Advanced Prostate Cancer

KEY TERMINOLOGY

Term	Definition
DISEASE STATES	
Biochemical recurrence without metastatic disease	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
Hormone-sensitive prostate cancer	prostate cancer that has either not yet been treated with ADT or is still responsive to ADT
Castration-resistant prostate cancer	disease progression despite ADT and a castrate level of testosterone (<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
High volume metastatic disease	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
High-risk metastatic disease	disease that has a poorer prognosis in the presence of two of the three following high-risk features: Gleason >8, >3 bone lesions, or measurable visceral metastases
De novo metastatic disease	metastatic disease that is present at the time of initial prostate cancer diagnosis rather than recurring after previous treatment of localized cancer
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

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

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

METASTATIC CASTRATION RESISTANT PROSTATE CANCER

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

Offer germline and somatic tumor genetic testing

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

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

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

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