Oncology Grand Rounds

New Agents and Strategies in Prostate Cancer

Tuesday, June 30, 2020

5:00 PM – 6:30 PM ET

Faculty

Robert Dreicer, MD, MS
Kara M Olivier, NP, APRN-BC
Victoria Sinibaldi, RN, MS, CS, CANP, BC
Matthew R Smith, MD, PhD

Moderator

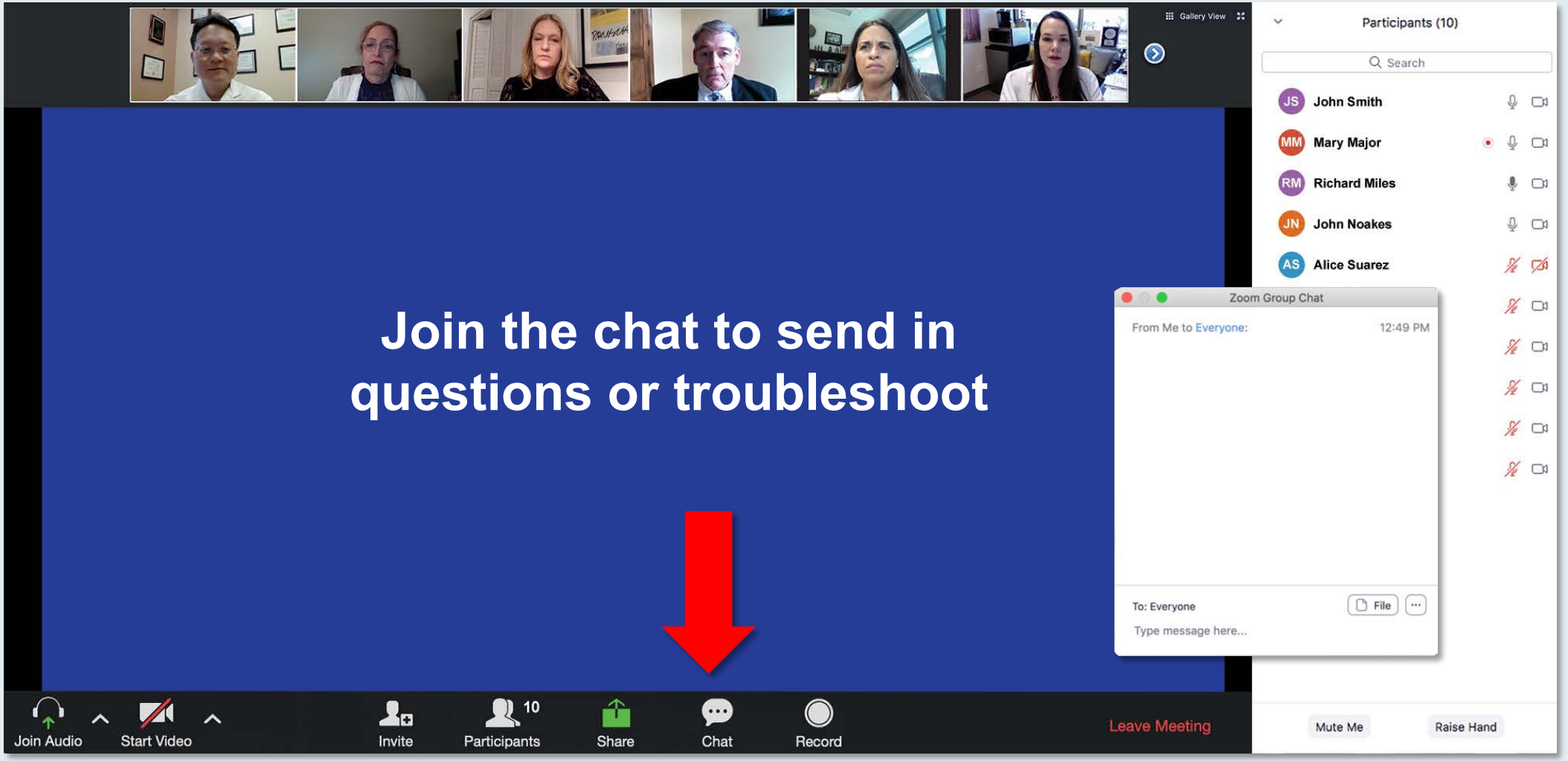
Neil Love, MD

Jointly provided by USF Health

RTP RESEARCH TO PRACTICE

Familiarizing yourself with the Zoom interface

How to participate in the chat



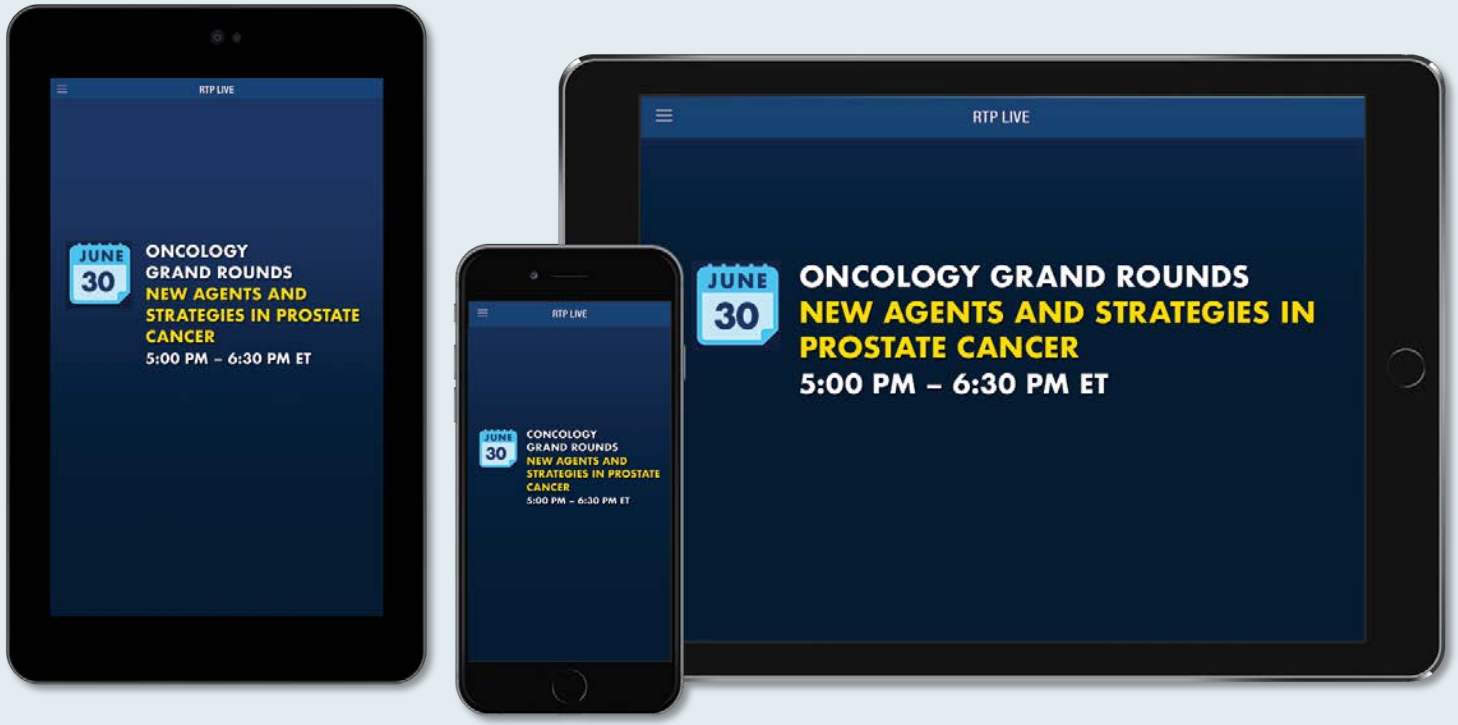
About the Enduring Program

- This webinar is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based video/PowerPoint program.
  An email will be sent to all attendees when the activity is available.
- To learn more about our education programs visit our website, www.ResearchToPractice.com

Make the Meeting Even More Relevant to You

Download the RTP Live app on your smartphone or tablet to access program information, including slides being presented during the program:

www.ResearchToPractice.com/RTPLiveApp



ONCOLOGY TODAY

WITH DR NEIL LOVE

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Conversations with the Investigators: Prostate Cancer

Wednesday, July 1, 2020
5:00 PM – 6:00 PM ET

Faculty

Robert Dreicer, MD, MS
Daniel P Petrylak, MD
Christopher Sweeney, MBBS

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

COVID-19 AND LUNG CANCER

What We Know, What We Don't Know and What It All Means for Current Patient Care – *A Live CME Webinar*

Thursday, July 2, 2020
12:00 PM – 1:00 PM ET

Moderator
Neil Love, MD

Faculty
Leora Horn, MD, MSc
Naiyer A Rizvi, MD
Lecia V Sequist, MD, MPH

Oncology Grand Rounds

New Agents and Strategies in Prostate Cancer

Tuesday, June 30, 2020

5:00 PM – 6:30 PM ET

Faculty

Robert Dreicer, MD, MS
Kara M Olivier, NP, APRN-BC
Victoria Sinibaldi, RN, MS, CS, CANP, BC
Matthew R Smith, MD, PhD

Moderator

Neil Love, MD

Jointly provided by USF Health

RTP RESEARCH TO PRACTICE

Robert Dreicer, MD, MS
University of Virginia School of Medicine
Charlottesville, Virginia

Kara M Olivier, NP, APRN-BC
Claire and John Bertucci Center for Genitourinary Cancers
Boston, Massachusetts

Victoria Sinibaldi, RN, MS, CS, CANP, BC
Johns Hopkins Hospital
Baltimore, Maryland

Matthew R Smith, MD, PhD
Massachusetts General Hospital Cancer Center
Boston, Massachusetts

Agenda

Case 1: 56-year-old man

Discussion: Overview of prostate cancer treatment

Case 2: 75-year-old man

Discussion: Management of M0 prostate cancer

Case 3: 57-year-old man

Discussion: Management of metastatic hormone-sensitive prostate cancer

Case 4: 56-year-old man

Discussion: Management of metastatic castration-resistant prostate cancer; emerging agents and strategies

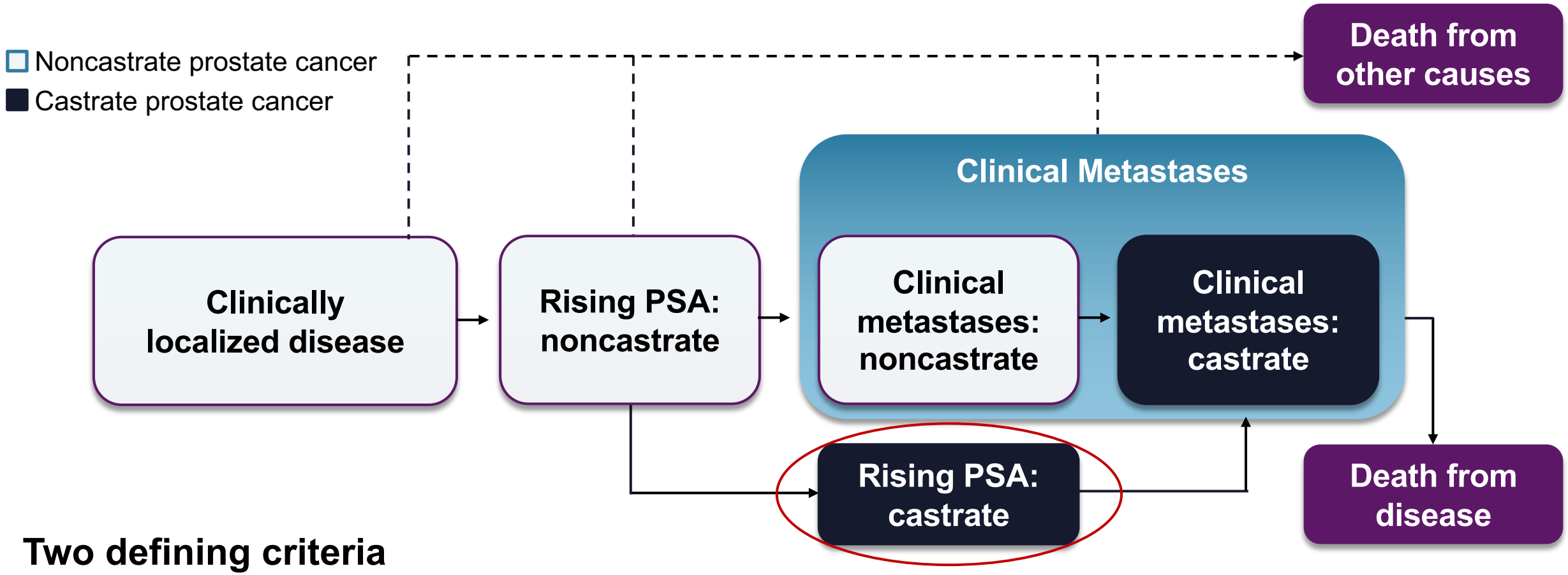
Case 1: 56-year-old man (from the practice of Ms Olivier)

- 12/2019: Gleason 5+4
- Treatments:
  - Radical prostatectomy
  - Androgen deprivation
  - Salvage radiation therapy
  - Secondary endocrine treatment (abiraterone/prednisone)

Overview of Prostate Cancer

- Natural history of prostate cancer; biology; PSA
- Hormonal strategies
- Local and systemic treatments

Clinical Disease States Model of Prostate Cancer[1]



Two defining criteria

- Rising PSA in the setting of castrate testosterone levels (<50 ng/dL)
- No radiographically identifiable metastasis

1. Adapted from Scher HI et al. *J Clin Oncol.* 2008;26:1148-1159.

Abiraterone may be challenging to administer to a patient …

a. With Crohn’s disease
b. With diabetes
c. With peripheral neuropathy
d. On a proton pump inhibitor
e. All of the above

Men with complete testosterone suppression have minimal or no sexual libido.

a. Agree

b. Disagree

c. I don’t know

Prostate Cancer

- Prostate cancer is still a major health problem in the US.
- Approximately 191,930 new cases; approximately 33,330 deaths are expected to occur in 2020.
- With these large numbers, it is more likely that nurses will be seeing these patients in their practice.
- It becomes imperative that nurses keep abreast of current patient issues, current treatments, their associated side effects, and nursing interventions that can help to mitigate problems and ensure quality care.
- Treatment depends on diagnosis (stage and grade of the tumor), co-morbidies, prior therapies, performance status and patient's desires in terms of goals of treatment and QOL.
- Patient-centered strategies to optimize symptom management and improve patient adherence to therapies and outcomes are of paramount importance.

Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

Considerations

- Side effects of ADT in young men related to muscle loss, fatigue and sexual health impact quality of life.
- Prioritize access to adequate support for management of sexual health and mental health.
- Ongoing discussion regarding rationale for treatment and how it’s related to long term survival.

Courtesy of Kara M Olivier, NP, APRN-BC

Balancing the benefits/risks of treatment

- Improved survival
- Delayed progression
- Psychological benefits of receiving treatment

Benefits

Shared decision making: goals of patient

- Expense: COST $$$$... ↓ QOL
- ED and ↓ libido
- Hot flashes
- Changes in mood/ ↓cognition
- ↓ strength/ muscle mass
- Osteoporosis
- Anemia, fatigue
- Metabolic syndrome
- Cardiac risk, DM

Risks

Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

Agenda

Case 1: 56-year-old man

Discussion: Overview of prostate cancer treatment

Case 2: 75-year-old man

Discussion: Management of M0 prostate cancer

Case 3: 57-year-old man

Discussion: Management of metastatic hormone-sensitive prostate cancer

Case 4: 56-year-old man

Discussion: Management of metastatic castration-resistant prostate cancer; emerging agents and strategies

Case 2: 75-year-old man with M0 prostate cancer (from the practice of Ms Sinibaldi)

- 2001: High-risk PCa (Gleason 3+4 = 7) → Radical prostatectomy (+ left SV, -nodes) → salvage RT → Clinical trial of HT + docetaxel, with eventual biochemical progression
- Intermittent HT (LHRH + bicalutamide), ultimately requiring CHT
- 2015: Enzalutamide 160mg added LHRH therapy
  - Poor tolerance even with dose reduction to 80 mg and subsequently to 80 mg every other day
  - Significant fatigue, severe diarrhea, nausea and vomiting
  - 2018: Discontinuation of the AR targeted therapy, continue LHRH alone
- Asymptomatic, good PS, PSA rising
- 3/2020
  - PSA 12.01 ng/ml
  - PSADT < 7 months
  - CT and bone scan: NED
- Initiated darolutamide

Management of Nonmetastatic Castration-Resistant Prostate Cancer (CRPC)

Types of hormonal treatment

- Androgen deprivation
- Antiandrogens
  - Enzalutamide, darolutamide, apalutamide

Men with detectable PSA levels after radical prostatectomy almost always die of metastatic disease.

a. Agree

b. Disagree

c. I don’t know

There is no discernible difference in the side-effect profiles of enzalutamide, darolutamide and apalutamide.

a. Agree

b. Disagree

c. I don’t know

Definition of nmCRPC

- Patients with rising PSA despite ongoing ADT and no detectable metastases by conventional imaging (bone scan and CT or MRI)
- Most patients with nmCRPC are presumed to have occult metastatic disease not detected by conventional imaging

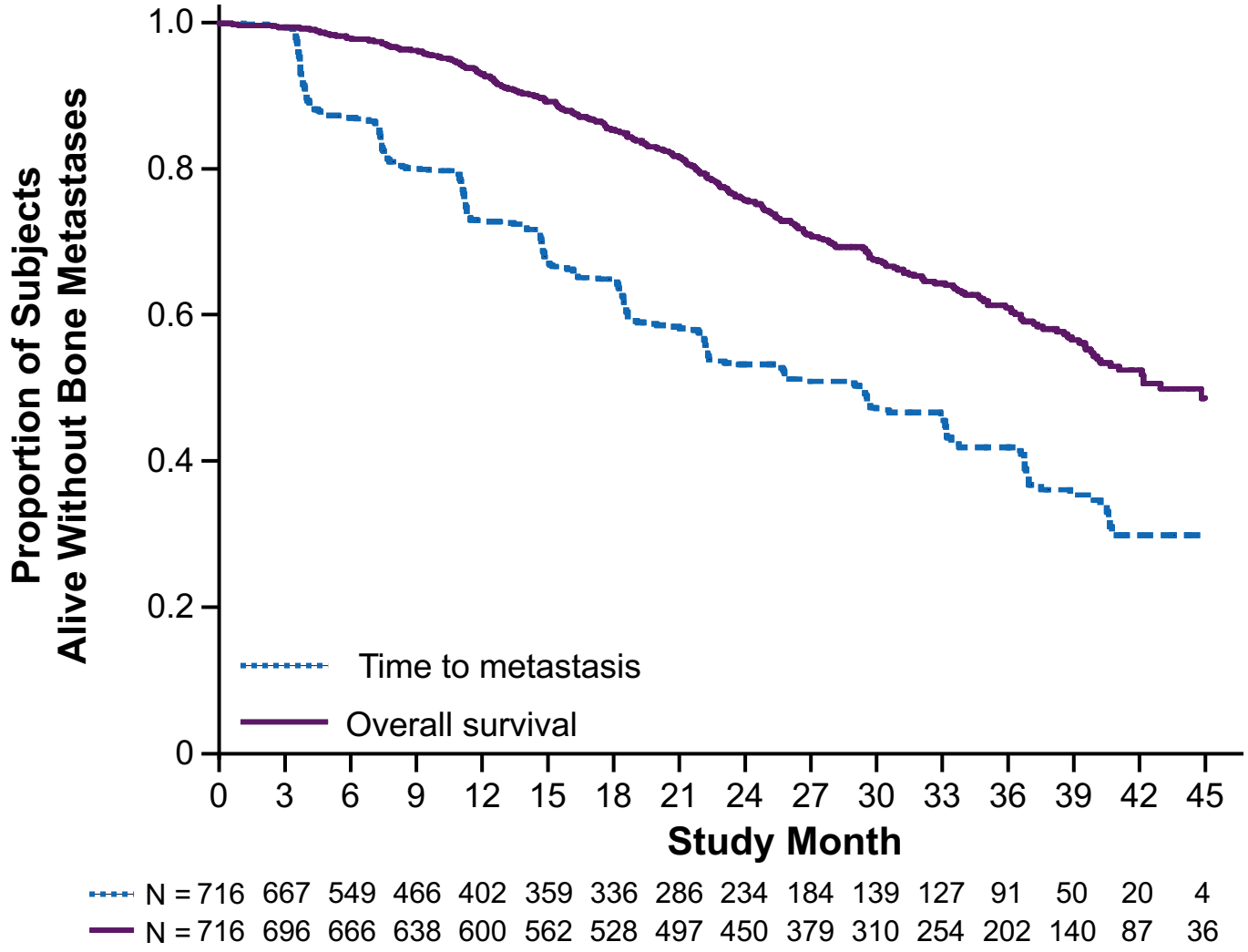
Courtesy of Matthew R Smith, MD, PhD

Context

- Men with nmCRPC are at significant risk for metastatic disease and prostate cancer–specific death[1]
- Metastases are a major cause of morbidity and mortality[2,3]
- Prevention of metastases represents an important unmet medical need

1. Smith MR et al. *J Clin Oncol*. 2013;31:3800-3806. 2. Scher HI et al. *PLoS One*. 2015;10;e0139440. 3. Gartrell BA et al. *Nat Rev Clin Oncol*. 2014;11:335-345.

nmCRPC Is a Deadly Disease[1]

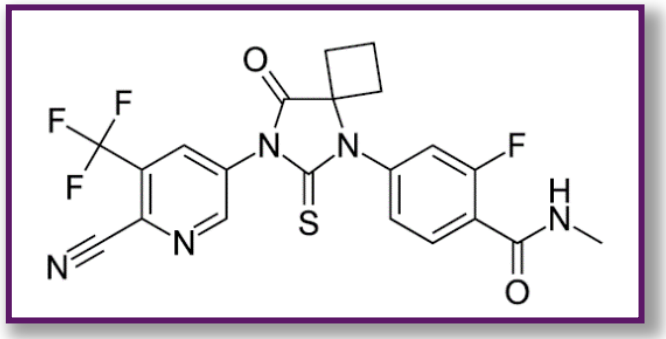


- **Median time to metastasis:** 29.5 months
- **Median overall survival:** 44.8 months

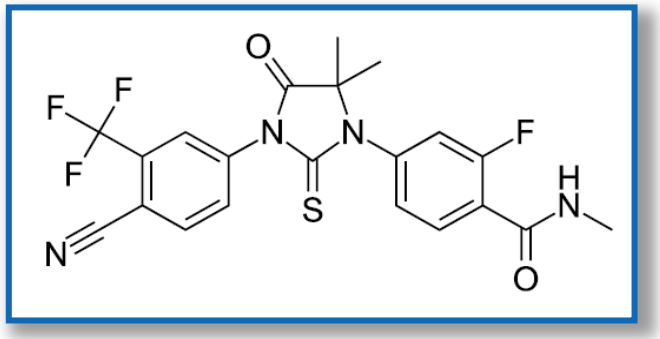
1. Smith MR et al. *Lancet*. 2012;379:39-46.

Next-Generation Androgen Receptor Inhibitors[1,2]

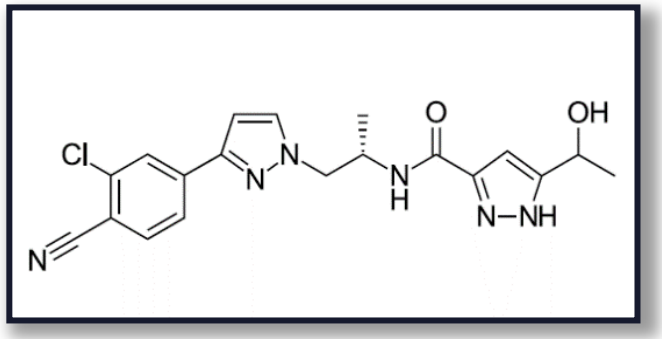
Apalutamide



Enzalutamide



Darolutamide



- Apalutamide and enzalutamide have similar structures
- Darolutamide is structurally distinct from apalutamide and enzalutamide, characterized by low blood–brain barrier penetration[1,2,] and may have improved tolerability

1. Zurth C et al. *J Clin Oncol*. 2018;36(Suppl 6):Abstract 345.
2. Sandmann S et al. American Society of Clinical Oncology 2019 Genitourinary Cancers Symposium (ASCO GU 2019). Abstract 156.

Oral Anti Androgens Approved For M0 Prostate Cancer – How do you choose?

- Enzalutamide
  - Cautious with patients with a history of falls and seizure
- Apalutamide
  - Risk of rash
- Darolutamide
  - Mild fatigue

*For all patients monitor CBC/diff, comprehensive metabolic panel and PSA.

Courtesy of Kara M Olivier, NP, APRN-BC

Nursing implications: oral agents

- Nurses need to be aware that there needs to be a shift in management from provider to patient
- Nurses need to become familiar with the oral agents and develop educational strategies to ensure patient understanding of medication, dosing and administration, potential side effects, symptom management, self care measures, proactive follow-up.
- Stress the import' of need to keep scheduled visits and contact the health care provider when side effects develop. If side effects are not reported, necessary adjustments will not be made and serious consequences can occur and have impact on their life and further therapy.

Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

Nursing implications: oral agents (cont.')

- Nurses need to be aware of factors that affect patient compliance and reporting
- Patients are often reluctant to notify the provider because they fear that their therapy may be interrupted or dose lowered
  - Most side effects resolve with brief interruption of therapy
  - Any necessary dose reduction is simply to customize a dose that the individual needs
  - A dose reduction does not necessarily decrease the efficacy of the treatment
- Communication, education, organization, and trusting relationship are key!!

Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

FDA Approval of Apalutamide[1]

Apalutamide approved on 2/14/2018

First drug approved by the FDA for nmCRPC

First approval based on metastasis-free survival


The NEW ENGLAND JOURNAL of MEDICINE

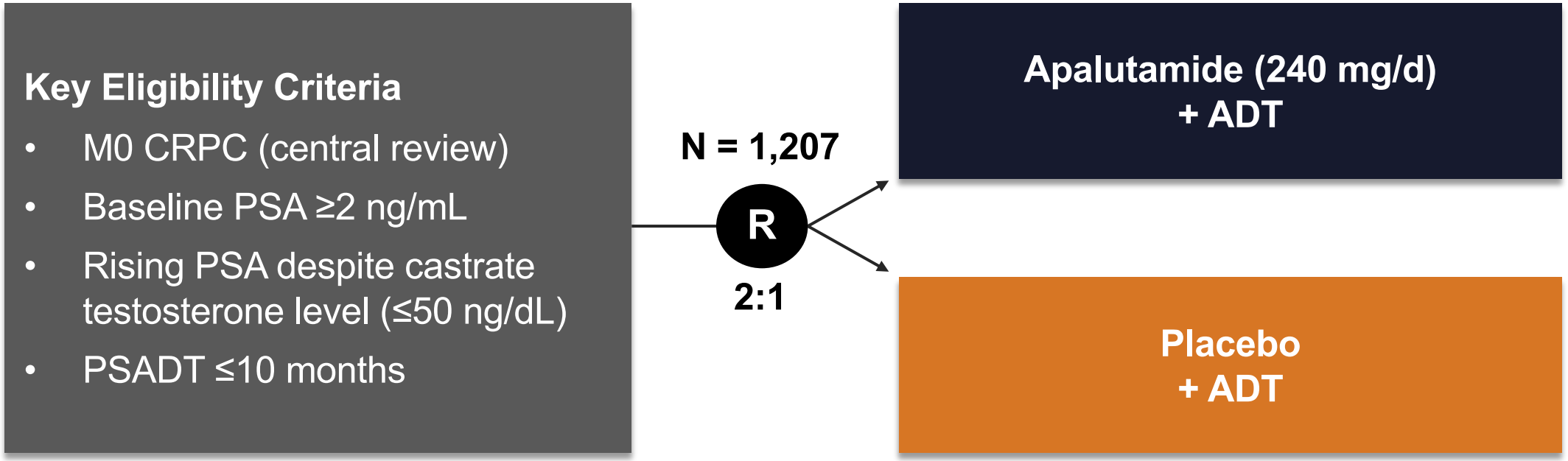
Metastasis-free Survival — A New End Point in Prostate Cancer Trials

Julia A. Beaver, M.D., Paul G. Kluetz, M.D., and Richard Pazdur, M.D.

N ENGL J MED 378;26 NEJM.ORG JUNE 28, 2018

1. Beaver JA et al. *N Engl J Med*. 2018;378:2458-2460.

SPARTAN: Apalutamide vs Placebo Study Design[1,2]

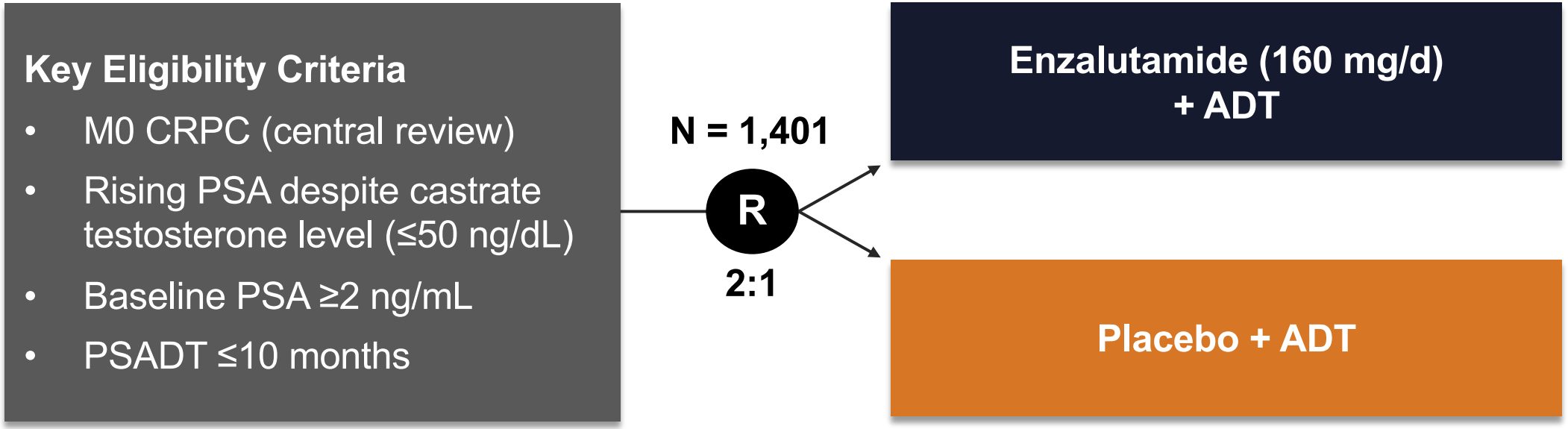


- **Primary endpoint:** MFS
- **Secondary endpoints:** Safety, time to PSA progression, time to symptomatic progression, OS, PSA response, QOL

78% of patients in placebo group received subsequent approved therapy for mCRPC

1. Small EJ et al. ASCO GU 2018. Abstract 161. 2. Smith MR et al. *N Eng J Med.* 2018; 378:1408-1418.

PROSPER: Enzalutamide vs Placebo Study Design[1,2]

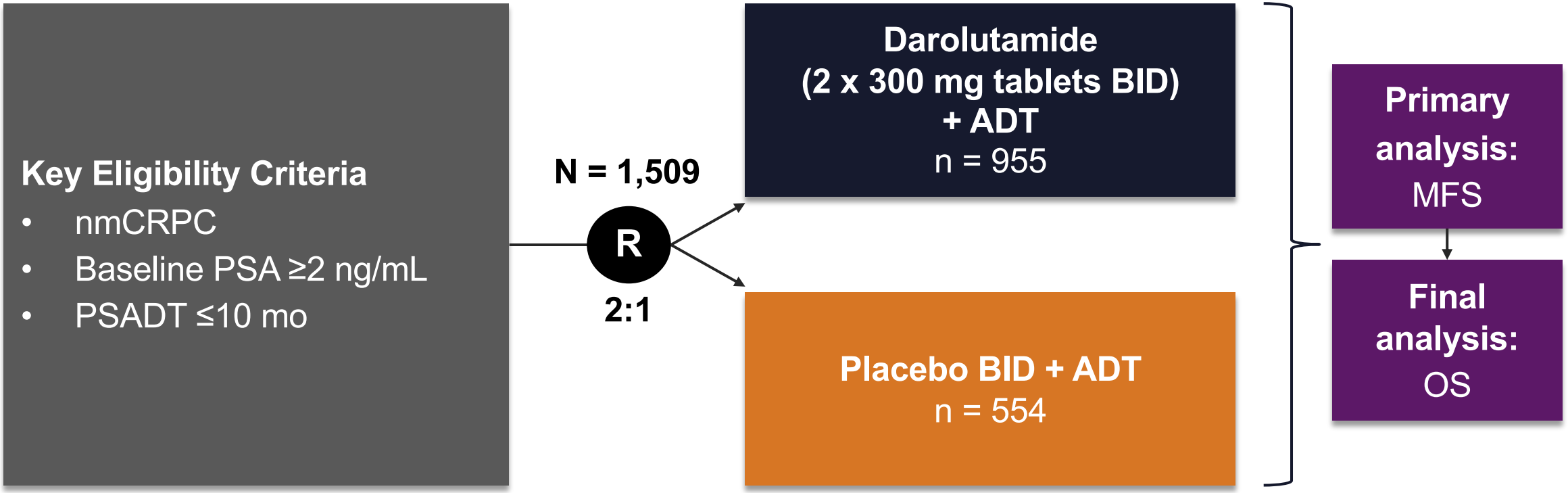


- **Primary endpoint:** MFS (defined as time from randomization to radiographic progression or death within 112 days of treatment discontinuation)
- **Secondary endpoints:** Safety, time to PSA progression, time to use of new antineoplastic therapy, OS, PSA response, and QOL

48% of patients in placebo group received subsequent approved therapy for mCRPC

1. Hussain M et al. ASCO GU 2018. Abstract 3. 2. Hussain M et al. *N Engl J Med.* 2018;378:2465-2474.

ARAMIS: Darolutamide vs Placebo Study Design[1,2]



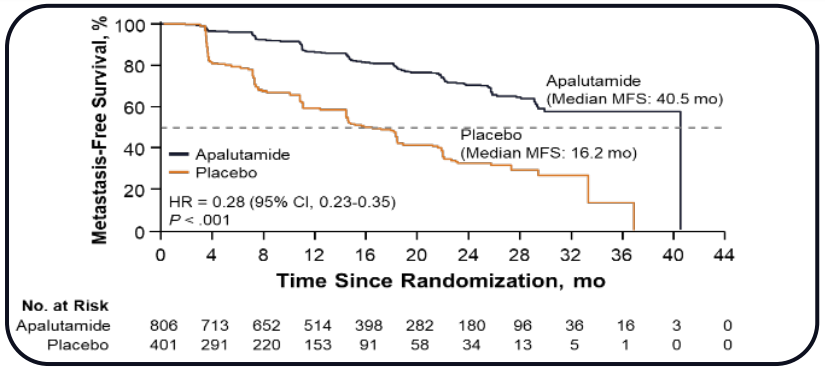
- **Primary endpoint:** MFS
- **Secondary endpoints:** OS, time to first symptomatic skeletal event, time to initiation of first cytotoxic chemotherapeutic, time to pain progression, safety, and tolerability

37% of patients in placebo group received subsequent approved therapy for mCRPC

1. Fizazi K et al. ASCO GU 2019 Abstract 140. 2. Fizazi K et al. *N Engl J Med*. 2019;380:1235-1246.

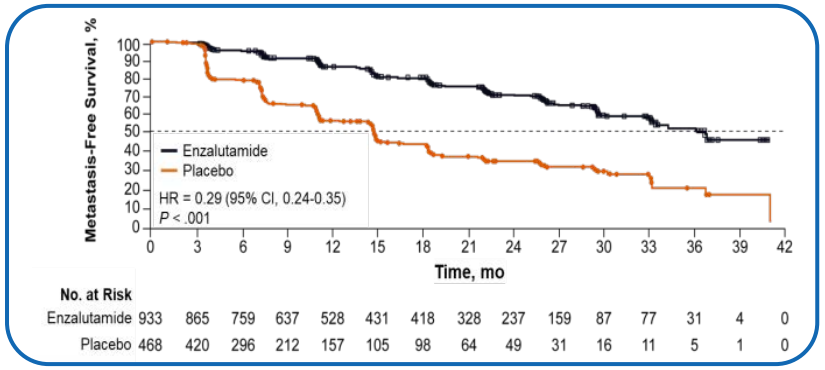
Primary Endpoint: Metastasis-Free Survival

SPARTAN[1]
Apalutamide



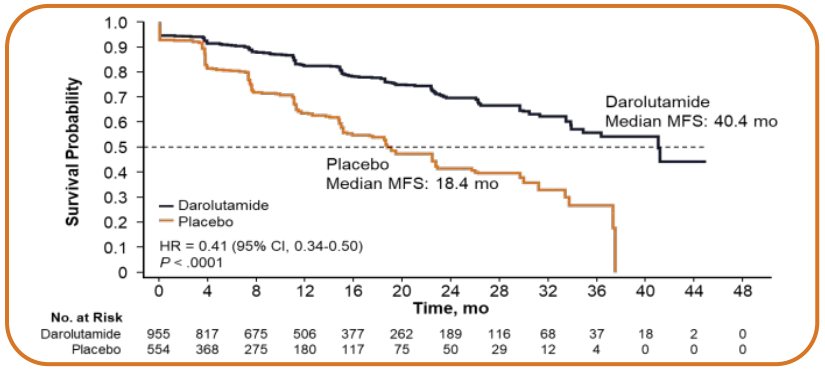
- 72% reduction of distant progression or death
- Median MFS: APA 40.5 vs PBO 16.2 months
- 24-month MFS benefit

PROSPER[2]
Enzalutamide



- 71% reduction of distant progression or death
- Median MFS: ENZA 36.6 vs PBO 14.7 months
- 22-month MFS benefit

ARAMIS[3]
Darolutamide



- 59% reduction of distant progression or death
- Median MFS: DARO 40.4 vs PBO 18.4 months
- 22-month MFS benefit

1. Smith MR et al. *N Engl J Med*. 2018;378:1408-1418. 2. Hussain M et al. *N Engl J Med*. 2018;378:2465-2474. 3. Fizazi K et al. *N Engl J Med*. 2019;380:1235-1246.

Adverse Events of Interest

Safety[a]	SPARTAN[1]		PROSPER[2]		ARAMIS[3]	
	APA (n = 803)	PBO (n = 398)	ENZA (n = 930)	PBO (n = 465)	DARO (n = 954)	PBO (n = 554)
Any AEs, n (%)	775 (96.5)	371 (93.2)	808 (87)	360 (77)	794 (83.2)	426 (76.9)
Any serious AEs, n (%)	199 (24.8)	92 (23.1)	226 (24)	85 (18)	237 (24.8)	111 (20.0)
AEs leading to discontinuation, %	11.0	7.0	9.0	6.0	8.9	8.7
AEs leading to death, n (%)	10 (1.2)	1 (0.3)	32 (3.4)	3 (0.7)	37 (3.9)	18 (3.2)
AEs (all grades), %						
Fatigue	30.4	21.1	33.0	14.0	12.1	8.7
Hypertension	24.8	19.8	12.0	5.0	6.6	5.2
Rash	23.8	5.5	0	0	2.9	0.9
Falls	15.6	9.0	11.0	4.0	4.2	4.7
Fractures	11.7	6.5	N/A	N/A	4.2	3.6
Mental impairment disorders	5.1	3.0	5.0	2.0	0.4	0.2

[a] AE reporting every 4 weeks in SPARTAN and every 16 weeks in PROSPER and ARAMIS.

1. Smith MR et al. *N Engl J Med*. 2018;378:1408-1418. 2. Hussain M et al. *N Engl J Med*. 2018;378:2465-2474. 3. Fizazi K et al. *N Engl J Med*. 2019;380:1235-1246.

Agenda

Case 1: 56-year-old man

Discussion: Overview of prostate cancer treatment

Case 2: 75-year-old man

Discussion: Management of M0 prostate cancer

Case 3: 57-year-old man

Discussion: Management of metastatic hormone-sensitive prostate cancer

Case 4: 56-year-old man

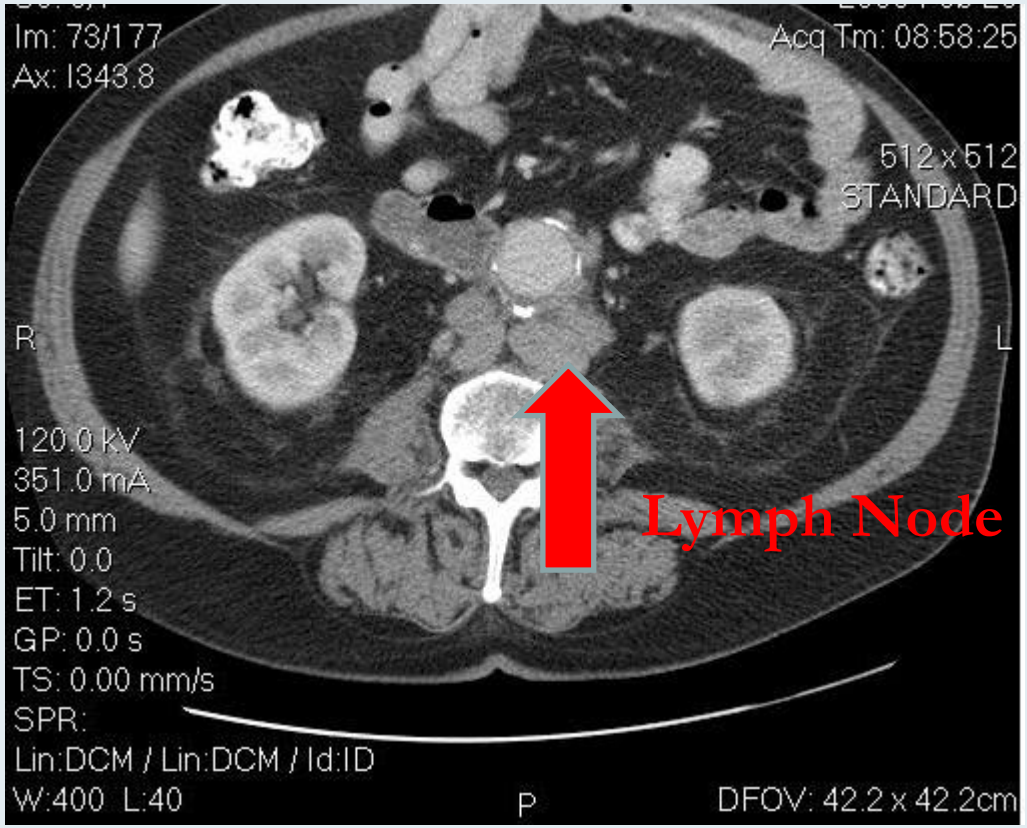
Discussion: Management of metastatic castration-resistant prostate cancer; emerging agents and strategies

Case 3: 57-year-old man with de novo metastatic prostate cancer (from the practice of Ms Olivier)

- 10/2019: Diagnosed with metastatic prostate cancer to lymph nodes
- 11/2019: TRUS-biopsies: Gleason 4+4=8 (4+3, 3+4 in multiple cores), PSA 45.9
- 12/2019: mpMRI: 1.6-cm PI-RADS 5 lesion with abutment of the capsule, multiple enlarged iliac nodes (largest 2.6 cm) consistent with metastasis
  - CT scan: 0.7 cm retrocaval node
  - Bone scan: Negative for metastatic disease
- 12/2019: GnRH antagonist + degarelix
  - PSA after 1 month: 14.4
  - PSA after 2 months: 5.6
  - PSA after 3 months: 1.07
- 2/2020: Transitioned to LHRH agonist (leuprolide)
- 3/2020: Completed RT, initiates enzalutamide
  - PSA after 1 month: 0.10
  - Fatigue but otherwise active

57-year-old man with de novo metastatic prostate cancer (from the practice of Ms Olivier)

Abdominal/Pelvic CT



Strategies in the Management of Metastatic Hormone-Sensitive Prostate Cancer

- De novo metastatic disease versus recurrent disease
- Risks and benefits of androgen deprivation
- Additional benefits
  - Enzalutamide, darolutamide, apalutamide, abiraterone
- Chemotherapy versus oral endocrine therapy
- COVID-19 considerations

Men who have metastatic prostate cancer on initial diagnosis have the greatest chance for sustained response with androgen deprivation and…

a. An antiandrogen

b. Docetaxel

c. Either an antiandrogen or docetaxel — no difference

d. I don’t know

Selected FDA Approved Drugs in Advanced Prostate Cancer

- Docetaxel: cytotoxic/taxane (fatigue, diarrhea, peripheral neuropathy, muscle cramps)
- Cabazitaxel: cytotoxic/taxane (fatigue, myelosupression)
- Abiraterone: lyase inhibitor (dramatically inhibits testosterone production) LFT abnormalities, hypertension
- Enzalutamide: androgen receptor antagonist (fatigue, cognitive issues)
- Apalutamide: androgen receptor antagonist (fatigue, cognitive issues)

Courtesy of Robert Dreicer, MD, MS

Clinical Decision-Making Hormone-Sensitive Metastatic Disease

- Patient factors
  - Performance status
  - Co-morbidities, i.e. pre-existing peripheral neuropathy
  - I hate taking pills doc etc.
- Disease factor
  - Extent of disease, volume of disease, presence/absence of visceral i.e. liver metastases
  - Non AR biology, i.e. poor psa expresser, significant neuroendocrine features
- Economic factors
  - Non viable co-pay or oral agents

Courtesy of Robert Dreicer, MD, MS

Choosing Oral Antiandrogen

- Age
- Comorbidities
  - Diabetes
  - History of seizure
  - Falls
  - Performance status
  - Concomitant medications

Courtesy of Kara M Olivier, NP, APRN-BC

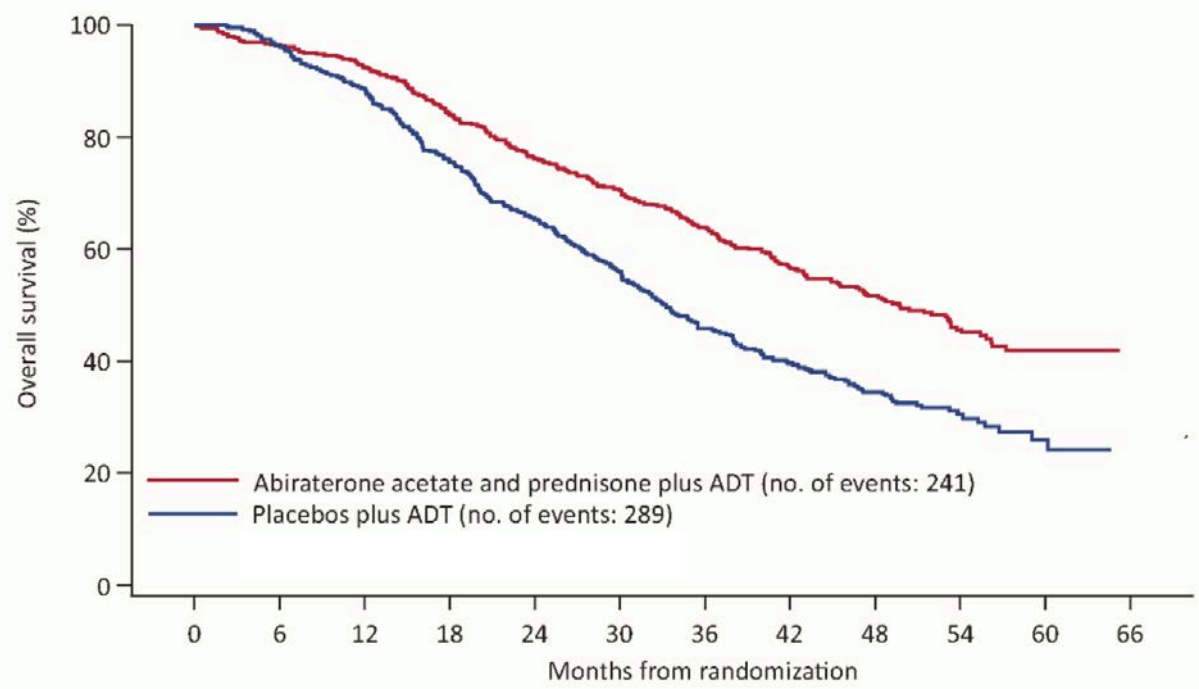
Monitoring

- Evaluation two weeks after initiating treatment with physical exam and safety laboratory monitoring
  - CBC/differential, comprehensive metabolic panel
- Based on tolerability can move to monthly follow up with serial labs and PSA
- Restaging scans within six months of initiating treatment

Courtesy of Kara M Olivier, NP, APRN-BC

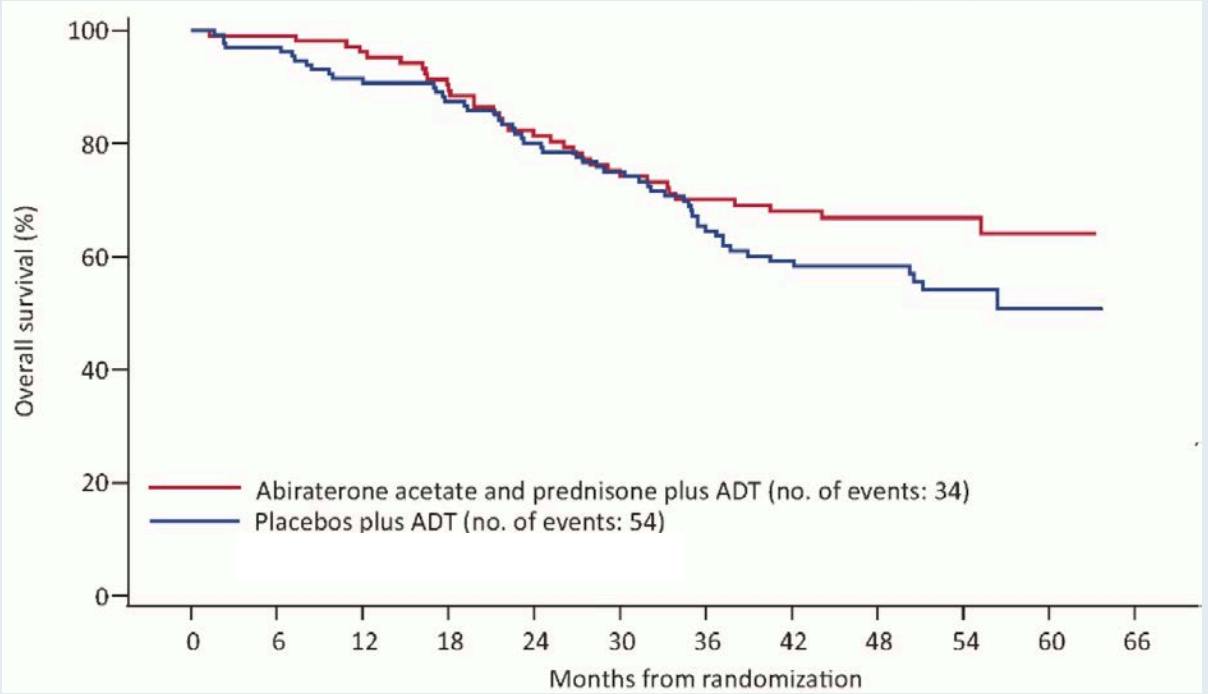
LATITUDE Final Overall Survival Analysis By Volume of Disease (CHAARTED definition*)

High-Volume Disease



	ADT + AA + P (n = 487)	ADT + Placebo (n = 468)	HR	*P*-value
mOS	49.7 mo	33.3 mo	0.62	<0.0001

Low-Volume Disease



	ADT + AA + P (n = 110)	ADT + Placebo (n = 133)	HR	*P*-value
mOS	Not reached	Not reached	0.72	0.1242

*CHAARTED definition of low vs high volume: Presence of visceral mets and/or ≥ bone mets, with one outside the vertebral column or pelvis

Fizazi K et al. Lancet Oncol 2019;20:686-700. *Chi et al 2019 GU Cancers Symposium;* Abstract 141.

Summary Results for ADT + Enzalutamide (ARCHES) and Apalutamide (TITAN) in Metastatic HSPC

	ARCHES (N = 1150)		TITAN (N = 1052)	
Characteristics	• 2/3rd High Volume • 17% prior docetaxel • 25% prior RP/XRT		• 2/3rd High Volume; • 10% prior docetaxel • 17% prior RP/XRT	
	ADT + Enzalutamide (n = 574)	**ADT (n = 576)**	**ADT + Apalutamide (n = 955)**	**ADT (n = 554)**
Radiographic PFS	NR	19.0 mo	NR	22.1 mo
	HR (overall): 0.39 • HR (prior docetaxel): 0.52 • HR (high volume): 0.43 • HR (low volume): 0.25		**HR (overall): 0.48** • HR (prior docetaxel): 0.47 • HR (high volume): 0.53 • HR (low volume): 0.36	
Overall Survival	NR	NR	NR	NR
	HR: 0.81 (Immature)		**HR (overall): 0.67** • HR (prior docetaxel): 1.27 • HR (high volume): 0.68 • HR (low volume): 0.67	

NR, not reached

Armstrong AJ et al. *J Clin Oncol* 2019;[Epub ahead of print]. Chi KN et al. *N Engl J Med* 2019;381(1):13-24.

Agenda

Case 1: 56-year-old man

Discussion: Overview of prostate cancer treatment

Case 2: 75-year-old man

Discussion: Management of M0 prostate cancer

Case 3: 57-year-old man

Discussion: Management of metastatic hormone-sensitive prostate cancer

Case 4: 56-year-old man

Discussion: Management of metastatic castration-resistant prostate cancer; emerging agents and strategies

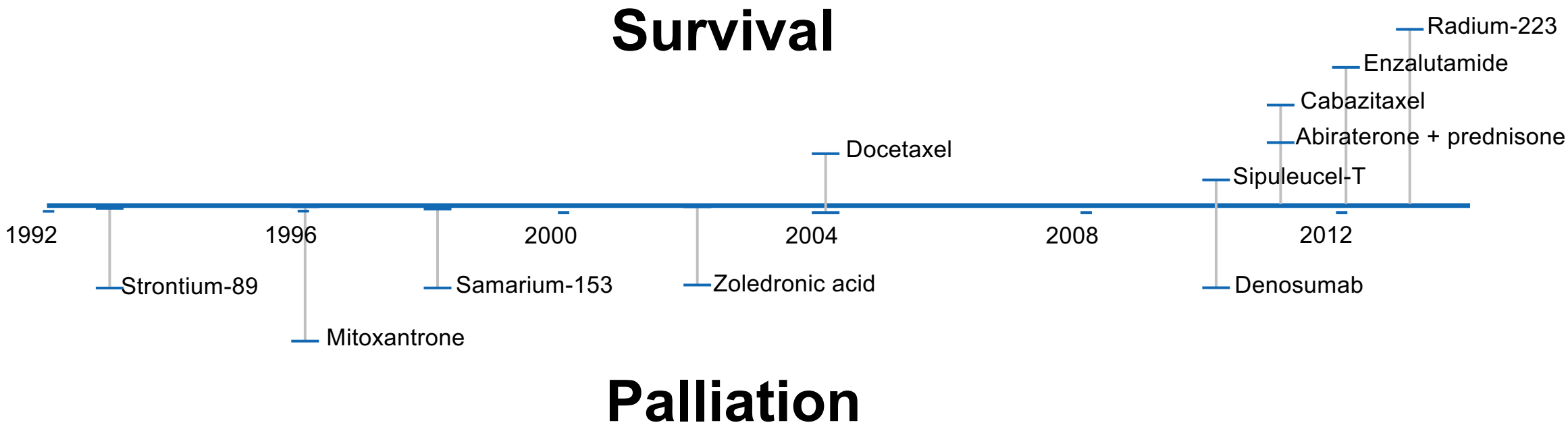
Case 4: 56-year-old man with metastatic castration resistant prostate cancer (from the practice of Ms Sinibaldi)

- ~2015: Diagnosed with metastatic prostate cancer, with diffuse bony metastases and significant retroperitoneal lymphadenopathy (Initial PSA: 1550)
- LHRH + bicalutamide + docetaxel x 6 (completed 12/2015)
  - PSA nadir 9 → 20 in 2017
- 2017: Abiraterone/prednisone → PD
- 5/2019: Symptomatic bone pain (PSA: 75.5) →Palliative EBRT to areas of painful mets
- 06/2019: Radium-223 x 1 before developing worsening multifocal bone pain
- 07/2019: Cabazitaxel + prednisone 10 mg
- 3/30/20 Follow-up: PSA 98→20, near complete resolution of pain (off narcotics)
- Currently, recommending a treatment break, with close PSA monitoring
  - Options upon disease progression: Cabazitaxel, radium-223, enzalutamide

Management of Metastatic Castration-Resistant Prostate Cancer (mCRPC)

- Radium-223
- Sipuleucel-T
- Cabazitaxel
- Evolving treatment paradigms
  - Lutetium 177 PSMA radionuclide therapy
  - PARP inhibitors
    - Genomic evaluation
    - Approved PARP inhibitors: Olaparib, rucaparib

Timeline of FDA Approvals in Metastatic Castration-Resistant Prostate Cancer



Metastatic disease was defined by conventional imaging (eg, bone scan, CT scans)

Courtesy of Matthew R Smith, MD, PhD

Metastatic Castration-Resistant Prostate Cancer (mCRPC)

- Defined: evidence of metastatic disease, with “castrate levels” of testosterone (< 50 ng/dL) with evidence of progression on imaging studies and/or rising PSA

Courtesy of Robert Dreicer, MD, MS

Therapeutic Decision Making in Metastatic Castration-Resistant Prostate Cancer (mCRPC)

- mCRPC space increasingly impacted by movement of primarily AR directed therapies early in the treatment course
  - Known resistance pathways of AR resistance limits utility of crossover of current agents
- Clinical factors
  - Symptoms yes/no
  - Biochemical or overt radiographic progression
  - Prior therapies
  - Durability of initial ADT response

Courtesy of Robert Dreicer, MD, MS

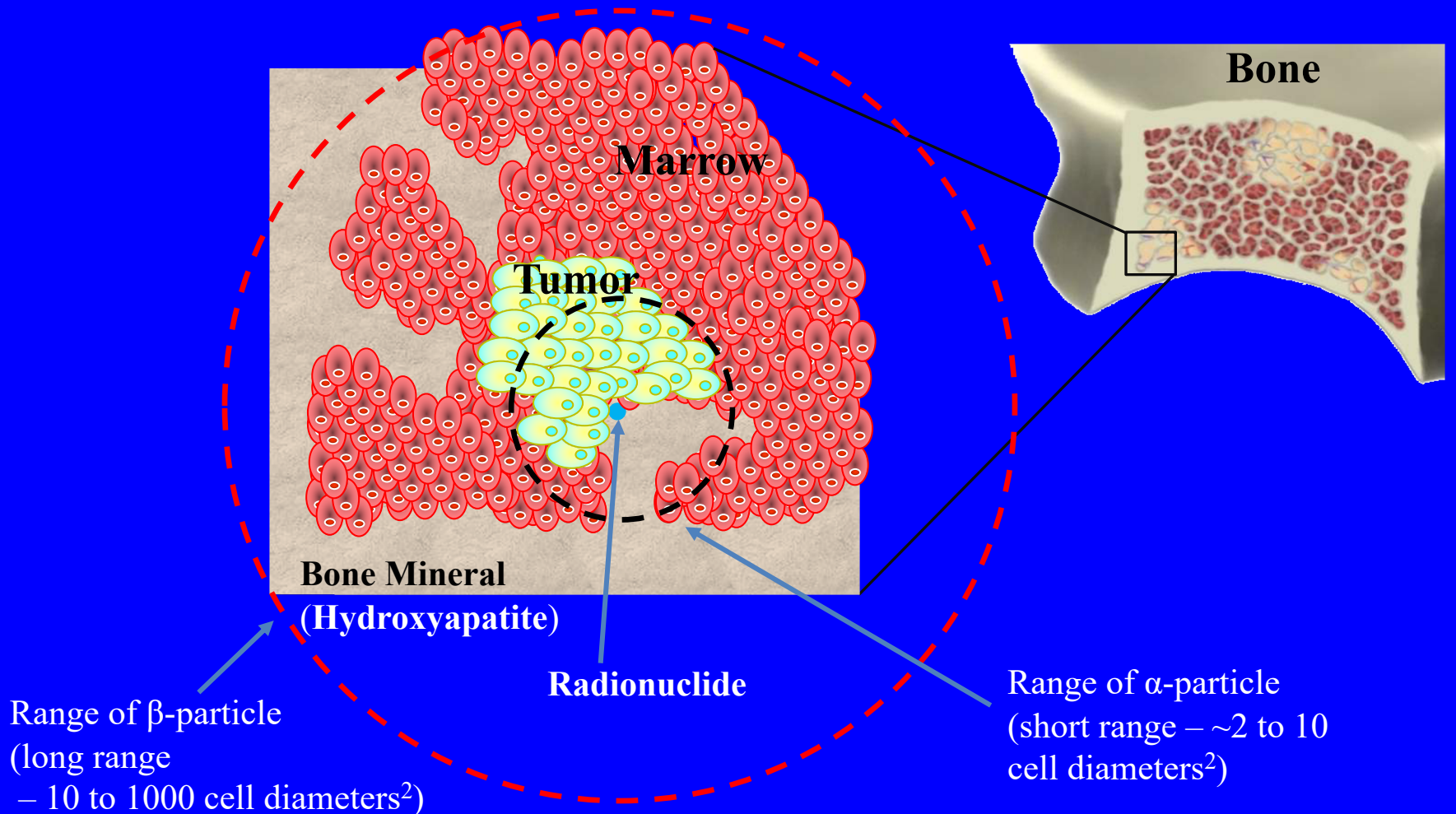
Selected FDA Approved Drugs in Advanced Prostate Cancer

- Sipuleucel-T
  - autologous cellular immunotherapy designed to stimulate a patient's own immune system against prostate cancer, MOA unknown
  - Minimal toxicity, apharesis required
- Radium-223
  - Radiopharmaceutical, alpha particle
  - GI toxicity, typically mild, important to remind patients re: lack of PSA activity
  - Administered by nuclear medicine or radiation oncology physicians
  - Important to monitor patients monthly as NO activity against non bone metastatic sites

Courtesy of Robert Dreicer, MD, MS

Range of an α-emitting Radiopharmaceutical Compared to a β-emitter

Short range of α-particles could reduce bone marrow exposure[1]



References: 1. Henriksen G, et al. *Cancer Res*. 2002;62:3120–3125. **2.** Brechbiel MW. *Dalton Trans*. 2007;43:4918-4928.

Nursing implications: Radium-223

- Rad-223 is safe and effective and targets tumor cells in the bone.
- Rad-223 -form of liquid radiation, administered IV, given every 4 weeks x6.
- Explain characteristics of RAD-223- has a short range that does limit damage to healthy cells.
- Data using this modality have shown improvement in QOL with improvement in pain, improved OS (by 3.6 months), delay in SSEs.
- Patients often focus on PSA. Point out that a decline in PSA is not an expected result of Rad-223; Patient benefits have been observed in the absence of a decreasing PSA.

Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

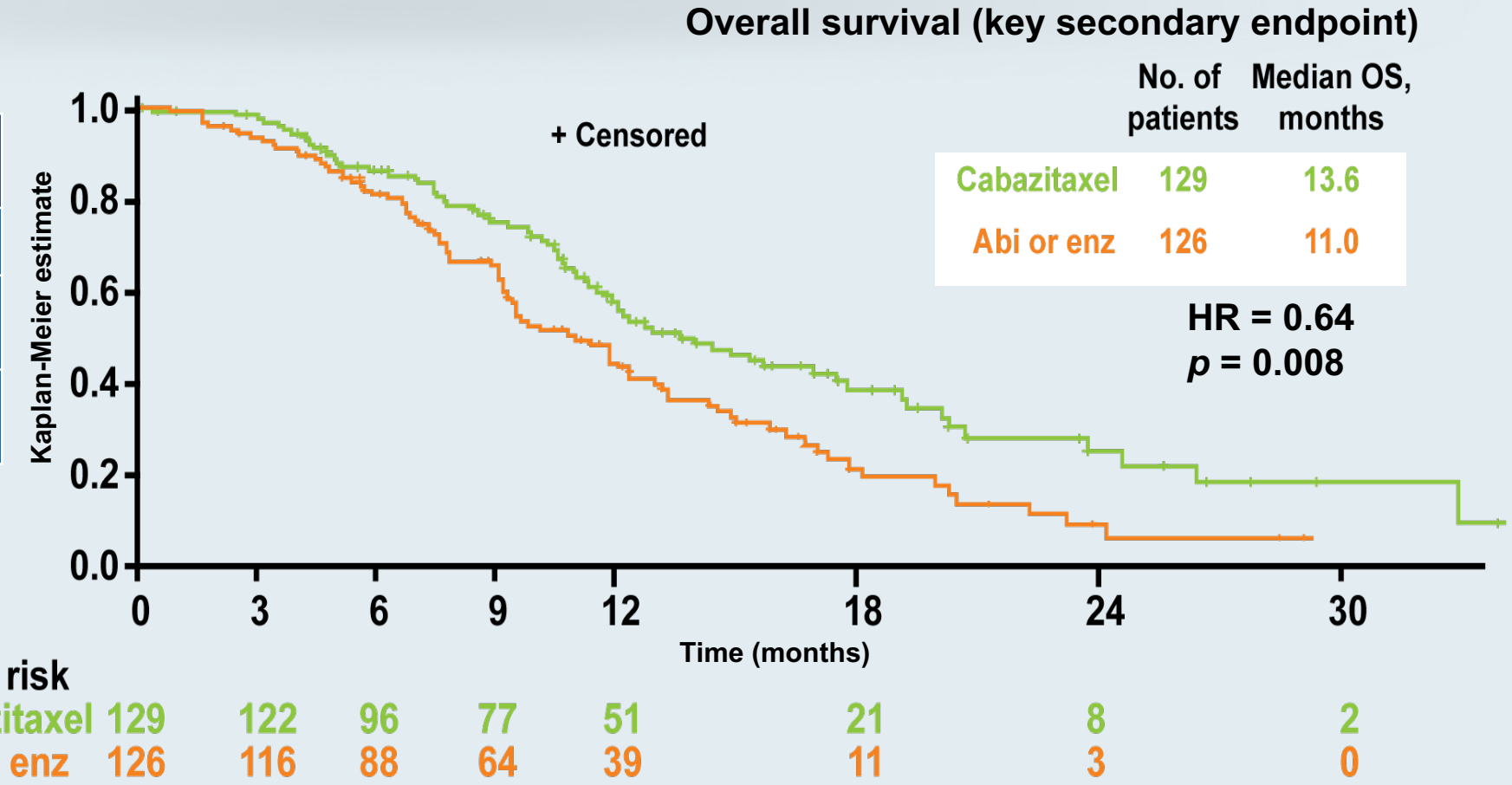
Nursing implications: Radium-223

- Fatigue
- GI: Nausea, Vomiting, Diarrhea
- Peripheral edema
- Pancytopenia: Anemia, Lymphopenia, leukopenia, thrombocytopenia, neutropenia
- Black tarry stools
- CP, Chills, Cough
- Erythema at the injection site

Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

CARD: Cabazitaxel vs Abiraterone or Enzalutamide in mCRPC Previously Treated with Docetaxel and an Androgen-Signaling-Targeted Inhibitor

Summary of AEs	Cabazitaxel	Abi or Enza
Grade ≥3 AE	56.3%	52.4%
AE leading to Tx discontinuation	19.8%	8.9%
AE leading to death	5.6%	11.3%



- CARD met its primary objective: Cabazitaxel more than doubled rPFS versus abiraterone or enzalutamide

de Wit R et al; CARD Investigators. *N Engl J Med* 2019;381(26):2506-18.

Nursing Implications: Cabazitaxel chemotherapy

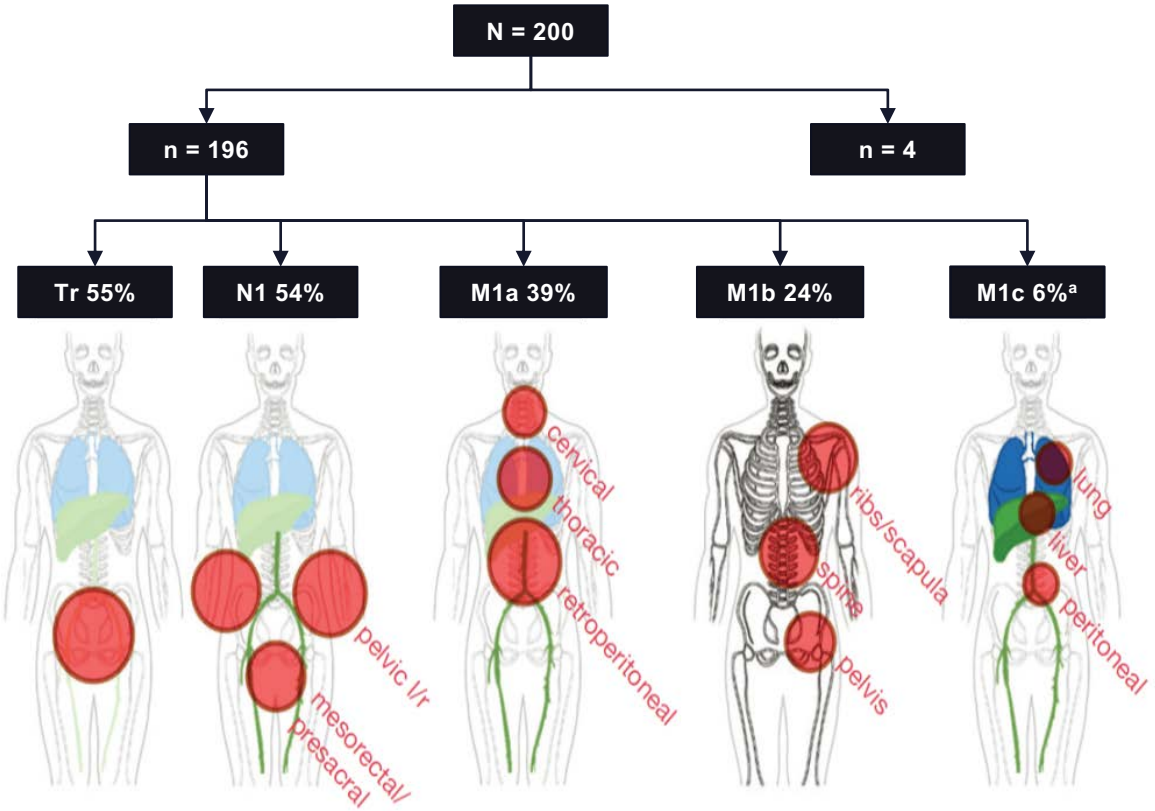
- Impt.' to know the results of the CARD trial: Improved benefit of use of cabazitaxel over abiraterone or enzalutamide as SOC in patients who had prior docetaxel within 12 months: improved pFS and overall survival
- Patient improvement: Mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.
- Dosing and administration: 20 mg/m2 IV Q 21 days (7 -10 cycles or until DLT or PD)
- Close monitoring for S/E imperative: **fatigue**, hypersensitivity reactions, nausea/vomiting, renal failure, **neutropenia w/wo fever**, **diarrhea**, **constipation,** hypotension, neuropathy, **hematuria**/cystitis, belching, heartburn, back pain.

Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

Novel Agents for mCRPC

- Poly(ADP-ribose) polymerase (PARP) inhibitors
  - Directed at targeting cancers with defective DNA-damage repair
  - Prostate cancer, most common defects in BRCA 1, BRCA 2 and ATM genes
  - Side effects include progressive anemia, fatigue, GI side effects indigestion, nausea/vomiting, diarrhea, headaches
- PSMA (prostate specific membrane antigen) targeted therapies
  - In combination with a number of molecules: Lutetium, radioactive iodine, T cell targeting combinations

PSMA-PET Results in Patients With High-Risk nmCRPC (nmCRPC, Negative Conventional Imaging, PSADT <10 mo)[1]



The size of the red circle is proportional to lesion prevalence.

PSMA-PET was positive in 196 of 200 (98%) patients; 55% of patients had any distant metastatic disease

Category Based on miTNM Stage, n (%)	All patients (N = 200)
M0	**91 (46)**
T0N0M0 (no PC lesion)	4 (2)
TrN0M0	48 (24)
T0N1M0	13 (7)
TrN1M0	26 (13)
Any M1	**109 (55)**
T0N0M1	31 (16)
T0N1M1	42 (21)
TrN0M1	9 (5)
TrN1M1	27 (14)
N/M disease extent	
Unifocal (1 lesion)	29 (15)
Oligometastatic (2-3 lesions)	28 (14)
Multiple/disseminated (≥ 4 lesions)	91 (46)

[a] Lung (n = 4), liver (n = 5), peritoneum (n = 4), connective tissue (n = 1).

1. Fendler WP et al. *Clin Cancer Res*. 2019;25:7448-7454.

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

Press Release – May 19, 2020

On May 19, 2020, the Food and Drug Administration approved olaparib for adult patients with deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC), who have progressed following prior treatment with enzalutamide or abiraterone.

Efficacy was investigated in PROfound (NCT02987543), an open-label, multicenter trial randomizing (2:1) 256 patients to olaparib 300 mg twice daily and 131 patients to investigator's choice of enzalutamide or abiraterone acetate. All patients received a GnRH analog or had prior bilateral orchiectomy. Patients were divided into two cohorts based on their HRR gene mutation status. Patients with mutations in either *BRCA1*, *BRCA2*, or *ATM* were randomized in Cohort A (N=245); patients with mutations among 12 other genes involved in the HRR pathway were randomized in Cohort B (N=142); those with co-mutations (Cohort A gene and a Cohort B gene) were assigned to Cohort A.

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-olaparib-hrr-gene-mutated-metastatic-castration-resistant-prostate-cancer

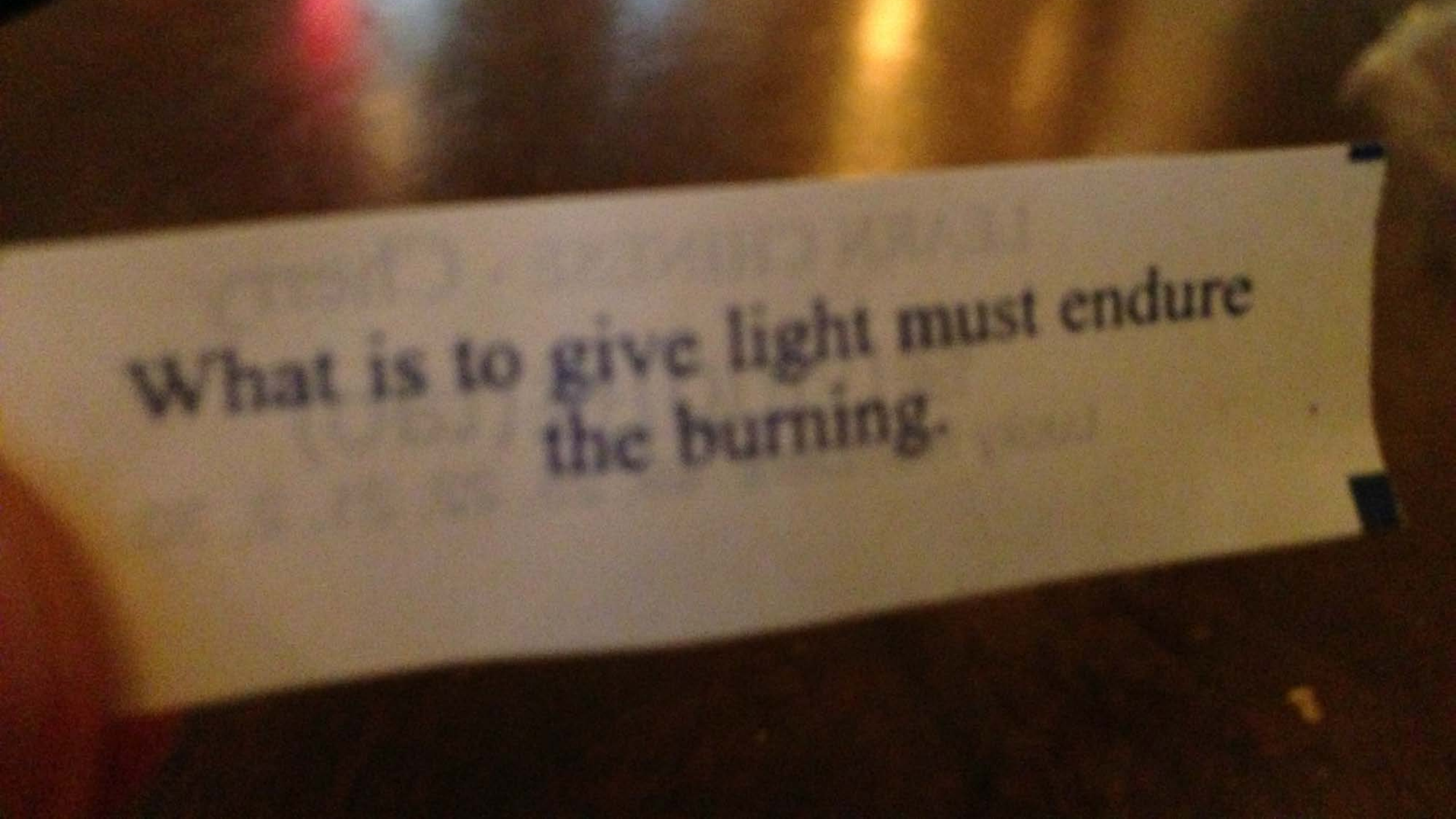
FDA grants accelerated approval to rucaparib for BRCA-mutated metastatic castration-resistant prostate cancer

Press Release – May 15, 2020

The Food and Drug Administration granted accelerated approval to rucaparib for patients with deleterious *BRCA* mutation (germline and/or somatic)-associated metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy.

Efficacy was investigated in TRITON2 (NCT02952534), an ongoing, multi-center, single arm clinical trial in 115 patients with *BRCA*-mutated (germline and/or somatic) mCRPC who had been treated with androgen receptor-directed therapy and taxane-based chemotherapy. Patients received rucaparib 600 mg orally twice daily and concomitant GnRH analog or had prior bilateral orchiectomy.

https://www.fda.gov/drugs/fda-grants-accelerated-approval-rucaparib-brca-mutated-metastatic-castration-resistant-prostate


What is to give light must endure
the burning.

Thank you for joining us!

CNE (NCPD) credit information will be emailed to each participant tomorrow morning.