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REAL-WORLD COMPARISON OF ACHIEVING UNDETECTABLE PROSTATE-SPECIFIC ANTIGEN RESPONSE IN PATIENTS WITH MCSPC TREATED WITH APALUTAMIDE WITHOUT DOCETAXEL VS DAROLUTAMIDE WITHOUT DOCETAXEL

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BACKGROUND AND METHODS

Objective

- To compare the proportion of patients with a decline in PSA value ≤0.2 ng/mL (PSA0.2 response) by 6 months between patients treated with apalutamide (APA) without docetaxel and darolutamide (DARO) without docetaxel in a nationally representative sample of androgen receptor pathway inhibitors (ARPI)-naïve patients with metastatic castration-sensitive prostate cancer (mCSPC)

Background

- Apalutamide and darolutamide are ARPIs approved for use with ADT in patients with mCSPC (also known as metastatic hormone-sensitive prostate cancer)[1,2]
- In Phase 3 studies, apalutamide (TITAN)[3] and darolutamide (ARANOTE)[4] demonstrated statistically significant reduction in disease progression as compared to ADT alone in patients with mCSPC[3,4]
- Currently, there are no clinical trials or real-world studies that directly compare survival outcomes between these approved agents in patients with mCSPC

Methods

- **Study design:** Retrospective, longitudinal analysis
- **Primary endpoint:** PSA0.2 response by 6 months
- **Data sources:** Linked data from a clinical urology database (Precision Point Specialty Analytics; PPS) and an administrative claims database (Komodo Research Database; KRD)
- **Statistical analyses:** Potentially confounding baseline demographic and clinical variables were balanced using inverse-probability of treatment weighting (IPTW). Weighted Cox proportional hazards models were used to evaluate and compare PSA0.2 between apalutamide and darolutamide cohorts
- **Compliance and power:** Data were de-identified, HIPAA compliant, and had a sufficient sample size to compare outcomes

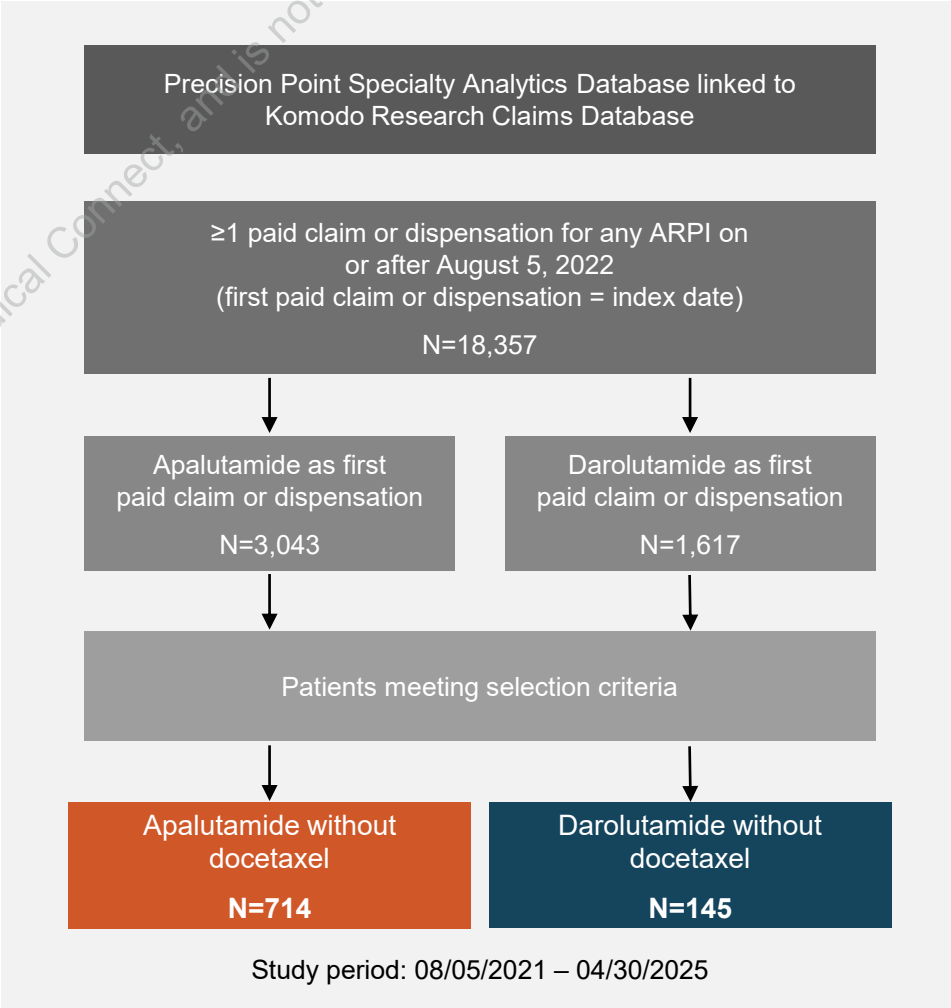
ARPI: androgen receptor pathway inhibitor; ADT: androgen deprivation therapy; IPTW: inverse-probability of treatment weighting; mCSPC: metastatic castration-sensitive prostate cancer; PSA: prostate-specific antigen.

1. U.S. Food and Drug Administration. FDA approves apalutamide for metastatic castration-sensitive prostate cancer. 2019. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-apalutamide-metastatic-castration-sensitive-prostate-cancer. Accessed 8 Jan 2025; 2. U.S. Food and Drug Administration. FDA approves darolutamide for metastatic castration-sensitive prostate cancer. 2025. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-darolutamide-metastatic-castration-sensitive-prostate-cancer. Accessed 23 Sep 2025; 3. Chi KN, et al. N Engl J Med. 2019;381(1):13–24; 4. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281.

PATIENT SELECTION FLOWCHART

Patient selection criteria:

- Adult patients meeting criteria for mCSPC
- No prior use of an ARPI
- No prior use of other advanced prostate cancer treatments including chemotherapy, immunotherapy, poly-ADP ribose polymerase inhibitor (PARPi), and radiopharmaceutical therapy
- No other primary cancer
- Detectable PSA level (>0.2 ng/mL) in the most recent measurement within the 13-week period prior to and including the index date
- No evidence of docetaxel use within 90 days prior to and 30 days after the index date



ARPI: androgen receptor pathway inhibitor; mCSPC: metastatic castration-sensitive prostate cancer; PARPi: poly-ADP ribose polymerase inhibitor; PSA: prostate-specific antigen.

PATIENT CHARACTERISTICS

	Apalutamide without docetaxel N=714	Darolutamide without docetaxel N=145	Standardized difference, %
Median age, years	**75.0**	**74.0**	**4.9**
Race			
White	**59.6%**	**58.8%**	**1.7**
Black	**21.2%**	**21.6%**	**0.9**
Other	**13.7%**	**15.0%**	**3.7**
Unknown	**5.5%**	**4.7%**	**3.8**
Medicare-insured	**79.7%**	**81.5%**	**4.5**
Year of index date			
2022	**15.6%**	**15.7%**	**0.2**
2023	**45.4%**	**41.9%**	**7.1**
2024	**29.3%**	**33.1%**	**8.2**
2025	**9.6%**	**9.3%**	**1.3**
Median time between metastasis and index, months	**1.9**	**2.0**	**1.3**
Median time between prostate cancer diagnosis and index, months	**51.5**	**62.3**	**0.1**
***De novo* mCSPC**	**38.3%**	**35.6%**	**5.8**
Concurrent use of ADT	**98.1%**	**97.4%**	**4.3**
Metastasis type			
Bone	**52.2%**	**50.5%**	**3.4**
Nodal	**51.0%**	**49.2%**	**3.7**
Visceral	**15.3%**	**15.5%**	**0.8**
PSA level, ng/mL			
>0.2 to ≤2	**34.1%**	**31.7%**	**5.1**
>2 to ≤10	**32.5%**	**35.2%**	**5.8**
>10 to <20	**9.8%**	**9.6%**	**0.7**
≥20	**23.6%**	**23.5%**	**0.4**
Mean Quan-CCI score	**10.1**	**9.9**	**3.8**

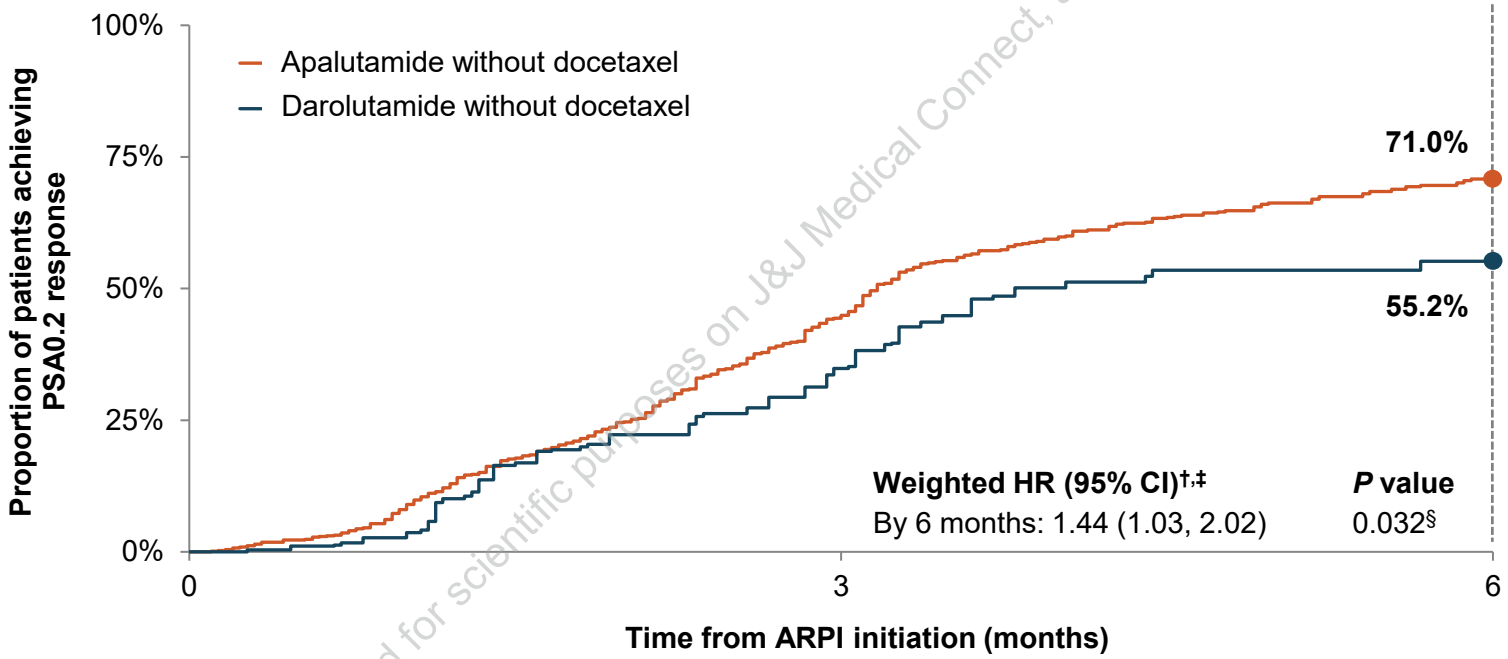
Weighted baseline characteristics

- Overall, 714 patients initiating apalutamide without docetaxel and 145 patients initiating darolutamide without docetaxel were identified
- The median age was 75.0 years and 74.0 years in the apalutamide and darolutamide cohorts, respectively
- The majority of patients were white (apalutamide: 59.6%, daroluatmide: 58.8%), and received Medicare insurance (apalutamide: 79.7%, darolutamide: 81.5%)
- The median time between metastasis and index was 1.9 months for apalutamide patients and 2.0 months for darolutamide patients
- Baseline characteristics were well-balanced between the weighted cohorts, with standardized differences <10%

ADT: androgen deprivation therapy; mCSPC: metastatic castration-sensitive prostate cancer; PSA: prostate-specific antigen; Quan-CCI: Quan-Charlson Comorbidity Index.

PSA0.2 RESPONSE

- By 6 months post-index, patients with mCSPC initiated on apalutamide without docetaxel had a statistically significant **44% increased likelihood in achieving PSA0.2 response** compared to patients initiated on darolutamide without docetaxel



Patients at risk, n (%)	3 months	6 months
Apalutamide without docetaxel	285 (40.0)	114 (16.0)
Darolutamide without docetaxel	63 (43.4)	33 (22.5)

†Propensity scores were generated using probability estimates from a logistic regression model using the following predictors: age (continuous), race, geographic region, payer, year of index date, time between metastasis and index date (continuous), time between first observed PC diagnosis and index date (continuous), *de novo* mCSPC, concurrent use of ADT, prior use of first-generation antiandrogens, bone antiresorptive therapy, most recent PSA level (categorical), earliest Gleason score (categorical), types of metastases (bone, nodal, visceral, and metastasis in multiple sites) and Quan-CCI score (continuous). Each patient was attributed an inverse-probability of treatment weight that was defined as follows: 1/(propensity score) for the apalutamide cohort and 1/(1-propensity score) for the darolutamide cohort. Normalized inverse-probability of treatment weights were truncated at the 95th percentiles. ‡A hazard ratio >1 indicates that the apalutamide cohort had a higher PSA0.2 rate compared with the darolutamide cohort. §Significant at the 5% level.
ADT: androgen deprivation therapy; ARPI: androgen receptor pathway inhibitor; CI: confidence interval; HR: hazard ratio; mCSPC: metastatic castration-sensitive prostate cancer; PSA: prostate-specific antigen; Quan-CCI: Quan-Charlson Comorbidity Index.

LIMITATIONS

- The potential for misclassification or miscoding in both EMR and claims data may introduce measurement bias in patient selection and outcome assessment
- IPTW only accounts for observed covariates and residual confounding may be present
- For the PSA endpoint, only testing performed within PPS network was captured, and therefore PSA testing done outside these clinics was not available. This may result in underestimation of PSA0.2 response rates, but is expected to be non-differential with respect to index treatment received

IPTW: inverse-probability of treatment weighting; PSA: prostate-specific antigen.

CONCLUSIONS

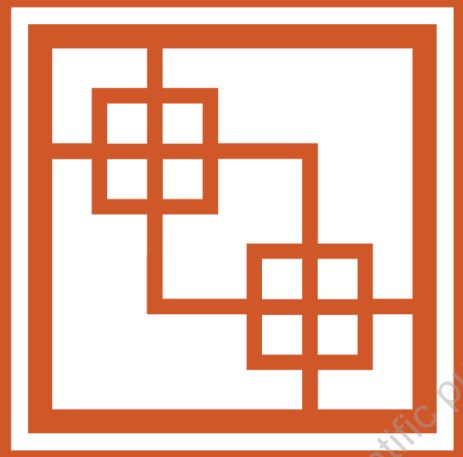
Key takeaway

- Patients with mCSPC initiated on apalutamide without docetaxel had a 44% higher rate of PSA0.2 response compared to patients initiated on darolutamide without docetaxel by 6 months post-index

Conclusions

- A significantly higher proportion of patients with mCSPC who initiated apalutamide without docetaxel experienced an early deep PSA response compared to patients who initiated darolutamide without docetaxel
- These results suggest that apalutamide remains an effective option for achieving early and deep PSA response, even in the absence of treatment intensification with docetaxel
- These findings may hold substantial long-term clinical significance and could contribute to informing treatment strategies, based on the established association between early PSA response and survival outcomes

mCSPC: metastatic castration-sensitive prostate cancer; PSA: prostate-specific antigen.



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