Comparative Effectiveness of Radioligand Therapy in PSMA-Positive mCRPC - Insights from Real-World Data

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Objective

- To assess the real-world effectiveness of radioligand therapy compared with other second-line therapies in PSMA-positive mCRPC patients in a rapidly expanding therapeutic market, projected to reach USD 91.9 billion by 2034.[1]

Methodology

- This retrospective cohort study analyzed de-identified Optum® Market Clarity data from an index period between January 1, 2023, and December 31, 2024.
- Incident PSMA-positive mCRPC patients were identified using ICD-10 diagnosis codes for prostate cancer (C61*) with metastatic disease codes (C77*, C78*, C79*). PSMA positivity was confirmed using PSMA PET imaging (CPT/HCPCS codes), and evidence of castration was established using CPT/NDC codes for medical or surgical castration.
- **Inclusion Criteria:** Male patients aged ≥18 years with prior exposure to androgen receptor pathway inhibitors (ARPIs; Abiraterone, Enzalutamide, Darolutamide, Apalutamide) and taxane-based chemotherapy (Docetaxel, Cabazitaxel).
  - Cohort 1 (Radioligand Therapy): Patients who completed ≥3 cycles of radioligand therapy.
  - Cohort 2 (Other Second-line Therapies): Patients initiating other second-line therapies (PARP inhibitors; Olaparib, Rucaparib), immunotherapy (Pembrolizumab, Sipuleucel-T), or Radium-223.
- **Exclusion Criteria:**
  - Cohort 1: Radioligand therapy during baseline or ARPI/taxane use within 28 days before radioligand therapy initiation.
  - Cohort 2: Other second-line therapies during baseline or ARPI/taxane use within 28 days before other second-line therapies initiation.
- **Index date:** Date of first claim (drug of interest).
- Continuous eligibility was observed for 6 months baseline and 12 months follow-up period.
- Propensity score matching (1:1) was done on age, race, and Charlson Comorbidity Index (CCI).
- Treatment effectiveness was evaluated using prostate-specific antigen (PSA) responses in 12 months follow-up period, defined as PSA50 (≥50% decline) and PSA80 (≥80% decline) from baseline.
- Progression-free survival (PFS) was defined as the number of days from the index date to initiation of a subsequent therapy (ARPI, taxanes, PARP inhibitors, Radium-223, immunotherapy, radioligand therapy) during follow-up due to disease progression or symptom worsening.
- Average survival days were defined as the mean number of days a patient survived from the index date until the date of death or the end of the follow-up period, whichever occurred first.

Results

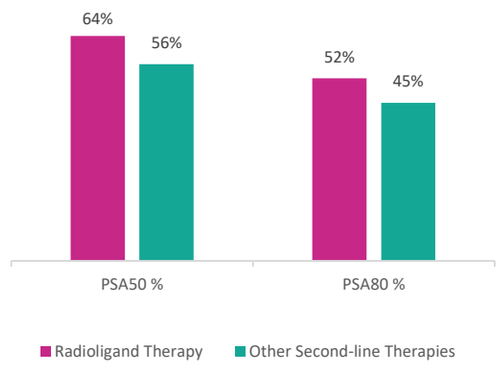

Figure 1. PSA50 and PSA80 Responses with Radioligand Therapy vs Second-Line Therapies

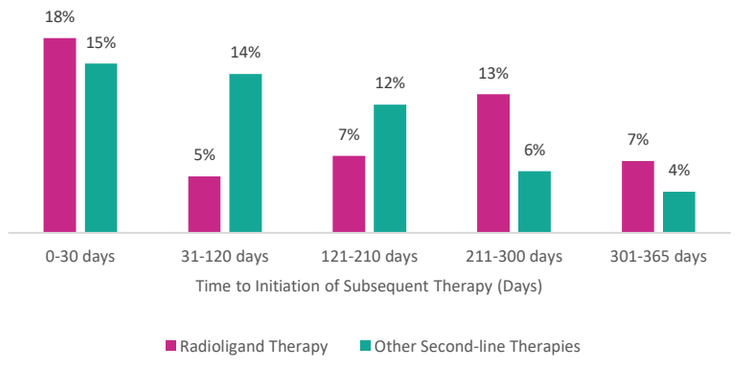

Figure 2. Time to Initiation of Subsequent Therapy: Radioligand vs Other Second-Line Therapies

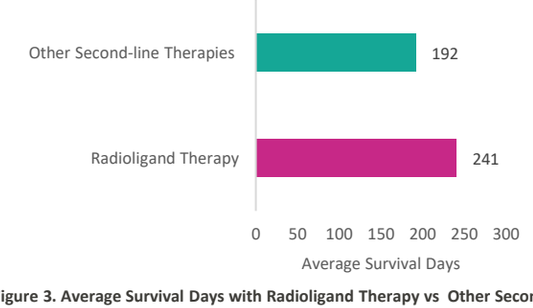

Figure 3. Average Survival Days with Radioligand Therapy vs Other Second-Line Therapies

- A total of 28,191 male patients (aged ≥18 years) with incident mCRPC were identified.
- Among 28,191 mCRPC patients, 63% (n = 17,794) were aged ≥70 years, 29% (n = 8,228) were 60-69 years, and 8% (n = 2,169) were 30-59 years; differences across age groups were statistically significant (χ^2 test, $p < 0.0001$).
- After applying exclusion criteria and continuous eligibility, 330 patients in Cohort 1 and 417 patients in Cohort 2 were included in the analysis. After PSM matching, 259 patients were matched in each cohort.
- Radioligand therapy showed higher PSA50 (64% vs 56%) and PSA80 (52% vs 45%) response rates than other second-line therapies; however, the difference in PSA change was not statistically significant based on a Mann-Whitney U test ($p = 0.132$). **(Figure 1).**
- Out of 518 patients, 214 initiated a subsequent therapy during follow-up due to increasing disease burden or symptom progression. Among these 18% patients in radioligand therapy cohort and 15% patients in other second-line therapies cohort had initiated subsequent therapy within 30 days from the index date (χ^2 test, $p = 0.529$).
- Patients receiving radioligand therapy demonstrated statistically significantly higher PFS rates at 31–120 days (14% vs 5%, χ^2 test, $p = 0.0015$) and 121–210 days (12% vs 7%, χ^2 test, $p = 0.05$) compared with other second-line therapies, indicating improved early disease control. Initiation at later intervals (211–300 days) occurred more frequently among radioligand therapy patients (χ^2 test, $p = 0.03$), while differences at 301–365 days were not statistically significant (χ^2 test, $p = 0.239$), consistent with longer treatment exposure and delayed progression **(Figure 2).**
- On comparing average survival days, patients on radioligand therapy had shown longer duration (241 days vs 192 days) compared to patients on other second-line of therapies**.** However, the difference was not statistically significant (Mann–Whitney U test, $p = 0.323$). **(Figure 3).**

Conclusions

- In this real-world analysis, radioligand therapy was associated with higher PSA50 and PSA80 response rates, a longer average survival days, and favorable progression-free survival compared with other second-line treatments.

Limitation

- The smaller sample size, due to few claims of new radioligand therapy and patients were considered receiving 2nd line therapy for study ,may have contributed to non-statistically significant differences in PSA change from baseline to follow-up and survival outcomes.

References: 1. https://www.fortunebusinessinsights.com/metastatic-castration-resistant-prostate-cancer-therapeutics-market-112690
2. Kulkarni, Harshad, et al. "Real-World Single-Center Response, Survival and Safety Analysis of Pluvicto in Metastatic Castration-Resistant Prostate Cancer." (2024): 242538-242538..
3. Wei, Xiao X., et al. "Real-world outcomes among patients with metastatic castration-resistant prostate cancer (mCRPC) receiving guideline-recommended therapies after treatment with 177Lu-PSMA-617: A real-world prostate cancer disease observation (PRECISION) data platform analysis." (2025): e17035-e17035.

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