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Overall Survival in Patients with Metastatic Castration Sensitive Prostate Cancer Treated With Apalutamide versus Abiraterone Acetate – A Head-to-Head Analysis of Real-World Patients in the United States

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Benjamin Lowentritt[1], Mehmet A. Bilen[2], Ibrahim Khilfeh[3], Carmine Rossi[4], Shawn Du[3], Frederic Kinkead[4], Lilian Diaz[4], Dominic Pilon[4], Lorie Ellis[3], Neal Shore[5]

[1]Chesapeake Urology, Towson, Maryland, USA; [2]Winship Cancer Institute of Emory University, Atlanta, Georgia, USA; [3]Janssen Scientific Affairs, LLC, a Johnson & Johnson company, Horsham, Pennsylvania, USA; [4]Analysis Group, Inc., Montréal, Québec, Canada; [5]Carolina Urologic Research Center, Myrtle Beach, South Carolina, USA

Key Takeaway

By 24 months post-treatment initiation, patients with mCSPC initiating apalutamide had a statistically significant 26% reduction in the risk of death when compared to patients initiating abiraterone acetate

Conclusions

In ARPI-naïve patients with mCSPC, patients treated with apalutamide were 26% more likely to survive at 24 months post-treatment initiation compared to those treated with abiraterone acetate

Overall survival observed in the apalutamide cohort of this real-world study at 24 months is consistent with overall survival observed at 24 months in the phase 3 TITAN study[5]

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Poster

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Disclosures

B. Lowentritt is an employee of Chesapeake Urology Associates and has received consulting fees from Janssen Scientific Affairs, LLC, a Johnson & Johnson company. M. Bilen is an employee of the Winship Cancer Institute of Emory University and has received consulting fees from Janssen Scientific Affairs, LLC, a Johnson & Johnson company. I. Khilfeh, S. Du, and L. Ellis are employees of Janssen Scientific Affairs, LLC, a Johnson & Johnson company 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 Janssen Scientific Affairs, LLC, a Johnson & Johnson company. N. Shore is an employee of Carolina Urologic Research Center and has received consulting fees from Janssen Scientific Affairs, LLC, a Johnson & Johnson company.

Background

- Apalutamide and abiraterone acetate are androgen receptor pathway inhibitors (ARPIs), approved for use in combination with androgen deprivation therapy (ADT) for the treatment of metastatic castration-sensitive prostate cancer (mCSPC)[1,2]
- Apalutamide (TITAN)[3] and abiraterone acetate (LATITUDE)[4] demonstrated statistically significant reduction in disease progression and death as compared to ADT alone in patients with mCSPC in phase 3 trials[3-5]
- There are currently no clinical trials or real-world studies that have directly compared progression or survival outcomes between these approved agents in patients with mCSPC

Objectives

- To compare the proportion of ARPI-naïve patients surviving by 24 months for patients with mCSPC who newly initiated apalutamide versus abiraterone acetate
- Null hypothesis: In ARPI-naïve patients with mCSPC, overall survival by 24 months post-apalutamide initiation is not different than overall survival by 24 months post-abiraterone acetate initiation.
- Alternative hypothesis: In ARPI-naive patients with mCSPC, overall survival by 24 months post-apalutamide initiation is different than overall survival by 24 months post-abiraterone acetate initiation.

Methods

- This study attempted to apply best practices from the US Food and Drug Administration guidance document entitled "Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products Guidance for Industry"[6]

Data sources

- Clinical data from Precision Point Specialty (PPS) Analytics from 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: 17 September 2018 - 31 December 2023)
- Electronic medical record (EMR) data from PPS were robust and captured longitudinal laboratory data including prostate-specific antigen (PSA) test results, and castration resistance, which were not available in administrative claims data, and necessary to identify mCSPC patients
- Mortality data from the KRD were updated monthly and captured >90% of all oncology-specific US deaths as identified by the US Centers for Disease Control and Prevention.[7] These data are curated from multiple third-party sources that aggregate their data from national and state governments, public listings (e.g., cemetery, funeral home), private claims and obituary data
- Patients with mCSPC were identified using PPS which provides the castration resistance designation and PSA test results necessary to exclude patients with evidence of castration resistance and confirm mCSPC status.
- Data were de-identified and Health Insurance Portability and Accountability Act (HIPAA) compliant

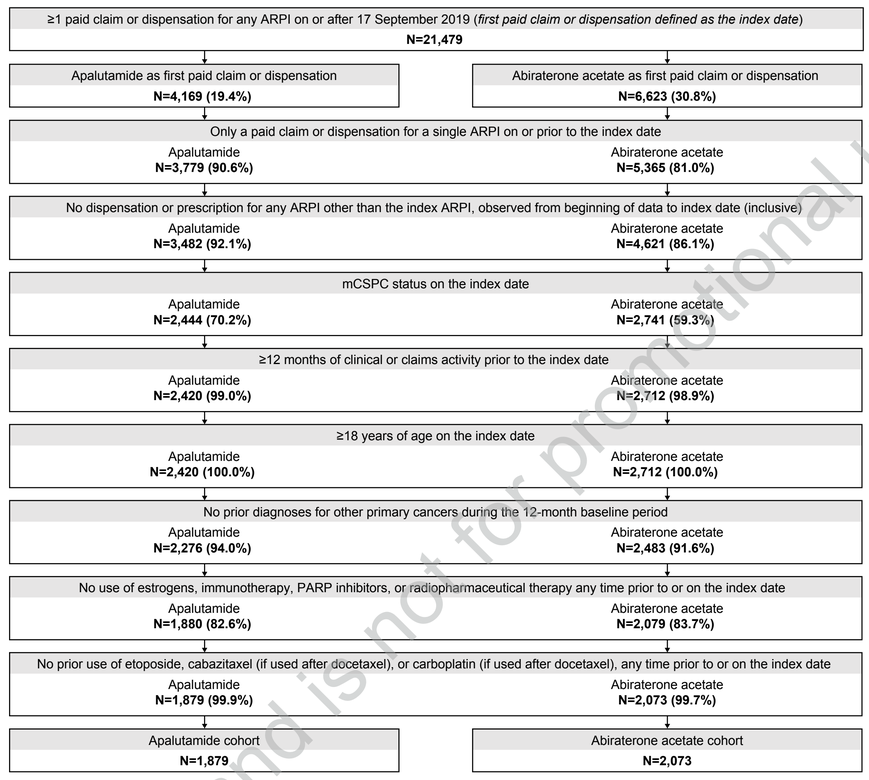
Study design

- A power calculation was performed to verify that the sample size was sufficient to detect statistically significant differences in survival between the apalutamide and abiraterone acetate cohorts
- A retrospective longitudinal causal analysis of ARPI-naïve patients with mCSPC was conducted utilizing propensity score-weighted cohorts of patients initiated on apalutamide or abiraterone acetate, following an intention-to-treat design
- Patients were selected into 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 on or after 17 September 2019 (the US Food and Drug Administration approval date for apalutamide[1] which followed abiraterone acetate approval on 7 February 2018[2])
- Baseline patient characteristics were evaluated in the 12 months before the index date
- The observation period was defined as the index date to the latter of end of clinical activity (in PPS) or claims activity (in KRD), with both not exceeding 31 December 2023
- Treatment patterns were observed from the index date for a period spanning up to 24 months

Patient selection criteria

- Patients were assessed as having 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 incorporating presence of ADT (as identified in both PPS and KRD)[8] and PSA levels and clinical notes abstracted from the EMR by PPS
- 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

Figure 1: Patient Flowchart



ARPI: androgen receptor pathway inhibitor; mCSPC: metastatic castration-sensitive prostate cancer; PARP: poly ADP ribose polymerase.

Study outcome

- The primary outcome was the proportion of patients who survived by 24-months post-index ARPI initiation

Statistical analysis

- Based on the propensity score (PS), inverse probability of treatment weighting (IPTW) was used to account for differences in baseline characteristics between the apalutamide and abiraterone acetate cohorts[9]
- The PS was obtained from a logistic regression model where index treatment was the dependent variable and with the following baseline characteristics as independent variables: age, race, geographic region, payer type, index year, time between metastasis and index date, time between PC diagnosis and index date, *de novo* PC, metastases type, ADT use overlapping index date, prior first-generation antiandrogen use, prior chemotherapy use, Quan-Charlson comorbidity index, baseline PSA level, and initial Gleason score
- Baseline characteristics between treatment cohorts were considered balanced after weighting[10], as indicated by standardized differences of less than 10%
- A weighted Kaplan-Meier analysis was conducted to evaluate the proportion of patients surviving by 24-months after the index date
- Weighted Cox proportional hazards models were used to evaluate the causal relationship between the index ARPI treatment and overall survival

Results

Baseline characteristics

- Overall, 1,879 patients with mCSPC who initiated apalutamide and 2,073 patients with mCSPC who initiated abiraterone acetate were identified (**Figure 1**)
- Generally, baseline patient characteristics were well-balanced between the weighted cohorts, with standardized differences of less than 10% (**Table 1**)

Table 1: Baseline Characteristics

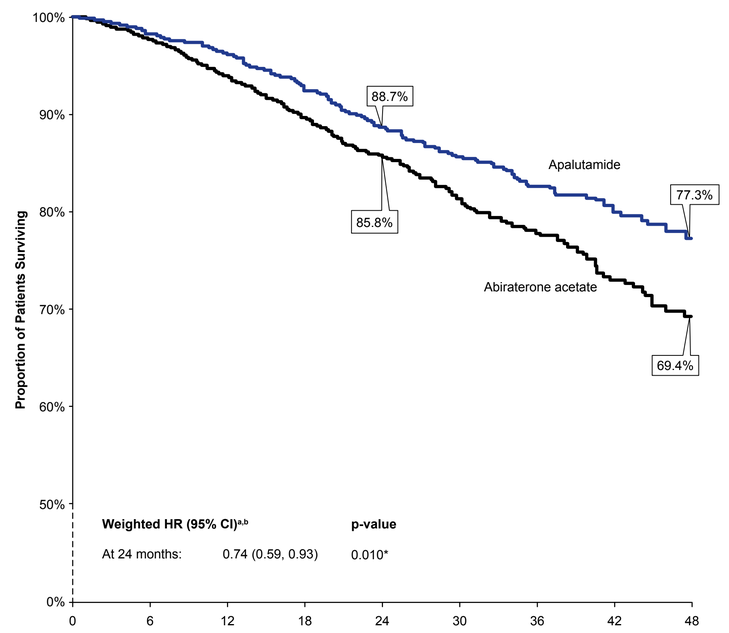
	Non-Weighted Population			Weighted Population[a]		
	Apalutamide N=1,879	Abiraterone acetate N=2,073	Standardized Difference, %	Apalutamide N=1,879	Abiraterone acetate N=2,073	Standardized Difference, %
Age, mean ± SD [median]	72.9 ± 9.1 [73.0]	71.2 ± 9.2 [71.0]	18.4	72.1± 9.3 [72.0]	71.9 ± 9.1 [72.0]	2.5
Race, n (%)						
White	1,139 (60.6)	1,325 (63.9)	6.8	1,159 (61.7)	1,295 (62.5)	1.6
Black or African American	416 (22.1)	317 (15.3)	17.6	359 (19.1)	374 (18.0)	2.8
Hispanic or Latino	136 (7.2)	151 (7.3)	0.2	141 (7.5)	152 (7.3)	0.6
Other	71 (3.8)	114 (5.5)	8.2	85 (4.5)	100 (4.8)	1.3
Unknown	117 (6.2)	166 (8.0)	6.9	134 (7.1)	152 (7.3)	0.7
Geographic region, n (%)						
South	1,068 (56.8)	744 (35.9)	43.0	900 (47.9)	923 (44.5)	6.8
Midwest	421 (22.4)	686 (33.1)	24.0	515 (27.4)	602 (29.0)	3.6
Northeast	212 (11.3)	353 (17.0)	16.5	247 (13.1)	296 (14.3)	3.3
West	178 (9.5)	290 (14.0)	14.1	217 (11.5)	253 (12.2)	2.0
index year, n (%)						
2019-2020	405 (21.6)	504 (24.3)	6.6	414 (22.0)	473 (22.8)	1.8
2021	447 (23.8)	466 (22.5)	3.1	444 (23.6)	484 (23.3)	0.8
2022	519 (27.6)	528 (25.5)	4.9	514 (27.4)	555 (26.8)	1.3
2023	508 (27.0)	575 (27.7)	1.6	506 (27.0)	562 (27.1)	0.4
Time between metastasis and index date, months, mean ± SD [median]	9.0 ± 17.9 [2.3]	11.3 ± 17.6 [3.4]	13.0	9.7 ± 17.6 [2.5]	10.2 ± 17.1 [2.8]	2.5
Time between PC diagnosis and index date, months, mean ± SD [median]	39.3 ± 46.9 [14.9]	37.1 ± 46.9 [13.3]	4.6	37.4 ± 45.5 [14.1]	35.5 ± 47.7 [12.8]	0.3
Metastasis type[b], n (%)						
Bone	1,311 (69.8)	1,339 (64.6)	11.1	1,249 (66.5)	1,373 (66.2)	0.6
Nodal	960 (51.1)	1,103 (53.2)	4.2	994 (52.9)	1,097 (52.9)	0.1
Visceral	335 (17.8)	571 (27.5)	23.4	396 (21.1)	477 (23.0)	4.7
Metastasis in multiple sites	536 (28.5)	405 (19.5)	21.2	477 (25.4)	492 (23.7)	3.9
Quan-CCI, mean ± SD [median]	8.5 ± 3.0 [8.0]	8.6 ± 2.9 [8.0]	1.4	8.5 ± 3.0 [8.0]	8.5 ± 2.9 [8.0]	0.7
***De novo* PC[c], n (%)**	1,040 (55.3)	1,259 (60.7)	10.9	1,100 (58.5)	1,223 (59.0)	1.0
Concurrent use of ADT with index ARPI[d], n (%)	1,542 (82.1)	1,395 (67.3)	34.5	1,443 (76.8)	1,535 (74.0)	6.4
Duration of ADT episode overlapping with index date, months, mean ± SD [median]	4.4 ± 8.5 [1.8]	5.1 ± 8.3 [2.0]	8.6	4.5 ± 8.0 [1.8]	5.0 ± 8.3 [1.9]	6.4
Prior use of first-generation ARPI[e], n (%)	297 (15.8)	437 (21.1)	13.6	343 (18.2)	396 (19.1)	2.2
Prior use of chemotherapy[f], n (%)	30 (1.6)	102 (4.9)	18.8	51 (2.7)	72 (3.5)	4.6
Most recent PSA level, ng/mL, n (%)						
≤0.2	325 (17.3)	246 (11.9)	15.4	288 (15.3)	298 (14.4)	2.7
>0.2 to ≤2	309 (16.4)	265 (12.8)	10.4	286 (15.2)	296 (14.3)	2.7
>2 to ≤5	214 (11.4)	161 (7.8)	12.3	186 (9.9)	194 (9.3)	1.9
>5 to ≤10	194 (10.3)	141 (6.8)	12.6	168 (9.0)	172 (8.3)	2.3
>10	558 (29.7)	541 (26.1)	8.0	533 (28.4)	577 (27.8)	1.3
Unknown	279 (14.8)	719 (34.7)	47.2	417 (22.2)	537 (25.9)	8.7
Earliest Gleason score[g], n (%)						
≤6	110 (5.9)	85 (4.1)	8.1	94 (5.0)	97 (4.7)	1.6
7	370 (19.7)	355 (17.1)	6.6	355 (18.9)	383 (18.5)	1.1
8	263 (14.0)	320 (15.4)	4.1	276 (14.7)	311 (15.0)	0.9
9	405 (21.6)	430 (20.7)	2.0	408 (21.7)	446 (21.5)	0.6
10	56 (3.0)	66 (3.2)	1.2	60 (3.2)	65 (3.2)	0.3
Unknown	675 (35.9)	817 (39.4)	7.2	685 (36.5)	771 (37.2)	1.5

ADT: androgen deprivation therapy; ARPI: androgen receptor pathway inhibitor; CCI: Charlson Comorbidity Index; PC: prostate cancer; PSA: prostate-specific antigen; SD: standard deviation.
Notes:
[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 first observed PC diagnosis and date of metastasis.
[d]Concurrent ADT use was defined as an episode of continuous ADT use overlapping with the index date (using a 60-day gap to define discontinuation).
[e]Prior use of first-generation ARPI was defined as any prescription for bicalutamide, nilutamide, or flutamide in the 12 months preceding the index date.
[f]Prior chemotherapy use was defined as any administration at any time prior to (and excluding) the index date.
[g]Gleason score was evaluated at any time prior to and including the index date.

Overall survival

- By 24 months post-index, apalutamide patients had a statistically significant 26% reduction in their risk of death compared with patients initiated on abiraterone acetate (hazard ratio [HR]=0.74, 95% confidence interval [CI]: 0.59, 0.93; p=0.010; **Figure 2**)
- This result was consistent when evaluating overall survival using all available follow-up (HR=0.72, 95% CI: 0.59, 0.88; nominal p<0.001 [not adjusted for multiple comparison and statistical significance not established for time points beyond primary endpoint])

Figure 2: Comparison of Overall Survival among Patients with mCSPC



Number At Risk, n (%)[c]

Apalutamide	1,897 (100)	1,631 (86.8)	1,329 (70.8)	1,026 (54.6)	739 (39.3)	507 (27.0)	333 (17.7)	192 (10.2)	82 (4.4)
Abiraterone acetate	2,073 (100)	1,770 (85.4)	1,415 (68.3)	1,112 (53.6)	771 (37.2)	498 (24.0)	312 (15.0)	185 (8.9)	68 (3.3)

ADT: androgen deprivation therapy; CI: confidence interval; HR: hazard ratio; mCSPC: metastatic castration-sensitive prostate cancer; PC: prostate cancer; PSA: prostate-specific antigen.
*Significant at the 5% level.
Notes:
[a]Propensity scores were generated using probability estimates from a logistic regression models using the following predictors: age (continuous), race, geographic region, payer, year of index date, time between metastasis and index date (continuous and categorical), time between PC diagnosis and index date (continuous), *de novo* PC, ADT use overlapping with index date, first-generation antiandrogen use, chemotherapy use, types of metastases (bone, nodal, visceral, and metastasis in multiple sites), Quan-Charlson comorbidity index (continuous), most recent PSA level (categorical), and earliest Gleason score (categorical). 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]A hazard ratio <1 indicates that the apalutamide cohort had a lower rate of death compared to the abiraterone acetate cohort.
[c]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.

Treatment patterns

- The mean (median) follow-up period was 16.8 (19.5) months in patients who initiated apalutamide and 16.3 (19.0) months in patients who initiated abiraterone acetate
- Using a 90-day gap in treatment to define discontinuation, the mean (median) duration of continuous index ARPI use was 9.3 (6.6) months in patients who initiated apalutamide and 10.7 (8.9) months in patients who initiated abiraterone acetate

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
- The generalizability of the study in certain settings may be limited due to the database representing the community urology perspective, and may not be representative of the entire population of patients with mCSPC in the US
- While comparisons with US Centers for Disease Control (CDC) estimates of overall survival has demonstrated that KRD captured >90% of all deaths in oncology settings between 2018 and 2023[7], it is possible that not all deaths are captured in the data
- Abiraterone acetate is only indicated for high-risk mCSPC, which may result in residual differences relative to the apalutamide treatment cohort after IPTW adjustments
- Regression analyses could only adjust for documented covariates and unknown confounders may be present
- In phase 3 trials[3,4], overall survival was assessed at pre-specified numbers of events. In this study, survival was assessed by 24 months for evaluation of statistical comparison. Studies assessing longer follow-up in these patient cohorts may be needed to estimate the full magnitude of therapeutic effect for these agents

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