IP26-22

Real-world comparison of prostate-specific antigen response in Black patients with metastatic castration-sensitive prostate cancer treated with apalutamide or enzalutamide

Benjamin Lowentritt[1], Shawn Du[2], Ibrahim Khilfeh[2], Dominic Pilon[3], Sabree Burbage[2], Carmine Rossi[3], Frederic Kinkead[3], Lilian Diaz [3], Gordon Brown[4]

[1]Chesapeake Urology, Towson, MD, USA; [2]Johnson & Johnson, Horsham, PA, USA; [3]Analysis Group, Inc., Montréal, QC, Canada; [4]New Jersey Urology, Cherry Hill, NJ, USA

Key Takeaway

By 6-months post-treatment initiation, Black patients with mCSPC initiating apalutamide were 42% more likely to achieve PSA90 compared to Black patients initiating enzalutamide

Conclusions

PSA90 response was attained earlier and in more Black patients treated with apalutamide than those treated with enzalutamide

The significant increase in PSA90 response rates among Black patients initiating apalutamide relative to enzalutamide in this study was consistent with the main findings from a race agnostic population using the same linked clinical data and insurance claims data[6]

The proportions of patients attaining a PSA90 response by 6- and 12-months following initiation of apalutamide in this real-world study are consistent with those observed in patients with mCSPC enrolled in the phase III TITAN study[15]

Please scan QR code

Poster

https://www.congresshub.com/Oncology/AUA2025/Apalutamide/Lowentritt

This QR code is intended to provide scientific information for individual reference and the information should not be altered or reproduced in any way.

Acknowledgements
This study was sponsored by Johnson & Johnson.

Disclosures
B. Lowentritt is an employee of Chesapeake Urology Associates and has received consulting fees from Johnson & Johnson. I. Khilfeh, S. Du, and S. Burbage are employees of Johnson & Johnson and stockholders of Johnson & Johnson. C. Rossi, F. Kinkead, L. Díaz, and D. Pilon are employees of Analysis Group, Inc., a consulting company that has provided paid consulting services to Johnson & Johnson. G. Brown is an employee of New Jersey Urology and has received consulting fees from Johnson & Johnson.

Background

- Deep prostate-specific antigen (PSA) response (≥90% reduction in PSA [PSA90]) is an important early response indicator of radiographic progression-free survival (rPFS) and overall survival (OS) in patients with metastatic castration-sensitive prostate cancer (mCSPC)[1,2]
- Apalutamide and enzalutamide, two androgen receptor pathway inhibitors (ARPIs), have demonstrated significant improvements in rPFS and OS, in combination with androgen deprivation therapy (ADT), versus placebo plus ADT in the TITAN and ARCHES trials[3-5]
- Previous real-world studies in the United States (US) using clinical data linked with administrative claims showed that apalutamide was associated with 21%–56% higher PSA90 response rates than enzalutamide among patients with mCSPC at 6-months post-treatment initiation[6,7]
- Due to lower representation in trials[8] and greater barriers to accessing treatment[9,10], there is limited information regarding the efficacy of ARPIs in treating Black patients with mCSPC
- This study aimed to demonstrate the robustness of real-world PSA response in a cohort of Black patients with mCSPC

Objectives

- To compare the proportion of ARPI-naïve patients with a PSA90 response by 6 months among Black patients with mCSPC who newly initiated apalutamide versus enzalutamide

Methods

Data sources

- Clinical data from Precision Point Specialty (PPS) Analytics from >90 private, community-based urology practices in the US collected as part of routine care were linked with insurance claims data from the Komodo Research Database (KRD; study period: 17 September 2018 - 31 December 2023)
- Data are de-identified and Health Insurance Portability and Accountability Act (HIPAA) compliant

Study design

- A retrospective, longitudinal casual analysis of ARPI-naïve Black patients with mCSPC was conducted utilizing propensity score-weighted cohorts of patients initiated on apalutamide or enzalutamide
- Patients were assigned to mutually exclusive treatment cohorts based on the first dispensation or paid pharmacy claim for apalutamide or enzalutamide
- The index date was defined as the first dispensation or paid pharmacy claim for apalutamide or enzalutamide after 16 December 2019 (the US Food and Drug Administration approval date for enzalutamide[11] which followed apalutamide approval on 17 September 2019)[12]
- Baseline patient characteristics were evaluated in the 12 months preceding 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 (i.e., apalutamide, abiraterone acetate, darolutamide, or enzalutamide) or a radiopharmaceutical agent, end of insurance or clinical activity, or end of data availability (31 December 2023)

Study outcomes

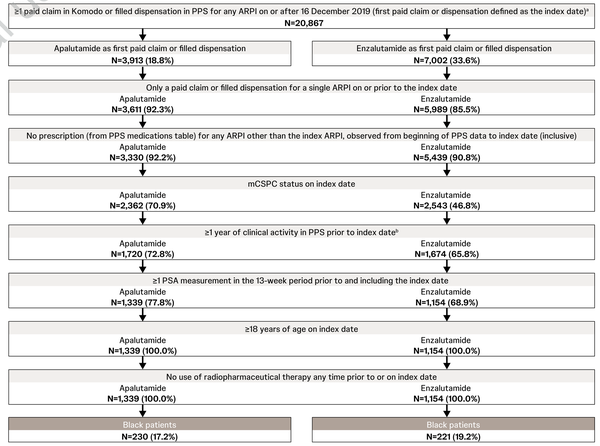
- The primary outcome was the proportion of patients who achieved PSA90 from the most recent baseline value by 6 months post-index
- As an exploratory outcome, the proportion of patients who achieved PSA90 using all available follow-up was also assessed

Statistical analysis

- Inverse probability of treatment weighting (IPTW), based on patients' propensity score, was used to account for differences in baseline characteristics between the apalutamide and enzalutamide cohorts[13]
- Balancing of baseline characteristics between treatment cohorts after weighting was confirmed by standardized differences <10% which indicates balance[14]
- A weighted Kaplan-Meier analysis was conducted to evaluate the proportion of patients achieving PSA90 by 6-months after the index date
- Weighted Cox proportional hazards models were used to evaluate the causal relationship between the index ARPI treatment and PSA90

Patient selection

Figure 1: Patient Selection Flowchart



ARPI: androgen receptor pathway inhibitor; mCSPC: metastatic castration-sensitive prostate cancer; PPS: Precision Point Specialty; PSA: prostate-specific antigen.
Notes: a. The Food and Drug Administration (FDA) approved enzalutamide as treatment for mCSPC on 16 December 2019. b. Clinical activity was defined as the period from the first to last record in the Precision Point Specialty (PPS) electronic medical records (EMR) database. Patients with no observation period after the index date were excluded.

Results

Baseline characteristics

- Overall, 230 Black patients with mCSPC who initiated apalutamide and 221 Black patients with mCSPC who initiated enzalutamide were identified (**Figure 1**)
- Baseline patient characteristics were generally well-balanced between the weighted cohorts, with standardized differences <10% (**Table 1**)

Table 1: Baseline Characteristics

	Weighted Population[a,b]		
	Apalutamide N=230	Enzalutamide N=221	Standardized Difference[c]
Age, mean ± SD [median]	71.0 ± 8.5 [70.0]	71.4 ± 8.6 [71.0]	4.7
Geographic region, n (%)			
South	157 (68.4)	146 (66.1)	4.8
Midwest	52 (22.6)	54 (24.5)	4.4
Northeast	18 (7.8)	18 (8.0)	0.9
West	3 (1.2)	3 (1.3)	1.3
Payer type, n (%)			
Medicare	176 (76.5)	173 (78.1)	3.7
Commercial	46 (19.8)	43 (19.3)	1.2
Medicaid	8 (3.3)	6 (2.5)	4.6
Unknown	1 (0.3)	0 (0.0)	0.0
Year of treatment initiation (index date), n (%)			
2019-2020	49 (21.3)	51 (23.1)	4.4
2021	52 (22.8)	52 (23.7)	2.2
2022	70 (30.4)	63 (28.4)	4.4
2023	59 (25.6)	55 (24.8)	1.8
Time between metastasis and treatment initiation, months, mean ± SD [median]	11.3 ± 20.0 [3.4]	11.8 ± 16.9 [3.4]	2.6
Time between PC diagnosis and treatment initiation, months, mean ± SD [median]	52.7 ± 45.5 [47.6]	54.0 ± 46.4 [45.3]	2.9
Metastasis type, n (%)			
Bone	147 (63.9)	142 (64.1)	0.3
Nodal	127 (55.2)	117 (53.0)	4.4
Visceral	41 (17.7)	43 (19.3)	4.0
De novo PC, n (%)	81 (35.4)	76 (34.4)	2.0
Prior use of ADT, n (%)	206 (89.4)	197 (89.1)	0.9
Cumulative duration of prior ADT use, months, mean ± SD [median]	9.8 ± 12.6 [5.6]	11.3 ± 13.4 [6.3]	11.1
Prior use of first generation ARPI, n (%)	35 (15.0)	34 (15.2)	0.5
Prior use of chemotherapy, n (%)	4 (1.5)	4 (1.9)	2.8
Baseline PSA level, ng/mL, mean ± SD [median]	23.6 ± 54.8 [2.7]	23.4 ± 48.1 [2.7]	0.3
Earliest Gleason score, n (%)			
≤6	25 (11.0)	24 (11.0)	0.0
7	66 (28.8)	60 (27.2)	3.5
8	28 (12.2)	31 (14.0)	5.3
9	47 (20.5)	45 (20.3)	0.5
10	3 (1.2)	3 (1.5)	1.8
Unknown	61 (26.3)	58 (26.1)	0.6

ADT: androgen deprivation therapy; ARPI: androgen receptor pathway inhibitor; PC: prostate cancer; PSA: prostate-specific antigen; SD: standard deviation.
Notes: a. Propensity scores were generated using probability estimates from a logistic regression models using the following predictors: age (categorical), 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 PC, previous ADT use, first-generation antiandrogen use, chemotherapy use, types of metastases (bone, nodal, visceral), most recent PSA level (continuous), baseline testosterone level (categorized as <50 ng/dL or ≥50ng/dL; patients without a testosterone measurement were grouped into the <50 ng/dL category), and earliest Gleason score (categorized as ≤6, 7, 8, 9, 10 and unknown). 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 enzalutamide cohort. Normalized inverse-probability of treatment weights were truncated at the 95th percentiles. 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. c. Standardized differences <10% indicate that the variable was balanced between the apalutamide and enzalutamide cohorts.

PSA testing patterns

- PSA testing occurred at similar frequency in both the apalutamide and the enzalutamide cohort (**Table 2**)
  - By 6 months post-index, 77.0% of apalutamide patients and 77.7% of enzalutamide patients had a post-index PSA measurement

Table 2: Follow-Up PSA Testing

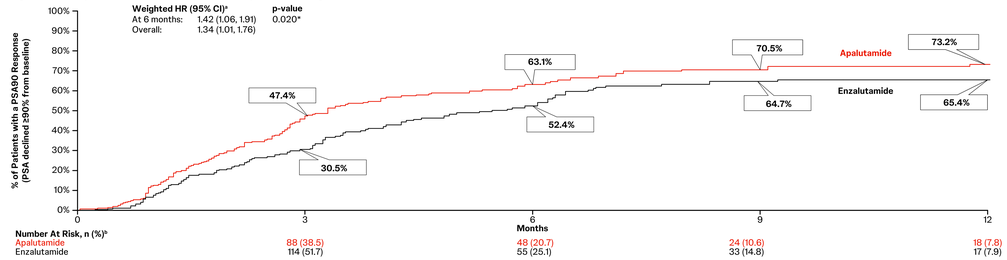
	Weighted Population[a]	
	Apalutamide N=230	Enzalutamide N=221
Patients with ≥1 PSA test, n (%)	185 (80.3)	174 (78.5)
Within 3 months of treatment	159 (69.3)	135 (61.3)
Within 6 months of treatment	177 (77.0)	172 (77.7)
Number of follow-up PSA tests per year, mean ± SD [median]	3.9 ± 3.5 [3.4]	3.9 ± 3.8 [3.2]
Patients with PSA test on average every 3 months, n (%)	87 (38.0)	72 (32.7)
Patients with PSA test on average every 6 months, n (%)	167 (72.8)	168 (75.9)

PSA: prostate-specific antigen; SD: standard deviation.
Note: 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.

PSA outcomes

- By 6 months post-index, Black patients initiating apalutamide had a statistically significant 42% increase in their probability of achieving a PSA90 response compared with Black patients initiated on enzalutamide (hazard ratio [HR]=1.42, 95% confidence interval [CI]: 1.06, 1.91; p=0.020; **Figure 2**)
- This result was consistent when evaluating PSA90 using all available follow-up (HR=1.34, CI: 1.01, 1.76)
  - This analysis was not adjusted for multiple comparisons, and statistical significance was not established for time points beyond the primary endpoint
- PSA90 response was attained earlier in patients treated with apalutamide (3.3 months) than those treated with enzalutamide (5.5 months)

Figure 2: Comparison of Time to PSA90 Response Among Black Patients with mCSPC



CI: confidence interval; HR: hazard ratio; mCSPC: metastatic castration-sensitive prostate cancer; PSA: prostate-specific antigen.
* Significant at the 5% level.
Note: a. A hazard ratio >1 indicates that the apalutamide cohort had a higher rate of PSA90 response compared to the enzalutamide 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.

Limitations

- Miscoding or misclassification in the clinical record or through the insurance claims may introduce selection and information biases despite efforts to match the study populations
- Regression analyses could only adjust for documented covariates and unknown confounders may be present

References
1. Chowdhury S, et al. *Ann Oncol.* 2023;34(5):477-485. 2. Matsubara N, et al. *Eur Urol.* 2020;77(4):494-500. 3. Chi KN, et al. *N Engl J Med.* 2019;381(1):13-24. 4. Chi KN, et al. *J Clin Oncol.* 2021;39(20):2294-2303. 5. Armstrong AJ, et al. *J Clin Oncol.* 2022;40(15):1616-1622. 6. Lowentritt B, et al. *Reviews in Urology.* 2024;23(2):e29-e40. 7. Lowentritt B, et al. *Urol Oncol.* 2023;41(5):253-e251. 8. Pittell H, et al. *JAMA Network Open.* 2023;6(7):e2322515. 9. Ma T, et al. *JAMA Network Open.* 2023;6(12):e2345906. 10. Barocas DF, et al. *BJU Int.* 2010;106(3):322-328. 11. U.S. Food and Drug Administration. FDA approves enzalutamide for metastatic castration-sensitive prostate cancer. 2018. 12. U.S. Food and Drug Administration. FDA approves apalutamide for metastatic castration-sensitive prostate cancer. 2019. 13. Austin PC. *Multivariate Behav Res.* 2011;46(3):399-424. 14. *Austin PC. Stat Med.* 2009;28(25):3083-3107. 15. Chowdhury S. *Ann Oncol.* 2023;34(5):477-485.

Prostate Cancer

Presented at the American Urological Association (AUA) Annual Meeting 2025; April 26–29, 2025; Las Vegas, Nevada