Janssen Oncology

PHARMACEUTICAL COMPANIES OF Johnson & Johnson

PI R

# Push back early. Extend life.[1–3]

**Doublet therapy with ERLEADA® + ADT provides robust and long-term benefits in mHSPC,** including for synchronous high-volume disease—offering **a net clinical benefit** in terms of survival and potential AEs vs. placebo + ADT **that triplet therapy (NHT + ADT + docetaxel) is less likely to offer.***[2–6]

ADT, androgen deprivation therapy; AE, adverse event; mHSPC, metastatic hormone-sensitive prostate cancer, NHT, novel hormonal therapy.

ERLEADA® is indicated:[1]

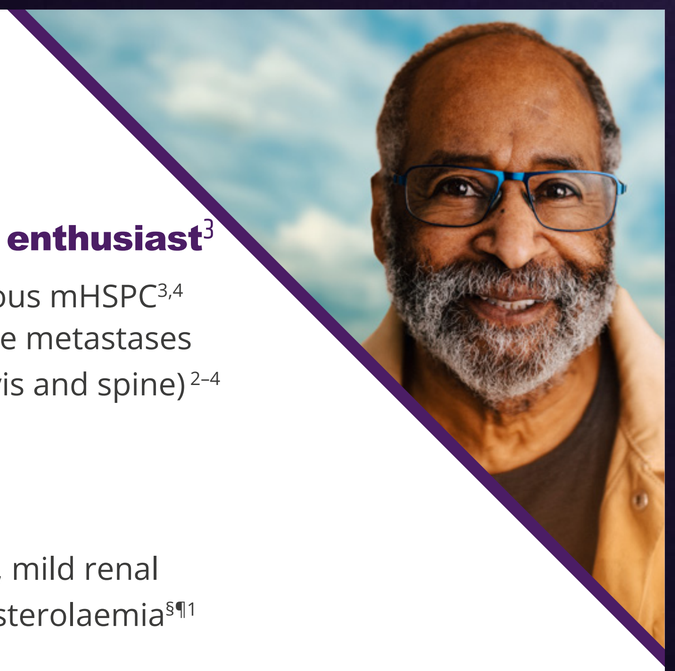
- in adult men for the treatment of non-metastatic castration-resistant prostate cancer (nmCRPC) who are at high risk of developing metastatic disease
- in adult men for the treatment of metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT)

*Triplet therapy includes docetaxel + ADT + NHTs (abiraterone acetate or darolutamide). The net clinical benefit vs. triplet therapy is due to the lower frequency of adverse events (grades 3–5) with ERLEADA® + ADT.[6]

Full prescribing information, adverse events reporting, and references can be found through accessing the buttons at the top right-hand corner of each page

CP-444974 | Date of preparation: March 2024

# How can ERLEADA® + ADT benefit patients like Khaled and Tarek*?



## Khaled,
### 75-year-old classic car enthusiast[3]

Current diagnosis: Synchronous mHSPC[3,4]
Disease volume: High† (9 bone metastases [on bone scan] including pelvis and spine)[2–4]
Disease risk: High‡[2,3]
PSA: 124 ng/mL[3]
Gleason score: 8 (4+4)[2,3]
Comorbidities: Hypertension, mild renal insufficiency and hypercholesterolaemia§¶[1]

Khaled has **synchronous high-volume mHSPC**, which has a poor prognosis.[4]

He wants to extend the time he has left, and continue restoring his classic car.

## Tarek,
### 64-year-old restaurant owner[3]

Current diagnosis: Metachronous mHSPC[3,4]
Disease volume: Low† (3 bone metastases)[2–4]
Disease risk: High‡[2,3]
PSA: 16 ng/mL[3]
Gleason score: 8 (4+4)[2,3]
Comorbidities: Moderate hepatic impairment (Child-Pugh B)‖[1]

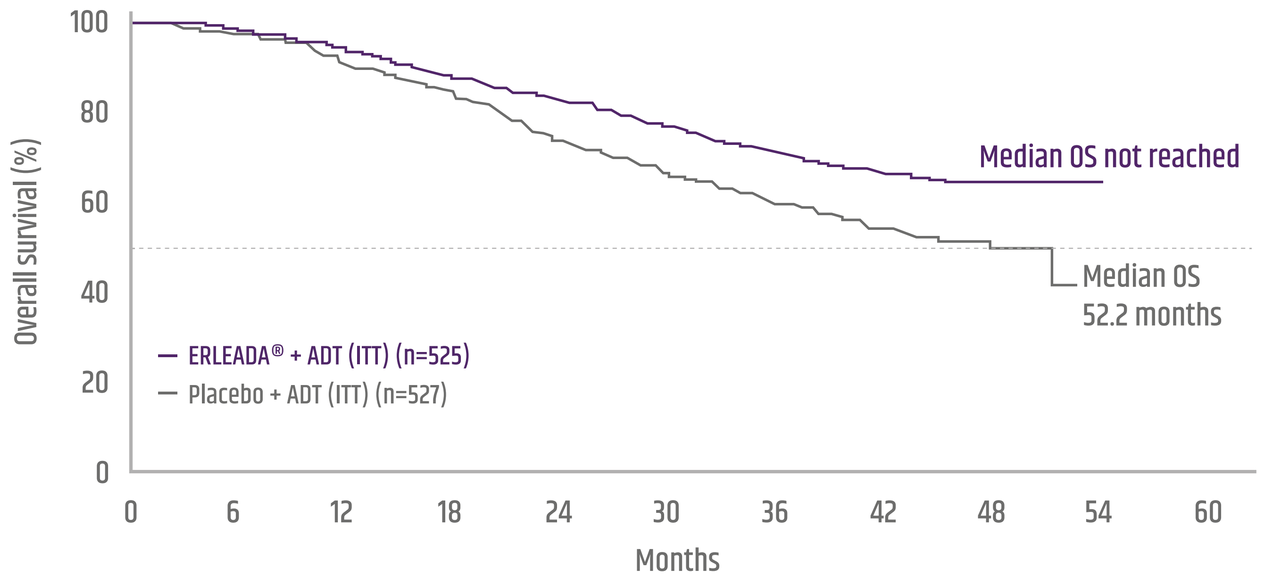
Tarek fears that the side effects of treatment may prevent him from running his business.

He wants to slow the progression of his mHSPC, without slowing down himself.

ADT, androgen deprivation therapy; mHSPC, metastatic hormone-sensitive prostate cancer; PSA, prostate-specific antigen. *Fictional patients based on the clinical characteristics of mHSPC patients included in the TITAN study.[2,3] †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.[3] ‡In TITAN, patients were considered to be high risk if they had a Gleason score of ≥8, ≥1 lesion on bone scan and the presence of measurable visceral metastasis.[3] §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] ‖No dose adjustment is necessary for patients with baseline mild or moderate hepatic impairment (Child-Pugh Class A and B, respectively).[1]

# Upfront use of ERLEADA® + ADT in mHSPC extends life vs. placebo + ADT[2,7]

TITAN OS (ITT population)*[2]




No. at risk

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ERLEADA® + ADT | 525 | 513 | 489 | 452 | 425 | 394 | 362 | 227 | 52 | 3 | 0 |
| Placebo + ADT | 527 | 510 | 474 | 436 | 374 | 339 | 301 | 181 | 43 | 0 | 0 |

Adapted from Chi KN, *et al.* 2021.[2]

TITAN OS (after adjustment for crossover)*[2]

At 44.0 months' median follow-up[2]

**35%**

reduction in the risk of death
in the ITT population vs. placebo + ADT
(HR=0.65; 95% CI: 0.53–0.79; p<0.0001)[2]

In a statistical extrapolation of the TITAN study, ERLEADA® + ADT offers a predicted median OS of:

~6 years vs. 3.3 years with placebo + ADT†[7]

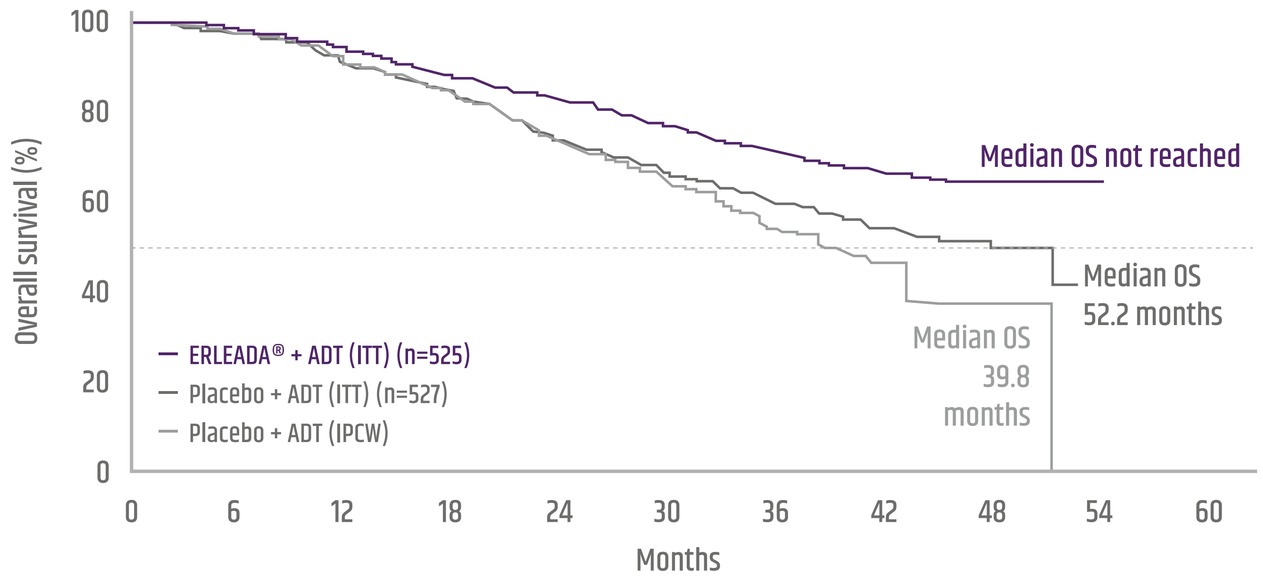
In a network meta-analysis, doublet therapy with ERLEADA® + ADT offers:

Comparable OS benefits to triplet therapy (NHT + ADT + docetaxel)‡[5]

ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; HRQoL, health-related quality of life; IPCW, inverse probability of censoring weighting; ITT, intention to treat; mHSPC, metastatic hormone-sensitive prostate cancer; NHT, novel hormonal therapy; OS, overall survival; RCT, randomised controlled trial; rPFS, radiographic progression-free survival. *Data are from TITAN, a double-blind, randomised, placebo-controlled international Phase III study evaluating ERLEADA® + ADT vs. placebo + ADT in patients with mHSPC, regardless of their disease stage at baseline (N=1052). Patients with severe angina, myocardial infarction, congestive heart failure, arterial or venous thromboembolic events, a history of or predisposition to seizure, or recent ventricular arrhythmias were excluded. Dual primary endpoints of the TITAN study were radiographic progression-free survival (rPFS) and overall survival (OS). rPFS was estimated as the time from randomisation to first imaging-based documentation of disease progression or death, whichever occurred first. Median follow-up of 44.0 months.[2,3] †In a statistical extrapolation of the TITAN study, using validated survival models. Predicted median OS of 71.5 months with ERLEADA® + ADT vs. 39.5 months with placebo + ADT.[7] ‡Triplet therapy includes docetaxel + ADT + NHTs (abiraterone acetate or darolutamide). Results from a meta-analysis of ten Phase 3 RCTs that investigated an NHT + ADT + docetaxel or docetaxel + ADT alone and compared the effect on survival outcomes of available systemic treatments for mHSPC (abiraterone acetate + ADT, enzalutamide + ADT, ERLEADA® + ADT, docetaxel + ADT, and docetaxel + darolutamide + ADT).[5]

# Upfront use of ERLEADA® + ADT in mHSPC extends life vs. placebo + ADT[2,7]

TITAN OS (ITT population)*[2]




| No. at risk | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ERLEADA® + ADT | 525 | 513 | 489 | 452 | 425 | 394 | 362 | 227 | 52 | 3 | 0 |
| Placebo + ADT | 527 | 510 | 474 | 436 | 374 | 339 | 301 | 181 | 43 | 0 | 0 |

Adapted from Chi KN, *et al.* 2021.[2]

TITAN OS (after adjustment for crossover)*[2]

**At 44.0 months' median follow-up[2]**

**48%**

reduction in the risk of death after adjustment for crossover (208/527 patients on placebo + ADT crossed over to ERLEADA® + ADT) vs. placebo + ADT

(HR=0.52; 95% CI: 0.42–0.64; p<0.0001)[2]

In a statistical extrapolation of the TITAN study, ERLEADA® + ADT offers a predicted median OS of:

~6 years vs. 3.3 years with placebo + ADT†[7]

In a network meta-analysis, doublet therapy with ERLEADA® + ADT offers:

Comparable OS benefits to triplet therapy (NHT + ADT + docetaxel)‡[5]

ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; HRQoL, health-related quality of life; IPCW, inverse probability of censoring weighting; ITT, intention to treat; mHSPC, metastatic hormone-sensitive prostate cancer; NHT, novel hormonal therapy; OS, overall survival; RCT, randomised controlled trial; rPFS, radiographic progression-free survival. *Data are from TITAN, a double-blind, randomised, placebo-controlled international Phase III study evaluating ERLEADA® + ADT vs. placebo + ADT in patients with mHSPC, regardless of their disease stage at baseline (N=1052). Patients with severe angina, myocardial infarction, congestive heart failure, arterial or venous thromboembolic events, a history of or predisposition to seizure, or recent ventricular arrhythmias were excluded. Dual primary endpoints of the TITAN study were radiographic progression-free survival (rPFS) and overall survival (OS). rPFS was estimated as the time from randomisation to first imaging-based documentation of disease progression or death, whichever occurred first. Median follow-up of 44.0 months.[2,3] †In a statistical extrapolation of the TITAN study, using validated survival models. Predicted median OS of 71.5 months with ERLEADA® + ADT vs. 39.5 months with placebo + ADT.[7] ‡Triplet therapy includes docetaxel + ADT + NHTs (abiraterone acetate or darolutamide). Results from a meta-analysis of ten Phase 3 RCTs that investigated an NHT + ADT + docetaxel or docetaxel + ADT alone and compared the effect on survival outcomes of available systemic treatments for mHSPC (abiraterone acetate + ADT, enzalutamide + ADT, ERLEADA® + ADT, docetaxel + ADT, and docetaxel + darolutamide + ADT).[5]

# Upfront use of ERLEADA® + ADT in mHSPC extends life vs. placebo + ADT, regardless of disease volume[2,4,7]

## In patients with synchronous high-volume mHSPC[4,7]

**Synchronous high-volume mHSPC[4]**

**32%**

reduction in the risk of death vs. placebo + ADT, at 44 months' median follow-up[2,4]

(HR=0.68; 95% CI: 0.53–0.87; p=0.002)*[4]

**Synchronous high-volume mHSPC[7]**

**>1.5 years**

(52.1 months)

longer predicted median OS

(vs. 33.4 months with placebo + ADT)†[7]

## In patients with metachronous and/or low-volume mHSPC[4,7]

**Metachronous low-volume mHSPC[4]**

**78%**

reduction in the risk of death vs. placebo + ADT, at 44 months' median follow-up[2,4]

(HR=0.22; 95% CI: 0.09–0.55; p=0.001)*[4]

**Low-volume mHSPC[7]**

**5.5 years**

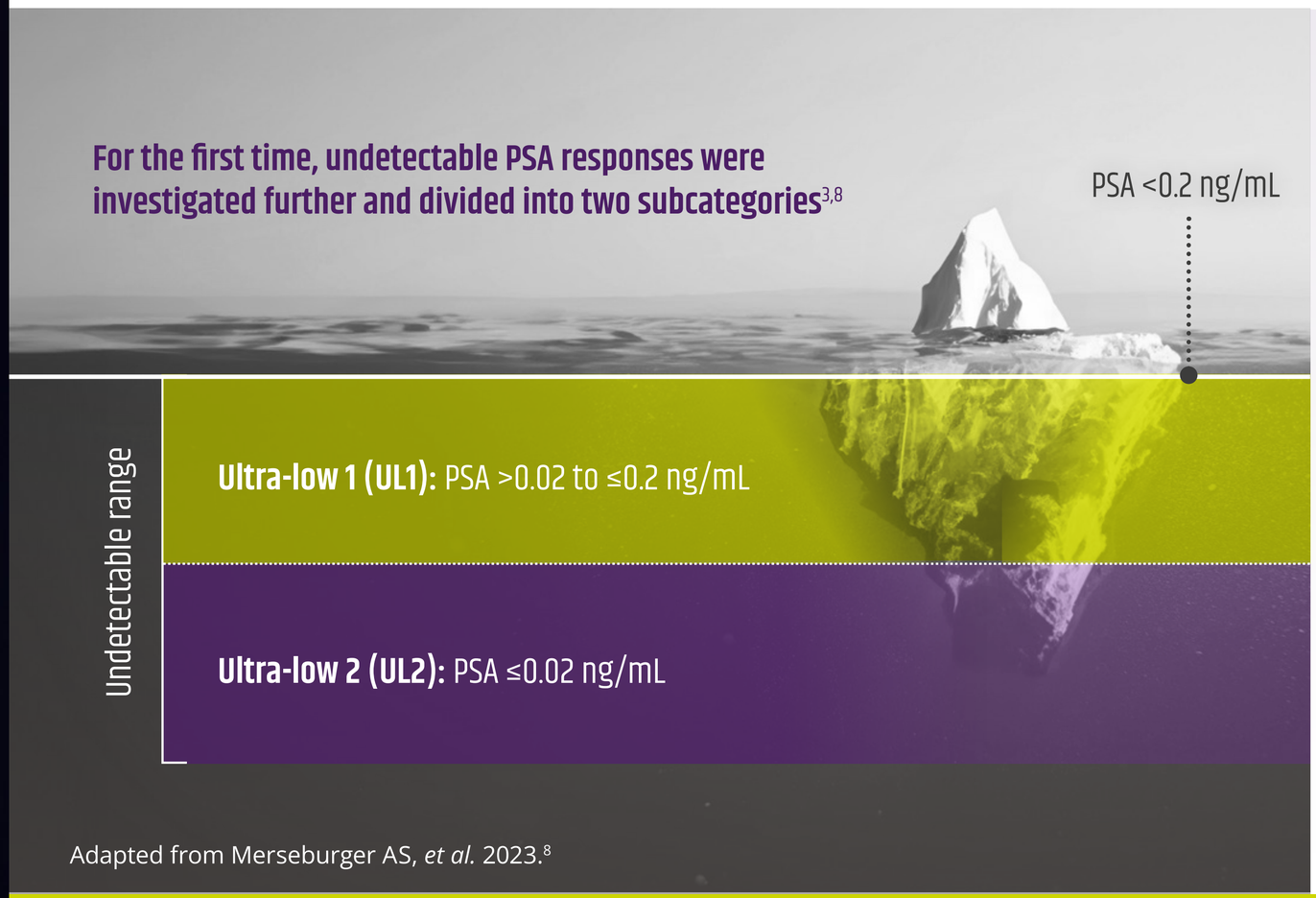
(113.7 months)

longer predicted median OS

(vs. 47.3 months with placebo + ADT)†[7]

ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; ITT, intention to treat; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival. *In a *post-hoc* analysis of TITAN subgroup data.[4] †In a statistical extrapolation of the TITAN study, using validated survival models.[7]

# Upfront use of ERLEADA® + ADT in mHSPC takes undetectable PSA responses to a new low*[8]




Adapted from Merseburger AS, *et al.* 2023.[8]

- UL2 PSA (≤0.02 ng/mL) is 10x lower than the current threshold for undetectable PSA[8]
- ERLEADA® + ADT can reduce PSA levels to ≤0.02 ng/mL, even in patients with high-volume disease[8]

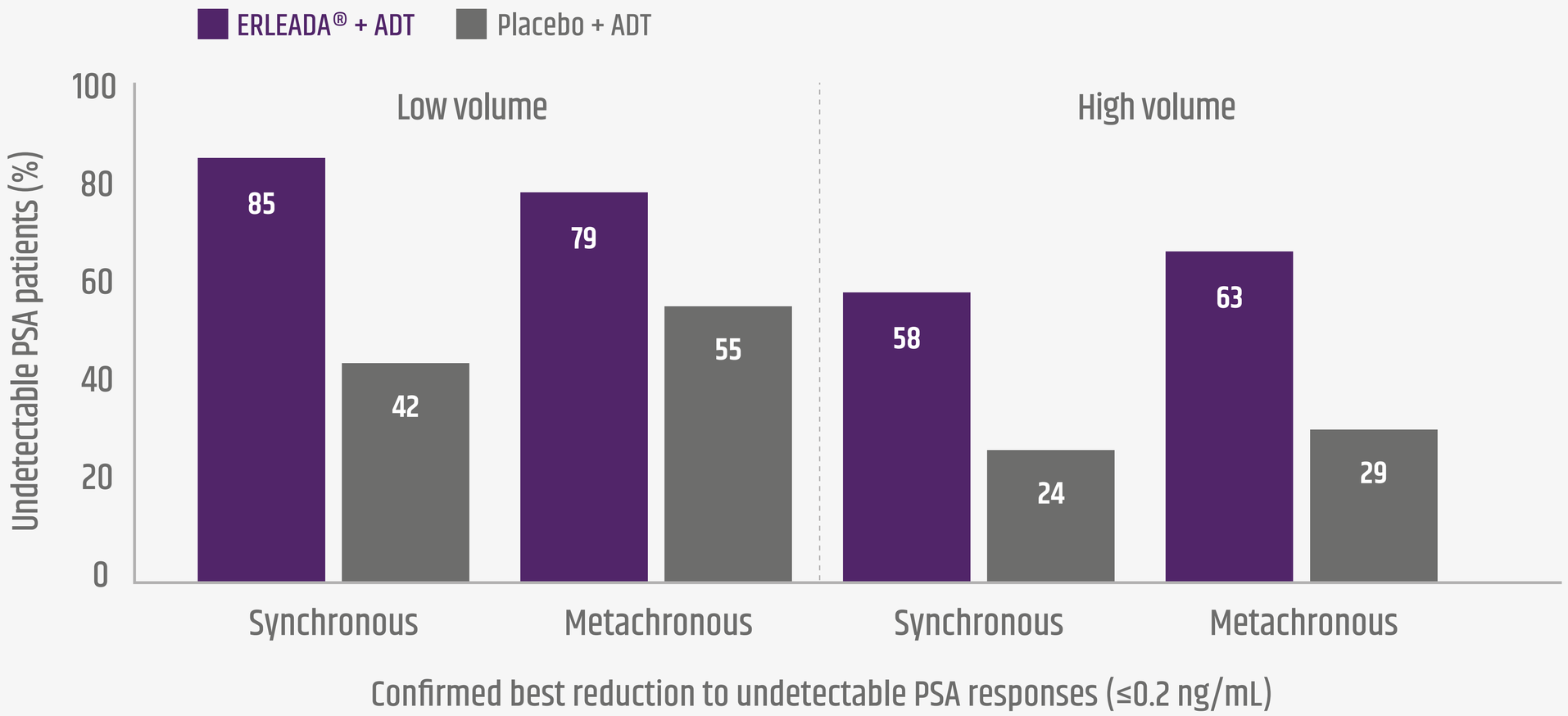
**Undetectable PSA responses by disease volume**[9] +

**Rapid UL1 or UL2 PSA responses**[8] +

**A UL1 or UL2 PSA response with ERLEADA® + ADT translates into superior clinical benefits,† regardless of disease volume,** vs. those not achieving such a response[8,9]

ADT, androgen deprivation therapy; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival; TTCR, time to castration resistance; UL, ultra-low; UL1, ultra-low 1 (PSA: >0.02 to ≤0.2 ng/mL); UL2, ultra-low 2 (PSA: ≤0.02 ng/mL). *In a *post-hoc* analysis of the TITAN study, patients with evaluable PSA values.[8] †Superior clinical benefits include improved OS, rPFS and delayed TTCR.[8]

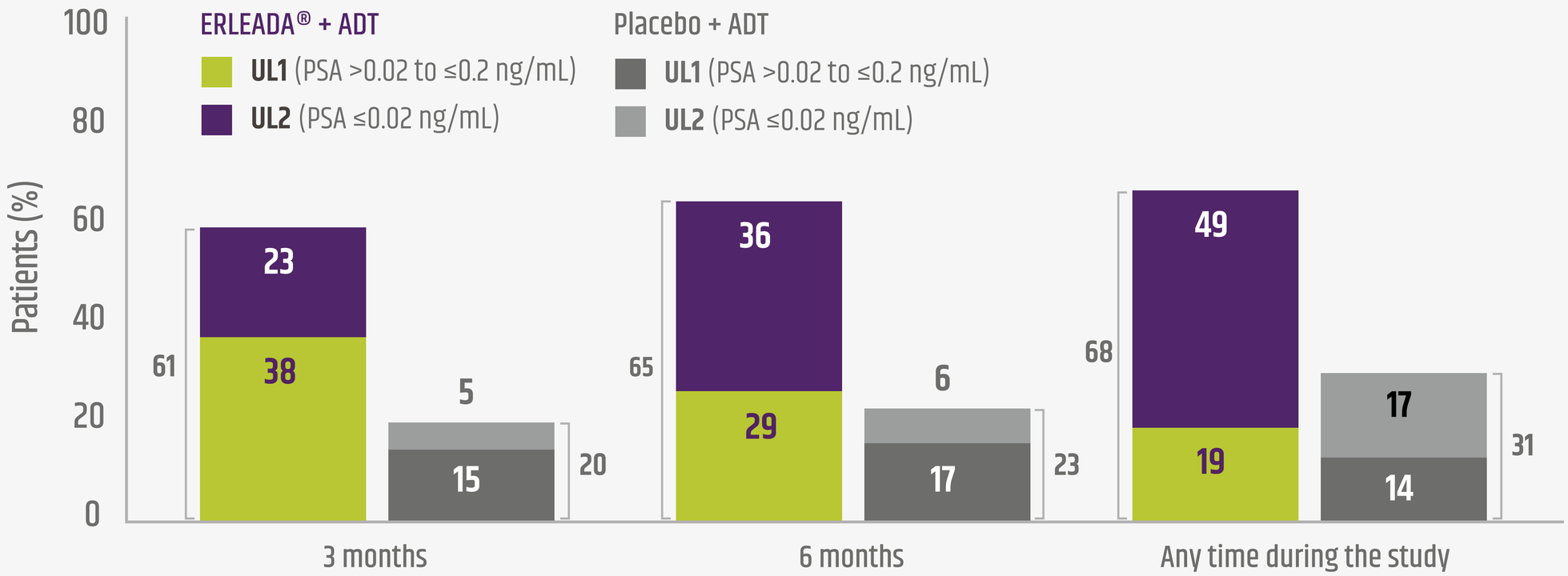
## Undetectable PSA responses (≤0.2 ng/mL) by disease volume and timing of metastasis, at any time during the study[9]




Adapted from Merseburger AS, *et al.* 2023 (supplementary appendix).[9]

- **~80%** of patients with **metachronous low-volume mHSPC achieved undetectable PSA responses** with ERLEADA® + ADT vs. 55% with placebo + ADT[9]
- More than half **(58%)** of patients with **synchronous high-volume mHSPC achieved undetectable PSA responses** with ERLEADA® + ADT vs. 24% with placebo + ADT[9]

## Patients achieving UL1 and UL2 PSA responses over time[8]

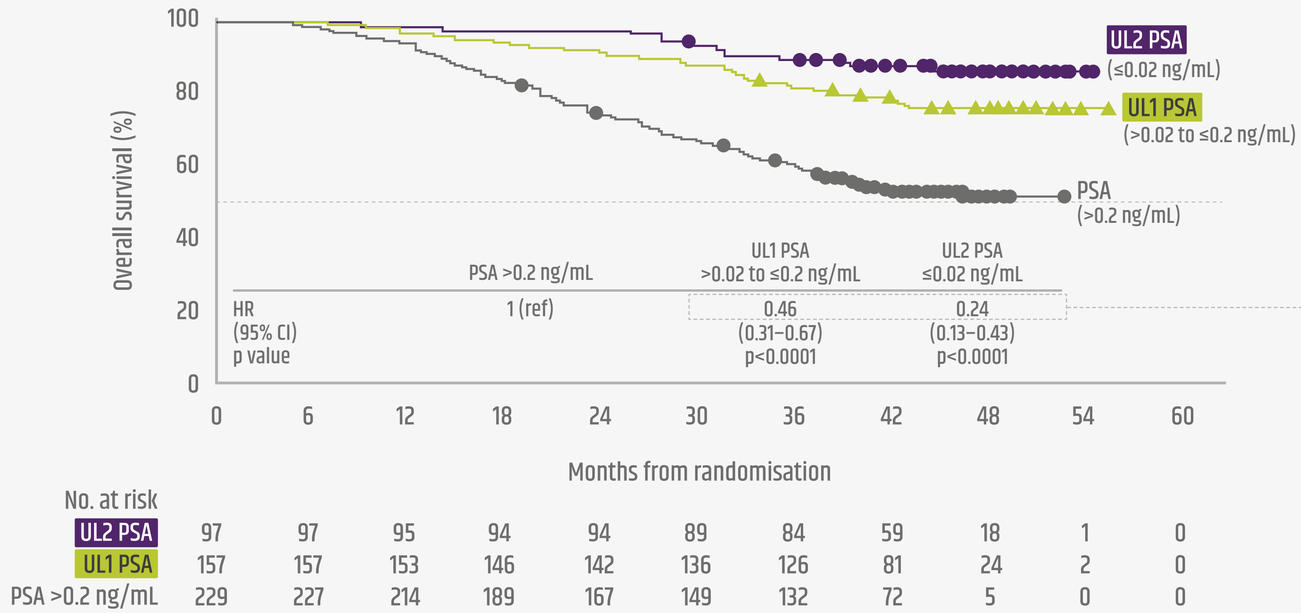



Adapted from Merseburger AS, *et al.* 2023.[8]

# **Upfront use of ERLEADA® + ADT offers undetectable PSA responses that translate into extended survival** vs. those not achieving such a response[8]

## OS by undetectable PSA responses at 3 months with ERLEADA® + ADT

(44.0 months' median follow-up)*[8]




Adapted from Merseburger AS, *et al.* 2023.[8]

- Patients treated with ERLEADA® + ADT who achieved undetectable PSA responses at Month 3 experienced a reduction in the risk of death vs. those not achieving such a response[8]

**UL1 PSA**
**54%**
reduction in the risk of death with a UL1 PSA response[8]

**UL2 PSA**
**76%**
reduction in the risk of death with a UL2 PSA response[8]

ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival; TTCR, time to castration resistance; UL, ultra low; UL1, ultra-low 1 (PSA: >0.02 to ≤0.2 ng/mL); UL2, ultra-low 2 (PSA: ≤0.02 ng/mL). *Patients treated with ERLEADA® + ADT who achieved undetectable PSA responses at 3 months were split into the subgroups based on the level of PSA decline.[8]

# Upfront use of ERLEADA® + ADT in mHSPC delays progression vs. placebo + ADT[3,8]

**At 22.7 months' median follow-up[3]**

**52%**

reduction in the risk of radiographic progression or death (rPFS) at 2 years vs. placebo + ADT

(HR=0.48; 95% CI: 0.39–0.60; p<0.001)[3]

Patients (%) with rPFS at 22.7 months[3]

**68.2%** vs. **47.5%**

**ERLEADA® + ADT** | **placebo + ADT**

**72% reduction**

in the risk of radiographic progression or death (rPFS) with ERLEADA® + ADT in patients achieving a UL2 PSA response (≤0.02 ng/mL) at Month 3 vs. those not achieving such a response

(at a median follow-up of 22.7 months; HR=0.28; 95% CI: 0.14–0.54; p=0.0002)*[8]

**rPFS by PSA response at 3 months*†[8]** +

- ERLEADA® + ADT reduces the risk of rPFS vs. placebo + ADT, regardless of disease volume[3]

**47% reduction**

in the risk of rPFS vs. placebo + ADT in high-volume mHSPC patients like Khaled

(median rPFS not reached vs. 14.9 months; HR=0.53; 95% CI: 0.41–0.67)[3]

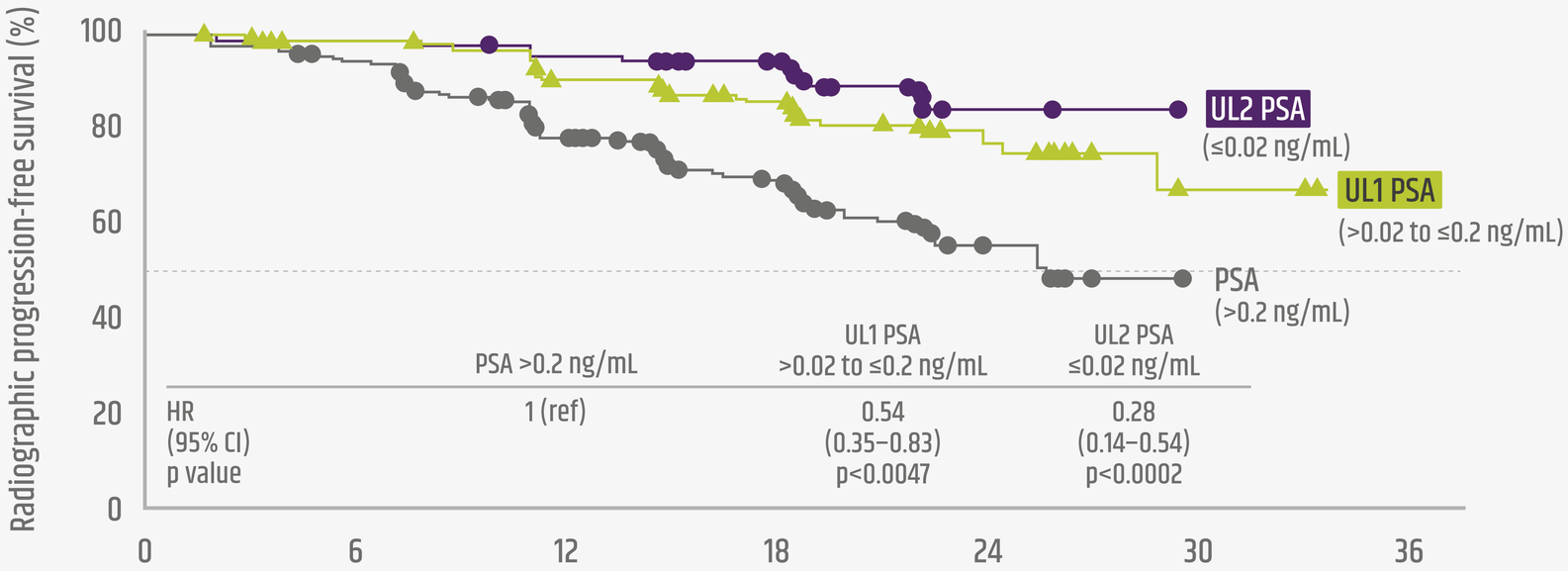
**64% reduction**

in the risk of rPFS vs. placebo + ADT in low-volume mHSPC patients like Tarek

(median rPFS not reached vs. 30.5 months; HR=0.36; 95% CI: 0.22–0.57)[3]

ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival; TTCR, time to castration resistance; UL, ultra low; UL1, ultra-low 1 (PSA: >0.02 to ≤0.2 ng/mL); UL2, ultra-low 2 (PSA: ≤0.02 ng/mL). *In a *post-hoc* analysis of the TITAN study, patients with evaluable PSA values.[8] †Patients treated with ERLEADA® + ADT who achieved undetectable PSA responses at 3 months were split into the subgroups based on the level of PSA decline.[8]

# rPFS by PSA response at 3 months in patients on ERLEADA® + ADT*†[8]




| No. at risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| UL2 PSA | 97 | 90 | 84 | 76 | 27 | 0 | 0 |
| UL1 PSA | 157 | 153 | 133 | 107 | 34 | 2 | 0 |
| PSA >0.2 ng/mL | 229 | 210 | 161 | 121 | 23 | 0 | 0 |

Adapted from Merseburger AS, *et al*. 2023.[8]

*In a *post-hoc* analysis of the TITAN study, patients with evaluable PSA values.[8] †Patients treated with ERLEADA® + ADT who achieved undetectable PSA responses at 3 months were split into the subgroups based on the level of PSA decline.[8]

# Upfront use of ERLEADA® + ADT in mHSPC significantly delays time to castration resistance (TTCR) and the need for chemotherapy vs. placebo + ADT[2,8]

**At a median follow-up of 44.0 months:**[2]

Patients developing castration resistance (%)*[2]

**36.4%** vs. **71.2%**

**ERLEADA® + ADT** | **placebo + ADT**

Patients needing cytotoxic chemotherapy (%)*[2]

**13.1%** vs. **23.9%**

**ERLEADA® + ADT** | **placebo + ADT**

**80% reduction**

in TTCR with ERLEADA® + ADT in patients achieving a UL2 PSA response (≤0.02 ng/mL) at Month 3 vs. those not achieving such a response

(at a median follow-up of 44.0 months; HR=0.20; 95% CI: 0.11–0.38; p<0.0001)[†8]

**TTCR by PSA responses at 3 months**[†‡8]

- ERLEADA® + ADT significantly delays time to castration resistance (TTCR) vs. placebo + ADT, regardless of disease volume[2,4]

**60% reduction**

in TTCR vs. placebo + ADT

for synchronous high-volume mHSPC patients like Khaled

(median TTCR 38.8 months vs. 8.3 months; HR=0.40; 95% CI: 0.32–0.50; p<0.001)[4]

**82% reduction**

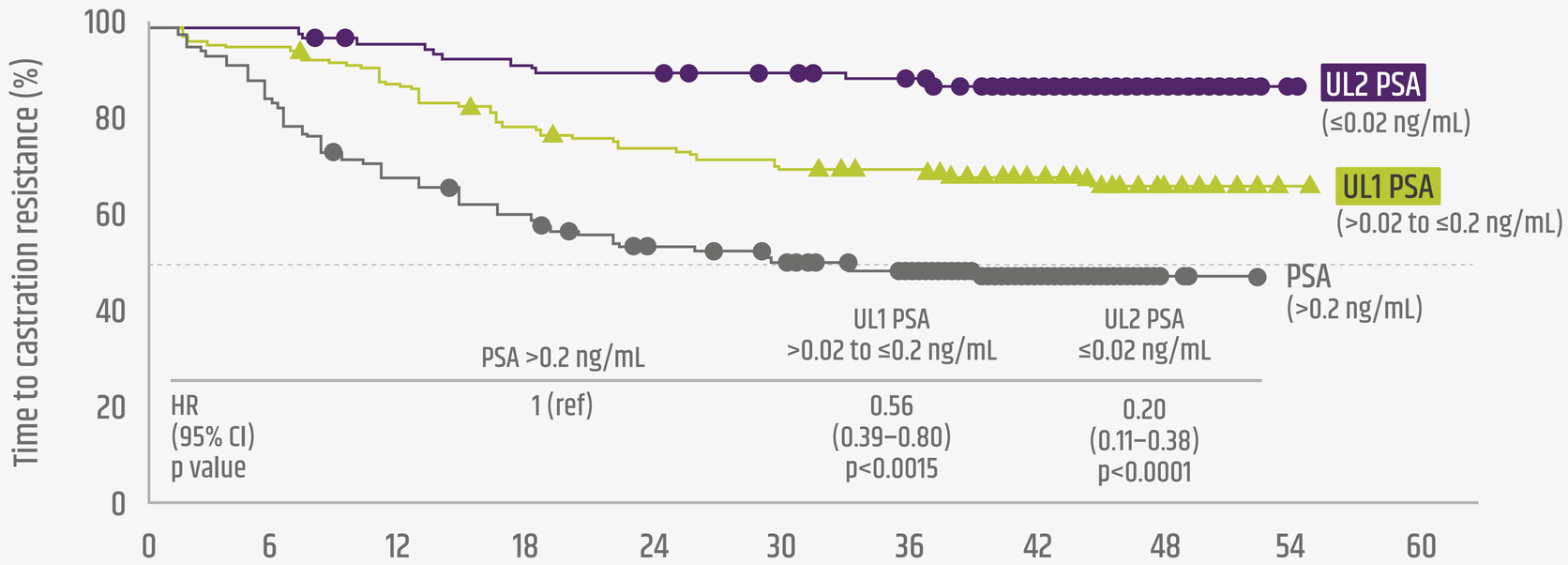
in TTCR vs. placebo + ADT

for metachronous low-volume mHSPC patients like Tarek

(median TTCR not reached vs. 22.1 months; HR=0.18; 95% CI: 0.08–0.41; p<0.001)[4]

ADT, androgen deprivation therapy; CI, confidence interval; HR, hazard ratio; ITT, intention to treat; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival; TTCR, time to castration resistance; UL, ultra low; UL2, ultra-low 2 (PSA: ≤0.02 ng/mL). *In the ITT population of the TITAN study, median time to castration resistance was not reached with ERLEADA® + ADT vs. 11.4 months with placebo + ADT (HR=0.34; 95% CI: 0.29–0.41; p<0.0001) and median time to cytotoxic chemotherapy was not reached in either arm (HR=0.47; 95% CI: 0.35–0.63; p<0.0001).[2] †In a *post-hoc* analysis of patients from the TITAN study with evaluable PSA values.[8] ‡Patients treated with ERLEADA® + ADT who achieved undetectable PSA responses at 3 months were split into the subgroups based on the level of PSA decline.[8]

# TTCR by PSA responses at 3 months with ERLEADA® + ADT*†[8]




| 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 |

Adapted from Merseburger AS, *et al.* 2023.[8]

*In a *post-hoc* analysis of patients from the TITAN study with evaluable PSA values.[8] †Patients treated with ERLEADA® + ADT who achieved undetectable PSA responses at 3 months were split into the subgroups based on the level of PSA decline.[8]

# Upfront use of ERLEADA® + ADT in mHSPC extends its benefits through to the next line of therapy[1,2,10–14]

**At 44.0 months' median follow-up**

**38%**

reduction in the risk of second progression or death (PFS2) vs. placebo + ADT

(median PFS2 not reached vs. 44.0 months with placebo + ADT; HR=0.62; 95% CI: 0.51–0.75; p<0.0001)*[2]

- ERLEADA® + ADT reduces the risk of second progression or death (PFS2) vs. placebo + ADT, regardless of disease volume*[2,4]

**36%** reduction
in the risk of second progression or death vs. placebo + ADT for synchronous high-volume mHSPC

(median PFS2 not reached vs. 33.1 months; HR=0.64; 95% CI: 0.51–0.82; p<0.001)[4]

**78%** reduction
in the risk of second progression or death vs. placebo + ADT for metachronous low-volume mHSPC

(median PFS2 not reached for either arm; HR=0.22; 95% CI: 0.09–0.56; p=0.002)[4]

- **ERLEADA® + ADT has a significantly lower frequency of androgen receptor (AR) aberrations** at the end of treatment vs. placebo + ADT†[10]
  - AR aberrations are a key step in the progression towards castration and can negatively impact response to treatment[11]
  - In the TITAN study, the frequency of total AR aberrations was significantly lower with ERLEADA® + ADT vs. placebo + ADT at end of treatment (48% vs. 67%; p=0.04)[10]
- **After progression to mCRPC, the opportunity to prescribe ERLEADA® + ADT is lost forever**[1,12–14]

## Keep other treatment options open for later stages of prostate cancer[2,12–14]

ADT, androgen deprivation therapy; AR, androgen receptor; CI, confidence interval; EOT, end of treatment; HR, hazard ratio; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; PFS2, second progression-free survival. *PFS2 was defined as time from random assignment to the first occurrence of investigator-determined disease progression (PSA progression, progression on imaging or clinical progression) on first subsequent therapy or death.[2] †In TITAN study, AR aberrations at baseline and end of treatment (EOT) were evaluated for associations of end of treatment AR aberrations with outcomes in the study. Detection of any AR aberration at EOT was significantly associated with duration on first subsequent therapy (2.0 [1.0–4.0], p=0.03).[10]

# Upfront use of ERLEADA® + ADT in mHSPC maintains HRQoL from baseline and vs. placebo + ADT[2,15]

- Regimens including docetaxel may negatively impact patients' HRQoL for up to 2 years*[16]
  - In the STAMPEDE study in mHSPC,* the addition of docetaxel to ADT was associated with early declines in HRQoL from baseline, that were observed for 2 years post randomisation[16]

## Upfront use of ERLEADA® + ADT offers:

**Maintained HRQoL from baseline†[2]**

**Improved or stable energy levels vs. placebo + ADT‡[17]**

**Maintained low baseline pain and fatigue scores at ~2 years' median follow-up§[18]**

ADT, androgen deprivation therapy; BFI, Brief Fatigue Inventory; FACT-P, Functional Assessment of Cancer Therapy-Prostate questionnaire; HRQoL, health-related quality of life; mHSPC, metastatic hormone-sensitive prostate cancer; QoL, quality of life; SF, short form; TTD, time to deterioration. *A group of patients with high-risk locally advanced or mHSPC within the randomised controlled STAMPEDE trial were contemporaneously enrolled to compare QoL outcomes with abiraterone acetate + prednisone or prednisolone + ADT (n=342) vs. docetaxel + ADT (n=173).[16] †Patient-reported HRQoL was assessed using the Functional Assessment of Cancer Therapy-Prostate (FACT-P) questionnaire.[2] ‡Patient-reported energy levels were assessed using the BFI, comprising 9 questions addressing fatigue and interference from fatigue rated 0 (no fatigue/interference) to 10 (fatigue/interference as bad as you can imagine). BFI was completed at baseline and averaged over 7 consecutive days every 28 days, then again at Months 4, 8 and 12 post-completion of study treatment.[17] §At a median follow-up of 22.7 months. Patient-reported outcomes for pain and fatigue were evaluated using the BFI-SF and BFI-TTD were estimated by the Kaplan-Meier method; hazard ratios and 95% confidence intervals were calculated using Cox proportional hazards model.[18]

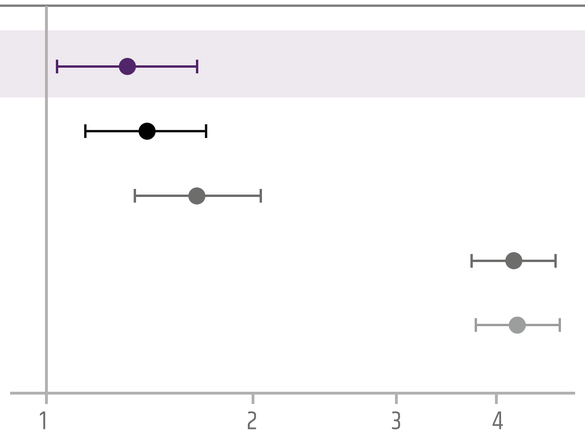
# ERLEADA® + ADT offers an established and generally well-tolerated safety profile in patients with mHSPC*[1,2]

In a network meta-analysis on the safety of systemic treatments for mHSPC, ERLEADA® + ADT:[19]

- Ranked better than docetaxel-based regimens for grade ≥3 AEs and serious AEs[19]
- Had the lowest relative risk of grade ≥3 AEs and serious AEs vs. other doublet and triplet regimens[19]

## Relative risk for aggregated outcomes for sAEs following systemic therapies vs. ADT alone[19]

| Treatments | RR (95% CrI) | p value (RR<1) |
|---|---|---|
| ERLEADA® + ADT | 1.26 (1.03–1.53) | 1.3 |
| Abiraterone acetate + ADT | 1.33 (1.12–1.57) | 0.1 |
| Enzalutamide + ADT | 1.54 (1.28–1.84) | 0.0 |
| Docetaxel + ADT | 3.78 (3.35–4.26) | 0.0 |
| Darolutamide + docetaxel + ADT | 3.83 (3.39–4.31) | 0.0 |




Adapted from Di Maio M, *et al.* 2023.[19]

In a meta-analysis, ERLEADA® + ADT was

**>3x more likely**

to produce a net clinical benefit than triplet therapy,† due to the lower frequency of adverse events (grades 3–5)[6]

**TEAEs of interest in the safety population**[2]

ADT, androgen deprivation therapy; AE, adverse event; CrI, credible interval; mHSPC, metastatic hormone-sensitive prostate cancer; NHT, novel hormonal therapy; RR, relative risk; sAE, serious adverse event; SCARs, severe cutaneous adverse reactions; TEAE, treatment-emergent adverse event. *The following AEs occurred in ≥5% of patients in the TITAN safety population, after a median follow-up of 44.0 months: rash (17.6% vs. 2.3% vs. 11.1%); pruritus (8.2% vs. 2.5% vs. 3.8%); fatigue (13.5% vs. 8.7% vs. 6.7%); hot flush (12.8% vs. 9.9% vs. 1.4%) and hypertension (5.3% vs. 4.0% vs. 2.4%) of all grades were observed with ERLEADA® + ADT, placebo + ADT and crossover (placebo to ERLEADA®) + ADT, respectively.[20] For more detailed safety information, please refer to the Summary of Product Characteristics.[1] Post-marketing reports of SCARs including drug reaction with eosinophilia and systemic symptoms (DRESS) and Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), which can be life-threatening or fatal, have been observed in association with ERLEADA® treatment.[1] For more information, please refer to SmPC sections 4.4 and 4.8. †Doublets include approved NHT-based regimens and triplets include docetaxel + ADT + NHTs (abiraterone acetate or darolutamide). Estimated probabilities for a net clinical benefit were 66.8% for ERLEADA® + ADT, 20.0% for docetaxel + darolutamide + ADT, 2.6% for docetaxel + ADT, 63.3% for abiraterone acetate + ADT, and 78.7% for enzalutamide + ADT.[6]

## TEAEs of interest in the safety population[2]

| Category | ERLEADA® + ADT (n=524) | | Placebo + ADT (n=527) | | Crossover to ERLEADA® + ADT (n=208) | |
|---|---|---|---|---|---|---|
| **Median treatment duration, months (range)*** | **39.3 (0–55.7)** | | **20.2 (0.1–37.0)** | | **15.4 (0.6–18.2)** | |
| **Total exposure, patient-years** | **1,358.9** | | **793.3** | | **243.6** | |
| **TEAEs by group term, event (event rate/100 patient-years of exposure)†** | **All grades‡** | **Grade 3–4‡** | **All grades** | **Grade 3–4** | **All grades** | **Grade 3–4** |
| Any TEAE of interest | 543 (40.3) | 103 (7.6) | 178 (22.4) | 21 (2.7) | 102 (41.9) | 16 (6.5) |
| Skin rash§ | 331 (24.4) | 40 (2.9) | 66 (8.3) | 5 (0.6) | 44 (18.1) | 8 (33.3) |
| Fracture¶ | 83 (6.1) | 21 (1.5) | 33 (4.2) | 4 (0.5) | 5 (2.1) | 0 |
| Fall | 63 (4.6) | 9 (0.7) | 54 (6.8) | 5 (0.6) | 14 (5.7) | 0 |
| Ischaemic heart disease‖ | 45 (3.3) | 21 (1.5) | 13 (1.6) | 5 (0.7) | 1 (0.4) | 1 (0.4) |
| Ischaemic cerebrovascular disorders# | 18 (1.3) | 11 (0.8) | 10 (1.3) | 2 (0.3) | 7 (2.9) | 7 (2.8) |
| Seizure** | 3 (0.2) | 1 (0.1) | 2 (0.3) | 0 | 0 | 0 |

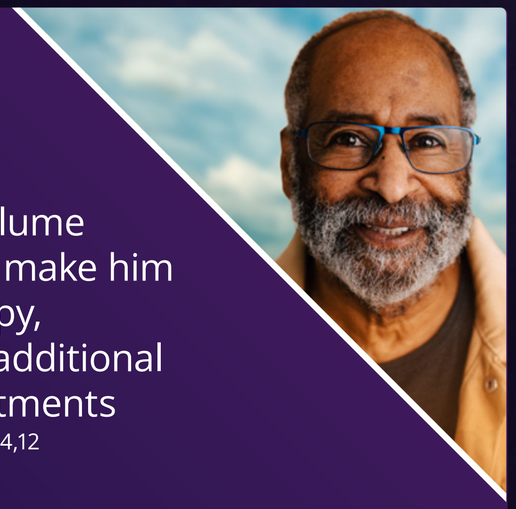
Adapted from Chi KN, *et al.* 2021.[2]

*Patients received treatment until disease progression or unacceptable toxicity.[2] †Event rate per 100 patient-years of exposure is calculated as 100 times the number of distinct events with the group term/total patient-years of exposure (total days of exposure/365.25) for the treatment group. AEs occurred from the time of the first dose of the study intervention through 30 days after the last dose. AEs were graded according to National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.3. One patient who was assigned to the ERLEADA® + ADT group withdrew consent before treatment.[2] ‡The worst toxicity grade is included. Patients with missing toxicity grades were counted in the all-grade column.[2] §Skin rash was a grouped term including rash, maculopapular rash, conjunctivitis, dermatitis, stomatitis, pruritic rash urticaria, papular rash, skin exfoliation, blister, mouth ulceration, drug eruption, erythema multiforme, exfoliative rash, toxic skin eruption, papule, skin reaction, butterfly rash, generalised exfoliative dermatitis, genital rash, erythematous rash, macular rash, systemic lupus erythematosus rash, oral mucosal blistering, follicular rash, pustular rash, and vesicular rash.[2] ¶Fracture was a grouped term including rib fracture, spinal compression fracture, hand fracture, femoral neck fracture, foot fracture, femur fracture, thoracic vertebral fracture, traumatic fracture, upper limb fracture, wrist fracture, ankle fracture, fracture, hip fracture, spinal fracture, radius fracture, acetabulum fracture, fracture pain, clavicle fracture, comminuted fracture, compression fracture, forearm fracture, humerus fracture, patella fracture, pelvic fracture, sternal fracture, stress fracture, ulna fracture, fibula fracture, lower limb fracture, skull fracture and tibia fracture.[2] ‖Ischaemic heart disease was a group term including angina pectoris, myocardial infarction, acute myocardial infarction, coronary artery stenosis, coronary artery arteriosclerosis, myocardial ischaemia, coronary artery disease, coronary artery occlusion, acute coronary syndrome, abnormal cardiac stress test, ischaemic cardiomyopathy, unstable angina and increased troponin.[2] #Ischaemic cardiovascular disorder was a group term including cerebrovascular accident, transient ischaemic attack, ischaemic stroke, cerebrovascular disorder, lacunar infarction, cerebral ischaemia, hemiplegia, vascular encephalopathy, carotid artery stenosis and carotid arteriosclerosis.[2] **Seizure was a group term including seizure and tongue biting.[2]

# ERLEADA® + ADT is a standard of care for mHSPC, recommended by international guidelines*[21–23]

The 2023 EAU guidelines state that the choice of treatment for mHSPC is driven by:[21]

- The nature of the disease
  - Low/high-volume
  - Synchronous/metachronous
- Fitness for docetaxel
- Patient preference
- Specific side effects
- Availability
- Logistics
- Cost



Khaled has synchronous high-volume disease. His comorbidities might make him less able to tolerate chemotherapy, and he does not want to attend additional time-consuming hospital appointments associated with chemotherapy.[2–4,12]

Tarek has metachronous low-volume disease. He is relatively fit and could tolerate chemotherapy, but he worries about hospital appointments for infusions disrupting his life and fears that nausea and fatigue might leave him unable to run his restaurant.[2–4,12]

**ERLEADA® + ADT is recommended by both EAU and ESMO guidelines for the first-line treatment of mHSPC, regardless of disease volume[21–23]**

ADT, androgen deprivation therapy; EAU, European Association for Urology; ESMO, European Society for Medical Oncology; mHSPC, metastatic hormone-sensitive prostate cancer. *ESMO and EAU guidelines.[21–23]

# Choose ERLEADA® + ADT upfront in mHSPC for benefits that extend through to the next line of therapy[1,2]

- Significantly prolongs OS with a 35% reduction in the risk of death vs. placebo + ADT (median OS not reached vs. 52.2 months; HR=0.65; 95% CI: 0.53 –0.79; p<0.0001) at ~4 years' median follow-up*[2]
- Predicted median OS of 6 years vs. 3.3 years with placebo + ADT, as shown in a statistical extrapolation of the TITAN study†[7]
- Undetectable PSA responses (UL1 and UL2) that translate into clinical benefits vs. those not achieving such responses‡[8]
- Keeps subsequent treatment options open upon disease progression[2,12–14]
- Maintains HRQoL from baseline and stable energy levels vs. placebo + ADT*[2,17]
- >3x more likely to produce a net clinical benefit than triplet therapy,§ due to the lower frequency of AEs (Grades 3–5) with ERLEADA® + ADT[6,19]
- An established and generally well-tolerated safety profile at ~4 years' median follow-up*¶[2]

ADT, androgen deprivation therapy; AE, adverse event; HRQoL, health-related quality of life; mHSPC, metastatic hormone-sensitive prostate cancer; NHT, novel hormonal therapy; OS, overall survival; PSA, prostate-specific antigen; rPFS, radiographic progression-free survival; SCARS, severe cutaneous adverse reactions; TTCR, time to castration resistance; UL1, ultra-low 1 (PSA: >0.02 to ≤0.2 ng/mL); UL2, ultra-low 2 (PSA: ≤0.02 ng/mL). *Data are from TITAN, a double-blind, randomised, placebo-controlled, international Phase III study evaluating ERLEADA® + ADT vs. placebo + ADT in patients with mHSPC, regardless of their disease stage at baseline (N=1052). Patients with severe angina, myocardial infarction, congestive heart failure, arterial or venous thromboembolic events, a history of or predisposition to seizure or recent ventricular arrhythmias were excluded. Dual primary endpoints were radiographic progression-free survival (rPFS) and overall survival (OS). rPFS was estimated as the time from randomisation to first imaging-based documentation of disease progression or death, whichever occurred first. Median follow-up was 44.0 months.[2,3] †In a statistical extrapolation of the TITAN study, using validated survival models. Predicted median OS of 71.5 months with ERLEADA® + ADT vs. 39.5 months with placebo + ADT.[7] ‡Patients on ERLEADA®+ ADT with undetectable PSA responses at 3 months had improved outcomes (OS, rPFS, TTCR and time to PSA progression) vs. those with a PSA response of >0.2 ng/mL, regardless of disease volume. Patients achieving a UL2 PSA response (≤0.02 ng/mL) before or by 6 months had a lower risk of death vs. those achieving after 6 months or never.[8] §Triplet therapy includes docetaxel + ADT + NHTs (abiraterone acetate or darolutamide).[6] ¶The following AEs occurred in ≥5% of patients in the TITAN safety population: rash (17.6% vs. 2.3% vs. 11.1%); pruritus (8.2% vs. 2.5% vs. 3.8%); fatigue (13.5% vs. 8.7% vs. 6.7%); hot flush (12.8% vs. 9.9% vs. 1.4%) and hypertension (5.3% vs. 4.0% vs. 2.4%) of all grades were observed with ERLEADA® + ADT, placebo + ADT and crossover (placebo to ERLEADA®) + ADT, respectively.[20] For more detailed safety information, please refer to the Summary of Product Characteristics.[1] Post-marketing reports of SCARs including drug reaction with eosinophilia and systemic symptoms (DRESS) and Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN), which can be life-threatening or fatal, have been observed in association with ERLEADA® treatment.[1] For more information, please refer to SmPC sections 4.4 and 4.8.[1]

# ERLEADA® prescribing information

Scan the QR code to view the full SmPC

# References


1. ERLEADA®. Summary of Product Characteristics (January 2024). Janssen-Cilag International NV. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/erleada. Accessed: March 2024.
2. Chi KN, *et al. J Clin Oncol* 2021;39:2294–2303.
3. Chi KN, *et al. N Engl J Med* 2019;381:13–24.
4. Merseburger AS, *et al. Eur J Can* 2023;193:113290.
5. Fallara G, *et al. Cancer Treat Rev* 2022;110:102441.
6. Menges D, *et al. Eur Urol Oncol* 2022;5:605–616.
7. Agarwal N, *et al.* ASCO Genitourinary Cancers Symposium 2024. 25–27 January. Poster: 223.
8. Merseburger AS, *et al.* European Society for Medical Oncology 2023. 20–24 October. Poster: 1786.
9. Merseburger AS, *et al*. European Society for Medical Oncology 2023. 20–24 October. Poster: 1786. (Supplementary appendix).
10. Chi KN, *et al. Genitourinary tumours, prostate* 2019; 30:v347–v348.
11. Sumiyoshi T, *et al. Sci Rep* 2019;9:4030.
12. Docetaxel. Summary of Product Characteristics (December 2023). Sanofi-Aventis. Available at: https://www.ema.europa.eu/en/documents/product-information/taxotere-epar-product-information_en.pdf. Accessed: March 2024.
13. Abiraterone acetate. Summary of Product Characteristics (June 2022). Janssen-Cilag International NV. Available at: https://www.ema europa.eu/en/documents/product-information/zytiga-epar-product-information_en.pdf. Accessed: March 2024.
14. Enzalutamide. Summary of Product Characteristics (June 2022). Astellas Pharma Europe BV. Available at: https://www.ema.europa.eu/en/documents/product-information/xtandi-epar-product-information_en.pdf. Accessed: March 2024.
15. Agarwal N, *et al. Lancet Oncol* 2019;20:1518–1530.
16. Rush HL, *et al. J Clin Oncol* 2022;40:825–836.
17. Agarwal N, *et al.* ASCO virtual annual congress. 4–8 June 2021. Poster 5068.
18. Agarwal N, *et al. J Urol* 2021;206:914–923.
19. Di Maio M, *et al.* European Multidisciplinary Congress on Urological Cancers 2023. 02–05 November. Poster: P107.
20. Chi KN, *et al. J Clin Oncol* 2021;39:2294–2303 (supplementary appendix).
21. Mottet N, *et al.* EAU Guidelines. Presented at the EAU Annual Congress Milan 2023. Available at: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2023_2023-06-13-141145.pdf. Accessed: March 2024.
22. Parker C, *et al.* ESMO Guidelines. *Ann Oncol* 2020;31:1119–1134.
23. Fizazi K, Gillessen S. *Ann Oncol* 2023;34:557–563.