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Real-life data on [177Lu]Lu- PSMA-617 : Descriptive analysis on the largest metastatic castration - resistant prostate cancer (mCRPC) cohort treated in France

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Note: this is poster is an encore of the original presented at ASCO-GU. Consent has been obtained from French authors.

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 and ≥1 NHA.
- From December 01, 2021 to October 28, 2023 (DCO 2), 1340 TEP-PSMA-positive mCRPC patients were included in this EAP.
- Considering the population from the VISION study, patients from this EAP had a poorer ECOG, more metastasis and were more heavily pre-treated.
- For those included until February 28, 2023 (DCO 1), patients received a median of 4 cycles. The median imaging-based PFS is 7.3 months.
- Despite an altered general condition, safety data were similar to VISION, and no new safety signal was identified.
- [177Lu]Lu-PSMA-617 tends to be used earlier in patients With mCRPC compared to the beginning of this EAP.

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 added to standard of care prolonged radiographic-based progression-free survival (rPFS) and overall survival (OS) in patients with PSMA-positive mCRPC**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.
- This work is a descriptive analysis on the largest mCRPC cohort of patients with mCRPC treated with [177Lu]Lu -PSMA-617 in EAP in France. These data are preliminary and will be updated as patients are still included, treated and followed -up. This analysis was conducted with a data cut-off (DCO) of October 28, 2023.

METHODS

- [177Lu]Lu-PSMA-617 was given to patients with progressive mCRPC overexpressing PSMA, previously treated with ≥1 taxane and ≥1 next-generation hormonal agent (NHA) Patients were selected for PSMA positivity based on PSMA positron -emission tomography . They received intravenous infusions of [177Lu]Lu-PSMA-617 at a dose of 7.4 GBq ± 10% once every six weeks for six cycles.
- 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 February 28 , 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 December 01, 2021 to October 31, 2023 (data cut-off 2, DCO2).

RESULTS

Patients included

- Since December 01, 2021, 1340 patients with mCRPC and TEP-PSMA-positive imaging, pretreated with 1-2 taxane chemotherapy and ≥1 NHA were included in this EAP. Patient characteristics are described in Table 1.
- Efficacy data were assessed from 696 patients included from December 01, 2021 to February 28, 2023 only, for a minimal follow -up time .
- In perspective of the VISION study population, patients from this EAP were older (73.4 *vs.* 70.0), with a poorer ECOG performance status (ECOG PS) (ECOG PS 0-1, 87.4% *vs.* 92.6%), and a higher prevalence of lymph node metastasis (60.9% *vs.* 49.7%) (Table 1).

Table 1. Characteristics of the patients at baseline

Characteristics	DCO 2 General Population n = 1340	DCO 1 Efficacy Population n = 696
Age - years		
Median (range)	73.4 (44-92)	72.8 (46-92)
≥ 75 years–n (%)	466 (34.8)	258 (37.1)
≥ 85 years–n (%)	71 (5.3)	36 (5.2)
ECOG performance status score (ECOG PS) –n (%)		
0-1	1171	593 (85.2)
0	367 (27.4)	178 (25.6)
1	(804 (60.0)	415 (59.6)
2	159 (11.9)	96 (13.8)
3	9 (0.7)	7 (1.0)
Sites of disease–n (%)		
Bone	1252 (93.4)	652 (93.7)
Lymph node	816 (60.9)	440 (63.2)
Liver	125 (9.3)	81 (11.6)
Lung	124 (9.3)	73 (10.5)
Brain	21 (1.6)	12 (1.7)
Bone only	425 (31.7)	202 (29.0)
Bone + lymph node	510 (38.1)	267 (38.4)
Bone + lymph node + lung	61 (4.6)	36 (5.2)
Bone + lymph node + liver	53 (4.0)	32 (4.6)
Bone + lymph node + others	55 (4.1)	30 (4.3)
Prostate-specific antigen (PSA)–ng/ml		
Median (range)	63.0 (0-6972)	81.9 (0-4562)
100% of PSMA-positive lesions–n (%)		
Yes	1041 (77.7)	527 (75.7)
Creatinine clearance –n (%)		
≥ 60	1204 (89.9)	629 (90.4)
30 -60	116 (8.7)	57 (8.2)
Time between TEP PSMA and patient inclusion		
Median in months (range)	0.5 (00-14.5)	0.5 (0.0 -8.2)

Previous treatments received

- In perspective of the VISION study population, a higher proportion of patients received ≥ 2 NHA and 2 taxanes (Table 2).

Table 2. Previous treatments

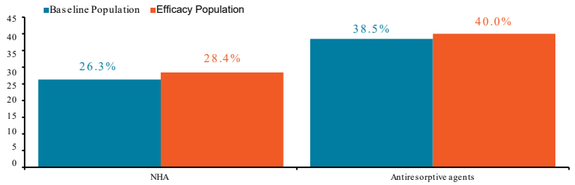
Treatments	DCO 2 General Population n=1340 (%)	DCO 1 Efficacy Population n=696 (%)
Next-generation hormonal agent – n (%)		
One More than one	467 (35.4) 862 (64.3)	228 (32.8) 468 (67.2)
Taxane chemotherapy– n (%)		
One taxane	547 (40.8)	227 (32.6)
More than one taxane	758 (56.6)	451 (64.8)
Chemo-naïve (contra-indication)	35 (2.6)	18 (2.6)
Internal radiotherapy– n (%)		
Yes	47 (3.5)	11
- 223Radium	38	11*
- other 177Lutetium-PSMA	9	0#
Retreated patient within EAP#	13	0#
PARP inhibitors		
Previously received PARPi	52 (3.9)	30 (4.3)
Number of major systemic treatments received **		
Median	3	4

* Excluding surgery, external radiotherapy, ADT and new class of investigational medicine products
\# The retreated patients are counted once and excluded from DCO2 to avoid misleading information in terms of efficacy

Concomitant treatments

- 1085 patients received a concomitant treatment. Almost all of them received ADT. The distribution is shown in Figure 1. Data on concomitant treatments are similar for both populations. **Less patients received NHA in parallel compared to VISION trial.**

Figure 1. Concomitant treatments



[177 Lu]Lu-PSMA-617 administration

- On February 28, 2023, among the 696 patients included in the efficacy analysis, 99 are still under treatment. **Patients received a median of 4 cycles** (*vs.* 5 in VISION trial). **18.7% patients had a decreased activity.**

N° cycles of [177Lu]Lu -PSMA-617	Efficacy Population n=696 (%)
1	70 (10.1)
2	99 (14.2)
3	99 (14.2)
4	93 (13.4)
5	116 (16.7)
6	219 (31.5)

Efficacy (n=696 patients included from December 01, 2021 to February 28, 2023)

- Imaging follow -up was performed according to investigators' choice. In most cases, both CT scan + bone scan. In some cases by PET-PSMA (Figure 2). Number of patients assessed with standard *vs.* molecular imaging will be subsequently reported.

Figure 2. Imaging -based PFS

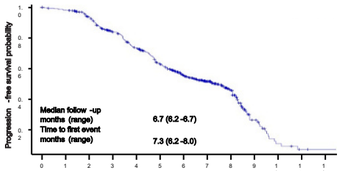
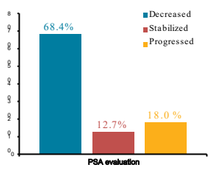


Figure 3. Best PSA response



- A minority of patients (4.9%) did not report any improvement in their symptoms (mainly pain). Approximately one fifty (18.1%) of patients experienced an early and sustained biochemical progression.

Safety (n=1321 patients included from December 01, 2021 to October 31, 2023)

- Most adverse effects (AE) were considered as expected (n=244/344) and no safety signal was identified, despite a poor condition at baseline.
- **The most frequent reported AE was hematotoxicity (n=192/344)** (Table 3).
- According to EMA Important Medical Event (IME) list, thrombocytopenia and neutropenia are classified as serious AEs. Anemia grade 3 and higher (CT-EAE) are classified as serious AEs.

Table 3. Hematological adverse events

Treatment related AE (n=192)	Thrombocytopenia (63/192)	Anemia (58/192)	Neutropenia (30/192)	Leucopenia (20/192)
Serious–n (%)	62/63 (98.4)	40/58 (69.0)	30/30 (100.0)	20/20 (100.0)
Non-serious–n (%)	1/63 (1.6)	18/58 (31.0)	0/30 (0.0)	0/20 (0.0)

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Disclosures

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