### 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 least annually or at intervals determined by lack of response to therapy

Offer germline and somatic tumor genetic testing

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### 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

**Clinicians SHOULD**

Obtain baseline labs and review location of metastatic disease, disease-related symptoms, and performance status

Assess the extent of metastatic disease using conventional imaging at least annually or at intervals determined by lack of response to therapy

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### Treatment (cont.)

**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

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### Treatment

**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

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### Key Terminology

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DISEASE STATES</strong></td>
<td></td>
</tr>
<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>
</tr>
<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>
</tr>
<tr>
<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>
</tr>
<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>
</tr>
<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, ≥3 bone lesions, or measurable visceral metastases</td>
</tr>
<tr>
<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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### Disease Management

| PSA doubling time | the number of months required for the PSA value to increase two-fold |
| Conventional imaging | CT, MRI, and 99mTc-methylene diphosphonate bone scan |

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

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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

BIOCHEMICAL RECURRENCE WITHOUT METASTATIC DISEASE

Prognosis
Clinicians SHOULD
Inform patients regarding the risk of developing metastatic disease and follow patients with serial PSA measurements and clinical evaluation
Perform periodic staging evaluations consisting of cross sectional imaging (CT, MRI) and technetium bone scan in patients who are at higher risk for development of metastases
Clinicians MAY
Utilize novel PET-CT scans as an alternative to or in the setting of negative conventional imaging
Consider radiographic assessments based on overall PSA and PSA kinetics

Treatment
Clinicians SHOULD
Offer observation or clinical trial enrollment
Clinicians SHOULD NOT
Routinely initiate ADT
Clinicians MAY
Offer intermittent ADT in lieu of continuous ADT if ADT is initiated in the absence of metastatic disease

METASTATIC HORMONE SENSITIVE PROSTATE CANCER

Prognosis
Clinicians SHOULD
Assess the extent of metastatic disease (bone, lymph node and visceral metastasis) using conventional imaging
Assess the extent of metastatic disease (high versus low volume)
Assess if the patient is experiencing symptoms from metastatic disease
Obtain a baseline PSA and serial PSAs at a minimum of three to six month intervals after initiation of ADT and consider periodic conventional imaging
Offer genetic counseling and germline testing regardless of age and family history

Treatment
Clinicians SHOULD
Offer ADT with either LHRH agonists or antagonists or surgical castration
Offer continued ADT in combination with either androgen pathway directed therapy (abiraterone acetate plus prednisone, apalutamide, enzalutamide) or chemotherapy (docetaxel)
Clinicians MAY
Offer primary radiotherapy to the prostate in combination with ADT in selected patients with low-volume metastatic disease
Clinicians SHOULD NOT
Offer first generation antiandrogens in combination with LHRH agonists, except to block testosterone flare
Offer oral androgen pathway directed therapy without ADT