UNIVERSITY of WASHINGTON

Real-World Comparative Effectiveness of Lutetium Lu-177-PSMA-617 Versus Cabazitaxel for Metastatic Castration-Resistant Prostate Cancer

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Background

- Prostate cancer is the most common non-skin cancer and the second leading cause of cancer-related deaths among men in the United States; 8% present with metastasis disease [1,2]
- Metastatic hormone castration prostate cancer (mCRPC) is the terminal stage of prostate cancer and remains fatal despite expanding treatment options.
- Cabazitaxel is a standard second-line chemotherapy option after docetaxel and ARPI therapy[3]
- Lutetium-177-PSMA-617 (Lu-PSMA) received FDA approval in 2022 for PSMA-positive mCRPC after prior ARPI and taxane therapy, based on the VISION trial[4]
- However, the VISION trial did not include chemotherapy in its control arm, leaving the Lu-PSMA vs cabazitaxel comparison unresolved for US clinical practice[5]
- Existing real-world studies are largely non-US, single-center, or underpowered; hence, a large US-based comparative study is needed

Objective

- To compare survival outcomes of Lu-PSMA versus cabazitaxel in US patients with mCRPC previously treated with docetaxel and at least one ARPI

Methods

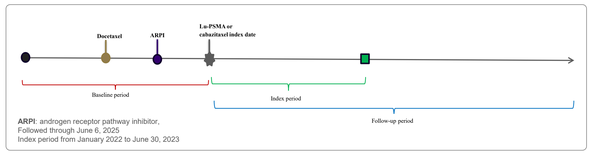
Data Source

- Komodo Health Administrative Claims Database

Study design

- Retrospective cohort study informed by the target trial emulation (TTE) framework

***Figure 1*. Study design schematic**



ARPI: androgen receptor pathway inhibitor,
Followed through June 6, 2025
Index period from January 2022 to June 30, 2023

Study Population

- **Inclusion criteria**
  - Men aged ≥18 years with mCRPC who initiated Lu-PSMA or cabazitaxel between January 2022 and June 2024
  - Prior docetaxel and at least one ARPI at any time before index treatment
  - 12 months of continuous insurance enrollment before index treatment date
- **Exclusion criteria**
  - Initiation of Lu-PSMA and cabazitaxel on the same day
  - Evidence of other cancer types

Treatment groups

- Lu-PSMA
- Cabazitaxel

Outcomes & Follow-up

- **Overall survival (OS)**
  - Time from index treatment to death from any cause
- **Progression-free survival (PFS)**:
  - Time from index treatment to new systemic mCRPC treatment or death.
- Patients were followed from index date to the earliest of outcome, end of study period or loss of insurance enrollment

Analysis

- Cox proportional hazards models to estimate survival outcomes
- Propensity score weighting using average treatment effect on the treated (ATT) weights was estimated via a generalized boosted model (GBM) with 5,000 regression tress to adjust for baseline confounders
  - ATT weights chosen because PSMA screening is required for Lu-PSMA eligibility
  - Balance assessed using standardized mean difference (SMD <0.1)
- Sensitivity analysis with 1:1 greedy propensity score matching

Results

***Table 1*. Select Baseline Characteristics**

Characteristics	Unweighted population				Weighted population[a]			
	Overall (n=2,843)	Lu-PSMA (n=954)	Cabazitaxel (n=1,889)	SMD	Overall (n=2,843)	Lu-PSMA (n=954)	Cabazitaxel (n=1,889)	SMD
Age, mean (SD)	71.0 (8.2)	72.4 (7.8)	70.3 (8.3)	0.27	72.1 (7.7)	72.4 (7.8)	72.0 (7.7)	0.046
Region, n (%)								
Midwest	862 (30.3)	347 (36.4)	515 (27.3)	0.189	1,029 (36.2)	347 (36.4)	682 (36.1)	0.0015
Northeast	671 (23.6)	210 (22.0)	461 (24.4)	0.058	644 (22.6)	210 (22.0)	434 (23.0)	0.021
South	820 (28.8)	241 (25.3)	579 (30.7)	0.12	730 (25.7)	241 (25.3)	489 (25.9)	0.018
West	489 (17.2)	156 (16.4)	333 (17.6)	0.035	440 (15.5)	156 (16.4)	284 (15.0)	0.047
Insurance type, n (%)								
Commercial	542 (19.1)	153 (16.0)	389 (20.6)	0.12	461 (16.2)	153 (16.0)	307 (16.3)	0.0062
Medicaid	185 (6.5)	39 (4.1)	146 (7.7)	0.18	125 (4.4)	39 (4.1)	86 (4.6)	0.026
Medicare	2,104 (74.0)	759 (79.6)	1,345 (71.2)	0.21	2,243 (78.9)	759 (79.6)	1,484 (78.6)	0.024
Unknown	12 (0.4)	3 (0.3)	9 (0.5)	0.029	14 (0.5)	3 (0.3)	11 (0.6)	0.040
Index treatment year, n (%)								
2022	953 (33.5)	165 (17.3)	788 (41.7)	0.65	499 (17.5)	165 (17.3)	333 (17.7)	0.021
2023	1,325 (46.6)	497 (52.1)	828 (43.8)	0.17	1,512 (53.2)	497 (52.1)	1,015 (53.7)	0.033
2024	565 (19.9)	292 (30.6)	273 (14.5)	0.35	832.7 (29.3)	292 (30.6)	540 (28.6)	0.052
De novo metastasis[b], n (%)	1,146 (40.3)	361 (37.8)	785 (41.6)	0.077	1,089 (38.3)	361 (37.8)	728 (38.5)	0.0012
Location of metastasis, n (%)								
Bone	2,619 (92.1)	866 (90.8)	1,753 (92.8)	0.070	2,587 (91.0)	866 (90.8)	1,721 (91.1)	0.0010
Visceral	947 (33.3)	241 (25.3)	706 (37.4)	0.28	747 (26.3)	241 (25.3)	506 (26.8)	0.034
Lymph	1,108 (39.0)	392 (41.1)	716 (37.9)	0.065	1,145 (40.3)	392 (41.1)	753 (39.8)	0.035
Bone + Visceral	894 (31.4)	227 (23.8)	667 (35.3)	0.27	700 (24.6)	227 (23.8)	473 (25.0)	0.028
ADT use, n (%)	2,547 (89.6)	847 (88.8)	1,700 (90.0)	0.038	2,540 (89.4)	847 (88.8)	1,693 (89.6)	0.021
CCI score, mean (SD)[c]	2.2 (2.3)	2.1 (2.2)	2.2 (2.3)	0.019	2.1 (2.2)	2.1 (2.2)	2.1 (2.2)	0.019
CCI category, n (%)[c]								
None: 0	823 (28.9)	270 (28.3)	553 (29.3)	0.14	799 (28.1)	270 (28.3)	529 (28.0)	0.0083
Mild: 1-2	994 (35.0)	350 (36.7)	644 (34.1)	0.13	1,060 (37.3)	350 (36.7)	710 (37.6)	0.0003
Moderate: 3-4	565 (19.9)	184 (19.3)	381 (20.2)	0.002	564 (19.8)	184 (19.3)	380 (20.1)	0.030
Severe: ≥5	461 (16.2)	150 (15.7)	311 (16.5)	0.007	420 (14.8)	150 (15.7)	270 (14.3)	0.042
ECI score, mean (SD)	8.3 (9.2)	8.1 (9.1)	8.3 (9.2)	0.013	8.1 (9.0)	8.1 (9.1)	8.0 (9.0)	0.018
Prior treatments[d], n (%)								
Docetaxel	2,137 (75.2)	689 (72.2)	1,448 (76.7)	0.099	2,042 (71.8)	689 (72.2)	1,353 (71.6)	0.019
ARPI	1,841 (64.8)	587 (61.5)	1,254 (66.4)	0.10	1,756 (61.8)	587 (61.5)	1,169 (61.9)	0.0018
Docetaxel + ARPI	1,368 (48.1)	425 (44.5)	943 (49.9)	0.11	1,255 (44.1)	425 (44.5)	830 (43.9)	0.019
Opioid use	2,012 (70.8)	638 (66.9)	1,374 (72.7)	0.12	1,937 (68.1)	638 (66.9)	1,299 (68.8)	0.030
First-generation antiandrogen	190 (6.7)	50 (5.2)	140 (7.4)	0.097	149 (5.2)	50 (5.2)	99 (5.2)	0.0031
Bone health agents	2,218 (78.0)	703 (73.7)	1,515 (80.2)	0.15	2,123 (74.7)	703 (73.7)	1,420 (75.2)	0.016
ED visit, n (%)	921 (32.4)	277 (29.0)	644 (34.1)	0.11	839 (29.5)	277 (29.0)	562 (29.8)	0.0037

ADT: androgen deprivation therapy, **ARPI**: androgen receptor pathway inhibitors, **CCI**: Charlson comorbidity index, **ECI**: Elixhauser comorbidity index, **ED**: emergency department, **SD**: standard deviation, **SMD**: standardized mean difference
[a]Weights normalized to sum up to 1 within each treatment group and scaled to original population. Frequency counts rounded to nearest integer and might not add up to total patients per treatment group

***Figure 2*. Unadjusted Overall Survival**

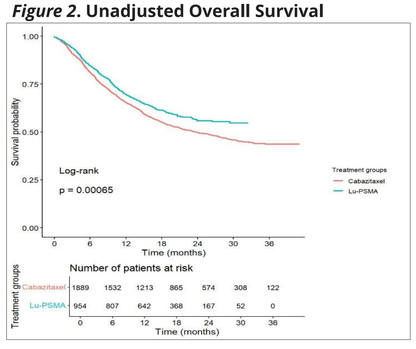


***Figure 3*. Unadjusted Progression-free Survival**

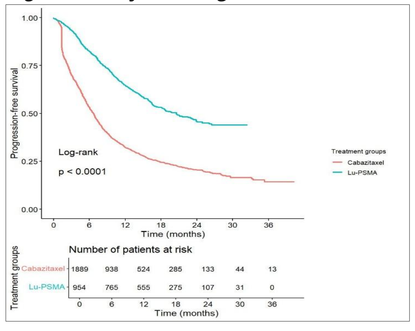


***Figure 4*. Weighted Overall Survival**

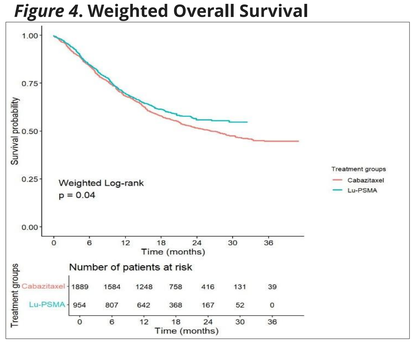
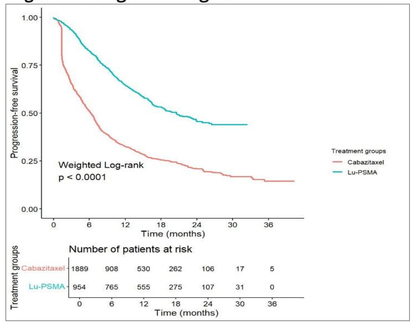


***Figure 5*. Weighted Progression-free survival**



Results (continued)

Cohort characteristics

- 2,843 patients included: 954 Lu-PSMA, 1,889 cabazitaxel; all covariate SMDs below 0.1 after weighting
- 37.6% of cabazitaxel patients subsequently crossed over to Lu-PSMA; no crossover occurred in the Lu-PSMA arm
- Lu-PSMA patients were older, had less visceral disease (25.3% vs 37.4%), and had been on treatment longer from diagnosis (62 vs 55 months)
- 37.6% of cabazitaxel patients subsequently crossed over to Lu-PSMA; no crossover occurred in the Lu-PSMA arm

Overall survival

- **Weighted median OS**: not reached (Lu-PSMA) vs 26.4 months (cabazitaxel; 95% CI: 22.0 to 30.9)
- **Adjusted HR**: 0.87 (95% CI: 0.76 to 0.99; p=0.039); confirmed in matched analysis (HR: 0.86; p=0.030)

Progression-free survival

- **Weighted median PFS**: 20.6 months (Lu-PSMA; 95% CI: 17.3 to 23.9) vs 6.2 months (cabazitaxel; 95% CI: 5.5 to 6.8 months)
- **Adjusted HR**: 0.41 (95% CI: 0.36 to 0.46; p<0.0001); similar pattern in matched analysis (HR: 0.39; p<0.0001)

Lu-PSMA was associated with a 13% lower risk of death and a 59% lower risk of progression or death vs cabazitaxel in patients with mCRPC previously treated with docetaxel and at least one ARPI

Discussion

Strengths

- Largest US real-world head-to-head comparison of Lu-PSMA vs cabazitaxel (n=2,843)
- Target trial emulation with GBM propensity scoring strengthens causal inference
- Nationally representative database across multiple payer types
- Results replicated in matched sensitivity analysis
- Active comparator (cabazitaxel), providing a more conservative and clinically meaningful benchmark than the VISION trial

Limitations

- Claims data lack key clinical variables: PSA, ECOG status, Gleason score, and PSMA-PET result
- PFS is a claims-based proxy (next systemic therapy or death), not imaging-based rPFS; direct comparisons with trial PFS estimates should be made with caution
- Crossover (37.6%) from cabazitaxel to Lu-PSMA likely attenuates the observed OS difference toward the null

Conclusion

- In this large US real-world cohort of 2,843 patients, Lu-PSMA was associated with superior overall survival and progression-free survival compared to cabazitaxel in post-docetaxel, post-ARPI mCRPC patients

References

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