**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 or PSMA PET imaging at intervals of 6 to 12 months

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

**Treatment**

Clinicians SHOULD
- Offer apalutamide, darolutamide, or enzalutamide with continued ADT to patients at high risk for developing metastatic disease
- 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; platinum-based chemotherapy may be offered for patients who cannot use or obtain a PARP inhibitor
- Offer pembrolizumab to patients with mismatch repair deficient or microsatellite instability high mCRPC

Clinicians MAY
- 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

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**Prognosis (cont.)**

Clinicians SHOULD
- 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; platinum-based chemotherapy may be offered for patients who cannot use or obtain a PARP inhibitor
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**Treatment (cont.)**

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**DISEASE STATES**

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<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, &gt;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>
</tr>
</tbody>
</table>

**DISEASE MANAGEMENT**

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSA doubling time</td>
<td>the number of months required for the PSA value to increase two-fold</td>
</tr>
<tr>
<td>Conventional imaging</td>
<td>CT, MRI, and 99mTc-methylene diphosphonate bone scan</td>
</tr>
</tbody>
</table>

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

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, and/or preferably PSMA PET imaging in patients who are at higher risk for development of metastases
• Utilize PSMA PET imaging preferentially, where available, as an alternative to conventional imaging due to its greater sensitivity or in the setting of negative conventional imaging

Clinicians MAY
• 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 (lymph node, bone, and visceral metastases)
• 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 three- to six-month intervals after initiation of ADT and consider periodic conventional imaging
• Offer germline testing, and consider somatic testing and genetic counseling

Clinicians MAY
• Consider radiographic assessments based on overall PSA and PSA kinetics

Treatment
Clinicians SHOULD
• Offer ADT with either LHRH agonists or antagonists or surgical castration
• Offer ADT in combination with either androgen pathway directed therapy or chemotherapy (docetaxel)
• Offer ADT in combination with docetaxel and either abiraterone acetate plus prednisone or darolutamide in selected patients with de novo mHSPC

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