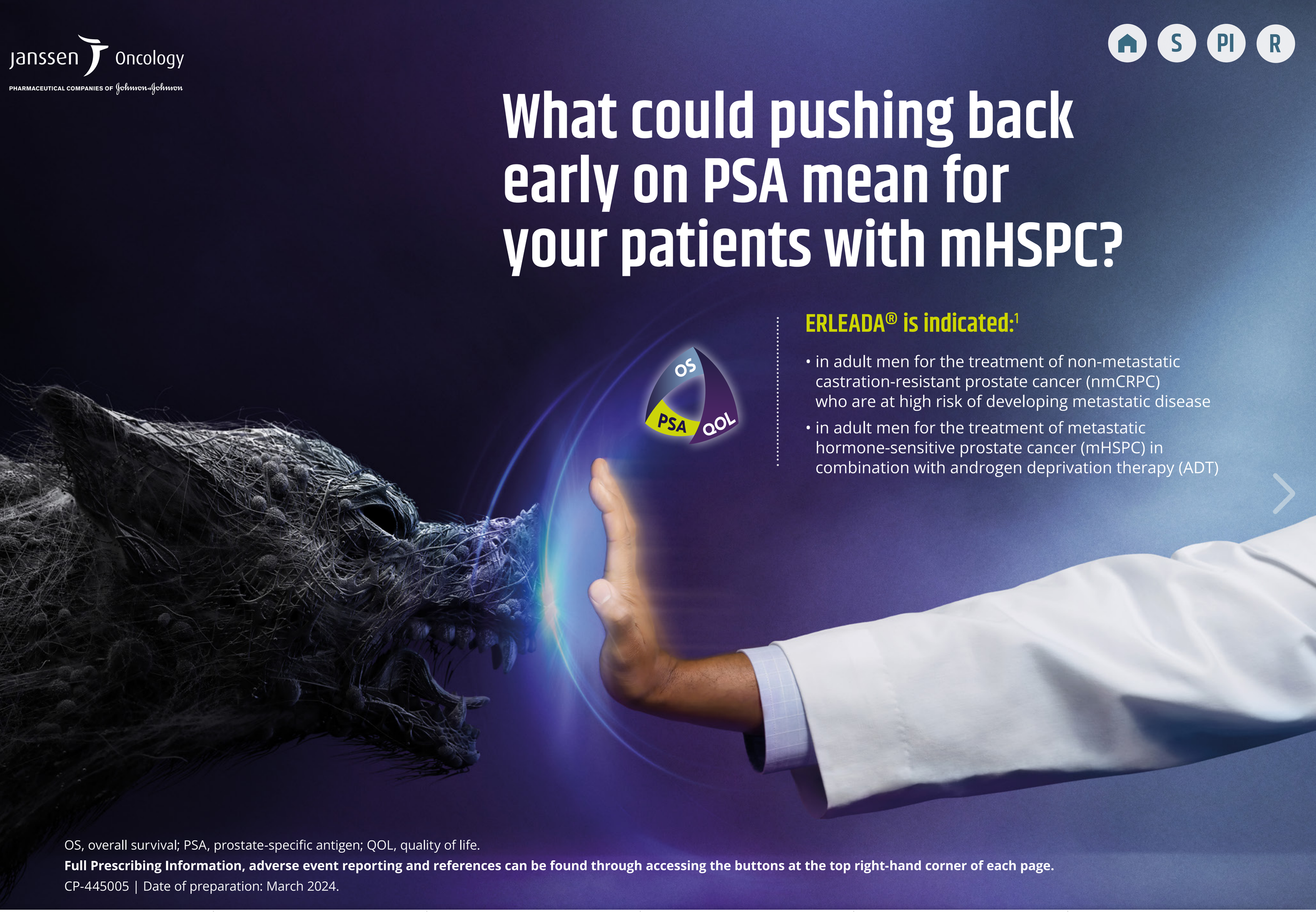
Janssen Oncology
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

S PI R

What could pushing back early on PSA mean for your patients with mHSPC?



ERLEADA® is indicated:[1]

- in adult men for the treatment of non-metastatic castration-resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease
- in adult men for the treatment of metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT)

OS, overall survival; PSA, prostate-specific antigen; QOL, quality of life.

Full Prescribing Information, adverse event reporting and references can be found through accessing the buttons at the top right-hand corner of each page.

CP-445005 | Date of preparation: March 2024.

A deep PSA response is an early marker for patient prognosis in mHSPC[2–6]

Rapid and deep PSA response correlates significantly with **extended survival** in patients with mHSPC, regardless of disease volume*[2,3]

Rapid and deep PSA response correlates significantly with **lower risk of HRQoL decline** in patients with mHSPC*[6]

Deep PSA response[2]	• PSA90 (PSA ≥90% decline from baseline) • Undetectable PSA (PSA reduction to ≤0.2 ng/mL)

HRQoL, health-related quality of life; mHSPC; metastatic hormone-sensitive prostate cancer; OS, overall survival; PSA, prostate-specific antigen; QOL, quality of life. *Compared to patients who don't achieve rapid and deep PSA responses.[2,3,6]

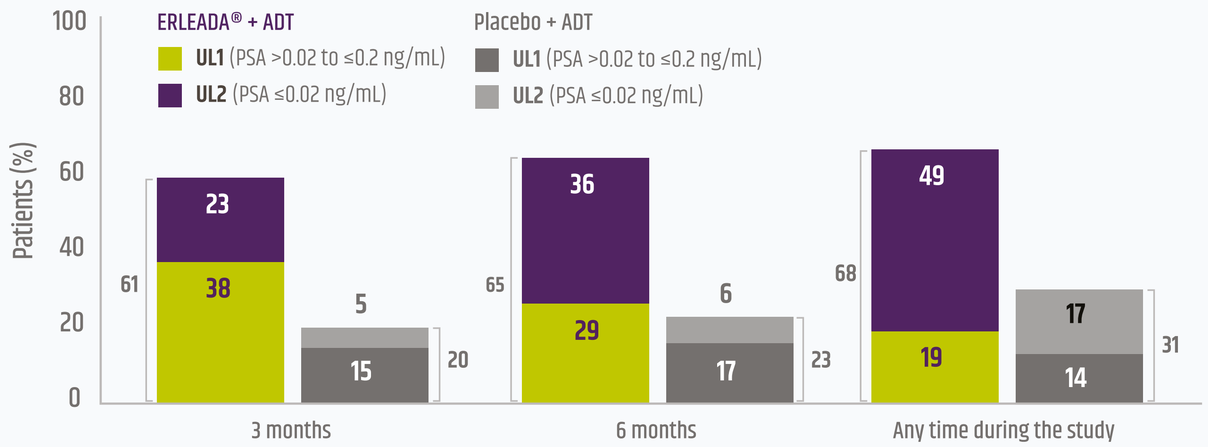
With ERLEADA® + ADT, >2x more patients with mHSPC achieved undetectable PSA vs. placebo + ADT[3]

Undetectable PSA response was investigated further and divided into two subcategories:[3]

Ultra-low 1 (UL1): >0.02 – ≤0.2 ng/mL

Ultra-low 2 (UL2): ≤0.02 ng/mL

Undetectable PSA at month 3, 6 and any time during the study[3]



Adapted from Merseburger AS, *et al.* 2023.[3]

A greater proportion of patients on ERLEADA® + ADT achieved undetectable PSA at 3 months than placebo + ADT[3]

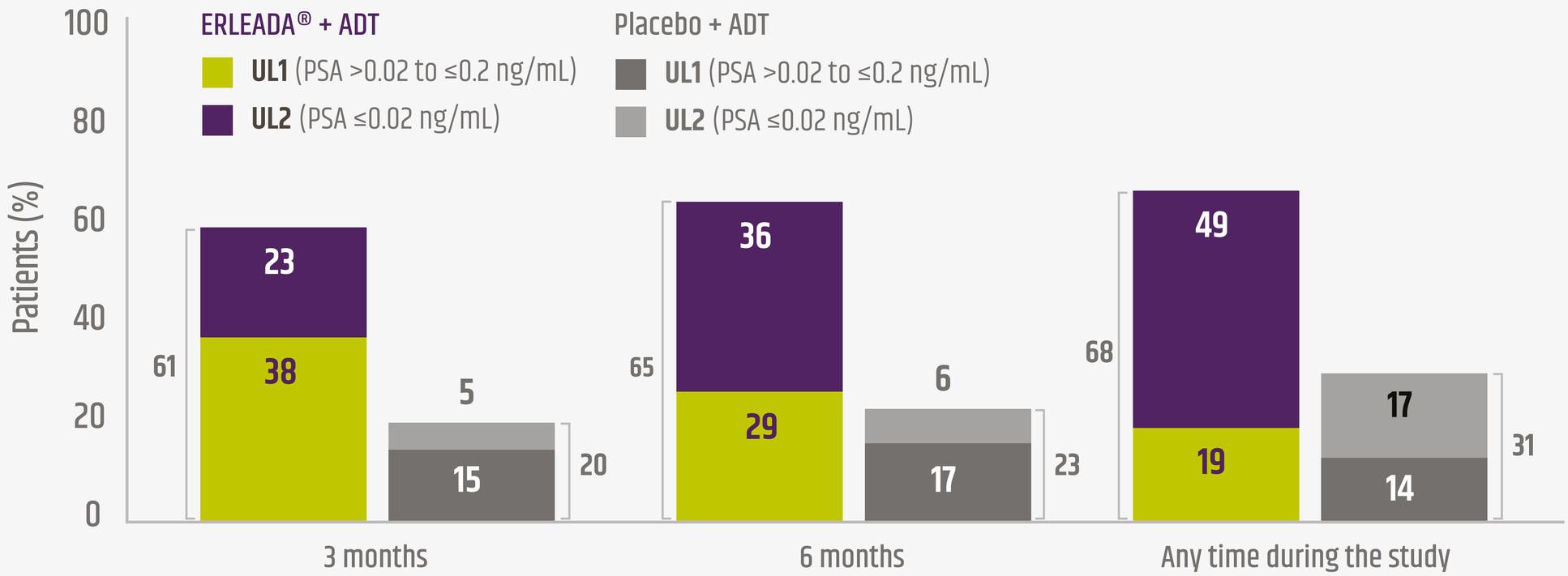
Achieving undetectable PSA with ERLEADA® + ADT is associated with an even greater OS benefit than not achieving such a response[2,3]

Patients were able to achieve undetectable PSA responses with ERLEADA® + ADT **regardless of disease volume and timing of metastasis presentation**[7]

Undetectable PSA by subgroup

ADT, androgen-deprivation therapy; HRQoL, health-related quality of life; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PSA, prostate-specific antigen; QOL, quality of life
UL1, ultra-low 1; UL2, ultra-low 2.

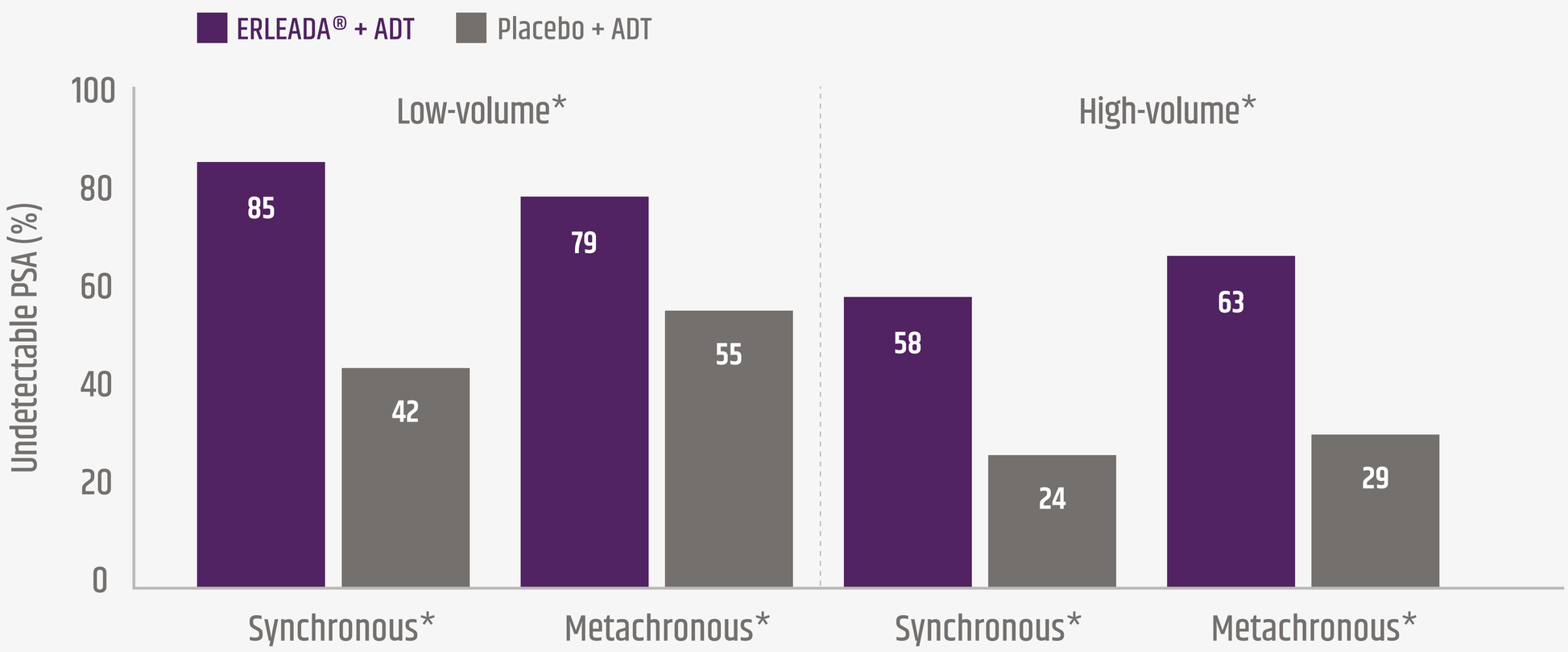
Undetectable PSA at month 3, 6 and any time during the study[3]



Adapted from Merseburger AS, *et al.* 2023.[3]

ADT, androgen-deprivation therapy; PSA, prostate-specific antigen; UL1, ultra-low 1; UL2, ultra-low 2.

Patients with confirmed best PSA reduction to ≤0.2 ng/mL (undetectable) at any time during the study[7]



Adapted from Merseburger AS, *et al.* 2023 (supplementary).[7]

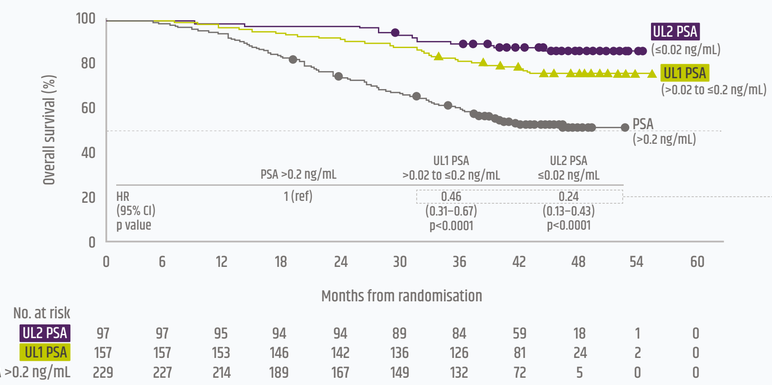
ADT, androgen-deprivation therapy; PSA, prostate-specific antigen. *High-volume disease was defined as either visceral metastases with ≥1 bone lesion or ≥4 bone lesions including one outside of the vertebral column or pelvis. Patients who did not meet the high-volume disease criteria were considered to have low-volume disease. Synchronous disease was defined as metastases at initial diagnosis; metachronous disease was defined as metastases developed after localised disease.[8]

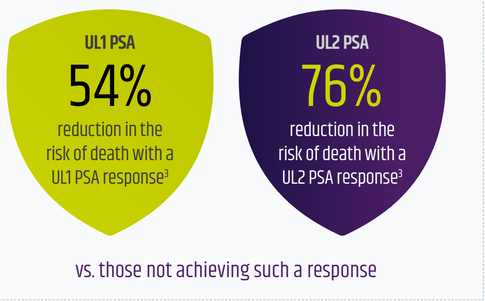
ERLEADA® + ADT offers the reassurance of rapid and deep PSA responses that correlate significantly with extended overall survival[2,3]

Undetectable PSA response with ERLEADA® + ADT at 3 months was associated with greater OS

vs. patients who did not achieve such a PSA response[2,3]

Undetectable PSA and OS in patients treated with ERLEADA® + ADT (44.0 months' median follow-up)[3]





Adapted from Merseburger AS, *et al.* 2023.[3]

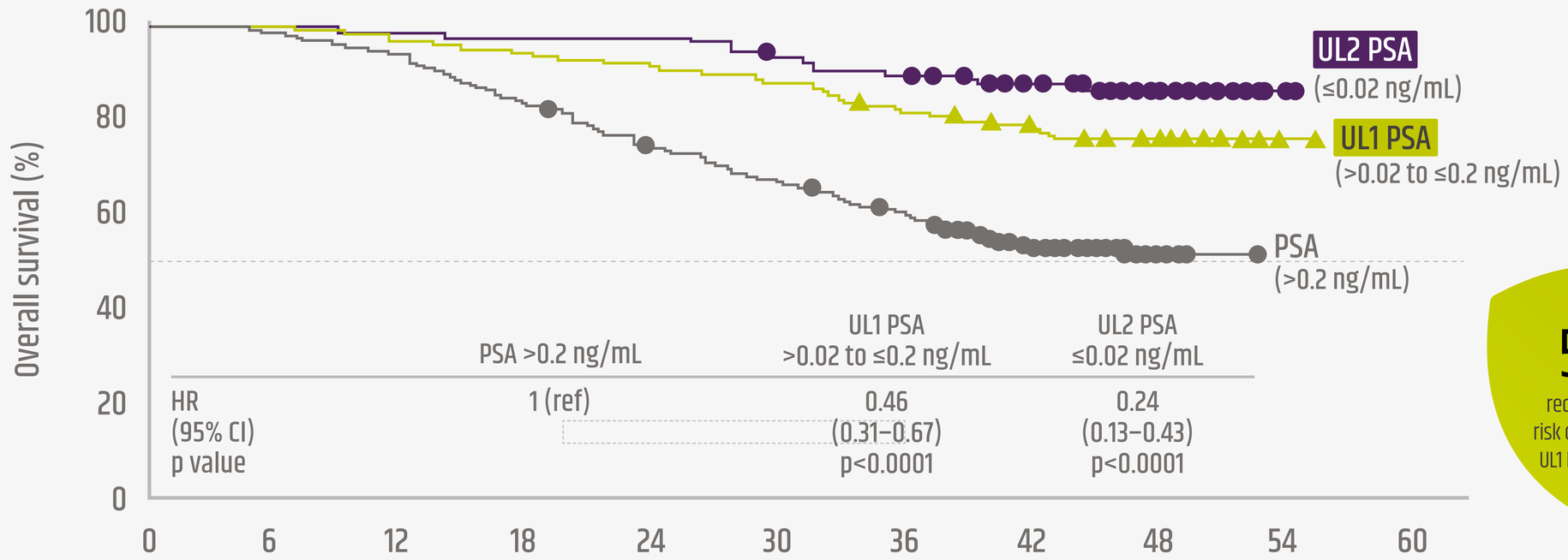
- ERLEADA® + ADT reduced the risk of death in patients achieving undetectable PSA at 3 months vs. not achieving such a response[3]
- The clinical benefits of ERLEADA® + ADT were more pronounced in patients achieving an UL2 PSA response vs. not achieving such a response[3]

OS benefit favoured ERLEADA® + ADT vs. placebo + ADT **regardless of disease volume and timing of metastasis presentation***[8]

- Hazard ratios for OS in metachronous/high-volume and synchronous/low-volume subgroups were very similar to those in the synchronous/high-volume subgroup (HR=0.68; 95% CI: 0.53–0.87, p=0.002), supporting the consistency of benefit across the three subgroups.[8] In the metachronous/low-volume subgroup, risk of death was reduced by 78% with ERLEADA® + ADT vs. placebo + ADT (HR=0.22; 95% CI: 0.09–0.55, p=0.001)[8]

ADT, androgen-deprivation therapy; CI, confidence interval; HR, hazard ratio; HRQoL, health-related quality of life; mHSPC, metastatic hormone-sensitive prostate cancer; MOA, mode of action; OS, overall survival; PSA, prostate-specific antigen; QOL, quality of life; UL1, ultra-low 1; UL2, ultra-low 2. *High-volume disease was defined as either visceral metastases with ≥1 bone lesion or ≥4 bone lesions including one outside of the vertebral column or pelvis. Patients who did not meet the high-volume disease criteria were considered to have low-volume disease. Synchronous disease was defined as metastases at initial diagnosis; metachronous disease was defined as metastases developed after localised disease.[8]

Undetectable PSA and OS in patients treated with ERLEADA® + ADT (44.0 months' median follow-up)[3]



No. at risk

UL2 PSA	97	97	95	94	94	89	84	59	18	1	0
UL1 PSA	157	157	153	146	142	136	126	81	24	2	0
PSA >0.2 ng/mL	229	227	214	189	167	149	132	72	5	0	0

UL1 PSA
54%
reduction in the risk of death with a UL1 PSA response[3]

UL2 PSA
76%
reduction in the risk of death with a UL2 PSA response[3]

vs. those not achieving such a response

Adapted from Merseburger AS, *et al.* 2023.[3]

ADT, androgen-deprivation therapy; CI, confidence interval; HR, hazard ratio; OS, overall survival; PSA, prostate-specific antigen; UL1, ultra-low 1; UL2, ultra-low 2.

ERLEADA® + ADT provides rapid and deep PSA responses that correlate significantly with maintained HRQoL in mHSPC[6]

In TITAN, rapid and deep PSA declines with ERLEADA® + ADT were associated with:[6]

Reduced risk of decline in:

HRQoL

Total FACT-P score*

HR=0.54; 95% CI: 0.38–0.76;
Events/N: 54/127

Physical wellbeing

Physical wellbeing score*

HR=0.63; 95% CI: 0.45–0.89;
Events/N: 65/128

Reduced risk of progression in:

Pain

BPI-SF worst pain intensity*

HR=0.70; 95% CI: 0.49–1.00;
Events/N: 58/169

Fatigue

BFI worst fatigue intensity*

HR=0.76; 95% CI: 0.53–1.10;
Events/N: 56/212

...vs. patients who did not achieve such a PSA response

ADT, androgen-deprivation therapy; BFI, Brief Fatigue Inventory; BPI-SF, Brief Pain Inventory-Short Form; CI, confidence interval; FACT-P, Functional Assessment of Cancer Therapy – Prostate; HR, hazard ratio; HRQoL, health-related quality of life; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PSA, prostate-specific antigen; QOL, quality of life. *Based on meaningful change thresholds from baseline in patient-reported outcomes: FACT-P total: ≥10 points; Physical well-being: ≥3 points; BPI-SF worst pain: ≥30% baseline, BFI worst fatigue: ≥2 points.[6]

ERLEADA® specificity and high affinity receptor binding may underlie the superior PSA response achieved in patients with mHSPC

vs. enzalutamide + ADT[9,10]

Real-world patients with mHSPC who received ERLEADA® + ADT were more likely to achieve deep and rapid PSA responses which were associated with improved long-term survival outcomes vs. those receiving enzalutamide + ADT[9,11]

ERLEADA® has been shown to selectively* inhibit androgen receptor (AR) translocation and subsequent signalling[10]

ERLEADA® binds AR with 1.3-fold greater affinity than enzalutamide†[10]

This mechanism of action, along with that of ADT, may underlie the superior PSA decline patients with mHSPC achieved with ERLEADA® + ADT vs. enzalutamide + ADT[9,10]

ADT, androgen-deprivation therapy; mHSPC, metastatic hormone-sensitive prostate cancer; MOA, mode of action; PSA, prostate-specific antigen; RWE, real-world evidence. *ERLEADA® binding is selective for AR vs. for other nuclear hormone receptors (e.g., estrogen, progesterone, or glucocorticoid receptors).[10] †Based on ligand-binding studies in whole-cell assay (LNCaP/AR(cs)) xenograft tumour models treated with ERLEADA® vs. vehicle or bicalutamide.[10]

See PSA through the patient's eyes

mHSPC can strike indiscriminately[1,2]

ERLEADA® + ADT improves clinical outcomes in mHSPC while maintaining quality of life.[2,3,6,13]

Tarek, 71*

Metachronous mHSPC

View Tarek's case study »

Khaled, 63*

Synchronous mHSPC

View Khaled's case study »

ADT, androgen-deprivation therapy; mHSPC, metastatic hormone-sensitive prostate cancer; PSA, prostate-specific antigen.*Fictional patient based on the clinical characteristics of mHSPC patients included in the TITAN study.[12]

See PSA through the patient's eyes

Elevated PSA levels are associated with higher levels of anxiety in patients with prostate cancer.[14]

Tarek*

Age: 71[15]

History: Localised prostate cancer treated with radiotherapy and radical prostatectomy[12,15]

Current diagnosis: Metachronous metastatic hormone-sensitive prostate cancer (mHSPC)[15]

Disease volume:†
Low – 2 bone metastases on bone scan[15]

PSA: 18.6 ng/mL[12]

Gleason score: 8 (4+4)[12]

Comorbidities:
Borderline diabetes[16]

Many patients monitor their PSA level, documenting the results of their PSA tests and watching for changes to help them cope with uncertainty.[17]

Could a rapid and deep PSA response with ERLEADA® + ADT give your patients with mHSPC the reassurance they need?[2,3]

ADT, androgen-deprivation therapy; mHSPC, metastatic hormone-sensitive prostate cancer; PSA, prostate-specific antigen.*Fictional patient based on the clinical characteristics of mHSPC patients included in the TITAN study.[12] †In TITAN, high-volume disease was defined as visceral metastases and ≥1 bone lesion or ≥4 bone lesions with ≥1 outside of the vertebral column/pelvis. Low-volume disease was defined as the presence of bone lesions not meeting high-volume definition.[8] ‡Fictional quotes reflecting real patients' feelings.[17] ¶In mHSPC, ERLEADA® is taken in combination with ADT.[1]

See PSA through the patient's eyes

Elevated PSA levels are associated with higher levels of anxiety in patients with prostate cancer.[14]

Khaled*

Age: 63[15]

History: No previous history of prostate cancer[13,15]

Current diagnosis: Synchronous metastatic hormone-sensitive prostate cancer (mHSPC)[15]

Disease volume:† High – liver metastases‡; 6 bone metastases on bone scan[12,15]

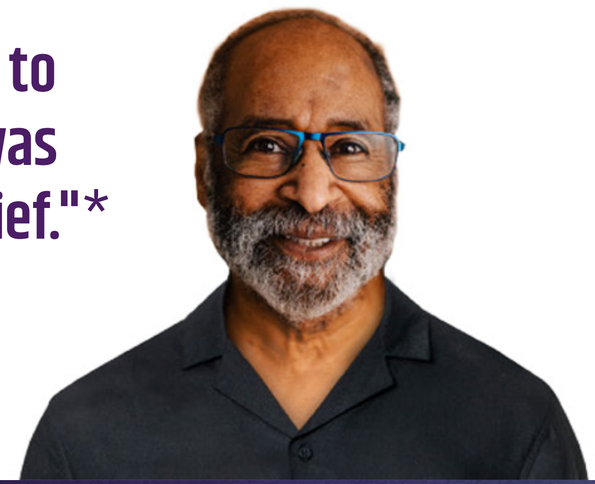
Disease risk:¶ High[12]

PSA: 124 ng/mL[15]

Gleason score: 8 (4+4)[15]

Comorbidities:§# Hypertension, mild renal insufficiency and hypercholesterolaemia[1,16]
– active smoker (15 packs a month)

"As my PSA started to come down, it was such a relief."*



When patients' PSA levels drop, it is often accompanied by a sense of relief and can have a positive impact on how they feel about their prostate cancer.[14,18]

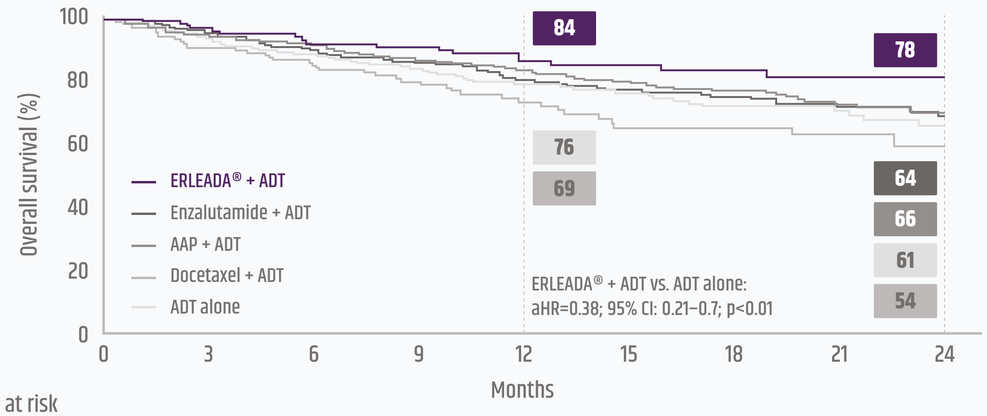
Could a rapid and deep PSA response with ERLEADA® + ADT make the difference for your patients with mHSPC?[2,3]

ADT, androgen-deprivation therapy; mHSPC, metastatic hormone-sensitive prostate cancer; PSA, prostate-specific antigen. *Fictional patient based on the clinical characteristics of mHSPC patients included in the TITAN study.[12] †In TITAN, high-volume disease was defined as visceral metastases and ≥1 bone lesion or ≥4 bone lesions with ≥1 outside of the vertebral column/pelvis. Low-volume disease was defined as the presence of bone lesions not meeting high-volume definition.[8] ‡No dose adjustment is necessary for patients with baseline mild or moderate hepatic impairment. ERLEADA® is not recommended in patients with severe hepatic impairment as there are no data in this patient population and apalutamide is primarily hepatically eliminated.[1] ¶In TITAN, patients were considered to be high risk if they had a Gleason score of ≥8, ≥1 lesion on bone scanning and the presence of measurable visceral metastasis.[13,19] §If ERLEADA® is prescribed, patients with clinically significant cardiovascular disease should be monitored for risk factors such as hypercholesterolaemia, hypertriglyceridaemia, or other cardio-metabolic disorders.[1] #No dose adjustment is necessary for patients with mild to moderate renal impairment. Caution is required in patients with severe renal impairment as ERLEADA® has not been studied in this patient population.[1] ||In mHSPC, ERLEADA® is taken in combination with ADT.[1]

In the real-world setting, rapid and deep PSA responses favoured **ERLEADA® + ADT** vs. other novel hormonal therapies (NHTs)[20]

A greater proportion of patients achieved undetectable PSA at 3 months with ERLEADA® + ADT vs. AAP + ADT and enzalutamide + ADT, which translated into longer OS vs. the other NHTs*[9,20]

OS by initial treatment compared to ADT alone[9,20]



No. at risk

ERLEADA® + ADT (N=165)	**144**	**132**	**107**	**85**	**63**	**51**	**37**	**23**	**12**
Enzalutamide + ADT (N=643)	394	342	283	225	169	120	93	56	35
AAP + ADT (N=1064)	555	490	429	351	270	206	153	102	70
Docetaxel + ADT (N=293)	131	113	93	69	50	39	32	20	12
ADT alone (N=543)	308	252	198	150	113	86	65	41	27

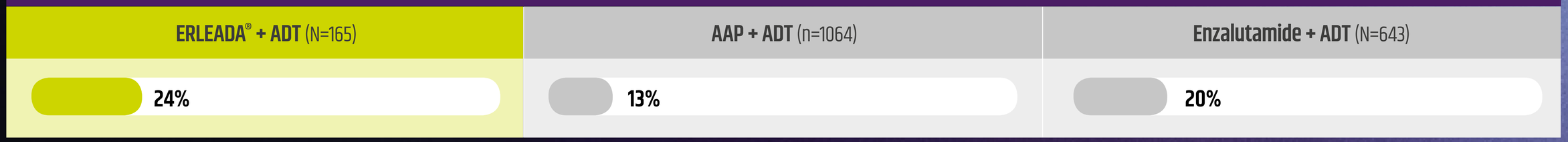
Adapted from Maughan BL, *et al*. 2024.[20]

ERLEADA® + ADT reduced the risk of death by:*[20]

ERLEADA® + ADT
50%
vs. enzalutamide + ADT
(aHR=0.50;
95% CI: 0.28–0.92;
p<0.05)

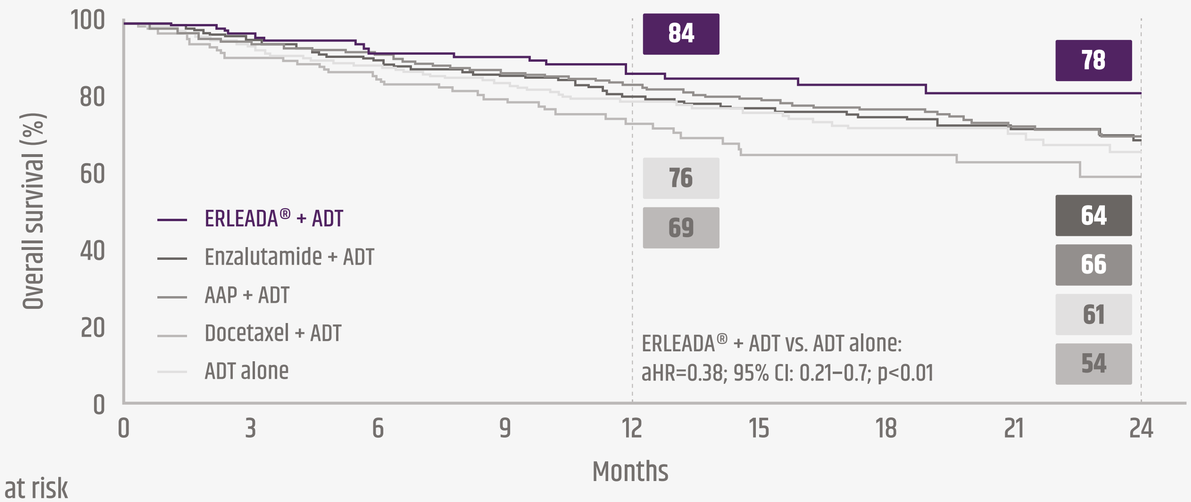
ERLEADA® + ADT
49%
vs. AAP + ADT
(aHR=0.51;
95% CI: 0.29–0.90;
p<0.05)

Undetectable PSA at 3 months[9]



AAP, abiraterone acetate + prednisone; ADT, androgen-deprivation therapy; aHR, adjusted hazard ratio; CI, confidence interval; HR, hazard ratio; mHSPC, metastatic hormone-sensitive prostate cancer; MOA, mode of action; NHT, novel hormonal therapy; PSA, prostate-specific antigen. *Data from a retrospective, observational cohort study evaluated clinical outcomes in adult patients with mHSPC using the ConcertAI RWD 360 prostate cancer dataset. All patients with newly diagnosed mHSPC from 1 Jan 2018 to 30 Sept 2022 were enrolled and followed up until 31 Mar 2023. Outcomes were assessed using the Kaplan-Meier method.[20]

OS by initial treatment compared to ADT alone[9,20]



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TITAN is a robust, large-scale, double-blind, randomised, placebo-controlled, international, Phase III study that included a broad population of patients with mHSPC, regardless of their disease status at baseline[13,15,16]

PRIOR TREATMENT:[16]

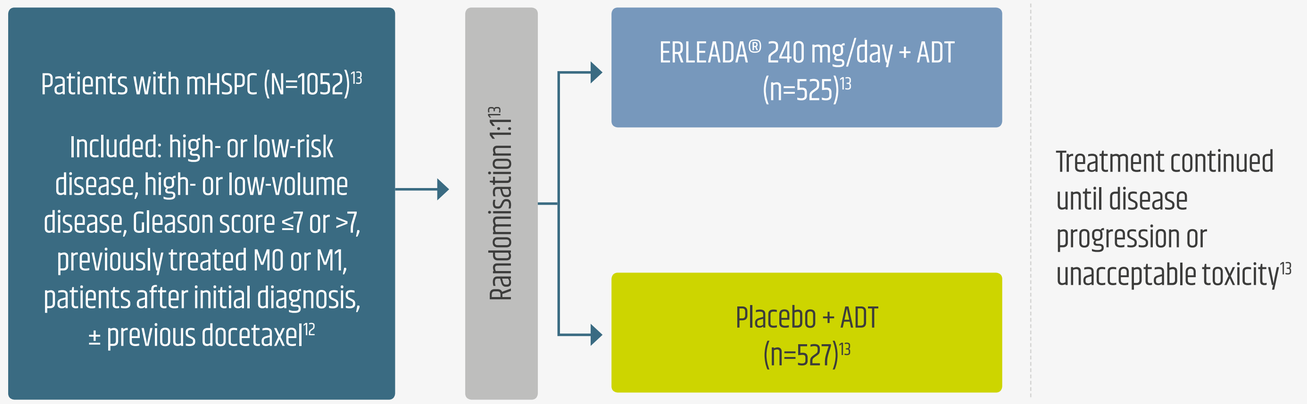
- Previous docetaxel (≤6 cycles, with no evidence of progression during treatment or before randomisation)
- ADT for ≤6 months
- One course of radiation or surgery completed before randomisation

PRIMARY ENDPOINT OUTCOMES*

- ERLEADA® + ADT significantly reduced risk of death by 35% vs. placebo (median OS not reached vs. 52.2 months; HR=0.65; 95% CI: 0.53–0.79; p<0.0001) and by 48% after adjustment for crossover (HR=0.52; 95% CI: 0.42–0.64; p<0.0001)[13]
- rPFS at 24 months was 68.2% for ERLEADA® + ADT and 47.5% for placebo + ADT (HR=0.48 for radiographic progression or death, 95% CI: 0.39–0.60; p<0.001), for a 52% lower risk of radiographic progression or death with ERLEADA®[16]

POST-HOC ANALYSES

- PROs were assessed at baseline, at specific treatment cycles and post progression using standardised questionnaires[6,13]
- PSA decline and time to subsequent deterioration in PROs were calculated at 3 and 6 months (landmark analyses)[6]
- PSA kinetics evaluated at final analysis; Cox proportional-hazards models and Kaplan-Meier methods were used to evaluate time-to-event data and association of OS with achievement of PSA responses[2]



DUAL PRIMARY ENDPOINTS:[16]	SECONDARY ENDPOINTS:[16]	EXPLORATORY ENDPOINTS:[16]	OTHER ENDPOINTS INCLUDED:[13]
• OS • rPFS	• Time to initiation of cytotoxic chemotherapy • Time to pain progression • Time to chronic opioid use • Time to skeletal-related event	• Time to PSA progression • Second progression-free survival (PFS2) • Time to symptomatic progression	• PROs (HRQoL)

ADT, androgen deprivation therapy; HRQoL, health-related quality of life; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PFS2, second progression-free survival; PRO, patient-reported outcome; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival.*OS from final analysis; median follow-up of 44.0 months.[2] rPFS from first prespecified interim analysis; median follow-up 22.7 months.[16]

ERLEADA® prescribing information

Scan the QR code to view the full SmPC

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