Head-to-head comparison of overall survival in subgroups of patients with metastatic castration-sensitive prostate cancer initiating apalutamide or abiraterone acetate – A real-world study

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Background and methods

A causal analysis using retrospective data comparing 24-month survival outcomes in ARPI-naïve patients with mCSPC initiating apalutamide versus abiraterone acetate, overall, and in key clinical subgroups

OBJECTIVE

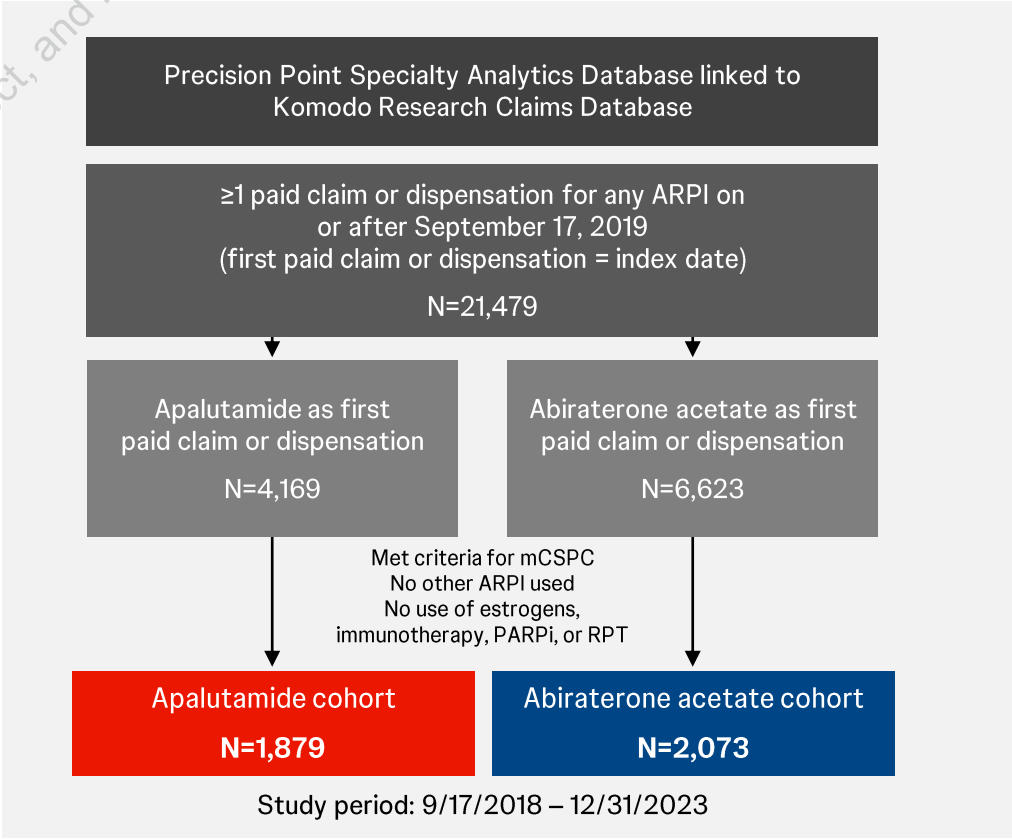
- Compare overall survival (OS) at 24 months between patients treated with apalutamide (APA) and abiraterone acetate (ABI) in a nationally representative sample of androgen receptor pathway inhibitors (ARPI)-naïve patients with metastatic castration-sensitive prostate cancer (mCSPC), overall, and in important subgroups

BACKGROUND

- Apalutamide and abiraterone acetate are ARPIs approved for use with ADT in patients with mCSPC (also known as metastatic hormone-sensitive prostate cancer)[1,2]
- In Phase 3 trials, 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[3–5]
- Currently, there are no clinical trials or real-world studies that directly compare survival outcomes between these approved agents in patients with mCSPC, or among subgroups

METHODS

- **Study design:** Retrospective, longitudinal, intention-to-treat analysis
- **Data sources:** Linked data from a clinical urology database (Precision Point Specialty Analytics; PPS) and an administrative claims database (Komodo Research Database; KRD)
- **Patient selection:** Adult patients with ARPI-naïve mCSPC were excluded if they were castration resistant, had prior use of an ARPI or other advanced treatment, or had another primary cancer
- **Statistical analyses:** Potentially confounding baseline demographic and clinical variables, overall, and in each subgroup were balanced using inverse-probability of treatment weighting (IPTW). Weighted Cox proportional hazards models were used to evaluate and compare OS between apalutamide and abiraterone acetate cohorts
- **Compliance & power:** Data were de-identified, HIPAA compliant, and had a sufficient sample size to compare OS



ARPI, androgen receptor pathway inhibitor; ADT, androgen deprivation therapy; IPTW: inverse-probability of treatment weighting; mCSPC, metastatic castration-sensitive prostate cancer; PARPi, poly-ADP ribose polymerase inhibitor; RPT, radiopharmaceutical therapy.

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 on 8 Jan 2025; 2. U.S. Food and Drug Administration. FDA approves abiraterone acetate in combination with prednisone for high-risk metastatic castration-sensitive prostate cancer. 2018. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-abiraterone-acetate-combination-prednisone-high-risk-metastatic-castration-sensitive. Accessed on 8 Jan 2025; 3. Chi KN, et al. J Clin Oncol. 2021;39(20):2294-2303. 4. Fizazi K, et al. Lancet Oncol. 2019;20(5):686-700. 5. Chi KN, et al. N Engl J Med. 2019;381(1):13-24.

Results

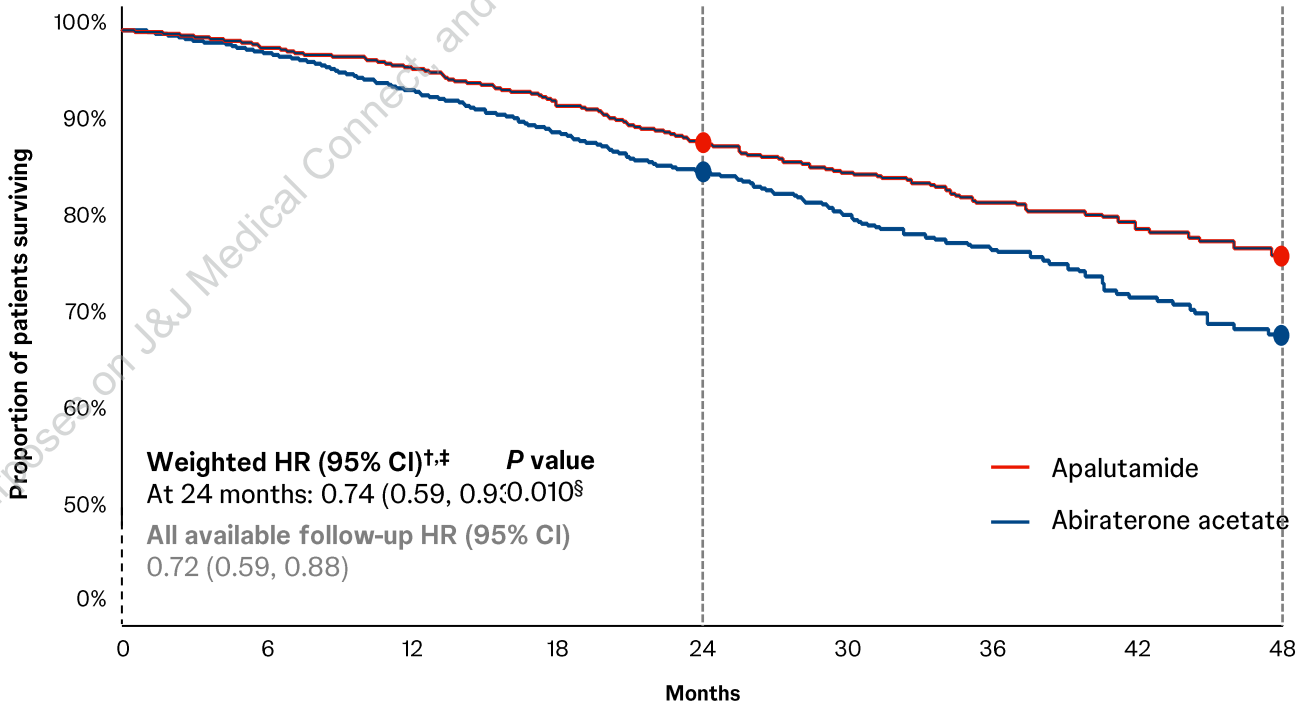
Patient population

- Adult patients with ARPI-naïve mCSPC
- The patient population was well-balanced between cohorts

Select patient characteristics*	Apalutamide N=1,810	Abiraterone acetate N=2,073	Standardized difference, %
Mean age, years	72.1	71.9	2.5
Race			
White	61.7%	62.5%	1.6
Black	19.1%	18.0%	2.8
Hispanic/Latino	7.5%	7.3%	0.6
Other	4.5%	4.8%	1.3
Unknown	7.1%	7.3%	0.7
Medicare-insured	74.2%	73.5%	1.7
Year of index date			
2019-2020	22.0%	22.8%	1.8
2021	23.6%	23.3%	0.8
2022	27.4%	26.8%	1.3
2023	27.0%	27.1%	0.4
Mean Quan-CCI	8.5	8.5	0.7
Metastasis type			
Bone	66.5%	66.2%	0.6
Nodal	52.9%	52.9%	0.1
Visceral	21.1%	23.0%	4.7
Multiple sites	25.4%	23.7%	3.9
***De novo* PC**	58.5%	59.0%	1.0
Concurrent use of ADT	76.8%	74.0%	6.4

Overall survival

By 24 months post-index, patients with mCSPC taking apalutamide had a statistically significant **26% reduction in the risk of death** compared with patients initiated on abiraterone acetate



Overall survival	24 months	48 months
Apalutamide	**88.7%**	**77.3%**
Abiraterone acetate	85.8%	69.4%

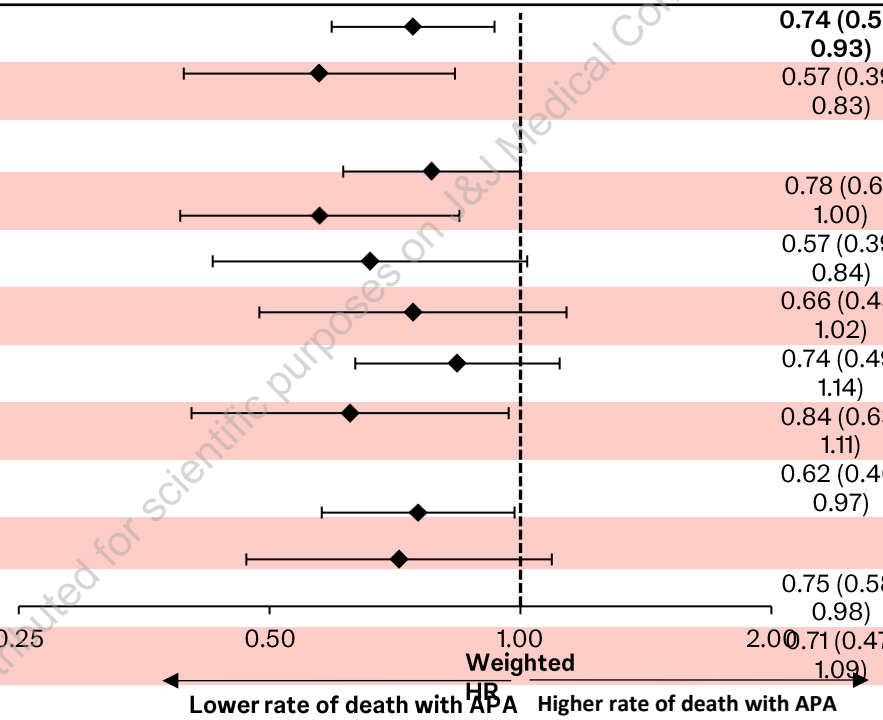
*After inverse probability of treatment weighting. †Propensity scores were generated using probability estimates from a logistic regression model using the following predictors: age (continuous), race, geographic region, payer, year of index date, time between metastasis and index date (continuous and categorical), time between PC diagnosis and index date (continuous), *de novo* prostate cancer, ADT use overlapping with index date, first-generation anti-androgen 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. ‡A hazard ratio <1 indicates that the apalutamide cohort had a lower rate of death compared with the abiraterone acetate 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; Quan-CCI, Quan-Charlson comorbidity index.

Results

Subgroup analysis of OS

- Weighted HRs generally indicate a lower rate of death with APA compared to ABI among key clinical subgroups

Subgroup	Apalutamide (N)	Abiraterone acetate (N)	Weighted HR (95% CI)†,‡
Overall	**1,879**	**2,073**	**0.74 (0.59, 0.93)**
≥3 months between metastasis and index date	803	1,081	0.57 (0.39, 0.83)
Metastasis type			
Bone metastasis	1,311	1,339	0.78 (0.61, 1.00)
Nodal metastasis	960	1,103	0.57 (0.39, 0.84)
Visceral metastasis	335	571	0.66 (0.43, 1.02)
Metastasis in multiple sites	536	405	0.74 (0.49, 1.14)
De novo PC	1,040	1,259	0.84 (0.63, 1.11)
>6 months between ADT initiation and index date	601	668	0.62 (0.40, 0.97)
Earliest Gleason score			
≤8	1,418	1,577	0.75 (0.58, 0.98)
9-10	461	496	0.71 (0.47, 1.09)



*After inverse probability of treatment weighting. †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 and categorical), time between PC diagnosis and index date (continuous), *de novo* prostate cancer, ADT use overlapping with index date, first-generation anti-androgen 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. ‡A hazard ratio <1 indicates that the apalutamide cohort had a lower rate of death compared with the abiraterone acetate cohort. ADT, androgen deprivation therapy; ABI, abiraterone acetate; APA, apalutamide; CI, confidence interval; HR, hazard ratio; OS, overall survival.

KEY TAKEAWAY

Initiation of apalutamide resulted in statistically significant improved OS by 24 months relative to patients who initiated abiraterone acetate. This finding of OS benefit at 24 months was generally consistent in key clinical subgroups.

CONCLUSION

By 24 months, treatment with apalutamide resulted in statistically significant 26% reduction in the risk of death as compared to treatment with abiraterone acetate (HR: 0.74 [95% CI: 0.59, 0.93]; p=0.010).