Abstract 24-7844

Third interim analysis (IA3) of the DARolutamide ObservationaL (DAROL) Study in Patients with Non-Metastatic Castration-Resistant Prostate Cancer (nmCRPC)

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Disclosures

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Introduction and Objective

- **Darolutamide is a structurally distinct and highly potent ARI** with **low blood–brain barrier penetration** and **limited potential for DDIs**[1–5]

- In patients with nmCRPC, darolutamide **significantly improved median MFS** by ~2 years and **reduced risk of death** by 31% vs placebo, with a **favorable tolerability** profile in the phase 3 ARAMIS study (NCT02200614)[6,7]

- **DAROL** (NCT04122976) is assessing **real-world safety and effectiveness** of darolutamide in patients with nmCRPC
  - We report results from the **prespecified IA3**

ARI, androgen receptor inhibitor; DDI, drug–drug interaction; IA3, interim analysis 3; MFS, metastasis-free survival; nmCRPC, nonmetastatic castration-resistant prostate cancer.

1. Moilanen A-M, et al. *Sci Rep* 2015;5:12007; 2. Zurth C, et al. *Clin Pharmacokinet* 2022;61:565–575; 3. Williams SCR, et al. *Target Oncol* 2023;18:403–413; 4. Zurth C, et al. *Eur J Drug Metab Pharmacokinet* 2019;44:747–759; 5. Shore N, et al. *Target Oncol* 2019;14:527–539; 6. Fizazi K, et al. *N Engl J Med* 2019;380:1235–1246; 7. Fizazi K, et al. *N Engl J Med* 2020;383:1040–1049.

DAROL Trial Design

Ongoing, global, prospective, open-label, single-arm, noninterventional study

Key eligibility criteria

- Confirmed nmCRPC:
  - Disease progression despite treatment with ADT
  - No evidence of metastasis on conventional imaging
- Decision to initiate darolutamide treatment made before enrollment

Darolutamide*

600 mg orally twice daily

FPFV January 30, 2020
LPFV July 7, 2023

Prespecified analyses	IA1	IA2	IA3	IA4	Final
Patients	100	300	**550**	800	800
Treatment duration†	≥6 months	≥6 months	**≥6 months**	≥12 months	≥36 months
	✓	✓	✓		

Data cut-off date for IA3: July 17, 2023

Primary endpoint

- Safety: frequency, severity, and seriousness of TEAEs

Key secondary/ exploratory endpoints

- MFS
- OS
- PSA progression
- PSA response rates

*Treatment is according to investigator's routine clinical practice, based on recommendations in the local product information; †Unless patient discontinued earlier.
ADT, androgen-deprivation therapy; FPFV, first patient, first visit; IA, interim analysis; IQR, interquartile range; LPFV, last patient, first visit; MFS, metastasis-free survival; nmCRPC, nonmetastatic castration-resistant prostate cancer; OS, overall survival; PSA, prostate-specific antigen; TEAE, treatment-emergent adverse event.

Demographics and Baseline Characteristics

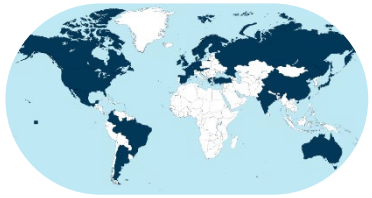
Demographics and patient characteristics

550 patients*

Median age **79 years**
(IQR 73–84; range 29–98)

North America
n=191 (34.7%)

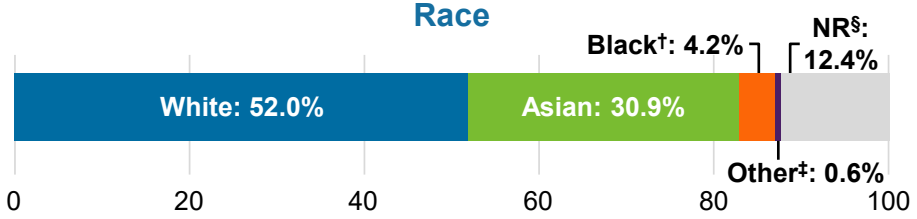
Europe
n=199 (36.2%)



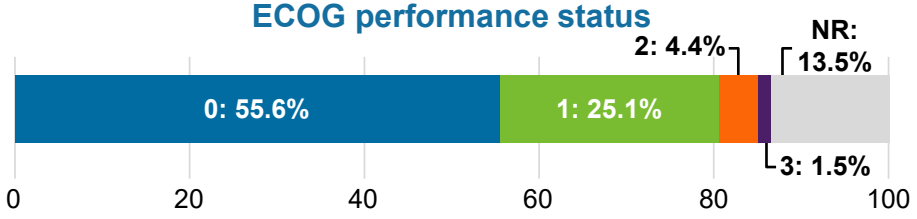
Latin America
n=8 (1.5%)

Asia Pacific
n=152 (27.6%)

Race

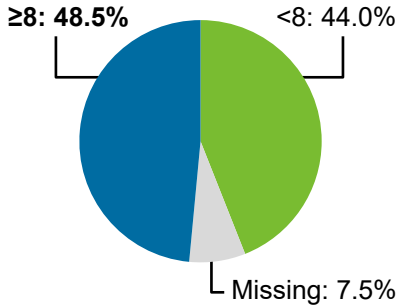


ECOG performance status

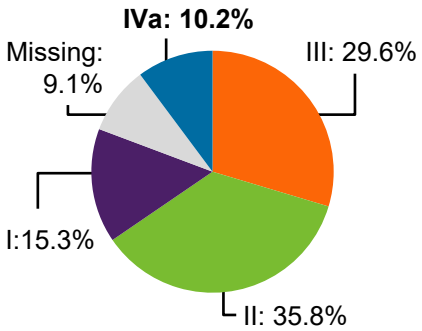


Disease characteristics at initial diagnosis

Gleason score



AJCC stage

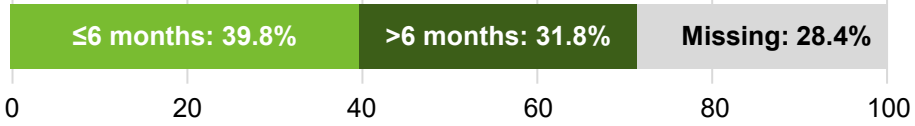


Baseline PSA and PSADT

	Minimum	Q1	Median	Q3	Maximum
PSA, ng/mL	0	2.3	**4.0**	9.3	248.0
PSADT, months	0	3.1	**5.3**	8.9	668.4

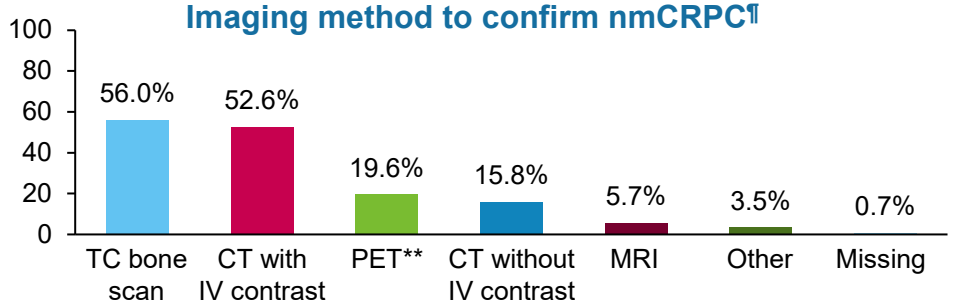
PSA category

PSADT category



nmCRPC status

Imaging method to confirm nmCRPC¶



Local or regional lymph node involvement	N0	434 (78.9%)
	N1	62 (11.3%)
	Unknown/missing	54 (9.8%)

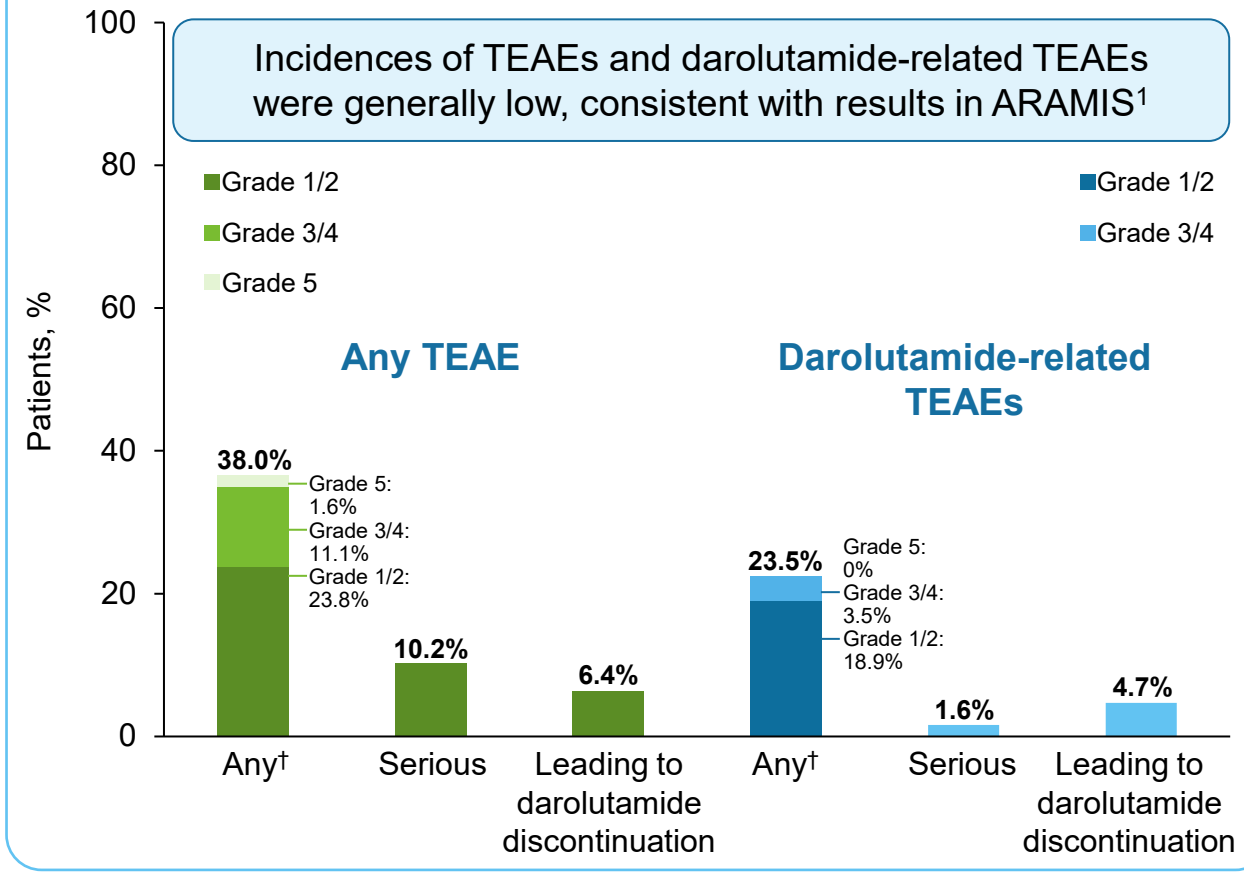
*Safety analysis set includes all patients who have taken ≥1 dose of darolutamide and completed ≥6 months of treatment or discontinued treatment); †Black or African American patients were all enrolled in the USA (12.0% of US participants) and therefore are underrepresented globally; ‡Other includes two Native Americans or Alaska Natives and one Native Hawaiian, or other Pacific Islander; §Patient did not complete self-reported race query. ¶Patients may have had >1 imaging method to confirm nmCRPC; hence percentages total >100%.
**PET comprises axumin PET, choline PET, CT/PET, prostate-specific membrane antigen PET, fluorodeoxyglucose PET, and PET with other tracer.
AJCC, American Joint Committee on Cancer; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; IV, intravenous; MRI, magnetic resonance imaging; nmCRPC, nonmetastatic castration-resistant prostate cancer; NR, not recorded; PET, positron emission tomography; PSA, prostate-specific antigen; PSADT, prostate-specific antigen doubling time; Q, quartile; TC, technetium-99m.

Primary Endpoint: Safety*

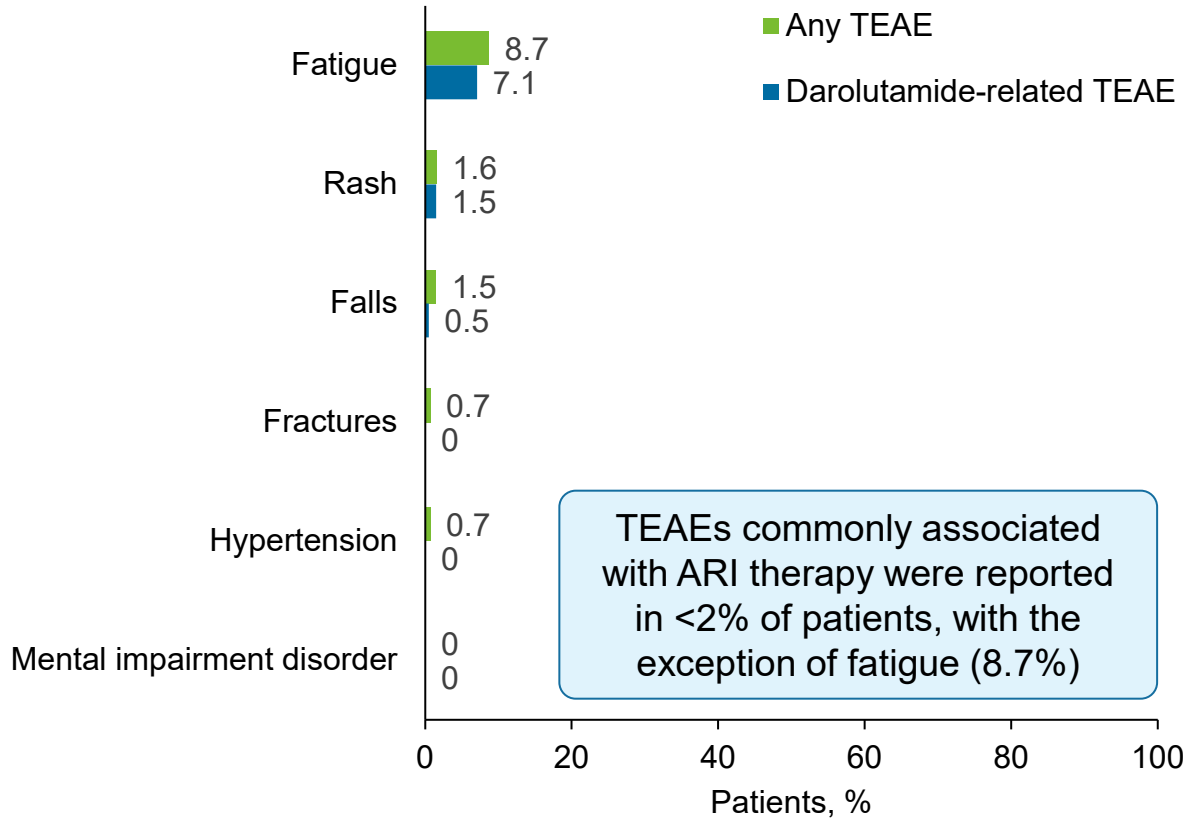
Median follow-up was 16.5 months (IQR 12.5–23.1)

TEAE overview

Incidences of TEAEs and darolutamide-related TEAEs were generally low, consistent with results in ARAMIS[1]



TEAEs commonly associated with ARI therapy‡



TEAEs commonly associated with ARI therapy were reported in <2% of patients, with the exception of fatigue (8.7%)

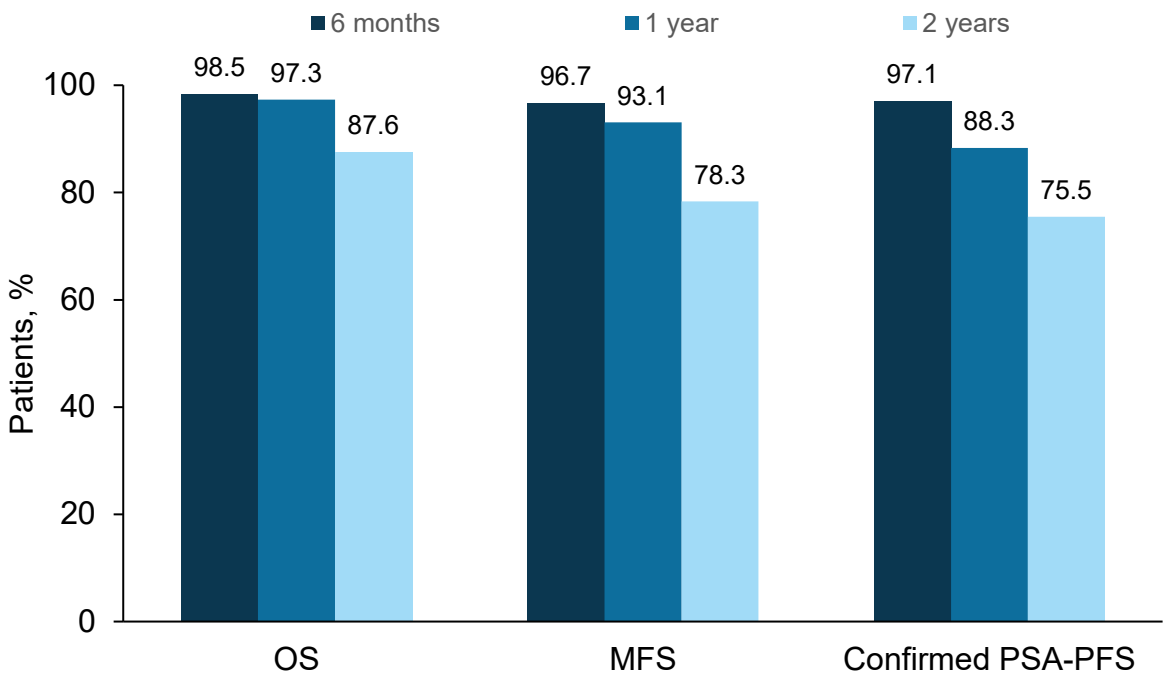
*Safety analysis set includes all patients enrolled in the study who have taken ≥1 dose of darolutamide and completed ≥6 months of treatment or discontinued treatment.
†Grade missing for eight patients (1.5%) for any TEAE and six patients (1.1%) for darolutamide-related TEAEs.
‡Data were updated from the abstract.
ARI, androgen receptor inhibitor; TEAE, treatment-emergent adverse event.

1. Fizazi K, et al. *N Engl J Med* 2019;380:1235–1246.

Effectiveness Outcomes

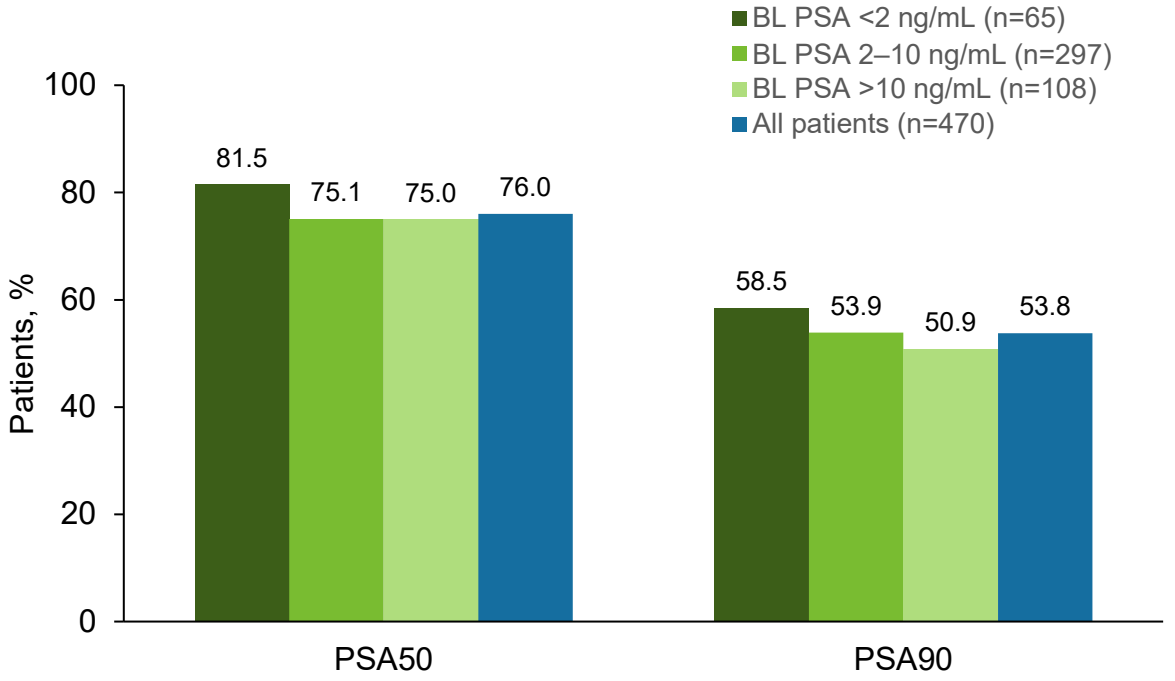
MFS, OS, and PSA outcomes indicate effectiveness in the real-world setting, consistent with ARAMIS[1,2]
Median treatment duration was 14.9 months (IQR 10.4–20.9)

Landmark survival rates*



OS, MFS, and PSA-PFS medians have not been reached in IA3

PSA response at any time during follow-up†



Most patients achieved a PSA response, regardless of baseline PSA value

*Assessed in 471 patients who took ≥1 dose of darolutamide, did not violate eligibility criteria, and had ≥1 post-baseline assessment after receiving darolutamide.
†Data were updated from the abstract.
BL, baseline; IA3, interim analysis 3; MFS, metastasis-free survival; OS, overall survival; PSA, prostate-specific antigen; PSA-PFS, PSA progression-free survival; PSA50, ≥50% reduction in PSA from baseline; PSA90, ≥90% reduction in PSA from baseline.
1. Fizazi K, et al. *N Engl J Med* 2019;380:1235–1246; 2. Fizazi K, et al. *N Engl J Med* 2020;383:1040–1049.

Conclusions

- Under real-world conditions, **darolutamide shows a favorable safety profile** in patients with nmCRPC, consistent with ARAMIS[1]
  - The **incidences of TEAEs were generally low**, with no new safety signals in IA3

- The MFS, OS, and PSA outcomes in IA3 indicate the **real-world effectiveness of darolutamide** in patients with nmCRPC, consistent with ARAMIS[1]

- Further analyses with more patients and longer follow-up are planned, which will provide mature effectiveness outcomes

IA3, interim analysis 3; MFS, metastasis-free survival; nmCRPC, nonmetastatic castration-resistant prostate cancer; OS, overall survival; PSA, prostate-specific antigen; TEAE, treatment-emergent adverse event.

1. Fizazi K, et al. *N Engl J Med* 2019;380:1235–1246.

Acknowledgments

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Thank you for your attention

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