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 or PSMA PET imaging at intervals of 6 to 12 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
- Perform imaging at least annually in mCRPC patients without PSA progression or new symptoms
- Order PSMA PET imaging in mCRPC patients, who are considering ^{177}Lu-PSMA-617, with disease progression having previously received docetaxel and androgen pathway inhibitor
- Offer germline (if not already performed) and somatic genetic testing

Treatment

Clinicians SHOULD

- Offer continued ADT with abiraterone acetate plus prednisone, docetaxel, or enzalutamide in mCRPC patients who have not received prior androgen receptor pathway inhibitors
- Offer radium-223 to patients with symptoms from bony metastases from mCRPC and without known visceral disease or lymphadenopathy >3cm
- Offer ^{177}Lu-PSMA-617 to patients with progressive mCRPC having previously received docetaxel and androgen pathway inhibitor with a positive PSMA PET imaging study

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; 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

AUA/SUO
Advanced Prostate Cancer Algorithm

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, 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

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