Thank you for joining us.
The program will begin momentarily.

Role of Hormonal Therapy in the Management of Prostate Cancer

Tuesday, September 15, 2020
9:00 AM – 10:00 AM ET

ONS Oncology Nursing Society
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Faculty

Andrew J Armstrong, MD, ScM
Molly Kim, MSN, NP-C
Ellen Leidig, MSN, FNP-BC, RN
William K Oh, MD

Moderator

Neil Love, MD

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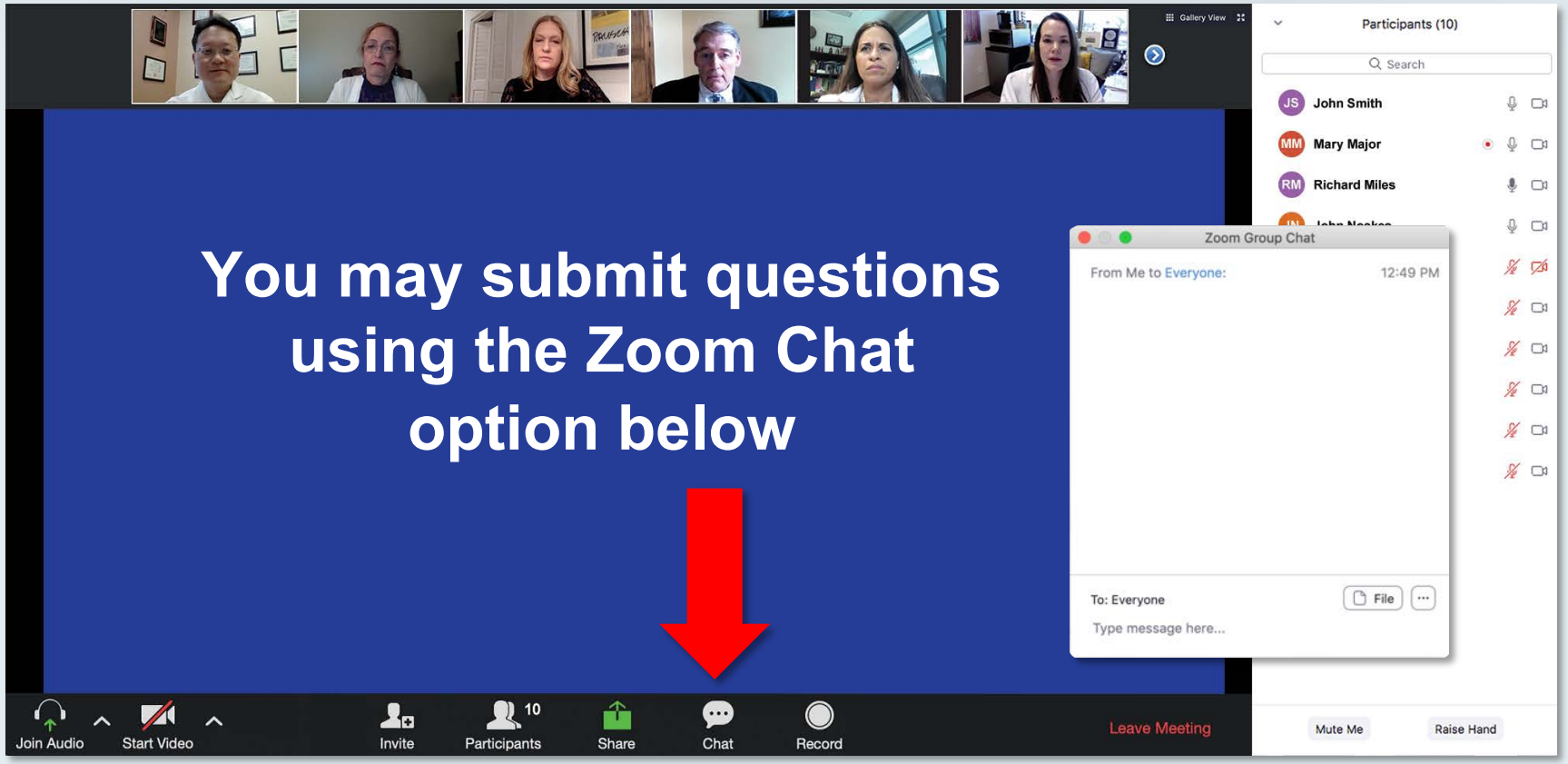
Dr Love and Faculty Encourage You to Ask Questions



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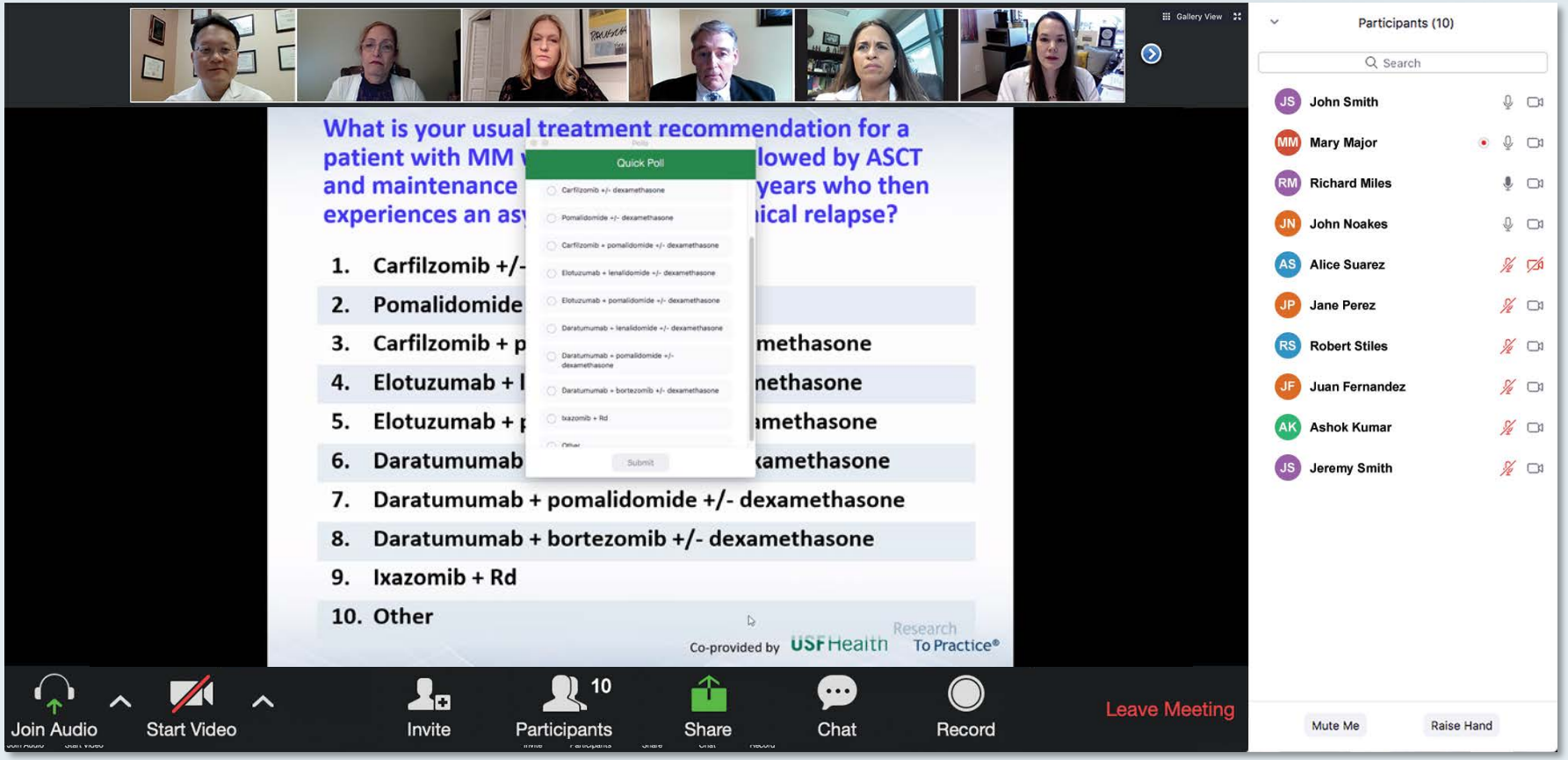

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Upcoming Live Webinars

Tuesday, September 15, 2020
5:00 PM – 6:00 PM ET

Management of Locally Advanced Non-Small Cell Lung Cancer

Faculty
Kelly EH Goodwin, MSN, RN, ANP-BC
David R Spigel, MD
Heather Wakelee, MD
Elizabeth S Waxman, RN, MSN, ANP-BC

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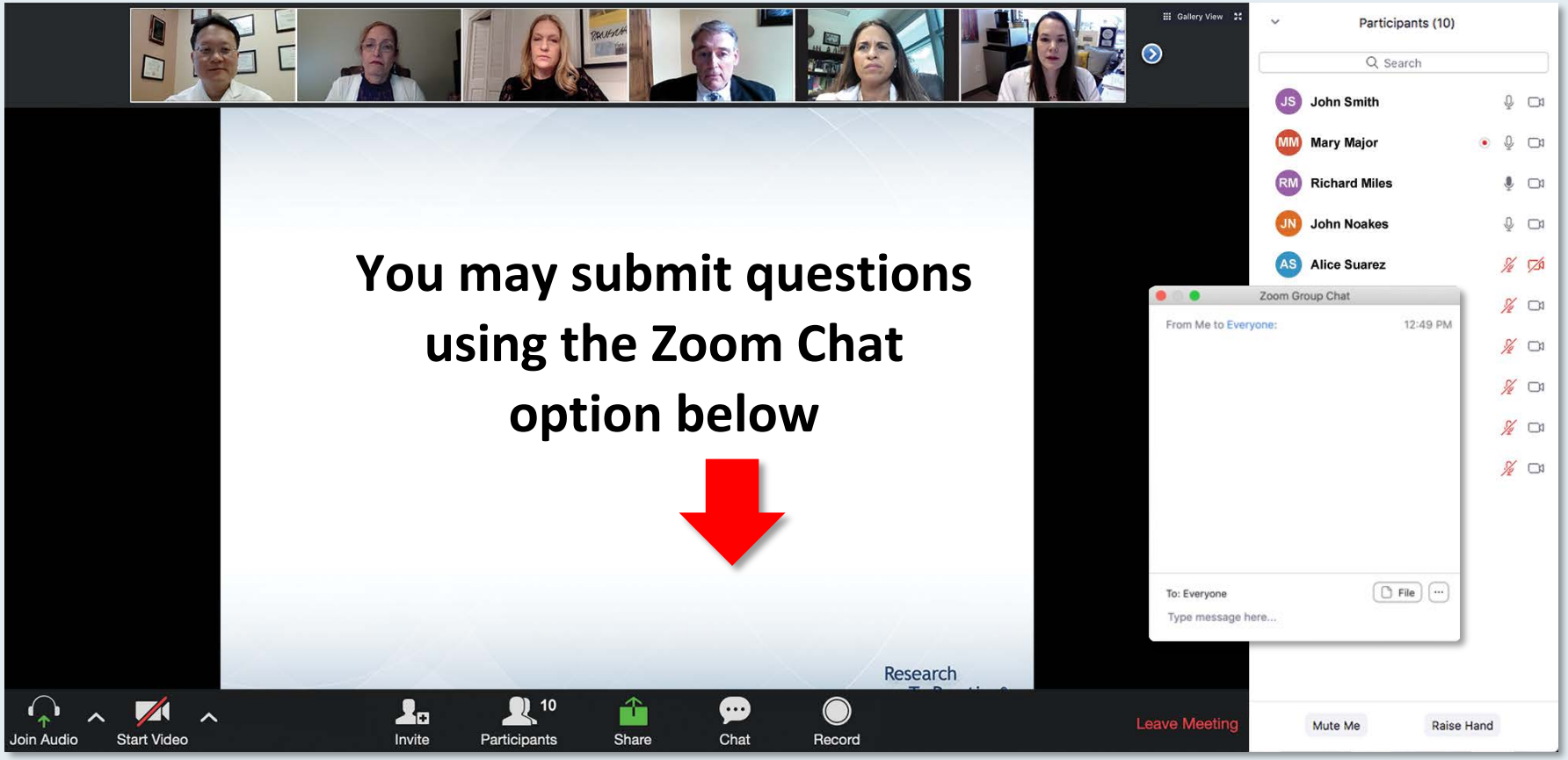

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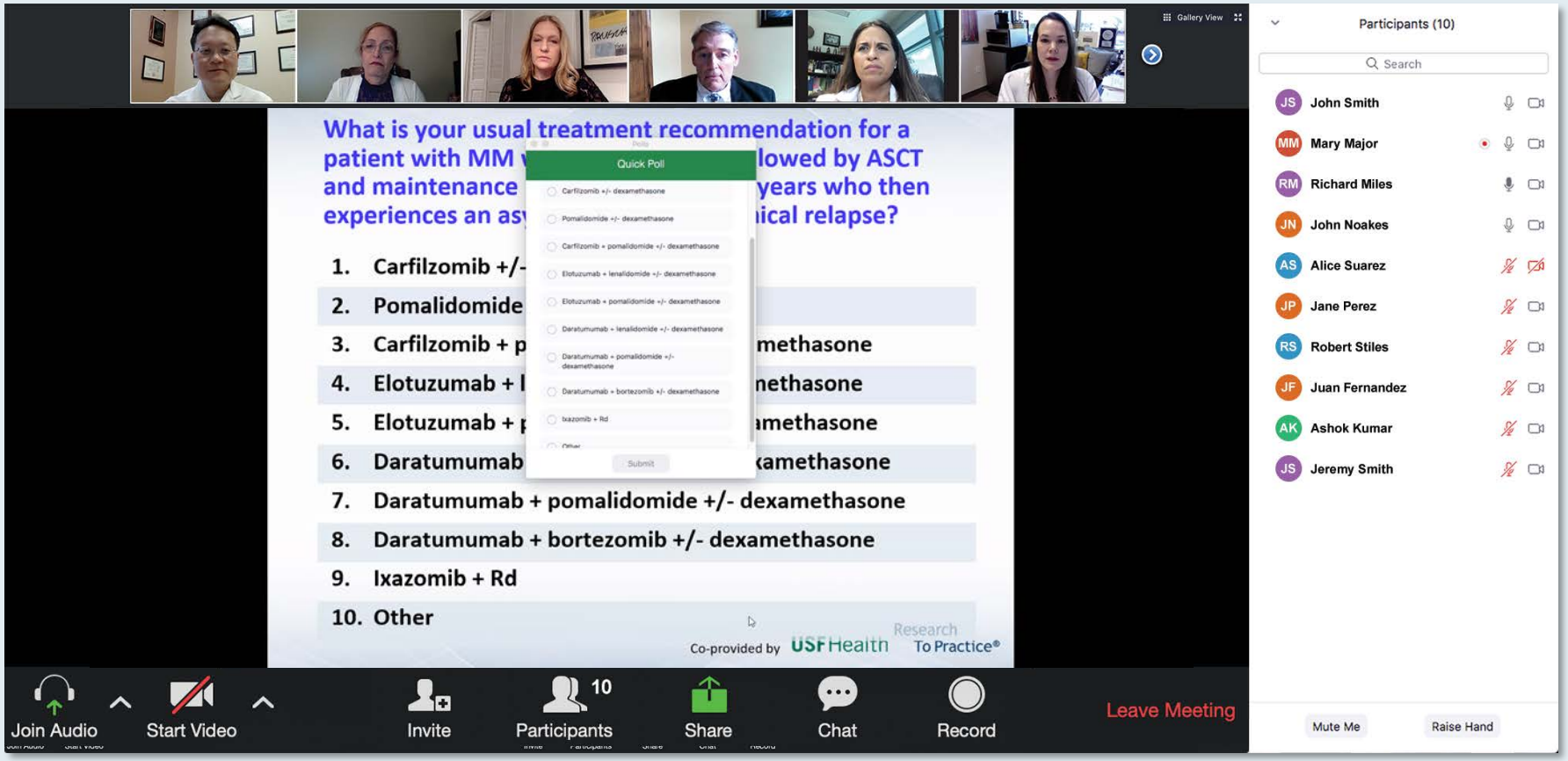

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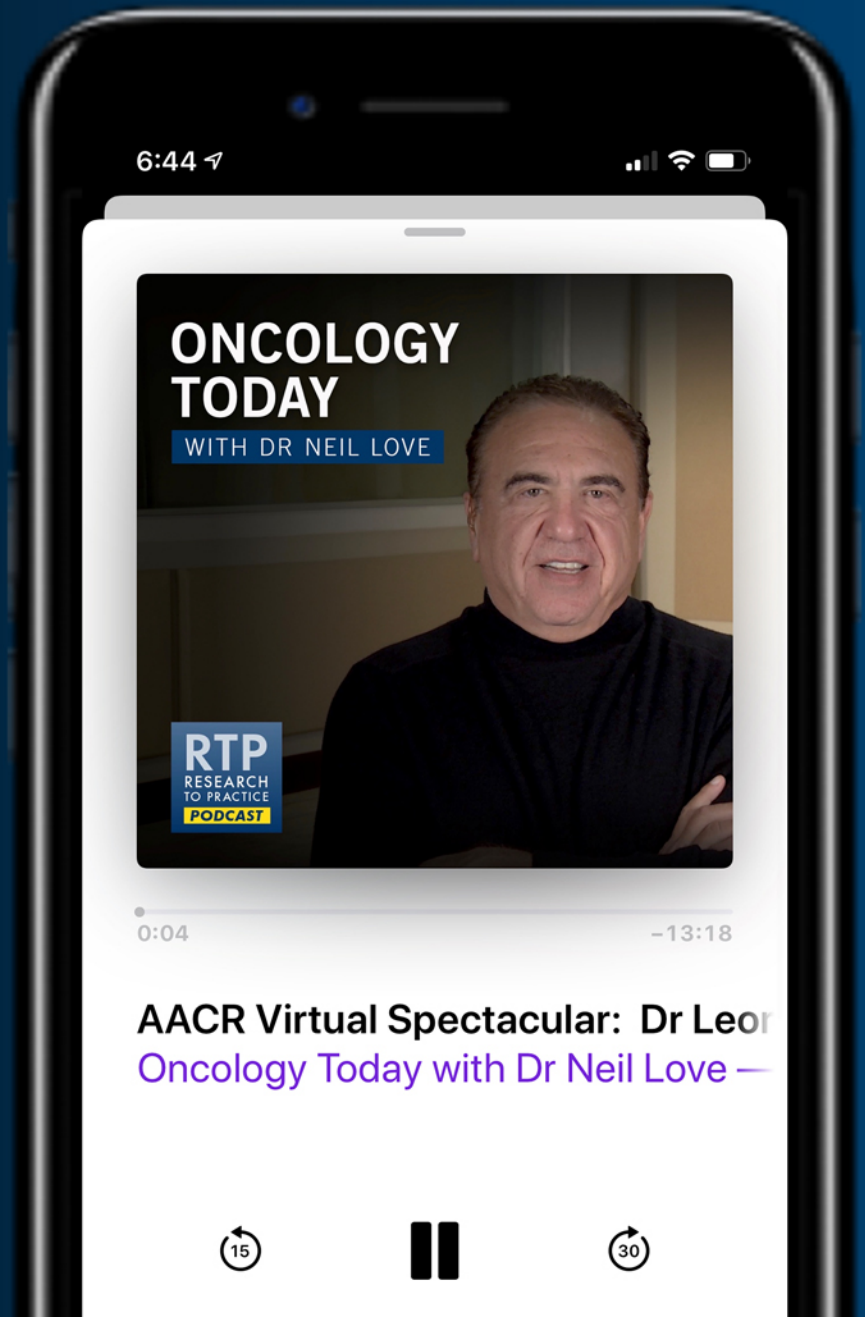

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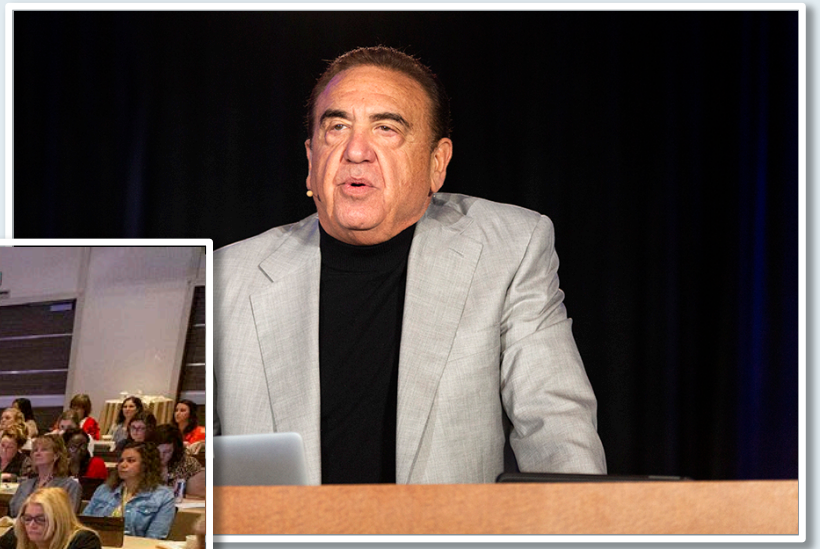

Role of Hormonal Therapy in the Management of Prostate Cancer

Case 1: A 73-year-old man with metastatic hormone-sensitive prostate cancer (mHSPC)

- Biology of prostate cancer and the androgen receptor
- Overview of androgen deprivation therapy (ADT) and its role in the management of prostate cancer
- Clinical and patient factors guiding the use of ADT alone or in combination with other treatment modalities
- Educating patients on the secondary side effects associated with ADT
- Addition of chemotherapy versus secondary hormonal therapy to ADT for the management of mHSPC
- Monitoring for and management of cardiovascular and CNS-related events in patients receiving hormonal therapy

Case 2: A 55-year-old man with metastatic castration-resistant prostate cancer (mCRPC)

- Definition of castration-resistant disease and current role of secondary hormonal therapies in the treatment of mCRPC
- Nonhormonal interventions (sipuleucel-T, radium 223, taxanes)

Case 3: A 77-year-old man with M0 prostate cancer

- Management of initial PSA relapse
- Management of PSA progression; choice of antiandrogen therapy

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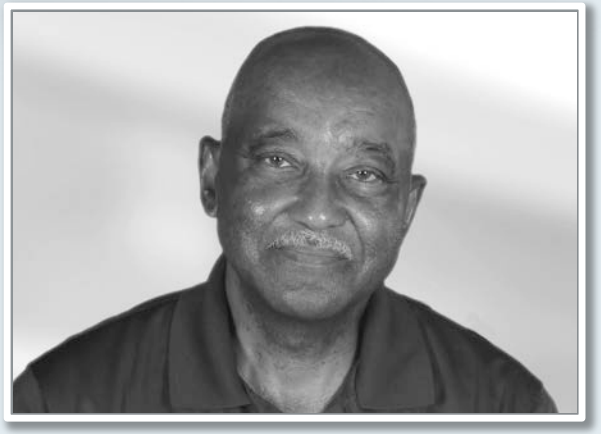
Case Presentation: A 73-year-old man with hormone-sensitive metastatic prostate cancer



Special Considerations

- Wife died 1 year ago from breast cancer at the age of 72
- Has no close family
- Currently out of work as a chef in a restaurant and is very concerned about finances as well as exposure to COVID-19
- Never underwent PSA or rectal exam
- Presents with back pain and is found to have multiple bone metastases, high PSA and an enlarged prostate (biopsy: Gleason 6 [3 + 3] prostate cancer)

Key Treatment Decision: ADT alone or with enzalutamide, apalutamide, abiraterone or docetaxel

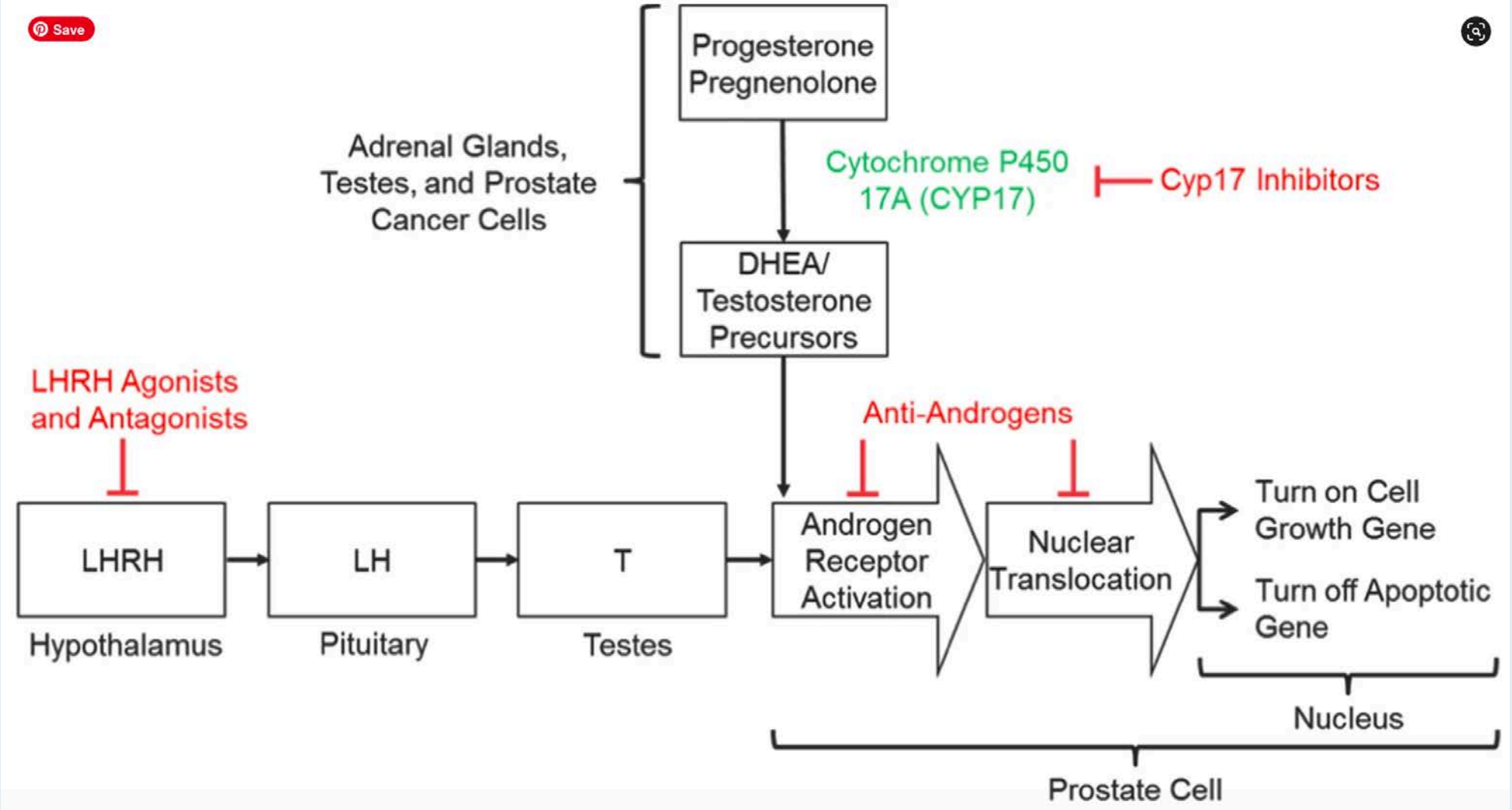
In general, which treatment strategy would be best for this patient?

a. Androgen deprivation therapy (ADT) alone
b. ADT plus chemotherapy
c. ADT plus secondary hormonal therapy
d. Other

To what extent do you believe the COVID-19 pandemic would affect this decision?

a. Significantly
b. Somewhat
c. Minimally or not at all

Mechanisms of Androgen Signaling Inhibition



Crawford DE et al. *Prostate Cancer and Prostatic Diseases* 2019;22:24-38.

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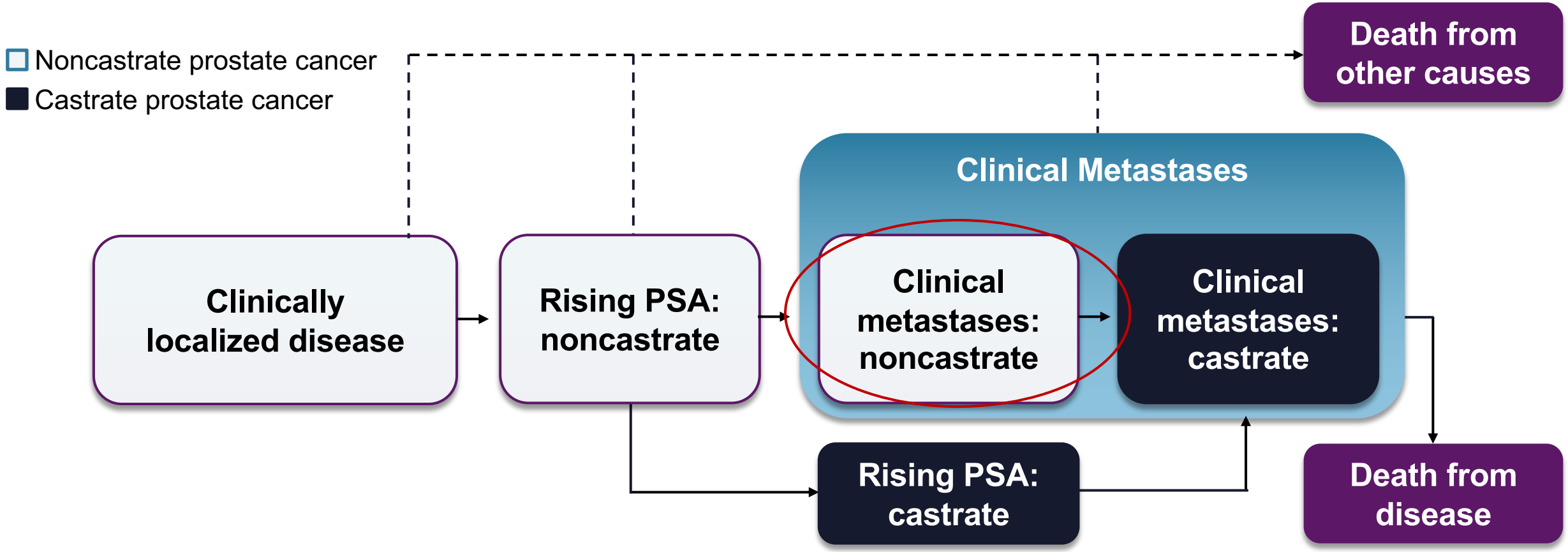
Clinical Disease States Model of Prostate Cancer[1]



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

Courtesy of Matthew R Smith, MD, PhD

Clinical Decision-Making in Hormone-Sensitive Metastatic Disease

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

Courtesy of Robert Dreicer, MD, MS

Treatment Options for mHSPC 2020

- ADT plus docetaxel
- ADT plus abiraterone acetate & prednisone
- ADT plus apalutamide
- ADT plus enzalutamide
- ADT alone?
- Treat the primary in addition to one of above?
- Treat oligometastatic sites?

How to decide?

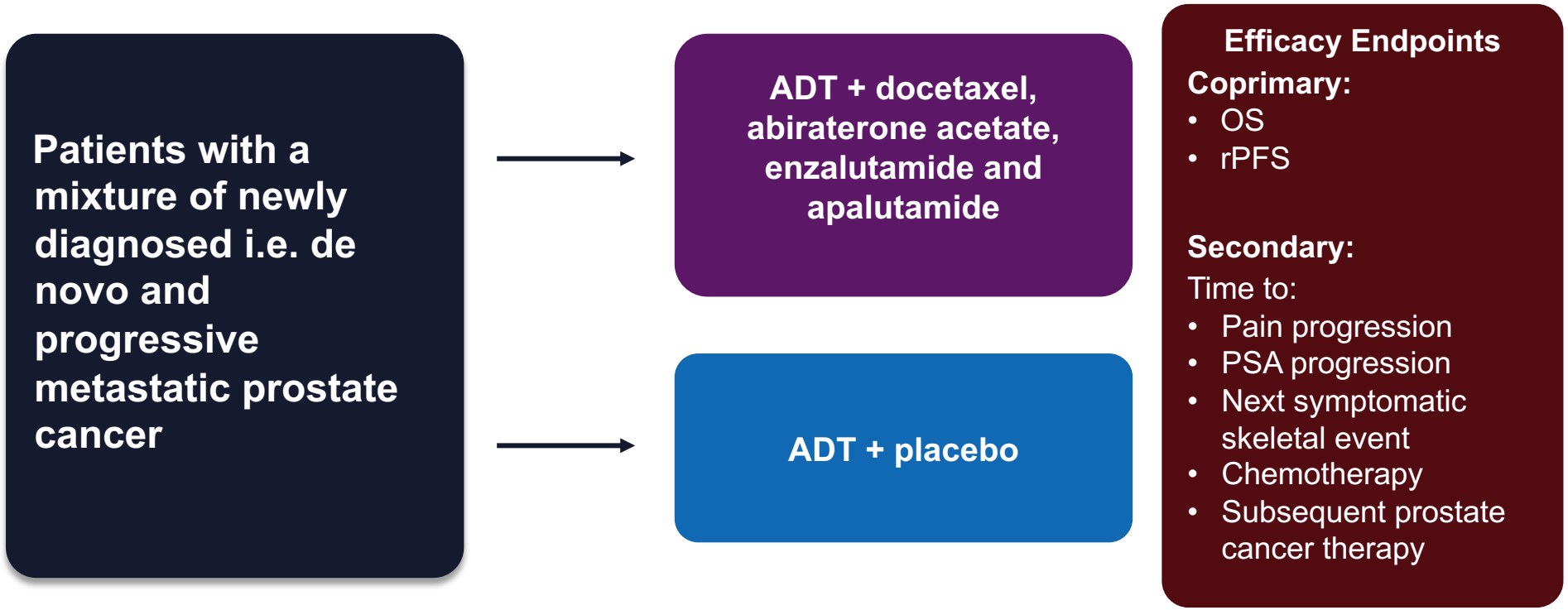
Courtesy of Neal Shore, MD

Choosing Oral Antiandrogen Therapy

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

Courtesy of Kara M Olivier, NP, APRN-BC

Phase 3 Studies in Hormone-Sensitive Metastatic Prostate Cancer



Survival benefit from combo therapy from 6 randomized studies is a median increase in greater than 1 year

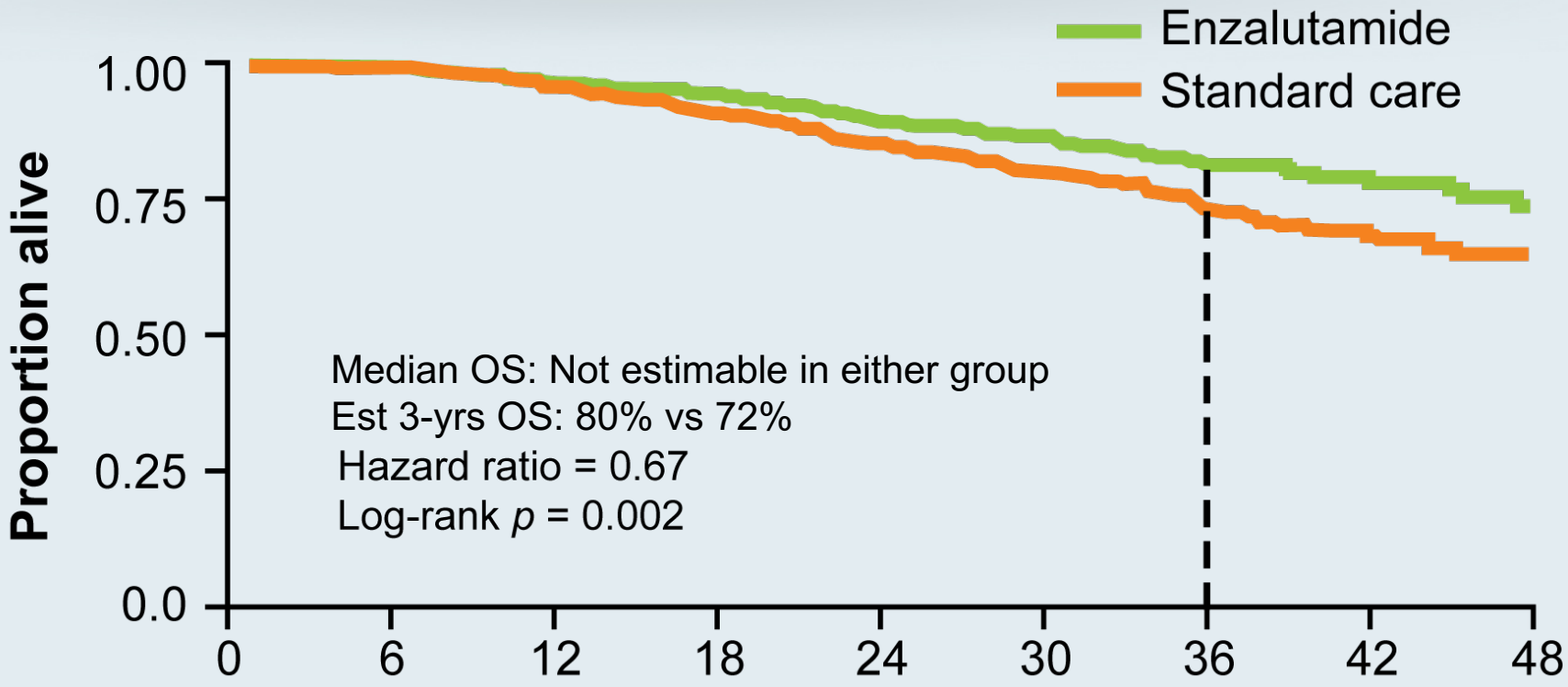
Sweeney CJ et al. *N Engl J Med*. 2015;373:737-746, Fizazi K et al. *N Engl J Med.* 2017;377:352-360 , James N, et al. Lancet. 2015, . James ND, et al. N Engl J Med 2017;377:338-351, Armstrong A, et al JCO 2019, Chi K et al. NEJM 2019

Courtesy of Robert Dreicer, MD

ENZAMET: ADT + Enzalutamide or Standard Nonsteroidal Antiandrogen
Primary Endpoint: Overall Survival

A Mixed Bag

- High and Low Volume
- *De novo* vs Metach
- Concurrent Docetaxel
- Many Permutations



Number at risk

Standard care	562	551	531	501	452	311	174	86	32
Enzalutamide	563	558	541	527	480	340	189	106	45

Davis ID et al. *N Engl J Med* 2019;381(2):121-31.

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

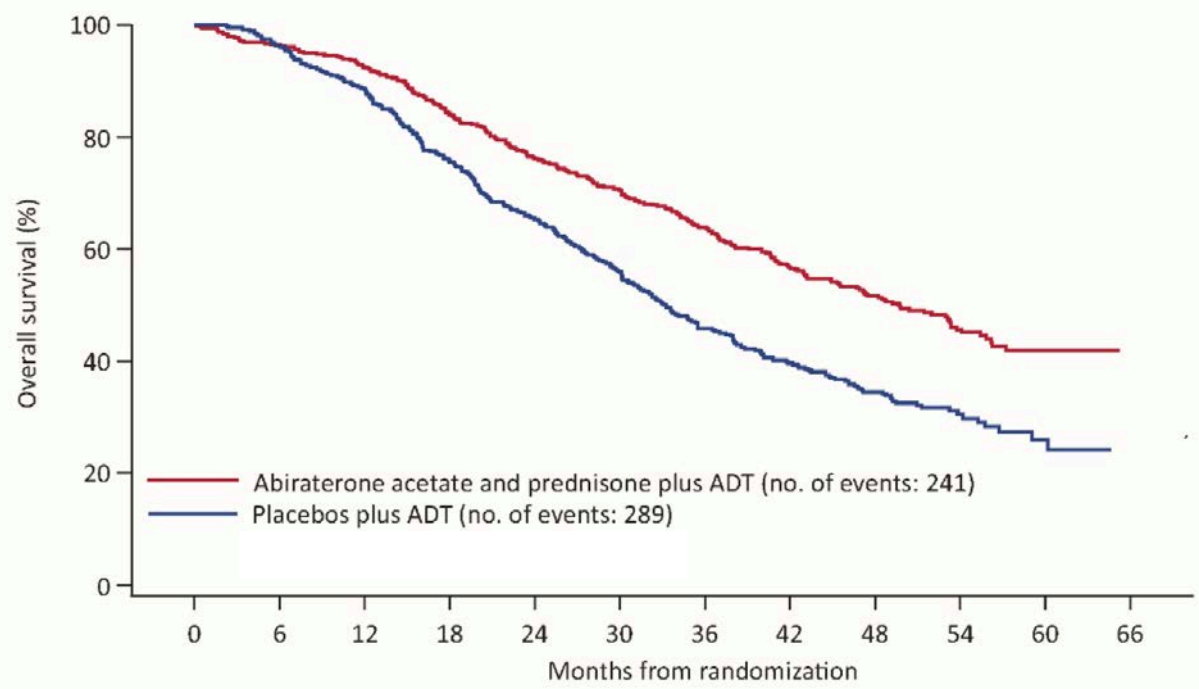
	ARCHES (N = 1150)		TITAN (N = 1052)	
Characteristics	• 2/3rd high volume • 17% prior docetaxel • 25% prior RP/XRT		• 2/3rd high volume • 10% prior docetaxel • 17% prior RP/XRT	
	ADT + enzalutamide (n = 574)	**ADT (n = 576)**	**ADT + apalutamide (n = 525)**	**ADT (n = 527)**
Radiographic PFS	NR	19.0 mo	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.

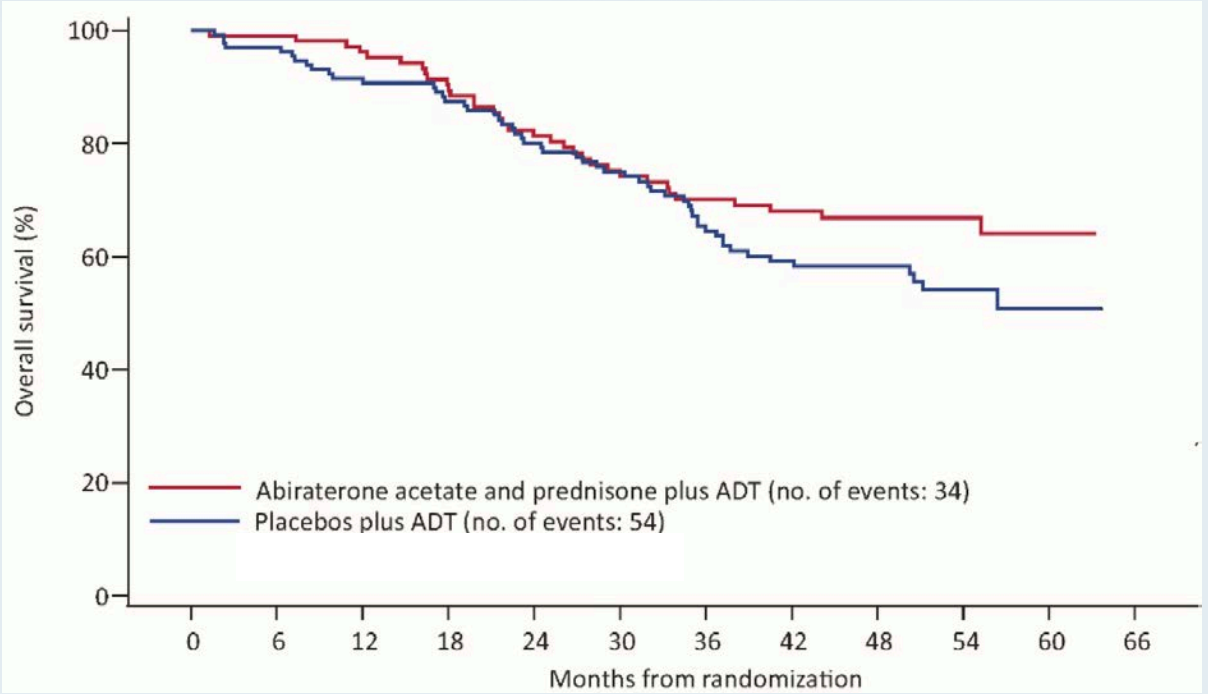
LATITUDE Final Overall Survival Analysis By Volume of Disease (CHAARTED definition*)

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

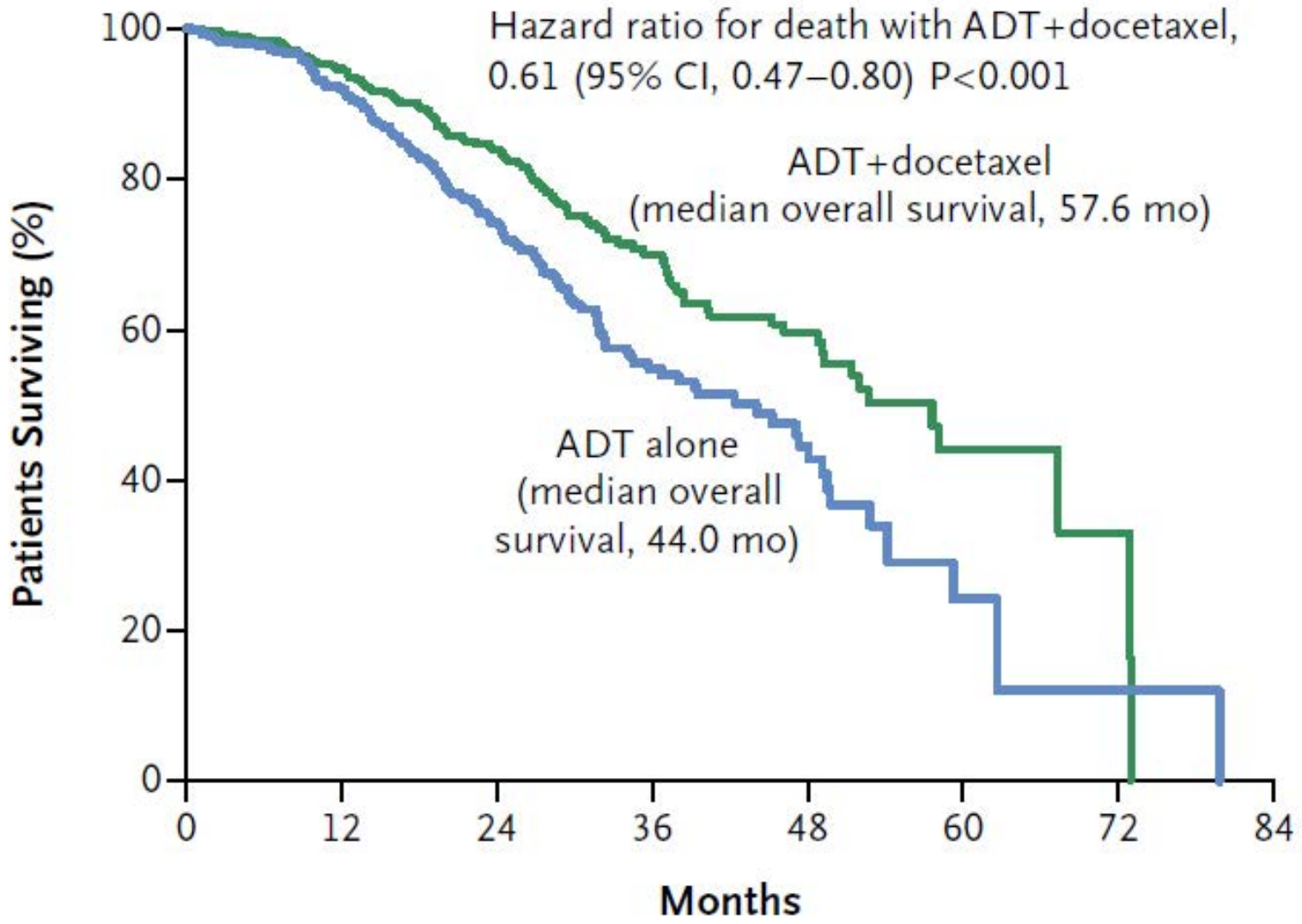


	ADT + AA + P (n = 110)	ADT + Placebo (n = 133)	HR	*p*-value
mOS	Not reached	Not reached	0.72	0.1242

*CHAARTED definition of low vs high volume: Presence of visceral mets and/or ≥ 4 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.

CHAARTED: Docetaxel for mHSPC



Sweeney et al. *N Engl J Med* 2015;373:737-46.

Courtesy of Matthew R Smith, MD, PhD

Summary of Risks of mHSPC Rx:

No head-to-head trials showing one is more effective than the other in terms of overall survival

Agent	Side Effects	Quality of Life	Financial Costs
Abiraterone	• Hypertension • Liver dysfunction • Hyperkalemia • Fluid retention/edema	• Stable over time • Potentially maintains better QOL over time	• Next cheapest option • Available in generic • Continuous treatment
Enzalutamide	• Fatigue • Hypertension • Seizure risk • Cardiac risk	• Stable over time	• More expensive • Not available in generic • Continuous treatment
Apalutamide	• Rash • Hypothyroidism • Fracture	• Stable over time	• More expensive • Not available in generic • Continuous treatment

Courtesy of David F Penson, MD, MPH

In general, which treatment strategy would be best for this patient?

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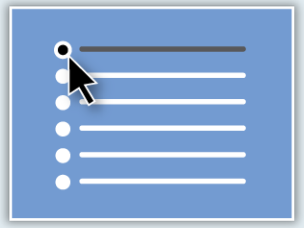

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To what extent do you believe the COVID-19 pandemic would affect this decision?

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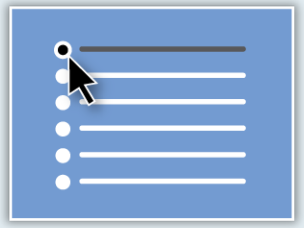

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For a patient with prostate cancer for whom androgen deprivation therapy (ADT) is being initiated, what potential side effects do you generally counsel him about?
(Ms Kim)

A patient who has recently started ADT for prostate cancer complains that he has been experiencing hot flashes that have interrupted his sleep and contributed to fatigue. What would you recommend? (Ms Leidig)

 ANDREW J ARMSTRONG, MD, SCM	Exercise first during the day, consider megace, an SSRI, ceiling/bedside fan, low-dose vitamin E
 CELESTIA S HIGANO, MD	Venlafaxine 37.5 mg BID
 MOLLY KIM, MSN, NP-C	Discuss role of black cohosh vs venlafaxine for relief of hot flashes
 ELLEN LEIDIG, MSN, FNP-BC, RN	Recommend black cohosh or flaxseed oil, behavioral modification (use of fan and cold glass of water). If ineffective, we may prescribe interventions such as venlafaxine, gabapentin or megace
 WILLIAM K OH, MD	Black cohosh → venlafaxine
 A OLIVER SARTOR, MD	Oxybutynin at 5 mg starting dose

In what situations is ADT combined with radiation therapy for patients with locally advanced prostate cancer? (Ms Leidig)

In general, how do you respond to a patient who is receiving ADT for prostate cancer and asks how long he can expect to experience side effects after treatment has been discontinued?

 ANDREW J ARMSTRONG, MD, SCM	3 to 12 months (sometimes longer due to age, duration of ADT)
 CELESTIA S HIGANO, MD	Depends on several factors, but about 3 to 6 months
 MOLLY KIM, MSN, NP-C	Varies by patient (side effects dissipate as testosterone recovers)
 ELLEN LEIDIG, MSN, FNP-BC, RN	Varies by patient (age, pretreatment testosterone levels, etc)
 WILLIAM K OH, MD	Side effects may last as long as duration patient was on ADT
 A OLIVER SARTOR, MD	Side effects dependent on testosterone recovery, which depends on duration of therapy and other factors

Do you generally recommend nutritional supplements for patients with prostate cancer who are starting ADT? If so, which supplements would you recommend? (Ms Kim)

 ANDREW J ARMSTRONG, MD, SCM	Yes (vitamin D3 at least 800 IU plus calcium 1,200 mg/d)
 CELESTIA S HIGANO, MD	Yes (calcium 1,200 mg/d and vitamin D 1,000 IU/d)
 MOLLY KIM, MSN, NP-C	Yes (refer to nutritionist)
 ELLEN LEIDIG, MSN, FNP-BC, RN	Yes (calcium 1,200 mg and vitamin D 800 IU daily)
 WILLIAM K OH, MD	No (diet but not supplements per se)
 A OLIVER SARTOR, MD	Calcium 1,000 mg per day and vitamin D at least 400 IU per day

A 73-year-old man presents with a PSA of 660 ng/dL and difficulty urinating, and biopsy confirms Gleason 8 prostate cancer. Scans show limited bone metastases in the ribs and pelvis. Which therapy would you recommend adding to ADT for this patient? (Dr Armstrong)

An 85-year-old man with a remote history of a hemorrhagic stroke is found to have metastatic prostate cancer with a PSA of 1,200 ng/dL and diffuse bone metastases. He prefers to avoid chemotherapy if possible. Which therapy would you recommend adding to ADT for this patient? (Dr Armstrong)

How would you compare the rapidity of responses observed with secondary hormonal therapy (eg, abiraterone, enzalutamide or apalutamide) to that with docetaxel in patients receiving those agents in combination with ADT for metastatic hormone-sensitive prostate cancer (mHSPC)?

 ANDREW J ARMSTRONG, MD, SCM	Secondary hormonal therapy yields more rapid responses
 CELESTIA S HIGANO, MD	Cannot distinguish since ADT itself will result in rapid responses alone
 MOLLY KIM, MSN, NP-C	Docetaxel yields more rapid responses
 ELLEN LEIDIG, MSN, FNP-BC, RN	About the same
 WILLIAM K OH, MD	Docetaxel yields more rapid responses
 A OLIVER SARTOR, MD	Secondary hormonal therapy yields more rapid responses

How would you compare the global tolerability/toxicity of abiraterone, enzalutamide and apalutamide for patients with mHSPC?

Do you believe intermittent ADT is as effective and safe as continuous ADT in men receiving long-term treatment for metastatic prostate cancer?

In general, do you initiate calcium and vitamin D supplementation for your patients with prostate cancer preparing to receive secondary hormonal therapy?

 ANDREW J ARMSTRONG, MD, SCM	Yes
 CELESTIA S HIGANO, MD	Yes
 MOLLY KIM, MSN, NP-C	Yes
 ELLEN LEIDIG, MSN, FNP-BC, RN	Yes
 WILLIAM K OH, MD	Yes
 A OLIVER SARTOR, MD	Yes

In general, do you initiate antiresorptive agents such as zoledronic acid or denosumab for your patients with prostate cancer preparing to receive secondary hormonal therapy?

 ANDREW J ARMSTRONG, MD, SCM	Yes, but only in the mCRPC setting, not mHSPC unless they have osteopenia/osteoporosis or a prior fracture
 CELESTIA S HIGANO, MD	Yes
 MOLLY KIM, MSN, NP-C	Yes, in patients with mCRPC to the bone or if patient has osteopenia/osteoporosis
 ELLEN LEIDIG, MSN, FNP-BC, RN	Yes (as appropriate, would obtain DXA scan and based on results treat with antiresorptive agents)
 WILLIAM K OH, MD	Yes
 A OLIVER SARTOR, MD	Yes

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- Clinical and patient factors guiding the use of ADT alone or in combination with other treatment modalities
- Educating patients on the secondary side effects associated with ADT
- Addition of chemotherapy versus secondary hormonal therapy to ADT for the management of mHSPC
- Monitoring for and management of cardiovascular and CNS-related events in patients receiving hormonal therapy

Case 2: A 55-year-old man with metastatic castration-resistant prostate cancer (mCRPC)

- Definition of castration-resistant disease and current role of secondary hormonal therapies in the treatment of mCRPC
- Nonhormonal interventions (sipuleucel-T, radium 223, taxanes)

Case 3: A 77-year-old man with M0 prostate cancer

- Management of initial PSA relapse
- Management of PSA progression; choice of antiandrogen therapy

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Case Presentation: A 55-year-old man with castration-resistant metastatic prostate cancer

Special Considerations

- Grandson who is 4 years old currently lives with him and his wife
- Interested in alternative, complementary strategies, particularly supplements and diet, but is open to other approaches
- Previous history
  - Radical prostatectomy
  - PSA recurrence: Radiation therapy
  - Further progression: ADT plus docetaxel
  - Further progression: Widespread bone metastases

Key Treatment Decision: Choice of systemic therapy — enzalutamide, abiraterone, chemotherapy, sipuleucel-T, radium-223

In general, which treatment would be best for this patient?

a. Sipuleucel-T
b. Chemotherapy
c. Enzalutamide
d. Apalutamide
e. Abiraterone
f. Radium-223
g. Other

To what extent do you believe the COVID-19 pandemic would affect this decision?

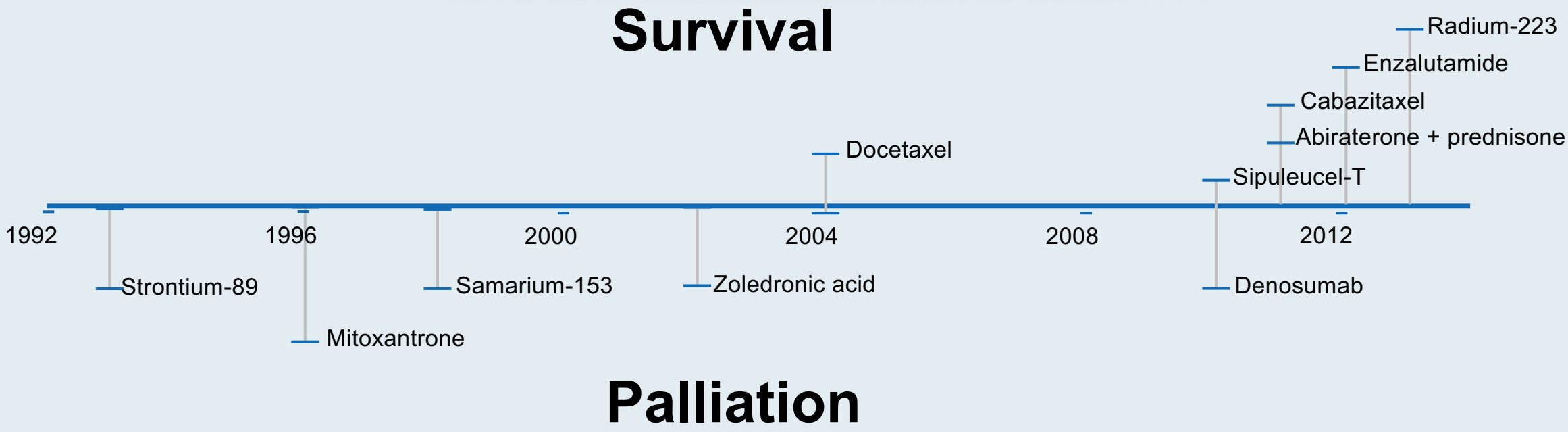
a. Significantly
b. Somewhat
c. Minimally or not at all

Therapeutic Decision-Making in 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

Timeline of FDA Approvals in mCRPC

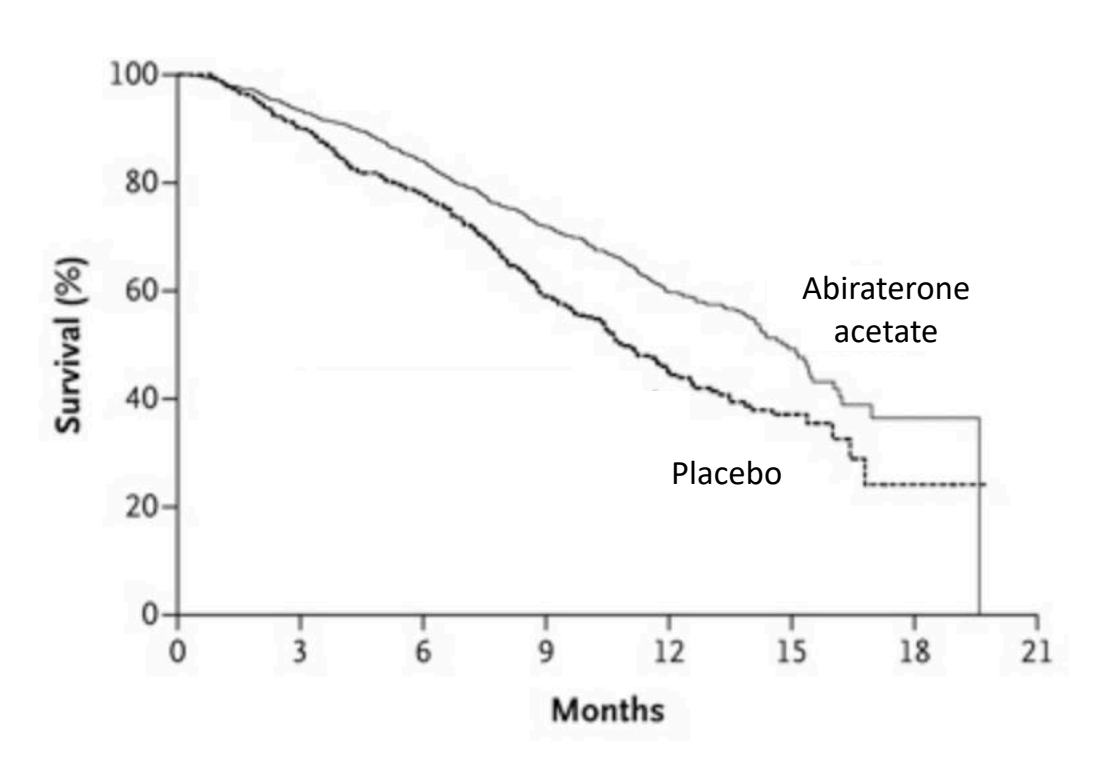


Metastatic disease was defined by conventional imaging (eg, bone scan, CT scans)

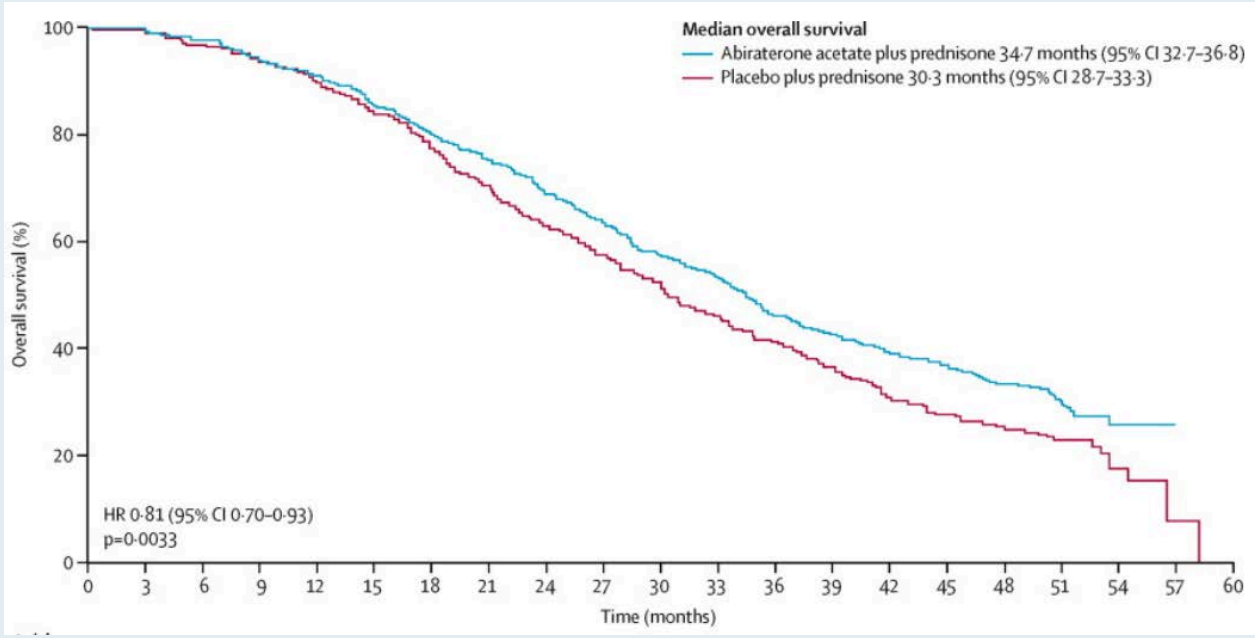
Courtesy of Matthew R Smith, MD, PhD

Phase III Trials of Abiraterone Acetate for mCRPC: Overall Survival

COU-AA-301: Previously Treated with Docetaxel



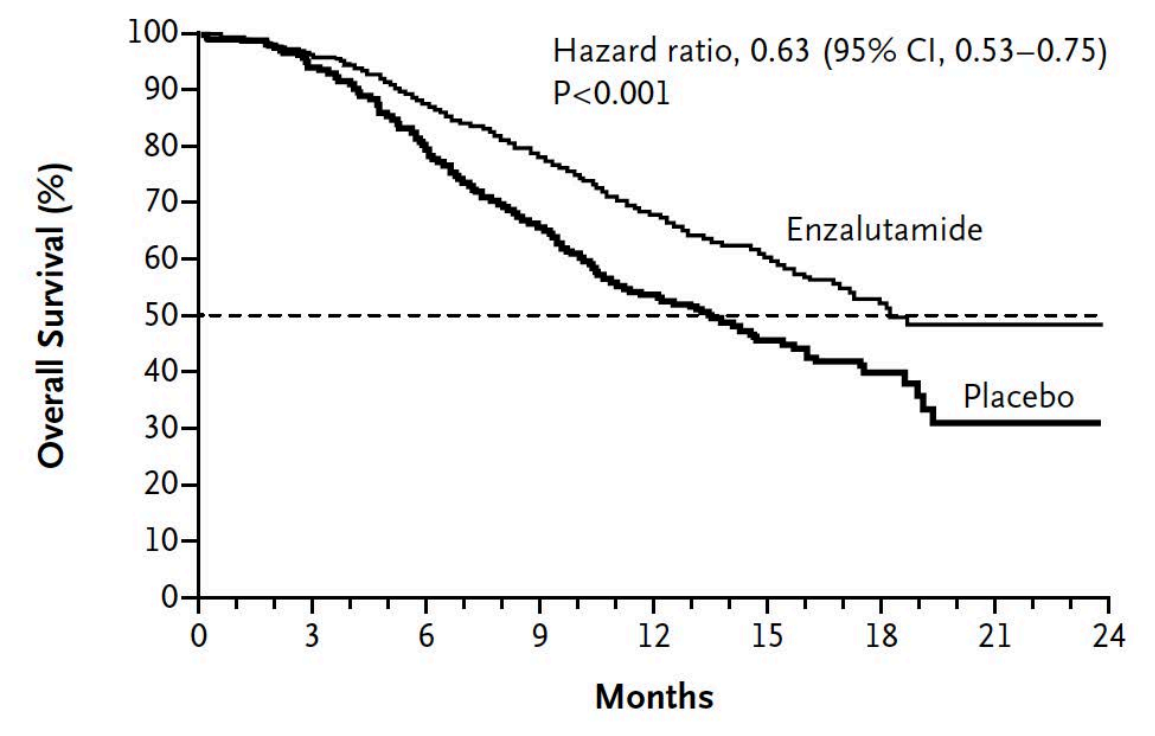
COU-AA-302: No Prior Chemotherapy



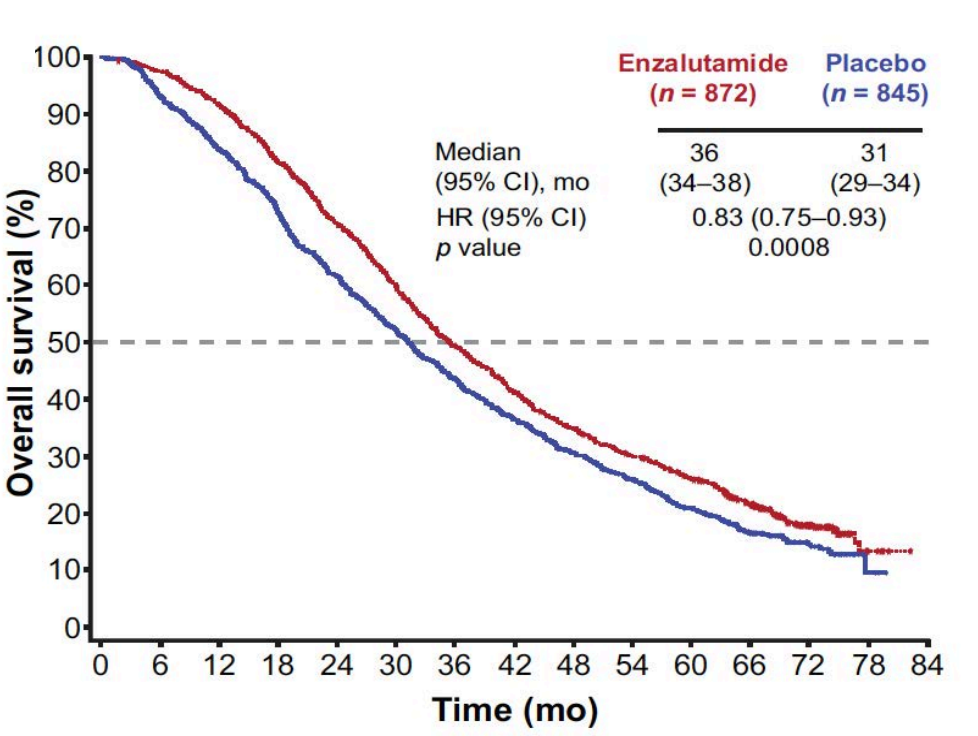
de Bono JS et al. *N Engl J Med* 2011;364(21):1995-2005; Ryan CJ et al. *Lancet Oncol* 2015;16(2):152-60.

Phase III Trials of Enzalutamide for mCRPC: Overall Survival

AFFIRM: Previously Treated with Docetaxel



PREVAIL: No Prior Chemotherapy



Scher HI et al. *N Engl J Med* 2012; 367(13):1187-97; Armstrong AJ et al. *Eur Urol* 2020;78:347-57.

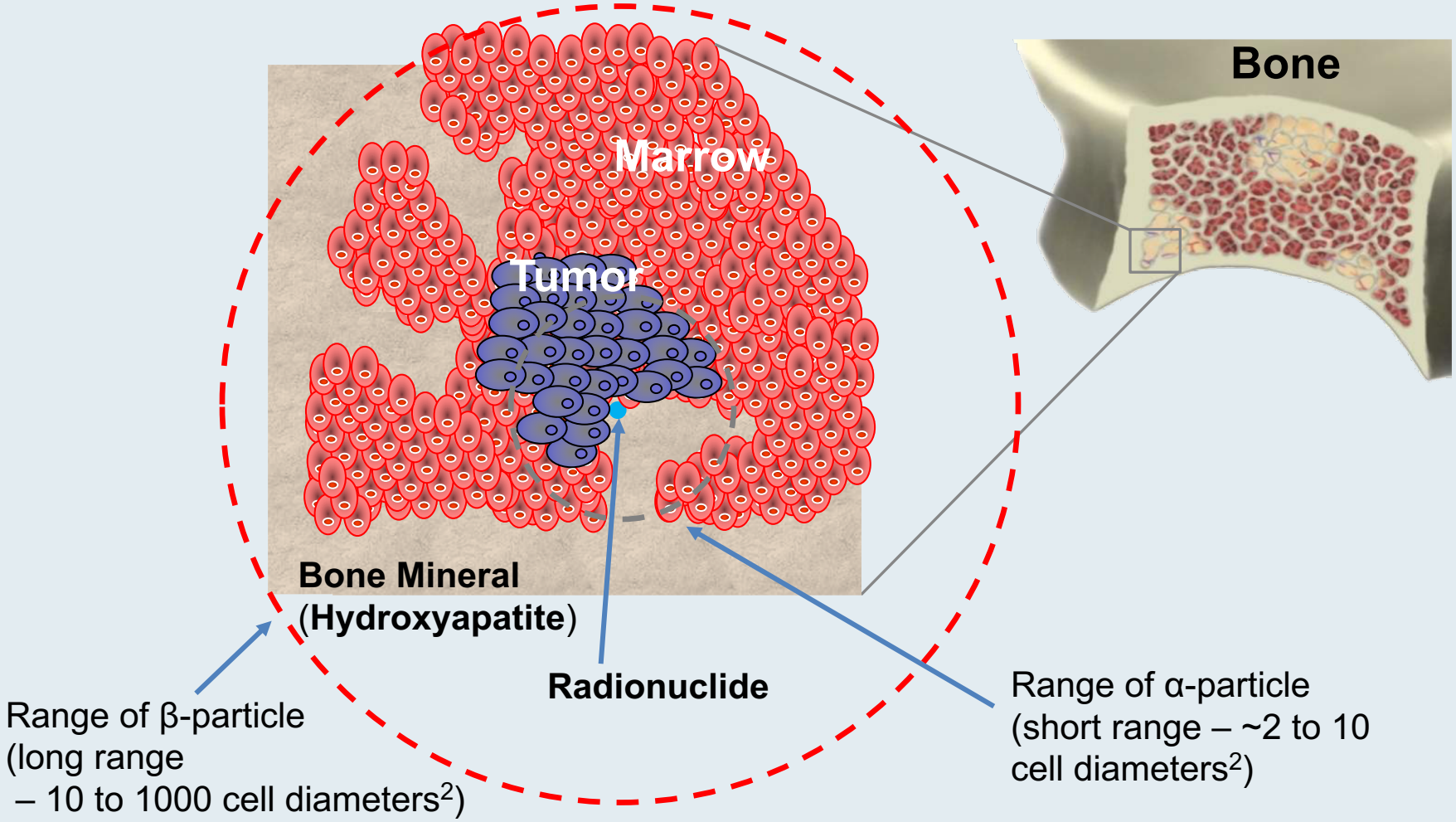
Selected FDA-Approved Drugs in Advanced Prostate Cancer

- 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 metastastic 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]

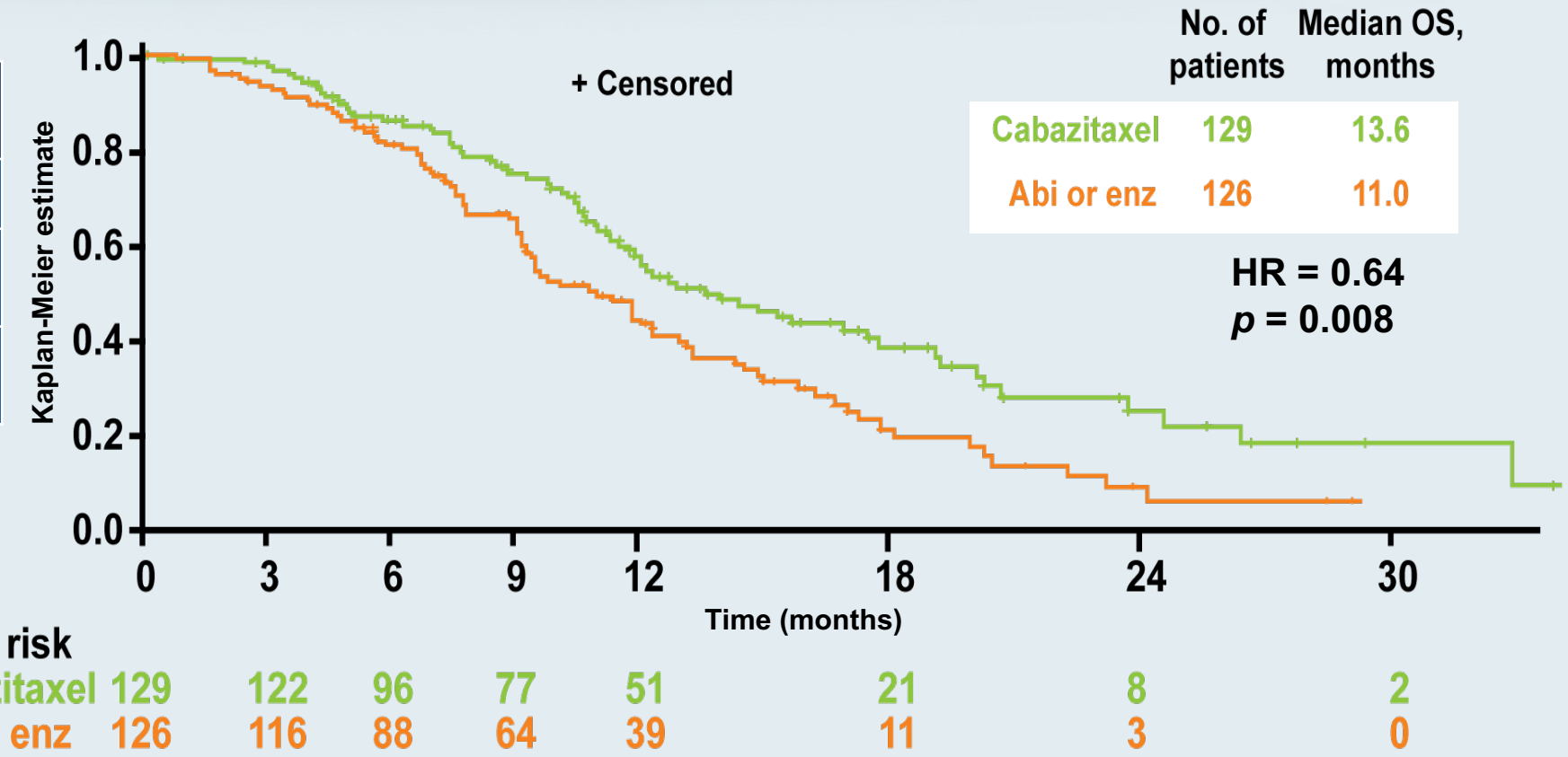


References: 1. Henriksen G, et al. *Cancer Res*. 2002;62:3120–3125. **2.** Brechbiel MW. *Dalton Trans*. 2007;43:4918-4928.

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%

Overall survival (key secondary endpoint)



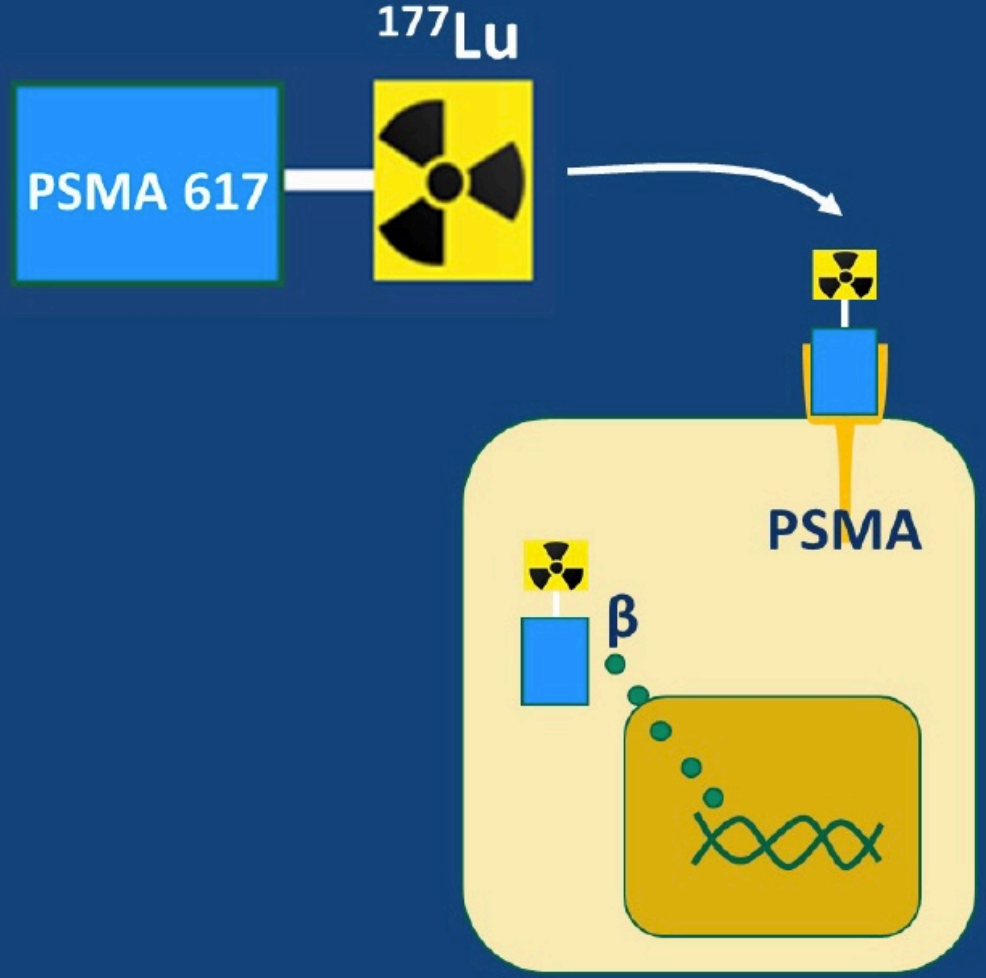
- CARD met its primary objective: Cabazitaxel more than doubled rPFS versus abiraterone or enzalutamide

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

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

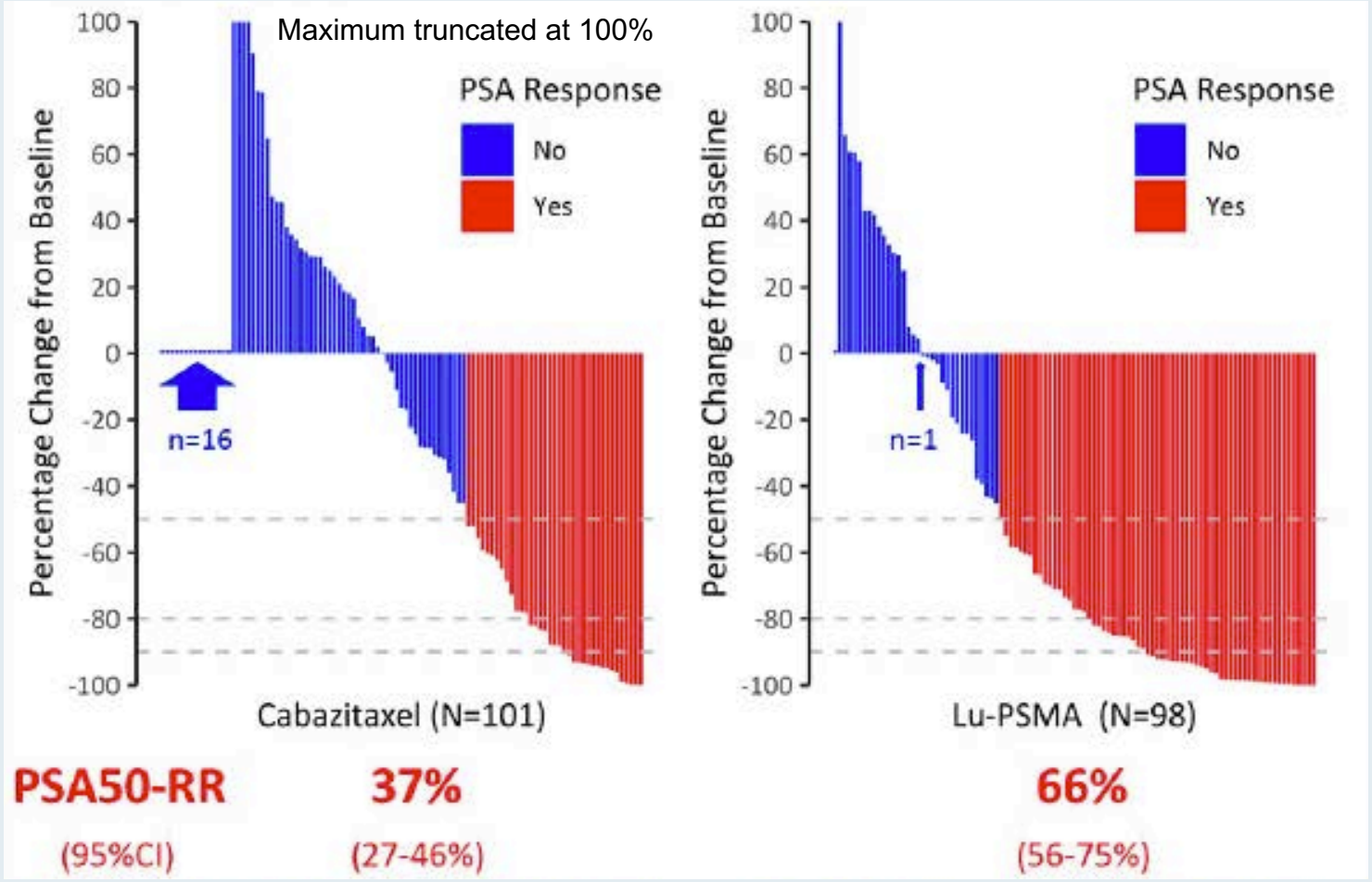
^{177}Lu-PSMA-617 is a small molecule RLT targeting PSMA



Wise DR. ASCO 2020 Highlights of the Day: Genitourinary Cancer (Prostate)

TheraP Study: ^{177}Lu-PSMA-617 (Lu-PSMA) Theranostic versus Cabazitaxel for Metastatic Castration-Resistant Prostate Cancer (mCRPC) Progressing After Docetaxel

Best PSA Response



Hofman MS et al. ASCO 2020;Abstract 5500.

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

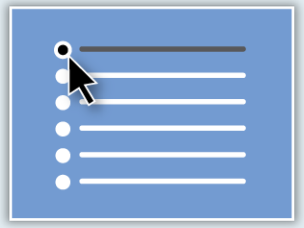
The Food and Drug Administration granted accelerated approval to rucaparib for patients with deleterious *BRCA* mutation (germline and/or somatic)-associated metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor-directed therapy and a taxane-based chemotherapy.

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

In general, which treatment would be best for this patient?

a. Sipuleucel-T
b. Chemotherapy
c. Enzalutamide
d. Apalutamide
e. Abiraterone
f. Radium-223
g. Other

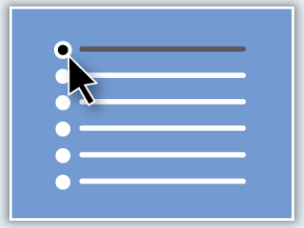


To what extent do you believe the COVID-19 pandemic would affect this decision?

a. Significantly

b. Somewhat

c. Minimally or not at all



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A 67-year-old man receiving 3 blood pressure medications for refractory hypertension presents with metastatic castration-resistant prostate cancer (mCRPC) with moderately symptomatic metastatic disease to the bone, liver and lung. He states that he does not want chemotherapy, at least initially. He has received only ADT with leuprolide for the past 5 years. What would you recommend? (Dr Oh)

 ANDREW J ARMSTRONG, MD, SCM	Enzalutamide
 CELESTIA S HIGANO, MD	Docetaxel
 MOLLY KIM, MSN, NP-C	Abiraterone
 ELLEN LEIDIG, MSN, FNP-BC, RN	Abiraterone
 WILLIAM K OH, MD	Enzalutamide
 A OLIVER SARTOR, MD	Enzalutamide

An 82-year-old man with mCRPC is currently receiving leuprolide and enzalutamide. His PSA has declined from 120 ng/mL to 0.2 ng/mL over 3 months, and he has experienced a marked improvement in symptoms. During a routine clinic visit, his wife notes that he seems more fatigued and weaker than usual and mentions that he has tripped 3 times in the past 2 months, once resulting in a significant fall. What would you recommend? (Dr Oh)

 ANDREW J ARMSTRONG, MD, SCM	Addition of physical therapy and exercise program
 CELESTIA S HIGANO, MD	Continue enzalutamide at a reduced dose
 MOLLY KIM, MSN, NP-C	Continue enzalutamide at a reduced dose
 ELLEN LEIDIG, MSN, FNP-BC, RN	Continue enzalutamide at a reduced dose
 WILLIAM K OH, MD	Continue enzalutamide at a reduced dose
 A OLIVER SARTOR, MD	Continue enzalutamide at a reduced dose

Role of Hormonal Therapy in the Management of Prostate Cancer

Case 1: A 73-year-old man with metastatic hormone-sensitive prostate cancer (mHSPC)

- Biology of prostate cancer and the androgen receptor
- Overview of androgen deprivation therapy (ADT) and its role in the management of prostate cancer
- Clinical and patient factors guiding the use of ADT alone or in combination with other treatment modalities
- Educating patients on the secondary side effects associated with ADT
- Addition of chemotherapy versus secondary hormonal therapy to ADT for the management of mHSPC
- Monitoring for and management of cardiovascular and CNS-related events in patients receiving hormonal therapy

Case 2: A 55-year-old man with metastatic castration-resistant prostate cancer (mCRPC)

- Definition of castration-resistant disease and current role of secondary hormonal therapies in the treatment of mCRPC
- Nonhormonal interventions (sipuleucel-T, radium 223, taxanes)

Case 3: A 77-year-old man with M0 prostate cancer

- Management of initial PSA relapse
- Management of PSA progression; choice of antiandrogen therapy

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Case Presentation: A 77-year-old man with M0 prostate cancer

Special Considerations

- Sedentary and overweight with Type 2 diabetes on oral agents
- 2015: Radical prostatectomy for primary Gleason 7 (4 + 3) prostate cancer
- 2016: Salvage radiation therapy to pelvis; PSA undetectable
- 9 months later PSA is detected

Key Treatment Decision 1: Treat or observe?

- ADT administered and PSA becomes undetectable
- 2019: PSA progression; negative workup

Key Treatment Decision 2: Add novel antiandrogen?

The patient wants to delay starting treatment for 6 to 12 months. How would you respond?

a. It’s acceptable to delay treatment for 6 to 12 months

b. Recommend treatment now

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Balancing the Benefits and Risks of Treatment

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

Benefits

Shared decision making: goals of patient

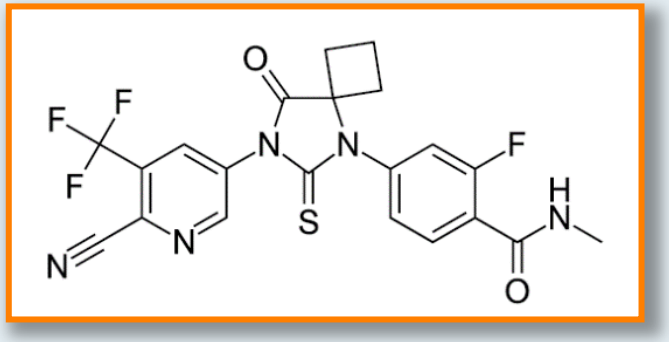
- Expense: COST $$$$... ↓ QOL
- ED and ↓ libido
- Hot flashes
- Changes in mood/ ↓cognition
- ↓ strength/ muscle mass
- Osteoporosis
- Anemia, fatigue
- Metabolic syndrome
- Cardiac risk, DM

Risks

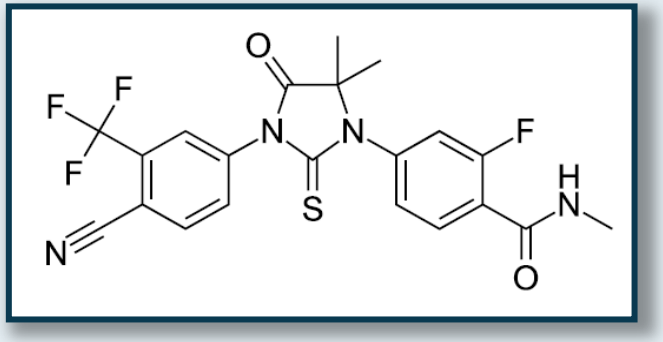
Courtesy of Victoria Sinibaldi, RN, MS, CS, CANP, BC

Next-Generation Androgen Receptor Inhibitors[1,2]

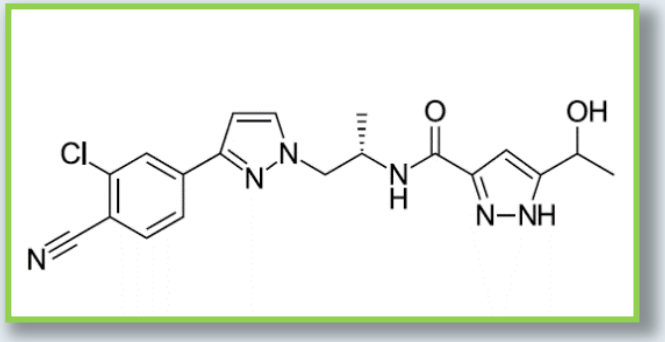
Apalutamide



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.

Courtesy of Matthew R Smith, MD, PhD

Oral Anti-androgen Agents Approved for M0 Prostate Cancer: How Do You Choose?

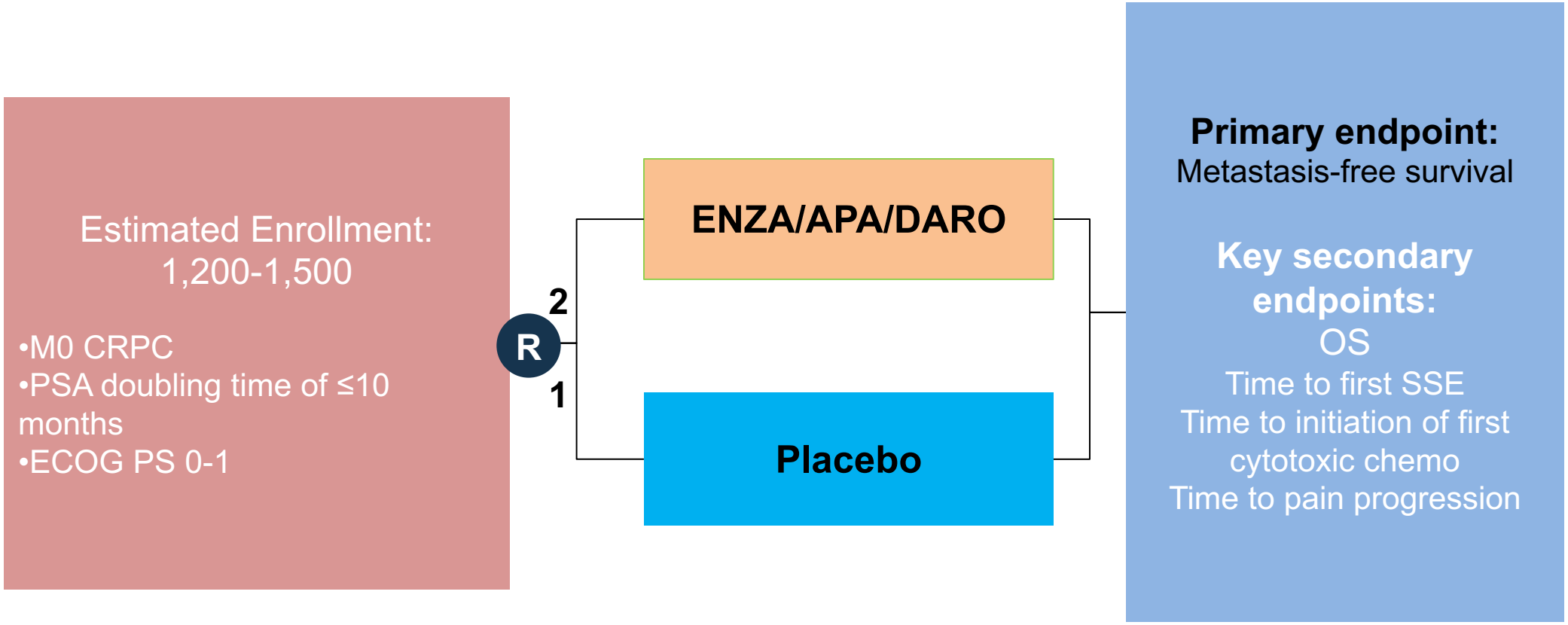
- Enzalutamide
  - Cautious with patients with a history of falls and seizure
- Apalutamide
  - Risk of rash
- Darolutamide
  - Mild fatigue

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

Courtesy of Kara M Olivier, NP, APRN-BC

PROSPER/SPARTAN/ARAMIS Study Design:
in High-Risk M0 CRPC

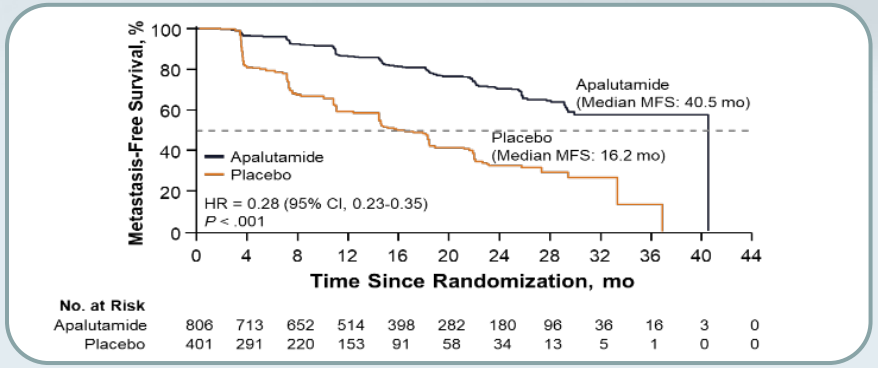
Similar trials with Enzalutamide (PROSPER), Apalutamide (SPARTAN) and Darolutamide (ARAMIS)



Courtesy of Karim Fizazi, MD. PhD

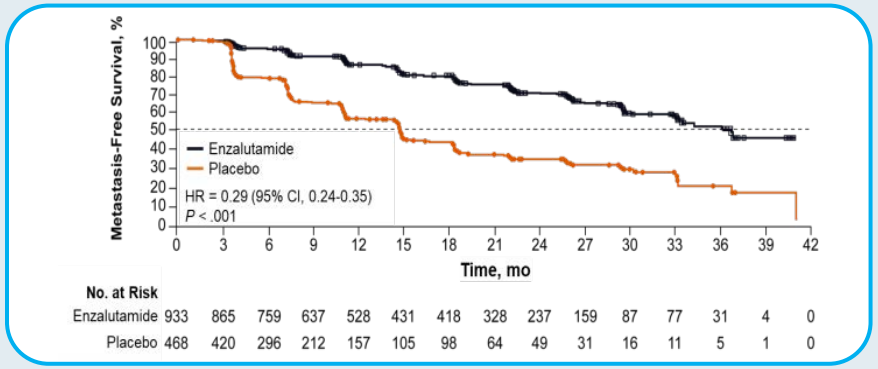
Primary Endpoint: Metastasis-Free Survival

SPARTAN[1]
Apalutamide



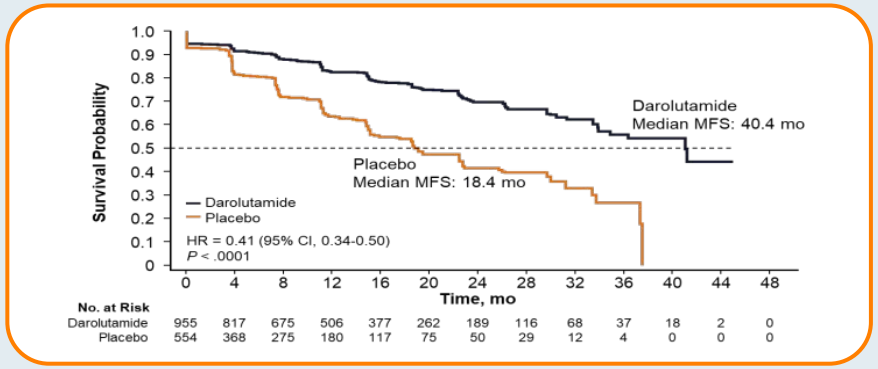
- 72% reduction of distant progression or death
- Median MFS: APA 40.5 vs PBO 16.2 months
- 24-month MFS benefit

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

Courtesy of Matthew R Smith, MD, PhD

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.

Safety in the 3 M0 CRPC trials

AE, n (%, unless indicated)	SPARTAN[1]		PROSPER[2,3]		ARAMIS[4]	
	Apalutamide (n=803)	Placebo (n=398)	Enzalutamide (n=930)	Placebo (n=465)	Darolutamide (n=954)	Placebo (n=554)
Fatigue	224 (30)	84 (21)	303 (33)	64 (14)	115 (12)	48 (9)
Cognitive disorder	–	–	–	–	4 (<1)	1 (<1)
Memory impairment	–	–	–	–	5 (1)	7 (1)
Mental impairment disorder	41 (5)	12 (3)	48 (5)	9 (2)	–	–
Seizure/convulsion†	2 (<1)	0 (0)	3 (<1)	0 (0)	2 (<1)	1 (<1)
Bone fracture	94 (12)	26 (7)	4%	1%	40 (4)	20 (4)
Falls‡	125 (16)	36 (9)	106 (11)	19 (4)	40 (4)	26 (5)
Hypertension	199 (25)	79 (20)	111 (12)	24 (5)	63 (7)	29 (5)
Coronary artery disorder	–	–	–	–	31 (3)	14 (3)
Heart failure	–	–	–	–	18 (2)	5 (1)
Major adverse cardiovascular event	–	–	48 (5)	13 (3)	–	–
Rash	191 (24)	22 (6)	–	–	28 (3)	5 (1)
Weight decreased	129 (16)	25 (6)	55 (6)	7 (2)	34 (4)	12 (2)
Hypothyroidism	65 (8)	8 (2)	–	–	2 (<1)	0 (0)

Courtesy of Karim Fizazi, MD. PhD

Major Cardiovascular Events in M0 CRPC Trials — Apalutamide and Enzalutamide

	SPARTAN[1]		PROSPER[2]	
	APA (n = 803)	PBO (n = 398)	ENZA (n = 933)	PBO (n = 468)
Safety	AE reporting every 4 weeks		AE reporting every 4 months	
AEs, %				
Any grade	97%	93%	87%	77%
Grade ≥ 3	45%	34%	31%	23%
Serious AEs	25%	23%	24%	13%
AEs leading to discontinuation	11%	7%	9%	6%
AEs leading to death	1.2% (n=10)	0.3% (n=1)	3.4% (n=32)	0.6% (n=3)
Major CV event	1*	1*	5%	3%
Seizures	0.24% (n= 2)	0	0.32% (n = 3)	0

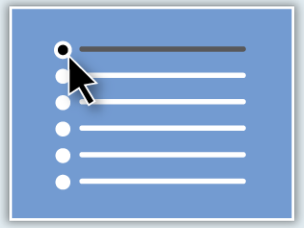
1. Smith MR, et al. *N Engl J Med,* 2018
2. Hussain M, et al. *N Engl J Med*. 2018

Courtesy of David F Penson, MD, MPH

The patient wants to delay starting treatment for 6 to 12 months. How would you respond?

a. It’s acceptable to delay treatment for 6 to 12 months

b. Recommend treatment now



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A 72-year-old man has been receiving leuprolide for 3 years because of a rising PSA after radical prostatectomy. His PSA is 7 ng/mL, testosterone is undetectable and his PSA doubling time is 6 months. He has negative bone and CT scans of the abdomen and pelvis and feels well. He states that he wants to be aggressive in terms of treating his cancer in order to live as long as possible. What would you recommend? (Dr Oh)

Management of Locally Advanced Non-Small Cell Lung Cancer

Tuesday, September 15, 2020
5:00 PM – 6:00 PM ET

Faculty

Kelly EH Goodwin, MSN, RN, ANP-BC
David R Spigel, MD
Heather Wakelee, MD
Elizabeth S Waxman, RN, MSN, ANP-BC

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Thank you for joining us!

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

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