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Intensifying Metastatic Hormone-Sensitive Prostate Cancer Treatment

The Role of Triplet Therapy

Initially, metastatic hormone-sensitive prostate cancer (mHSPC) treatment was focused on a single therapeutic modality, i.e. androgen deprivation therapy (ADT)[1]

However, the treatment landscape for mHSPC is rapidly expanding, and combining chemotherapy, radiotherapy (RT), or an androgen receptor axis-targeted therapeutic agent (ARAT) with ADT has been found to improve clinical outcomes in men with mHSPC[1,2]

This has led to the evolution of more intensive treatment regimens involving doublet—i.e. administration of ADT with a chemotherapeutic or ARAT—and triplet—i.e. administration of ADT with a chemotherapeutic and ARAT—therapies with various molecules[2]

Which molecules have already been evaluated in clinical trials?[3–12]

- Docetaxel (CHAARTED, STAMPEDE trials)
- Abiraterone (LATITUDE, STAMPEDE trials)
- Enzalutamide (ENZAMET, ARCHES trials)
- Apalutamide (TITAN trial)
- Docetaxel + Abiraterone (PEACE-1 trial)
- Docetaxel + Darolutamide (ARASENS trial)

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Triplet therapy for mHSPC: the evidence

PEACE-1 trial[11]

Patients with:
- mHSPC discovered at diagnosis
- Eastern Cooperative Oncology Group (ECOG) score: 0–2

- Standard of care (SOC; ADT alone or with Docetaxel)
- SOC + RT
- SOC + Abiraterone + Prednisone
- SOC + Abiraterone + Prednisone + RT

Patients receiving abiraterone had longer:
- OS
- Radiographic progression-free survival (rPFS)

Over 1.5 years survival benefit seen in men with high-volume disease

Among patients receiving ADT + Docetaxel:
- Longer OS
- Grade 3 or worse AEs occurred in:

52% of those not receiving Abiraterone

63% of those receiving Abiraterone

Most common AEs

Hypertension 22%

Neutropenia 10%

Hepatotoxicity 6%

ARASENS trial[12,13]

Patients with:
- mHSPC
- ECOG score of 0 or 1

86.1% With metastatic disease at time of diagnosis

- Darolutamide + Docetaxel + ADT
- Placebo + Docetaxel + ADT

32.5% Lower risk of death

Delayed onset of:
- Hormonal resistance
- Pain
- Cancer-related secondary symptoms
- Additional therapy requirements

= Frequency of grade 3 or 4 AE similar in both groups

Neutropenia was the most common AE

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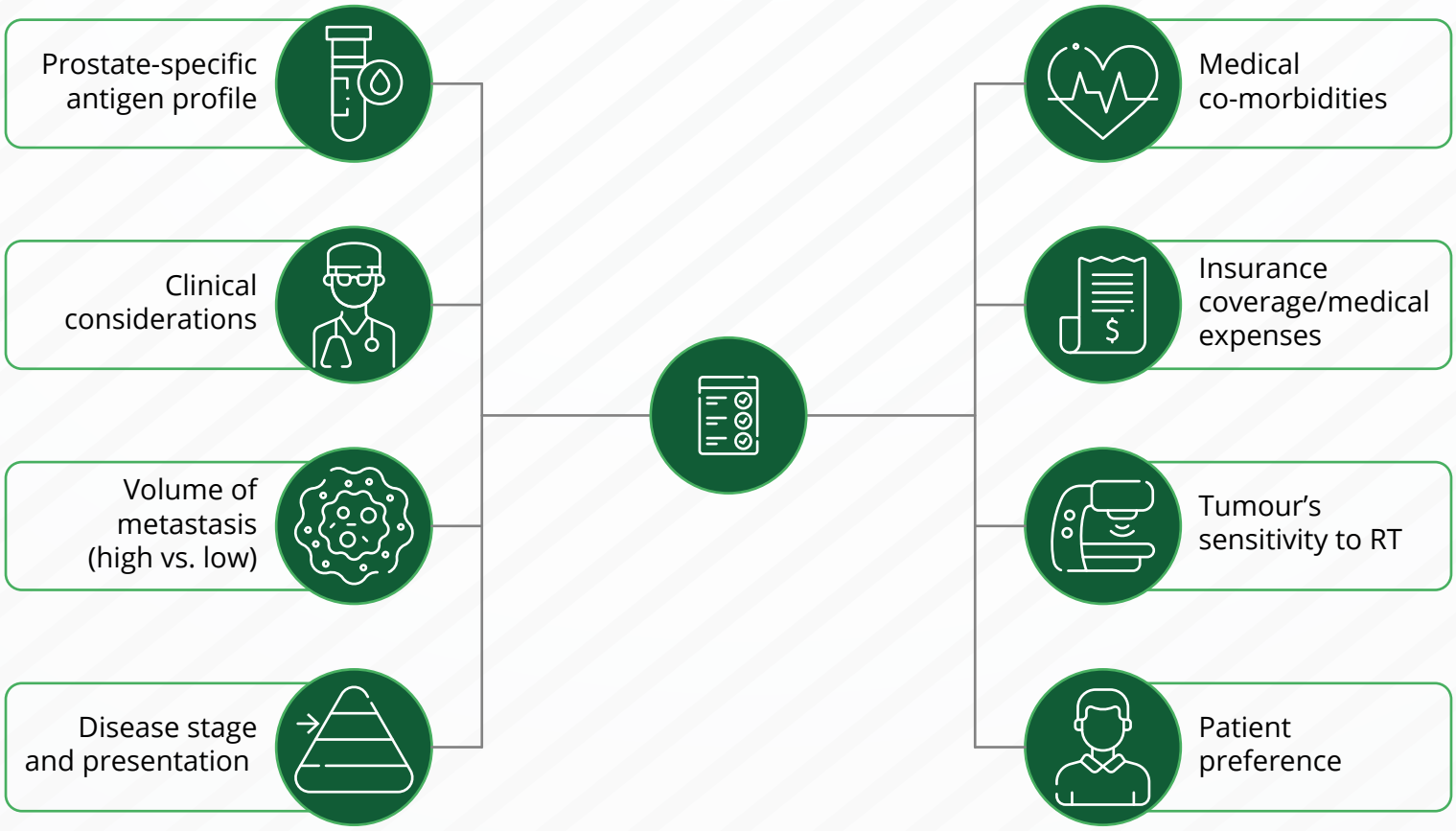
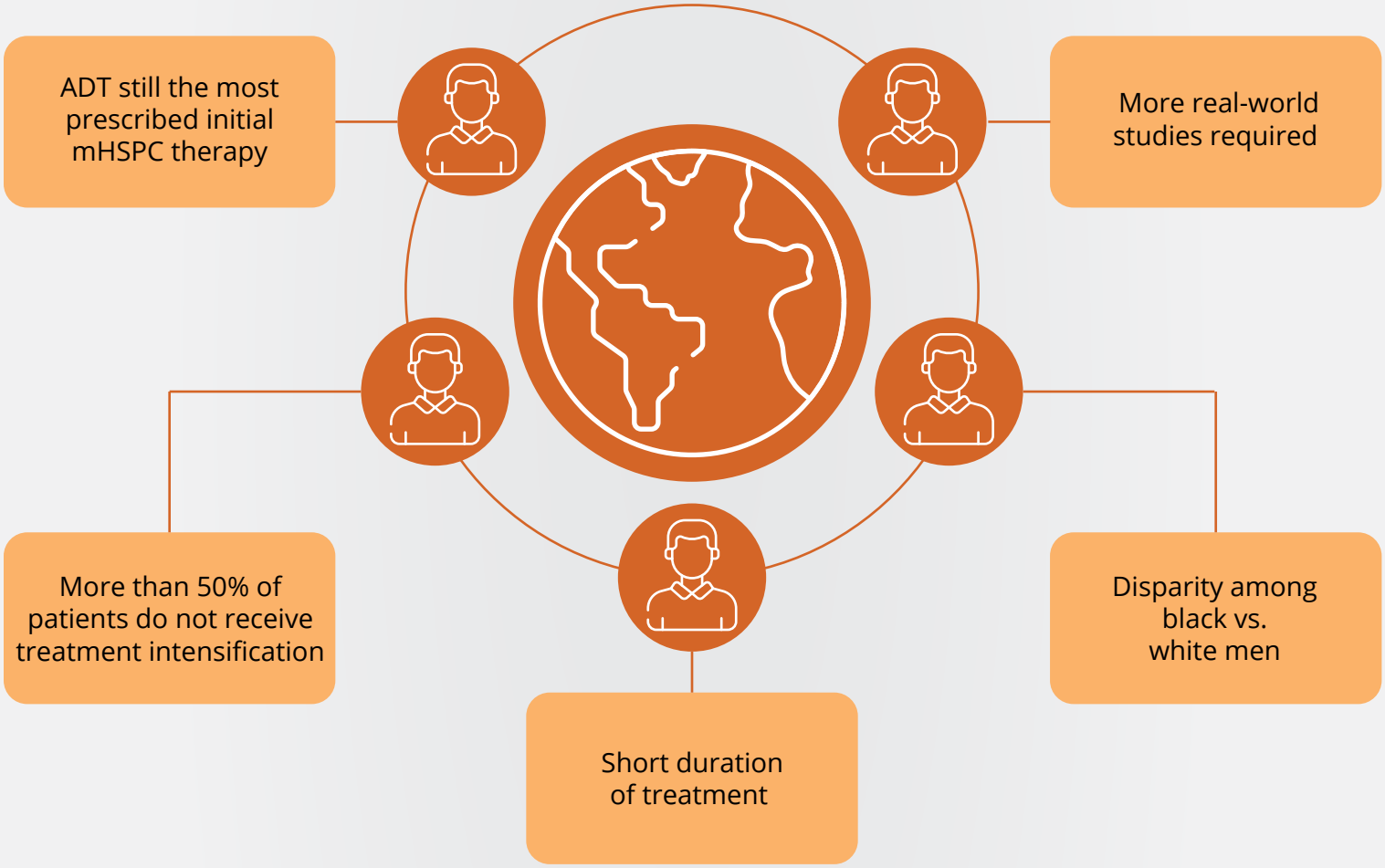
Which factors determine the treatment intensification strategy to be used for each patient?[14–16]



Gaps in treatment intensification in the real world[17–20]



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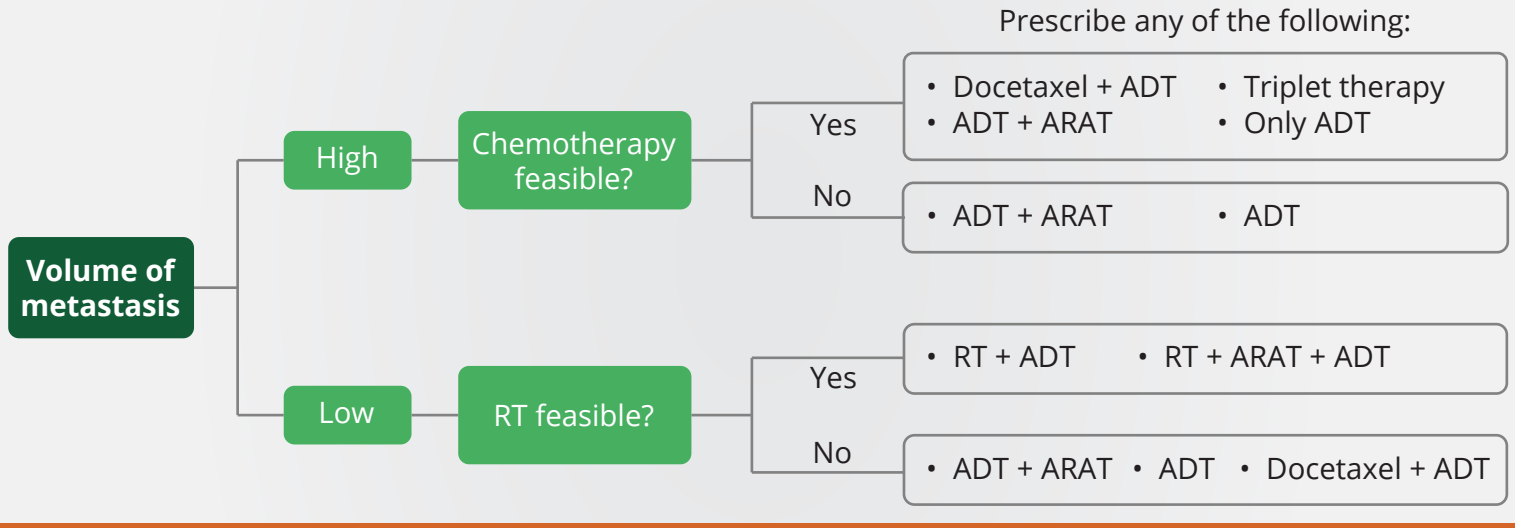
A new approach to treatment intensification[16]



Considerations for treatment intensification in patients with mHSPC

Objectives:
• Delay progression • Prolong OS • Maintain quality of life

Though triplet therapy has been proved more effective, it may not necessarily be the new SOC

Healthcare providers should evaluate each patient and prescribe treatment intensification accordingly

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