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General Cancer 1

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Topics for Today

- **Prostate Cancer**
  - –Localized
  - –Advanced
- **Kidney Cancer**
  - –Localized

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ARS Q1:

A 38-year-old man is referred for prostate cancer screening. According to the AUA Guidelines, the next step is:

a) Advise against screening
b) Initiate yearly screening
c) Initiate yearly screening if positive family history or African American
d) Initiate biennial screening
e) Screen now and repeat in five years

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Answer: A

A. Advise against screening.

- This is index patient 1 (age < 40). The Panel recommends against PSA screening in men under age 40 years. Due to the relatively low prevalence of clinically detectable prostate cancer in men < 40 years, the absence of any evidence demonstrating benefits of screening and the known harms, screening is discouraged for men < 40 years of age.

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Potential Harms of PSA Screening

- Prostate biopsy has risks of hematuria, hematochezia, hematospermia, dysuria and retention, pain and infection.
- **Hematuria** and **hematospermia** are the most frequently observed side effects.
- Hematospermia after biopsy occurs in 10% to 70% of patients while hematuria is seen 14% to 50% of the time.

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Potential Harms of PSA Screening

- While the risk of hospitalization due to bleeding complications remains low, infectious complications are increasing steadily over time, possibly due to fluoroquinolone resistance.
- 30-day risk of hospitalization after biopsy for any cause has been estimated to be approximately 4%, of which three in four are for infections.
- ***The use of routine fecal culture and sensitivity tailored antibiotic prophylaxis may be one approach to reduce infection rates.***

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ARS Q2:

A 61-year-old man has a T1c, Gleason 7 prostate cancer with a PSA of 9.1 ng/ml. He has moderate LUTS and prostate volume of 42 ml. Before any treatment decisions are made, he should undergo:

a) CT scan of abdomen and pelvis
b) Bone scan
c) Urodynamics
d) Assessment of life expectancy
e) Molecular testing

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Answer: D

D. Assessment of life expectancy.

- This patient has intermediate-risk clinically localized prostate cancer. According to the AUA Guidelines for the management of clinically localized prostate cancer, as a standard, an assessment of the patient's life expectancy, overall health status, and tumor characteristics should be performed prior to making any treatment decisions.

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Early Detection of Prostate Cancer

AUA Guideline 2013, Reviewed and Validity Confirmed 2018

Four Index Patients

1. Men < 40 years of age
2. Men age 40 – 54 years
3. Men age 55 – 69 years
4. Men age 70+ years

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Index Patient 1: Age < 40 years

Panel recommends against PSA screening in men under age 40 years

- Prevalence of prostate cancer in men under age 40 years is extremely low. Population based studies reveal the prevalence of prostate cancer in men below age 40 years to be about 0.1%
- None of the prospective randomized studies evaluating the benefits of PSA based screening for prostate cancer included men under age 40 years. Hence there are no data available to estimate the benefit of prostate cancer screening in this population.
- However, the harms that can accrue from screening, which include the side effects of diagnostic biopsies and subsequent treatment apply to men in this age group.
- ***Due to the relatively low prevalence of clinically detectable prostate cancer in men < 40 years, the absence of any evidence demonstrating benefits of screening and the known harms, screening is discouraged for men < 40 years of age.***

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Index Patient 2: Age 40-54

Panel does not recommend routine screening in men between ages 40 to 54 years at average risk

- Panel recommends that screening, as routine practice, not be encouraged in men age 40 to 54 years who are not at increased risk for the disease (i.e., family history, race).
- There is no high-quality evidence to support this practice in the general population (PLCO and ERSPC did not include men under age 55 years).
- While the evidence of benefit of screening of men age 40 to 55 years indicates that the effect size is marginal at best, at least in terms of prostate-cancer specific mortality, the weight and quality of the evidence demonstrating the harms of screening remains high.
- The harms of screening in this population were at least equal to the benefits, if not higher and, to this end, the **Panel recommends that screening should not be routine practice.**

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Index Patient 2: Age 40-54

Panel does not recommend routine screening in men between ages 40 to 54 years at average risk

- For men younger than age 55 years at higher risk, decisions regarding prostate cancer screening should be individualized. Those at higher risk may include men of **African American race**; and those with a **family history of metastatic or lethal adenocarcinomas** (e.g., prostate, male and female breast cancer, ovarian, pancreatic) spanning multiple generations, affecting multiple first-degree relatives, and that developed at younger ages.
- In the future it is possible that individuals at high risk of developing a lethal prostate cancer phenotype may be identifiable at an early age through **genetic testing and/or new biomarkers**. *These individuals could then be targeted for more intense screening even at a young age.*

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Index Patient 3: Age 55-69

Panel strongly recommends shared decision-making for men age 55 to 69 years that are considering PSA screening and proceeding based on men's values and preferences.

- Evidence for screening benefit in this setting is moderate and is derived from RCTs.
  - ERSPC showed a relative risk reduction of prostate cancer-specific death of 21% at a median follow-up of 11 years. While the absolute reduction in prostate cancer-specific mortality was relatively small (0.10 deaths per 1,000 person-years or 1.07 deaths per 1,000 men randomized), this may represent an underestimate of benefit given the length of follow-up of the study and the degree of non-compliance in the intervention arm.
- To reduce the harms of screening, a routine screening interval of two years or more may be preferred over annual screening in those men who have participated in shared decision-making and decided on screening.

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Index Patient 4: Age 70+

Panel does not recommend routine PSA screening in men age 70+ years or any man with less than a 10 to 15 year life expectancy.

- A *small subgroup* of men age 70+ years who are in excellent health may benefit from PSA screening, but evidence to support the magnitude of benefit in this age group is extremely limited.
- ERSPC: no reduction in mortality among men age 70 years or older. Although men in this age group have a higher prevalence of prostate cancer and a higher incidence of fatal tumors, they also have increased competing mortality compared to younger men, and no compelling evidence of a treatment benefit, especially in men with a limited life expectancy below 10 to 15 years.
- Therefore, given the lack of direct evidence for benefit of screening beyond age 70 years, and especially beyond age 74 years, as well as higher quality data regarding harms, **the Panel discourages routine screening in this age group.**

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Contemporary Prostate Cancer Grading

Epstein et al., Eur Urol (2015)

Grade Group	Gleason Score
1	≤ 6
2	3 + 4 = 7
3	4 + 3 = 7
4	8
5	9 - 10

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Risk Stratification for Localized Prostate Cancer

AUA/ASTRO/SUO Guideline 2017

Very Low Risk	PSA <10 ng/ml AND Grade Group 1 AND clinical stage T1-T2a AND <34% of biopsy cores positive AND no core with >50% involved, AND PSA density <0.15 ng/ml/cc
Low Risk	PSA <10 ng/ml AND Grade Group 1 AND clinical stage T1-T2a
Intermediate Risk	PSA 10-<20 ng/ml OR Grade Group 2-3 OR clinical stage T2b-c · Favorable: Grade Group 1 (with PSA 10-<20) OR Grade Group 2 (with PSA<10) · Unfavorable: Grade Group 2 (with either PSA 10-<20 or clinical stage T2b-c) OR Grade Group 3 (with PSA < 20)
High Risk	PSA ≥20 ng/ml OR Grade Group 4-5 OR clinical stage ≥T3*

*Clinical stage T3 cancer is considered locally advanced and, therefore, outside the scope of this guideline.

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Care Options by Cancer Severity/Risk Group

AUA/ASTRO/SUO Guideline 2017

- Very Low Risk: PSA < 10 AND Grade Group 1 AND clinical stage T1-T2a AND ≤ 1/3 of biopsy cores positive AND no core with > 50% involved, AND PSA density <0.15 ng/ml/cc
- Low Risk: PSA < 10 AND Grade Group 1 AND clinical stage T1-T2a

Prostate Cancer Severity	Amount of Prostate Cancer on Biopsy	PSA (ng/ml); PSAD	Clin Stage (DRE)	Pathology Grade
Very Low Risk	≤1/3 of cores; ≤50% per core	<10; <0.15	T1-T2a	Gleason score ≤6 (Grade Group 1)
Low Risk	Any	<10; any psad		

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ARS Q3:

An otherwise healthy 65-year old man elects active surveillance for T1c, PSA 8.2 ng/dL, Gleason score 6 (1 of 12 cores positive) prostate cancer. His DRE remains normal and has subsequent serial PSA values of 7.1, 9.2, and 7.9 ng/dL at 6, 12, and 18 months respectively. The next step is:

a) Bone scan
b) TRUS and prostate biopsy
c) Definitive local therapy
d) ProstaScint scan
e) Endorectal MRI scan

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Answer: B

B. TRUS and prostate biopsy.

- Localized prostate cancer patients undergoing active surveillance should be encouraged to have a confirmatory biopsy within the initial two years and surveillance biopsies thereafter. (Clinical Principle)

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Care Options by Cancer Severity

Very Low-/Low-Risk Prostate Cancer

Active Surveillance – Very Low-Risk

- Clinicians should recommend active surveillance as the **best** available care option. [Guideline Statement 7]

Active Surveillance – Low Risk

- Clinicians should recommend active surveillance as the ***preferable*** care option. [Guideline Statement 8]
- Clinicians may offer definitive treatment (i.e. radical prostatectomy or radiotherapy) to select patients who may have a high probability of progression. [Guideline Statement 9]
  - Clinical predictors for increased risk of higher grade disease or reclassification of subsequent biopsy include PSA density > 0.15, obesity as measured by BMI, African American race, and extensive Gleason 6 cancer on systematic biopsy cores.

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Care Options by Cancer Severity

Very Low-/Low-Risk Prostate Cancer

Definitive Treatment for Low-Risk Prostate Cancer

- Clinicians should not add ADT along with radiotherapy except to reduce prostate size for brachytherapy. [Guideline Statement 10]
- Clinicians should inform patients considering whole gland cryosurgery that side effects are considerable and survival benefit has not been shown compared to active surveillance. [Guideline Statement 11]
- Clinicians should inform patients who are considering focal therapy or HIFU that these interventions are not standard care options because comparative outcome evidence is lacking. [Guideline Statement 12]

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Care Options by Cancer Severity

Intermediate-Risk Prostate Cancer

PSA 10 - < 20 ng/ml OR Grade Group 2-3 OR clinical stage T2b-c

- Favorable: Grade Group 1 (with PSA 10-<20) OR Grade Group 2 (with PSA<10)
- Unfavorable: Grade Group 2 (with either PSA 10-<20 or clinical stage T2b-c) OR Grade Group 3 (with PSA < 20)

PCa Intermediate Risk Sub-Group	Pathology Grade Group	PSA (ng/ml)	Clin Stage (DRE)
Favorable	1	10-20	T1-T2a
	2	<10	
Unfavorable	2	<10	T2b
	2	10-20	Any T1-2
	3	<20	Any T1-2

Amount of Pca on biopsy not included in sub-categorization due to lack of such strata in RCT evidence

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Zumsteg 2013, 2016; Mathieu 2017

Care Options by Cancer Severity

Guideline Statement 15

Staging in Intermediate-Risk Patients

- Clinicians should consider staging unfavorable intermediate-risk localized prostate cancer patients with cross sectional imaging (CT or MRI) and bone scan. (Expert Opinion)

Unfavorable: Grade Group 2 (with either PSA 10-<20 or clinical stage T2b-c) OR Grade Group 3 (with PSA < 20)

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Care Options by Cancer Severity

Guideline Statement 16

Standard Treatment Option

- Clinicians should recommend **radical prostatectomy** or **radiotherapy plus androgen deprivation therapy** (ADT) as standard treatment options for patients with intermediate-risk localized prostate cancer. (Strong Recommendation; Evidence Level: Grade A)

PSA 10 - < 20 ng/ml OR Grade Group 2-3 OR clinical stage T2b-c

- Favorable: Grade Group 1 (with PSA 10-<20) OR Grade Group 2 (with PSA<10)
- Unfavorable: Grade Group 2 (with either PSA 10-<20 or clinical stage T2b-c) OR Grade Group 3 (with PSA < 20)

Care Option Summary

Intermediate-Risk Prostate Cancer

Evidence Level/ Recommendation Strength	Care Option Advisability Based on Prostate Cancer Severity Subgroup	
	Favorable Intermediate Risk	Unfavorable Intermediate Risk
A / Strong	Radical Prostatectomy *OR* Radiotherapy with ADT	Radical Prostatectomy *OR* Radiotherapy with ADT
B / Moderate	Radiotherapy* without ADT	NA
C / Conditional	Active Surveillance *OR* Cryosurgery (whole gland)	Cryosurgery (whole gland)
No evidence / clinical principle or expert opinion	Focal Ablative Therapy *OR* HIFU	Focal Ablative Therapy *OR* HIFU

** Radiotherapy includes external 3-D conformal or IMRT, alone or combined with LDR or HDR radiotherapy*

PSA 10 - < 20 ng/ml OR Grade Group 2-3 OR clinical stage T2b-c

- Favorable: Grade Group 1 (with PSA 10-<20) OR Grade Group 2 (with PSA<10)
- Unfavorable: Grade Group 2 (with either PSA 10-<20 or clinical stage T2b-c) OR Grade Group 3 (with PSA < 20)

HIGH RISK PROSTATE CANCER

Risk Stratification

The Panel did not substratify high-risk patients into high-risk and very high-risk (as has been proposed by the NCCN). The rationale to not further substratify is not based upon differences in outcome, but rather the lack of clinical utility as a context for decisions about treatment options is generally similar between high-risk and very high-risk men.

High Risk: PSA ≥ 20 ng/ml OR Grade Group 4-5 OR clinical stage ≥ T3

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Care Options by Cancer Severity

Guideline Statement 22

Staging High-Risk Patients

- Clinicians should stage high-risk localized prostate cancer patients with cross sectional imaging (CT or MRI) and bone scan.
  (Clinical Principle)

High Risk: PSA ≥ 20 ng/ml OR Grade Group 4-5 OR clinical stage ≥ T3

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Care Options by Cancer Severity

Guideline Statement 23

Standard Therapy

- Clinicians should recommend radical prostatectomy ***or*** radiotherapy plus ADT as standard treatment options for patients with high-risk localized prostate cancer.
  (Strong Recommendation; Evidence Level: Grade A)

High Risk: PSA ≥ 20 ng/ml OR Grade Group 4-5 OR clinical stage ≥ T3

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Recommended Approaches

Prostatectomy

- Clinicians should inform localized prostate cancer patients that robotic/laparoscopic or perineal techniques are associated with less blood loss than retropubic prostatectomy. [Guideline Statement 36]
- Clinicians should counsel localized prostate cancer patients that nerve-sparing is associated with better erectile function recovery than non-nerve sparing. [Guideline Statement 37]
- Clinicians should not treat localized prostate cancer patients who have elected to undergo radical prostatectomy with neoadjuvant ADT or other systemic therapy outside of clinical trials. [Guideline Statement 38]

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Recommended Treatment Approaches

Radiotherapy

- Clinicians may offer *single modality* external beam radiotherapy or brachytherapy for patients who elect radiotherapy for low-risk localized prostate cancer. [Guideline Statement 42]
- Clinicians may offer *external beam radiotherapy or brachytherapy alone or in combination* for favorable intermediate-risk localized prostate cancer. [Guideline Statement 43]
- Clinicians should offer **24-36 months of ADT** as an *adjunct* to either external beam radiotherapy alone or external beam radiotherapy combined with brachytherapy to patients electing radiotherapy for high-risk localized prostate cancer. [Guideline Statement 44]

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Recommended Treatment Approaches

Whole Gland Cryosurgery

- Clinicians may consider whole gland cryosurgery in low- and intermediate-risk localized prostate cancer patients who are not suitable for either radical prostatectomy or radiotherapy due to comorbidities yet have >10 year life expectancy. [Guideline Statement 50]
- Clinicians should inform localized prostate cancer patients considering whole gland cryosurgery that cryosurgery has similar progression-free survival as did non-dose escalated external beam radiation (also given with neoadjuvant hormonal therapy) in low- and intermediate-risk disease, but conclusive comparison of cancer mortality is lacking. [Guideline Statement 51]
- **Defects from prior transurethral resection of the prostate are a relative contraindication for whole gland cryosurgery due to the increased risk of urethral sloughing.** [Guideline Statement 52]

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Recommended Treatment Approaches

HIFU and Focal Therapy

- Clinicians should inform those localized prostate cancer patients considering focal therapy or HIFU that these treatment options lack robust evidence of efficacy. [Guideline Statement 57]
- **Clinicians should inform localized prostate cancer patients who are considering HIFU that even though HIFU is approved by the FDA for the destruction of prostate tissue, it is <u>not</u> approved explicitly for the treatment of prostate cancer.** [Guideline Statement 58]
- Clinicians should advise localized prostate cancer patients considering HIFU that tumor location may influence oncologic outcome. Limiting apical treatment to minimize morbidity increases the risk of cancer persistence. [Guideline Statement 59]
- **As prostate cancer is often multifocal, clinicians should inform localized prostate cancer patients considering focal therapy that focal therapy may not be curative and that further treatment for prostate cancer may be necessary.** [Guideline Statement 60]

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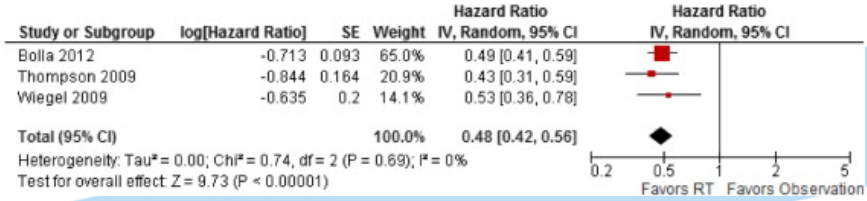
Adjuvant and Salvage Radiotherapy after Prostatectomy

Guideline Statement 1

- Patients who are being considered for management of localized prostate cancer with RP should be informed of the potential for adverse pathologic findings that portend a higher risk of cancer recurrence and that these findings may suggest a potential benefit of additional therapy after surgery. (Clinical Principle)



Meta-analysis of biochemical recurrence data from SWOG 8794, EORTC 22911, and ARO 96–02.

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ASTRO/AUA Guideline: Published 2013

Adjuvant and Salvage Radiotherapy after Prostatectomy

Guideline Statement 2

- Patients with adverse pathologic findings including **seminal vesicle invasion, positive surgical margins, and extraprostatic extension** should be informed that adjuvant radiotherapy, compared to RP only, reduces the risk of biochemical (PSA) recurrence, local recurrence, and clinical progression of cancer.
- They should also be informed that the impact of adjuvant radiotherapy on subsequent metastases and overall survival is less clear; one of two randomized controlled trials that addressed these outcomes indicated a benefit but the other trial did not demonstrate a benefit. However, the other trial was not powered to test the benefit regarding metastases and overall survival. (Clinical Principle)

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ASTRO/AUA Guideline: Published 2013

Adjuvant and Salvage Radiotherapy after Prostatectomy

Guideline Statement 3

- Physicians should offer adjuvant radiotherapy to patients with adverse pathologic findings at prostatectomy including seminal vesicle invasion, positive surgical margins, or extraprostatic extension because of demonstrated reductions in biochemical recurrence, local recurrence and clinical progression. (Standard; Evidence Strength: Grade A)

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ASTRO/AUA Guideline: Published 2013

Adjuvant and Salvage Radiotherapy after Prostatectomy

Guideline Statements 5 - 7

- **Clinicians should define biochemical recurrence as a detectable or rising PSA value after surgery that is ≥ 0.2 ng/ml with a second confirmatory level ≥ 0.2 ng/ml.** (Recommendation; Evidence Strength: Grade C)
- A restaging evaluation in the patient with a PSA recurrence may be considered. (Option; Evidence Strength: Grade C)
- Physicians should offer **salvage radiotherapy** to patients with PSA or local recurrence after radical prostatectomy in whom there is no evidence of distant metastatic disease. (Recommendation; Evidence Strength: Grade C)

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ASTRO/AUA Guideline: Published 2013

Failure After Radiation

- **Phoenix Consensus**:
  - PSA nadir + 2 ng/mL for EBRT +/- ADT
  - Recurrence evaluation should be considered when PSA has been confirmed to be increasing after radiation even if the increase above nadir is not yet 2 ng/mL, especially in candidates for salvage local therapy who are young and healthy.
  - Rapid PSA increase may warrant evaluation (prostate biopsy) prior to meeting the Phoenix definition, especially in younger or healthier men.
- **PSA "bounce" may be seen within 3 years of radiation**

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NCCN Guidelines 2018

Prostate Cancer: Advanced

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Castration-Resistant Prostate Cancer

A rising PSA despite medical or surgical castration is one of the first clinical presentations of CRPC.

- Prostate Cancer Clinical Trials Working Group 2 (PCWG2) defines PSA only failure as a rising PSA > 2 ng/mL higher than the nadir; the rise has to be at least 25% over nadir, and the rise has to be confirmed by a second PSA at least 3 weeks later.
- Patient is required to have castrate levels of testosterone (< 50 ng/mL) and no radiographic evidence of metastatic disease.
- These patients represent a relatively common clinical presentation and the earliest clinical manifestation of castration resistance.

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AUA CRPC Guidelines 2018

Hormonal Therapy - Mechanisms of Action

1. Ablation at source
   - Orchiectomy
2. Inhibition of androgen synthesis
   - Ketoconazole, Aminoglutethimide, Abiraterone
3. Blockade of androgen action
   - Cyproterone acetate, Flutamide, Bicalutamide, Nilutamide
4. Inhibition of LH-RH +/- LH release
   - DES, Leuprolide, Goserlin, Triptorelin, Histrelin, Cetrorelix, Abarelix, Degarelix

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Complications of ADT

- **Hot flashes**
  - 50-80% of men
  - Megestrol acetate 20 mg/bid
  - Cyproterone acetate 50-300 mg/day
  - Estrogen compounds effective but associated with DVT/gynecomastia
- **Sexual dysfunction**
  - 20% will maintain sexual activity
  - Libido affected more so than erection
- **Cognitive function**
  - Strong suggestions of link
- **Muscle/fat ratio**
  - Expect 1.8 – 3.8% weight gain (5-15 lbs)
  - Obesity portends a worse cancer prognosis
  - Exercise regimen/healthy diet

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Complications of ADT

- **Diabetes or metabolic syndrome**
  - Cluster of cardiac risk factors related to insulin resistance
  - Differs from “classic metabolic syndrome” – subcutaneous fat/HDL
- **Anemia**
  - Normochromic, normocytic anemia
  - Common, 90% men on CAB have 10% decrease in Hgb
  - Does respond to erythropoietin

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Complications of ADT

- **Cardiovascular morbidity**
  - Risk seems to be the greatest in men with lower risk cancer
    - Population based studies (20% higher risk of event) [1]
    - Older men with RP + hormones had increased cardiac death risk (5.5 vs 2%)[2]
    - Not seen in ADT + radiation for local advanced CaP [3]
  - Metabolic syndrome and AHA guidelines
- **Gynecomastia**
  - Only prophylactic radiation (10 Gy) is effective
  - Liposuction, subcutaneous mastectomy, tamoxifen once occurs

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[1]Saigal et al. *Cancer* 2007; 110:1493
[2]*Tsai et al. J Natl Cancer Inst* 2007; 99:1516
[3]Efstathiou et al. *J Clin Oncol* 2008; 27:92

Index Patients

Based on the presence or absence of metastatic disease, degree of symptoms, patient performance status (as defined by ECOG scale), and prior treatment with docetaxel-based chemotherapy.

1. Asymptomatic non-metastatic CRPC
2. Asymptomatic or minimally-symptomatic, mCRPC without prior docetaxel chemotherapy
3. Symptomatic, mCRPC with good performance status and no prior docetaxel chemotherapy
4. Symptomatic, mCRPC with poor performance status and no prior docetaxel chemotherapy
5. Symptomatic, mCRPC with good performance status and prior docetaxel chemotherapy
6. Symptomatic, mCRPC with poor performance status and prior docetaxel chemotherapy

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ECOG Performance Status

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

* As published in Am. J. Clin. Oncol.:

Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982.

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ARS Q4:

A 61-year-old man has non-metastatic CRPC, PSA doubling time ≤ 10 months, and is asymptomatic. The next best step is:

a) Observation
b) Abiraterone + prednisone
c) Apalutamide
d) Enzalutamide + ADT
e) Docetaxel

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Answer: D

D. Enzalutamide + ADT

- Standard treatment for Index Patient 1: apalutamide or enzalutamide with continued androgen deprivation for patients at high risk for developing metastatic disease (Evidence Level Grade A)

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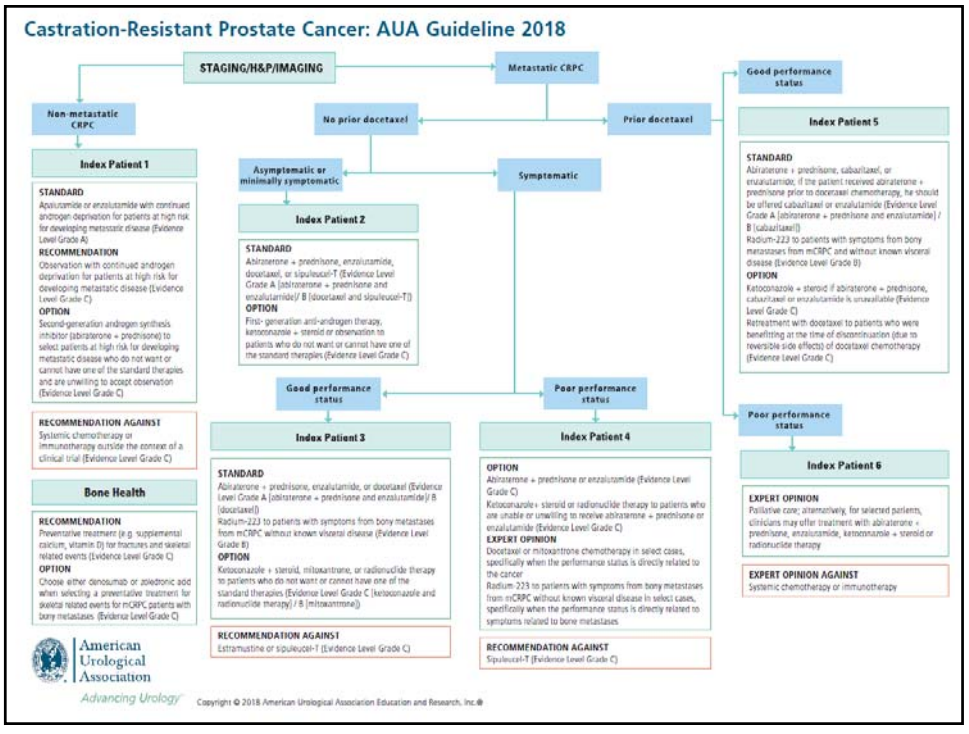
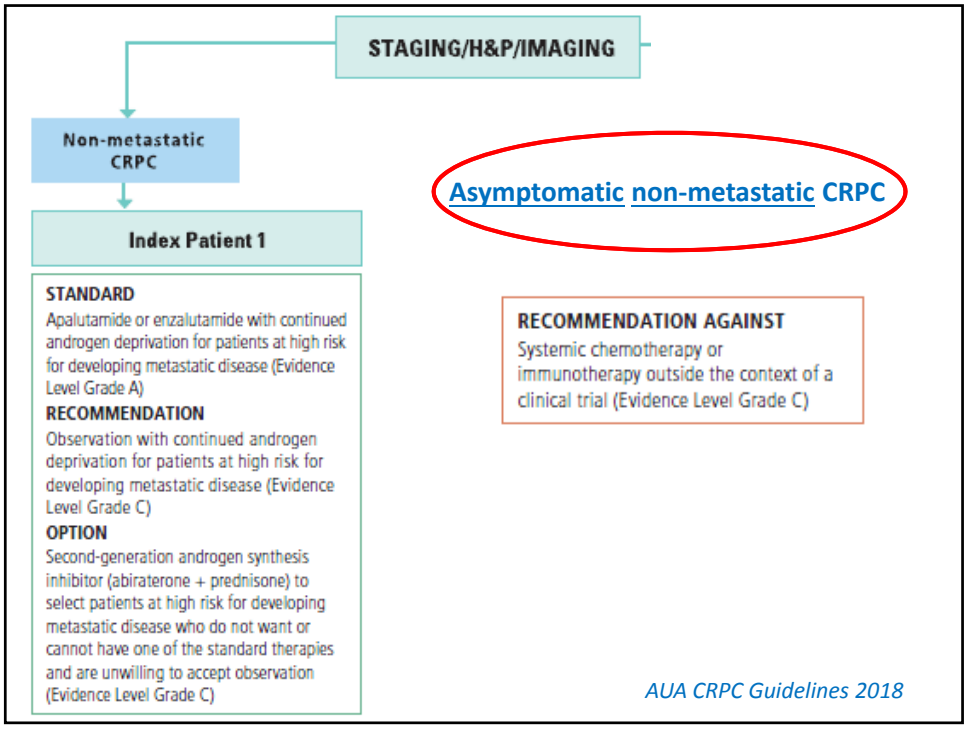
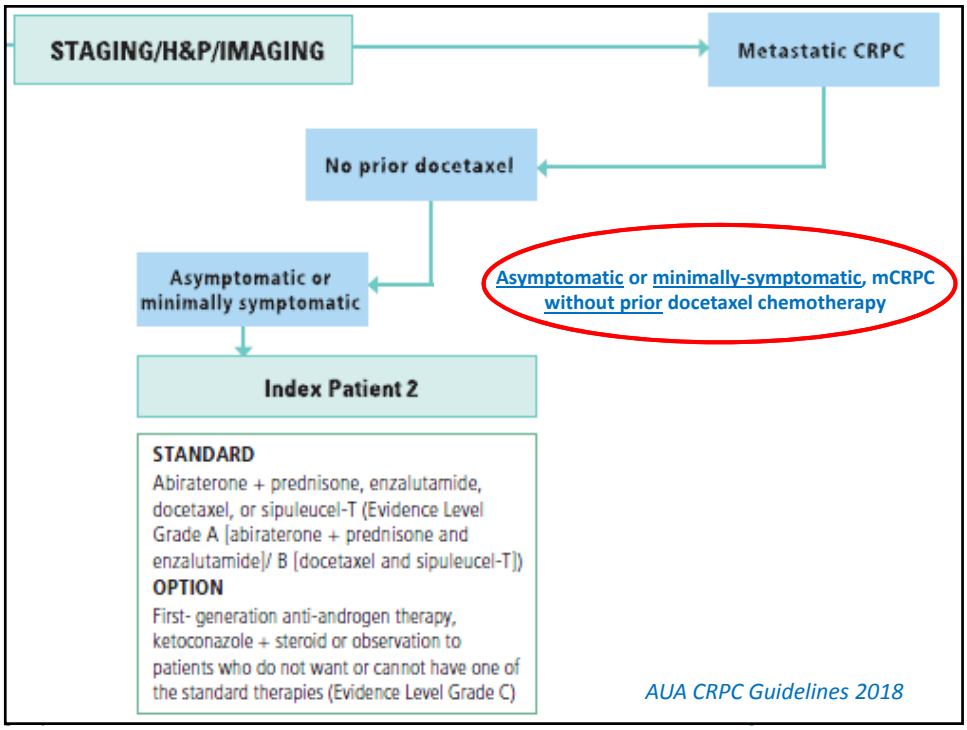
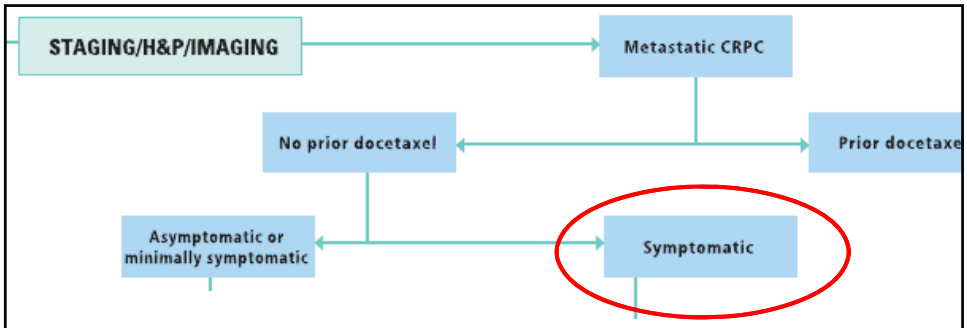


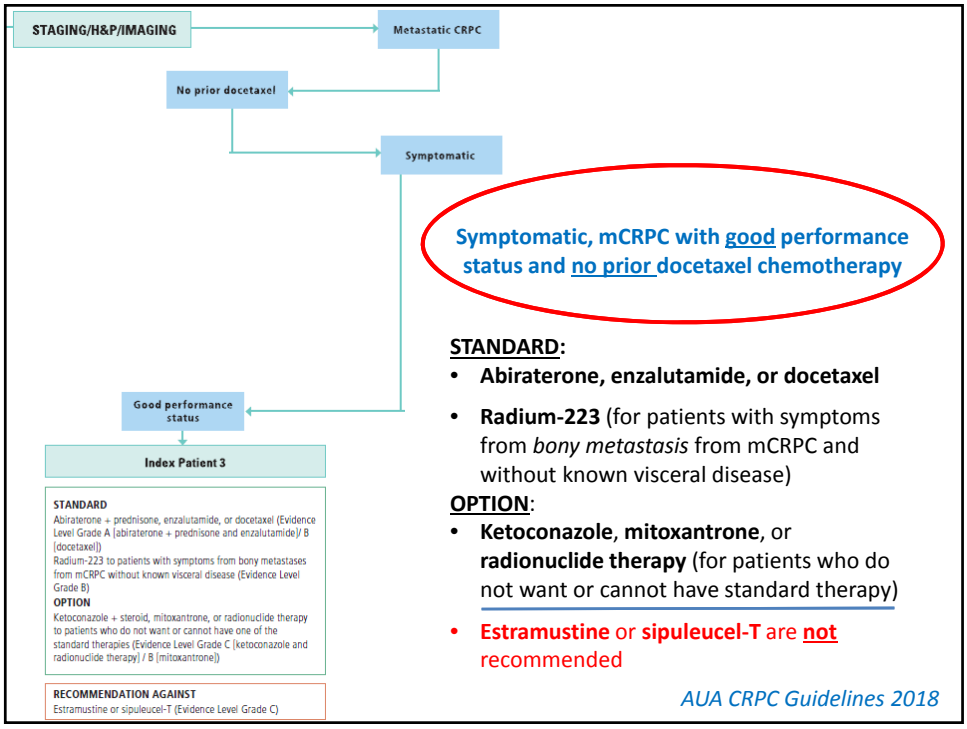






- **Patient must have symptoms that are clearly attributable to metastatic disease burden, not any other medical condition.**
- **If having pain, the patient should require regular opiate pain medications for symptoms attributable to documented metastases in order to achieve an acceptable level of pain control.**
- **If patients require regular narcotic medications for pain relief, then they are symptomatic from their prostate cancer and should be included in this category.**

AUA CRPC Guidelines 2018



Symptomatic, mCRPC with good performance status and no prior docetaxel chemotherapy

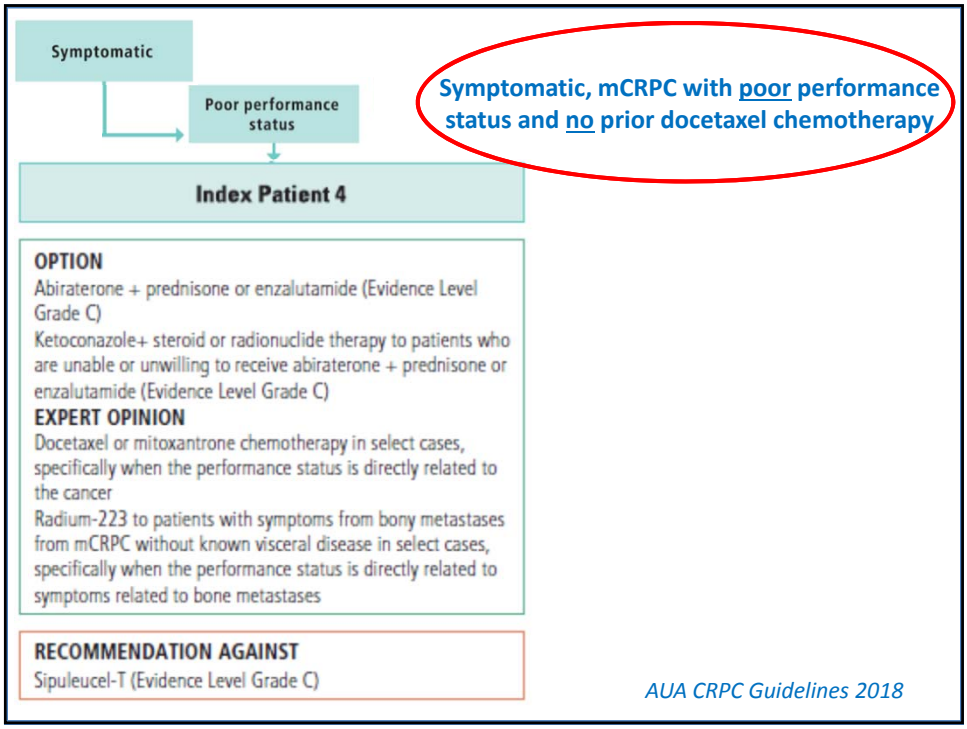
STANDARD:

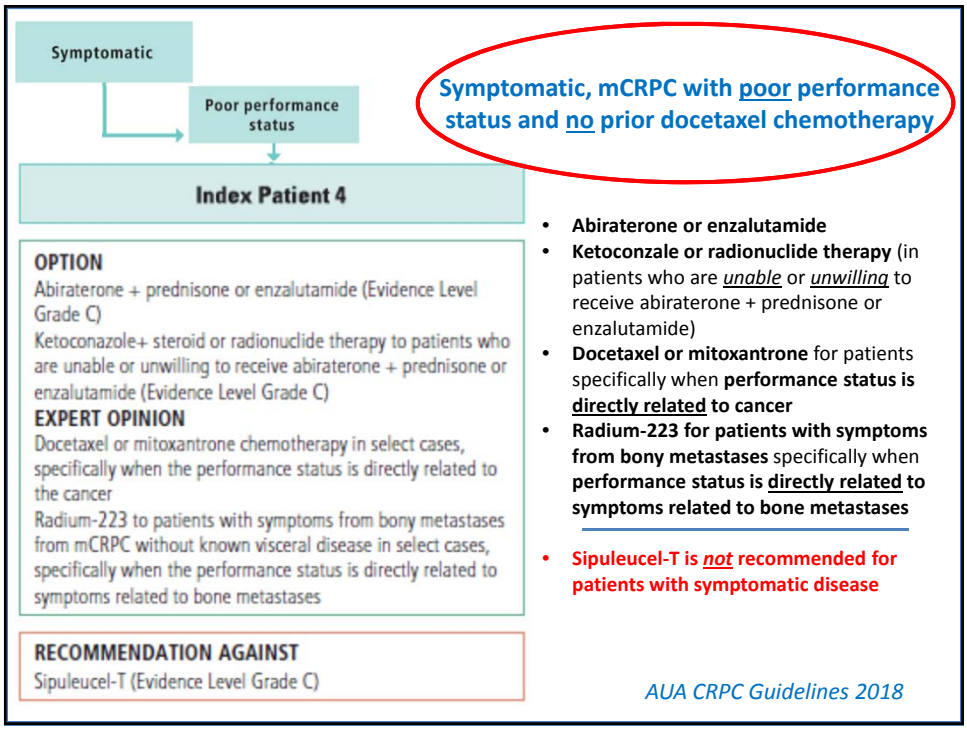
- **Abiraterone, enzalutamide, or docetaxel**
- **Radium-223** (for patients with symptoms from *bony metastasis* from mCRPC and without known visceral disease)

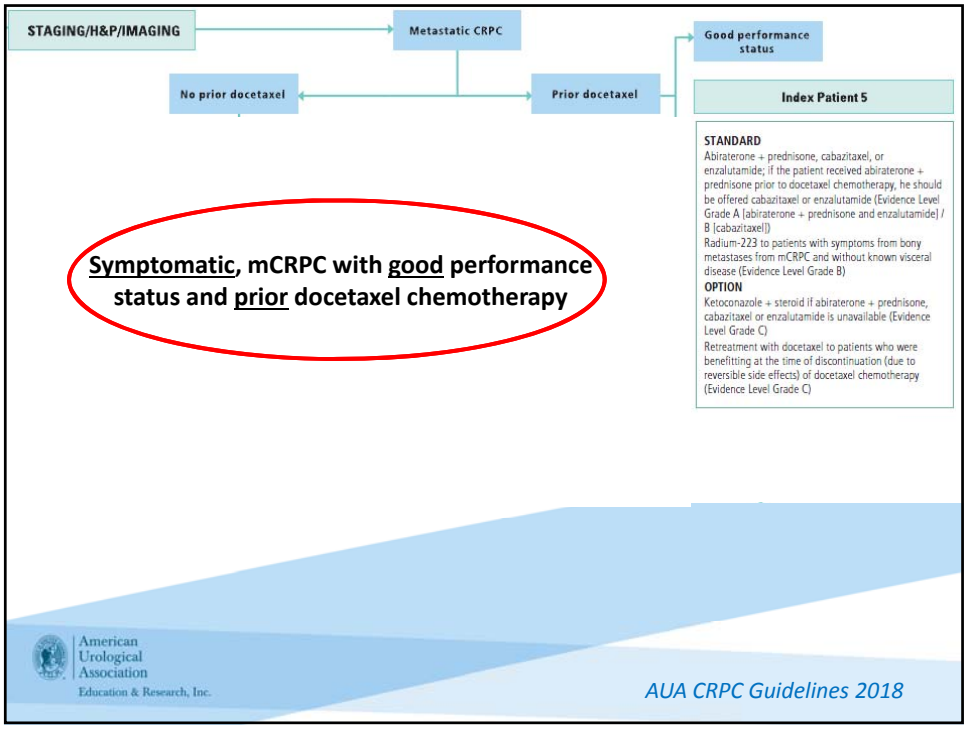
OPTION:

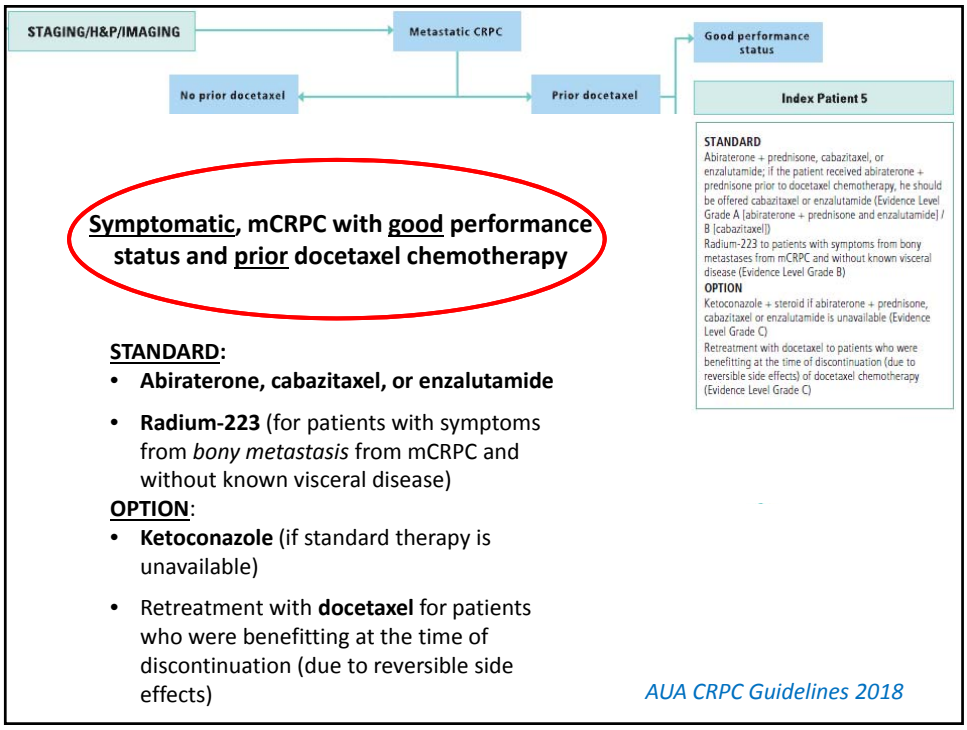
- **Ketoconazole**, **mitoxantrone**, or **radionuclide therapy** (for patients who do not want or cannot have standard therapy)
- **Estramustine** or **sipuleucel-T** are **not** recommended

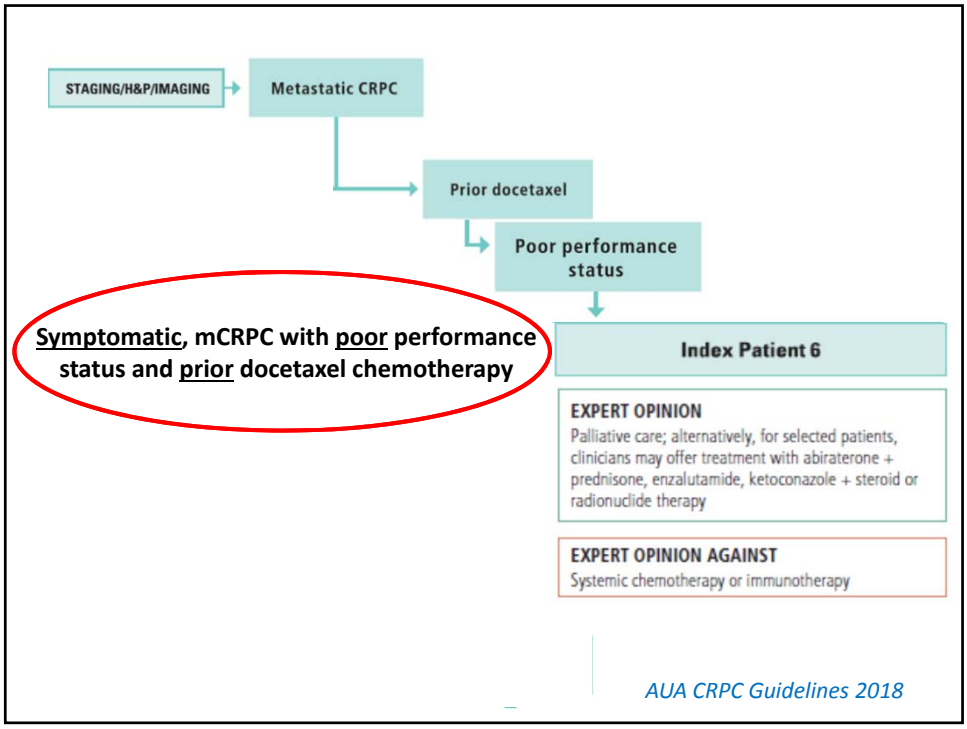
AUA CRPC Guidelines 2018

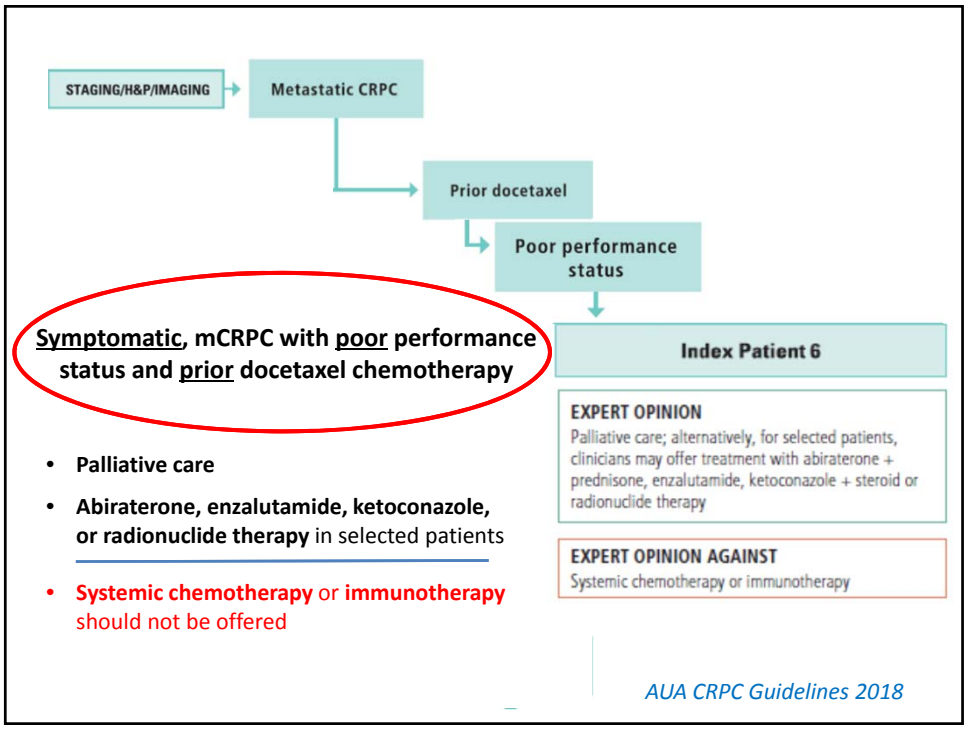












Castrate-Resistant Prostate Cancer

Bone Health

- Clinicians should offer *preventative* treatment (e.g. **supplemental calcium**, **vitamin D**) for fractures and skeletal related events to CRPC patients. (Recommendation; Evidence Level Grade C)
- Clinicians may choose either **denosumab** or **zoledronic** acid when selecting a *preventative* treatment for skeletal related events for mCRPC patients ***with*** bony metastases. (Option; Evidence Level Grade C)

Bone Health

RECOMMENDATION
Preventative treatment (e.g. supplemental calcium, vitamin D) for fractures and skeletal related events (Evidence Level Grade C)

OPTION
Choose either denosumab or zoledronic acid when selecting a preventative treatment for skeletal related events for mCRPC patients with bony metastases (Evidence Level Grade C)

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Kidney Cancer: Localized

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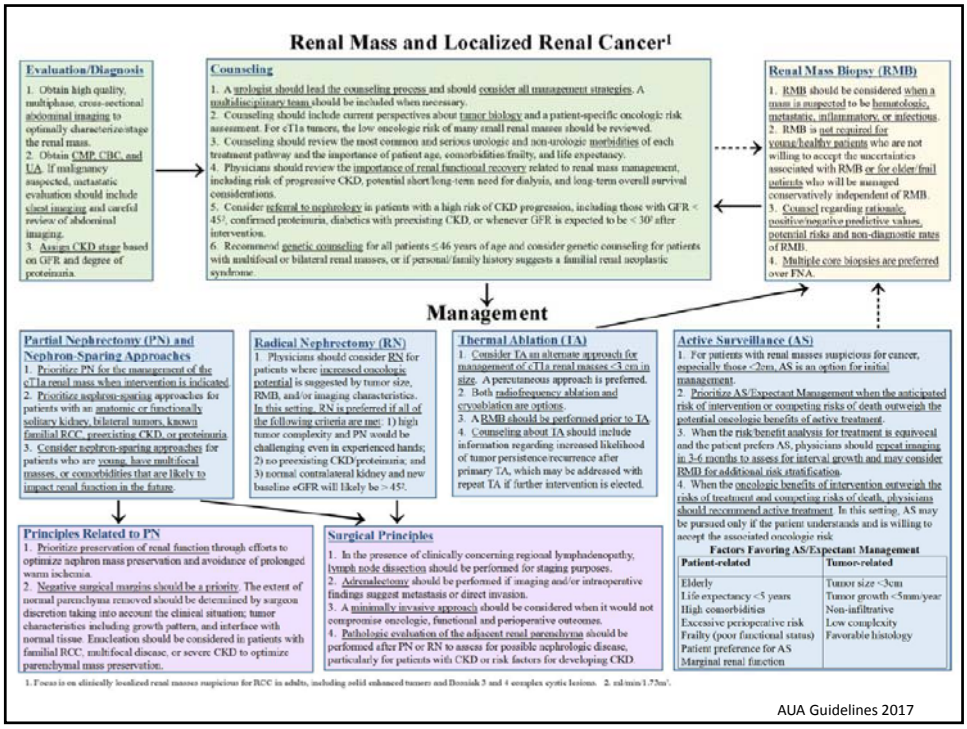

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Primary Tumor (T)	
TX	Primary tumor cannot be assessed.
T0	No evidence of primary tumor.
T1	Tumor ≤7 cm in greatest dimension, limited to the kidney.
T1a	Tumor ≤4 cm in greatest dimension, limited to the kidney.
T1b	Tumor >4 cm but not >7 cm in greatest dimension, limited to the kidney.
T2	Tumor >7 cm in greatest dimension, limited to the kidney.
T2a	Tumor >7 cm but ≤10 cm in greatest dimension, limited to the kidney.
T2b	Tumor >10 cm, limited to the kidney.

AJCC TNM Staging System for Kidney Cancer

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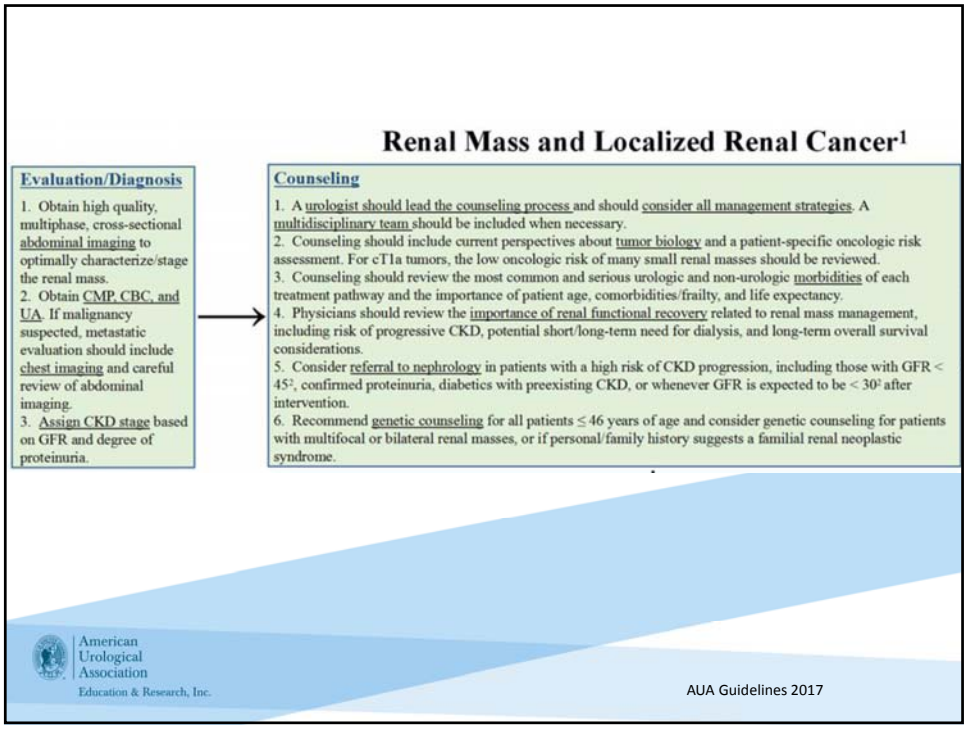

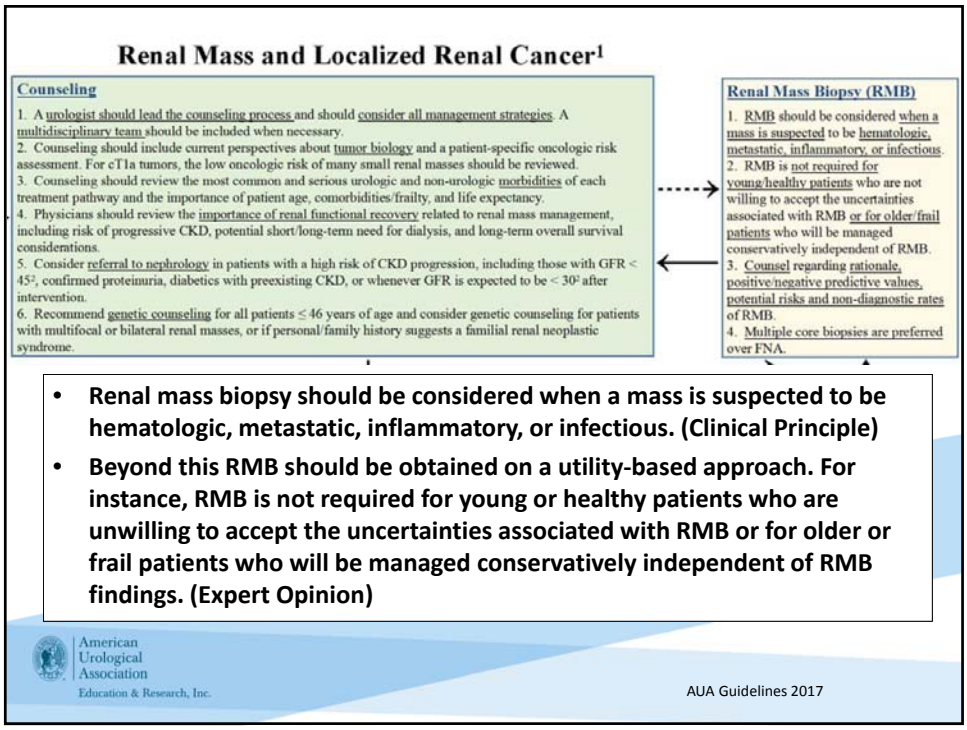

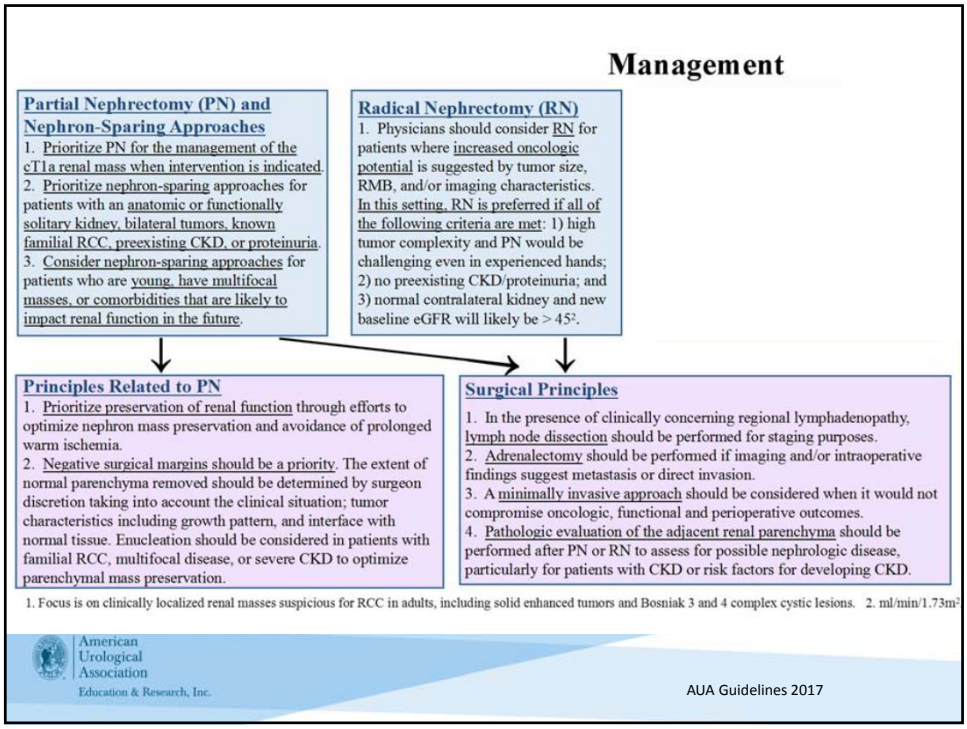

Statement 14

- **Physicians should prioritize PN for the management of the cT1a renal mass when intervention is indicated. In this setting, PN minimizes the risk of CKD or CKD progression and is associated with favorable oncologic outcomes, including excellent local control. (Moderate Recommendation; Evidence Level: Grade B)**
- **EORTC 30904 and AHRQ Metanalysis: PN provides similar oncologic outcomes as RN for appropriately selected patients. PN also provides more favorable LRF survival when compared to single session of TA**
- **Many SRM's have low oncologic risk and RN is therapeutic overkill, and should be avoided if possible**
- **Morbidity: PN can be associated with urologic complications but most can be successfully managed with conservative measures**

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ARS Q5:

A 65-year-old male with good performance status desires treatment of a 2.8 cm left renal mass, but he does not want surgery. The next step is:

a) Renal mass biopsy
b) Percutaneous cryoablation
c) Percutaneous radiofrequency ablation
d) Laparoscopic cryoablation
e) Laparoscopic radiofrequency ablation

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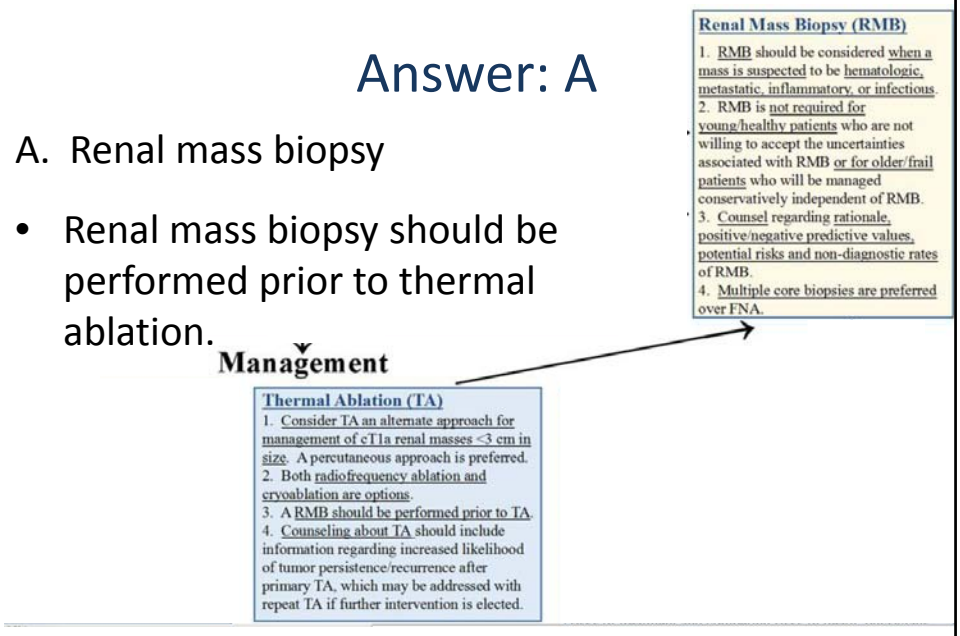
Answer: A

A. Renal mass biopsy

- Renal mass biopsy should be performed prior to thermal ablation.



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Active Surveillance (AS)

1. **For patients with renal masses suspicious for cancer, especially those < 2 cm, AS is an option for initial management.**
2. **Prioritize AS/Expectant Management when the anticipated risk of intervention or competing risks of death outweigh the potential oncologic benefits of active treatment.**
3. **When the risk/benefit analysis for treatment is equivocal and the patient prefers AS, physicians should repeat imaging in 3-6 months to assess for interval growth and may consider RMB for additional risk stratification.**
4. **When the oncologic benefit of intervention outweigh the risks of treatment and competing risks of death, physicians should recommend active treatment. In this setting, AS may be pursued only if the patient understands and is willing to accept the associated oncologic risk.**

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Factors Favoring AS/Expectant Management

Patient-related	Tumor-related
Elderly	Tumor size <3cm
Life expectancy <5 years	Tumor growth <5mm/year
High comorbidities	Non-infiltrative
Excessive perioperative risk	Low complexity
Frailty (poor functional status)	Favorable histology
Patient preference for AS	
Marginal renal function	

- **For patients with small solid or Bosniak 3/4 complex cystic renal masses, especially those <2cm, AS is an option for initial management (*Even in healthy patients).***
- **Shared-decision making about AS/Expectant Management versus Intervention requires careful consideration of the anticipated risks of intervention and competing risks of death versus the potential oncologic benefits of active treatment.**

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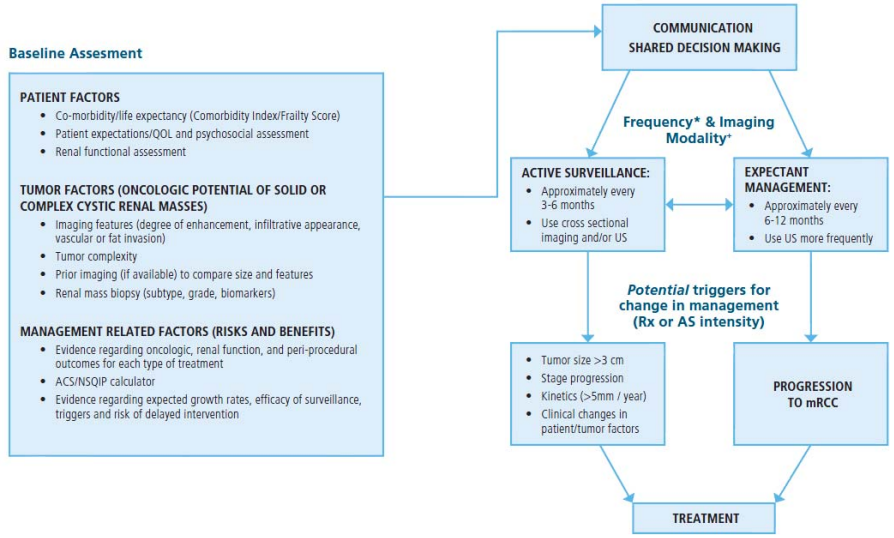
Algorithm for active surveillance or expectant management of localized renal masses suspicious for malignancy



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* Consider concurrent renal functional assessment (sCr, proteinuria), metabolic assessment (LFTs) and chest imaging

+ Consider alternatives to contrast when possible or necessary (doppler, diffusion weighted images etc.)