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)
- **Apatlutamide** (TITAN trial)
- **Docetaxel + Abiraterone** (PEACE-1 trial)
- **Docetaxel + Darolutamide** (ARASENS trial)
**PEACE-1 trial**

- **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

**Most common AEs**

- Hypertension 22%
- Neutropenia 10%
- Hepatotoxicity 6%

**ARASENS trial**

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

- **With metastatic disease at time of diagnosis:** 86.1%

**Darolutamide + Docetaxel + ADT**

**Placebo + Docetaxel + ADT**

- 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

Visit https://hspc.knowledgehub.wiley.com/ for additional resources
Which factors determine the treatment intensification strategy to be used for each patient? 14–16

**Clinical considerations**

- Prostate-specific antigen profile
- Volume of metastasis (high vs. low)
- Disease stage and presentation

**Medical co-morbidities**

- Tumour's sensitivity to RT
- Tumour coverage/medical expenses
- Patient preference

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**Gaps in treatment intensification in the real world** 17–20

- ADT still the most prescribed initial mHSPC therapy
- More than 50% of patients do not receive treatment intensification
- Short duration of treatment
- More real-world studies required
- Disparity among black vs. white men

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A new approach to treatment intensification

Prescribe any of the following:

- Docetaxel + ADT
- ADT + ARAT
- Triplet therapy
- Only ADT
- RT + ADT
- RT + ARAT + ADT
- ADT + ARAT
- ADT
- RT
- Docetaxel + ADT

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

References: