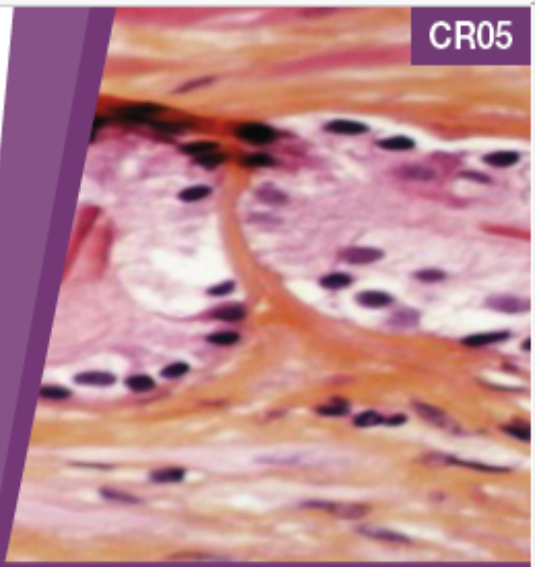
CR05

DAROLUTAMIDE

COMPARATIVE REAL-WORLD EVIDENCE ON DAROLUTAMIDE, ENZALUTAMIDE, AND APALUTAMIDE FOR NONMETASTATIC CASTRATION-RESISTANT PROSTATE CANCER PATIENTS IN THE UNITED STATES (DEAR)

Kirollos S. Hanna, PharmD,[1] on behalf of Alicia K. Morgans, MD,[2] Neal D. Shore, MD,[3] Nasreen Khan, PhD,[4] Nicolae Constantinovici, MD,[5] Javeed Khan, MSc,[5] Guifang Chen, MSc,[4] Julie Xu, MSc,[7] Jorge Ortiz, MD,[4] Daniel J George, MD[8]

[1]Mayo Clinic College of Medicine, Maple Grove, Minnesota, USA; [2]Dana-Farber Cancer Institute, Boston, MA, USA; [3]Carolina Urologic Research Center, Myrtle Beach, SC, USA; [4]Bayer HealthCare, Whippany, NJ, USA; [5]Bayer Consumer Care AG, Basel, Switzerland; [6]Bayer plc, Reading, United Kingdom; [7]Bayer Canada, Mississauga, ON, Canada; [8]Duke Cancer Institute, Durham, NC, USA



INTRODUCTION

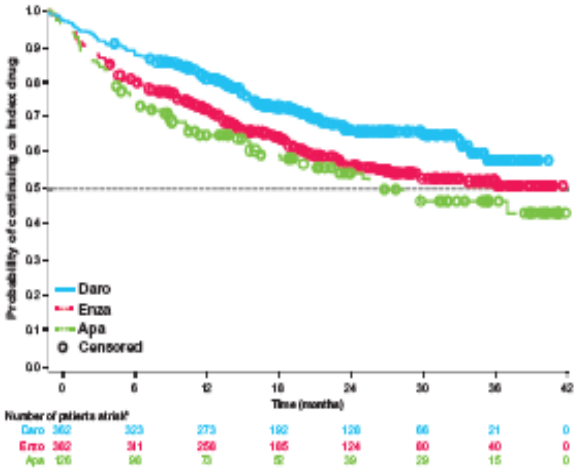
- Novel androgen receptor inhibitors (ARIs), including darolutamide, enzalutamide, and apalutamide, are the standard of care for non-metastatic castration-resistant prostate cancer (nmCRPC)
- DEAR is the first study comparing real-world utilization, outcomes, and occurrence of adverse events between these agents in men with nmCRPC

METHODS

- Retrospective chart review cohort study using electronic medical records from the Precision Point Specialty network of US urology practices
- Outcomes: proportion of patients who discontinued initial ARI treatment/ progressed to mCRPC, time to initial ARI discontinuation/progression to mCRPC, and incidence of adverse events (AEs)

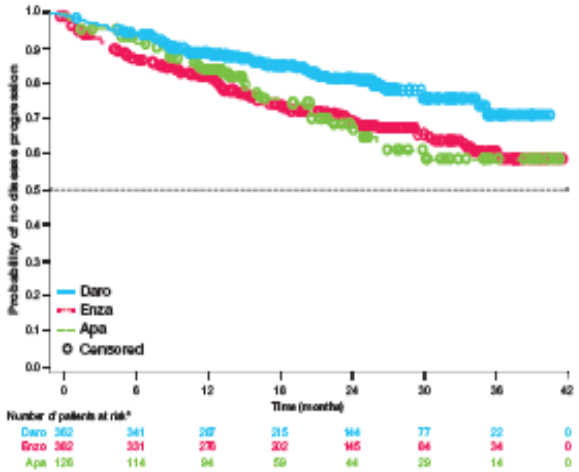
Darolutamide was associated with lower risk of treatment discontinuation[a]

Discontinuation of initial ARI treatment was lower for darolutamide (30.4%) than for enzalutamide (40.8%) or apalutamide (46.0%)



Darolutamide was associated with lower risk of progression to mCRPC

The proportion of patients who progressed to mCRPC was lower for darolutamide (17.7%) than for enzalutamide (28.3%) and apalutamide (27.8%)



[a]Earliest occurrence of ARI treatment stop, switch to another ARI, or death; *At-risk patients were calculated at the start of each time point.
Apa, apalutamide; Daro, darolutamide; Enza, enzalutamide

CONCLUSIONS

- Darolutamide was associated with longer times to treatment discontinuation and lower risk of progression to mCRPC than enzalutamide and apalutamide in a real-world setting

SCAN ME FOR MORE INFO

Medical writing services were provided by Sidrah Rahman, MSc, of Adelphi Communications Ltd (Bollington, UK), funded by Bayer, in accordance with Good Publications Practice 2022 guidelines.
HOPA Annual Conference 2024, Tampa Convention Center, Tampa, Florida, USA; April 3–6, 2024

Comparative Real-world Evidence on Darolutamide, Enzalutamide, and Apalutamide for non-Metastatic Castration-Resistant Prostate Cancer Patients in the United States (DEAR)

Supplementary material

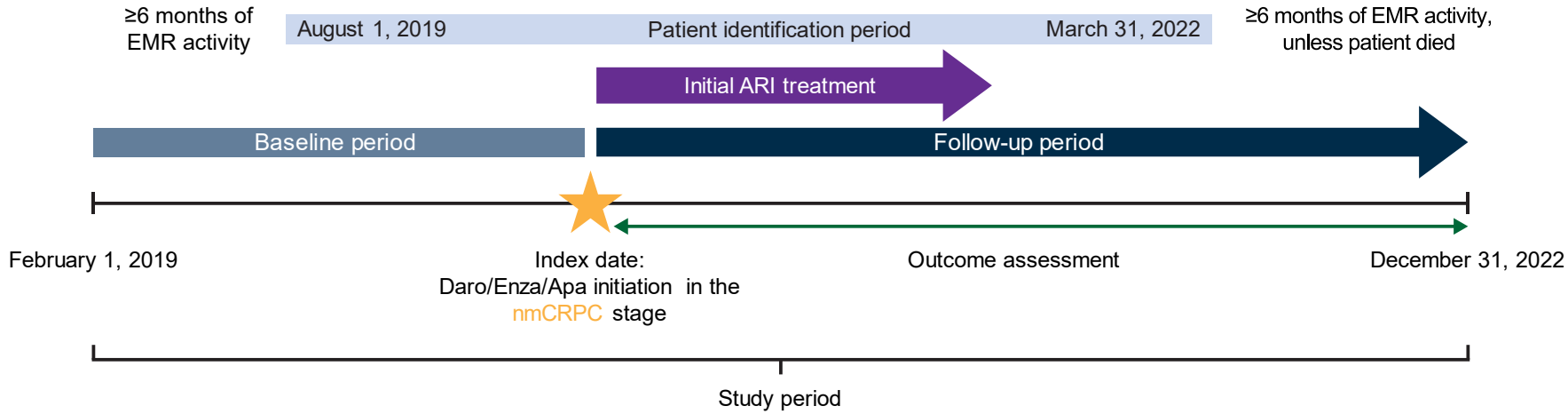
Kirollos S. Hanna, PharmD,[1] on behalf of Alicia K. Morgans, MD,[2] Neal D. Shore, MD,[3] Nasreen Khan, PhD,[4] Niculae Constantinovici, MD,[5] Javeed Khan, MSc,[6] Guifang Chen, MSc,[4] Julie Xu, MSc,[7] Jorge Ortiz, MD, Daniel J George, MD[8]

[1]Mayo Clinic College of Medicine, Maple Grove, Minnesota, USA; [2] Dana-Farber Cancer Institute, Boston, MA, USA; [3]Carolina Urologic Research Center, Myrtle Beach, SC, USA; [4]Bayer HealthCare, Whippany, NJ, USA; [5]Bayer Consumer Care AG, Basel, Switzerland; [6]Bayer plc, Reading, United Kingdom; [7]Bayer Canada, Mississauga, ON, Canada; [8]Duke Cancer Institute, Durham, NC, USA

Poster presented at HOPA Annual Conference 2024, Tampa Convention Center, Tampa, Florida, U.S; April 3–6, 2024

Study design

- Patients were classified into 3 treatment cohorts based on the first prescribed ARI in the nmCRPC stage (darolutamide, enzalutamide, or apalutamide)



ARI, androgen receptor inhibitor; EMR, electronic medical record; nmCRPC, non-metastatic castration-resistant prostate cancer

Patient Population

Inclusion criteria

- Men aged ≥18 years at the index date AND
- Diagnosed with nmCRPC before their first ever ARI treatment initiation
  AND with a minimum
  6-month baseline period and a ≥6-month follow-up period, unless the patient died earlier

Exclusion criteria

- Evidence of metastatic disease before or 30 days after the index date
  OR
- Prior history of other primary cancers, except non-melanoma skin cancer, in the 5 years before the index date
  OR
- Prior use of a novel antihormonal agent (darolutamide, enzalutamide, apalutamide, or abiraterone acetate)
  OR
- Initiation of multiple ARIs recorded on the same date
  OR
- Evidence of inclusion in clinical trials during the study period

Outcomes and analysis

- For each ARI cohort, the overall proportion of patients who discontinued initial treatment and who progressed to mCRPC during the study, the reasons for discontinuation, and the proportion of patients with adverse events were described
- Kaplan-Meier estimates of time to discontinuation of initial treatment and time to progression were calculated
- Cox proportional hazards models were used to compare time to treatment discontinuation and time to progression to mCRPC between treatment cohorts, before and after adjusting for baseline factors:
    - Age, race, insurance coverage, index year, PSA, PSA doubling time, time from nmCRPC diagnosis to index date, and Gleason score

mCRPC, metastatic castration-resistant prostate cancer; PSA, prostate-specific antigen.

Observed baseline characteristics and duration of follow-up were similar across the 3 treatment cohorts

	Darolutamide (n=362)	Enzalutamide (n=382)	Apalutamide (n=126)
Age, years, n (%)			
≤74	109 (30.1)	118 (30.9)	36 (28.6)
75–84	154 (42.5)	160 (41.9)	56 (44.4)
≥85	99 (27.3)	104 (27.2)	34 (27.0)
Race, n (%)			
White	238 (65.7)	254 (66.5)	93 (73.8)
Black/African American	80 (22.1)	82 (21.5)	25 (19.8)
Other	6 (1.7)	15 (3.9)	5 (4.0)
Unknown	38 (10.5)	31 (8.1)	3 (2.4)
Insurance coverage			
Commercial	103 (28.5)	88 (23.0)	32 (25.4)
Public	247 (68.2)	287 (75.1)	94 (74.6)
Unknown	12 (3.3)	7 (1.8)	0

Time from diagnosis of PC to the index date and time from nmCRPC diagnosis to the index date varied slightly across cohorts

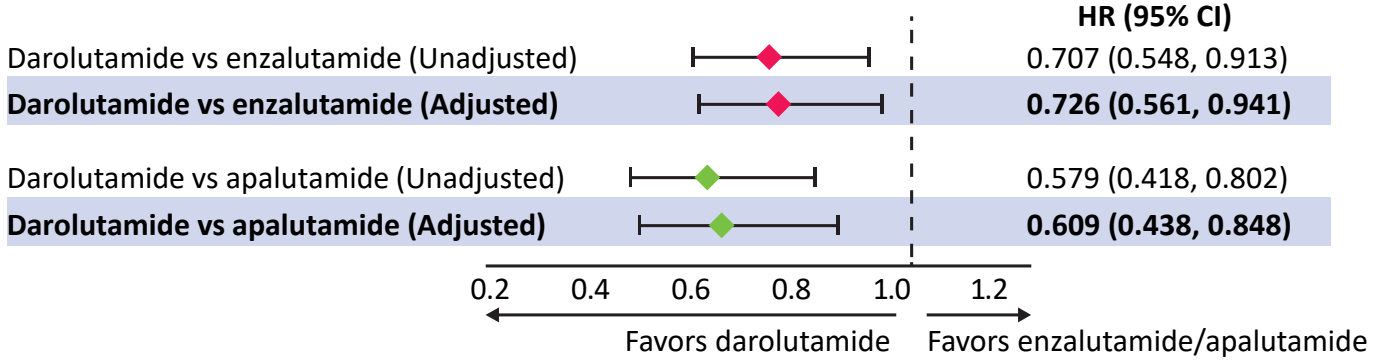
	Darolutamide (n=362)	Enzalutamide (n=382)	Apalutamide (n=126)
PSA,[a] ng/mL, n (%)			
<2.0	127 (35.1)	134 (35.1)	47 (37.3)
≥2.0 and <10.0	148 (40.9)	135 (35.3)	48 (38.1)
≥10.0	65 (18.0)	76 (19.9)	27 (21.4)
Missing	22 (6.1)	37 (9.7)	4 (3.2)
PSADT,[a] months, n (%)			
≤6	120 (33.1)	119 (31.2)	37 (29.4)
>6 and ≤10	64 (17.7)	51 (13.4)	31 (24.6)
>10	85 (23.5)	81 (21.2)	28 (22.2)
Missing	93 (25.7)	131 (34.3)	30 (23.8)
Gleason score at initial PC diagnosis, n (%)			
4–7	161 (44.5)	139 (36.4)	45 (35.7)
8–10	133 (36.7)	153 (40.1)	58 (46.0)
Missing	68 (18.8)	90 (23.6)	23 (18.3)
Time from PC diagnosis to index date, median (range), months[c]	94.7 (–3.1, 350.3)	77.1 (–12.2, 384.1)	82.1 (4.9, 388.1)
Time from nmCRPC to index date, median (range), months	5.3 (0, 247.9)	3.4 (0, 130.0)	6.5 (0, 131.2)
Follow-up, median (range), months	22.2 (2.2, 40.3)	22.7 (0.9, 41.5)	23.3 (2.6, 41.7)
Patients starting at approved ARI dose,[d] n (%)	351 (97.0)	360 (94.2)	124 (98.4)

[a]Value closest to index date (darolutamide, n=340; enzalutamide, n=345; apalutamide, n=122); [b]PSADT is calculated using the Sloan Kettering methodology, which is based on ≥3 PSA values ≥0.2 ng/mL taken ≥1 month apart, within the 12 months before index date; (darolutamide, n=269; enzalutamide, n=251; apalutamide, n=96). PSADT values >100 ng/mL were capped at 100; [c]4 patients (0.5%) had a record of PC diagnosis after the index ARI treatment start date. This is likely a data artifact resulting from the limitation of how disease history is recorded in the EMR system. These patients are included in all analyses; [d]Darolutamide, 1200 mg; enzalutamide, 160 mg; apalutamide, 240 mg.

PC, prostate cancer; PSADT, prostate-specific antigen doubling time.

Adjusting for baseline factors[a], fewer patients discontinued darolutamide versus enzalutamide or apalutamide

- Patients receiving darolutamide had a 27.4% and 39.1% lower risk of discontinuation of initial ARI treatment[b] over time compared with enzalutamide and apalutamide, respectively

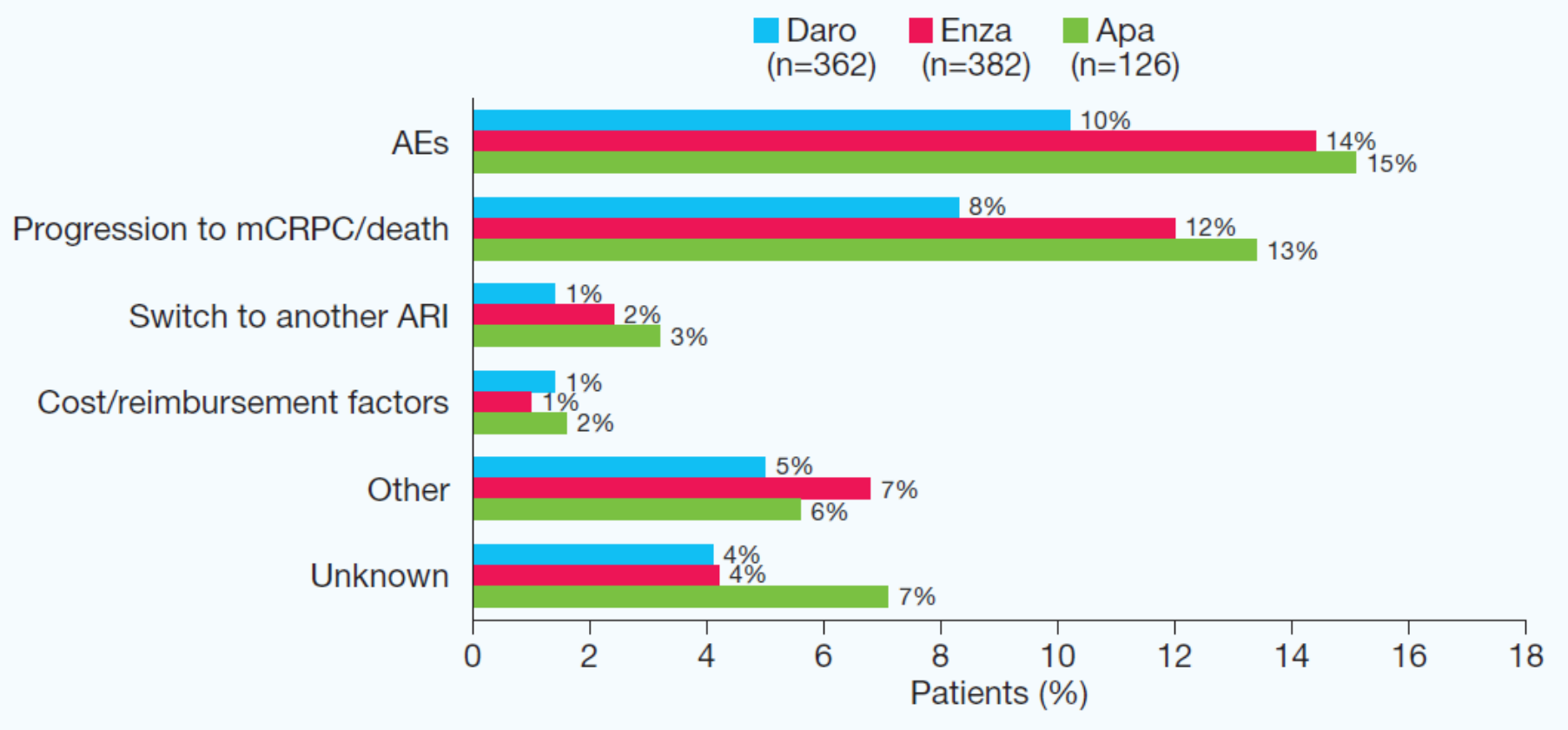


A total of 791 patients (darolutamide, n=328; enzalutamide, n=341; apalutamide, n=122) were included in this analysis, after excluding 79 patients with unknown insurance coverage and/or missing baseline PSA values.

[a]Results (HR; 95% CI) for other model covariates were age (reference group, ≥85 years): ≤74 years (0.72; 0.52, 1.00), 75 to 84 years (0.66; 0.50, 0.87); race (reference group, White): Black (0.68; 0.50, 0.93), other (0.92; 0.63, 1.36); insurance coverage (reference group, public insurance): commercial (0.76; 0.58, 1.01); index year (reference group, 2019-2020): 2021 to 2022 (0.84; 0.64, 1.10); baseline PSA (reference group, ≥10 ng/mL): <2 ng/mL (0.52; 0.38, 0.72), ≥2 to <10 ng/mL (0.78; 0.59, 1.04); baseline PSADT (reference group, ≤6 months): >6 to ≤10 months (1.18; 0.84, 1.66), >10 months (0.81; 0.58, 1.14), missing (1.23; 0.91, 1.66); time from CRPC to index date in months (1.00; 0.99, 1.01); Gleason score (reference group, 8-10): 4 to 7 (0.82; 0.63, 1.07), missing (1.12; 0.83, 1.51).[b]Earliest occurrence of ARI treatment stop, switch to another ARI, or death.

CI, confidence interval; HR, hazard ratio.

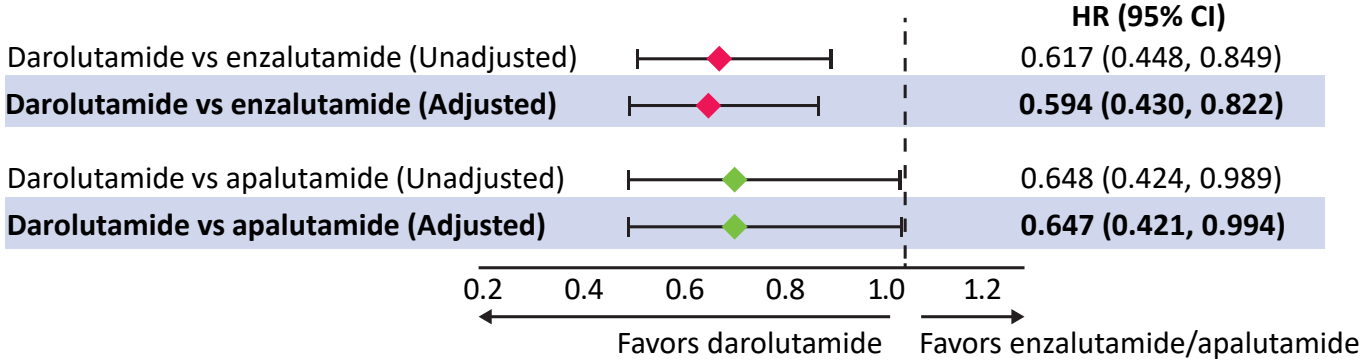
The most common reason for discontinuation was the occurrence of AEs



AE, adverse event.

Adjusting for baseline factors[a], darolutamide was associated with lower risk of progression to mCRPC

- Patients on darolutamide had a 40.6% and 35.3% lower risk of progression to mCRPC[b] over time compared with enzalutamide and apalutamide, respectively



A total of 791 patients (darolutamide, n=328; enzalutamide, n=341; apalutamide, n=122) were included in this analysis, after excluding 79 patients with unknown insurance coverage and/or missing baseline PSA values.

[a]Results (HR; 95% CI) for other model covariates were age (reference group, ≥85 years): ≤74 years (0.88; 0.59, 1.33), 75 to 84 years (0.87; 0.61, 1.23); race (reference group, White): Black (0.61; 0.41, 0.90), other (0.73; 0.43, 1.21); insurance coverage (reference group, public insurance): commercial (0.95; 0.68, 1.32); index year (reference group, 2019-2020): 2021 to 2022 (1.28; 0.93, 1.78); baseline PSA (reference group, ≥10 ng/mL): <2 ng/mL (0.53; 0.35, 0.80), ≥2 to <10 ng/mL (0.77; 0.54, 1.10); baseline PSADT (reference group, ≤6 months): >6 to ≤10 months (0.84; 0.56, 1.27), >10 months (0.44; 0.28, 0.69), missing (0.73; 0.50, 1.05); time from CRPC to index date in months (1.00; 0.99, 1.01); Gleason score (reference group, 8-10): 4 to 7 (0.94; 0.68, 1.29), missing (0.81; 0.55, 1.20).[b]Earliest occurrence of ARI treatment stop, switch to another ARI, or death.

Patients receiving darolutamide had a lower incidence of AEs compared with enzalutamide and apalutamide

AE,[a] n (%)	Darolutamide (n=362)	Enzalutamide (n=382)	Apalutamide (n=126)
Any AE[b]	90 (24.9)	112 (29.3)	38 (30.2)
CNS-related AEs[b,c]	54 (14.9)	75 (19.6)	20 (15.9)
Fatigue	41 (11.3)	53 (13.9)	14 (11.1)
Dizziness	4 (1.1)	11 (2.9)	3 (2.4)
Cognitive disorder	4 (1.1)	7 (1.8)	2 (1.6)
Fall	3 (0.8)	5 (1.3)	1 (0.8)
Other AEs[b,d]	51 (14.1)	53 (13.9)	20 (15.9)
Pain	17 (4.7)	10 (2.6)	3 (2.4)
Rash	8 (2.2)	3 (0.8)	10 (7.9)
Diarrhea	7 (1.9)	9 (2.4)	4 (3.2)
Nausea	8 (2.2)	8 (2.1)	4 (3.2)
Vomiting	5 (1.4)	6 (1.6)	0

[a]AEs recorded during each ARI treatment and up to 30 days after discontinuation; [b]Some patients experienced multiple AEs; [c]CNS-related AEs recorded in ≥1% of patients overall. Other CNS-related AEs occurring in <1% of patients were headache, insomnia, anxiety, confusion, ataxia, and memory issue; [d]Other AEs recorded in ≥1% of patients overall. Other AEs occurring in <1% of patients included hot flash, hypertension, liver issues, weight loss, and cardiovascular.
CNS, central nervous system.

Limitations

- While the analysis adjusts for observed differences in baseline characteristics between the 3 ARI treatment cohorts, unobserved confounding factors may also influence treatment duration and clinical outcomes in the absence of randomization
- Other limitations may include the ability to generalize results to other patient populations, although limitations related to the mismeasurement or missingness of study variables would affect results only to the extent that cohorts were affected differently

Conclusions

- This is the first RWE study assessing treatment discontinuation and underlying reasons for discontinuation, progression to mCRPC, and incidence of AEs for the 3 ARIs approved for nmCRPC: darolutamide, enzalutamide, and apalutamide
- Observed baseline characteristics and median duration of follow-up (~2 years) were similar across the 3 ARI treatment cohorts
- Results suggest that treatment with darolutamide was associated with lower risks of treatment discontinuation and progression to mCRPC compared with enzalutamide and apalutamide
- In addition, a lower proportion of patients had AEs on darolutamide compared with enzalutamide and apalutamide
- Future studies are needed to confirm these results in other populations or using other data sources