Poster FPN 1628P

Factors Influencing Clinical and Biological Response in Patients Treated with [177Lu]Lu-PSMA-617 under France's Early Access Program.

Vincent Habouzit [1], Marine Claudin [2], Fanny Borrelly [3], Capucine Richard [4], Clément Bailly [5], Paul Schwartz [6], Elise Mairal [7], Stephanie Chêne [8], Kevin Hébert [9]

[1] Centre Hospitalier Universitaire, Saint-Etienne, France ; [2] Centre Hospitalier Universitaire, Nancy, France ; [3] Centre Hospitalier Universitaire, Nîmes, France ; [4] Institut Curie, Paris, France ; [5] Centre Hospitalier Universitaire, Nancy, France ; [6] Institut Bergonié, Bordeaux, France ; [7] Centre Jean Perrin, Clermont-Ferrand, France ; [8] Advanced Accelerator Applications, Rueil-Malmaison, France ; [9] Institut du Cancer de Montpellier, Montpellier, France

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.
- From December 01, 2021 to September 30, 2023, **1048 PSMA-PET-positive mCRPC patients** were included in this EAP. They were classified as **responders (n=466; 44.5%) and non-responders (n=582; 55.5%) based on clinical and biological follow-up.**
- The characteristics of the patients, their disease, and the therapeutic sequences recorded in the EAP database were compared between the two populations using a bivariate analysis. Patients classified as **clinico-biological responders** are therefore more likely to:
  . Have not developed **brain metastases** and have **100% of PSMA-positive lesions.**
  . Have received **concomitant treatment**, in particular **ARPI** or **biphosphonates**.
  . Have had a **reduction in opioid analgesic** treatment during follow-up.
  . Have received all **six courses of treatment**.
- Further analysis showed that **PSMA-PET lesion positivity, concomitant treatment, particularly concurrent ARPI administration also contribute to enhance imaging and symptom-based progression free survival.**

Scan to obtain:
- Poster

https://bit.ly/Habouzit1628P

Copies of this poster obtained through Quick Response (QR) code are for personal use only and may not be reproduced without permission of the authors.

Dr Vincent HABOUZIT : vincent.habouzit@chu-st-etienne.fr

This study is sponsored by Novartis Pharma AG
Poster presented at ESMO Congress, held in Barcelona, Spain (13-17 September 2024)

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.
- Various factors related to patients, their disease, and the treatment sequence may impact the treatment's effectiveness. This work is a retrospective analysis that aims to evaluate the **influence of these factors on the clinical and biological response** of patients receiving [177Lu]Lu-PSMA-617 under France's early access program.

METHODS

- [177Lu]Lu-PSMA-617 was given to **patients with progressive mCRPC overexpressing PSMA, previously treated with ≥1 taxane chemotherapy and ≥1 ARPI**. Patients included had received at least one of the six planned cycles of intravenous infusions of [177Lu]Lu-PSMA-617 (7.4 GBq ± 10%) administered every six weeks.
- In order to ensure a minimum of 6-month follow-up after the first injection, the efficacy data focused on patients included from December 01, 2021 to September 30, 2023 (data cut-off 1, DCO 1). Patient's baseline characteristics 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).
- Patients were categorized into two groups: **Responders** (experiencing reduced PSA levels and improved clinical symptoms) and **Non-responders** (experiencing PSA progression and/or worsening clinical symptoms). Response evaluation was conducted by the referring nuclear medicine physician during routine care follow-up visits. Group characteristics were compared using bivariate analysis. Additionally, the impact of factors associated with treatment response on progression-free survival (PFS) was evaluated.

RESULTS

- From the December 01, 2021 to June 30, 2024, 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, **684 were classified as responders (30.4%) and 1567 as non-responders (69.6%)**. Patients characteristics from both subgroups are described in **Table 1**.

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

Characteristics	Non-responders (n=1567)	Responders (n=684)
Age - years		
Median (range)	73.7 (37-93)	73.3 (44-92)
≥ 75 years – n (%)	652 (41.6)	274 (40.1)
≥ 85 years – n (%)	85 (5.4)	30 (4.4)
ECOG performance status score (ECOG PS) – n (%)		
0-1	1357 (86.7)	597 (87.3)
0	448 (28.6)	180 (26.3)
1	909 (58.1)	417 (61.0)
2	195 (12.5)	84 (12.3)
3	12 (0.9)	3 (0.4)
Sites of disease – n (%)		
Bone	1456 (92.9)	639 (93.4)
Lymph node	936 (59.7)	418 (61.1)
Liver	142 (9.1)	50 (7.3)
Lung	133 (8.5)	56 (8.2)
Brain	22 (1.4)	7 (1.0)
Bone only	515 (32.9)	216 (31.6)
Bone + lymph node	583 (37.2)	262 (38.3)
Bone + lymph node + lung	58 (3.7)	33 (4.8)
Bone + lymph node + liver	63 (4.0)	22 (3.2)
Bone + lymph node + others	71 (4.5)	42 (6.1)
Prostate-specific antigen (PSA) – ng/ml		
Median (range)	48.0 (0-6972)	64.0 (0-4293)
100% of PSMA-positive lesions – n (%)		
Yes	1130 (72.2)	578 (84.5)
Time between inclusion and positive PET - months		
Median (range)	0.5 (0-55)	0.5 (0-15)

- Efficacy data and statistical comparison were assessed from 1048 patients included until September 30, 2023, including **466 responders (44.5%) and 582 non-responders (55.5%)**.

Statistical comparison of the two sub-groups

- Among all the parameters, a significant difference between the two groups (p<0.05) was observed for the criteria listed in **Table 2**.

Table 2. Factors statistically significantly associated with treatment responses (n=1048)

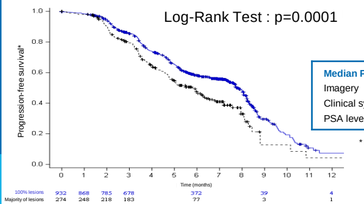
Characteristics	Non-responders (n=582)	Responders (n=466)	Odd-Ratio ; P-value
Sites of disease – n (%)			
Brain	15 (2.6)	**4 (0.9)**	**0.33** [0.11-0.99]; 0.038
100% of PSMA-positive lesions – n (%)			
Yes	423 (72.7)	**395 (84.8)**	**2.07** [1.51-2.82]; <0.001
Number of cycles administered – n			
Median	3.0	**6.0**	**0.52** [0.47-0.57]; <0.0001
During follow-up – n (%)			
≥ 1 reduction in activity	123 (21.1)	**123 (26.4)**	**1.34** [1.01-1.78]; 0.046
≥ 1 concomittant treatment	499 (85.7)	**436 (93.6)**	**2.42** [1.56-3.74]; <0.001
≥ 1 ARPI	106 (18.2)	**151 (32.4)**	**1.96** [1.47-2.63]; <0.001
≥ 1 biphosphonates	19 (3.3)	**34 (7.3)**	**2.14** [1.20-3.80]; 0.008
≥ 1 reduction of opioid analgesics	75 (12.9)	**184 (39.5)**	**4.41** [3.25-5.99]; <0.001

- Patients classified as clinico-biological responders are therefore more likely to:
  . Have not developed brain metastases and have 100% of PSMA-positive lesions.
  . Have received all six courses of treatment (and at least one reduction in activity).
  . Have received concomitant treatment, in particular ARPI or biphosphonates.
  . Have had at least one reduction in opioid analgesic treatment during follow-up.

Comparison of median progression-free survival (PFS)

- We further evaluated the impact of factors associated with clinical and biological treatment responses on progression-free survival (PFS), as assessed by imaging, clinical examination, and PSA evaluation during routine care follow-up.
- Our results suggest that **lesions positivity to PSMA (Figure 1), the use of concomitant treatment, particularly concomitant ARPI (Figure 2)**, contribute to **increased PFS**
- Additionally, it has also been observed that patients who have received a **single course of taxane chemotherapy** have a longer survival without symptom progression (**Figure 3**).

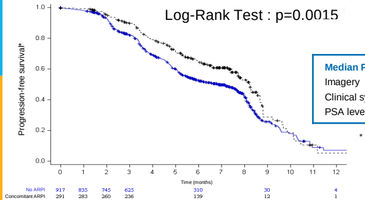
Figure 1. 100% lesion positivity to PSMA enhances imaging and symptom-based median PFS



	100% (n=944)	Majority (n=276)	P-Value
Median PFS – months			
Imagery	**7.8**	**5.8**	0.0001
Clinical symptoms	**8.2**	**6.6**	0.0035
PSA level	3.8	3.6	0.1634

* Progression-free survival confirmed by imagery as assessed during routine care follow-up

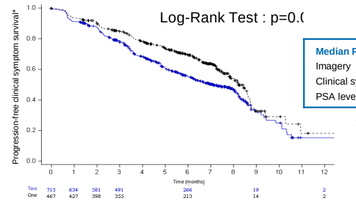
Figure 2. Administration of concomitant ARPI enhances imaging, symptom and PSA-based PFS



	ARPI (n=291)	No ARPI (n=931)	P-Value
Median PFS – months			
Imagery	**8.2**	**6.9**	0.0015
Clinical symptoms	**8.8**	**7.3**	<0.0001
PSA level	**4.7**	**3.6**	0.0396

* Progression-free survival confirmed by imagery as assessed during routine care follow-up

Figure 3. Single taxane chemotherapy pretreatment enhances symptom-based PFS



	1 regimen (n=468)	2 regimens (n=720)	P-Value
Median PFS – months			
Imagery	7.9	7.2	0.1617
Clinical symptoms	**8.2**	**7.1**	0.0003
PSA level	4.3	3.6	0.0881

* Progression-free clinical symptom survival as assessed during routine care follow-up

Acknowledgements

The authors thank the patients and their families, and all site investigators and personnel who participated in the study. Under the direction of the authors, Fabien Duval, PhD, of KPL Agency, Paris, France, provided medical writing assistance, which was funded by Advanced Accelerator Applications, in accordance with Good Publication Practice 4 (GPP4) guidelines (https:// www.ismpp.org/gpp-2022)..

Disclosures

VH: Sanofi, Sirtex, Boston Scientific, Pfizer; **MC**: Advanced Accelerator Applications-Novartis; **FB**: None; **CR**: None; **CB**: Boston Scientifics, Advanced Accelerator Applications-Novartis, Sirtex, Telix; **PS**: Advanced Accelerator Applications-Novartis, Eisai; **EM**: None; **SC**: Advanced Accelerator Applications-Novartis; **KH**: Advanced Accelerator Applications-Novartis; Astellas

References

1. **Paschalis A.** *et al.* Prostate-specific membrane antigen heterogeneity and DNA repair defects in prostate cancer. Eur Urol 2019; 76: 469-478
2. **Sartor O.** *et al.* Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. *N Engl J Med.* 2021; 385(12):1091-1103