Poster 2395P

Retreatment with [177Lu]Lu-PSMA-617 in mCRPC patients treated under the French Early Access Program (EAP)

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KEY FINDINGS & CONCLUSIONS

- An Early Access Program (EAP) has been granted to [177Lu]Lu-PSMA-617 in France, for patients with progressive mCRPC expressing PSMA, previously treated with ≥1 taxane chemotherapy and ≥1 ARPI. This retrospective analysis focuses on patients retreated beyond 6 cycles.
- As of April 29, 2025, **134 patients had received a second schedule**, including 4 who had subsequently initiated a third schedule.
- Minor patient characteristics differences were observed between their first and second schedule of treatment.
- During the second schedule, **retreated patients received less frequently a concomitant treatment** and more specifically concomitant ARPI than during the first.
- **Most retreated patients experienced clinical improvement** and **PSA decrease** during the second schedule follow-up.
- **No new signal of adverse events occured** during the retreatment period

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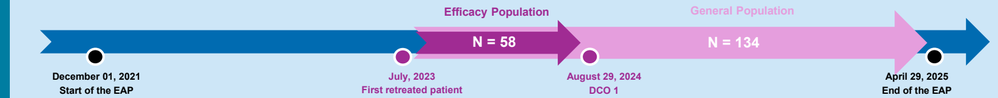
INTRODUCTION

- [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 a benefice of 5.3 months of PFS and 4 months of OS with [177Lu]Lu-PSMA-617 versus standard of care.[2]
- However, most patients eventually progress, leading to more research to answer the question : **"Can extended cycles or retreatment maintain safety and efficacy?"**. Subsequent studies have shown that retreatment with [177Lu]Lu-PSMA-617 preserves efficacy, with PSA declines ≥ 50% observed in 37-64% of patients. Importantly, toxicity remains manageable, without significant increase in severe adverse events. These findings suggest [177Lu]Lu-PSMA-617 retreatment as a safe and effective therapeutic strategy for patients who have progressed.[3-5]
- This work is a descriptive analysis comparing the **characteristics, safety, and efficacity of [177Lu]Lu-PSMA-617** in patients retreated beyond 6 cycles with [177Lu]Lu-PSMA-617. While previous studies have been conducted on limited patient cohorts, our analysis involves the **largest global cohort to date**.
- These are exploratory results, generating hypotheses that will need to be validated by further studies.

METHODS

[177Lu]Lu-PSMA-617 was given to patients with mCRPC, positive on [68Ga]Ga-PSMA-11 PET, previously treated with ≥1 chemotherapy and ≥1 androgen receptor pathway inhibitor (ARPI). Treatment consisted of up to 6 cycles (7.4 GBq) every 6 weeks during initial treatment and retreatment.

Of the 134 patients who received an additional course of [177Lu]Lu-PSMA-617 following the initial treatment, 4 subsequently underwent a third schedule. Various parameters were assessed within the retreated population.



RESULTS

Retreatment experience in France

GENERAL POPULATION

- As of April 29, 2025, 134 patients had received a second schedule, including 4 who had subsequently initiated a third schedule.
- Of the 46 centers in France, 23 have retreated patients (50%)
  - Majority of these centers are experienced centers
  - Median number of retreated patients per center : 4 [1;15]

Patient characteristics

- Patient characteristics are described in Table 1.

Table 1. Patient characteristics at baseline

Characteristics	First schedule (not yet retreated) (n = 134)	Second schedule (retreatment) (n = 134)	Third schedule (retreatment) (n = 4)
Age - years			
Median (range)	**72.4** (55.2 – 86.7)	**73.5** (56.1 – 88.7)	**74.3** (65.0 – 77.8)
≥ 75 years – n (%)	47 (35.1)	55 (42.3)	2 (50.0)
≥ 85 years – n (%)	4 (3.0)	6 (4.6)	0 (0.0)
ECOG performance status score – n (%)			
0-1	**124 (92.5)**	**120 (89.6)**	**4 (100.0)**
Sites of disease – n (%)			
Bone	119 (88.8)	121 (90.3)	4 (100.0)
Lymph node	87 (64.9)	79 (59.0)	2 (50.0)
Liver	5 (3.7)	7 (5.2)	1 (25.0)
Lung	15 (11.2)	13 (9.7)	1 (25.0)
Brain	1 (0.7)	3 (2.2)	0 (0.0)
100% of PSMA-positive lesions – n (%)			
Yes	**103 (76.9)**	**93 (69.4)**	**2 (50.0)**
Creatinine clairance – n (%)			
≥ 60	124 (92.5)	116 (86.6)	3 (75.0)
30 – 60	**10 (7.5)**	**18 (13.4)**	**1 (25.0)**

- **Some** differences were observed at the initiation of the various treatment schedules within the retreated patients.
- **Fewer** of them had 100% PSMA-positive lesions, and ECOG status ≤ 1. Increasing number of patients were presenting renal impairment. This suggests a decline in patient condition at the start of the second schedule, compared to the first schedule.

Previous treatments received

GENERAL POPULATION

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

Table 2. Previous treatments received

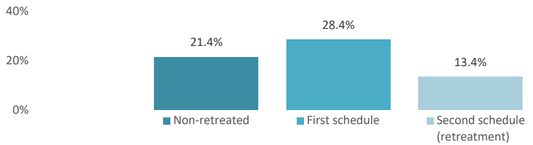
Characteristics	First schedule (not yet retreated) (n = 134)	Second schedule (retreatment) (n = 134)	Third schedule (retreatment) (n = 4)
ARPI– n (%)			
1	57 (42.5)	48 (35.8)	1 (25.0)
≥ 2	**77 (57.5)**	**86 (64.2)**	3 (75.0)
Taxane-chemotherapy– n (%)			
1	59 (44.0)	57 (42.5)	0 (0.0)
≥ 2	**75 (56.0)**	**77 (57.5)**	4 (100.0)

- 2 patients received taxane-chemotherapy between two schedules and 9 patients received ARPI.

Concomitant ARPI treatment

GENERAL POPULATION

Figure 1. Concomitant ARPI treatment



- In the initial treatment schedule, the 134 retreated patients were more likely to have received **concomitant ARPI** (compared to non-retreated patients).
- However, **fewer patients received a concomitant ARPI during their second schedule (retreatment) than during their first schedule**.

Treatment administrations

EFFICACY POPULATION

- During the first schedule, patients received a median of 6 (1-6) administration of [177Lu]Lu-PSMA-617 and 3 (1-6) during their second schedule.
- The patient who received the highest number of cycles received 13 cycles with a total activity of 92.02 GBq administered.

Progression-Free Survival (n = 58 patients from efficacy population)

With an 8-months follow-up

EFFICACY POPULATION

Table 3.

Schedule		Imaging-based evaluation First (n=134)	Imaging-based evaluation Second (n=58)	Clinical evaluation First (n=134)	Clinical evaluation Second (n=58)	PSA evaluation First (n=134)	PSA evaluation Second (n=58)
Patient proportion without progression at 6 months – n (%)		127 (94.8)	41 (70.7)	125 (93.3)	46 (79.3)	95 (70.9)	27 (46.6)
Best response obtained	Improvement	75.6	38.2	65.4	30.9	95.5	67.9
	Stabilization	21.4	36.2	33.8	63.6	2.3	10.7
	Progression	0.8	19.1	0.8	5.5	2.3	19.6

- Most retreated patients showed :
  - Disease **stabilization** (clinical evaluation) during second schedule
  - PSA **decrease** during second schedule

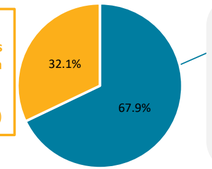
Treatment discontinuation (n = 134 patients from second schedule)

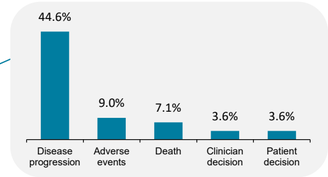
GENERAL POPULATION

- From the General Population, 56 patients received a second schedule and completed an end of treatment form. The other 78 patients were still being monitored at the end of the EAP. Among them, **1/3 received the planned 6 cycles**. The causes of treatment discontinuation are described in Figure 2.

Figure 2. Causes of early treatment discontinuation

Nearly 1/3 of retreated patients received the extra 6 cycles during the 2nd schedule (retreatment period)





- In the first schedule : 15/134 patients were affected by at least 1 related AE (total of AEs = 25)
  - 8 patients experienced hematotoxicities (11/25 AEs)
  - 2 patients experienced renal disorders (2/25 AEs)
- In the second schedule: only 3/134 patients were affected by at least 1 related AE (total of AEs = 5). All those AEs were hematotoxicites considered to be expected
- In the 4 patients who initiated the 3rd schedule, no AEs were reported to date

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Conflicts of interest

PB : AdAcAp-Novartis, Amgen, Astellas, AstraZeneca, Bayer, Bristol-Myers Squibb, Eisai, Gilead, Ipsen, Johnson&Johnson, Merck, MSD, Novartis, Pfizer, Seagen ; **DT** : None ; **FS** : AdAcAp-Novartis, Curium, Bayer, Telix, Blue Earth Diagnostics, Astellas, Ipsen, Netcancer ; **CP** : None ; **SC** : AdAcAp-Novartis ; **AD** : AdAcAp-Novartis ; **PR** : AdAcAp-Novartis, Astellas, Curium, Johnson&Johnson, Netcancer, Siemens Healthcare.

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