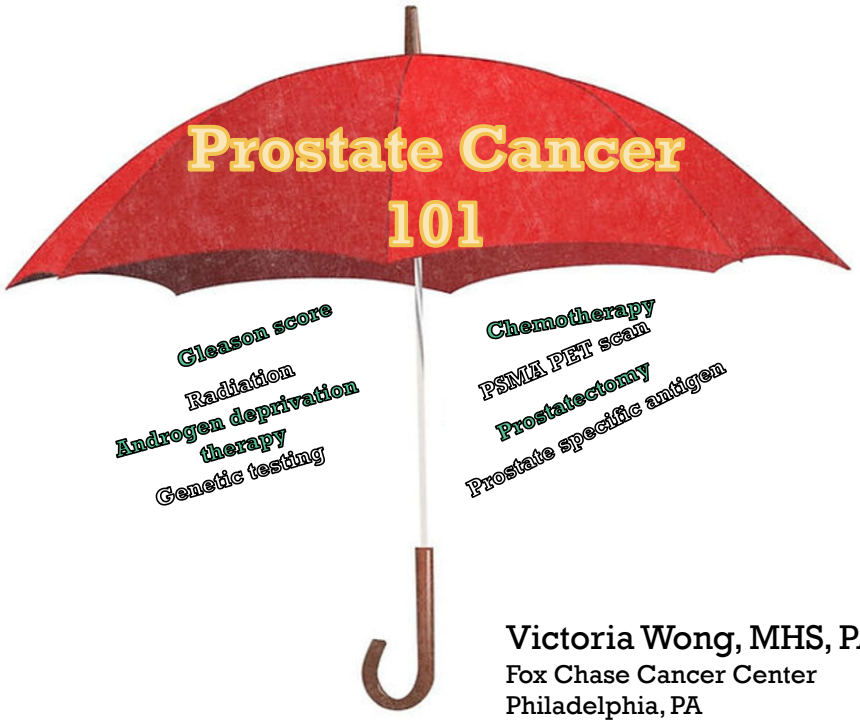


Victoria Wong, MHS, PA-C
Fox Chase Cancer Center
Philadelphia, PA

OBJECTIVES

- Review the incidence and screening of prostate cancer
- Describe the diagnosis and treatment of prostate cancer
- Review recommendations for prostate cancer survivorship

SEER DATABASE

	Common Types of Cancer	Estimated New Cases 2022	Estimated Deaths 2022
1.	Breast Cancer (Female)	287,850	43,250
2.	Prostate Cancer	268,490	34,500
3.	Lung and Bronchus Cancer	236,740	130,180
4.	Colorectal Cancer	151,030	52,580
5.	Melanoma of the Skin	99,780	7,650
6.	Bladder Cancer	81,180	17,100
7.	Non-Hodgkin Lymphoma	80,470	20,250
8.	Kidney and Renal Pelvis Cancer	79,000	13,920
9.	Uterine Cancer	65,950	12,550
10.	Pancreatic Cancer	62,210	49,830

Prostate cancer represents 14.0% of all new cancer cases in the U.S.

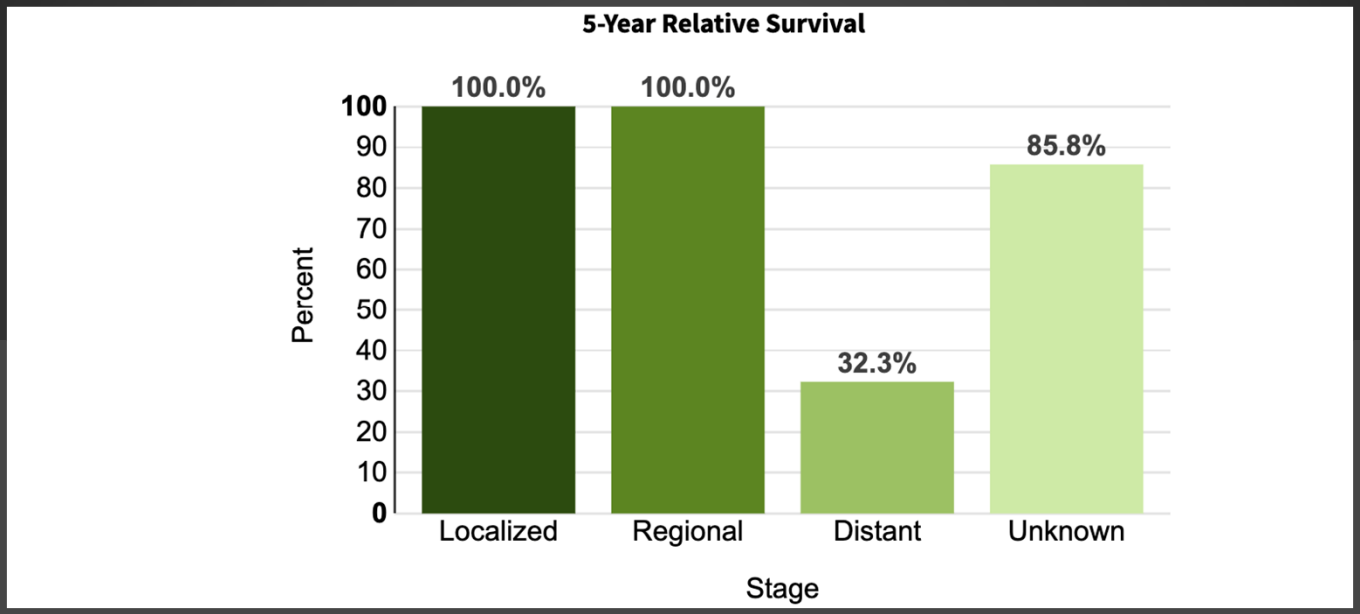
Cancer of the prostate - cancer stat facts. SEER. https://seer.cancer.gov/statfacts/html/prost.html. Accessed March 28, 2023.

GENERAL STATISTICS

- 1/8 males will be diagnosed with prostate cancer
- More likely to develop in older men and in non-Hispanic African American men.
  - The average age of diagnosis is 67.
- 14% of all new cancer cases
- 2nd leading cause of cancer-related death in American men (5.7% of all cancer deaths)

Cancer of the prostate - cancer stat facts. SEER. https://seer.cancer.gov/statfacts/html/prost.html. Accessed March 28, 2023.

5-YEAR RELATIVE SURVIVAL



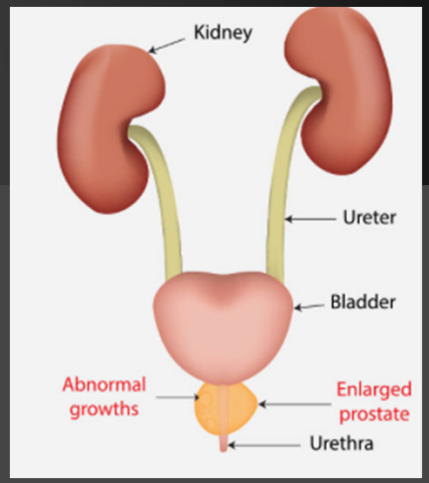
RISK FACTORS

- Age
- Geography
- Occupational
  - Agent orange
  - Cadmium exposure
- Inherited genetic factors (5-10%)
  - BRCA 1 or BRCA 2
  - HOXB13
  - ATM
- Family history
  - Prostate, breast, ovarian, pancreatic, colon, melanoma
  - Relative diagnosed at earlier age (before 60)
- Race/nationality
  - African American men at higher risk
  - Also more likely to have an advanced stage when diagnosed

Prostate cancer causes & risk factors. Memorial Sloan Kettering Cancer Center. https://www.mskcc.org/cancer-care/types/prostate/risk-factors. Accessed March 28, 2023.

CLINICAL MANIFESTATIONS

- Most men are asymptomatic, found by screening PSA
  - Most localized disease at diagnosis.
- Urinary symptoms: frequency, nocturia, weak stream, dribbling
- Advanced: bone pain, lymphedema, symptoms related to cord compression, weight loss, fatigue, anemia



Prostate Cancer: Causes, Symptoms And Treatment https://www.netmeds.com/health-library/post/prostate-cancer-causes-symptoms-and-treatment. Accessed March 28, 2023.

PSA SCREENING

PSA SCREENING

U.S. Preventive Services TASK FORCE

Population	Men aged 55 to 69 y	Men 70 y and older
Recommendation	The decision to be screened for prostate cancer should be an individual one.	Do not screen for prostate cancer. Grade: D

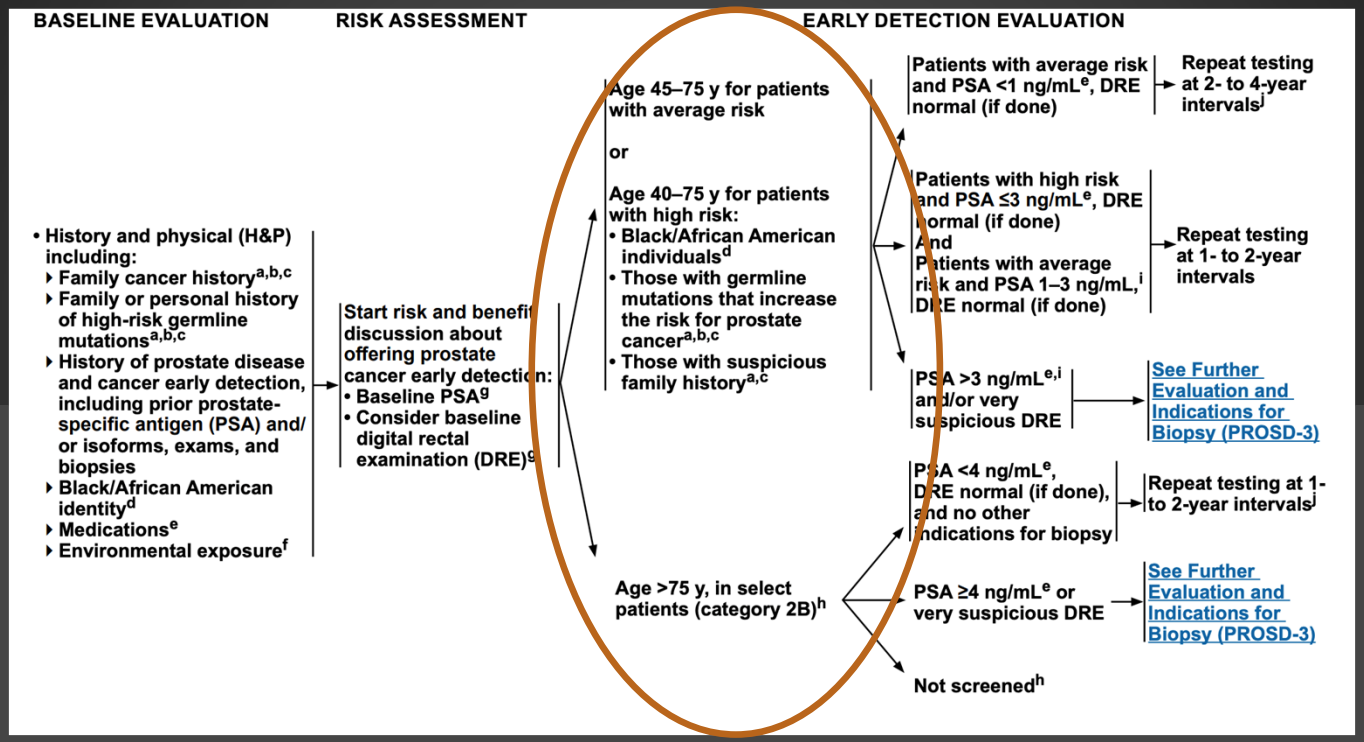
American Cancer Society®

- **Age 50 for men who are at average risk** of prostate cancer and are expected to live at least 10 more years.
- **Age 45 for men at high risk** of developing prostate cancer. This includes African Americans and men who have a first-degree relative (father or brother) diagnosed with prostate cancer at an early age (younger than age 65).
- **Age 40 for men at even higher risk** (those with more than one first-degree relative who had prostate cancer at an early age).

Prostate Cancer Screening. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/prostate-cancer-screening. Accessed March 28, 2023.

American Cancer Society Recommendations for Prostate Cancer Early Detection. https://www.cancer.org/cancer/prostate-cancer/detection-diagnosis-staging/acs-recommendations.html. Accessed March 28, 2023.

National Comprehensive Cancer Network®



Prostate Cancer Early Detection. https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf. Accessed March 28, 2023.

PSA IS NOT PERFECT

- PSA generally considered elevated if ≥ 4.0 ng/mL
  - Sensitivity of 21%, specificity of 91% for detection of any prostate cancer
  - Sensitivity 51% for detection of high grade prostate cancer

  = some men with PSA levels < 4 ng/mL will have prostate cancer
- May be elevated in benign prostatic hyperplasia, infection, inflammation
- 5-alpha reductase inhibitors can decrease PSA by up to 50%

Screening For Prostate Cancer. https://www.uptodate.com/contents/screening-for-prostate-cancer. Accessed March 24, 2023.

DRE DIGITAL RECTAL EXAM

❌ U.S. Preventive Services TASK FORCE

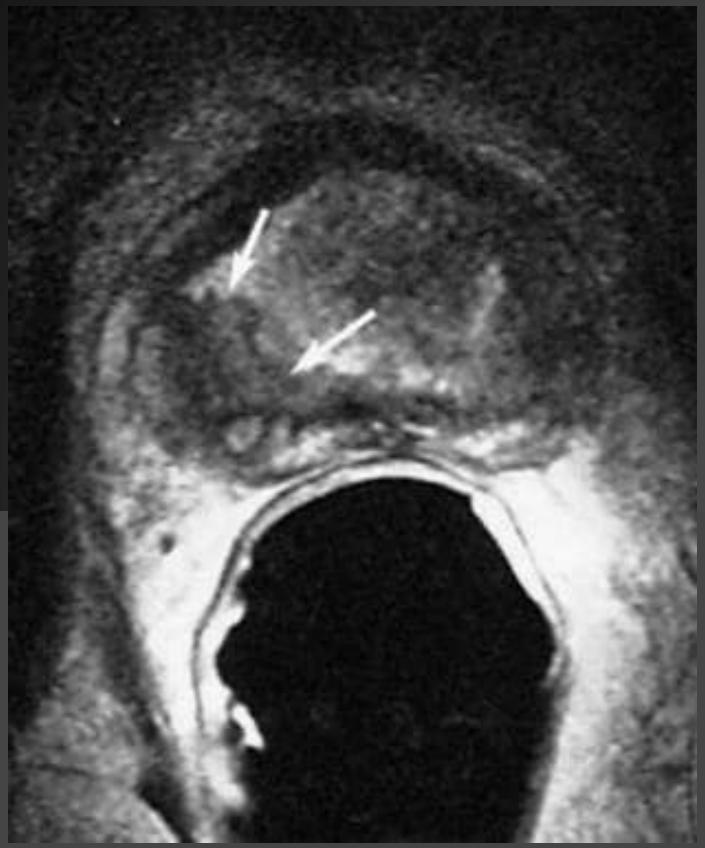
"The use of digital rectal examination as a screening modality is not recommended because there is a lack of evidence on the benefits"

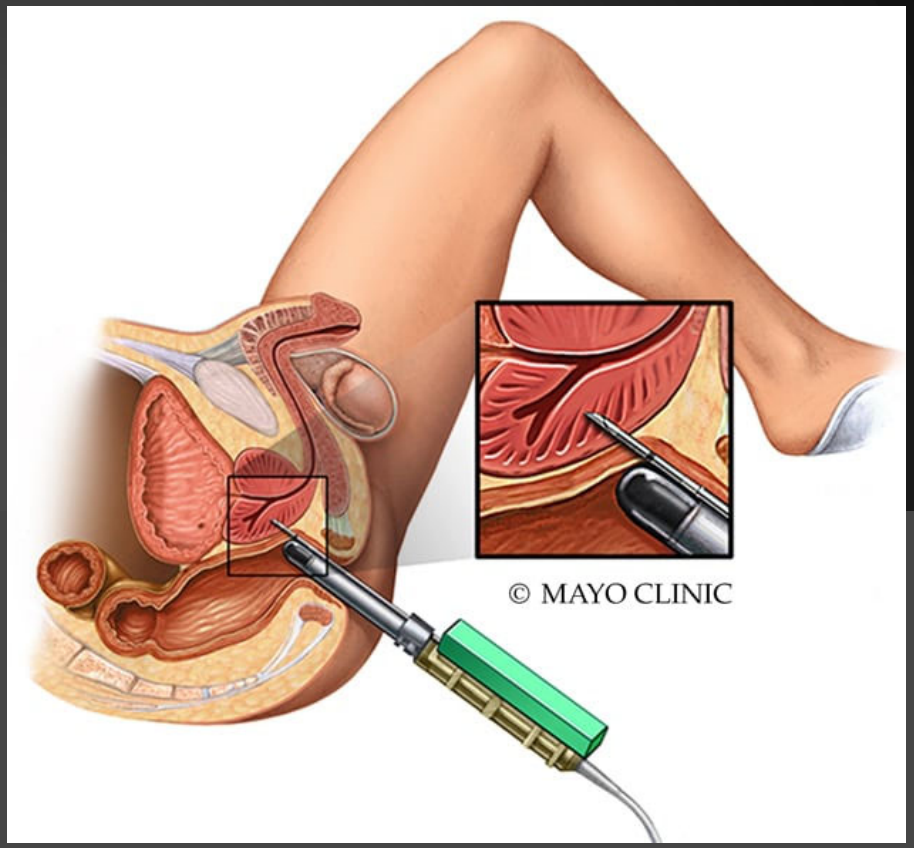
❌ NCCN National Comprehensive Cancer Network®

"The best evidence supports the use of serum PSA for the early detection of prostate cancer. DRE should not be used as a stand-alone test.

American Cancer Society®

"DRE is less effective than the PSA blood test in finding prostate cancer, but it can sometimes find cancers in men with normal PSA levels. For this reason, it might be included as a part of prostate cancer screening."





Prostate Cancer Imaging. https://emedicine.medscape.com/article/379996-overview. Accessed March 28, 2023.

Ultrasound-guided transperineal prostate biopsy. https://www.mayoclinic.org/medical-professionals/urology/news/ultrasound-guided-transperineal-prostate-biopsy/mac-20473283. Accessed March 28, 2023.

STAGING

American Joint Committee on Cancer (AJCC)
TNM Staging System For Prostate Cancer (8th ed., 2017)
***Table 1.* Definitions for T, N, M**
Clinical T (cT)

T	Primary Tumor
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Clinically inapparent tumor that is not palpable
T1a	Tumor incidental histologic finding in 5% or less of tissue resected
T1b	Tumor incidental histologic finding in more than 5% of tissue resected
T1c	Tumor identified by needle biopsy found in one or both sides, but not palpable
T2	Tumor is palpable and confined within prostate
T2a	Tumor involves one-half of one side or less
T2b	Tumor involves more than one-half of one side but not both sides
T2c	Tumor involves both sides
T3	Extraprostatic tumor that is not fixed or does not invade adjacent structures
T3a	Extraprostatic extension (unilateral or bilateral)
T3b	Tumor invades seminal vesicle(s)
T4	Tumor is fixed or invades adjacent structures other than seminal vesicles such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall.

Pathological T (pT)

T	Primary Tumor
T2	Organ confined
T3	Extraprostatic extension
T3a	Extraprostatic extension (unilateral or bilateral) or microscopic invasion of bladder neck
T3b	Tumor invades seminal vesicle(s)
T4	Tumor is fixed or invades adjacent structures other than seminal vesicles such as external sphincter, rectum, bladder, levator muscles, and/or pelvic wall

Note: There is no pathological T1 classification.
Note: Positive surgical margin should be indicated by an R1 descriptor, indicating residual microscopic disease.

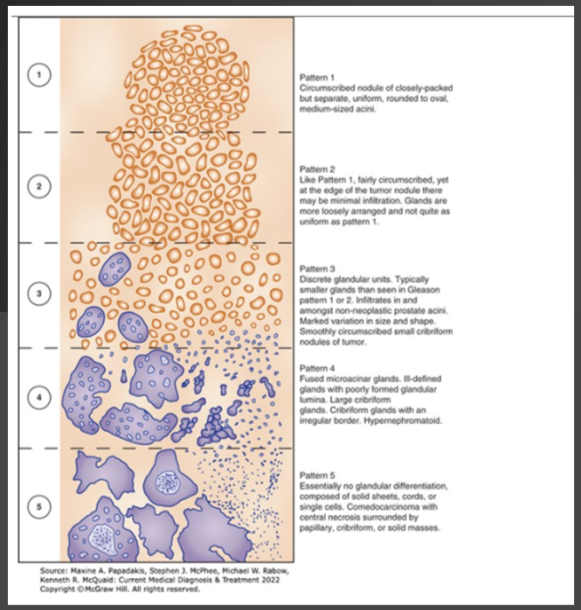
N	Regional Lymph Nodes
NX	Regional lymph nodes cannot be assessed
N0	No positive regional nodes
N1	Metastases in regional node(s)

M	Distant Metastasis
M0	No distant metastasis
M1	Distant metastasis
M1a	Nonregional lymph node(s)
M1b	Bone(s)
M1c	Other site(s) with or without bone disease

Note: When more than one site of metastasis is present, the most advanced category is used. M1c is most advanced.

National Comprehensive Cancer Network. Prostate Cancer (2022). https://www.nccn.org/patients/guidelines/content/PDF/prostate-early-patient.pdf. Accessed March 24, 2023.

GLEASON SCORE + GRADE GROUPS



Guide 2 Grade Groups	
1	• Gleason score 6 or less • Gleason pattern 1+3, 2+3, 3+3
2	• Gleason score 7 • Gleason pattern 3+4
3	• Gleason score 7 • Gleason pattern 4+3
4	• Gleason score 8 • Gleason pattern 4+4, 3+5, 5+3
5	• Gleason score 9 or 10 • Gleason pattern 4+5, 5+4, 5+5

RISK STRATIFICATION

- PSA
- Tissue
- Imaging
  - MRI
  - CT
  - PET
  - Bone scan

INITIAL RISK STRATIFICATION AND STAGING WORKUP FOR CLINICALLY LOCALIZED DISEASE[d]

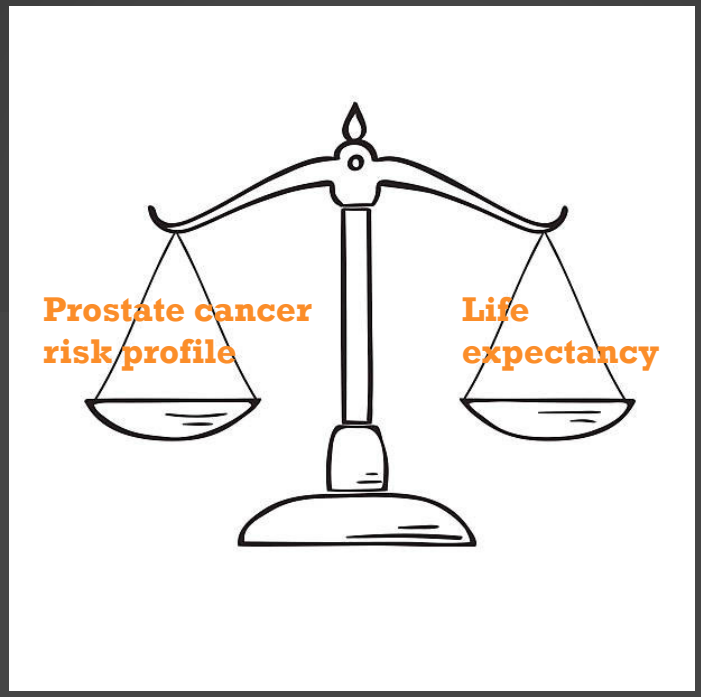
Risk Group	Clinical/Pathologic Features See Staging (ST-1)			Additional Evaluation[g,h]	Initial Therapy
Very low[e]	Has all of the following: • cT1c • Grade Group 1 • PSA <10 ng/mL • Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core • PSA density <0.15 ng/mL/g			• Consider confirmatory mpMRI ± prostate biopsy if MRI not performed initially. All patients should undergo a confirmatory prostate biopsy within 1-2 years of their diagnostic biopsy.	See PROS-3
Low[e]	Has all of the following but does not qualify for very low risk: • cT1–cT2a • Grade Group 1 • PSA <10 ng/mL			• Consider confirmatory mpMRI ± prostate biopsy and/or molecular tumor analysis if MRI not performed initially to establish candidacy for active surveillance. All patients should undergo a confirmatory prostate biopsy within 1-2 years of their diagnostic biopsy.	See PROS-4
Intermediate[e]	Has all of the following: • No high-risk group features • No very-high-risk group features • Has one or more intermediate risk factors (IRFs): ▸ cT2b–cT2c ▸ Grade Group 2 or 3 ▸ PSA 10–20 ng/mL	Favorable intermediate	Has all of the following: • 1 IRF • Grade Group 1 or 2 • <50% biopsy cores positive (eg, <6 of 12 cores)[f]	• Consider confirmatory mpMRI ± prostate biopsy and/or molecular tumor analysis if MRI not performed initially for those considering active surveillance. All patients should undergo a confirmatory prostate biopsy within 1-2 years of their diagnostic biopsy.	See PROS-5
		Unfavorable intermediate	Has one or more of the following: • 2 or 3 IRFs • Grade Group 3 • ≥ 50% biopsy cores positive (eg, ≥ 6 of 12 cores)[f]	Bone and soft tissue imaging[i,j] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-6
High	Has no very-high-risk features and has exactly one high-risk feature: • cT3a OR • Grade Group 4 or Grade Group 5 OR • PSA >20 ng/mL			Bone and soft tissue imaging[i,j] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-7
Very high	Has at least one of the following: • cT3b–cT4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • >4 cores with Grade Group 4 or 5			Bone and soft tissue imaging[i,j] • If regional or distant metastases are found, see PROS-8 or PROS-12	See PROS-7

See Footnotes for Initial Risk Stratification and Staging Workup for Clinically Localized Disease (PROS-2A)

National Comprehensive Cancer Network. Prostate Cancer (Version 1.2023). https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed March 25, 2023.

Active surveillance
Radiation
Surgery
Hormonal Therapy
Chemotherapy
SPIN

ACTIVE SURVEILLANCE



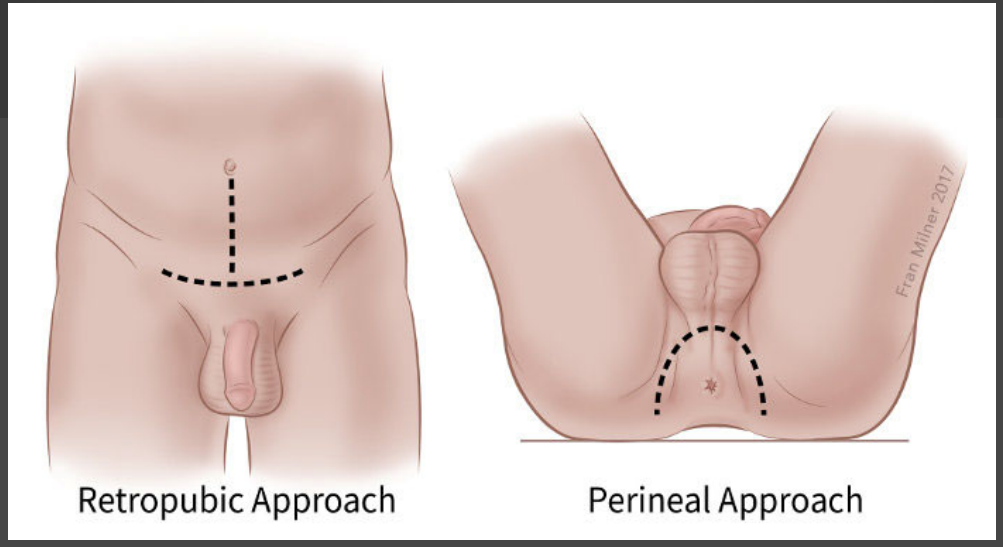
ACTIVE SURVEILLANCE ≠ NOTHING

- "Active surveillance involves actively monitoring the course of disease with the expectation to intervene with curative intent if the cancer progresses." – NCCN
- Advantages:
  - 50-68% may safely avoid treatment for at least 10 years
  - Quality of life, avoid side effects
  - "Unnecessary treatment of small, indolent cancers will be reduced"

National Comprehensive Cancer Network. Prostate Cancer (Version 1.2023). https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed March 25, 2023.

SURGERY

- Radical prostatectomy and lymph node dissection
  - Open with retropubic (suprapubic) approach or with perineal approach

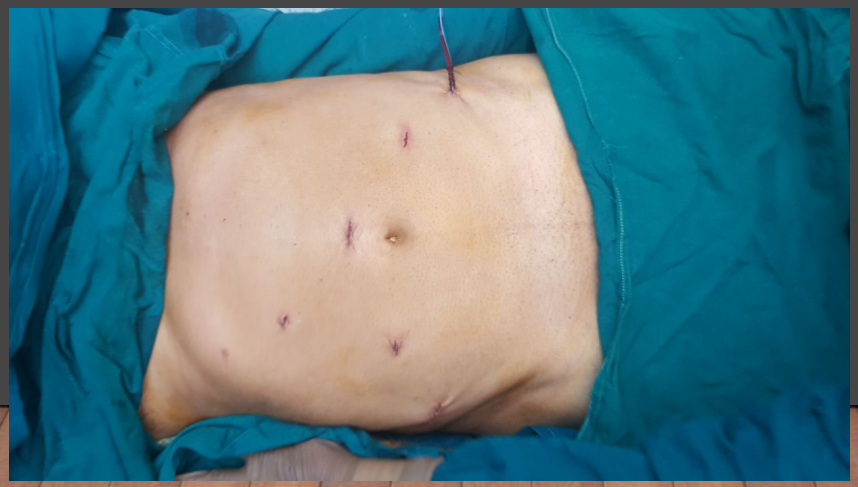


Surgery For Prostate Cancer. https://www.cancer.org/cancer/prostate-cancer/treating/surgery.html. Accessed March 25, 2023.

Radical Prostatectomy. https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/radical-prostatectomy. Accessed March 25, 2023

SURGERY

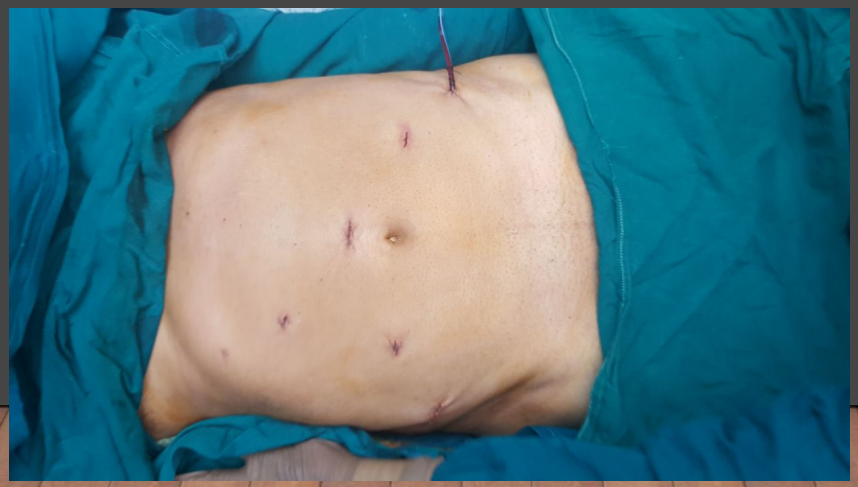
- Radical prostatectomy and lymph node dissection
  - Open with retropubic (suprapubic) approach or with perineal approach
  - Laparoscopic radical prostatectomy
  - Robotic-assisted laparoscopic prostatectomy



Robotic Radical Prostatectomy. https://www.roboticsurgeonpune.com/robotic-surgeon-pune/terms/Robotic-Radical-Prostatectomy/4514. Accessed March 25, 2023.

SURGERY

- Radical prostatectomy and lymph node dissection
  - Open with retropubic (suprapubic) approach or with perineal approach
  - Laparoscopic radical prostatectomy
  - Robotic-assisted laparoscopic prostatectomy



Laparoscopic Advantages:

- Less blood loss and pain
- Shorter hospital stays (usually no more than a day)
- Faster recovery times
- Less catheter time

Robotic Radical Prostatectomy. https://www.roboticsurgeonpune.com/robotic-surgeon-pune/terms/Robotic-Radical-Prostatectomy/4514. Accessed March 25, 2023.

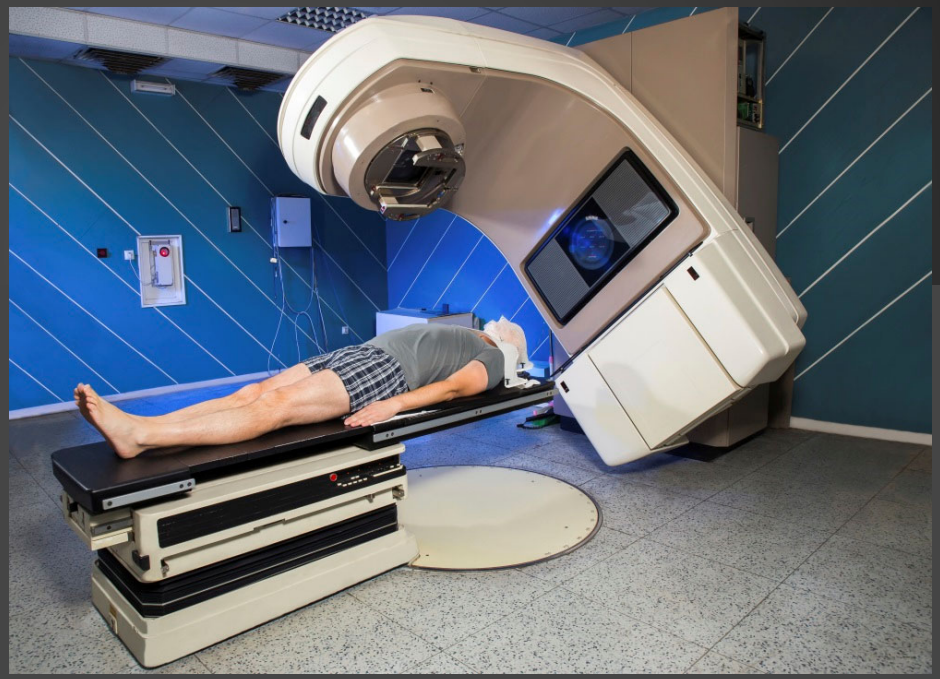
SURGERY

- Radical prostatectomy and lymph node dissection
  - Open with retropubic (suprapubic) approach or with perineal approach
  - Laparoscopic radical prostatectomy
  - Robotic-assisted laparoscopic prostatectomy
- Transurethral resection of the prostate (TURP)

Surgery For Prostate Cancer. https://www.cancer.org/cancer/prostate-cancer/treating/surgery.html. Accessed March 25, 2023.

RADIATION THERAPY

- External beam radiation
- Brachytherapy



How is Prostate Cancer Treated? https://www.cdc.gov/cancer/prostate/basic_info/treatment.htm. Accessed March 27, 2023.

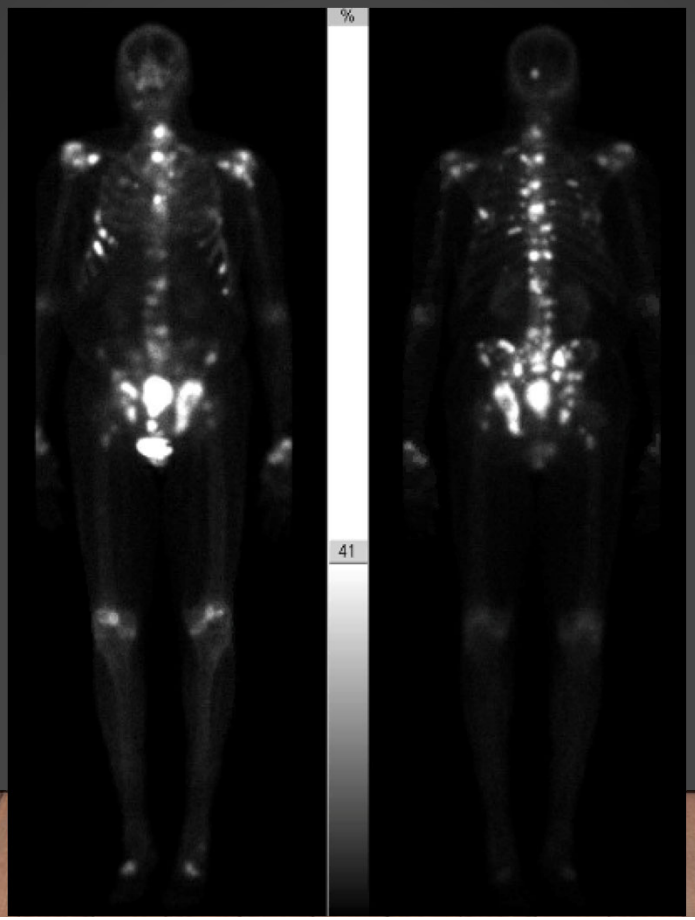
Prostate Brachytherapy. https://www.mayoclinic.org/tests-procedures/prostate-brachytherapy/about/pac-20384949. Accessed March 25, 2023

RADIATION SIDE EFFECTS

- Fatigue
- Radiation proctitis
- Radiation cystitis / urethritis
- Dermatitis
- Erectile dysfunction

Radiation Therapy for Prostate Cancer. https://www.cancer.org/cancer/prostate-cancer/treating/radiation-therapy.html. Accessed March 27, 2023

ADVANCED DISEASE



SYSTEMIC THERAPIES

- Hormonal therapy
- Chemotherapy
- Targeted therapy
- *Immunotherapy*

ANDROGEN RECEPTOR (AR)

- AR is highly expressed on prostate cancer cells.
- Androgens (testosterone and dihydrotestosterone (DHT)) stimulate prostate cancer cells to grow.
- When androgens attach to AR → stimulation of prostate cell growth
- Androgen deprivation therapy can suppress castrate-sensitive prostate cancer

Hormone Therapy for Prostate Cancer https://www.cancer.org/cancer/prostate-cancer/treating/hormone-therapy.html. Accessed March 12, 2023

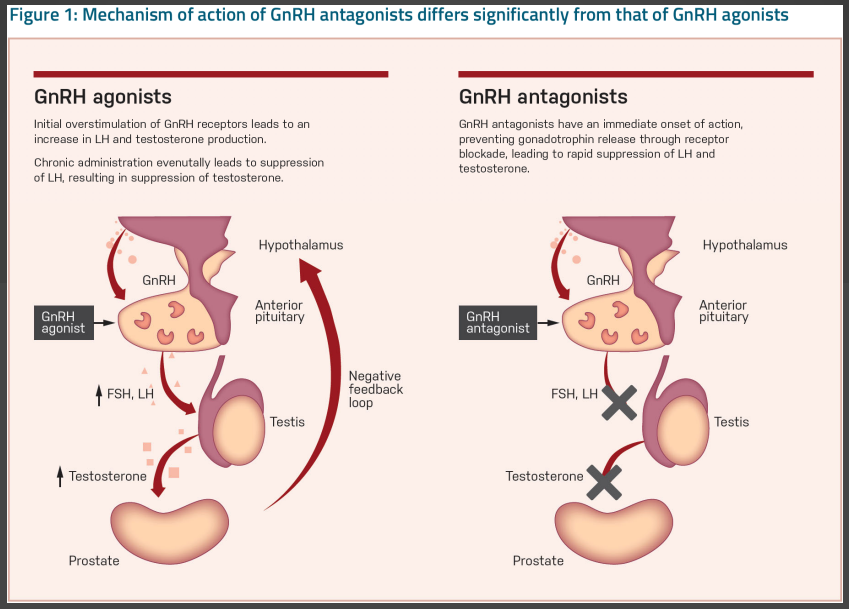
Fujita K, Nonomura N. Role of Androgen Receptor in Prostate Cancer: A Review. *World J Mens Health.* 2019;37(3):288-295. doi:10.5534/wjmh.180040

HORMONAL THERAPY

- Androgen deprivation therapy
  - Surgical: Orchiectomy
  - Medical: GnRH agonist / antagonist- injections or oral
- Goal is to suppress testosterone

HORMONAL THERAPY

Figure 1: Mechanism of action of GnRH antagonists differs significantly from that of GnRH agonists



HORMONAL THERAPY- SIDE EFFECTS

- Fatigue
- Hot Flashes
- Decreased libido/ED
- Weakening bones (osteoporosis)/ bone fractures
- Weight gain
- Mood changes
- Loss of muscle mass
- Breast tenderness
- Increased risk of diabetes and cardiovascular disease
- Unfortunately more!

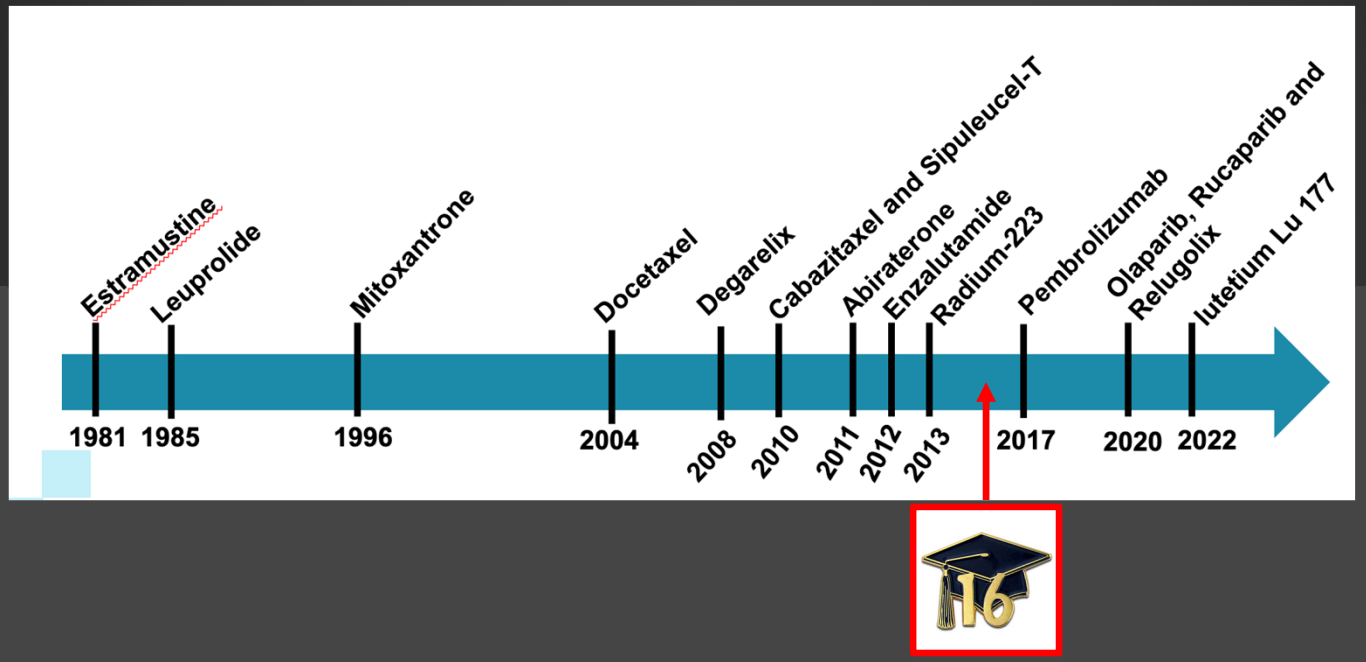
National Comprehensive Cancer Network. Prostate Cancer (2022). https://www.nccn.org/patients/guidelines/content/PDF/prostate-early-patient.pdf. Accessed March 24, 2023

CASTRATION RESISTANT DISEASE

- PSA rise despite serum testosterone <50 ng/dL (castrate levels)
- Prostate cancer adapts to survive under castration levels of androgen (AR point mutations, AR amplification, changes in androgen biosynthesis, changes in AR cofactor)

National Comprehensive Cancer Network. Prostate Cancer (Version 1.2023). https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed March 24, 2023.

M1 CRPC – FDA APPROVED TREATMENTS



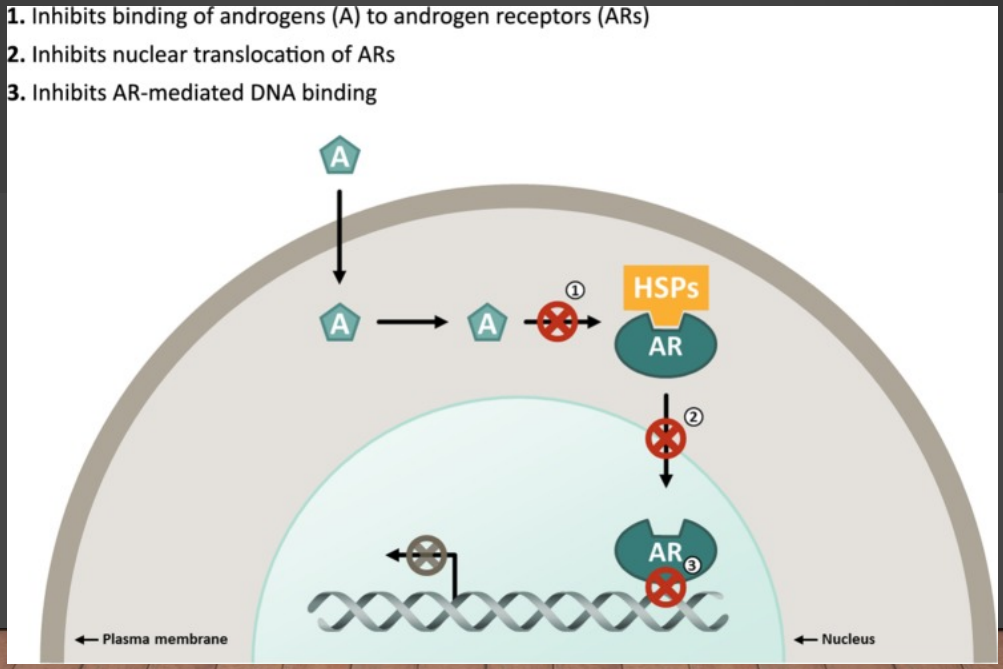
- Slide adopted with permission by Dr. Fern Anari, MD

INDIVIDUAL PATIENT = INDIVIDUAL TREATMENT DECISION

- Burden of disease
- Aggressiveness of disease
- Symptoms
- Performance status

ANDROGEN RECEPTOR INHIBITORS

- Enzalutamide, apalutamide, darolutamide



Saad F. Evidence for the efficacy of enzalutamide in postchemotherapy metastatic castrate-resistant prostate cancer. *Ther Adv Urol.* 2013;5(4):201-210. doi:10.1177/1756287213490054

ANDROGEN RECEPTOR INHIBITORS

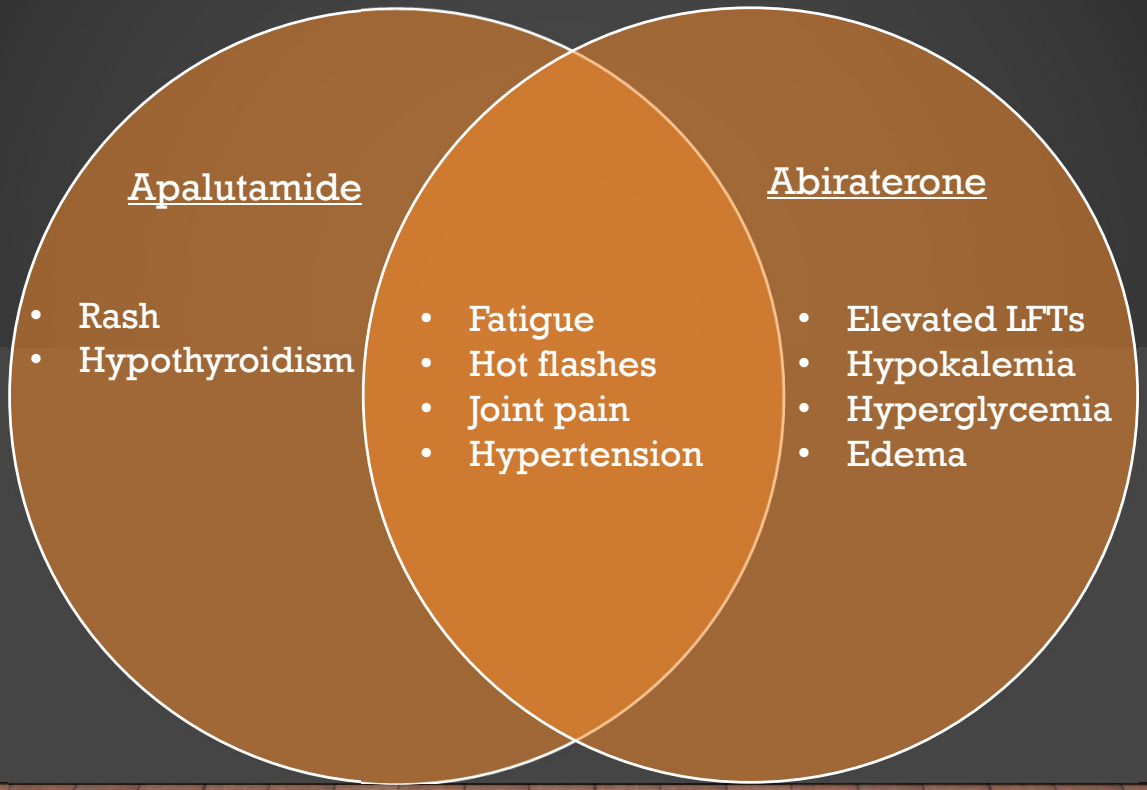
- Enzalutamide, apalutamide, darolutamide

ANDROGEN BIOSYNTHESIS INHIBITOR

- Abiraterone

How Abiraterone Works. https://www.zytigahcp.com/how-zytiga-works. Accessed March 29, 2023.

ADVERSE EFFECTS



CHEMOTHERAPY

- Docetaxel
- Cabazitaxel

- National Comprehensive Cancer Network. Prostate Cancer (Version 1.2023). https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed March 24, 2023.

DOCETAXEL ADVERSE EFFECTS

- Anemia
- Neutropenia
- Thrombocytopenia
- Infection
- Allergic reaction
- Fluid retention
- Neuropathy
- Rash
- Alopecia
- Hepatotoxicity
- Nail changes
- Nausea/vomiting
- Diarrhea
- Stomatitis/Pharyngitis
- Taste disturbance
- Fatigue

https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020449s071lbl.pdf. Accessed March 24 2023.

DOCETAXEL ADVERSE EFFECTS

- Anemia
- Neutropenia → hold if neutrophils <1500 cells/mm^3
- Thrombocytopenia
- Infection
- Allergic reaction → pre-medications
- Fluid retention
- Neuropathy → gabapentin
- Rash
- Alopecia
- Nail changes
- Nausea/vomiting → anti-emetics
- Diarrhea → anti-diarrheal
- Stomatitis/Pharyngitis → mouth rinse/magic mouthwash
- Taste Disturbance
- Fatigue

- https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/020449s071lbl.pdf. Accessed March 24 2023.

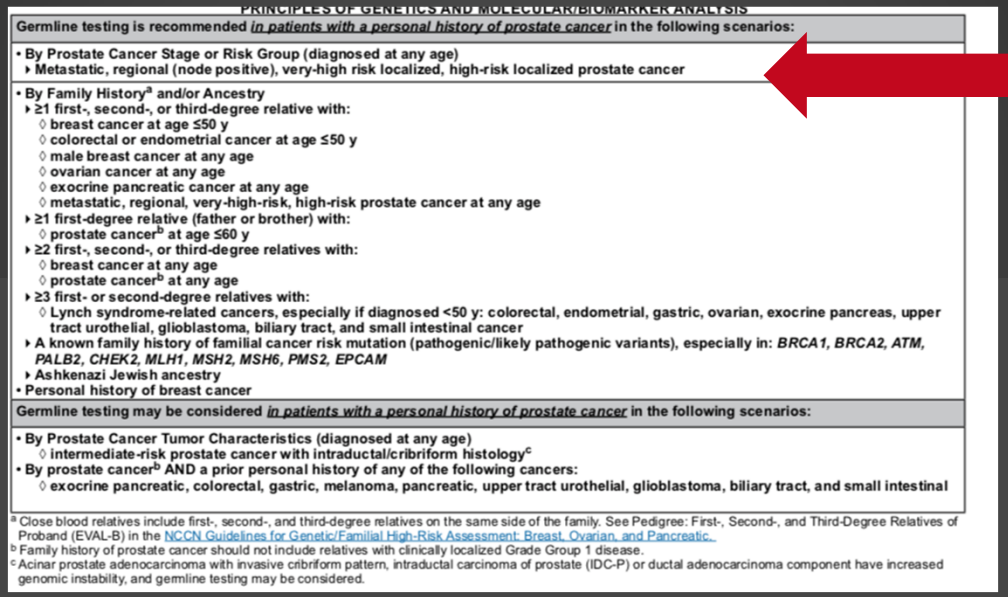
TRIPLET THERAPY

- Chemotherapy + 2nd generation anti-androgen + androgen deprivation therapy

(docetaxel + darolutamide + androgen deprivation therapy)

FDA approves darolutamide tablets for metastatic hormone-sensitive prostate cancer. U.S. Food and Drug Administration. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-darolutamide-tablets-metastatic-hormone-sensitive-prostate-cancer. Accessed March 24, 2023.

MOLECULAR AND GENETIC TESTING



PRINCIPLES OF GENETICS AND MOLECULAR/BIOMARKER ANALYSIS

Germline testing is recommended *in patients with a personal history of prostate cancer* in the following scenarios:

- **By Prostate Cancer Stage or Risk Group (diagnosed at any age)**
  - **Metastatic, regional (node positive), very-high risk localized, high-risk localized prostate cancer**
- **By Family History[a] and/or Ancestry**
  - **≥1 first-, second-, or third-degree relative with:**
    - **breast cancer at age ≤50 y**
    - **colorectal or endometrial cancer at age ≤50 y**
    - **male breast cancer at any age**
    - **ovarian cancer at any age**
    - **exocrine pancreatic cancer at any age**
    - **metastatic, regional, very-high-risk, high-risk prostate cancer at any age**
  - **≥1 first-degree relative (father or brother) with:**
    - **prostate cancer[b] at age ≤60 y**
  - **≥2 first-, second-, or third-degree relatives with:**
    - **breast cancer at any age**
    - **prostate cancer[b] at any age**
  - **≥3 first- or second-degree relatives with:**
    - **Lynch syndrome-related cancers, especially if diagnosed <50 y: colorectal, endometrial, gastric, ovarian, exocrine pancreas, upper tract urothelial, glioblastoma, biliary tract, and small intestinal cancer**
  - **A known family history of familial cancer risk mutation (pathogenic/likely pathogenic variants), especially in: *BRCA1, BRCA2, ATM, PALB2, CHEK2, MLH1, MSH2, MSH6, PMS2, EPCAM***
  - **Ashkenazi Jewish ancestry**
- **Personal history of breast cancer**

Germline testing may be considered *in patients with a personal history of prostate cancer* in the following scenarios:

- **By Prostate Cancer Tumor Characteristics (diagnosed at any age)**
  - **intermediate-risk prostate cancer with intraductal/cribriform histology[c]**
- **By prostate cancer[b] AND a prior personal history of any of the following cancers:**
  - **exocrine pancreatic, colorectal, gastric, melanoma, pancreatic, upper tract urothelial, glioblastoma, biliary tract, and small intestinal**

[a] Close blood relatives include first-, second-, and third-degree relatives on the same side of the family. See Pedigree: First-, Second-, and Third-Degree Relatives of Proband (EVAL-B) in the NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic.

[b] Family history of prostate cancer should not include relatives with clinically localized Grade Group 1 disease.

[c] Acinar prostate adenocarcinoma with invasive cribriform pattern, intraductal carcinoma of prostate (IDC-P) or ductal adenocarcinoma component have increased genomic instability, and germline testing may be considered.

National Comprehensive Cancer Network. Prostate Cancer (Version 1.2023). https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed March 24, 2023.

MOLECULAR AND GENETIC TESTING

- Somatic testing
  - Tissue testing
  - Liquid biopsy
- Homologous recombination DNA repair genes: *BRCA1, BRCA2, ATM, PALB2, FANCA, RAD51D, CHEK2*, and *CDK12*
- Testing for Microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) or tumor mutational burden (TMB) is recommended in patients with metastatic castration-resistant prostate cancer.

National Comprehensive Cancer Network. Prostate Cancer (Version 4.2022). https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed August 25, 2022.

TARGETED THERAPY FOR PROSTATE CANCER

FDA grants accelerated approval to rucaparib for BRCA-mutated metastatic castration-resistant prostate cancer

FDA approves olaparib for HRR gene-mutated metastatic castration-resistant prostate cancer

Center for Drug Evaluation and Research. FDA approves Olaparib for HRR gene-mutated metastatic castration-resis. U.S. Food and Drug Administration. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-olaparib-hrr-gene-mutated-metastatic-castration-resistant-prostate-cancer. Accessed March 20, 2023
Center for Drug Evaluation and Research. FDA grants accelerated approval to Rucaparib for BRCA-mutated metastat. U.S. Food and Drug Administration. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-rucaparib-brca-mutated-metastatic-castration-resistant-prostate. Accessed March 20, 2023

PARP INHIBITORS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer

C.C. Pritchard, J. Mateo, M.F. Walsh, N. De Sarkar, W. Abida, H. Beltran, A. Garofalo, R. Gulati, S. Carreira, R. Eeles, O. Elemento, M.A. Rubin, D. Robinson, R. Lonigro, M. Hussain, A. Chinnaiyan, J. Vinson, J. Filipenko, L. Garraway, M.-E. Taplin, S. AlDubayan, G.C. Han, M. Beightol, C. Morrissey, B. Nghiem, H.H. Cheng, B. Montgomery, T. Walsh, S. Casadei, M. Berger, L. Zhang, A. Zehir, J. Vijai, H.I. Scher, C. Sawyers, N. Schultz, P.W. Kantoff, D. Solit, M. Robson, E.M. Van Allen, K. Offit, J. de Bono, and P.S. Nelson

Pritchard CC, Mateo J, Walsh MF, et al. Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer. *N Engl J Med*. 2016;375(5):443-453. doi:10.1056/NEJMoa1603144

PARP INHIBITORS

11.8% had a mutation in DNA repair gene

- BRCA2 5.3%
- CHEK2 1.9%
- ATM 1.6%
- BRCA1 0.9%
- RAD51D 0.4%
- PALB2 0.4%

Pritchard CC, Mateo J, Walsh MF, et al. Inherited DNA-Repair Gene Mutations in Men with Metastatic Prostate Cancer. *N Engl J Med*. 2016;375(5):443-453. doi:10.1056/NEJMoa1603144

IMMUNOTHERAPY

FDA grants accelerated approval to pembrolizumab for first tissue/site agnostic indication

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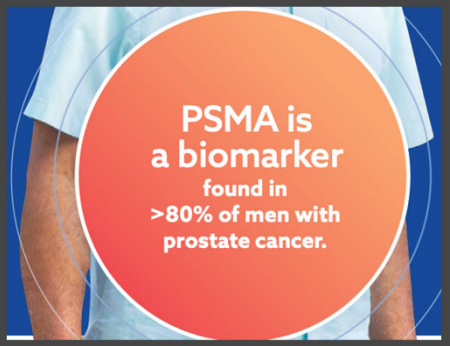
Listen to the FDA D.I.S.C.O. podcast about this approval

On May 23, 2017, the U.S. Food and Drug Administration granted accelerated approval to pembrolizumab ( ) for adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options or with MSI-H or dMMR colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-pembrolizumab-first-tissuesite-agnostic-indication. Accessed March 12, 2023

LUTETIUM LU 177 VIPIVOTIDE TETRAXETAN

- 177Lu-PSMA-617 delivers β-particle radiation to PSMA-expressing cells and their surrounding microenvironment.
- Improvement in overall survival and progression free survival
- AEs: fatigue, dry mouth, anemia, nausea and constipation.



https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pluvicto-metastatic-castration-resistant-prostate-cancer. Accessed March 23, 2023
Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer. *N Engl J Med*. 2021;385(12):1091-1103. doi:10.1056/NEJMoa2107322

INDIVIDUAL PATIENT = INDIVIDUAL TREATMENT DECISION

- History of neuropathy → docetaxel may cause neuropathy
- History of uncontrolled diabetes → abiraterone is taken with prednisone (though low dose)
- History of seizures → enzalutamide increased risk of seizures
- Worried about compliance → abiraterone is taken on an empty stomach and prednisone is taken with food

SURVIVORSHIP

5-Year Relative Survival
96.8%

ACS GUIDELINES

- Health promotion
  - Maintain healthy weight
  - Healthy diet: fruits, vegetables, whole grains, low saturated fat
  - Promote increased physical activity- 150 minutes per week (may include weight bearing exercise)
  - Intake of at least 600 IU of vitamin D per day and adequate dietary sources of calcium (not to exceed 1,200 mg/d).
  - Limit alcohol < 2 drinks per day
  - Assess for tobacco use -> refer to smoking cessation

Resnick MJ, Lacchetti C, Penson DF; American Society of Clinical Oncology. Prostate cancer survivorship care guidelines: American Society of Clinical Oncology practice guideline endorsement. J Oncol Pract. 2015 May;11(3):e445-9. doi: 10.1200/JOP.2015.004606. Epub 2015 Mar 31

- Surveillance for recurrence
  - Measure PSA level at appropriate interval
    - *"ASCO qualifying statement: Prostate cancer specialists may recommend more frequent PSA monitoring during the early survivorship experience for some men, particularly men with higher risk of prostate cancer recurrence and/or men who may be candidates for salvage therapy. The exact schedule for PSA measurement should be determined by both the prostate cancer specialist and primary care physician in collaboration.*
- Screening for second primary cancers
  - Hematuria- rule out bladder cancer
  - Rectal bleeding- rule out colorectal cancer
  - *"ASCO qualifying statement: Patients and physicians should be informed of the increased risk of bladder and colorectal cancer (CRC) after pelvic radiation therapy."*

PHYSICAL AND PSYCHOSOCIAL

- Anemia
- Bowel dysfunction
- Fracture risk/osteoporosis
- Cardiovascular and metabolic effects
  - CV risk factors, blood pressure monitoring, lipid profiles and glucose monitoring
- Distress, depression, anxiety monitoring
  - "PSA anxiety"

- Sexual dysfunction and body image (ED up to 90%!!)
  - Can refer to urologist, sexual health specialist, psychotherapist after phosphodiesterase type 5 inhibitors
- Urinary dysfunction
  - Difficulty emptying, incontinence, frequency/nocturia
  - Post-prostatectomy incontinence
    - PT for pelvic floor rehabilitation
    - Male urethral sling or artificial urinary sphincter for incontinence.

CONCLUSIONS

- Prostate cancer is the second most common cancer in the US. The 5-year relative survival rate is 96.8%
- Different recommendations exist for PSA screening- most aggressive guideline recommends starting at age 45 for average risk
- Treatment options for localized disease includes: surgery, radiation, active surveillance. Advanced treatment options include androgen deprivation therapy with a combination of second-generation androgen inhibitor, chemotherapy, targeted therapy
- Given the high cure rate, prostate cancer survivors need to be monitored for detection of disease recurrence, early detection of second primary cancers, assessment and management of physical and psychosocial long-term and late effects of treatment.

Thank you!