Prostate Cancer

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.

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

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.

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INITIAL EVALUATION

- Prostate biopsy[1, 2]
- Digital rectal exam (DRE)
- Prostate specific antigen (PSA)
- Gleason score
- Lifestyle risk assessment[3]

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

Life expectancy less than 5 years and asymptomatic

Follow up annually, no further work up until symptoms present (*e.g.*, bone pain or voiding dysfunction)

Symptomatic

STAGING WORK-UP

- Bone scan if any of the following are present:
  - PSA greater than 15 ng/mL
  - cT3-cT4 disease
  - Bone pain
  - Positive nodes on CT/MRI imaging
  - Gleason scores of 8 to 10
  - Adverse histologies (*e.g.*, small cell and/or neuroendocrine)
- CT **or** MRI considered for high risk patients
- Biopsy suspicious lesion(s) if clinically indicated

PRESENTING CLINICAL STAGE

cT1a

cT1b, cT1c, cT2a, cT2b

See Page 3

cT3a

cT3b, cT4

See Page 4

Any TN1, M0

Any T or N, M1[4]

[1] Perform prostate biopsy if not previously done. If done, MD Anderson review of prostate biopsy results.
[2] See MD Anderson Approved Biomarker algorithm
[3] See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
[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 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.

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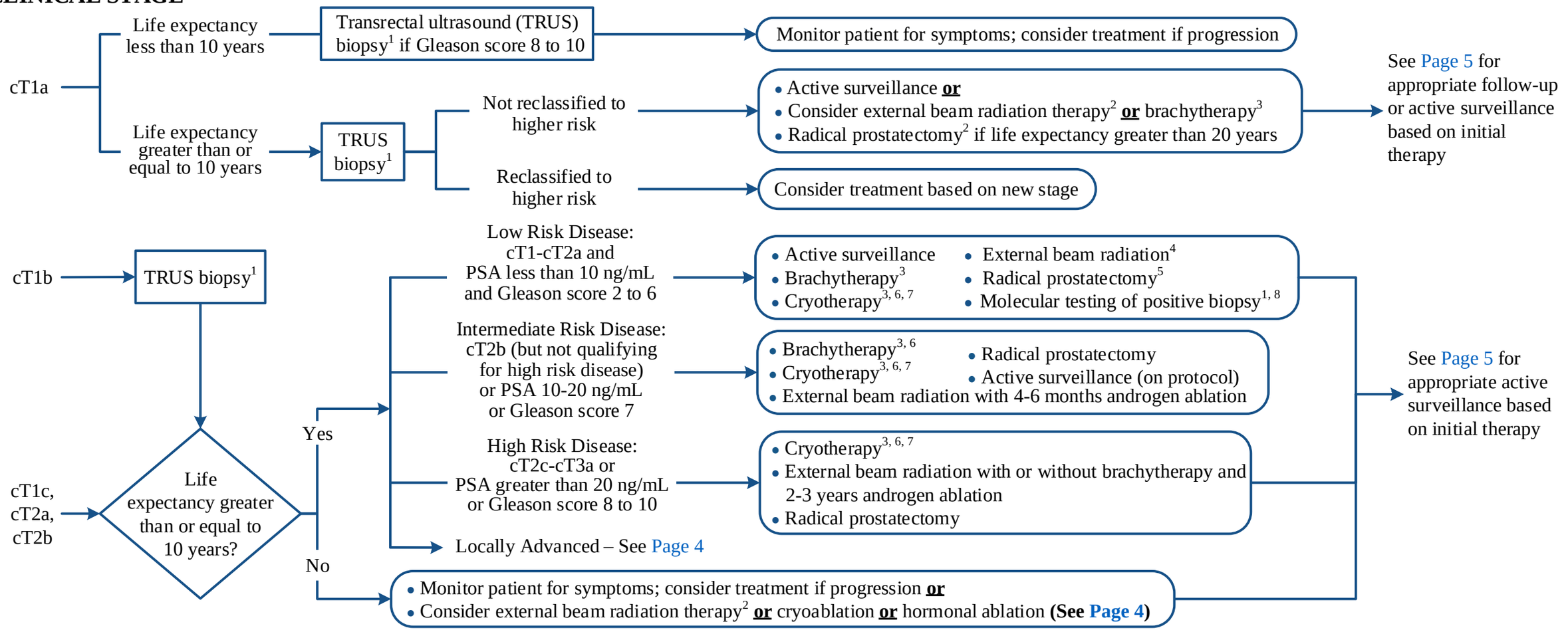
PRESENTING CLINICAL STAGE

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

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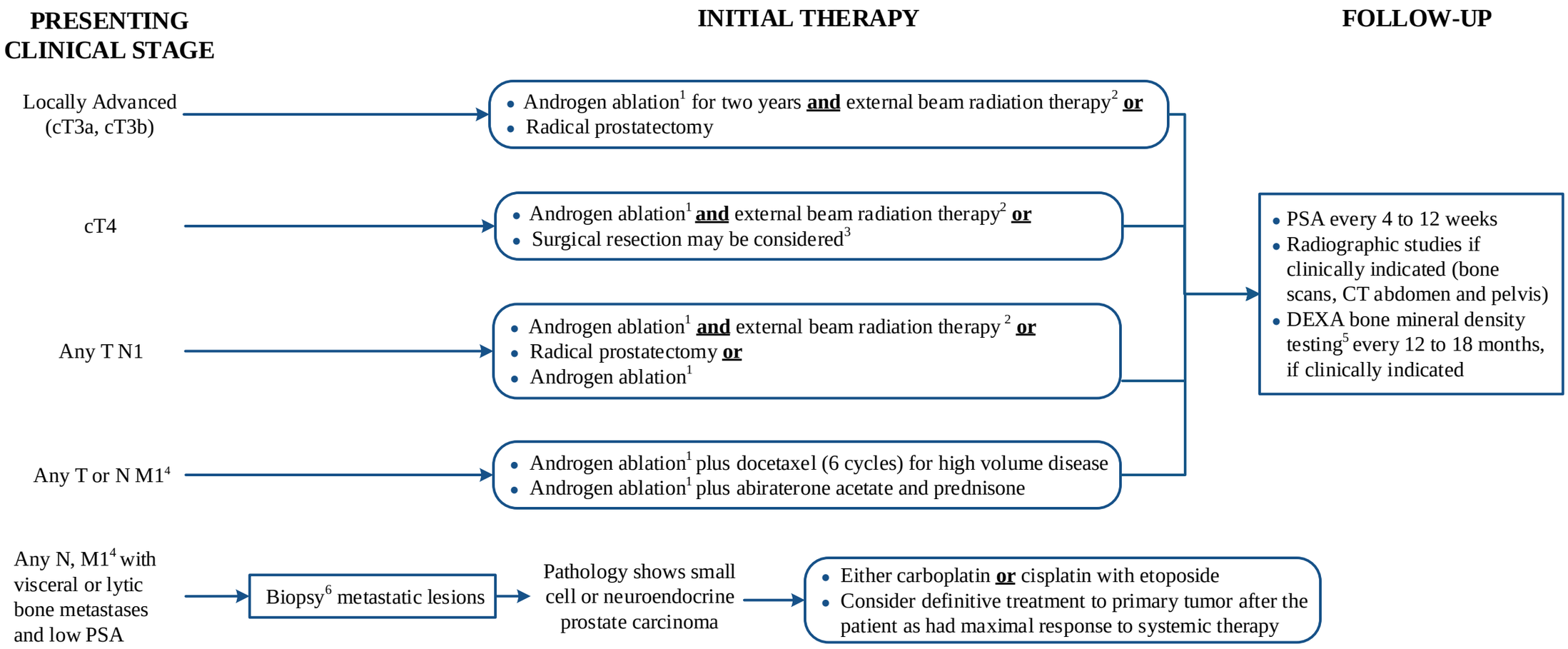

[1] Luteinizing hormone releasing hormone (LHRH) agonist or antagonist
[2] 3D conformal radiotherapy or intensity modulated radiotherapy (IMRT) are standard for external beam radiotherapy
[3] Based on pathologic findings after radical prostatectomy (*e.g.*, path stage, margin status, Gleason score, age), 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

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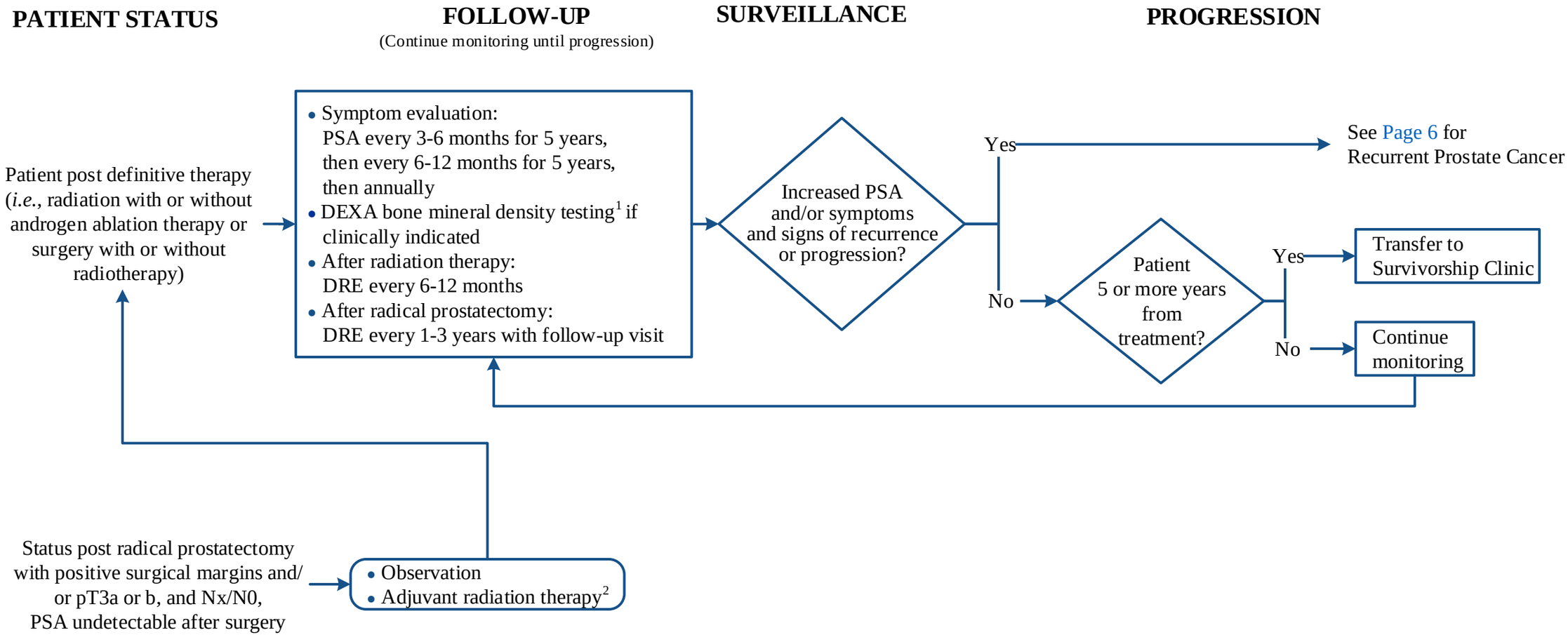

[1] DEXA scan for patients less than 70 years of age who have received at least 12 months of androgen ablation therapy or those greater than or equal to 70 years who have received at least 6 months of androgen ablation therapy

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PROGRESSION

Patient increasing PSA[1] and/or signs or symptoms of disease progression

- 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 disease[2]
- 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 testing[3] if clinically indicated

No Metastatic Disease

Evidence or high likelihood of local recurrence[1]?

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

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

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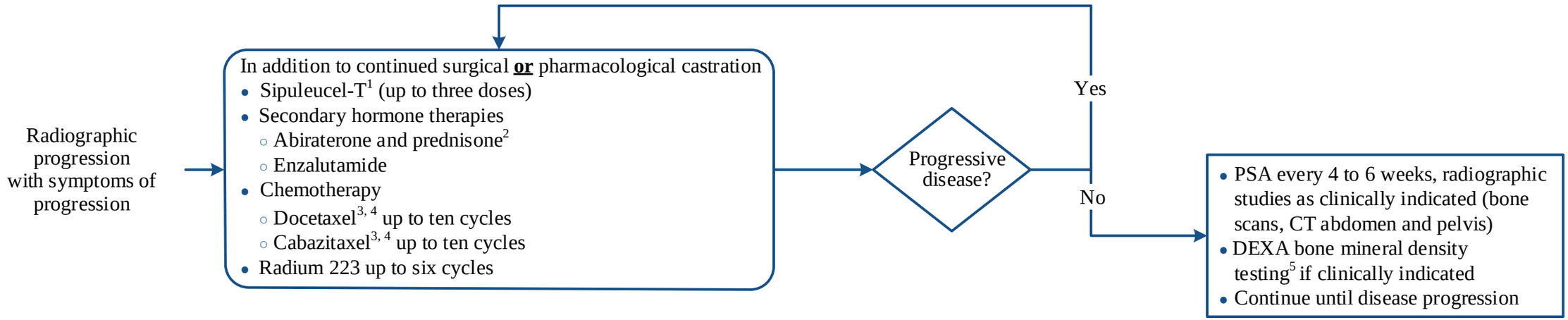
CASTRATION RESISTANT



[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 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.

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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:

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