020 ^a | 2.25 | [1.14, 4.44] | 31/39 (79.5) | 12/12 (100.0) |
| | <500 | 0.050 | 2.11 | [1.00, 4.46] | 34/42 (81.0) | 9/9 (100.0) |
| | <700 | 0.121 | 1.85 | [0.85, 4.04] | 35/43 (81.4) | 8/8 (100.0) |
| | <1000 | 0.200 | 1.71 | [0.75, 3.87] | 36/44 (81.8) | 7/7 (100.0) |
| | <1300 | 0.379 | 1.52 | [0.60, 3.90] | 38/46 (82.6) | 5/5 (100.0) |
| | <1600 | 0.287 | 1.76 | [0.62, 4.99] | 39/47 (83.0) | 4/4 (100.0) |
| | <2300 | 0.062 | 4.03 | [0.93, 17.41] | 41/49 (83.7) | 2/2 (100.0) |
| | <3700 | 0.481 | 2.06 | [0.28, 15.40] | 42/50 (84.0) | 1/1 (100.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Final Version

Table 4.4: rPFS multivariate Cox proportional hazards model - with optimal cut points - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Lymph Node SUVmax (g/ml) <86 vs. >=86 ^c | 0.12 | [0.03, 0.50] | 0.003 ^a |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^c Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 4.4-s: rPFS univariate Cox proportional hazards model - candidate cut points - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - Optimal cut | <86 | 0.003 ^a | 0.12 | [0.03, 0.50] | 176/245 (71.8) | 2/13 (15.4) |
| SUVmax (g/ml) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <11 | 0.017 ^a | 0.65 | [0.45, 0.93] | 40/56 (71.4) | 138/202 (68.3) |
| | <12 | 0.009 ^a | 0.62 | [0.44, 0.89] | 42/58 (72.4) | 136/200 (68.0) |
| | <13 | 0.008 ^a | 0.63 | [0.45, 0.89] | 45/61 (73.8) | 133/197 (67.5) |
| | <14 | <.001 ^a | 0.56 | [0.40, 0.77] | 53/70 (75.7) | 125/188 (66.5) |
| | <15 | <.001 ^a | 0.58 | [0.42, 0.80] | 57/76 (75.0) | 121/182 (66.5) |
| | <16 | <.001 ^a | 0.56 | [0.41, 0.77] | 63/82 (76.8) | 115/176 (65.3) |
| | <17 | <.001 ^a | 0.56 | [0.41, 0.76] | 68/89 (76.4) | 110/169 (65.1) |
| | <18 | <.001 ^a | 0.54 | [0.40, 0.73] | 73/96 (76.0) | 105/162 (64.8) |
| | <19 | <.001 ^a | 0.55 | [0.41, 0.74] | 75/99 (75.8) | 103/159 (64.8) |
| | <20 | <.001 ^a | 0.52 | [0.39, 0.71] | 79/103 (76.7) | 99/155 (63.9) |
| | <21 | <.001 ^a | 0.50 | [0.37, 0.68] | 84/111 (75.7) | 94/147 (63.9) |
| | <22 | <.001 ^a | 0.53 | [0.40, 0.72] | 86/115 (74.8) | 92/143 (64.3) |
| | <23 | <.001 ^a | 0.55 | [0.41, 0.75] | 88/118 (74.6) | 90/140 (64.3) |
| | <24 | <.001 ^a | 0.55 | [0.41, 0.75] | 90/120 (75.0) | 88/138 (63.8) |
| | <25 | <.001 ^a | 0.53 | [0.39, 0.71] | 95/126 (75.4) | 83/132 (62.9) |
| | <26 | <.001 ^a | 0.49 | [0.36, 0.66] | 100/132 (75.8) | 78/126 (61.9) |
| | <27 | <.001 ^a | 0.47 | [0.35, 0.64] | 104/137 (75.9) | 74/121 (61.2) |
| | <28 | <.001 ^a | 0.47 | [0.35, 0.64] | 107/140 (76.4) | 71/118 (60.2) |
| | <30 | <.001 ^a | 0.47 | [0.34, 0.64] | 109/142 (76.8) | 69/116 (59.5) |
| | <31 | <.001 ^a | 0.43 | [0.32, 0.59] | 113/146 (77.4) | 65/112 (58.0) |
| | <33 | <.001 ^a | 0.43 | [0.32, 0.59] | 113/147 (76.9) | 65/111 (58.6) |
| | <34 | <.001 ^a | 0.43 | [0.31, 0.58] | 116/152 (76.3) | 62/106 (58.5) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.4-s: rPFS univariate Cox proportional hazards model - candidate cut points - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|--------------|---------------------------------|---------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <35 | <.001 ^a | 0.44 | [0.32, 0.61] | 117/154 (76.0) | 61/104 (58.7) |
| | <36 | <.001 ^a | 0.45 | [0.33, 0.62] | 119/157 (75.8) | 59/101 (58.4) |
| | <37 | <.001 ^a | 0.47 | [0.34, 0.64] | 120/159 (75.5) | 58/99 (58.6) |
| | <38 | <.001 ^a | 0.47 | [0.34, 0.65] | 124/166 (74.7) | 54/92 (58.7) |
| | <39 | <.001 ^a | 0.45 | [0.32, 0.63] | 130/172 (75.6) | 48/86 (55.8) |
| | <40 | <.001 ^a | 0.41 | [0.29, 0.58] | 136/179 (76.0) | 42/79 (53.2) |
| | <41 | <.001 ^a | 0.41 | [0.29, 0.59] | 138/182 (75.8) | 40/76 (52.6) |
| | <42 | <.001 ^a | 0.44 | [0.31, 0.63] | 139/185 (75.1) | 39/73 (53.4) |
| | <43 | <.001 ^a | 0.43 | [0.30, 0.62] | 140/186 (75.3) | 38/72 (52.8) |
| | <44 | <.001 ^a | 0.40 | [0.28, 0.58] | 143/189 (75.7) | 35/69 (50.7) |
| | <45 | <.001 ^a | 0.46 | [0.31, 0.66] | 143/192 (74.5) | 35/66 (53.0) |
| | <46 | <.001 ^a | 0.48 | [0.33, 0.69] | 143/193 (74.1) | 35/65 (53.8) |
| | <47 | <.001 ^a | 0.46 | [0.31, 0.68] | 147/198 (74.2) | 31/60 (51.7) |
| | <48 | <.001 ^a | 0.49 | [0.33, 0.72] | 147/199 (73.9) | 31/59 (52.5) |
| | <49 | <.001 ^a | 0.50 | [0.34, 0.74] | 148/201 (73.6) | 30/57 (52.6) |
| | <50 | <.001 ^a | 0.50 | [0.34, 0.75] | 149/203 (73.4) | 29/55 (52.7) |
| | <51 | <.001 ^a | 0.49 | [0.32, 0.73] | 150/204 (73.5) | 28/54 (51.9) |
| | <52 | <.001 ^a | 0.50 | [0.33, 0.75] | 150/205 (73.2) | 28/53 (52.8) |
| | <53 | <.001 ^a | 0.48 | [0.31, 0.74] | 153/210 (72.9) | 25/48 (52.1) |
| | <54 | <.001 ^a | 0.47 | [0.30, 0.72] | 154/211 (73.0) | 24/47 (51.1) |
| | <55 | <.001 ^a | 0.45 | [0.29, 0.70] | 156/213 (73.2) | 22/45 (48.9) |
| | <56 | 0.001 ^a | 0.48 | [0.31, 0.75] | 156/215 (72.6) | 22/43 (51.2) |
| | <57 | 0.004 ^a | 0.51 | [0.32, 0.81] | 157/218 (72.0) | 21/40 (52.5) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.4-s: rPFS univariate Cox proportional hazards model - candidate cut points - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|---------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <59 | 0.006 ^a | 0.52 | [0.33, 0.83] | 157/219 (71.7) | 21/39 (53.8) |
| | <61 | 0.003 ^a | 0.50 | [0.31, 0.79] | 158/220 (71.8) | 20/38 (52.6) |
| | <65 | 0.002 ^a | 0.47 | [0.28, 0.76] | 160/223 (71.7) | 18/35 (51.4) |
| | <66 | 0.003 ^a | 0.46 | [0.27, 0.77] | 162/226 (71.7) | 16/32 (50.0) |
| | <67 | 0.002 ^a | 0.43 | [0.25, 0.74] | 163/227 (71.8) | 15/31 (48.4) |
| | <70 | 0.003 ^a | 0.43 | [0.25, 0.74] | 164/229 (71.6) | 14/29 (48.3) |
| | <71 | 0.004 ^a | 0.44 | [0.25, 0.77] | 165/230 (71.7) | 13/28 (46.4) |
| | <72 | 0.008 ^a | 0.46 | [0.26, 0.82] | 165/231 (71.4) | 13/27 (48.1) |
| | <73 | 0.005 ^a | 0.43 | [0.24, 0.78] | 166/232 (71.6) | 12/26 (46.2) |
| | <74 | 0.003 ^a | 0.39 | [0.21, 0.73] | 167/233 (71.7) | 11/25 (44.0) |
| | <77 | <.001 ^a | 0.30 | [0.15, 0.61] | 170/236 (72.0) | 8/22 (36.4) |
| | <78 | <.001 ^a | 0.20 | [0.08, 0.49] | 173/239 (72.4) | 5/19 (26.3) |
| | <81 | <.001 ^a | 0.16 | [0.06, 0.44] | 174/240 (72.5) | 4/18 (22.2) |
| | <82 | 0.001 ^a | 0.19 | [0.07, 0.52] | 174/241 (72.2) | 4/17 (23.5) |
| | <83 | 0.001 ^a | 0.20 | [0.07, 0.53] | 174/242 (71.9) | 4/16 (25.0) |
| | <84 | 0.002 ^a | 0.21 | [0.08, 0.57] | 174/243 (71.6) | 4/15 (26.7) |
| | <85 | 0.003 ^a | 0.17 | [0.06, 0.55] | 175/244 (71.7) | 3/14 (21.4) |
| | <86 | 0.003 ^a | 0.12 | [0.03, 0.50] | 176/245 (71.8) | 2/13 (15.4) |
| | <87 | 0.004 ^a | 0.13 | [0.03, 0.51] | 176/246 (71.5) | 2/12 (16.7) |
| | <92 | 0.005 ^a | 0.13 | [0.03, 0.53] | 176/247 (71.3) | 2/11 (18.2) |
| | <98 | 0.008 ^a | 0.15 | [0.04, 0.61] | 176/248 (71.0) | 2/10 (20.0) |
| SUVmax (g/ml) - All cuts | <3 | 0.492 | 1.99 | [0.28, 14.22] | 1/2 (50.0) | 177/256 (69.1) |
| | <4 | 0.861 | 0.92 | [0.34, 2.47] | 4/6 (66.7) | 174/252 (69.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Table 4.4-s: rPFS univariate Cox proportional hazards model - candidate cut points - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - All cuts | <5 | 0.159 | 0.60 | [0.29, 1.22] | 8/11 (72.7) | 170/247 (68.8) |
| | <6 | 0.245 | 0.72 | [0.42, 1.25] | 14/19 (73.7) | 164/239 (68.6) |
| | <7 | 0.132 | 0.69 | [0.42, 1.12] | 18/25 (72.0) | 160/233 (68.7) |
| | <8 | 0.131 | 0.71 | [0.46, 1.11] | 23/32 (71.9) | 155/226 (68.6) |
| | <9 | 0.234 | 0.78 | [0.51, 1.18] | 27/38 (71.1) | 151/220 (68.6) |
| | <10 | 0.283 | 0.80 | [0.54, 1.20] | 30/44 (68.2) | 148/214 (69.2) |
| | <11 | 0.017 ^a | 0.65 | [0.45, 0.93] | 40/56 (71.4) | 138/202 (68.3) |
| | <12 | 0.009 ^a | 0.62 | [0.44, 0.89] | 42/58 (72.4) | 136/200 (68.0) |
| | <13 | 0.008 ^a | 0.63 | [0.45, 0.89] | 45/61 (73.8) | 133/197 (67.5) |
| | <14 | <.001 ^a | 0.56 | [0.40, 0.77] | 53/70 (75.7) | 125/188 (66.5) |
| | <15 | <.001 ^a | 0.58 | [0.42, 0.80] | 57/76 (75.0) | 121/182 (66.5) |
| | <16 | <.001 ^a | 0.56 | [0.41, 0.77] | 63/82 (76.8) | 115/176 (65.3) |
| | <17 | <.001 ^a | 0.56 | [0.41, 0.76] | 68/89 (76.4) | 110/169 (65.1) |
| | <18 | <.001 ^a | 0.54 | [0.40, 0.73] | 73/96 (76.0) | 105/162 (64.8) |
| | <19 | <.001 ^a | 0.55 | [0.41, 0.74] | 75/99 (75.8) | 103/159 (64.8) |
| | <20 | <.001 ^a | 0.52 | [0.39, 0.71] | 79/103 (76.7) | 99/155 (63.9) |
| | <21 | <.001 ^a | 0.50 | [0.37, 0.68] | 84/111 (75.7) | 94/147 (63.9) |
| | <22 | <.001 ^a | 0.53 | [0.40, 0.72] | 86/115 (74.8) | 92/143 (64.3) |
| | <23 | <.001 ^a | 0.55 | [0.41, 0.75] | 88/118 (74.6) | 90/140 (64.3) |
| | <24 | <.001 ^a | 0.55 | [0.41, 0.75] | 90/120 (75.0) | 88/138 (63.8) |
| | <25 | <.001 ^a | 0.53 | [0.39, 0.71] | 95/126 (75.4) | 83/132 (62.9) |
| | <26 | <.001 ^a | 0.49 | [0.36, 0.66] | 100/132 (75.8) | 78/126 (61.9) |
| | <27 | <.001 ^a | 0.47 | [0.35, 0.64] | 104/137 (75.9) | 74/121 (61.2) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.4-s: rPFS univariate Cox proportional hazards model - candidate cut points - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|---------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - All cuts | <28 | <.001 ^a | 0.47 | [0.35, 0.64] | 107/140 (76.4) | 71/118 (60.2) |
| | <30 | <.001 ^a | 0.47 | [0.34, 0.64] | 109/142 (76.8) | 69/116 (59.5) |
| | <31 | <.001 ^a | 0.43 | [0.32, 0.59] | 113/146 (77.4) | 65/112 (58.0) |
| | <33 | <.001 ^a | 0.43 | [0.32, 0.59] | 113/147 (76.9) | 65/111 (58.6) |
| | <34 | <.001 ^a | 0.43 | [0.31, 0.58] | 116/152 (76.3) | 62/106 (58.5) |
| | <35 | <.001 ^a | 0.44 | [0.32, 0.61] | 117/154 (76.0) | 61/104 (58.7) |
| | <36 | <.001 ^a | 0.45 | [0.33, 0.62] | 119/157 (75.8) | 59/101 (58.4) |
| | <37 | <.001 ^a | 0.47 | [0.34, 0.64] | 120/159 (75.5) | 58/99 (58.6) |
| | <38 | <.001 ^a | 0.47 | [0.34, 0.65] | 124/166 (74.7) | 54/92 (58.7) |
| | <39 | <.001 ^a | 0.45 | [0.32, 0.63] | 130/172 (75.6) | 48/86 (55.8) |
| | <40 | <.001 ^a | 0.41 | [0.29, 0.58] | 136/179 (76.0) | 42/79 (53.2) |
| | <41 | <.001 ^a | 0.41 | [0.29, 0.59] | 138/182 (75.8) | 40/76 (52.6) |
| | <42 | <.001 ^a | 0.44 | [0.31, 0.63] | 139/185 (75.1) | 39/73 (53.4) |
| | <43 | <.001 ^a | 0.43 | [0.30, 0.62] | 140/186 (75.3) | 38/72 (52.8) |
| | <44 | <.001 ^a | 0.40 | [0.28, 0.58] | 143/189 (75.7) | 35/69 (50.7) |
| | <45 | <.001 ^a | 0.46 | [0.31, 0.66] | 143/192 (74.5) | 35/66 (53.0) |
| | <46 | <.001 ^a | 0.48 | [0.33, 0.69] | 143/193 (74.1) | 35/65 (53.8) |
| | <47 | <.001 ^a | 0.46 | [0.31, 0.68] | 147/198 (74.2) | 31/60 (51.7) |
| | <48 | <.001 ^a | 0.49 | [0.33, 0.72] | 147/199 (73.9) | 31/59 (52.5) |
| | <49 | <.001 ^a | 0.50 | [0.34, 0.74] | 148/201 (73.6) | 30/57 (52.6) |
| | <50 | <.001 ^a | 0.50 | [0.34, 0.75] | 149/203 (73.4) | 29/55 (52.7) |
| | <51 | <.001 ^a | 0.49 | [0.32, 0.73] | 150/204 (73.5) | 28/54 (51.9) |
| | <52 | <.001 ^a | 0.50 | [0.33, 0.75] | 150/205 (73.2) | 28/53 (52.8) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.4-s: rPFS univariate Cox proportional hazards model - candidate cut points - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - All cuts | <53 | <.001 ^a | 0.48 | [0.31, 0.74] | 153/210 (72.9) | 25/48 (52.1) |
| | <54 | <.001 ^a | 0.47 | [0.30, 0.72] | 154/211 (73.0) | 24/47 (51.1) |
| | <55 | <.001 ^a | 0.45 | [0.29, 0.70] | 156/213 (73.2) | 22/45 (48.9) |
| | <56 | 0.001 ^a | 0.48 | [0.31, 0.75] | 156/215 (72.6) | 22/43 (51.2) |
| | <57 | 0.004 ^a | 0.51 | [0.32, 0.81] | 157/218 (72.0) | 21/40 (52.5) |
| | <59 | 0.006 ^a | 0.52 | [0.33, 0.83] | 157/219 (71.7) | 21/39 (53.8) |
| | <61 | 0.003 ^a | 0.50 | [0.31, 0.79] | 158/220 (71.8) | 20/38 (52.6) |
| | <65 | 0.002 ^a | 0.47 | [0.28, 0.76] | 160/223 (71.7) | 18/35 (51.4) |
| | <66 | 0.003 ^a | 0.46 | [0.27, 0.77] | 162/226 (71.7) | 16/32 (50.0) |
| | <67 | 0.002 ^a | 0.43 | [0.25, 0.74] | 163/227 (71.8) | 15/31 (48.4) |
| | <70 | 0.003 ^a | 0.43 | [0.25, 0.74] | 164/229 (71.6) | 14/29 (48.3) |
| | <71 | 0.004 ^a | 0.44 | [0.25, 0.77] | 165/230 (71.7) | 13/28 (46.4) |
| | <72 | 0.008 ^a | 0.46 | [0.26, 0.82] | 165/231 (71.4) | 13/27 (48.1) |
| | <73 | 0.005 ^a | 0.43 | [0.24, 0.78] | 166/232 (71.6) | 12/26 (46.2) |
| | <74 | 0.003 ^a | 0.39 | [0.21, 0.73] | 167/233 (71.7) | 11/25 (44.0) |
| | <77 | <.001 ^a | 0.30 | [0.15, 0.61] | 170/236 (72.0) | 8/22 (36.4) |
| | <78 | <.001 ^a | 0.20 | [0.08, 0.49] | 173/239 (72.4) | 5/19 (26.3) |
| | <81 | <.001 ^a | 0.16 | [0.06, 0.44] | 174/240 (72.5) | 4/18 (22.2) |
| | <82 | 0.001 ^a | 0.19 | [0.07, 0.52] | 174/241 (72.2) | 4/17 (23.5) |
| | <83 | 0.001 ^a | 0.20 | [0.07, 0.53] | 174/242 (71.9) | 4/16 (25.0) |
| | <84 | 0.002 ^a | 0.21 | [0.08, 0.57] | 174/243 (71.6) | 4/15 (26.7) |
| | <85 | 0.003 ^a | 0.17 | [0.06, 0.55] | 175/244 (71.7) | 3/14 (21.4) |
| | <86 | 0.003 ^a | 0.12 | [0.03, 0.50] | 176/245 (71.8) | 2/13 (15.4) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

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Table 4.4-s: rPFS univariate Cox proportional hazards model - candidate cut points - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|-------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - All cuts | <87 | 0.004 ^a | 0.13 | [0.03, 0.51] | 176/246 (71.5) | 2/12 (16.7) |
| | <92 | 0.005 ^a | 0.13 | [0.03, 0.53] | 176/247 (71.3) | 2/11 (18.2) |
| | <98 | 0.008 ^a | 0.15 | [0.04, 0.61] | 176/248 (71.0) | 2/10 (20.0) |
| | <100 | 0.014 ^a | 0.17 | [0.04, 0.70] | 176/249 (70.7) | 2/9 (22.2) |
| | <104 | 0.020 ^a | 0.10 | [0.01, 0.70] | 177/250 (70.8) | 1/8 (12.5) |
| | <105 | 0.025 ^a | 0.11 | [0.01, 0.76] | 177/251 (70.5) | 1/7 (14.3) |
| | <119 | 0.039 ^a | 0.13 | [0.02, 0.90] | 177/252 (70.2) | 1/6 (16.7) |
| | <146 | 0.977 | 0.00 | [0.00,] | 178/254 (70.1) | 0/4 (0.0) |
| | <160 | 0.980 | 0.00 | [0.00,] | 178/255 (69.8) | 0/3 (0.0) |
| | <190 | 0.977 | 0.00 | [0.00,] | 178/256 (69.5) | 0/2 (0.0) |
| | <207 | 0.981 | 0.00 | [0.00,] | 178/257 (69.3) | 0/1 (0.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is '<'

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Table 4.5: rPFS multivariate Cox proportional hazards model - with optimal cut points - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|---|--------------|--------------|--------------------|
| Soft Tissue SUVmax (g/ml) <51 vs. >=51 ^c | 0.35 | [0.14, 0.86] | 0.022 ^a |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^c Reference is '<'
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Table 4.5-s: rPFS univariate Cox proportional hazards model - candidate cut points - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|--------------|---------------------------------|---------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - Optimal cut | <51 | 0.022 ^a | 0.35 | [0.14, 0.86] | 117/162 (72.2) | 5/11 (45.5) |
| SUVmax (g/ml) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <11 | 0.045 ^a | 0.67 | [0.45, 0.99] | 38/48 (79.2) | 84/125 (67.2) |
| | <12 | 0.010 ^a | 0.61 | [0.42, 0.89] | 42/54 (77.8) | 80/119 (67.2) |
| | <13 | 0.001 ^a | 0.54 | [0.37, 0.78] | 47/59 (79.7) | 75/114 (65.8) |
| | <14 | 0.002 ^a | 0.57 | [0.39, 0.81] | 56/71 (78.9) | 66/102 (64.7) |
| | <15 | 0.007 ^a | 0.61 | [0.42, 0.87] | 56/73 (76.7) | 66/100 (66.0) |
| | <16 | 0.017 ^a | 0.65 | [0.45, 0.93] | 58/76 (76.3) | 64/97 (66.0) |
| | <17 | 0.021 ^a | 0.65 | [0.46, 0.94] | 62/82 (75.6) | 60/91 (65.9) |
| | <18 | 0.024 ^a | 0.66 | [0.46, 0.95] | 62/83 (74.7) | 60/90 (66.7) |
| | <19 | 0.019 ^a | 0.65 | [0.45, 0.93] | 65/86 (75.6) | 57/87 (65.5) |
| | <20 | 0.017 ^a | 0.65 | [0.45, 0.93] | 68/89 (76.4) | 54/84 (64.3) |
| | <21 | 0.024 ^a | 0.66 | [0.45, 0.95] | 73/97 (75.3) | 49/76 (64.5) |
| | <22 | 0.033 ^a | 0.67 | [0.46, 0.97] | 75/99 (75.8) | 47/74 (63.5) |
| | <23 | 0.012 ^a | 0.62 | [0.43, 0.90] | 78/103 (75.7) | 44/70 (62.9) |
| | <24 | 0.013 ^a | 0.62 | [0.43, 0.91] | 80/106 (75.5) | 42/67 (62.7) |
| | <25 | 0.010 ^a | 0.61 | [0.41, 0.89] | 82/109 (75.2) | 40/64 (62.5) |
| | <26 | 0.009 ^a | 0.60 | [0.41, 0.88] | 83/110 (75.5) | 39/63 (61.9) |
| | <28 | 0.006 ^a | 0.57 | [0.38, 0.85] | 88/116 (75.9) | 34/57 (59.6) |
| | <29 | 0.005 ^a | 0.55 | [0.37, 0.84] | 91/120 (75.8) | 31/53 (58.5) |
| | <30 | 0.003 ^a | 0.53 | [0.35, 0.81] | 92/121 (76.0) | 30/52 (57.7) |
| | <31 | 0.003 ^a | 0.52 | [0.34, 0.80] | 93/123 (75.6) | 29/50 (58.0) |
| | <32 | 0.028 ^a | 0.62 | [0.41, 0.95] | 93/126 (73.8) | 29/47 (61.7) |
| | <33 | 0.027 ^a | 0.62 | [0.40, 0.95] | 94/129 (72.9) | 28/44 (63.6) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Table 4.5-s: rPFS univariate Cox proportional hazards model - candidate cut points - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <35 | 0.008 ^a | 0.54 | [0.34, 0.85] | 98/135 (72.6) | 24/38 (63.2) |
| | <36 | 0.046 ^a | 0.61 | [0.38, 0.99] | 102/142 (71.8) | 20/31 (64.5) |
| | <46 | 0.047 ^a | 0.50 | [0.25, 0.99] | 113/157 (72.0) | 9/16 (56.3) |
| | <49 | 0.014 ^a | 0.36 | [0.16, 0.81] | 116/160 (72.5) | 6/13 (46.2) |
| | <51 | 0.022 ^a | 0.35 | [0.14, 0.86] | 117/162 (72.2) | 5/11 (45.5) |
| | <54 | 0.047 ^a | 0.40 | [0.16, 0.99] | 117/163 (71.8) | 5/10 (50.0) |
| SUVmax (g/ml) - All cuts | <2 | 0.165 | 0.24 | [0.03, 1.78] | 1/1 (100.0) | 121/172 (70.3) |
| | <3 | 0.030 ^a | 0.33 | [0.12, 0.90] | 4/4 (100.0) | 118/169 (69.8) |
| | <4 | 0.007 ^a | 0.28 | [0.11, 0.70] | 5/5 (100.0) | 117/168 (69.6) |
| | <5 | 0.425 | 0.73 | [0.34, 1.57] | 7/8 (87.5) | 115/165 (69.7) |
| | <6 | 0.113 | 0.59 | [0.31, 1.13] | 10/12 (83.3) | 112/161 (69.6) |
| | <7 | 0.623 | 0.88 | [0.53, 1.47] | 18/22 (81.8) | 104/151 (68.9) |
| | <8 | 0.206 | 0.76 | [0.49, 1.17] | 27/34 (79.4) | 95/139 (68.3) |
| | <9 | 0.165 | 0.74 | [0.49, 1.13] | 30/39 (76.9) | 92/134 (68.7) |
| | <10 | 0.107 | 0.71 | [0.47, 1.08] | 32/42 (76.2) | 90/131 (68.7) |
| | <11 | 0.045 ^a | 0.67 | [0.45, 0.99] | 38/48 (79.2) | 84/125 (67.2) |
| | <12 | 0.010 ^a | 0.61 | [0.42, 0.89] | 42/54 (77.8) | 80/119 (67.2) |
| | <13 | 0.001 ^a | 0.54 | [0.37, 0.78] | 47/59 (79.7) | 75/114 (65.8) |
| | <14 | 0.002 ^a | 0.57 | [0.39, 0.81] | 56/71 (78.9) | 66/102 (64.7) |
| | <15 | 0.007 ^a | 0.61 | [0.42, 0.87] | 56/73 (76.7) | 66/100 (66.0) |
| | <16 | 0.017 ^a | 0.65 | [0.45, 0.93] | 58/76 (76.3) | 64/97 (66.0) |
| | <17 | 0.021 ^a | 0.65 | [0.46, 0.94] | 62/82 (75.6) | 60/91 (65.9) |
| | <18 | 0.024 ^a | 0.66 | [0.46, 0.95] | 62/83 (74.7) | 60/90 (66.7) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Table 4.5-s: rPFS univariate Cox proportional hazards model - candidate cut points - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - All cuts | <19 | 0.019 ^a | 0.65 | [0.45, 0.93] | 65/86 (75.6) | 57/87 (65.5) |
| | <20 | 0.017 ^a | 0.65 | [0.45, 0.93] | 68/89 (76.4) | 54/84 (64.3) |
| | <21 | 0.024 ^a | 0.66 | [0.45, 0.95] | 73/97 (75.3) | 49/76 (64.5) |
| | <22 | 0.033 ^a | 0.67 | [0.46, 0.97] | 75/99 (75.8) | 47/74 (63.5) |
| | <23 | 0.012 ^a | 0.62 | [0.43, 0.90] | 78/103 (75.7) | 44/70 (62.9) |
| | <24 | 0.013 ^a | 0.62 | [0.43, 0.91] | 80/106 (75.5) | 42/67 (62.7) |
| | <25 | 0.010 ^a | 0.61 | [0.41, 0.89] | 82/109 (75.2) | 40/64 (62.5) |
| | <26 | 0.009 ^a | 0.60 | [0.41, 0.88] | 83/110 (75.5) | 39/63 (61.9) |
| | <28 | 0.006 ^a | 0.57 | [0.38, 0.85] | 88/116 (75.9) | 34/57 (59.6) |
| | <29 | 0.005 ^a | 0.55 | [0.37, 0.84] | 91/120 (75.8) | 31/53 (58.5) |
| | <30 | 0.003 ^a | 0.53 | [0.35, 0.81] | 92/121 (76.0) | 30/52 (57.7) |
| | <31 | 0.003 ^a | 0.52 | [0.34, 0.80] | 93/123 (75.6) | 29/50 (58.0) |
| | <32 | 0.028 ^a | 0.62 | [0.41, 0.95] | 93/126 (73.8) | 29/47 (61.7) |
| | <33 | 0.027 ^a | 0.62 | [0.40, 0.95] | 94/129 (72.9) | 28/44 (63.6) |
| | <35 | 0.008 ^a | 0.54 | [0.34, 0.85] | 98/135 (72.6) | 24/38 (63.2) |
| | <36 | 0.046 ^a | 0.61 | [0.38, 0.99] | 102/142 (71.8) | 20/31 (64.5) |
| | <37 | 0.056 | 0.62 | [0.38, 1.01] | 103/143 (72.0) | 19/30 (63.3) |
| | <38 | 0.104 | 0.66 | [0.40, 1.09] | 103/144 (71.5) | 19/29 (65.5) |
| | <39 | 0.211 | 0.73 | [0.45, 1.19] | 103/145 (71.0) | 19/28 (67.9) |
| | <40 | 0.169 | 0.70 | [0.42, 1.16] | 104/146 (71.2) | 18/27 (66.7) |
| | <41 | 0.203 | 0.72 | [0.43, 1.20] | 105/148 (70.9) | 17/25 (68.0) |
| | <43 | 0.229 | 0.72 | [0.42, 1.23] | 107/150 (71.3) | 15/23 (65.2) |
| | <44 | 0.162 | 0.67 | [0.38, 1.17] | 108/151 (71.5) | 14/22 (63.6) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

Output ID: T-4-5-S 2021-08-30 20:31

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-cut-hr.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 4.5-s: rPFS univariate Cox proportional hazards model - candidate cut points - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - All cuts | <45 | 0.071 | 0.55 | [0.29, 1.05] | 112/155 (72.3) | 10/18 (55.6) |
| | <46 | 0.047 ^a | 0.50 | [0.25, 0.99] | 113/157 (72.0) | 9/16 (56.3) |
| | <49 | 0.014 ^a | 0.36 | [0.16, 0.81] | 116/160 (72.5) | 6/13 (46.2) |
| | <51 | 0.022 ^a | 0.35 | [0.14, 0.86] | 117/162 (72.2) | 5/11 (45.5) |
| | <54 | 0.047 ^a | 0.40 | [0.16, 0.99] | 117/163 (71.8) | 5/10 (50.0) |
| | <59 | 0.066 | 0.39 | [0.14, 1.06] | 118/165 (71.5) | 4/8 (50.0) |
| | <62 | 0.068 | 0.27 | [0.07, 1.10] | 120/167 (71.9) | 2/6 (33.3) |
| | <80 | 0.144 | 0.35 | [0.09, 1.43] | 120/168 (71.4) | 2/5 (40.0) |
| | <90 | 0.240 | 0.31 | [0.04, 2.20] | 121/170 (71.2) | 1/3 (33.3) |
| | <108 | 0.607 | 0.60 | [0.08, 4.28] | 121/171 (70.8) | 1/2 (50.0) |
| | <166 | 0.979 | 0.00 | [0.00,] | 122/172 (70.9) | 0/1 (0.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is '<'.

Output ID: T-4-5-S 2021-08-30 20:31

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 5.1: OS univariate Cox proportional hazards model - Whole Body (Body-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|---|--------------|--------------|--------------------|
| Whole Body | | | |
| SUVmean | 0.92 | [0.89, 0.95] | <.001 ^a |
| SUVmax | 0.99 | [0.99, 1.00] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 1.39 | [1.27, 1.52] | <.001 ^a |
| Tumor load | 1.03 | [1.02, 1.04] | <.001 ^a |
| Bone | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.35 | [0.20, 0.61] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.50 | [0.37, 0.66] | <.001 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.77 | [0.61, 0.97] | 0.026 ^a |
| Soft Tissue | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.79 | [0.64, 0.98] | 0.035 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-5-1 2021-08-30 17:30

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 5.2: OS univariate Cox proportional hazards model - Bone (Bone-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Bone | | | |
| SUVmean | 0.91 | [0.88, 0.95] | <.001 ^a |
| SUVmax | 0.99 | [0.99, 1.00] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 1.29 | [1.17, 1.43] | <.001 ^a |
| Tumor load | 1.02 | [1.01, 1.04] | <.001 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-5-2 2021-08-30 17:30

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 5.3: OS univariate Cox proportional hazards model - Liver (Liver-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Liver | | | |
| SUVmean | 0.97 | [0.91, 1.04] | 0.429 |
| SUVmax | 1.00 | [0.98, 1.01] | 0.709 |
| Volume of segmented PSMA positive tumors | 1.82 | [1.24, 2.67] | 0.002 ^a |
| Tumor load | 1.04 | [1.01, 1.08] | 0.020 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-5-3 2021-08-30 17:31

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 5.4: OS univariate Cox proportional hazards model - Lymph Node (Lymph Node-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Lymph node | | | |
| SUVmean | 0.94 | [0.91, 0.97] | <.001 ^a |
| SUVmax | 0.99 | [0.98, 0.99] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 1.17 | [0.76, 1.80] | 0.466 |
| Tumor load | 0.99 | [0.96, 1.02] | 0.636 |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-5-4 2021-08-30 17:31

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 5.5: OS univariate Cox proportional hazards model - Soft Tissue (Soft Tissue-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Soft tissue | | | |
| SUVmean | 0.97 | [0.94, 1.00] | 0.050 |
| SUVmax | 0.99 | [0.98, 1.00] | 0.018 ^a |
| Volume of segmented PSMA positive tumors | 1.56 | [1.03, 2.37] | 0.035 ^a |
| Tumor load | 1.03 | [0.99, 1.06] | 0.155 |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-5-5 2021-08-30 17:31

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 6.1: OS multivariate Cox proportional hazards model - Whole Body (Body-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Whole body | | | |
| SUVmean | 0.90 | [0.85, 0.96] | <.001 ^a |
| SUVmax | 1.00 | [0.99, 1.00] | 0.210 |
| Volume of segmented PSMA positive tumors | 1.05 | [0.73, 1.50] | 0.807 |
| Tumor load | 1.03 | [0.99, 1.08] | 0.135 |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.36 | [0.20, 0.63] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.50 | [0.37, 0.67] | <.001 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.78 | [0.60, 1.00] | 0.046 ^a |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.79 | [0.63, 1.00] | 0.045 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-6-1 2021-08-30 19:11

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 6.1: OS multivariate Cox proportional hazards model - Whole Body (Body-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward/forward selection | | | |
| Whole body | 0.88 | [0.84, 0.91] | <.001 ^a |
| SUVmean | 1.04 | [1.03, 1.05] | <.001 ^a |
| Tumor load | | | |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.38 | [0.22, 0.67] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.49 | [0.37, 0.66] | <.001 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.74 | [0.58, 0.94] | 0.014 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-6-1 2021-08-30 19:11

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Source data: adsl.xpt, adtte.xpt

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Final Version

Table 6-1-b-s: OS multivariate Cox proportional hazards model - backward selection - Whole Body (Body-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Whole body | | | |
| SUVmean | 0.90 | [0.85, 0.96] | <.001 ^a |
| SUVmax | 1.00 | [0.99, 1.00] | 0.210 |
| Volume of segmented PSMA positive tumors | 1.05 | [0.73, 1.50] | 0.807 |
| Tumor load | 1.03 | [0.99, 1.08] | 0.135 |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.36 | [0.20, 0.63] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.50 | [0.37, 0.67] | <.001 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.78 | [0.60, 1.00] | 0.046 ^a |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.79 | [0.63, 1.00] | 0.045 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-6-1-B-S 2021-08-30 19:11

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Source data: adsl.xpt, adtte.xpt

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Table 6-1-b-s: OS multivariate Cox proportional hazards model - backward selection - Whole Body (Body-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|----------------------------------|--------------|--------------|--------------------|
| Step 1 | | | |
| Whole body | 0.90 | [0.85, 0.95] | <.001 ^a |
| SUVmean | 1.00 | [0.99, 1.00] | 0.208 |
| SUVmax | 1.04 | [1.03, 1.05] | <.001 ^a |
| Tumor load | | | |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.36 | [0.20, 0.63] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.50 | [0.37, 0.67] | <.001 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.78 | [0.60, 0.99] | 0.045 ^a |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.80 | [0.63, 1.00] | 0.047 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-6-1-B-S 2021-08-30 19:11

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Source data: adsl.xpt, adtte.xpt

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Table 6-1-b-s: OS multivariate Cox proportional hazards model - backward selection - Whole Body (Body-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Step 2 | | | |
| Whole body | 0.87 | [0.84, 0.91] | <.001 ^a |
| SUVmean | 1.04 | [1.03, 1.05] | <.001 ^a |
| Tumor load | | | |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.38 | [0.22, 0.66] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.50 | [0.38, 0.68] | <.001 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.78 | [0.61, 1.00] | 0.051 |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.81 | [0.64, 1.01] | 0.060 |
| Final multivariate model from the backward selection | | | |
| Whole body | 0.88 | [0.84, 0.91] | <.001 ^a |
| SUVmean | 1.04 | [1.03, 1.05] | <.001 ^a |
| Tumor load | | | |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.38 | [0.22, 0.67] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.49 | [0.37, 0.66] | <.001 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.74 | [0.58, 0.94] | 0.014 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

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Source data: adsl.xpt, adtte.xpt

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Table 6-1-f-s: OS multivariate Cox proportional hazards model - forward selection - Whole Body (Body-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Whole body | 0.88 | [0.84, 0.91] | <.001 ^a |
| SUVmean | 1.04 | [1.03, 1.05] | <.001 ^a |
| Tumor load | | | |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.38 | [0.22, 0.67] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.49 | [0.37, 0.66] | <.001 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.74 | [0.58, 0.94] | 0.014 ^a |
| Step 1 - Candidate | | | |
| Whole body | | | 0.273 |
| SUVmax | | | 0.914 |
| Volume of segmented PSMA positive tumors | | | |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | | | 0.059 |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

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Table 6-1-f-s: OS multivariate Cox proportional hazards model - forward selection - Whole Body (Body-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward/forward selection | | | |
| Whole body | 0.88 | [0.84, 0.91] | <.001 ^a |
| SUVmean | 1.04 | [1.03, 1.05] | <.001 ^a |
| Tumor load | | | |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.38 | [0.22, 0.67] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.49 | [0.37, 0.66] | <.001 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.74 | [0.58, 0.94] | 0.014 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-6-1-F-S 2021-08-30 19:12

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 6.2: OS multivariate Cox proportional hazards model - Bone (Bone-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Bone | | | |
| SUVmean | 0.87 | [0.80, 0.94] | <.001 ^a |
| SUVmax | 1.00 | [0.99, 1.01] | 0.506 |
| Volume of segmented PSMA positive tumors | 1.36 | [0.86, 2.14] | 0.190 |
| Tumor load | 1.00 | [0.94, 1.06] | 0.991 |
| Final multivariate model from the backward/forward selection | | | |
| Bone | | | |
| SUVmean | 0.89 | [0.85, 0.93] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 1.36 | [1.23, 1.50] | <.001 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-2 2021-08-30 19:12

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 6-2-b-s: OS multivariate Cox proportional hazards model - backward selection - Bone (Bone-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Bone | | | |
| SUVmean | 0.87 | [0.80, 0.94] | <.001 ^a |
| SUVmax | 1.00 | [0.99, 1.01] | 0.506 |
| Volume of segmented PSMA positive tumors | 1.36 | [0.86, 2.14] | 0.190 |
| Tumor load | 1.00 | [0.94, 1.06] | 0.991 |
| Step 1 | | | |
| Bone | | | |
| SUVmean | 0.87 | [0.81, 0.94] | <.001 ^a |
| SUVmax | 1.00 | [0.99, 1.01] | 0.506 |
| Volume of segmented PSMA positive tumors | 1.35 | [1.22, 1.50] | <.001 ^a |
| Final multivariate model from the backward selection | | | |
| Bone | | | |
| SUVmean | 0.89 | [0.85, 0.93] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 1.36 | [1.23, 1.50] | <.001 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-2-B-S 2021-08-30 19:12

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-hr.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
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Table 6-2-f-s: OS multivariate Cox proportional hazards model - forward selection - Bone (Bone-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Bone | | | |
| SUVmean | 0.89 | [0.85, 0.93] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 1.36 | [1.23, 1.50] | <.001 ^a |
| Step 1 - Candidate | | | |
| Bone | | | |
| SUVmax | | 0.506 | |
| Tumor load | | 0.991 | |
| Final multivariate model from the backward/forward selection | | | |
| Bone | | | |
| SUVmean | 0.89 | [0.85, 0.93] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 1.36 | [1.23, 1.50] | <.001 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-2-F-S 2021-08-30 19:13

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-hr.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 6.3: OS multivariate Cox proportional hazards model - backward/forward selection - Liver (Liver-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|----------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 16.22 | [1.13, 232.91] | 0.040 ^a |
| Tumor load | 0.82 | [0.64, 1.05] | 0.110 |
| Final multivariate model from the backward/forward selection | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 1.82 | [1.24, 2.67] | 0.002 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-3 2021-08-30 19:13

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-hr.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 6-3-b-s: OS multivariate Cox proportional hazards model - backward selection - Liver (Liver-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|----------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 16.22 | [1.13, 232.91] | 0.040 ^a |
| Tumor load | 0.82 | [0.64, 1.05] | 0.110 |
| Final multivariate model from the backward selection | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 1.82 | [1.24, 2.67] | 0.002 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-3-B-S 2021-08-30 19:13

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Final Version

Table 6-3-f-s: OS multivariate Cox proportional hazards model - forward selection - Liver (Liver-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 1.82 | [1.24, 2.67] | 0.002 ^a |
| Step 1 - Candidate | | | |
| Liver | | | |
| SUVmean | 0.174 | | |
| SUVmax | 0.307 | | |
| Tumor load | 0.119 | | |
| Final multivariate model from the backward/forward selection | | | |
| Liver | | | |
| Volume of segmented PSMA positive tumors | 1.82 | [1.24, 2.67] | 0.002 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-3-F-S 2021-08-30 19:14

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 6.4: OS multivariate Cox proportional hazards model - Lymph Node (Lymph Node-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Lymph Node | 0.97 | [0.92, 1.02] | 0.252 |
| SUVmean | 0.99 | [0.98, 1.00] | 0.281 |
| Final multivariate model from the backward/forward selection | | | |
| Lymph Node | 0.93 | [0.90, 0.96] | <.001 ^a |
| SUVmean | 1.77 | [1.20, 2.62] | 0.004 ^a |
| Volume of segmented PSMA positive tumors | | | |

Note: The hazard ratios for tumor volume are computed for a 1000cc increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-4 2021-08-30 19:14

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-hr.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 6-4-b-s: OS multivariate Cox proportional hazards model - backward selection - Lymph Node (Lymph Node-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Lymph Node | 0.97 | [0.92, 1.02] | 0.252 |
| SUVmean | 0.99 | [0.98, 1.00] | 0.281 |
| Final multivariate model from the backward selection | | | |
| Lymph Node | 0.94 | [0.91, 0.97] | <.001 ^a |
| SUVmean | | | |

Note: The hazard ratios for tumor volume are computed for a 1000cc increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-4-B-S 2021-08-30 19:14

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-hr.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Final Version

Table 6-4-f-s: OS multivariate Cox proportional hazards model - forward selection - Lymph Node (Lymph Node-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Lymph Node SUVmean | 0.94 | [0.91, 0.97] | <.001 ^a |
| Step 1 - Candidate | | | |
| Lymph Node SUVmax | 0.281 | | |
| Volume of segmented PSMA positive tumors | 0.004 ^a | | |
| Tumor load | 0.026 ^a | | |
| Step 2 - Candidate | | | |
| Lymph Node SUVmax | 0.068 | | |
| Tumor load | 0.194 | | |
| Final multivariate model from the backward/forward selection | | | |
| Lymph Node SUVmean | 0.93 | [0.90, 0.96] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 1.77 | [1.20, 2.62] | 0.004 ^a |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-4-F-S 2021-08-30 19:14

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-hr.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 6.5: OS multivariate Cox proportional hazards model - Soft Tissue (Soft Tissue-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Soft Tissue | | | |
| SUVmax | 0.99 | [0.98, 1.00] | 0.008 ^a |
| Volume of segmented PSMA positive tumors | 1.77 | [1.19, 2.65] | 0.005 ^a |
| Final multivariate model from the backward/forward selection | | | |
| Soft Tissue | | | |
| SUVmax | 0.99 | [0.98, 1.00] | 0.008 ^a |
| Volume of segmented PSMA positive tumors | 1.77 | [1.19, 2.65] | 0.005 ^a |

Note: The hazard ratios for tumor volume are computed for a 1000cc increase, those for SUVmean and SUVmax for a 1g/ml increase.

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-5 2021-08-30 19:15

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-hr.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 6-5-b-s: OS multivariate Cox proportional hazards model - backward selection - Soft Tissue (Soft Tissue-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Soft Tissue | | | |
| SUVmax | 0.99 | [0.98, 1.00] | 0.008 ^a |
| Volume of segmented PSMA positive tumors | 1.77 | [1.19, 2.65] | 0.005 ^a |
| Final multivariate model from the backward selection | | | |
| Soft Tissue | | | |
| SUVmax | 0.99 | [0.98, 1.00] | 0.008 ^a |
| Volume of segmented PSMA positive tumors | 1.77 | [1.19, 2.65] | 0.005 ^a |

Note: The hazard ratios for tumor volume are computed for a 1000cc increase, those for SUVmean and SUVmax for a 1g/ml increase.

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-5-B-S 2021-08-30 19:15

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-hr.sas

Source data: adsl.xpt, adtte.xpt

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Final Version

Table 6-5-f-s: OS multivariate Cox proportional hazards model - forward selection - Soft Tissue (Soft Tissue-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Soft Tissue | 0.99 | [0.98, 1.00] | 0.008 ^a |
| SUVmax | 1.77 | [1.19, 2.65] | 0.005 ^a |
| Volume of segmented PSMA positive tumors | | | |
| Step 1 - Candidate | | | |
| Soft Tissue | | | 0.421 |
| SUVmean | | | 0.450 |
| Tumor load | | | |
| Final multivariate model from the backward/forward selection | | | |
| Soft Tissue | 0.99 | [0.98, 1.00] | 0.008 ^a |
| SUVmax | 1.77 | [1.19, 2.65] | 0.005 ^a |
| Volume of segmented PSMA positive tumors | | | |

Note: The hazard ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-6-5-F-S 2021-08-30 19:16

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-hr.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Final Version

Table 7.1: OS multivariate Cox proportional hazards model - with optimal cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|---|--------------|--------------|--------------------|
| Whole body | | | |
| SUVmean (g/ml) <18 vs. >=18 ^c | 0.06 | [0.01, 0.43] | 0.005 ^a |
| Tumor load (g) <200 vs. >=200 ^c | 1.75 | [1.07, 2.84] | 0.025 ^a |
| Bone | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.36 | [0.20, 0.63] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.48 | [0.36, 0.64] | <.001 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.75 | [0.59, 0.95] | 0.018 ^a |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

^c Reference is '<'

Output ID: T-7-1 2021-08-30 20:59

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-cut-hr2.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmean (g/ml) - Optimal cut | <18 | 0.005 ^a | 0.06 | [0.01, 0.42] | 340/530 (64.2) | 1/18 (5.6) |
| SUVmean (g/ml) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <7 | 0.002 ^a | 0.71 | [0.57, 0.88] | 167/241 (69.3) | 174/307 (56.7) |
| | <8 | <.001 ^a | 0.65 | [0.52, 0.81] | 212/308 (68.8) | 129/240 (53.8) |
| | <9 | <.001 ^a | 0.56 | [0.44, 0.71] | 253/367 (68.9) | 88/181 (48.6) |
| | <10 | <.001 ^a | 0.50 | [0.38, 0.66] | 282/413 (68.3) | 59/135 (43.7) |
| | <11 | <.001 ^a | 0.48 | [0.35, 0.67] | 300/447 (67.1) | 41/101 (40.6) |
| | <12 | <.001 ^a | 0.42 | [0.29, 0.61] | 312/468 (66.7) | 29/80 (36.3) |
| | <13 | <.001 ^a | 0.33 | [0.20, 0.54] | 324/490 (66.1) | 17/58 (29.3) |
| | <14 | <.001 ^a | 0.21 | [0.10, 0.44] | 334/509 (65.6) | 7/39 (17.9) |
| | <15 | <.001 ^a | 0.26 | [0.12, 0.55] | 334/515 (64.9) | 7/33 (21.2) |
| | <16 | <.001 ^a | 0.13 | [0.04, 0.40] | 338/522 (64.8) | 3/26 (11.5) |
| | <17 | <.001 ^a | 0.10 | [0.02, 0.39] | 339/526 (64.4) | 2/22 (9.1) |
| | <18 | 0.005 ^a | 0.06 | [0.01, 0.42] | 340/530 (64.2) | 1/18 (5.6) |
| SUVmean (g/ml) - All cuts | <2 | 0.974 | 164085.8 | [0.00,] | 0/2 (0.0) | 341/546 (62.5) |
| | <3 | 0.627 | 0.80 | [0.33, 1.95] | 5/8 (62.5) | 336/540 (62.2) |
| | <4 | 0.318 | 0.80 | [0.52, 1.24] | 22/32 (68.8) | 319/516 (61.8) |
| | <5 | 0.105 | 0.80 | [0.60, 1.05] | 62/90 (68.9) | 279/458 (60.9) |
| | <6 | 0.052 | 0.80 | [0.63, 1.00] | 104/153 (68.0) | 237/395 (60.0) |
| | <7 | 0.002 ^a | 0.71 | [0.57, 0.88] | 167/241 (69.3) | 174/307 (56.7) |
| | <8 | <.001 ^a | 0.65 | [0.52, 0.81] | 212/308 (68.8) | 129/240 (53.8) |
| | <9 | <.001 ^a | 0.56 | [0.44, 0.71] | 253/367 (68.9) | 88/181 (48.6) |
| | <10 | <.001 ^a | 0.50 | [0.38, 0.66] | 282/413 (68.3) | 59/135 (43.7) |
| | <11 | <.001 ^a | 0.48 | [0.35, 0.67] | 300/447 (67.1) | 41/101 (40.6) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

Output ID: T-7-1-S 2021-08-30 21:12

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|------------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmean (g/ml) - All cuts | <12 | <.001 ^a | 0.42 | [0.29, 0.61] | 312/468 (66.7) | 29/80 (36.3) |
| | <13 | <.001 ^a | 0.33 | [0.20, 0.54] | 324/490 (66.1) | 17/58 (29.3) |
| | <14 | <.001 ^a | 0.21 | [0.10, 0.44] | 334/509 (65.6) | 7/39 (17.9) |
| | <15 | <.001 ^a | 0.26 | [0.12, 0.55] | 334/515 (64.9) | 7/33 (21.2) |
| | <16 | <.001 ^a | 0.13 | [0.04, 0.40] | 338/522 (64.8) | 3/26 (11.5) |
| | <17 | <.001 ^a | 0.10 | [0.02, 0.39] | 339/526 (64.4) | 2/22 (9.1) |
| | <18 | 0.005 ^a | 0.06 | [0.01, 0.42] | 340/530 (64.2) | 1/18 (5.6) |
| | <19 | 0.963 | 0.00 | [0.00, 2.51E253] | 341/533 (64.0) | 0/15 (0.0) |
| | <20 | 0.968 | 0.00 | [0.00, 4.18E296] | 341/537 (63.5) | 0/11 (0.0) |
| | <22 | 0.956 | 0.00 | [0.00, 6.18E196] | 341/539 (63.3) | 0/9 (0.0) |
| | <23 | 0.959 | 0.00 | [0.00, 1.16E210] | 341/540 (63.1) | 0/8 (0.0) |
| | <24 | 0.965 | 0.00 | [0.00, 2.26E250] | 341/542 (62.9) | 0/6 (0.0) |
| | <25 | 0.972 | 0.00 | [0.00,] | 341/544 (62.7) | 0/4 (0.0) |
| | <26 | 0.963 | 0.00 | [0.00, 1.93E217] | 341/545 (62.6) | 0/3 (0.0) |
| | <33 | 0.969 | 0.00 | [0.00, 1.74E254] | 341/546 (62.5) | 0/2 (0.0) |
| | <38 | 0.969 | 0.00 | [0.00, 1.13E233] | 341/547 (62.3) | 0/1 (0.0) |
| Tumor load (g) - Optimal cut | <200 | 0.002 ^a | 2.14 | [1.33, 3.45] | 18/43 (41.9) | 323/505 (64.0) |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <200 | 0.002 ^a | 2.14 | [1.33, 3.45] | 18/43 (41.9) | 323/505 (64.0) |
| | <300 | 0.004 ^a | 1.70 | [1.18, 2.44] | 33/64 (51.6) | 308/484 (63.6) |
| | <400 | <.001 ^a | 1.92 | [1.36, 2.70] | 37/78 (47.4) | 304/470 (64.7) |
| | <500 | <.001 ^a | 1.96 | [1.42, 2.72] | 42/90 (46.7) | 299/458 (65.3) |
| | <600 | <.001 ^a | 1.88 | [1.38, 2.57] | 47/97 (48.5) | 294/451 (65.2) |
| | <700 | <.001 ^a | 1.83 | [1.36, 2.46] | 53/107 (49.5) | 288/441 (65.3) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <800 | <.001 ^a | 1.77 | [1.33, 2.35] | 58/114 (50.9) | 283/434 (65.2) |
| | <900 | <.001 ^a | 1.87 | [1.42, 2.48] | 62/125 (49.6) | 279/423 (66.0) |
| | <1000 | <.001 ^a | 1.76 | [1.35, 2.30] | 70/135 (51.9) | 271/413 (65.6) |
| | <1100 | <.001 ^a | 1.82 | [1.40, 2.37] | 73/144 (50.7) | 268/404 (66.3) |
| | <1200 | <.001 ^a | 1.78 | [1.38, 2.29] | 81/156 (51.9) | 260/392 (66.3) |
| | <1300 | <.001 ^a | 1.76 | [1.37, 2.25] | 87/165 (52.7) | 254/383 (66.3) |
| | <1400 | <.001 ^a | 1.80 | [1.41, 2.29] | 90/172 (52.3) | 251/376 (66.8) |
| | <1500 | <.001 ^a | 1.80 | [1.41, 2.29] | 92/175 (52.6) | 249/373 (66.8) |
| | <1600 | <.001 ^a | 1.88 | [1.47, 2.39] | 92/179 (51.4) | 249/369 (67.5) |
| | <1700 | <.001 ^a | 1.87 | [1.48, 2.37] | 99/191 (51.8) | 242/357 (67.8) |
| | <1800 | <.001 ^a | 1.78 | [1.41, 2.24] | 105/198 (53.0) | 236/350 (67.4) |
| | <1900 | <.001 ^a | 1.88 | [1.49, 2.37] | 106/205 (51.7) | 235/343 (68.5) |
| | <2000 | <.001 ^a | 1.92 | [1.53, 2.43] | 106/207 (51.2) | 235/341 (68.9) |
| | <2100 | <.001 ^a | 1.90 | [1.51, 2.39] | 108/210 (51.4) | 233/338 (68.9) |
| | <2200 | <.001 ^a | 1.88 | [1.50, 2.37] | 110/213 (51.6) | 231/335 (69.0) |
| | <2300 | <.001 ^a | 1.84 | [1.46, 2.31] | 115/220 (52.3) | 226/328 (68.9) |
| | <2400 | <.001 ^a | 1.87 | [1.49, 2.34] | 117/226 (51.8) | 224/322 (69.6) |
| | <2500 | <.001 ^a | 1.84 | [1.47, 2.31] | 121/233 (51.9) | 220/315 (69.8) |
| | <2600 | <.001 ^a | 1.84 | [1.48, 2.30] | 126/240 (52.5) | 215/308 (69.8) |
| | <2700 | <.001 ^a | 1.80 | [1.44, 2.24] | 130/244 (53.3) | 211/304 (69.4) |
| | <2800 | <.001 ^a | 1.78 | [1.43, 2.22] | 131/245 (53.5) | 210/303 (69.3) |
| | <2900 | <.001 ^a | 1.73 | [1.39, 2.15] | 134/248 (54.0) | 207/300 (69.0) |
| | <3000 | <.001 ^a | 1.69 | [1.36, 2.11] | 139/256 (54.3) | 202/292 (69.2) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <3100 | <.001 ^a | 1.69 | [1.36, 2.11] | 141/259 (54.4) | 200/289 (69.2) |
| | <3200 | <.001 ^a | 1.67 | [1.34, 2.07] | 146/265 (55.1) | 195/283 (68.9) |
| | <3300 | <.001 ^a | 1.66 | [1.34, 2.06] | 150/272 (55.1) | 191/276 (69.2) |
| | <3400 | <.001 ^a | 1.70 | [1.37, 2.11] | 150/274 (54.7) | 191/274 (69.7) |
| | <3500 | <.001 ^a | 1.76 | [1.42, 2.19] | 151/278 (54.3) | 190/270 (70.4) |
| | <3600 | <.001 ^a | 1.74 | [1.40, 2.16] | 152/279 (54.5) | 189/269 (70.3) |
| | <3700 | <.001 ^a | 1.74 | [1.41, 2.16] | 153/281 (54.4) | 188/267 (70.4) |
| | <3800 | <.001 ^a | 1.79 | [1.45, 2.22] | 157/289 (54.3) | 184/259 (71.0) |
| | <3900 | <.001 ^a | 1.82 | [1.47, 2.25] | 158/292 (54.1) | 183/256 (71.5) |
| | <4000 | <.001 ^a | 1.85 | [1.49, 2.29] | 159/295 (53.9) | 182/253 (71.9) |
| | <4100 | <.001 ^a | 1.83 | [1.48, 2.27] | 163/301 (54.2) | 178/247 (72.1) |
| | <4200 | <.001 ^a | 1.83 | [1.48, 2.27] | 166/306 (54.2) | 175/242 (72.3) |
| | <4300 | <.001 ^a | 1.86 | [1.50, 2.30] | 169/312 (54.2) | 172/236 (72.9) |
| | <4500 | <.001 ^a | 1.82 | [1.47, 2.25] | 173/316 (54.7) | 168/232 (72.4) |
| | <4600 | <.001 ^a | 1.81 | [1.46, 2.25] | 174/317 (54.9) | 167/231 (72.3) |
| | <4700 | <.001 ^a | 1.82 | [1.47, 2.25] | 175/319 (54.9) | 166/229 (72.5) |
| | <4900 | <.001 ^a | 1.79 | [1.45, 2.22] | 177/321 (55.1) | 164/227 (72.2) |
| | <5000 | <.001 ^a | 1.78 | [1.43, 2.20] | 178/322 (55.3) | 163/226 (72.1) |
| | <5100 | <.001 ^a | 1.84 | [1.48, 2.28] | 179/326 (54.9) | 162/222 (73.0) |
| | <5200 | <.001 ^a | 1.80 | [1.46, 2.23] | 183/331 (55.3) | 158/217 (72.8) |
| | <5300 | <.001 ^a | 1.83 | [1.48, 2.27] | 185/336 (55.1) | 156/212 (73.6) |
| | <5400 | <.001 ^a | 1.87 | [1.51, 2.32] | 185/338 (54.7) | 156/210 (74.3) |
| | <5500 | <.001 ^a | 1.88 | [1.52, 2.33] | 186/340 (54.7) | 155/208 (74.5) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <5600 | <.001 ^a | 1.87 | [1.51, 2.32] | 187/342 (54.7) | 154/206 (74.8) |
| | <5700 | <.001 ^a | 1.91 | [1.54, 2.37] | 189/346 (54.6) | 152/202 (75.2) |
| | <5800 | <.001 ^a | 1.88 | [1.51, 2.33] | 191/348 (54.9) | 150/200 (75.0) |
| | <5900 | <.001 ^a | 1.85 | [1.49, 2.29] | 193/350 (55.1) | 148/198 (74.7) |
| | <6000 | <.001 ^a | 1.82 | [1.46, 2.25] | 195/352 (55.4) | 146/196 (74.5) |
| | <6100 | <.001 ^a | 1.80 | [1.45, 2.23] | 196/353 (55.5) | 145/195 (74.4) |
| | <6300 | <.001 ^a | 1.82 | [1.46, 2.26] | 198/357 (55.5) | 143/191 (74.9) |
| | <6400 | <.001 ^a | 1.78 | [1.44, 2.22] | 201/360 (55.8) | 140/188 (74.5) |
| | <6500 | <.001 ^a | 1.80 | [1.45, 2.24] | 202/362 (55.8) | 139/186 (74.7) |
| | <6600 | <.001 ^a | 1.75 | [1.41, 2.18] | 205/365 (56.2) | 136/183 (74.3) |
| | <6700 | <.001 ^a | 1.77 | [1.42, 2.20] | 207/369 (56.1) | 134/179 (74.9) |
| | <6800 | <.001 ^a | 1.80 | [1.45, 2.24] | 209/372 (56.2) | 132/176 (75.0) |
| | <6900 | <.001 ^a | 1.79 | [1.44, 2.23] | 210/373 (56.3) | 131/175 (74.9) |
| | <7000 | <.001 ^a | 1.78 | [1.43, 2.21] | 212/375 (56.5) | 129/173 (74.6) |
| | <7100 | <.001 ^a | 1.73 | [1.38, 2.15] | 215/378 (56.9) | 126/170 (74.1) |
| | <7200 | <.001 ^a | 1.75 | [1.40, 2.18] | 215/379 (56.7) | 126/169 (74.6) |
| | <7300 | <.001 ^a | 1.74 | [1.39, 2.17] | 216/380 (56.8) | 125/168 (74.4) |
| | <7400 | <.001 ^a | 1.78 | [1.43, 2.22] | 216/382 (56.5) | 125/166 (75.3) |
| | <7600 | <.001 ^a | 1.81 | [1.45, 2.26] | 216/383 (56.4) | 125/165 (75.8) |
| | <7700 | <.001 ^a | 1.80 | [1.44, 2.25] | 217/384 (56.5) | 124/164 (75.6) |
| | <7800 | <.001 ^a | 1.82 | [1.45, 2.27] | 218/386 (56.5) | 123/162 (75.9) |
| | <7900 | <.001 ^a | 1.79 | [1.43, 2.24] | 220/388 (56.7) | 121/160 (75.6) |
| | <8100 | <.001 ^a | 1.77 | [1.41, 2.21] | 223/391 (57.0) | 118/157 (75.2) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <8200 | <.001 ^a | 1.75 | [1.40, 2.19] | 225/393 (57.3) | 116/155 (74.8) |
| | <8300 | <.001 ^a | 1.75 | [1.40, 2.19] | 226/394 (57.4) | 115/154 (74.7) |
| | <8400 | <.001 ^a | 1.73 | [1.38, 2.17] | 227/395 (57.5) | 114/153 (74.5) |
| | <8600 | <.001 ^a | 1.80 | [1.43, 2.25] | 227/397 (57.2) | 114/151 (75.5) |
| | <8700 | <.001 ^a | 1.77 | [1.41, 2.22] | 229/399 (57.4) | 112/149 (75.2) |
| | <8900 | <.001 ^a | 1.75 | [1.39, 2.20] | 230/400 (57.5) | 111/148 (75.0) |
| | <9000 | <.001 ^a | 1.73 | [1.38, 2.17] | 231/401 (57.6) | 110/147 (74.8) |
| | <9100 | <.001 ^a | 1.69 | [1.35, 2.13] | 233/403 (57.8) | 108/145 (74.5) |
| | <9200 | <.001 ^a | 1.66 | [1.32, 2.08] | 235/405 (58.0) | 106/143 (74.1) |
| | <9400 | <.001 ^a | 1.65 | [1.31, 2.08] | 236/406 (58.1) | 105/142 (73.9) |
| | <9500 | <.001 ^a | 1.68 | [1.33, 2.12] | 236/407 (58.0) | 105/141 (74.5) |
| | <9700 | <.001 ^a | 1.69 | [1.34, 2.13] | 238/410 (58.0) | 103/138 (74.6) |
| | <9900 | <.001 ^a | 1.71 | [1.35, 2.15] | 238/411 (57.9) | 103/137 (75.2) |
| | <10000 | <.001 ^a | 1.66 | [1.32, 2.10] | 241/414 (58.2) | 100/134 (74.6) |
| | <10100 | <.001 ^a | 1.62 | [1.28, 2.05] | 244/417 (58.5) | 97/131 (74.0) |
| | <10200 | <.001 ^a | 1.66 | [1.31, 2.10] | 244/418 (58.4) | 97/130 (74.6) |
| | <10400 | <.001 ^a | 1.65 | [1.30, 2.08] | 245/419 (58.5) | 96/129 (74.4) |
| | <10600 | <.001 ^a | 1.64 | [1.29, 2.08] | 247/422 (58.5) | 94/126 (74.6) |
| | <10900 | <.001 ^a | 1.67 | [1.31, 2.12] | 247/423 (58.4) | 94/125 (75.2) |
| | <11100 | <.001 ^a | 1.66 | [1.31, 2.11] | 248/424 (58.5) | 93/124 (75.0) |
| | <11200 | <.001 ^a | 1.68 | [1.33, 2.14] | 248/425 (58.4) | 93/123 (75.6) |
| | <11300 | <.001 ^a | 1.68 | [1.32, 2.13] | 250/428 (58.4) | 91/120 (75.8) |
| | <11500 | <.001 ^a | 1.69 | [1.33, 2.15] | 251/430 (58.4) | 90/118 (76.3) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|---------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <11600 | <.001 ^a | 1.72 | [1.35, 2.19] | 251/431 (58.2) | 90/117 (76.9) |
| | <11700 | <.001 ^a | 1.69 | [1.33, 2.16] | 253/433 (58.4) | 88/115 (76.5) |
| | <11900 | <.001 ^a | 1.70 | [1.33, 2.17] | 254/434 (58.5) | 87/114 (76.3) |
| | <12200 | <.001 ^a | 1.69 | [1.32, 2.16] | 255/435 (58.6) | 86/113 (76.1) |
| | <12300 | <.001 ^a | 1.67 | [1.31, 2.14] | 256/436 (58.7) | 85/112 (75.9) |
| | <12500 | <.001 ^a | 1.66 | [1.30, 2.13] | 257/437 (58.8) | 84/111 (75.7) |
| | <12700 | <.001 ^a | 1.61 | [1.26, 2.07] | 260/440 (59.1) | 81/108 (75.0) |
| | <12900 | <.001 ^a | 1.65 | [1.28, 2.12] | 262/443 (59.1) | 79/105 (75.2) |
| | <13000 | <.001 ^a | 1.62 | [1.25, 2.08] | 264/445 (59.3) | 77/103 (74.8) |
| | <13100 | <.001 ^a | 1.60 | [1.24, 2.06] | 265/446 (59.4) | 76/102 (74.5) |
| | <13400 | <.001 ^a | 1.60 | [1.24, 2.07] | 266/447 (59.5) | 75/101 (74.3) |
| | <13500 | <.001 ^a | 1.63 | [1.26, 2.11] | 267/450 (59.3) | 74/98 (75.5) |
| | <13700 | <.001 ^a | 1.63 | [1.25, 2.11] | 269/452 (59.5) | 72/96 (75.0) |
| | <13800 | <.001 ^a | 1.61 | [1.24, 2.09] | 270/453 (59.6) | 71/95 (74.7) |
| | <13900 | 0.001 ^a | 1.55 | [1.19, 2.03] | 273/456 (59.9) | 68/92 (73.9) |
| | <14000 | 0.002 ^a | 1.54 | [1.18, 2.01] | 274/457 (60.0) | 67/91 (73.6) |
| | <14100 | 0.001 ^a | 1.55 | [1.19, 2.03] | 275/458 (60.0) | 66/90 (73.3) |
| | <14400 | 0.002 ^a | 1.53 | [1.17, 2.01] | 276/459 (60.1) | 65/89 (73.0) |
| | <14700 | 0.003 ^a | 1.51 | [1.15, 1.98] | 277/460 (60.2) | 64/88 (72.7) |
| | <14800 | 0.003 ^a | 1.51 | [1.15, 1.99] | 278/461 (60.3) | 63/87 (72.4) |
| | <14900 | 0.001 ^a | 1.59 | [1.21, 2.10] | 280/465 (60.2) | 61/83 (73.5) |
| | <15000 | <.001 ^a | 1.65 | [1.25, 2.17] | 280/466 (60.1) | 61/82 (74.4) |
| | <15100 | <.001 ^a | 1.68 | [1.27, 2.21] | 281/468 (60.0) | 60/80 (75.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company

68Ga-PSMA-11 Quantitative analysis

Final Version

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <15400 | <.001 ^a | 1.63 | [1.23, 2.17] | 283/470 (60.2) | 58/78 (74.4) |
| | <15500 | <.001 ^a | 1.72 | [1.30, 2.29] | 283/472 (60.0) | 58/76 (76.3) |
| | <15600 | <.001 ^a | 1.70 | [1.28, 2.26] | 284/473 (60.0) | 57/75 (76.0) |
| | <15800 | <.001 ^a | 1.75 | [1.31, 2.32] | 284/474 (59.9) | 57/74 (77.0) |
| | <15900 | <.001 ^a | 1.84 | [1.38, 2.45] | 284/475 (59.8) | 57/73 (78.1) |
| | <16000 | <.001 ^a | 1.88 | [1.41, 2.50] | 285/477 (59.7) | 56/71 (78.9) |
| | <16100 | <.001 ^a | 1.90 | [1.42, 2.54] | 286/478 (59.8) | 55/70 (78.6) |
| | <16200 | <.001 ^a | 1.89 | [1.41, 2.53] | 287/479 (59.9) | 54/69 (78.3) |
| | <16400 | <.001 ^a | 1.86 | [1.38, 2.49] | 288/480 (60.0) | 53/68 (77.9) |
| | <16600 | <.001 ^a | 1.82 | [1.35, 2.46] | 290/482 (60.2) | 51/66 (77.3) |
| | <16800 | <.001 ^a | 1.80 | [1.33, 2.45] | 293/485 (60.4) | 48/63 (76.2) |
| | <16900 | <.001 ^a | 1.76 | [1.29, 2.40] | 294/486 (60.5) | 47/62 (75.8) |
| | <17000 | <.001 ^a | 1.72 | [1.26, 2.35] | 295/487 (60.6) | 46/61 (75.4) |
| | <17100 | <.001 ^a | 1.70 | [1.24, 2.32] | 296/488 (60.7) | 45/60 (75.0) |
| | <17200 | 0.001 ^a | 1.67 | [1.22, 2.30] | 297/489 (60.7) | 44/59 (74.6) |
| | <18000 | 0.002 ^a | 1.64 | [1.19, 2.26] | 298/490 (60.8) | 43/58 (74.1) |
| | <18500 | <.001 ^a | 1.74 | [1.26, 2.40] | 299/492 (60.8) | 42/56 (75.0) |
| | <18800 | 0.001 ^a | 1.70 | [1.23, 2.36] | 300/493 (60.9) | 41/55 (74.5) |
| | <18900 | 0.002 ^a | 1.68 | [1.21, 2.34] | 301/494 (60.9) | 40/54 (74.1) |
| | <19300 | 0.004 ^a | 1.64 | [1.17, 2.29] | 303/496 (61.1) | 38/52 (73.1) |
| | <19800 | 0.001 ^a | 1.75 | [1.25, 2.46] | 303/497 (61.0) | 38/51 (74.5) |
| | <19900 | 0.002 ^a | 1.71 | [1.21, 2.40] | 304/498 (61.0) | 37/50 (74.0) |
| | <20100 | 0.008 ^a | 1.61 | [1.14, 2.29] | 306/500 (61.2) | 35/48 (72.9) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company

68Ga-PSMA-11 Quantitative analysis

Final Version

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <20700 | 0.003 ^a | 1.70 | [1.20, 2.41] | 306/501 (61.1) | 35/47 (74.5) |
| | <21200 | 0.004 ^a | 1.69 | [1.19, 2.41] | 307/502 (61.2) | 34/46 (73.9) |
| | <21400 | 0.004 ^a | 1.69 | [1.18, 2.43] | 308/503 (61.2) | 33/45 (73.3) |
| | <21600 | 0.003 ^a | 1.74 | [1.21, 2.51] | 309/504 (61.3) | 32/44 (72.7) |
| | <22100 | 0.003 ^a | 1.77 | [1.22, 2.56] | 310/506 (61.3) | 31/42 (73.8) |
| | <22500 | 0.003 ^a | 1.78 | [1.23, 2.60] | 311/507 (61.3) | 30/41 (73.2) |
| | <22600 | 0.001 ^a | 1.86 | [1.28, 2.71] | 311/508 (61.2) | 30/40 (75.0) |
| | <22900 | 0.002 ^a | 1.85 | [1.26, 2.70] | 312/509 (61.3) | 29/39 (74.4) |
| | <23000 | 0.002 ^a | 1.83 | [1.24, 2.70] | 313/510 (61.4) | 28/38 (73.7) |
| | <23200 | <.001 ^a | 1.97 | [1.34, 2.91] | 313/511 (61.3) | 28/37 (75.7) |
| | <23400 | 0.001 ^a | 1.91 | [1.29, 2.83] | 314/512 (61.3) | 27/36 (75.0) |
| | <23800 | 0.002 ^a | 1.88 | [1.26, 2.81] | 315/513 (61.4) | 26/35 (74.3) |
| | <23900 | 0.004 ^a | 1.83 | [1.21, 2.75] | 316/514 (61.5) | 25/34 (73.5) |
| | <24000 | 0.006 ^a | 1.78 | [1.18, 2.70] | 317/515 (61.6) | 24/33 (72.7) |
| | <24300 | 0.014 ^a | 1.71 | [1.12, 2.61] | 318/516 (61.6) | 23/32 (71.9) |
| | <24400 | 0.004 ^a | 1.85 | [1.21, 2.83] | 318/517 (61.5) | 23/31 (74.2) |
| | <24900 | 0.010 ^a | 1.77 | [1.15, 2.73] | 319/518 (61.6) | 22/30 (73.3) |
| | <25100 | 0.004 ^a | 1.90 | [1.23, 2.92] | 319/519 (61.5) | 22/29 (75.9) |
| | <25800 | 0.007 ^a | 1.84 | [1.18, 2.86] | 320/520 (61.5) | 21/28 (75.0) |
| | <26000 | 0.010 ^a | 1.81 | [1.15, 2.85] | 321/521 (61.6) | 20/27 (74.1) |
| | <26200 | 0.022 ^a | 1.72 | [1.08, 2.73] | 322/522 (61.7) | 19/26 (73.1) |
| Tumor load (g) - All cuts | <100 | 0.208 | 1.57 | [0.78, 3.17] | 8/19 (42.1) | 333/529 (62.9) |
| | <200 | 0.002 ^a | 2.14 | [1.33, 3.45] | 18/43 (41.9) | 323/505 (64.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-cut-hr2.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <300 | 0.004 ^a | 1.70 | [1.18, 2.44] | 33/64 (51.6) | 308/484 (63.6) |
| | <400 | <.001 ^a | 1.92 | [1.36, 2.70] | 37/78 (47.4) | 304/470 (64.7) |
| | <500 | <.001 ^a | 1.96 | [1.42, 2.72] | 42/90 (46.7) | 299/458 (65.3) |
| | <600 | <.001 ^a | 1.88 | [1.38, 2.57] | 47/97 (48.5) | 294/451 (65.2) |
| | <700 | <.001 ^a | 1.83 | [1.36, 2.46] | 53/107 (49.5) | 288/441 (65.3) |
| | <800 | <.001 ^a | 1.77 | [1.33, 2.35] | 58/114 (50.9) | 283/434 (65.2) |
| | <900 | <.001 ^a | 1.87 | [1.42, 2.48] | 62/125 (49.6) | 279/423 (66.0) |
| | <1000 | <.001 ^a | 1.76 | [1.35, 2.30] | 70/135 (51.9) | 271/413 (65.6) |
| | <1100 | <.001 ^a | 1.82 | [1.40, 2.37] | 73/144 (50.7) | 268/404 (66.3) |
| | <1200 | <.001 ^a | 1.78 | [1.38, 2.29] | 81/156 (51.9) | 260/392 (66.3) |
| | <1300 | <.001 ^a | 1.76 | [1.37, 2.25] | 87/165 (52.7) | 254/383 (66.3) |
| | <1400 | <.001 ^a | 1.80 | [1.41, 2.29] | 90/172 (52.3) | 251/376 (66.8) |
| | <1500 | <.001 ^a | 1.80 | [1.41, 2.29] | 92/175 (52.6) | 249/373 (66.8) |
| | <1600 | <.001 ^a | 1.88 | [1.47, 2.39] | 92/179 (51.4) | 249/369 (67.5) |
| | <1700 | <.001 ^a | 1.87 | [1.48, 2.37] | 99/191 (51.8) | 242/357 (67.8) |
| | <1800 | <.001 ^a | 1.78 | [1.41, 2.24] | 105/198 (53.0) | 236/350 (67.4) |
| | <1900 | <.001 ^a | 1.88 | [1.49, 2.37] | 106/205 (51.7) | 235/343 (68.5) |
| | <2000 | <.001 ^a | 1.92 | [1.53, 2.43] | 106/207 (51.2) | 235/341 (68.9) |
| | <2100 | <.001 ^a | 1.90 | [1.51, 2.39] | 108/210 (51.4) | 233/338 (68.9) |
| | <2200 | <.001 ^a | 1.88 | [1.50, 2.37] | 110/213 (51.6) | 231/335 (69.0) |
| | <2300 | <.001 ^a | 1.84 | [1.46, 2.31] | 115/220 (52.3) | 226/328 (68.9) |
| | <2400 | <.001 ^a | 1.87 | [1.49, 2.34] | 117/226 (51.8) | 224/322 (69.6) |
| | <2500 | <.001 ^a | 1.84 | [1.47, 2.31] | 121/233 (51.9) | 220/315 (69.8) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <2600 | <.001 ^a | 1.84 | [1.48, 2.30] | 126/240 (52.5) | 215/308 (69.8) |
| | <2700 | <.001 ^a | 1.80 | [1.44, 2.24] | 130/244 (53.3) | 211/304 (69.4) |
| | <2800 | <.001 ^a | 1.78 | [1.43, 2.22] | 131/245 (53.5) | 210/303 (69.3) |
| | <2900 | <.001 ^a | 1.73 | [1.39, 2.15] | 134/248 (54.0) | 207/300 (69.0) |
| | <3000 | <.001 ^a | 1.69 | [1.36, 2.11] | 139/256 (54.3) | 202/292 (69.2) |
| | <3100 | <.001 ^a | 1.69 | [1.36, 2.11] | 141/259 (54.4) | 200/289 (69.2) |
| | <3200 | <.001 ^a | 1.67 | [1.34, 2.07] | 146/265 (55.1) | 195/283 (68.9) |
| | <3300 | <.001 ^a | 1.66 | [1.34, 2.06] | 150/272 (55.1) | 191/276 (69.2) |
| | <3400 | <.001 ^a | 1.70 | [1.37, 2.11] | 150/274 (54.7) | 191/274 (69.7) |
| | <3500 | <.001 ^a | 1.76 | [1.42, 2.19] | 151/278 (54.3) | 190/270 (70.4) |
| | <3600 | <.001 ^a | 1.74 | [1.40, 2.16] | 152/279 (54.5) | 189/269 (70.3) |
| | <3700 | <.001 ^a | 1.74 | [1.41, 2.16] | 153/281 (54.4) | 188/267 (70.4) |
| | <3800 | <.001 ^a | 1.79 | [1.45, 2.22] | 157/289 (54.3) | 184/259 (71.0) |
| | <3900 | <.001 ^a | 1.82 | [1.47, 2.25] | 158/292 (54.1) | 183/256 (71.5) |
| | <4000 | <.001 ^a | 1.85 | [1.49, 2.29] | 159/295 (53.9) | 182/253 (71.9) |
| | <4100 | <.001 ^a | 1.83 | [1.48, 2.27] | 163/301 (54.2) | 178/247 (72.1) |
| | <4200 | <.001 ^a | 1.83 | [1.48, 2.27] | 166/306 (54.2) | 175/242 (72.3) |
| | <4300 | <.001 ^a | 1.86 | [1.50, 2.30] | 169/312 (54.2) | 172/236 (72.9) |
| | <4500 | <.001 ^a | 1.82 | [1.47, 2.25] | 173/316 (54.7) | 168/232 (72.4) |
| | <4600 | <.001 ^a | 1.81 | [1.46, 2.25] | 174/317 (54.9) | 167/231 (72.3) |
| | <4700 | <.001 ^a | 1.82 | [1.47, 2.25] | 175/319 (54.9) | 166/229 (72.5) |
| | <4900 | <.001 ^a | 1.79 | [1.45, 2.22] | 177/321 (55.1) | 164/227 (72.2) |
| | <5000 | <.001 ^a | 1.78 | [1.43, 2.20] | 178/322 (55.3) | 163/226 (72.1) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <5100 | <.001 ^a | 1.84 | [1.48, 2.28] | 179/326 (54.9) | 162/222 (73.0) |
| | <5200 | <.001 ^a | 1.80 | [1.46, 2.23] | 183/331 (55.3) | 158/217 (72.8) |
| | <5300 | <.001 ^a | 1.83 | [1.48, 2.27] | 185/336 (55.1) | 156/212 (73.6) |
| | <5400 | <.001 ^a | 1.87 | [1.51, 2.32] | 185/338 (54.7) | 156/210 (74.3) |
| | <5500 | <.001 ^a | 1.88 | [1.52, 2.33] | 186/340 (54.7) | 155/208 (74.5) |
| | <5600 | <.001 ^a | 1.87 | [1.51, 2.32] | 187/342 (54.7) | 154/206 (74.8) |
| | <5700 | <.001 ^a | 1.91 | [1.54, 2.37] | 189/346 (54.6) | 152/202 (75.2) |
| | <5800 | <.001 ^a | 1.88 | [1.51, 2.33] | 191/348 (54.9) | 150/200 (75.0) |
| | <5900 | <.001 ^a | 1.85 | [1.49, 2.29] | 193/350 (55.1) | 148/198 (74.7) |
| | <6000 | <.001 ^a | 1.82 | [1.46, 2.25] | 195/352 (55.4) | 146/196 (74.5) |
| | <6100 | <.001 ^a | 1.80 | [1.45, 2.23] | 196/353 (55.5) | 145/195 (74.4) |
| | <6300 | <.001 ^a | 1.82 | [1.46, 2.26] | 198/357 (55.5) | 143/191 (74.9) |
| | <6400 | <.001 ^a | 1.78 | [1.44, 2.22] | 201/360 (55.8) | 140/188 (74.5) |
| | <6500 | <.001 ^a | 1.80 | [1.45, 2.24] | 202/362 (55.8) | 139/186 (74.7) |
| | <6600 | <.001 ^a | 1.75 | [1.41, 2.18] | 205/365 (56.2) | 136/183 (74.3) |
| | <6700 | <.001 ^a | 1.77 | [1.42, 2.20] | 207/369 (56.1) | 134/179 (74.9) |
| | <6800 | <.001 ^a | 1.80 | [1.45, 2.24] | 209/372 (56.2) | 132/176 (75.0) |
| | <6900 | <.001 ^a | 1.79 | [1.44, 2.23] | 210/373 (56.3) | 131/175 (74.9) |
| | <7000 | <.001 ^a | 1.78 | [1.43, 2.21] | 212/375 (56.5) | 129/173 (74.6) |
| | <7100 | <.001 ^a | 1.73 | [1.38, 2.15] | 215/378 (56.9) | 126/170 (74.1) |
| | <7200 | <.001 ^a | 1.75 | [1.40, 2.18] | 215/379 (56.7) | 126/169 (74.6) |
| | <7300 | <.001 ^a | 1.74 | [1.39, 2.17] | 216/380 (56.8) | 125/168 (74.4) |
| | <7400 | <.001 ^a | 1.78 | [1.43, 2.22] | 216/382 (56.5) | 125/166 (75.3) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <7600 | <.001 ^a | 1.81 | [1.45, 2.26] | 216/383 (56.4) | 125/165 (75.8) |
| | <7700 | <.001 ^a | 1.80 | [1.44, 2.25] | 217/384 (56.5) | 124/164 (75.6) |
| | <7800 | <.001 ^a | 1.82 | [1.45, 2.27] | 218/386 (56.5) | 123/162 (75.9) |
| | <7900 | <.001 ^a | 1.79 | [1.43, 2.24] | 220/388 (56.7) | 121/160 (75.6) |
| | <8100 | <.001 ^a | 1.77 | [1.41, 2.21] | 223/391 (57.0) | 118/157 (75.2) |
| | <8200 | <.001 ^a | 1.75 | [1.40, 2.19] | 225/393 (57.3) | 116/155 (74.8) |
| | <8300 | <.001 ^a | 1.75 | [1.40, 2.19] | 226/394 (57.4) | 115/154 (74.7) |
| | <8400 | <.001 ^a | 1.73 | [1.38, 2.17] | 227/395 (57.5) | 114/153 (74.5) |
| | <8600 | <.001 ^a | 1.80 | [1.43, 2.25] | 227/397 (57.2) | 114/151 (75.5) |
| | <8700 | <.001 ^a | 1.77 | [1.41, 2.22] | 229/399 (57.4) | 112/149 (75.2) |
| | <8900 | <.001 ^a | 1.75 | [1.39, 2.20] | 230/400 (57.5) | 111/148 (75.0) |
| | <9000 | <.001 ^a | 1.73 | [1.38, 2.17] | 231/401 (57.6) | 110/147 (74.8) |
| | <9100 | <.001 ^a | 1.69 | [1.35, 2.13] | 233/403 (57.8) | 108/145 (74.5) |
| | <9200 | <.001 ^a | 1.66 | [1.32, 2.08] | 235/405 (58.0) | 106/143 (74.1) |
| | <9400 | <.001 ^a | 1.65 | [1.31, 2.08] | 236/406 (58.1) | 105/142 (73.9) |
| | <9500 | <.001 ^a | 1.68 | [1.33, 2.12] | 236/407 (58.0) | 105/141 (74.5) |
| | <9700 | <.001 ^a | 1.69 | [1.34, 2.13] | 238/410 (58.0) | 103/138 (74.6) |
| | <9900 | <.001 ^a | 1.71 | [1.35, 2.15] | 238/411 (57.9) | 103/137 (75.2) |
| | <10000 | <.001 ^a | 1.66 | [1.32, 2.10] | 241/414 (58.2) | 100/134 (74.6) |
| | <10100 | <.001 ^a | 1.62 | [1.28, 2.05] | 244/417 (58.5) | 97/131 (74.0) |
| | <10200 | <.001 ^a | 1.66 | [1.31, 2.10] | 244/418 (58.4) | 97/130 (74.6) |
| | <10400 | <.001 ^a | 1.65 | [1.30, 2.08] | 245/419 (58.5) | 96/129 (74.4) |
| | <10600 | <.001 ^a | 1.64 | [1.29, 2.08] | 247/422 (58.5) | 94/126 (74.6) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|---------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <10900 | <.001 ^a | 1.67 | [1.31, 2.12] | 247/423 (58.4) | 94/125 (75.2) |
| | <11100 | <.001 ^a | 1.66 | [1.31, 2.11] | 248/424 (58.5) | 93/124 (75.0) |
| | <11200 | <.001 ^a | 1.68 | [1.33, 2.14] | 248/425 (58.4) | 93/123 (75.6) |
| | <11300 | <.001 ^a | 1.68 | [1.32, 2.13] | 250/428 (58.4) | 91/120 (75.8) |
| | <11500 | <.001 ^a | 1.69 | [1.33, 2.15] | 251/430 (58.4) | 90/118 (76.3) |
| | <11600 | <.001 ^a | 1.72 | [1.35, 2.19] | 251/431 (58.2) | 90/117 (76.9) |
| | <11700 | <.001 ^a | 1.69 | [1.33, 2.16] | 253/433 (58.4) | 88/115 (76.5) |
| | <11900 | <.001 ^a | 1.70 | [1.33, 2.17] | 254/434 (58.5) | 87/114 (76.3) |
| | <12200 | <.001 ^a | 1.69 | [1.32, 2.16] | 255/435 (58.6) | 86/113 (76.1) |
| | <12300 | <.001 ^a | 1.67 | [1.31, 2.14] | 256/436 (58.7) | 85/112 (75.9) |
| | <12500 | <.001 ^a | 1.66 | [1.30, 2.13] | 257/437 (58.8) | 84/111 (75.7) |
| | <12700 | <.001 ^a | 1.61 | [1.26, 2.07] | 260/440 (59.1) | 81/108 (75.0) |
| | <12900 | <.001 ^a | 1.65 | [1.28, 2.12] | 262/443 (59.1) | 79/105 (75.2) |
| | <13000 | <.001 ^a | 1.62 | [1.25, 2.08] | 264/445 (59.3) | 77/103 (74.8) |
| | <13100 | <.001 ^a | 1.60 | [1.24, 2.06] | 265/446 (59.4) | 76/102 (74.5) |
| | <13400 | <.001 ^a | 1.60 | [1.24, 2.07] | 266/447 (59.5) | 75/101 (74.3) |
| | <13500 | <.001 ^a | 1.63 | [1.26, 2.11] | 267/450 (59.3) | 74/98 (75.5) |
| | <13700 | <.001 ^a | 1.63 | [1.25, 2.11] | 269/452 (59.5) | 72/96 (75.0) |
| | <13800 | <.001 ^a | 1.61 | [1.24, 2.09] | 270/453 (59.6) | 71/95 (74.7) |
| | <13900 | 0.001 ^a | 1.55 | [1.19, 2.03] | 273/456 (59.9) | 68/92 (73.9) |
| | <14000 | 0.002 ^a | 1.54 | [1.18, 2.01] | 274/457 (60.0) | 67/91 (73.6) |
| | <14100 | 0.001 ^a | 1.55 | [1.19, 2.03] | 275/458 (60.0) | 66/90 (73.3) |
| | <14400 | 0.002 ^a | 1.53 | [1.17, 2.01] | 276/459 (60.1) | 65/89 (73.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <14700 | 0.003 ^a | 1.51 | [1.15, 1.98] | 277/460 (60.2) | 64/88 (72.7) |
| | <14800 | 0.003 ^a | 1.51 | [1.15, 1.99] | 278/461 (60.3) | 63/87 (72.4) |
| | <14900 | 0.001 ^a | 1.59 | [1.21, 2.10] | 280/465 (60.2) | 61/83 (73.5) |
| | <15000 | <.001 ^a | 1.65 | [1.25, 2.17] | 280/466 (60.1) | 61/82 (74.4) |
| | <15100 | <.001 ^a | 1.68 | [1.27, 2.21] | 281/468 (60.0) | 60/80 (75.0) |
| | <15400 | <.001 ^a | 1.63 | [1.23, 2.17] | 283/470 (60.2) | 58/78 (74.4) |
| | <15500 | <.001 ^a | 1.72 | [1.30, 2.29] | 283/472 (60.0) | 58/76 (76.3) |
| | <15600 | <.001 ^a | 1.70 | [1.28, 2.26] | 284/473 (60.0) | 57/75 (76.0) |
| | <15800 | <.001 ^a | 1.75 | [1.31, 2.32] | 284/474 (59.9) | 57/74 (77.0) |
| | <15900 | <.001 ^a | 1.84 | [1.38, 2.45] | 284/475 (59.8) | 57/73 (78.1) |
| | <16000 | <.001 ^a | 1.88 | [1.41, 2.50] | 285/477 (59.7) | 56/71 (78.9) |
| | <16100 | <.001 ^a | 1.90 | [1.42, 2.54] | 286/478 (59.8) | 55/70 (78.6) |
| | <16200 | <.001 ^a | 1.89 | [1.41, 2.53] | 287/479 (59.9) | 54/69 (78.3) |
| | <16400 | <.001 ^a | 1.86 | [1.38, 2.49] | 288/480 (60.0) | 53/68 (77.9) |
| | <16600 | <.001 ^a | 1.82 | [1.35, 2.46] | 290/482 (60.2) | 51/66 (77.3) |
| | <16800 | <.001 ^a | 1.80 | [1.33, 2.45] | 293/485 (60.4) | 48/63 (76.2) |
| | <16900 | <.001 ^a | 1.76 | [1.29, 2.40] | 294/486 (60.5) | 47/62 (75.8) |
| | <17000 | <.001 ^a | 1.72 | [1.26, 2.35] | 295/487 (60.6) | 46/61 (75.4) |
| | <17100 | <.001 ^a | 1.70 | [1.24, 2.32] | 296/488 (60.7) | 45/60 (75.0) |
| | <17200 | 0.001 ^a | 1.67 | [1.22, 2.30] | 297/489 (60.7) | 44/59 (74.6) |
| | <18000 | 0.002 ^a | 1.64 | [1.19, 2.26] | 298/490 (60.8) | 43/58 (74.1) |
| | <18500 | <.001 ^a | 1.74 | [1.26, 2.40] | 299/492 (60.8) | 42/56 (75.0) |
| | <18800 | 0.001 ^a | 1.70 | [1.23, 2.36] | 300/493 (60.9) | 41/55 (74.5) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <18900 | 0.002 ^a | 1.68 | [1.21, 2.34] | 301/494 (60.9) | 40/54 (74.1) |
| | <19300 | 0.004 ^a | 1.64 | [1.17, 2.29] | 303/496 (61.1) | 38/52 (73.1) |
| | <19800 | 0.001 ^a | 1.75 | [1.25, 2.46] | 303/497 (61.0) | 38/51 (74.5) |
| | <19900 | 0.002 ^a | 1.71 | [1.21, 2.40] | 304/498 (61.0) | 37/50 (74.0) |
| | <20100 | 0.008 ^a | 1.61 | [1.14, 2.29] | 306/500 (61.2) | 35/48 (72.9) |
| | <20700 | 0.003 ^a | 1.70 | [1.20, 2.41] | 306/501 (61.1) | 35/47 (74.5) |
| | <21200 | 0.004 ^a | 1.69 | [1.19, 2.41] | 307/502 (61.2) | 34/46 (73.9) |
| | <21400 | 0.004 ^a | 1.69 | [1.18, 2.43] | 308/503 (61.2) | 33/45 (73.3) |
| | <21600 | 0.003 ^a | 1.74 | [1.21, 2.51] | 309/504 (61.3) | 32/44 (72.7) |
| | <22100 | 0.003 ^a | 1.77 | [1.22, 2.56] | 310/506 (61.3) | 31/42 (73.8) |
| | <22500 | 0.003 ^a | 1.78 | [1.23, 2.60] | 311/507 (61.3) | 30/41 (73.2) |
| | <22600 | 0.001 ^a | 1.86 | [1.28, 2.71] | 311/508 (61.2) | 30/40 (75.0) |
| | <22900 | 0.002 ^a | 1.85 | [1.26, 2.70] | 312/509 (61.3) | 29/39 (74.4) |
| | <23000 | 0.002 ^a | 1.83 | [1.24, 2.70] | 313/510 (61.4) | 28/38 (73.7) |
| | <23200 | <.001 ^a | 1.97 | [1.34, 2.91] | 313/511 (61.3) | 28/37 (75.7) |
| | <23400 | 0.001 ^a | 1.91 | [1.29, 2.83] | 314/512 (61.3) | 27/36 (75.0) |
| | <23800 | 0.002 ^a | 1.88 | [1.26, 2.81] | 315/513 (61.4) | 26/35 (74.3) |
| | <23900 | 0.004 ^a | 1.83 | [1.21, 2.75] | 316/514 (61.5) | 25/34 (73.5) |
| | <24000 | 0.006 ^a | 1.78 | [1.18, 2.70] | 317/515 (61.6) | 24/33 (72.7) |
| | <24300 | 0.014 ^a | 1.71 | [1.12, 2.61] | 318/516 (61.6) | 23/32 (71.9) |
| | <24400 | 0.004 ^a | 1.85 | [1.21, 2.83] | 318/517 (61.5) | 23/31 (74.2) |
| | <24900 | 0.010 ^a | 1.77 | [1.15, 2.73] | 319/518 (61.6) | 22/30 (73.3) |
| | <25100 | 0.004 ^a | 1.90 | [1.23, 2.92] | 319/519 (61.5) | 22/29 (75.9) |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is '<'

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <25800 | 0.007 ^a | 1.84 | [1.18, 2.86] | 320/520 (61.5) | 21/28 (75.0) |
| | <26000 | 0.010 ^a | 1.81 | [1.15, 2.85] | 321/521 (61.6) | 20/27 (74.1) |
| | <26200 | 0.022 ^a | 1.72 | [1.08, 2.73] | 322/522 (61.7) | 19/26 (73.1) |
| | <26600 | 0.064 | 1.59 | [0.97, 2.59] | 324/524 (61.8) | 17/24 (70.8) |
| | <27500 | 0.117 | 1.49 | [0.90, 2.47] | 325/525 (61.9) | 16/23 (69.6) |
| | <27800 | 0.203 | 1.40 | [0.83, 2.35] | 326/526 (62.0) | 15/22 (68.2) |
| | <28200 | 0.237 | 1.38 | [0.81, 2.36] | 327/527 (62.0) | 14/21 (66.7) |
| | <28700 | 0.286 | 1.35 | [0.78, 2.35] | 328/528 (62.1) | 13/20 (65.0) |
| | <29800 | 0.453 | 1.25 | [0.70, 2.22] | 329/529 (62.2) | 12/19 (63.2) |
| | <30900 | 0.659 | 1.15 | [0.63, 2.09] | 330/530 (62.3) | 11/18 (61.1) |
| | <31000 | 0.425 | 1.28 | [0.70, 2.33] | 330/531 (62.1) | 11/17 (64.7) |
| | <31300 | 0.649 | 1.16 | [0.62, 2.17] | 331/532 (62.2) | 10/16 (62.5) |
| | <31700 | 0.403 | 1.31 | [0.70, 2.45] | 331/533 (62.1) | 10/15 (66.7) |
| | <32200 | 0.771 | 1.11 | [0.55, 2.24] | 333/535 (62.2) | 8/13 (61.5) |
| | <32400 | 0.589 | 1.21 | [0.60, 2.45] | 333/536 (62.1) | 8/12 (66.7) |
| | <32700 | 0.739 | 1.14 | [0.54, 2.40] | 334/537 (62.2) | 7/11 (63.6) |
| | <34000 | 0.399 | 1.38 | [0.65, 2.92] | 334/538 (62.1) | 7/10 (70.0) |
| | <34800 | 0.160 | 1.71 | [0.81, 3.62] | 334/539 (62.0) | 7/9 (77.8) |
| | <35600 | 0.344 | 1.48 | [0.66, 3.31] | 335/540 (62.0) | 6/8 (75.0) |
| | <37100 | 0.060 | 2.17 | [0.97, 4.87] | 335/541 (61.9) | 6/7 (85.7) |
| | <39600 | 0.056 | 2.37 | [0.98, 5.74] | 336/542 (62.0) | 5/6 (83.3) |
| | <39700 | 0.149 | 2.07 | [0.77, 5.55] | 337/543 (62.1) | 4/5 (80.0) |
| | <41100 | 0.223 | 2.03 | [0.65, 6.33] | 338/544 (62.1) | 3/4 (75.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.1-s: OS univariate Cox proportional hazards model - candidate cut points - Whole Body (Body-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---------------------------|------------------------|---------|--------------|---------------|---------------------------------|-------------|
| | | | | | <cut point | >=cut point |
| Tumor load (g) - All cuts | <43600 | 0.379 | 1.87 | [0.46, 7.51] | 339/545 (62.2) | 2/3 (66.7) |
| | <47700 | 0.995 | 0.99 | [0.14, 7.08] | 340/546 (62.3) | 1/2 (50.0) |
| | <54100 | 0.151 | 4.23 | [0.59, 30.25] | 340/547 (62.2) | 1/1 (100.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

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68Ga-PSMA-11 Quantitative analysis

Final Version

Table 7.2: OS multivariate Cox proportional hazards model - with optimal cut points - Bone (Bone-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|--|--------------|--------------|--------------------|
| Bone | | | |
| SUVmean (g/ml) <18 vs. >=18 ^c | 0.11 | [0.02, 0.77] | 0.027 ^a |
| Volume of segmented PSMA positive tumors (cc) <3000 vs. >=3000 ^c | 2.01 | [1.18, 3.44] | 0.011 ^a |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is '<'.

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ut-hr2.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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68Ga-PSMA-11 Quantitative analysis

Final Version

Table 7.2-s: OS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmean (g/ml) - Optimal cut | <18 | 0.025 ^a | 0.11 | [0.01, 0.76] | 327/498 (65.7) | 1/10 (10.0) |
| SUVmean (g/ml) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <5 | 0.030 ^a | 0.76 | [0.60, 0.97] | 88/125 (70.4) | 240/383 (62.7) |
| | <6 | <.001 ^a | 0.66 | [0.53, 0.82] | 148/204 (72.5) | 180/304 (59.2) |
| | <7 | <.001 ^a | 0.67 | [0.54, 0.84] | 198/281 (70.5) | 130/227 (57.3) |
| | <8 | <.001 ^a | 0.60 | [0.46, 0.77] | 249/355 (70.1) | 79/153 (51.6) |
| | <9 | <.001 ^a | 0.52 | [0.38, 0.71] | 279/402 (69.4) | 49/106 (46.2) |
| | <10 | <.001 ^a | 0.47 | [0.33, 0.67] | 295/429 (68.8) | 33/79 (41.8) |
| | <11 | <.001 ^a | 0.40 | [0.25, 0.65] | 310/457 (67.8) | 18/51 (35.3) |
| | <12 | <.001 ^a | 0.37 | [0.21, 0.64] | 315/468 (67.3) | 13/40 (32.5) |
| | <13 | <.001 ^a | 0.28 | [0.13, 0.59] | 321/481 (66.7) | 7/27 (25.9) |
| | <14 | 0.007 ^a | 0.21 | [0.07, 0.64] | 325/491 (66.2) | 3/17 (17.6) |
| | <15 | 0.010 ^a | 0.22 | [0.07, 0.69] | 325/492 (66.1) | 3/16 (18.8) |
| | <16 | 0.025 ^a | 0.20 | [0.05, 0.82] | 326/497 (65.6) | 2/11 (18.2) |
| | <18 | 0.025 ^a | 0.11 | [0.01, 0.76] | 327/498 (65.7) | 1/10 (10.0) |
| SUVmean (g/ml) - All cuts | <2 | 0.986 | 0.99 | [0.37, 2.66] | 4/5 (80.0) | 324/503 (64.4) |
| | <3 | 0.154 | 0.58 | [0.27, 1.23] | 7/8 (87.5) | 321/500 (64.2) |
| | <4 | 0.773 | 0.95 | [0.67, 1.35] | 35/53 (66.0) | 293/455 (64.4) |
| | <5 | 0.030 ^a | 0.76 | [0.60, 0.97] | 88/125 (70.4) | 240/383 (62.7) |
| | <6 | <.001 ^a | 0.66 | [0.53, 0.82] | 148/204 (72.5) | 180/304 (59.2) |
| | <7 | <.001 ^a | 0.67 | [0.54, 0.84] | 198/281 (70.5) | 130/227 (57.3) |
| | <8 | <.001 ^a | 0.60 | [0.46, 0.77] | 249/355 (70.1) | 79/153 (51.6) |
| | <9 | <.001 ^a | 0.52 | [0.38, 0.71] | 279/402 (69.4) | 49/106 (46.2) |
| | <10 | <.001 ^a | 0.47 | [0.33, 0.67] | 295/429 (68.8) | 33/79 (41.8) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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68Ga-PSMA-11 Quantitative analysis

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Table 7.2-s: OS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|------------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmean (g/ml) - All cuts | <11 | <.001 ^a | 0.40 | [0.25, 0.65] | 310/457 (67.8) | 18/51 (35.3) |
| | <12 | <.001 ^a | 0.37 | [0.21, 0.64] | 315/468 (67.3) | 13/40 (32.5) |
| | <13 | <.001 ^a | 0.28 | [0.13, 0.59] | 321/481 (66.7) | 7/27 (25.9) |
| | <14 | 0.007 ^a | 0.21 | [0.07, 0.64] | 325/491 (66.2) | 3/17 (17.6) |
| | <15 | 0.010 ^a | 0.22 | [0.07, 0.69] | 325/492 (66.1) | 3/16 (18.8) |
| | <16 | 0.025 ^a | 0.20 | [0.05, 0.82] | 326/497 (65.6) | 2/11 (18.2) |
| | <18 | 0.025 ^a | 0.11 | [0.01, 0.76] | 327/498 (65.7) | 1/10 (10.0) |
| | <19 | 0.964 | 0.00 | [0.00, 2.65E238] | 328/502 (65.3) | 0/6 (0.0) |
| | <22 | 0.971 | 0.00 | [0.00, 3.16E304] | 328/504 (65.1) | 0/4 (0.0) |
| | <23 | 0.962 | 0.00 | [0.00, 9.77E207] | 328/505 (65.0) | 0/3 (0.0) |
| | <26 | 0.969 | 0.00 | [0.00, 6.29E255] | 328/506 (64.8) | 0/2 (0.0) |
| | <52 | 0.963 | 0.00 | [0.00, 6.04E197] | 328/507 (64.7) | 0/1 (0.0) |
| Volume of segmented PSMA positive tumors (cc) - Optimal cut | <3000 | 0.008 ^a | 2.07 | [1.21, 3.53] | 314/491 (64.0) | 14/17 (82.4) |
| Volume of segmented PSMA positive tumors (cc) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <100 | <.001 ^a | 1.64 | [1.29, 2.10] | 89/161 (55.3) | 239/347 (68.9) |
| | <200 | <.001 ^a | 1.64 | [1.31, 2.05] | 124/218 (56.9) | 204/290 (70.3) |
| | <300 | <.001 ^a | 1.81 | [1.45, 2.26] | 146/258 (56.6) | 182/250 (72.8) |
| | <400 | <.001 ^a | 1.84 | [1.48, 2.29] | 163/289 (56.4) | 165/219 (75.3) |
| | <500 | <.001 ^a | 1.94 | [1.56, 2.42] | 182/318 (57.2) | 146/190 (76.8) |
| | <600 | <.001 ^a | 1.87 | [1.50, 2.33] | 192/331 (58.0) | 136/177 (76.8) |
| | <700 | <.001 ^a | 1.96 | [1.57, 2.45] | 200/345 (58.0) | 128/163 (78.5) |
| | <800 | <.001 ^a | 1.84 | [1.47, 2.32] | 215/364 (59.1) | 113/144 (78.5) |
| | <900 | <.001 ^a | 1.88 | [1.49, 2.37] | 220/371 (59.3) | 108/137 (78.8) |
| | <1000 | <.001 ^a | 1.94 | [1.53, 2.45] | 227/383 (59.3) | 101/125 (80.8) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.2-s: OS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Volume of segmented PSMA positive tumors (cc) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <1100 | <.001 ^a | 1.82 | [1.43, 2.31] | 236/392 (60.2) | 92/116 (79.3) |
| | <1200 | <.001 ^a | 1.70 | [1.32, 2.18] | 245/402 (60.9) | 83/106 (78.3) |
| | <1300 | <.001 ^a | 1.76 | [1.37, 2.27] | 250/409 (61.1) | 78/99 (78.8) |
| | <1400 | <.001 ^a | 1.60 | [1.22, 2.10] | 261/421 (62.0) | 67/87 (77.0) |
| | <1500 | 0.001 ^a | 1.60 | [1.21, 2.11] | 267/429 (62.2) | 61/79 (77.2) |
| | <1600 | 0.006 ^a | 1.50 | [1.12, 1.99] | 271/433 (62.6) | 57/75 (76.0) |
| | <1700 | 0.009 ^a | 1.50 | [1.11, 2.05] | 280/444 (63.1) | 48/64 (75.0) |
| | <1800 | 0.012 ^a | 1.49 | [1.09, 2.02] | 281/445 (63.1) | 47/63 (74.6) |
| | <1900 | 0.013 ^a | 1.50 | [1.09, 2.07] | 285/451 (63.2) | 43/57 (75.4) |
| | <2400 | 0.042 ^a | 1.53 | [1.02, 2.30] | 303/475 (63.8) | 25/33 (75.8) |
| | <2500 | 0.006 ^a | 1.81 | [1.18, 2.76] | 305/479 (63.7) | 23/29 (79.3) |
| | <2600 | 0.002 ^a | 2.04 | [1.31, 3.18] | 307/482 (63.7) | 21/26 (80.8) |
| | <2700 | 0.006 ^a | 1.91 | [1.20, 3.03] | 309/484 (63.8) | 19/24 (79.2) |
| | <2800 | 0.013 ^a | 1.82 | [1.13, 2.94] | 310/485 (63.9) | 18/23 (78.3) |
| | <2900 | 0.014 ^a | 1.85 | [1.14, 3.02] | 311/486 (64.0) | 17/22 (77.3) |
| | <3000 | 0.008 ^a | 2.07 | [1.21, 3.53] | 314/491 (64.0) | 14/17 (82.4) |
| | <3100 | 0.011 ^a | 2.06 | [1.18, 3.59] | 315/492 (64.0) | 13/16 (81.3) |
| Volume of segmented PSMA positive tumors (cc) - All cuts | <100 | <.001 ^a | 1.64 | [1.29, 2.10] | 89/161 (55.3) | 239/347 (68.9) |
| | <200 | <.001 ^a | 1.64 | [1.31, 2.05] | 124/218 (56.9) | 204/290 (70.3) |
| | <300 | <.001 ^a | 1.81 | [1.45, 2.26] | 146/258 (56.6) | 182/250 (72.8) |
| | <400 | <.001 ^a | 1.84 | [1.48, 2.29] | 163/289 (56.4) | 165/219 (75.3) |
| | <500 | <.001 ^a | 1.94 | [1.56, 2.42] | 182/318 (57.2) | 146/190 (76.8) |
| | <600 | <.001 ^a | 1.87 | [1.50, 2.33] | 192/331 (58.0) | 136/177 (76.8) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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68Ga-PSMA-11 Quantitative analysis

Final Version

Table 7.2-s: OS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| Volume of segmented PSMA positive tumors (cc) - All cuts | <700 | <.001 ^a | 1.96 | [1.57, 2.45] | 200/345 (58.0) | 128/163 (78.5) |
| | <800 | <.001 ^a | 1.84 | [1.47, 2.32] | 215/364 (59.1) | 113/144 (78.5) |
| | <900 | <.001 ^a | 1.88 | [1.49, 2.37] | 220/371 (59.3) | 108/137 (78.8) |
| | <1000 | <.001 ^a | 1.94 | [1.53, 2.45] | 227/383 (59.3) | 101/125 (80.8) |
| | <1100 | <.001 ^a | 1.82 | [1.43, 2.31] | 236/392 (60.2) | 92/116 (79.3) |
| | <1200 | <.001 ^a | 1.70 | [1.32, 2.18] | 245/402 (60.9) | 83/106 (78.3) |
| | <1300 | <.001 ^a | 1.76 | [1.37, 2.27] | 250/409 (61.1) | 78/99 (78.8) |
| | <1400 | <.001 ^a | 1.60 | [1.22, 2.10] | 261/421 (62.0) | 67/87 (77.0) |
| | <1500 | 0.001 ^a | 1.60 | [1.21, 2.11] | 267/429 (62.2) | 61/79 (77.2) |
| | <1600 | 0.006 ^a | 1.50 | [1.12, 1.99] | 271/433 (62.6) | 57/75 (76.0) |
| | <1700 | 0.009 ^a | 1.50 | [1.11, 2.05] | 280/444 (63.1) | 48/64 (75.0) |
| | <1800 | 0.012 ^a | 1.49 | [1.09, 2.02] | 281/445 (63.1) | 47/63 (74.6) |
| | <1900 | 0.013 ^a | 1.50 | [1.09, 2.07] | 285/451 (63.2) | 43/57 (75.4) |
| | <2000 | 0.060 | 1.38 | [0.99, 1.94] | 290/456 (63.6) | 38/52 (73.1) |
| | <2100 | 0.109 | 1.35 | [0.94, 1.94] | 296/463 (63.9) | 32/45 (71.1) |
| | <2200 | 0.113 | 1.36 | [0.93, 1.99] | 299/468 (63.9) | 29/40 (72.5) |
| | <2300 | 0.085 | 1.41 | [0.95, 2.07] | 300/470 (63.8) | 28/38 (73.7) |
| | <2400 | 0.042 ^a | 1.53 | [1.02, 2.30] | 303/475 (63.8) | 25/33 (75.8) |
| | <2500 | 0.006 ^a | 1.81 | [1.18, 2.76] | 305/479 (63.7) | 23/29 (79.3) |
| | <2600 | 0.002 ^a | 2.04 | [1.31, 3.18] | 307/482 (63.7) | 21/26 (80.8) |
| | <2700 | 0.006 ^a | 1.91 | [1.20, 3.03] | 309/484 (63.8) | 19/24 (79.2) |
| | <2800 | 0.013 ^a | 1.82 | [1.13, 2.94] | 310/485 (63.9) | 18/23 (78.3) |
| | <2900 | 0.014 ^a | 1.85 | [1.14, 3.02] | 311/486 (64.0) | 17/22 (77.3) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-cut-hr2.sas

Source data: adsl.xpt, adtte.xpt

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Table 7.2-s: OS univariate Cox proportional hazards model - candidate cut points - Bone (Bone-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|------------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Volume of segmented PSMA positive tumors (cc) - All cuts | <3000 | 0.008 ^a | 2.07 | [1.21, 3.53] | 314/491 (64.0) | 14/17 (82.4) |
| | <3100 | 0.011 ^a | 2.06 | [1.18, 3.59] | 315/492 (64.0) | 13/16 (81.3) |
| | <3200 | 0.084 | 1.74 | [0.93, 3.27] | 318/495 (64.2) | 10/13 (76.9) |
| | <3400 | 0.216 | 1.56 | [0.77, 3.14] | 320/497 (64.4) | 8/11 (72.7) |
| | <3500 | 0.421 | 1.36 | [0.64, 2.88] | 321/498 (64.5) | 7/10 (70.0) |
| | <3600 | 0.707 | 1.17 | [0.52, 2.62] | 322/499 (64.5) | 6/9 (66.7) |
| | <3700 | 0.811 | 0.89 | [0.33, 2.38] | 324/501 (64.7) | 4/7 (57.1) |
| | <3900 | 0.847 | 1.10 | [0.41, 2.96] | 324/502 (64.5) | 4/6 (66.7) |
| | <4000 | 0.245 | 1.79 | [0.67, 4.82] | 324/503 (64.4) | 4/5 (80.0) |
| | <4400 | 0.533 | 1.56 | [0.39, 6.26] | 326/505 (64.6) | 2/3 (66.7) |
| | <4900 | 0.963 | 0.00 | [0.00, 8.38E198] | 328/507 (64.7) | 0/1 (0.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is '<'.

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Table 7.3: OS multivariate Cox proportional hazards model - with optimal cut points - Liver (Liver-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|---|--------------|--------------|--------------------|
| Liver Volume of segmented PSMA positive tumors (cc) <200 vs. >=200 ^c | 2.13 | [1.17, 3.88] | 0.013 ^a |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^c Reference is '<'.

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ut-hr2.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.3-s: OS univariate Cox proportional hazards model - candidate cut points - Liver (Liver-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|---------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Volume of segmented PSMA positive tumors (cc) - Optimal cut | <200 | 0.013 ^a | 2.13 | [1.17, 3.88] | 40/55 (72.7) | 15/17 (88.2) |
| Volume of segmented PSMA positive tumors (cc) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <200 | 0.013 ^a | 2.13 | [1.17, 3.88] | 40/55 (72.7) | 15/17 (88.2) |
| Volume of segmented PSMA positive tumors (cc) - All cuts | <100 | 0.080 | 1.64 | [0.94, 2.85] | 35/48 (72.9) | 20/24 (83.3) |
| | <200 | 0.013 ^a | 2.13 | [1.17, 3.88] | 40/55 (72.7) | 15/17 (88.2) |
| | <400 | 0.060 | 1.85 | [0.98, 3.53] | 43/58 (74.1) | 12/14 (85.7) |
| | <500 | 0.081 | 1.90 | [0.92, 3.90] | 46/62 (74.2) | 9/10 (90.0) |
| | <700 | 0.119 | 1.82 | [0.86, 3.87] | 47/63 (74.6) | 8/9 (88.9) |
| | <1000 | 0.008 ^a | 2.84 | [1.32, 6.12] | 47/64 (73.4) | 8/8 (100.0) |
| | <1200 | 0.018 ^a | 2.84 | [1.20, 6.72] | 49/66 (74.2) | 6/6 (100.0) |
| | <1300 | 0.070 | 2.37 | [0.93, 6.01] | 50/67 (74.6) | 5/5 (100.0) |
| | <1600 | 0.031 ^a | 3.11 | [1.11, 8.72] | 51/68 (75.0) | 4/4 (100.0) |
| | <2300 | 0.002 ^a | 11.06 | [2.44, 50.08] | 53/70 (75.7) | 2/2 (100.0) |
| | <3700 | 0.105 | 5.40 | [0.70, 41.54] | 54/71 (76.1) | 1/1 (100.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Table 7.4: OS multivariate Cox proportional hazards model - with optimal cut points - Lymph Node (Lymph Node-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|---|--------------|--------------|--------------------|
| Lymph Node | | | |
| SUVmean (g/ml) | | | |
| <20 vs. >=20 ^c | 0.08 | [0.01, 0.59] | 0.013 ^a |
| Volume of segmented PSMA positive tumors (cc) | | | |
| No optimal cuts | | | |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^c Reference is '<'.

Output ID: T-7-4 2021-08-30 21:27

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Table 7.4-s: OS univariate Cox proportional hazards model - candidate cut points - Lymph Node (Lymph Node-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|---|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmean (g/ml) - Optimal cut | <20 | 0.013 ^a | 0.08 | [0.01, 0.59] | 240/357 (67.2) | 1/12 (8.3) |
| SUVmean (g/ml) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <5 | 0.024 ^a | 0.73 | [0.55, 0.96] | 70/92 (76.1) | 171/277 (61.7) |
| | <6 | 0.015 ^a | 0.72 | [0.56, 0.94] | 95/127 (74.8) | 146/242 (60.3) |
| | <7 | 0.004 ^a | 0.69 | [0.53, 0.89] | 122/164 (74.4) | 119/205 (58.0) |
| | <8 | 0.002 ^a | 0.67 | [0.52, 0.87] | 145/198 (73.2) | 96/171 (56.1) |
| | <9 | <.001 ^a | 0.63 | [0.48, 0.83] | 165/229 (72.1) | 76/140 (54.3) |
| | <10 | <.001 ^a | 0.58 | [0.43, 0.77] | 181/252 (71.8) | 60/117 (51.3) |
| | <11 | <.001 ^a | 0.56 | [0.41, 0.77] | 192/270 (71.1) | 49/99 (49.5) |
| | <12 | 0.002 ^a | 0.58 | [0.41, 0.82] | 201/287 (70.0) | 40/82 (48.8) |
| | <13 | <.001 ^a | 0.52 | [0.35, 0.76] | 212/303 (70.0) | 29/66 (43.9) |
| | <14 | <.001 ^a | 0.44 | [0.27, 0.71] | 224/323 (69.3) | 17/46 (37.0) |
| | <15 | 0.010 ^a | 0.47 | [0.26, 0.83] | 229/336 (68.2) | 12/33 (36.4) |
| | <16 | 0.017 ^a | 0.44 | [0.23, 0.87] | 232/343 (67.6) | 9/26 (34.6) |
| | <17 | 0.007 ^a | 0.35 | [0.17, 0.75] | 234/346 (67.6) | 7/23 (30.4) |
| | <18 | 0.007 ^a | 0.26 | [0.10, 0.69] | 237/352 (67.3) | 4/17 (23.5) |
| | <19 | 0.006 ^a | 0.20 | [0.06, 0.63] | 238/353 (67.4) | 3/16 (18.8) |
| | <20 | 0.013 ^a | 0.08 | [0.01, 0.59] | 240/357 (67.2) | 1/12 (8.3) |
| | <22 | 0.017 ^a | 0.09 | [0.01, 0.65] | 240/358 (67.0) | 1/11 (9.1) |
| SUVmean (g/ml) - All cuts | <2 | 0.850 | 0.87 | [0.22, 3.52] | 2/3 (66.7) | 239/366 (65.3) |
| | <3 | 0.366 | 1.39 | [0.68, 2.82] | 8/13 (61.5) | 233/356 (65.4) |
| | <4 | 0.392 | 0.86 | [0.61, 1.22] | 38/53 (71.7) | 203/316 (64.2) |
| | <5 | 0.024 ^a | 0.73 | [0.55, 0.96] | 70/92 (76.1) | 171/277 (61.7) |
| | <6 | 0.015 ^a | 0.72 | [0.56, 0.94] | 95/127 (74.8) | 146/242 (60.3) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

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Table 7.4-s: OS univariate Cox proportional hazards model - candidate cut points - Lymph Node (Lymph Node-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|------------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmean (g/ml) - All cuts | <7 | 0.004 ^a | 0.69 | [0.53, 0.89] | 122/164 (74.4) | 119/205 (58.0) |
| | <8 | 0.002 ^a | 0.67 | [0.52, 0.87] | 145/198 (73.2) | 96/171 (56.1) |
| | <9 | <.001 ^a | 0.63 | [0.48, 0.83] | 165/229 (72.1) | 76/140 (54.3) |
| | <10 | <.001 ^a | 0.58 | [0.43, 0.77] | 181/252 (71.8) | 60/117 (51.3) |
| | <11 | <.001 ^a | 0.56 | [0.41, 0.77] | 192/270 (71.1) | 49/99 (49.5) |
| | <12 | 0.002 ^a | 0.58 | [0.41, 0.82] | 201/287 (70.0) | 40/82 (48.8) |
| | <13 | <.001 ^a | 0.52 | [0.35, 0.76] | 212/303 (70.0) | 29/66 (43.9) |
| | <14 | <.001 ^a | 0.44 | [0.27, 0.71] | 224/323 (69.3) | 17/46 (37.0) |
| | <15 | 0.010 ^a | 0.47 | [0.26, 0.83] | 229/336 (68.2) | 12/33 (36.4) |
| | <16 | 0.017 ^a | 0.44 | [0.23, 0.87] | 232/343 (67.6) | 9/26 (34.6) |
| | <17 | 0.007 ^a | 0.35 | [0.17, 0.75] | 234/346 (67.6) | 7/23 (30.4) |
| | <18 | 0.007 ^a | 0.26 | [0.10, 0.69] | 237/352 (67.3) | 4/17 (23.5) |
| | <19 | 0.006 ^a | 0.20 | [0.06, 0.63] | 238/353 (67.4) | 3/16 (18.8) |
| | <20 | 0.013 ^a | 0.08 | [0.01, 0.59] | 240/357 (67.2) | 1/12 (8.3) |
| | <22 | 0.017 ^a | 0.09 | [0.01, 0.65] | 240/358 (67.0) | 1/11 (9.1) |
| | <23 | 0.047 ^a | 0.14 | [0.02, 0.98] | 240/361 (66.5) | 1/8 (12.5) |
| | <25 | 0.967 | 0.00 | [0.00, 5.49E263] | 241/364 (66.2) | 0/5 (0.0) |
| | <30 | 0.974 | 0.00 | [0.00,] | 241/366 (65.8) | 0/3 (0.0) |
| | <38 | 0.968 | 0.00 | [0.00, 2.9E248] | 241/367 (65.7) | 0/2 (0.0) |
| | <52 | 0.976 | 0.00 | [0.00,] | 241/368 (65.5) | 0/1 (0.0) |
| Volume of segmented PSMA positive tumors (cc) - All cuts | <100 | 0.253 | 1.17 | [0.90, 1.52] | 156/243 (64.2) | 85/126 (67.5) |
| | <200 | 0.969 | 0.99 | [0.72, 1.37] | 194/295 (65.8) | 47/74 (63.5) |
| | <300 | 0.641 | 1.09 | [0.76, 1.55] | 205/316 (64.9) | 36/53 (67.9) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Table 7.4-s: OS univariate Cox proportional hazards model - candidate cut points - Lymph Node (Lymph Node-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|---------|--------------|---------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| Volume of segmented PSMA positive tumors (cc) - All cuts | <400 | 0.866 | 1.04 | [0.69, 1.56] | 215/331 (65.0) | 26/38 (68.4) |
| | <500 | 0.965 | 0.99 | [0.63, 1.57] | 221/339 (65.2) | 20/30 (66.7) |
| | <600 | 0.744 | 1.09 | [0.65, 1.84] | 226/347 (65.1) | 15/22 (68.2) |
| | <700 | 0.733 | 1.10 | [0.63, 1.93] | 228/350 (65.1) | 13/19 (68.4) |
| | <800 | 0.099 | 1.67 | [0.91, 3.07] | 230/355 (64.8) | 11/14 (78.6) |
| | <900 | 0.064 | 2.04 | [0.96, 4.33] | 234/360 (65.0) | 7/9 (77.8) |
| | <1100 | 0.380 | 1.49 | [0.61, 3.61] | 236/362 (65.2) | 5/7 (71.4) |
| | <1200 | 0.931 | 0.94 | [0.23, 3.78] | 239/365 (65.5) | 2/4 (50.0) |
| | <1300 | 0.544 | 1.54 | [0.38, 6.21] | 239/366 (65.3) | 2/3 (66.7) |
| | <1900 | 0.920 | 0.90 | [0.13, 6.45] | 240/367 (65.4) | 1/2 (50.0) |
| | <3100 | 0.432 | 2.20 | [0.31, 15.69] | 240/368 (65.2) | 1/1 (100.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Table 7.5: OS multivariate Cox proportional hazards model - with optimal cut points - Soft Tissue (Soft Tissue-Full Analysis Set)

| Predictor variables | Hazard ratio | 95% CI | p-value |
|---|--------------|--------------|--------------------|
| Soft Tissue | | | |
| SUVmax (g/ml) <59 vs. >=59 ^c | 0.27 | [0.09, 0.85] | 0.026 ^a |
| Volume of segmented PSMA positive tumors (cc) | | | |
| No optimal cuts | | | |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^c Reference is '<'.

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.5-s: OS univariate Cox proportional hazards model - candidate cut points - Soft Tissue (Soft Tissue-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - Optimal cut | <59 | 0.026 ^a | 0.27 | [0.09, 0.85] | 151/222 (68.0) | 3/11 (27.3) |
| SUVmax (g/ml) - Candidate cuts (p<0.05 and 10 or more patients in each subgroup) | <25 | 0.046 ^a | 0.70 | [0.50, 0.99] | 108/153 (70.6) | 46/80 (57.5) |
| | <26 | 0.036 ^a | 0.69 | [0.49, 0.98] | 109/154 (70.8) | 45/79 (57.0) |
| | <27 | 0.021 ^a | 0.65 | [0.46, 0.94] | 114/161 (70.8) | 40/72 (55.6) |
| | <28 | 0.023 ^a | 0.66 | [0.46, 0.94] | 115/162 (71.0) | 39/71 (54.9) |
| | <29 | 0.017 ^a | 0.63 | [0.43, 0.92] | 119/167 (71.3) | 35/66 (53.0) |
| | <30 | 0.011 ^a | 0.61 | [0.41, 0.89] | 120/168 (71.4) | 34/65 (52.3) |
| | <31 | 0.007 ^a | 0.58 | [0.39, 0.86] | 122/170 (71.8) | 32/63 (50.8) |
| | <32 | 0.026 ^a | 0.64 | [0.43, 0.95] | 122/174 (70.1) | 32/59 (54.2) |
| | <33 | 0.043 ^a | 0.66 | [0.44, 0.99] | 124/178 (69.7) | 30/55 (54.5) |
| | <34 | 0.007 ^a | 0.55 | [0.35, 0.85] | 130/185 (70.3) | 24/48 (50.0) |
| | <35 | 0.026 ^a | 0.61 | [0.39, 0.94] | 130/187 (69.5) | 24/46 (52.2) |
| | <36 | 0.033 ^a | 0.59 | [0.37, 0.96] | 135/195 (69.2) | 19/38 (50.0) |
| | <44 | 0.045 ^a | 0.56 | [0.32, 0.99] | 141/205 (68.8) | 13/28 (46.4) |
| | <49 | 0.028 ^a | 0.43 | [0.20, 0.91] | 147/215 (68.4) | 7/18 (38.9) |
| | <50 | 0.034 ^a | 0.41 | [0.18, 0.94] | 148/217 (68.2) | 6/16 (37.5) |
| | <51 | 0.022 ^a | 0.35 | [0.14, 0.86] | 149/218 (68.3) | 5/15 (33.3) |
| | <52 | 0.033 ^a | 0.38 | [0.16, 0.92] | 149/219 (68.0) | 5/14 (35.7) |
| | <54 | 0.023 ^a | 0.31 | [0.12, 0.85] | 150/220 (68.2) | 4/13 (30.8) |
| | <59 | 0.026 ^a | 0.27 | [0.09, 0.85] | 151/222 (68.0) | 3/11 (27.3) |
| SUVmax (g/ml) - All cuts | <2 | 0.012 ^a | 0.08 | [0.01, 0.57] | 1/1 (100.0) | 153/232 (65.9) |
| | <3 | 0.913 | 1.07 | [0.34, 3.35] | 3/5 (60.0) | 151/228 (66.2) |
| | <4 | 0.800 | 1.12 | [0.46, 2.74] | 5/7 (71.4) | 149/226 (65.9) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

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Table 7.5-s: OS univariate Cox proportional hazards model - candidate cut points - Soft Tissue (Soft Tissue-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|----------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - All cuts | <5 | 0.817 | 0.92 | [0.45, 1.88] | 8/12 (66.7) | 146/221 (66.1) |
| | <6 | 0.598 | 1.17 | [0.66, 2.07] | 13/22 (59.1) | 141/211 (66.8) |
| | <7 | 0.386 | 1.22 | [0.78, 1.90] | 23/39 (59.0) | 131/194 (67.5) |
| | <8 | 0.615 | 1.10 | [0.75, 1.62] | 34/54 (63.0) | 120/179 (67.0) |
| | <9 | 0.573 | 1.11 | [0.77, 1.60] | 39/61 (63.9) | 115/172 (66.9) |
| | <10 | 0.716 | 1.07 | [0.75, 1.53] | 42/66 (63.6) | 112/167 (67.1) |
| | <11 | 0.568 | 1.11 | [0.78, 1.56] | 46/74 (62.2) | 108/159 (67.9) |
| | <12 | 0.958 | 1.01 | [0.73, 1.40] | 56/85 (65.9) | 98/148 (66.2) |
| | <13 | 0.452 | 0.88 | [0.64, 1.22] | 62/91 (68.1) | 92/142 (64.8) |
| | <14 | 0.377 | 0.87 | [0.63, 1.19] | 71/103 (68.9) | 83/130 (63.8) |
| | <15 | 0.434 | 0.88 | [0.64, 1.21] | 73/106 (68.9) | 81/127 (63.8) |
| | <16 | 0.346 | 0.86 | [0.63, 1.18] | 77/111 (69.4) | 77/122 (63.1) |
| | <17 | 0.303 | 0.85 | [0.62, 1.16] | 82/119 (68.9) | 72/114 (63.2) |
| | <18 | 0.297 | 0.84 | [0.61, 1.16] | 83/120 (69.2) | 71/113 (62.8) |
| | <19 | 0.351 | 0.86 | [0.63, 1.18] | 84/123 (68.3) | 70/110 (63.6) |
| | <20 | 0.374 | 0.87 | [0.63, 1.19] | 87/127 (68.5) | 67/106 (63.2) |
| | <21 | 0.288 | 0.84 | [0.61, 1.16] | 94/137 (68.6) | 60/96 (62.5) |
| | <22 | 0.264 | 0.83 | [0.60, 1.15] | 96/139 (69.1) | 58/94 (61.7) |
| | <23 | 0.133 | 0.77 | [0.55, 1.08] | 102/146 (69.9) | 52/87 (59.8) |
| | <24 | 0.088 | 0.74 | [0.53, 1.04] | 105/150 (70.0) | 49/83 (59.0) |
| | <25 | 0.046 ^a | 0.70 | [0.50, 0.99] | 108/153 (70.6) | 46/80 (57.5) |
| | <26 | 0.036 ^a | 0.69 | [0.49, 0.98] | 109/154 (70.8) | 45/79 (57.0) |
| | <27 | 0.021 ^a | 0.65 | [0.46, 0.94] | 114/161 (70.8) | 40/72 (55.6) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

Output ID: T-7-5-S 2021-08-30 21:38

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-cut-hr2.sas

Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.5-s: OS univariate Cox proportional hazards model - candidate cut points - Soft Tissue (Soft Tissue-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--------------------------|------------------------|--------------------|--------------|--------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - All cuts | <28 | 0.023 ^a | 0.66 | [0.46, 0.94] | 115/162 (71.0) | 39/71 (54.9) |
| | <29 | 0.017 ^a | 0.63 | [0.43, 0.92] | 119/167 (71.3) | 35/66 (53.0) |
| | <30 | 0.011 ^a | 0.61 | [0.41, 0.89] | 120/168 (71.4) | 34/65 (52.3) |
| | <31 | 0.007 ^a | 0.58 | [0.39, 0.86] | 122/170 (71.8) | 32/63 (50.8) |
| | <32 | 0.026 ^a | 0.64 | [0.43, 0.95] | 122/174 (70.1) | 32/59 (54.2) |
| | <33 | 0.043 ^a | 0.66 | [0.44, 0.99] | 124/178 (69.7) | 30/55 (54.5) |
| | <34 | 0.007 ^a | 0.55 | [0.35, 0.85] | 130/185 (70.3) | 24/48 (50.0) |
| | <35 | 0.026 ^a | 0.61 | [0.39, 0.94] | 130/187 (69.5) | 24/46 (52.2) |
| | <36 | 0.033 ^a | 0.59 | [0.37, 0.96] | 135/195 (69.2) | 19/38 (50.0) |
| | <37 | 0.052 | 0.62 | [0.38, 1.00] | 135/196 (68.9) | 19/37 (51.4) |
| | <38 | 0.073 | 0.64 | [0.40, 1.04] | 135/197 (68.5) | 19/36 (52.8) |
| | <39 | 0.113 | 0.68 | [0.42, 1.10] | 135/198 (68.2) | 19/35 (54.3) |
| | <40 | 0.079 | 0.64 | [0.39, 1.05] | 136/199 (68.3) | 18/34 (52.9) |
| | <41 | 0.052 | 0.60 | [0.36, 1.01] | 138/201 (68.7) | 16/32 (50.0) |
| | <43 | 0.078 | 0.62 | [0.36, 1.06] | 139/203 (68.5) | 15/30 (50.0) |
| | <44 | 0.045 ^a | 0.56 | [0.32, 0.99] | 141/205 (68.8) | 13/28 (46.4) |
| | <45 | 0.055 | 0.53 | [0.28, 1.01] | 144/210 (68.6) | 10/23 (43.5) |
| | <46 | 0.056 | 0.52 | [0.26, 1.02] | 145/212 (68.4) | 9/21 (42.9) |
| | <49 | 0.028 ^a | 0.43 | [0.20, 0.91] | 147/215 (68.4) | 7/18 (38.9) |
| | <50 | 0.034 ^a | 0.41 | [0.18, 0.94] | 148/217 (68.2) | 6/16 (37.5) |
| | <51 | 0.022 ^a | 0.35 | [0.14, 0.86] | 149/218 (68.3) | 5/15 (33.3) |
| | <52 | 0.033 ^a | 0.38 | [0.16, 0.92] | 149/219 (68.0) | 5/14 (35.7) |
| | <54 | 0.023 ^a | 0.31 | [0.12, 0.85] | 150/220 (68.2) | 4/13 (30.8) |

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is '<'.

Output ID: T-7-5-S 2021-08-30 21:38

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

Table 7.5-s: OS univariate Cox proportional hazards model - candidate cut points - Soft Tissue (Soft Tissue-Full Analysis Set)

| Predictor variables | Cut point ^b | p-value | Hazard ratio | 95% CI | # of events / # of patients (%) | |
|--|------------------------|--------------------|--------------|---------------|---------------------------------|--------------|
| | | | | | <cut point | >=cut point |
| SUVmax (g/ml) - All cuts | <59 | 0.026 ^a | 0.27 | [0.09, 0.85] | 151/222 (68.0) | 3/11 (27.3) |
| | <60 | 0.031 ^a | 0.21 | [0.05, 0.87] | 152/224 (67.9) | 2/9 (22.2) |
| | <61 | 0.026 ^a | 0.11 | [0.01, 0.76] | 153/225 (68.0) | 1/8 (12.5) |
| | <62 | 0.043 ^a | 0.13 | [0.02, 0.93] | 153/226 (67.7) | 1/7 (14.3) |
| | <75 | 0.056 | 0.15 | [0.02, 1.05] | 153/227 (67.4) | 1/6 (16.7) |
| | <80 | 0.101 | 0.19 | [0.03, 1.38] | 153/228 (67.1) | 1/5 (20.0) |
| | <90 | 0.981 | 0.00 | [0.00,] | 154/230 (67.0) | 0/3 (0.0) |
| | <108 | 0.977 | 0.00 | [0.00,] | 154/231 (66.7) | 0/2 (0.0) |
| | <166 | 0.975 | 0.00 | [0.00,] | 154/232 (66.4) | 0/1 (0.0) |
| Volume of segmented PSMA positive tumors (cc) - All cuts | <100 | 0.189 | 1.35 | [0.86, 2.13] | 132/204 (64.7) | 22/29 (75.9) |
| | <200 | 0.228 | 1.44 | [0.80, 2.59] | 142/218 (65.1) | 12/15 (80.0) |
| | <300 | 0.060 | 1.85 | [0.97, 3.52] | 144/222 (64.9) | 10/11 (90.9) |
| | <500 | 0.136 | 1.79 | [0.83, 3.83] | 147/225 (65.3) | 7/8 (87.5) |
| | <600 | 0.421 | 1.44 | [0.59, 3.53] | 149/227 (65.6) | 5/6 (83.3) |
| | <800 | 0.128 | 2.17 | [0.80, 5.87] | 150/229 (65.5) | 4/4 (100.0) |
| | <900 | 0.085 | 2.74 | [0.87, 8.62] | 151/230 (65.7) | 3/3 (100.0) |
| | <1600 | 0.009 ^a | 6.67 | [1.62, 27.49] | 152/231 (65.8) | 2/2 (100.0) |
| | <3800 | 0.159 | 4.15 | [0.57, 30.03] | 153/232 (65.9) | 1/1 (100.0) |

^a Indicates statistical significance (2-sided) at the 0.05 level.^b Reference is '<'.

Output ID: T-7-5-S 2021-08-30 21:38

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Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Table 8.1: ORR univariate logistic regression model - Whole Body (Body-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|---|------------|--------------|--------------------|
| Whole Body | | | |
| SUVmean | 1.24 | [1.15, 1.34] | <.001 ^a |
| SUVmax | 1.01 | [1.01, 1.02] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 0.98 | [0.75, 1.28] | 0.891 |
| Tumor load | 1.03 | [1.00, 1.05] | 0.043 ^a |
| Bone | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 3.60 | [1.58, 8.16] | 0.002 ^a |
| Liver | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 1.79 | [0.82, 3.88] | 0.142 |
| Lymph Node | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.10 | [0.04, 0.23] | <.001 ^a |
| Soft Tissue | | | |
| Presence of PSMA positive tumors Yes vs. No ^b | 0.52 | [0.32, 0.85] | 0.009 ^a |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-8-1 2021-08-30 17:31

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 8.2: ORR univariate logistic regression model - Bone (Bone-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|---------|
| Bone | | | |
| -SUVmean | 1.06 | [0.99, 1.12] | 0.079 |
| SUVmax | 1.00 | [1.00, 1.01] | 0.342 |
| Volume of segmented PSMA positive tumors | 0.82 | [0.58, 1.14] | 0.233 |
| Tumor load | 0.99 | [0.96, 1.03] | 0.778 |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-8-2 2021-08-30 17:32

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-univ-hr-log.sas

Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 8.3: ORR univariate logistic regression model - Liver (Liver-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|---------|
| Liver | | | |
| SUVmean | 1.19 | [0.95, 1.49] | 0.134 |
| SUVmax | 1.03 | [0.99, 1.08] | 0.187 |
| Volume of segmented PSMA positive tumors | 0.21 | [0.01, 5.27] | 0.344 |
| Tumor load | 0.96 | [0.83, 1.11] | 0.569 |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-8-3 2021-08-30 17:32

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-univ-hr-log.sas

Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 8.4: ORR univariate logistic regression model - Lymph Node (Lymph Node-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|----------------|--------------------|
| Lymph node | | | |
| SUVmean | 1.26 | [1.16, 1.36] | <.001 ^a |
| SUVmax | 1.04 | [1.02, 1.05] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 33.40 | [5.58, 200.06] | <.001 ^a |
| Tumor load | 1.41 | [1.20, 1.66] | <.001 ^a |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-8-4 2021-08-30 17:32

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 8.5: ORR univariate logistic regression model - Soft Tissue (Soft Tissue-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Soft tissue | | | |
| SUVmean | 1.07 | [1.00, 1.14] | 0.039 ^a |
| SUVmax | 1.02 | [1.00, 1.04] | 0.029 ^a |
| Volume of segmented PSMA positive tumors | 0.90 | [0.34, 2.36] | 0.835 |
| Tumor load | 1.00 | [0.93, 1.07] | 0.973 |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-8-5 2021-08-30 17:32

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Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 9.1: ORR multivariate logistic regression model - Whole Body (Body-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Whole body | | | |
| SUVmean | 1.43 | [1.24, 1.65] | <.001 ^a |
| SUVmax | 0.98 | [0.96, 0.99] | 0.007 ^a |
| Tumor load | 1.00 | [0.97, 1.03] | 0.998 |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.69 | [1.01, 7.22] | 0.049 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.11 | [0.04, 0.28] | <.001 ^a |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.62 | [0.35, 1.12] | 0.113 |
| Final multivariate model from the backward/forward selection | | | |
| Whole body | | | |
| SUVmean | 1.43 | [1.24, 1.65] | <.001 ^a |
| SUVmax | 0.98 | [0.96, 0.99] | 0.009 ^a |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 3.06 | [1.12, 8.38] | 0.030 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.55 | [1.02, 6.34] | 0.045 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.10 | [0.04, 0.25] | <.001 ^a |

Note: The odds ratios for tumor load are computed for a 1000g increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-9-1 2021-08-30 19:17

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Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 9-1-b-s: ORR multivariate logistic regression model - backward selection - Whole Body (Body-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Whole body | | | |
| SUVmean | 1.43 | [1.24, 1.65] | <.001 ^a |
| SUVmax | 0.98 | [0.96, 0.99] | 0.007 ^a |
| Tumor load | 1.00 | [0.97, 1.03] | 0.998 |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.69 | [1.01, 7.22] | 0.049 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.11 | [0.04, 0.28] | <.001 ^a |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.62 | [0.35, 1.12] | 0.113 |
| Step 1 | | | |
| Whole body | | | |
| SUVmean | 1.43 | [1.24, 1.65] | <.001 ^a |
| SUVmax | 0.98 | [0.96, 0.99] | 0.006 ^a |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.69 | [1.01, 7.19] | 0.048 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.11 | [0.04, 0.27] | <.001 ^a |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.62 | [0.35, 1.12] | 0.113 |

Note: The odds ratios for tumor load are computed for a 1000g increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-9-1-B-S 2021-08-30 19:17

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 9-1-b-s: ORR multivariate logistic regression model - backward selection - Whole Body (Body-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Whole body | | | |
| SUVmean | 1.42 | [1.23, 1.63] | <.001 ^a |
| SUVmax | 0.98 | [0.96, 1.00] | 0.011 ^a |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.69 | [1.01, 7.19] | 0.048 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.10 | [0.04, 0.25] | <.001 ^a |

Note: The odds ratios for tumor load are computed for a 1000g increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

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Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 9-1-f-s: ORR multivariate logistic regression model - forward selection - Whole Body (Body-Response
Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Whole body | | | |
| SUVmean | 1.42 | [1.23, 1.63] | <.001 ^a |
| SUVmax | 0.98 | [0.96, 1.00] | 0.011 ^a |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.69 | [1.01, 7.19] | 0.048 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.10 | [0.04, 0.25] | <.001 ^a |
| Step 1 - Candidate | | | |
| Whole body | | | |
| Volume of segmented PSMA positive tumors | | | 0.999 |
| Tumor load | | | 0.949 |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | | | 0.041 ^a |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | | | 0.112 |
| Step 2 - Candidate | | | |
| Whole body | | | |
| Volume of segmented PSMA positive tumors | | | 0.742 |
| Tumor load | | | 0.660 |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | | | 0.075 |

Note: The odds ratios for tumor load are computed for a 1000g increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-9-1-F-S 2021-08-30 19:18

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Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 9-1-f-s: ORR multivariate logistic regression model - forward selection - Whole Body (Body-Response
Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Final multivariate model from the backward/forward selection | | | |
| Whole body | 1.43 | [1.24, 1.65] | <.001 ^a |
| SUVmean | 0.98 | [0.96, 0.99] | 0.009 ^a |
| SUVmax | | | |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 3.06 | [1.12, 8.38] | 0.030 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.55 | [1.02, 6.34] | 0.045 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.10 | [0.04, 0.25] | <.001 ^a |

Note: The odds ratios for tumor load are computed for a 1000g increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

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Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 9.2: ORR multivariate logistic regression model - Bone (Bone-Response Evaluable Analysis Set)

No variable with p<0.05 in the univariate analysis

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...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_AN
ALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas
Source data: adsl.xpt, adrs.xpt, adpsa.xpt
Data Cutoff Date: 27JAN2021

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Table 9-2-b-s: ORR multivariate logistic regression model - backward selection - Bone (Bone-Response Evaluable Analysis Set)

No variable with p<0.05 in the univariate analysis

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...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_AN
ALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas
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Final Version

Table 9-2-f-s: ORR multivariate logistic regression model - forward selection - Bone (Bone-Response Evaluable Analysis Set)

No variable with p<0.05 in the univariate analysis

Output ID: T-9-2-F-S 2021-08-30 19:18
...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_AN
ALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas
Source data: adsl.xpt, adrs.xpt, adpsa.xpt
Data Cutoff Date: 27JAN2021

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Final Version

Table 9.3: ORR multivariate logistic regression model - backward/forward selection - Liver (Liver-Response
Evaluable Analysis Set)

No variable with p<0.05 in the univariate analysis

Output ID: T-9-3 2021-08-30 19:19
...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_AN
ALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas
Source data: adsl.xpt, adrs.xpt, adpsa.xpt
Data Cutoff Date: 27JAN2021

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Table 9-3-b-s: ORR multivariate logistic regression model - backward selection - Liver (Liver-Response Evaluable Analysis Set)

No variable with p<0.05 in the univariate analysis

Output ID: T-9-3-B-S 2021-08-30 19:19
...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_AN
ALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas
Source data: adsl.xpt, adrs.xpt, adpsa.xpt
Data Cutoff Date: 27JAN2021

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Final Version

Table 9-3-f-s: ORR multivariate logistic regression model - forward selection - Liver (Liver-Response Evaluable Analysis Set)

No variable with p<0.05 in the univariate analysis

Output ID: T-9-3-F-S 2021-08-30 19:19
...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_AN
ALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas
Source data: adsl.xpt, adrs.xpt, adpsa.xpt
Data Cutoff Date: 27JAN2021

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Final Version

Table 9.4: ORR multivariate logistic regression model - Lymph Node (Lymph Node-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|-----------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Lymph Node | | | |
| SUVmean | 1.21 | [1.07, 1.38] | 0.003 ^a |
| SUVmax | 1.00 | [0.98, 1.02] | 0.896 |
| Volume of segmented PSMA positive tumors | 12.31 | [0.06, 2654.44] | 0.360 |
| Tumor load | 0.95 | [0.59, 1.52] | 0.834 |
| Final multivariate model from the backward/forward selection | | | |
| Lymph Node | | | |
| SUVmean | 1.21 | [1.12, 1.31] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 7.26 | [1.45, 36.46] | 0.016 ^a |

Note: The odds ratios for tumor volume are computed for a 1000cc increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-9-4 2021-08-30 19:19

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Final Version

Table 9-4-b-s: ORR multivariate logistic regression model - backward selection - Lymph Node (Lymph Node-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|-----------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Lymph Node | 1.21 | [1.07, 1.38] | 0.003 ^a |
| SUVmean | 1.00 | [0.98, 1.02] | 0.896 |
| SUVmax | 12.31 | [0.06, 2654.44] | 0.360 |
| Volume of segmented PSMA positive tumors | 0.95 | [0.59, 1.52] | 0.834 |
| Tumor load | | | |
| Step 1 | | | |
| Lymph Node | 1.22 | [1.11, 1.34] | <.001 ^a |
| SUVmean | 12.12 | [0.05, 2750.23] | 0.367 |
| Volume of segmented PSMA positive tumors | 0.95 | [0.59, 1.53] | 0.845 |
| Tumor load | | | |
| Final multivariate model from the backward selection | | | |
| Lymph Node | 1.21 | [1.12, 1.31] | <.001 ^a |
| SUVmean | 7.26 | [1.45, 36.46] | 0.016 ^a |
| Volume of segmented PSMA positive tumors | | | |

Note: The odds ratios for tumor volume are computed for a 1000cc increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-9-4-B-S 2021-08-30 19:20

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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68Ga-PSMA-11 Quantitative analysis

Final Version

Table 9-4-f-s: ORR multivariate logistic regression model - forward selection - Lymph Node (Lymph Node-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|---------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Lymph Node SUVmean | 1.21 | [1.12, 1.31] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 7.26 | [1.45, 36.46] | 0.016 ^a |
| Step 1 - Candidate | | | |
| Lymph Node SUVmax | | | 0.912 |
| Tumor load | | | 0.848 |
| Final multivariate model from the backward/forward selection | | | |
| Lymph Node SUVmean | 1.21 | [1.12, 1.31] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 7.26 | [1.45, 36.46] | 0.016 ^a |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-9-4-F-S 2021-08-30 19:20

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

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Table 9.5: ORR multivariate logistic regression model - Soft Tissue (Soft Tissue-Response Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Soft Tissue | | | |
| SUVmean | 1.01 | [0.89, 1.14] | 0.868 |
| SUVmax | 1.02 | [0.98, 1.05] | 0.309 |
| Final multivariate model from the backward/forward selection | | | |
| Soft Tissue | | | |
| SUVmax | 1.02 | [1.00, 1.04] | 0.029 ^a |

Note: The odds ratios for SUVmean and SUVmax are computed for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-9-5 2021-08-30 19:20

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 9-5-b-s: ORR multivariate logistic regression model - backward selection - Soft Tissue (Soft Tissue-Response Evaluatable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Soft Tissue | | | |
| SUVmean | 1.01 | [0.89, 1.14] | 0.868 |
| SUVmax | 1.02 | [0.98, 1.05] | 0.309 |
| Final multivariate model from the backward selection | | | |
| Soft Tissue | | | |
| SUVmax | 1.02 | [1.00, 1.04] | 0.029 ^a |

Note: The odds ratios for SUVmean and SUVmax are computed for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-9-5-B-S 2021-08-30 19:21

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Final Version

Table 9-5-f-s: ORR multivariate logistic regression model - forward selection - Soft Tissue (Soft Tissue-Response
Evaluable Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Soft Tissue SUVmax | 1.02 | [1.00, 1.04] | 0.029 ^a |
| Step 1 - Candidate | | | |
| Soft Tissue SUVmean | 0.868 | | |
| Volume of segmented PSMA positive tumors | 0.518 | | |
| Tumor load | 0.565 | | |
| Final multivariate model from the backward/forward selection | | | |
| Soft Tissue SUVmax | 1.02 | [1.00, 1.04] | 0.029 ^a |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-9-5-F-S 2021-08-30 19:21

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Final Version

Table 10.1: PSA response univariate logistic regression model - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Whole Body | | | |
| SUVmean | 1.33 | [1.23, 1.44] | <.001 ^a |
| SUVmax | 1.03 | [1.02, 1.04] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 0.90 | [0.73, 1.11] | 0.315 |
| Tumor load | 1.01 | [0.99, 1.03] | 0.338 |
| Bone | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 1.28 | [0.60, 2.73] | 0.526 |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.27 | [1.20, 4.31] | 0.012 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.64 | [0.41, 0.99] | 0.046 ^a |
| Soft Tissue | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.91 | [0.61, 1.36] | 0.636 |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-10-1 2021-08-30 17:33

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-univ-hr-log.sas

Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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68Ga-PSMA-11 Quantitative analysis

Final Version

Table 10.2: PSA response univariate logistic regression model - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Bone | | | |
| SUVmean | 1.32 | [1.21, 1.45] | <.001 ^a |
| SUVmax | 1.02 | [1.01, 1.03] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 0.90 | [0.71, 1.14] | 0.367 |
| Tumor load | 1.01 | [0.98, 1.04] | 0.603 |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-10-2 2021-08-30 17:33

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-univ-hr-log.sas

Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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68Ga-PSMA-11 Quantitative analysis

Final Version

Table 10.3: PSA response univariate logistic regression model - Liver (Liver-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|---------|
| Liver | | | |
| SUVmean | 1.09 | [0.94, 1.27] | 0.256 |
| SUVmax | 1.01 | [0.97, 1.05] | 0.713 |
| Volume of segmented PSMA positive tumors | 0.17 | [0.01, 2.11] | 0.169 |
| Tumor load | 0.92 | [0.80, 1.06] | 0.260 |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-10-3 2021-08-30 17:33

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-univ-hr-log.sas

Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 10.4: PSA response univariate logistic regression model - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|---------------|--------------------|
| Lymph node | | | |
| SUVmean | 1.17 | [1.09, 1.24] | <.001 ^a |
| SUVmax | 1.03 | [1.02, 1.04] | <.001 ^a |
| Volume of segmented PSMA positive tumors | 4.07 | [1.26, 13.14] | 0.019 ^a |
| Tumor load | 1.16 | [1.04, 1.29] | 0.007 ^a |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-10-4 2021-08-30 17:34

..\BIOMETRY\PROJECTS\PSMA617\VISION\QUANTITATIVE_ANALYSIS\PRODUCTION\TLF\PGM\t-eff-univ-hr-log.sas

Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 10.5: PSA response univariate logistic regression model - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Soft tissue | | | |
| SUVmean | 1.04 | [0.99, 1.10] | 0.129 |
| SUVmax | 1.02 | [1.00, 1.04] | 0.043 ^a |
| Volume of segmented PSMA positive tumors | 0.63 | [0.20, 1.97] | 0.424 |
| Tumor load | 0.98 | [0.91, 1.06] | 0.573 |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-10-5 2021-08-30 17:34

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-univ-hr-log.sas

Source data: adsl.xpt, adtte.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Final Version

Table 11.1: PSA response multivariate logistic regression model - Whole Body (Body-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Whole body | 1.29 | [1.15, 1.45] | <.001 ^a |
| SUVmean | 1.01 | [0.99, 1.02] | 0.454 |
| SUVmax | | | |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.40 | [1.19, 4.84] | 0.014 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.85 | [0.52, 1.38] | 0.513 |
| Final multivariate model from the backward/forward selection | | | |
| Whole body | 1.34 | [1.23, 1.45] | <.001 ^a |
| SUVmean | | | |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.42 | [1.21, 4.86] | 0.013 ^a |

Note: The odds ratios for SUVmean and SUVmax are computed for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-11-1 2021-08-30 19:21

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Final Version

Table 11-1-b-s: PSA response multivariate logistic regression model - backward selection - Whole Body
(Body-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Whole body | | | |
| SUVmean | 1.29 | [1.15, 1.45] | <.001 ^a |
| SUVmax | 1.01 | [0.99, 1.02] | 0.454 |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.40 | [1.19, 4.84] | 0.014 ^a |
| Lymph Node | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 0.85 | [0.52, 1.38] | 0.513 |
| Step 1 | | | |
| Whole body | | | |
| SUVmean | 1.30 | [1.16, 1.45] | <.001 ^a |
| SUVmax | 1.01 | [0.99, 1.02] | 0.419 |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.37 | [1.18, 4.76] | 0.016 ^a |
| Final multivariate model from the backward selection | | | |
| Whole body | | | |
| SUVmean | 1.34 | [1.23, 1.45] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | 2.42 | [1.21, 4.86] | 0.013 ^a |

Note: The odds ratios for tumor load are computed for a 1000g increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-11-1-B-S 2021-08-30 19:21

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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68Ga-PSMA-11 Quantitative analysis

Final Version

Table 11-1-f-s: PSA response multivariate logistic regression model - forward selection - Whole Body (Body-PFS
Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Whole body | 1.34 | [1.23, 1.45] | <.001 ^a |
| Liver | | | |
| Presence of PSMA positive tumors | 2.42 | [1.21, 4.86] | 0.013 ^a |
| Yes vs. No ^b | | | |
| Step 1 - Candidate | | | |
| Whole body | | | 0.418 |
| SUVmax | | | 0.511 |
| Volume of segmented PSMA positive tumors | | | 0.346 |
| Tumor load | | | |
| Bone | | | 0.604 |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | | | |
| Lymph Node | | | 0.471 |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | | | |
| Soft Tissue | | | 0.901 |
| Presence of PSMA positive tumors | | | |
| Yes vs. No ^b | | | |
| Final multivariate model from the backward/forward selection | | | |
| Whole body | 1.34 | [1.23, 1.45] | <.001 ^a |
| SUVmean | | | |
| Liver | | | |
| Presence of PSMA positive tumors | 2.42 | [1.21, 4.86] | 0.013 ^a |
| Yes vs. No ^b | | | |

Note: The odds ratios for tumor load are computed for a 1000g increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

^b Reference is 'Yes'

Output ID: T-11-1-F-S 2021-08-30 19:22

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Final Version

Table 11.2: PSA response multivariate logistic regression model - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Bone | | | |
| SUVmean | 1.41 | [1.21, 1.65] | <.001 ^a |
| SUVmax | 0.99 | [0.98, 1.01] | 0.319 |
| Final multivariate model from the backward/forward selection | | | |
| Bone | | | |
| SUVmean | 1.32 | [1.21, 1.45] | <.001 ^a |

Note: The odds ratios for SUVmean and SUVmax are computed for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-11-2 2021-08-30 19:22

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 11-2-b-s: PSA response multivariate logistic regression model - backward selection - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Bone | | | |
| SUVmean | 1.41 | [1.21, 1.65] | <.001 ^a |
| SUVmax | 0.99 | [0.98, 1.01] | 0.319 |
| Final multivariate model from the backward selection | | | |
| Bone | | | |
| SUVmean | 1.32 | [1.21, 1.45] | <.001 ^a |

Note: The odds ratios for SUVmean and SUVmax are computed for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-11-2-B-S 2021-08-30 19:22

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

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Table 11-2-f-s: PSA response multivariate logistic regression model - forward selection - Bone (Bone-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Bone SUVmean | 1.32 | [1.21, 1.45] | <.001 ^a |
| Step 1 - Candidate | | | |
| Bone SUVmax | 0.318 | | |
| Volume of segmented PSMA positive tumors | 0.128 | | |
| Tumor load | 0.143 | | |
| Final multivariate model from the backward/forward selection | | | |
| Bone SUVmean | 1.32 | [1.21, 1.45] | <.001 ^a |

Note: The odds ratios for tumor load are computed for a 1000g increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-11-2-F-S 2021-08-30 19:23

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Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 11.3: PSA response multivariate logistic regression model - backward/forward selection - Liver (Liver-PFS
Full Analysis Set)

No variable with p<0.05 in the univariate analysis

Output ID: T-11-3 2021-08-30 19:23
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ALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas
Source data: adsl.xpt, adrs.xpt, adpsa.xpt
Data Cutoff Date: 27JAN2021

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Table 11-3-b-s: PSA response multivariate logistic regression model - backward selection - Liver (Liver-PFS Full Analysis Set)

No variable with p<0.05 in the univariate analysis

Output ID: T-11-3-B-S 2021-08-30 19:23
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ALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas
Source data: adsl.xpt, adrs.xpt, adpsa.xpt
Data Cutoff Date: 27JAN2021

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Table 11-3-f-s: PSA response multivariate logistic regression model - forward selection - Liver (Liver-PFS Full Analysis Set)

No variable with p<0.05 in the univariate analysis

Output ID: T-11-3-F-S 2021-08-30 19:24
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ALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas
Source data: adsl.xpt, adrs.xpt, adpsa.xpt
Data Cutoff Date: 27JAN2021

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Table 11.4: PSA response multivariate logistic regression model - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|---------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Lymph Node SUVmean | 1.08 | [0.96, 1.21] | 0.192 |
| SUVmax | 1.01 | [0.99, 1.03] | 0.244 |
| Volume of segmented PSMA positive tumors | 0.40 | [0.00, 55.61] | 0.718 |
| Tumor load | 1.11 | [0.73, 1.70] | 0.616 |
| Final multivariate model from the backward/forward selection | | | |
| Lymph Node SUVmean | 1.17 | [1.09, 1.24] | <.001 ^a |

Note: The odds ratios for tumor volume are computed for a 1000cc increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-11-4 2021-08-30 19:24

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Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 11-4-b-s: PSA response multivariate logistic regression model - backward selection - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|---------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Lymph Node | 1.08 | [0.96, 1.21] | 0.192 |
| SUVmean | 1.01 | [0.99, 1.03] | 0.244 |
| SUVmax | 0.40 | [0.00, 55.61] | 0.718 |
| Volume of segmented PSMA positive tumors | 1.11 | [0.73, 1.70] | 0.616 |
| Tumor load | | | |
| Step 1 | | | |
| Lymph Node | 1.09 | [0.97, 1.21] | 0.152 |
| SUVmean | 1.01 | [0.99, 1.03] | 0.241 |
| SUVmax | 1.03 | [0.94, 1.14] | 0.488 |
| Tumor load | | | |
| Step 2 | | | |
| Lymph Node | 1.09 | [0.97, 1.22] | 0.145 |
| SUVmean | 1.01 | [0.99, 1.04] | 0.159 |
| SUVmax | | | |
| Final multivariate model from the backward selection | | | |
| Lymph Node | 1.17 | [1.09, 1.24] | <.001 ^a |
| SUVmean | | | |

Note: The odds ratios for tumor volume are computed for a 1000cc increase, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-11-4-B-S 2021-08-30 19:24

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Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 11-4-f-s: PSA response multivariate logistic regression model - forward selection - Lymph Node (Lymph Node-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Lymph Node SUVmean | 1.17 | [1.09, 1.24] | <.001 ^a |
| Step 1 - Candidate | | | |
| Lymph Node SUVmax | 0.156 | | |
| Volume of segmented PSMA positive tumors | 0.348 | | |
| Tumor load | 0.305 | | |
| Final multivariate model from the backward/forward selection | | | |
| Lymph Node SUVmean | 1.17 | [1.09, 1.24] | <.001 ^a |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-11-4-F-S 2021-08-30 19:25

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Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 11.5: PSA response multivariate logistic regression model - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Soft Tissue | 1.02 | [1.00, 1.04] | 0.043 ^a |
| SUVmax | | | |
| Final multivariate model from the backward/forward selection | | | |
| Soft Tissue | 1.02 | [1.00, 1.04] | 0.043 ^a |
| SUVmax | | | |

Note: The odds ratios for SUVmax are computed for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-11-5 2021-08-30 19:25

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 11-5-b-s: PSA response multivariate logistic regression model - backward selection - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Initial multivariate model from selected covariates based on univariate models | | | |
| Soft Tissue SUVmax | 1.02 | [1.00, 1.04] | 0.043 ^a |
| Final multivariate model from the backward selection | | | |
| Soft Tissue SUVmax | 1.02 | [1.00, 1.04] | 0.043 ^a |

Note: The odds ratios for SUVmax are computed for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-11-5-B-S 2021-08-30 19:25

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\QUANTITATIVE_ANALYSIS\\PRODUCTION\\TLF\\PGM\\t-eff-multbf-or.sas

Source data: adsl.xpt, adrs.xpt, adpsa.xpt

Data Cutoff Date: 27JAN2021

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Table 11-5-f-s: PSA response multivariate logistic regression model - forward selection - Soft Tissue (Soft Tissue-PFS Full Analysis Set)

| Predictor variables | Odds ratio | 95% CI | p-value |
|--|------------|--------------|--------------------|
| Final multivariate model from the backward selection | | | |
| Soft Tissue SUVmax | 1.02 | [1.00, 1.04] | 0.043 ^a |
| Step 1 - Candidate | | | |
| Soft Tissue SUVmean | 0.542 | | |
| Volume of segmented PSMA positive tumors | 0.191 | | |
| Tumor load | 0.237 | | |
| Final multivariate model from the backward/forward selection | | | |
| Soft Tissue SUVmax | 1.02 | [1.00, 1.04] | 0.043 ^a |

Note: The odds ratios for tumor volume and tumor load are computed for a 1000cc and 1000g increase respectively, those for SUVmean and SUVmax for a 1g/ml increase

^a Indicates statistical significance (2-sided) at the 0.05 level.

Output ID: T-11-5-F-S 2021-08-30 19:26

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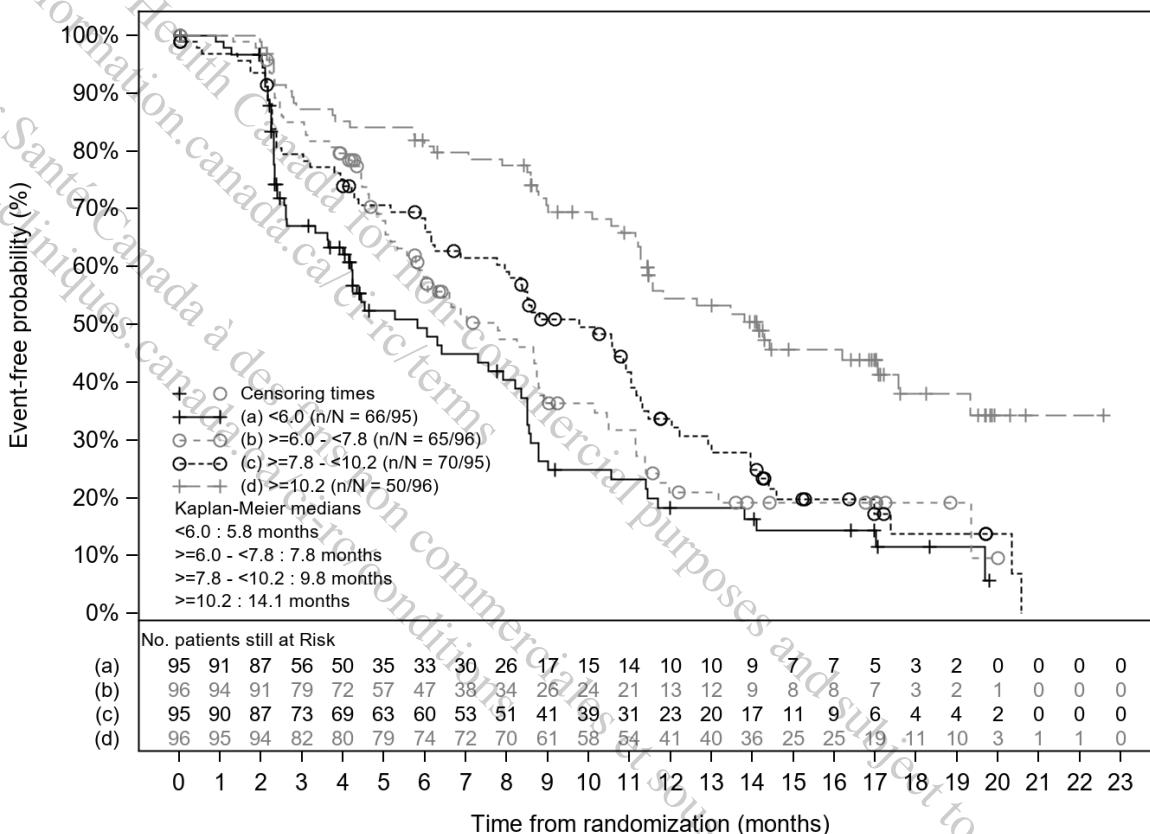
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Data Cutoff Date: 27JAN2021

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Figure 2-1-1 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by SUV mean (g/mL) quartiles in whole body (Body - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-1-1 2021-08-30 12:24

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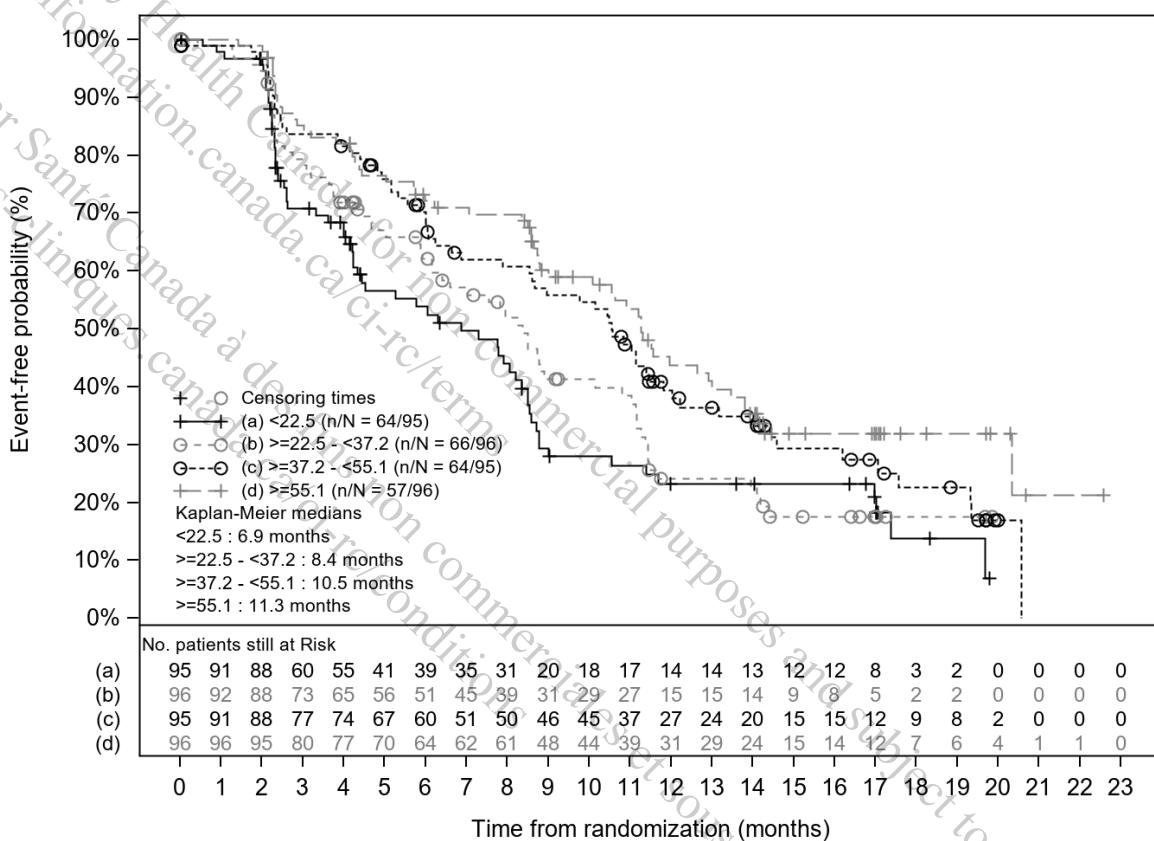
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Data Cutoff Date: 27JAN2021

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Figure 2-1-2 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by SUV max (g/mL) quartiles in whole body (Body - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-1-2 2021-08-30 12:24

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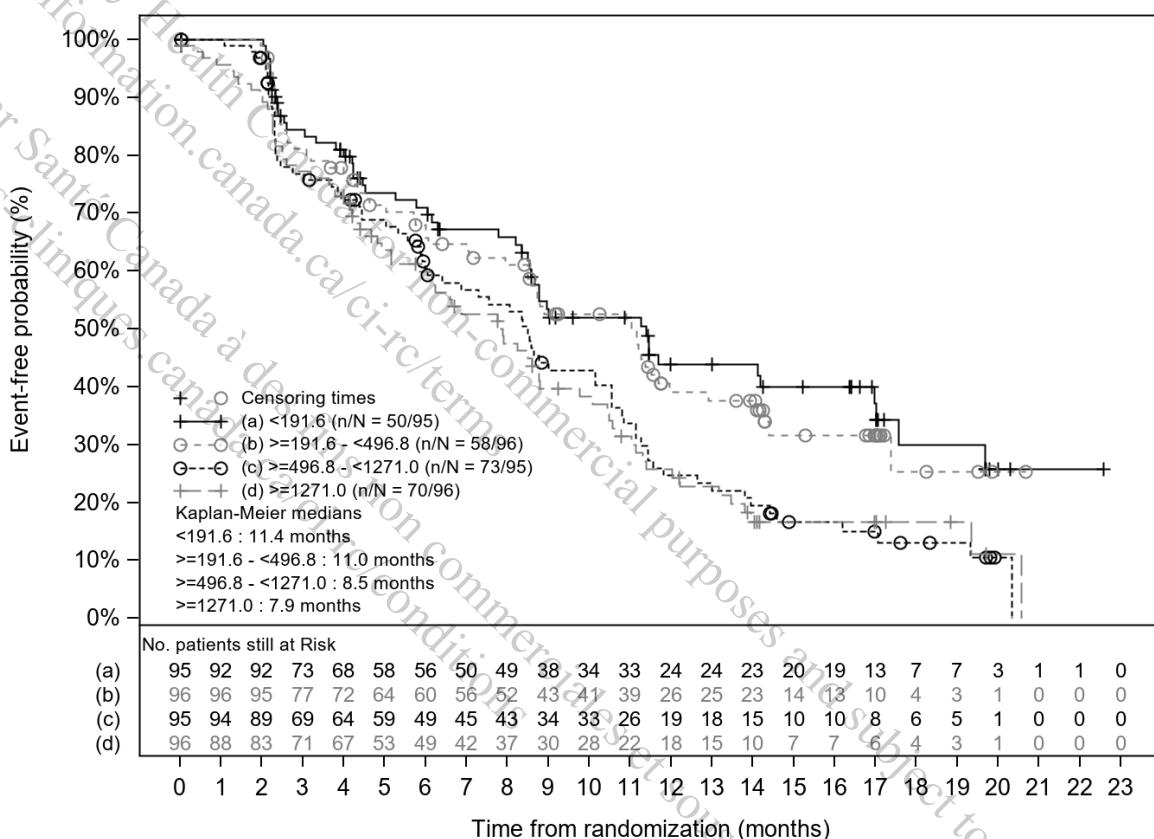
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Data Cutoff Date: 27JAN2021

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Figure 2-1-3 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by tumor volume (cc) quartiles in whole body (Body - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-1-3 2021-08-30 12:24

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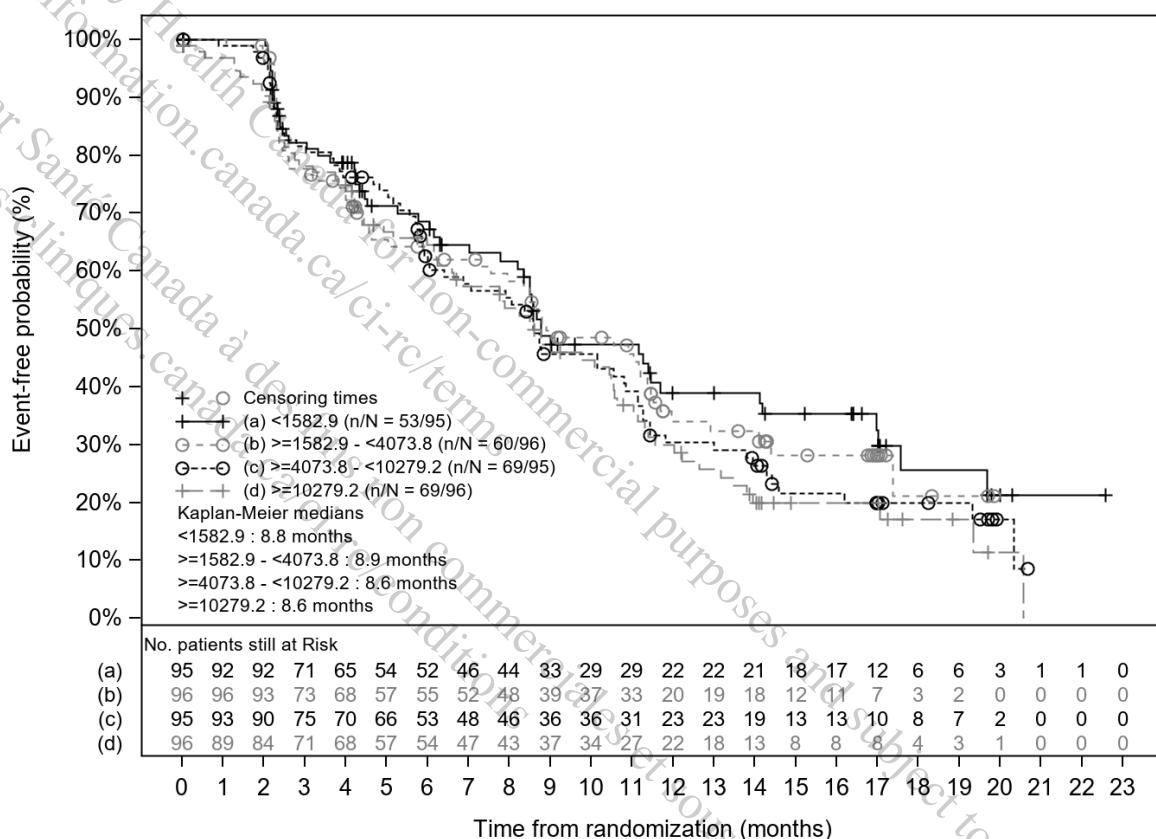
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Data Cutoff Date: 27JAN2021

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Figure 2-1-4 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by tumor load (g) quartiles in whole body (Body - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-1-4 2021-08-30 12:25

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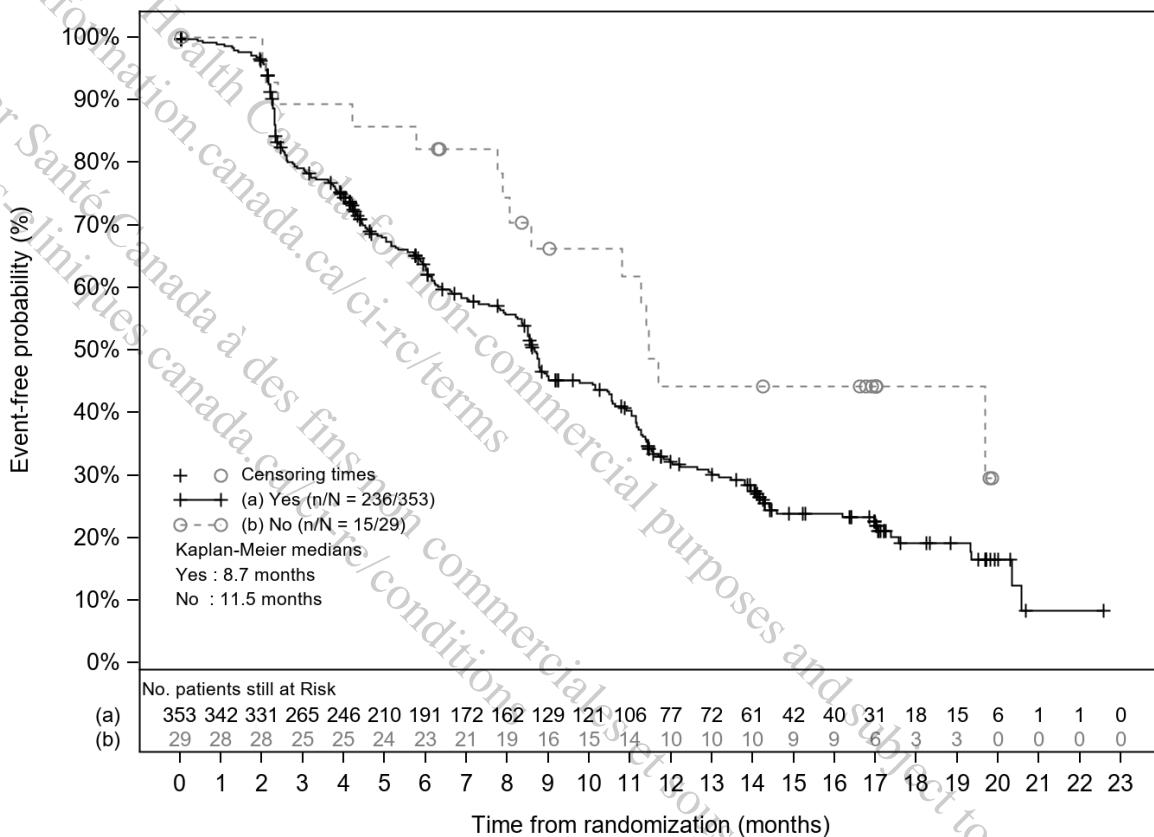
Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Figure 2-1-5 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by presence of PSMA positive tumors in bone (Body - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-1-5 2021-08-30 12:25

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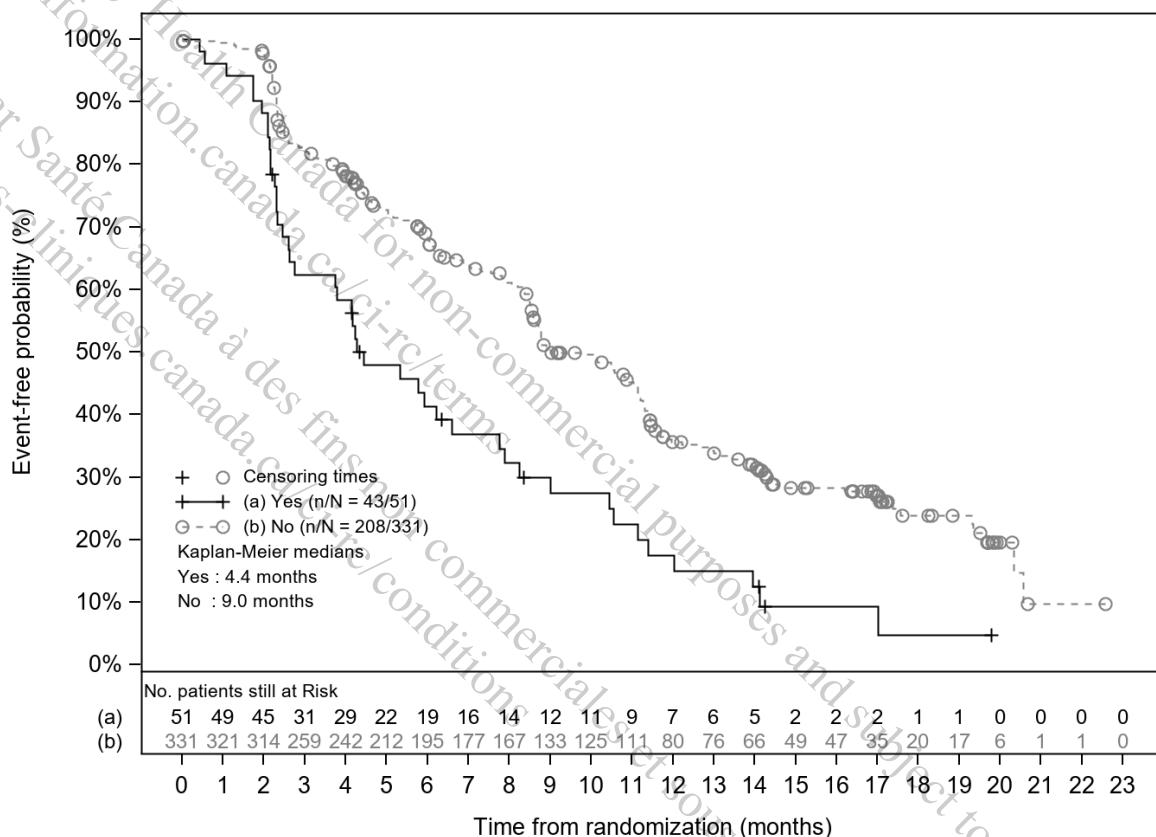
Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Figure 2-1-6 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by presence of PSMA positive tumors in liver (Body - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-1-6 2021-08-30 12:25

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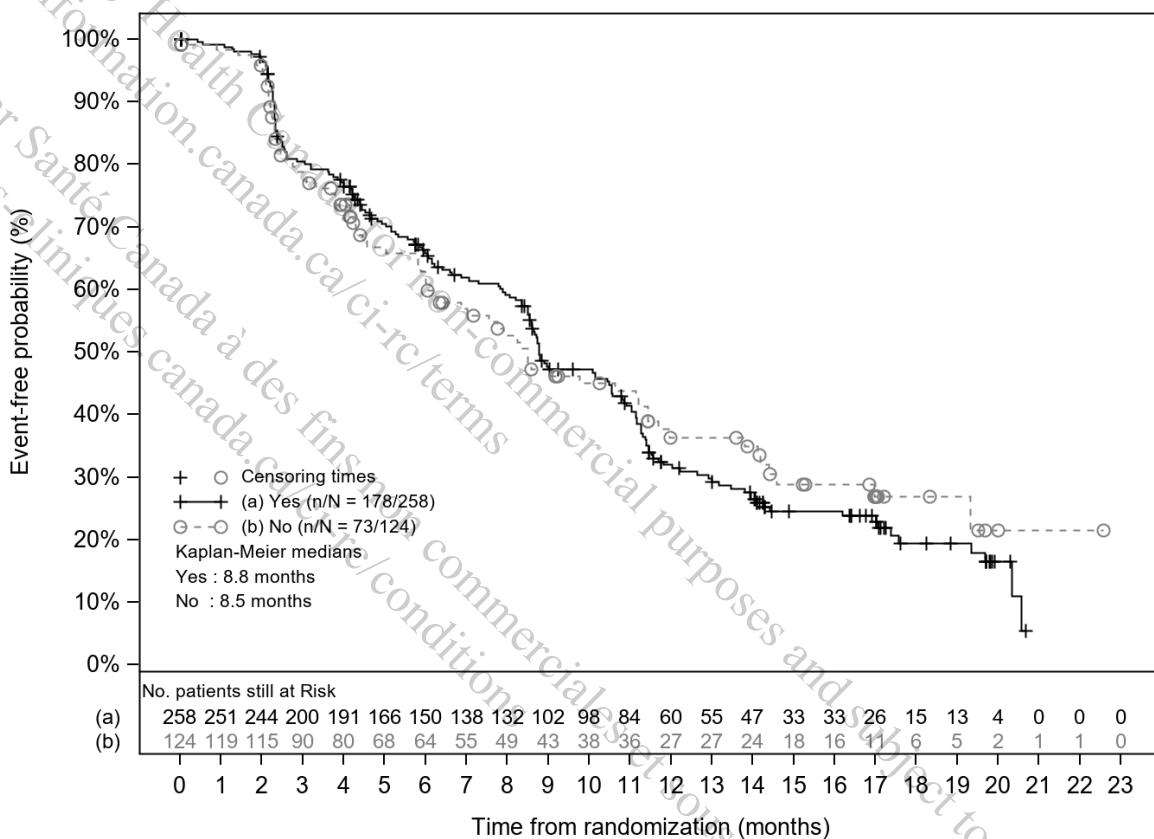
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Data Cutoff Date: 27JAN2021

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Figure 2-1-7 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by presence of PSMA positive tumors in lymph node (Body - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-1-7 2021-08-30 12:25

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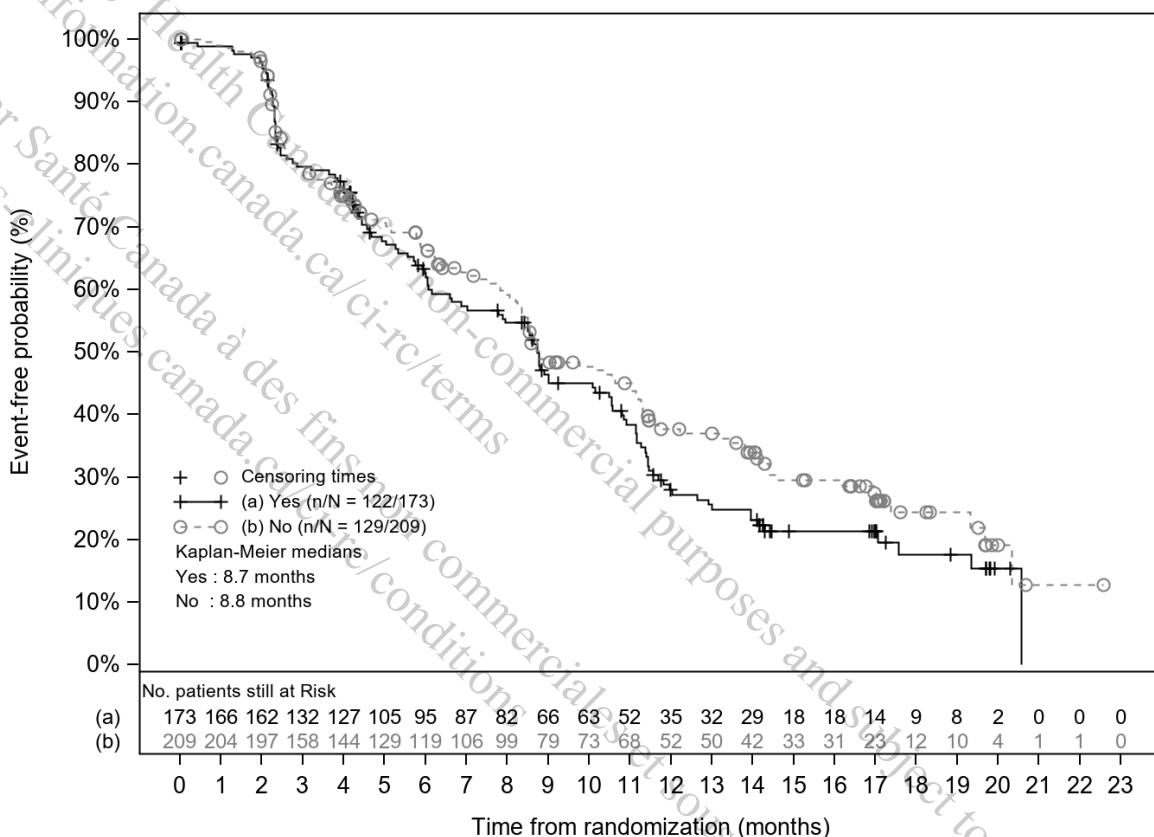
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Data Cutoff Date: 27JAN2021

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Figure 2-1-8 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by presence of PSMA positive tumors in soft tissue (Body - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-1-8 2021-08-30 12:25

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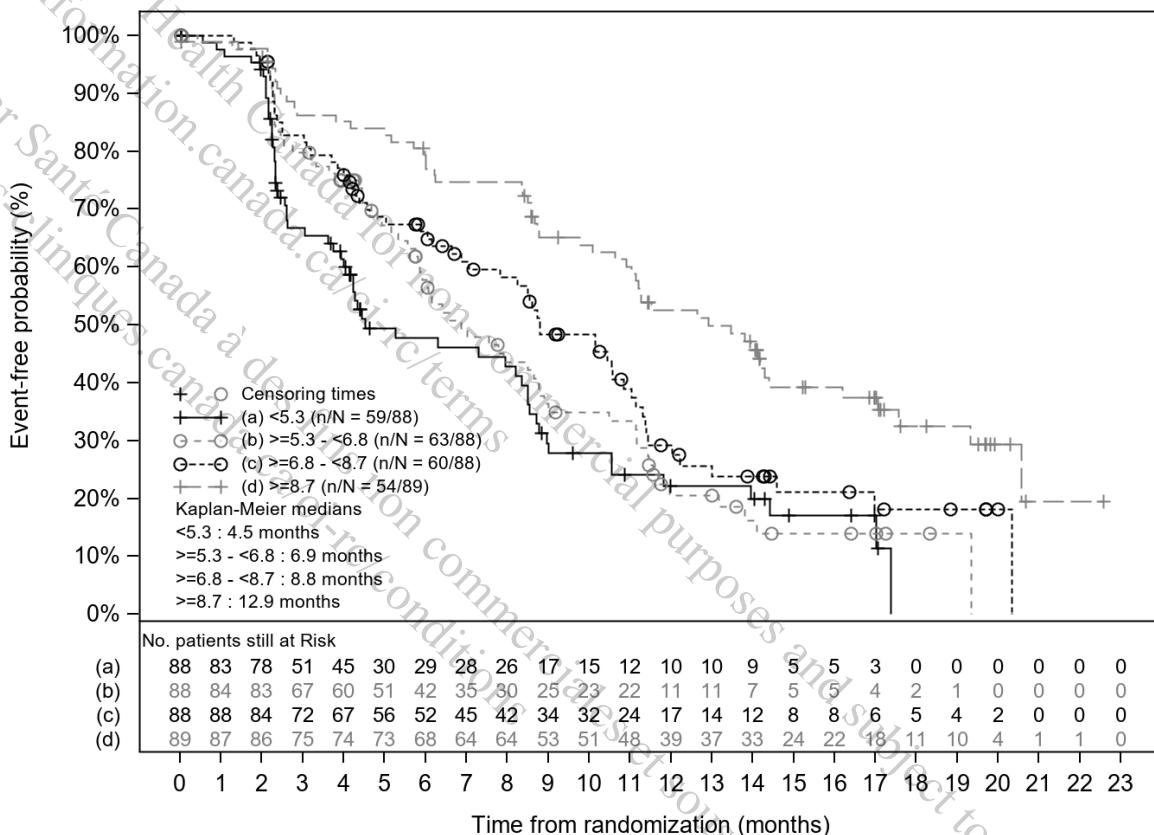
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Data Cutoff Date: 27JAN2021

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Figure 2-2-1 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by SUV mean (g/mL) quartiles in bone (Bone - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-2-1 2021-08-30 12:25

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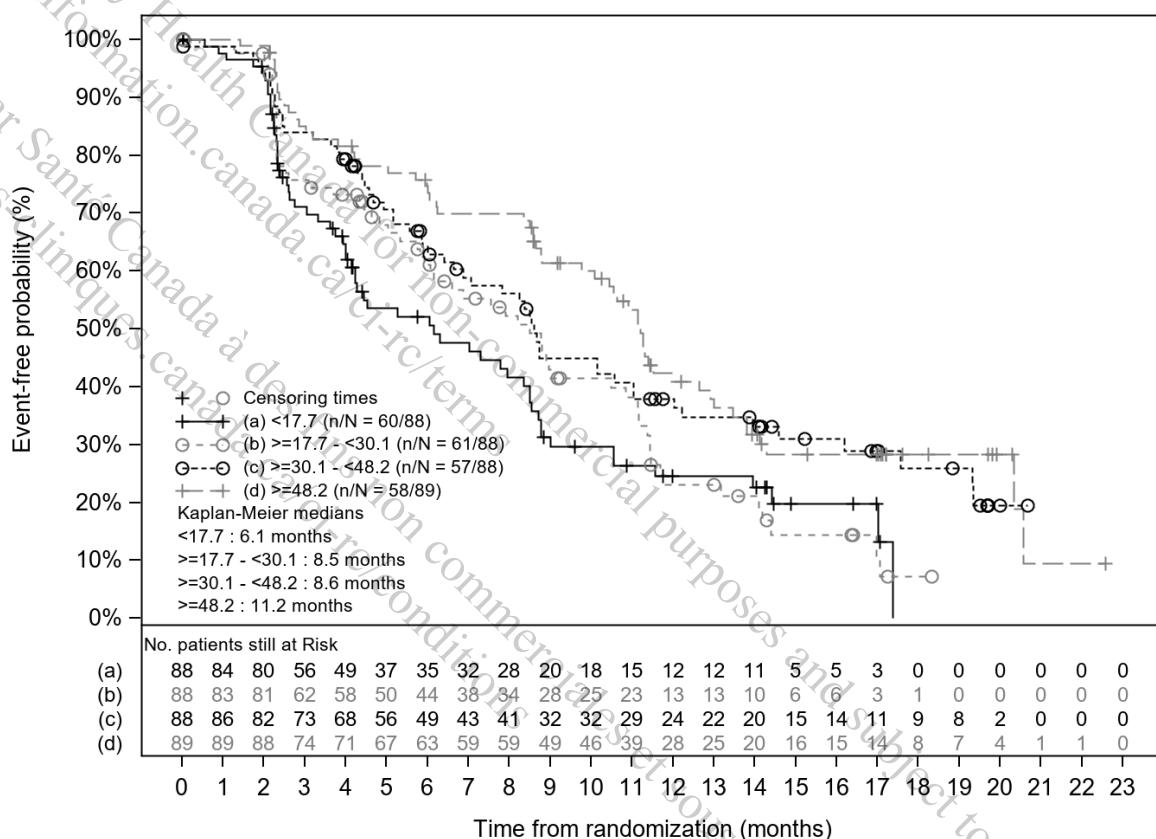
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Data Cutoff Date: 27JAN2021

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Figure 2-2-2 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by SUV max (g/mL) quartiles in bone (Bone - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-2-2 2021-08-30 12:25

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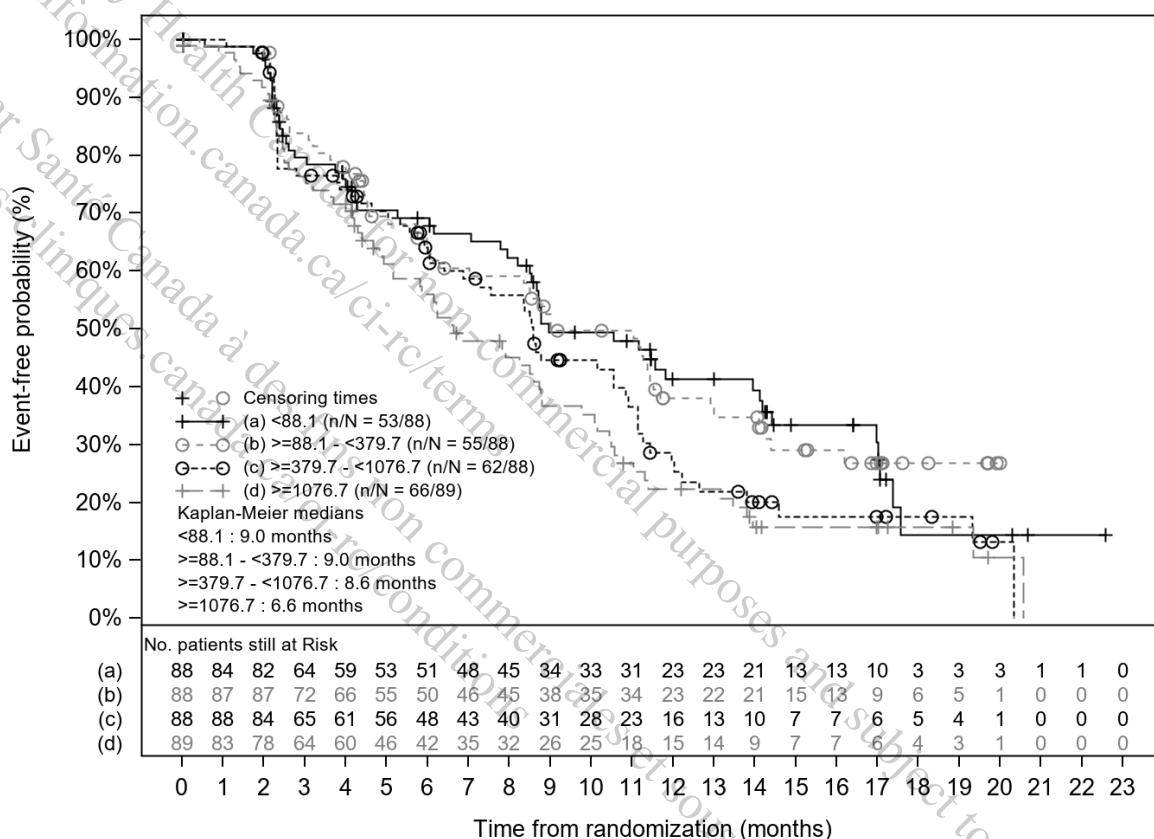
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Data Cutoff Date: 27JAN2021

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Figure 2-2-3 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by tumor volume (cc) quartiles in bone (Bone - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-2-3 2021-08-30 12:25

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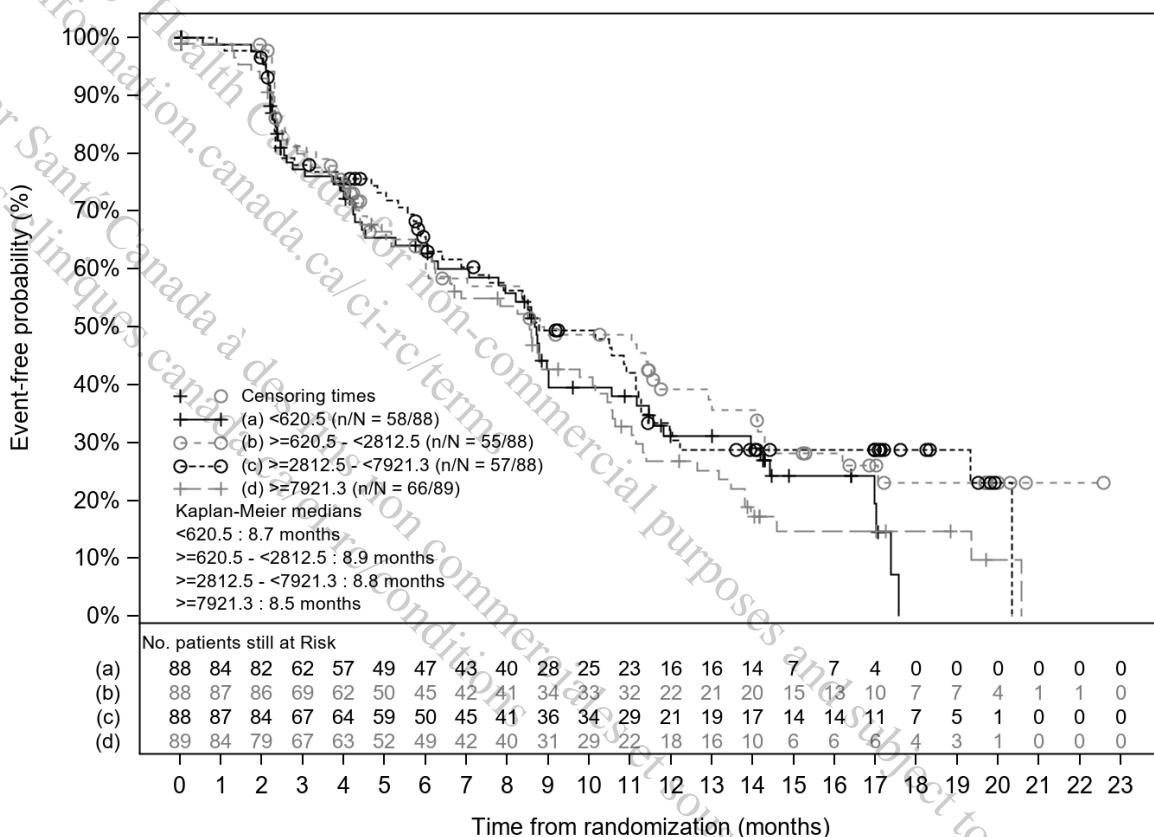
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Data Cutoff Date: 27JAN2021

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Figure 2-2-4 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by tumor load (g) quartiles in bone (Bone - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-2-4 2021-08-30 12:25

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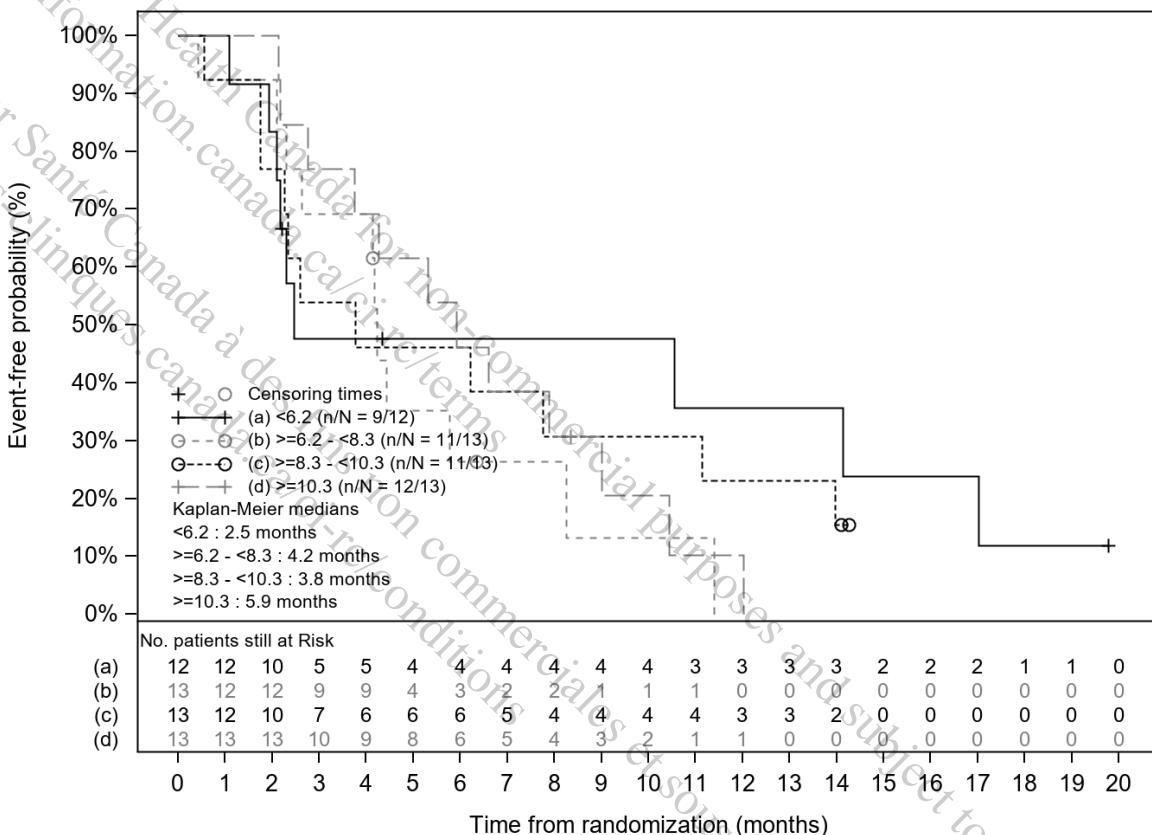
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Data Cutoff Date: 27JAN2021

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Figure 2-3-1 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by SUV mean (g/mL) quartiles in liver (Liver - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-3-1 2021-08-30 12:25

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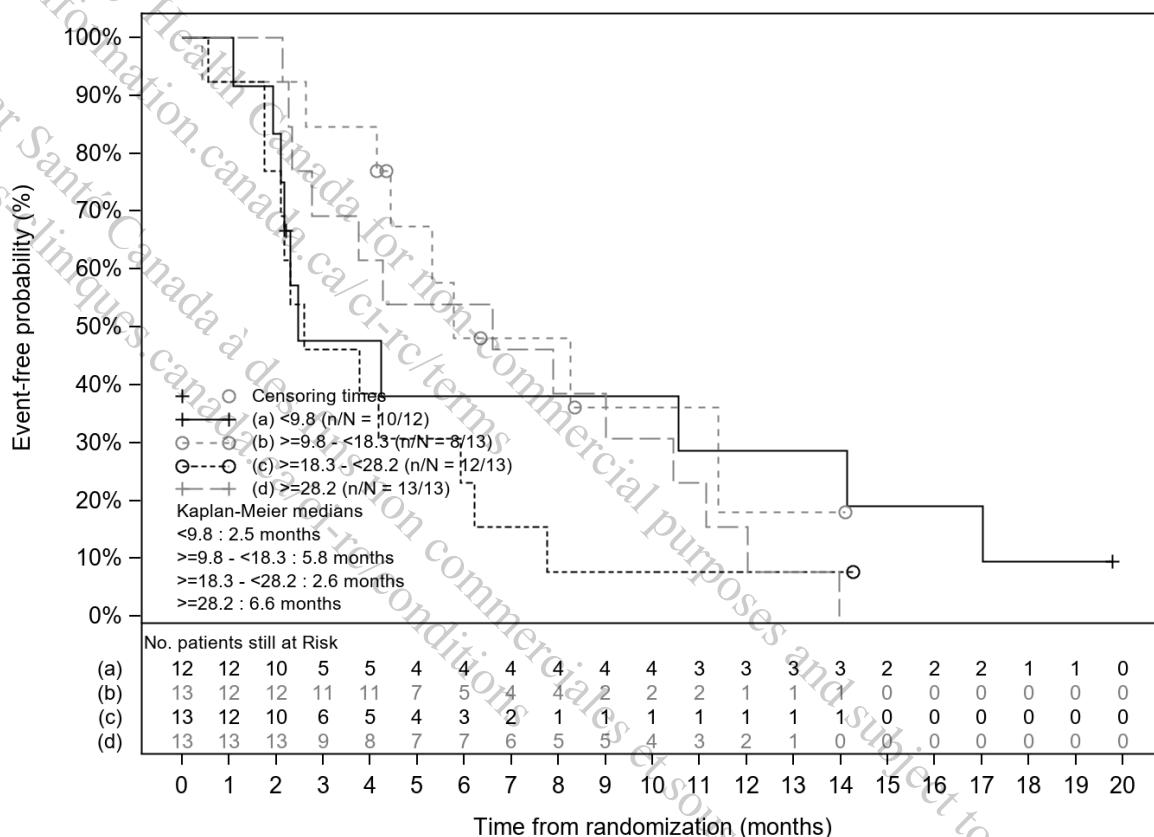
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Figure 2-3-2 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by SUV max (g/mL) quartiles in liver (Liver - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-3-2 2021-08-30 12:25

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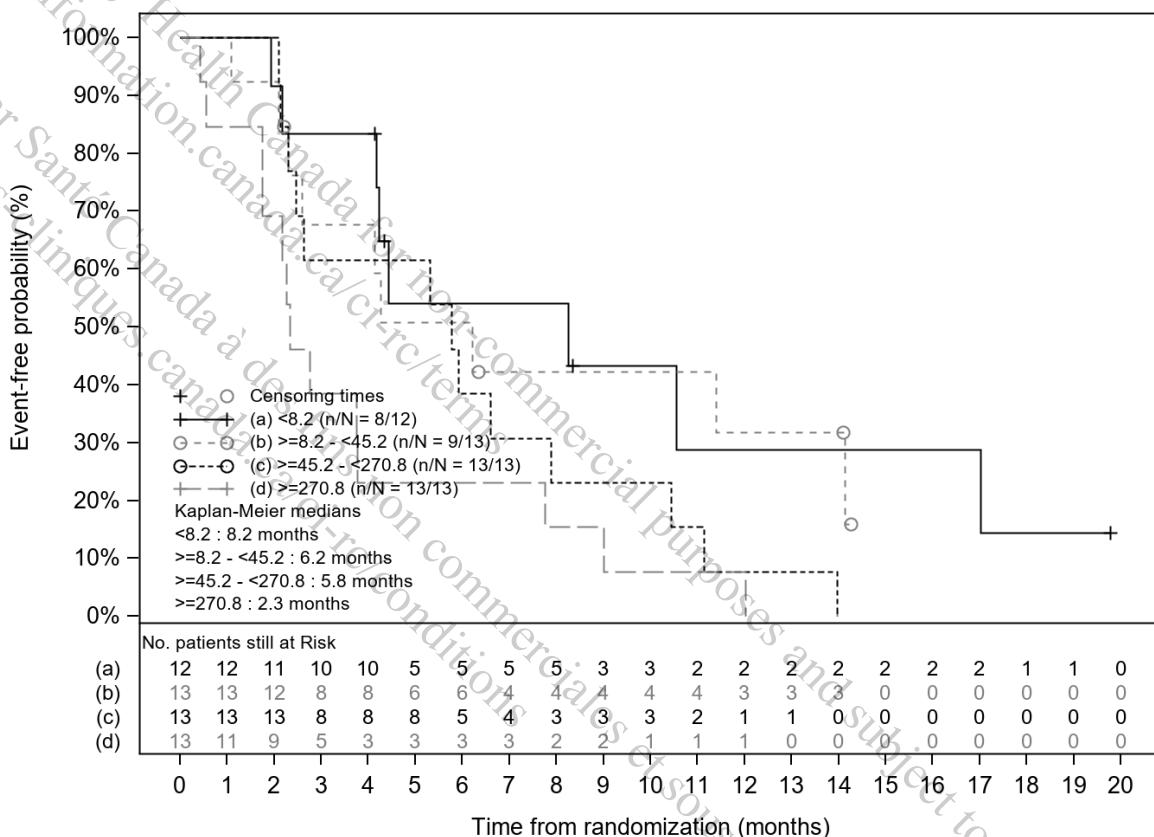
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Data Cutoff Date: 27JAN2021

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Figure 2-3-3 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by tumor volume (cc) quartiles in liver (Liver - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-3-3 2021-08-30 12:25

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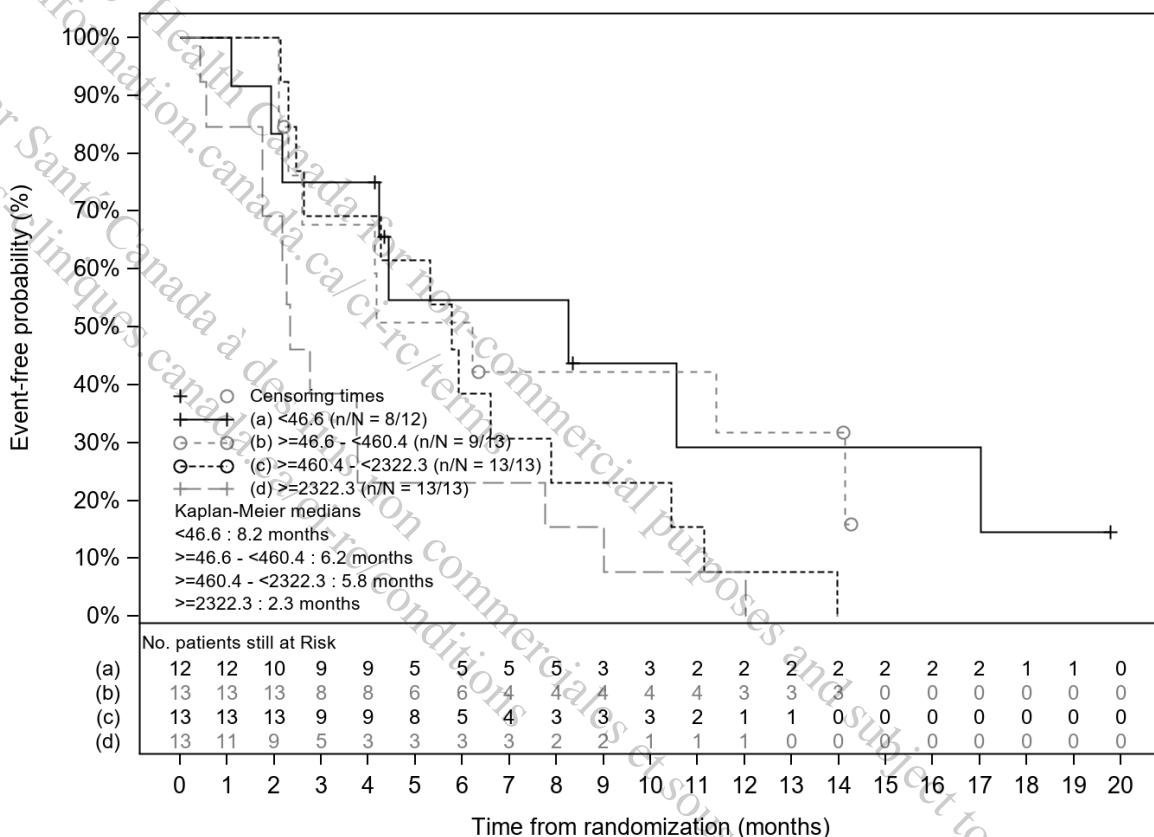
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Data Cutoff Date: 27JAN2021

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Figure 2-3-4 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by tumor load (g) quartiles in liver (Liver - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-3-4 2021-08-30 12:25

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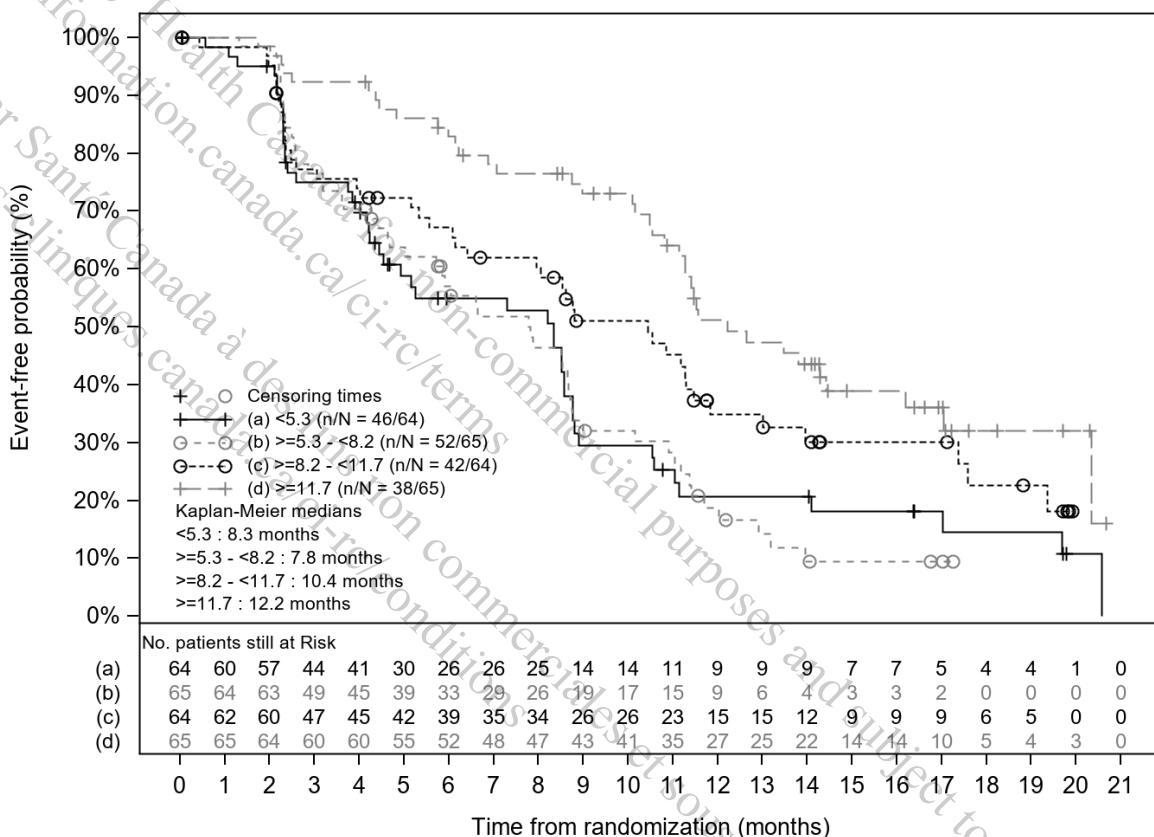
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Figure 2-4-1 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by SUV mean (g/mL) quartiles in lymph node (Lymph node - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-4-1 2021-08-30 12:25

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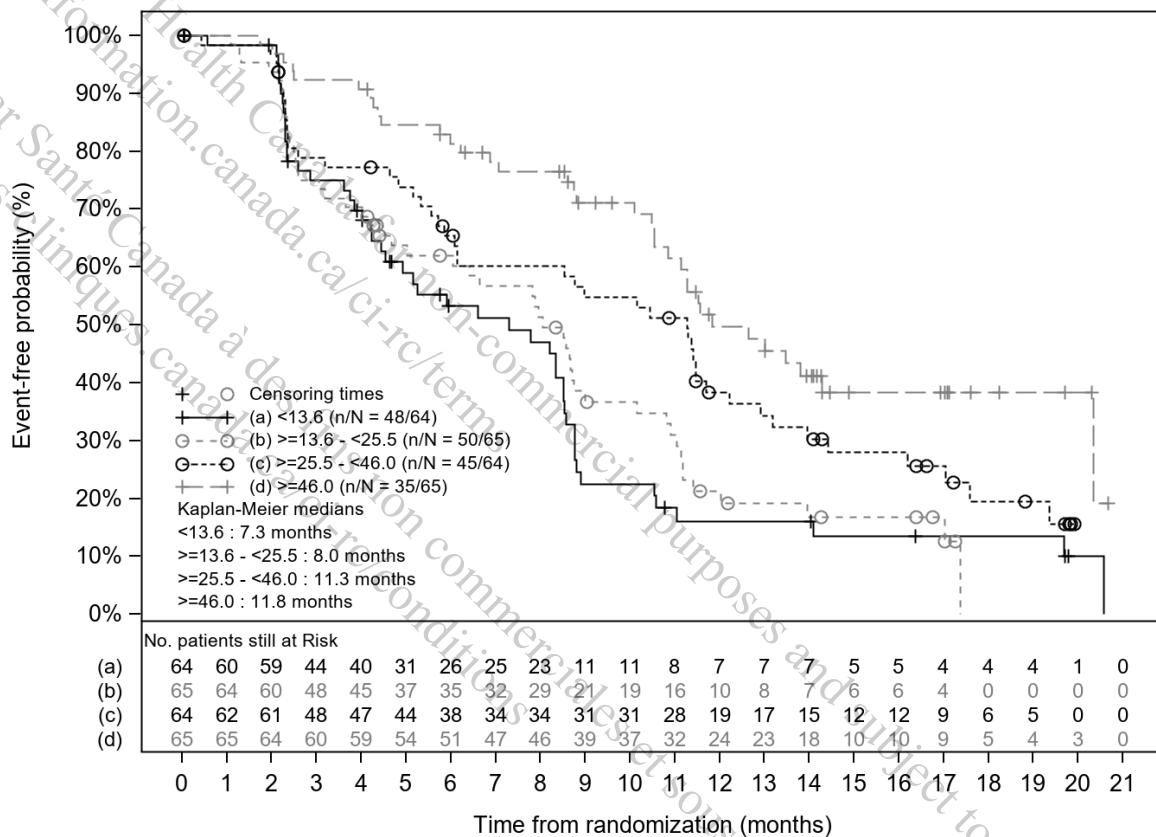
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Data Cutoff Date: 27JAN2021

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Figure 2-4-2 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by SUV max (g/mL) quartiles in lymph node (Lymph node - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-4-2 2021-08-30 12:25

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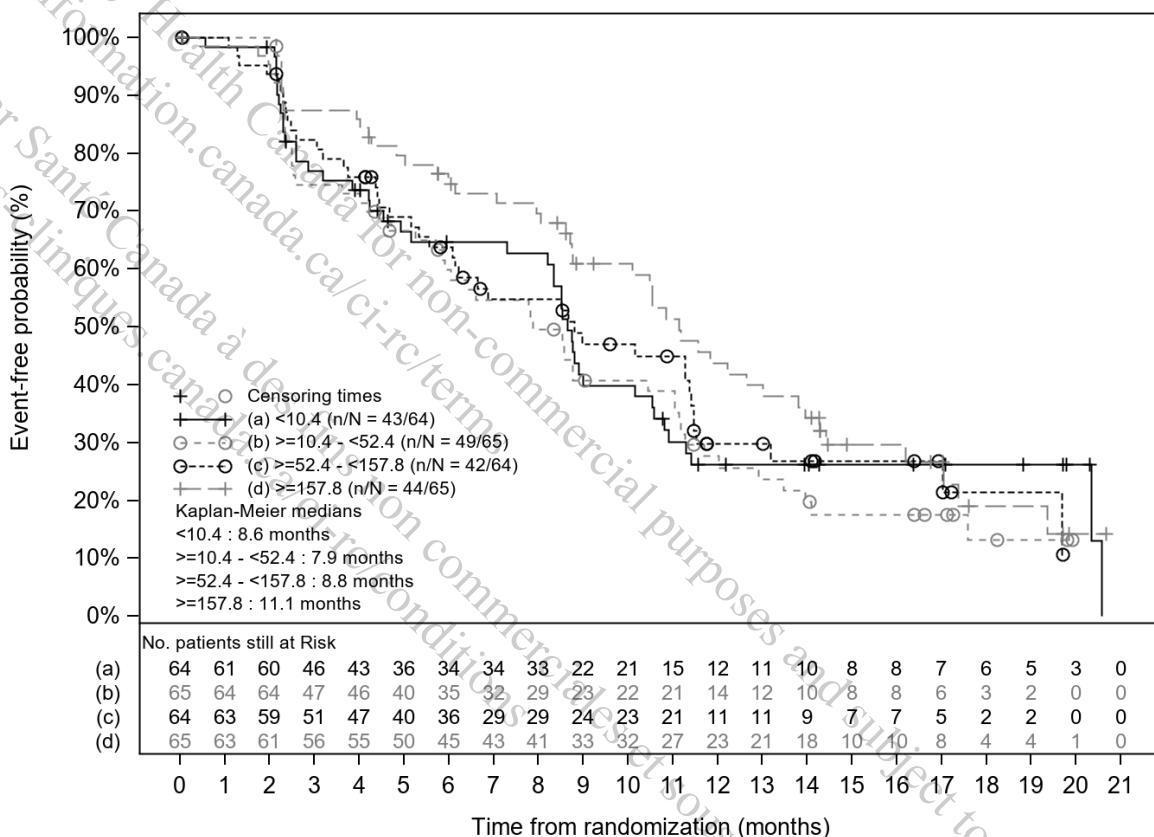
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Data Cutoff Date: 27JAN2021

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Figure 2-4-3 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by tumor volume (cc) quartiles in lymph node (Lymph node - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-4-3 2021-08-30 12:26

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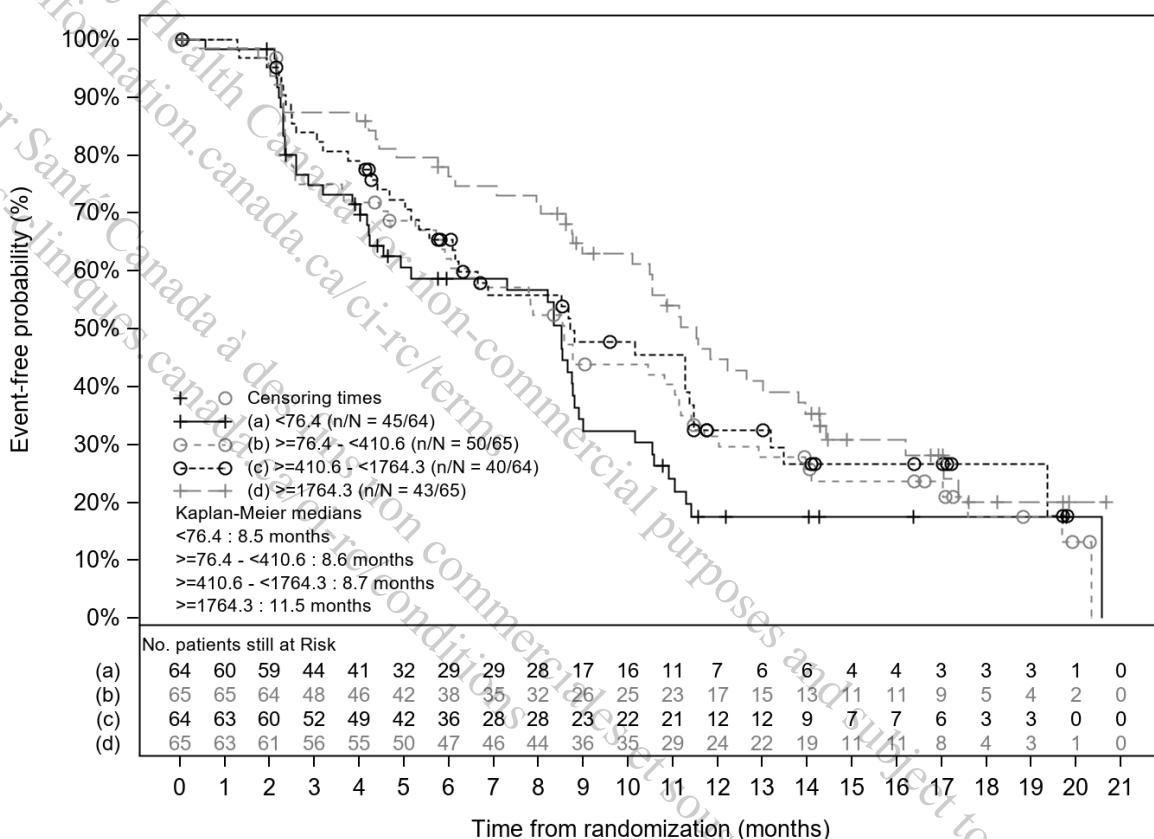
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Data Cutoff Date: 27JAN2021

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Figure 2-4-4 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by tumor load (g) quartiles in lymph node (Lymph node - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-4-4 2021-08-30 12:26

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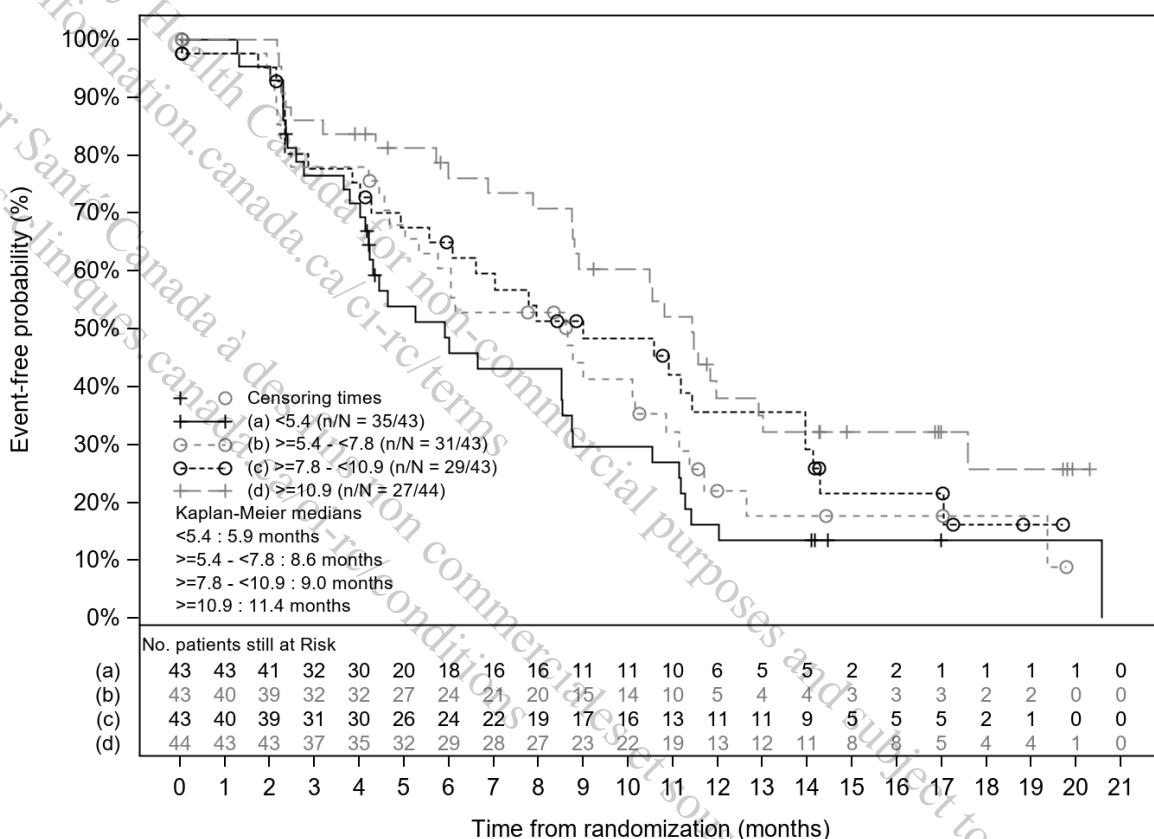
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Data Cutoff Date: 27JAN2021

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Figure 2-5-1 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by SUV mean (g/mL) quartiles in soft tissue (Soft tissue - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-5-1 2021-08-30 12:26

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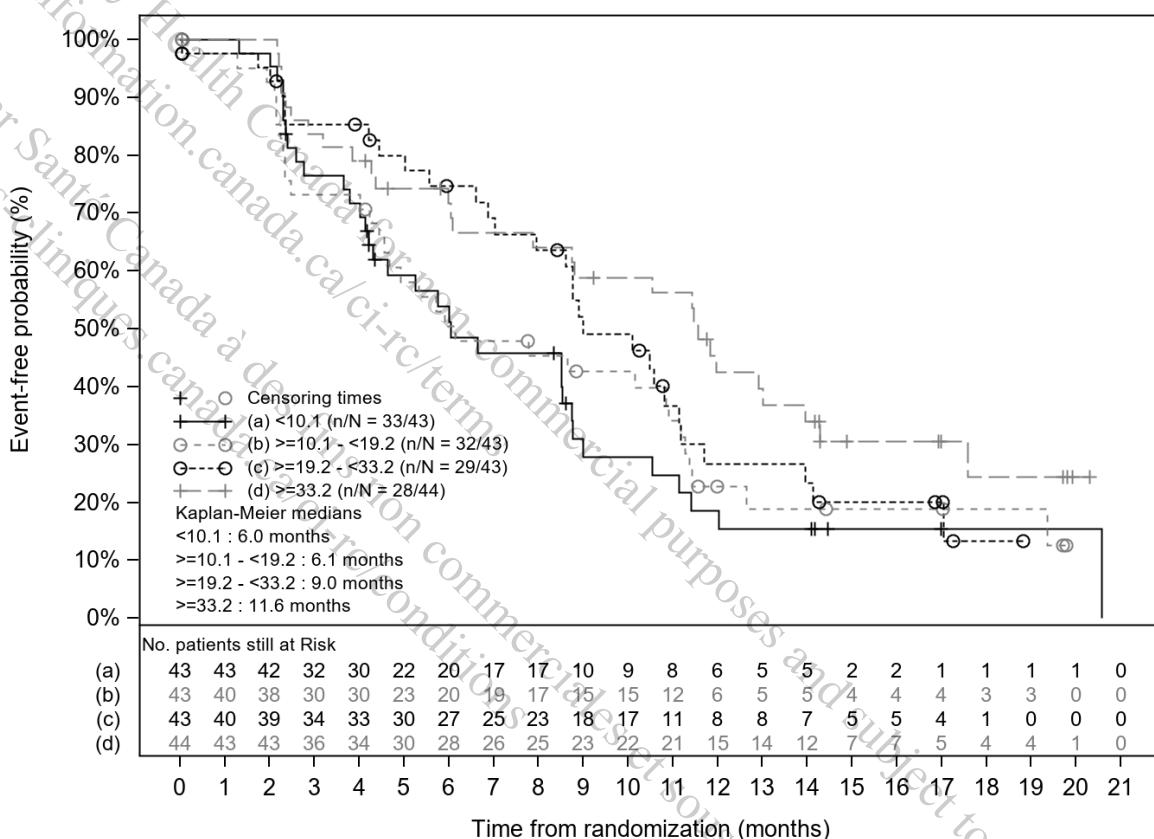
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Data Cutoff Date: 27JAN2021

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Figure 2-5-2 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by SUV max (g/mL) quartiles in soft tissue (Soft tissue - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-5-2 2021-08-30 12:26

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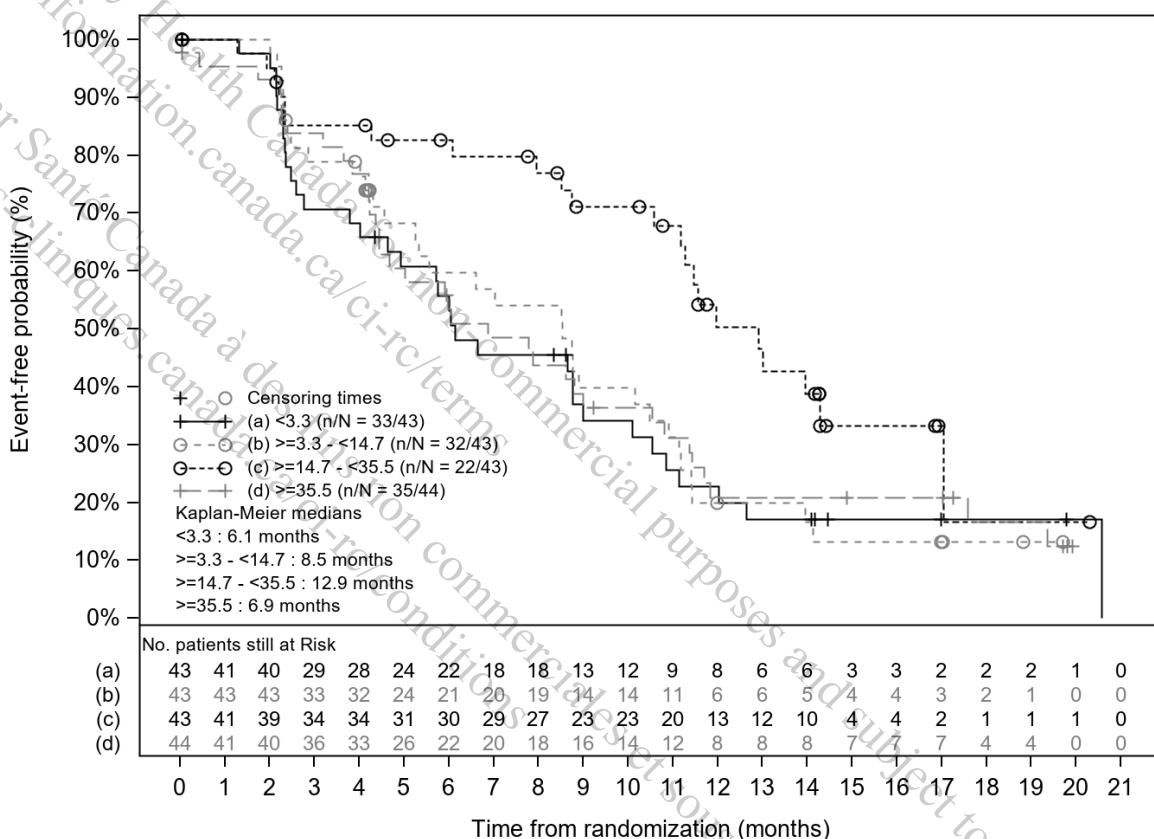
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Data Cutoff Date: 27JAN2021

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Figure 2-5-3 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by tumor volume (cc) quartiles in soft tissue (Soft tissue - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-5-3 2021-08-30 12:26

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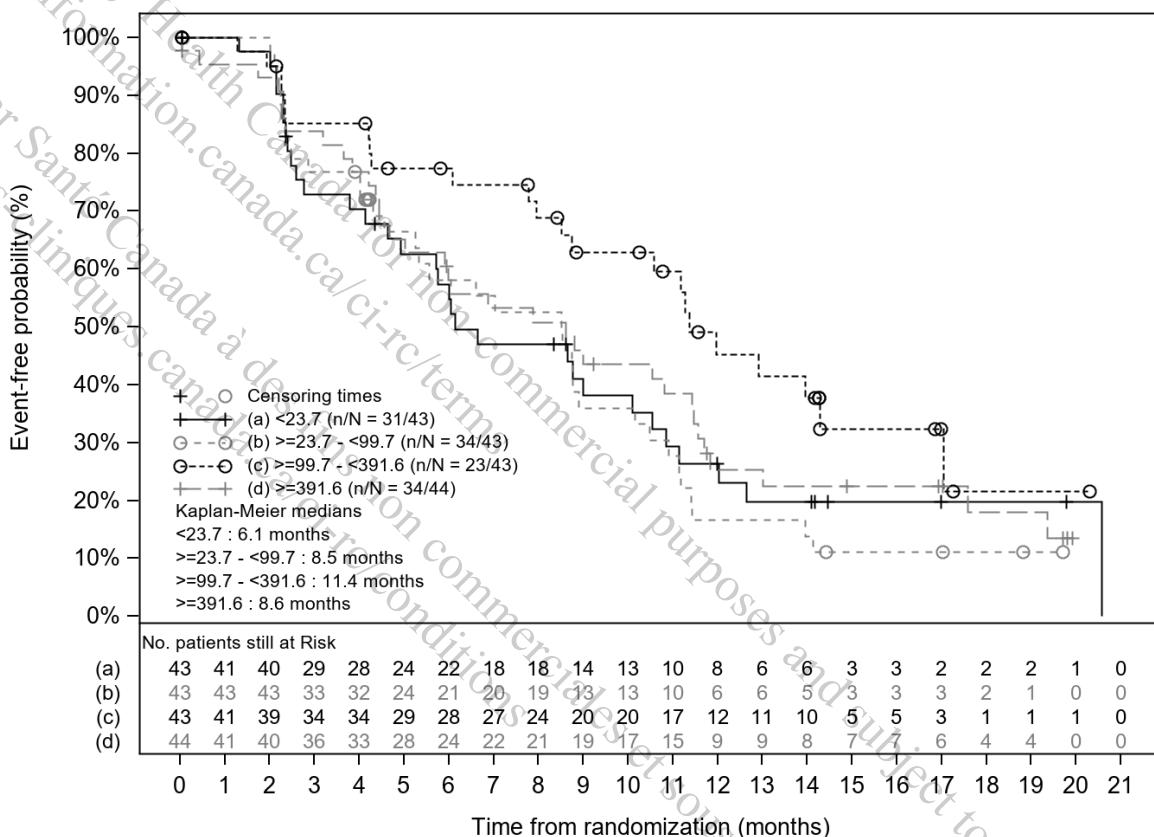
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Data Cutoff Date: 27JAN2021

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Figure 2-5-4 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by tumor load (g) quartiles in soft tissue (Soft tissue - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-2-5-4 2021-08-30 12:26

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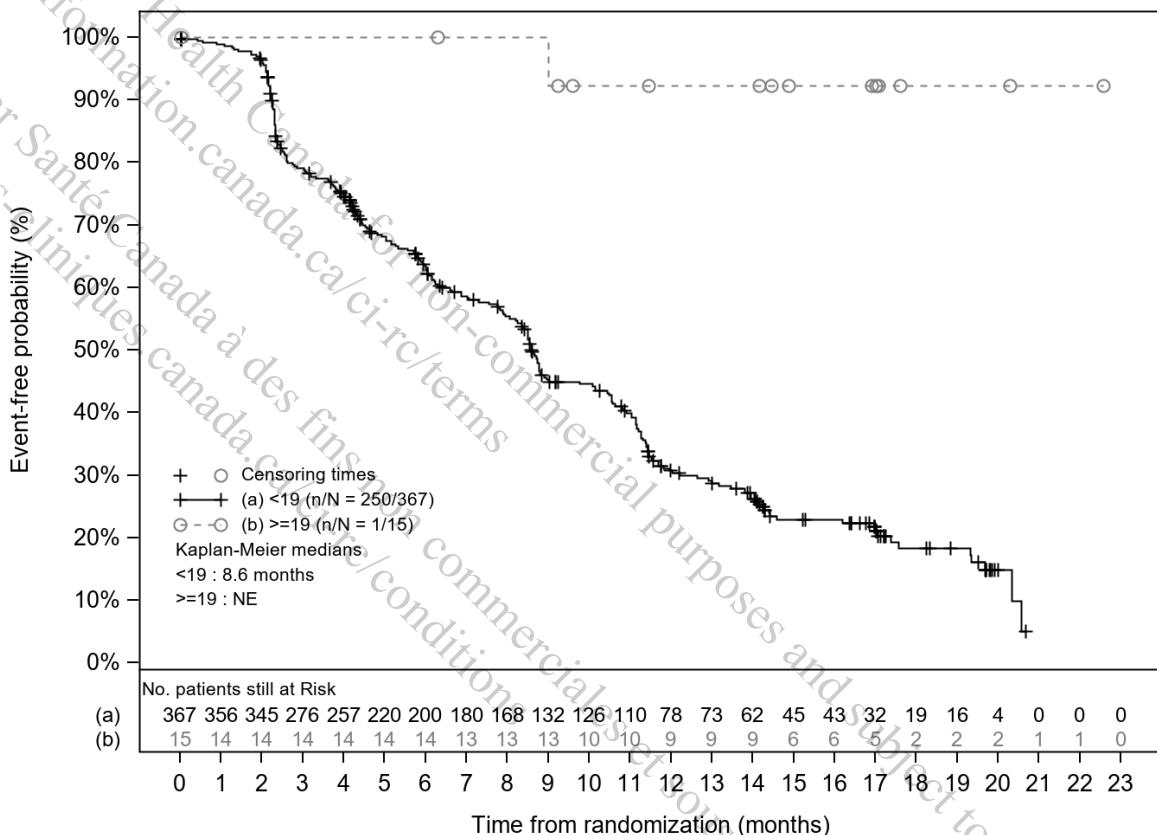
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Data Cutoff Date: 27JAN2021

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Figure 4-1-1 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by optimal cut point of SUV mean (g/mL) in whole body (Body - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-4-1-1 2021-08-30 12:28

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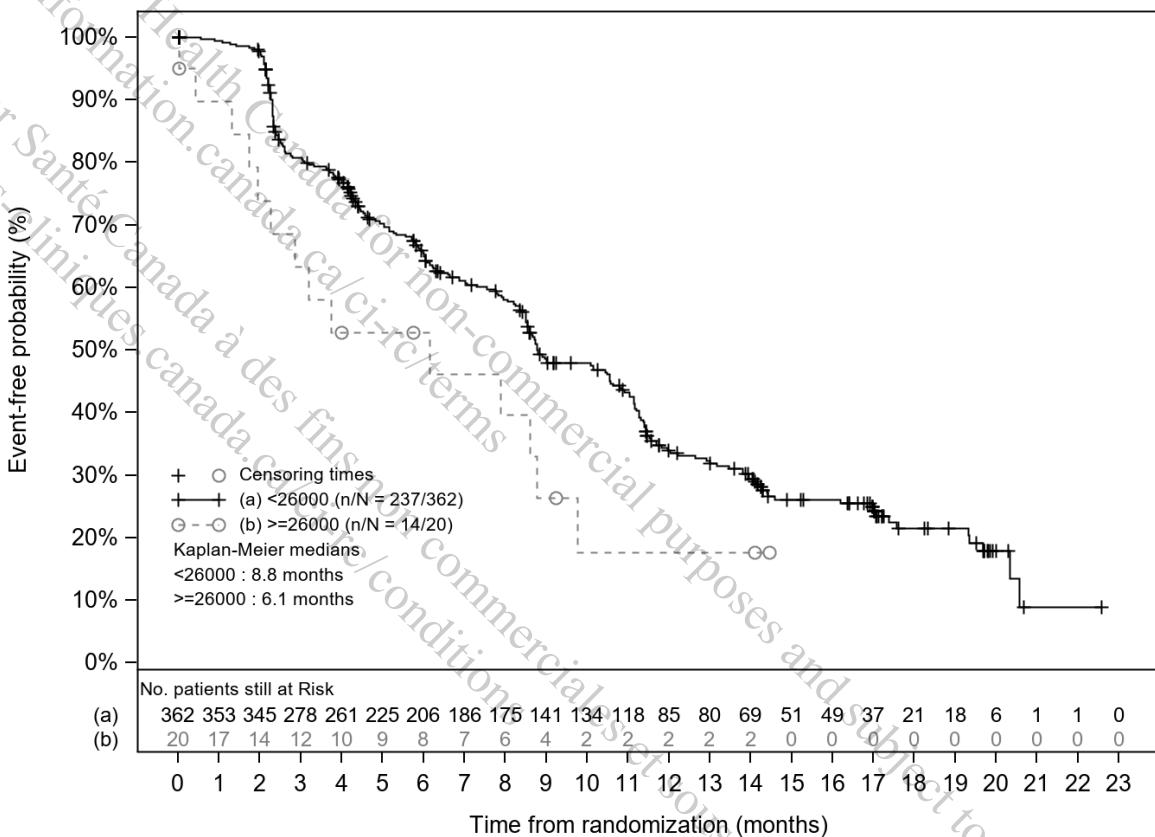
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Data Cutoff Date: 27JAN2021

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Figure 4-1-2 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by optimal cut point of tumor load (g) in whole body (Body - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-4-1-2 2021-08-30 12:28

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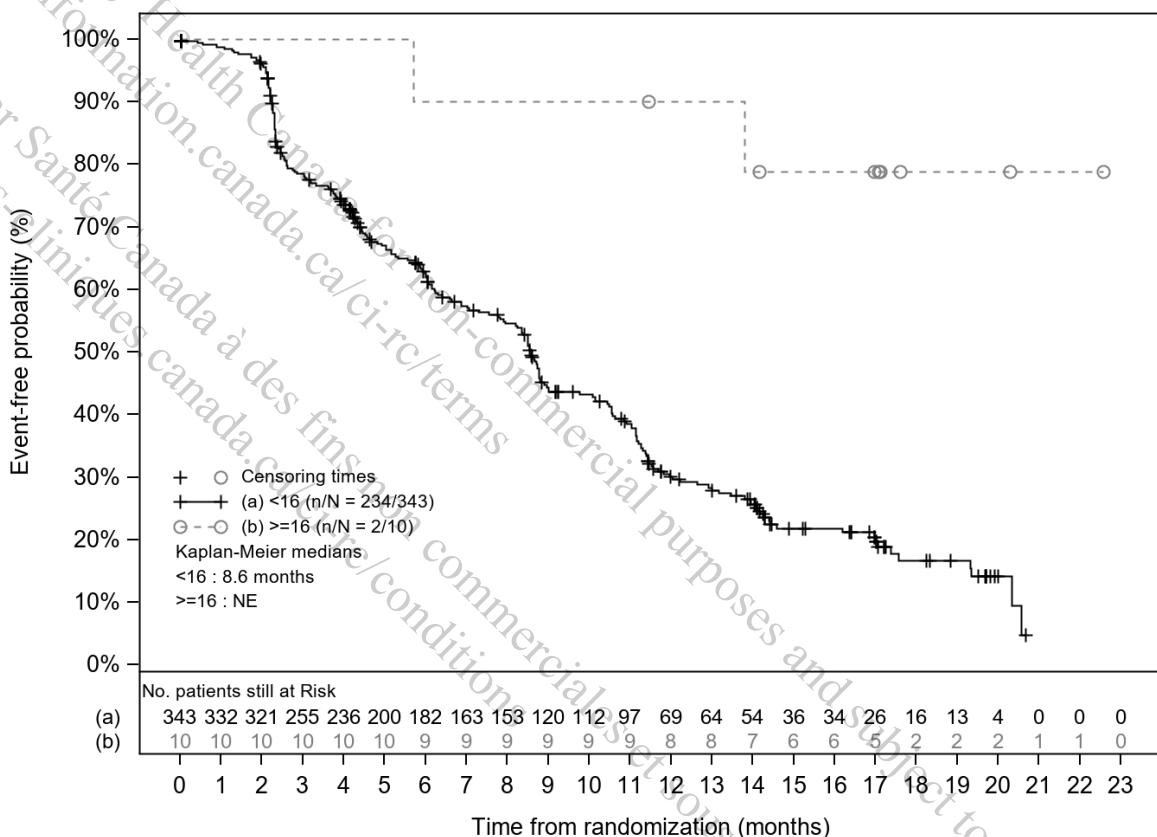
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Data Cutoff Date: 27JAN2021

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Figure 4-2-1 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by optimal cut point of SUV mean (g/mL) in bone (Bone - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-4-2-1 2021-08-30 12:28

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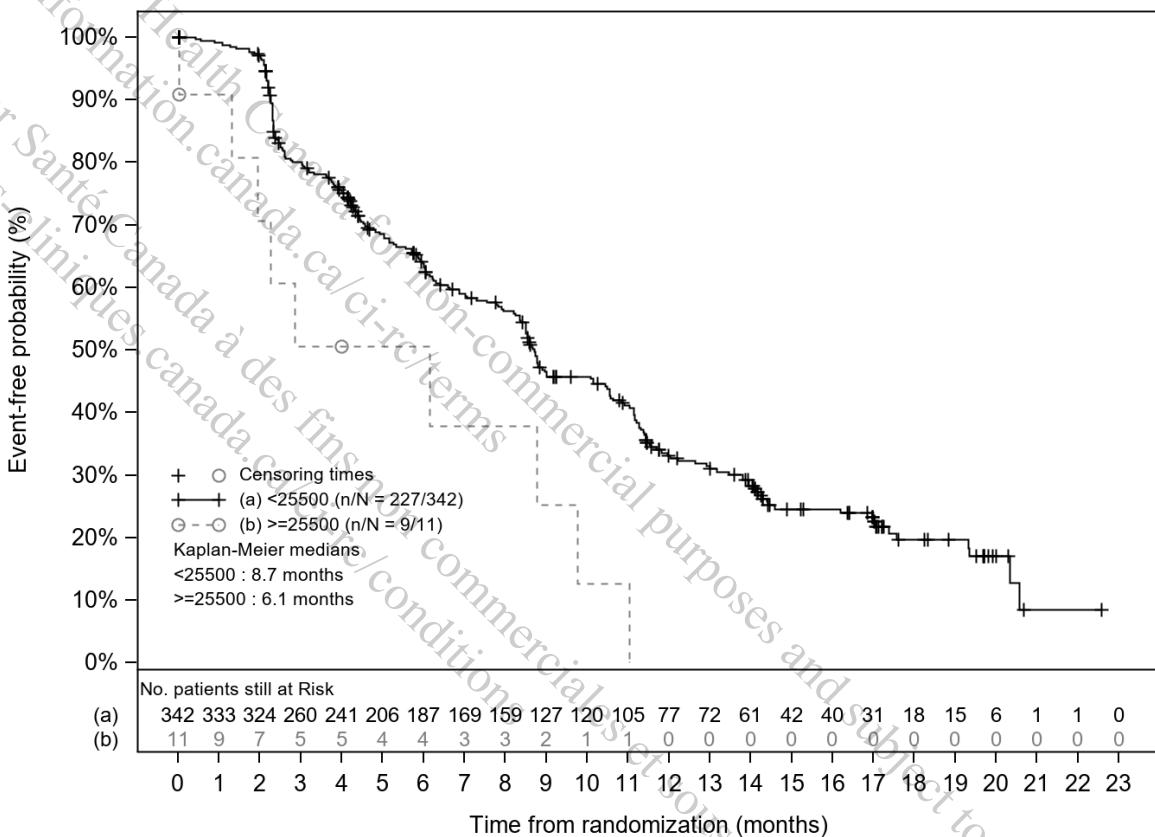
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Data Cutoff Date: 27JAN2021

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Final Version

Figure 4-2-2 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by optimal cut point of tumor load (g) in bone (Bone - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-4-2-2 2021-08-30 12:28

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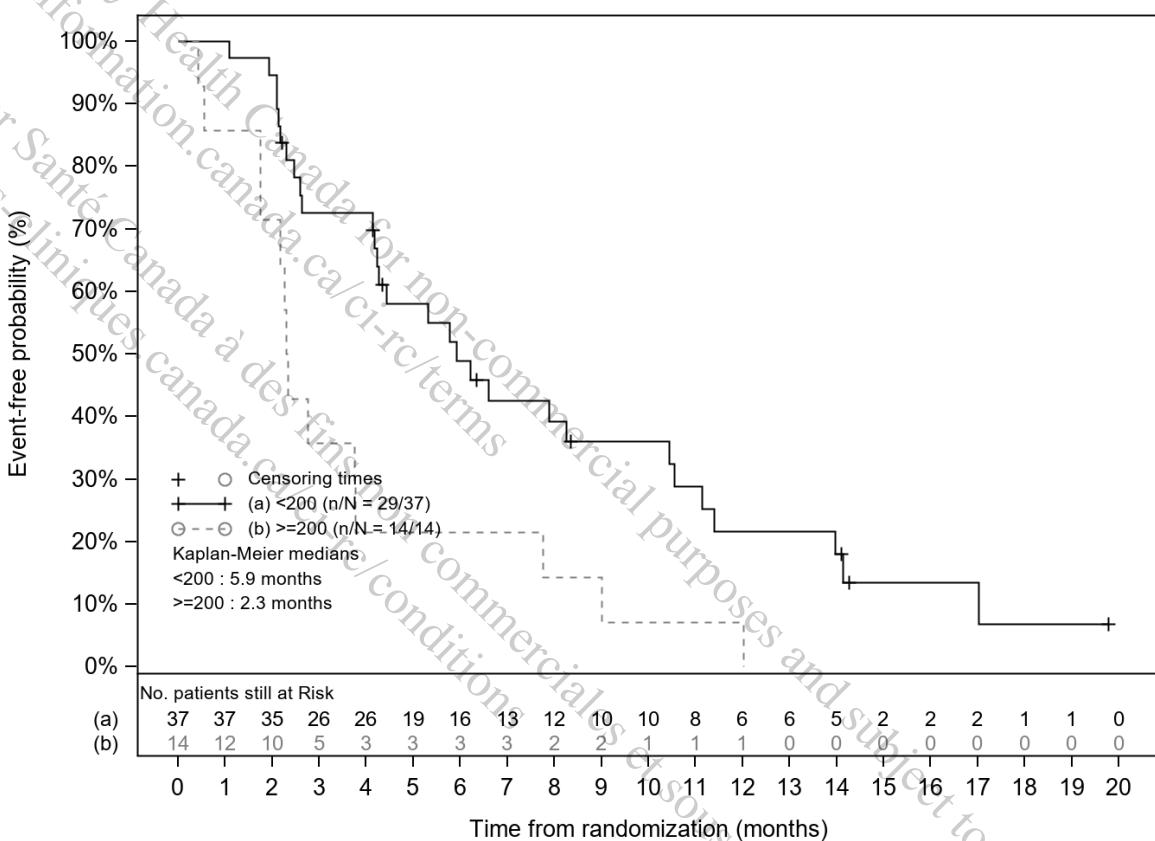
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Data Cutoff Date: 27JAN2021

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Figure 4-3-1 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by optimal cut point of tumor volume (cc) in liver (Liver - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-4-3-1 2021-08-30 12:28

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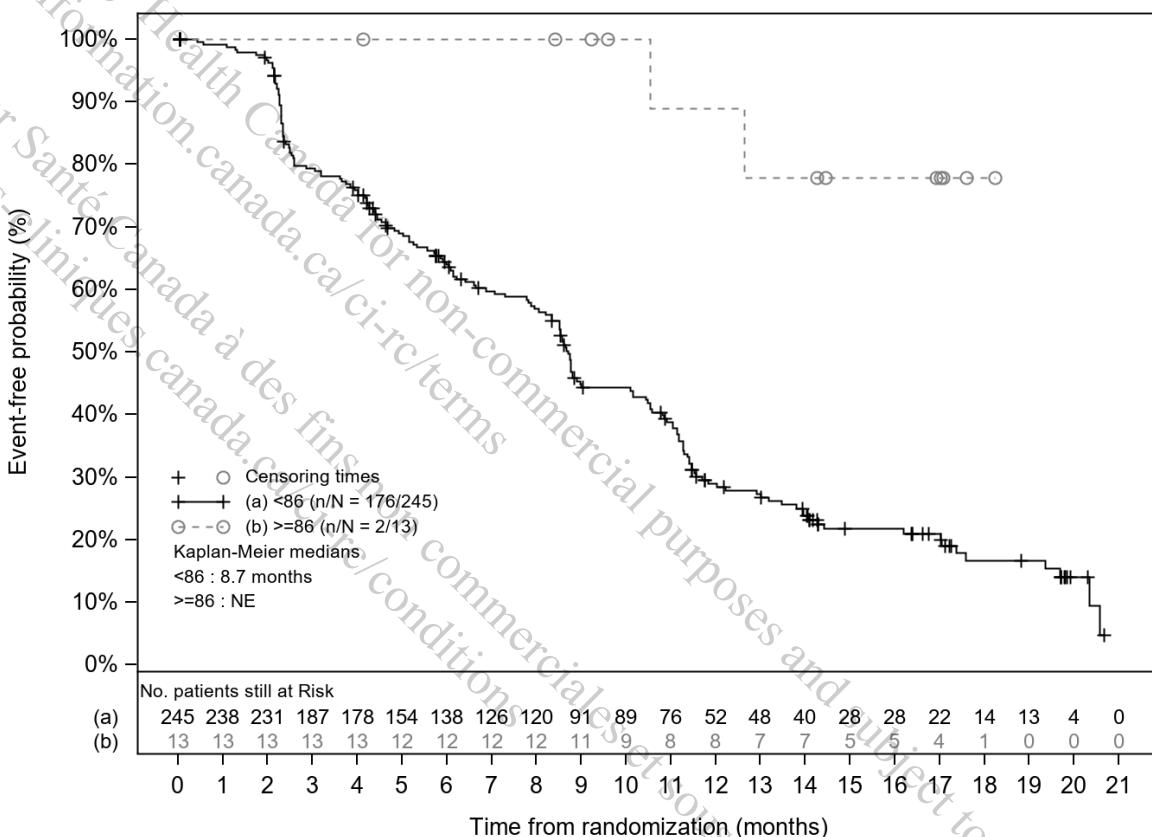
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Data Cutoff Date: 27JAN2021

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Figure 4-4-1 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by optimal cut point of SUV max (g/mL) in lymph node (Lymph node - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-4-4-1 2021-08-30 12:29

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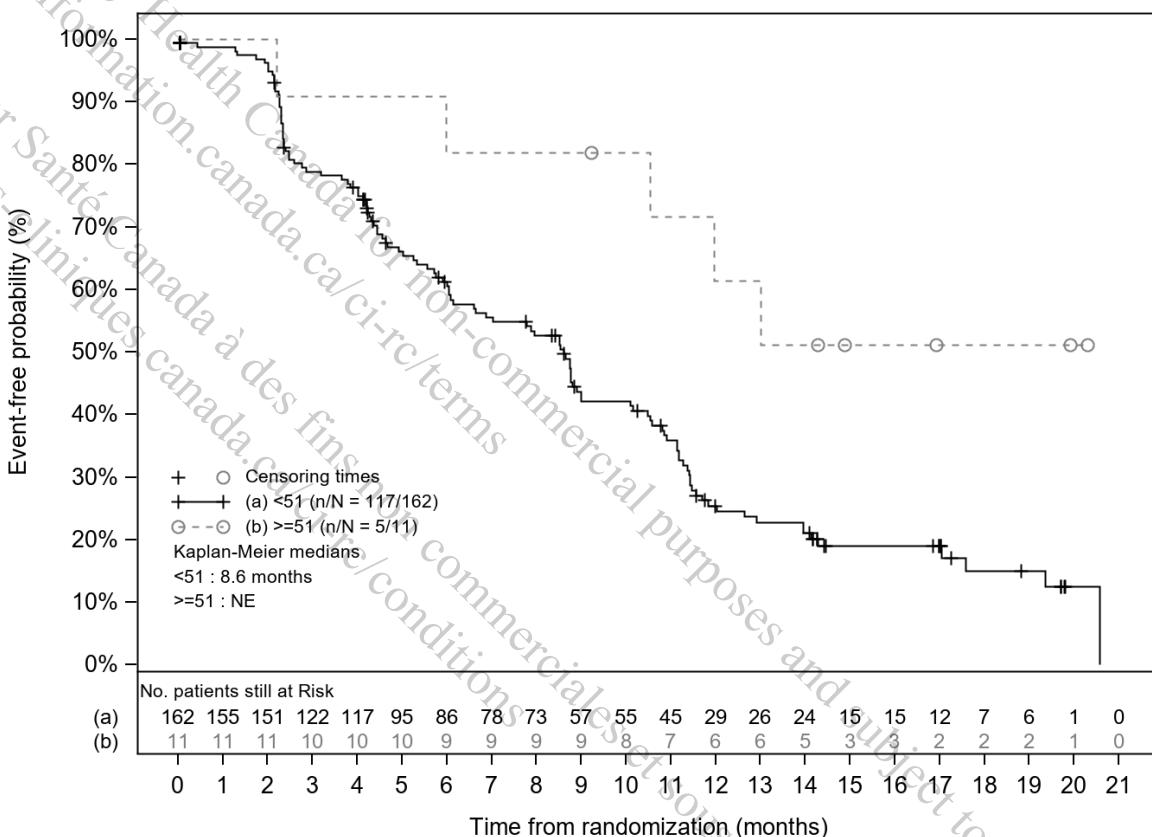
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Data Cutoff Date: 27JAN2021

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Figure 4-5-1 Kaplan-Meier plot for radiographic progression-free survival based on independent central review by optimal cut point of SUV max (g/mL) in soft tissue (Soft tissue - PFS Full analysis set)



n/N: Number of events/number of patients

Output ID: F-4-5-1 2021-08-30 12:29

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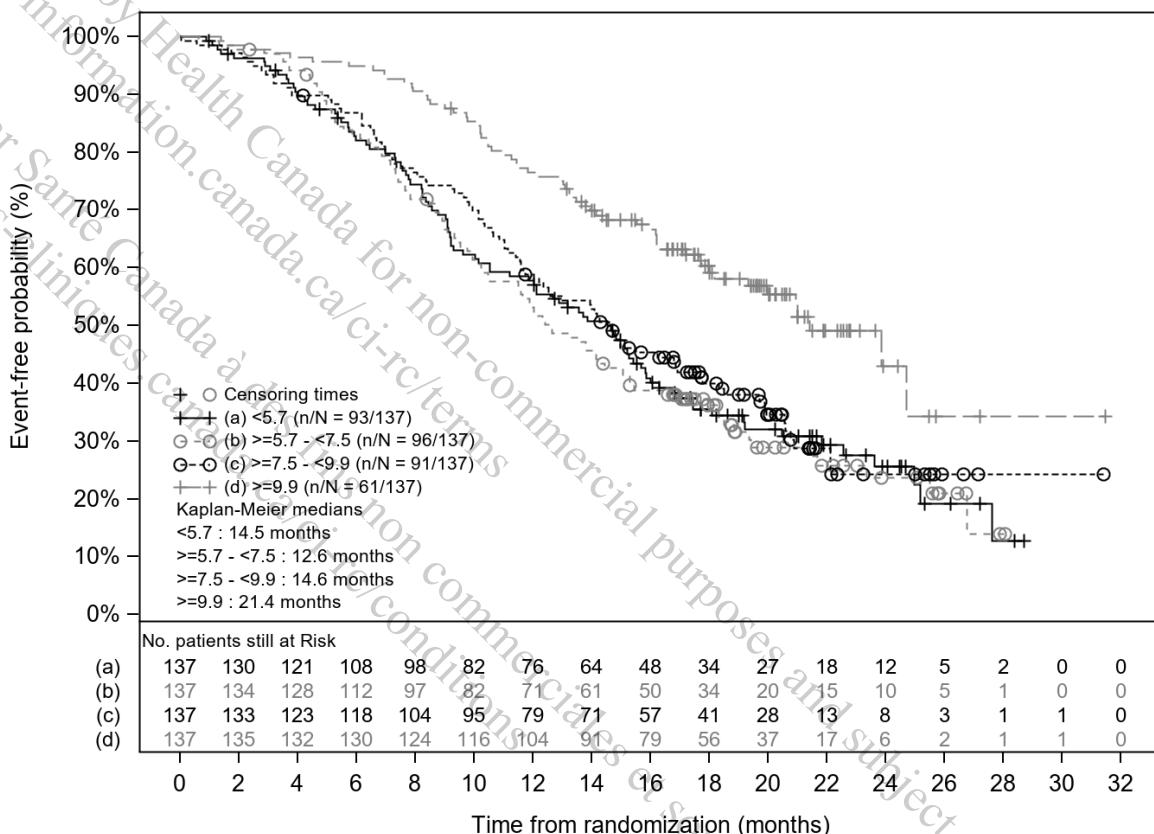
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Data Cutoff Date: 27JAN2021

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Figure 5-1-1 Kaplan-Meier plot for OS by SUV mean quartiles (g/mL) quartiles in whole body (Body - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-1-1 2021-08-30 12:26

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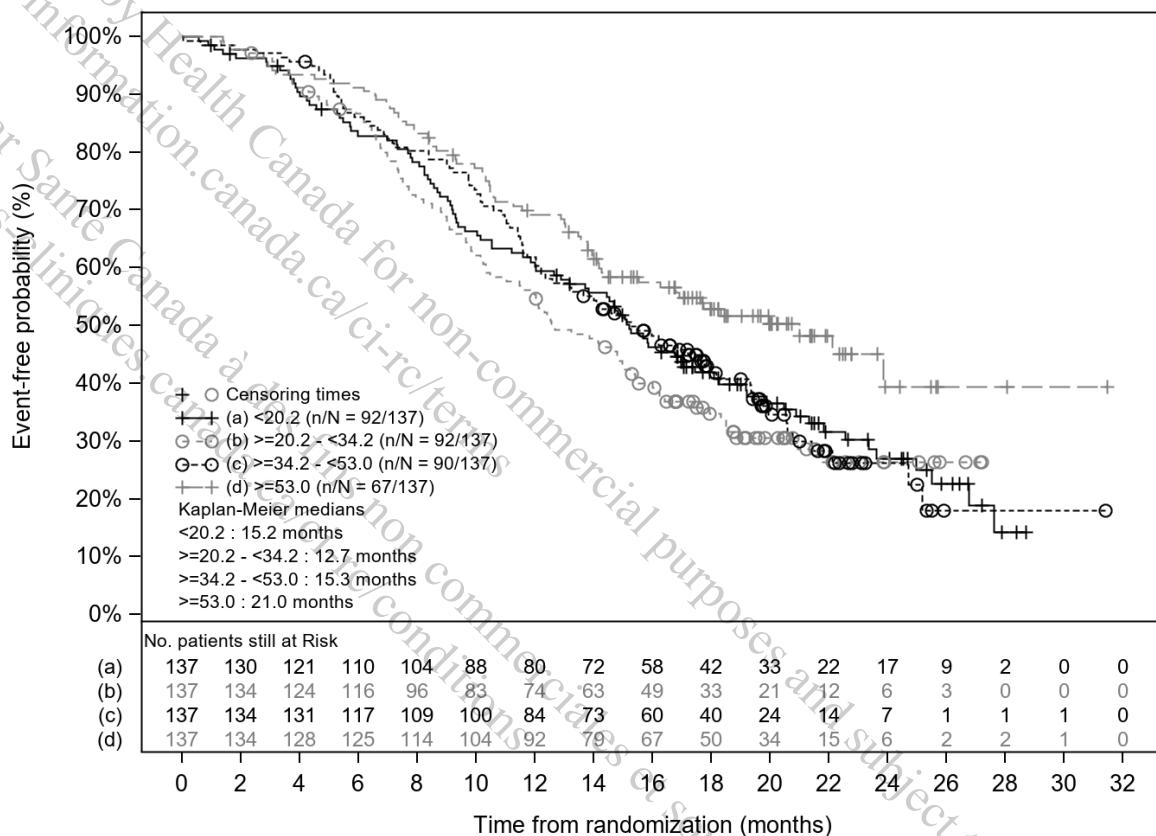
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Data Cutoff Date: 27JAN2021

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Final Version

Figure 5-1-2 Kaplan-Meier plot for OS by SUV max (g/mL) quartiles in whole body (Body - Full analysis set)



n/N: Number of events/number of patients

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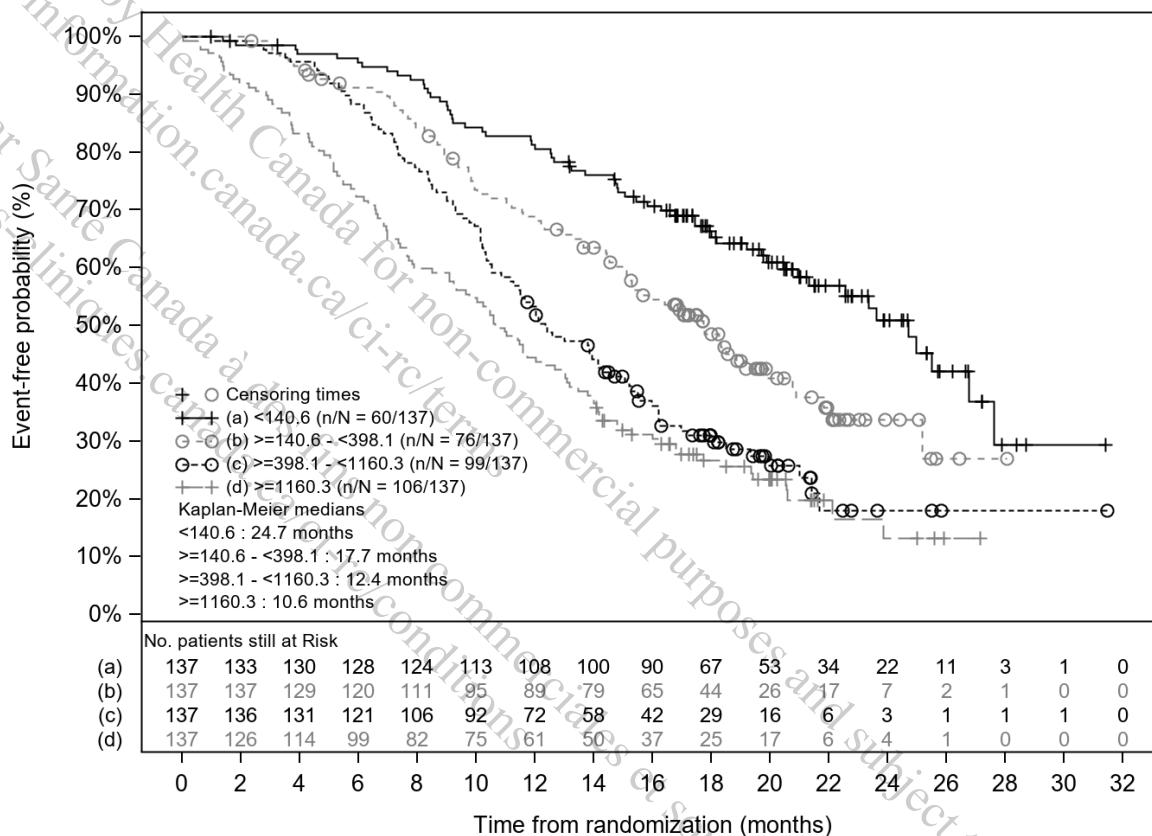
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Data Cutoff Date: 27JAN2021

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Figure 5-1-3 Kaplan-Meier plot for OS by tumor volume (cc) quartiles in whole body (Body - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-1-3 2021-08-30 12:26

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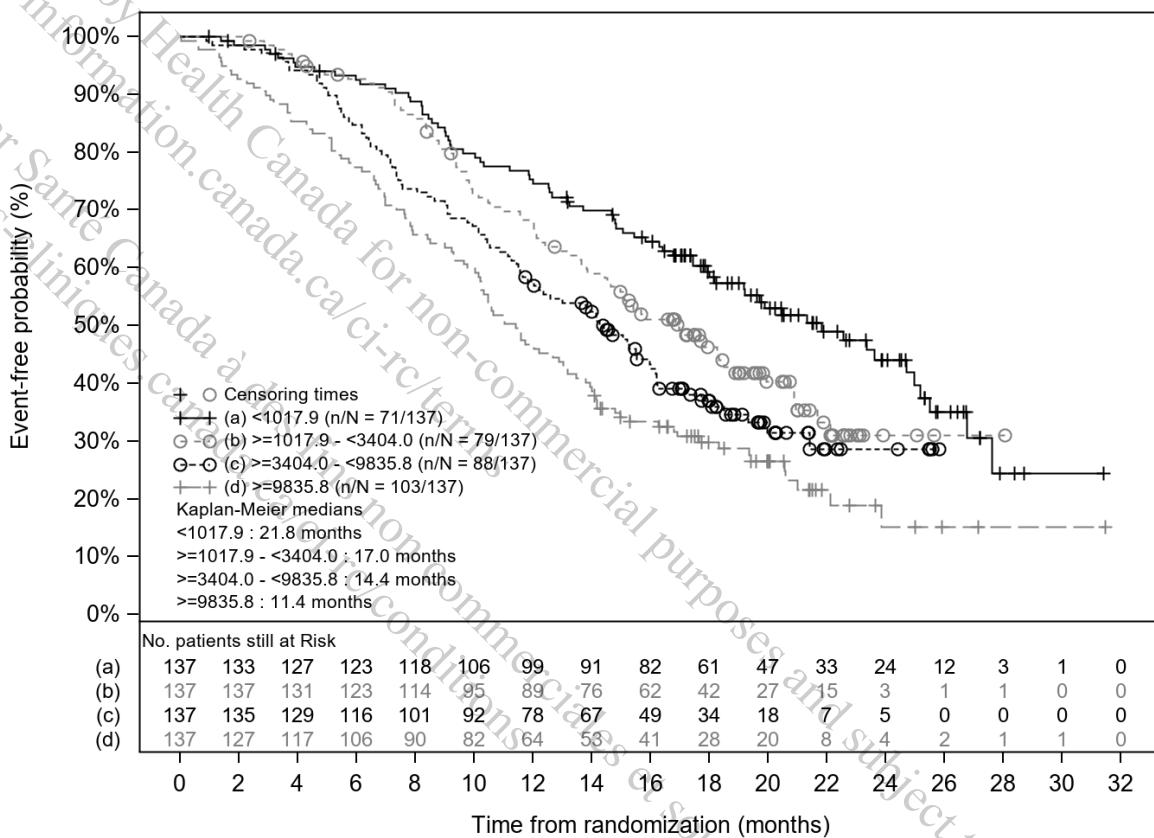
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Figure 5-1-4 Kaplan-Meier plot for OS by tumor load (g) quartiles in whole body (Body - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-1-4 2021-08-30 12:26

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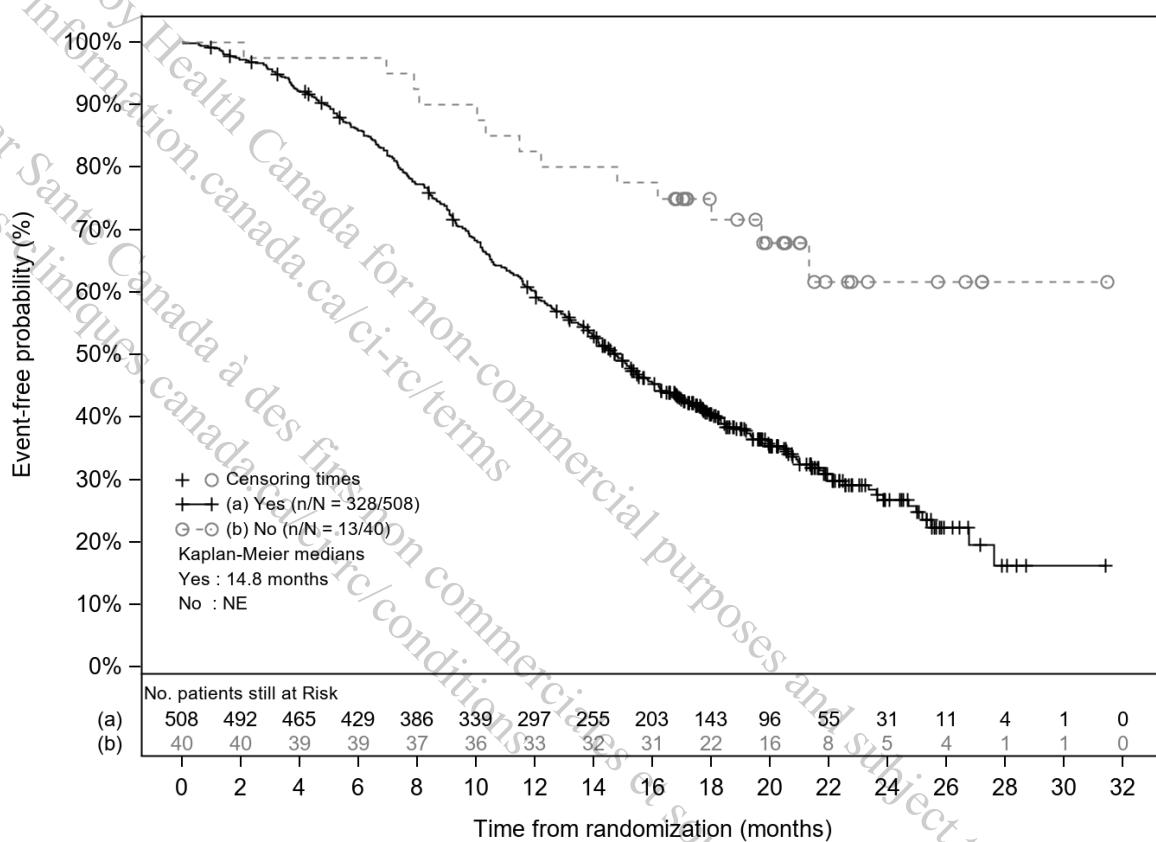
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Data Cutoff Date: 27JAN2021

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Figure 5-1-5 Kaplan-Meier plot for OS by presence of PSMA positive tumors in bone (Body - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-1-5 2021-08-30 12:26

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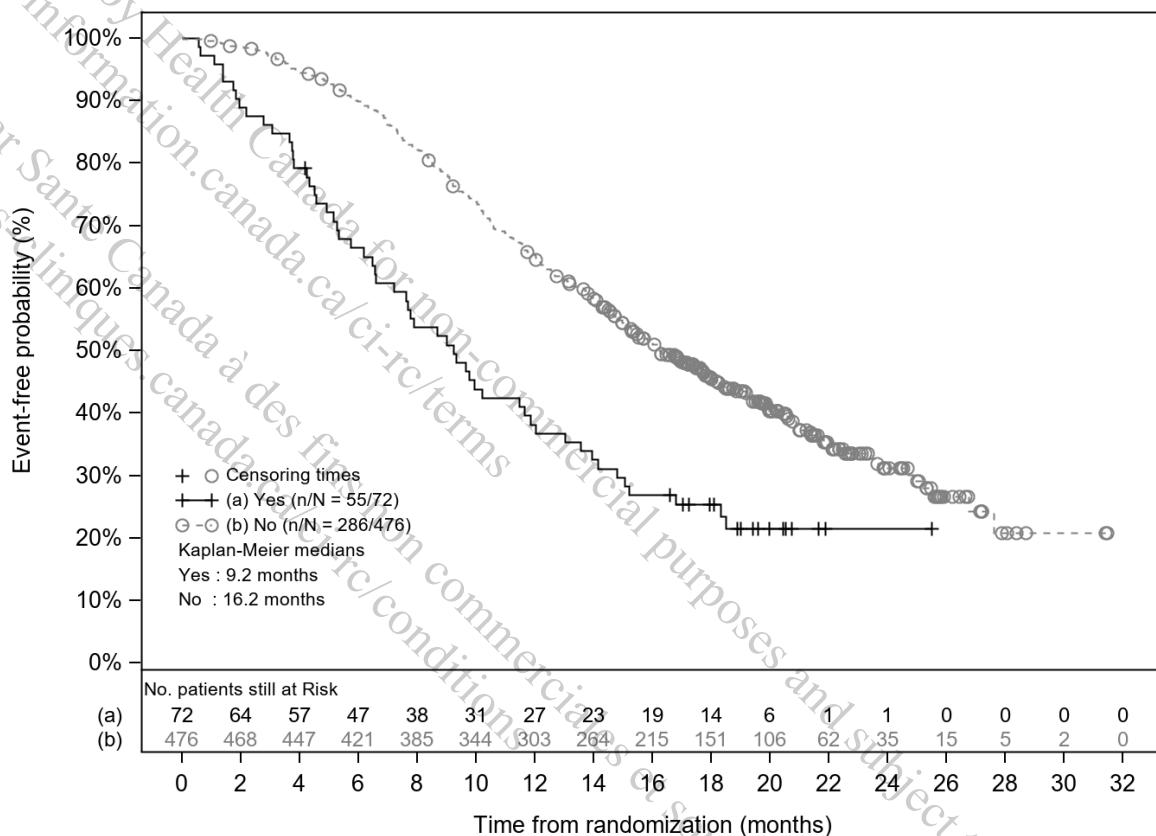
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Data Cutoff Date: 27JAN2021

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Figure 5-1-6 Kaplan-Meier plot for OS by presence of PSMA positive tumors in liver (Body - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-1-6 2021-08-30 12:26

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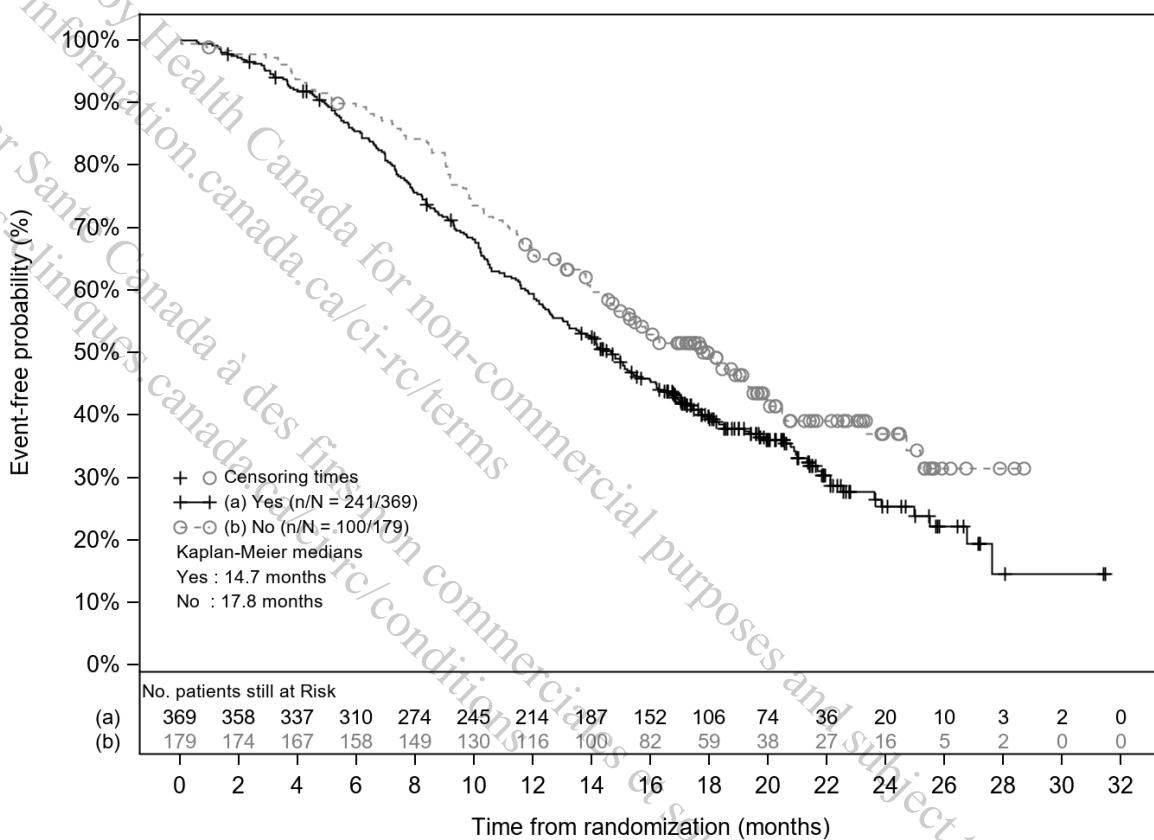
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Data Cutoff Date: 27JAN2021

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Figure 5-1-7 Kaplan-Meier plot for OS by presence of PSMA positive tumors in lymph node (Body - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-1-7 2021-08-30 12:26

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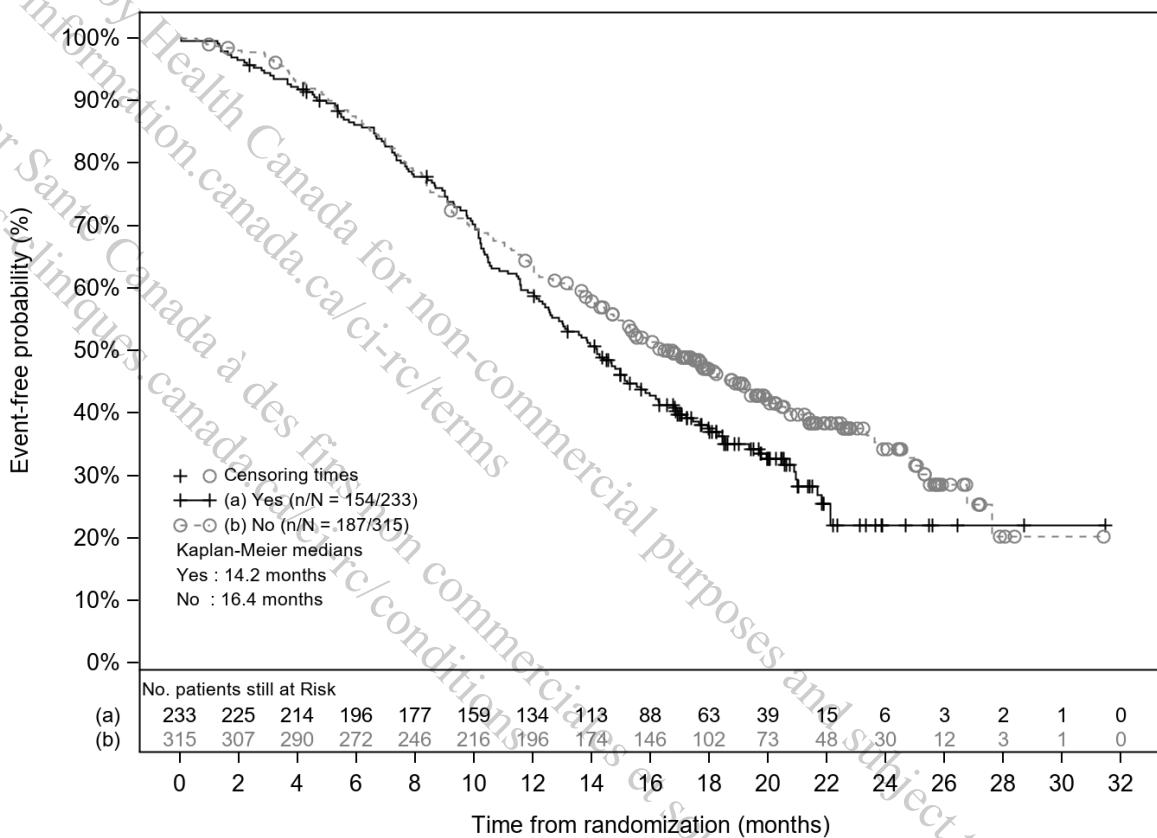
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Data Cutoff Date: 27JAN2021

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Figure 5-1-8 Kaplan-Meier plot for OS by presence of PSMA positive tumors in soft tissue (Body - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-1-8 2021-08-30 12:27

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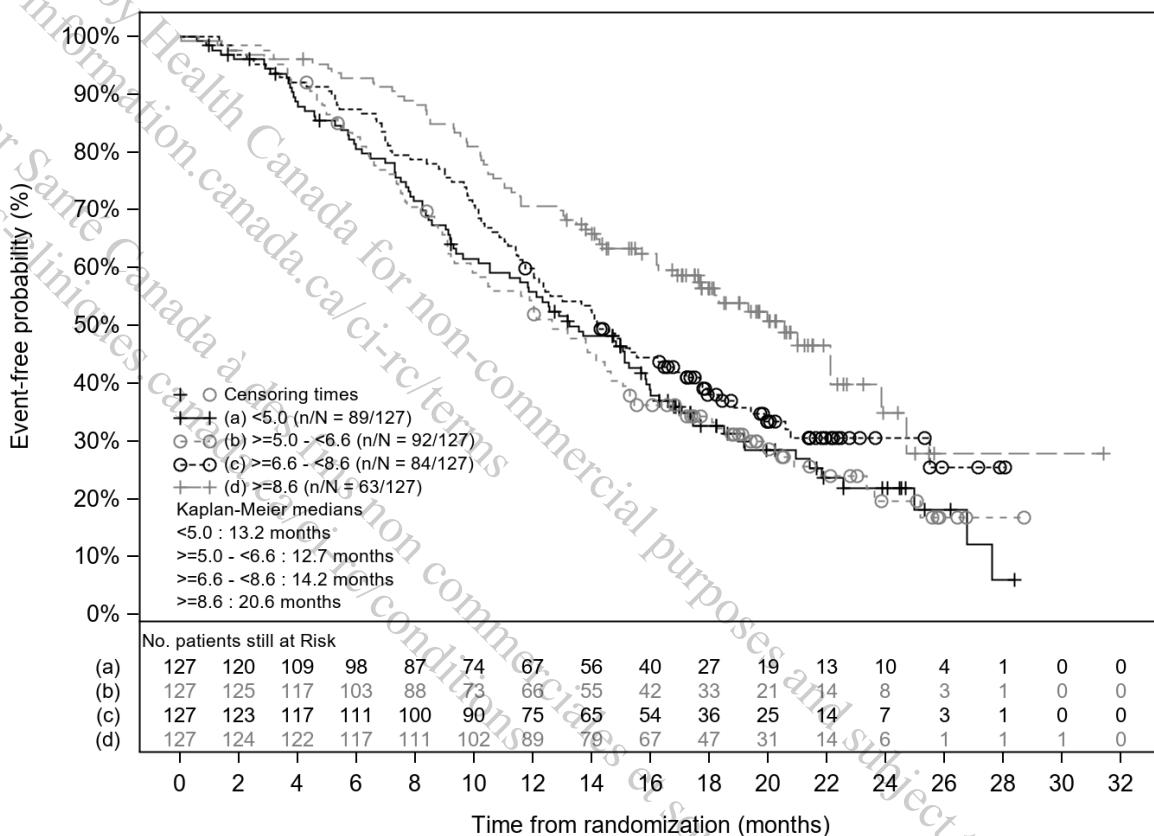
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Data Cutoff Date: 27JAN2021

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Figure 5-2-1 Kaplan-Meier plot for OS by SUV mean (g/mL) quartiles in bone (Bone - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-2-1 2021-08-30 12:27

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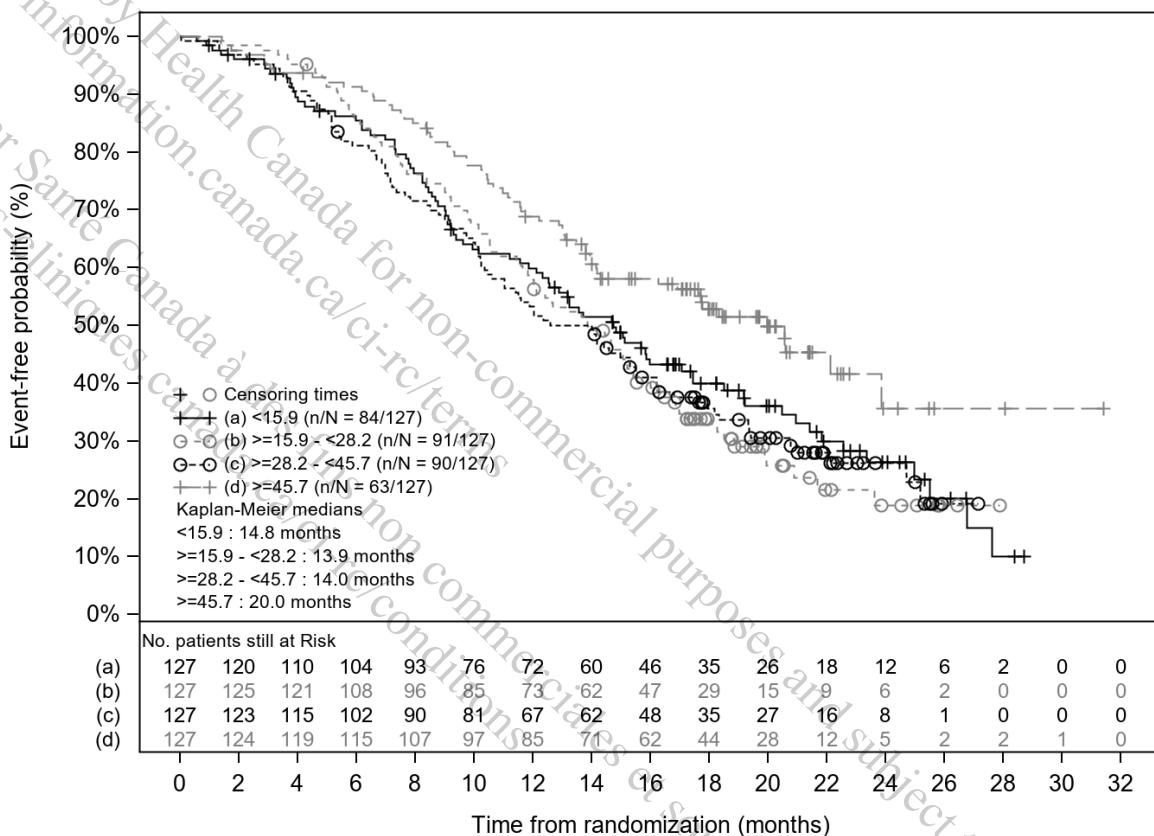
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Data Cutoff Date: 27JAN2021

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68Ga-PSMA-11 Quantitative analysis

Final Version

Figure 5-2-2 Kaplan-Meier plot for OS by SUV max (g/mL) quartiles in bone (Bone - Full analysis set)



n/N: Number of events/number of patients

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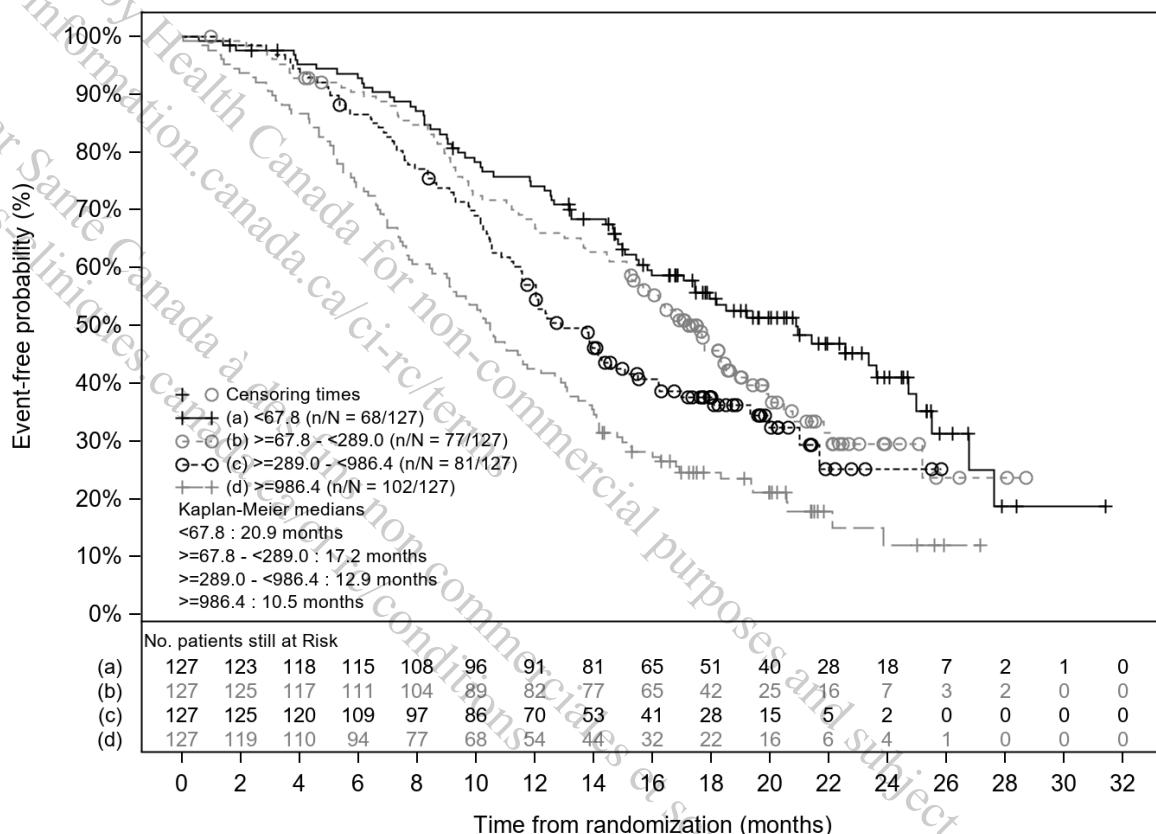
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Data Cutoff Date: 27JAN2021

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Figure 5-2-3 Kaplan-Meier plot for OS by tumor volume (cc) quartiles in bone (Bone - Full analysis set)



n/N: Number of events/number of patients

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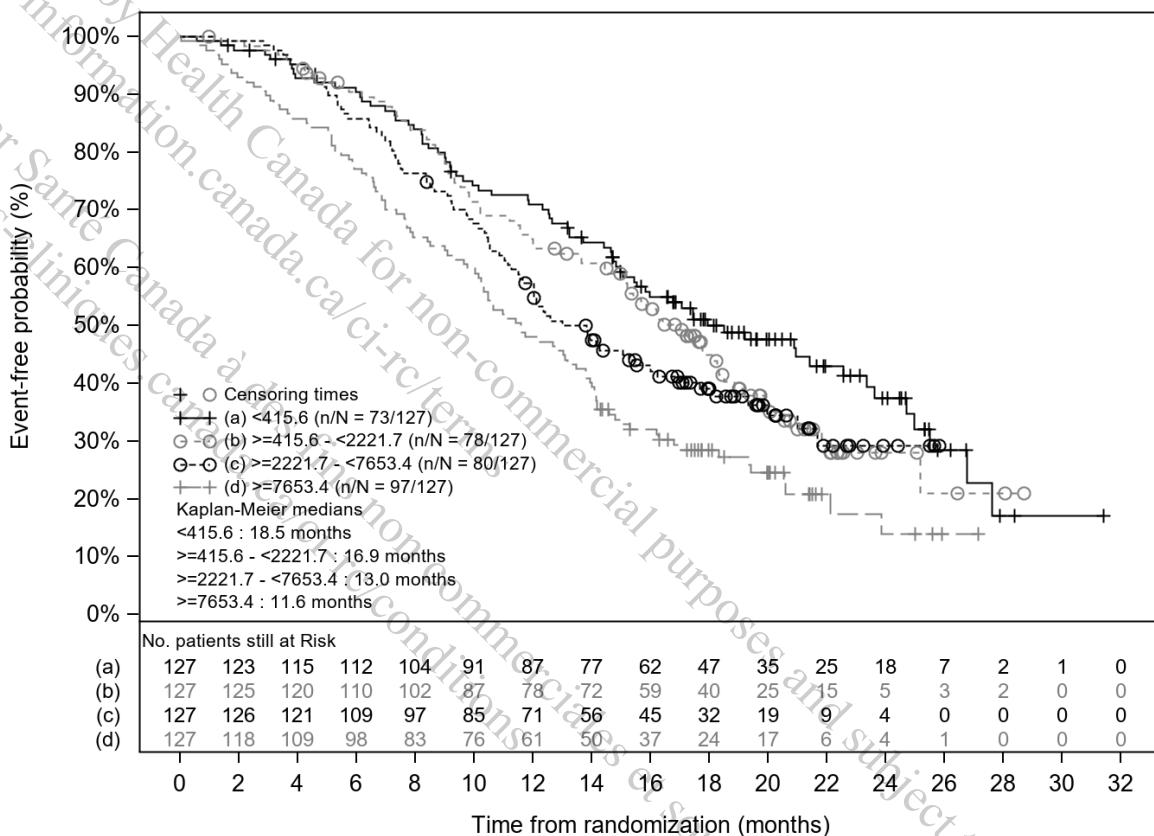
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Data Cutoff Date: 27JAN2021

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Figure 5-2-4 Kaplan-Meier plot for OS by tumor load (g) quartiles in bone (Bone - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-2-4 2021-08-30 12:27

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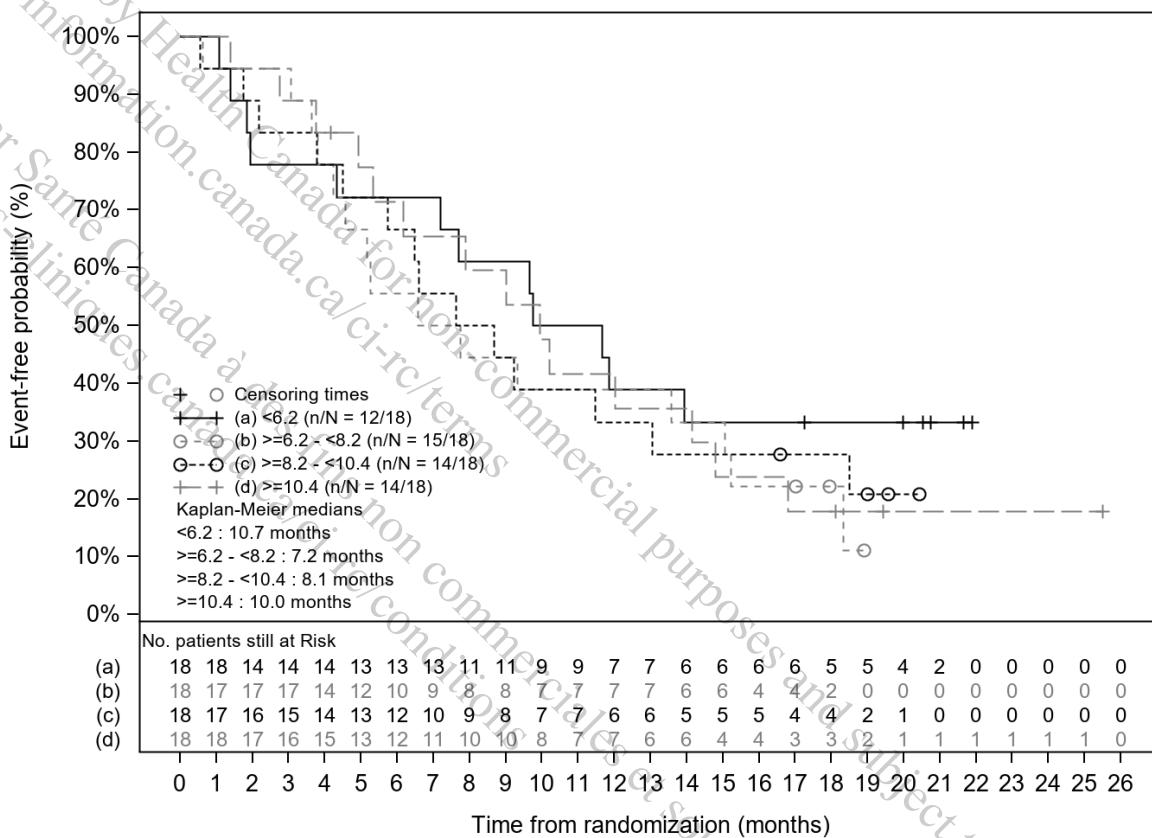
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Data Cutoff Date: 27JAN2021

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Figure 5-3-1 Kaplan-Meier plot for OS by SUV mean (g/mL) quartiles in liver (Liver - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-3-1 2021-08-30 12:27

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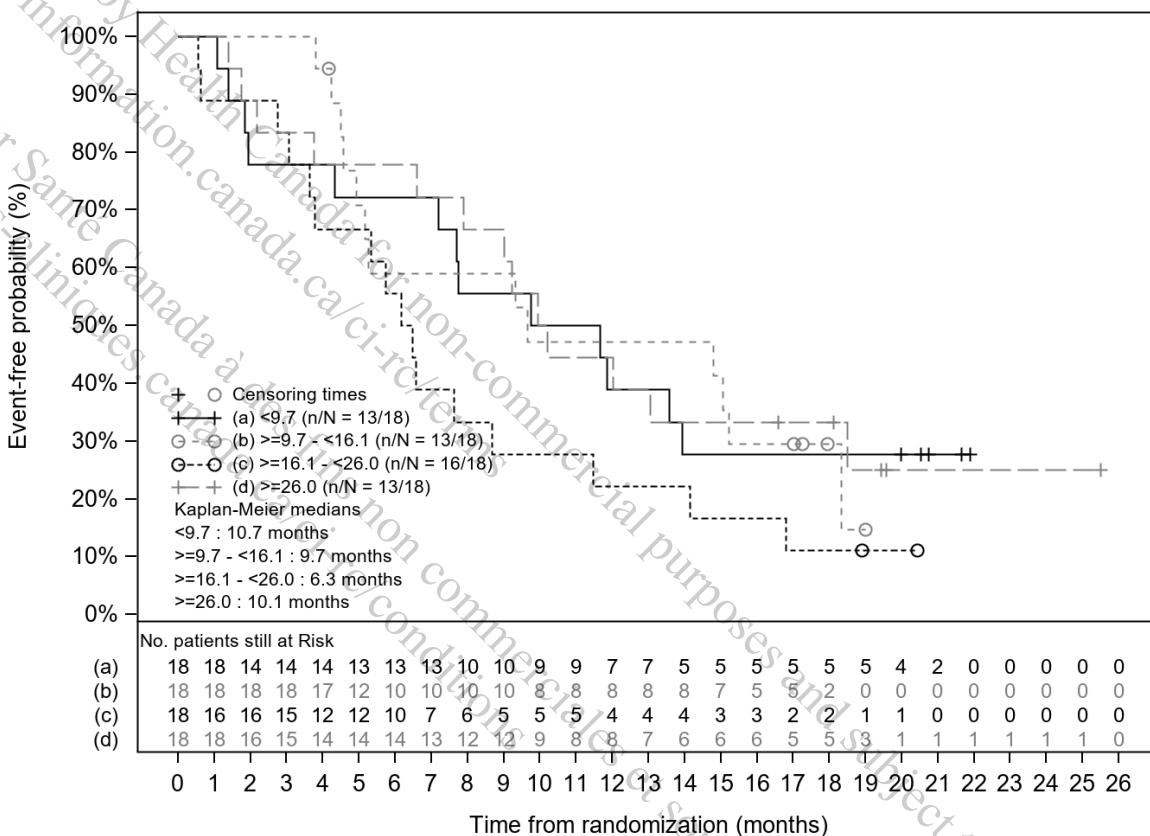
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Data Cutoff Date: 27JAN2021

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Figure 5-3-2 Kaplan-Meier plot for OS by SUV max (g/mL) quartiles in liver (Liver - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-3-2 2021-08-30 12:27

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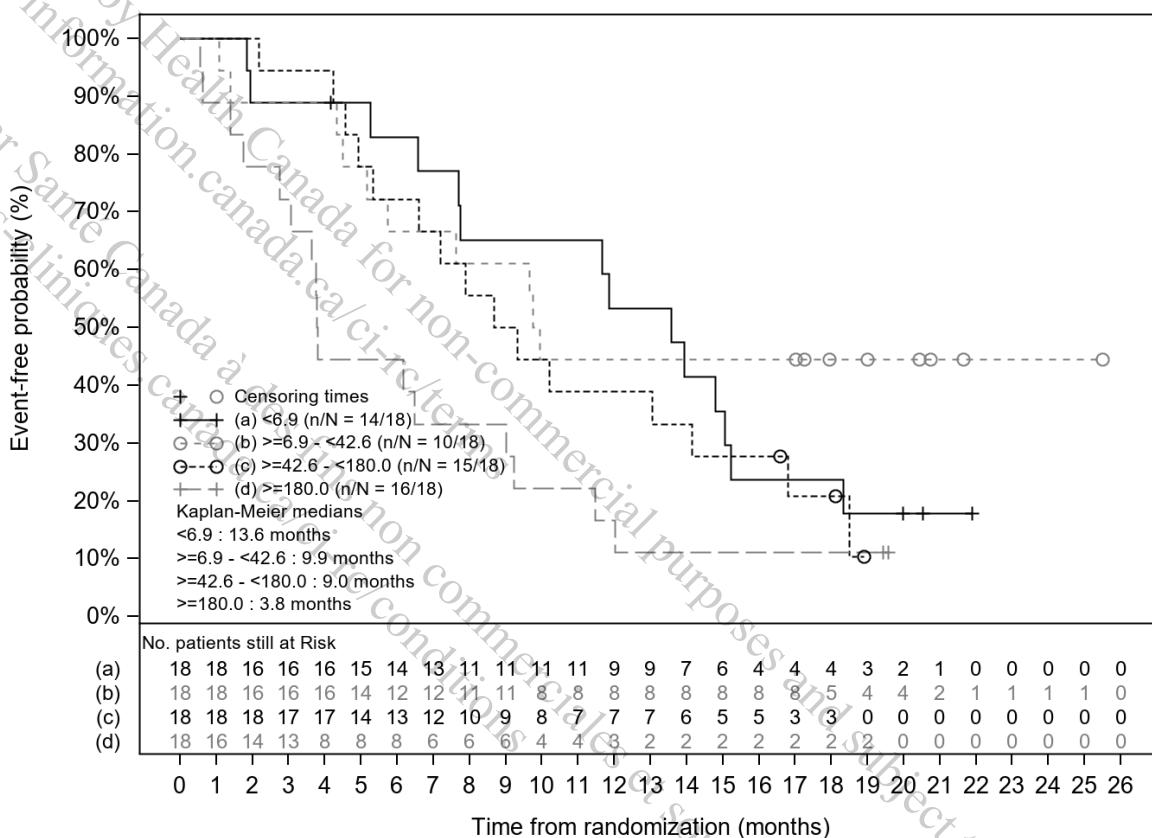
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Data Cutoff Date: 27JAN2021

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Final Version

Figure 5-3-3 Kaplan-Meier plot for OS by tumor volume (cc) quartiles in liver (Liver - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-3-3 2021-08-30 12:27

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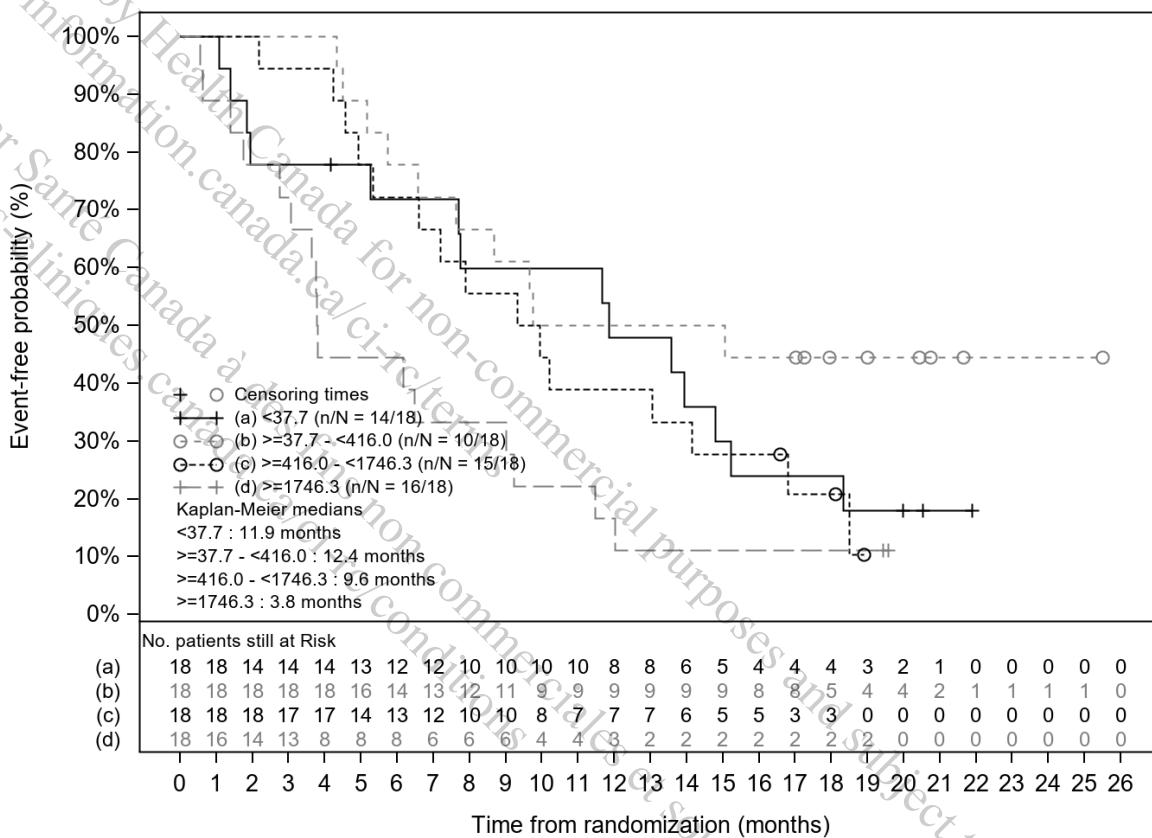
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Data Cutoff Date: 27JAN2021

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Final Version

Figure 5-3-4 Kaplan-Meier plot for OS by tumor load (g) quartiles in liver (Liver - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-3-4 2021-08-30 12:27

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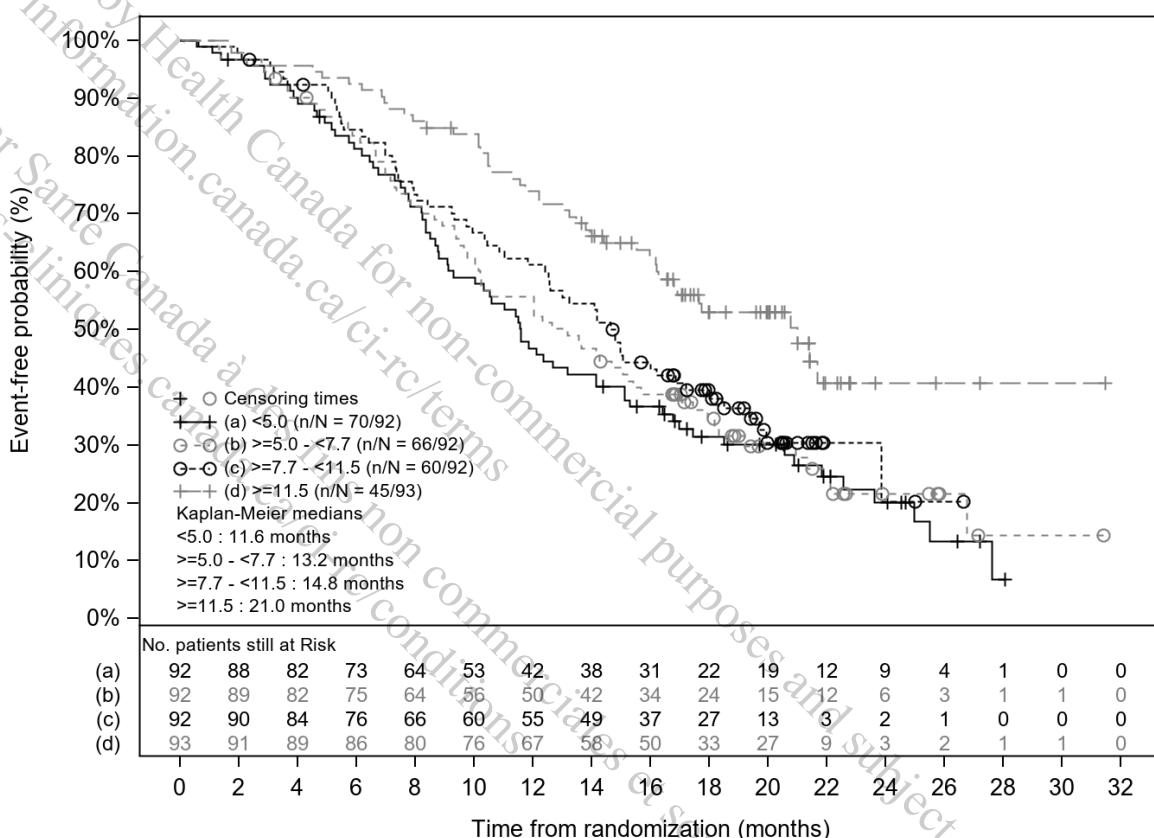
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Data Cutoff Date: 27JAN2021

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68Ga-PSMA-11 Quantitative analysis

Final Version

Figure 5-4-1 Kaplan-Meier plot for OS by SUV mean (g/mL) quartiles in lymph node (Lymph node - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-4-1 2021-08-30 12:27

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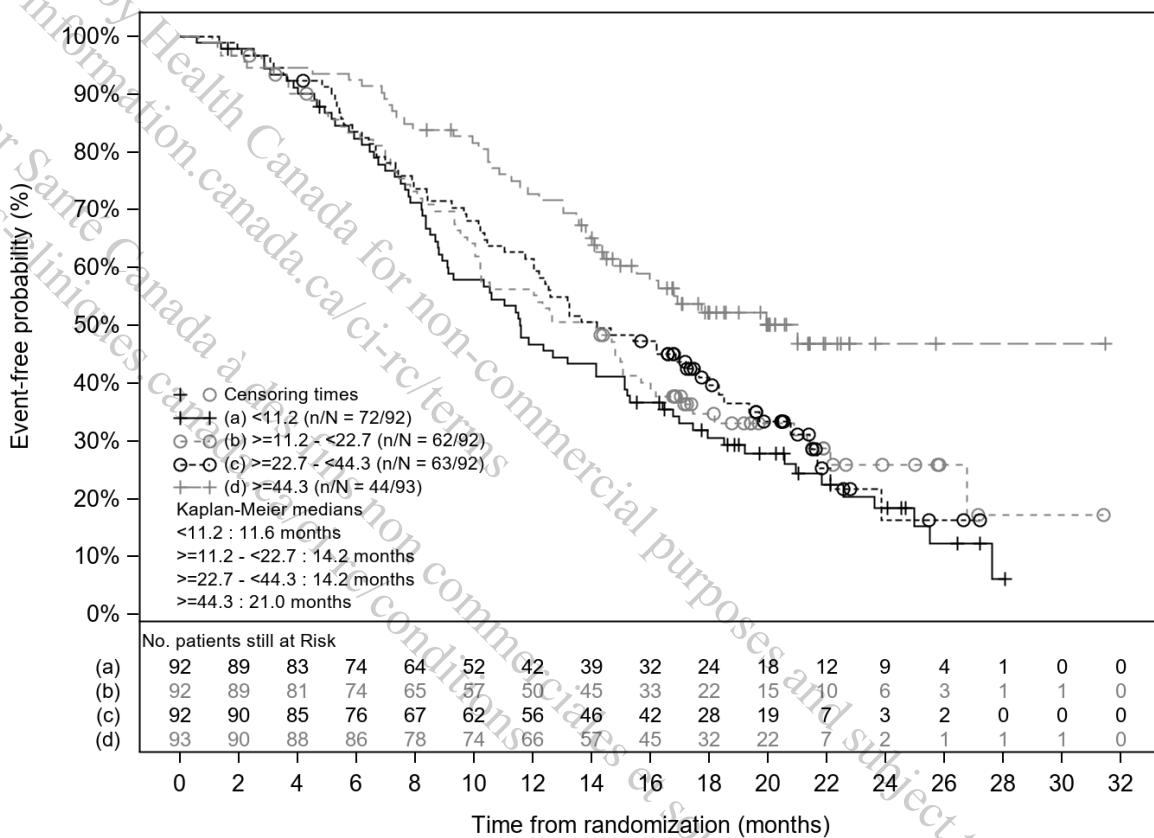
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Data Cutoff Date: 27JAN2021

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Final Version

Figure 5-4-2 Kaplan-Meier plot for OS by SUV max (g/mL) quartiles in lymph node (Lymph node - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-4-2 2021-08-30 12:27

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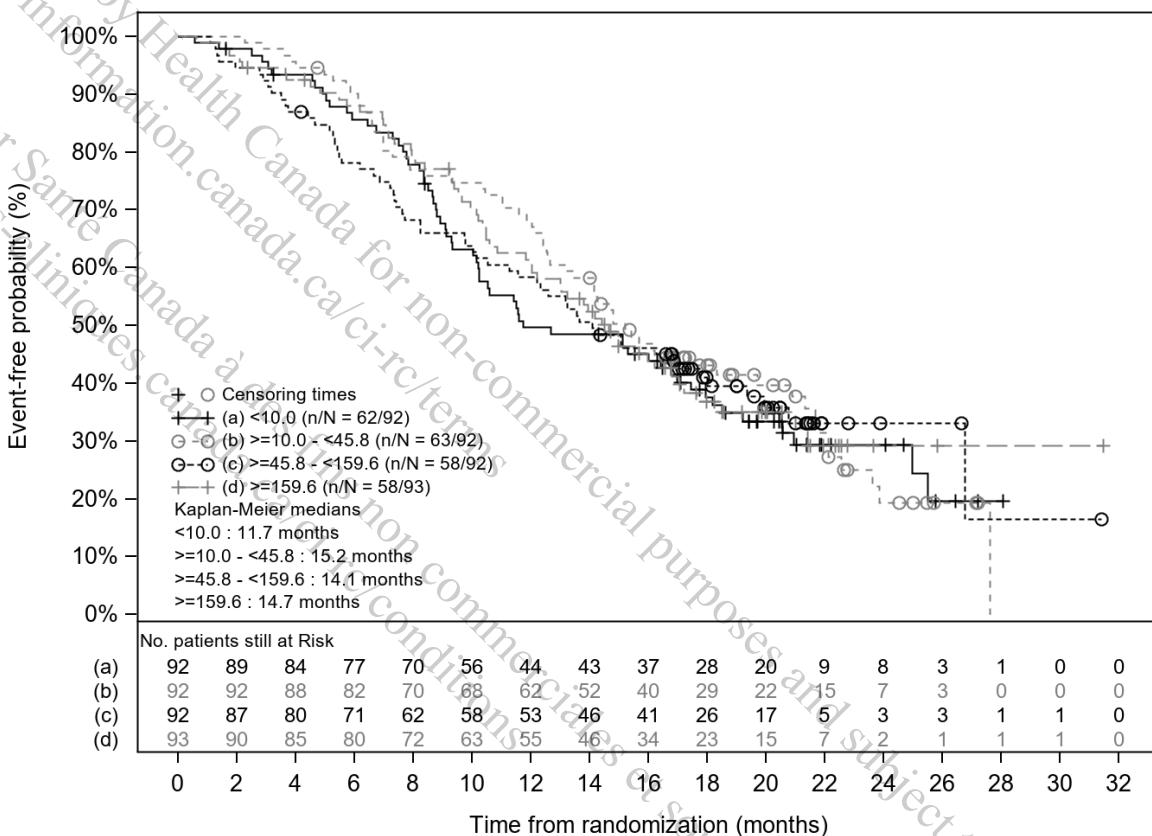
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Data Cutoff Date: 27JAN2021

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Final Version

Figure 5-4-3 Kaplan-Meier plot for OS by tumor volume (cc) quartiles in lymph node (Lymph node - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-4-3 2021-08-30 12:28

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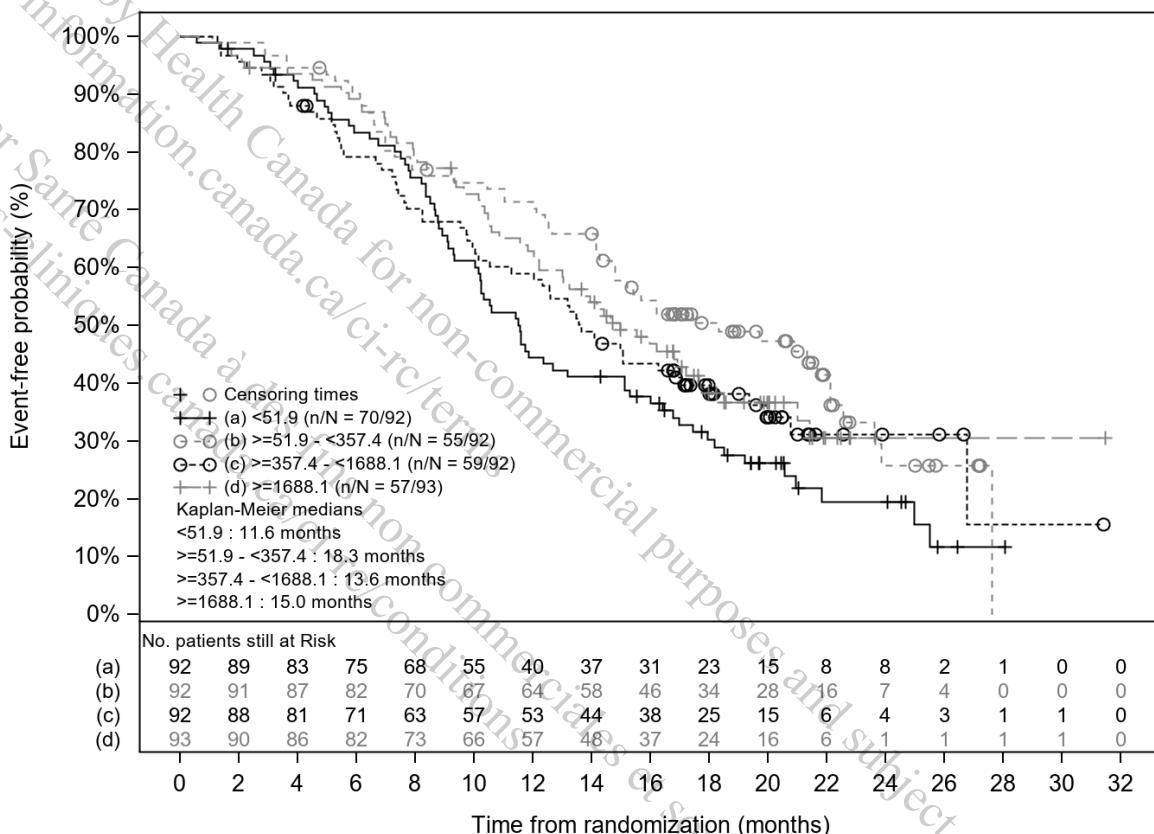
Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Figure 5-4-4 Kaplan-Meier plot for OS by tumor load (g) quartiles in lymph node (Lymph node - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-4-4 2021-08-30 12:28

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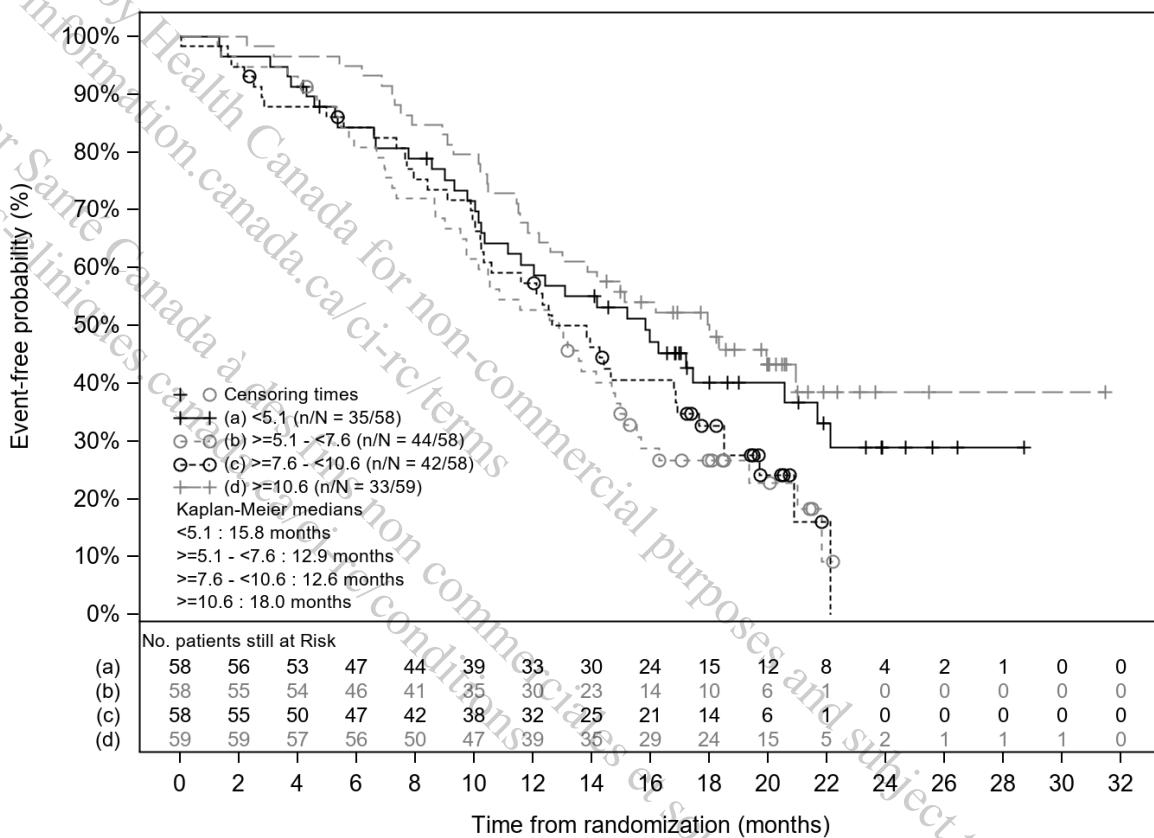
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Data Cutoff Date: 27JAN2021

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Figure 5-5-1 Kaplan-Meier plot for OS by SUV mean (g/mL) quartiles in soft tissue (Soft tissue - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-5-1 2021-08-30 12:28

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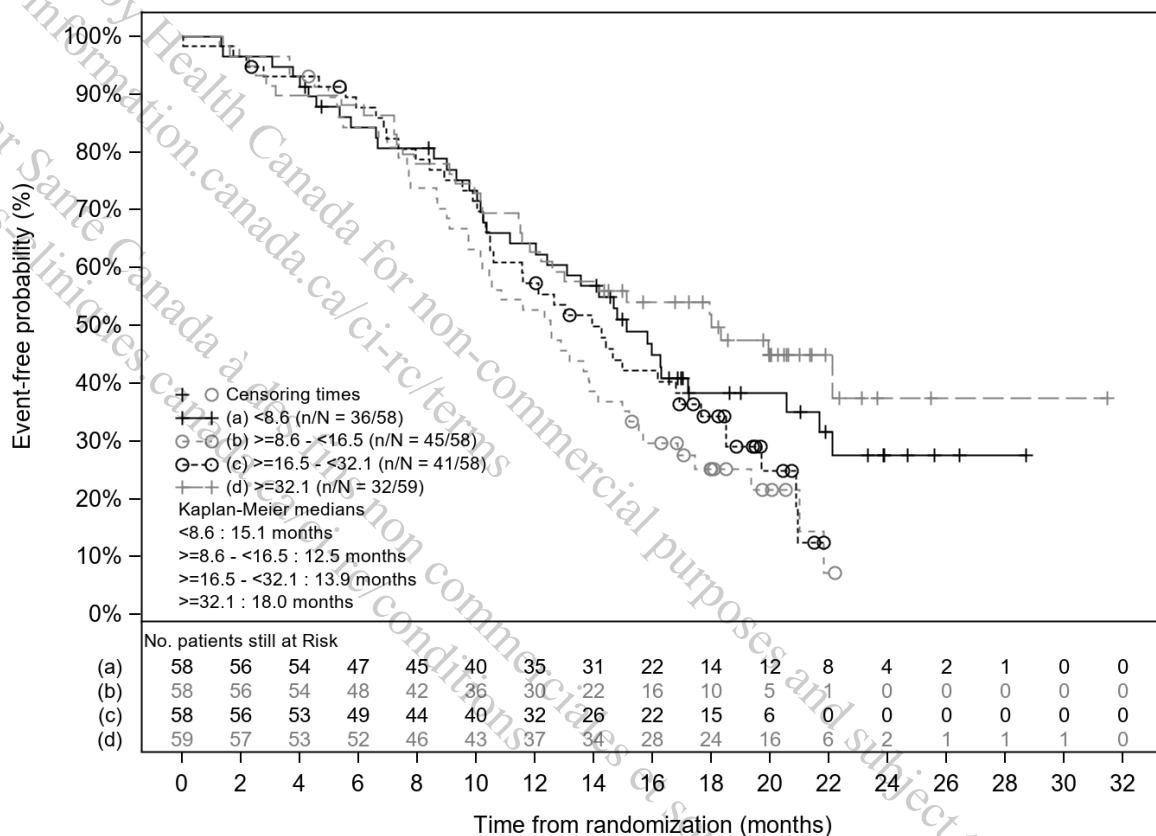
Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Figure 5-5-2 Kaplan-Meier plot for OS by SUV max (g/mL) quartiles in soft tissue (Soft tissue - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-5-2 2021-08-30 12:28

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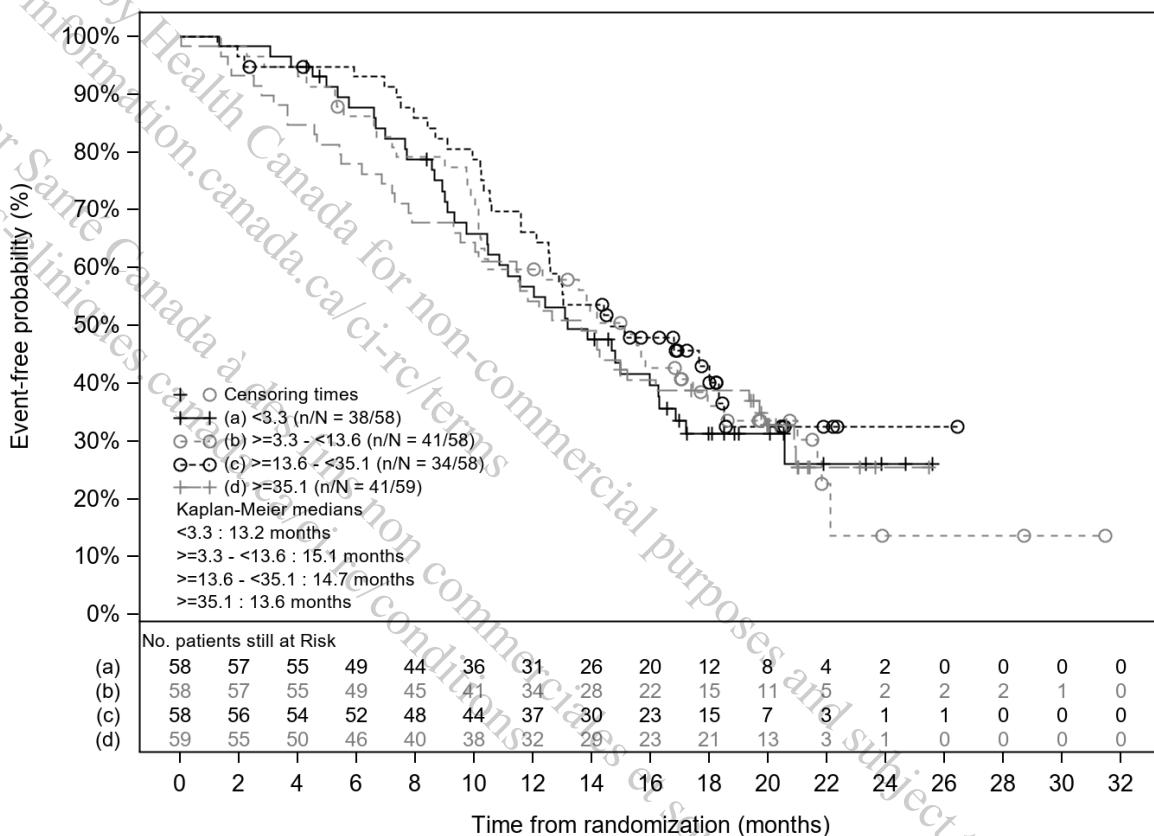
Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Figure 5-5-3 Kaplan-Meier plot for OS by tumor volume (cc) quartiles in soft tissue (Soft tissue - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-5-3 2021-08-30 12:28

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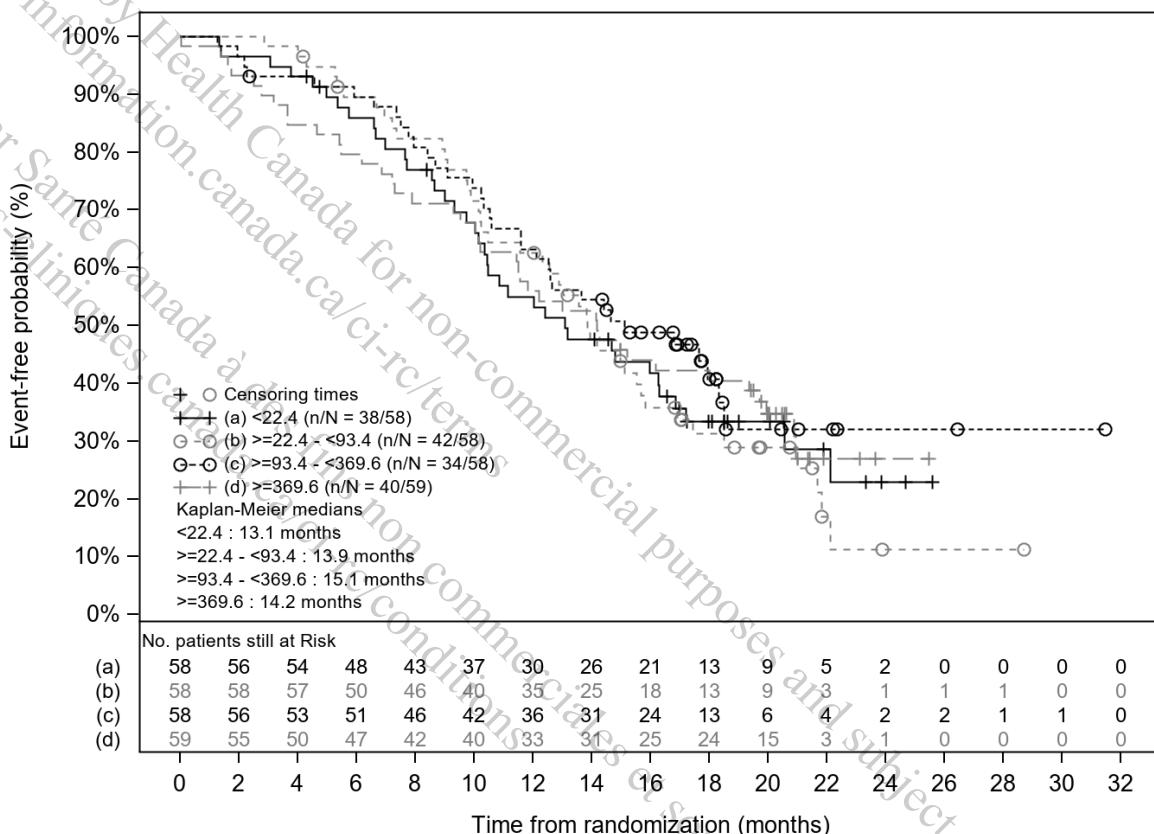
Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Figure 5-5-4 Kaplan-Meier plot for OS by tumor load (g) quartiles in soft tissue (Soft tissue - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-5-5-4 2021-08-30 12:28

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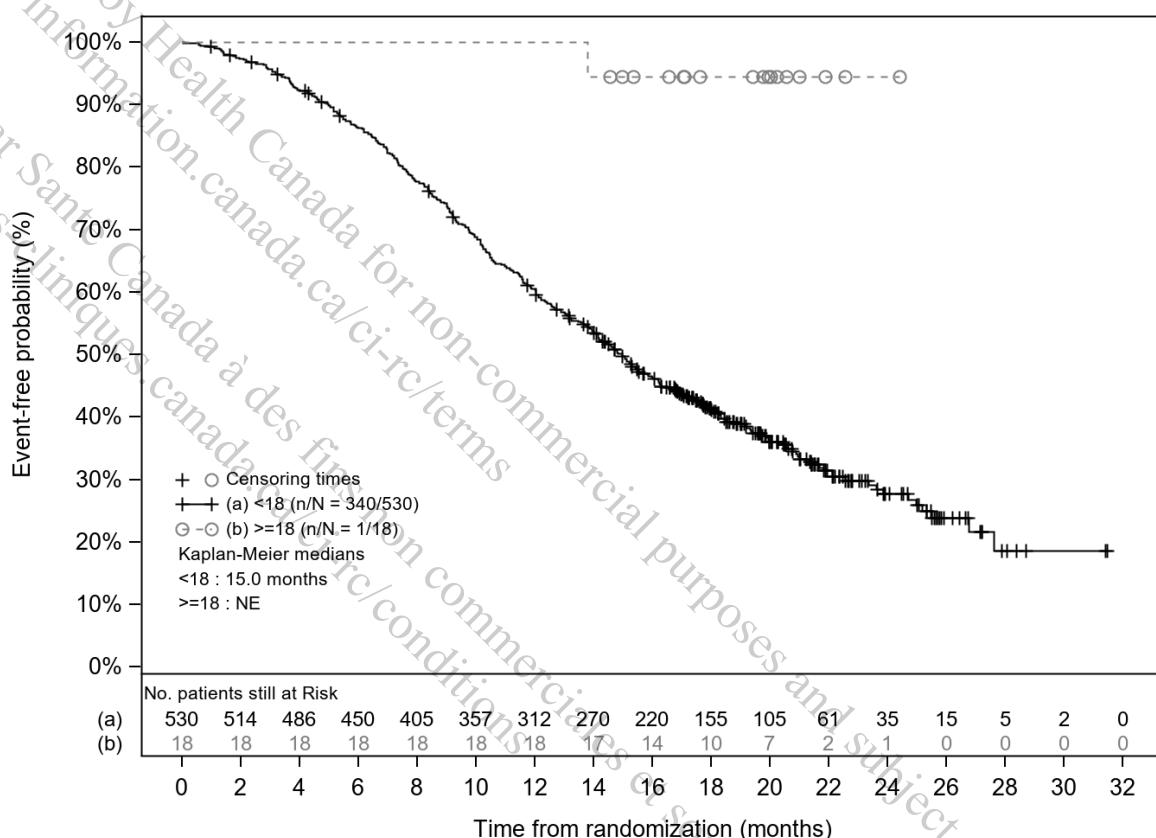
Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Figure 7-1-1 Kaplan-Meier plot for OS by optimal cut point of SUV mean (g/mL) in whole body (Body - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-7-1-1 2021-08-30 12:29

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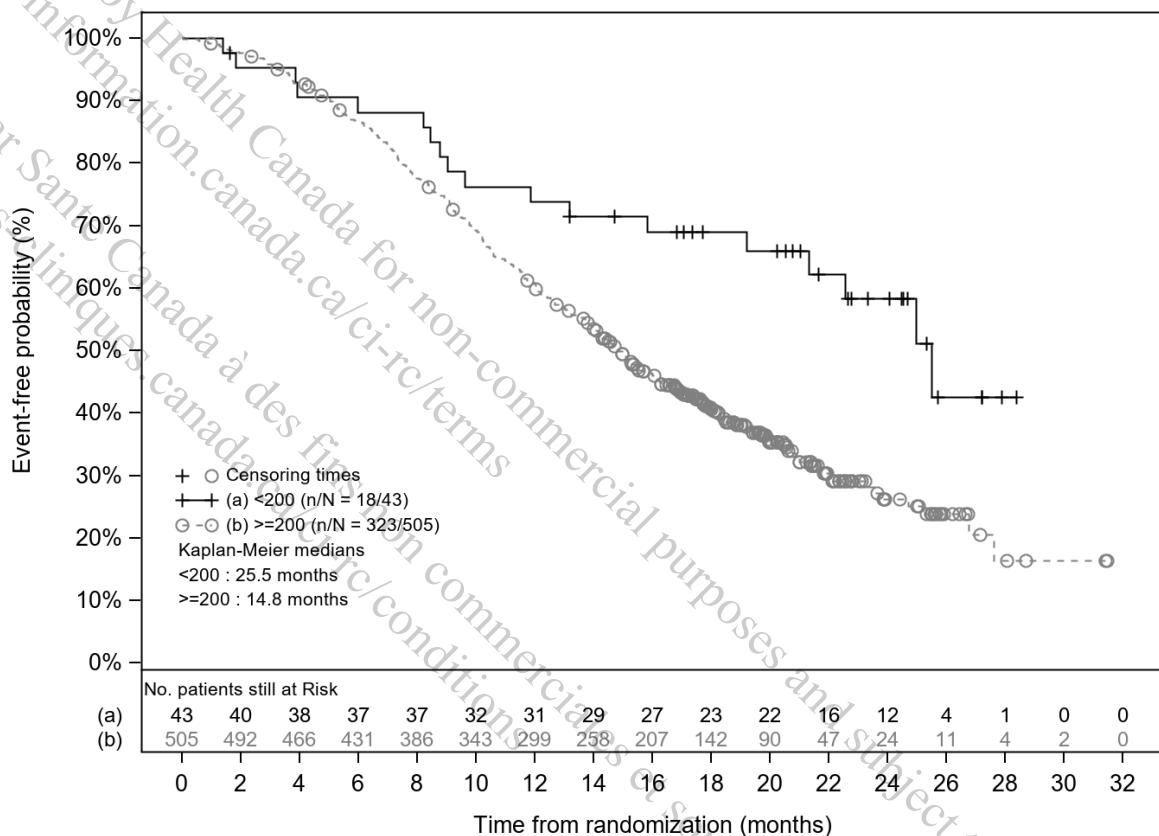
Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Figure 7-1-2 Kaplan-Meier plot for OS by optimal cut point of tumor load (g) in whole body (Body - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-7-1-2 2021-08-30 12:29

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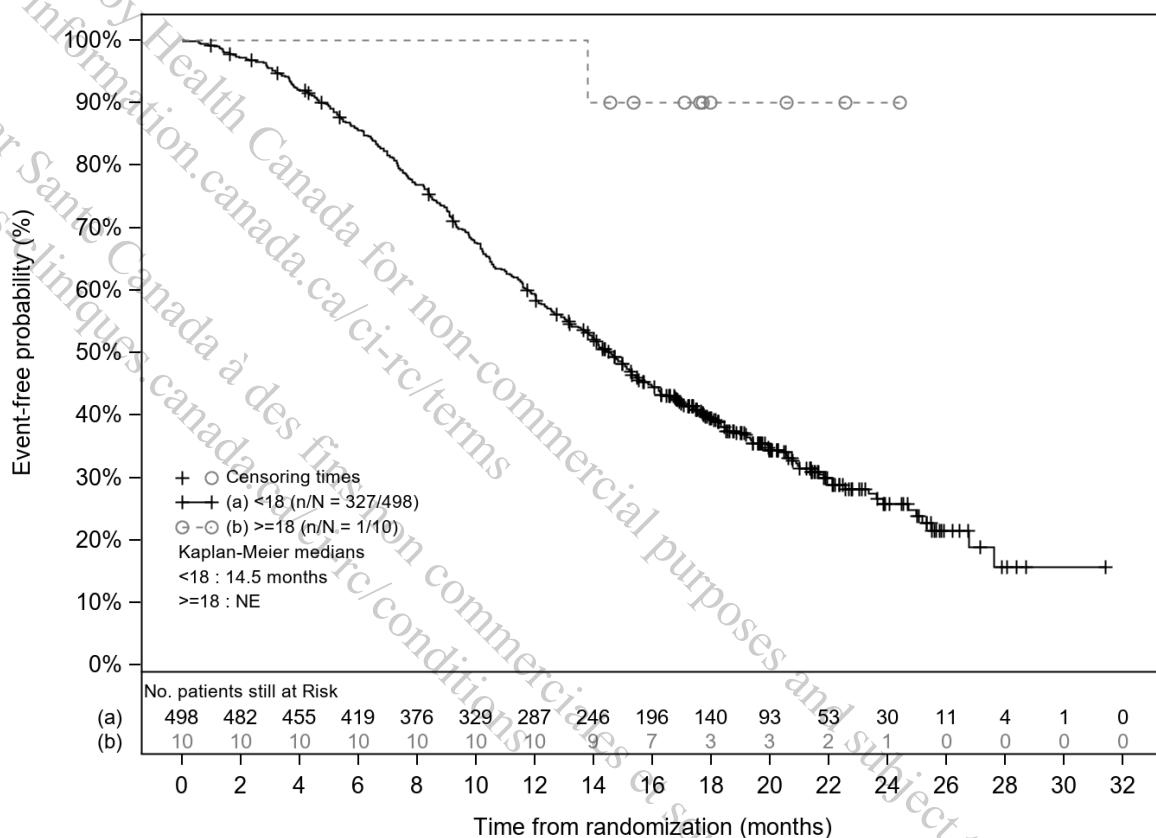
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Data Cutoff Date: 27JAN2021

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Figure 7-2-1 Kaplan-Meier plot for OS by optimal cut point of SUV mean (g/mL) in bone (Bone - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-7-2-1 2021-08-30 12:29

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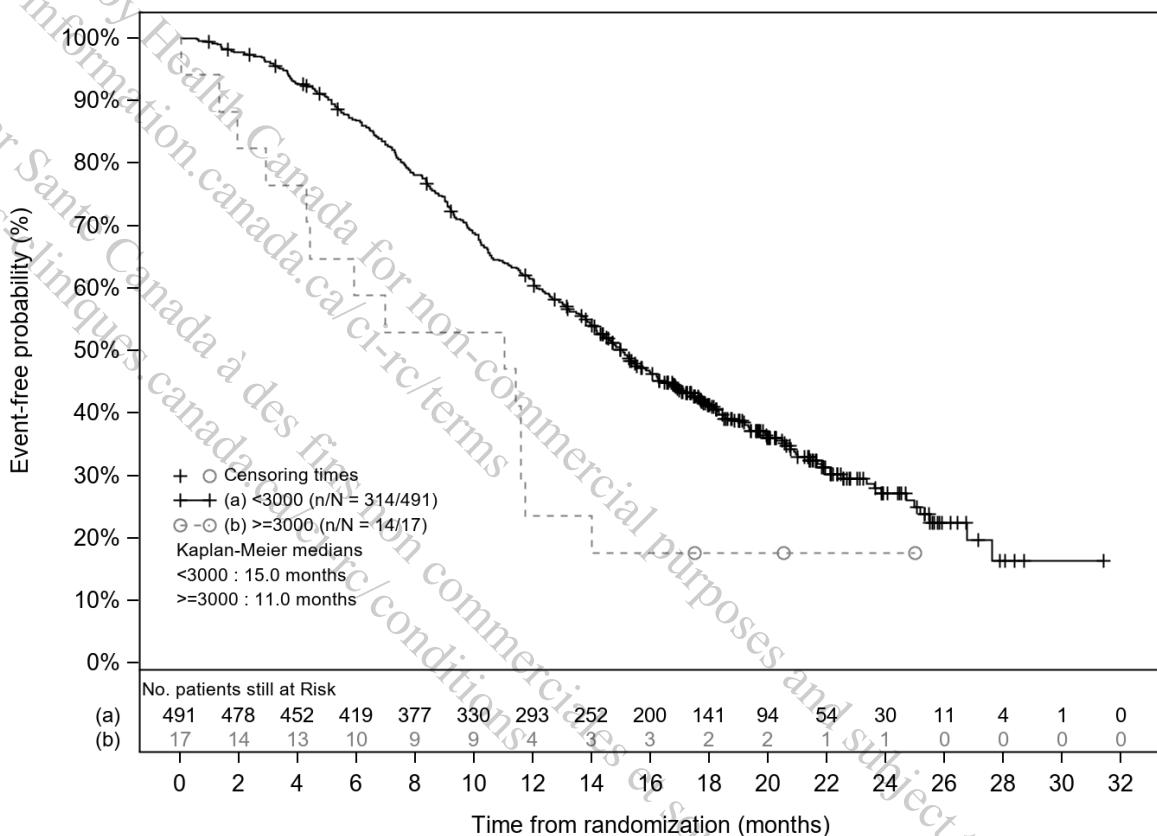
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Data Cutoff Date: 27JAN2021

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Figure 7-2-2 Kaplan-Meier plot for OS by optimal cut point of tumor volume (cc) in bone (Bone - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-7-2-2 2021-08-30 12:29

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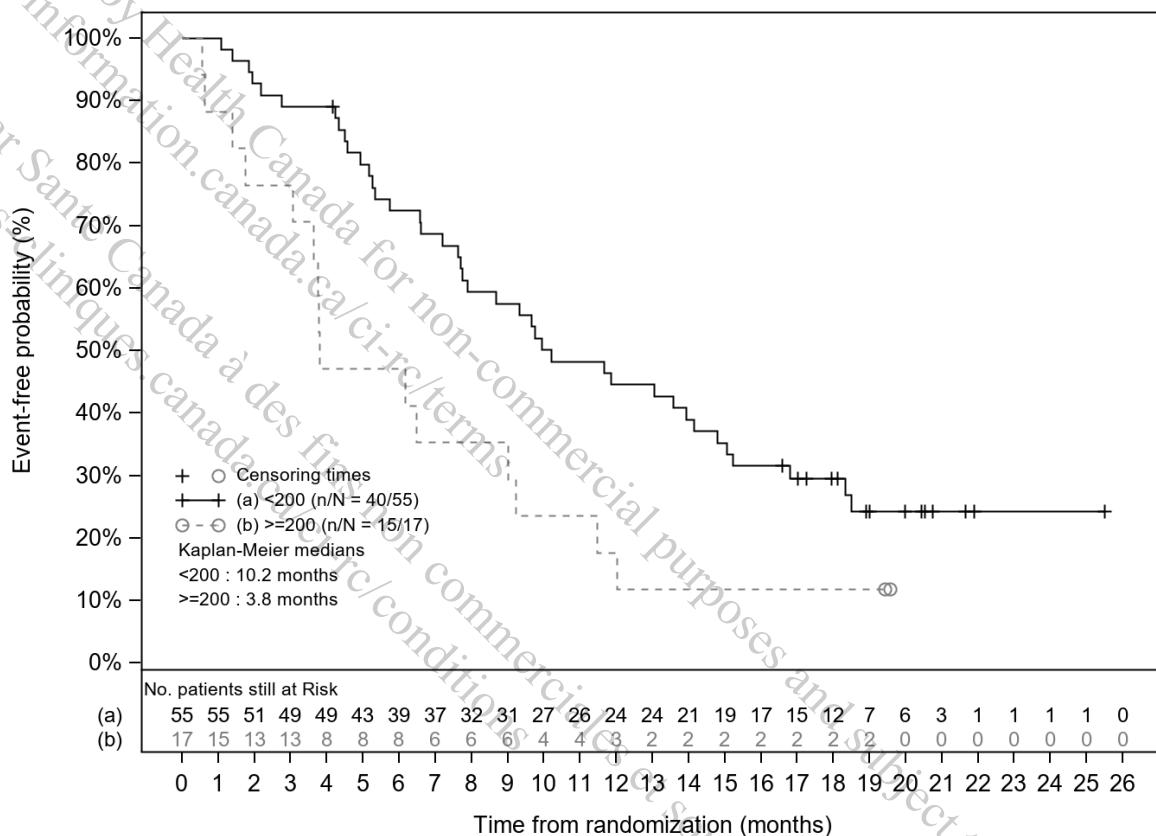
Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Figure 7-3-1 Kaplan-Meier plot for OS by optimal cut point of tumor volume (cc) in liver (Liver - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-7-3-1 2021-08-30 12:29

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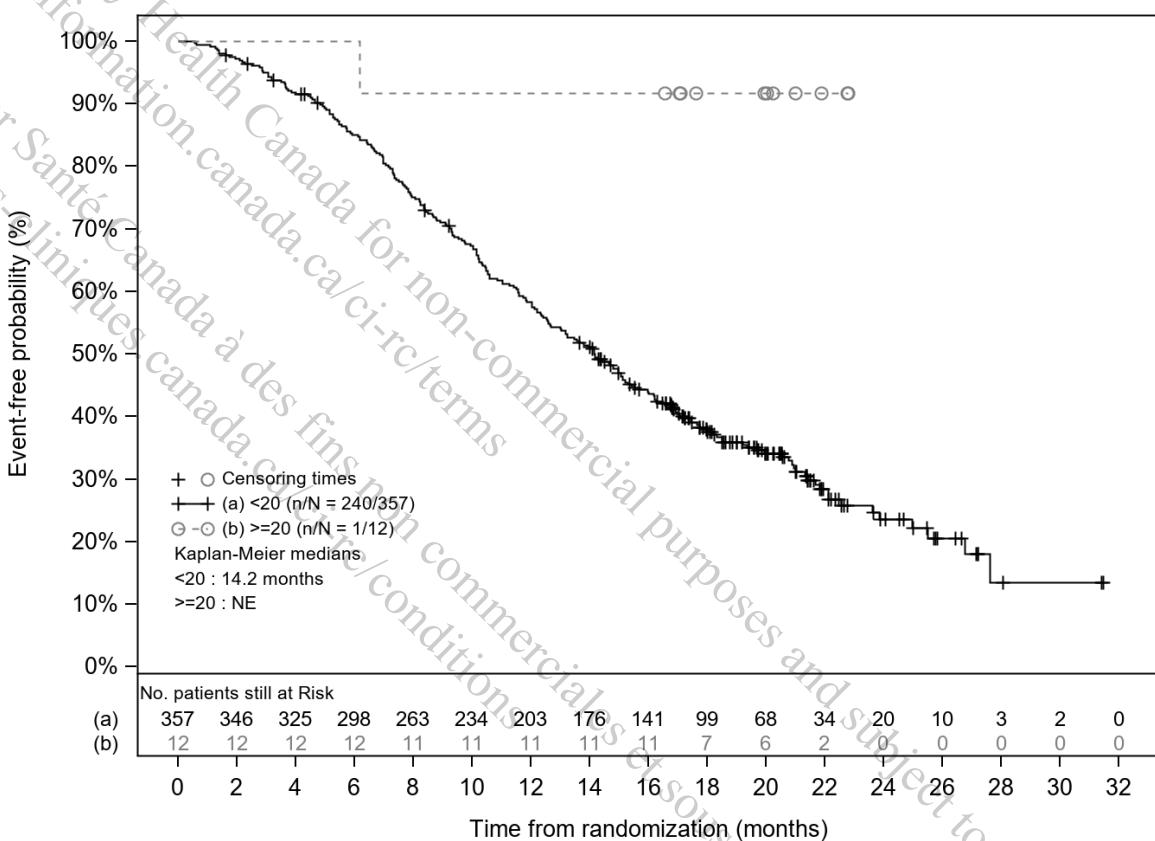
Source data: adsl.xpt, adtte.xpt

Data Cutoff Date: 27JAN2021

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Figure 7-4-1 Kaplan-Meier plot for OS by optimal cut point of SUV mean (g/mL) in lymph node (Lymph node - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-7-4-1 2021-08-30 12:29

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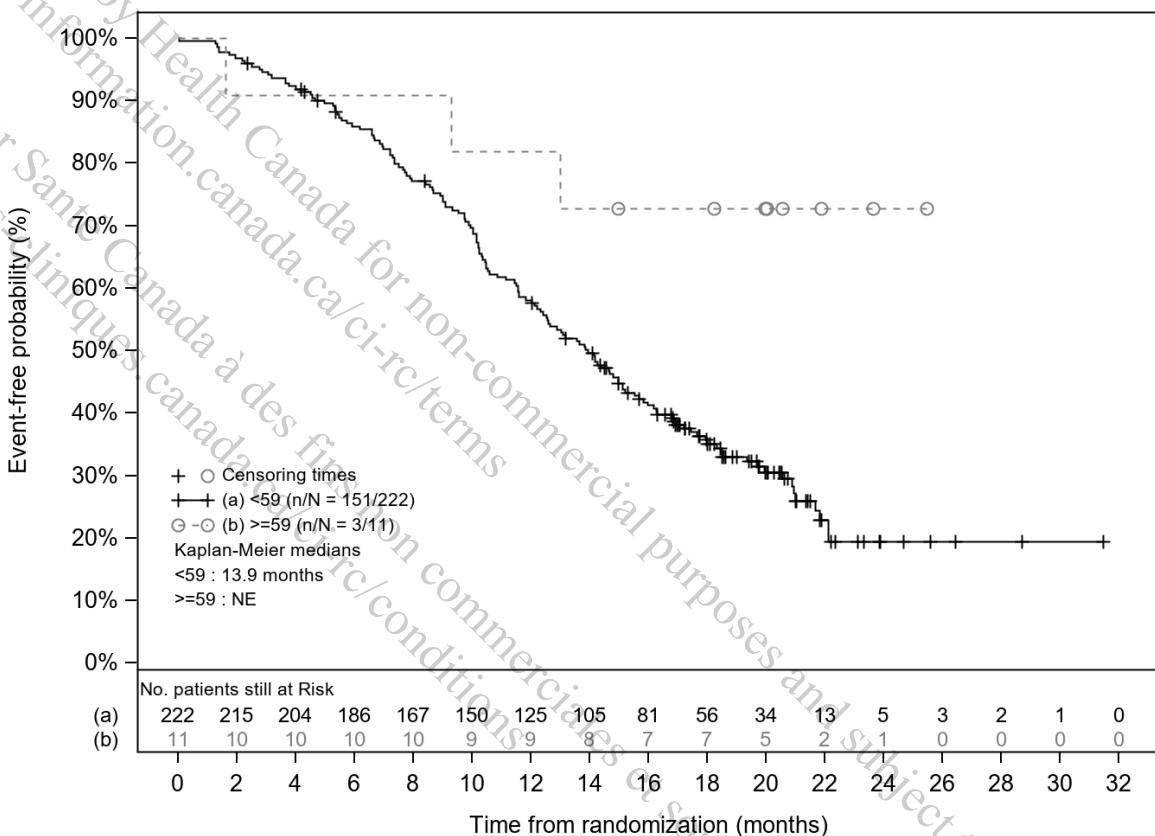
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Data Cutoff Date: 27JAN2021

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Figure 7-5-1 Kaplan-Meier plot for OS by optimal cut point of SUV max (g/mL) in soft tissue (Soft tissue - Full analysis set)



n/N: Number of events/number of patients

Output ID: F-7-5-1 2021-08-30 12:29

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