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CAAA617A1US13 Study Results Abstract for Public Disclosure

Title

Real-World Characteristics, Treatment Patterns, and Clinical Outcomes Among Patients Receiving Lutetium-177 Vipivotide Tetraxetan

Keywords

Lutetium-177 (^{177}Lu) vipivotide tetraxetan, ^{177}Lu-PSMA-617, clinical outcomes, prostate cancer, prostate-specific antigen

Rationale and background

This study was designed to better understand the characteristics, treatment patterns, and clinical outcomes among patients in the United States (US) treated with lutetium-177 (^{177}Lu) vipivotide tetraxetan (^{177}Lu-PSMA-617) in the real-world setting. Of particular interest was understanding the profile of patients who were receiving ^{177}Lu-PSMA-617 in real-world clinical practice, what other therapies they were receiving before and after ^{177}Lu-PSMA-617, what clinical outcomes they experienced with ^{177}Lu-PSMA-617, whether these outcomes differed between patients with different numbers and types of therapy prior to ^{177}Lu-PSMA-617, and what outcomes patients who proceeded to receive other therapies after ^{177}Lu-PSMA-617 experienced.

Research question and objectives

What are the characteristics, treatment patterns, and outcomes among patients receiving ^{177}Lu-PSMA-617 in real-world clinical practice, do outcomes differ between patients with different numbers and types of therapy prior to ^{177}Lu-PSMA-617, and what outcomes do patients who go to receive other therapies after ^{177}Lu-PSMA-617 experience?

Primary objective

1. To describe the characteristics and treatment patterns among patients receiving ^{177}Lu-PSMA-617 in US real-world clinical practice

Secondary objectives

1. To describe the prostate-specific antigen (PSA) reduction outcomes among patients receiving ^{177}Lu-PSMA-617 in US real-world clinical practice, overall and among subgroups of patients defined by their prior therapy use (i.e., the number and type of therapies received prior to ^{177}Lu-PSMA-617)
2. To describe the PSA reduction outcomes among patients receiving ^{177}Lu-PSMA-617 in US real-world clinical practice who go on to receive subsequent therapies post-^{177}Lu-PSMA-617, overall and by type of therapy received

Study design

This was a retrospective observational study to assess the characteristics, treatment patterns, and clinical outcomes among patients treated with ^{177}Lu-PSMA-617 in real-world clinical practice across the US. All data were extracted from the PRECISION (PRostatE Cancer dISease observatION) data platform.

This study involved three data refreshes and three separate sets of analysis in which the key objective analyses were repeated. These are designated Analysis 1, Analysis 2, and Analysis 3 in this report.

Setting

The study included all adult patients with evidence of treatment with ^{177}Lu-PSMA-617 in PRECISION. The index date was the date of ^{177}Lu-PSMA-617 initiation, which had to occur within the identification period of March 23, 2022 (the date of ^{177}Lu-PSMA-617 approval) to the data cut-off date (April 30, 2024 for Analysis 1; June 30, 2024 for Analysis 2 and Analysis 3). The baseline period was the period prior to ^{177}Lu-PSMA-617 initiation and included all available data for each included patient. The follow-up period was from the index date until the first occurrence of death, loss to follow-up, or the end of the study period.

Patient characteristics and all study outcomes were assessed in the overall study population as well as in subgroups defined according to the number and type of prior therapies received:

- 1 androgen receptor pathway inhibitor (ARPI) and 1 taxane: patients with evidence of 1 ARPI and 1 taxane therapy prior to ^{177}Lu-PSMA-617 initiation
- Delayed: patients with evidence of 1 ARPI and 1 taxane therapy plus ≥1 additional ARPI or taxane prior to ^{177}Lu-PSMA-617 initiation

In addition, patient characteristics and outcomes were assessed in subgroups of patients receiving subsequent therapies. The index date for this analysis was the date of initiation of the subsequent therapy, which had to occur ≥14 days after the last treatment date with ^{177}Lu-PSMA-617. The baseline period was the period prior to initiation of the subsequent therapy. The subsequent therapies were defined as follows:

- Any guideline-recommended therapy: any guideline-recommended therapy for metastatic castration-resistant prostate cancer (mCRPC) post-^{177}Lu-PSMA-617 discontinuation (i.e., abiraterone, enzalutamide, darolutamide, apalutamide, cabazitaxel, docetaxel, pembrolizumab, sipuleucel-T, niraparib, olaparib, talazoparib, rucaparib, radium-223; carboplatin, cisplatin, etoposide, and mitoxantrone also included for Analysis 3)
- ARPI or taxane: any ARPI or taxane therapy post-^{177}Lu-PSMA-617 discontinuation (i.e., abiraterone, enzalutamide, darolutamide, apalutamide, cabazitaxel, docetaxel)
    - ARPI: any ARPI post-^{177}Lu-PSMA-617 discontinuation (i.e., abiraterone, enzalutamide, darolutamide, apalutamide)
    - Taxane: any taxane therapy post-^{177}Lu-PSMA-617 discontinuation (i.e., cabazitaxel, docetaxel)

Subjects and study size, including dropouts

For Analysis 1, a total of 1,247 patients met the eligibility criteria and were included in the study. Analysis 2 included a total of 943 patients, and Analysis 3 included 1,141 patients.

Variables and data sources

The primary outcome variables of interest were patient characteristics, treatments received before and after ^{177}Lu-PSMA-617, and dosing/duration for ^{177}Lu-PSMA-617. The secondary variables of interest were PSA reduction outcomes: PSA reduction of ≥50% (PSA50), ≥80% (PSA80), and ≥90% (PSA90).

The PRECISION data platform is a comprehensive, longitudinal dataset of patient-level data derived from patient registries, electronic medical records and insurance claims, harmonized and de-duplicated across multiple US data sources. The platform represents advanced prostate cancer population treated in community, academic, urology and medical oncology settings.

Statistical methods

Descriptive statistics were generated for patient characteristics, treatment patterns, and clinical outcomes. Continuous variables were described using mean and standard deviation (if normally distributed) or median and interquartile range (if skewed). Categorical variables were described by the number and percentage of patients in each category.

Results

Analysis 1

Overall, 1,247 patients met the eligibility criteria for Analysis 1, of whom 117 were treated with ^{177}Lu-PSMA-617 after 1 ARPI and 1 taxane and 193 had delayed ^{177}Lu-PSMA-617 treatment. A total of 179 patients went on to receive subsequent treatment with a guideline-recommended therapy, of whom 145 received a subsequent ARPI or taxane (83 ARPI, 62 taxane). The mean age in the overall study population was 73 years and 66% of patients were White.

Among the 35 patients treated with ^{177}Lu-PSMA-617 after 1 ARPI and 1 taxane who had sufficient information for PSA reduction evaluation, 54.5%, 39.4%, and 21.2% achieved PSA50, PSA80, and PSA90, respectively. Of the 86 patients with delayed ^{177}Lu-PSMA-617 treatment who had sufficient information for PSA reduction evaluation, 41.8%, 31.3%, and 26.9% achieved PSA50, PSA80, and PSA90, respectively.

With regard to the subsequent therapy analyses, among the 34 patients who proceeded to receive a subsequent guideline-recommended therapy and had sufficient information for PSA reduction evaluation, PSA50, PSA80, and PSA90 were achieved in 50.0%, 35.3%, and 26.5% of patients, respectively. Of the 18 patients who received an ARPI as their subsequent therapy, 61.1%, 55.6%, and 38.9% achieved PSA50, PSA80, and PSA90, respectively; among the 12 patients who received a taxane, 25.0%, 16.7%, and 16.7% achieved PSA50, PSA80, and PSA90, respectively.

Analysis 2

Overall, 943 patients met the eligibility criteria for Analysis 2, of whom 431 were treated with ^{177}Lu-PSMA-617 after ≥1 ARPI and ≥1 taxane and comprised the overall study population for this analysis. Among these patients, 177 were treated with ^{177}Lu-PSMA-617 after 1 ARPI and 1 taxane and 254 had delayed ^{177}Lu-PSMA-617 treatment. A total of 152 patients went on to receive subsequent treatment with a guideline-recommended therapy, of whom 135 received a subsequent ARPI or taxane (93 ARPI, 42 taxane).

Among the overall study population, the mean age was 72 years and 72% of patients were White. The majority (42.9%) of these patients received one dose of ^{177}Lu-PSMA-617 and the median duration of ^{177}Lu-PSMA-617 therapy was 84 days. Following discontinuation of ^{177}Lu-PSMA-617, 20.2% of these patients proceeded to subsequent treatment with a guideline-recommended therapy, 51.7% of whom subsequently received ARPIs and 37.9% taxanes.

Among the 61 patients treated with ^{177}Lu-PSMA-617 after 1 ARPI and 1 taxane who had sufficient information for PSA reduction evaluation, 52.5%, 34.4%, and 24.6% achieved PSA50, PSA80, and PSA90, respectively. Of the 105 patients with delayed ^{177}Lu-PSMA-617 treatment who had sufficient information for PSA reduction evaluation, 50.5%, 32.4%, and 24.8% achieved PSA50, PSA80, and PSA90, respectively.

In the subsequent therapy analyses, among the 56 patients who proceeded to receive a subsequent guideline-recommended therapy and had sufficient information for PSA reduction evaluation, 44.6%, 30.4%, and 17.9% achieved PSA50, PSA80, and PSA90, respectively. Of the 32 patients who received an ARPI as their subsequent therapy, 53.1%, 34.4%, and 25.0% achieved PSA50, PSA80, and PSA90, respectively; among the 18 patients who received a taxane, 16.7%, 11.1%, and 0.0% achieved PSA50, PSA80, and PSA90, respectively.

Analysis 3

Overall, 1,141 patients met the eligibility criteria for Analysis 3 and comprised the overall study population for this analysis. Among these patients, 241 were treated with ^{177}Lu-PSMA-617 after 1 ARPI and 1 taxane and 383 had delayed ^{177}Lu-PSMA-617 treatment. A total of 250 patients went on to receive subsequent treatment with a guideline-recommended therapy, of whom 226 received a subsequent ARPI or taxane (137 ARPI, 89 taxane). The mean age in the overall study population was 73 years and 71% of patients were White. The majority of these patients (48.6%) received one dose of ^{177}Lu-PSMA-617 and the median duration of therapy was 71 days. Following discontinuation of ^{177}Lu-PSMA-617, 21.9% of patients proceeded to subsequent treatment with a guideline-recommended therapy, 60.6% of whom subsequently received ARPIs and 39.4% taxanes.

Among the 74 patients treated with ^{177}Lu-PSMA-617 after 1 ARPI and 1 taxane who had sufficient information for PSA reduction evaluation, 50.0%, 31.1%, and 25.7% achieved PSA50, PSA80, and PSA90, respectively. Of the 143 patients with delayed ^{177}Lu-PSMA-617 treatment who had sufficient information for PSA reduction evaluation, 51.0%, 29.4%, and 22.4% achieved PSA50, PSA80, and PSA90, respectively.

In the subsequent therapy analyses, among the 104 patients who proceeded to receive a subsequent guideline-recommended therapy and had sufficient information for PSA reduction evaluation, 41.3%, 27.9%, and 16.3% achieved PSA50, PSA80, and PSA90, respectively. Of the 57 patients who received an ARPI as their subsequent therapy, 52.6%, 35.1%, and 19.3% achieved PSA50, PSA80, and PSA90, respectively; among the 38 patients who received a taxane, 26.3%, 18.4%, and 10.5% achieved PSA50, PSA80, and PSA90, respectively.

Discussion

This is one of the first real-world studies of ^{177}Lu-PSMA-617. Across all three analyses of the study, the majority of patients initiated ^{177}Lu-PSMA-617 treatment late in their treatment journey (after 1 ARPI and 1 taxane therapy plus ≥1 additional ARPI or taxane) rather than after 1 ARPI and 1 taxane (the earliest time per the current indication). The results of Analysis 1 indicate that higher proportions of patients receiving ^{177}Lu-PSMA-617 earlier in their treatment journey (e.g., after 1 ARPI and 1 taxane) achieved PSA reductions of ≥50% and ≥80% when compared with those receiving ^{177}Lu-PSMA-617 after more ARPI/taxane therapy lines. Analysis 2 and Analysis 3 found similar PSA reduction rates between treatment cohorts. In addition, across all three analyses, 40–50% of patients who went on to receive other guideline-recommended therapies for mCRPC after ^{177}Lu-PSMA-617 discontinuation achieved a PSA reduction of ≥50%, suggesting that ^{177}Lu-PSMA-617 treatment does not a preclude response to subsequent therapies.

Despite multiple refreshes, data problems and inadequacies limited the interpretability of some of the study results, particularly around treatment patterns. Future studies are thus required to confirm and build on this research.

Conclusion

Patients receiving ^{177}Lu-PSMA-617 in this real-world study had promising outcomes, with approximately half of all patients experiencing at least a PSA50 response. Patients who initiated therapy with ^{177}Lu-PSMA-617 earlier in their treatment journey tended to have higher rates of PSA reduction outcomes than those initiating ^{177}Lu-PSMA-617 after more therapy lines. Patients who initiated other therapies after ^{177}Lu-PSMA-617 also experienced PSA responses, suggesting that concerns about the effectiveness of potential future therapy options should not preclude early treatment with ^{177}Lu-PSMA-617. Future research is required to confirm these findings.