NON-METASTATIC CASTRATION RESISTANT PROSTATE CANCER

Prognosis

Clinicians SHOULD

- Obtain serial PSA measurements at 3- to 6-month intervals and calculate PSADT 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

Treatment

Clinicians SHOULD

- Offer continued ADT with abiraterone acetate plus prednisone or enzalutamide in mCRPC patients who have not received prior ARPIs
- Offer docetaxel in mCRPC patients with disease progression following treatment with an ARPI
- 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 in mCRPC patients with disease progression following treatment with an ARPI (with or without prior docetaxel), and a positive PSMA PET/CT

Treatment (cont.)

Clinicians SHOULD (cont.)

- Recommend cabazitaxel rather than an alternative androgen pathway inhibitor in mCRPC patients who received prior docetaxel chemotherapy and an ARPI
- Offer pembrolizumab to patients with dMMR or MSI-H mCRPC

Clinicians MAY

- Offer sipuleucel-T to asymptomatic/minimally symptomatic patients
- Offer cabazitaxel in mCRPC patients who received prior docetaxel chemotherapy in the mHSPC or mCRPC setting
- Offer a PARP inhibitor to select patients with deleterious germline or somatic HRR gene-mutated mCRPC who have progressed on progressed on prior ARPI; platinum-based chemotherapy may be offered as an alternative for patients who cannot use or obtain a PARP inhibitor
- Offer a PARP inhibitor in combination with an ARPI to select patients with deleterious germline or somatic HRR gene-mutated mCRPC

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; ARPI: androgen receptor pathway inhibitor; CT: computed tomography; HRR: homologous recombination repair; dMMR: mismatch repair deficient; LHRH: luteinizing hormone-releasing hormone; mCRPC: metastatic castration-resistant prostate cancer; MRI: magnetic resonance imaging; MSI-H: microsatellite instability-high; PET: positron emission tomography; PARP: poly (ADP-ribose) polymerase; PSA: prostate-specific antigen; PSMA: prostate-specific membrane 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
- Offer germline testing for all patients and somatic tumor testing for metastatic disease

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 imaging, preferentially with PSMA PET and/or CT, MRI, and technetium bone scan in patients who are at higher risk for development of metastases
- Utilize PSMA PET imaging preferentially in patients with PSA recurrence after exhaustion of local therapy

Clinicians MAY

- Consider radiographic assessments based on overall PSA and PSA kinetics

Treatment

Clinicians SHOULD

- Risk stratify patients as low- or high-risk. High-risk patients generally are defined as patients with PSADT ≤ 9 months
- Offer observation for patients with low-risk features
- Offer ADT with enzalutamide for patients with high-risk features

Clinicians MAY

- Offer intermittent ADT in lieu of continuous therapy in the setting of a favorable therapy response in patients with high-risk features and no metastatic disease in whom ADT+/- ARPI is initiated

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 and stratify based on low- versus high-volume
- Assess if the patient is experiencing symptoms from metastatic disease
- Obtain a baseline PSA and serial PSAs at 3- to 6-month intervals after initiation of ADT and consider periodic imaging

Treatment

Clinicians SHOULD

- Offer ADT with either LHRH agonists or antagonists or surgical castration
- Offer ADT in addition to androgen pathway-directed therapy with abiraterone acetate plus prednisone, apalutamide, enzalutamide, or darolutamide
- Offer ADT in combination with docetaxel and either abiraterone acetate plus prednisone or darolutamide in select patients with mHSPC

Clinicians MAY

- Offer primary radiotherapy to the prostate in combination with ADT +/- ARPI in select patients
- Offer the combination of ADT, abiraterone, and niraparib in patients with HRR gene alterations

Clinicians SHOULD NOT

- Offer first generation antiandrogens in combination with LHRH agonists, except to block testosterone flare