Prostate cancer

PROSTATE CANCER

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October 2023

NIH Intramural Research Program
Our Research Changes Lives

ONE PROGRAM, MANY PEOPLE, INFINITE POSSIBILITIES

Outline

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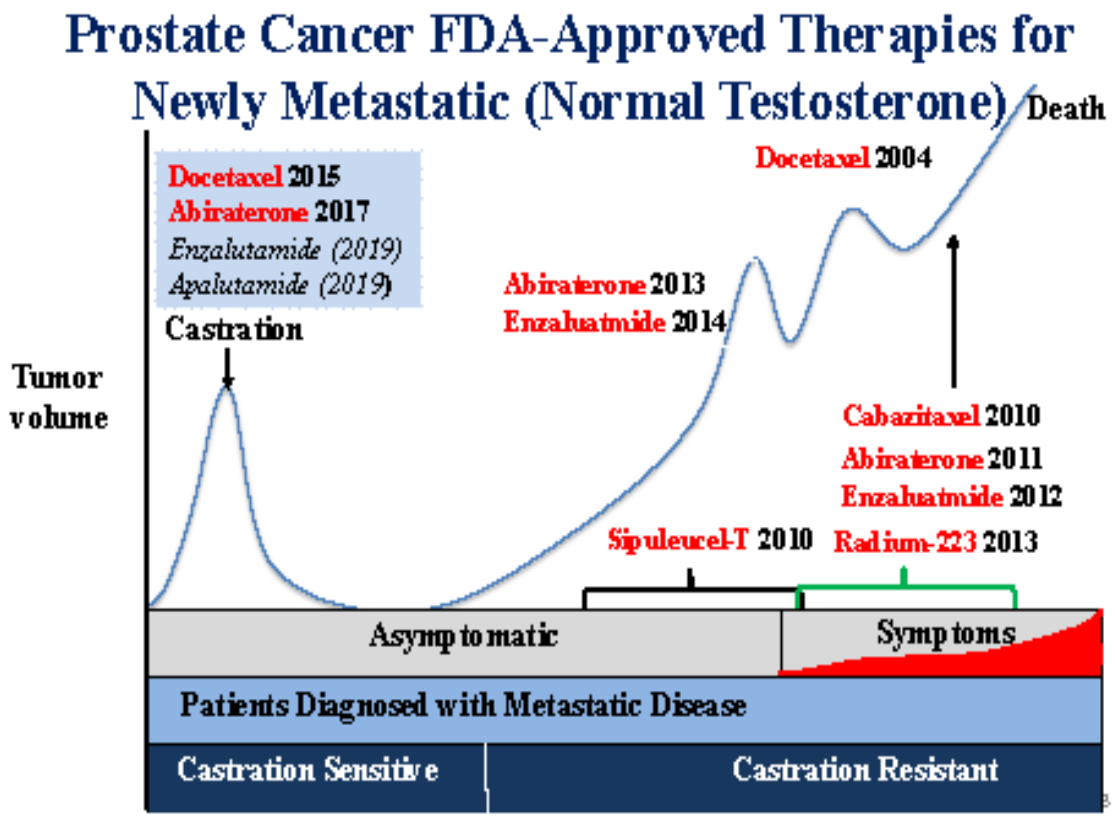
1. Prostate Cancer overview
2. Therapies for localized prostate cancer
3. Metastatic Castrate-Resistant Prostate Cancer
4. Future Directions

FDA approved therapies



Cancer statistics

Cancer Statistics 2023

Estimated New Cases

Males			Females		
Prostate	288,300	29%	Breast	297,790	31%
Lung & bronchus	117,550	12%	Lung & bronchus	120,790	13%
Colon & rectum	81,860	8%	Colon & rectum	71,160	8%
Urinary bladder	62,420	6%	Uterine corpus	66,200	7%
Melanoma of the skin	58,120	6%	Melanoma of the skin	33,490	4%
Kidney & renal pelvis	52,360	5%	Non-Hodgkin lymphoma	35,670	4%
Non-Hodgkin lymphoma	44,880	4%	Thyroid	31,180	3%
Oral cavity & pharynx	39,290	4%	Pancreas	30,920	3%
Leukemia	35,670	4%	Kidney & renal pelvis	29,440	3%
Pancreas	33,130	3%	Leukemia	23,940	3%
All Sites	**1,010,310**	**100%**	**All Sites**	**948,000**	**100%**

Estimated Deaths

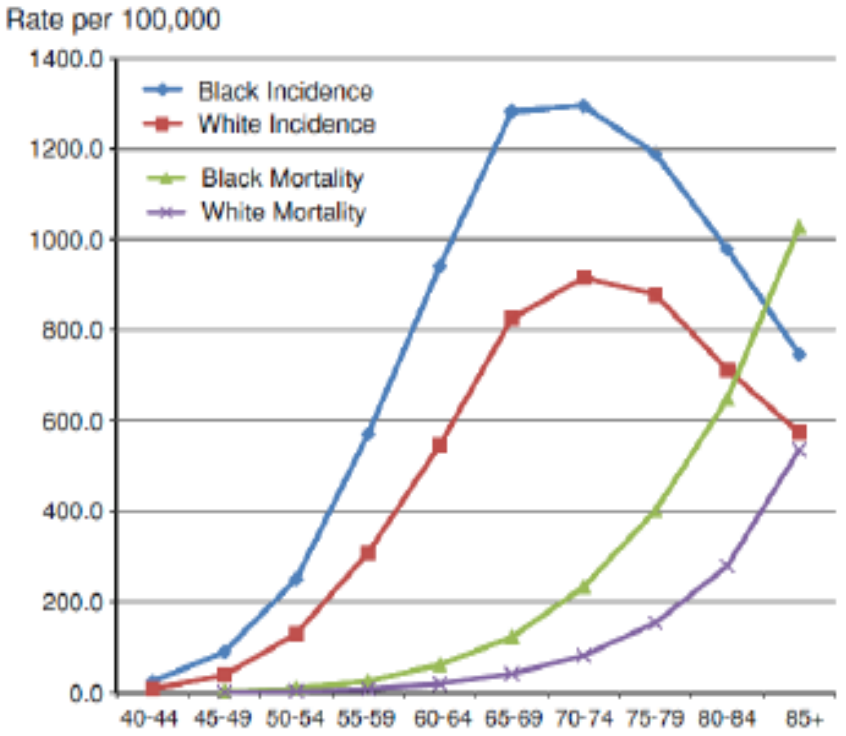
Males			Females		
Lung & bronchus	67,160	21%	Lung & bronchus	59,910	21%
Prostate	34,700	11%	Breast	43,170	15%
Colon & rectum	28,470	9%	Colon & rectum	24,080	8%
Pancreas	26,020	8%	Pancreas	23,330	8%
Liver & intrahepatic bile duct	19,000	6%	Ovary	13,270	5%
Leukemia	13,500	4%	Uterine corpus	13,030	5%
Esophagus	12,920	4%	Liver & intrahepatic bile duct	10,380	4%
Urinary bladder	12,160	4%	Leukemia	9,810	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,400	3%
Brain & other nervous system	11,020	3%	Brain & other nervous system	7,970	3%
All Sites	**322,080**	**100%**	**All Sites**	**287,740**	**100%**

CA A Cancer J Clinicians, Volume: 73, Issue: 1, Pages: 17-48, First published: 12 January 2023, DOI: (10.3322/caac.21763)

Risks

Risks

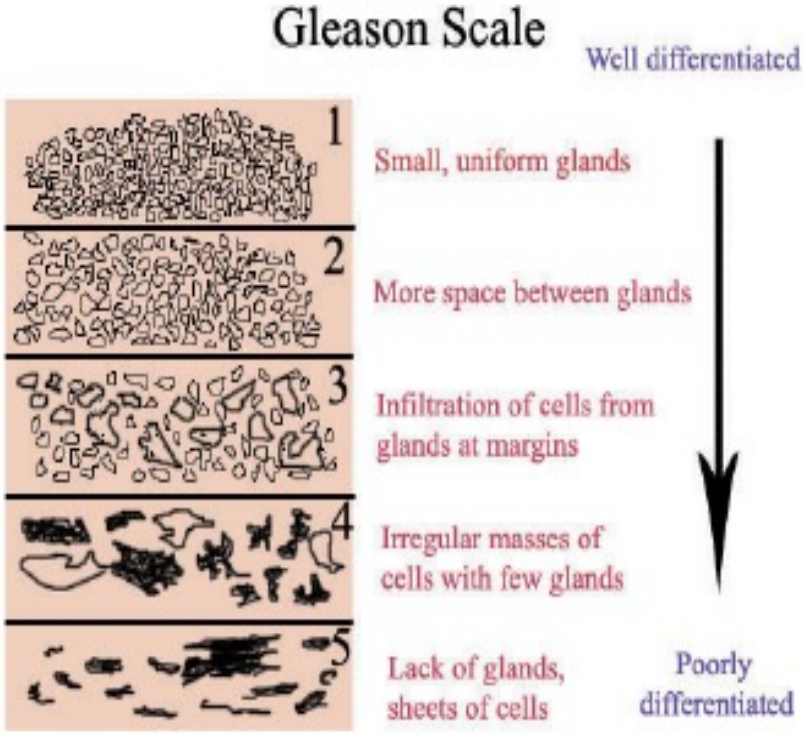
- Age
- Family history
- Genetic predisposition
  - *BRCA*
- Environmental
- Obesity
- Race



Brawley. World J Urol. 2012;30:195-200

Gleason grading

Gleason Grading



- Primary Grade
  - Greater 50%
- Secondary Grade
  - <50% but ≥5%

Grade

Grade Group

In 2014, the International Society of Urological Pathology released supplementary guidance and a revised prostate cancer grading system, called the Grade Groups.

The Grade Group system is simpler, with just five grades, 1 through 5.

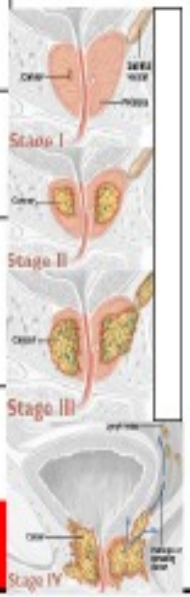
Risk Group*	Grade Group	Gleason Score
Low/Very Low	Grade Group 1	Gleason Score ≤ 6
Intermediate (Favorable/Unfavorable)	Grade Group 2	Gleason Score 7 (3 + 4)
	Grade Group 3	Gleason Score 7 (4 + 3)
High/Very High	Grade Group 4	Gleason Score 8
	Grade Group 5	Gleason Score 9-10

https://www.pcf.org/about-prostate-cancer/diagnosis-staging-prostate-cancer/gleason-score-isup-grade/

Staging

Staging

Stage	TNM	Description
I (A)	T1a (incidental)	Localized
II (B)	T1b, ***T1c***, T2a,b,c (within prostate)	
III (C)	T3a (through capsule) T3b (seminal vesicles)	Locally Advanced
IV (D)	T4 (fixed, invades)	
	N1, M1	Metastatic



MRI

Multiparametric MRI

- Studies show targeted MR/ultrasound fusion biopsies are associated with increased detection of high-risk prostate cancer
- Studies have also reported mpMRI as a useful modality for predicting pathological outcomes in patients with high-risk prostate cancer
- Approach to prostate cancer screening is to target populations at risk of developing prostate cancer based on their genetic predisposition

Jeong IG et al. J Urol 2013; 190: 2054-2060
Zhang Q et al. J Transl Med 2018; 15:230

Diagnosis

ORIGINAL ARTICLE

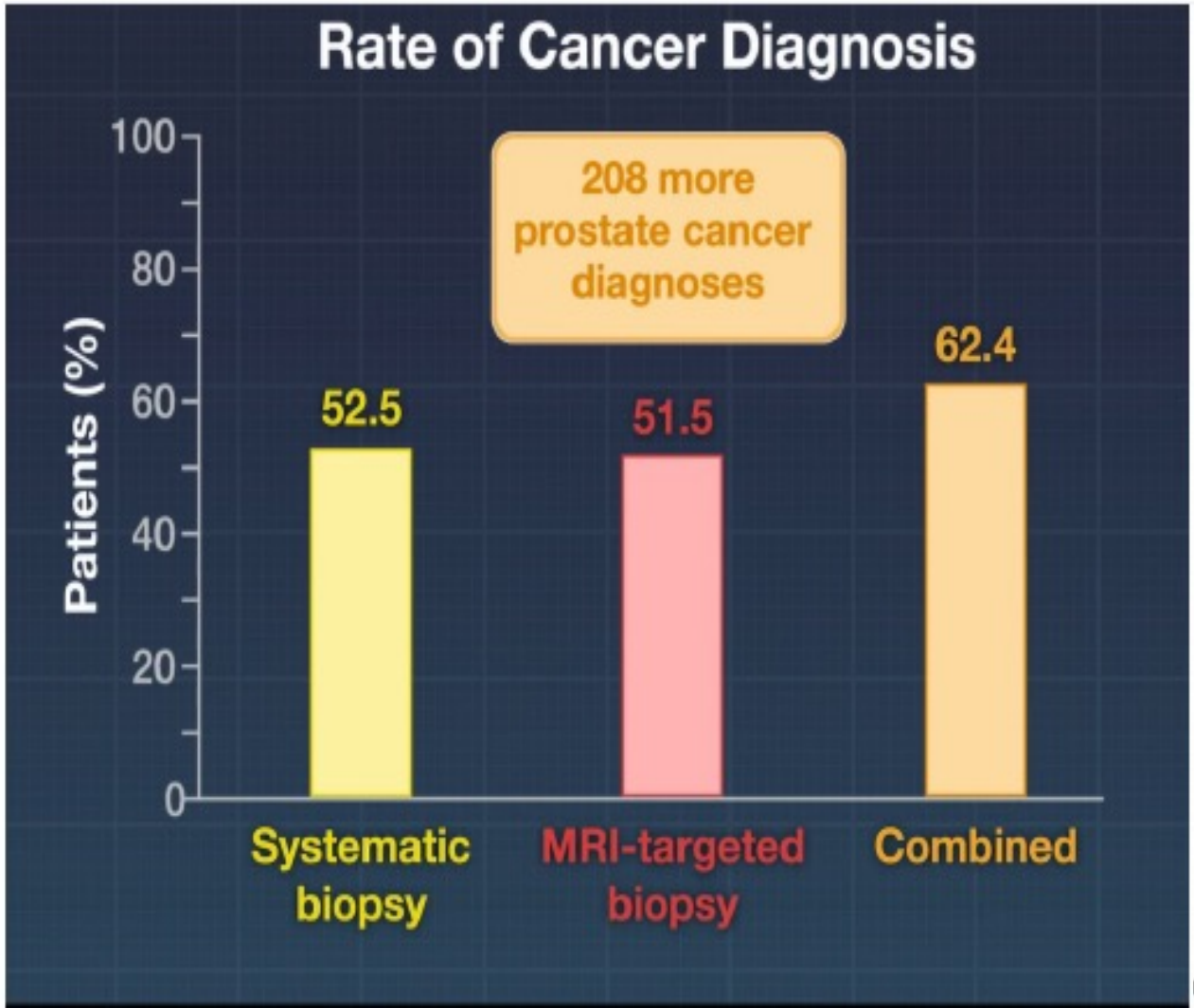
MRI-Targeted, Systematic, and Combined Biopsy for Prostate Cancer Diagnosis

Michael Ahdoot, M.D., Andrew R. Wilbur, B.S., Sarah E. Reese, Ph.D., Amir H. Lebastchi, M.D., Sherif Mehralivand, M.D., Patrick T. Gomella, M.D., Jonathan Bloom, M.D., Sandeep Gurram, M.D., Minhaj Siddiqui, M.D., Paul Pinsky, Ph.D., Howard Parnes, M.D., W. Marston Linehan, M.D., et al.

Article Figures/Media Metrics

March 5, 2020
N Engl J Med 2020; 382:917-928
DOI: 10.1056/NEJMoa1910038

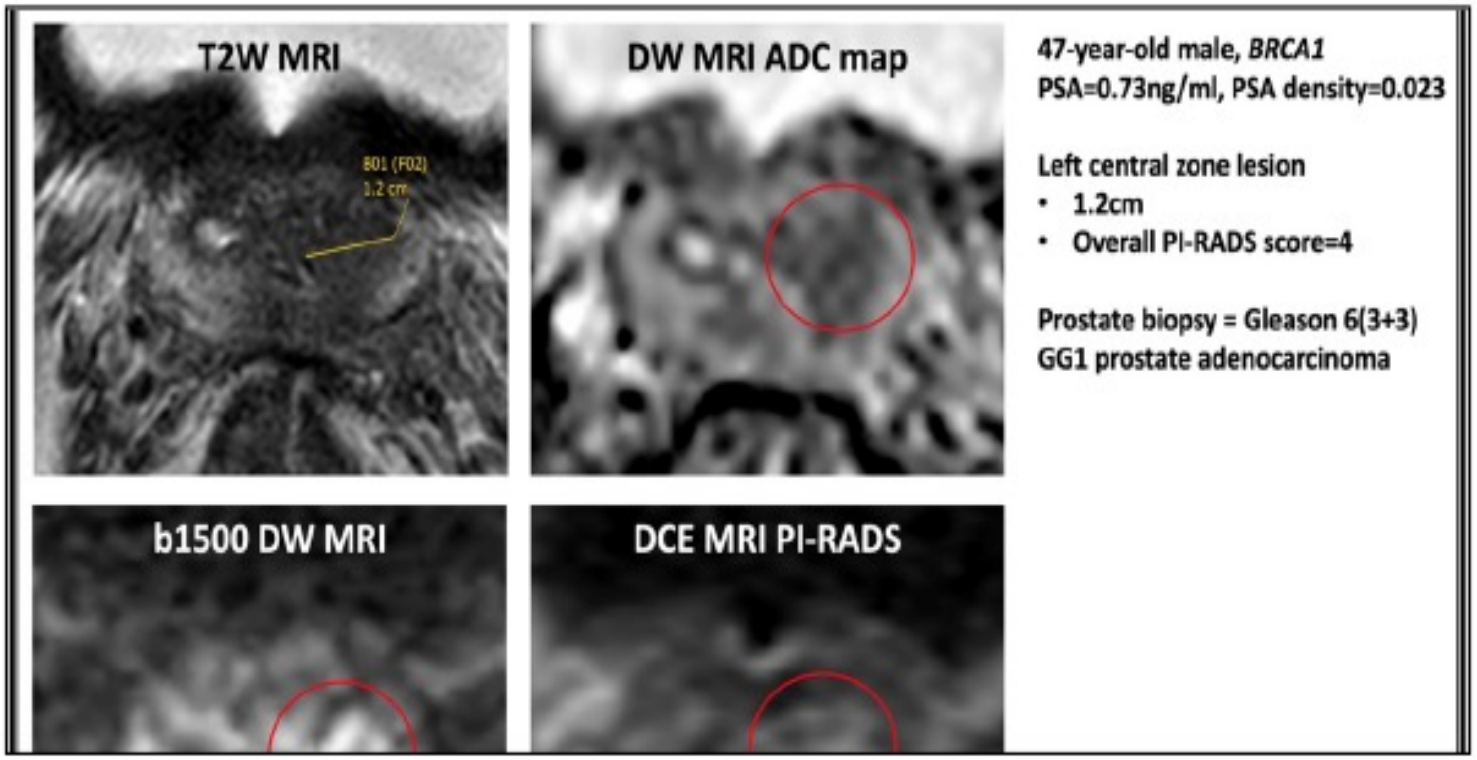
Diagnosis rate



Pinto P. et al. NEJM 2020

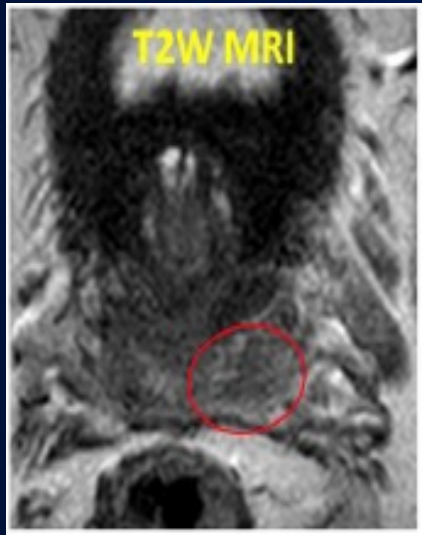
Imaging

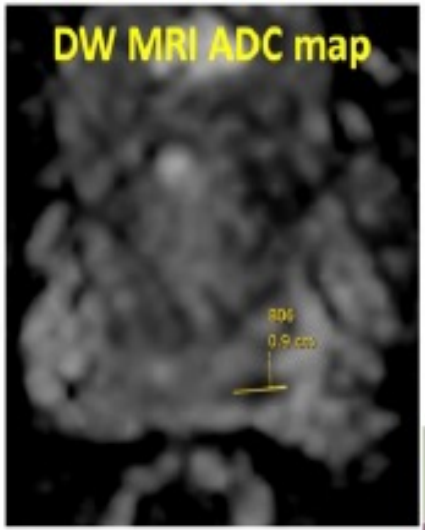
Imaging: Prostate MRI



Images Courtesy of Dr. Baris Turkbey and the Molecular Imaging Branch

MRI

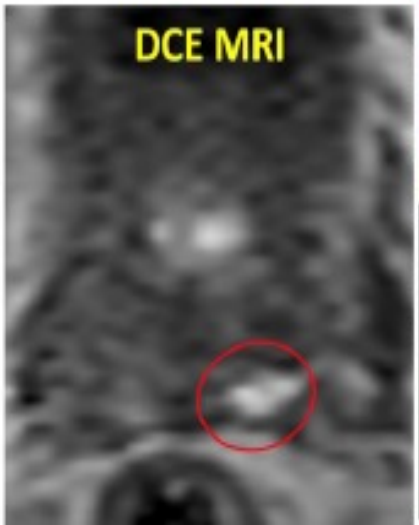


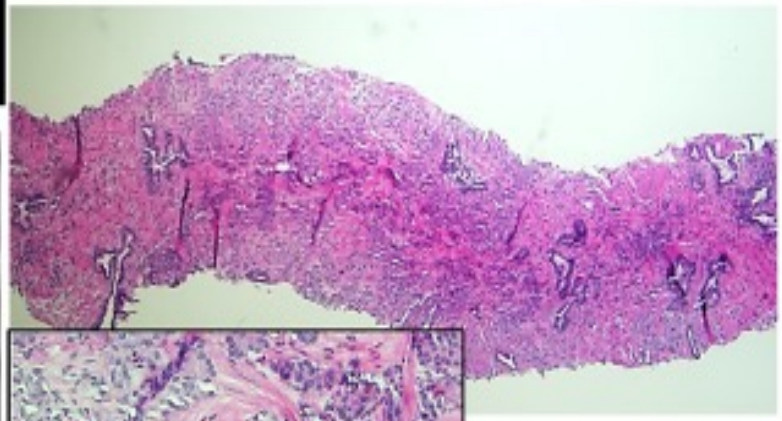


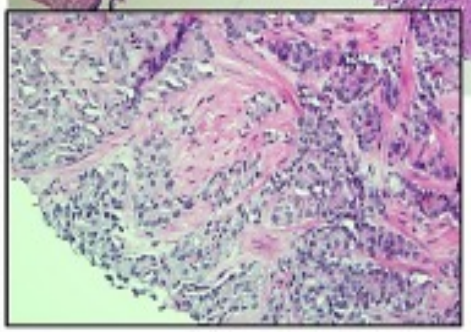
63-year-old male, *MSH2*
PSA=5.7ng/ml, PSA density=0.158

Left base peripheral zone lesion
(PI-RADS score = 4)

Prostate biopsy = Gleason 7(4+3)
GG3 prostatic adenocarcinoma with
cribriform and poorly formed glands

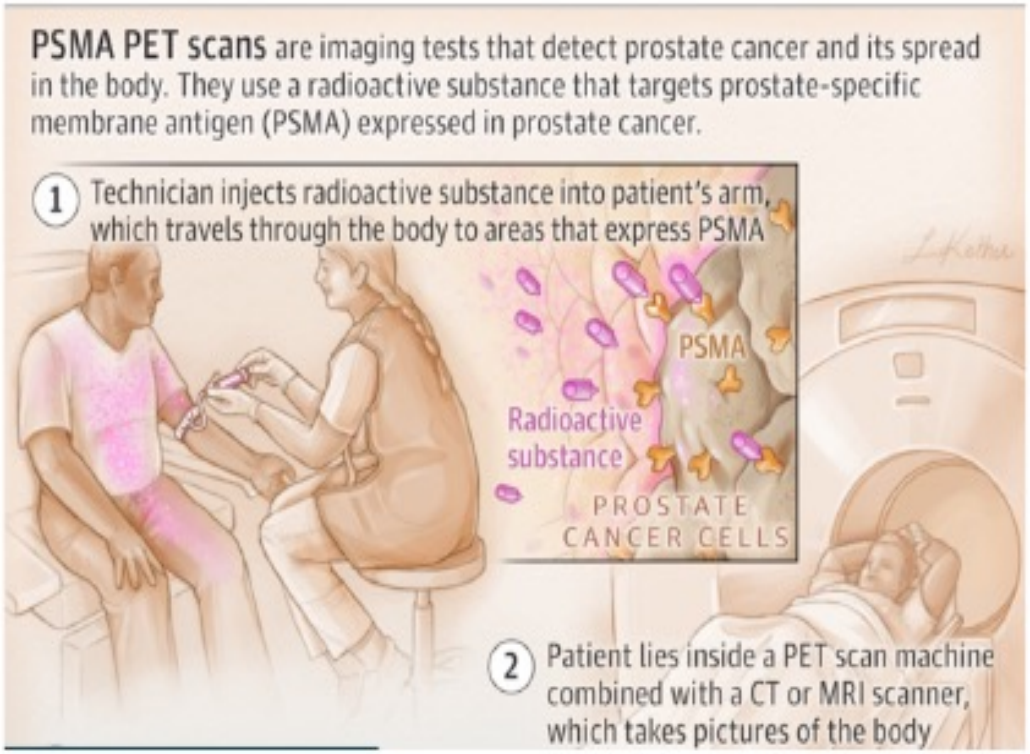






PSMA PET/CT

Imaging: PSMA PET/CT



Kwon DH et al. JAMA Oncol. 2022;8(12):1860

FDA approved PET imaging

FDA approved PSMA-targeted PET imaging

- FDA approved the first PSMA-targeted PET imaging drug, Ga 68 PSMA-11, on December 1, 2020
- FDA approved 18F-DCFPyL in 2021
- Indication is for suspected metastatic disease or recurrent disease after definitive treatment

PET/CT

PRIOR PSMA PET/CT PRIOR TO PROSTATECTOMY. PSA= 6.3 ng/mL (3-29-2022)

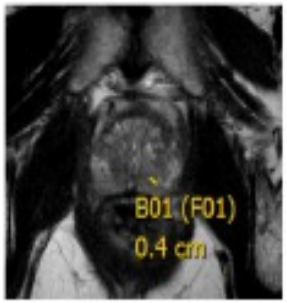
18F-DCFPyL-PET/CT imaging

- No DCFPyL-avid lymph nodes
- No DCFPyL-avid bone lesions

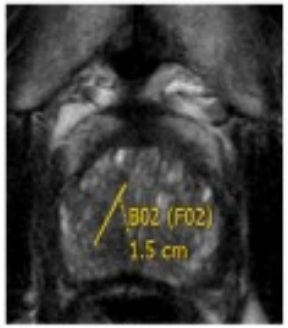
Right apical posterior prostate:
SUV 10.5
(not seen on MRI)

-Right apical-mid central prostate: SUV 36.6
-Left apical posterior prostate: SUV 10.2
Both concordant with MRI

MRI (3-30-2022)



Left apical peripheral zone lesion (PIRADS 3)
NIH Score: Low-moderate



Right apical-mid transition zone lesion
(PIRADS 3)

Therapy principles

Principles Guiding Therapy of Localized Prostate Cancer

- Patients with a life expectancy of at least 10 years are more likely to benefit
- Patients older than 75 years have other competing causes of mortality
- Eradication of the cancer is the goal of therapy
- Low grade/stage tumors may just require active surveillance

Watchful waiting

Watchful Waiting

- Observation with palliative treatment for symptoms
- No PSA monitoring
- Ideal for patients with poor life expectancy who are likely to die from causes other than prostate cancer

Active surveillance

Active Surveillance

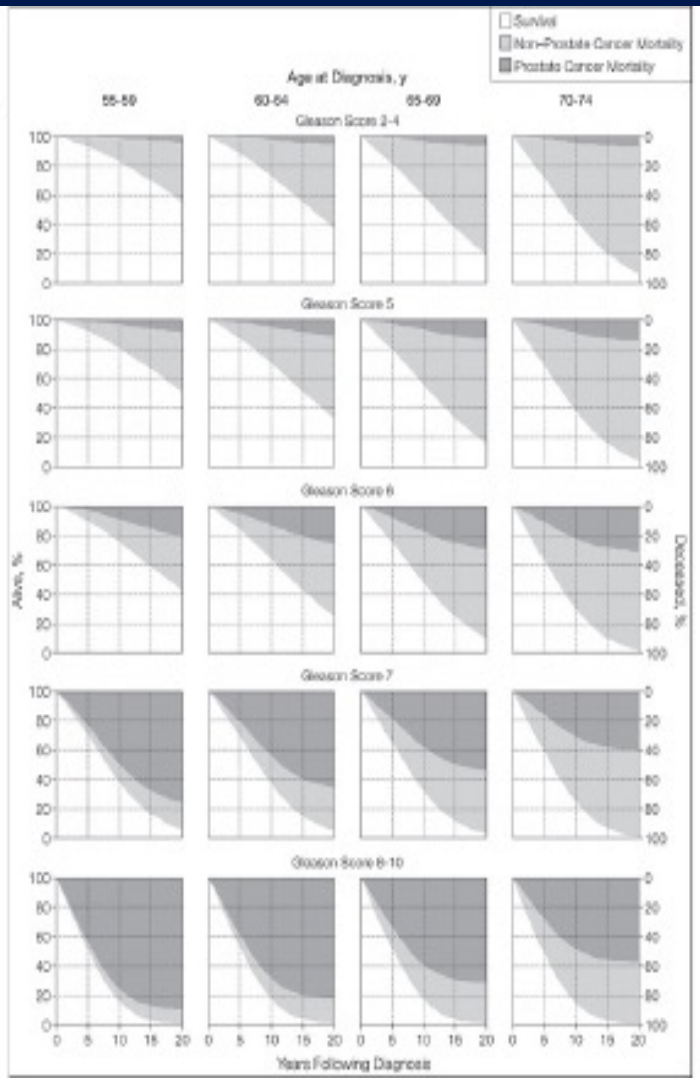
- Periodic PSA monitoring
- Prostate MRIs and prostate biopsies
- Conversion to active treatment when signs of disease progression develop

Ideal candidate

Who is the Ideal Candidate for Watchful Waiting/Active Surveillance?

The probability of prostate cancer mortality is low with:

- Lower Gleason score
- Advanced age



Albertsen, P. C. et al. JAMA 2005;293:2095-101

Management

Management of Locally Advanced Prostate Cancer

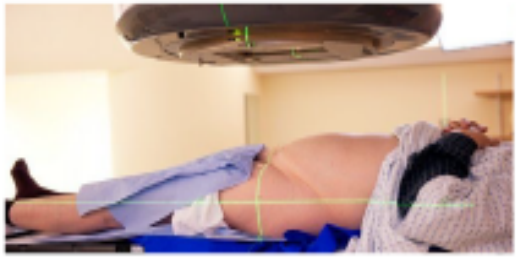
- Surgery with Androgen Deprivation Therapy (ADT)
  - Neoadjuvant is usually on a clinical trial
- Surgery with adjuvant RT
- Radiotherapy with ADT (6 months-18 months)

Radiation therapy

Radiation Therapy-External Beam

- The principle is to deliver therapeutic dose of radiation to the tumor but minimize damage to adjacent structures

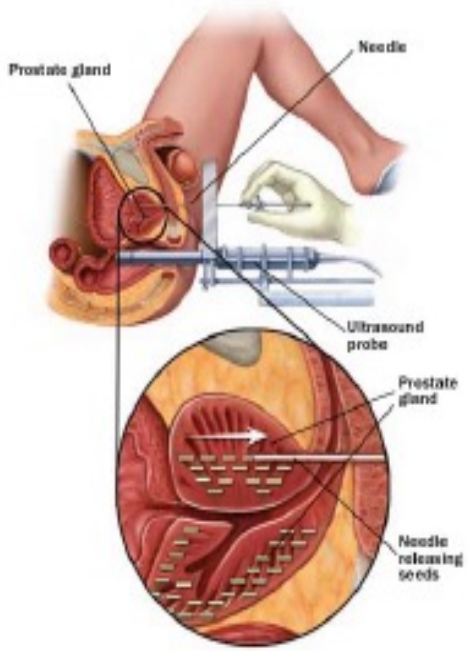
- Modalities of external beam radiotherapy
  - 3-dimensional conformal radiation therapy (3D-CRT)
  - Intensity modulated radiation therapy (IMRT)
  - Image-guided radiation therapy (IGRT)
  - Proton-beam radiation therapy



Brachytherapy

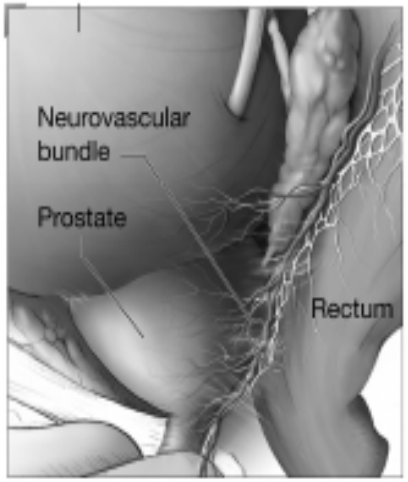
Radiation Therapy-Brachytherapy

- Direct implantation of radiation seeds
- Maximizes radiotherapy to the tumor
  - limits damage to the surrounding structures
- One time treatment



Complications

Radiation Therapy-Complications



- Gastrointestinal
  - Less common with brachytherapy
- Genitourinary
  - Incidence of erectile dysfunction varies widely
- Secondary malignancies
  - Slight increased risk with bladder and to a lesser extent with rectal cancer

Radiotherapy

Radiotherapy with ADT

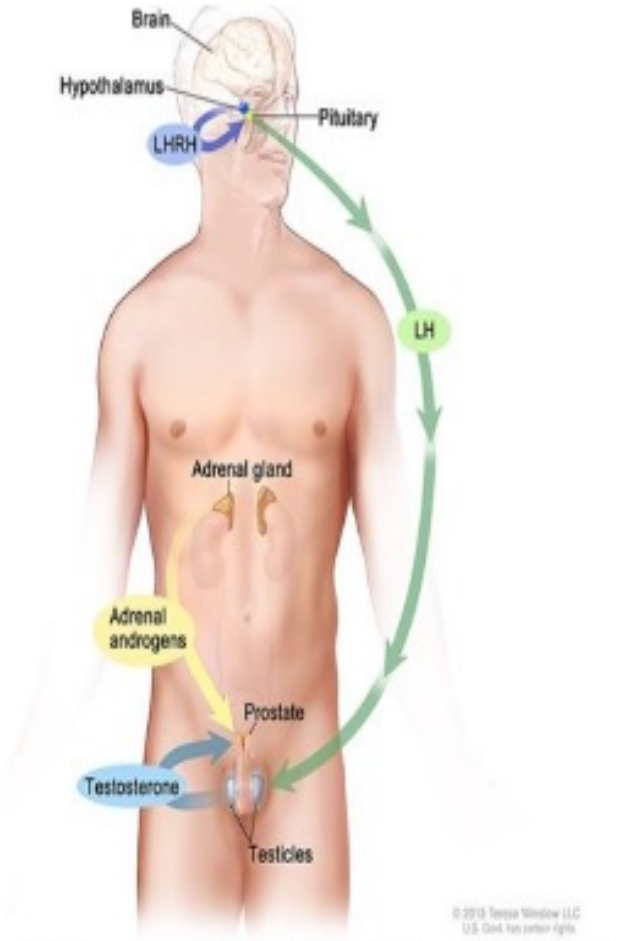
- EORTC 22863 randomized 415 men with high grade locally advanced prostate cancer
  - EBRT ± goserelin for 3 years
- ADT group had better
  - 10-yr disease free-survival (22.7 vs.44.7%, p<0.0001)
  - 10-yr overall survival (39.8 vs. 58.1%, p=0.0004)
  - 10-yr disease-specific mortality (30.4 vs. 10.3%, p<0.0001)

Bolla M. et al. Lancet Oncol. 2010;11:1066-73

ADT-castration

ADT-Castration

Type	Method
Surgical	Bilateral Orchidectomy
Medical	1. Gonadotropin releasing hormone (GnRH) agonists • Goserelin • Leuprolide 2. GnRH receptor antagonists • Degarelix
	Antiandrogens • Bicalutamide, flutamide



https://www.cancer.gov/types/prostate/prostate-hormone-therapy-fact-sheet

ADT radiotherapy

Radiotherapy with ADT

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Bolla M. et al. Lancet Oncol. 2010;11:1066-73

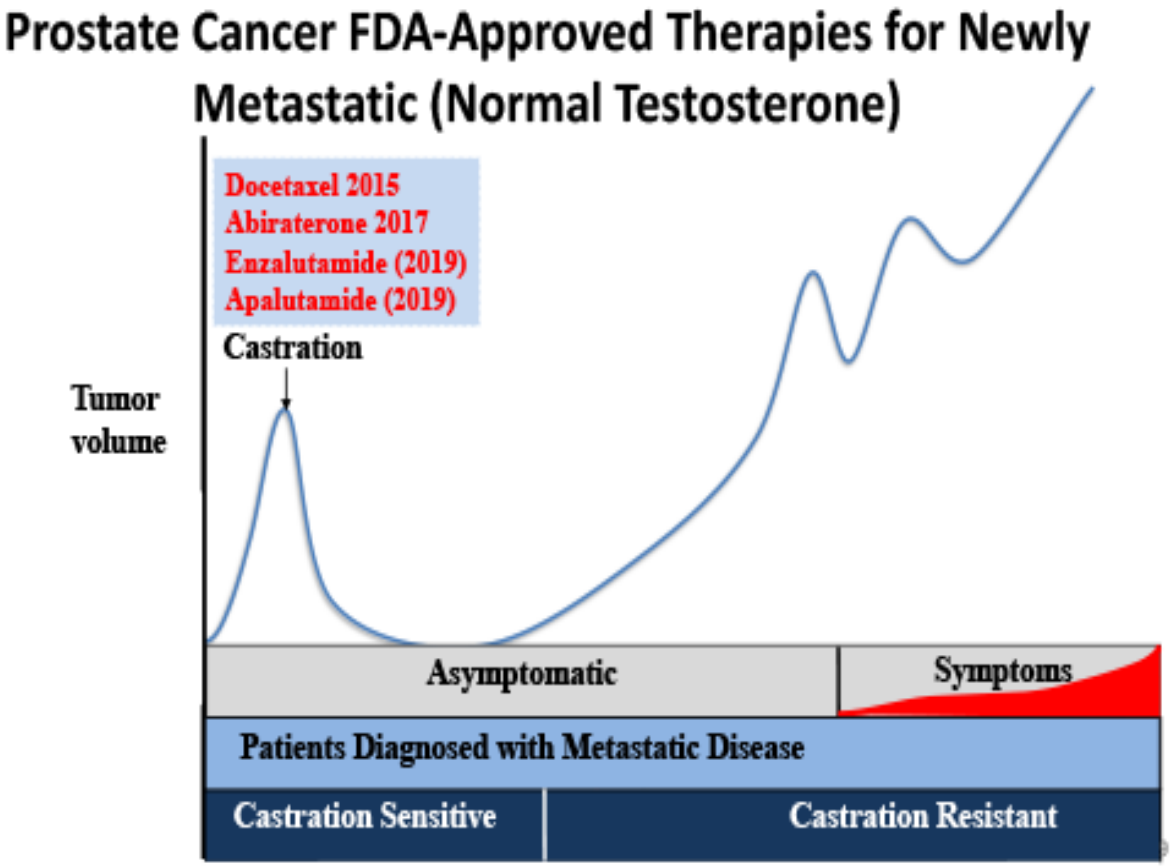
Biochemical recurrence

Biochemical Recurrence after Initial Prostatectomy or RT

- Rising PSA without local recurrence or metastases on CONVENTIONAL imaging (CT and bone scan)

- Treatment options include watchful waiting, prostatectomy, RT, and ADT or clinical trial

FDA approved therapies



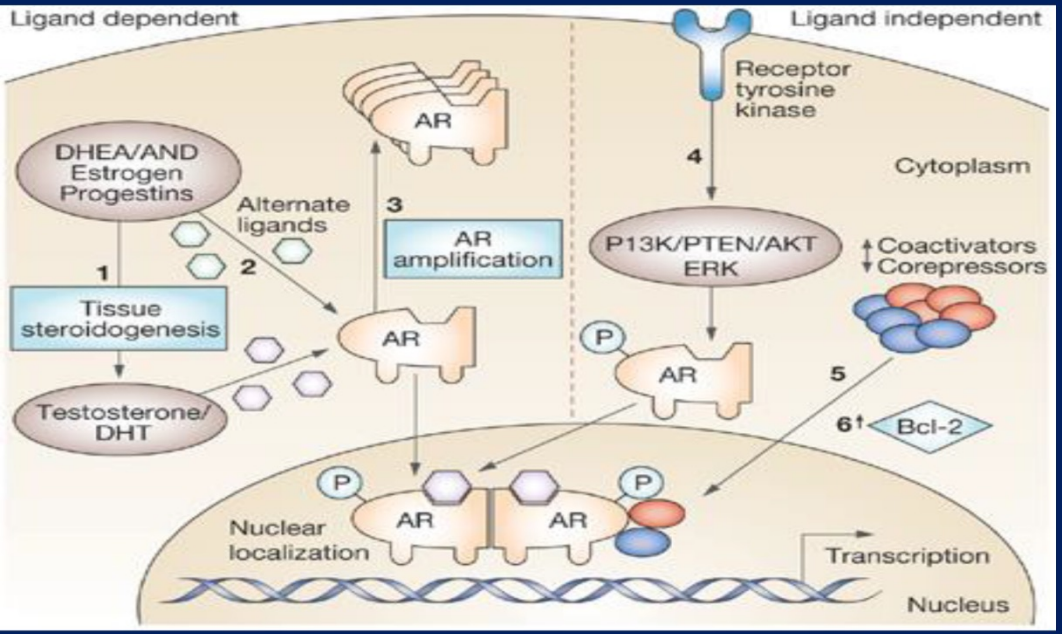
Castrate-resistance prostate cancer

What is Castration-Resistance Prostate Cancer?

- Progressive disease despite castrate levels of testosterone (≤50 ng/dL)
- Progression could be based on PSA rises or imaging
- The androgen receptor (AR) drives prostate cancer growth
  - Depriving the tumor of testosterone is the primary therapy for metastatic disease

Anti-androgen therapy

So why do we use Anti-Androgen therapy in CRPC?



Resistance Mechanisms:

- AR Amplification
- Secondary androgen production
- Ligand independent growth
- Intranuclear changes

Harris W P *et al. Nat Clin Pract Urol, 2009*

Considerations for treatment

Considerations for treatment

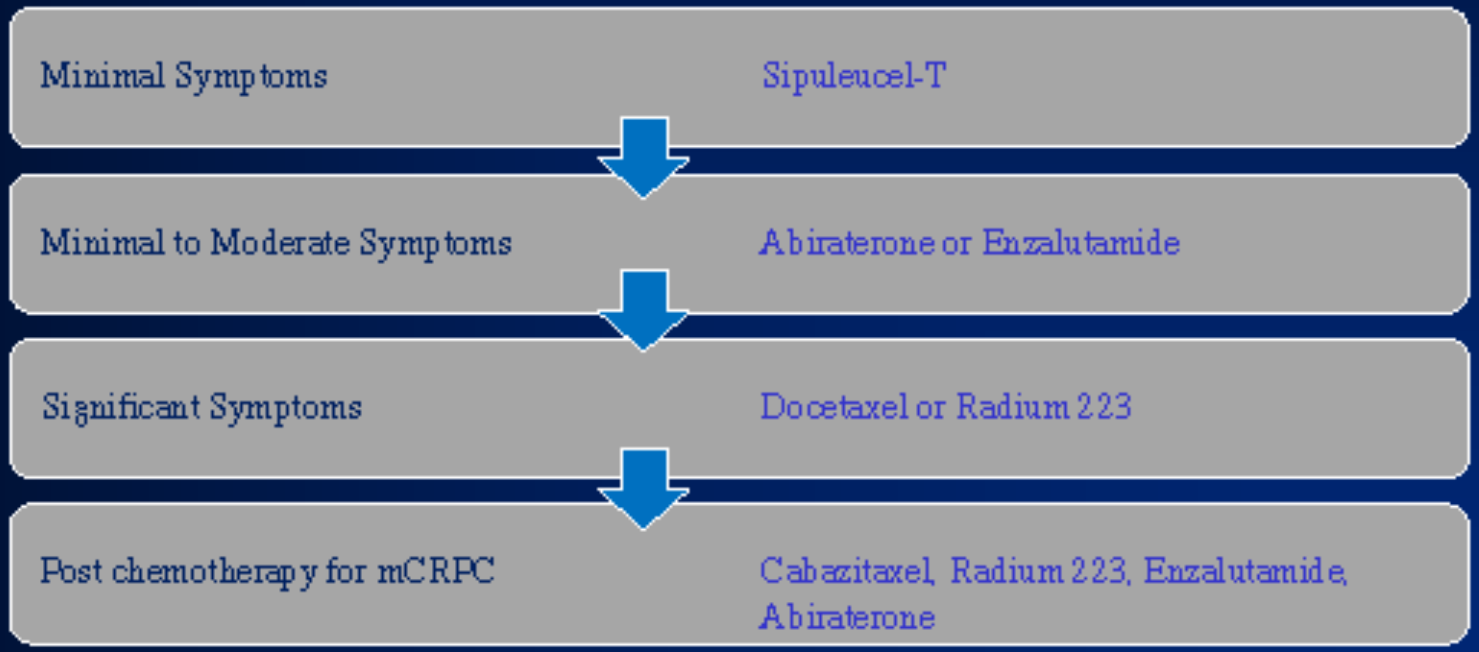
Key disease questions:

- Previous therapies
- Pace of disease (time of progression on ADT, pace of metastases)
- Symptoms (none, moderate or significant)

Key patient characteristics:

- Age
- Comorbidities
- Quality of life preferences
- Treatment logistics

One Possible Decision Algorithm for Treatment of mCRPC: Normal Pace of Disease*



*Initial response to ADT 1-2 years or longer
*Metastasis on scans shows slow progression

9

Decision algorithm

One Possible Decision Algorythm for Treatment of mCRPC: Normal Pace of Disease*

Minimal Symptoms	Sipuleucel-T

*Initial response to ADT 1-2 years or longer
*Metastasis on scans shows slow progression

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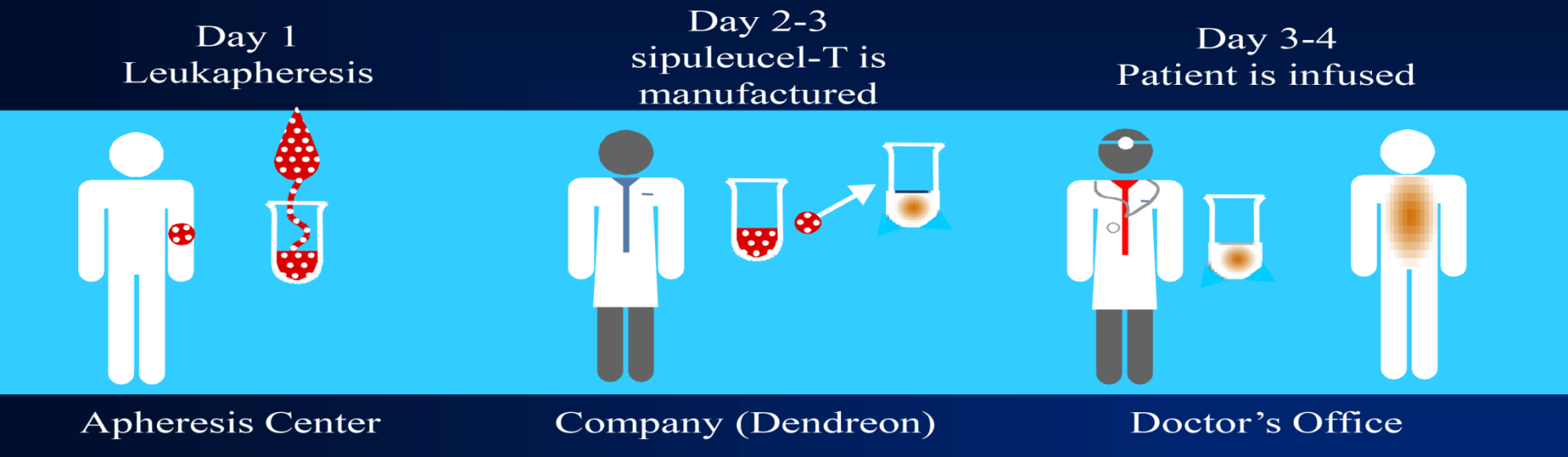
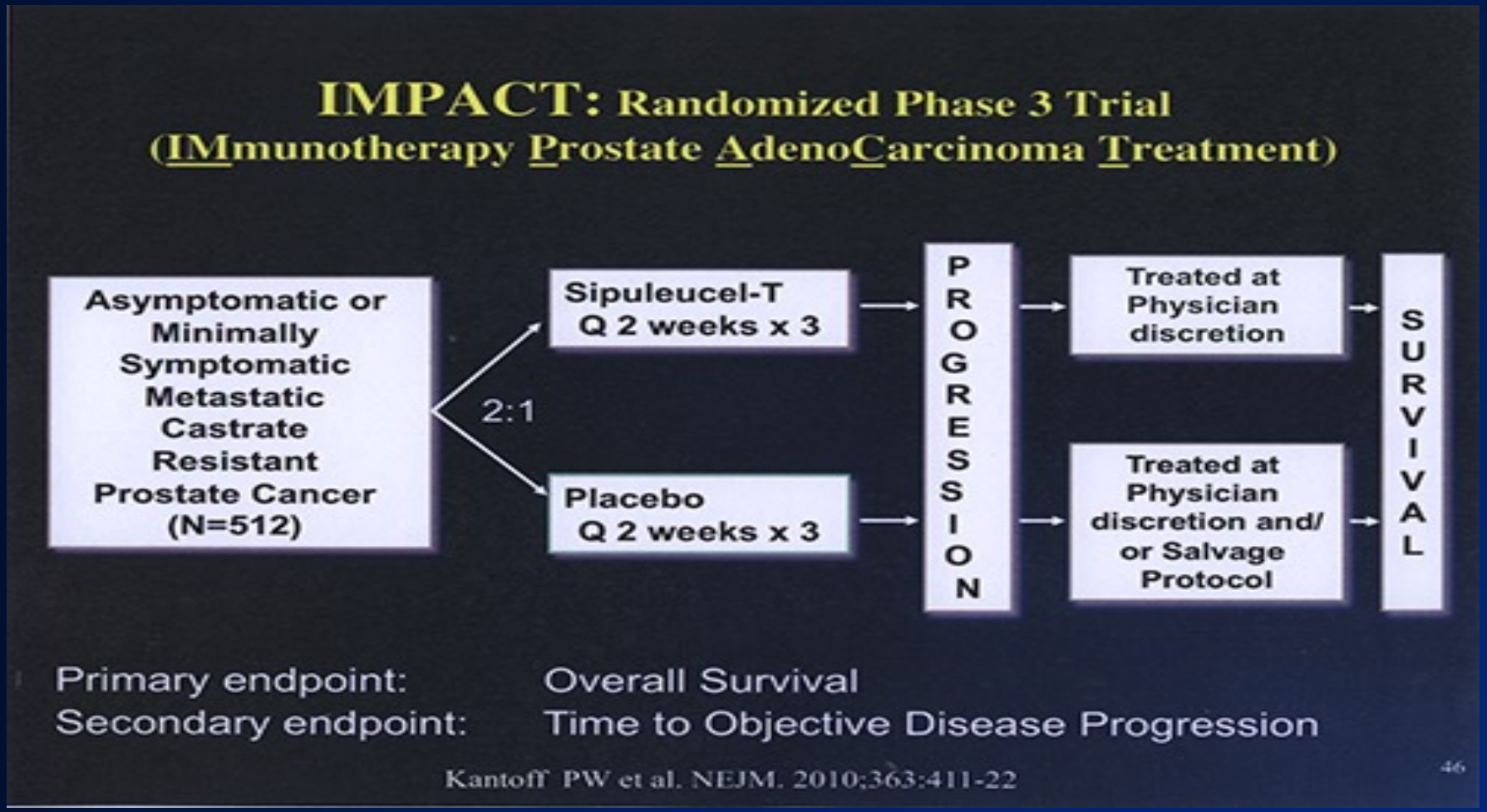
Therapeutic Cancer Vaccine: Sipuleucel-T

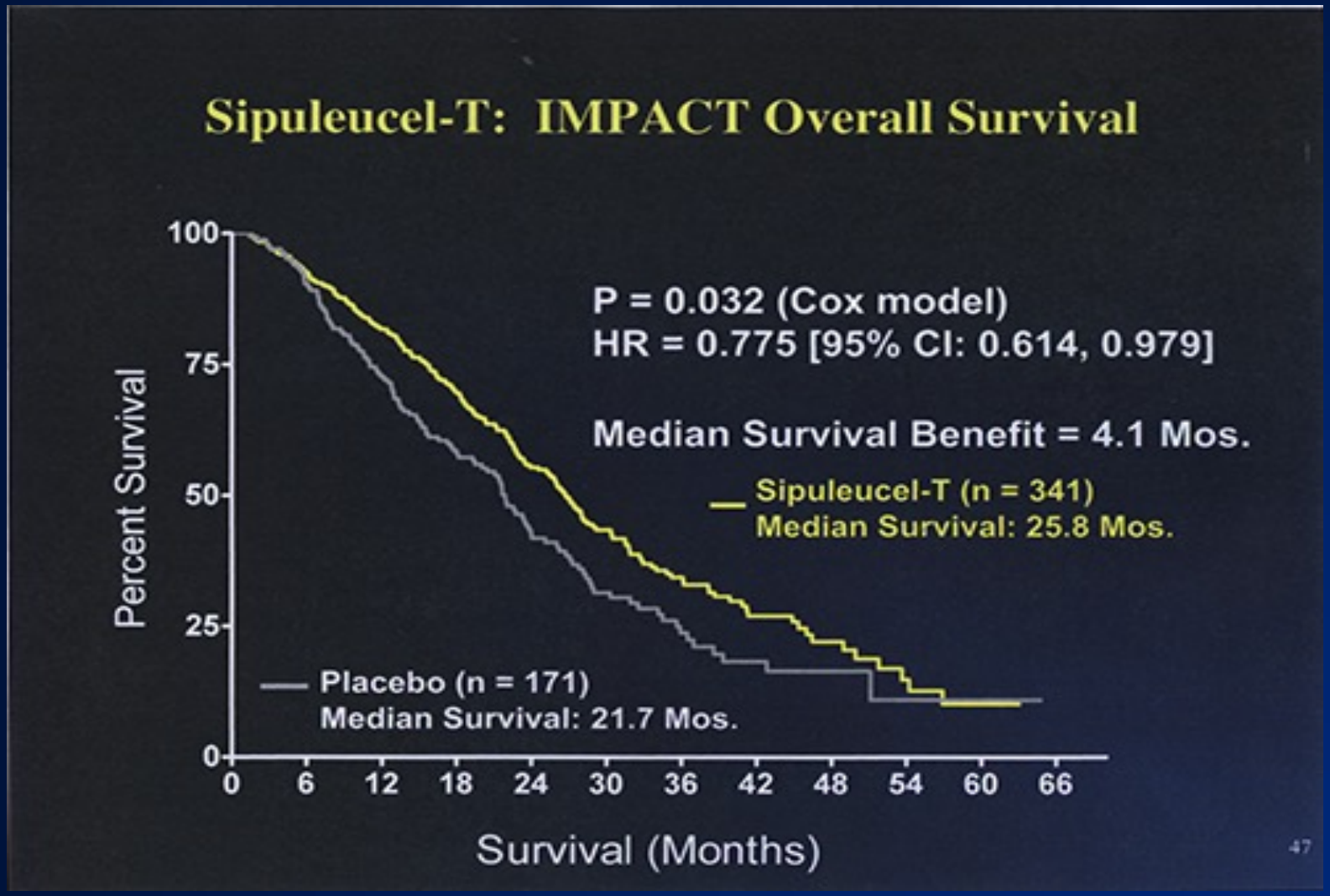
Therapeutic Cancer Vaccine: Sipuleucel-T



IMPACT: Randomized Phase 3 Trial

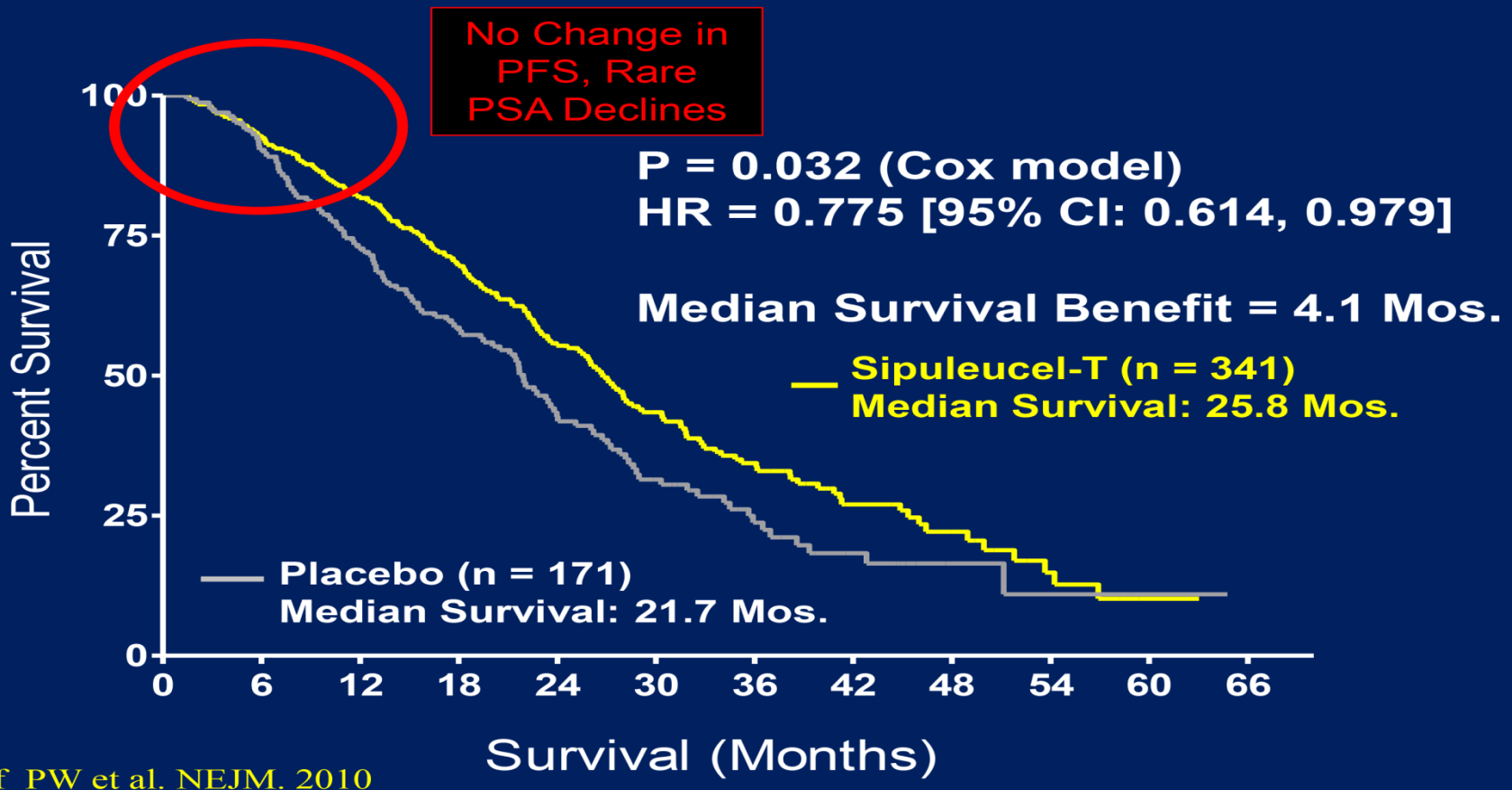


Sipuleucel-T: IMPACT Overall Survival



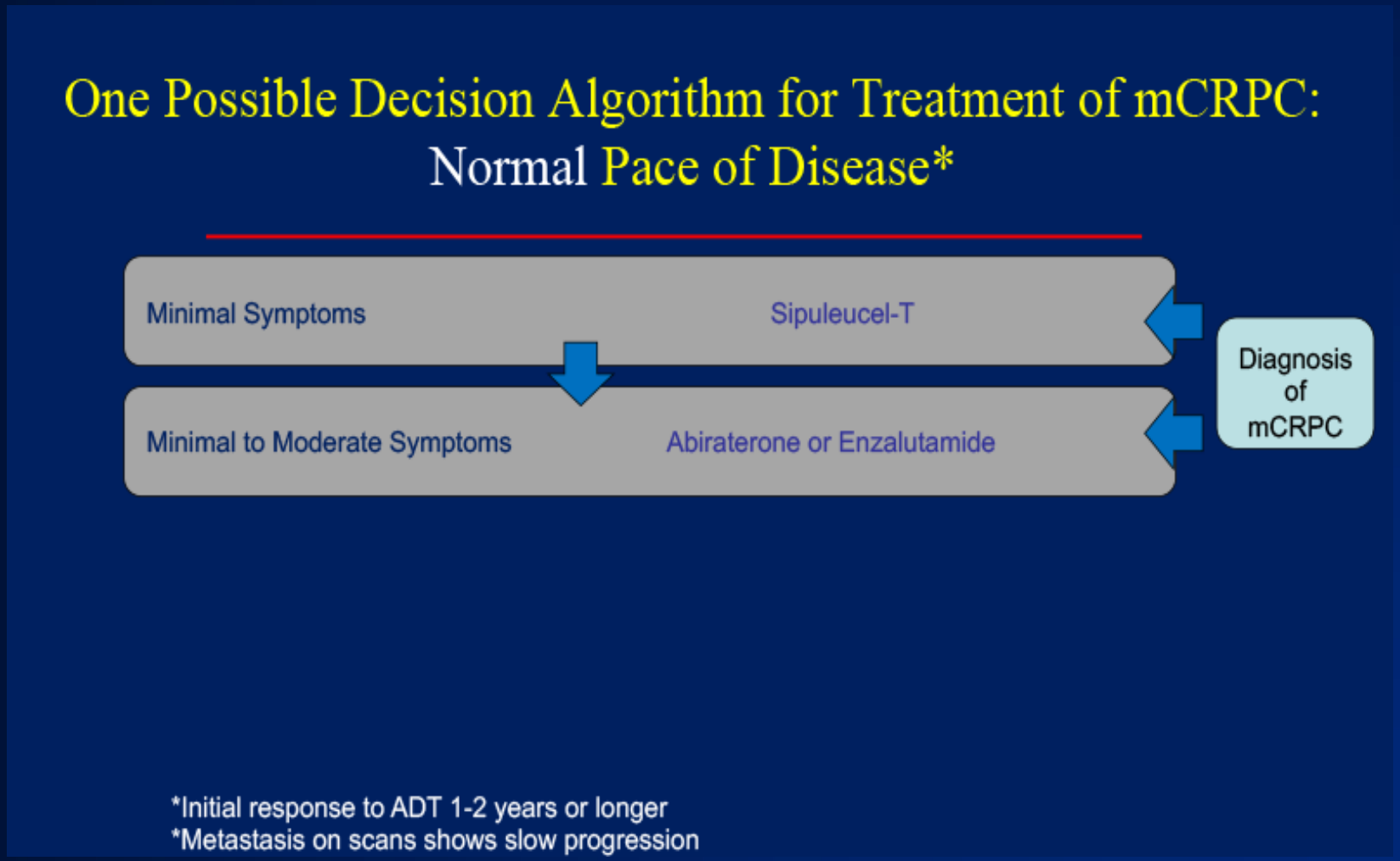
Sipuleucel-T

Sipuleucel-T: IMPACT Overall Survival



Kantoff PW et al. NEJM. 2010

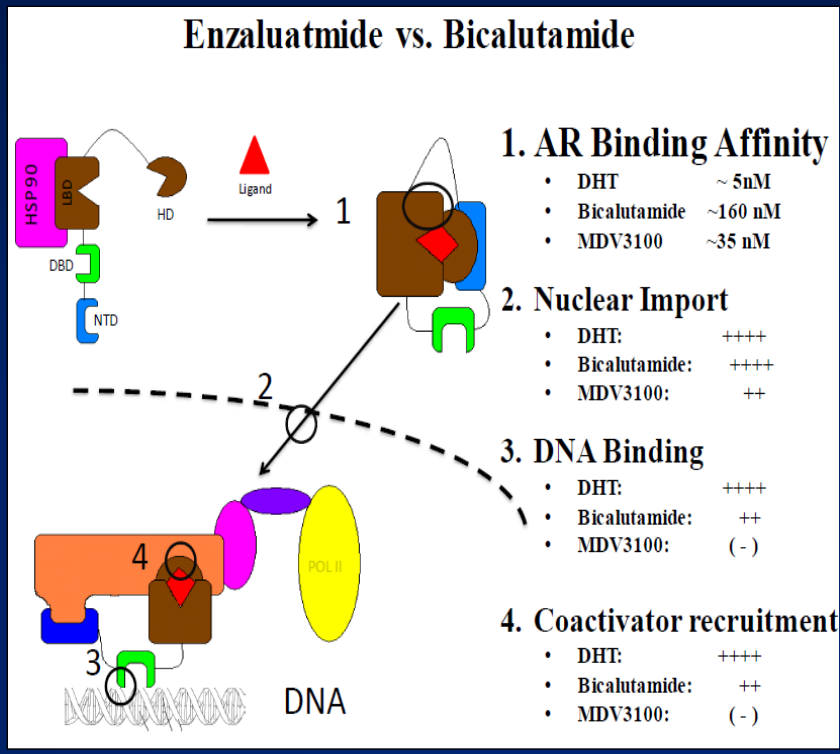
Algorithm


One Possible Decision Algorithm for Treatment of mCRPC:
Normal Pace of Disease*
Minimal Symptoms
Sipuleucel-T
Minimal to Moderate Symptoms
Abiraterone or Enzalutamide
Diagnosis of mCRPC
*Initial response to ADT 1-2 years or longer
*Metastasis on scans shows slow progression

Enzalutamide

A small molecule AR antagonist

- Affinity 30 folds of bicalutamide
- Prevent nuclear translocation
- Prevents co-activator recruitment



Enzalutamide Toxicity

Cardiovascular: Peripheral edema (15%)

Central nervous system: Fatigue (51%), headache (12%)

Endocrine & metabolic: Hot flashes (20%)

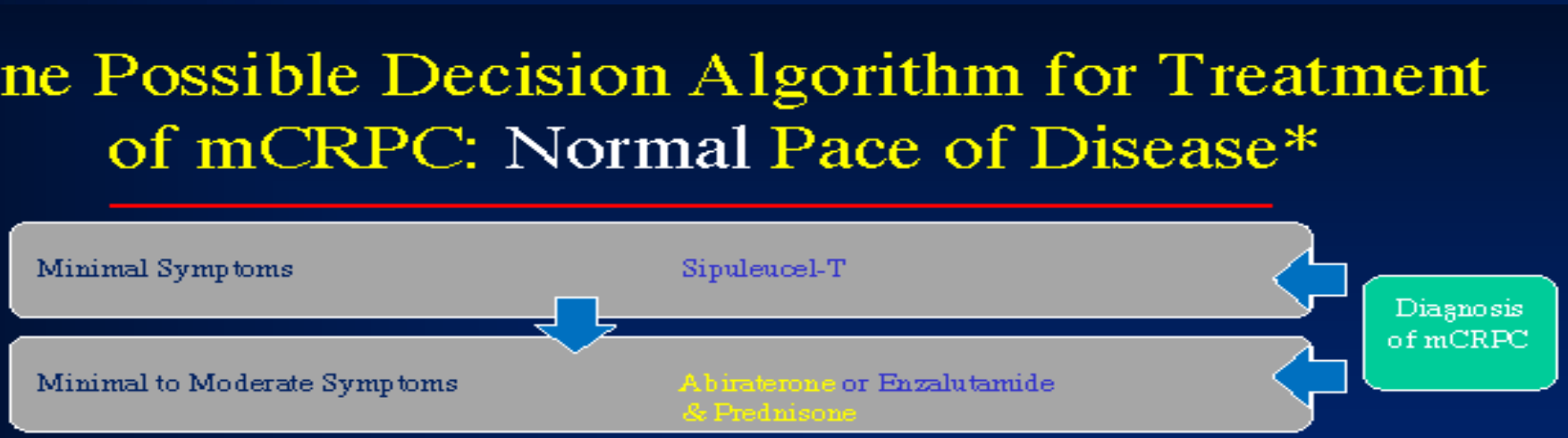
Gastrointestinal: Diarrhea (22%)

Hematologic: Neutropenia (15%; grades 3/4: 1%)

Neuromuscular & skeletal: Back pain (26%), arthralgia (21%), musculoskeletal pain (15%)

Respiratory: Upper respiratory tract infection (11%)

Algorithm


One Possible Decision Algorithm for Treatment of mCRPC: Normal Pace of Disease*
Minimal Symptoms
Sipuleucel-T
Minimal to Moderate Symptoms
Abiraterone or Enzalutamide & Prednisone
Diagnosis of mCRPC
*Initial response to ADT 1-2 years or longer
*Metastasis on scans shows slow progression
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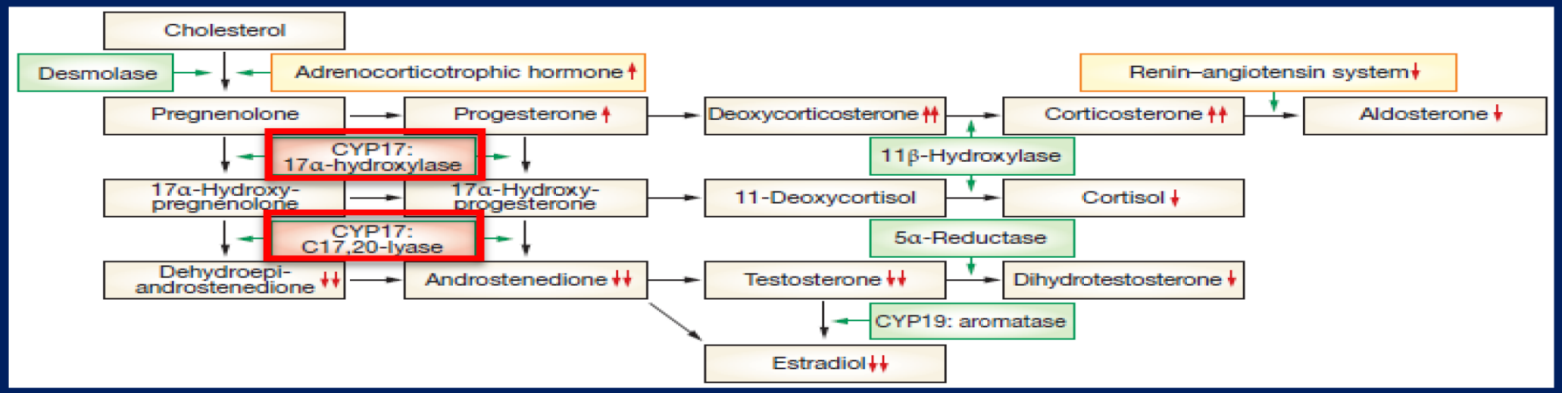
Abiraterone rationale

Rationale for Abiraterone in CRPC

- There is up-regulation of androgen biosynthesis enzymes in CRPC



- Blocks androgen synthesis by the adrenal glands, testes and within the prostate tumor tissue

Reid et al. Nat Clin Pract Urol. 2008

Abiraterone Toxicity

Cardiovascular: Edema (25% to 27%), hypertension (9% to 22%; grades 3/4: 1% to 4%)

Central nervous system: Fatigue (39%), insomnia (14%)

Dermatologic: Bruise (13%)

Endocrine & metabolic: Increased serum triglycerides (63%), hyperglycemia (57%), hypernatremia (33%), hypokalemia (17% to 28%; grades 3/4: 3% to 5%), hypophosphatemia (24%; grades 3/4: 7%), hot flash (19% to 22%)

Gastrointestinal: Constipation (23%), diarrhea (18% to 22%), dyspepsia (6% to 11%)

Genitourinary: Urinary tract infection (12%)

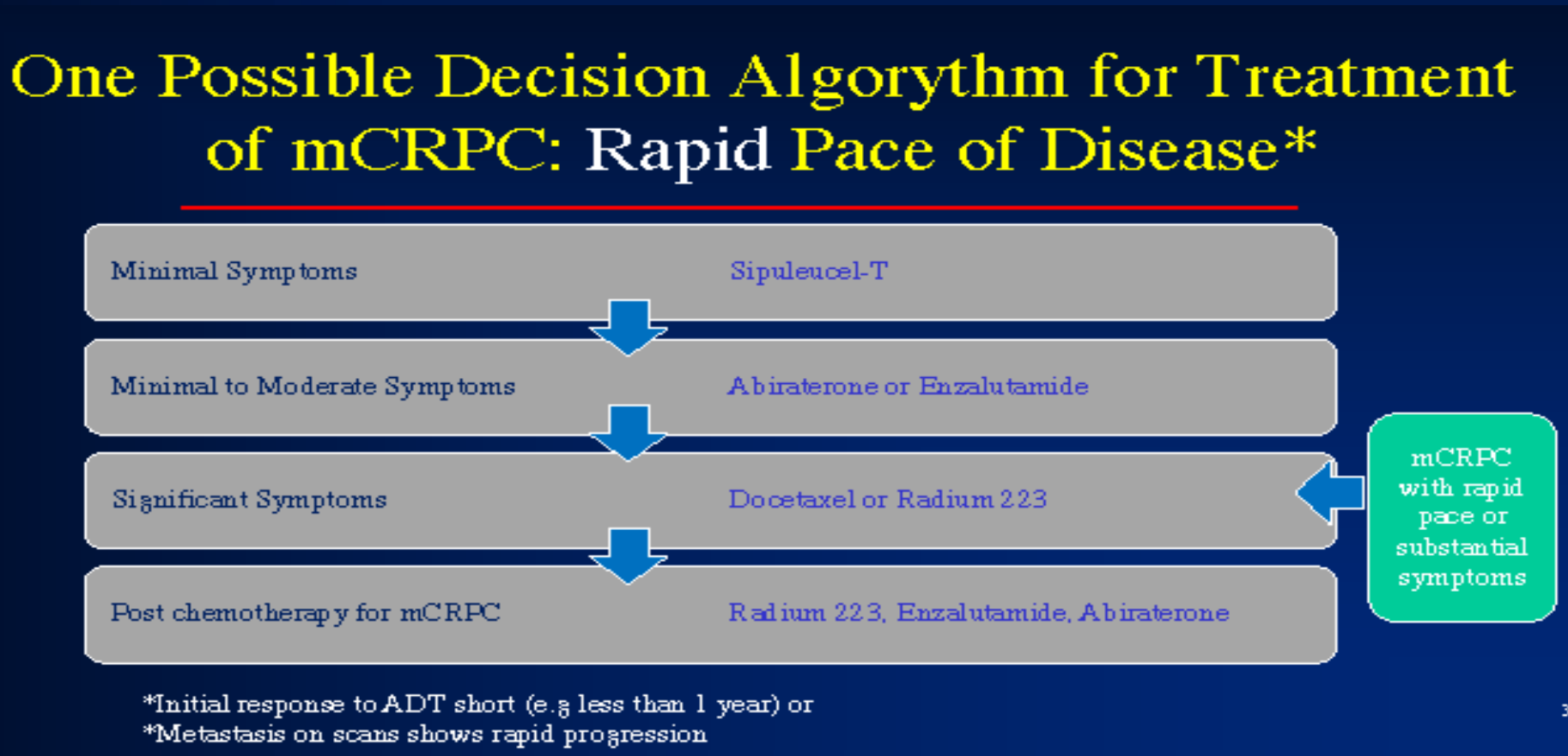
Hematologic: Lymphocytopenia (38%; grades 3/4: 9%)

Hepatic: Increased serum ALT (11% to 42%; grades 3/4: 1% to 6%), increased serum AST (31% to 37%; grades 3/4: 2% to 3%)

Neuromuscular & skeletal: Joint swelling (30%, including joint discomfort), myalgia (26%)

Respiratory: Cough (11% to 17%), upper respiratory infection (5% to 13%), dyspnea (12%), nasopharyngitis (11%)

Algorithm


One Possible Decision Algorythm for Treatment of mCRPC: Rapid Pace of Disease*
Minimal Symptoms
Sipuleucel-T
Minimal to Moderate Symptoms
Abiraterone or Enzalutamide
Significant Symptoms
Docetaxel or Radium 223
Post chemotherapy for mCRPC
Radium 223, Enzalutamide, Abiraterone
mCRPC with rapid pace or substantial symptoms
*Initial response to ADT short (e.g less than 1 year) or
*Metastasis on scans shows rapid progression

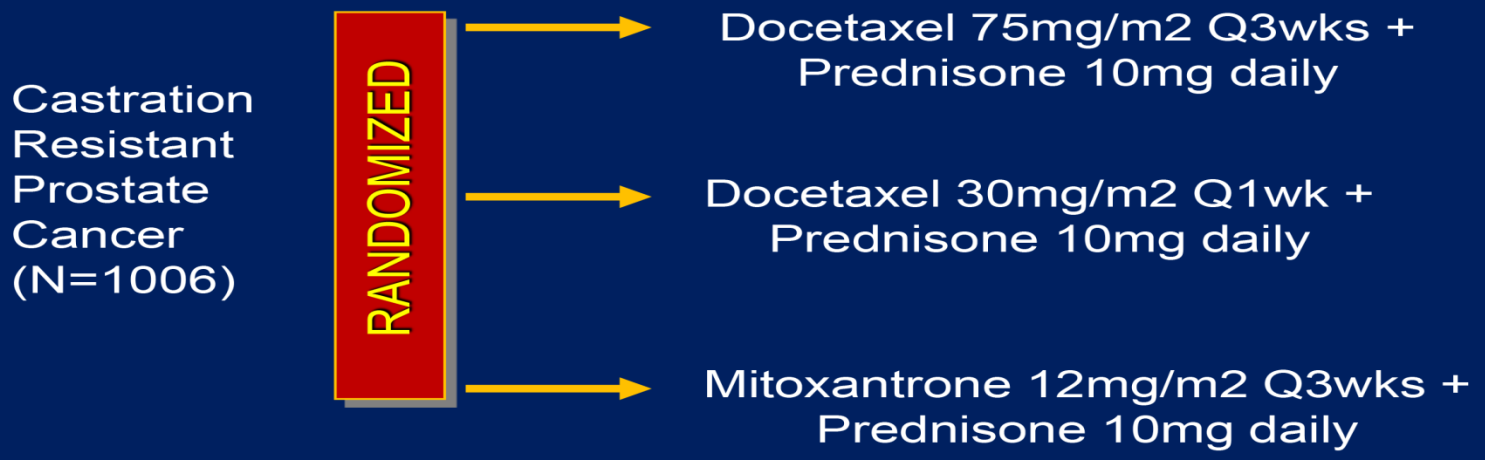
Docetaxel

Docetaxel

- In 1960s, crude extract of the bark of the Pacific yew tree, Taxus brevifolia, was shown to have suppressive activity in preclinical tumor models.
- By 1971, paclitaxel was identified as the active constituent of the bark extract.
- Taxanes exhibit antimicrotubule and antitumor activity
- *Emerging data suggests that taxanes inhibit AR translocation via microtubules*

Phase III study

TAX327: A Multicenter, Randomized Phase III Study of 3 weekly Docetaxel + Prednisone vs. Weekly Docetaxel + Prednisone vs. Mitoxantrone + Prednisone



Tannock IF et al. NEJM. 2004.

Docetaxel Toxicity

Central nervous system: Central nervous system toxicity (20% to 58%; severe: 6%; including neuropathy)

Dermatologic: Alopecia (56% to 76%), dermatological reaction (20% to 48%; severe: ≤5%), nail disease (11% to 41%)

Endocrine & metabolic: Fluid retention (13% to 60%; severe: 7% to 9%; dose dependent)

Gastrointestinal: Stomatitis (19% to 53%; severe 1% to 8%), diarrhea (23% to 43%; severe: 5% to 6%), nausea (34% to 42%), vomiting (22% to 23%)

Hematologic & oncologic: Neutropenia (84% to 99%; grade 4: 75% to 86%; nadir [median]: 7 days, duration [severe neutropenia]: 7 days; dose dependent), leukopenia (84% to 99%; grade 4: 32% to 44%), anemia (65% to 97%; dose dependent; grades 3/4: 8% to 9%), thrombocytopenia (8% to 14%; grade 4: 1%; dose dependent), febrile neutropenia (5% to 14%; dose dependent)

Hepatic: Increased serum transaminases (4% to 19%)

Hypersensitivity: Hypersensitivity (1% to 21%; with premedication 15%)

Infection: Infection (1% to 34%; dose dependent)

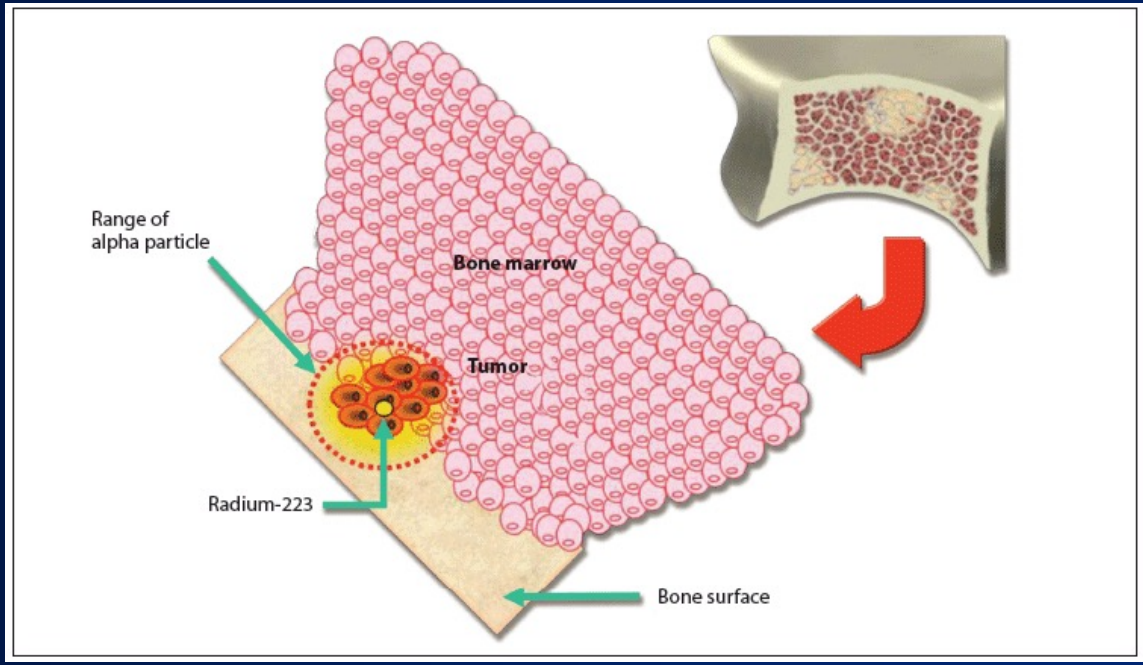
Neuromuscular & skeletal: Weakness (53% to 66%; severe 13% to 18%), myalgia (3% to 23%), neuromuscular reaction (16%)

Respiratory: Pulmonary reaction (41%)

Radium-223 (Alpharadin)

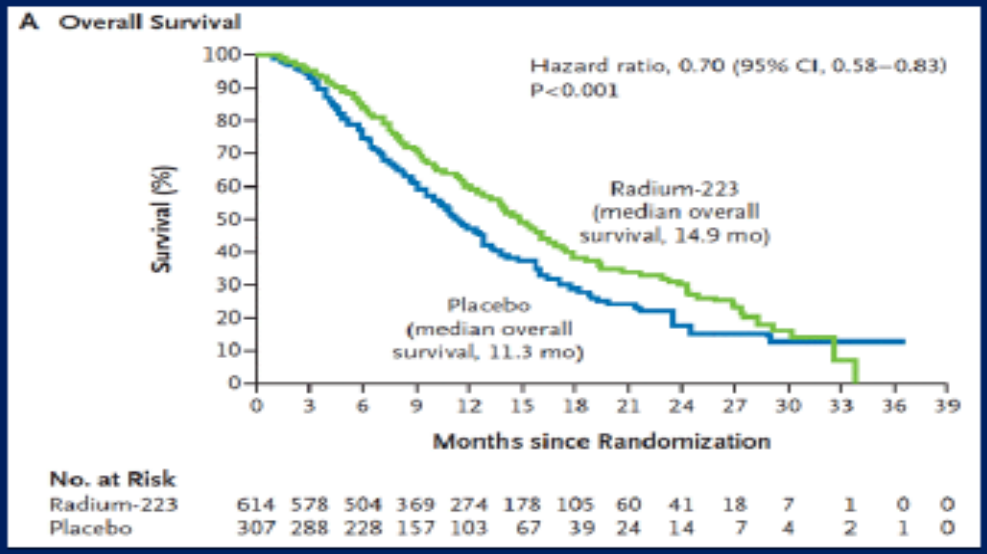
Bone –targeting radiopharmaceutical

High energy alpha-particles with short range (<100μm) hence less bone marrow toxicity



ALSYMPCA trial

ALSYMPCA: Randomized Phase III Study of Radium-223 vs. Placebo in mCRPC with bone metastases



Parker C. et al. NEJM, 2013.

Radium 223 AEs

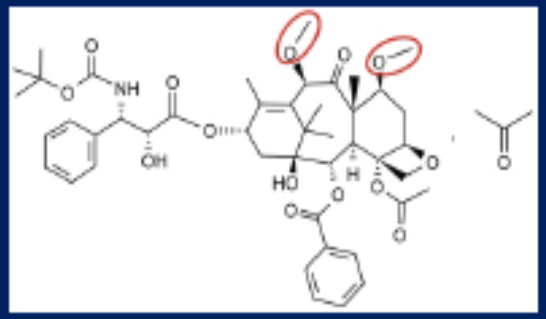
Radium 223 AEs

- Cardiovascular: Peripheral edema (13%)
- Gastrointestinal: Nausea (36%), diarrhea (25%), vomiting (19%)
- Hematologic: Anemia (93%; grades 3/4: 6%), lymphocytopenia (72%; grades 3/4: 20%), leukopenia (35%; grades 3/4: 3%), thrombocytopenia (31%; grades 3/4: 1% to 6%), neutropenia (18%; grades 3/4: 1% to 3%)

Cabazitaxel

Cabazitaxel

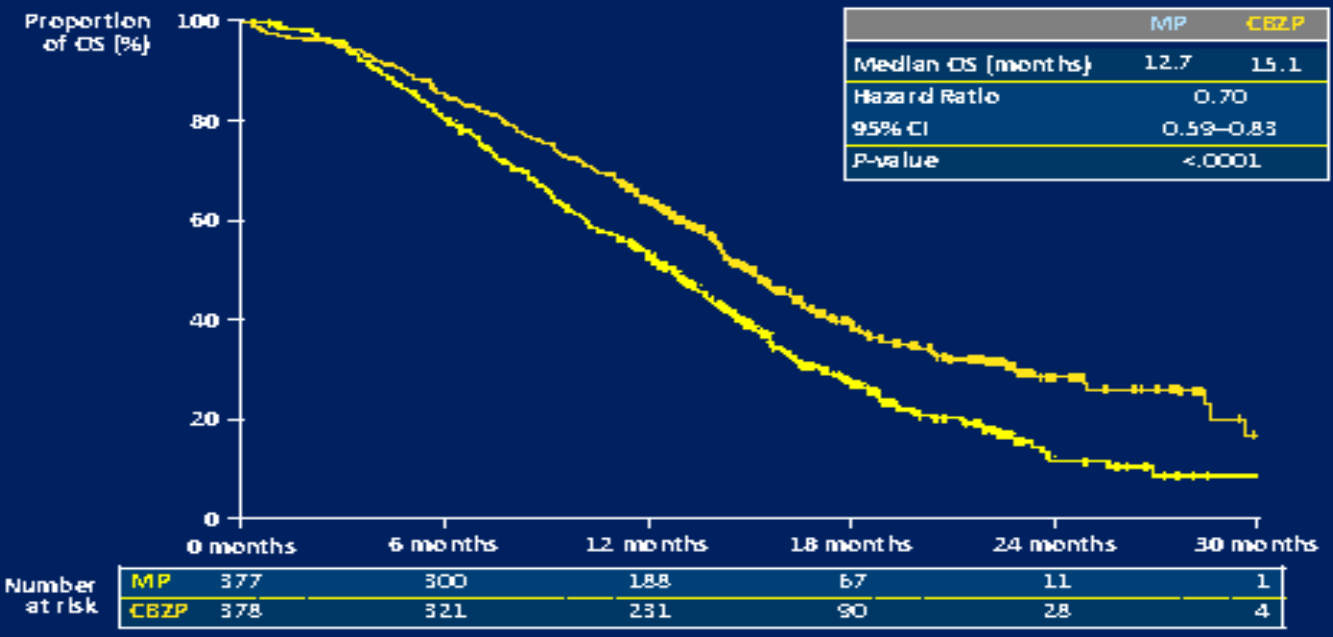
- Novel taxane active in docetaxel resistant cell lines
  - Less affinity for P-glycoprotein pump



Methoxyl side chain instead of hydroxyl groups found in docetaxel

TROPIC

TROPIC: Overall Survival



de Bono JS. et al. Lancet 2010

50

Cabazitaxel toxicity

Cabazitaxel Toxicity

- Central nervous system: Fatigue (37%), fever (12%)
- Gastrointestinal: Diarrhea (47%; grades 3/4: 6%), nausea (34%), vomiting (22%), constipation (20%), abdominal pain (17%), anorexia (16%), taste alteration (11%)
- Hematologic: Anemia (98%; grades 3/4: 11%), leukopenia (96%; grades 3/4: 69%), neutropenia (94%; grades 3/4: 82%; nadir: 12 days [range: 4-17 days]), thrombocytopenia (48%; grades 3/4: 4%)
- Neuromuscular & skeletal: Weakness (20%), back pain (16%), peripheral neuropathy (13%; grades 3/4: <1%), arthralgia (11%)
- Renal: Hematuria (17%)
- Respiratory: Dyspnea (12%), cough (11%)

Should strongly consider the use of growth factor

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Targeted radioligand therapy

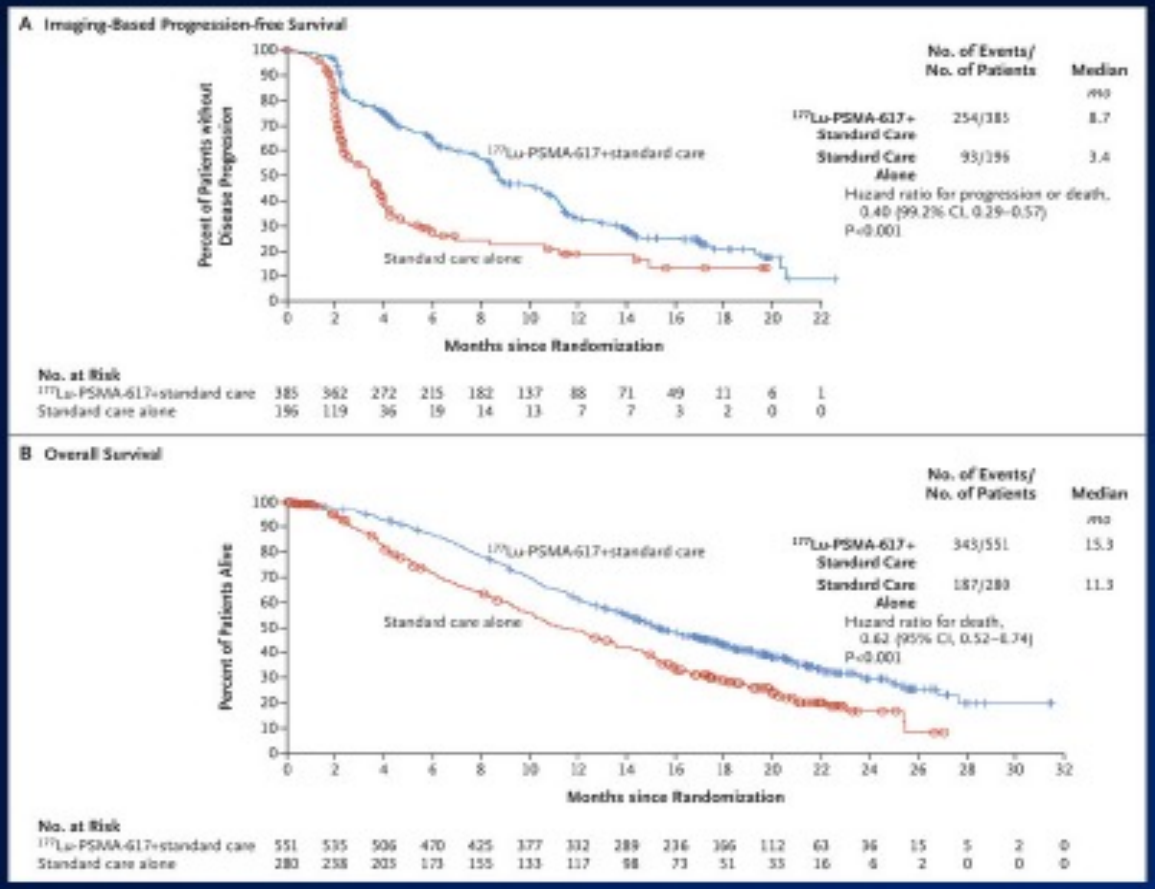
Targeted Radioligand Therapy: ^{77}Lu-PSMA-617

- For the treatment patients with PSMA-positive mCRPC who have been treated with AR pathway inhibition and taxane-based chemotherapy

- The most common adverse reactions (≥20%) were fatigue, dry mouth, nausea, anemia, decreased appetite, and constipation

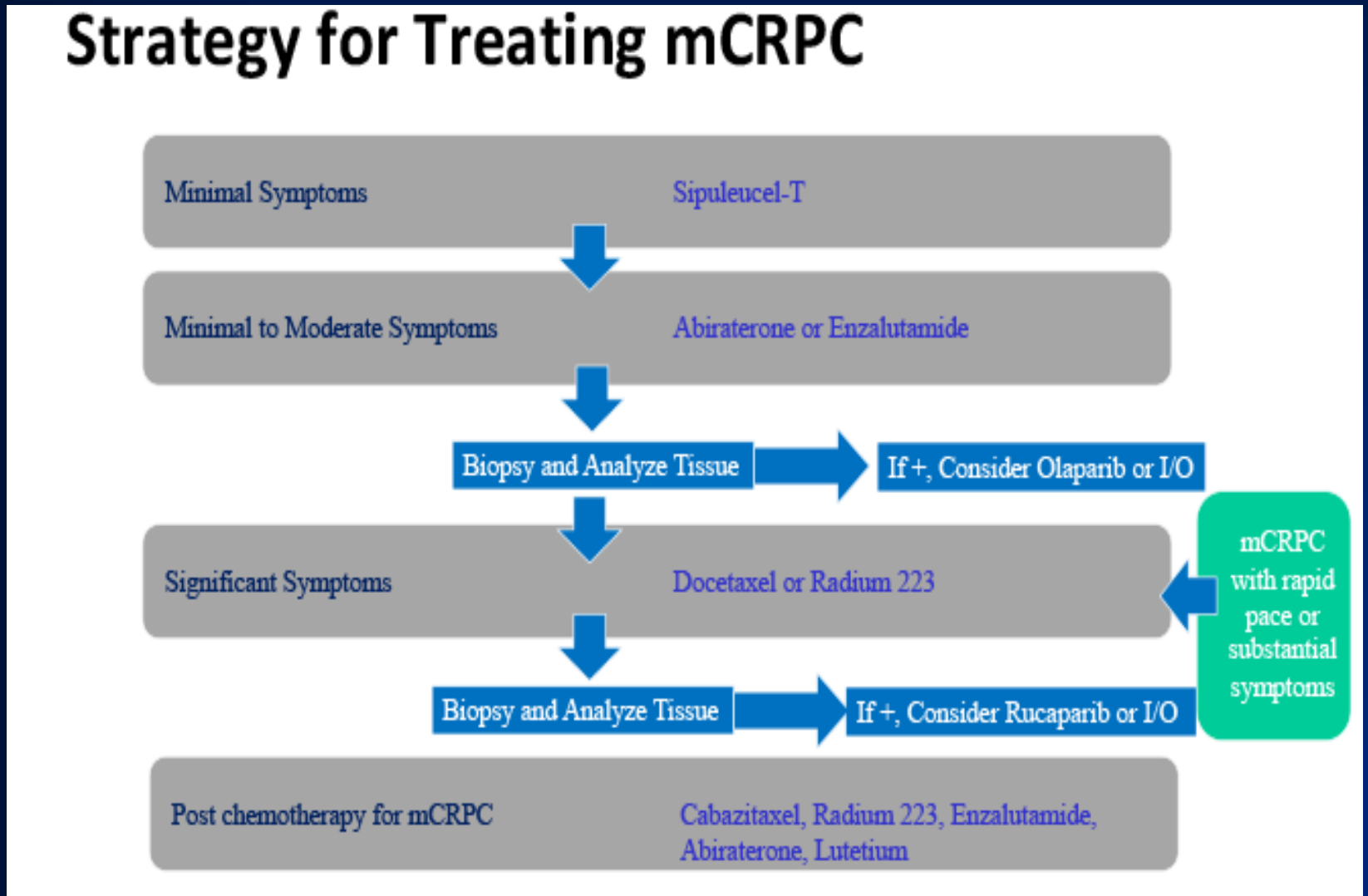
Survival curve

Lu-177-PSMA



Sartor, O et al. NEJM, 2021

Treatments


Strategy for Treating mCRPC
Minimal Symptoms
Sipuleucel-T
Minimal to Moderate Symptoms
Abiraterone or Enzalutamide
Biopsy and Analyze Tissue
If +, Consider Olaparib or I/O
Significant Symptoms
Docetaxel or Radium 223
mCRPC with rapid pace or substantial symptoms
Biopsy and Analyze Tissue
If +, Consider Rucaparib or I/O
Post chemotherapy for mCRPC
Cabazitaxel, Radium 223, Enzalutamide, Abiraterone, Lutetium

Germline testing

Current Guidelines for Germline Testing in Prostate Cancer

Testing Criteria	Additional Criteria
Known high-risk family history/genes	By family history and ancestry ≥1 close blood relative with: – breast cancer at age ≤50 y – triple-negative breast cancer at any age – male breast cancer at any age – ovarian cancer at any age – pancreatic cancer at any age – metastatic high- or very-high-risk group ≥2 close blood relatives with either breast or prostate cancer (any grade) at any age
High-risk, very high-risk, regional, or metastatic prostate cancer	Regardless of family history
Ashkenazi Jewish ancestry	
Family History of high-risk germline mutations (eg: *BRCA1/2*, Lynch mutation)	Should include *MLH1*, *MSH2*, *MSH6*, and *PMS2* (for Lynch syndrome) and homologous recombination genes (*BRCA1/2*, *ATM*, *PALB2*, and *CHEK2*)
Intermediate-risk prostate cancer AND intraductal/cribriform histology OR Personal history of exocrine pancreatic cancer, breast cancer, colorectal, gastric, melanoma, pancreatic cancer, upper tract urothelial cancer, glioblastoma, biliary tract cancer, and small intestinal	

NCCN Guidelines. Prostate Cancer. V1.2023. www.nccn.org
NCCN Guidelines. Genetic/familial High-Risk Assessment: Breast, Ovarian, and Pancreatic V2.2023. www.nccn.org

Olaparib

The NEW ENGLAND JOURNAL of MEDICINE

AL ARTICLE
nd Safety of the
73 SARS-CoV-2 Vaccine

AHA Scientific Sessions 2020

EDITORIAL
SARS-CoV-2 Vaccination — An Ounce (Actually, Much Less) of Prevention

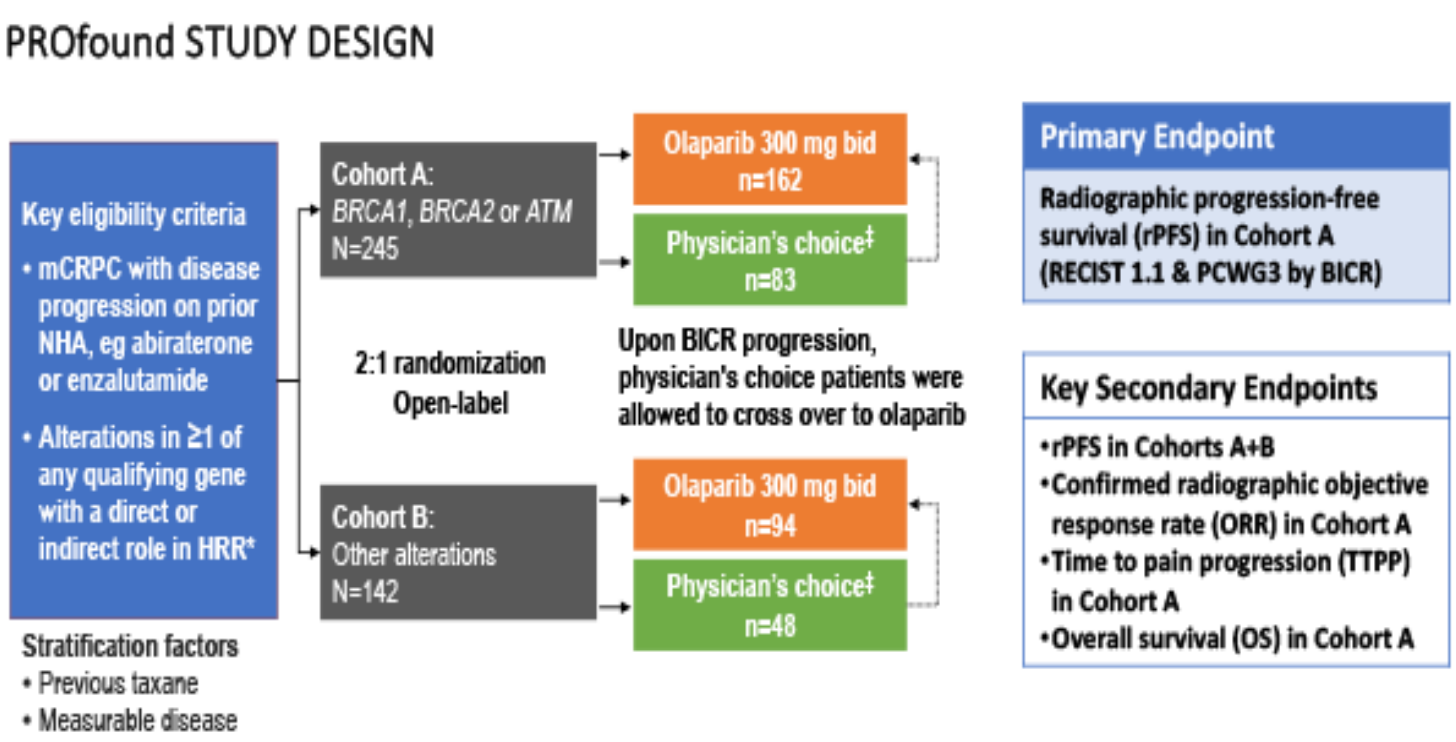
EDITORIAL
Hiding in Plain Sight — Somatic Mutation in Human Disease

ORIGINAL ARTICLE

Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

Maha Hussain, M.D., Joaquin Mateo, M.D., Karim Fizazi, M.D., Fred Saad, M.D., Neal Shore, M.D., Shahneen Sandhu, M.D., Kim N. Chi, M.D., Oliver Sartor, M.D., Neeraj Agarwal, M.D., David Olmos, M.D., Antoine Thiery-Vuillemin, M.D., Przemyslaw Twardowski, M.D., et al., for the PROfound Trial Investigators*

PROfound STUDY



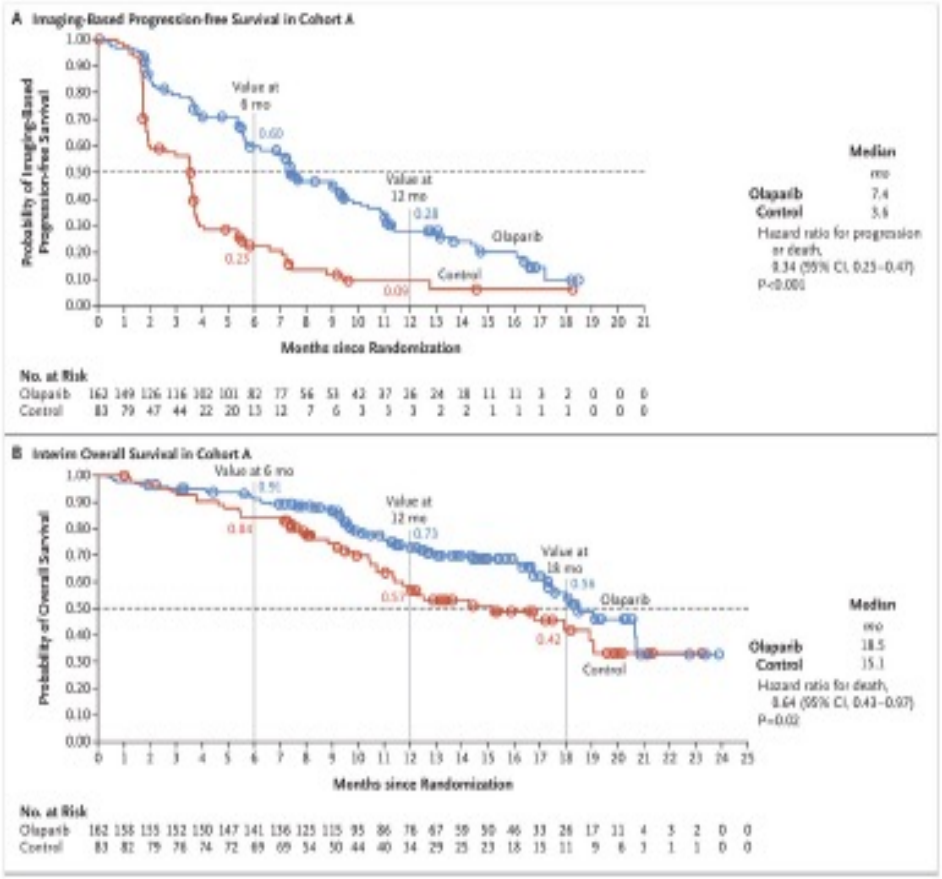
*An investigational Clinical Trial Assay, based on the FoundationOne® CDx next-generation sequencing test
Developed in partnership with Foundation Medicine Inc, and used to prospectively select patients harboring alterations in *BRCA1*, *BRCA2*, *ATM*, *BARD1*, *BRIP1*, *CDK12*, *CHEK1*, *CHEK2*, *FANCL*, *PALB2*, *PPP2R2A*, *RAD51B*, *RAD51C*, *RAD51D* or *RAD54L* in their tumor tissue

‡Physician's choice of either enzalutamide (160 mg qd) or abiraterone (1000 mg qd plus prednisone [5 mg bid])
BICR, blinded independent central review

Hussain, M et al. ESMO, 2019

Kaplan-Meier

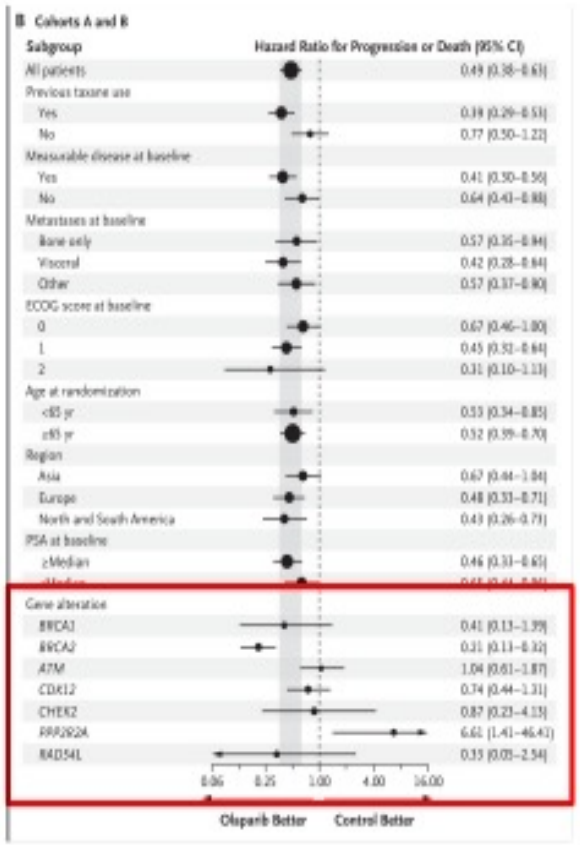
Kaplan–Meier Estimates of Imaging-Based PFS and Interim OS

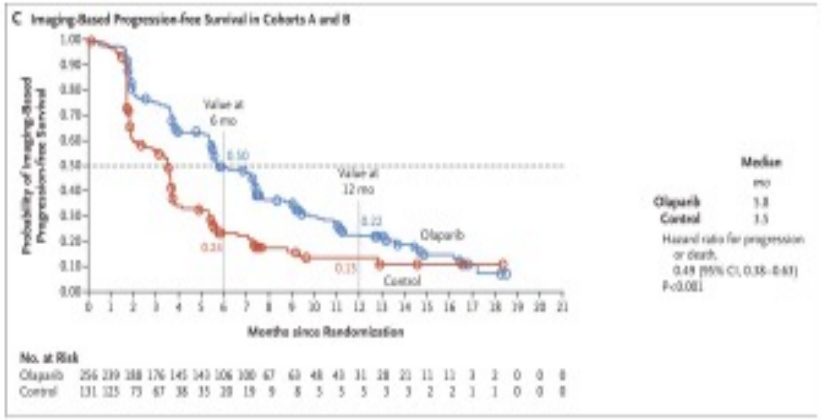


Hussain, M et al. NEJM. 2020

Olaparib

Olaparib for metastatic castrate-resistant prostate cancer (mCRPC)

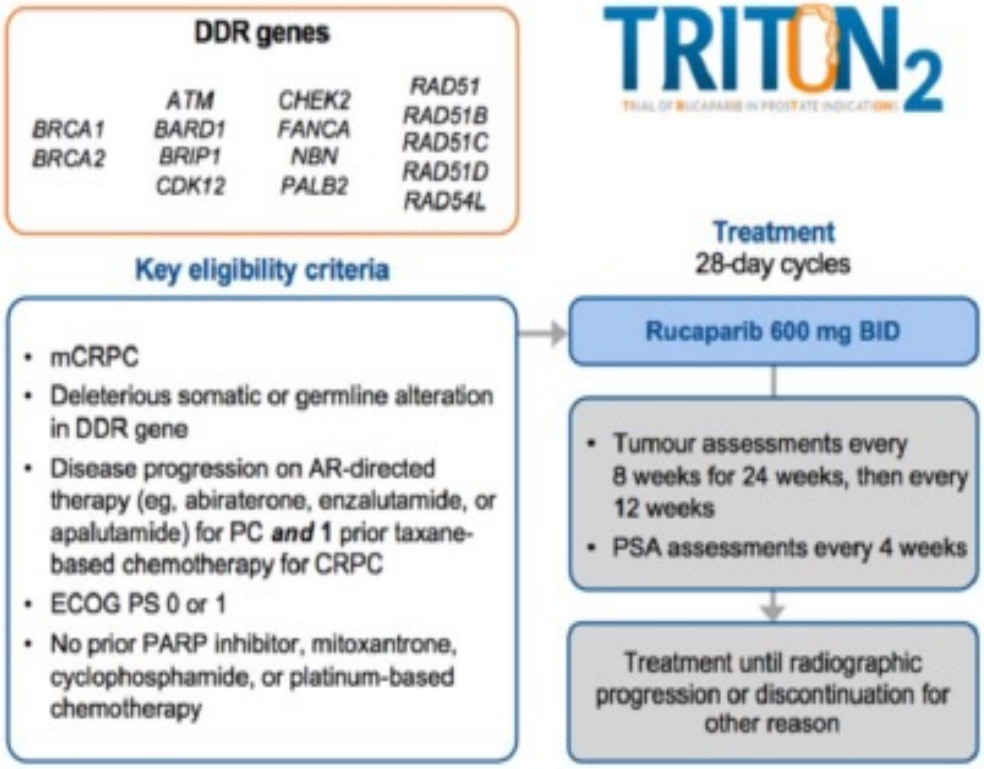




FDA approval: deleterious or suspected deleterious germline or somatic HRR gene-mutated mCRPC, after treatment with enzalutamide or abiraterone

Hussain, M et al. NEJM. 2020

TRITON2

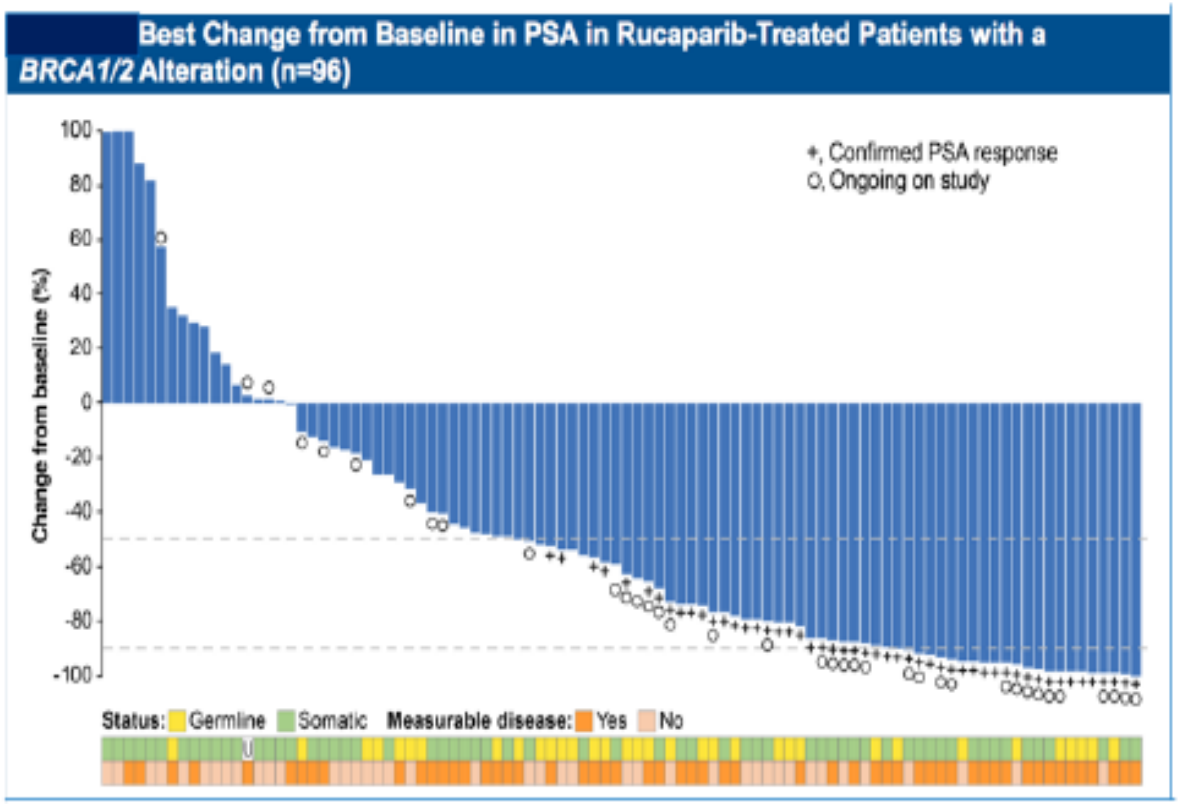


FDA breakthrough therapy designation for patients with *BRCA1/2*-mutated mCRPC who have received >=1 prior AR-directed therapy and a taxane based chemotherapy

Abida W et al. ESMO, 2019

Rucaparib

Phase II TRITON2: Rucaparib in mCRPC



Abida W et al. ESMO, 2019

MSI high prostate cancer

MSI High Prostate Cancer

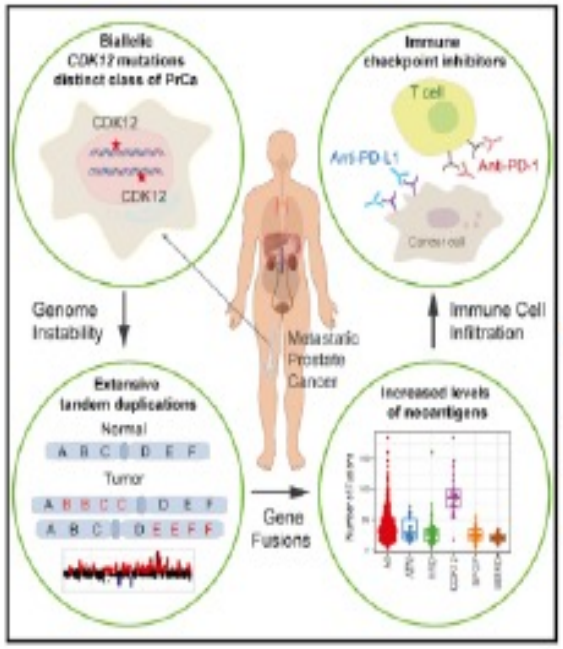
- Approval of pembrolizumab
- Incidence
  - Localized PC ~2%
  - Autopsy series of mCRPC ~12%
    - Pritchard et al., *Nature Com* 2014
  - Ongoing testing suggests 5-6% of mCRPC

Lemery et al. NEJM. 2017

Inactivation of *CDK12* Delineates a Distinct Immunogenic Class of Advanced Prostate Cancer

Yi-Mi Wu, Marcin Cieślik, Robert J. Lonigro, Pankaj Vats, Melissa A. Reimers, Xuhong Cao, Yu Ning, Lisha Wang, Lakshmi P. Kunju, Navonil de Sarkar, Elisabeth I. Heath, Jonathan Chou, Felix Y. Feng, Peter S. Nelson, Johann S. de Bono, Weiping Zou, Bruce Montgomery, Ajjai Alva, PCF/SU2C International Prostate Cancer Dream Team, Dan R. Robinson, and Arul M. Chinnaiyan

Graphical Abstract



Highlights

- *CDK12* biallelic inactivating mutations define a distinct subtype of prostate cancer
- *CDK12* loss is associated with genomic instability and focal tandem duplications
- *CDK12* loss leads to increased gene fusions, neoantigen burden, and T cell infiltration
- Patients with *CDK12* mutant tumors may benefit from immune checkpoint inhibition

Wu YM et al. Cell. 2018

CDK12 inactivation

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  - Ongoing testing suggests 5-6% of mCRPC

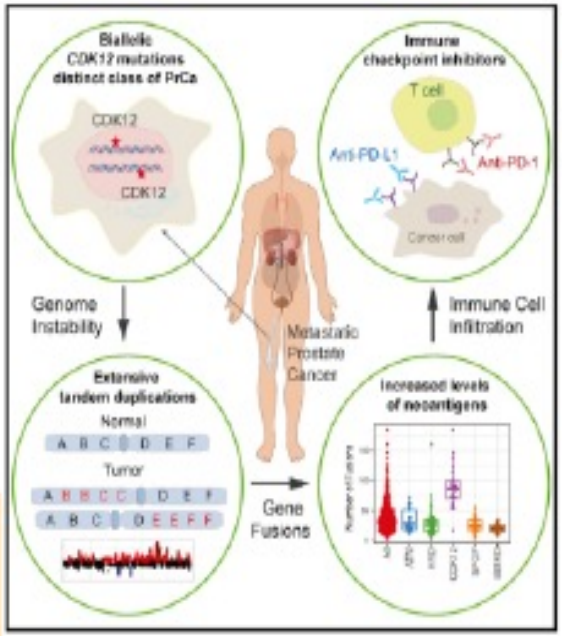
Lemery et al., *NEJM* 2017

Pembrolizumab for high tumor mutational burden (2020)
10 mutations/megabase
FDA Approval June 2020

Inactivation of *CDK12* Delineates a Distinct Immunogenic Class of Advanced Prostate Cancer

Yi-Mi Wu,[1,2,20] Marcin Cieslik,[1,2,20] Robert J. Lonigro,[1] Pankaj Vats,[1] Melissa A. Reimers,[2] Xuhong Cao,[1] Yu Ning,[1] Lisha Wang,[1] Lakshmi P. Kunju,[1,2,4] Navonil de Sarkar,[1] Elisabeth I. Heath,[6,7] Jonathan Chou,[6] Felix Y. Feng,[8,9,10,11] Peter S. Nelson,[5,12,13] Johann S. de Bono,[14,15] Weiping Zou,[1,2,16] Bruce Montgomery,[12,17] Ajjai Alva,[1,3] PCF/SU2C International Prostate Cancer Dream Team, Dan R. Robinson,[1,2,*] and Arul M. Chinnaiyan[1,2,4,18,19,21,*]

Graphical Abstract



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- Patients with *CDK12* mutant tumors may benefit from immune checkpoint inhibition

Wu YM *et al. Cell, 2018*

Future Directions

Future Directions

- mpMRI screening in men be used for diagnosis and monitoring of prostate cancer
- Imaging may facilitate detection of prostate cancer below conventional PSA thresholds particularly in a high genetic risk setting
- New combination strategies in mCRPC

Acknowledgements

THANK YOU

William D. Figg PharmD
James L. Gulley MD, PhD
Ravi A. Madan MD
Lisa M. Cordes PharmD
Anna Couvillon, CRNP
Katherine Lee-Wisdom, RN
Amy Hankin, PA-C
Monique Nikki Williams, CRNP
Moniquea Smith, PCC

Baris Turkbey, MD
Pete Choyke, MD
Yolanda McKinney, RN
Maria Merino, MD
Antoun Toubaji, MD
Peter Pinto, MD
Michele Reed, RN

The Genitourinary Malignancies Branch,
The Center for Immuno-Oncology, and
the Molecular Imaging Branch

All Clinical Trial Participants
and their Families