Prostate Cancer

This Prostate Cancer treatment consensus algorithm is used as a framework for the application of individualized therapy for patients with prostate cancer at the MD Anderson Cancer Center. The faculty and members of the Genitourinary Center apply this general algorithm to individual patients accommodating patient preference and physician experience in the context of a specific knowledge of prostate cancer.

Note: Consider Clinical Trials as treatment options for eligible patients.
Prostate Cancer

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INITIAL DIAGNOSIS

STAGING WORKUP

PRESENTING
CLINICAL STAGE

Bone scan if:
- PSA greater than 15 ng/mL or
- cT3-cT4 disease or
- Bone pain or
- Positive nodes on CT/MRI imaging or
- Gleason scores of 8-10 or
- Adverse histologies (e.g. small cell and/or neuroendocrine)
- CT or MRI considered for high risk patients based on NCCN guidelines
- FNA if clinically indicated

Follow up annually, no further work up until symptoms, for example, bone pain or voiding dysfunction

Symptomatic

Life expectancy greater than or equal to 5 years, or symptomatic from local or metastatic disease

Life expectancy less than 5 years and asymptomatic

Prostate biopsy, DRE, PSA, Gleason score

See Page 3 of this algorithm

See Page 4 of this algorithm

Any T or N, M1

Any N M1 with Visceral or lytic bone metastases and low PSA

Any TN1, M0

cT3a

cT3b, cT4

cT1a

cT1b, cT1c, cT2a, cT2b

1 Perform prostate biopsy if not previously done. If done, MDACC review of prostate biopsy results.

2 Refer to Appendix A – Approved MD Anderson Prostate Biomarkers on page 9.


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### PRESENTING CLINICAL STAGE

- **cT1a**
  - Life expectancy greater than or equal to 10 years
  - TRUS biopsy

- **cT1b**
  - Life expectancy less than 10 years
  - TRUS biopsy

- **cT1c, cT2a, cT2b**
  - Life expectancy greater than or equal to 10 years?
  - Yes
  - Low Risk Disease:
    - TRUS biopsy
    - cT1-cT2a and PSA less than 10 ng/mL
    - Gleason score 2-6

  - Intermediate Risk Disease:
    - cT2b (but not qualifying for high risk disease) or
    - PSA 10-20 ng/mL or
    - Gleason score 7

  - High Risk Disease:
    - cT2c-cT3a or
    - PSA greater than 20 ng/mL or
    - Gleason score 8-10

- No

### INITIAL THERAPY

- **cT1a**
  - TRUS biopsy
  - Not reclassified to higher risk
  - Reclassified to higher risk

- **cT1b**
  - Life expectancy greater than or equal to 10 years

- **cT1c, cT2a, cT2b**
  - Life expectancy greater than or equal to 10 years?
  - Yes
  - Monitor patient for symptoms; consider treatment if progression

- **No**
  - Consider treatment based on new stage

### Life Expectancy

- **Yes**
  - Active surveillance
  - Consider external beam radiotherapy or brachytherapy
  - Radical prostatectomy if life expectancy greater than 20 years

- **No**
  - Monitor patient for symptoms; consider treatment if progression
  - Consider external beam radiotherapy or cryoablation or hormonal ablation

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1. Refer to Appendix A – Approved MD Anderson Prostate Biomarkers on page 9.
2. All localized treatments: length of follow-up and quality of data differ with each treatment and should be discussed with your treatment team.
3. Brachytherapy and cryotherapy eligibility limited by prostate size, pubic bone geometry, baseline urinary function.
4. External beam radiation should be dose escalated using either IMRT (intensity modulated radiation therapy), or proton therapy. Inflammatory bowel disease and peri-rectal disease may be contraindications.
5. Radical prostatectomy is performed by open retropubic or robot assisted technique. These technique choices, eligibility for a nerve sparing procedure, and the need for a pelvic lymph node dissection should be discussed with your treatment team.
6. External beam radiation and brachytherapy radical prostatectomy have longer duration of follow-up and may be preferred over cryotherapy.

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**Note:** Consider Clinical Trials as treatment options for eligible patients.

### PRESENTING CLINICAL STAGE

- **Locally Advanced** (cT3a, cT3b, cT4)
  - *Life Expectancy greater than or equal to 5 years or symptomatic?*
    - **Yes**
      - *Consider 6-12 months androgen ablation* (See Page 5 or 6)
      - *Consider radical prostatectomy in selected cases or on protocol*
    - **No**
      - *Consider androgen ablation* (See Page 5 or 6)

- **Any T, N1**
  - *Consider androgen ablation* (See Page 5 or 6)

- **Any T, N or M1**
  - *Androgen ablation* (See Page 5 or 6)

- **Any N, M1 with visceral or lytic bone metastases and low PSA**
  - *Biopsy metastatic lesions*
  - *Pathology shows Small Cell component and/or neuroendocrine markers*
    - *External beam radiotherapy with androgen ablation* or
    - *Androgen ablation* (See Page 6, Box A) or
    - *Consider radical prostatectomy in selected cases or on protocol*

### INITIAL THERAPY

- **Consider:**
  - Radiotherapy or
  - Consider radical prostatectomy or
  - Clinical trial

### FOLLOW-UP

- *PSA every 3 months, Radiographic studies if clinically indicated (bone scans, CT of abdomen and pelvis)*

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1. 3D conformal radiotherapy or intensity modulated radiotherapy (IMRT) are standard for external beam radiotherapy.
2. Based on pathologic findings after radical prostatectomy (e.g. path stage, margin status, Gleason score, age), consider adjuvant external beam radiotherapy.
4. Refer to Appendix A – Approved MD Anderson Prostate Biomarkers on page 9.
**Prostate Cancer**

Follow-up androgen ablative therapy

**Intermittent androgen ablation**
- Follow up visit every 3 months with PSA and testosterone, repeat imaging if rising PSA and/or clinical progression, and liver function tests every month for 3 months if on anti-androgens.

**High volume bone disease**
- Androgen ablative therapy with LHRH analogue plus docetaxel for 6 cycles

**Rising PSA or other signs of progression?**

- Yes
  - If on anti-androgen alone, add LHRH agonist; if progression, go to Box C on page 6
  - If on LHRH agonist alone, switch to continuous androgen ablation and add anti-androgen; if progression, go to Box B on Page 6

- No
  - Continue follow up and current treatment

**Androgen-independent salvage therapy**

- For Continuous Androgen Ablation, see Box A on Page 6

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**Note:** Consider Clinical Trials as treatment options for eligible patients.

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1 Consider intermittent androgen ablation for rising PSA only. If skeletal metastases are present, recommend 7 to 14 days of anti-androgen prior to initiation of LHRH agonist to prevent flare.

2 Consider baseline bone density scan and bisphosphonate therapy every 6 months to minimize osteoporosis associated with LHRH agonist use.

3 Check liver function tests 1 month after initiation of anti-androgen and then with each 3 month follow up visit thereafter.

4 Visceral metastasis and/or greater than or equal to 4 bone metastasis
Prostate Cancer

ANDROGEN ABLATIVE THERAPY

Continuous androgen ablation with LHRH agonist alone1,2 or with anti-androgen3

Radiographic progression with symptoms of progression?

Yes

Progression

• Chemotherapy (Docetaxel and Glucocorticoids) or
• Consider Xofigo
• Consider Clinical trial or
• Consider Supportive care

Pathology shows adenocarcinoma

No

Progression without visceral or lytic bone metastases

• Secondary hormone therapies or noncytotoxics Anti-androgen3, Diethylstilbestrol, Abiraterone, Enzalutamide, Sipuleucel-T, Ketoconazole, or Low-dose Glucorticoids if not previously given
• Clinical trial or
• Observation

Progression with only or predominately visceral metastasis

• Radio-isotopes such as Xofigo, Strontium 89, Samarium 153
• Salvage chemotherapy4 or
• Secondary hormone therapies or noncytotoxics Anti-androgen3, Enzalutamide, Diethylstilbestrol, Abiraterone, Sipuleucel-T, Ketoconazole, or low dose Glucorticoids if not previously given

Progression with only or predominately lytic osteoblastic bone metastases

Appropriately elevated PSA5

Yes

Biopsy metastatic lesion

Pathology shows small cell component and/or neuroendocrine component

• Cisplatin and Etoposide or
• Carboplatin/Docetaxel
• Clinical Trial or
• Palliative Care

No

Rising PSA2

Discontinue antiandrogen

Decreasing PSA?

Yes

No

No progression

Follow-up

Return to clinic every 3 months:
• Routine labs, PSA, testosterone, and liver function tests.
• Repeat imaging if rising PSA and/or clinical progression.

FOLLOW-UP

Radiographic progression without symptoms of progression

ANDROGEN-INDEPENDENT SALVAGE THERAPY

Yes

Pathology shows small cell component and/or neuroendocrine component

No

Clinical trial or
• Palliative radiotherapy or
• Cabazitaxel or
• Supportive care

Yes

Discontinue antiandrogen

Decreasing PSA?

No

No progression

Return to clinic every 3 months:
• Routine labs, PSA, testosterone, and liver function tests.
• Repeat imaging if rising PSA and/or clinical progression.

Note: Consider Clinical Trials as treatment options for eligible patients.

1 If skeletal metastases are present, recommend 7 to 14 days of antiandrogen prior to initiation of LHRH agonist to prevent flare.
2 Consider baseline bone density scan and bisphosphonate therapy every 6 months to minimize osteoporosis associated with LHRH agonist use.
3 Check Liver Function Tests 1 month after initiation of antiandrogen and then with each 3 month follow up visit thereafter.
4 If testosterone greater than or equal to 50 on LHRH analogue, consider orchiectomy or GNRH receptor antagonist to achieve testosterone less than or equal to 49.
5 Appropriately elevated PSA corresponds to radiographic volume of disease related to PSA.
6 Cytoxan with Vincristine and Dexamethasone; Carboplatin with Taxane; KAVE.

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**Prostate Cancer**

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**Note:** Consider Clinical Trials as treatment options for eligible patients.

**PATIENT STATUS**

- Patient on active surveillance
  - Consider active surveillance protocol
  - PSA and DRE every 6 months
  - TRUS biopsy at baseline and annually (option to skip years if 1-2 negative biopsies in a row)
  - Consider active surveillance support group
  - Consider MRI pelvis with endo-rectal coil or targeted MRI/US fusion biopsy of suspicious lesion(s)

**ACTIVE SURVEILLANCE**

**PROGRESSION**

PSA trend and/or repeat biopsy indicates reclassification to higher risk, or symptomatic, or unable to tolerate further biopsies

Refer to appropriate stage on Pages 3 or 4 of this guideline

**FOLLOW UP**

(Continue monitoring until progression)

- Symptom evaluation
  - PSA every 3-6 months for 5 years, then every 6-12 months for 5 years, then annually
  - After radiotherapy:
    - DRE every 6-12 months
  - After radical prostatectomy:
    - DRE every 1-3 years with follow-up visit

**Signs of recurrence or progression?**

- Yes
  - See Page 8 for Recurrent Prostate Cancer
- No

**Patient 5 or more years from treatment?**

- Yes
  - Transfer to Survivorship Clinic
- No, continue monitoring

**Consider randomized clinical trials supporting the long-term survival benefits of adjuvant radiation weighed against the side effects**

**Patient post definitive therapy (i.e. radiotherapy or radical prostatectomy)**

**Status post radical prostatectomy with positive surgical margins and/or pT3a or b, and Nx/N0, PSA undetectable after surgery**
Prostate Cancer (Recurrence)

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Note: Consider Clinical Trials as treatment options for eligible patients.

PROGRESSION

- Bone scan, abdominal and pelvic CT
- Bone scan and CT scans positive?
  - Yes
  - Androgen ablation (See Page 5 for intermittent or Page 6 for continuous)
  - No
  - Consider prostate biopsy
    - Biopsy positive?
      - Yes
      - Observation
      - No or not done
      - Androgen ablation

SALVAGE THERAPY

- Bone scan, abdominal and pelvic CT, MRI pelvis with endo-rectal coil, TRUS
- Consider prostate bed biopsy
- Consider Prostascint scan with co-registration
- Bone scan and CT scans positive?
  - Yes
  - Androgen ablation (See Page 5 for intermittent or Page 6 for continuous)
  - No
  - Observation
  - External beam radiotherapy
  - Androgen ablation

1 Rising PSA after radical prostatectomy is greater than 0.2 ng/mL.
Rising PSA after radiotherapy or brachytherapy PSA is greater than 2.0 ng/mL above the nadir (lowest value post treatment off androgen deprivation, or medical castration therapy [ADT])

2 Numerous studies indicate that salvage external beam radiotherapy is most effective if delivered with a PSA less than 0.5 ng/mL.
### APPENDIX A: Prostate Cancer Molecular Markers – MD ANDERSON APPROVED

<table>
<thead>
<tr>
<th>DISEASE SITE</th>
<th>CELL TYPE</th>
<th>BIOMARKER</th>
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<tbody>
<tr>
<td>GU</td>
<td>Prostate</td>
<td>• PSA</td>
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<tr>
<td></td>
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<td>• PAP</td>
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<td>• CgA</td>
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1 Literature support for MD Anderson approved Biomarkers is available and can be found under Clinical Management Algorithms → “Biomarkers – MD Anderson Approved”
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SUGGESTED READINGS

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Prostate Cancer

This practice consensus algorithm is based on majority expert opinion of the GU Center Faculty at the University of Texas, MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following medical oncologists, radiation oncologist, and urologic oncologists:

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Note: Consider Clinical Trials as treatment options for eligible patients.

DEVELOPMENT CREDITS

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‡ Core Development Team