Prostate-specific antigen response in Black patients with metastatic castration-sensitive prostate cancer treated with apalutamide versus abiraterone acetate – A real-world comparison

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Key Takeaway

By 6-months post-treatment initiation, Black patients with mCSPC initiating apalutamide were 66% more likely to achieve PSA90 compared to Black patients initiating abiraterone acetate

Conclusions

- PSA90 response was attained earlier and in more Black patients treated with apalutamide than those treated with abiraterone acetate
- The significant increase in PSA90 response rates among Black patients initiating apalutamide relative to abiraterone acetate in this study was consistent with the main findings from a race agnostic population using the same linked clinical data and insurance claims data[7]
- 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[12]

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Disclosures

G. Brown is an employee of New Jersey Urology 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. Diaz, 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 Associates 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 abiraterone acetate, 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 LATITUDE 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 53%–67% higher PSA90 response rates than abiraterone acetate among patients with mCSPC at 6-months post-treatment initiation[6,7]
- This study aimed to demonstrate the robustness of real-world PSA response in a cohort of Black patients with mCSPC

Objective

- 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 abiraterone acetate

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 causal analysis of ARPI-naïve Black patients with mCSPC was conducted utilizing propensity score-weighted cohorts of patients initiated on apalutamide or abiraterone acetate
- Patients were assigned to mutually exclusive treatment cohorts based on the first dispensation or paid pharmacy claim for apalutamide or abiraterone acetate
- The index date was defined as the first dispensation or paid pharmacy claim for apalutamide or abiraterone acetate after 17 September 2019 (the US Food and Drug Administration approval date for apalutamide[8] which followed abiraterone acetate approval on 7 February 2018[9])
- 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)

Patient selection

- Concurrent use of ADT was not required for patients to be included in either the apalutamide or abiraterone acetate cohort and concurrent use of prednisone was not required for patients to be included in the abiraterone acetate cohort

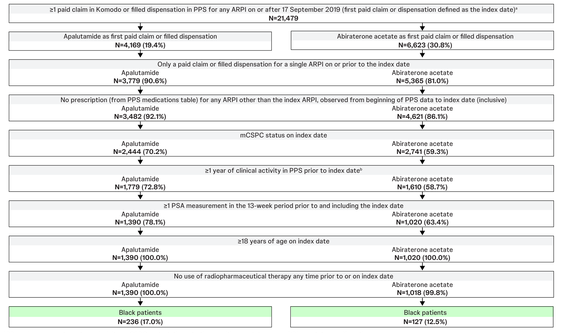
Study outcomes

- 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 abiraterone acetate cohorts[10]
- Balancing of baseline characteristics between treatment cohorts after weighting was confirmed by standardized differences <10% which indicates balance[11]
- 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

Figure 1: Patient Selection Flowchart



ARPI: androgen receptor pathway inhibitor; mCSPC: metastatic castration-sensitive prostate cancer; PSA: prostate-specific antigen.
Notes: a. The Food and Drug Administration (FDA) approved apalutamide as treatment for mCSPC on 17 September 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, 236 Black patients with mCSPC who initiated apalutamide and 127 Black patients with mCSPC who initiated abiraterone acetate 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=236	Abiraterone acetate N=127	Standardized Difference[c]
Age, mean ± SD [median]	70.1 ± 8.8 [69.0]	69.2 ± 8.9 [68.0]	9.5
Geographic region, n (%)			
South	169 (71.7)	89 (70.4)	2.8
Midwest	42 (17.8)	21 (16.6)	3.0
Northeast	22 (9.3)	13 (10.3)	3.2
West	3 (1.3)	3 (2.7)	10.4
Payer type, n (%)			
Medicare	167 (70.7)	85 (67.1)	7.7
Commercial	59 (24.9)	34 (26.8)	4.4
Medicaid	10 (4.1)	6 (4.6)	2.5
Unknown	1 (0.3)	2 (1.5)	0.0
Year of treatment initiation (index date), n (%)			
2019-2020	50 (21.2)	26 (20.7)	1.1
2021	49 (20.6)	25 (20.1)	1.2
2022	72 (30.7)	37 (29.2)	3.3
2023	65 (27.6)	38 (30.0)	5.3
Time between metastasis and treatment initiation, months, mean ± SD [median]	10.0 ± 19.7 [3.1]	10.6 ± 16.0 [4.0]	3.8
Time between PC diagnosis and treatment initiation, months, mean ± SD [median]	51.0 ± 46.0 [45.0]	51.3 ± 52.8 [31.4]	0.7
Metastasis type, n (%)			
Bone	140 (59.2)	69 (54.7)	9.1
Nodal	140 (59.5)	79 (62.6)	6.3
Visceral	34 (14.4)	15 (11.6)	8.4
De novo PC, n (%)	90 (38.2)	51 (40.2)	4.0
Prior use of ADT, n (%)	209 (88.7)	110 (86.6)	6.6
Cumulative duration of prior ADT use, months, mean ± SD [median]	9.5 ± 13.0 [4.9]	11.9 ± 18.0 [6.1]	14.8
Prior use of first generation ARPI, n (%)	37 (15.7)	19 (15.3)	1.0
Prior use of chemotherapy, n (%)	4 (1.5)	2 (1.7)	2.0
Baseline PSA level, ng/mL, mean ± SD [median]	23.8 ± 53.7 [3.3]	24.1 ± 57.5 [2.4]	0.6
Earliest Gleason score, n (%)			
≤6	23 (9.7)	13 (9.8)	0.3
7	70 (29.5)	36 (28.1)	3.2
8	31 (13.1)	20 (15.9)	7.9
9	47 (20.0)	24 (19.3)	1.9
10	2 (0.8)	1 (0.8)	0.4
Unknown	63 (26.7)	33 (26.1)	1.5

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 missing). 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 abiraterone acetate 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 abiraterone acetate cohorts.

PSA testing patterns

- PSA testing occurred at a similar frequency in both the apalutamide and the abiraterone acetate cohort (**Table 2**)
  - By 6 months post-index, 78.4% of apalutamide patients and 76.5% of abiraterone acetate patients had a post-index PSA measurement

PSA outcomes

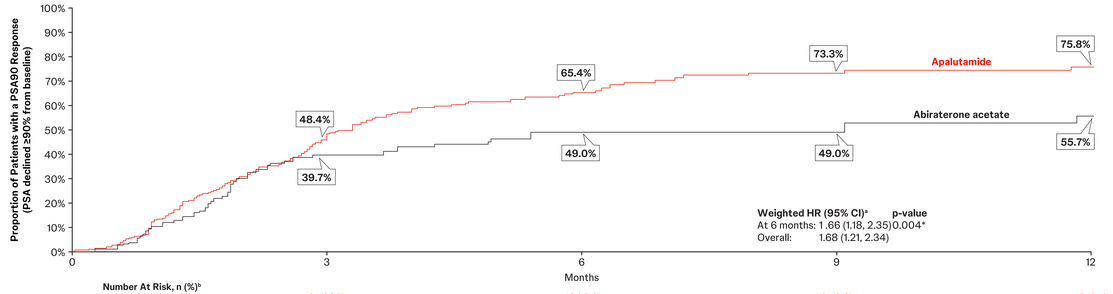
- By 6 months post-index, Black patients initiating apalutamide had a statistically significant 66% increase in their probability of achieving a PSA90 response compared with Black patients initiated on abiraterone acetate (hazard ratio [HR]=1.66, 95% confidence interval [CI]: 1.18, 2.35; p=0.004; **Figure 2**)
- This result was consistent when evaluating PSA90 using all available follow-up (HR=1.68, CI: 1.21, 2.34)
  - Not adjusted for multiple comparison and statistical significance not established for time points beyond primary endpoint
- PSA90 response was attained earlier in patients treated with apalutamide (3.3 months) than for those treated with abiraterone acetate (9.1 months)

Table 2: Follow-Up PSA Testing

	Non-weighted Population		Weighted Population[a]	
	Apalutamide N=236	Abiraterone acetate N=127	Apalutamide N=236	Abiraterone acetate N=127
Patients with ≥1 PSA test, n (%)	193 (81.8)	99 (78.0)	193 (81.9)	100 (79.0)
Within 3 months of treatment	165 (69.9)	88 (69.3)	164 (69.4)	88 (69.4)
Within 6 months of treatment	186 (78.8)	96 (75.6)	185 (78.4)	97 (76.5)
Number of follow-up PSA tests per year, mean ± SD [median]	4.0 ± 3.5 [3.4]	5.1 ± 5.0 [4.1]	4.0 ± 3.6 [3.4]	5.3 ± 5.1 [4.1]
Patients with PSA test on average every 3 months, n (%)	93 (39.4)	64 (50.4)	93 (39.3)	65 (51.4)
Patients with PSA test on average every 6 months, n (%)	175 (74.2)	92 (72.4)	175 (74.2)	94 (74.2)

ADT: androgen deprivation therapy; PC: prostate cancer; 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.

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.
Notes: a. A hazard ratio >1 indicates that the apalutamide cohort had a higher rate of PSA90 response compared to the abiraterone acetate 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
- Abiraterone acetate is indicated for high-risk mCSPC only, which may result in residual differences relative to the apalutamide treatment cohort after weighting

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