Poster FPN 1651P

Characteristics, tolerance, and effectiveness of patients aged more or less than 75 years treated with [177Lu]Lu-PSMA-617 as part of France's early access program

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KEY FINDINGS & CONCLUSIONS

- An early access program (EAP) has been granted to [177Lu]Lu-PSMA-617 in France, for patients (pts) with progressive mCRPC expressing PSMA, previously treated with ≥1 taxane chemotherapy and ≥1 ARPI.
- From December 01, 2021 to June 30, 2024, **2251 PSMA-PET-positive mCRPC patients were included in this EAP**.
- Among them, **1334 were aged ≤ 75 years old (59.3%) and 917 were > 75 years old (40.7%).**
- Elderly patients have a poorer general condition, higher PSA level and altered renal function.
- These patients aged > 75 years old were also more likely to be pretreated with >1 ARPI and external radiotherapy. During follow-up they received **less frequently opioid analgesic treatment.**
- No significant difference was observed between the two groups regarding the administration of concomitant treatments and the median time to imaging PFS was not statistically different between the two groups.
- **Elderly patients were most likely to have received all doses (43% vs. 38%).** Side effects seemed to be more frequent as a cause for discontinuation in elderly patients (18% vs. 9%).

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INTRODUCTION

- [177Lu]Lu-PSMA-617 is a radiopharmaceutical with binding affinity to the **prostate specific membrane antigen (PSMA)**, expressed in 90% of **metastatic castration resistant prostate cancer (mCRPC)** [1].
- The VISION study showed that [177Lu]Lu-PSMA-617 combined with best standard of care, **prolonged progression-free survival (rPFS), overall survival, and delayed time to worsening in health-related quality of life** in patients with PSMA-positive mCRPC, previously treated with at least one taxane-based chemotherapy and one androgen receptor pathway inhibitors (ARPI) [2]. A cohort temporary authorization for use (ATUc) has been granted to [177Lu]Lu-PSMA-617 by French Health Authorities for patients in this indication. This **early access program** (EAP) began on December 01, 2021 and is still in progress.
- [177Lu]Lu-PSMA-617 safety profile in the elderly is not known. This work is a retrospective analysis comparing the **characteristics, safety, and efficacity of [177Lu]Lu-PSMA-617** in patients aged > 75 years old treated in France as part of early access program, compared to patients aged ≤ 75 years old.

METHODS

- [177Lu]Lu-PSMA-617 was given to **patients with progressive mCRPC overexpressing PSMA, previously treated with ≥1 taxane chemotherapy and ≥1 ARPI**. They received intravenous infusions of [177Lu]Lu-PSMA-617 once every six weeks for up to six cycles.
- In order to ensure a minimum of 6-month follow-up after the first injection and to obtain a homogeneous population providing a greater robustness in the presented results, the efficacy data focused on patients included from December 01, 2021 to September 30, 2023 (data cut-off 1, DCO 1). Patient's characteristics and safety data were described from the total patient population included in this EAP, from the December 01, 2021 to June 30, 2024 (data cut-off 2, DCO 2).

RESULTS

- Since December 01, 2021, 2251 patients with mCRPC and PSMA-PET-positive imaging, pretreated with 1-2 taxane chemotherapy and ≥1 ARPI were included in this EAP. Among them, **1334 were aged ≤ 75 years old (59.3%) and 917 were > 75 years old (40.7%)**. Patients characteristics are described in **Table 1**.

Table 1. Characteristics of the patients at baseline (n=2251)

Characteristics	≤ 75 years old (n=1334)	> 75 years old (n=917)	P-Value
Age - years			
Median (range)	68.8 (37-75)	79.2 (75-93)	N/A
≥ 75 years – n (%)	9 (0.7)	917 (100.0)	N/A
≥ 85 years – n (%)	0 (0.0)	115 (12.5)	N/A
ECOG performance status score – n (%)			
0-1	1182 (88.6)	772 (84.2)	<0.001
0	438 (32.8)	190 (20.7)	
1	744 (55.8)	582 (63.5)	
2	139 (10.4)	140 (15.3)	
3	11 (0.8)	4 (0.4)	
Sites of disease – n (%)			
Bone	1246 (93.4)	849 (92.6)	0.452
Lymph node	824 (61.8)	530 (57.8)	0.059
Liver	109 (8.2)	83 (9.1)	0.463
Lung	113 (8.5)	76 (8.3)	0.878
Brain	22 (1.6)	7 (0.8)	0.067
Bone only	419 (31.4)	312 (34.0)	N/A
Bone + lymph node	512 (38.4)	333 (36.3)	N/A
Bone + lymph node + lung	51 (3.8)	40 (4.4)	N/A
Bone + lymph node + liver	52 (3.9)	33 (3.6)	N/A
Bone + lymph node + others	77 (5.8)	36 (3.9)	N/A
Prostate-specific antigen (PSA) – ng/ml			
Median (range)	**48.0 (0-6680)**	**59.9 (0-6972)**	0.0308
100% of PSMA-positive lesions – n (%)			
Yes	1005 (75.5)	703 (76.7)	0.765
Creatinine clairance – n (%)			
≥ 60	**1246 (93.4)**	**780 (85.1)**	<0.001
30 - 60	**74 (5.5)**	**122 (13.3)**	
Albuminemia – n (%)			
< 3.0 g/dL	22 (1.7)	17 (1.9)	0.534 (NS)

- Patients > 75 years tend to have a **poorer general condition.** They also tend to have fewer lymph node and brain metastases (the results are not significant but near 0.05 threshold).
- **PSA levels are higher** in patients aged > 75 years (59.9 ng/ml vs. 48.0 ng/ml). In addition, a **smaller proportion of patients over 75 years old have a creatinine clearance ≥ 60**.

Previous treatments recieved

- Anterior treatments have been compared in the two populations. Results are described in **Table 2**.

Table 2. Previous treatments recieved (n=2251)

Characteristics	≤ 75 years old (n=1334)	> 75 years old (n=917)	P-Value
Next-generation hormonal agent – n (%)			
One	609 (45.7)	366 (39.9)	0.007
More than one	**725 (54.3)**	**551 (60.1)**	
Taxane chemotherapy – n (%)			
One taxane	624 (46.8)	465 (50.7)	0.021
More than one taxane	**700 (52.5)**	**427 (46.6)**	
Chemo-naïve (contra-indication)	10 (0.7)	25 (2.7)	
Treatment combination – n (%)			
2 hormonal agents + 2 chemotherapies	**327 (24.5)**	**209 (22.8)**	<0.001
External radiotherapy – n (%)			
Yes	**614 (46.1)**	**462 (50.4)**	0.044
Internal radiotherapy – n (%)			
Yes	37 (2.8)	32 (3.5)	0.330
Immunotherapy – n (%)			
Yes	72 (5.4)	35 (3.8)	0.082
PARP inhibitors – n (%)			
Yes	**80 (6.0)**	**29 (3.2)**	0.002
Number of systemic treatments			
Median	4	4	0.312

- Elderly patients were **more likely to receive >1 ARPI and external radiotherapy**. However, taxane chemotherapy, PARP inhibitors, and treatment combinations (2 ARPI + 2 chemotherapies) were less frequent in this population.
- Patients > 75 years received **less frequently opioid analgesic treatment** (19.6% vs. 32.3%, data not shown) during follow-up.

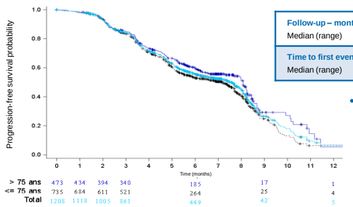
Concomitant treatment

- **No significant difference** was observed between the two groups regarding the concomitant administration of ARPI, androgen deprivation, biphosphonates or denosumab (data not shown).

Efficacy (n=1222 patients included from December 01, 2021 to September 30, 2023)

- Imaging follow-up was carried out according to the investigators' choice, in most cases both CT-PET and bone scintigraphy and in some cases PSMA-PET or PET-Choline (**Figure 1**).

Figure 1. Imaging-based PFS



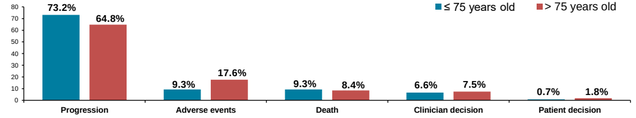
	≤ 75 years old (n=743)	> 75 years old (n=479)	P-Value
Follow-up – months			
Median (range)	6.64 (6.21-6.64)	6.74 (6.27-6.82)	
Time to first event – months			
Median (range)	7.20 (5.88-7.72)	8.08 (7.33-8.25)	0.1043

- The median time to imaging PFS was not statistically different between the two groups. Similarly, PFS of symptoms and PFS of PSA levels were not significantly different between patients > 75 or ≤ 75 years old (data not shown).

End of treatment (n=1059 patients included from December 01, 2021 to September 30, 2023)

- The following data have not been evaluated statistically. Among patients who stopped treatment, 422 received all six doses and went to every follow-up visit (39.8%). Elderly patients were most likely to have received all doses (43% vs. 38%). The other causes of treatment interruption are described in **Figure 2**.

Figure 2. Causes of treatment interruption



- **Side effects seemed to be more frequent as a cause for discontinuation in elderly patients**. However, there was no significant difference in the occurrence of AEs during follow-up: 2.4% of patients aged >75 years and 1.6% of those ≤ 75 years experienced at least 1 AE during follow-up (p=0.102).

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Conflicts of interest

DT: Novartis; **JF**: Boston Scientific; **LA**: None; **CM**: Advanced Accelerator Applications-Novartis, Curium, Bayer, AstraZeneca, Janssen, Astellas, Pfizer; **ASC**: Advanced Accelerator Applications-Novartis; **SC**: Advanced Accelerator Applications-Novartis; **CB**: Boston Scientific, Advanced Accelerator Applications-Novartis, Sirtex Medical, Telix Radiopharmaceuticals; **MB**: Advanced Accelerator Applications-Novartis; **LM**: Astellas, Janssen, MSD, BMS, Ipsen, AstraZeneca, Pfizer, Merck, Advanced Accelerator Applications-Novartis, Sanofi; **ML**: None

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