Specialty Networks

ADVANCED PROSTATE CANCER (APC) CLINICAL GUIDELINE

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PRINCIPLES OF DISEASE MANAGEMENT

1. Consider clinical trials when appropriate
2. Evaluate biological and functional age, overall health and comorbidities when choosing advanced therapies
3. Leverage multi-modality strategies during the disease course with the goal of delivering all life-extending agents at the recommended course of therapy
4. Therapies should be modified based on imaging/radiographic evidence or clinical progression, not on PSA progression alone
5. Early patient identification and therapeutic intervention is recommended as earlier treatment leads to superior outcomes
6. Consider next generation imaging (NGI) in addition to T99 bone scan and CT/MRI per RADAR 3
7. Reimaging to verify METS not required for reimbursement if previous positive imaging exists
8. Evaluate sites of disease when choosing therapy
9. Bicalutamide (Casodex) is not recommended apart from management of flare due to lack of evidence supporting overall survival
10. Use of novel hormonal agents (NHA) requires use of androgen deprivation therapy (ADT) or bilateral orchiectomy

GENETIC TESTING

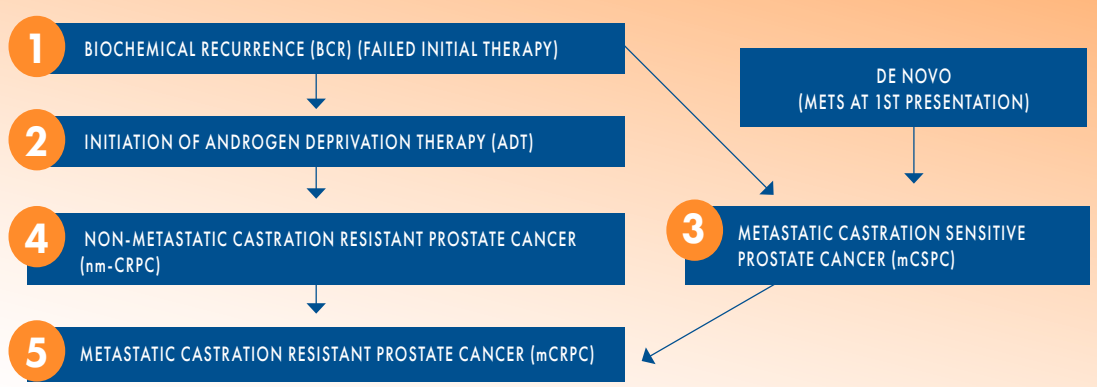
- When possible, collect family history on all prostate cancer patients to determine need for testing
- Recommend genetic germline testing (DNA damage repair defects) for patients with positive family history, high risk disease or metastatic disease
- Consider testing (tissue or blood) for somatic mutations (HRRm*/DDR †, ARV7 status) at disease progression
- MSI-H (microsatellite instability-high) patients may receive pembrolizumab

* homologous recombination repair gene mutation
† DNA damage response

PRODUCT REFERENCE

- Axumin (fluciclovine F18)
- Casodex (bicalutamide)
- Eligard (leuprolide)
- Erleada (apalutamide)
- Firmagon (degarelix)
- Jevtana (cabazitaxel)
- Keytruda (pembrolizumab)
- Lupron (leuprolide)
- Lynparza (olaparib)
- Nubeqa (darolutamide)
- Prolia (denosumab)
- Provenge (sipuleucel-T)
- Rubraca (rucaparib)
- Taxotere (docetaxel)
- Xofigo (radium-223)
- Xgeva (denosumab)
- Xtandi (enzalutamide)
- Yonsa (abiraterone)
- Zometa (zoledronic acid)
- Zytiga (abiraterone)

GUIDELINE DISEASE STATE MAP



Specialty Networks

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The information contained within is the consensus of the UroGPO Medical Advisory Group and is intended only as a suggested guideline for the management of prostate cancer. UroGPO Members are encouraged to review, discuss and make adjustments as they see fit.

11/2022

1 BIOCHEMICAL RECURRENCE

BIOCHEMICAL RECURRENCE (BCR) SURVEILLANCE
- Testing every 3 months
  - Total PSA
  - PSA Doubling Time (rising PSA)
- Follow RADAR 3 BCR imaging guidelines
  - 1st scan PSA = 5-10 ng/ml
  - 2nd scan PSA = 20 ng/ml
  - Subsequent scan PSA doubling
  - Consider Next Generation Imaging (NGI) PSA ≥ 0.5
- Consider imaging every 1-2 years
- Evaluate for Local Salvage Therapy

DETECTABLE METS — NO → (back to BCR surveillance) / YES ↓

2 INITIATION OF ANDROGEN DEPRIVATION THERAPY

On ADT? — YES ↓

INITIATE BONE HEALTH PLAN
- Vitamin D and Calcium per bone therapy protocol
- DEXA at initiation
- Consider **PROLIA or RECLAST** if indicated (**alendronate** as non-preferred alternative)
- Yearly DEXA recommended

MONITOR DISEASE PROGRESSION
- Testing every 3 months
  - Total PSA and Testosterone
  - PSA Doubling Time (rising PSA)
- New Symptoms/Clinical Progression
- Continue RADAR 3 BCR imaging guidelines

CASTRATION SENSITIVE? — YES → (back to monitor) / NO →

CRPC IF:
- Testosterone <50 ng/dl **and**
- Confirmed PSA elevation over nadir on continuous ADT

and/or
- Progression on Imaging

POSITIVE FOR METS? — YES → **5** METASTATIC CASTRATION RESISTANT PROSTATE CANCER (mCRPC) / NO →

3 METASTATIC CASTRATION SENSITIVE PROSTATE CANCER (mCSPC)

RECURRENT (FAILED PRIMARY THERAPY) | **DE NOVO (METS AT 1ST PRESENTATION)**

DETECTABLE METS? — YES ↓

INITIATE ADT AND ERLEADA or XTANDI or ABIRATERONE
or in certain circumstances

HIGH VOLUME*
- CONSIDER ADT + 6 cycles **docetaxel**

*CHAARTED definition: 4 or more bone lesions with ≥1 outside axial skeletal and/or visceral mets

LOW VOLUME LOCALIZED DISEASE
- CONSIDER† treatment of primary & oligomets
- CONSIDER† radiotherapy or surgical resection for regional lymph nodes

† Review national guidelines for specific criteria

MONITOR DISEASE PROGRESSION

4 NON-METASTATIC CASTRATION RESISTANT PROSTATE CANCER (nm-CRPC)

CRPC IF: TESTOSTERONE <50 NG/DL **and** CONFIRMED PSA ELEVATION OVER NADIR ON CONTINUOUS ADT

MONITOR DISEASE PROGRESSION
- Testing every 3 months
  - Total PSA and Testosterone
  - PSA Doubling Time (rising PSA)
- New Symptoms/Clinical Progression

INITIATE RADAR 3 nm-CRPC IMAGING PROTOCOLS
- 1st scan PSA = 2 ng/ml
- 2nd scan PSA = 5 ng/ml
- Subsequent scan at each PSA doubling
- Consider Next Generation Imaging (NGI)

CONTINUE BONE HEALTH PLAN

Before therapy initiation, consider repeat imaging if none in past 6-12 months, especially consider NGI in appropriate patients

DETECTABLE METS? — NO → **ERLEADA or NUBEQA or XTANDI** for patients at high risk of mets based on PSADT and clinical factors

YES ↓

- Recommend imaging upon PSA rise or symptom progression
- Consider Next Generation Imaging (NGI) in the setting of PSA rise when M1 therapies would be appropriate
- Continue Bone Health Plan

5 METASTATIC CASTRATION RESISTANT PROSTATE CANCER (mCRPC)

† consider layered therapy when clinically appropriate

+ SYMPTOMS & SIGNS ASSOCIATED WITH ADVANCED PROSTATE CANCER ARE MULTI-FACTORIAL AND MANIFEST IN WAYS BEYOND PAIN: Fatigue, generalized weakness; Weakness in extremities; Impaired mobility; Interference with daily activities; Loss of appetite; Loss of bladder and bowel function; Dyspnea; Neurologic Impairment; Mild sensory loss, numbness; Pain and discomfort; Interference with sleep; Anemia, neutropenia, thrombocytopenia

SOFT TISSUE/ LYMPH NODE PREDOMINANT

ASYMPTOMATIC or MINIMALLY SYMPTOMATIC
- **PROVENGE** † recommended as 1st agent (no cancer-related narcotic use)
- **XTANDI or ABIRATERONE**

SYMPTOMATIC
- **XTANDI or ABIRATERONE**

BONE MET PREDOMINANT

Initiate or continue XGEVA or ZOMETA

ASYMPTOMATIC
- **PROVENGE** † recommended as 1st agent (no cancer-related narcotic use)
- **XTANDI or ABIRATERONE**

MINIMALLY SYMPTOMATIC
- **PROVENGE** † recommended as 1st agent (no cancer-related narcotic use)
- **XOFIGO** † (with documented symptoms+) **or XTANDI or ABIRATERONE**

SYMPTOMATIC
- **XOFIGO** † (with documented symptoms+) **or XTANDI or ABIRATERONE**

VISCERAL METS^
- **DOCETAXEL or XTANDI**

^ platinum based therapy for neuroendocrine tumors / small cell disease

No peer review data showing durable responses for back to back hormonal usage

LYNPARZA - HRR positive (post **XTANDI or ABIRATERONE**)

or

Positive for homologous recombination repair mutations? — YES → **RUBRACA** - BRCA 1/2 positive (post ≥ 1 novel hormone and post-taxane chemo)

NO ↓

DOCETAXEL (if not yet received)

JEVTANA