## Advanced Prostate Cancer

### KEY TERMINOLOGY

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td><strong>DISEASE STATES</strong></td>
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<tr>
<td>Biochemical recurrence without metastatic disease</td>
<td>A rise in PSA in prostate cancer patients after treatment with surgery or radiation (PSA of 0.2ng/mL and a confirmatory value of 0.2ng/mL or greater following radical prostatectomy and nadir + 2.0ng/mL following radiation); this may occur in patients who do not have symptoms</td>
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<tr>
<td>Hormone-sensitive prostate cancer</td>
<td>Prostate cancer that has either not yet been treated with ADT or is still responsive to ADT</td>
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<td>Castration-resistant prostate cancer</td>
<td>Disease progression despite ADT and a castrate level of testosterone (&lt;50 ng/dL); progression may present as either a continuous rise in serum PSA levels, the progression of pre-existing or new radiographic disease, and/or clinical progression with symptoms</td>
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<tr>
<td>High volume metastatic disease</td>
<td>Presence of visceral metastases and/or greater than or equal to four bone metastases with at least one outside of the vertebral column and pelvis</td>
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<tr>
<td>High-risk metastatic disease</td>
<td>Disease that has a poorer prognosis in the presence of two of the three following high-risk features: Gleason &gt;8, &gt;3 bone lesions, or measurable visceral metastases</td>
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<td>De novo metastatic disease</td>
<td>Metastatic disease that is present at the time of initial prostate cancer diagnosis rather than recurring after previous treatment of localized cancer</td>
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<tr>
<td><strong>DISEASE MANAGEMENT</strong></td>
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<tr>
<td>PSA doubling time</td>
<td>The number of months required for the PSA value to increase two-fold</td>
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<tr>
<td>Conventional imaging</td>
<td>CT, MRI, and 99mTc-methylene diphosphonate bone scan</td>
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ADT: androgen deprivation therapy; CT: computed tomography; HRR: homologous recombination repair; LHRH: luteinizing hormone-releasing hormone; mCRPC: metastatic castration-resistant prostate cancer; MRI: magnetic resonance imaging; PET: positron emission tomography; PSA: prostate specific antigen

### Early Evaluation

Clinicians SHOULD

- Obtain tissue diagnosis from primary tumor or site of metastases when clinically feasible in patients without prior histologic confirmation
- Discuss treatment options based on patient life expectancy, comorbidities, preferences, and tumor characteristics
- Treat patients incorporating a multidisciplinary approach
- Optimize pain control or other symptom support and encourage engagement with professional or community-based resources, including patient advocacy groups

### Bone Health

Clinicians SHOULD

- Discuss the risk of osteoporosis associated with ADT and assess the risk of fragility fracture
- Recommend preventative treatment for fractures and skeletal-related events, including supplemental calcium, vitamin D, smoking cessation, and weight-bearing exercise, to patients on ADT
- Recommend preventative treatments with bisphosphonates or denosumab to patients at high fracture risk due to bone loss and recommend referral to physicians who have familiarity with the management of osteoporosis
- Prescribe a bone-protective agent (denosumab or zoledronic acid) for mCRPC patients with bony metastases to prevent skeletal-related events
### Prognosis and Treatment for Non-Metastatic Castration-Resistant Prostate Cancer

**Prognosis**
- Clinicians SHOULD
  - Obtain serial PSA measurements at three to six month intervals and calculate PSA doubling time starting at time of development of castration-resistance
  - Assess for development of metastatic disease using conventional imaging at intervals of six to twelve months

**Treatment**
- Clinicians SHOULD
  - Offer apalutamide, darolutamide, or enzalutamide with continued ADT to patients at high risk for developing metastatic disease
- Clinicians MAY
  - Recommend observation with continued ADT, particularly for those at lower risk for developing metastatic disease
- Clinicians SHOULD NOT
  - Offer systemic chemotherapy or immunotherapy outside the context of a clinical trial

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### Prognosis and Treatment for Metastatic Castration-Resistant Prostate Cancer

**Prognosis**
- Clinicians SHOULD
  - Offer continued ADT with abiraterone acetate plus prednisone, docetaxel, or enzalutamide
  - Consider prior treatment in sequencing agents and recommend therapy with an alternative mechanism of action
  - Offer radium-223 to patients with symptoms from bony metastases from mCRPC and without known visceral disease or lymphadenopathy >3cm

**Treatment**
- Clinicians SHOULD (cont.)
  - Recommend cabazitaxel rather than an alternative androgen pathway directed therapy in patients who received prior docetaxel and abiraterone acetate plus prednisone or enzalutamide
  - Offer a PARP inhibitor to patients with deleterious or suspected deleterious germline or somatic HRR gene-mutated mCRPC following prior treatment with enzalutamide or abiraterone, and/or a taxane-based chemotherapy
  - Offer pembrolizumab to patients with mismatch repair deficient or microsatellite instability high CRPC
  - Offer sipuleucel-T to asymptomatic/minimally symptomatic patients
  - Offer cabazitaxel to patients who received prior docetaxel with or without prior abiraterone acetate plus prednisone or enzalutamide
  - Offer platinum-based chemotherapy to patients with deleterious or suspected deleterious germline or somatic HRR gene-mutated mCRPC following prior treatment with enzalutamide or abiraterone acetate, and/or a taxane-based chemotherapy who cannot use/obtain a PARP inhibitor