This Prostate Cancer treatment consensus algorithm is used as a framework for the application of individualized therapy for patients with prostate cancer at 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.
STAGING WORK-UP

- Bone scan if any of the following are present:
  - PSA > 15 ng/mL
  - cT3-cT4 disease
  - Bone pain
  - Positive nodes on CT/MRI imaging
  - Gleason groups 4 and 5
  - Adverse histologies (e.g., small cell and/or neuroendocrine)
- If not completed prior to biopsy and if needed for clinical decision making, multi-parametric MRI or CT pelvis with contrast if MRI cannot be done
- Biopsy suspicious lesion(s) if clinically indicated

PRESENTING CLINICAL STAGE

- cT1a – cT3a See Page 3
- cT3b, cT4 AnyTN1, M0 AnyT or N, M1 See Page 4

INITIAL EVALUATION

- Prostate biopsy\(^1,2\) with Gleason grading\(^3\)
- History and Physical
- Digital rectal exam (DRE)
- Prostate specific antigen (PSA)
- Expanded Prostate Cancer Index Composite (EPIC)
- Family history with referral to genetic counseling and germline mutation testing as indicated\(^4\)
- Lifestyle risk assessment\(^5\)

- Life expectancy ≥ 5 years or symptomatic from local or metastatic disease

- Life expectancy < 5 years and asymptomatic

Follow up annually; no imaging or treatment until symptoms present (e.g., bone pain or voiding dysfunction)

Symptomatic?

Yes

No

\(^1\) Perform prostate biopsy if not previously done. If previously done, MD Anderson to review prostate biopsy results.

\(^2\) See MD Anderson Approved Biomarker algorithm

\(^3\) See Appendix A: Prognostic Groups Based on Gleason Scores

\(^4\) Men meeting any one of the following suggested criteria should undergo genetic counseling and genetic testing:
- All men with prostate carcinoma (PCA) from families meeting established testing or syndromic criteria for the following syndromes: hereditary breast and ovarian cancer (HBOC), hereditary prostate carcinoma (HPC) and Lynch Syndrome (LS)
- Men with PCA with two or more close blood relatives on the same side of the family with a cancer in the following syndromes: HBOC, HPC and LS
- All men with mCRPC should consider genetic testing

\(^5\) See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

\(^6\) For all M1, platinum-based chemotherapy and/or a PARP (poly ADP ribose polymerase) inhibitor should be considered
Prostate Cancer

INITIAL THERAPY

Active surveillance or
Consider external beam radiation therapy or Radical prostatectomy if life expectancy > 20 years

Monitor patient for symptoms; consider treatment if progression

Active surveillance or
Consider external beam radiation therapy or Radical prostatectomy or Molecular testing of positive biopsy

External beam radiation or Radical prostatectomy

Consider treatment based on new stage

Low Risk Disease: cT1-cT2a and PSA < 10 ng/mL and Gleason group 1

Intermediate Risk Disease: cT2b-cT3a or PSA 10-20 ng/mL or Gleason group 2 and 3

High Risk Disease: cT3a or PSA > 20 ng/mL or Gleason group 4 and 5

Locally Advanced

Multidisciplinary Algorithm Based on Clinical and Molecular Testing

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

Presenting Clinical Stage

Life expectancy < 10 years

Transrectal ultrasound (TRUS) biopsy if Gleason group 4 and 5

Life expectancy ≥ 10 years

TRUS biopsy

No

Yes

cT1a

cT1b

cT1c-cT3a

TRUS biopsy

Not reclassified to higher risk

Reclassified to higher risk

Monitor patient for symptoms; consider treatment if progression

See Page 5 for surveillance and follow-up

See Page 5 for surveillance and follow-up

See Page 4

Radical prostatectomy is performed by open retropubic or robot assisted technique.

External beam radiation and brachytherapy radical prostatectomy have longer duration of follow-up and may be preferred over cryotherapy. Cryotherapy is usually not recommended as first line definitive treatment.

May provide assistance to patients considering active surveillance versus treatment options.

Luteinizing hormone releasing hormone (LHRH) agonist or antagonist.

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Department of Clinical Effectiveness

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Prostate Cancer

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

**INITIAL THERAPY**

**PRESENTING CLINICAL STAGE**

- Locally Advanced cT3b
  - External beam radiation therapy\(^1\) and 18-36 months of androgen ablation\(^2\) or
  - External beam radiation therapy\(^1\) with brachytherapy and 12 months of androgen ablation\(^2\)
  - Radical prostatectomy

- cT4
  - Androgen ablation\(^2\) and external beam radiation therapy\(^1\)
  - Surgical resection may be considered\(^3\) with possible perioperative and/or intraoperative radiation therapy

- Any TN1
  - Androgen ablation\(^2\) and external beam radiation therapy\(^1\) or
  - Radical prostatectomy or
  - Androgen ablation\(^2\)

- Any T or N, M\(^1\)\(^4\)
  - Androgen ablation\(^2\) plus docetaxel (6 cycles) for high volume disease or
  - Androgen ablation\(^2\) plus abiraterone acetate and prednisone
  - Local therapy consisting of radiation therapy or surgery may be considered on protocol

- Any N, M\(^1\)\(^4\) with visceral or lytic bone metastases and low PSA
  - Biopsy\(^6\) of metastatic lesions
  - Pathology shows small cell or neuroendocrine prostate carcinoma? Yes
    - Either carboplatin or cisplatin with etoposide
    - Consider definitive treatment to primary tumor after the patient as had maximal response to systemic therapy
  - No
    - Treatment as indicated by clinical stage

**FOLLOW-UP**

- PSA every 4 to 12 weeks
- Radiographic studies if clinically indicated (bone scans, CT abdomen and pelvis with contrast)
- Dual energy x-ray absorptiometry (DEXA) bone mineral density scan\(^5\) every 12 to 18 months, if clinically indicated

---

1. 3D conformal radiation therapy, intensity modulated radiation therapy (IMRT) or proton therapy are standard for external beam radiation therapy
2. Luteinizing hormone releasing hormone (LHRH) agonist or antagonist
3. Based on pathologic findings after radical prostatectomy (e.g., path stage, margin status, Gleason score, age), consider adjuvant external beam radiation therapy
4. For all M1, platinum-based chemotherapy and/or a PARP (poly ADP ribose polymerase) inhibitor should be considered
5. DEXA scan is indicated for patients < 70 years of age who have received at least 12 months of androgen ablation therapy or for patients ≥ 70 years who have received at least 6 months of androgen ablation therapy
6. See MD Anderson Approved Biomarker algorithm

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**PATIENT STATUS**

- Symptom evaluation: PSA every 3-6 months for 5 years, then every 6-12 months for 5 years, then annually
- DEXA bone mineral density scan if clinically indicated
- After radiation therapy: DRE every 6-12 months
- After radical prostatectomy: DRE every 1-3 years with follow-up visit

**SURVEILLANCE**

- observation
- Adjuvant radiation therapy

**PROGRESSION**

- Increased PSA and/or signs of recurrence or progression?
  - Yes
  - No

**FOLLOW-UP**

- Patient ≥ 2 Years from treatment?
  - Yes
  - Transfer to Survivorship Clinic
  - No
  - Continue monitoring

---

1 DEXA scan is indicated for patients < 70 years of age who have received at least 12 months of androgen ablation therapy or for patients ≥ 70 years who have received at least 6 months of androgen ablation therapy.

2 External beam radiation therapy should be considered based on pathological findings after radical prostatectomy (e.g., path stage, margin status, Gleason score/grade, age) when PSA is 0 ng/mL. If not considered after surgery, external beam radiation therapy should be performed at or below a PSA level of 0.5 ng/mL.
**PROGRESSION**

- **Increasing PSA**
  - Bone scan, and
  - CT abdomen/pelvis with contrast or CT abdomen with contrast and MRI pelvis, and
  - Chest x-ray or CT chest with contrast
  - Consider F18-Fluciclovine PET/CT with contrast

- **Metastatic Disease**
  - Yes
    - Hormone sensitive disease?
    - Yes
      - Consider docetaxel for 6 cycles in high volume disease
      - Add AR inhibitor (prior to initiation to prevent flare) plus abiraterone acetate and prednisone
    - No
      - See Page 7

- **No Metastatic Disease**
  - Evidence or high likelihood of local recurrence?
    - Yes
      - Consider salvage therapies (radiation if prior surgery)
      - Salvage surgery or ablative procedures (if previous radiation)
    - No
      - Calculate PSA doubling time
        - Less than 6 months
          - Androgen ablation intermittently
          - Observation
        - Greater than 9 months
          - Observation (recommended)
          - Androgen ablation intermittently

**SALVAGE THERAPY**

- **Orchiectomy or LHRH agonist or antagonist**
  - with or without androgen receptor (AR) inhibitor (e.g., bicalutamide, flutamide)
  - Consider docetaxel for 6 cycles in high volume disease
  - Add AR inhibitor (prior to initiation to prevent flare) plus abiraterone acetate and prednisone

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

**Disclaimer:** This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care.
Radiographic progression with symptoms of progression

In addition to continued surgical or pharmacological castration
- Sipuleucel-T\(^1\) (up to three doses)
- Secondary hormone therapies
  - Axitinib and prednisone\(^2\)
  - Enzalutamide
- Chemotherapy
  - Docetaxel\(^3\) up to 10 cycles
  - Cabazitaxel\(^3\) up to 10 cycles
  - Radium 223 up to 6 cycles
- Radiation therapy for symptomatic/progressive local and/or metastatic disease

Progressive disease?

Yes

- PSA every 4 to 6 weeks, radiographic studies as clinically indicated (bone scans, CT abdomen and pelvis)
- DEXA bone mineral density scan\(^5\) if clinically indicated
- Continue until disease progression

No

- PSA every 4 to 6 weeks, radiographic studies as clinically indicated (bone scans, CT abdomen and pelvis)
- DEXA bone mineral density scan\(^5\) if clinically indicated
- Continue until disease progression

---

\(^1\) Recommended for early Castrate Resistant Prostate Cancer (CRPC) asymptomatic patients that do not have evidence of rapid disease progression

\(^2\) Other possible secondary hormone therapy options include ketoconazole plus hydrocortisone when abiraterone unavailable, diethylstilbestrol (DES) with low dose prophylactic anticoagulants, low dose corticosteroids, bicalutamide, nilutamide, flutamide

\(^3\) Addition of carboplatin to either docetaxel or cabazitaxel recommended for patients meeting Aggressive Variant Prostate Cancer Criteria. Aggressive Variant Prostate Cancer Criteria is defined as a subset of patients with advanced castration-resistant prostate cancer who may eventually evolve into an androgen receptor (AR)–independent phenotype, with a clinical picture associated with the development of rapidly progressive disease involving visceral sites and hormone refractoriness, often in the setting of a low or modestly rising serum prostate-specific antigen level. Biopsies performed in such patients may vary, ranging from poorly differentiated carcinomas to mixed adenocarcinoma-small cell carcinomas to pure small cell carcinomas. These aggressive tumors often demonstrate low or absent AR protein expression and in some cases, express markers of neuroendocrine differentiation.

\(^4\) May consider other chemotherapy options as per Thall et al. (2007) after progression of disease on docetaxel/cabazitaxel with or without carboplatin

\(^5\) DEXA scan for patients < 70 years of age who have received at least 12 months of androgen ablation therapy or those ≥ 70 years who have received at least 6 months of androgen ablation therapy
APPENDIX A: Prognostic Groups Based on Gleason Scores

<table>
<thead>
<tr>
<th>Prognostic Group</th>
<th>Corresponding Gleason Score</th>
<th>Risk Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>6</td>
<td>Low</td>
</tr>
<tr>
<td>Group 2</td>
<td>$3 + 4 = 7$</td>
<td>Intermediate Favorable</td>
</tr>
<tr>
<td>Group 3</td>
<td>$4 + 3 = 7$</td>
<td>Intermediate Unfavorable</td>
</tr>
<tr>
<td>Group 4</td>
<td>8</td>
<td>High</td>
</tr>
<tr>
<td>Group 5</td>
<td>9 - 10</td>
<td>High</td>
</tr>
</tbody>
</table>


SUGGESTED READINGS
SUGGESTED READINGS - continued


Continued on next page


**SUGGESTED READINGS - continued**
DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Genitourinary Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

Ana Aparicio, MD (Genitourinary Medical Oncology)
John Araujo, MD (Genitourinary Medical Oncology)†
Tharakeswara Bathala, MD (Abdominal Imaging)
Brian Chapin, MD (Urology)
Seungtaek Choi, MD (Radiation Oncology)†
Paul Corn, MD, PhD (Genitourinary Medical Oncology)†
John W. Davis, MD (Urology)†
Colin P. Dinney, MD (Urology)
Olga N. Fleckenstein* Steven J. Frank, MD (Radiation Oncology)
Ashish Kamat, MD (Urology)
Eric Jonasch, MD (Genitourinary Medical Oncology)

Deborah A. Kuban, MD (Radiation Oncology)
Christopher J. Logothetis, MD (Genitourinary Medical Oncology)
Surena Matin, MD (Urology)
Curtis A Pettaway, MD (Urology)
Louis L Pisters, MD (Urology)
Devaki Shilpa Sursi, MBBS (Nuclear Medicine)
Chad Tang, MD (Radiation Oncology)
Shi-Ming Tu, MD (Genitourinary Medical Oncology)
John F. Ward, MD (Urology)
Mary Lou Warren, DNP, APRN, CNS-CC*
Amado Zurita-Saavedra, MD (Genitourinary Medical Oncology)

† Core Development Team
* Clinical Effectiveness Development Team