P3 PROSTATE CANCER FORUM 2026

Perspectives, Possibilities, Progress

Personalising Treatment in mHSPC: ARI Clinical Landscape

Vincent Khoo, Royal Marsden & St Georges NHS Foundation Hospitals

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Disclosures

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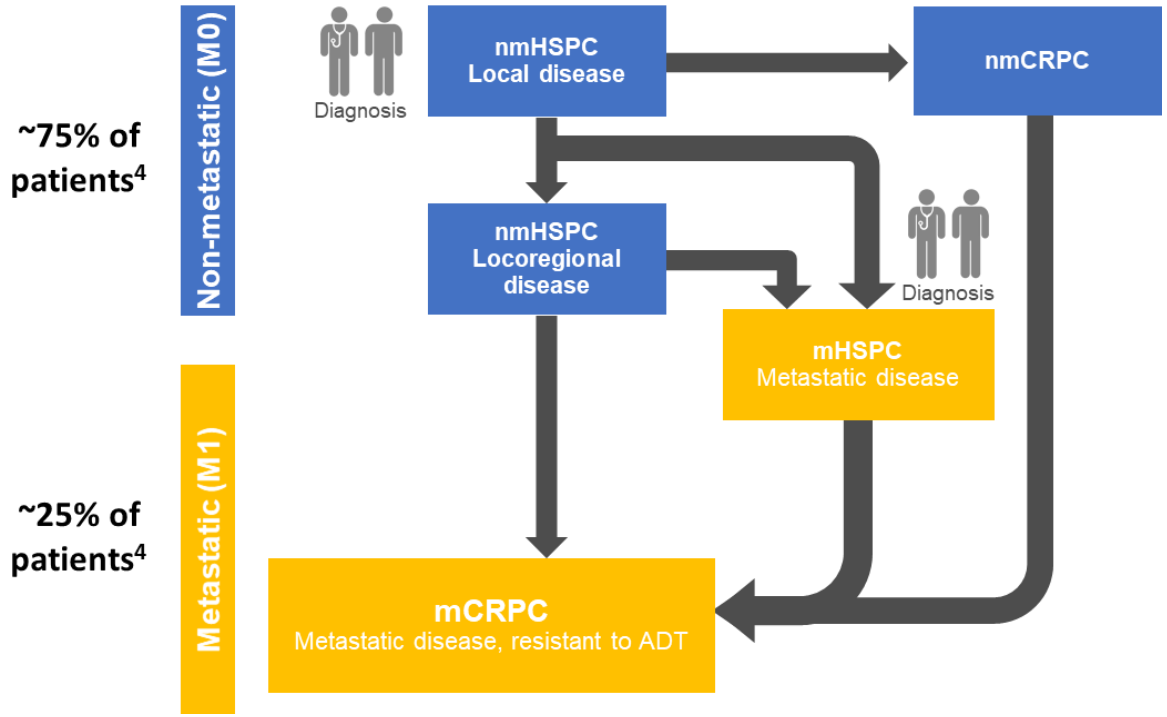
- Novartis
- Ovidius

The unmet medical need in patients with mHSPC

mHSPC, metastatic hormone-sensitive prostate cancer.

Defining mHSPC

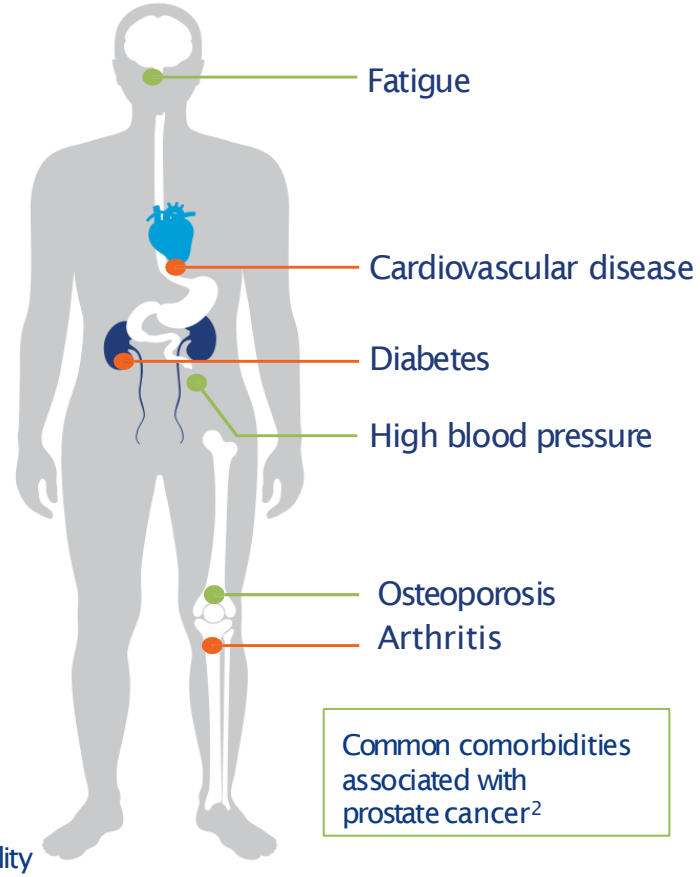
- In **m**etastatic **h**ormone-**s**ensitive **p**rostate **c**ancer, the disease responds to androgen deprivation therapy (ADT) and patients have 1 or more metastases on conventional imaging[1–3]
  - Patients with mHSPC can be classified as having either de novo or recurrent disease[5]
  - Metastatic disease can be further defined based on the volume of metastases or risk factors associated with poor prognosis[6,7]



ADT, androgen deprivation therapy; nmHSPC, non-metastatic hormone-sensitive prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer; mCRPC, metastatic castration-resistant prostate cancer.

1. Ng K, et al. Oncol Thera. 2020;8(2):209–230; 2. Rosen RD, Sapra A. TNM Classification. Treasure Island, FL: StatPearls Publishing; 2022; 3. Bouchelouche K et al. Curr Urol Rep. 2010;11(3):180–190; 4. Liede A, et al. ESMO Open. 2016;1:e000040; 5. Armstrong AJ, et al. J Clin Oncol. 2019;37(32):2974–2986; 6. Sweeney CJ, et al. N Engl J Med. 2015; 373:737–746; 7. Fizazi K, et al. N Engl J Med. 2017;377:352–360.

What do mHSPC patients look like?

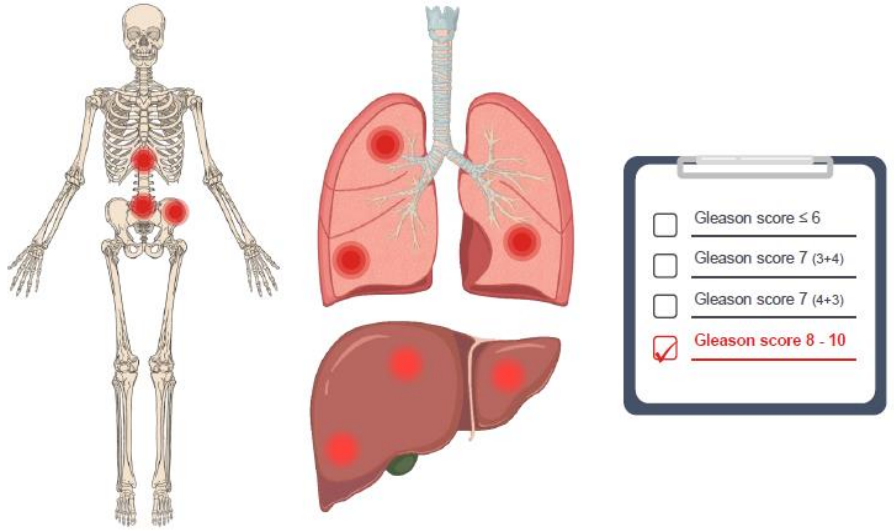


- The prevalence of prostate cancer in the UK is highest in males aged 75 to 79 years[1]
- Due to age and lifestyle patients are likely to have a significant comorbidity burden requiring polypharmacy on top of their anti-cancer treatment[3]
- Metastatic sites and burden of disease will vary between mHSPC patients, as will their functional status and presence of cancer-related symptoms[3]
- When prescribing darolutamide or other second generation ARIs, **both efficacy and tolerability** are significant clinical considerations to ensure patients can maintain their quality of life and avoid AEs that require further healthcare resource use[3]

AE, adverse event; ARI, androgen receptor inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer; UK, United Kingdom.
1. CRUK prostate cancer statistics. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer#heading-Zero (accessed May 2026); 2. Benzo RM. Support Care Cancer. 2023;31(8):496; 3. Based on speaker's own experience.

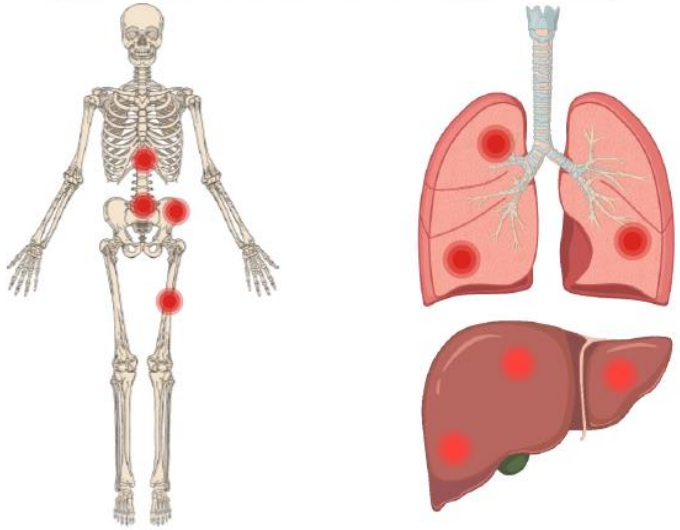
Disease burden in mHSPC varies between patients

High-risk Disease According to LATITUDE Study (at least 2 of the following criteria) [1]



- ≥ 3 bone mets
- Visceral mets
- Gleason score ≥ 8

High-volume Disease According to CHAARTED Study (at least 1 of the following criteria) [2]



- ≥ 4 bone mets (with ≥ 1 outside the pelvis/column)
- Visceral mets

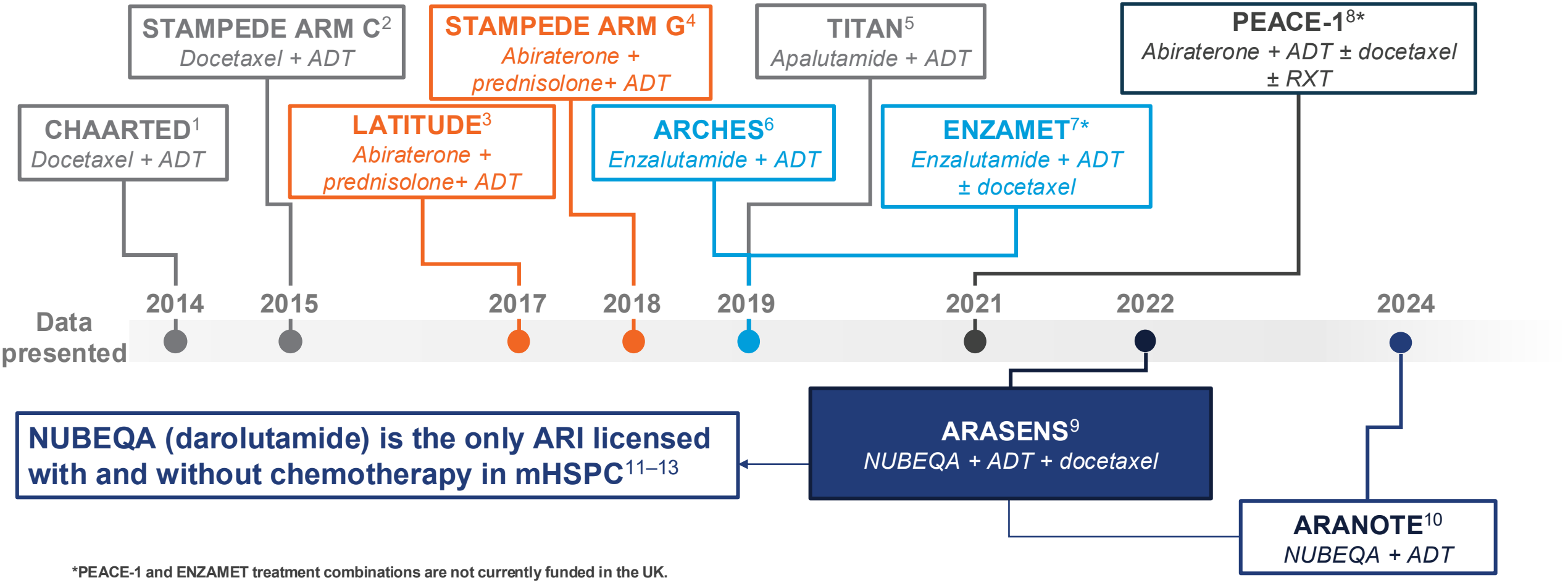
Metastatic disease burden has been defined based on volume of metastases per CHAARTED trial criteria[2] and based on risk factors associated with poor prognosis per LATITUDE trial criteria[1]

Metastatic sites and burden of disease will vary between mHSPC patients, as will their functional status and presence of cancer-related symptoms[3]

mHSPC, metastatic hormone-sensitive prostate cancer.

1. Fizazi K et al. Lancet Oncol. 2019;20:686–700; 2. Kyriakopoulos CE et al. J Clin Oncol. 2018;36:1080–1087; 3. Dodkins J, et al. Eur J Cancer. 2025;220:115335.

Key clinical trials in the setting of mHSPC



***PEACE-1 and ENZAMET treatment combinations are not currently funded in the UK.**

ADT, androgen deprivation therapy; ARI, androgen receptor inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer; RXT, radiotherapy.

1. Sweeney C, et al. NEJM. 2015 10.1056/NEJMoa1503747; 2. James ND, et al. J Clin Oncol 2015;33(suppl_15):5001; 3. Fizazi K, et al. J Clin Oncol 2017;35(suppl):Abstract LBA-3; 4. Hoyle A, et al. Ann Oncol 2018;29(suppl_8):Abstract 3982; 5. Chi KN, et al. J Clin Oncol. 2019;37(suppl_15):Abstract 5006; 6. Armstrong AJ, et al. J Clin Oncol 2019;37(7_suppl):Abstract 687; 7. Sweeney C, et al. J Clin Oncol 2019;37(18_suppl):Abstract LBA-2; 8. Fizazi K, et al. Ann Oncol. 2021;32(suppl_5):Abstract LBA-5_PR); 9. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02799602 (accessed May 2026); 10. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04736199 (accessed May 2026); 11. Nubeqa. Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/11324/smpc (accessed May 2026) 12. Xtandi. Summary of Product Characteristics. Available at https://www.medicines.org.uk/emc/product/10318/smpc (accessed May 2026); 13. Erleada. Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/9832/smpc (accessed May 2026).

What are your therapeutic goals for advanced prostate cancer patients?

An efficacious treatment option while maintaining QoL

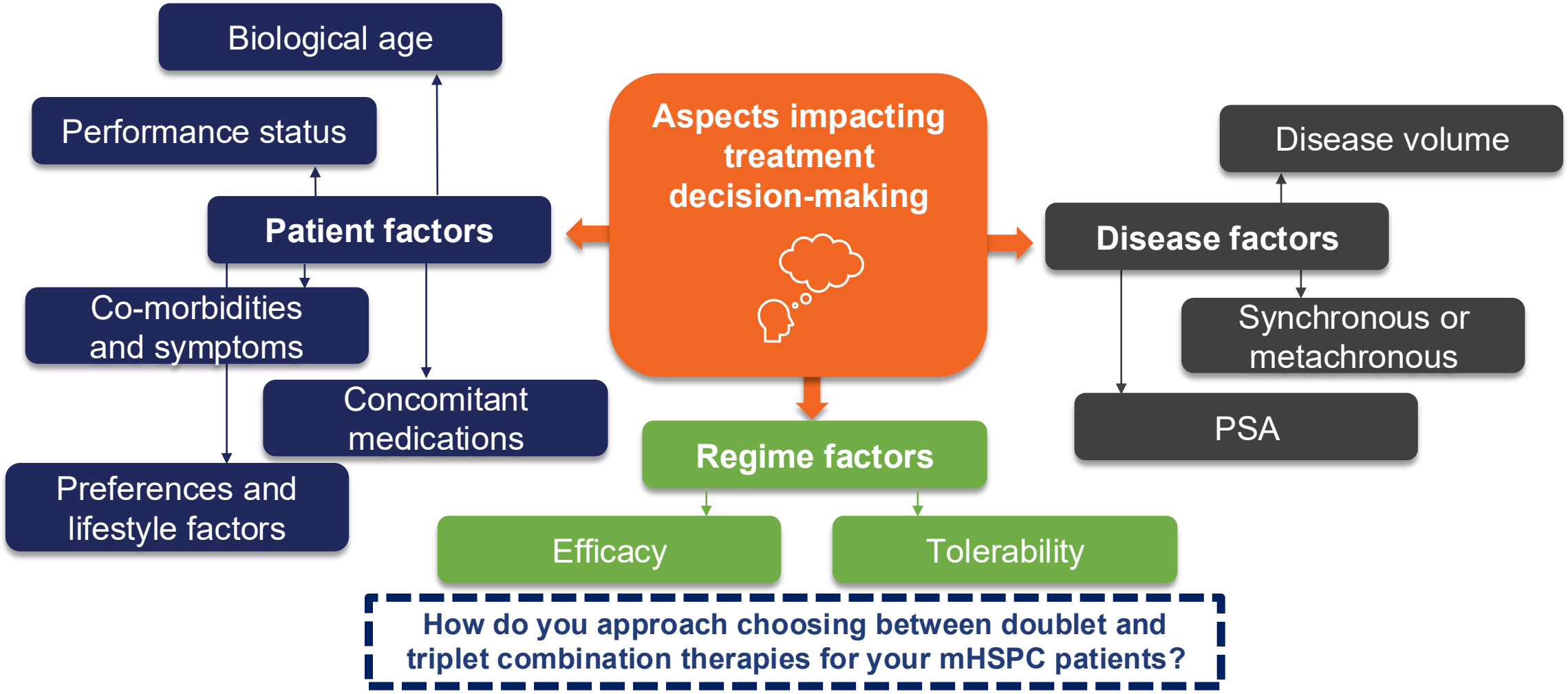
Minimise treatment-related adverse events as much as possible

Have a treatment they can remain on for an extended period of time

Minimise interactions with drugs prescribed for common comorbidities

QoL, quality of life.
Based on speaker's own opinions and experience.

What parameters do you consider when choosing a treatment for an mHSPC patient?



mHSPC, metastatic hormone-sensitive prostate cancer; PSA, prostate-specific antigen.
Based on speaker's own opinions and experience.

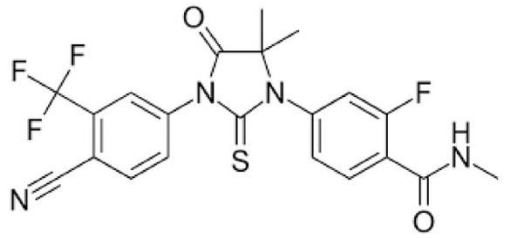
Second-generation ARIs – the clinical data landscape in mHSPC: Doublet therapy

ARI, androgen receptor inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer.

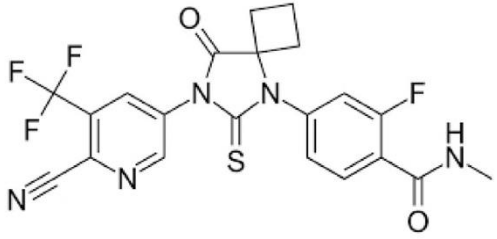
Key features of darolutamide

- Darolutamide is a second-generation ARI, **structurally distinct from apalutamide and enzalutamide (other ARIs)**[1]

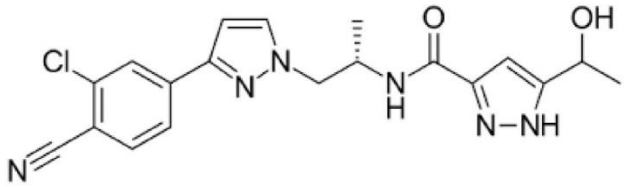
Enzalutamide



Apalutamide



Darolutamide



Adapted from Heidegger I, et al. (2020)[1]

Darolutamide indications for the UK[2]

Darolutamide is indicated for the treatment of adult men with:

- Non-metastatic castration-resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease
- Metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy
- mHSPC in combination with docetaxel

ARI, androgen receptor inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer; nmCRPC, non-metastatic castration-resistant prostate cancer; UK, United Kingdom.

1. Heidegger I, et al. Urol Oncol. 2020;38(4):129–136; 2. NUBEQA (Darolutamide). Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/11324/smpc (accessed May 2026).

Darolutamide is clinically proven in Phase III studies across three indications in mHSPC and nmCRPC[1–4]

All three indications are NICE-recommended

ARAMIS[3]	ARASENS[2]	ARANOTE[4]
Darolutamide + ADT in nmCRPC	**Darolutamide + ADT + docetaxel in mHSPC**	**Darolutamide + ADT in mHSPC**
Delayed tumour progression by 22 months Reduced the risk of death by >30%[c] vs. ADT + placebo *Absolute risk at 3 years, 5.7%*	Extended overall survival by >30%[b] vs. ADT + docetaxel *Absolute risk at 4 years, 12.3%*	Reduced the risk of radiographic progression or death by 46%[a] vs. ADT + placebo *Absolute risk at 2 years, 18.2%*
2019	2022	2025

*The eligibility criteria for treatment with Darolutamide for patients with high-risk nmCRPC is: no metastases detected in conventional imaging, pelvic lymph nodes up to 2 cm permissible; castration-resistant prostate carcinoma (testosterone <1.7 nmol/L PSA increase while on ADT, PSA ≥ 2ng/ml); PSA doubling time of ≤ 10 months (this list is not exhaustive)[4]

[a]Absolute risk at 2 years, 18.2%, HR: 0.54; 95% CI: 0.41–0.71; p<0.0001[1]; [b]Absolute risk at 4 years, 12.3%, HR: 0.68; 95% CI: 0.57–0.80; p<0.0001[1]; [c]Absolute risk at 3 years, 5.7%. HR: 0.69; 95% CI: 0.53–0.88; p=0.003[1]

ADT, androgen deprivation therapy; mHSPC, metastatic hormone-sensitive prostate cancer; NICE, National Institute for Health and Care Excellence; nmCRPC, non-metastatic castration-resistant prostate cancer; PSA, prostate-specific antigen.

1. NUBEQA (Darolutamide) Summary of Product Characteristics. Available at https://www.medicines.org.uk/emc/product/11324/smpc (accessed May 2026); 2. Smith M, et al. N Engl J Med. 2022;386(12); 3. Fizazi K et al. N Engl J Med. 2019;380(13)1235–1246; 4.Saad, F, et al. J Clin Oncol. 2024;42(36);4271–81.

Efficacy and safety of darolutamide plus ADT in patients with mHSPC from the Phase III ARANOTE Trial

ADT, androgen deprivation therapy; mHSPC, metastatic hormone-sensitive prostate cancer.

ARANOTE trial design[1–2]

Patients (N=669)

- mHSPC*
- ECOG PS: 0–2

Stratification Factors:

- Visceral metastases (assessed by central review): present/absent
- Prior local therapy: Yes/No

2:1 randomisation

Darolutamide 600 mg BID + ADT (n=446)

Placebo + ADT (n=223)

- *Data cutoff: June 7, 2024*
- *ClinicalTrials.gov: NCT04736199*

Primary Endpoint: rPFS (central review)

Secondary Endpoints:

- Overall survival
- Time to initiation of subsequent antineoplastic therapy
- Time to CRPC
- Time to PSA progression
- Rates of undetectable PSA (<0.2 ng/mL)
- Time to pain progression (BPI-SF)
- Safety

Other Pre-Specified Endpoints include:

- Time to deterioration of FACT-P total

*Metastatic disease confirmed by conventional imaging method either by a positive ^{99m}Tc-phosphonate bone scan, or soft tissue or visceral metastases, either by contrast-enhanced abdominal/pelvic/chest CT or MRI scan assessed by central review.

ADT, androgen deprivation therapy; BID, twice a day; BPI-SF, Brief Pain Inventory – Short Form; CRPC, castration-resistant prostate cancer; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FACT-P, Functional Assessment of Cancer Therapy – Prostate; mHSPC, metastatic hormone-sensitive prostate cancer; MRI, magnetic resonance imaging; PSA, prostate-specific antigen; rPFS, radiological progression-free survival.

1. Clinicaltrials.gov identifier: NCT04736199. Available at: https://clinicaltrials.gov/ct2/show/NCT04736199 (accessed May 2026); 2. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281.

ARANOTE eligibility criteria

Key eligibility criteria[1]

Inclusion criteria

- Documented metastatic disease confirmed by conventional imaging method - central review*
- Started ADT (LHRH agonist/antagonist or orchidectomy) with or without first-generation anti-androgen (≤12 weeks before randomisation)
- ECOG performance status 0, 1, or 2
- Adequate bone marrow, liver, and renal function
- Included both de novo and recurrent disease

Exclusion criteria

- Regional lymph node metastases only (N1, below the aortic bifurcation)
- Baseline superscan
- Prior treatment with:
  - LHRH agonist or antagonist started >12 weeks before study treatment starts except neoadjuvant and/or adjuvant therapy for a duration of ≤24 months and completed ≥12 months prior to randomisation
  - Second-generation ARIs or other investigational ARIs
  - CYP17 enzyme inhibitors as antineoplastic treatment
  - Chemotherapy (docetaxel or immunotherapy for PC)
  - Radiotherapy in the 2 weeks prior to randomisation

*Metastatic disease confirmed by conventional imaging method either by a positive ^{99m}Tc-phosphonate bone scan, or soft tissue or visceral metastases, either by contrast-enhanced abdominal/pelvic/chest CT or MRI scan assessed by central review.

ADT, androgen deprivation therapy; ARI, androgen receptor inhibitor; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; LHRH, luteinising hormone-releasing hormone; MRI, magnetic resonance imaging; PC, prostate cancer.

1. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281.

ARANOTE trial: Key patient demographics and baseline characteristics[1]

		Darolutamide + ADT (n=446)	Placebo + ADT (n=223)
Age, median (range), years		70 (43-93)	70 (45-91)
Race, n (%)	White	251 (56.3)	125 (56.1)
	Asian	144 (32.3)	65 (29.1)
	Black	41 (9.2)	24 (10.8)
	Other	10 (2.2)	9 (4.0)
Region, n (%)	Asia	141 (31.6)	63 (28.3)
	Latin America	119 (26.7)	72 (32.3)
	Europe and Rest of World	186 (41.7)	88 (39.5)
ECOG PS, n (%)	0	235 (52.7)	98 (43.9)
	1–2	211 (47.3)	125 (56.1)
Gleason score ≥8 at initial diagnosis, n (%)		311 (69.7)	146 (65.5)
Serum PSA, median (range), ng/mL		21.4 (0.02–15,915)	21.2 (0.02–8533)
Metastases at initial diagnosis, n (%)	Yes - De novo	317 (71.1)	168 (75.3)
	No - Recurrent	100 (22.4)	45 (20.2)
Disease volume, n (%)*	High	315 (70.6)	157 (70.4)
	Low	131 (29.4)	66 (29.6)
Visceral metastases, n (%)	Yes	53 (11.9)	27 (12.1)
	No	393 (88.1)	196 (87.9)
Prior local therapy, n (%)	Yes	80 (17.9)	40 (17.9)
	No	366 (82.1)	183 (82.1)

- Approximately 70% of patients had de novo disease and 70% of patients had high-volume disease

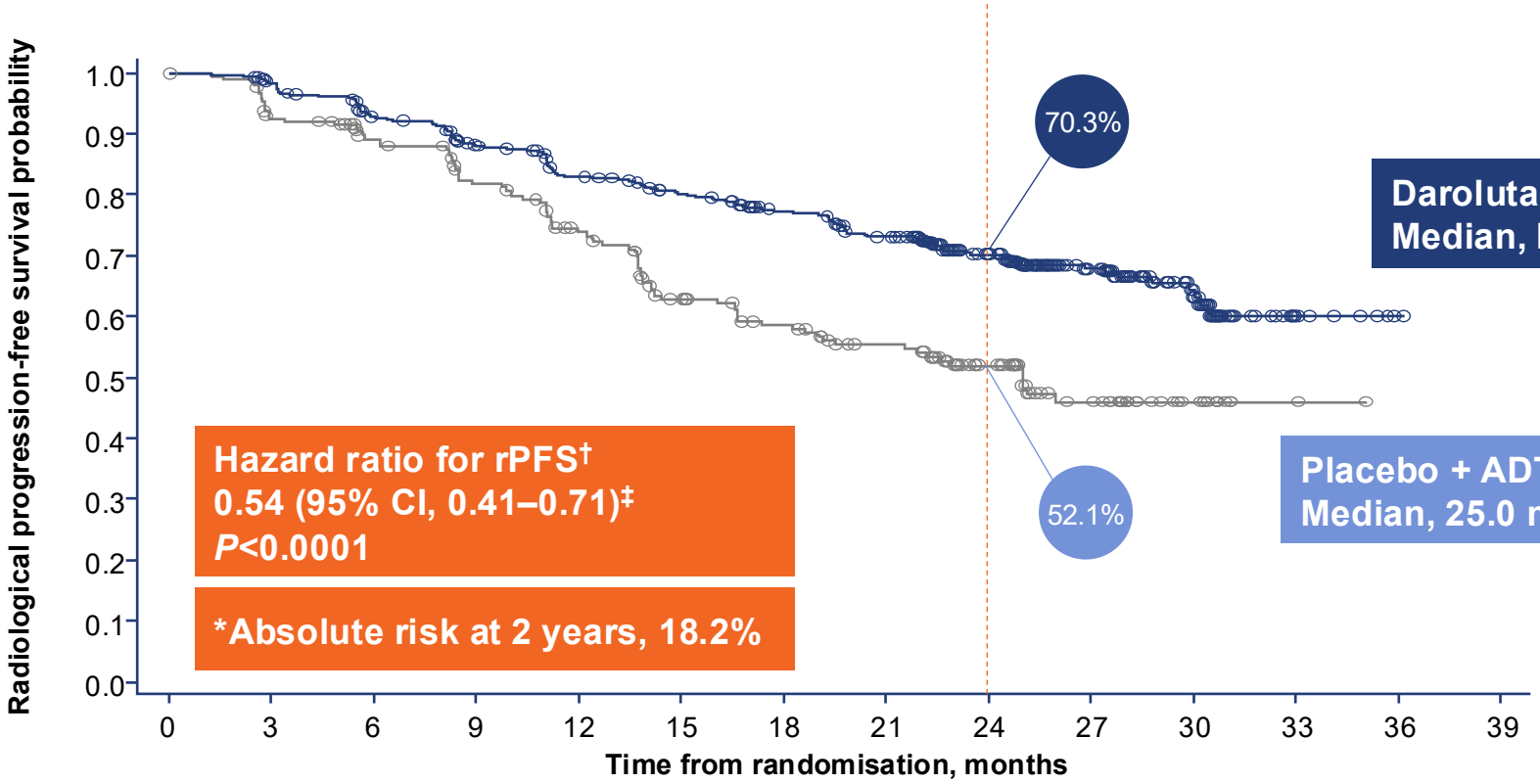
*Disease volume defined by CHAARTED criteria: presence of visceral metastases and/or ≥4 bone metastases with ≥1 beyond vertebral bodies and pelvis.[2]

ADT, androgen deprivation therapy; ECOG PS, Eastern Cooperative Oncology Group Performance Status; PSA, prostate-specific antigen.

1. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281; 2. Sweeney CJ, et al. N Engl J Med. 2015;373:737–746.

Darolutamide + ADT significantly reduced the risk of radiographic progression or death by 46%*[1,2]

Primary Endpoint: rPFS



No. of patients at risk

Darolutamide	446	422	388	358	330	309	285	262	186	113	54	9	1	0
Placebo	223	197	178	158	137	109	96	83	58	32	12	2	0	0

Adapted from Saad F, et al. (2024)[1]

- **Median follow-up:** Darolutamide group 25.3 months; placebo group 25.0 months
- The rPFS rates at 24 months were 70.3% in the darolutamide group and 52.1% in the placebo group

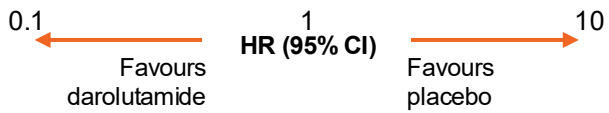
*Absolute risk at 2 years, 18.2%, HR: 0.54; 95% CI: 0.41–0.71; p<0.0001[1]; †Primary analysis occurred after 222 events (darolutamide 128; placebo 94); ‡HR and 95% CI were calculated using the Cox model stratified on visceral metastases (Y/N) and prior therapy (Y/N).

ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; mo, months; NR, not reached; rPFS, radiographic progression-free survival; Y/N, yes/no.

1. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281.

The rPFS benefit with darolutamide + ADT was consistent across all subgroups

		Darolutamide (n=446)		Placebo (n=223)		Stratified HR (95% CI)
		Events/Patients, n/N	Median, months	Events/Patients, n/N	Median, months	
Overall population		128/446	NR	94/223	25.0	0.54 (0.41-0.71)
Age subgroups, years	**<65**	37/118	NR	32/65	14.2	0.44 (0.27-0.71)
	65–74	53/193	NR	35/96	NR	0.64 (0.41-0.98)
	75–84	29/117	NR	22/52	NR	0.48 (0.27-0.83)
	≥85	9/18	27.4	5/10	19.2	0.51 (0.16-1.66)
Baseline PSA values	**< median**	58/216	NR	44/111	26.0	0.55 (0.37-0.81)
	≥ median	67/220	NR	47/108	22.9	0.55 (0.38-0.80)
ECOG PS at baseline	**0**	61/235	NR	37/98	NR	0.55 (0.37-0.83)
	≥1	67/211	NR	57/125	22.6	0.56 (0.39-0.79)
Gleason score at initial diagnosis	**Missing/not assessed**	5/13	NR	4/10	13.8	
	<8	32/122	NR	30/67	22.9	0.46 (0.28-0.75)
	≥8	91/311	NR	60/146	25.1	0.58 (0.42-0.81)
Disease volume	**High volume**	113/315	30.2	75/157	19.2	0.60 (0.44-0.80)
	Low volume	15/131	NR	19/66	NR	0.30 (0.15-0.60)
Race	**White**	76/251	NR	55/125	22.2	0.52 (0.36-0.73)
	Asian	38/144	NR	24/65	25.0	0.59 (0.35-0.98)
	Black	10/41	NR	10/24	NR	0.51 (0.21-1.23)
	Other	4/10	NR	5/9	13.7	
Geographic region	**Europe and RoW**	56/186	NR	39/88	22.6	0.50 (0.33-0.75)
	Asia	37/141	NR	23/63	25.0	0.60 (0.35-1.01)
	Latin America	35/119	NR	32/72	25.1	0.56 (0.35-0.90)
Visceral metastases	**Yes**	21/53	NR	13/27	25.0	0.71 (0.35-1.41)
	No	107/393	NR	81/196	25.0	0.52 (0.39-0.69)
Prior local therapy	**Yes**	19/80	NR	18/40	19.5	0.34 (0.17-0.66)
	No	109/366	NR	76/183	25.0	0.59 (0.44-0.79)



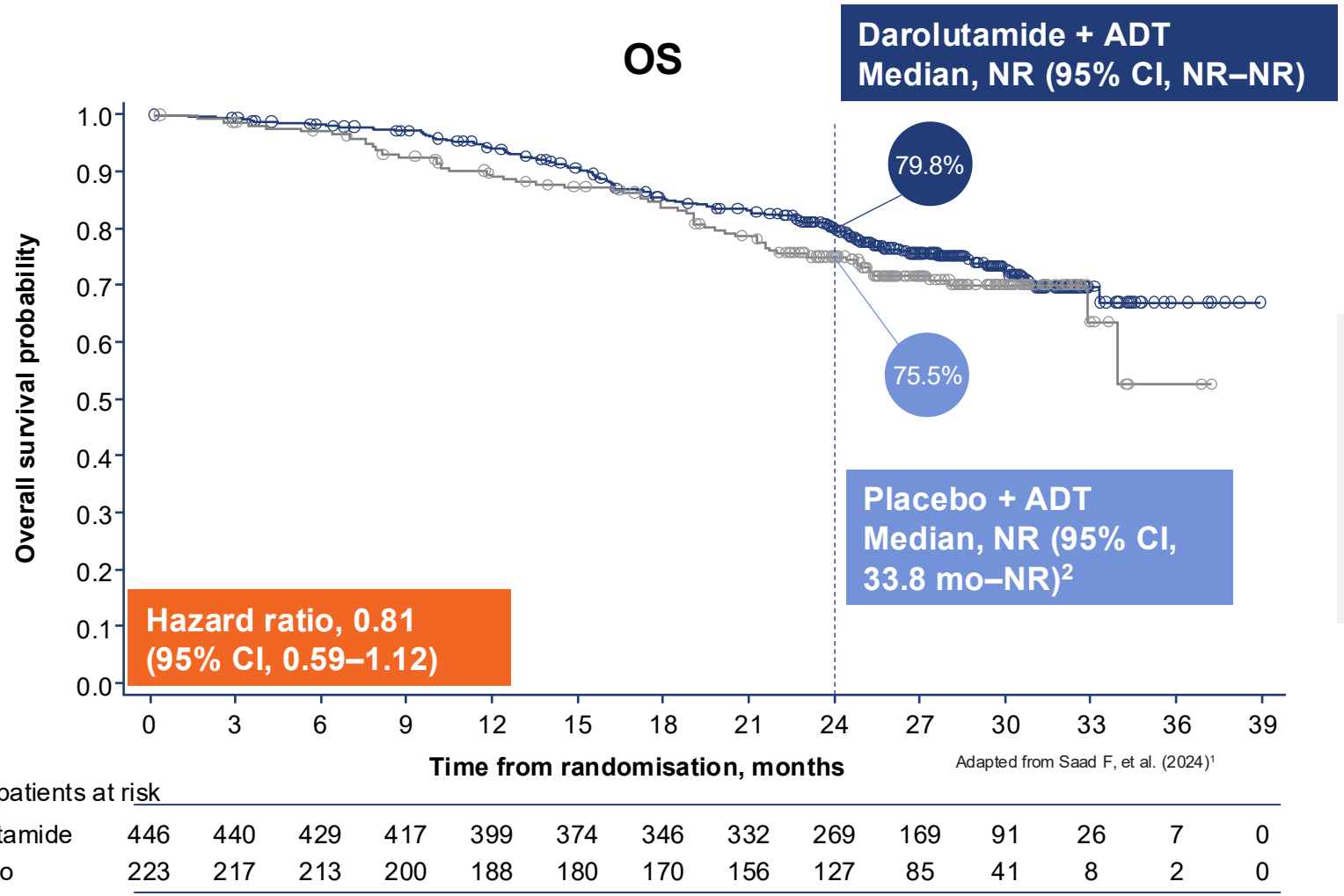
The rPFS benefit with darolutamide + ADT was consistent across all subgroups, including high- and low-volume disease

HR and 95% CI were calculated from univariate analysis using unstratified Cox regression.

ADT, androgen deprivation therapy; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group Performance Status; HR, hazard ratio; NR, not reached; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival; RoW, rest of world.

1. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281.

ARANOTE overall survival at the time of primary analysis[1]



No. of patients at risk

Darolutamide	446	440	429	417	399	374	346	332	269	169	91	26	7	0
Placebo	223	217	213	200	188	180	170	156	127	85	41	8	2	0

Secondary endpoints at the time of primary analysis

- The ARANOTE study's primary endpoint is rPFS, clinically accepted for efficient evaluation of treatment effectiveness[1,3,4]
- There is a correlation of outcomes between rPFS and OS[3,4]

ADT, androgen deprivation therapy; CI, confidence interval; mHSPC, metastatic hormone-sensitive prostate cancer; mo, months; NR, not reached; OS, overall survival; rPFS, radiographic progression-free survival.

1. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281; 2. NUBEQA (darolutamide) UK Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/11324/smpc#gref (accessed May 2026); 3. Halabi S, et al. J Clin Oncol. 2024;42:1044–1054; 4. Shore N, et al. Eur J Cancer. 2025;223:115513.

Surrogate endpoints in cancer trials[1]

➢ Validated surrogate endpoints allow cancer trials to quickly and reliably measure efficacy of treatments[1]

rPFS is a clinically meaningful endpoint in cancer trials

rPFS is an important, accepted clinical endpoint that provides an efficient and early assessment of a treatment's efficacy[2,3]

- rPFS can guide real-world treatment decisions[4]

rPFS is a reliable surrogate for OS

Studies have shown a correlation between rPFS and OS[1,3]

Surrogacy endpoints are accepted by regulatory bodies

71%
of FDA approvals were based on surrogate endpoints[5]

~66%
of supporting trials for market access authorisation did not use OS as a primary endpoint[6]

Previously, rPFS had been validated as a surrogate for OS in mHSPC patients treated with ADT and docetaxel, but not with ARPIs[1,3]

ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; EMA, European Medicines Agency; FDA, US Food and Drug Administration; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; rPFS, radiographic progression-free survival.

1. Halabi S, et al. J Clin Oncol. 2024;42:1044–54; 2. Rathkopf DA, et al. JAMA Oncol. 2018;4(5):694–701; 3. Morris MJ, et al. Cancers. 2024;130(20):3426–3435; 4. Shore N, et al. Eur J Cancer. 2025;223:115513; 5. Chitkara A, et al. J Clin Oncol. 2023;41:e13658; 6. Kordecka A, et al. Value Health. 2019;22:884–90.

The Shore et al. (2025) surrogacy analysis validates the use of rPFS as a reliable surrogate for OS in ARPI trials*[2]

Halabi et al. STOPCAP/ICECaP collaboration (2024) investigated rPFS as a surrogate for OS in mHSPC[1]

Key takeaway

- Using individual patient data (~6400 patients), rPFS was identified as a valid surrogate for OS in mHSPC
- Analysis focused on trials utilising ADT or docetaxel as treatment options, not ARPIs

Aim of Shore et al. 2025[2]

Explore if rPFS continues to be a valid surrogate endpoint for OS when ARPIs are added

*These studies show different clinical scenarios, include different patient populations, and are not intended to compare therapies.
ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; rPFS, radiographic progression-free survival.
1. Halabi S, et al. J Clin Oncol. 2024;42:1044–54; 2. Shore N, et al. Eur J Cancer. 2025;223:115513.

The Shore et al. (2025) surrogacy analysis validates the use of rPFS as a reliable surrogate for OS in ARPI trials*[1]

Methodology

Systematic literature review

35 treatment comparisons identified

31 trials, that reported rPFS and/or OS

18,900 patients

Statistical analysis

Assessed the relationship between rPFS and OS using bivariate random-effects meta-analysis (BRMA) following NICE guidelines[2]

Predictive validity

Evaluated the accuracy of OS predictions based on rPFS using leave-one-out cross-validation

Sensitivity analyses

Tested the robustness of the results by conducting 4 sensitivity analyses to provide additional confidence in the findings

*These studies show different clinical scenarios, include different patient populations, and are not intended to compare therapies.

ARPI, androgen receptor pathway inhibitor; BRMA, bivariate random-effects meta-analysis; NICE, National Institute for Health and Care Excellence; OS, overall survival; rPFS, radiographic progression-free survival.

1. Shore N, et al. Eur J Cancer. 2025;223:115513; 2. Bujkiewicz S, et al. NICE DSU technical support document 20: multivariate meta-analysis of summary data for combining treatment effects on correlated outcomes and evaluating surrogate endpoints. Available at: http://www.nicedsu.org.uk/ (accessed May 2026).

ARANOTE secondary endpoints[1,2]

Secondary Endpoint	Darolutamide (n=446)		Placebo (n=223)		Hazard Ratio[a] (95% Confidence Interval [CI]); p-value (two-sided)[b]
	n (%)	Median, months	n (%)	Median, months	
OS	103 (23.1)	NR	60 (26.9)	NR	0.813 (0.591-1.118); P=0.2014
Time to initiation of subsequent anti-cancer therapy for prostate cancer	68 (15.2)	NR	74 (33.2)	NR	0.401 (0.288-0.558); p<0.0001*
Time to CRPC[d]	154 (34.5)	NR	143 (64.1)	13.8	0.404 (0.321-0.508); p<0.0001*
Time to PSA progression	93 (20.9)	NR	108 (48.4)	16.8	0.306 (0.231-0.405); p<0.0001*
Time to pain progression[c]	124 (27.8)	NR	79 (35.4)	29.9	0.721 (0.544-0.957); p=0.0115*

Adapted from: Saad F, et al. ESMO Congress 2024. September 13-17, 2024; Barcelona, Spain. Abstract LBA68[3]

Secondary endpoints at the time of primary analysis

[a]Hazard ratio <1 favours darolutamide.
[b]Based on stratified log-rank test except for PSA undetectable rates.
[c]This secondary efficacy endpoint was listed after time to PSA progression as per the hierarchical gatekeeping procedure order.
[d]Results of patients progressing to mCRPC.
*Nominal p-values (two-sided) are provided for descriptive purposes only.

The p-value for OS did not reach statistical significance at the time of the primary analysis. Therefore (as per hierarchical methodology) a formal testing for statistical significance of the remaining secondary endpoints was not conducted; nominal p-values (two-sided) are provided for descriptive purposes only[2]

CI, confidence interval; (m)CRPC, (metastatic) castration-resistance prostate cancer; NR; not reached; OS, overall survival; PSA, prostate-specific antigen.

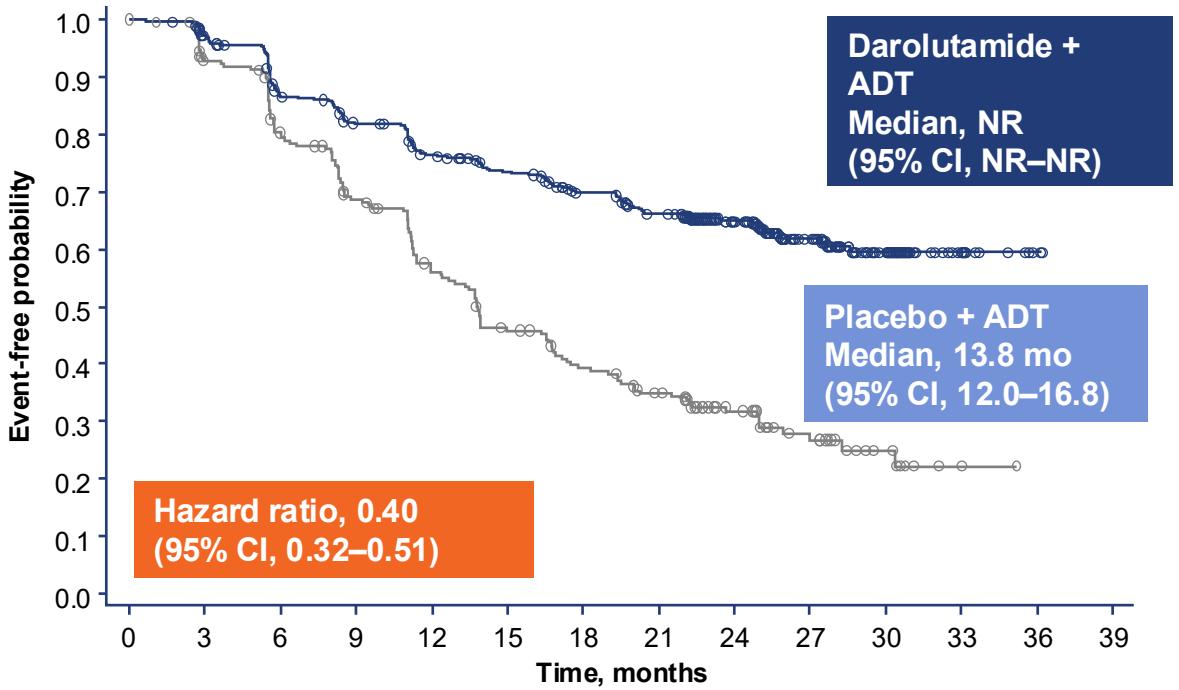
1. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281; 2. NUBEQA (darolutamide) UK Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/11324/smpc#gref (accessed May 2026); 3. Saad F, et al. Presented at ESMO Congress 2024. September 13–17, 2024; Barcelona, Spain. Abstract LBA68.

ARANOTE: Time to mCRPC and time to pain progression in mHSPC[1,2]

- The p-value for OS did not reach statistical significance at the time of the primary analysis. Therefore (as per hierarchical methodology) a formal testing for statistical significance of the remaining secondary endpoints was not conducted

Secondary endpoints at the time of primary analysis

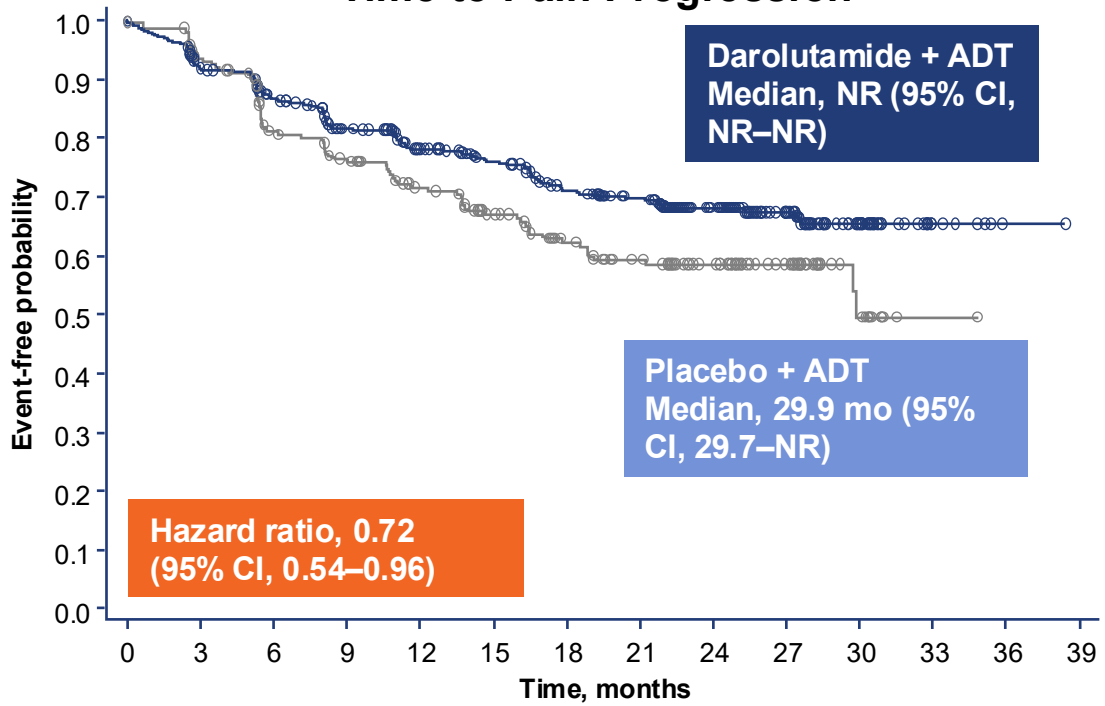
Time to mCRPC[1]



No. of patients at risk

Darolutamide	446	417	364	339	312	293	268	245	177	110	51	14	2	0
Placebo	223	197	167	139	110	88	73	61	42	25	10	2	0	0

Time to Pain Progression[2]



No. of patients at risk

Darolutamide	446	385	349	310	278	254	225	209	150	90	36	7	1	0
Placebo	223	195	159	146	127	106	87	74	55	31	11	1	0	0

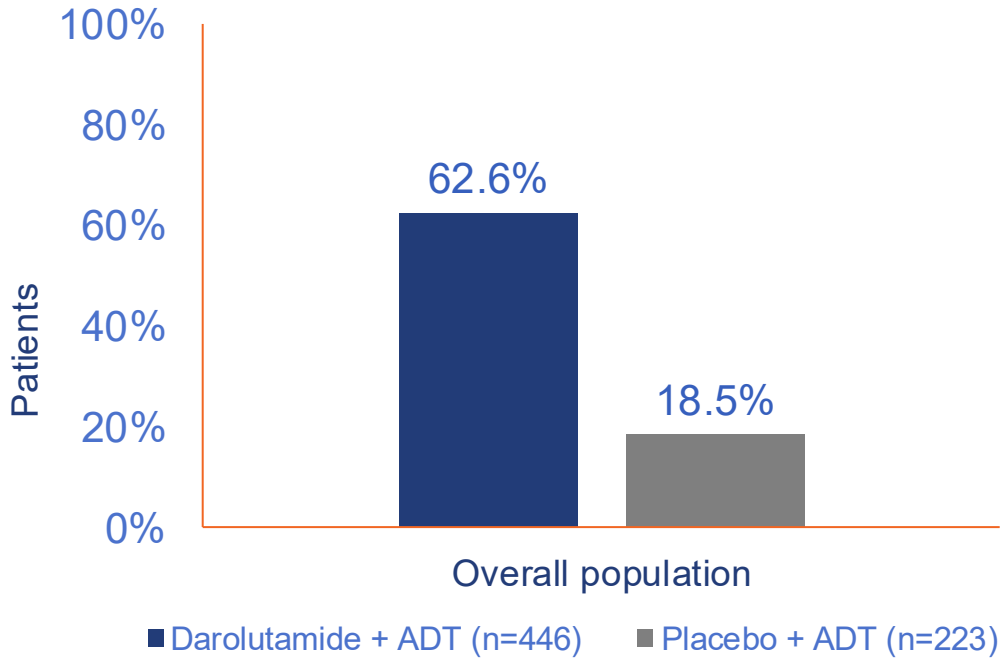
ADT, androgen deprivation therapy; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; mo, months; NR, not reached; OS, overall survival.

1. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281; 2. Saad F, et al. Presented at ESMO Congress 2024. September 13–17, 2024; Barcelona, Spain. Abstract LBA68.

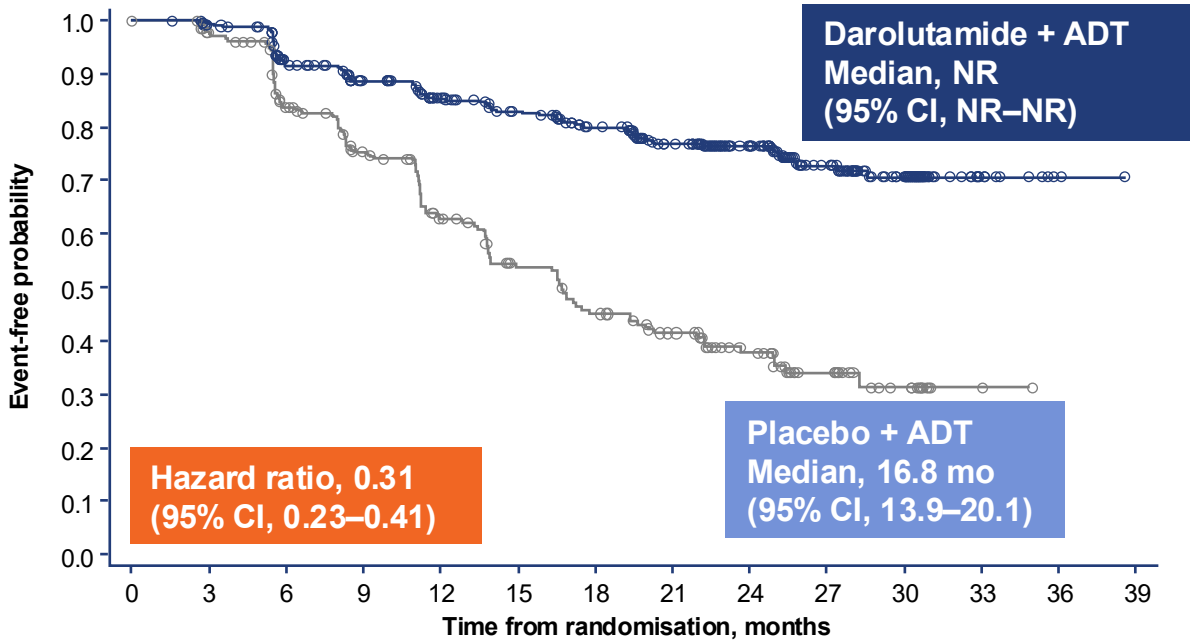
62.6% of patients in the darolutamide arm achieved an undetectable PSA rate[1]

Secondary endpoints at the time of primary analysis

PSA <0.2 ng/mL at any time during treatment



Time to PSA progression



No. of patients at risk

Darolutamide	446	408	357	330	301	280	256	220	158	95	48	12	2	0
Placebo	223	195	158	130	102	81	67	54	36	20	9	2	0	0

- **The p-value for OS did not reach statistical significance at the time of the primary analysis. Therefore (as per hierarchical methodology) a formal testing for statistical significance of the time to PSA progression was not conducted**

ADT, androgen deprivation therapy; CI, confidence interval; mo, months; NR, not reached; OS, overall survival; PSA, prostate-specific antigen.

1. Saad F, et al. Presented at ESMO Congress 2024. September 13–17, 2024; Barcelona, Spain. Abstract LBA68.

ARANOTE subsequent life-prolonging anticancer therapy[a,1]

No. (%) of patients[b]	Darolutamide + ADT (n=446)	Placebo + ADT (n=223)
Discontinued study treatment, n (%)	203 (45.5)	160 (71.7)
Received subsequent life-prolonging anticancer therapy, n/n (%)[c]	66/203 (32.5)	68/160 (42.5)
Docetaxel	46/203 (22.7)	46/160 (28.8)
Abiraterone acetate	26/203 (12.8)	21/160 (13.1)
Enzalutamide	6/203 (3.0)	12/160 (7.5)
Apalutamide	3/203 (1.5)	0
Cabazitaxel	2/203 (1.0)	1/160 (0.6)
Radium-223 dichloride ▼	2/203 (1.0)	0
Olaparib	1/203 (0.5)	0

Patients receiving darolutamide + ADT had a lower proportion of patients receiving subsequent life-prolonging anticancer therapy compared to those on placebo + ADT

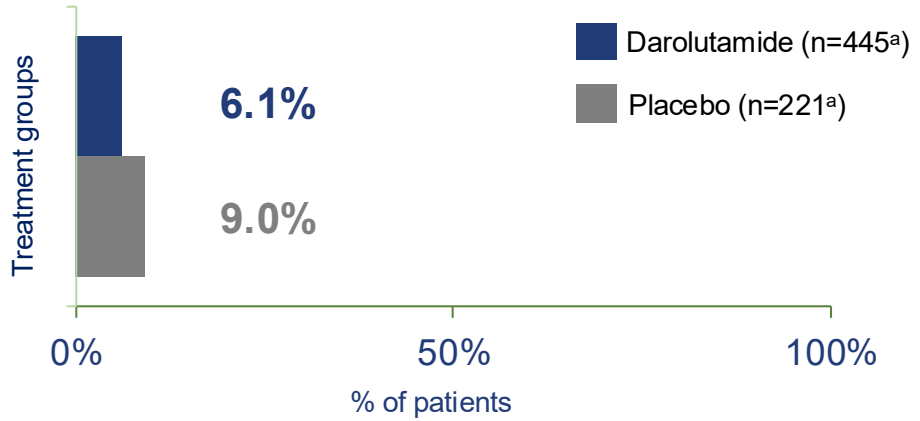
[a]Subsequent life-prolonging therapies for prostate cancer are defined as abiraterone acetate, apalutamide, enzalutamide, docetaxel, cabazitaxel, radium-223, sipuleucel-T, lutetium-177–PSMA-617, rucaparib, and olaparib. [b]Patients could receive more than one subsequent life-prolonging anticancer therapy. [c]Four patients who started life-prolonging therapy before study treatment discontinuation are included.
ADT, androgen deprivation therapy.
1. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281.

Darolutamide is the only 2nd-generation ARI in mHSPC with fewer discontinuations vs. placebo when added to ADT in a Phase III clinical trial[1–3]

Safety analysis

TEAE, no. of patients (%)[1]	Darolutamide + ADT (n=445[a])[1]	Placebo + ADT (n=221[a])[1]
Any AE	405 (91.0)	199 (90.0)
Serious AE	105 (23.6)	52 (23.5)
Grade 3 or 4 AE	137 (30.8)	67 (30.3)
Grade 5 AE	21 (4.7)	12 (5.4)

TEAEs leading to permanent discontinuation of darolutamide/placebo[1]



Darolutamide + ADT had lower discontinuation rates due to AEs vs. placebo[1]

[a]Two patients who were randomised to the placebo group but received darolutamide are analysed in the darolutamide group for the safety analysis set.
ADT, androgen deprivation therapy; AE, adverse event; ARI, androgen receptor inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer; TEAE, treatment-emergent adverse event.
1. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281; 2. Chi K, et al. N Eng J Med. 2019;381(1):13–24; 3. Armstrong, et al. J Clin Oncol. 2019;37(32):2974–2986.

Darolutamide is the only 2nd-generation ARI in mHSPC with lower levels of fatigue vs. placebo when added to ADT in a Phase III clinical trial[1–3]

Most common adverse events, occurring in ≥5% of patients in either group[1]	Darolutamide + ADT (n=445[a])[1]		Placebo + ADT (n=221[a])[1]	
	n (%)	Grade 3/4	n (%)	Grade 3/4
Anaemia	91 (20.4)	14 (3.1)	39 (17.6)	8 (3.6)
Arthralgia	55 (12.4)	5 (1.1)	25 (11.3)	0
UTI	52 (11.7)	8 (1.8)	17 (7.7)	1 (0.5)
Back pain	43 (9.7)	5 (1.1)	23 (10.4)	2 (0.9)
Increased AST	43 (9.7)	10 (2.2)	17 (7.7)	1 (0.5)
Constipation	42 (9.4)	0	16 (7.2)	0
Hot flush	41 (9.2)	0	16 (7.2)	0
Increase ALT	40 (9.0)	9 (2.0)	18 (8.1)	1 (0.5)
Pain in extremity	38 (8.5)	1 (0.2)	20 (9.0)	4 (1.8)

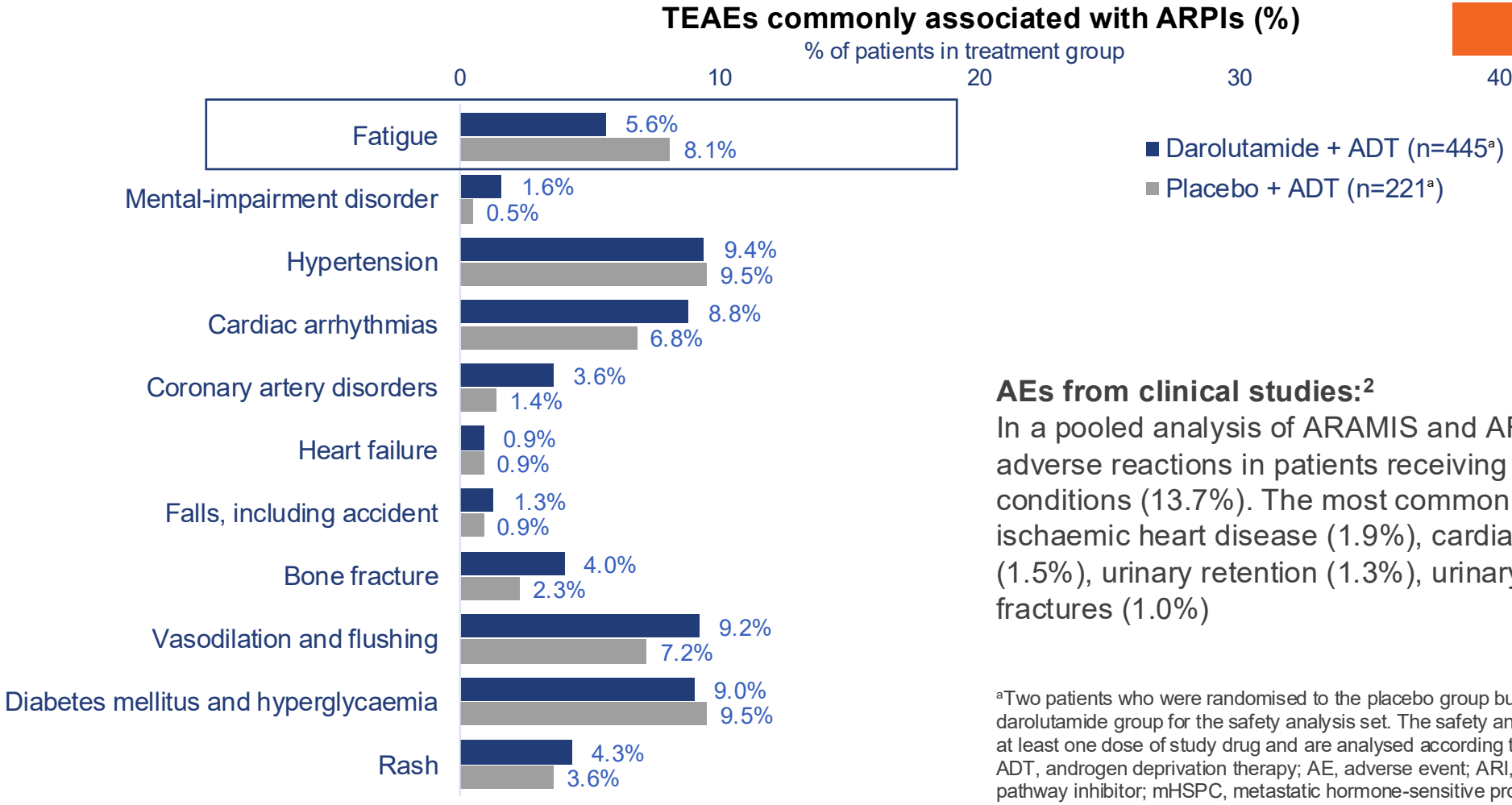
Most common adverse events, occurring in ≥5% of patients in either group[1]	Darolutamide + ADT (n=445[a])[1]		Placebo + ADT (n=221[a])[1]	
	n (%)	Grade 3/4	n (%)	Grade 3/4
Hypertension	38 (8.5)	19 (4.3)	19 (8.6)	8 (3.6)
Bone pain	33 (7.4)	9 (2.0)	27 (12.2)	3 (1.4)
Increased weight	33 (7.4)	4 (0.9)	17 (7.7)	1 (0.5)
COVID-19	32 (7.2)	1 (0.2)	15 (6.8)	2 (0.9)
Increased ALP	30 (6.7)	0	13 (5.9)	3 (1.4)
Insomnia	28 (6.3)	0	6 (2.7)	1 (0.5)
Hyperglycaemia	27 (6.1)	1 (0.2)	8 (3.6)	0
Fatigue	25 (5.6)	0	18 (8.1)	1 (0.5)
Increased creatinine	21 (4.7)	2 (0.4)	15 (6.8)	0
Headache	18 (4.0)	0	14 (6.3)	2 (0.9)

[a]Two patients who were randomised to the placebo group but received darolutamide are analysed in the darolutamide group for the safety analysis set.
ADT, androgen deprivation therapy; ALP, alkaline phosphatase; ALT, alanine aminotransferase; ARI, androgen receptor inhibitor; AST, aspartate aminotransferase; mHSPC, metastatic hormone-sensitive prostate cancer; UTI, urinary tract infection.

1. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281; 2. Chi K, et al. N Eng J Med. 2019;381(1):13–24; 3. Armstrong, et al. J Clin Oncol. 2019;37(32):2974–2986.

Darolutamide is the only 2nd-generation ARI in mHSPC with lower levels of fatigue vs. placebo when added to ADT in a Phase III clinical trial[1–3]

Safety analysis



AEs from clinical studies:[2]

In a pooled analysis of ARAMIS and ARANOTE, the most common adverse reactions in patients receiving darolutamide was fatigue/asthenic conditions (13.7%). The most common serious adverse reactions were ischaemic heart disease (1.9%), cardiac arrhythmias (1.8%), pneumonia (1.5%), urinary retention (1.3%), urinary tract infection (1.1%) and fractures (1.0%)

[a]Two patients who were randomised to the placebo group but received darolutamide are analysed in the darolutamide group for the safety analysis set. The safety analysis set included all randomized patients who received at least one dose of study drug and are analysed according to the treatment they received.

ADT, androgen deprivation therapy; AE, adverse event; ARI, androgen receptor inhibitor; ARPI, androgen receptor pathway inhibitor; mHSPC, metastatic hormone-sensitive prostate cancer; TEAE, treatment-emergent adverse event.

1. Saad F, et al. J Clin Oncol. 2024;42(36):4271–4281; 2. NUBEQA (darolutamide) UK Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/11324/smpc#gref (accessed May 2026); 3. Chi K, et al. N Eng J Med. 2019;381(1):13–24; 4. Armstrong, et al. J Clin Oncol. 2019;37(32):2974–2986.

Conclusions

- Darolutamide is clinically proven in Phase III studies across three indications in mHSPC and nmCRPC[1–4]
- Darolutamide + ADT significantly reduced the risk of radiographic progression or death by 46%* (absolute risk at 2 years: 18.2%)[4]
- Darolutamide is the only 2nd-generation ARI in mHSPC with lower levels of fatigue and fewer discontinuations vs. placebo when added to ADT in a Phase III clinical trial[4–6]
- Darolutamide is the only 2nd-generation ARI with proven efficacy for treatment of patients with mHSPC, both with and without docetaxel[1,2,4,7,8]

*HR: 0.54; 95% CI: 0.41–0.71; p<0.0001[1]

1. NUBEQA (darolutamide) Summary of Product Characteristics. Available at https://www.medicines.org.uk/emc/product/11324/smpc (accessed May 2026); 2. Smith M, et al. N Engl J Med. 2022;386(12); 3. Fizazi K et al. N Engl J Med. 2019;380(13)1235–1246; 4. Saad, F, et al. J Clin Oncol. 2024;42(36);4271–81; 5. Chi K, et al. N Eng J Med. 2019;381(1):13–24; 6. Armstrong, et al. J Clin Oncol. 2019;37(32):2974–2986; 7. XTANDI (enzalutamide) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/10318/smpc (accessed May 2026; 8. ERLEADA (apalutamide) Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/9832/smpc (accessed May 2026).

NUBEQA (darolutamide) Prescribing Information

NUBEQA® (darolutamide) 300 mg film-coated tablets
Prescribing Information – United Kingdom
(Refer to full Summary of Product Characteristics (SmPC) before prescribing)

Presentation: Each film-coated tablet contains 300 mg of darolutamide. **Indication(s):** NUBEQA is indicated for the treatment of adult men with non-metastatic castration resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease or with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy or with mHSPC in combination with docetaxel. **Posology & method of administration:** Treatment should be initiated and supervised by a specialist physician experienced in treatment of prostate cancer. Medical castration with a luteinising hormone-releasing hormone (LHRH) analogue should be continued during treatment of patients not surgically castrated. For oral use. The tablets should be taken whole with food. ***Adults:*** 600 mg darolutamide (two tablets of 300 mg) taken twice daily, equivalent to a total daily dose of 1200 mg. When used in combination with docetaxel in mHSPC patients, the first of 6 cycles of docetaxel should be administered within 6 weeks after the start of darolutamide treatment. Treatment with darolutamide should be continued until disease progression or unacceptable toxicity even if a cycle of docetaxel is delayed, interrupted, or discontinued. If a patient experiences a ≥ Grade 3 toxicity or an intolerable adverse reaction related to darolutamide, dosing should be withheld or reduced to 300 mg twice daily until symptoms improve. Treatment may then be resumed at a dose of 600 mg twice daily. ***Children & adolescents:*** There is no relevant use of darolutamide in the paediatric population. ***Elderly:*** No dose adjustment is necessary. ***Renal Impairment:*** No dose adjustment is necessary for patients with mild or moderate renal impairment. For patients with severe renal impairment (eGFR 15-29 mL/min/1.73 m2) not receiving haemodialysis, the recommended starting dose is 300 mg twice daily. ***Hepatic Impairment:*** No dose adjustment is necessary for patients with mild hepatic impairment. The available data on darolutamide pharmacokinetics in moderate hepatic impairment is limited. Darolutamide has not been studied in patients with severe hepatic impairment. For patients with moderate and severe hepatic impairment (Child-Pugh Classes B and C), the recommended starting dose is 300 mg twice daily. **Contra-indications:** Hypersensitivity to the active substance or to any of the excipients. Women who are or may become pregnant. **Warnings & precautions:** Monitor for signs and symptoms of ischaemic heart disease. Optimise management of cardiovascular risk factors. Discontinue darolutamide for Grade 3-4 ischaemic heart disease. Seizure occurred in patients receiving darolutamide. Advise patients of the risk of developing a seizure while receiving darolutamide. Consider discontinuation of darolutamide in patients who develop a seizure during treatment. Cases of idiosyncratic drug-induced liver injury (DILI) with increases in alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) to ≥5 and ≥20 x upper limit of normal (ULN) have been reported. Idiosyncratic DILI has been reported in clinical trials and the post-marketing setting. Liver function test abnormalities were reversible upon darolutamide discontinuation. In case of liver function test abnormalities suggestive of idiosyncratic drug-induced liver injury, permanently discontinue darolutamide. The available data in patients with severe renal impairment are limited. As exposure might be increased those patients should be closely monitored for adverse reactions. The available data in patients with moderate hepatic impairment are limited, and darolutamide has not been studied in patients with severe hepatic impairment. As exposure might be increased those patients should be closely monitored for adverse reactions. Patients with clinically significant cardiovascular disease in the past 6 months including stroke, myocardial infarction, severe/unstable angina pectoris, coronary/peripheral artery bypass graft, and symptomatic congestive heart failure were excluded from the clinical studies. Therefore, the safety of darolutamide in these patients has not been established. Use of strong CYP3A4 and P-gp inducers during treatment with darolutamide may decrease the plasma concentration of darolutamide and is not recommended, unless there is no therapeutic alternative. Selection of an alternate concomitant medicinal product with less potential to induce CYP3A4 or P-gp should be considered. Patients should be monitored for adverse reactions of BCRP, OATP1B1 and OATP1B3 substrates as co-administration with darolutamide may increase the plasma concentrations of these substrates. Co-administration with rosuvastatin should be avoided unless there is no therapeutic alternative. In patients with a history of risk factors for QT prolongation and in patients receiving concomitant medicinal products that might prolong the QT interval, physicians should assess the benefit-risk ratio including the potential for Torsade de pointes prior to initiating NUBEQA. NUBEQA 300mg film-coated tablets contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose galactose malabsorption should not take this medicinal product. **Interactions:** For the effect of other medicinal products on the action of darolutamide (e.g CYP3A4, P-gp inducers and CYP3A4, P-gp and BCRP inhibitors, UGT1A9 inhibitors and docetaxel) and the action of darolutamide on other medicinal products (BCRP, OATP1B1, OATP1B3 substrates, P-gp substrates, docetaxel, CYP3A4 substrates and other medicinal products that prolong the QT interval) refer to the relevant SmPCs. **Pregnancy & lactation:** Darolutamide is not indicated in women of childbearing potential, and it is not to be used in women who are, or may be, pregnant or breast-feeding. Unknown whether darolutamide or its metabolites are present in semen. If the patient is engaged in sexual activity with a woman of childbearing potential, a highly effective contraceptive method (<1% failure rate per year) should be used during and for 1 week after completion of treatment. Unknown whether darolutamide or its metabolites are excreted in human milk. No studies in animals have been conducted to evaluate the excretion of darolutamide or its metabolites into milk. A risk to the breast-fed child cannot be excluded. There are no human data on the effect of darolutamide on fertility. Based on animal studies, darolutamide may impair fertility in males of reproductive potential. **Effects on ability to drive and use machines:** Darolutamide has no or negligible influence on the ability to drive and use machines. **Undesirable effects:** *Adverse reactions observed in patients with nmCRPC and mHSPC* *Very common:* fatigue/asthenic conditions, neutrophil count decreased, bilirubin increased, ALT increased, AST increased, anaemia. *Common:* ischaemic heart disease, heart failure, rash, pain in extremity, fractures. *Serious adverse reactions:* cardiac arrhythmias, urinary retention, urinary tract infection, pneumonia, fractures, seizure. *Adverse reactions observed in patients with mHSPC treated with darolutamide in combination with docetaxel*. *Very common:* hypertension, rash, blood bilirubin increased, ALT increased, AST increased. *Serious adverse reactions:* fractures, ischaemic heart disease, seizure, febrile neutropenia, neutrophil count decreased, pneumonia. Prescribers should consult the SmPC in relation to other side effects (see section 4.8 of SmPC). **Overdose:** In the event of intake of a higher than recommended dose, treatment with darolutamide can be continued with the next dose as scheduled. There is no specific antidote for darolutamide and symptoms of overdose are not established. **Legal Category:** POM**. Package Quantities & Basic NHS Costs:** Pack of 112 film-coated tablets, £4,040. **MA Number(s):** PLGB 00010/0677. **Further information available from:** Bayer plc, 400 South Oak Way, Reading RG2 6AD, United Kingdom. Telephone: 0118 206 3000. **Date of preparation:** June 2025

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in Google Play or Apple App Store.
Adverse events should also be reported to Bayer plc.
Tel: 0118 206 3500, Fax: 0118 206 3703, Email: pvuk@bayer.com

Xofigo▼ (radium-223 dichloride) Prescribing Information

▼ Xofigo® 1100 kBq/mL solution for injection (radium223 dichloride)
Prescribing Information (Refer to full Summary of Product Characteristics (SmPC) before prescribing)

Presentation: Each vial contains 6 mL of solution (6.6 MBq radium223 dichloride at the reference date). Each mL of solution contains 1100 kBq radium Ra 223 dichloride (radium-223 dichloride), corresponding to 0.58 ng radium-223 at the reference date. **Indication(s):** Xofigo monotherapy or in combination with luteinising hormone releasing hormone (LHRH) analogue is indicated for the treatment of adult patients with metastatic castration-resistant prostate cancer (mCRPC), symptomatic bone metastases and no known visceral metastases, in progression after at least two prior lines of systemic therapy for mCRPC (other than LHRH analogues), or ineligible for any available systemic mCRPC treatment. **Posology & method of administration:** Xofigo should be administered only by persons authorised to handle radiopharmaceuticals in designated clinical settings, and after evaluation of the patient by a qualified physician. Xofigo is for intravenous use and must be administered by slow injection (generally up to 1 minute). The intravenous access line or cannula must be flushed with isotonic sodium chloride 9 mg/mL (0.9%) solution for injection before and after injection of Xofigo. ***Adults:*** The dose regimen of Xofigo is an activity of 55 kBq per kg body weight, given at 4 week intervals for 6 injections. ***Hepatic impairment:*** No dose adjustment is considered necessary in patients with hepatic impairment. ***Renal impairment:*** No dose adjustment is considered necessary in patients with renal impairment. ***Elderly patients:*** No dose adjustment is considered necessary in elderly patients. ***Children & adolescents:*** There is no relevant use of this medicinal product in the paediatric population for prostate cancer. **Contra-indications:** Xofigo is contraindicated in combination with abiraterone acetate and prednisone/prednisolone. **Warnings & precautions:** The safety and efficacy of Xofigo in combination with cancer therapies other than LHRH analogues have not been established; an increased risk of mortality and fractures is possible. The combination of radium-223 with other systemic cancer therapies other than LHRH analogues is not recommended. The use of Xofigo is not recommended for treatment of adults with CRPC and only asymptomatic bone metastases. In adults with CRPC and mildly symptomatic bone metastases the benefit of treatment should be carefully assessed to outweigh the risks considering that high osteoblastic activity is likely to be required for treatment benefit. In clinical studies, patients with fewer than 6 bone metastases had an increased risk of fractures and did not have a statistically significant survival benefit. A pre-specified subgroup analysis also showed that overall survival was not significantly improved in patients with a total ALP < 220 U/L. Therefore, in patients with a low level of osteoblastic bone metastases treatment with radium-223 is not recommended. Bone marrow suppression, notably thrombocytopenia, neutropenia, leukopenia and pancytopenia, have been reported in patients treated with Xofigo. Haematological evaluation of patients must be performed at baseline and prior to every dose of Xofigo. In case there is no recovery in values for absolute neutrophil count (ANC), platelets and haemoglobin within 6 weeks after the last administration of Xofigo despite receiving standard of care, further treatment with Xofigo should only be continued after a careful benefit/risk evaluation. Patients with evidence of compromised bone marrow should be treated with caution. Safety and efficacy of Xofigo have not been studied in patients with Crohn's disease and ulcerative colitis. Due to faecal excretion of Xofigo, radiation may lead to aggravation of acute inflammatory bowel disease. Therefore, Xofigo should only be administered after a careful benefit-risk assessment in patients with acute inflammatory bowel disease. In patients with untreated imminent or established spinal cord compression, treatment with standard of care, as clinically indicated, should be completed before starting or resuming treatment with Xofigo. Xofigo increases the risk of bone fractures, especially in patients with medical history of osteoporosis and in patients with <6 bone metastases. Prior to starting radium-223 bone status and baseline risk of fractures of patients (e.g. osteoporosis, less than 6 bone metastases, medication increasing fracture risk, low body mass index) should be carefully assessed, and closely monitored for at least 24 months. Preventive measures should be considered before starting or resuming treatment with Xofigo. In patients with a high baseline risk of fracture, the benefit of treatment should be carefully assessed to outweigh the risk. In patients with bone fractures, orthopaedic stabilisation of fractures should be performed before starting or resuming treatment with Xofigo. In patients treated with bisphosphonates and Xofigo, an increased risk of development of osteonecrosis of the jaw (ONJ) cannot be excluded. Xofigo contributes to a patient's overall long-term cumulative radiation exposure which may be associated with an increased risk of cancer and hereditary defects. In particular, the risk for osteosarcoma, myelodysplastic syndrome and leukaemias may be increased. Xofigo increases the incidence of diarrhoea, nausea, and vomiting which may result in dehydration. Oral intake and fluid status of patients should be carefully monitored. Patients should be advised to seek medical advice if they experience severe or persistent diarrhoea, nausea, vomiting. Patients who display signs or symptoms of dehydration or hypovolemia should be promptly treated. This medicinal product can contain up to 2.35 mmol (54 mg) sodium per dose, depending on the required volume, and must be taken into consideration by patients on a controlled sodium diet. **Interactions:** No clinical interaction studies have been performed. Interactions with calcium and phosphate cannot be excluded. Safety and efficacy of concomitant chemotherapy with Xofigo have not been established. **Fertility, pregnancy & lactation:** Xofigo is not indicated in women. Results from animal studies, indicate there is a potential risk that radiation from Xofigo could cause adverse effects on fertility. Male patients should seek advice on conservation of sperm prior to treatment. Due to potential effects on spermatogenesis associated with radiation, men should be advised to use effective contraceptive methods during and up to 6 months after treatment with Xofigo. **Effects on ability to drive and use machines:** There is no evidence, nor is it expected, that Xofigo will affect the ability to drive or use machines. **Undesirable effects:** Very common: Thrombocytopenia, diarrhoea, vomiting, nausea, bone fracture. Common: Neutropenia, pancytopenia, leukopenia and injection site reactions. Uncommon: Lymphopenia, osteoporosis. Serious: Thrombocytopenia and neutropenia. Prescribers should consult the SmPC in relation to other side effects. **Overdose:** No specific antidote. In the event of an inadvertent overdose, general supportive measures, including monitoring for potential haematological and gastrointestinal toxicity should be undertaken. **Incompatibilities:** Do not mix with other medicinal products. **Special Precautions for Storage:** Store in accordance with national regulation on radioactive materials. **Legal Category:** POM. **Package Quantities & Basic NHS Costs:** Single vial pack £4040. **MA Number(s):** PLGB 00010/0710. **Further information available from:** Bayer plc, 400 South Oak Way, Reading, Berkshire, RG2 6AD United Kingdom. Telephone: 0118 206 3000. **Date of preparation: February 2025**

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Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in Google Play or Apple App Store.
Adverse events should also be reported to Bayer plc.
Tel: 0118 206 3500, Fax: 0118 206 3703, Email: pvuk@bayer.com