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.

Note: Consider Clinical Trials as treatment options for eligible patients.
Perform prostate biopsy if not previously done. If done, MD Anderson review of prostate biopsy results.

If done, MD Anderson review of prostate biopsy results.

See MD Anderson Approved Biomarker algorithm.

See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice.

All M1 should undergo genetic testing to look for germline mutations in DNA damage repair pathway genes. If present, should obtain genetic counseling for family members; platinum-based chemotherapy and/or a PARP (poly ADP ribose polymerase) inhibitor should be considered during the course of that patient’s disease.

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

This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers.

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Prostate Cancer

INITIAL THERAPY

Monitor patient for symptoms; consider treatment if progression

- Active surveillance
- Consider external beam radiation therapy \(^2\) or brachytherapy \(^3\)
- Radical prostatectomy \(^2\) if life expectancy greater than 20 years

Consider treatment based on new stage

- Active surveillance
- Brachytherapy \(^3\)
- Cryotherapy \(^3,6,7\)
- External beam radiation \(^4\)
- Radical prostatectomy \(^7\)
- Molecular testing of positive biopsy \(^1,8\)

Active surveillance

- Brachytherapy \(^3,6,7\)
- Cryotherapy \(^3,6,7\)
- Radical prostatectomy
- Active surveillance (on protocol)
- External beam radiation with 4-6 months androgen ablation

Active surveillance

- Brachytherapy \(^3,6,7\)
- Cryotherapy \(^3,6,7\)
- Radical prostatectomy
- External beam radiation with or without brachytherapy and 2-3 years androgen ablation
- Radical prostatectomy

See Page 5 for appropriate follow-up or active surveillance based on initial therapy

See Page 5 for appropriate active surveillance based on initial therapy

1 See MD Anderson Approved Biomarker algorithm
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, and baseline urinary function
4 External beam radiation should be dose escalated using either intensity modulated radiation therapy (IMRT), 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.
7 Usually not recommended as first line definitive treatment
8 May provide assistance to patients considering active surveillance or radical therapy

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

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

### PRESENTING CLINICAL STAGE

<table>
<thead>
<tr>
<th>Locally Advanced (cT3a, cT3b)</th>
<th>INITIAL THERAPY</th>
<th>FOLLOW-UP</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Androgen ablation(^1) for two years and external beam radiation therapy(^2) or</td>
<td></td>
<td>• PSA every 4 to 12 weeks</td>
</tr>
<tr>
<td>• Radical prostatectomy</td>
<td></td>
<td>• Radiographic studies if clinically indicated (bone scans, CT abdomen and pelvis)</td>
</tr>
</tbody>
</table>

| cT4 | | • DEXA bone mineral density testing\(^5\) every 12 to 18 months, if clinically indicated |
| Any T N1 | | |
| • Androgen ablation\(^1\) and external beam radiation therapy\(^2\) or | | |
| • Surgical resection may be considered\(^3\) | | |
| • Radical prostatectomy or Androgen ablation\(^1\) | | |

| Any T or N M1\(^4\) | | |
| • Androgen ablation\(^1\) plus docetaxel (6 cycles) for high volume disease | | |
| • Androgen ablation\(^1\) plus abiraterone acetate and prednisone | | |

| Any N, M1\(^4\) with visceral or lytic bone metastases and low PSA | Pathology shows small cell or neuroendocrine prostate carcinoma | • Either carboplatin or cisplatin with etoposide |
| Biopsy\(^6\) metastatic lesions | • Consider definitive treatment to primary tumor after the patient as had maximal response to systemic therapy |

\(^1\) Luteinizing hormone releasing hormone (LHRH) agonist or antagonist
\(^2\) 3D conformal radiotherapy or intensity modulated radiotherapy (IMRT) are standard for external beam radiotherapy
\(^3\) Based on pathologic findings after radical prostatectomy (e.g., path stage, margin status, Gleason score, age), consider adjuvant external beam radiotherapy
\(^4\) All M1 should undergo genetic testing to look for germline mutations in DNA damage repair pathway genes. If present, should obtain genetic counseling for their family; platinum-based chemotherapy and/or a PARP (poly ADP ribose polymerase) inhibitor should be considered during the course of that patient’s disease.
\(^5\) DEXA scan for patients less than 70 years of age who have received at least 12 months of androgen ablation therapy or those greater than or equal to 70 years who have received at least 6 months of androgen ablation therapy
\(^6\) See MD Anderson Approved Biomarker algorithm
PATIENT STATUS

Patient post definitive therapy (i.e., radiation with or without androgen ablation therapy or surgery with or without radiotherapy)

Surveillance

Based on pathologic findings after radical prostatectomy (e.g., path stage, margin status, Gleason score, age), consider adjuvant external beam radiotherapy

PROGRESSION

See Page 6 for Recurrent Prostate Cancer

Surveillance

Increased PSA and/or symptoms and signs of recurrence or progression?

Yes

Patient 5 or more years from treatment?

Yes

Transfer to Survivorship Clinic

No

Continue monitoring

No

Increased PSA and/or symptoms and signs of recurrence or progression?

Yes

Observation

Adjuvant radiation therapy

No

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
- DEXA bone mineral density testing if clinically indicated
- After radiation therapy:
  - DRE every 6-12 months
- After radical prostatectomy:
  - DRE every 1-3 years with follow-up visit

PSA:
- Every 3-6 months for 5 years
- Then every 6-12 months for 5 years
- Then annually

DEXA bone mineral density testing:
- If clinically indicated

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

Surveillance

1. DEXA scan for patients less than 70 years of age who have received at least 12 months of androgen ablation therapy or those greater than or equal to 70 years who have received at least 6 months of androgen ablation therapy

2. Based on pathologic findings after radical prostatectomy (e.g., path stage, margin status, Gleason score, age), consider adjuvant external beam radiotherapy

Department of Clinical Effectiveness V11
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No Evidence or high likelihood of local recurrence⁵:

- Bone scan, and
- CT abdomen/pelvis or
- CT abdomen and
- MRI pelvis, and
- Chest x-ray or CT chest

Metastatic Disease

Hormone sensitive disease:
- Orchectomy or LHRH agonist or antagonist with or without androgen receptor (AR) inhibitor (e.g., bicalutamide, flutamide)
- Consider docetaxel 6 cycles in high volume disease²
- Add AR inhibitor (prior to initiation to prevent flare) plus abiraterone acetate and prednisone

SALVAGE THERAPY

- PSA every 4 to 12 weeks
- Radiographic studies if clinically indicated (bone scans, CT abdomen and pelvis)
- DEXA bone mineral density testing³ if clinically indicated

No Evidence or high likelihood of local recurrence⁵:

- Consider salvage therapies (radiation if prior surgery)
- Salvage surgery or ablative procedures (if previous radiation)

Calculate PSA doubling time

Less than 6 months

- Androgen ablation intermittently
- Observation

Greater than 9 months

- Observation (recommended)
- Androgen ablation intermittently

Patient increasing PSA¹ and/or signs or symptoms of disease progression

LHRH = luteinizing hormone releasing hormone

¹ Evidence or high likelihood of local recurrence: biopsy strongly recommended

² Patients were classified as high volume if they had more than three areas of presumed pathologic uptake on bone scan, involvement of the appendicular skeleton, or visceral involvement (Thall et al 2007)

³ DEXA scan for patients less than 70 years of age who have received at least 12 months of androgen ablation therapy or those greater than or equal to 70 years who have received at least 6 months of androgen ablation therapy

Note: Consider Clinical Trials as treatment options for eligible patients.
Radiographic progression with symptoms of progression

In addition to continued surgical or pharmacological castration
- Sipuleucel-T\(^1\) (up to three doses)
- Secondary hormone therapies
  - Abiraterone and prednisone\(^2\)
  - Enzalutamide
- Chemotherapy
  - Docetaxel\(^3,4\) up to ten cycles
  - Cabazitaxel\(^3,4\) up to ten cycles
  - Radium 223 up to six cycles

Progressive disease?

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

No

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 caboplatin 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 caboplatin
5 DEXA scan for patients less than 70 years of age who have received at least 12 months of androgen ablation therapy or those greater than or equal to 70 years who have received at least 6 months of androgen ablation therapy.
SUGGESTED READINGS


SUGGESTED READINGS - continued


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