Access to theranostics in metastatic castration-resistant prostate cancer in hospital settings in France

Study carried out under the framework of MR-006 reference methodology

TheranoPRO study – Additional analyses

Report Version V2.0, 31 January 2025

Table of contents

Study overview

Study overview

Additional objectives

Using France hospital discharge PMSI database

Obj. 1 and 2

1. To describe the **characteristics of mCRPC patients treated with ^{177}LuPSMA-617, with or without history of cabazitaxel** treatment before **^{177}LuPSMA-617**.
2. To describe **characteristics of mCRPC patients with or without hospitals stays between each ^{177}LuPSMA-617 administration.**

Obj. 3 and 4

3. To **identify factors influencing the choice to initiate ^{177}LuPSMA-617 or cabazitaxel.**
4. To describe **hospital stays occurring between each administration of treatment** in patients treated with **^{177}LuPSMA-617 vs. patients treated with cabazitaxel**.

Populations

Adult male patients living in France or DROM

Cohort of patients treated with ^{177}LuPSMA-617 in 2023 [Cohort 3]

Cohort of patients eligible to RLT and with an initiation of ^{177}LuPSMA-617 or cabazitaxel in 2022-2023

Sub-cohort of cohort 1

- Initiating ^{177}LuPSMA-617 or cabazitaxel in 2022-2023, without history of the other treatment (in 2015-2023)
- With ≥ 1 hospital stay with evidence of chemotherapy for PC before initiation, in 2015-2023

Periods

Historical period	7-year look-back period
Inclusion period	Year 2023
Index date (obj. 1 and 2)	First hospital stay with administration of ^{177}LuPSMA-617 in 2022-2023 period
Index date (obj. 3 and 4)	First hospital stay with administration of ^{177}LuPSMA-617 or cabazitaxel in 2022-2023 period
Follow-up period	Until 31 December 2023

Overview of the different cohorts of the TheranoPRO study

Patients with ≥ 1 chemotherapy for PC

- **Patients without ^{177}LuPSMA-617**
- **Patients with ^{177}LuPSMA-617***

Cohort 1
N = 12,130 [2022]
N = 12,427 [2023]

- **With an initiation of ^{177}LuPSMA-617 or cabazitaxel in 2022-2023**
  - **Sub-cohort 1**
    N = 523 [^{177}LuPSMA-617]
    N = 2875 [cabazitaxel]
    → **With ≥2 cures of treatment and ≥8 months of follow-up**
    N = 200 [^{177}LuPSMA-617]
    N = 1792 [cabazitaxel]
- **Without an initiation of ^{177}LuPSMA-617 or cabazitaxel in 2022-2023**

Patients without chemotherapy for PC

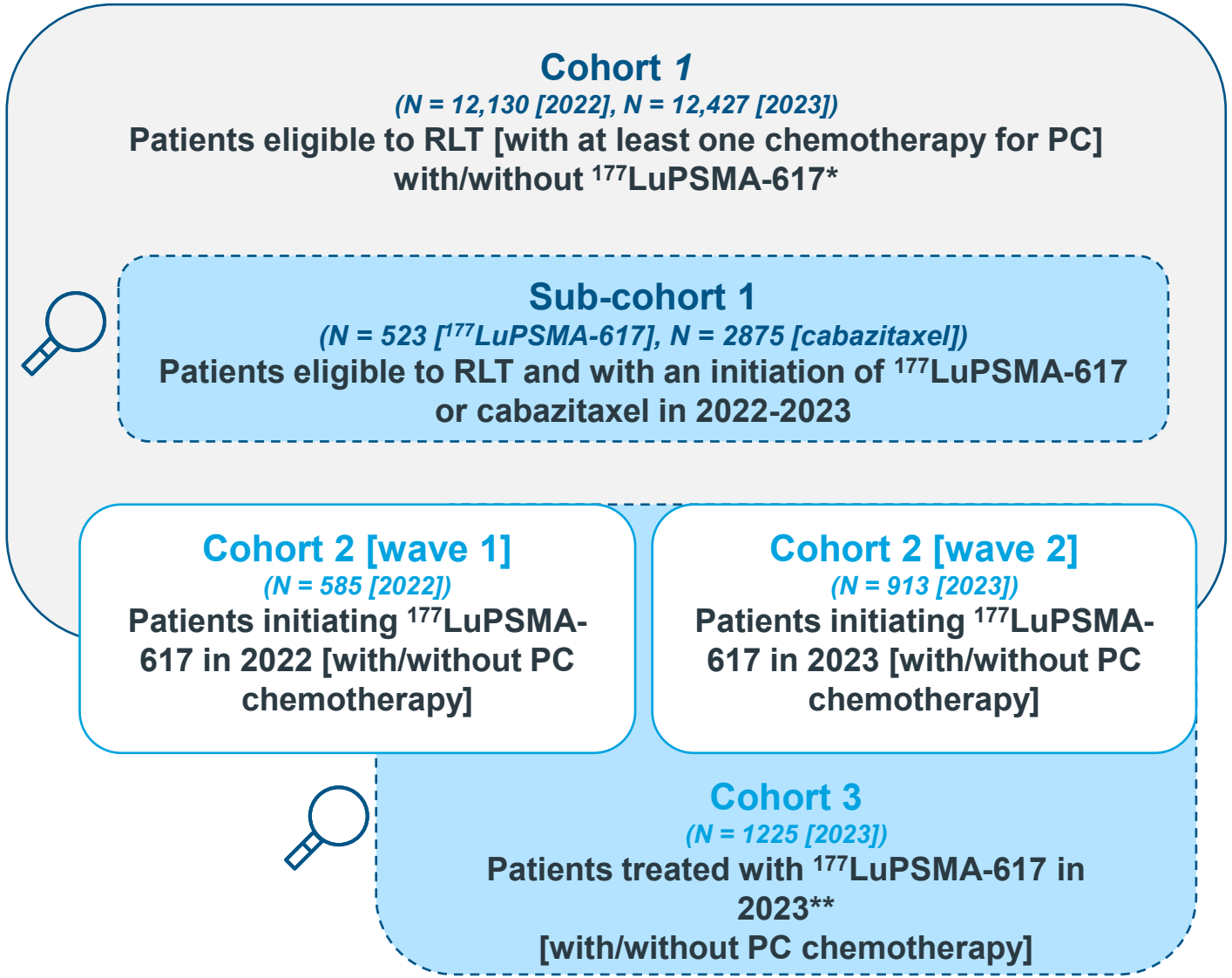
- **Patients with ^{177}LuPSMA-617**
- **Patients without ^{177}LuPSMA-617**

Cohort 2**
N = 585 initiators [2022]
N = 913 initiators [2023]

- **Last administration of ^{177}LuPSMA-617 in 2022**
- **≥ 1 administration of ^{177}LuPSMA-617 in 2023*****
  - **Cohort 3**
    N = 1225
    → **With ≥2 cures of treatment and ≥8 months of follow-up**
    N = 493

**At least one administration of ^{177}LuPSMA-617 in 2022 or 2023*
***Initiation of ^{177}LuPSMA-617 in 2022 or 2023*
****Patients with an initiation of ^{177}LuPSMA-617 in 2022 with current use in 2023 or initiation in 2023).*

Overview of the different cohorts of the TheranoPRO study



**At least one administration of ^{177}LuPSMA-617 in 2022 or 2023;*
***Initiation of ^{177}LuPSMA-617 in 2022 with current use in 2023 or initiation in 2023*

Identification of mCRPC patients treated with ^{177}LuPSMA-617 - [Cohort 3]

Inclusion criteria

- Male patients;
- Patients aged **≥18 years at index date;**
- **Patients with ≥ 1 administration of** ^{177}LuPSMA-617 **in 2023**
  - ^{177}LuPSMA-617 identified through UCD7 codes (9002980, 9001699).

Exclusion criteria

- Deceased before index date;
- Not living in France or DROM at index date.

Identification of mPC patients eligible to RLT and initiating ^{177}LuPSMA-617 or cabazitaxel - [Sub-cohort of Cohort 1]

Inclusion criteria

- Male patients;
- Patients aged **≥18 years at index date**;
- Having at least one hospital stay in PMSI-MCO with **evidence of chemotherapy for treatment of PC** during the study period (including historical and inclusion periods) [proxy for mCRPC patients eligible for RLT]
- Having **at least one hospital stay** during the **inclusion period;**
- **Initiating ^{177}LuPSMA-617 or cabazitaxel in 2022 or 2023** after evidence of chemotheray for treatment of PC.

Exclusion criteria

- Deceased patients during the historical period (i.e., between 2015 and 2021).
- Not living in France or DROM at index date.
- **Having administration of ^{177}LuPSMA-617, cabazitaxel or other RLT (excluding ^{177}LuPSMA-617) before initation of ^{177}LuPSMA-617 and cabazitaxel[1].**

[1] Note: To select patients at the same stage of the disease (candidates for second-line treatment).

Outcomes (1/2)

Additional objectives – Focus on mCRPC patients treated with ^{177}LuPSMA-617 in 2023 [Cohort 3]

	Study endpoints
Additional objective 1 ***Baseline characteristics of mCRPC patients receiving ^{177}LuPSMA-617, with or without prior history of cabazitazel***	• **Demographics and clinical profile** ○ Age, region of residence ○ Clinical history and comorbidities [Charlson comorbidity index] ○ Distances from region of residence to hospital of RLT infusion
Secondary objective 2 ***Baseline characteristics of patients with or without hospitals stays between each ^{177}LuPSMA-617 administration*** *Note: analyzes performed in patients with at least 2 cures and at least 8 months of potential follow-up (i.e. patients included up to 30/04/2023 maximum)*	• **Demographics, clinical profile and distances in patients with or without overnight all-cause MCO stays.**

Outcomes (2/2)

Additional objectives – Focus on mPC patients eligible to RLT and initiating ^{177}LuPSMA-617 or cabazitaxel [Sub-cohort of Cohort 1]

	Study endpoints
Additional objective 3 ***Identify factors influencing the choice to initiate ^{177}LuPSMA-617 or cabazitaxel***	• **Logistic regression model for the identification of factors associated to the initiation of ^{177}LuPSMA-617 or cabazitaxel in patients living in mainland France.** • **Variables included in the model:** • **Demographics and clinical profile** ○ Age and region of residence ○ Clinical history and comorbidities ○ Last chemotherapy for PC performed in a RLT center ○ Calendar semester of treatment initiation ○ Delay from first chemotherapy for PC to treatment initiation • **Distances** from the place of residence to the nearest RLT center of the region of residence.
Additional objective 4 ***To describe hospital stays occurring between each administration of treatment in patients treated with ^{177}LuPSMA-617 vs. patients treated with cabazitaxel*** *Note: analyzes performed in patients with at least 2 cures and at least 8 months of potential follow-up [i.e. included until 30/04/2023]*	For patients [living in mainland France] treated with ^{177}LuPSMA-617 and cabazitaxel, respectively: • **All-cause hospitalizations in MCO** ○ Number and duration of hospitalizations with a duration ≥1 day (i.e. one night spent at hospital) ○ All-cause emergency department visits (followed by a hospitalization) ○ Hospitalizations in intensive care unit / oncology unit. • Requirement for **transfusions** in MCO *Note: the cures observed after a delivery of the other treatment (^{177}LuPSMA-617 for patient in cabazitaxel group and vice versa) were not considered.*

Analyses for the additional objectives

Statistical considerations

- **Descriptive analyses were performed for additional objectives 1, 2 and 4.**
  - Number and percentage of patients per category (categorical variable)
  - Mean (standard deviation), median (quartiles), min and max (quantitative variable)

- **Logistic regression model [additional objective 3]** was performed for identifying factors influencing the choice to initiate ^{177}LuPSMA-617 or cabazitaxel.
  - **Independent variable:** initiation of ^{177}LuPSMA-617 or cabazitaxel [reference used in model: cabazitaxel]
  - **Dependent variables:** demographic and clinical profile of the patient, and distances
  - Stepwise backward variable selection, tests for collinearity between variables.

Nota bene:

Due to GDPR regulation, all counts ≤ 10 were masked.

Stratifications were performed only if sufficient sample size.

Study Results

Description of characteristics of mCRPC patients receiving ^{177}LuPSMA-617 with/without prior history of cabazitaxel administration

Additional objective 1

Population: *patients living in mainland France and DROM treated with ^{177}LuPSMA-617 in 2023* ***[Cohort 3, N= 1225 patients]***

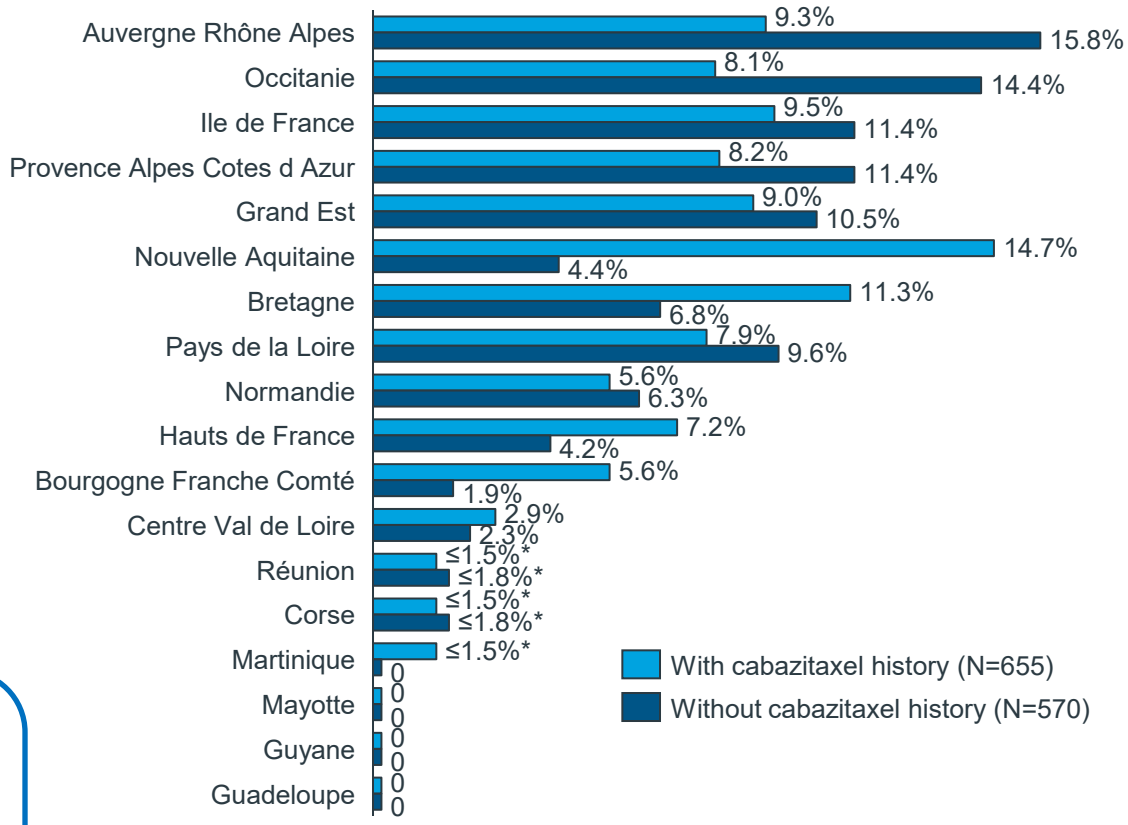
Characteristics of users of ^{177}LuPSMA-617 in 2023 with/without prior history of cabazitaxel administration (1/3)

- Demographic characteristics: age, region of residence

	Patients with cabazitaxel history (N=655)	Patients without cabazitaxel history (N=570)	TOTAL (N=1225)
Age at index date (years)			
Mean (SD)	72.1 (7.39)	72.5 (8.18)	72.3 (7.77)
Median (Q1-Q3)	**73.0 (67.0-77.0)**	**73.0 (67.0-78.0)**	73.0 (67.0-78.0)
Min-Max	45.0-90.0	37.0-92.0	37.0-92.0
Age at index date (categories), n (%)			
18-54 years	12 (1.8%)	≤10 (≤1.8%)	22 (1.8%)
55-64 years	87 (13.3%)	78 (13.7%)	165 (13.5%)
65-74 years	292 (44.6%)	246 (43.2%)	538 (43.9%)
75-84 years	237 (36.2%)	203 (35.6%)	440 (35.9%)
≥85 years	27 (4.1%)	[33;42] (5.8%;7.4%)	60 (4.9%)

- No difference of age between patients with and without prior history of cabazitaxel administration before ^{177}LuPSMA-617.
- Patients living in **Nouvelle Aquitaine and Bretagne regions** had **more often received a prior treatment with cabazitaxel before ^{177}LuPSMA-617.**
- While in **Auvergne Rhône Alpes and Occitanie regions**, **patients were less frequently treated with cabazitaxel before ^{177}LuPSMA-617.**

Region of residence:



*Region with a number ≤10 patients (GDPR rules).

Characteristics of users of ^{177}LuPSMA-617 in 2023 with/without prior history of cabazitaxel administration (1/3)

- France – Ranking of regions of residence from higher to lower history of cabazitaxel administration before ^{177}LuPSMA-617 administration

	Number of patients with cabazitaxel history	Total number of patients	% of patients with cabazitaxel history	Ratio vs France*
Nouvelle Aquitaine	96	121	79,3%	1,48
Bourgogne Franche Comté	37	48	77,1%	1,44
Hauts de France	47	71	66,2%	1,24
Bretagne	74	113	65,5%	1,22
Centre Val de Loire	19	32	59,4%	1,11
Normandie	37	73	50,7%	0,95
Grand Est	59	119	49,6%	0,93
Ile de France	62	127	48,8%	0,91
Pays de la Loire	52	107	48,6%	0,91
Provence Alpes Cotes d Azur	54	119	45,4%	0,85
Auvergne Rhone Alpes	61	151	40,4%	0,76
Occitanie	53	135	39,3%	0,73
Corse**	≤10	≤10	≤1.5%	-
DROM				-
Guadeloupe	-	-	-	-
Guyane	-	-	-	-
Martinique**	≤10	≤10	≤1.5%	-
Mayotte	-	-	-	-
Réunion**	≤10	≤10	≤1.5%	-

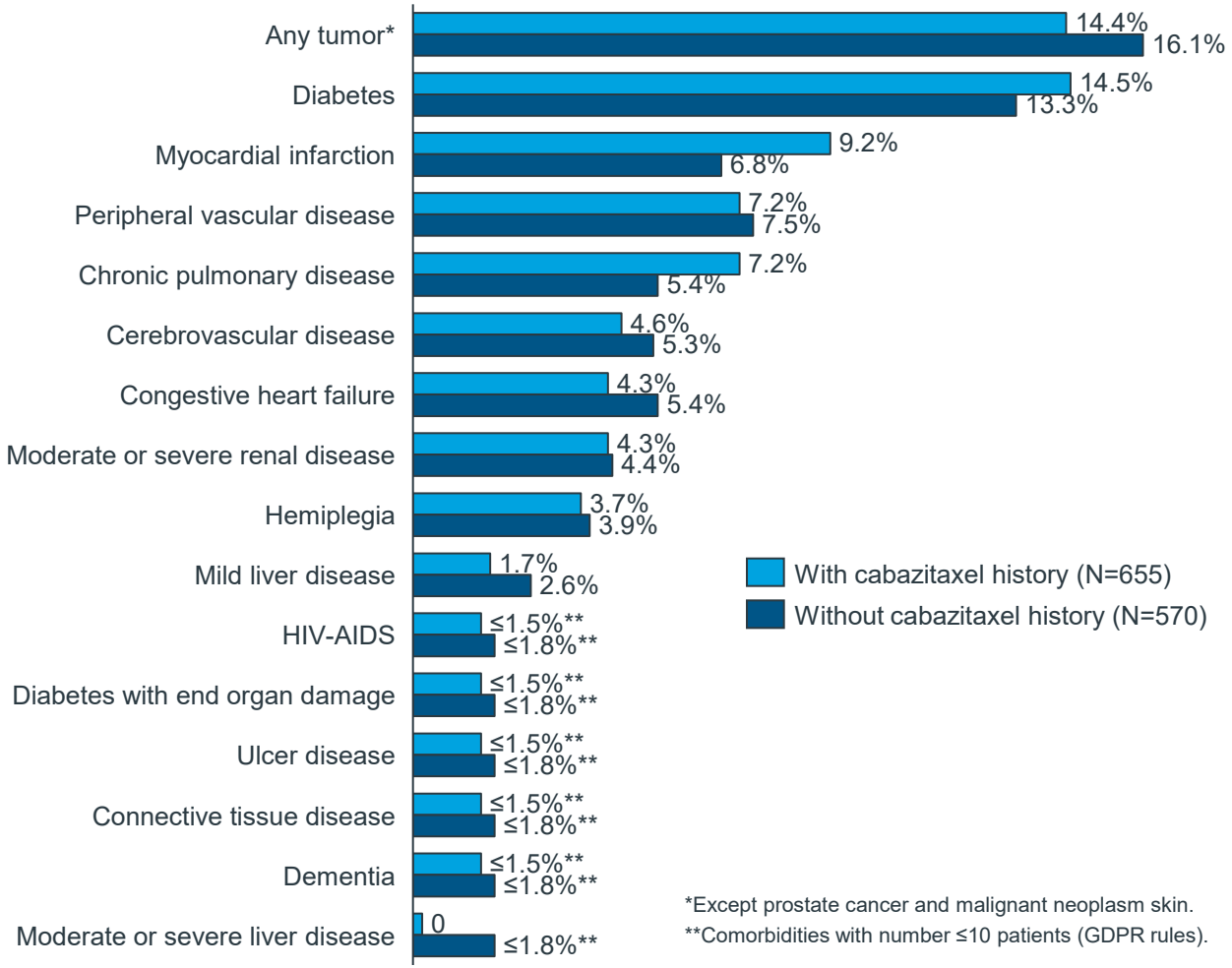
*Ratio vs France = Percentage of patients with cabazitaxel in the region / Percentage of patients with cabazitaxel in France.
**Region with a number ≤10 patients (GDPR rules).

Characteristics of users of ^{177}LuPSMA-617 in 2023 with /without prior history of cabazitaxel administration (2/3)

- Clinical profile [CCI and comorbidities included in the CCI]

	Patients with cabazitaxel history (N=655)	Patients without cabazitaxel history (N=570)	TOTAL (N=1225)
CCI score at index date			
Mean (SD)	11.4 (0.95)	11.5 (1.08)	11.5 (1.01)
Median (Q1-Q3)	**11.0 (11.0-11.0)**	**11.0 (11.0-12.0)**	11.0 (11.0-11.0)
Min-Max	11.0-19.0	11.0-18.0	11.0-19.0
CCI score at index date (categories), n (%)			
11	494 (75.4%)	427 (74.9%)	921 (75.2%)
12-13	131 (20.0%)	102 (17.9%)	233 (19.0%)
14-15	[20;29] (3.1%;4.4%)	[31;40] (5.4%;7.0%)	59 (4.8%)
≥ 16	≤10 (≤1.5%)	≤10 (≤1.8%)	12 (1.0%)

- **No difference of in terms of comorbidities between patients with / without prior history of cabazitaxel administration.**



Characteristics of users of ^{177}LuPSMA-617 in 2023 with / without prior history of cabazitaxel administration (3/3)

❑ Distance between place of residence and hospital of first ^{177}LuPSMA-617 administration

	Patients with cabazitaxel history (N=655)	Patients without cabazitaxel history (N=570)	Total (N=1,225)
	Hospital of first administration of 177LuPSMA-617* (N= 651)	Hospital of first administration of 177LuPSMA-617* (N= 564)	Hospital of first administration of 177LuPSMA-617* (N= 1215)
Distance from residence (km)			
Mean (SD)	91.6 (86.13)	69.0 (88.20)	81.1 (87.78)
Median (Q1-Q3)	**72.5 (29.1-129.2)**	**46.3 (14.4-88.8)**	60.7 (21.2-110.4)
Min-Max	1.2-760.7	1.3-955.1	1.2-955.1
Distance from residence, in categories, n (%)			
[0-50 km[	**235 (36.1%)**	**294 (52.1%)**	529 (43.5%)
[50-150 km[	294 (45.2%)	216 (38.3%)	510 (42.0%)
150 km and more	122 (18.7%)	54 (9.6%)	176 (14.5%)

* Patients residing in Corse or DROM and treated in mainland France were excluded from these analyses.

Note: Regions considered for residence and ^{177}LuPSMA-617 administration are the regions identified at index date (first administration of ^{177}LuPSMA-617 identified in 2022-2023).

- Patients with cabazitaxel history traveled more distance from their region of residence for receiving ^{177}LuPSMA-617 than those without prior cabazitaxel administration.

Description of mCRPC patients with / without hospital stays occurring between each administration of ^{177}LuPSMA-617

Additional objective 2

Population: *patients living in mainland France and DROM with at 2 cures of ^{177}LuPSMA-617 in 2023 and at least 8 months of potential follow-up [i.e. included until 30/04/2023]* ***[Cohort 3, N=493 patients]***

IQVIA

Characteristics of users of ^{177}LuPSMA-617 in 2023 with / without hospitalizations [overnight all-cause MCO stays] occurring between each administration of ^{177}LuPSMA-617 (1/4)

- Demographic characteristics: age

	Patients with hospital stays between administration (N=95)	Patients without hospital stays between administration (N=389)	TOTAL (N=493)
Age at index date (years)			
Mean (SD)	72.9 (8.04)	71.6 (7.91)	71.9 (7.94)
Median (Q1-Q3)	**74.0 (68.0-79.0)**	**72.0 (66.0-76.0)**	72.0 (67.0-77.0)
Min-Max	54.0-88.0	45.0-91.0	45.0-91.0
Age at index date (categories), n (%)			
18-54 years	≤10 (≤10.5%)	≤10 (≤2.5%)	≤10 (≤2.0%)
55-64 years	14 (14.7%)	62 (15.6%)	76 (15.4%)
65-74 years	34 (35.8%)	189 (47.5%)	223 (45.2%)
75-84 years	**40 (42.1%)**	**118 (29.6%)**	158 (32.0%)
≥85 years	≤10 (≤10.5%)	[19;28] (4.8%;7.0%)	[26;35] (5.3%;7.1%)
^{177}LuPSMA-617 administration in region of residence, n (%)	76 (80.0%)	337 (84.7%)	413 (83.8%)

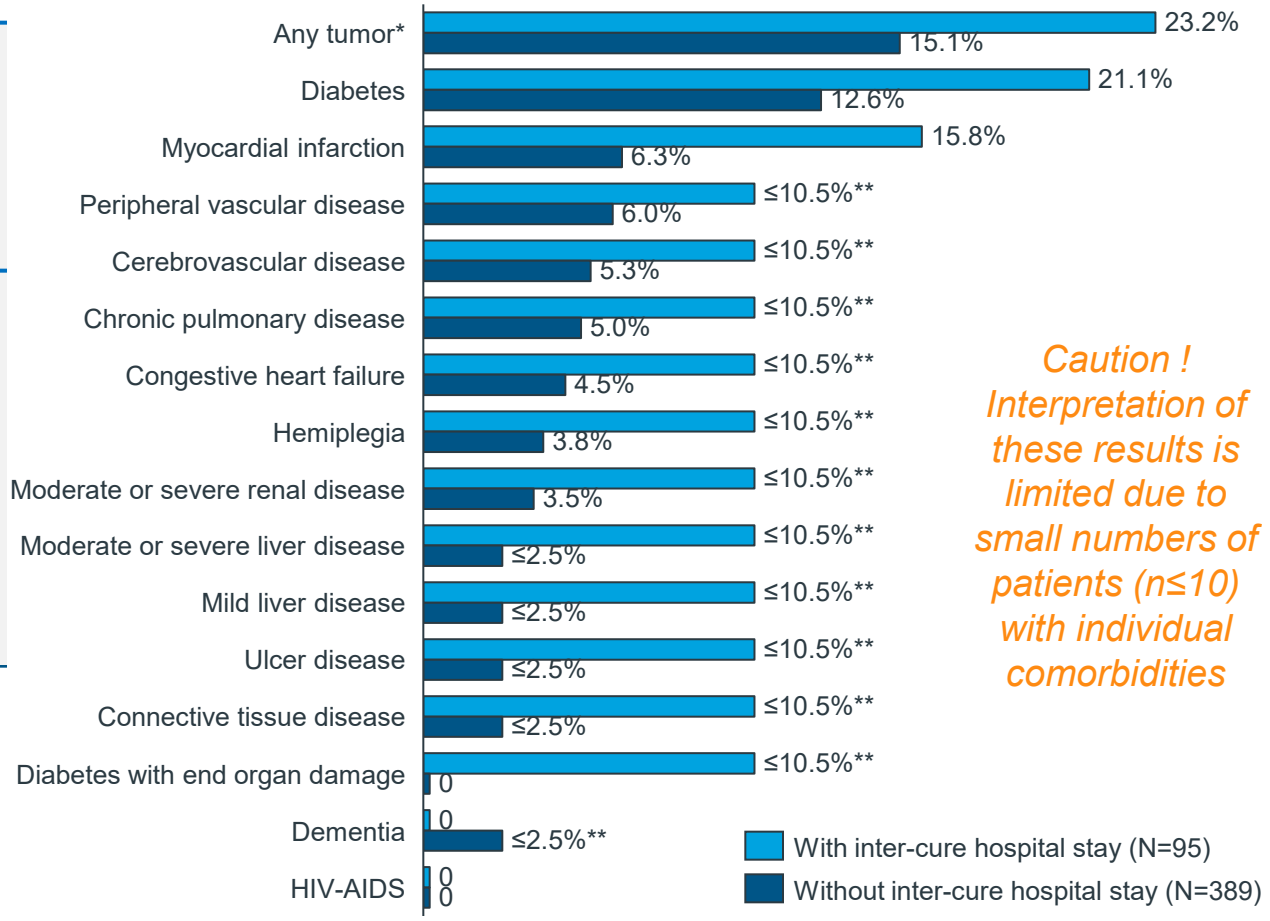
- **Patients with at least one hospital stay were slightly older than patients without hospital stay between administration of each treatment** [median age: 74.0 vs. 72.0].
- Due to low number of patients with hospital stays between each administration of treatment, the repartition of patients by region of residence is not presented (n≤10 patients for the majority of the regions in the subgroup of patients with at least one inter-cure hospital stay).

Characteristics of users of ^{177}LuPSMA-617 in 2023 with / without hospitalizations [overnight all-cause MCO stays] occurring between each administration of ^{177}LuPSMA-617 (2/4)

- Clinical profile [Comorbidities included in the CCI]

	Patients with hospital stays between administration of ^{177}LuPSMA-617 (N=95)	Patients without hospital stays between administration of ^{177}LuPSMA-617 (N=389)	TOTAL (N=493)
CCI score at index date			
Mean (SD)	11.6 (1.16)	11.4 (0.95)	11.4 (1.00)
Median (Q1-Q3)	11.0 (11.0-12.0)	11.0 (11.0-11.0)	11.0 (11.0-11.0)
Min-Max	11.0-16.0	11.0-19.0	11.0-19.0
CCI score at index date (categories), n (%)			
11	68 (71.6%)	314 (78.9%)	382 (77.5%)
12-13	18 (18.9%)	67 (16.8%)	85 (17.2%)
14-15	≤10 (≤10.5%)	[11;16] (2.8%;4.0%)	[16;25] (3.2%;5.1%)
≥ 16	≤10 (≤10.5%)	≤10 (≤2.5%)	≤10 (≤2.0%)

- **Patients with hospital stays between administration were reported with higher CCI scores (CCI≥14: 9.5% vs. 4.3%) compared to patients without hospital stays. They were more reported with:**
  - A history of another tumor (23.2% vs. 15.1%).
  - A history of diabetes (21.1% vs. 12.6%) and myocardial infarction (15.8% vs. 6.3%).



*Except prostate cancer and malignant neoplasm skin.

**Comorbidities with number ≤10 patients (GDPR rules).

Caution ! Interpretation of these results is limited due to small numbers of patients (n≤10) with individual comorbidities

Characteristics of users of ^{177}LuPSMA-617 in 2023 with / without hospitalizations [overnight all-cause MCO stays] occurring between each administration of ^{177}LuPSMA-617 (3/4)

- History of chemotherapy

PC treatments before start date of ^{177}LuPSMA-617	Patients with hospital stays between administration of ^{177}LuPSMA-617 (N=95)	Patients without hospital stays between administration of ^{177}LuPSMA-617 (N=389)	TOTAL (N=493)
At least one administration of chemotherapy, n (%)	[85;94] (89.5%;98.9%)	378 (95.0%)	465 (94.3%)
At least one cabazitaxel administration, n (%)	57 (60.0%)	246 (61.8%)	303 (61.5%)

- No difference between patients with at least hospital stay and those without hospital stay between each administration of treatment regarding the history of PC treatments before ^{177}LuPSMA-617 administration.

Characteristics of users of ^{177}LuPSMA-617 in 2023 with / without hospitalizations [overnight all-cause MCO stays] occurring between each administration of ^{177}LuPSMA-617 (4/4)

- ❑ Distance between place of residence and hospital of last chemotherapy administration
- ❑ Distance between place of residence and hospital of first ^{177}LuPSMA-617 administration

	Patients with hospital stays between administration of ^{177}LuPSMA-617 (N=95)		Patients without hospital stays between administration of ^{177}LuPSMA-617 (N=389)		TOTAL (N=493)	
	Hospital of last chemotherapy administered* (N = 84)	Hospital of first administration of ^{177}LuPSMA-617** (N= 92)	Hospital of last chemotherapy administered* (N = 377)	Hospital of first administration of ^{177}LuPSMA-617** (N= 395)	Hospital of last chemotherapy administered* (N = 493)	Hospital of first administration of ^{177}LuPSMA-617** (N= 487)
Distance from residence (km)						
Mean (SD)	48.1 (45.71)	96.8 (87.49)	53.7 (93.54)	90.1 (99.71)	52.6 (86.79)	91.4 (97.47)
Median (Q1-Q3)	35.1 (13.8-70.1)	68.7 (31.8-163.7)	30.2 (10.5-58.8)	64.3 (24.5-121.4)	30.6 (10.9-61.9)	64.9 (25.2-127.1)
Min-Max	3.6-217.0	4.1-383.3	1.1-850.8	1.6-871.3	1.1-850.8	1.6-871.3
Distance from residence, in categories, n (%)						
[0-50 km[	54 (64.3%)	34 (37.0%)	258 (68.4%)	160 (40.5%)	312 (67.7%)	194 (39.8%)
[50-150 km[	[20;29] (23.8%;34.5%)	31 (33.7%)	98 (26.0%)	167 (42.3%)	123 (26.7%)	198 (40.7%)
150 km and more	≤10 (≤11.9%)	27 (29.3%)	21 (5.6%)	68 (17.2%)	26 (5.6%)	95 (19.5%)

* Distances calculated only for patients identified with at least one previous chemotherapy for prostate cancer treatment before the first administration of ^{177}LuPSMA-617.
** Patients residing in Corse or DROM and treated in mainland France were excluded from these analyses.

Note: Regions considered for residence and ^{177}LuPSMA-617 administration are the regions identified at index date (first administration of ^{177}LuPSMA-617 identified in 2022-2023).

Factors influencing the choice to initiate ^{177}LuPSMA-617 or cabazitaxel

Additional objective 3

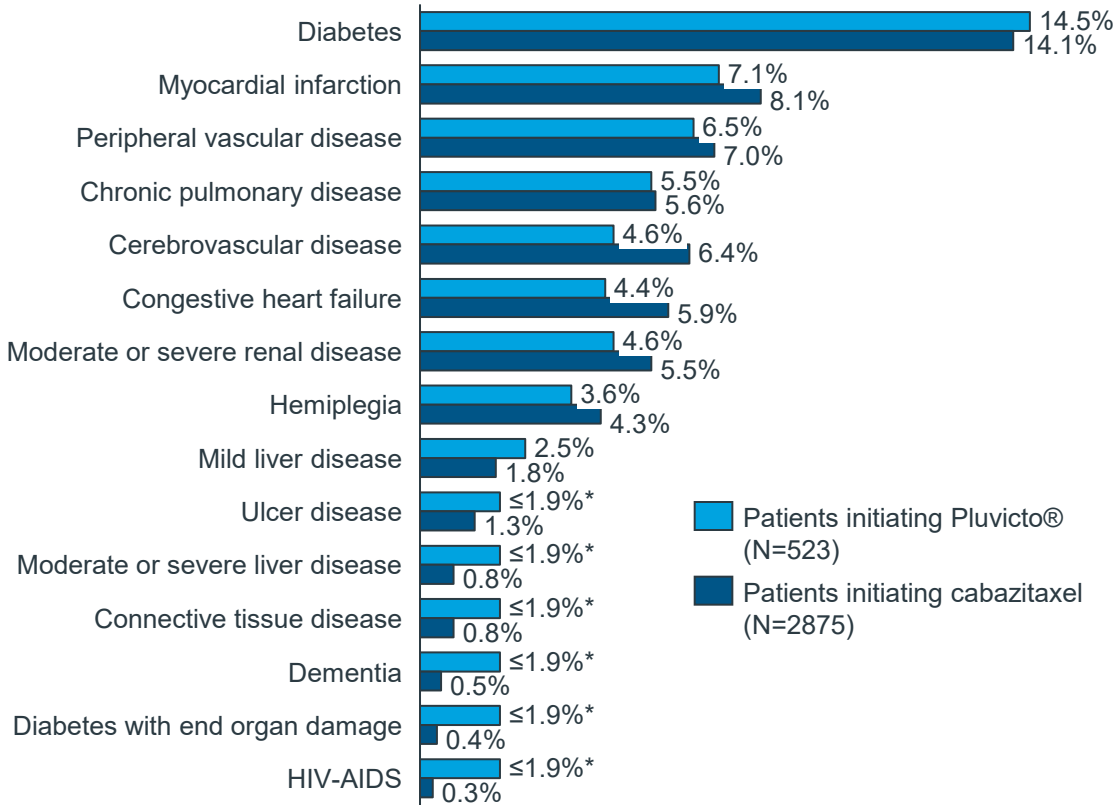
Population**: mPC patients [mainland France] eligible to RLT initiating ^{177}LuPSMA-617 or cabazitaxel in 2022-2023 **[Subcohort of Cohort 1, N=3398 patients (n=523 for ^{177}LuPSMA-617 / n=2875 for cabazitaxel)]

Description of patients' characteristics at initiation of ^{177}LuPSMA-617 or cabazitaxel for patients living in mainland France – *before inclusion in the model* (1/2)

- Demographic [age, region of residence] and clinical [comorbidities included in the CCI] characteristics

	Patients initiating ^{177}LuPSMA-617 (N=523)	Patients initiating cabazitaxel (N=2875)	*p-value**
Age at index date (years)			
Mean (SD)	72.2 (7.90)	72.8 (7.99)	0.087[1]
Median (Q1-Q3)	73.0 (67.0-78.0)	74.0 (68.0-78.0)	
Min-Max	37.0-91.0	41.0-95.0	
Age at index date (n, %)			
18-54 years	≤10 (≤1.9%)	64 (2.2%)	0.281[2]
55-64 years	67 (12.8%)	359 (12.5%)	
65-74 years	234 (44.7%)	1150 (40.0%)	
75-84 years	188 (35.9%)	1143 (39.8%)	
≥ 85 years	[24;33] (4.6%;6.3%)	159 (5.5%)	
Region of residence at index date (n, %)			<0.001[2]
Auvergne-Rhône-Alpes	90 (17.2%)	319 (11.1%)	
Bourgogne-Franche-Comté	≤10 (≤1.9%)	156 (5.4%)	
Bretagne	40 (7.6%)	192 (6.7%)	
Centre-Val de Loire	12 (2.3%)	125 (4.3%)	
Grand Est	54 (10.3%)	259 (9.0%)	
Hauts-de-France	23 (4.4%)	237 (8.2%)	
Île-de-France	49 (9.4%)	419 (14.6%)	
Normandie	36 (6.9%)	160 (5.6%)	
Nouvelle-Aquitaine	21 (4.0%)	344 (12.0%)	
Occitanie	77 (14.7%)	238 (8.3%)	
Pays de la Loire	58 (11.1%)	154 (5.4%)	
Provence-Alpes-Côtes d'Azur	51 (9.8%)	259 (9.0%)	
Corse	≤10 (≤1.9%)	13 (0.5%)	

*Comparative tests: [1]Wilcoxon test; [2]Chi2 test;



*Comorbidities with number ≤10 patients (GDPR rules).

No statistically significant difference for all comorbidities between those initiating ^{177}LuPSMA-617 / cabazitaxel (p>0.05).

Description of patients' characteristics at initiation of ^{177}LuPSMA-617 or cabazitaxel for patients living in mainland France – *before inclusion in the model* (2/2)

- History of chemotherapy and distances from region of residence to the nearest RLT center

	Patients initiating ^{177}LuPSMA-617 (N=523)	Patients initiating cabazitaxel (N=2875)	*p-value**
Delay from first chemotherapy for PC to treatment initiation (in years)			
Mean (SD)	1.8 (1.65)	1.4 (1.42)	<0.001[1]
Median (Q1 - Q3)	1.1 (0.8-2.2)	0.9 (0.6-1.6)	
Min-Max	0.2-8.8	0.0-8.5	
Delay from first chemotherapy for PC to treatment initiation (n, %)			
<1 year	221 (42.3%)	1558 (54.2%)	<0.001[2]
1-2 years	157 (30.0%)	753 (26.2%)	
≥2 years	145 (27.7%)	564 (19.6%)	
Calendar semester of treatment initiation (n, %)			<0.001[2]
January-June 2022	34 (6.5%)	572 (19.9%)	
July-December 2022	98 (18.7%)	758 (26.4%)	
January-June 2023	122 (23.3%)	869 (30.2%)	
July-December 2023	269 (51.4%)	676 (23.5%)	
Last chemotherapy for PC performed in a RLT center (n, %)	234 (44.7%)	489 (17.0%)	<0.001[2]
Distance between place of residence and nearest RLT center (in km)			
Mean (SD)	54.6 (48.02)	67.2 (51.58)	<0.001[1]
Median (Q1 - Q3)	43.3 (13.6-83.8)	60.9 (22.6-101.4)	
Min-Max	1.3-374.5	1.2-418.3	
Distance between place of residence and nearest RLT center (n, %)			
[0-50 km[	280 (53.5%)	1231 (42.8%)	<0.001[2]
[50-150 km[	222 (42.4%)	1459 (50.7%)	
150 km and more	21 (4.0%)	185 (6.4%)	

*Comparative tests: [1]Wilcoxon test; [2]Chi2 test.

Factors influencing the choice between to initiate ^{177}LuPSMA-617 or cabazitaxel (1/2)

- Multivariate logistic regression model [cabazitaxel used as reference for the variable to be explained for estimating the probability of receiving ^{177}LuPSMA-617] - Model performed in 3398 patients [n=523 for ^{177}LuPSMA-617 / n=2875 for cabazitaxel] (1/2)

Variable [Explanatory variables]	OR [95% CI]	*p-value*
Age at index date in years [ref: 18-54 years]*		
55-64 years	1.11 [0.51-2.39]	0.7987
65-74 years	1.30 [0.62-2.71]	0.4829
75-84 years	1.17 [0.56-2.45]	0.6715
≥85 years	1.26 [0.54-2.96]	0.5936
Last chemotherapy for PC performed in a RLT center [ref: No]	**3.95 [3.14-4.95]**	**<.0001**
Distance between place of residence and nearest RLT center [ref: [0-50[(km)]		
[50-100 km[	0.83 [0.64-1.06]	0.1282
100 km and more	0.75 [0.55-1.01]	0.0594
Delay from first chemotherapy for PC to treatment initiation years [ref: <1 year]		
1-2 years	**1.47 [1.15-1.88]**	**0.0019**
≥2 years	**1.96 [1.52-2.54]**	**<.0001**

*Variable forced in the model despite non-significance.
Comorbidities were not retained in the final model after the stepwise backward selection.

Factors associated significantly with the initiation of ^{177}LuPSMA-617 in comparison to cabazitaxel.

- **Having received the last chemotherapy for PC in a RLT center.**
- Having a **delay ≥1 year between first chemotherapy for PC and treatment initiation.**

On the contrary:

- **Patients living 100 km or more between their place of residence and the nearest RLT center** seemed **more likely to be treated with cabazitaxel than ^{177}LuPSMA-617** ***[p-value close to statistical significance threshold]***.

Factors influencing the choice between to initiate ^{177}LuPSMA-617 or cabazitaxel (2/2)

- Multivariate logistic regression model [cabazitaxel used as reference for the variable to be explained for estimating the probability of receiving ^{177}LuPSMA-617] - Model performed in 3398 patients [n=523 for ^{177}LuPSMA-617 / n=2875 for cabazitaxel] (2/2)

Variable [Explanatory variables]	OR [95% CI]	*p-value*
Calendar semester of treatment initiation [ref: January-June 2022]		
July-December 2022	**2.36 [1.55-3.59]**	**<.0001**
January-June 2023	**2.50 [1.66-3.77]**	**<.0001**
July-December 2023	**7.85 [5.30-11.61]**	**<.0001**
Region of residence at index date [ref: Ile de France]		
Auvergne-Rhône-Alpes	**2.52 [1.68-3.80]**	**<.0001**
Bourgogne-Franche-Comté	0.50 [0.23-1.05]	0.067
Bretagne	**1.98 [1.20-3.27]**	**0.0072**
Centre-Val de Loire	0.90 [0.44-1.82]	0.7593
Grand Est	**1.94 [1.23-3.08]**	**0.0047**
Hauts-de-France	0.90 [0.51-1.56]	0.6994
Normandie	**1.99 [1.19-3.33]**	**0.0086**
Nouvelle-Aquitaine	**0.51 [0.29-0.92]**	**0.0242**
Occitanie	**2.57 [1.67-3.96]**	**<.0001**
Pays de la Loire	**2.43 [1.51-3.91]**	**0.0003**
Provence-Alpes-Côtes d'Azur	**1.86 [1.18-2.95]**	**0.008**
Corse	1.77 [0.35-8.82]	0.487

Factors associated significantly with the initiation of ^{177}LuPSMA-617 in comparison to cabazitaxel.

- **Initiating the treatment in the most recent months** (year 2023).
- In comparison to IDF, **residing in Bretagne, Grand Est, Normandie, Occitanie, Pays de la Loire and PACA regions.**

On the contrary:

- Patients living in Nouvelle-Aquitaine regions were significantly more likely to initiate treatment with cabazitaxel treatment than with ^{177}LuPSMA-617 in comparison to patients living in IDF.

Description of hospital stays occuring between each administration of treatment in patients treated with ^{177}LuPSMA-617 or cabazitaxel

Additional objective 4

Population: *patients [mainland France] with at least 2 cures of treatment [^{177}LuPSMA-617 or cabazitaxel] in 2023 and at least 8 months of potential follow-up [i.e. included until 30/04/2023]* ***[Sub-cohort 1, N=1992 patients (n=200 for ^{177}LuPSMA-617 / n=1792 for cabazitaxel)]***

IQVIA

Analyzes for understanding treatment regimen of patients treated with ^{177}LuPSMA-617 or cabazitaxel

	Patients treated with ^{177}LuPSMA-617 (N=200)	Patients treated with cabazitaxel (N=1792)	*p-value**
Number of hospital stays with treatment administration (i.e. number of cures) per patient			
N	200	1792	<0.001[2]
Mean (SD)	4.9 (1.39)	7.1 (4.44)	
Median (Q1 - Q3)	6.0 (4.0-6.0)	6.0 (4.0-9.0)	
Min-Max	2.0-8.0	2.0-31.0	
Number of hospital stays with treatment administration (i.e. number of cures) per patient [categories], n (%)			
0	-	-	<0.001[2]
1	-	-	
2	[11;16] (5.5%;8.0%)	139 (7.8%)	
3	24 (12.0%)	203 (11.3%)	
4	33 (16.5%)	215 (12.0%)	
5	23 (11.5%)	186 (10.4%)	
6	103 (51.5%)	311 (17.4%)	
7 and more	≤10 (≤5.0%)	738 (41.2%)	
Delay between first and last cure (in days)			
N	200	1792 (100.0%)	<0.001[2]
Mean (SD)	185.4 (74.11)	140.5 (109.88)	
Median (Q1 - Q3)	209.0 (128.5-227.0)	107.0 (63.0-176.0)	
Range	42.0-602.0	7.0-713.0	
Delay between each cure per patient (in days)			
N	200	1792	<0.001[2]
Mean (SD)	48.2 (14.55)	23.1 (9.17)	
Median (Q1 - Q3)	43.9 (42.0-49.4)	21.2 (21.0-24.0)	
Range	39.3-185.0	1.0-199.0	

*Comparative tests: [1]Chi2 test; [2]Wilcoxon test.

In accordance with the marketing authorization of ^{177}LuPSMA-617 and cabazitaxel:

- Patients treated with cabazitaxel received on average more cures than patients treated with ^{177}LuPSMA-617 (mean number: 7.1 vs. 4.9), with a similar median number of 6 cures.
- Delay between each cure was twice as long for patients treated with ^{177}LuPSMA-617 vs. those treated with cabazitaxel.

→These expected differences must be taken into account when interpreting the results describing overnight stays occurring between administration of ^{177}LuPSMA-617 or cabazitaxel [hospital stays used as proxy for identifying potential adverse events related to treatment].

Comparison of hospital stays occuring between each administration of ^{177}LuPSMA-617 or cabazitaxel – *All cures* (1/2)

- MCO overnight stays [all-cause] – 2022 / 2023 years

	Patients treated with ^{177}LuPSMA-617 (N=200)	Patients treated with cabazitaxel (N=1792)	*p-value**
Number of overnight stays in MCO per patient			
N	200	1792	<0.001[2]
Mean (SD)	**0.6 (1.70)**	**1.9 (8.59)**	
Median (Q1 - Q3)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	
Min-Max	0.0-18.0	0.0-162.0	
≥ 1 overnight stay in MCO	**52 (26.0%)**	**721 (40.2%)**	<0.001[1]
Mean duration per patient in days			
N			0.034[2]
Mean (SD)	**7.8 (8.37)**	**10.0 (10.34)**	
Median (Q1 - Q3)	5.3 (3.0-8.8)	7.0 (4.0-12.0)	
Min-Max	2.0-52.0	2.0-116.0	
≥ 1 all-cause emergency department visit followed by all-cause overnight stay in MCO	**16 (8.0%)**	**384 (21.4%)**	<0.001[1]
≥ 1 overnight stay in intensive care unit in MCO	≤10 (≤5.0%)	101 (5.6%)	0.091[1]
≥ 1 overnight stay in oncology unit in MCO	**13 (6.5%)**	**224 (12.5%)**	0.008[1]

*Comparative tests: [1]Chi2 test; [2]Wilcoxon test.

- **In comparison to patients treated with ^{177}LuPSMA-617, patients treated with cabazitaxel had more often:**
  - **Overnight stays in MCO** (at least one overnight stay: 40.2% vs. 26.0%; mean number of overnight stays: 1.9 vs. 0.6).
    - **This finding was also associated with a higher mean duration of stays in patients treated with cabazitaxel vs. those treated with ^{177}LuPSMA-617** (mean duration: 10.0 vs. 7.8 days.
  - **Emergency visits before admission in MCO** (at least one all cause-emergency visit: 21.4% vs. 8.0%).
  - **Al least one overnight stay in oncology unit** (at least one all cause-emergency visit: 12.5% vs. 6.5%).

Note: Only the stays occurring between each cure of treatment were considered [i.e., exclusion of ^{177}LuPSMA-617 or cabazitaxel administration stays].

Comparison of hospital stays occuring between each administration of ^{177}LuPSMA-617 [Pluvicto®] or cabazitaxel – *All cures* (2/2)

- Focus on transfusion requirement in MCO – 2022 / 2023 years

	Patients treated with ^{177}LuPSMA-617 (N=200)	Patients treated with cabazitaxel (N=1792)	*p-value**
≥ 1 stay with transfusion requirement in MCO	**17 (8.5%)**	**362 (20.2%)**	<0.001[1]
Number of stays in MCO with transfusion requirement per patient			
N	200	1792	<0.001[2]
Mean (SD)	**0.3 (1.49)**	**1.5 (8.43)**	
Median (Q1 - Q3)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	
Min-Max	0.0-18.0	0.0-162.0	

*Comparative tests: [1]Chi2 test; [2]Wilcoxon test.

- **In comparison to patients treated with ^{177}LuPSMA-617, patients treated with cabazitaxel had more often:**
  - **Stays with transfusion requirement in MCO** (at least one stay: 20.2% vs. 8.5%; mean number of stays: 1.5 vs. 0.3).

^{177}LuPSMA-617 hospitalizations [overnight all-cause stays in MCO] occurring between each administration of ^{177}LuPSMA-617 (1/2)

	Overall (N=200)	Between administrations no. 1 and 2 (N=200)	Between administrations no. 2 and 3 (N=184)	Between administrations no. 3 and 4 (N=160)	Between administrations no. 4 and 5 (N=127)	Between administrations no. 5 and 6 (N=104)	Between administrations no. 6 and 7, or in the month after no. 6 (N=104)
Number of overnight stays in MCO per patient							
N	200	200	184	160	127	104	104
Mean (SD)	0.6 (1.70)	0.2 (1.32)	0.1 (0.51)	0.1 (0.38)	0.0 (0.15)	0.1 (0.82)	0.1 (0.27)
Median (Q1 - Q3)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Min-Max	0.0-18.0	0.0-18.0	0.0-4.0	0.0-2.0	0.0-1.0	0.0-8.0	0.0-2.0
≥ 1 overnight stay in MCO	**52 (26.0%)**	**13 (6.5%)**	**11 (6.0%)**	**12 (7.5%)**	**≤10 (≤7.9%)**	**≤10 (≤9.6%)**	**≤10 (≤9.6%)**
Mean duration per patient in days							
N	52	13	11	12	≤10	≤10	≤10
Mean (SD)	7.8 (8.37)	**7.0 (5.31)**	**6.7 (5.24)**	**4.3 (2.50)**	-	-	-
Median (Q1 - Q3)	5.3 (3.0-8.8)	5.0 (3.0-10.0)	6.0 (3.0-8.0)	3.0 (3.0-5.5)	-	-	-
Min-Max	2.0-52.0	2.0-19.0	2.0-18.0	2.0-10.0	-	-	-

- **The percentage of patients with at least one overnight stay remained globally similar over the cures** [results difficult to interpret from 4th cures].
- However, among patients with overnight stays, **the mean duration of stays decreased over the cures.**

Note: Only the stays occurring between each administration of ^{177}LuPSMA-617 were considered for the definition of hospitalizations [i.e., exclusion of ^{177}LuPSMA-617 administration stays].

^{177}LuPSMA-617 hospitalizations [overnight all-cause stays in MCO] occurring between each administration of ^{177}LuPSMA-617 (2/2)

❑ Focus on medical wards during hospitalizations with overnight stays in MCO between each administration of ^{177}LuPSMA-617

	Overall (N=200)	Between administrations no. 1 and 2 (N=200)	Between administrations no. 2 and 3 (N=184)	Between administrations no. 3 and 4 (N=160)	Between administrations no. 4 and 5 (N=127)	Between administrations no. 5 and 6 (N=104)	Between administrations no. 6 and 7, or in the month after no. 6 (N=104)
≥ 1 all-cause emergency department visit prior stay in MCO	16 (8.0%)	≤10 (≤5.0%)	≤10 (≤5.4%)	≤10 (≤6.3%)	-	≤10 (≤9.6%)	≤10 (≤9.6%)
≥ 1 overnight stay in intensive care unit in MCO	≤10 (≤5.0%)	-	≤10 (≤5.4%)	-	-	≤10 (≤9.6%)	≤10 (≤9.6%)
≥ 1 overnight stay in oncology unit in MCO	13 (6.5%)	≤10 (≤5.0%)	-	≤10 (≤6.3%)	-	≤10 (≤9.6%)	-

- Overall, few patients were hospitalized in emergency visits, in intensive care or oncology units between cures of treatment. Therefore, results are difficult to interpret in detail for each inter-cure.

^{177}LuPSMA-617 hospitalizations [MCO] with transfusion requirement occurring between each administration of ^{177}LuPSMA-617

	Overall (N=200)	Between administrations no. 1 and 2 (N=200)	Between administrations no. 2 and 3 (N=184)	Between administrations no. 3 and 4 (N=160)	Between administrations no. 4 and 5 (N=127)	Between administrations no. 5 and 6 (N=104)	Between administrations no. 6 and 7, or in the month after no. 6 (N=104)
≥ 1 stay with transfusion requirement in MCO	17 (8.5%)	≤10 (≤5.0%)	≤10 (≤5.4%)	≤10 (≤6.3%)	-	-	≤10 (≤9.6%)
Number of stays in MCO with transfusion requirement per patient							
N	200	200	184	160	127	104	104
Mean (SD)	0.3 (1.49)	0.1 (1.31)	0.0 (0.31)	0.0 (0.30)	0.0 (0.00)	0.0 (0.00)	0.0 (0.14)
Median (Q1 - Q3)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Min-Max	0.0-18.0	0.0-18.0	0.0-4.0	0.0-3.0	0.0-0.0	0.0-0.0	0.0-1.0

- Overall, few patients had at least one stay with transfusion requirement. Therefore, it is difficult to draw conclusions regarding the detailed results for each inter-cure.

Cabazitaxel hospitalizations [overnight all-cause stays in MCO] occurring between each administration of cabazitaxel (1/2)

	All cures (N=1792)	Between administrations no. 1 and 2 (N=1792)	Between administrations no. 2 and 3 (N=1653)	Between administrations no. 3 and 4 (N=1450)	Between administrations no. 4 and 5 (N=1235)	Between administrations no. 5 and 6 (N=1049)	Between administrations no. 6 and 7, or in the month after no. 6 (N=1049)
Number of overnight stays in MCO per patient							
N	1792	1792	1653	1450	1235	1049	1049
Mean (SD)	1.9 (8.59)	0.3 (2.90)	0.2 (2.41)	0.2 (1.79)	0.2 (1.20)	0.2 (1.62)	0.2 (1.49)
Median (Q1 - Q3)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Min-Max	0.0-162.0	0.0-84.0	0.0-54.0	0.0-48.0	0.0-24.0	0.0-32.0	0.0-40.0
≥ 1 overnight stay in MCO	721 (40.2%)	**122 (6.8%)**	82 (5.0%)	78 (5.4%)	63 (5.1%)	41 (3.9%)	**109 (10.4%)**
Mean duration per patient in days							
N	721	122	82	78	63	41	109
Mean (SD)	10.0 (10.34)	**10.0 (13.44)**	**7.1 (5.80)**	**7.2 (6.45)**	**5.7 (4.36)**	**5.8 (5.10)**	**9.1 (7.91)**
Median (Q1 - Q3)	7.0 (4.0-12.0)	7.0 (4.0-12.0)	5.3 (3.0-9.0)	4.3 (3.0-9.0)	4.0 (3.0-7.0)	4.0 (3.0-6.5)	6.0 (3.0-12.0)
Min-Max	2.0-116.0	2.0-128.0	2.0-31.0	2.0-28.0	2.0-19.0	2.0-23.0	2.0-37.0

- **The percentage of patients with at least one overnight stay between each cure was higher between 1st and 2nd cures, and increased between the 6th and 7th cures.**
  - This finding was associated with higher mean duration of stay per patient between the corresponding cures.

Note: Only the stays occurring between each administration of cabazitaxel were considered for the definition of hospitalizations [i.e., exclusion of cabazitaxel administration stays].

Cabazitaxel hospitalizations [overnight all-cause stays in MCO] occurring between each administration of cabazitaxel (2/2)

❑ Focus on medical wards during hospitalizations with overnight stays in MCO between each administration of cabazitaxel

	All cures (N=1792)	Between administrations no. 1 and 2 (N=1792)	Between administrations no. 2 and 3 (N=1653)	Between administrations no. 3 and 4 (N=1450)	Between administrations no. 4 and 5 (N=1235)	Between administrations no. 5 and 6 (N=1049)	Between administrations no. 6 and 7, or in the month after no. 6 (N=1049)
≥ 1 all-cause emergency department visit prior stay in MCO	384 (21.4%)	**64 (3.6%)**	**31 (1.9%)**	**46 (3.2%)**	**33 (2.7%)**	**17 (1.6%)**	**44 (4.2%)**
≥ 1 overnight stay in intensive care unit in MCO	101 (5.6%)	≤10 (≤0.6%)	≤10 (≤0.6%)	≤10 (≤0.7%)	≤10 (≤0.8%)	≤10 (≤1.0%)	**14 (1.3%)**
≥ 1 overnight stay in oncology unit in MCO	224 (12.5%)	**32 (1.8%)**	19 (1.1%)	14 (1.0%)	≤10 (≤0.8%)	≤10 (≤1.0%)	**28 (2.7%)**

- Patients were more often admitted in emergency visit, intensive care unit or oncology unit between 1st and 2nd cures, and between the 6th and 7th cures.

Cabazitaxel hospitalizations [MCO] with transfusion requirement occurring between each administration of cabazitaxel

	All cures (N=1792)	Between administrations no. 1 and 2 (N=1792)	Between administrations no. 2 and 3 (N=1653)	Between administrations no. 3 and 4 (N=1450)	Between administrations no. 4 and 5 (N=1235)	Between administrations no. 5 and 6 (N=1049)	Between administrations no. 6 and 7, or in the month after no. 6 (N=1049)
≥ 1 stay with transfusion requirement in MCO	362 (20.2%)	54 (3.0%)	50 (3.0%)	47 (3.2%)	39 (3.2%)	34 (3.2%)	**43 (4.1%)**
Number of stays in MCO with transfusion requirement per patient							
N	1792	1792	1653	1450	1235	1049	1049
Mean (SD)	1.5 (8.43)	0.1 (1.76)	0.2 (2.98)	0.2 (2.25)	0.2 (1.48)	0.2 (2.03)	0.2 (2.29)
Median (Q1 - Q3)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Min-Max	0.0-162.0	0.0-48.0	0.0-72.0	0.0-60.0	0.0-36.0	0.0-56.0	0.0-60.0

- The proportion of patients with at least one stay with transfusion requirement between cures of cabazitaxel increased between the 6th and 7th cures.