

Triplet Therapy in Metastatic Hormone-Sensitive Prostate Cancer

Updates on treatment recommendations from the American Society of Clinical Oncology Genitourinary Cancers Symposium, 2023

Androgen deprivation therapy (ADT) alone is not considered sufficient for treating metastatic hormone-sensitive prostate cancer (mHSPC)¹

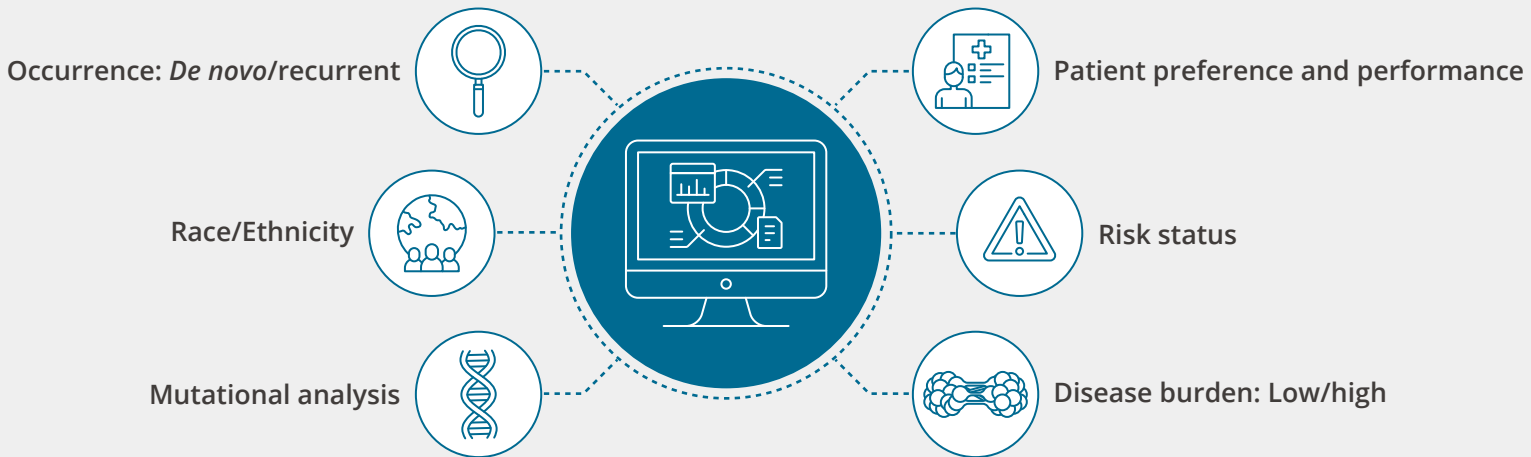


Should triplet therapy—involving ADT, a chemotherapeutic (docetaxel), and an androgen receptor axis-targeted therapeutic agent (darolutamide or abiraterone)—be prescribed as the standard of care for all cases of mHSPC?

Investigators of the **ARASENS** and **PEACE-1** trials sought to find an answer to this

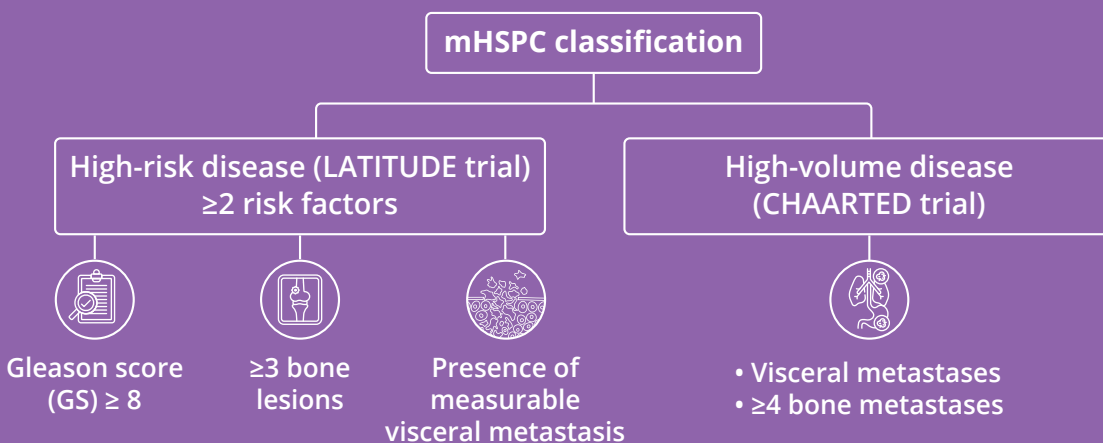
Findings from the trials¹

Patients' overall survival (OS) improved, but treatment should factor:

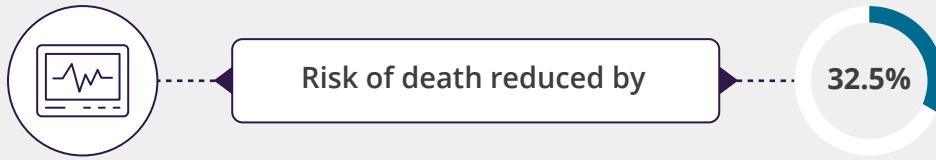


Addressing disease volume and risk can provide more information to clinicians

ARASENS subgroup analysis: Assessing efficacy and safety of darolutamide (DARO) + ADT + docetaxel (DOC)²



What was the effect of DARO + ADT + DOC treatment on clinical outcomes?²



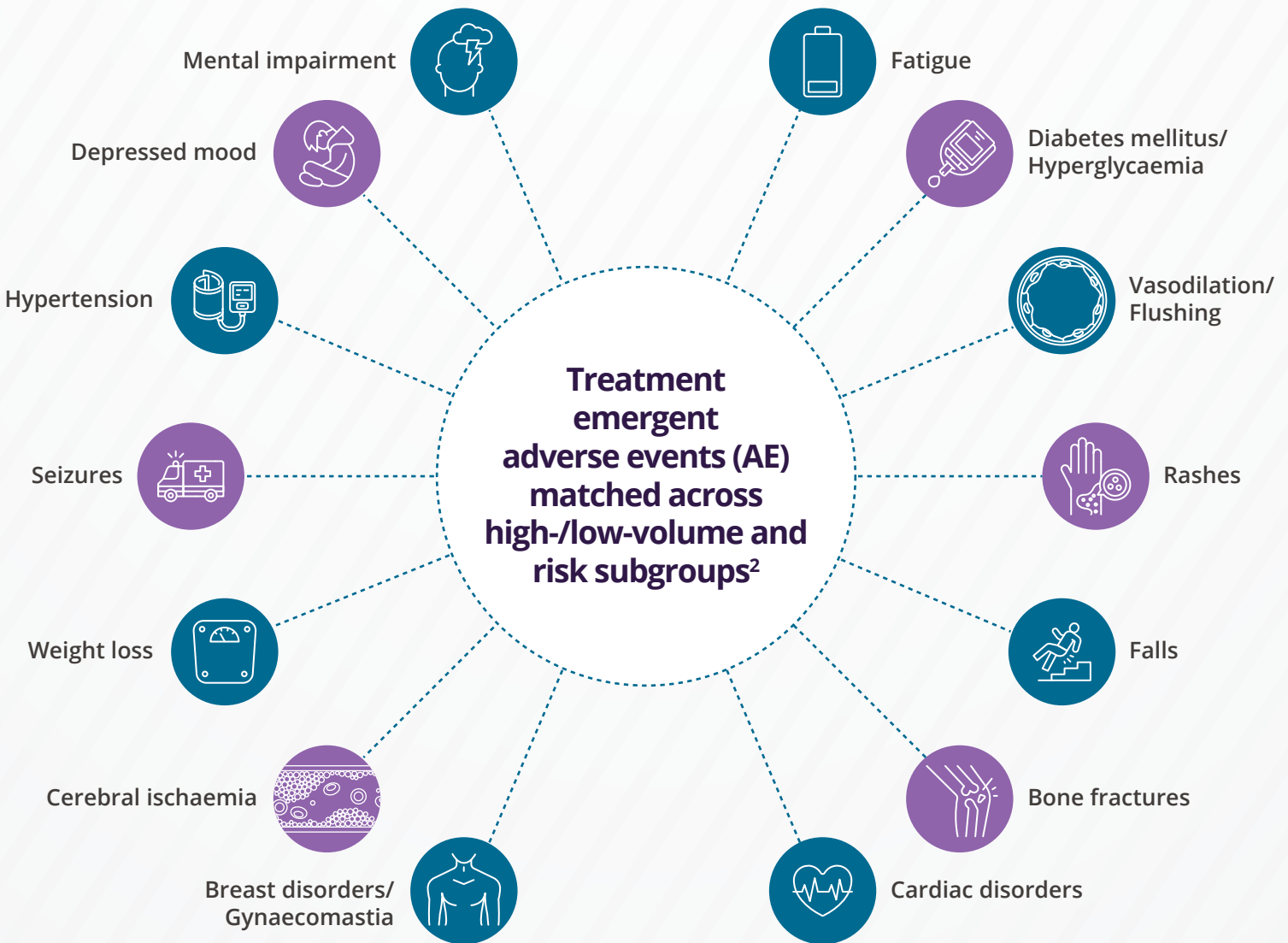
Prolonged OS across disease groups, with hazard ratio (HR) for death being:

High-volume	Low-volume
0.69	0.68
High-risk	Low-risk
0.71	0.62



HRs for progression to metastatic castration-resistant prostate cancer (mCRPC) across disease groups:

High-volume	Low-volume
0.41	0.21
High-risk	Low-risk
0.38	0.32



How effective is triplet therapy in elderly patients with mHSPC?³



Efficacy and safety profile of treatment regimen involving

Standard of care (SOC):
ADT +/- DOC



Abiraterone acetate + prednisone (AAP)

Radiotherapy (RXT)

AAP + RXT

Determined in men \geq 70 years old (older men) and $<$ 70 years old (younger men)

Effects in older vs. younger men³

Altered performance status per Eastern Cooperative Oncology Group Scale (Grade: 1-2)
36% vs. 26%

Increased:



Hypertension
56.5% vs. 38.2%



Diabetes mellitus type 2
15.5% vs. 11%



AAP OS benefit
HR = 0.80 vs. 0.71



Grade 3-5 adverse events (AE)
69% vs. 61%

Decreased:



Use of DOC
66% vs. 51%



Benefit of AAP on radiographic progression-free survival (rPFS; overall population)
HR = 0.65 vs. 0.49



OS (overall population)
HR = 0.95 vs. 0.73

No difference/comparable:



Visceral disease



GS



Tumour volume



Protein-specific antigen (PSA)



Benefit of AAP on rPFS when administered with ADT+DOC
HR = 0.55 vs. 0.5



AE in patients not receiving AAP
48% vs. 47%

Is it appropriate to use triplet therapy in older patients?³

Unless fit, older men benefit less from AAP + ADT + DOC therapy
Deteriorating performance status and comorbidities influence reduced benefit
Healthy older men require:

Geriatric assessment



Close monitoring for complications

What role does DOC have in triplet therapy moving forward?¹



At 84 months following treatment with AAP + ADT

Patient survival

79%

among those with high-risk M0

63%

among those with M1 low volume

34%

among those with M1 high volume



Meta-analysis of CHARTED, GETUG, and STAMPEDE data revealed that the DOC cohort had:

- Heterogenous response depending on volume and timing of M1 diagnosis
- Heterogenous response depending on volume and CT stage
- Greatest benefit in high-volume disease
- Significant improvements in quality of life

Planning treatment based on mHSPC disease progression¹

Progression



Consider abiraterone or enzalutamide



Consider poly-ADP ribose polymerase inhibitors (PARPi) depending on homologous recombination repair gene mutations

ADT monotherapy

Triplet therapy (ADT + DOC + ARPI)

ADT + chemotherapy (DOC)

ADT + androgen receptor pathway inhibitors (ARPI)

Progression



Consider Lu-prostate-specific membrane antigen radioligand therapy



Consider chemotherapy



Consider PARPi depending on homologous recombination repair mutations (HRRm)

Progression



Consider chemotherapy



Consider PARPi depending on HRRm

Considerations for mHSPC treatment

- ✓ Clinical trials evaluating triplet therapy in mHSPC show a favourable safety profile
- ✓ Older men, if healthy and slated for triplet therapy, should receive a geriatric assessment and regular monitoring for complications
- ✓ Developing predictive/prognostic tests and identifying biomarkers is necessary to determine which patients can benefit from DOC treatment
- ✓ Choice of treatment following progression to mHRPC should be tailored based on a patient's health status and needs

References:

1. ASCO GU Cancers Symposium. (2023). *Updates in mHSPC: ASCO Genitourinary Symposium 2023*.
2. Hussain, M. H., Tombal, B. F., Saad, F., Fizazi, K., Sternberg, C. N., Crawford, E. D., ... & Smith, M. R. (2023). Efficacy and safety of darolutamide (DARO) in combination with androgen-deprivation therapy (ADT) and docetaxel (DOC) by disease volume and disease risk in the phase 3 ARASENS study. *Journal of Clinical Oncology*, 41(6), Suppl. 15.
3. Mourey, L., Boyle, H. J., Roubaud, G., McDermott, R. S., Supiot, S., Tombal, B. F., ... & Carles, J. (2023). Efficacy and safety of abiraterone acetate plus prednisone and androgen deprivation therapy +/- docetaxel in older patients (≥70 years), with de novo metastatic-castration sensitive prostate cancer, compared to younger patients (<70 years): The PEACE-1 trial. Presented in: 2023 Genitourinary (GU) American Society of Clinical Oncology (ASCO) Annual Meeting, San Francisco, Feb 16–18, 2023.
4. López-Campos, F., González-San Segundo, C., Conde-Moreno, A. J., & Couñago, F. (2021). Metastatic hormone-sensitive prostate cancer: How should it be treated? *World Journal of Clinical Oncology*, 12(2), 43.

