



Clinical Development

lutetium (¹⁷⁷Lu) vipivotide tetraxetan

AAA617 ([¹⁷⁷Lu]Lu-PSMA-617)

SCE Appendix 1 **(Integrated Summary of Efficacy, data analyses)**

Document type: Clinical summary document appendix

Property of Advanced Accelerator Applications, a Novartis Company
Confidential

May not be used, divulged, published or otherwise disclosed
without the consent of Advanced Accelerator Applications

Table of Contents

Table of Contents.....	2
1 Organization of material.....	6
2 Efficacy data analyses (tables and figures)	7
Table 1 Baseline and Other Subgroup Characteristics (Full Analysis Set)	8
Table 2 Baseline and Other Subgroup Characteristics (PFS-Full Analysis Set)	10
Table 3 Overall Survival by Region (Full Analysis Set)	12
Table 4 Overall Survival by PSA Doubling Time at Baseline (Full Analysis Set)	13
Table 5 Overall Survival by Baseline Prostate-Specific Antigen (Full Analysis Set)	14
Table 6 Overall Survival by Number of prior NAADs (Full Analysis Set)	15
Table 7 Overall Survival by Number of prior immunotherapies (Full Analysis Set)	16
Table 8 Overall Survival by Number of prior taxane-containing regimens (Full Analysis Set)	17
Table 9 Overall Survival by Number of prior non-taxane cytotoxic chemotherapeutic therapies (Full Analysis Set)	18
Table 10 Overall Survival by Prior use of Bone Sparing Agents (Full Analysis Set)	19
Table 11 Overall Survival by Prior use of 223-Radium (Full Analysis Set)	20
Table 12 Overall Survival by Prior use of PARP inhibitors (Full Analysis Set)	21
Table 13 Overall Survival by Concurrent use of NAADs as part of BSC/BSoC treatment (Full Analysis Set)	22
Table 14 Overall Survival by Concurrent use of radiation therapy as part of BSC/BSoC treatment (Full Analysis Set)	23
Table 14.2.1.11 Analysis of overall survival using stratified log-rank test and cox regression model in the first 750 randomized (Full analysis set)	24
Table 14.2.1.12 Overall survival by cycles of Lu-PSMA-617 (FAS safety set)	25
Table 14.2.1.13 OS events and reasons for censoring in patients who withdrew consent to BSC/BSoC in patients randomized prior to 5 Mar 2019 (Full analysis set)	26
Table 14.2.1.14 OS events and reasons for censoring in patients who withdrew consent to BSC/BSoC (PFS Full analysis set)	27
Table 14.2.1.15 OS events and reasons for censoring in patients who withdrew consent to BSC/BSoC (Full analysis set)	28

Table 14.2.2.19 Analysis of radiographic progression-free survival based on independent central review using stratified log-rank test and cox regression model (Full analysis set)	29
Table 14.2.2.20 Radiographic progression-free survival based on independent central review by cycles of Lu-PSMA-617 (FAS safety set)	30
Table 14.2.2.21 rPFS per independent central review events and reasons for censoring in patients who withdrew consent to BSC/BSoC patients randomized prior to 5 Mar 2019 (Full analysis set)	31
Table 14.2.2.22 rPFS per independent central review events and reasons for censoring in patients who withdrew consent to BSC/BSoC (PFS Full analysis set)	32
Table 14.2.2.23 rPFS per independent central review events and reasons for censoring in patients who withdrew consent to BSC/BSoC (Full analysis set)	33
Table 14.2.3.1.1 RECIST 1.1 best overall response, disease control rate and duration of response based on independent central review - in patients with measurable disease at baseline (Response evaluable analysis set)	34
Table 14.2.5.1 Progression-free survival by cycles of Lu-PSMA-617 (FAS safety set)	35
Table 14.2.8.1.2.2 Time to worsening in FACT-P total score by cycles of Lu-PSMA-617 (FAS safety set)	36
Table 14.2.8.10.2.2 Time to worsening in FACT-G total score by cycles of Lu-PSMA-617 (FAS safety set)	37
Table 14.2.9.1.2.2 Time to worsening in BPI-SF pain intensity scale by cycles of Lu-PSMA-617 (FAS safety set)	38
Table 14.2.9.2.2.2 Time to worsening in BPI-SF pain interference scale by cycles of Lu-PSMA-617 (FAS safety set)	39
Table 14.3.12.2 Cancer related therapy (non-radiation) since discontinuation of randomized treatment - patients who withdrew consent to BSC/BSoC randomized prior to 5 Mar 2019 (Full analysis set)	40
Table 14.3.12.3 Cancer related therapy (non-radiation) since discontinuation of randomized treatment - patients who withdrew consent to BSC/BSoC (PFS Full analysis set)	42
Table 14.3.12.4 Cancer related therapy (non-radiation) since discontinuation of randomized treatment - patients who withdrew consent to BSC/BSoC (Full analysis set)	43
Table 14.3.13.2 Cancer related radiotherapy since discontinuation of randomized treatment - patients who withdrew consent to BSC/BSoC randomized prior to 5 Mar 2019 (Full analysis set)	45

Table 14.3.13.3 Cancer related radiotherapy since discontinuation of randomized treatment - patients who withdrew consent to BSC/BSoC (PFS Full analysis set)	46
Table 14.3.13.4 Cancer related radiotherapy since discontinuation of randomized treatment - patients who withdrew consent to BSC/BSoC (Full analysis set)	47
Table 15 Overall Survival by Concurrent use of Bone Sparing Agents as part of BSC/BSoC treatment (Full Analysis Set)	48
Table 16 Radiographic Progression-free Survival based on Independent Central Review by Region (PFS-Full Analysis Set)	49
Table 17 Radiographic Progression-free Survival based on Independent Central Review by PSA Doubling Time at Baseline (PFS-Full Analysis Set)	50
Table 18 Radiographic Progression-free Survival based on Independent Central Review by Baseline Prostate-Specific Antigen (PFS-Full Analysis Set)	51
Table 19 Radiographic Progression-free Survival based on Independent Central Review by Number of prior NAADs (PFS-Full Analysis Set)	52
Table 20 Radiographic Progression-free Survival based on Independent Central Review by Number of prior immunotherapies (PFS-Full Analysis Set)	53
Table 21 Radiographic Progression-free Survival based on Independent Central Review by Number of prior taxane-containing regimens (PFS-Full Analysis Set)	54
Table 22 Radiographic Progression-free Survival based on Independent Central Review by Number of prior non-taxane cytotoxic chemotherapeutic therapies (PFS-Full Analysis Set)	55
Table 23 Radiographic Progression-free Survival based on Independent Central Review by Prior use of Bone Sparing Agents (PFS-Full Analysis Set)	56
Table 24 Radiographic Progression-free Survival based on Independent Central Review by Prior use of 223-Radium (PFS-Full Analysis Set)	57
Table 25 Radiographic Progression-free Survival based on Independent Central Review by Prior use of PARP inhibitors (PFS-Full Analysis Set)	58
Table 26 Radiographic Progression-free Survival based on Independent Central Review by Concurrent use of NAADs as part of BSC/BSoC treatment (PFS-Full Analysis Set)	59
Table 27 Radiographic Progression-free Survival based on Independent Central Review by Concurrent use of radiation therapy as part of BSC/BSoC treatment (PFS-Full Analysis Set)	60

Table 28 Radiographic Progression-free Survival based on Independent Central Review by Concurrent use of Bone Sparing Agents as part of BSC/BSoC treatment (PFS-Full Analysis Set)	61
Table 29 OS sensitivity analyses- impact of dropout (Full analysis set)	62
Table 30 rPFS based on independent central review sensitivity analyses- impact of dropout (PFS-Full analysis set)	63
Figure 1 Forest Plot of Hazard Ratio with 95% Confidence Interval for Overall Survival from Subgroup Analysis (Full Analysis Set)	64
Figure 2 Forest Plot of Hazard Ratio with 95% Confidence Interval for Radiographic Progression-free Survival based on Independent Central Review from Subgroup Analysis (PFS-Full Analysis Set)	68
Figure 14.2.1.1.3 Kaplan-Meier plot for overall survival in the first 750 randomized (Full analysis set)	70
Figure 14.2.2.5 Kaplan-Meier plot for radiographic progression-free survival based on independent central review (Full analysis set)	71

1 Organization of material

SCE Appendix 1 contains the key data that supports the text portion of the Summary of Clinical Efficacy and is intended to be the major source of reference material when reviewing the summary document, in addition to the Clinical Study Report of study PSMA-617-01 (VISION). It includes all items given as the source of the text figures and tables and any other material that is provided in addition.

Disclosed by Health Canada for non-commercial purposes and subject to the Terms of Use
clinical-information.canada.ca/ci-rc/terms
Divulgué par Santé Canada à des fins non commerciales et sous réserve des conditions d'utilisation
renseignements-cliniques.canada.ca/ci-rc/conditions

2 Efficacy data analyses (tables and figures)

Disclosed by Health Canada for non-commercial purposes and subject to the Terms of Use
clinical-information.canada.ca/ci-rc/terms
Divulgué par Santé Canada à des fins non commerciales et sous réserve des conditions d'utilisation
renseignements-cliniques.canada.ca/ci-rc/conditions

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 1
Baseline and Other Subgroup Characteristics (Full Analysis Set)

	Lu-PSMA-617 +BSC/BSoC (N=551) n (%)	BSC/BSoC only (N=280) n (%)	Overall (N=831) n (%)
Region			
n	551	280	831
North America	393 (71.3)	209 (74.6)	602 (72.4)
Europe	158 (28.7)	71 (25.4)	229 (27.6)
Baseline PSA Doubling Time			
n (missing)	269 (282)	131 (149)	400 (431)
>0 - <=9 months	255 (94.8)	120 (91.6)	375 (93.8)
>9 months	14 (5.2)	11 (8.4)	25 (6.3)
Baseline PSA			
n	551	280	831
<=76.0 (ng/mL)	275 (49.9)	141 (50.4)	416 (50.1)
>76.0 (ng/mL)	276 (50.1)	139 (49.6)	415 (49.9)
Number of prior NAADs			
n	551	280	831
1	296 (53.7)	130 (46.4)	426 (51.3)
>=2	255 (46.3)	150 (53.6)	405 (48.7)
Number of prior immunotherapies			
n	551	280	831
0	414 (75.1)	200 (71.4)	614 (73.9)
>=1	137 (24.9)	80 (28.6)	217 (26.1)
Number of prior taxane-containing regimens			
n (missing)	512 (39)	264 (16)	776 (55)
1	342 (66.8)	165 (62.5)	507 (65.3)
>=2	170 (33.2)	99 (37.5)	269 (34.7)
Number of prior non-taxane cytotoxic chemotherapeutic therapies			
n	551	280	831
0	485 (88.0)	252 (90.0)	737 (88.7)
>=1	66 (12.0)	28 (10.0)	94 (11.3)
Prior use of bone sparing agents			
n	551	280	831
Yes	99 (18.0)	57 (20.4)	156 (18.8)
No	452 (82.0)	223 (79.6)	675 (81.2)

PSA: Prostate-specific antigen, NAAD: Novel androgen axis drugs, PARP: Poly ADP ribose polymerase
 Baseline PSA doubling time was derived for each patient as the natural log 2 divided by the sum of the fixed and random slopes of the random coefficient linear model between natural log of PSA and time of PSA measurement (in months). Patients with at least 3 PSA values prior to and at the time of screening were included in the model.

Patients with PSADT stable, non-increasing or decreasing are included in the category '>9 months'.

Output ID: T-1 2021-06-01 10:57

\FS\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-demo.sas
 Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 1
Baseline and Other Subgroup Characteristics (Full Analysis Set)

	Lu-PSMA-617 +BSC/BSoC (N=551) n (%)	BSC/BSoC only (N=280) n (%)	Overall (N=831) n (%)
Prior use of 223-Radium			
n	551	280	831
Yes	97 (17.6)	48 (17.1)	145 (17.4)
No	454 (82.4)	232 (82.9)	686 (82.6)
Prior use of PARP inhibitors			
n	551	280	831
Yes	30 (5.4)	16 (5.7)	46 (5.5)
No	521 (94.6)	264 (94.3)	785 (94.5)
Concurrent use of NAADs as part of BSC/BSoC treatment			
n	551	280	831
Yes	289 (52.5)	166 (59.3)	455 (54.8)
No	262 (47.5)	114 (40.7)	376 (45.2)
Concurrent use of radiation therapy as part of BSC/BSoC treatment			
n	551	280	831
Yes	75 (13.6)	31 (11.1)	106 (12.8)
No	476 (86.4)	249 (88.9)	725 (87.2)
Concurrent use of bone sparing agents as part of BSC/BSoC treatment			
n	551	280	831
Yes	240 (43.6)	125 (44.6)	365 (43.9)
No	311 (56.4)	155 (55.4)	466 (56.1)

PSA: Prostate-specific antigen, NAAD: Novel androgen axis drugs, PARP: Poly ADP ribose polymerase
 Baseline PSA doubling time was derived for each patient as the natural log 2 divided by the sum of the fixed and random slopes of the random coefficient linear model between natural log of PSA and time of PSA measurement (in months). Patients with at least 3 PSA values prior to and at the time of screening were included in the model.

Patients with PSADT stable, non-increasing or decreasing are included in the category '>9 months'.

Output ID: T-1 2021-06-01 10:57

\FSISTGENISAAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGMIt-demo.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 2
Baseline and Other Subgroup Characteristics (PFS-Full Analysis Set)

	Lu-PSMA-617 +BSC/BSoC (N=385) n (%)	BSC/BSoC only (N=196) n (%)	Overall (N=581) n (%)
Region			
n	385	196	581
North America	249 (64.7)	130 (66.3)	379 (65.2)
Europe	136 (35.3)	66 (33.7)	202 (34.8)
Baseline PSA Doubling Time			
n (missing)	182 (203)	82 (114)	264 (317)
>0 - <=9 months	175 (96.2)	73 (89.0)	248 (93.9)
>9 months	7 (3.8)	9 (11.0)	16 (6.1)
Baseline PSA			
n	385	196	581
<=76.0 (ng/mL)	177 (46.0)	91 (46.4)	268 (46.1)
>76.0 (ng/mL)	208 (54.0)	105 (53.6)	313 (53.9)
Number of prior NAADs			
n	385	196	581
1	209 (54.3)	97 (49.5)	306 (52.7)
>=2	176 (45.7)	99 (50.5)	275 (47.3)
Number of prior immunotherapies			
n	385	196	581
0	306 (79.5)	146 (74.5)	452 (77.8)
>=1	79 (20.5)	50 (25.5)	129 (22.2)
Number of prior taxane-containing regimens			
n (missing)	358 (27)	187 (9)	545 (36)
1	224 (62.6)	110 (58.8)	334 (61.3)
>=2	134 (37.4)	77 (41.2)	211 (38.7)
Number of prior non-taxane cytotoxic chemotherapeutic therapies			
n	385	196	581
0	347 (90.1)	183 (93.4)	530 (91.2)
>=1	38 (9.9)	13 (6.6)	51 (8.8)
Prior use of bone sparing agents			
n	385	196	581
Yes	66 (17.1)	35 (17.9)	101 (17.4)
No	319 (82.9)	161 (82.1)	480 (82.6)

PSA: Prostate-specific antigen, NAAD: Novel androgen axis drugs, PARP: Poly ADP ribose polymerase
 Baseline PSA doubling time was derived for each patient as the natural log 2 divided by the sum of the fixed and random slopes of the random coefficient linear model between natural log of PSA and time of PSA measurement (in months). Patients with at least 3 PSA values prior to and at the time of screening were included in the model.

Patients with PSADT stable, non-increasing or decreasing are included in the category '>9 months'.

Output ID: T-2 2021-06-01 10:58

\FS\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-demo.sas
 Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 2
Baseline and Other Subgroup Characteristics (PFS-Full Analysis Set)

	Lu-PSMA-617 +BSC/BSoC (N=385) n (%)	BSC/BSoC only (N=196) n (%)	Overall (N=581) n (%)
Prior use of 223-Radium			
n	385	196	581
Yes	63 (16.4)	36 (18.4)	99 (17.0)
No	322 (83.6)	160 (81.6)	482 (83.0)
Prior use of PARP inhibitors			
n	385	196	581
Yes	24 (6.2)	11 (5.6)	35 (6.0)
No	361 (93.8)	185 (94.4)	546 (94.0)
Concurrent use of NAADs as part of BSC/BSoC treatment			
n	385	196	581
Yes	193 (50.1)	124 (63.3)	317 (54.6)
No	192 (49.9)	72 (36.7)	264 (45.4)
Concurrent use of radiation therapy as part of BSC/BSoC treatment			
n	385	196	581
Yes	49 (12.7)	28 (14.3)	77 (13.3)
No	336 (87.3)	168 (85.7)	504 (86.7)
Concurrent use of bone sparing agents as part of BSC/BSoC treatment			
n	385	196	581
Yes	175 (45.5)	96 (49.0)	271 (46.6)
No	210 (54.5)	100 (51.0)	310 (53.4)

PSA: Prostate-specific antigen, NAAD: Novel androgen axis drugs, PARP: Poly ADP ribose polymerase
 Baseline PSA doubling time was derived for each patient as the natural log 2 divided by the sum of the fixed and random slopes of the random coefficient linear model between natural log of PSA and time of PSA measurement (in months). Patients with at least 3 PSA values prior to and at the time of screening were included in the model.

Patients with PSADT stable, non-increasing or decreasing are included in the category '>9 months'.

Output ID: T-2 2021-06-01 10:58

\FSISTGENISAAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGMIt-demo.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 3
Overall Survival by Region (Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)
North America	n/N (%)	247/393 (62.8)	137/209 (65.6)
	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	9.0 [7.8, 10.0]	4.7 [3.7, 6.2]
	Median OS [95% CI]	15.5 [14.1, 17.2]	12.5 [10.2, 14.4]
	75th percentile [95% CI]	26.8 [23.9, NE]	20.0 [17.9, 25.4]
	OS rates (%)		
	6 months (SE) [95% CI]	86.7 (1.72) [82.9, 89.7]	70.2 (3.38) [63.0, 76.2]
	12 months (SE) [95% CI]	63.2 (2.45) [58.1, 67.7]	52.0 (3.73) [44.4, 59.0]
	18 months (SE) [95% CI]	43.3 (2.59) [38.2, 48.3]	31.7 (3.56) [24.9, 38.7]
	Hazard Ratio ^a [95% CI]		0.66 [0.53, 0.82]
	Follow-up time (months)		
	Median [95% CI]	21.0 [20.2, 22.1]	20.0 [18.6, 21.9]
	Minimum-Maximum	0.0 - 31.5	0.0 - 27.1
Europe	n/N (%)	96/158 (60.8)	50/71 (70.4)
	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	8.6 [7.5, 10.0]	6.3 [4.3, 7.0]
	Median OS [95% CI]	14.8 [11.9, 18.5]	9.9 [7.3, 12.3]
	75th percentile [95% CI]	NE [21.0, NE]	16.3 [13.5, NE]
	OS rates (%)		
	6 months (SE) [95% CI]	86.6 (2.73) [80.2, 91.0]	75.4 (5.34) [63.1, 84.2]
	12 months (SE) [95% CI]	58.0 (3.97) [49.8, 65.3]	41.2 (6.14) [29.1, 52.8]
	18 months (SE) [95% CI]	42.3 (4.05) [34.3, 50.0]	20.8 (5.30) [11.6, 31.9]
	Hazard Ratio ^a [95% CI]		0.53 [0.37, 0.75]
	Follow-up time (months)		
	Median [95% CI]	19.6 [18.2, 20.1]	18.0 [17.2, 19.6]
	Minimum-Maximum	0.9 - 23.9	0.1 - 22.8

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (≤ 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-3 2021-06-01 10:58

\FS\STGENISAAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 4
Overall Survival by PSA Doubling Time at Baseline (Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)
PSADT:	n/N (%)	158/255 (62.0)	80/120 (66.7)
>0 - <=9 months	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	9.0 [7.8, 10.5]	4.3 [3.4, 6.3]
	Median OS [95% CI]	16.2 [14.2, 18.1]	11.3 [8.5, 13.6]
	75th percentile [95% CI]	23.9 [22.1, 27.6]	19.8 [16.8, NE]
OS rates (%)			
	6 months (SE) [95% CI]	88.1 (2.03) [83.5, 91.6]	69.2 (4.46) [59.5, 77.0]
	12 months (SE) [95% CI]	65.3 (3.01) [59.1, 70.8]	47.2 (4.86) [37.4, 56.3]
	18 months (SE) [95% CI]	44.9 (3.25) [38.4, 51.1]	29.6 (4.60) [20.9, 38.8]
Hazard Ratio ^a [95% CI]		0.59 [0.45, 0.78]	
Follow-up time (months)			
	Median [95% CI]	19.9 [19.4, 21.4]	19.8 [17.5, 21.2]
	Minimum-Maximum	0.0 - 27.6	0.0 - 27.1
PSADT:	n/N (%)	10/14 (71.4)	6/11 (54.5)
>9 months	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	9.7 [1.6, 17.9]	6.2 [2.5, 16.3]
	Median OS [95% CI]	18.2 [5.9, 25.2]	16.3 [4.7, NE]
	75th percentile [95% CI]	25.2 [17.9, NE]	NE [16.0, NE]
OS rates (%)			
	6 months (SE) [95% CI]	78.6 (10.97) [47.2, 92.5]	81.8 (11.63) [44.7, 95.1]
	12 months (SE) [95% CI]	64.3 (12.81) [34.3, 83.3]	71.6 (13.97) [35.0, 89.9]
	18 months (SE) [95% CI]	50.0 (13.36) [22.9, 72.2]	40.9 (15.59) [12.7, 67.9]
Hazard Ratio ^a [95% CI]		0.90 [0.32, 2.54]	
Follow-up time (months)			
	Median [95% CI]	23.9 [18.2, 27.2]	22.6 [5.5, 23.5]
	Minimum-Maximum	1.6 - 27.2	2.5 - 23.5

PSADT: Prostate-specific antigen doubling time

Patients with PSADT stable, non-increasing or decreasing are included in the category '>9 months'.

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-4 2021-06-01 10:58

\\\FS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rfps-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 5
Overall Survival by Baseline Prostate-Specific Antigen (Full Analysis Set)

	Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)	
BPSA: <=76.0 (ng/mL)	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] Median OS [95% CI] 75th percentile [95% CI]	149/275 (54.2) 11.6 [9.9, 12.6] 19.2 [17.1, 20.9] NE [25.5, NE]	81/141 (57.4) 8.6 [5.7, 11.3] 15.2 [12.9, 17.5] 23.0 [20.3, NE]
OS rates (%)			
6 months (SE) [95% CI]	92.3 (1.61) [88.5, 94.9]	81.3 (3.52) [73.2, 87.2]	
12 months (SE) [95% CI]	73.5 (2.67) [67.9, 78.4]	65.9 (4.33) [56.7, 73.7]	
18 months (SE) [95% CI]	53.5 (3.10) [47.2, 59.3]	40.2 (4.60) [31.1, 49.0]	
Hazard Ratio ^a [95% CI]		0.67 [0.51, 0.89]	
Follow-up time (months)			
Median [95% CI]	20.5 [19.8, 21.9]	20.3 [18.6, 21.9]	
Minimum-Maximum	0.0 - 31.4	0.0 - 27.1	
BPSA: >76.0 (ng/mL)	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] Median OS [95% CI] 75th percentile [95% CI]	194/276 (70.3) 7.2 [6.4, 7.9] 11.8 [10.5, 14.0] 21.8 [19.4, NE]	106/139 (76.3) 3.9 [2.9, 5.0] 8.3 [6.5, 9.9] 15.1 [11.5, 18.9]
OS rates (%)			
6 months (SE) [95% CI]	80.9 (2.38) [75.7, 85.1]	61.9 (4.34) [52.8, 69.7]	
12 months (SE) [95% CI]	49.7 (3.04) [43.6, 55.5]	32.7 (4.22) [24.6, 41.0]	
18 months (SE) [95% CI]	32.4 (2.94) [26.7, 38.2]	17.7 (3.56) [11.4, 25.2]	
Hazard Ratio ^a [95% CI]		0.55 [0.43, 0.70]	
Follow-up time (months)			
Median [95% CI]	20.0 [18.6, 21.0]	18.3 [17.4, 20.0]	
Minimum-Maximum	0.6 - 31.5	0.1 - 25.4	

BPSA: Baseline prostate-specific antigen

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-5 2021-06-01 10:58

\\\FSISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISIONSCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 6
Overall Survival by Number of prior NAADs (Full Analysis Set)

	Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)
#PNAAD: 1		
n/N (%)	182/296 (61.5)	83/130 (63.8)
Kaplan-Meier estimates (months)		
25th percentile [95% CI]	9.1 [7.9, 10.2]	6.3 [4.0, 8.3]
Median OS [95% CI]	15.3 [13.8, 17.1]	13.5 [10.6, 15.2]
75th percentile [95% CI]	27.6 [25.5, NE]	19.8 [16.5, NE]
OS rates (%)		
6 months (SE) [95% CI]	86.7 (1.98) [82.3, 90.1]	76.6 (3.94) [67.8, 83.3]
12 months (SE) [95% CI]	61.9 (2.85) [56.1, 67.2]	55.7 (4.70) [46.1, 64.4]
18 months (SE) [95% CI]	42.4 (2.97) [36.6, 48.2]	29.0 (4.45) [20.6, 37.9]
Hazard Ratio ^a [95% CI]		0.74 [0.57, 0.97]
Follow-up time (months)		
Median [95% CI]	20.3 [19.6, 21.4]	18.6 [17.4, 19.8]
Minimum-Maximum	0.0 - 28.7	0.0 - 27.1
#PNAAD: >=2		
n/N (%)	161/255 (63.1)	104/150 (69.3)
Kaplan-Meier estimates (months)		
25th percentile [95% CI]	8.4 [7.3, 9.6]	4.6 [3.7, 6.0]
Median OS [95% CI]	15.3 [13.2, 17.9]	10.1 [8.5, 12.3]
75th percentile [95% CI]	23.9 [22.1, NE]	20.0 [15.8, 25.4]
OS rates (%)		
6 months (SE) [95% CI]	86.5 (2.15) [81.7, 90.2]	67.1 (4.07) [58.5, 74.4]
12 months (SE) [95% CI]	61.4 (3.07) [55.1, 67.1]	43.3 (4.33) [34.7, 51.6]
18 months (SE) [95% CI]	43.7 (3.22) [37.3, 49.9]	28.6 (4.03) [21.0, 36.7]
Hazard Ratio ^a [95% CI]		0.52 [0.41, 0.67]
Follow-up time (months)		
Median [95% CI]	20.2 [19.6, 21.5]	20.3 [19.3, 21.7]
Minimum-Maximum	0.6 - 31.5	0.1 - 26.6

#PNAADs: Number of prior novel androgen axis drugs

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-6 2021-06-01 10:59

\NFS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISIONSCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 7
Overall Survival by Number of prior immunotherapies (Full Analysis Set)

	Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)
#PRIMM: 0	n/N (%) 255/414 (61.6) Kaplan-Meier estimates (months) 25th percentile [95% CI] 9.0 [7.8, 9.8] Median OS [95% CI] 15.2 [14.2, 17.1] 75th percentile [95% CI] 26.8 [23.9, NE] OS rates (%) 6 months (SE) [95% CI] 85.2 (1.75) [81.3, 88.2] 12 months (SE) [95% CI] 61.9 (2.40) [57.0, 66.4] 18 months (SE) [95% CI] 42.5 (2.52) [37.6, 47.4] Hazard Ratio ^a [95% CI] 0.58 [0.47, 0.73] Follow-up time (months) Median [95% CI] 20.2 [19.6, 20.7] Minimum-Maximum 0.0 - 31.5	134/200 (67.0) 5.3 [4.0, 6.5] 10.7 [9.3, 13.0] 18.5 [15.6, 20.3] 71.6 (3.41) [64.3, 77.6] 46.7 (3.82) [39.0, 53.9] 25.6 (3.42) [19.2, 32.4] 19.4 [18.0, 20.0] 0.0 - 27.1
#PRIMM: >=1	n/N (%) 88/137 (64.2) Kaplan-Meier estimates (months) 25th percentile [95% CI] 8.4 [7.3, 10.3] Median OS [95% CI] 15.3 [12.4, 18.5] 75th percentile [95% CI] 25.0 [21.4, NE] OS rates (%) 6 months (SE) [95% CI] 91.1 (2.45) [84.9, 94.9] 12 months (SE) [95% CI] 61.1 (4.22) [52.3, 68.8] 18 months (SE) [95% CI] 44.4 (4.39) [35.7, 52.8] Hazard Ratio ^a [95% CI] 0.72 [0.51, 1.01] Follow-up time (months) Median [95% CI] 21.4 [19.6, 23.9] Minimum-Maximum 0.6 - 28.7	53/80 (66.3) 5.1 [3.7, 8.9] 12.5 [9.2, 17.5] 23.0 [18.0, 25.5] 71.4 (5.28) [59.6, 80.3] 54.6 (5.86) [42.5, 65.2] 36.5 (5.85) [25.2, 47.8] 21.4 [18.0, 22.5] 0.0 - 25.5

#PRIMM: Number of prior immunotherapies

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-7 2021-06-01 10:59

\NFSISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISIONSCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 8
Overall Survival by Number of prior taxane-containing regimens (Full Analysis Set)

	Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)
#PTAX: 1	n/N (%) 206/342 (60.2) Kaplan-Meier estimates (months) 25th percentile [95% CI] 9.7 [8.4, 10.4] Median OS [95% CI] 16.2 [14.7, 18.1] 75th percentile [95% CI] NE [24.7, NE] OS rates (%) 6 months (SE) [95% CI] 87.3 (1.80) [83.3, 90.5] 12 months (SE) [95% CI] 65.1 (2.59) [59.8, 69.9] 18 months (SE) [95% CI] 45.3 (2.78) [39.8, 50.7] Hazard Ratio ^a [95% CI] 0.59 [0.46, 0.75] Follow-up time (months) Median [95% CI] 21.4 [20.2, 21.9] Minimum-Maximum 0.6 - 31.5	108/165 (65.5) 5.3 [4.0, 7.0] 11.8 [9.8, 14.4] 20.0 [17.5, NE] 73.5 (3.64) [65.6, 79.9] 49.9 (4.20) [41.4, 57.8] 31.4 (3.97) [23.8, 39.2] 20.3 [19.3, 21.9] 0.0 - 27.1
#PTAX: >=2	n/N (%) 113/170 (66.5) Kaplan-Meier estimates (months) 25th percentile [95% CI] 7.8 [6.6, 9.1] Median OS [95% CI] 13.6 [11.5, 15.4] 75th percentile [95% CI] 20.9 [19.4, NE] OS rates (%) 6 months (SE) [95% CI] 85.1 (2.75) [78.8, 89.7] 12 months (SE) [95% CI] 54.8 (3.87) [46.9, 62.0] 18 months (SE) [95% CI] 37.8 (3.88) [30.2, 45.3] Hazard Ratio ^a [95% CI] 0.73 [0.53, 0.99] Follow-up time (months) Median [95% CI] 19.4 [17.7, 19.9] Minimum-Maximum 0.0 - 28.4	70/99 (70.7) 5.1 [3.8, 6.5] 10.6 [8.3, 13.5] 18.0 [14.8, 25.5] 67.8 (4.92) [57.1, 76.4] 46.7 (5.26) [36.1, 56.6] 26.2 (4.78) [17.4, 35.9] 18.3 [17.2, 21.2] 0.1 - 25.5

#PTAX: Number of prior taxane-containing regimens

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-8 2021-06-01 10:59

\NFS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISIONSCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 9
Overall Survival by Number of prior non-taxane cytotoxic chemotherapeutic therapies (Full Analysis Set)

	Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)
#PNTAX: 0	n/N (%) 299/485 (61.6) Kaplan-Meier estimates (months) 25th percentile [95% CI] 8.7 [7.8, 9.5] Median OS [95% CI] 15.2 [14.2, 17.0] 75th percentile [95% CI] 25.5 [23.6, NE]	167/252 (66.3) 5.2 [4.1, 6.3] 11.3 [9.5, 13.5] 19.8 [17.3, 23.0]
OS rates (%)	6 months (SE) [95% CI] 86.7 (1.55) [83.3, 89.4] 12 months (SE) [95% CI] 61.9 (2.22) [57.4, 66.1] 18 months (SE) [95% CI] 43.2 (2.33) [38.6, 47.7]	71.5 (3.02) [65.1, 76.9] 49.3 (3.38) [42.5, 55.7] 29.2 (3.16) [23.2, 35.5]
Hazard Ratio ^a [95% CI]	0.61 [0.50, 0.74]	
Follow-up time (months)	Median [95% CI] 20.2 [19.7, 21.0] Minimum-Maximum 0.0 - 31.5	19.4 [18.0, 20.6] 0.0 - 27.1
#PNTAX: >=1	n/N (%) 44/66 (66.7) Kaplan-Meier estimates (months) 25th percentile [95% CI] 9.7 [6.4, 11.0] Median OS [95% CI] 16.2 [11.3, 18.2] 75th percentile [95% CI] 26.8 [18.3, 27.6]	20/28 (71.4) 4.6 [1.2, 10.7] 11.8 [4.6, 16.5] 20.0 [12.3, 25.4]
OS rates (%)	6 months (SE) [95% CI] 86.3 (4.24) [75.3, 92.6] 12 months (SE) [95% CI] 59.7 (6.12) [46.7, 70.5] 18 months (SE) [95% CI] 41.8 (6.25) [29.5, 53.6]	71.6 (9.13) [49.4, 85.4] 46.3 (10.19) [26.0, 64.4] 25.3 (8.90) [10.3, 43.5]
Hazard Ratio ^a [95% CI]	0.71 [0.42, 1.23]	
Follow-up time (months)	Median [95% CI] 20.5 [18.6, 25.5] Minimum-Maximum 1.3 - 27.6	24.5 [20.0, NE] 0.1 - 25.4

#PNTAX: Number of prior non-taxane cytotoxic chemotherapeutic therapies

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-9 2021-06-01 10:59

\NFSISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISIONSCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 10
Overall Survival by Prior use of Bone Sparing Agents (Full Analysis Set)

	Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)	
Prior BSA:	n/N (%)	66/99 (66.7)	43/57 (75.4)
Yes	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	8.3 [5.7, 10.2]	4.2 [3.4, 7.2]
	Median OS [95% CI]	14.8 [12.1, 16.9]	10.2 [6.2, 12.5]
	75th percentile [95% CI]	24.7 [19.9, NE]	19.0 [12.5, 25.5]
	OS rates (%)		
	6 months (SE) [95% CI]	83.6 (3.74) [74.7, 89.6]	65.9 (6.52) [51.5, 77.0]
	12 months (SE) [95% CI]	61.5 (4.98) [51.0, 70.4]	40.7 (6.81) [27.4, 53.6]
	18 months (SE) [95% CI]	39.7 (5.15) [29.7, 49.6]	26.5 (6.22) [15.3, 39.1]
	Hazard Ratio ^a [95% CI]	0.54 [0.36, 0.80]	
	Follow-up time (months)		
	Median [95% CI]	20.1 [18.9, 22.2]	22.0 [19.6, 26.6]
	Minimum-Maximum	0.6 - 31.5	0.1 - 26.6
Prior BSA:	n/N (%)	277/452 (61.3)	144/223 (64.6)
No	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	9.0 [8.0, 9.9]	5.6 [4.3, 6.8]
	Median OS [95% CI]	15.4 [14.1, 17.4]	12.3 [9.8, 14.2]
	75th percentile [95% CI]	26.8 [23.9, NE]	20.0 [16.8, NE]
	OS rates (%)		
	6 months (SE) [95% CI]	87.3 (1.57) [83.8, 90.0]	73.0 (3.17) [66.2, 78.7]
	12 months (SE) [95% CI]	61.7 (2.30) [57.0, 66.1]	51.3 (3.62) [44.0, 58.1]
	18 months (SE) [95% CI]	43.7 (2.41) [38.9, 48.3]	29.5 (3.39) [23.0, 36.2]
	Hazard Ratio ^a [95% CI]	0.64 [0.52, 0.79]	
	Follow-up time (months)		
	Median [95% CI]	20.4 [19.7, 21.4]	19.3 [18.0, 20.6]
	Minimum-Maximum	0.0 - 31.4	0.0 - 27.1

BSA: Bone sparing agents

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-10 2021-06-01 10:59

\NFS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISIONSCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 11
Overall Survival by Prior use of 223-Radium (Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)
Prior Radium:	n/N (%)	59/97 (60.8)	31/48 (64.6)
Yes	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	8.3 [6.6, 10.5]	5.2 [3.0, 8.6]
	Median OS [95% CI]	13.9 [11.6, 19.4]	12.4 [8.0, 16.0]
	75th percentile [95% CI]	NE [20.5, NE]	20.3 [15.2, NE]
	OS rates (%)		
	6 months (SE) [95% CI]	86.4 (3.51) [77.7, 91.9]	72.7 (6.71) [57.0, 83.5]
	12 months (SE) [95% CI]	56.7 (5.10) [46.1, 65.9]	54.5 (7.51) [38.8, 67.8]
	18 months (SE) [95% CI]	43.1 (5.18) [32.8, 52.9]	33.7 (7.18) [20.2, 47.7]
	Hazard Ratio ^a [95% CI]	0.73 [0.47, 1.13]	
	Follow-up time (months)		
	Median [95% CI]	20.0 [17.5, 22.1]	17.4 [16.2, 20.3]
	Minimum-Maximum	1.0 - 31.4	0.1 - 22.6
Prior Radium:	n/N (%)	284/454 (62.6)	156/232 (67.2)
No	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	9.0 [7.9, 9.8]	5.1 [4.0, 6.5]
	Median OS [95% CI]	15.7 [14.5, 17.2]	11.0 [9.4, 13.5]
	75th percentile [95% CI]	26.8 [23.6, NE]	19.8 [16.7, 22.3]
	OS rates (%)		
	6 months (SE) [95% CI]	86.7 (1.60) [83.2, 89.5]	71.3 (3.17) [64.5, 77.0]
	12 months (SE) [95% CI]	62.7 (2.29) [58.1, 67.0]	47.8 (3.54) [40.7, 54.5]
	18 months (SE) [95% CI]	43.1 (2.40) [38.4, 47.8]	27.9 (3.26) [21.7, 34.4]
	Hazard Ratio ^a [95% CI]	0.60 [0.49, 0.73]	
	Follow-up time (months)		
	Median [95% CI]	20.5 [19.7, 21.4]	19.8 [18.6, 21.4]
	Minimum-Maximum	0.0 - 31.5	0.0 - 27.1

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (≤ 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-11 2021-06-01 10:59

\\\FS\STGENISAAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 12
Overall Survival by Prior use of PARP inhibitors (Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)
Prior PARP:	n/N (%)	22/30 (73.3)	11/16 (68.8)
Yes	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	7.5 [2.9, 9.9]	4.5 [1.8, 9.1]
	Median OS [95% CI]	12.3 [8.4, 17.6]	9.1 [3.7, 18.9]
	75th percentile [95% CI]	22.1 [14.5, NE]	18.9 [9.1, 20.9]
	OS rates (%)		
	6 months (SE) [95% CI]	86.7 (6.21) [68.3, 94.8]	62.3 (13.37) [31.7, 82.4]
	12 months (SE) [95% CI]	56.7 (9.05) [37.3, 72.1]	46.8 (13.84) [19.6, 70.2]
	18 months (SE) [95% CI]	26.7 (8.58) [11.9, 44.0]	31.2 (12.89) [9.7, 55.9]
	Hazard Ratio ^a [95% CI]	0.60 [0.28, 1.28]	
	Follow-up time (months)		
	Median [95% CI]	18.6 [17.6, 23.7]	20.8 [20.0, NE]
	Minimum-Maximum	1.3 - 23.7	0.1 - 20.9
Prior PARP:	n/N (%)	321/521 (61.6)	176/264 (66.7)
No	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	9.0 [8.0, 9.8]	5.2 [4.2, 6.5]
	Median OS [95% CI]	15.4 [14.2, 17.1]	11.5 [9.9, 13.5]
	75th percentile [95% CI]	26.8 [24.7, NE]	20.0 [16.7, 23.0]
	OS rates (%)		
	6 months (SE) [95% CI]	86.6 (1.50) [83.4, 89.3]	72.0 (2.93) [65.8, 77.3]
	12 months (SE) [95% CI]	62.0 (2.15) [57.6, 66.0]	49.1 (3.30) [42.5, 55.4]
	18 months (SE) [95% CI]	44.0 (2.25) [39.5, 48.3]	28.7 (3.06) [22.9, 34.8]
	Hazard Ratio ^a [95% CI]	0.62 [0.51, 0.75]	
	Follow-up time (months)		
	Median [95% CI]	20.3 [19.8, 21.4]	19.6 [18.2, 21.1]
	Minimum-Maximum	0.0 - 31.5	0.0 - 27.1

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (≤ 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-12 2021-06-01 10:59

\FS\STGENISAAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 13
Overall Survival by Concurrent use of NAADs as part of BSC/BSoC treatment (Full Analysis Set)

	Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)	
Concur NAAD:	n/N (%)	166/289 (57.4)	110/166 (66.3)
Yes	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	10.3 [9.2, 12.0]	6.2 [4.0, 8.0]
	Median OS [95% CI]	17.8 [15.7, 20.6]	13.3 [10.7, 15.1]
	75th percentile [95% CI]	27.6 [25.0, NE]	20.3 [17.5, 25.5]
	OS rates (%)		
	6 months (SE) [95% CI]	89.2 (1.83) [85.1, 92.3]	75.8 (3.46) [68.3, 81.9]
	12 months (SE) [95% CI]	70.1 (2.70) [64.4, 75.0]	55.5 (4.07) [47.2, 63.0]
	18 months (SE) [95% CI]	49.9 (3.03) [43.8, 55.6]	32.2 (3.96) [24.6, 40.0]
	Hazard Ratio ^a [95% CI]	0.55 [0.43, 0.70]	
	Follow-up time (months)		
	Median [95% CI]	20.3 [19.6, 21.4]	19.6 [17.7, 20.8]
	Minimum-Maximum	1.3 - 31.5	0.1 - 27.1
Concur NAAD:	n/N (%)	177/262 (67.6)	77/114 (67.5)
No	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	7.6 [6.9, 8.4]	4.7 [3.7, 5.8]
	Median OS [95% CI]	12.4 [11.3, 14.3]	9.5 [6.8, 11.1]
	75th percentile [95% CI]	26.8 [19.9, NE]	16.7 [13.5, 25.4]
	OS rates (%)		
	6 months (SE) [95% CI]	83.8 (2.30) [78.7, 87.7]	64.5 (4.91) [54.0, 73.2]
	12 months (SE) [95% CI]	52.2 (3.13) [45.9, 58.1]	38.7 (5.03) [28.9, 48.4]
	18 months (SE) [95% CI]	35.3 (3.08) [29.3, 41.3]	23.3 (4.41) [15.3, 32.4]
	Hazard Ratio ^a [95% CI]	0.70 [0.53, 0.93]	
	Follow-up time (months)		
	Median [95% CI]	20.4 [18.9, 21.4]	20.0 [18.3, 22.6]
	Minimum-Maximum	0.0 - 28.4	0.0 - 25.4

Concur NAAD: Concurrent use of NAADs

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-13 2021-06-01 11:00

\NFSISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISIONSCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14
Overall Survival by Concurrent use of radiation therapy as part of BSC/BSoC treatment (Full Analysis Set)

	Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)	
Concur	n/N (%)	51/75 (68.0)	22/31 (71.0)
RT:	Kaplan-Meier estimates (months)		
Yes	25th percentile [95% CI] Median OS [95% CI] 75th percentile [95% CI]	11.0 [7.3, 11.9] 14.7 [12.9, 18.2] NE [19.3, NE]	5.1 [3.4, 7.7] 9.7 [6.5, 16.3] 20.9 [14.7, NE]
	OS rates (%)		
	6 months (SE) [95% CI] 12 months (SE) [95% CI] 18 months (SE) [95% CI]	89.3 (3.56) [79.8, 94.5] 65.3 (5.50) [53.4, 74.9] 40.5 (5.74) [29.3, 51.5]	73.3 (8.07) [53.7, 85.7] 43.3 (9.05) [25.6, 59.9] 31.8 (8.77) [15.9, 48.9]
	Hazard Ratio ^a [95% CI]	0.78 [0.46, 1.32]	
	Follow-up time (months)		
	Median [95% CI] Minimum-Maximum	22.6 [20.2, 25.7] 2.2 - 28.7	20.8 [15.4, 22.8] 0.8 - 23.2
Concur	n/N (%)	292/476 (61.3)	165/249 (66.3)
RT:	Kaplan-Meier estimates (months)		
No	25th percentile [95% CI] Median OS [95% CI] 75th percentile [95% CI]	8.6 [7.7, 9.3] 15.4 [14.1, 16.9] 25.5 [23.9, NE]	5.2 [4.0, 6.5] 11.8 [10.1, 13.5] 19.0 [16.8, 23.0]
	OS rates (%)		
	6 months (SE) [95% CI] 12 months (SE) [95% CI] 18 months (SE) [95% CI]	86.2 (1.59) [82.8, 89.0] 61.1 (2.26) [56.5, 65.4] 43.5 (2.36) [38.8, 48.1]	71.3 (3.06) [64.8, 76.8] 49.8 (3.43) [42.9, 56.3] 28.3 (3.17) [22.3, 34.7]
	Hazard Ratio ^a [95% CI]	0.60 [0.49, 0.73]	
	Follow-up time (months)		
	Median [95% CI] Minimum-Maximum	20.0 [19.5, 20.6] 0.0 - 31.5	19.8 [18.2, 20.6] 0.0 - 27.1

Concur RT: Concurrent use of radiation therapy

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-14 2021-06-01 11:00

\NFS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISIONSCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.1.11

Analysis of overall survival using stratified log-rank test and cox regression model in the first 750 randomized (Full analysis set)

	Lu-PSMA-617+ BSC/BSoC (N=497)	BSC/BSoC only (N=253)
Overall Survival (OS), n (%)		
Deaths	313 (63.0)	166 (65.6)
Censored	184 (37.0)	87 (34.4)
Reasons censored, n (%)		
Alive ^a	165 (33.2)	50 (19.8)
Lost to follow-up ^b	4 (0.8)	5 (2.0)
Withdrew consent ^c	15 (3.0)	32 (12.6)
Kaplan-Meier estimates (months)		
25th percentile [95% CI]	9.0 [7.9, 9.8]	5.3 [4.1, 6.7]
Median OS [95% CI]	15.4 [14.2, 17.1]	12.3 [10.1, 14.2]
75th percentile [95% CI]	26.8 [23.9, NE]	20.0 [17.5, 25.4]
OS rates (%)		
6 months (SE) [95% CI]	87.4 (1.50) [84.1, 90.0]	72.2 (3.01) [65.8, 77.6]
12 months (SE) [95% CI]	62.2 (2.20) [57.7, 66.3]	50.7 (3.39) [43.9, 57.2]
18 months (SE) [95% CI]	43.5 (2.28) [39.0, 48.0]	30.4 (3.18) [24.3, 36.7]
Hazard Ratio (Stratified Cox PH model) ^{d e}		
95% CI	0.63 [0.52, 0.77]	
Stratified Log-rank Test one-sided p-value ^e		<.001
Follow-up time (months) ^f		
Median [95% CI]	20.7 [20.1, 21.5]	19.8 [18.7, 21.2]
Minimum-Maximum	0.0 - 31.5	0.0 - 27.1

^a Patients without event and still on study at data cut-off date.^b Patients who discontinued the study for reasons other than withdrew consent.^c Patients who withdrew consent from the study.^d Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC.^e Both Cox PH model and Log-rank test are stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2); and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). IRT data for stratification are used.^f Follow-up time = (Date of event or censoring - randomization date + 1)/30,4375 (months) censoring for deaths.

Output ID: T-14-2-1-11 2021-06-01 11:03

\WFS\STGENISAAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-750.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.1.12
Overall survival by cycles of Lu-PSMA-617 (FAS safety set)

Number of cycles		Lu-PSMA-617+ BSC/BSoC (N=529)
1-3	n/N (%)	153/171 (89.5)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	5.0 [4.0, 5.7]
	Median OS [95% CI]	8.2 [7.0, 9.1]
	75th percentile [95% CI]	12.9 [11.2, 15.1]
	OS rates (%)	
	6 months (SE) [95% CI]	65.6 (3.70) [57.8, 72.3]
	12 months (SE) [95% CI]	27.8 (3.52) [21.2, 34.9]
	18 months (SE) [95% CI]	10.0 (2.41) [5.9, 15.3]
4	n/N (%)	52/69 (75.4)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	8.5 [7.4, 9.3]
	Median OS [95% CI]	11.0 [9.6, 12.6]
	75th percentile [95% CI]	17.0 [13.9, NE]
	OS rates (%)	
	6 months (SE) [95% CI]	98.6 (1.44) [90.2, 99.8]
	12 months (SE) [95% CI]	41.4 (5.97) [29.6, 52.7]
	18 months (SE) [95% CI]	24.4 (5.33) [14.8, 35.3]
1-4	n/N (%)	205/240 (85.4)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	6.1 [5.3, 6.9]
	Median OS [95% CI]	9.1 [8.3, 10.0]
	75th percentile [95% CI]	14.2 [12.3, 15.4]
	OS rates (%)	
	6 months (SE) [95% CI]	75.3 (2.82) [69.2, 80.3]
	12 months (SE) [95% CI]	31.8 (3.07) [25.9, 37.9]
	18 months (SE) [95% CI]	14.0 (2.36) [9.8, 19.0]
5-6	n/N (%)	116/289 (40.1)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	16.2 [14.7, 17.7]
	Median OS [95% CI]	24.7 [21.3, 27.6]
	75th percentile [95% CI]	NE [27.6, NE]
	OS rates (%)	
	6 months (SE) [95% CI]	100 (0.00) [100, 100]
	12 months (SE) [95% CI]	89.6 (1.80) [85.4, 92.6]
	18 months (SE) [95% CI]	69.3 (2.82) [63.4, 74.4]

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

Output ID: T-14-2-1-12 2021-06-01 11:04

\FS\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\T

LFPGMt-eff-os-rpfs-cycle.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.1.13

OS events and reasons for censoring in patients who withdrew consent to BSC/BSoC in patients randomized prior to 5 Mar 2019 (Full analysis set)

	Lu-PSMA-617+ BSC/BSoC (N=166) n (%)	BSC/BSoC only (N=84) n (%)
Patients that withdrew consent (treatment)	30 (18.1)	33 (39.3)
Overall Survival (OS)		
Deaths	19 (63.3)	20 (60.6)
Censored	11 (36.7)	13 (39.4)
Reasons censored		
Alive ^a	7 (23.3)	2 (6.1)
Lost to follow-up ^b	0	0
Withdrew consent ^c	4 (13.3)	11 (33.3)

^a Patients without event and still on study at data cut-off date.^b Patients who discontinued the study for reasons other than withdrew consent.^c Patients who withdrew consent from the study.

Output ID: T-14-2-1-13 2021-06-11 12:28

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-eff-os-rpfs-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.1.14
OS events and reasons for censoring in patients who withdrew consent to BSC/BSoC (PFS Full analysis set)

	Lu-PSMA-617+ BSC/BSoC (N=385) n (%)	BSC/BSoC only (N=196) n (%)
Patients that withdrew consent (treatment)	23 (6.0)	49 (25.0)
Overall Survival (OS)		
Deaths	14 (60.9)	28 (57.1)
Censored	9 (39.1)	21 (42.9)
Reasons censored		
Alive ^a	6 (26.1)	6 (12.2)
Lost to follow-up ^b	0	0
Withdrew consent ^c	3 (13.0)	15 (30.6)

^a Patients without event and still on study at data cut-off date.^b Patients who discontinued the study for reasons other than withdrew consent.^c Patients who withdrew consent from the study.

Output ID: T-14-2-1-14 2021-06-11 12:28

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-eff-os-rpfs-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.1.15
OS events and reasons for censoring in patients who withdrew consent to BSC/BSoC (Full analysis set)

	Lu-PSMA-617+ BSC/BSoC (N=551) n (%)	BSC/BSoC only (N=280) n (%)
Patients that withdrew consent (treatment)	53 (9.6)	82 (29.3)
Overall Survival (OS)		
Deaths	33 (62.3)	48 (58.5)
Censored	20 (37.7)	34 (41.5)
Reasons censored		
Alive ^a	13 (24.5)	8 (9.8)
Lost to follow-up ^b	0	0
Withdrew consent ^c	7 (13.2)	26 (31.7)

^a Patients without event and still on study at data cut-off date.^b Patients who discontinued the study for reasons other than withdrew consent.^c Patients who withdrew consent from the study.

Output ID: T-14-2-1-15 2021-06-11 12:28

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-eff-os-rpfs-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.2.19
Analysis of radiographic progression-free survival based on independent central review using stratified log-rank test and cox regression model (Full analysis set)

	Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)
Radiographic Progression-free Survival (rPFS), n (%)		
Events (Progression or Death)	339 (61.5)	116 (41.4)
Radiographic progressions	240 (43.6)	66 (23.6)
Deaths	99 (18.0)	50 (17.9)
Censored	212 (38.5)	164 (58.6)
Ongoing without event	131 (23.8)	30 (10.7)
Event documented after 2 or more missed tumor assessments	69 (12.5)	58 (20.7)
Adequate assessment not available ^a	12 (2.2)	76 (27.1)
Kaplan-Meier estimates (months)		
25th percentile [99.2% CI]	3.9 [2.6, 4.4]	2.1 [2.0, 2.3]
Median rPFS [99.2% CI]	8.8 [8.3, 11.0]	3.6 [2.5, 4.1]
75th percentile [99.2% CI]	17.1 [13.8, 20.6]	8.5 [4.6, NE]
rPFS rates (%)		
3 months (SE) [99.2% CI]	78.4 (1.80) [73.1, 82.7]	55.5 (3.92) [44.5, 65.1]
6 months (SE) [99.2% CI]	63.5 (2.14) [57.6, 68.9]	29.4 (4.00) [19.3, 40.2]
12 months (SE) [99.2% CI]	35.8 (2.35) [29.6, 42.0]	19.9 (4.04) [10.5, 31.4]
Hazard Ratio (Stratified Cox PH model) ^{b c}		0.43 [0.32, 0.58]
99.2% CI		
Stratified Log-rank Test one-sided p-value ^c		<.001
Follow-up time (months) ^d		
Median [95% CI]	14.3 [13.9, 16.4]	2.6 [2.3, 4.0]
Minimum-Maximum	0.0 - 28.4	0.0 - 27.1

^a Patients censored without adequate post-baseline evaluations or adequate baseline assessment.^b Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC.^c Both Cox PH model and Log-rank test are stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2); and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). IRT data for stratification are used.^d Follow-up time = (Date of event or censoring - randomization date + 1)/30.4375 (months) censoring for death or radiographic progression.

Output ID: T-14-2-2-19 2021-06-01 11:04

\FS\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-rpfs-adh.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.2.20
Radiographic progression-free survival based on independent central review by cycles of Lu-PSMA-617 (FAS safety set)

Number of cycles		Lu-PSMA-617+ BSC/BSoC (N=529)
1-3	n/N (%)	129/171 (75.4)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	2.3 [2.2, 2.3]
	Median rPFS [95% CI]	3.2 [2.6, 4.0]
	75th percentile [95% CI]	4.9 [4.5, 5.7]
	rPFS rates (%)	
	3 months (SE) [95% CI]	51.9 (4.00) [43.8, 59.4]
	6 months (SE) [95% CI]	15.8 (3.50) [9.7, 23.3]
	12 months (SE) [95% CI]	3.0 (1.89) [0.7, 8.5]
4	n/N (%)	52/69 (75.4)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	2.8 [2.3, 4.2]
	Median rPFS [95% CI]	6.4 [4.3, 7.9]
	75th percentile [95% CI]	8.8 [7.9, 10.6]
	rPFS rates (%)	
	3 months (SE) [95% CI]	72.5 (5.38) [60.3, 81.5]
	6 months (SE) [95% CI]	54.4 (6.27) [41.4, 65.7]
	12 months (SE) [95% CI]	5.2 (3.51) [1.0, 15.1]
1-4	n/N (%)	181/240 (75.4)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	2.3 [2.3, 2.4]
	Median rPFS [95% CI]	4.0 [3.2, 4.4]
	75th percentile [95% CI]	6.9 [5.7, 8.0]
	rPFS rates (%)	
	3 months (SE) [95% CI]	58.2 (3.28) [51.5, 64.3]
	6 months (SE) [95% CI]	29.1 (3.36) [22.7, 35.8]
	12 months (SE) [95% CI]	3.7 (1.74) [1.3, 8.3]
5-6	n/N (%)	144/289 (49.8)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	9.8 [8.7, 11.1]
	Median rPFS [95% CI]	13.8 [12.2, 17.0]
	75th percentile [95% CI]	NE [19.7, NE]
	rPFS rates (%)	
	3 months (SE) [95% CI]	96.8 (1.04) [94.0, 98.3]
	6 months (SE) [95% CI]	91.1 (1.70) [87.1, 93.9]
	12 months (SE) [95% CI]	57.7 (3.24) [51.1, 63.8]

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

Output ID: T-14-2-2-20 2021-06-01 11:04

\WFS\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\T

LF\PGM\lt-eff-os-rpfs-cycle.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.2.21
rPFS per independent central review events and reasons for censoring in patients who withdrew consent to
BSC/BSoC – patients randomized prior to 5 Mar 2019 (Full analysis set)

	Lu-PSMA-617+ BSC/BSoC (N=166) n (%)	BSC/BSoC only (N=84) n (%)
Patients that withdrew consent (treatment)	30 (18.1)	33 (39.3)
Radiographic Progression-free Survival (rPFS)	10 (33.3)	8 (24.2)
Radiographic progressions	6 (20.0)	2 (6.1)
Deaths	4 (13.3)	6 (18.2)
Censored	20 (66.7)	25 (75.8)
Ongoing without event	8 (26.7)	2 (6.1)
Event documented after 2 or more missed tumor assessments	10 (33.3)	1 (3.0)
Adequate assessment not available ^a	2 (6.7)	22 (66.7)

^a Patients censored without adequate post-baseline evaluations or adequate baseline assessment.

Output ID: T-14-2-2-21 2021-06-11, 12:28

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-eff-os-rpfs-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.2.22
rPFS per independent central review events and reasons for censoring in patients who withdrew consent to
BSC/BSoC (PFS Full analysis set)

	Lu-PSMA-617+ BSC/BSoC (N=385) n (%)	BSC/BSoC only (N=196) n (%)
Patients that withdrew consent (treatment)	23 (6.0)	49 (25.0)
Radiographic Progression-free Survival (rPFS)	12 (52.2)	15 (30.6)
Radiographic progressions	5 (21.7)	1 (2.0)
Deaths	7 (30.4)	14 (28.6)
Censored	11 (47.8)	34 (69.4)
Ongoing without event	8 (34.8)	2 (4.1)
Event documented after 2 or more missed tumor assessments	2 (8.7)	8 (16.3)
Adequate assessment not available ^a	1 (4.3)	24 (49.0)

^a Patients censored without adequate post-baseline evaluations or adequate baseline assessment.

Output ID: T-14-2-2-22 2021-06-11, 12:28

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-eff-os-rpfs-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.2.23

rPFS per independent central review events and reasons for censoring in patients who withdrew consent to BSC/BSoC (Full analysis set)

	Lu-PSMA-617+ BSC/BSoC (N=551) n (%)	BSC/BSoC only (N=280) n (%)
Patients that withdrew consent (treatment)	53 (9.6)	82 (29.3)
Radiographic Progression-free Survival (rPFS)	22 (41.5)	23 (28.0)
Radiographic progressions	11 (20.8)	3 (3.7)
Deaths	11 (20.8)	20 (24.4)
Censored	31 (58.5)	59 (72.0)
Ongoing without event	16 (30.2)	4 (4.9)
Event documented after 2 or more missed tumor assessments	12 (22.6)	9 (11.0)
Adequate assessment not available ^a	3 (5.7)	46 (56.1)

^a Patients censored without adequate post-baseline evaluations or adequate baseline assessment.

Output ID: T-14-2-2-23 2021-06-11, 12:29

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-eff-os-rpfs-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.3.1.1
RECIST 1.1 best overall response, disease control rate and duration of response based on independent central review - in patients with measurable disease at baseline (Response evaluable analysis set)

	Lu-PSMA-617+ BSC/BSoC (N=319)	BSC/BSoC only (N=120)
Patients with measurable disease at baseline, n (%)	184 (57.7)	64 (53.3)
Best Overall Response (BOR), n (%)		
Complete Response (CR)	17 (9.2)	0
Partial Response (PR)	77 (41.8)	2 (3.1)
Stable Disease (SD)	65 (35.3)	30 (46.9)
Progressive Disease (PD)	24 (13.0)	29 (45.3)
Unknown	1 (0.5)	3 (4.7)
Overall Response Rate (ORR: CR+PR), n (%)	94 (51.1)	2 (3.1)
Odds Ratio [95% CI] ^a	37.61 [8.84, 159.99]	
Two-sided p-value ^a	$<.001$	
Disease Control Rate (DCR CR+PR+SD>6 weeks), n (%)	159 (86.4)	32 (50.0)
Odds Ratio [95% CI] ^a	10.03 [4.50, 22.34]	
Two-sided p-value ^a	$<.001$	
Duration of Response (DoR) (months), n (%)		
n	94	2
Events (Progression or Death)	45 (47.9)	1 (50.0)
Radiographic progressions	29 (30.9)	1 (50.0)
Deaths	16 (17.0)	0
Censored	49 (52.1)	1 (50.0)
Ongoing without event	38 (40.4)	1 (50.0)
Event documented after 2 or more missed tumor assessments	11 (11.7)	0
Adequate assessment not available ^b	0	0
Kaplan-Meier estimates (months)		
25th percentile [95% CI]	6.9 [5.9, 8.6]	10.6 [NE, NE]
Median DOR [95% CI]	9.8 [9.2, 11.7]	10.6 [NE, NE]
75th percentile [95% CI]	18.0 [15.5, 18.0]	10.6 [NE, NE]
Mean DoR (months) ^c	12.7	10.6
SE DoR (months) ^c	0.009	0.000
EDoR (months) ^c	6.5	0.3
Ratio of EDoR and 95% CI ^c	19.45 [4.94, 76.67]	
Two-sided p-value ^c	$<.001$	

n: Total number of patients with a CR or PR.

^a Odds Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on logistic regression model stratifying for the randomization stratification factors, LDH ($\leq 260 \text{ IU/L}$ vs. $> 260 \text{ IU/L}$); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2); and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). IRT data for stratification are used. P-value based on Wald's Chi-Square test.

^b Patient censored without adequate post-baseline evaluations or adequate baseline assessment per RECIST 1.1.

^c Analyzed using mixture distribution methodology (Ellis et al. 2008). DoR: duration of response in responding patients (months); SE: standard error; EDoR: expected duration of response (months) equals Mean DoR X Overall Response Rate.

Output ID: T-14-2-3-1-1 2021-06-01 11:04

\FS\STGENISAAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-or.sas
Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.5.1
Progression-free survival by cycles of Lu-PSMA-617 (FAS safety set)

Number of cycles		Lu-PSMA-617+ BSC/BSoC (N=529)
1-3	n/N (%)	140/171 (81.9)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	2.3 [2.2, 2.3]
	Median PFS [95% CI]	2.7 [2.5, 3.3]
	75th percentile [95% CI]	4.2 [3.9, 4.6]
	PFS rates (%)	
	3 months (SE) [95% CI]	46.3 (3.99) [38.3, 53.9]
	6 months (SE) [95% CI]	9.6 (2.81) [5.0, 16.0]
	12 months (SE) [95% CI]	0.0 (NE) [NE, NE]
4	n/N (%)	57/69 (82.6)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	2.8 [2.3, 3.3]
	Median PFS [95% CI]	4.4 [3.3, 4.7]
	75th percentile [95% CI]	5.9 [4.7, 7.8]
	PFS rates (%)	
	3 months (SE) [95% CI]	72.5 (5.38) [60.3, 81.5]
	6 months (SE) [95% CI]	20.1 (5.39) [10.8, 31.5]
	12 months (SE) [95% CI]	0.0 (NE) [NE, NE]
1-4	n/N (%)	197/240 (82.1)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	2.3 [2.3, 2.4]
	Median PFS [95% CI]	3.3 [2.8, 3.7]
	75th percentile [95% CI]	4.6 [4.4, 5.2]
	PFS rates (%)	
	3 months (SE) [95% CI]	54.3 (3.31) [47.6, 60.5]
	6 months (SE) [95% CI]	12.9 (2.57) [8.3, 18.4]
	12 months (SE) [95% CI]	0.0 (NE) [NE, NE]
5-6	n/N (%)	201/289 (69.6)
	Kaplan-Meier estimates (months)	
	25th percentile [95% CI]	5.9 [5.1, 6.2]
	Median PFS [95% CI]	9.9 [8.6, 11.3]
	75th percentile [95% CI]	16.0 [14.3, 19.6]
	PFS rates (%)	
	3 months (SE) [95% CI]	96.5 (1.09) [93.6, 98.1]
	6 months (SE) [95% CI]	74.2 (2.61) [68.6, 78.9]
	12 months (SE) [95% CI]	37.3 (3.04) [31.4, 43.3]

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

Output ID: T-14-2-5-1 2021-06-01 11:04

\FS\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\T

LFPGMt-eff-os-rpfs-cycle.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.8.1.2.2
Time to worsening in FACT-P total score by cycles of Lu-PSMA-617 (FAS safety set)

Number of cycles	Lu-PSMA-617+ BSC/BSoC (N=529)
1-3	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 0.6 [0.5, 1.6] Median time to worsening [95% CI] 2.9 [2.1, 3.3] 75th percentile [95% CI] 4.6 [4.2, 5.3] Time to worsening rates (%) 3 months (SE) [95% CI] 47.6 (3.84) [40.0, 54.9] 6 months (SE) [95% CI] 16.3 (2.87) [11.2, 22.3] 12 months (SE) [95% CI] 5.0 (1.72) [2.4, 9.2]
4	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 1.7 [0.5, 3.2] Median time to worsening [95% CI] 5.4 [4.2, 6.0] 75th percentile [95% CI] 6.8 [6.0, 7.7] Time to worsening rates (%) 3 months (SE) [95% CI] 69.1 (5.60) [56.7, 78.6] 6 months (SE) [95% CI] 37.9 (5.92) [26.4, 49.3] 12 months (SE) [95% CI] 5.3 (2.92) [1.4, 13.1]
1-4	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 0.7 [0.6, 1.7] Median time to worsening [95% CI] 3.3 [2.8, 3.9] 75th percentile [95% CI] 5.7 [5.1, 6.3] Time to worsening rates (%) 3 months (SE) [95% CI] 53.8 (3.23) [47.3, 59.9] 6 months (SE) [95% CI] 22.5 (2.74) [17.4, 28.1] 12 months (SE) [95% CI] 5.1 (1.49) [2.7, 8.6]
5-6	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 3.3 [1.9, 5.0] Median time to worsening [95% CI] 9.2 [8.3, 11.1] 75th percentile [95% CI] 16.0 [14.4, 17.9] Time to worsening rates (%) 3 months (SE) [95% CI] 76.5 (2.50) [71.1, 80.9] 6 months (SE) [95% CI] 67.5 (2.76) [61.7, 72.5] 12 months (SE) [95% CI] 35.6 (2.95) [29.9, 41.4]

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

FACT-P total score (range 0-156) = PWB score + SFWB score + EWB score + FWB score + PCS score.

Worsening = worsening relative to baseline in FACT-P total score indicated by a ≥ 10 point decrease at any time up through EOT visit.Time to worsening is defined as time from randomization to the first occurring of a ≥ 10 point decrease in FACT-P total score compared to baseline, clinical disease progression, or death.

Output ID: T-14-2-8-1-2-2 2021-06-14 10:05

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-eff-wors-cycle.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.8.10.2.2
Time to worsening in FACT-G total score by cycles of Lu-PSMA-617 (FAS safety set)

Number of cycles	Lu-PSMA-617+ BSC/BSoC (N=529)
1-3	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 1.2 [0.6, 1.9] Median time to worsening [95% CI] 3.2 [2.6, 3.4] 75th percentile [95% CI] 4.8 [4.4, 5.8] Time to worsening rates (%) 3 months (SE) [95% CI] 52.9 (3.83) [45.1, 60.1] 6 months (SE) [95% CI] 18.1 (2.99) [12.6, 24.3] 12 months (SE) [95% CI] 6.2 (1.90) [3.2, 10.7]
4	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 2.1 [0.6, 4.5] Median time to worsening [95% CI] 5.6 [4.6, 6.0] 75th percentile [95% CI] 7.2 [6.3, 9.0] Time to worsening rates (%) 3 months (SE) [95% CI] 73.5 (5.35) [61.3, 82.4] 6 months (SE) [95% CI] 41.9 (6.05) [30.0, 53.3] 12 months (SE) [95% CI] 7.0 (3.32) [2.3, 15.3]
1-4	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 1.7 [0.7, 2.0] Median time to worsening [95% CI] 3.4 [3.2, 4.3] 75th percentile [95% CI] 6.0 [5.2, 6.9] Time to worsening rates (%) 3 months (SE) [95% CI] 58.8 (3.19) [52.3, 64.8] 6 months (SE) [95% CI] 24.9 (2.84) [19.6, 30.6] 12 months (SE) [95% CI] 6.5 (1.67) [3.8, 10.3]
5-6	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 5.0 [3.3, 6.3] Median time to worsening [95% CI] 10.3 [8.8, 11.4] 75th percentile [95% CI] 17.1 [15.2, 18.3] Time to worsening rates (%) 3 months (SE) [95% CI] 82.0 (2.26) [77.1, 86.0] 6 months (SE) [95% CI] 73.7 (2.59) [68.2, 78.4] 12 months (SE) [95% CI] 39.2 (3.03) [33.2, 45.1]

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

FACT-G total score (range 0-108) = PWB score + SFWB score + EWB score + FWB score.

Worsening = worsening relative to baseline in FACT-G total score indicated by a ≥ 9 point decrease at any time up through EOT visit.Time to worsening is defined as time from randomization to the first occurring of a ≥ 9 point decrease in FACT-G total score compared to baseline, clinical disease progression, or death.

Output ID: T-14-2-8-10-2-2 2021-06-14 10:05

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-eff-wors-cycle.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.9.1.2.2
Time to worsening in BPI-SF pain intensity scale by cycles of Lu-PSMA-617 (FAS safety set)

Number of cycles	Lu-PSMA-617+ BSC/BSoC (N=529)
1-3	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 1.5 [0.7, 1.9] Median time to worsening [95% CI] 3.2 [2.7, 3.8] 75th percentile [95% CI] 5.0 [4.6, 6.7] Time to worsening rates (%) 3 months (SE) [95% CI] 54.1 (3.83) [46.3, 61.2] 6 months (SE) [95% CI] 19.4 (3.08) [13.8, 25.8] 12 months (SE) [95% CI] 8.2 (2.15) [4.6, 13.0]
4	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 1.7 [0.6, 2.4] Median time to worsening [95% CI] 4.7 [3.1, 5.7] 75th percentile [95% CI] 6.5 [5.8, 7.9] Time to worsening rates (%) 3 months (SE) [95% CI] 64.7 (5.80) [52.1, 74.8] 6 months (SE) [95% CI] 32.4 (5.67) [21.6, 43.5] 12 months (SE) [95% CI] 3.2 (2.22) [0.6, 9.8]
1-4	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 1.6 [0.7, 1.9] Median time to worsening [95% CI] 3.3 [3.1, 4.2] 75th percentile [95% CI] 5.7 [5.1, 6.7] Time to worsening rates (%) 3 months (SE) [95% CI] 57.1 (3.21) [50.6, 63.1] 6 months (SE) [95% CI] 23.2 (2.76) [18.0, 28.8] 12 months (SE) [95% CI] 6.7 (1.67) [4.0, 10.5]
5-6	n/N (%) Kaplan-Meier estimates (months) 25th percentile [95% CI] 2.1 [1.6, 3.5] Median time to worsening [95% CI] 9.4 [8.5, 10.8] 75th percentile [95% CI] 15.2 [14.4, 17.4] Time to worsening rates (%) 3 months (SE) [95% CI] 73.4 (2.60) [67.9, 78.1] 6 months (SE) [95% CI] 66.8 (2.77) [61.0, 71.9] 12 months (SE) [95% CI] 36.2 (2.99) [30.3, 42.0]

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

BPI-SF (range 0-10): Brief Pain Inventory - Short Form

Time to worsening is defined as time from randomization to the first occurring of an increase of worsening threshold ($\geq 30\%$ of baseline or ≥ 2 -point increase) at any time up through EOT visit compared to baseline, clinical disease progression, or death.

Output ID: T-14-2-9-1-2-2 2021-06-14 10:05

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-eff-wors-cycle.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.2.9.2.2.2
Time to worsening in BPI-SF pain interference scale by cycles of Lu-PSMA-617 (FAS safety set)

Number of cycles	Lu-PSMA-617+ BSC/BSoC (N=529)
1-3	n/N (%) 167/171 (97.7) Kaplan-Meier estimates (months) 25th percentile [95% CI] 0.7 [0.5, 1.5] Median time to worsening [95% CI] 2.9 [2.4, 3.3] 75th percentile [95% CI] 4.6 [4.2, 5.3] Time to worsening rates (%) 3 months (SE) [95% CI] 47.2 (3.83) [39.5, 54.5] 6 months (SE) [95% CI] 16.4 (2.88) [11.2, 22.4] 12 months (SE) [95% CI] 6.3 (1.91) [3.2, 10.8]
4	n/N (%) 64/69 (92.8) Kaplan-Meier estimates (months) 25th percentile [95% CI] 2.2 [0.6, 3.2] Median time to worsening [95% CI] 5.6 [4.4, 6.0] 75th percentile [95% CI] 6.8 [6.0, 7.4] Time to worsening rates (%) 3 months (SE) [95% CI] 72.1 (5.44) [59.8, 81.2] 6 months (SE) [95% CI] 38.9 (5.99) [27.3, 50.4] 12 months (SE) [95% CI] 3.6 (2.47) [0.7, 10.9]
1-4	n/N (%) 231/240 (96.3) Kaplan-Meier estimates (months) 25th percentile [95% CI] 0.9 [0.6, 1.7] Median time to worsening [95% CI] 3.2 [2.9, 3.9] 75th percentile [95% CI] 5.7 [5.1, 6.5] Time to worsening rates (%) 3 months (SE) [95% CI] 54.3 (3.23) [47.8, 60.4] 6 months (SE) [95% CI] 22.9 (2.76) [17.7, 28.4] 12 months (SE) [95% CI] 5.7 (1.57) [3.1, 9.3]
5-6	n/N (%) 222/289 (76.8) Kaplan-Meier estimates (months) 25th percentile [95% CI] 1.7 [0.6, 3.2] Median time to worsening [95% CI] 8.8 [7.4, 10.4] 75th percentile [95% CI] 15.4 [14.7, 17.2] Time to worsening rates (%) 3 months (SE) [95% CI] 71.3 (2.66) [65.7, 76.1] 6 months (SE) [95% CI] 61.6 (2.86) [55.7, 66.9] 12 months (SE) [95% CI] 35.5 (2.96) [29.7, 41.3]

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

BPI-SF (range 0-10): Brief Pain Inventory - Short Form

Time to worsening is defined as time from randomization to the first occurring of 1) an increase of worsening threshold ($\geq 30\%$ of baseline or ≥ 2 -point increase) at any time up through EOT visit compared to baseline, 2) clinical disease progression, or 3) death.

Output ID: T-14-2-9-2-2 2021-06-14 10:06

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-eff-wors-cycle.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.3.12.2
Cancer related therapy (non-radiation) since discontinuation of randomized treatment - patients who withdrew consent to BSC/BSoC randomized prior to 5 Mar 2019 (Full analysis set)

ATC level 4 Preferred term	Lu-PSMA-617 +BSC/BSoC (N=30) n (%)	BSC/BSoC only (N=33) n (%)	Overall (N=63) n (%)
Number of patients with one or more cancer (non-radiation) related therapies	6 (20.0)	9 (27.3)	15 (23.8)
ANTI-ANDROGENS	1 (3.3)	1 (3.0)	2 (3.2)
ENZALUTAMIDE	1 (3.3)	1 (3.0)	2 (3.2)
ESTROGENS	0	1 (3.0)	1 (1.6)
ESTRADIOL	0	1 (3.0)	1 (1.6)
GLUCOCORTICOIDS	1 (3.3)	0	1 (1.6)
PREDNISONE	1 (3.3)	0	1 (1.6)
GONADOTROPIN RELEASING HORMONE ANALOGUES	0	1 (3.0)	1 (1.6)
GOSERELIN	0	1 (3.0)	1 (1.6)
MONOCLONAL ANTIBODIES	0	3 (9.1)	3 (4.8)
BEVACIZUMAB	0	1 (3.0)	1 (1.6)
IPILIMUMAB	0	1 (3.0)	1 (1.6)
NIVOLUMAB	0	1 (3.0)	1 (1.6)
PEMBROLIZUMAB	0	1 (3.0)	1 (1.6)
NOT CODED	0	2 (6.1)	2 (3.2)
INVESTIGATIONAL DRUG	0	2 (6.1)	2 (3.2)
OTHER ANTINEOPLASTIC AGENTS	2 (6.7)	0	2 (3.2)
CAR T-CELLS NOS	1 (3.3)	0	1 (1.6)
OLAPARIB	1 (3.3)	0	1 (1.6)
OTHER HORMONE ANTAGONISTS AND RELATED AGENTS	0	2 (6.1)	2 (3.2)
ABIRATERONE ACETATE	0	1 (3.0)	1 (1.6)
DEGARELIX ACETATE	0	1 (3.0)	1 (1.6)
OTHER IMMUNOSTIMULANTS	1 (3.3)	0	1 (1.6)
SIPULEUCEL-T	1 (3.3)	0	1 (1.6)
PLATINUM COMPOUNDS	1 (3.3)	4 (12.1)	5 (7.9)
CARBOPLATIN	1 (3.3)	3 (9.1)	4 (6.3)
CISPLATIN	0	2 (6.1)	2 (3.2)
PODOPHYLLOTOXIN DERIVATIVES	0	1 (3.0)	1 (1.6)
ETOPOSIDE	0	1 (3.0)	1 (1.6)

ATC levels are presented alphabetically; preferred terms within ATC level are sorted by descending frequency, as reported in the 'Lu-PSMA-617+BSC/BSoC' column.

Every patient is counted a single time for each applicable category.

Coded using WHODrug Global version Mar 2020 B3.

Output ID: T-14-3-12-2 2021-06-10 14:48

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-postrrt1-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.3.12.2
Cancer related therapy (non-radiation) since discontinuation of randomized treatment - patients who withdrew consent to BSC/BSoC randomized prior to 5 Mar 2019 (Full analysis set)

ATC level 4 Preferred term	Lu-PSMA-617 +BSC/BSoC (N=30) n (%)	BSC/BSoC only (N=33) n (%)	Overall (N=63) n (%)
PYRIMIDINE ANALOGUES	0	1 (3.0)	1 (1.6)
GEMCITABINE	0	1 (3.0)	1 (1.6)
TAXANES	4 (13.3)	2 (6.1)	6 (9.5)
CABAZITAXEL	3 (10.0)	2 (6.1)	5 (7.9)
DOCETAXEL	1 (3.3)	0	1 (1.6)
PACLITAXEL ALBUMIN	1 (3.3)	0	1 (1.6)
VARIOUS THERAPEUTIC RADIOPHARMACEUTICALS	2 (6.7)	3 (9.1)	5 (7.9)
LUTETIUM (177LU) PSMA-617	1 (3.3)	1 (3.0)	2 (3.2)
RADIUM RA 223 DICHLORIDE	1 (3.3)	2 (6.1)	3 (4.8)

ATC levels are presented alphabetically; preferred terms within ATC level are sorted by descending frequency, as reported in the 'Lu-PSMA-617+BSC/BSoC' column.

Every patient is counted a single time for each applicable category.

Coded using WHODrug Global version Mar 2020 B3.

Output ID: T-14-3-12-2 2021-06-10 14:48

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-postrt1-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.3.12.3
Cancer related therapy (non-radiation) since discontinuation of randomized treatment - patients who withdrew consent to BSC/BSoC (PFS Full analysis set)

ATC level 4 Preferred term	Lu-PSMA-617 +BSC/BSoC (N=23) n (%)	BSC/BSoC only (N=49) n (%)	Overall (N=72) n (%)
Number of patients with one or more cancer (non-radiation) related therapies	2 (8.7)	4 (8.2)	6 (8.3)
ANTI-ANDROGENS	0	1 (2.0)	1 (1.4)
ENZALUTAMIDE	0	1 (2.0)	1 (1.4)
OTHER HORMONE ANTAGONISTS AND RELATED AGENTS	1 (4.3)	0	1 (1.4)
ABIRATERONE	1 (4.3)	0	1 (1.4)
PLATINUM COMPOUNDS	1 (4.3)	1 (2.0)	2 (2.8)
CARBOPLATIN	1 (4.3)	1 (2.0)	2 (2.8)
TAXANES	0	1 (2.0)	1 (1.4)
CABAZITAXEL	0	1 (2.0)	1 (1.4)
VARIOUS THERAPEUTIC RADIOPHARMACEUTICALS	0	2 (4.1)	2 (2.8)
LUTETIUM (177Lu) PSMA-617	0	1 (2.0)	1 (1.4)
VARIOUS THERAPEUTIC RADIOPHARMACEUTICALS	0	1 (2.0)	1 (1.4)

ATC levels are presented alphabetically; preferred terms within ATC level are sorted by descending frequency, as reported in the 'Lu-PSMA-617+BSC/BSoC' column.

Every patient is counted a single time for each applicable category.

Coded using WHODrug Global version Mar 2020 B3.

Output ID: T-14-3-12-3 2021-06-10 12:23

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-postrt1-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.3.12.4
Cancer related therapy (non-radiation) since discontinuation of randomized treatment - patients who withdrew consent to BSC/BSoC (Full analysis set)

ATC level 4 Preferred term	Lu-PSMA-617 +BSC/BSoC (N=53) n (%)	BSC/BSoC only (N=82) n (%)	Overall (N=135) n (%)
Number of patients with one or more cancer (non-radiation) related therapies	8 (15.1)	13 (15.9)	21 (15.6)
ANTI-ANDROGENS	1 (1.9)	2 (2.4)	3 (2.2)
ENZALUTAMIDE	1 (1.9)	2 (2.4)	3 (2.2)
ESTROGENS	0	1 (1.2)	1 (0.7)
ESTRADIOL	0	1 (1.2)	1 (0.7)
GLUCOCORTICOIDS	1 (1.9)	0	1 (0.7)
PREDNISONE	1 (1.9)	0	1 (0.7)
GONADOTROPIN RELEASING HORMONE ANALOGUES	0	1 (1.2)	1 (0.7)
GOSERELIN	0	1 (1.2)	1 (0.7)
MONOCLONAL ANTIBODIES	0	3 (3.7)	3 (2.2)
BEVACIZUMAB	0	1 (1.2)	1 (0.7)
IPILIMUMAB	0	1 (1.2)	1 (0.7)
NIVOLUMAB	0	1 (1.2)	1 (0.7)
PEMBROLIZUMAB	0	1 (1.2)	1 (0.7)
NOT CODED	0	2 (2.4)	2 (1.5)
INVESTIGATIONAL DRUG	0	2 (2.4)	2 (1.5)
OTHER ANTINEOPLASTIC AGENTS	2 (3.8)	0	2 (1.5)
CAR T-CELLS NOS	1 (1.9)	0	1 (0.7)
OLAPARIB	1 (1.9)	0	1 (0.7)
OTHER HORMONE ANTAGONISTS AND RELATED AGENTS	1 (1.9)	2 (2.4)	3 (2.2)
ABIRATERONE	1 (1.9)	0	1 (0.7)
ABIRATERONE ACETATE	0	1 (1.2)	1 (0.7)
DEGARELIX ACETATE	0	1 (1.2)	1 (0.7)
OTHER IMMUNOSTIMULANTS	1 (1.9)	0	1 (0.7)
SIPULEUCEL-T	1 (1.9)	0	1 (0.7)
PLATINUM COMPOUNDS	2 (3.8)	5 (6.1)	7 (5.2)
CARBOPLATIN	2 (3.8)	4 (4.9)	6 (4.4)
CISPLATIN	0	2 (2.4)	2 (1.5)
PODOPHYLLOTOXIN DERIVATIVES	0	1 (1.2)	1 (0.7)
ETOPOSIDE	0	1 (1.2)	1 (0.7)

ATC levels are presented alphabetically; preferred terms within ATC level are sorted by descending frequency, as reported in the 'Lu-PSMA-617+BSC/BSoC' column.

Every patient is counted a single time for each applicable category.

Coded using WHODrug Global version Mar 2020 B3.

Output ID: T-14-3-12-4 2021-06-10 12:23

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-posttrt1-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.3.12.4
Cancer related therapy (non-radiation) since discontinuation of randomized treatment - patients who withdrew consent to BSC/BSoC (Full analysis set)

ATC level 4 Preferred term	Lu-PSMA-617 +BSC/BSoC (N=53) n (%)	BSC/BSoC only (N=82) n (%)	Overall (N=135) n (%)
PYRIMIDINE ANALOGUES	0	1 (1.2)	1 (0.7)
GEMCITABINE	0	1 (1.2)	1 (0.7)
TAXANES	4 (7.5)	3 (3.7)	7 (5.2)
CABAZITAXEL	3 (5.7)	3 (3.7)	6 (4.4)
DOCETAXEL	1 (1.9)	0	1 (0.7)
PACLITAXEL ALBUMIN	1 (1.9)	0	1 (0.7)
VARIOUS THERAPEUTIC RADIOPHARMACEUTICALS	2 (3.8)	5 (6.1)	7 (5.2)
LUTETIUM (177LU) PSMA-617	1 (1.9)	2 (2.4)	3 (2.2)
RADIUM RA 223 DICHLORIDE	1 (1.9)	2 (2.4)	3 (2.2)
VARIOUS THERAPEUTIC RADIOPHARMACEUTICALS	0	1 (1.2)	1 (0.7)

ATC levels are presented alphabetically; preferred terms within ATC level are sorted by descending frequency, as reported in the 'Lu-PSMA-617+BSC/BSoC' column.

Every patient is counted a single time for each applicable category.

Coded using WHODrug Global version Mar 2020 B3.

Output ID: T-14-3-12-4 2021-06-10 12:23

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-postrt1-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.3.13.2
Cancer related radiotherapy since discontinuation of randomized treatment - patients who withdrew consent to
BSC/BSoC randomized prior to 5 Mar 2019 (Full analysis set)

	Lu-PSMA-617 +BSC/BSoC (N=30)	BSC/BSoC only (N=33)	Overall (N=63)
Number of patients with one or more cancer related radiotherapies, n (%)	4 (13.3)	3 (9.1)	7 (11.1)
Number of radiotherapies	6	3	9
Site of radiotherapy, n (%)			
Back	2 (6.7)	1 (3.0)	3 (4.8)
Femur	1 (3.3)	1 (3.0)	2 (3.2)
Other	1 (3.3)	1 (3.0)	2 (3.2)
Upper extremity bone	1 (3.3)	0	1 (1.6)
Vertebral column	1 (3.3)	0	1 (1.6)

Site of radiotherapy are sorted in descending frequency, as reported in 'Lu-PSMA-617+BSC/BSoC' column.

Every patient is counted a single time for each site of radiotherapy.

Output ID: T-14-3-13-2 2021-06-10 14:56

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-postrrt2-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.3.13.3
Cancer related radiotherapy since discontinuation of randomized treatment - patients who withdrew consent to
BSC/BSoC (PFS Full analysis set)

	Lu-PSMA-617 +BSC/BSoC (N=23)	BSC/BSoC only (N=49)	Overall (N=72)
Number of patients with one or more cancer related radiotherapies, n (%)	1 (4.3)	0	1 (1.4)
Number of radiotherapies	2	0	2
Site of radiotherapy, n (%)			
Rib	1 (4.3)	0	1 (1.4)
Vertebral column	1 (4.3)	0	1 (1.4)

Site of radiotherapy are sorted in descending frequency, as reported in 'Lu-PSMA-617+BSC/BSoC' column.
Every patient is counted a single time for each site of radiotherapy.

Output ID: T-14-3-13-3 2021-06-10 14:56

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-postrrt2-wc.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 14.3.13.4
Cancer related radiotherapy since discontinuation of randomized treatment - patients who withdrew consent to
BSC/BSoC (Full analysis set)

	Lu-PSMA-617 +BSC/BSoC (N=53)	BSC/BSoC only (N=82)	Overall (N=135)
Number of patients with one or more cancer related radiotherapies, n (%)	5 (9.4)	3 (3.7)	8 (5.9)
Number of radiotherapies	8	3	11
Site of radiotherapy, n (%)			
Back	2 (3.8)	1 (1.2)	3 (2.2)
Vertebral column	2 (3.8)	0	2 (1.5)
Femur	1 (1.9)	1 (1.2)	2 (1.5)
Other	1 (1.9)	1 (1.2)	2 (1.5)
Rib	1 (1.9)	0	1 (0.7)
Upper extremity bone	1 (1.9)	0	1 (0.7)

Site of radiotherapy are sorted in descending frequency, as reported in 'Lu-PSMA-617+BSC/BSoC' column.
Every patient is counted a single time for each site of radiotherapy.

Output ID: T-14-3-13-4 2021-06-10 14:56

...\\BIOMETRY\\PROJECTS\\PSMA617\\VISION\\SCE\\PRODUCTION\\TLF\\PGM\\t-postrrt2-wc.sas
Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 15
Overall Survival by Concurrent use of Bone Sparing Agents as part of BSC/BSoC treatment (Full Analysis Set)

	Lu-PSMA-617+ BSC/BSoC (N=551)	BSC/BSoC only (N=280)
Concur	n/N (%)	152/240 (63.3)
BSA:	Kaplan-Meier estimates (months)	
Yes	25th percentile [95% CI] Median OS [95% CI] 75th percentile [95% CI]	9.1 [7.7, 10.0] 15.3 [13.2, 17.4] 25.0 [22.6, NE]
	OS rates (%)	
	6 months (SE) [95% CI] 12 months (SE) [95% CI] 18 months (SE) [95% CI]	88.7 (2.05) [84.0, 92.1] 62.0 (3.16) [55.5, 67.8] 43.6 (3.29) [37.1, 49.9]
	Hazard Ratio ^a [95% CI]	0.59 [0.45, 0.78]
	Follow-up time (months)	
	Median [95% CI] Minimum-Maximum	20.0 [19.4, 21.7] 0.0 - 31.4
Concur	n/N (%)	191/311 (61.4)
BSA:	Kaplan-Meier estimates (months)	
No	25th percentile [95% CI] Median OS [95% CI] 75th percentile [95% CI]	8.6 [7.4, 10.0] 15.3 [13.8, 17.6] 26.8 [23.6, NE]
	OS rates (%)	
	6 months (SE) [95% CI] 12 months (SE) [95% CI] 18 months (SE) [95% CI]	85.0 (2.03) [80.5, 88.6] 61.4 (2.78) [55.7, 66.6] 42.6 (2.92) [36.8, 48.2]
	Hazard Ratio ^a [95% CI]	0.64 [0.50, 0.82]
	Follow-up time (months)	
	Median [95% CI] Minimum-Maximum	20.5 [19.8, 21.4] 0.6 - 31.5

Concur BSA: Concurrent use of bone sparing agents

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-15 2021-06-01 11:00

\NFSISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISIONSCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 16

Radiographic Progression-free Survival based on Independent Central Review by Region (PFS-Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
North America	n/N (%)	163/249 (65.5)	60/130 (46.2)
	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.2 [3.1, 4.7]	2.1 [2.0, 2.3]
	Median rPFS [95% CI]	8.7 [7.9, 10.4]	3.6 [2.4, 4.0]
	75th percentile [95% CI]	17.0 [13.2, 19.7]	6.0 [4.3, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	81.4 (2.51) [75.8, 85.7]	56.1 (5.45) [44.8, 66.0]
	6 months (SE) [95% CI]	65.5 (3.11) [59.1, 71.3]	24.5 (5.58) [14.4, 35.9]
	12 months (SE) [95% CI]	32.6 (3.30) [26.3, 39.1]	19.6 (5.43) [10.3, 31.1]
	Hazard Ratio ^a [95% CI]	0.39 [0.28, 0.53]	
	Follow-up time (months)		
	Median [95% CI]	14.3 [14.1, 16.9]	3.9 [2.3, 5.4]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.8
Europe	n/N (%)	91/136 (66.9)	33/66 (50.0)
	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	3.6 [2.5, 5.2]	2.0 [1.9, 2.4]
	Median rPFS [95% CI]	9.0 [7.8, 11.3]	3.4 [2.2, 4.3]
	75th percentile [95% CI]	14.4 [12.0, 20.6]	10.6 [4.0, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	76.9 (3.70) [68.7, 83.3]	51.2 (7.47) [35.9, 64.7]
	6 months (SE) [95% CI]	63.0 (4.31) [53.9, 70.8]	33.4 (7.71) [19.1, 48.4]
	12 months (SE) [95% CI]	34.1 (4.52) [25.4, 43.0]	17.5 (7.93) [5.5, 35.1]
	Hazard Ratio ^a [95% CI]	0.43 [0.28, 0.65]	
	Follow-up time (months)		
	Median [95% CI]	17.0 [14.4, 18.2]	3.7 [2.3, 6.5]
	Minimum-Maximum	0.0 - 20.6	0.0 - 14.4

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (≤ 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-16 2021-06-01 11:00

\\\FS\STGENISAAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 17
Radiographic Progression-free Survival based on Independent Central Review by PSA Doubling Time at Baseline
(PFS-Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
PSADT:	n/N (%)	110/175 (62.9)	40/73 (54.8)
>0 - <=9 months	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.2 [2.6, 5.8]	2.1 [2.0, 2.4]
	Median rPFS [95% CI]	9.8 [8.3, 11.3]	3.1 [2.4, 4.2]
	75th percentile [95% CI]	17.1 [14.0, 19.7]	6.1 [4.0, 14.9]
	rPFS rates (%)		
	3 months (SE) [95% CI]	80.3 (3.07) [73.4, 85.6]	51.0 (7.18) [36.3, 64.0]
	6 months (SE) [95% CI]	66.3 (3.72) [58.5, 73.0]	27.6 (6.70) [15.6, 41.1]
	12 months (SE) [95% CI]	36.0 (4.08) [28.1, 43.9]	19.3 (6.17) [9.0, 32.5]
	Hazard Ratio ^a [95% CI]		0.37 [0.25, 0.55]
	Follow-up time (months)		
	Median [95% CI]	14.5 [13.9, 16.9]	10.8 [2.3, 12.0]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.6
PSADT:	n/N (%)	3/7 (42.9)	2/9 (22.2)
>9 months	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	2.6 [2.0, NE]	3.5 [2.5, NE]
	Median rPFS [95% CI]	14.0 [2.0, NE]	NE [2.5, NE]
	75th percentile [95% CI]	NE [2.6, NE]	NE [3.5, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	66.7 (19.25) [19.5, 90.4]	83.3 (15.21) [27.3, 97.5]
	6 months (SE) [95% CI]	66.7 (19.25) [19.5, 90.4]	66.7 (19.25) [19.5, 90.4]
	12 months (SE) [95% CI]	66.7 (19.25) [19.5, 90.4]	66.7 (19.25) [19.5, 90.4]
	Hazard Ratio ^a [95% CI]		0.82 [0.11, 6.24]
	Follow-up time (months)		
	Median [95% CI]	4.4 [0.0, 18.2]	3.8 [0.0, 14.4]
	Minimum-Maximum	0.0 - 18.2	0.0 - 14.4

PSADT: Prostate-specific antigen doubling time

Patients with PSADT stable, non-increasing or decreasing are included in the category '>9 months'.

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-17 2021-06-01 11:00

\WFS\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 18
Radiographic Progression-free Survival based on Independent Central Review by Baseline Prostate-Specific Antigen (rPFS-Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
BPSA:	n/N (%)	108/177 (61.0)	35/91 (38.5)
<=76.0 (ng/mL)	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.2 [2.6, 5.9]	2.1 [2.0, 2.4]
	Median rPFS [95% CI]	9.0 [8.5, 11.4]	3.9 [2.4, 6.1]
	75th percentile [95% CI]	19.7 [14.2, NE]	14.4 [5.6, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	79.7 (3.06) [72.9, 85.0]	60.9 (6.50) [47.0, 72.2]
	6 months (SE) [95% CI]	68.1 (3.60) [60.4, 74.5]	38.1 (7.37) [24.0, 52.2]
	12 months (SE) [95% CI]	38.5 (4.07) [30.5, 46.4]	29.1 (7.96) [14.8, 44.9]
	Hazard Ratio ^a [95% CI]		0.45 [0.30, 0.68]
	Follow-up time (months)		
	Median [95% CI]	15.3 [13.0, 17.1]	3.0 [2.1, 4.7]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.8
BPSA:	n/N (%)	146/208 (70.2)	58/105 (55.2)
>76.0 (ng/mL)	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	3.9 [2.6, 4.7]	2.1 [1.9, 2.2]
	Median rPFS [95% CI]	8.6 [6.9, 10.4]	2.9 [2.4, 3.9]
	75th percentile [95% CI]	14.0 [11.5, 17.1]	4.8 [4.0, 11.2]
	rPFS rates (%)		
	3 months (SE) [95% CI]	79.9 (2.85) [73.6, 84.8]	49.5 (5.91) [37.5, 60.4]
	6 months (SE) [95% CI]	61.7 (3.52) [54.4, 68.2]	20.7 (5.40) [11.3, 32.0]
	12 months (SE) [95% CI]	29.0 (3.47) [22.4, 35.9]	12.4 (4.96) [4.8, 23.9]
	Hazard Ratio ^a [95% CI]		0.38 [0.27, 0.52]
	Follow-up time (months)		
	Median [95% CI]	16.4 [14.2, 17.0]	5.4 [2.6, 10.8]
	Minimum-Maximum	0.0 - 20.3	0.0 - 17.2

BPSA: Baseline prostate-specific antigen

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-18 2021-06-01 11:00

\\\FS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 19
Radiographic Progression-free Survival based on Independent Central Review by Number of prior NAADs (PFS-Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
#PNAAD:	n/N (%)	138/209 (66.0)	42/97 (43.3)
1	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	3.6 [2.4, 4.5]	2.1 [2.0, 2.4]
	Median rPFS [95% CI]	8.9 [6.9, 11.1]	3.6 [2.4, 4.3]
	75th percentile [95% CI]	14.6 [13.8, 19.7]	14.4 [4.3, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	76.5 (3.01) [69.9, 81.8]	57.2 (6.27) [44.0, 68.4]
	6 months (SE) [95% CI]	60.9 (3.52) [53.6, 67.4]	35.3 (6.78) [22.4, 48.4]
	12 months (SE) [95% CI]	35.6 (3.68) [28.4, 42.8]	27.2 (7.30) [14.3, 41.9]
	Hazard Ratio ^a [95% CI]	0.51 [0.35, 0.73]	
	Follow-up time (months)		
	Median [95% CI]	15.2 [14.1, 17.1]	3.9 [2.3, 5.7]
	Minimum-Maximum	0.0 - 20.6	0.0 - 19.6
#PNAAD:	n/N (%)	116/176 (65.9)	51/99 (51.5)
>=2	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.3 [3.2, 6.0]	2.1 [1.9, 2.2]
	Median rPFS [95% CI]	8.7 [8.0, 10.5]	3.1 [2.3, 4.0]
	75th percentile [95% CI]	17.6 [11.6, NE]	5.6 [4.0, 11.2]
	rPFS rates (%)		
	3 months (SE) [95% CI]	83.7 (2.82) [77.2, 88.4]	51.4 (6.20) [38.7, 62.7]
	6 months (SE) [95% CI]	68.9 (3.59) [61.3, 75.4]	21.1 (5.79) [11.1, 33.3]
	12 months (SE) [95% CI]	30.4 (3.84) [23.1, 38.0]	12.7 (5.18) [4.8, 24.6]
	Hazard Ratio ^a [95% CI]	0.32 [0.23, 0.45]	
	Follow-up time (months)		
	Median [95% CI]	16.4 [14.3, 17.0]	4.3 [2.3, 10.8]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.8

#PNAADs: Number of prior novel androgen axis drugs

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-19 2021-06-01 11:01

\\\FS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 20
Radiographic Progression-free Survival based on Independent Central Review by Number of prior immunotherapies (PFS-Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
#PRIMM:	n/N (%)	199/306 (65.0)	65/146 (44.5)
0	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	3.8 [2.6, 4.6]	2.1 [2.0, 2.3]
	Median rPFS [95% CI]	8.8 [8.4, 10.8]	3.4 [2.5, 4.0]
	75th percentile [95% CI]	17.0 [13.9, 20.6]	11.2 [4.3, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	79.0 (2.37) [73.9, 83.2]	55.2 (5.14) [44.6, 64.6]
	6 months (SE) [95% CI]	64.3 (2.84) [58.4, 69.5]	30.9 (5.36) [20.9, 41.6]
	12 months (SE) [95% CI]	35.4 (3.03) [29.5, 41.4]	23.2 (5.62) [13.3, 34.8]
	Hazard Ratio ^a [95% CI]	0.44 [0.33, 0.59]	
	Follow-up time (months)		
	Median [95% CI]	15.3 [14.2, 17.0]	3.9 [2.4, 5.4]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.8
#PRIMM:	n/N (%)	55/79 (69.6)	28/50 (56.0)
>=1	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.2 [2.5, 6.0]	2.1 [2.0, 2.3]
	Median rPFS [95% CI]	8.5 [6.2, 10.5]	3.7 [2.1, 4.6]
	75th percentile [95% CI]	11.7 [10.9, 19.4]	6.0 [3.9, 14.9]
	rPFS rates (%)		
	3 months (SE) [95% CI]	82.8 (4.35) [72.2, 89.6]	51.8 (8.62) [33.9, 67.0]
	6 months (SE) [95% CI]	65.8 (5.57) [53.7, 75.5]	20.3 (7.99) [7.5, 37.4]
	12 months (SE) [95% CI]	24.5 (5.41) [14.7, 35.6]	10.1 (6.46) [1.9, 26.5]
	Hazard Ratio ^a [95% CI]	0.33 [0.20, 0.53]	
	Follow-up time (months)		
	Median [95% CI]	16.8 [13.0, 17.1]	4.7 [2.2, 15.6]
	Minimum-Maximum	0.0 - 19.5	0.0 - 15.6

#PRIMM: Number of prior immunotherapies

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-20 2021-06-01 11:01

\\\FS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 21
Radiographic Progression-free Survival based on Independent Central Review by Number of prior taxane-containing regimens (PFS-Full Analysis Set)

#PTAX:		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
1	n/N (%)	142/224 (63.4)	49/110 (44.5)
	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.2 [3.1, 5.7]	2.1 [2.0, 2.4]
	Median rPFS [95% CI]	8.9 [8.5, 11.0]	3.4 [2.4, 4.0]
	75th percentile [95% CI]	16.2 [13.9, NE]	14.4 [4.2, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	81.9 (2.63) [76.0, 86.4]	54.0 (6.04) [41.5, 64.9]
	6 months (SE) [95% CI]	67.1 (3.26) [60.3, 73.0]	25.7 (6.15) [14.7, 38.2]
	12 months (SE) [95% CI]	36.4 (3.61) [29.4, 43.5]	25.7 (6.15) [14.7, 38.2]
	Hazard Ratio ^a [95% CI]	0.39 [0.27, 0.54]	
	Follow-up time (months)		
	Median [95% CI]	14.3 [14.1, 16.8]	3.7 [2.3, 5.6]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.8
>=2	n/N (%)	94/134 (70.1)	40/77 (51.9)
	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.1 [2.4, 4.6]	2.1 [1.9, 2.2]
	Median rPFS [95% CI]	8.3 [6.2, 10.4]	3.5 [2.2, 4.0]
	75th percentile [95% CI]	14.4 [11.4, 19.4]	6.1 [3.9, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	77.6 (3.67) [69.4, 83.8]	52.3 (6.91) [38.1, 64.8]
	6 months (SE) [95% CI]	60.9 (4.38) [51.8, 68.9]	27.5 (6.83) [15.2, 41.3]
	12 months (SE) [95% CI]	28.4 (4.26) [20.4, 36.9]	13.8 (5.94) [4.8, 27.4]
	Hazard Ratio ^a [95% CI]	0.44 [0.30, 0.66]	
	Follow-up time (months)		
	Median [95% CI]	17.0 [14.4, 17.2]	4.3 [2.3, 11.5]
	Minimum-Maximum	0.0 - 20.7	0.0 - 17.2

#PTAX: Number of prior taxane-containing regimens

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-21 2021-06-01 11:01

\\\FS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 22
Radiographic Progression-free Survival based on Independent Central Review by Number of prior non-taxane cytotoxic chemotherapeutic therapies (PFS-Full Analysis Set)

#PNTAX:		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
0	n/N (%)	230/347 (66.3)	88/183 (48.1)
	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.2 [3.0, 4.8]	2.1 [2.0, 2.3]
	Median rPFS [95% CI]	8.8 [8.4, 10.6]	3.5 [2.5, 4.0]
	75th percentile [95% CI]	17.0 [13.9, 19.4]	8.4 [4.8, 14.9]
	rPFS rates (%)		
	3 months (SE) [95% CI]	80.2 (2.18) [75.5, 84.1]	55.4 (4.50) [46.1, 63.7]
	6 months (SE) [95% CI]	65.0 (2.65) [59.6, 70.0]	29.0 (4.65) [20.3, 38.3]
	12 months (SE) [95% CI]	34.2 (2.81) [28.7, 39.7]	19.9 (4.66) [11.7, 29.7]
	Hazard Ratio ^a [95% CI]	0.41 [0.32, 0.54]	
	Follow-up time (months)		
	Median [95% CI]	16.4 [14.3, 17.0]	3.9 [2.6, 5.6]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.8
>=1	n/N (%)	24/38 (63.2)	5/13 (38.5)
	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.0 [2.2, 4.6]	1.9 [1.9, 2.2]
	Median rPFS [95% CI]	8.2 [4.3, 11.0]	2.2 [1.9, 4.3]
	75th percentile [95% CI]	12.0 [9.0, NE]	4.3 [1.9, 4.3]
	rPFS rates (%)		
	3 months (SE) [95% CI]	76.2 (6.92) [59.3, 86.9]	33.3 (19.25) [4.6, 67.6]
	6 months (SE) [95% CI]	60.6 (8.33) [42.4, 74.6]	0.0 (NE) [NE, NE]
	12 months (SE) [95% CI]	22.7 (7.97) [9.5, 39.4]	0.0 (NE) [NE, NE]
	Hazard Ratio ^a [95% CI]	0.20 [0.07, 0.56]	
	Follow-up time (months)		
	Median [95% CI]	13.9 [6.3, 17.6]	1.7 [0.0, NE]
	Minimum-Maximum	0.4 - 19.8	0.0 - 4.3

#PNTAX: Number of prior non-taxane cytotoxic chemotherapeutic therapies

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-22 2021-06-01 11:01

\\\FS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 23
Radiographic Progression-free Survival based on Independent Central Review by Prior use of Bone Sparing Agents (rPFS-Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
Prior BSA:	n/N (%)	45/66 (68.2)	21/35 (60.0)
Yes	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.1 [2.6, 5.9]	2.2 [2.0, 3.6]
	Median rPFS [95% CI]	8.7 [6.0, 11.1]	3.7 [2.3, 4.3]
	75th percentile [95% CI]	13.0 [11.1, 20.6]	6.0 [3.9, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	79.4 (5.08) [67.2, 87.5]	63.4 (9.33) [42.4, 78.5]
	6 months (SE) [95% CI]	64.0 (6.20) [50.5, 74.7]	19.8 (9.15) [5.9, 39.6]
	12 months (SE) [95% CI]	25.7 (6.27) [14.5, 38.5]	6.6 (6.19) [0.5, 25.1]
	Hazard Ratio ^a [95% CI]	0.35 [0.20, 0.62]	
	Follow-up time (months)		
	Median [95% CI]	17.0 [11.6, 19.7]	4.7 [2.3, 19.6]
	Minimum-Maximum	0.0 - 20.6	0.0 - 19.6
Prior BSA:	n/N (%)	209/319 (65.5)	72/161 (44.7)
No	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.0 [2.8, 4.6]	2.1 [2.0, 2.2]
	Median rPFS [95% CI]	8.8 [8.2, 10.6]	3.4 [2.4, 4.0]
	75th percentile [95% CI]	17.0 [14.0, 19.4]	11.2 [4.6, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	79.9 (2.29) [74.9, 83.9]	52.0 (4.99) [41.8, 61.2]
	6 months (SE) [95% CI]	64.8 (2.77) [59.0, 69.9]	30.1 (5.12) [20.5, 40.3]
	12 months (SE) [95% CI]	34.5 (2.94) [28.8, 40.3]	23.0 (5.33) [13.5, 34.0]
	Hazard Ratio ^a [95% CI]	0.42 [0.31, 0.56]	
	Follow-up time (months)		
	Median [95% CI]	16.4 [14.3, 17.0]	3.7 [2.3, 5.4]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.8

BSA: Bone sparing agents

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-23 2021-06-01 11:01

\\\FS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 24
Radiographic Progression-free Survival based on Independent Central Review by Prior use of 223-Radium (PFS-Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
Prior Radium:	n/N (%)	43/63 (68.3)	19/36 (52.8)
Yes	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.4 [2.3, 6.9]	2.1 [1.9, 2.4]
	Median rPFS [95% CI]	10.5 [6.9, 11.3]	4.6 [2.1, 11.2]
	75th percentile [95% CI]	19.3 [11.3, NE]	14.9 [5.0, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	80.3 (5.09) [68.0, 88.3]	59.5 (9.10) [39.7, 74.7]
	6 months (SE) [95% CI]	68.2 (6.04) [54.8, 78.4]	39.9 (10.20) [20.5, 58.7]
	12 months (SE) [95% CI]	33.5 (6.34) [21.5, 45.9]	26.6 (10.26) [9.6, 47.3]
	Hazard Ratio ^a [95% CI]	0.49 [0.28, 0.87]	
	Follow-up time (months)		
	Median [95% CI]	14.9 [14.0, 18.8]	4.7 [2.6, 17.2]
	Minimum-Maximum	0.0 - 19.7	0.0 - 19.8
Prior Radium:	n/N (%)	211/322 (65.5)	74/160 (46.3)
No	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.0 [2.9, 4.5]	2.1 [2.0, 2.3]
	Median rPFS [95% CI]	8.7 [8.0, 10.4]	3.4 [2.4, 3.9]
	75th percentile [95% CI]	16.2 [13.8, 19.7]	6.0 [4.0, 14.4]
	rPFS rates (%)		
	3 months (SE) [95% CI]	79.7 (2.29) [74.8, 83.8]	52.7 (5.05) [42.3, 62.0]
	6 months (SE) [95% CI]	63.9 (2.78) [58.2, 69.1]	24.0 (4.92) [15.1, 34.1]
	12 months (SE) [95% CI]	33.1 (2.94) [27.5, 38.9]	17.1 (4.88) [8.9, 27.7]
	Hazard Ratio ^a [95% CI]	0.38 [0.28, 0.50]	
	Follow-up time (months)		
	Median [95% CI]	16.4 [14.2, 17.0]	3.7 [2.3, 5.4]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.6

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-24 2021-06-01 11:02

\NFS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISIONSCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 25
Radiographic Progression-free Survival based on Independent Central Review by Prior use of PARP inhibitors
(PFS-Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
Prior PARP:	n/N (%)	18/24 (75.0)	5/11 (45.5)
Yes	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	2.6 [1.3, 7.0]	2.1 [2.0, 2.3]
	Median rPFS [95% CI]	8.4 [2.6, 11.1]	2.3 [2.0, NE]
	75th percentile [95% CI]	12.2 [8.7, NE]	NE [2.2, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	72.5 (9.60) [48.6, 86.6]	40.0 (17.38) [9.8, 69.7]
	6 months (SE) [95% CI]	58.0 (10.73) [34.7, 75.6]	40.0 (17.38) [9.8, 69.7]
	12 months (SE) [95% CI]	29.0 (9.94) [11.9, 48.7]	40.0 (17.38) [9.8, 69.7]
	Hazard Ratio ^a [95% CI]	0.31 [0.11, 0.89]	
	Follow-up time (months)		
	Median [95% CI]	15.2 [14.3, 17.1]	2.3 [0.0, 5.4]
	Minimum-Maximum	0.0 - 17.1	0.0 - 5.4
Prior PARP:	n/N (%)	236/361 (65.4)	88/185 (47.6)
No	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.1 [3.1, 4.7]	2.1 [2.0, 2.2]
	Median rPFS [95% CI]	8.8 [8.3, 10.5]	3.5 [2.5, 4.0]
	75th percentile [95% CI]	17.0 [13.8, 19.7]	7.0 [4.6, 14.9]
	rPFS rates (%)		
	3 months (SE) [95% CI]	80.2 (2.13) [75.7, 84.1]	55.6 (4.52) [46.3, 63.9]
	6 months (SE) [95% CI]	65.0 (2.60) [59.7, 69.9]	28.0 (4.62) [19.4, 37.3]
	12 months (SE) [95% CI]	33.4 (2.76) [28.1, 38.9]	19.2 (4.56) [11.2, 28.8]
	Hazard Ratio ^a [95% CI]	0.41 [0.31, 0.53]	
	Follow-up time (months)		
	Median [95% CI]	16.4 [14.2, 17.0]	3.9 [2.6, 5.7]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.8

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-25 2021-06-01 11:02

\NFS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISIONSCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 26
Radiographic Progression-free Survival based on Independent Central Review by Concurrent use of NAADs as part of BSC/BSoC treatment (PFS-Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
Concur NAAD:	n/N (%)	122/193 (63.2)	57/124 (46.0)
Yes	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	4.3 [3.1, 5.7]	2.2 [2.0, 2.5]
	Median rPFS [95% CI]	10.2 [8.5, 11.2]	3.9 [3.1, 5.6]
	75th percentile [95% CI]	14.4 [13.2, 20.3]	14.4 [6.1, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	82.1 (2.82) [75.8, 86.9]	62.3 (5.20) [51.3, 71.6]
	6 months (SE) [95% CI]	67.0 (3.53) [59.6, 73.4]	37.9 (5.81) [26.6, 49.0]
	12 months (SE) [95% CI]	34.7 (3.90) [27.2, 42.4]	25.9 (5.96) [15.2, 38.0]
	Hazard Ratio ^a [95% CI]	0.46 [0.33, 0.65]	
	Follow-up time (months)		
	Median [95% CI]	15.2 [14.1, 17.0]	4.0 [2.6, 6.0]
	Minimum-Maximum	0.0 - 20.3	0.0 - 19.8
Concur NAAD:	n/N (%)	132/192 (68.8)	36/72 (50.0)
No	Kaplan-Meier estimates (months)		
	25th percentile [95% CI]	3.7 [2.3, 4.6]	2.0 [1.7, 2.1]
	Median rPFS [95% CI]	8.5 [7.1, 9.8]	2.3 [2.1, 3.6]
	75th percentile [95% CI]	16.2 [12.0, 19.7]	4.2 [2.7, 6.0]
	rPFS rates (%)		
	3 months (SE) [95% CI]	77.5 (3.06) [70.8, 82.8]	37.4 (7.61) [22.8, 51.9]
	6 months (SE) [95% CI]	62.2 (3.60) [54.7, 68.8]	8.4 (5.14) [1.8, 21.8]
	12 months (SE) [95% CI]	31.5 (3.64) [24.5, 38.7]	8.4 (5.14) [1.8, 21.8]
	Hazard Ratio ^a [95% CI]	0.25 [0.17, 0.38]	
	Follow-up time (months)		
	Median [95% CI]	16.4 [14.2, 17.0]	2.4 [2.0, 6.0]
	Minimum-Maximum	0.0 - 22.6	0.0 - 6.9

Concur NAAD: Concurrent use of NAADs

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-26 2021-06-01 11:02

\\\FS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 27
Radiographic Progression-free Survival based on Independent Central Review by Concurrent use of radiation therapy as part of BSC/BSoC treatment (PFS-Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
Concur	n/N (%)	37/49 (75.5)	16/28 (57.1)
RT:	Kaplan-Meier estimates (months)		
Yes	25th percentile [95% CI]	5.3 [3.1, 8.5]	2.1 [0.9, 2.5]
	Median rPFS [95% CI]	10.2 [7.3, 11.4]	2.7 [2.2, 4.3]
	75th percentile [95% CI]	13.0 [11.4, 19.3]	4.3 [2.7, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	89.8 (4.32) [77.2, 95.6]	46.5 (11.40) [23.8, 66.4]
	6 months (SE) [95% CI]	72.5 (6.53) [57.3, 83.0]	21.8 (10.19) [6.2, 43.4]
	12 months (SE) [95% CI]	30.5 (7.23) [17.3, 44.8]	10.9 (9.24) [0.9, 35.1]
	Hazard Ratio ^a [95% CI]	0.51 [0.27, 0.94]	
	Follow-up time (months)		
	Median [95% CI]	17.0 [14.1, NE]	4.3 [2.2, 14.4]
	Minimum-Maximum	2.0 - 20.3	0.0 - 14.4
Concur	n/N (%)	217/336 (64.6)	77/168 (45.8)
RT:	Kaplan-Meier estimates (months)		
No	25th percentile [95% CI]	3.8 [2.6, 4.4]	2.1 [2.0, 2.2]
	Median rPFS [95% CI]	8.7 [8.0, 10.5]	3.7 [2.4, 4.0]
	75th percentile [95% CI]	17.0 [14.0, NE]	7.0 [4.8, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	78.3 (2.30) [73.4, 82.4]	55.8 (4.77) [45.9, 64.5]
	6 months (SE) [95% CI]	63.4 (2.73) [57.8, 68.5]	28.7 (5.01) [19.4, 38.7]
	12 months (SE) [95% CI]	33.6 (2.86) [28.0, 39.2]	20.5 (5.01) [11.7, 31.0]
	Hazard Ratio ^a [95% CI]	0.39 [0.29, 0.51]	
	Follow-up time (months)		
	Median [95% CI]	15.2 [14.2, 17.0]	3.9 [2.4, 5.4]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.8

Concur RT: Concurrent use of radiation therapy

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-27 2021-06-01 11:02

\\\FS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Table 28
Radiographic Progression-free Survival based on Independent Central Review by Concurrent use of Bone
Sparing Agents as part of BSC/BSoC treatment (PFS-Full Analysis Set)

		Lu-PSMA-617+ BSC/BSoC (N=385)	BSC/BSoC only (N=196)
Concur	n/N (%)	122/175 (69.7)	48/96 (50.0)
BSA:	Kaplan-Meier estimates (months)		
Yes	25th percentile [95% CI]	3.3 [2.3, 4.4]	2.2 [2.0, 2.9]
	Median rPFS [95% CI]	8.5 [6.9, 10.2]	4.0 [3.4, 5.6]
	75th percentile [95% CI]	14.3 [11.7, 20.6]	10.6 [5.6, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	76.0 (3.27) [68.9, 81.7]	63.6 (5.71) [51.3, 73.6]
	6 months (SE) [95% CI]	61.9 (3.76) [54.0, 68.8]	34.4 (6.46) [22.1, 46.9]
	12 months (SE) [95% CI]	31.2 (3.79) [23.9, 38.7]	21.4 (6.54) [10.3, 35.2]
	Hazard Ratio ^a [95% CI]	0.51 [0.36, 0.72]	
	Follow-up time (months)		
	Median [95% CI]	16.9 [14.2, 17.1]	4.7 [3.0, 6.5]
	Minimum-Maximum	0.0 - 20.6	0.0 - 17.2
Concur	n/N (%)	132/210 (62.9)	45/100 (45.0)
BSA:	Kaplan-Meier estimates (months)		
No	25th percentile [95% CI]	4.3 [3.1, 5.7]	2.0 [1.9, 2.1]
	Median rPFS [95% CI]	9.8 [8.5, 11.3]	2.4 [2.1, 3.4]
	75th percentile [95% CI]	17.0 [13.5, 20.3]	4.8 [3.4, NE]
	rPFS rates (%)		
	3 months (SE) [95% CI]	83.0 (2.66) [77.1, 87.6]	43.0 (6.57) [30.0, 55.3]
	6 months (SE) [95% CI]	67.0 (3.40) [59.8, 73.1]	19.9 (5.98) [9.8, 32.6]
	12 months (SE) [95% CI]	34.8 (3.73) [27.6, 42.1]	16.6 (5.83) [7.2, 29.4]
	Hazard Ratio ^a [95% CI]	0.29 [0.20, 0.42]	
	Follow-up time (months)		
	Median [95% CI]	15.2 [14.0, 17.0]	2.6 [2.0, 4.3]
	Minimum-Maximum	0.0 - 22.6	0.0 - 19.8

Concur BSA: Concurrent use of bone sparing agents

n: Total number of events included in the analysis.

N: Total number of patients included in the analysis.

^a Hazard Ratio of Lu-PSMA-617+BSC/BSoC vs. BSC/BSoC based on stratified Cox PH model stratified for LDH (<= 260 IU/L vs. > 260 IU/L); presence of liver metastases (yes vs. no); ECOG score (0 or 1 vs. 2) and inclusion of NAAD in best supportive/standard of care at time of randomization (yes vs no). Stratification factors based on data from IRT.

Output ID: T-28 2021-06-01 11:02

\\\FS\ISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\t-eff-os-rpfs-sgp.sas

Data Cutoff Date: 27JAN2021

Table 29 OS sensitivity analyses- impact of dropout (Full analysis set)

Analysis	Scenarios	HR (95% CI)
Analysis per protocol	Censored as it is	0.62 (0.52, 0.74)
Extreme case	The selected extreme case scenario	0.66 (0.55, 0.79)
Multiple imputation under best subjects	Hazard in BSC/BSOC arm based on best 20% subjects across both arms	0.8 (0.67, 0.96)
Multiple imputation under best BSC/BSOC subjects	Hazard in BSC/BSOC arm based on best 20% BSC/BSOC subjects	0.76 (0.64, 0.91)
Multiple imputation under non-informative censoring	Hazard remains unchanged after censoring	0.63 (0.53, 0.76)
Multiple imputation under informative censoring	Hazard decrease by 38% in BSC/BSOC arm after censoring*	0.68 (0.56, 0.82)
Tipping point 1: largest upper 95% CI	Hazard decrease by 99% in BSC/BSOC arm after censoring*	0.84 (0.7, 1.00)
Tipping point 2: Extreme case	Hazard decrease by 27% in BSC/BSOC arm after censoring*	0.66 (0.55, 0.79)

*: risk of event remains unchanged after censoring in the investigational arm

This results are based on 1000 simulations implemented in the code placed in /vob/CAAA000A1/CAAA000A12301/csr_2/pgm/stats/os_sensitivity.R. The outputs are placed in the same folder in GPS.

Session Information

R version 3.6.1 (2019-07-05)

```
Platform: x86_64-pc-linux-gnu
Locale: LC_CTYPE=en_US.UTF-8;LC_NUMERIC=C;LC_TIME=en_US.UTF-8;
LC_COLLATE=en_US.UTF-8;LC_MONETARY=en_US.UTF-8;LC_MESSAGES=en_US.UTF-8;
LC_PAPER=en_US.UTF-8;LC_NAME=C;LC_ADDRESS=C;LC_TELEPHONE=C;LC_MEASUREMENT=en_US.UTF-8;
LC_IDENTIFICATION=C
```

Packages

```
Base: base, datasets, graphics, grDevices, methods, stats, utils
Other: data.table (v1.12.6), dplyr (v0.8.3), DT (v0.9), ggplot2 (v3.2.1), ggrepel (v0.2.3), gtools (v3.8.1),
haven (v2.2.0), ldbounds (v1.1-1.1), magrittr (v1.5), MatchIt (v3.0.2), mvtnorm (v1.0-11), purrr (v0.3.3), rtf
(v0.4-14), sandwich (v2.5-1), stringr (v1.4.0), survival (v3.1-7), survminer (v0.4.6), tidyverse (v1.0.0), viridis
(v0.5.1), viridisLite (v0.3.0)
Loaded (not attached): assertthat (v0.2.1), backports (v1.1.5), broom (v0.5.3), colorspace (v1.4-1),
compiler (v3.6.1), crayon (v1.3.4), digest (v0.6.22), evaluate (v0.14), forcats (v0.4.0), generics (v0.0.2),
ggsignif (v0.6.0), glue (v1.3.1), grid (v3.6.1), gridExtra (v2.3), gtable (v0.3.0), hms (v0.5.2), htmltools
(v0.4.0), htmlwidgets (v1.5.1), km.ci (v0.5-2), KMsurv (v0.1-5), knitr (v1.25), labeling (v0.3), lattice (v0.20-38),
lazyeval (v0.2.2), lifecycle (v0.1.0), MASS (v7.3-51.4), Matrix (v1.2-17), munsell (v0.5.0), nlme (v3.1-142),
pillar (v1.4.2), pkgconfig (v2.0.3), plyr (v1.8.4), R.methodsS3 (v1.7.1), R.oo (v1.23.0), R6 (v2.4.0),
Rcpp (v1.0.3), readr (v1.3.1), reshape2 (v1.4.3), rlang (v0.4.1), rmarkdown (v1.16), rstudioapi (v0.10),
scales (v1.0.0), splines (v3.6.1), stringi (v1.4.3), survMisc (v0.5.5), tibble (v2.1.3), tidyselect (v0.2.5), tools
(v3.6.1), vctrs (v0.2.0), withr (v2.1.2), xfun (v0.10), xtable (v1.8-4), yaml (v2.2.0), zeallot (v0.1.0), zoo
(v1.8-6)
```

Session Details

Working directory: /home/[Contact]
Output file: os_sensitivity.rtf

Table 30 rPFS based on independent central review sensitivity analyses- impact of dropout (PFS-Full analysis set)

Analysis	Scenarios	HR (99.2% CI)
Analysis per protocol	Censored as it is	0.4 (0.29, 0.57)
Extreme case	The selected extreme case scenario	0.42 (0.3, 0.6)
Multiple imputation under best subjects	Hazard in BSC/BSOC arm based on best 20% subjects across both arms	0.77 (0.55, 1.07)
Multiple imputation under best BSC/BSOC subjects	Hazard in BSC/BSOC arm based on best 20% BSC/BSOC subjects	0.56 (0.4, 0.79)
Multiple imputation under non-informative censoring	Hazard remains unchanged after censoring	0.4 (0.29, 0.56)
Multiple imputation under informative censoring	Hazard decrease by 60% in BSC/BSOC arm after censoring*	0.54 (0.38, 0.77)
Tipping point 1: 99.2% CI above 1	Hazard decrease by 85% in BSC/BSOC arm after censoring*	0.71 (0.5, 1.01)
Tipping point 2: Extreme case	Hazard decrease by 11% in BSC/BSOC arm after censoring*	0.42 (0.3, 0.59)

*: risk of event remains unchanged after censoring in the investigational arm

This results are based on 1000 simulations implemented in the code placed in /vob/CAAA000A1/CAAA000A12301/csr_2/pgm/stats/rpfs_sensitivity.R. The outputs are placed in the same folder in GPS.

Session Information

R version 3.6.1 (2019-07-05)

```
Platform: x86_64-pc-linux-gnu
Locale: LC_CTYPE=en_US.UTF-8;LC_NUMERIC=C;LC_TIME=en_US.UTF-8;LC_COLLATE=en_US.UTF-8;LC_MONETARY=en_US.UTF-8;LC_MESSAGES=en_US.UTF-8;LC_PAPER=en_US.UTF-8;LC_NAME=C;LC_ADDRESS=C;LC_TELEPHONE=C;LC_MEASUREMENT=en_US.UTF-8;LC_IDENTIFICATION=C
```

Packages

```
Base: base, datasets, graphics, grDevices, methods, stats, utils
Other: data.table (v1.12.6), dplyr (v0.8.3), DT (v0.9), ggplot2 (v3.2.1), ggpubr (v0.2.3), gtools (v3.8.1), haven (v2.2.0), ldbounds (v1.1-1.1), magrittr (v1.5), MatchIt (v3.0.2), mvtnorm (v1.0-11), purrr (v0.3.3), rtf (v0.4-14), sandwich (v2.5-1), stringr (v1.4.0), survival (v3.1-7), survminer (v0.4.6), tidyverse (v1.0.0), viridis (v0.5.1), viridisLite (v0.3.0)
Loaded (not attached): assertthat (v0.2.1), backports (v1.1.5), broom (v0.5.3), colorspace (v1.4-1), compiler (v3.6.1), crayon (v1.3.4), digest (v0.6.22), evaluate (v0.14), forecats (v0.4.0), generics (v0.0.2), ggsignif (v0.6.0), glue (v1.3.1), grid (v3.6.1), gridExtra (v2.3), gtable (v0.3.0), hms (v0.5.2), htmltools (v0.4.0), htmlwidgets (v1.5.1), km.ci (v0.5-2), KMsurv (v0.1-5), knitr (v1.25), labeling (v0.3), lattice (v0.20-38), lazyeval (v0.2.2), lifecycle (v0.1.0), MASS (v7.3-51.4), Matrix (v1.2-17), munsell (v0.5.0), nlme (v3.1-142), pillar (v1.4.2), pkgconfig (v2.0.3), plyr (v1.8.4), R.methodsS3 (v1.7.1), R.oo (v1.23.0), R6 (v2.4.0), Rcpp (v1.0.3), readr (v1.3.1), reshape2 (v1.4.3), rlang (v0.4.1), rmarkdown (v1.16), rstudioapi (v0.10), scales (v1.0.0), splines (v3.6.1), stringi (v1.4.3), survMisc (v0.5.5), tibble (v2.1.3), tidyselect (v0.2.5), tools (v3.6.1), vctrs (v0.2.0), withr (v2.1.2), xfun (v0.10), xtable (v1.8-4), yaml (v2.2.0), zeallot (v0.1.0), zoo (v1.8-6)
```

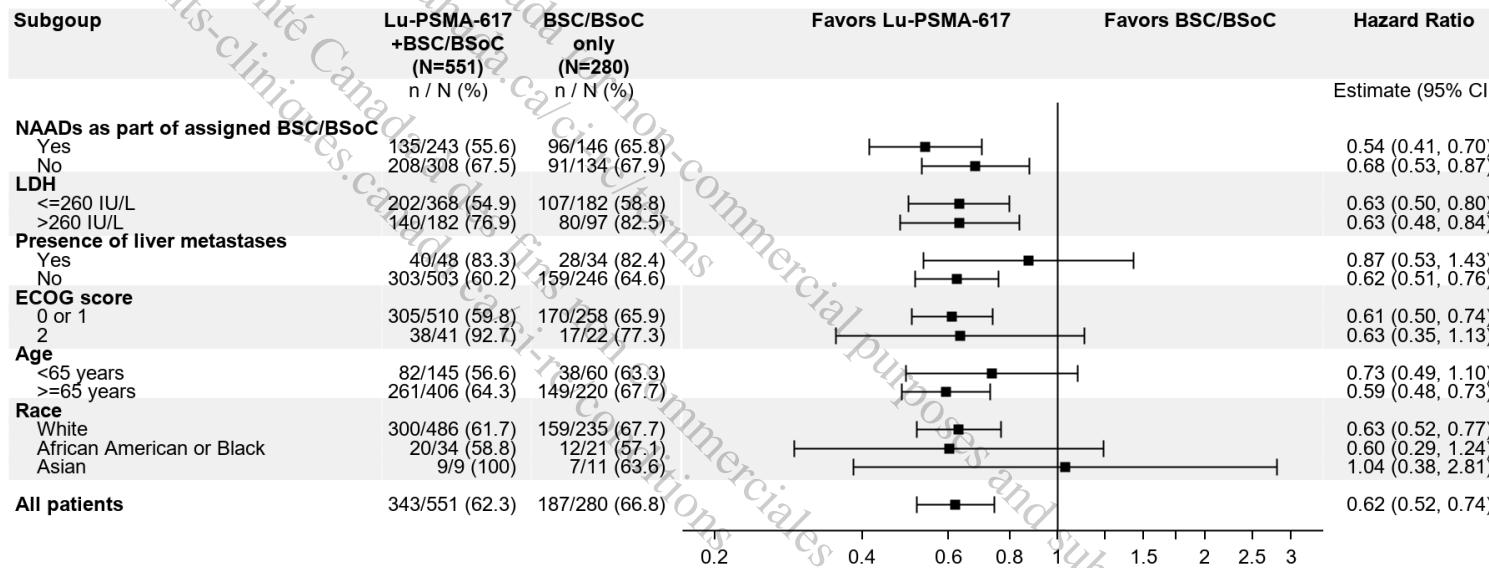
Session Details

Working directory: /home/[Contact]
Output file: rpfs_sensitivity.rtf

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Figure 1 Forest Plot of Hazard Ratio with 95% Confidence Interval for Overall Survival from Subgroup Analysis (Full Analysis Set)



n/N: Number of events/number of patients in treatment arm. Bold line shows no effect point.

Note: NAAD: Novel androgen axis drugs, PSADT: Prostate-specific antigen doubling time, PSA: Prostate-specific antigen, PARP: Poly ADP ribose polymerase

Output ID: F-1 2021-06-01 11:03

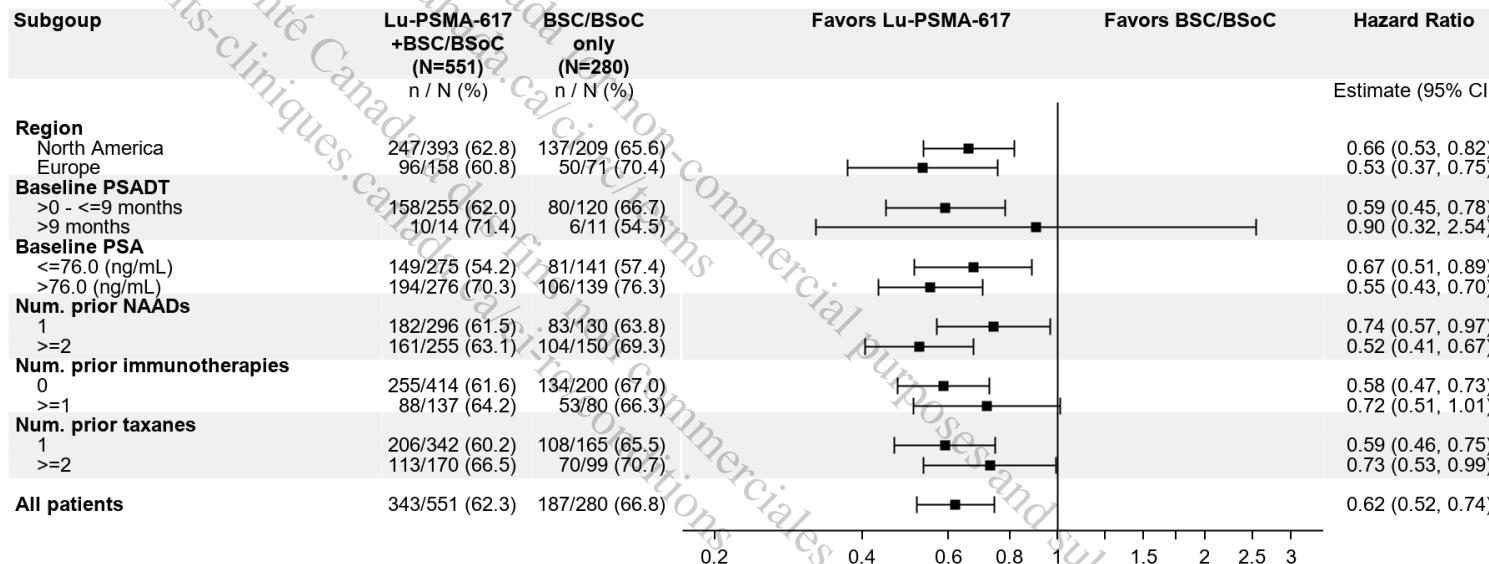
\WFSISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\f-forest.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Figure 1 Forest Plot of Hazard Ratio with 95% Confidence Interval for Overall Survival from Subgroup Analysis (Full Analysis Set)



n/N: Number of events/number of patients in treatment arm. Bold line shows no effect point.

Note: NAAD: Novel androgen axis drugs, PSADT: Prostate-specific antigen doubling time, PSA: Prostate-specific antigen, PARP: Poly ADP ribose polymerase

Output ID: F-1 2021-06-01 11:03

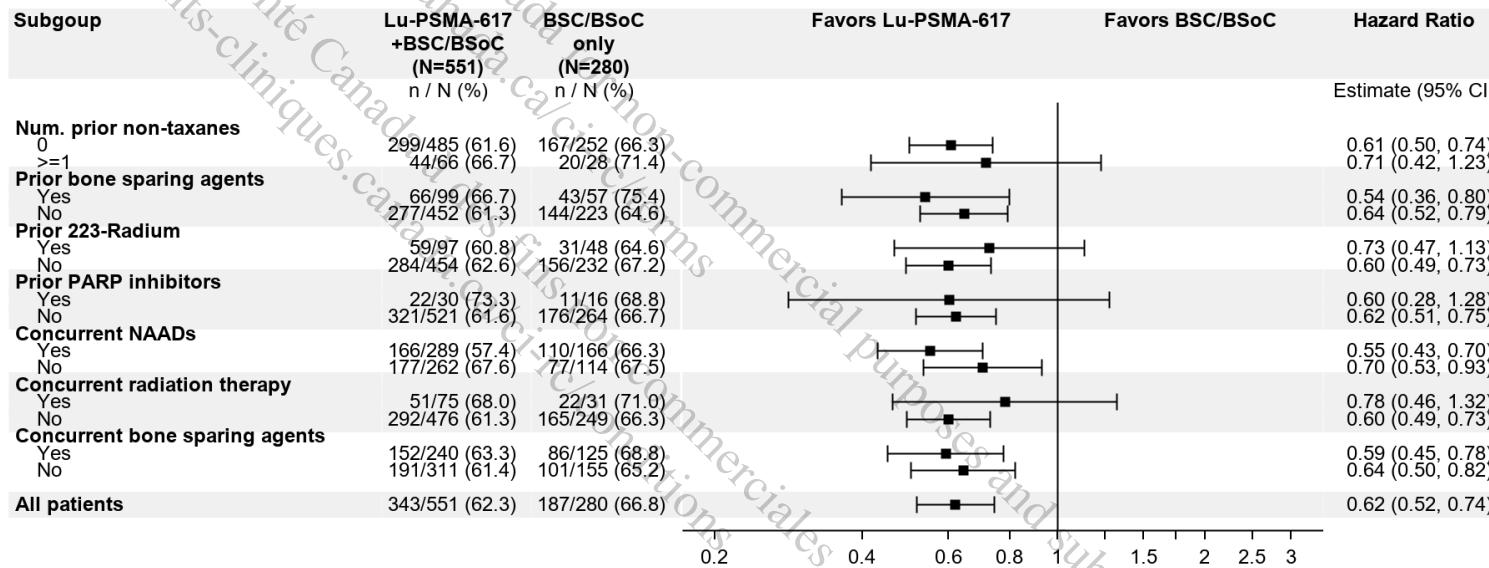
\WFSISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\f-forest.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Figure 1 Forest Plot of Hazard Ratio with 95% Confidence Interval for Overall Survival from Subgroup Analysis (Full Analysis Set)



n/N: Number of events/number of patients in treatment arm. Bold line shows no effect point.

Note: NAAD: Novel androgen axis drugs, PSADT: Prostate-specific antigen doubling time, PSA: Prostate-specific antigen, PARP: Poly ADP ribose polymerase

Output ID: F-1 2021-06-01 11:03

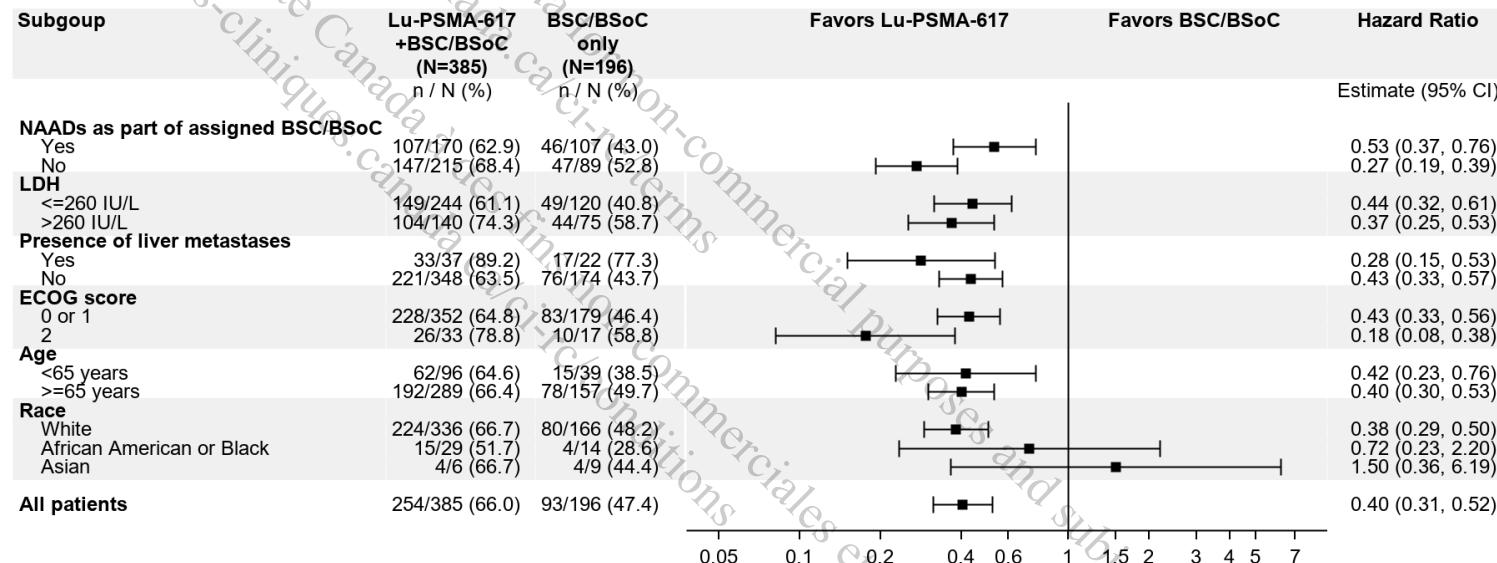
\WFSISTGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\f-forest.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Figure 2 Forest Plot of Hazard Ratio with 95% Confidence Interval for Radiographic Progression-free Survival based on Independent Central Review from Subgroup Analysis (PFS-Full Analysis Set)



n/N: Number of events/number of patients in treatment arm. Bold line shows no effect point.

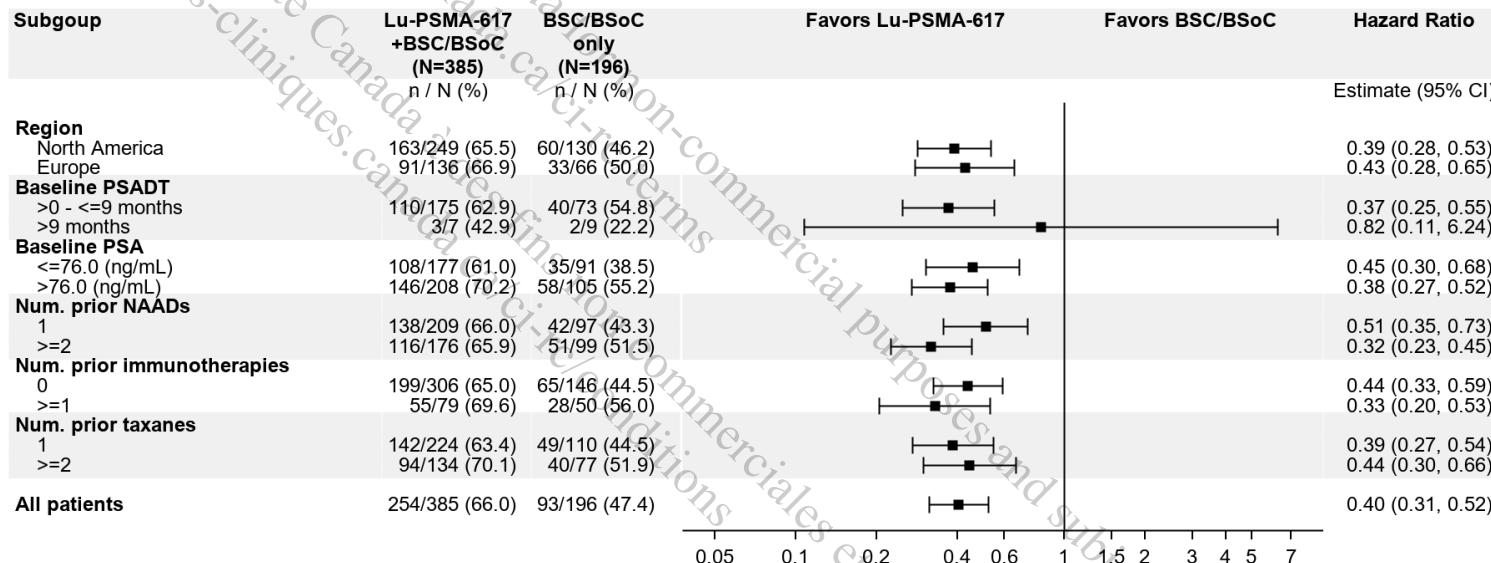
Note: NAAD: Novel androgen axis drugs, PSADT: Prostate-specific antigen doubling time, PSA: Prostate-specific antigen, PARP: Poly ADP ribose polymerase
Output ID: F-2 2021-06-01 11:03

\\\FS\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGMf-forest.sas
Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Figure 2 Forest Plot of Hazard Ratio with 95% Confidence Interval for Radiographic Progression-free Survival based on Independent Central Review from Subgroup Analysis (PFS-Full Analysis Set)



n/N: Number of events/number of patients in treatment arm. Bold line shows no effect point.

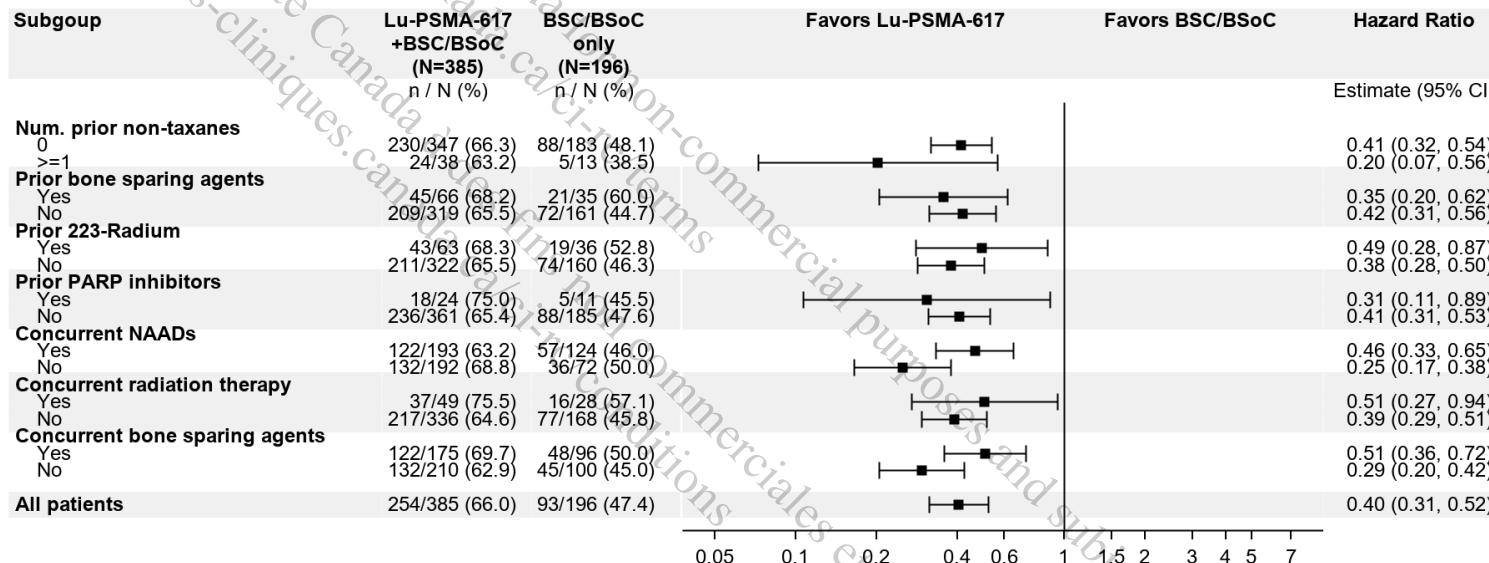
Note: NAAD: Novel androgen axis drugs, PSADT: Prostate-specific antigen doubling time, PSA: Prostate-specific antigen, PARP: Poly ADP ribose polymerase
Output ID: F-2 2021-06-01 11:03

\FS\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGMf-forest.sas
Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Figure 2 Forest Plot of Hazard Ratio with 95% Confidence Interval for Radiographic Progression-free Survival based on Independent Central Review from Subgroup Analysis (PFS-Full Analysis Set)



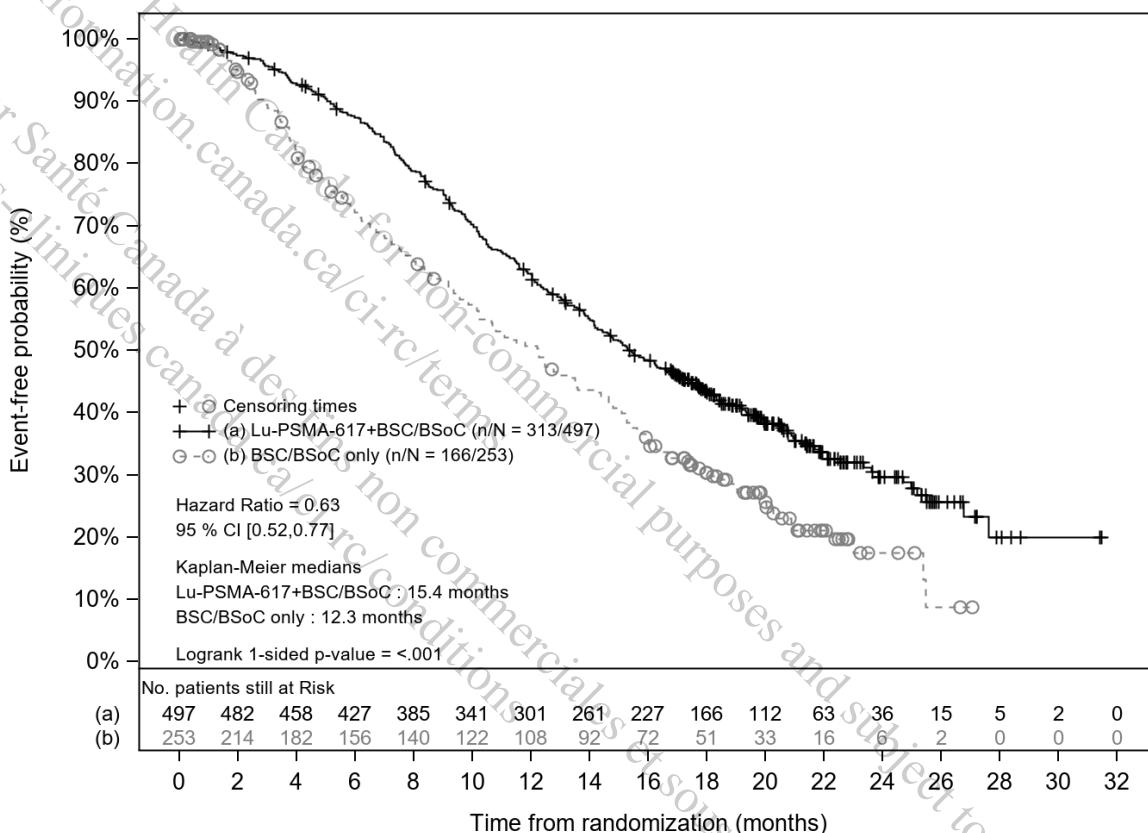
n/N: Number of events/number of patients in treatment arm. Bold line shows no effect point.

Note: NAAD: Novel androgen axis drugs, PSADT: Prostate-specific antigen doubling time, PSA: Prostate-specific antigen, PARP: Poly ADP ribose polymerase
Output ID: F-2 2021-06-01 11:03

\\\FS\STGENESIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGMf-forest.sas
Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Figure 14.2.1.1.3
Kaplan-Meier plot for overall survival in the first 750 randomized (Full analysis set)

Stratified log-rank test and stratified Cox model using strata per IRT defined by LDH level, presence of liver metastases, ECOG score and inclusion of NAAD in BSC/BSoC at time of randomization.

n/N: Number of events/number of patients in treatment arm.

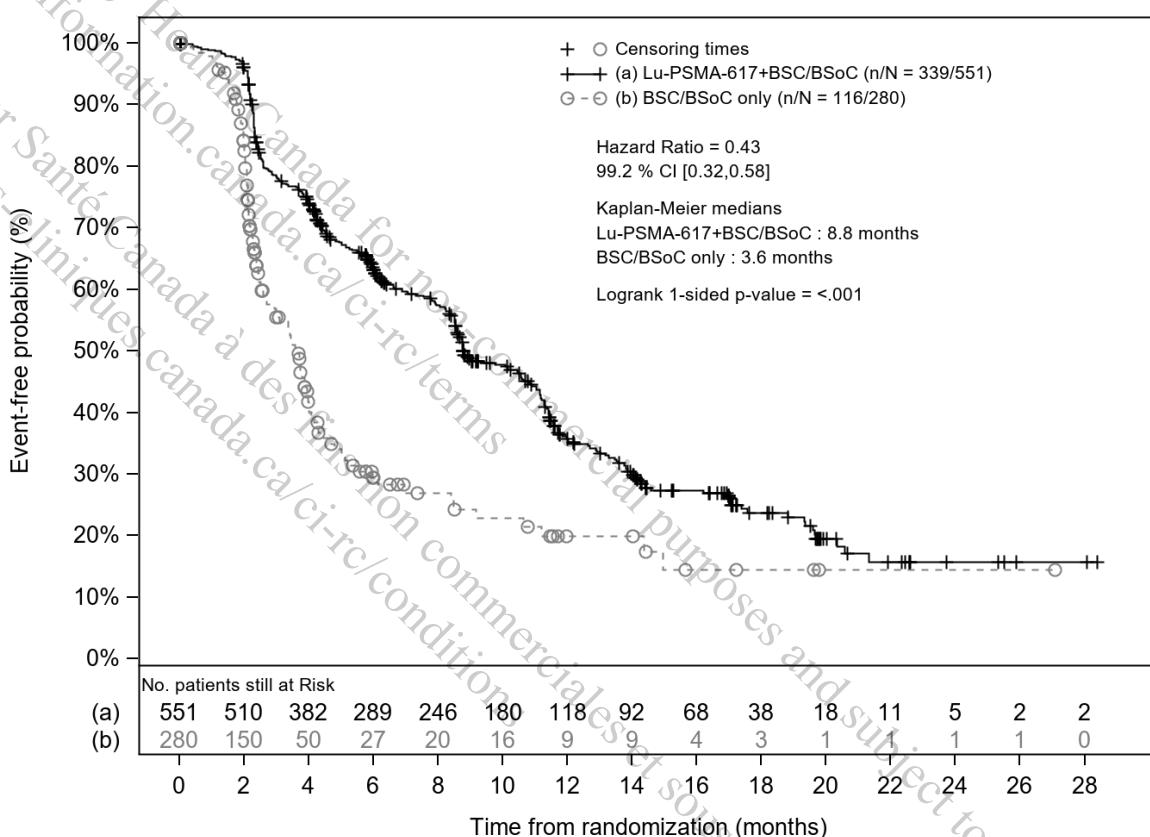
Output ID: F-14-2-1-1-3 2021-06-01 11:05

\FS\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\f-km-os-750.sas

Data Cutoff Date: 27JAN2021

Advanced Accelerator Applications, a Novartis Company
177Lu-PSMA-617 SCE

Final Version

Figure 14.2.2.5
Kaplan-Meier plot for radiographic progression-free survival based on independent central review (Full analysis set)

Stratified log-rank test and stratified Cox model using strata per IRT defined by LDH level, presence of liver metastases, ECOG score and inclusion of NAAD in BSC/BSoC at time of randomization.

n/N: Number of events/number of patients in treatment arm.

Output ID: F-14-2-2-5 2021-06-01 11:05

\FS\STGENIS\AAA\BIOMETRY\PROJECTS\PSMA617\VISION\SCE\PRODUCTION\TLF\PGM\f-km-adh.sas

Data Cutoff Date: 27JAN2021