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Real-World Comparison of Prostate-Specific Antigen Response in Metastatic Castration-Sensitive Prostate Cancer Patients Treated With Apalutamide Without Docetaxel vs Darolutamide Without Docetaxel

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Key Takeaway

Patients with mCSPC initiated on apalutamide without docetaxel had a 49% higher rate of PSA90 response compared to patients initiated on darolutamide without docetaxel by 6 months

Conclusions

- Earlier deep PSA response was observed in a significantly higher proportion of ARPI-naïve patients initiating apalutamide without docetaxel relative to those initiating darolutamide without docetaxel, suggesting larger therapeutic benefit for apalutamide among patients with mCSPC, even without treatment intensification
- Treatment efficacy in routine clinical practice may be influenced by molecular and treatment administration factors, including dosing frequency and food requirements, which can affect adherence and systemic exposure
- These findings combined with the demonstrated significant overall survival benefit[10] for apalutamide vs darolutamide without docetaxel may hold substantial long-term clinical significance and could contribute to informing treatment strategies for patients with mCSPC

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Disclosures
M. A. Bilen is an employee of the Winship Cancer Institute of Emory University and has received consulting fees from Johnson & Johnson. G. Brown is an employee of New Jersey Urology and has received consulting fees from Johnson & Johnson. M. Singhal and C. D. Morrow are employees and stockholders of Johnson & Johnson. C. Rossi, F. Kinkead, G. Wong, A. Palladino, and D. Pilon are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Johnson & Johnson. B. Lowentritt is an employee of Chesapeake Urology and has received consulting fees from Johnson & Johnson.

Background

- Apalutamide and darolutamide are two androgen receptor pathway inhibitors (ARPIs) approved for the treatment of metastatic castration-sensitive prostate cancer (mCSPC) in combination with androgen deprivation therapy (ADT), with darolutamide also approved in combinations with ADT and docetaxel[1–3]
- Post-hoc analyses of Phase 3 trials, including TITAN[4] and ARANOTE[5], have shown that early and sustained prostate-specific antigen (PSA) reductions ≥90% (PSA90) following treatment initiation has been associated with improved prognosis among patients with mCSPC
- Recently, real-world studies of patients with mCSPC have demonstrated that apalutamide is associated with a significantly higher likelihood of achieving PSA response and improved overall survival relative to enzalutamide, abiraterone acetate, and darolutamide without docetaxel[6–11]
- Given the prognostic significance of achieving PSA90, there is a need to evaluate the comparative effectiveness of apalutamide vs darolutamide in real-world clinical practice in the United States (US)

Objective

- To compare PSA90 response by 6 months post-treatment initiation for patients with mCSPC who newly initiated apalutamide without docetaxel vs darolutamide without docetaxel

Methods

Data sources

- Clinical data from Precision Point Specialty (PPS) Analytics from >90 private, community-based urology practices as part of routine clinical care in the US were linked with administrative claims data from the Komodo Research Database (KRD+; study period: August 5, 2021–April 30, 2025)
- Data were de-identified and Health Insurance Portability and Accountability Act (HIPAA) compliant

Study design

- A retrospective, longitudinal study of ARPI-naïve patients with mCSPC was conducted
- Patients were selected into mutually exclusive treatment cohorts based on the first dispensation or paid pharmacy claim for apalutamide or darolutamide
- The index date was defined as the first dispensation or paid pharmacy claim for apalutamide or darolutamide on or after August 5, 2022 (the initial US Food and Drug Administration [FDA] approval date for darolutamide)
- Baseline patient characteristics were evaluated in the 12 months prior to the index date
- The observation period spanned from the index date to the earliest of index treatment discontinuation (using a 90-day treatment gap to define discontinuation), initiation of a non-index ARPI (ie, apalutamide, enzalutamide, abiraterone acetate, or darolutamide) or a radiopharmaceutical agent, initiation of docetaxel >30 days post-index, end of clinical activity or data availability (April 30, 2025)

Patient selection criteria

- Patients were classified as mCSPC if they had a diagnosis code or clinical indicator for bone, nodal, or visceral metastasis, in the absence of castration resistance prior to or on the index date
- Castration resistance was assessed based on a previously published algorithm[12] incorporating presence of ADT (as identified in both PPS and KRD+), PSA levels, and clinical notes abstracted from the electronic medical record by PPS
- Patients were excluded if they were treated with docetaxel within 90 days prior to or 30 days post-index

Study outcomes

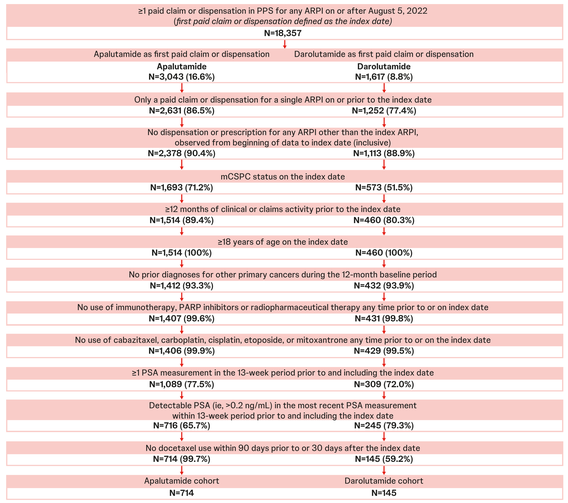
- The primary outcome was the proportion of patients who achieved a PSA90 response by 6 months following the initiation of apalutamide without docetaxel or darolutamide without docetaxel

Statistical analysis

- Inverse probability of treatment weighting, based on the propensity scores (PS), was used to account for differences in baseline characteristics between the apalutamide and darolutamide cohorts[13]
- The PS was obtained from a logistic regression model where index treatment was the dependent variable with the following baseline characteristics as independent variables: age, race, geographic region, payer type, index year, time between metastasis and index date, time between prostate cancer (PC) diagnosis and index date, *de novo* PC, metastases type, metastasis in multiple sites, concurrent ADT use, prior use of first-generation ARPI, prior use of bone antiresorptive therapy, Quan-Charlson Comorbidity Index, baseline PSA level, and initial Gleason score
- Baseline characteristics between treatment cohorts were considered well-balanced after weighting, as indicated by standardized differences of <10%[14]
- A weighted Kaplan-Meier analysis was conducted to assess the proportion of patients who achieved PSA90
- Weighted Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for PSA90 response between apalutamide and darolutamide cohorts

Patient selection criteria

Figure 1: Patient flowchart



ARPI, androgen receptor pathway inhibitor; mCSPC, metastatic castration-sensitive prostate cancer; PPS, Precision Point Specialty; PARP, poly (ADP-ribose) polymerase; PSA, prostate-specific antigen.

Results

Table 1: Baseline characteristics

	Weighted population[a]		
	Apalutamide without docetaxel N=714	Darolutamide without docetaxel N=145	Standardized difference (%)
Age, years, mean ± SD [median]	73.9 ± 8.2 [75.0]	74.3 ± 8.8 [74.0]	4.9
Race, n (%)			
White	425 (59.6)	85 (58.8)	1.7
Black	151 (21.2)	31 (21.6)	0.9
Other	98 (13.7)	22 (15.0)	3.7
Unknown	40 (5.5)	7 (4.7)	3.8
Geographic region, n (%)			
South	426 (59.7)	91 (62.7)	6.3
Midwest	169 (23.6)	32 (22.1)	3.8
Northeast	66 (9.2)	12 (8.4)	2.8
West	53 (7.5)	10 (6.8)	2.7
Payer type, n (%)			
Medicare	569 (79.7)	118 (81.5)	4.5
Commercial	120 (16.8)	24 (16.4)	1.2
Medicaid	21 (3.0)	3 (2.0)	6.5
Unknown	4 (0.6)	0 (0.2)	5.1
Year of index date, n (%)			
2022	112 (15.6)	23 (15.7)	0.2
2023	324 (45.4)	61 (41.9)	7.1
2024	209 (29.3)	48 (33.1)	8.2
2025	69 (9.6)	13 (9.3)	1.3
Time between metastasis and index date, months, median [IQR]	1.9 [0.7–6.1]	2.0 [0.5–5.5]	1.3
Time between PC diagnosis and index date, months, median [IQR]	51.5 [5.8–97.6]	62.3 [5.5–94.6]	0.1
Types of metastasis,[b] n (%)			
Visceral metastasis	109 (15.3)	23 (15.5)	0.8
Bone metastasis	373 (52.2)	73 (50.5)	3.4
Nodal metastasis	364 (51.0)	71 (49.2)	3.7
Metastasis in multiple sites	202 (28.3)	41 (28.5)	0.3
Quan-CCI, mean ± SD [median]	10.1 ± 3.4 [10.0]	9.9 ± 3.3 [10.0]	3.8
***De novo* PC,[c] n (%)**	274 (38.3)	52 (35.6)	5.8
Concurrent use of ADT with index ARPI,[d] n (%)	700 (98.1)	141 (97.4)	4.3
Prior use of first-generation ARPIs,[e] n (%)	75 (10.5)	15 (10.7)	0.4
Most recent PSA level,[f] ng/mL, n (%)			
>0.2 to ≤2	243 (34.1)	46 (31.7)	5.1
>2 to ≤10	232 (32.5)	51 (35.2)	5.8
>10 to ≤20	70 (9.8)	14 (9.6)	0.7
≥20	169 (23.6)	34 (23.5)	0.4
Initial Gleason score,[g] n (%)			
≤8	51 (7.1)	12 (8.0)	3.1
7	187 (26.1)	44 (30.5)	9.8
8	98 (13.8)	18 (12.7)	3.2
9	139 (19.4)	28 (19.3)	0.4
10	17 (2.3)	2 (1.5)	6.1
Unknown	223 (31.2)	41 (28.0)	7.0

ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; CCI, Charlson Comorbidity Index; IQR, interquartile range; PC, prostate cancer; PSA, prostate-specific antigen; SD, standard deviation.

[a]Of note, the number of patients reported in this weighted population represents the sum of weights for the corresponding non-weighted patients, rounded to the nearest integer. The proportions displayed were calculated before the rounding and may be slightly different than if they were calculated based on rounded numbers. [b]Types of metastases were defined at any time prior to (and including) the index date. Types of metastases were not mutually exclusive. [c]*De novo* PC was defined as ≤180 days between PC diagnosis and date of metastasis. [d]Concurrent use was defined as having a record for an ADT agent from 180 days before or after the index date. [e]Prior use of first-generation ARPIs was defined as any prescription for bicalutamide, nilutamide, or flutamide in the 12 months preceding index date. [f]Most recent PSA level was assessed within 13 weeks prior to or on the index date. [g]Gleason score was evaluated at any time prior to and including the index date.

Baseline characteristics

- Overall, 714 patients with mCSPC who initiated apalutamide without docetaxel and 145 patients with mCSPC who initiated darolutamide without docetaxel were identified (**Figure 1**)
- Baseline patient characteristics were well-balanced between the weighted cohorts (**Table 1**)

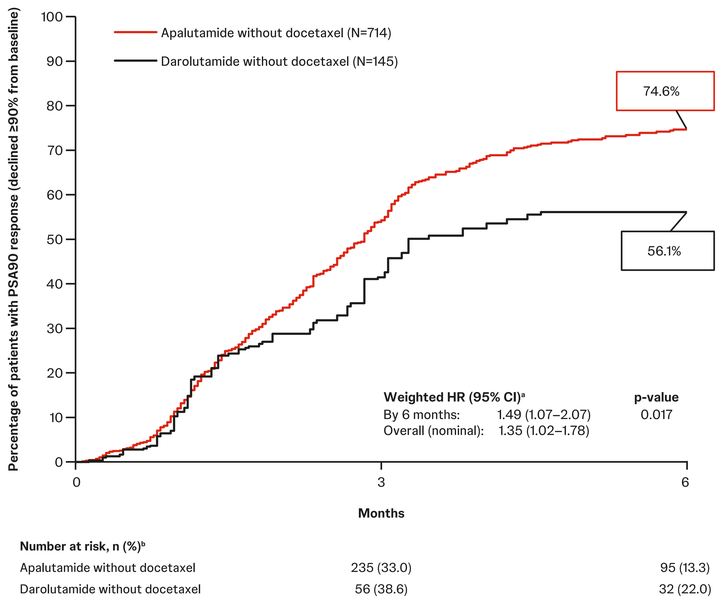
PSA90 response

- By 6 months, apalutamide patients had a 49% higher rate of PSA90 response compared to darolutamide patients (HR 1.49, 95% CI: 1.07–2.07; p=0.017; **Figure 2**)
- The median time-to-PSA90 response was 2.8 months for apalutamide patients and 3.3 months for darolutamide patients

Limitations

- Miscoding or misclassification in the clinical record or through the administrative claims can lead to selection and information biases despite efforts to balance the study populations
- PSA testing conducted outside of the PPS network was not captured, which may have led to an underestimation of PSA90 response rates
- Given the use of open source data, combination treatment with docetaxel may not be completely captured if administered outside of PPS network or hospitals that do not provide data to KRD+
- Darolutamide was used off-label prior to FDA approval for mCSPC without docetaxel on June 3, 2025; prior studies have demonstrated frequent off-label use without docetaxel during this time period[15]
- Regression analyses could only adjust for measured covariates and residual confounding may be present

Figure 2: Comparison of PSA90 among patients with mCSPC



CI, confidence interval; HR, hazard ratio; mCSPC, metastatic castration-sensitive prostate cancer; PSA, prostate-specific antigen.
[a]A HR >1 indicates that the apalutamide cohort has a higher PSA90 response rate compared to the darolutamide cohort. [b]Of note, the number of patients reported in this weighted population represents the sum of weights for the corresponding non-weighted patients, rounded to the nearest integer. The proportions displayed were calculated before the rounding and may be slightly different than if they were calculated based on rounded numbers.

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