

# Comparison of real-world overall survival in subgroups of patients with metastatic castration-sensitive prostate cancer treated with apalutamide or enzalutamide

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# Background and methods

## Retrospective causal analysis comparing 24-month survival outcomes in ARPI-naïve patients with mCSPC initiating apalutamide versus enzalutamide, overall, and in key clinical subgroups

### OBJECTIVE

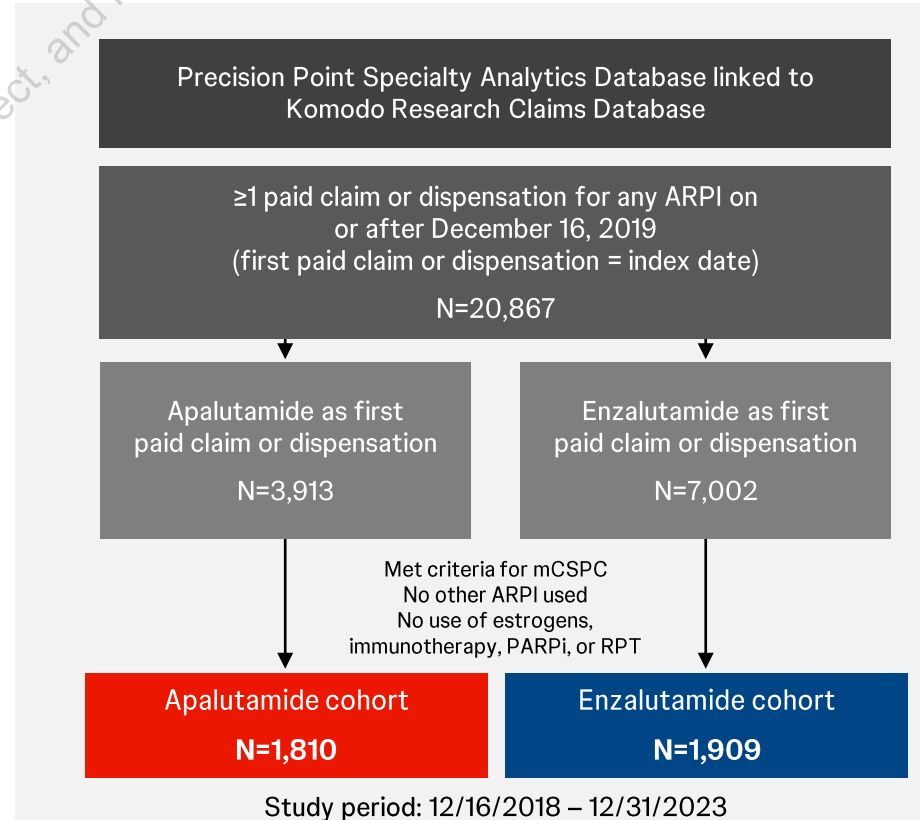
- Compare overall survival (OS) at 24 months between patients treated with apalutamide (APA) and enzalutamide (ENZ) in a nationally representative sample of androgen receptor pathway inhibitors (ARPI)-naïve patients with metastatic castration-sensitive prostate cancer (mCSPC), overall, and in important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

### BACKGROUND

- Apalutamide and enzalutamide are ARPIs approved for use with ADT in patients with mCSPC (also known as metastatic hormone-sensitive prostate cancer)<sup>1,2</sup>
- In Phase 3 studies, apalutamide (TITAN)<sup>3</sup> and enzalutamide (ARCHES)<sup>4</sup> demonstrated statistically significant reduction in disease progression and death as compared to ADT alone in patients with mCSPC<sup>3-6</sup>
- 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 enzalutamide 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 8 Jan 2025; 2. U.S. Food and Drug Administration. FDA approves enzalutamide for metastatic castration-sensitive prostate cancer. 2019. Available at: <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-enzalutamide-metastatic-castration-sensitive-prostate-cancer>. Accessed 8 Jan 2025; 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. 2019;37(32):2974-2986; 6. Armstrong AJ, et al. J Clin Oncol. 2022;40(15):1616-1622.

# Results

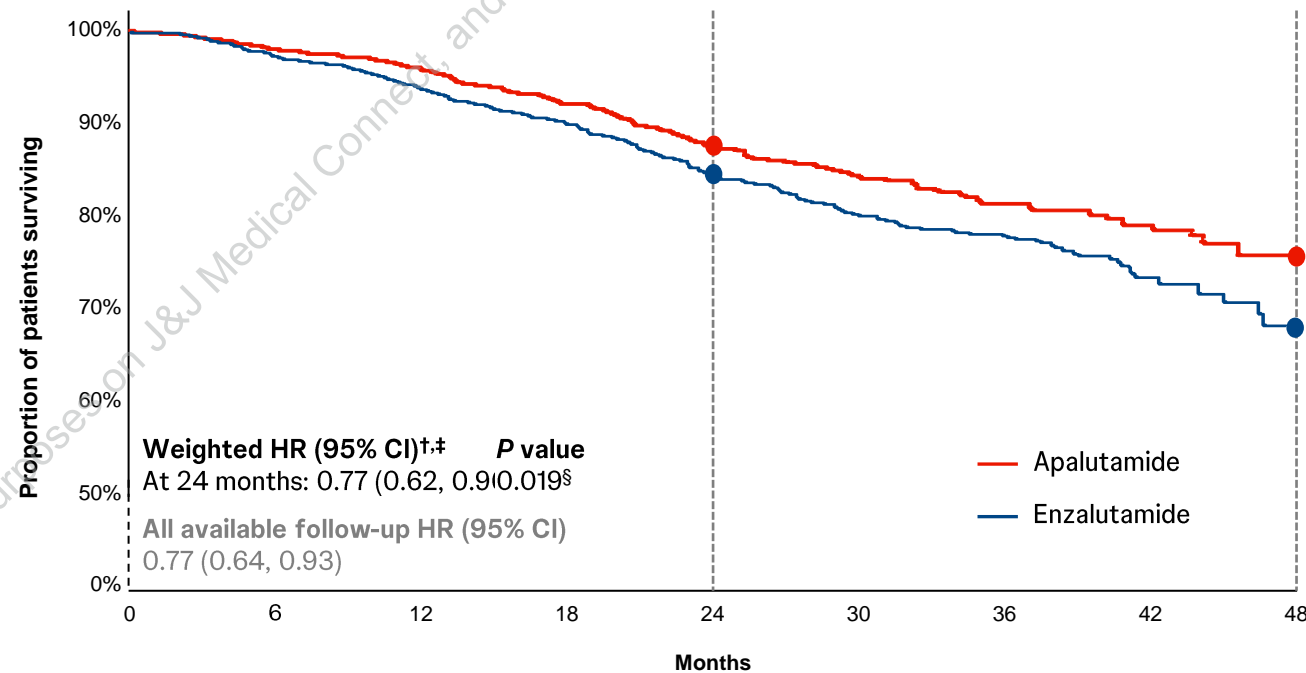
## Patient population

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

Select patient characteristics*	Apalutamide N=1,810	Enzalutamide N=1,909	Standardized difference, %
Mean age, years	73.0	73.0	0.1
<b>Race</b>			
White	59.8%	59.4%	0.8
Black	22.5%	22.7%	0.3
Hispanic/Latino	7.5%	7.6%	0.6
Other	4.4%	4.6%	1.2
Unknown	5.8%	5.7%	0.7
Medicare-insured	77.7%	77.9%	0.5
<b>Year of index date</b>			
2019-2020	21.6%	22.7%	2.7
2021	27.0%	27.5%	1.2
2022	27.3%	26.7%	1.2
2023	24.2%	23.1%	2.7
Mean Quan-CCI	8.6	8.6	1.1
<b>Metastasis type</b>			
Bone	71.9%	72.8%	2.1
Nodal	49.0%	48.1%	1.8
Visceral	19.7%	20.8%	2.9
Multiple sites	26.8%	26.1%	1.6
<b>De novo PC</b>	56.2%	56.2%	0.1
Concurrent use of ADT	79.2%	77.8%	3.3

## Overall survival

By 24 months post-index, patients with mCSPC taking apalutamide had a statistically significant **23% reduction in the risk of death** compared with patients initiated on enzalutamide



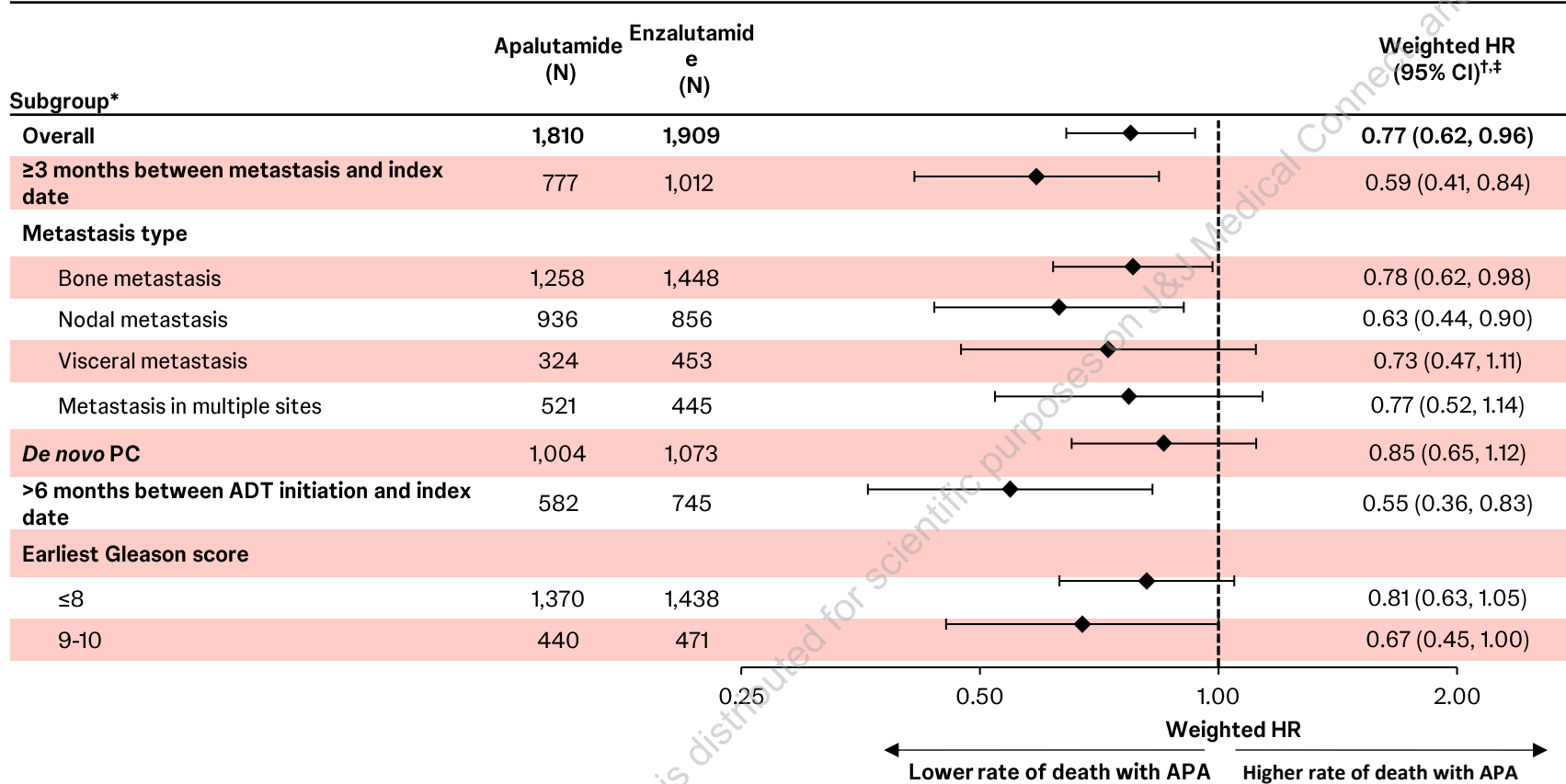
Overall survival	24 months	48 months
Apalutamide	87.6%	75.6%
Enzalutamide	84.6%	68.1%

\*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 enzalutamide 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 enzalutamide 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 ENZ among key clinical subgroups



\*After inverse probability of treatment weighting. <sup>†</sup>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 enzalutamide cohort. Normalized inverse-probability of treatment weights were truncated at the 95th percentiles. <sup>‡</sup>A hazard ratio <1 indicates that the apalutamide cohort had a lower rate of death compared with the enzalutamide cohort. ADT, androgen deprivation therapy; APA, apalutamide; CI, confidence interval; ENZ, enzalutamide; 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 enzalutamide. 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 23% reduction in the risk of death as compared to treatment with enzalutamide (HR: 0.77 [95% CI: 0.62, 0.96]; p=0.019).