A Conversation with the Investigators: Hormonal Therapy for Prostate Cancer

Monday, July 12, 2021
5:00 PM – 6:00 PM ET

Faculty

Simon Chowdhury, MD, PhD
Tanya B Dorff, MD
Matthew R Smith, MD, PhD

Moderator

Neil Love, MD

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Faculty

Simon Chowdhury, MD, PhD
Consultant Medical Oncologist
London, United Kingdom

Matthew R Smith, MD, PhD
Claire and John Bertucci Endowed Chair in Genitourinary Cancers
Professor of Medicine, Harvard Medical School
Director, Genitourinary Malignancies Program
Massachusetts General Hospital Cancer Center
Boston, Massachusetts

Tanya B Dorff, MD
Associate Clinical Professor of Medicine
City of Hope National Medical Center
Department of Medical Oncology and Developmental Therapeutics
Head, Genitourinary Cancer Program
Los Angeles, California

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Commercial Support

This activity is supported by educational grants from Astellas and Pfizer Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Exelixis Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Merck and Sanofi Genzyme.

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Dr Love — Disclosures

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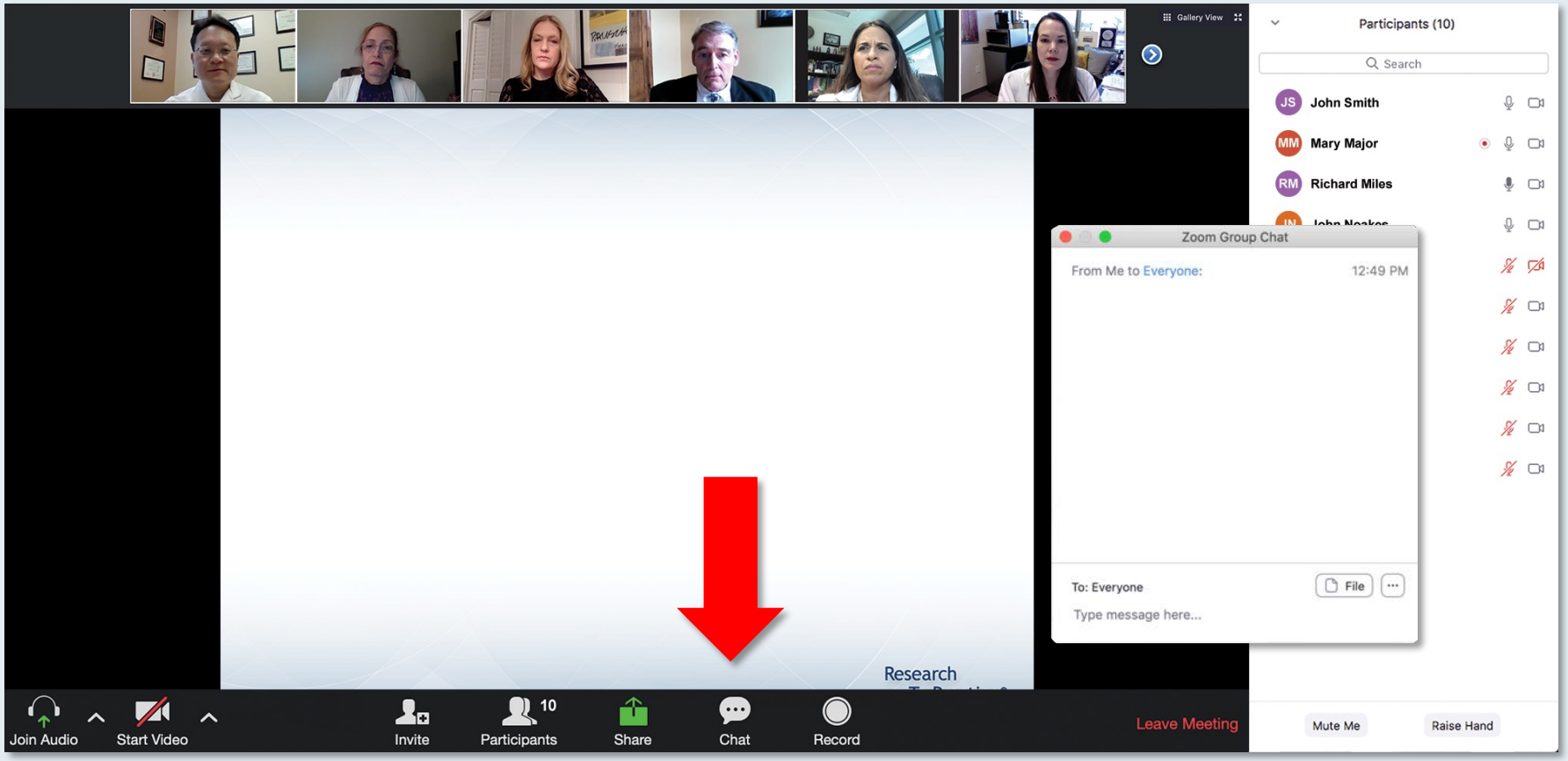

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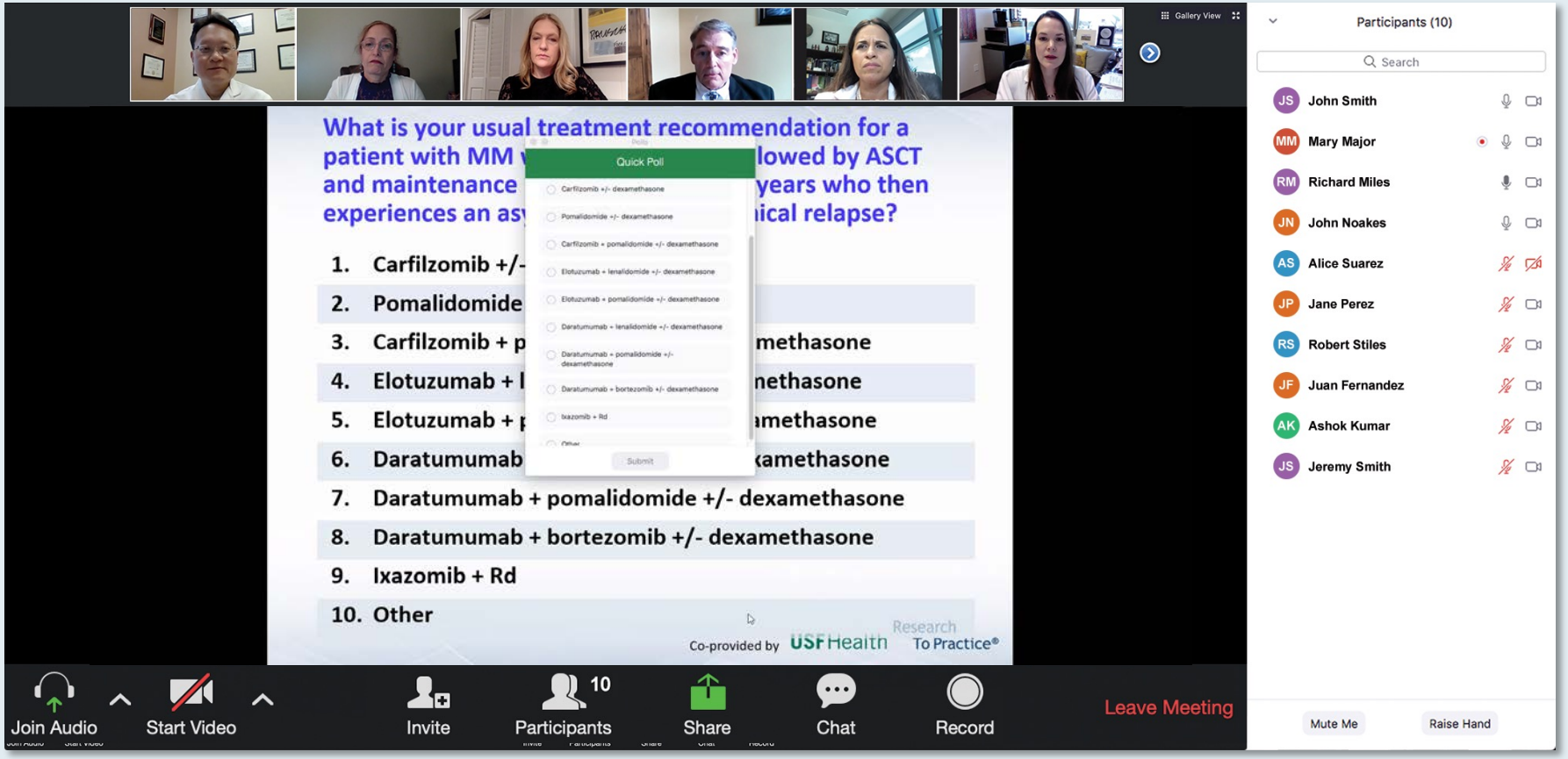
How to answer poll questions



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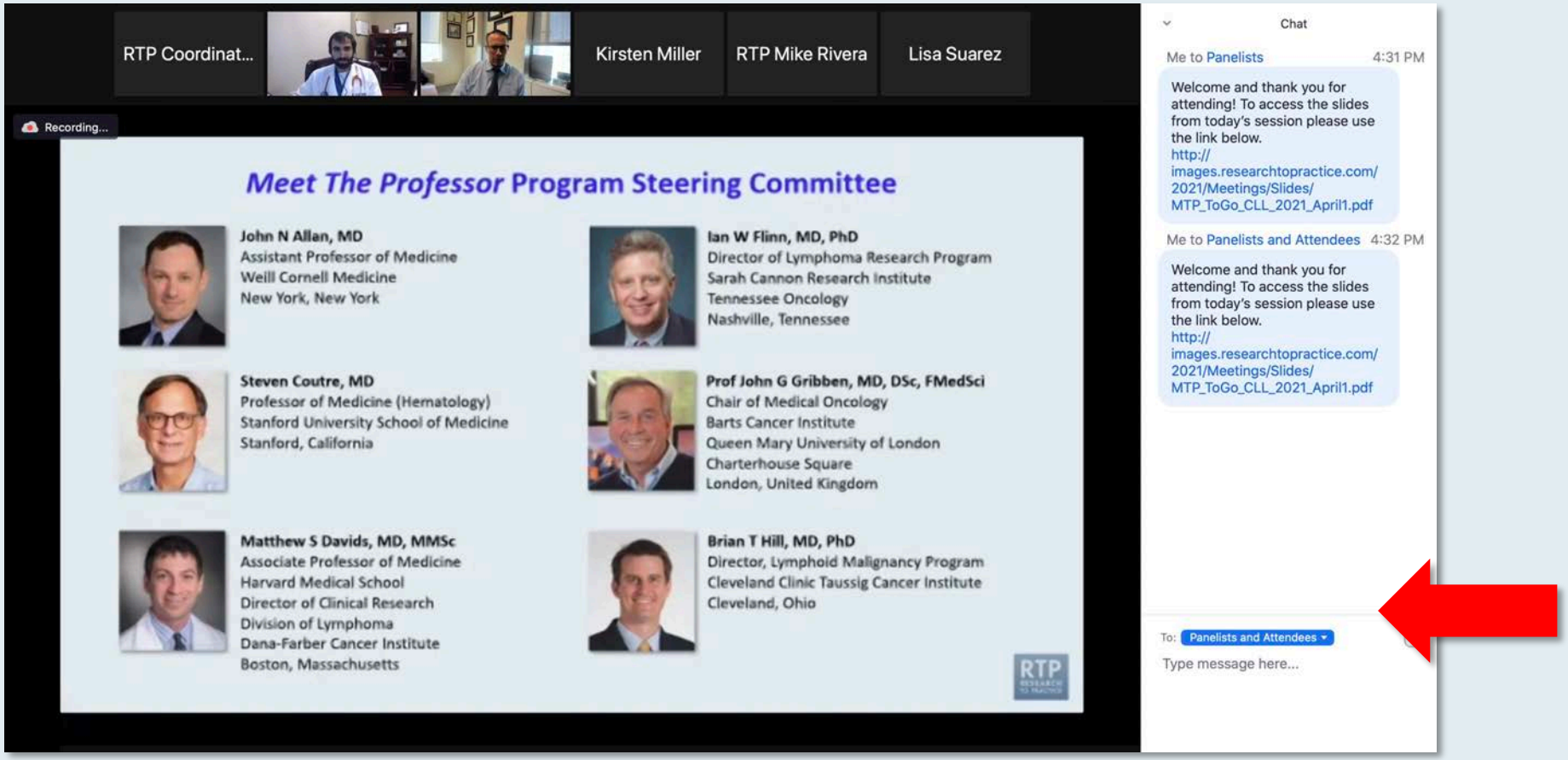
Familiarizing Yourself with the Zoom Interface

Expand chat submission box



Drag the white line above the submission box up to create more space for your message.

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Familiarizing Yourself with the Zoom Interface

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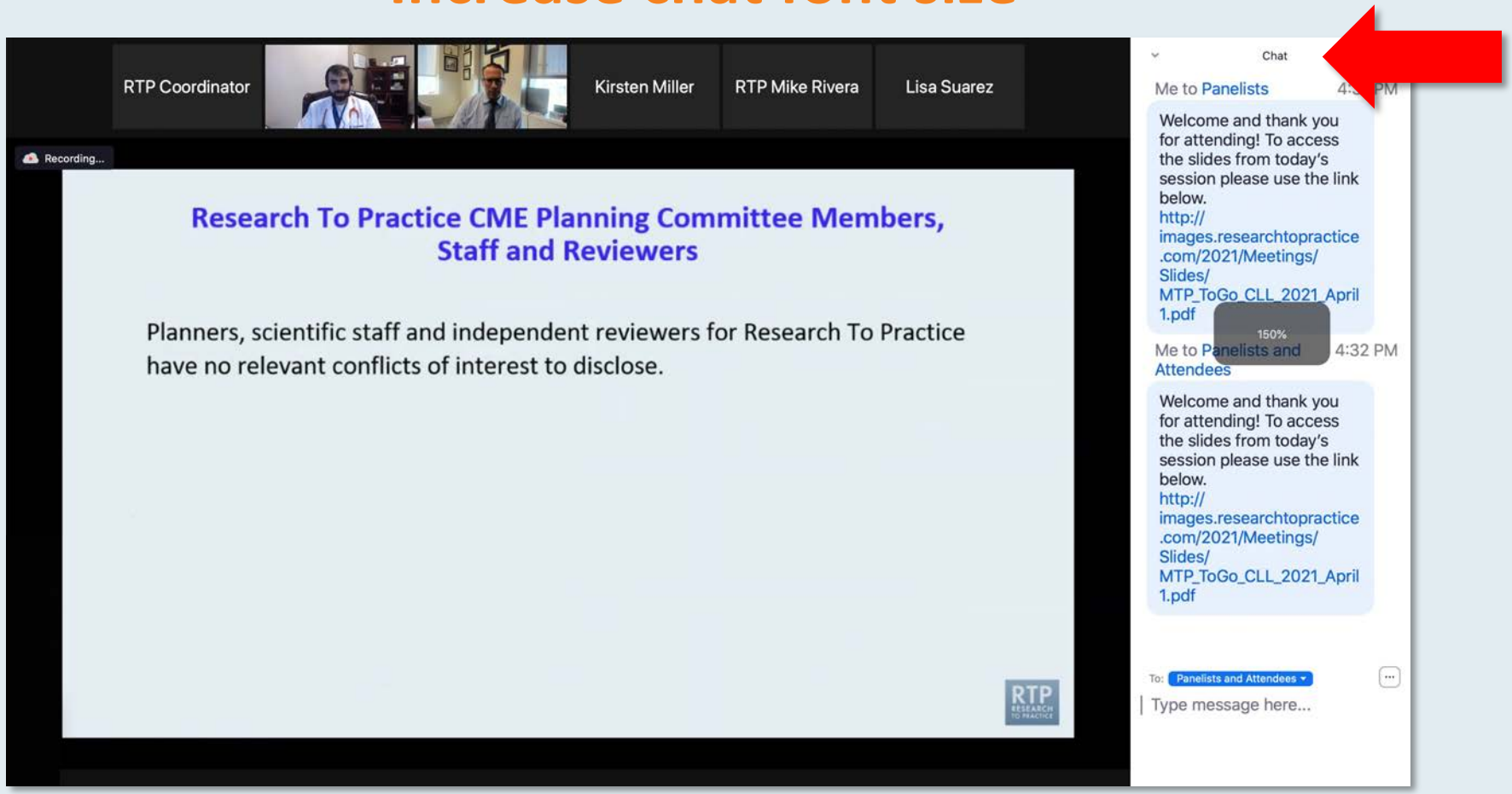

Press Command (for Mac) or Control (for PC) and the + symbol.
You may do this as many times as you need for readability.

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Side Effects of Hormonal Therapy in Prostate Cancer

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A Conversation with the Investigators: Chimeric Antigen Receptor T-Cell Therapy in Hematologic Cancers

Tuesday, July 13, 2021
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Caron Jacobson, MD
David G Maloney, MD, PhD
Nikhil C Munshi, MD

Moderator

Neil Love, MD

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Gail J Roboz, MD
Eytan M Stein, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with Advanced Gastrointestinal Cancers

Monday, July 19, 2021
5:00 PM – 6:00 PM ET

Faculty

Tanios Bekaii-Saab, MD

Moderator

Neil Love, MD

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RESEARCH TO PRACTICE

A Conversation with the Investigators: Metastatic Castration-Resistant Prostate Cancer

Tuesday, July 20, 2021
5:00 PM – 6:00 PM ET

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Emmanuel S Antonarakis, MD
Johann de Bono, MBChB, MSc, PhD
Julie N Graff, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

A Conversation with the Investigators: Bladder Cancer

Wednesday, July 21, 2021
5:00 PM – 6:00 PM ET

Faculty

Petros Grivas, MD, PhD
Daniel P Petrylak, MD
Arlene Siefker-Radtke, MD

Moderator

Neil Love, MD

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Optimizing the Selection and Sequencing of Therapy for Patients with Renal Cell Carcinoma

Thursday, July 22, 2021
5:00 PM – 6:00 PM ET

Faculty

David F McDermott, MD

Moderator

Neil Love, MD

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A Conversation with the Investigators: Endometrial and Cervical Cancers

Monday, July 26, 2021
5:00 PM – 6:00 PM ET

Faculty

Mansoor Raza Mirza, MD
David M O'Malley, MD
Angeles Alvarez Secord, MD, MHSc

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

What General Medical Oncologists Want to Know About Targeted Therapy for Non-Small Cell Lung Cancer

Tuesday, July 27, 2021
5:00 PM – 6:00 PM ET

Faculty

Professor Solange Peters, MD, PhD
Zofia Piotrowska, MD, MHS
Gregory J Riely, MD, PhD

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

What General Medical Oncologists Want to Know About Immunotherapy and Other Nontargeted Approaches for Lung Cancer

Wednesday, July 28, 2021
5:00 PM – 6:00 PM ET

Faculty

Mark Awad, MD, PhD
David R Spigel, MD
Heather Wakelee, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 2 to 3 business days.

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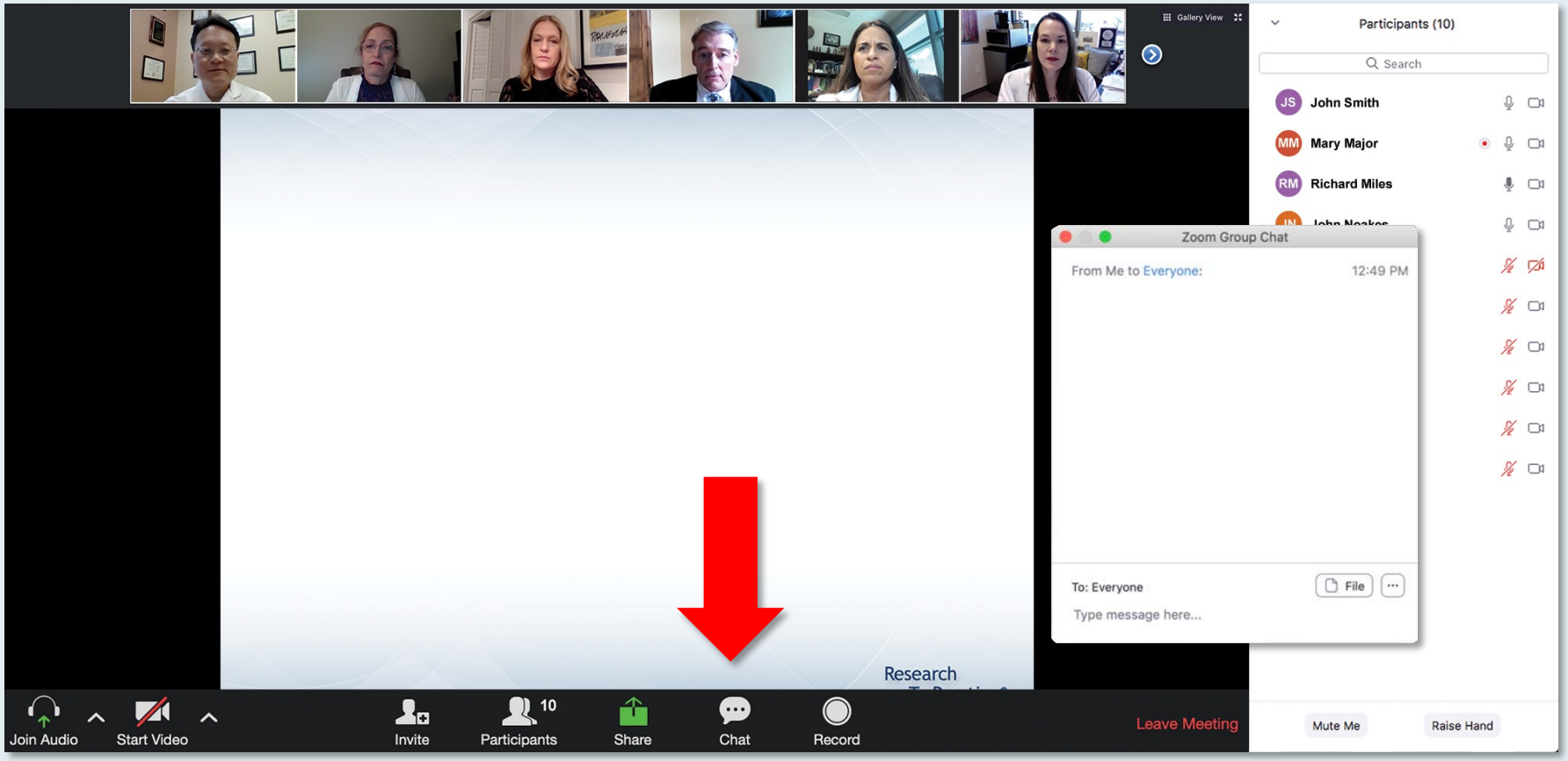

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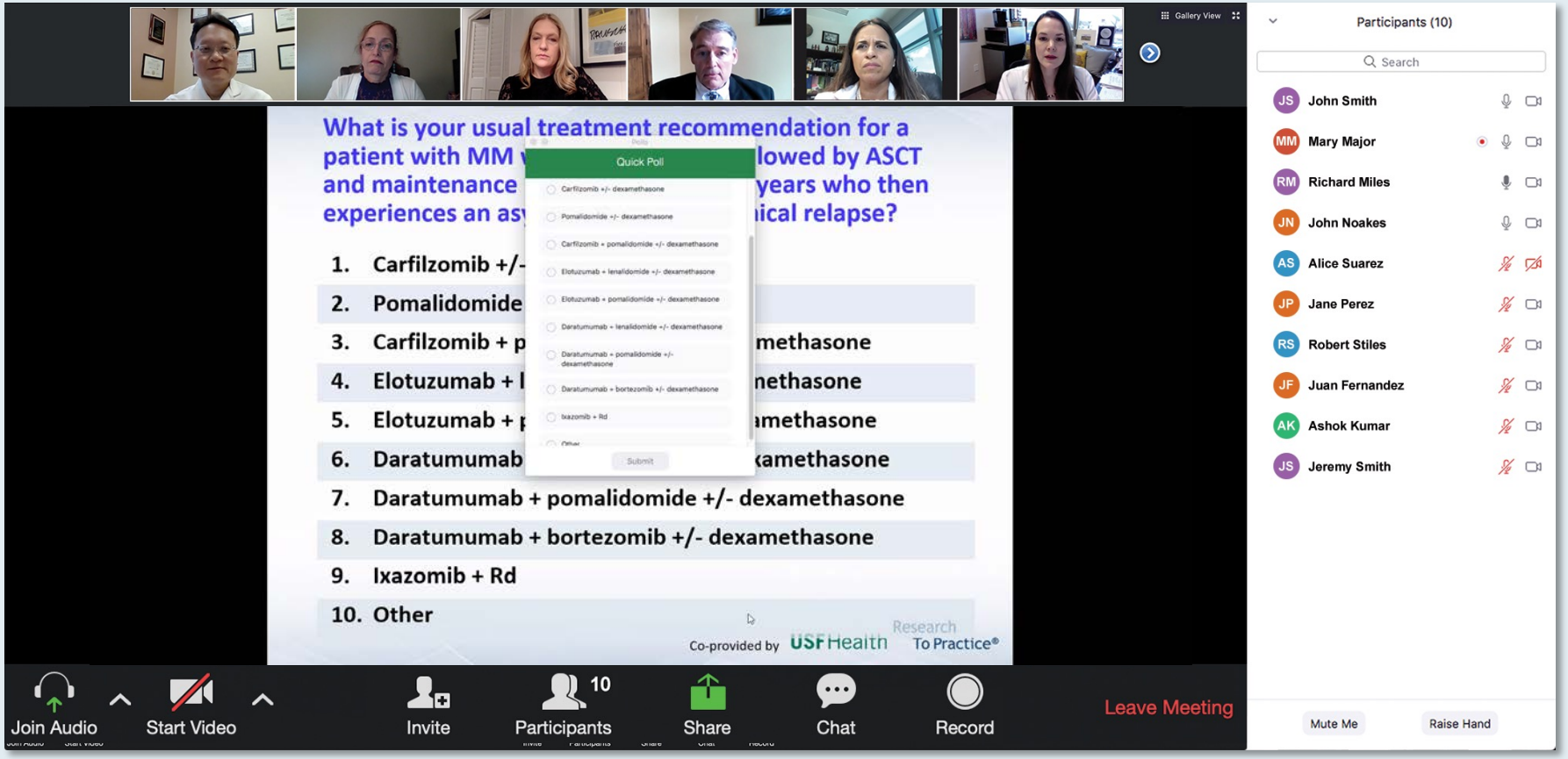

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RTP RESEARCH TO PRACTICE

Agenda

Module 1: Choice of Androgen Deprivation Therapy

- HERO study: Oral relugolix versus leuprolide acetate

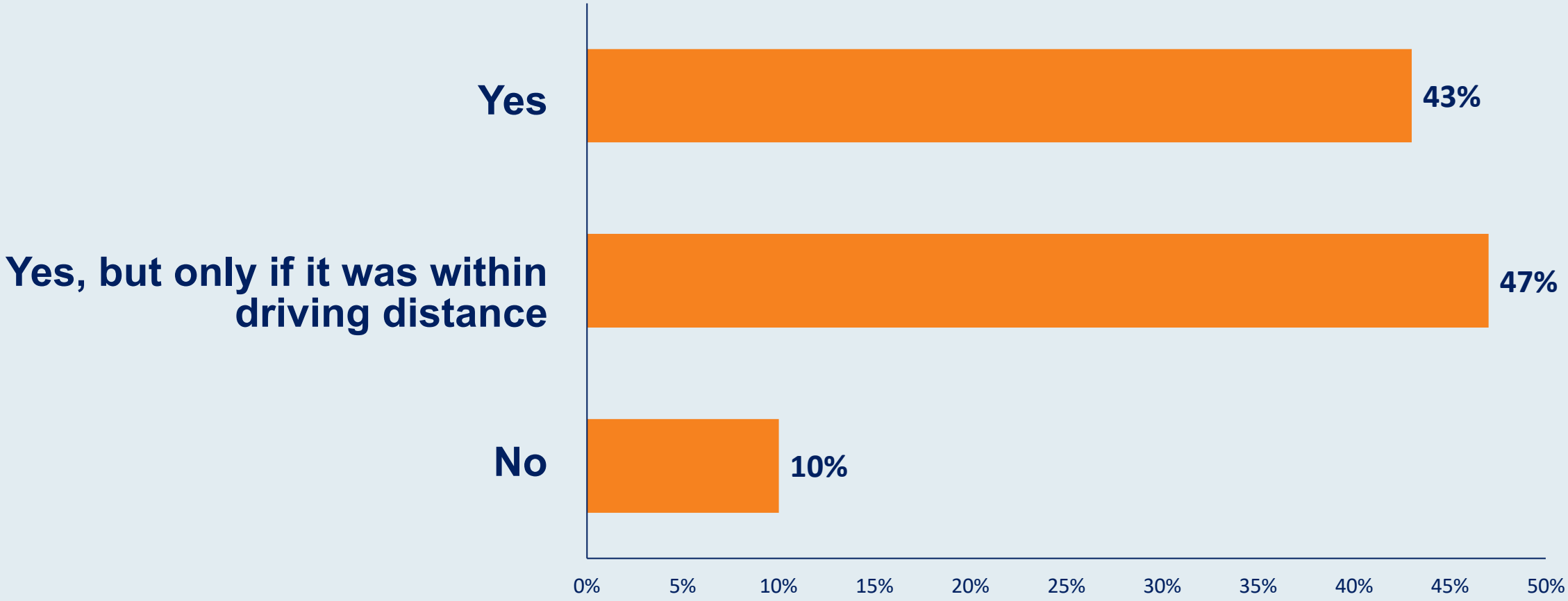
Module 2: Nonmetastatic Castration-Resistant Prostate Cancer (nmCRPC)

- Next-generation androgen receptor inhibitors (ie, apalutamide, darolutamide, enzalutamide)
- Phase III PROSPER, SPARTAN and ARAMIS trials: Long-term efficacy outcomes
- Differential side-effect profiles of abiraterone, enzalutamide, apalutamide and darolutamide
- Incidence of CNS-related adverse events with secondary hormonal therapy

Module 3: Metastatic Hormone-Sensitive PC (mHSPC)

- Real-world treatment patterns in mHSPC
- PEACE-1 study: Abiraterone with prednisone and/or local radiation therapy for men with de novo mHSPC
- ARCHES, ENZAMET and TITAN trials: Long-term results
- Ongoing Phase III trials assessing darolutamide-based therapy for men with mHSPC

If Research To Practice hosted a daylong multitumor live meeting, would you likely attend?



Premeeting survey: July 2021

Which would you prefer as the “lead song” at the next RTP event to be held in person?

1. Bad Company, “Leaving You”
2. Coldplay, “A Message”
3. U2, “Beautiful Day”
4. Tom Petty and the Heartbreakers, “Jammin’ Me”
5. Crosby, Stills & Nash, “Suite: Judy Blue Eyes”
6. None of the above

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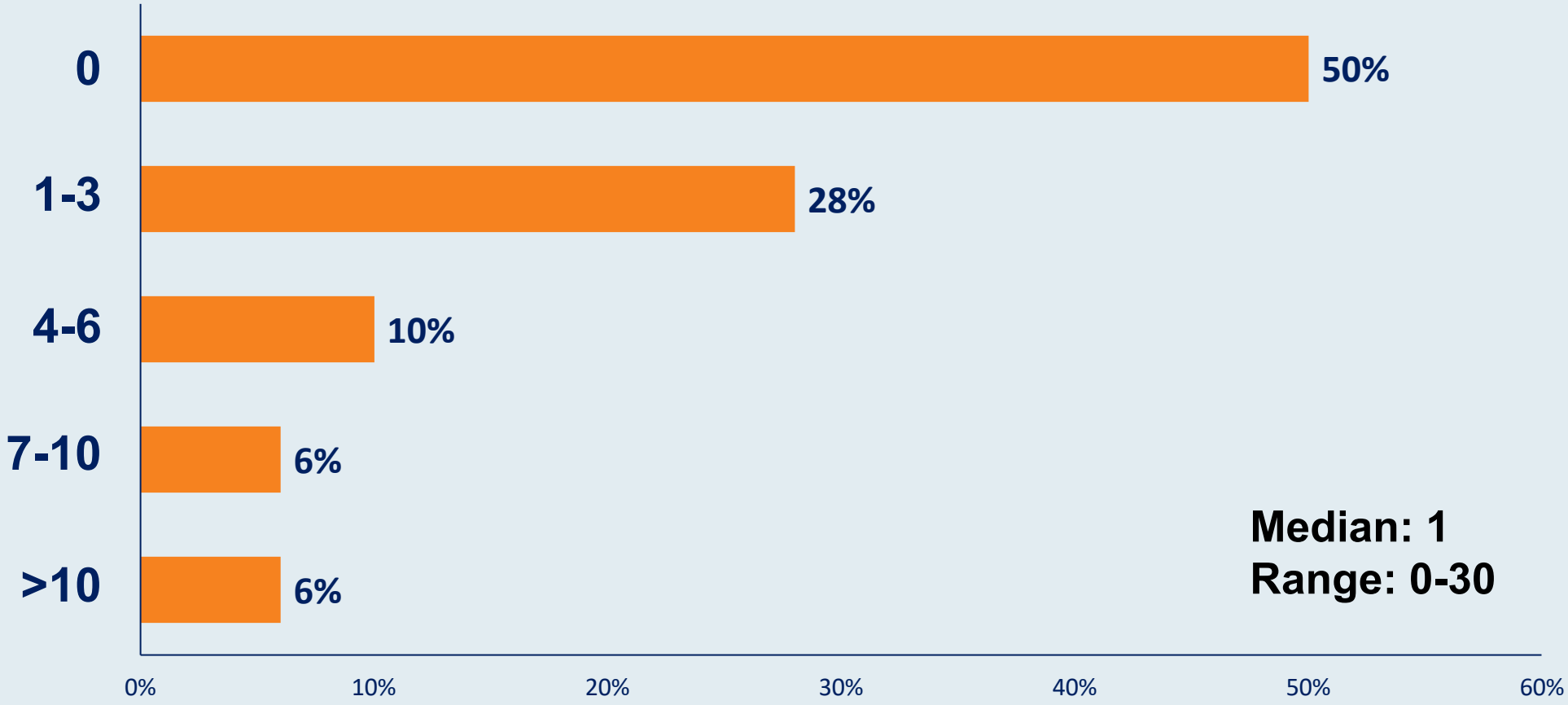
Approximately how many patients in your practice with PC have received or are receiving degarelix?



Premeeting survey: July 2021

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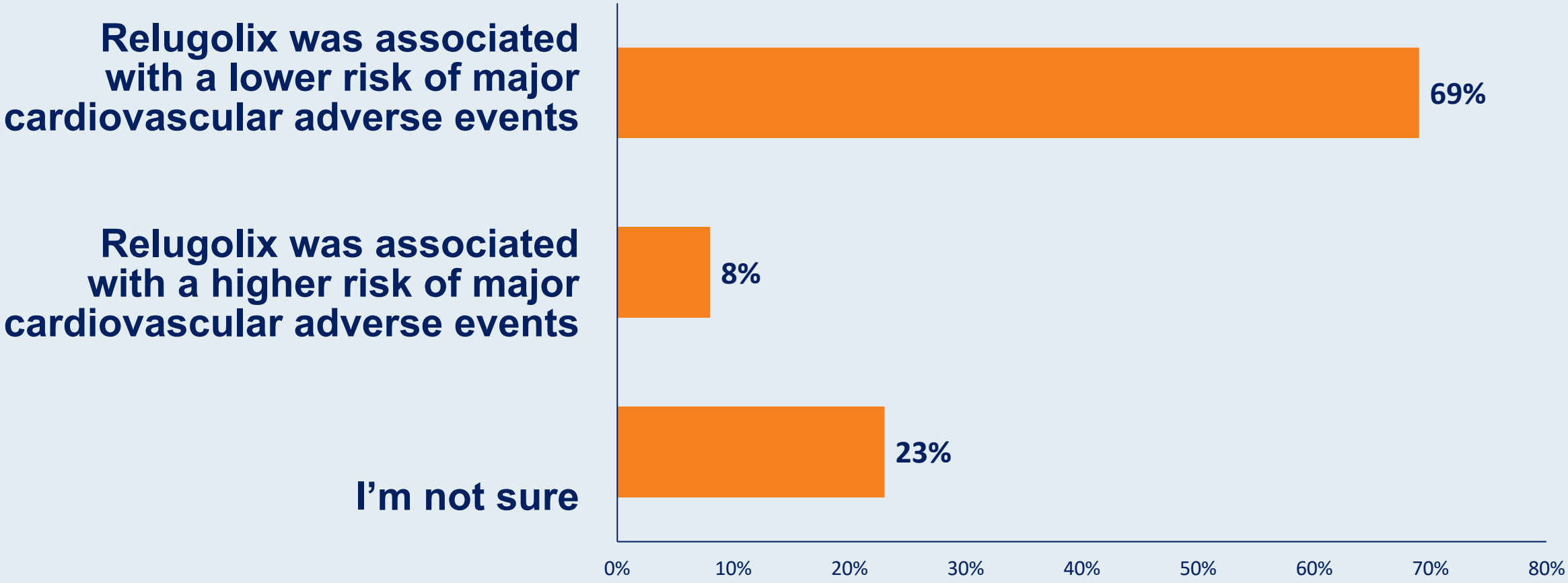
Which of the following statements is true regarding relugolix, an oral LHRH antagonist, as it was compared to standard leuprolide for patients with advanced PC in the Phase III HERO trial?



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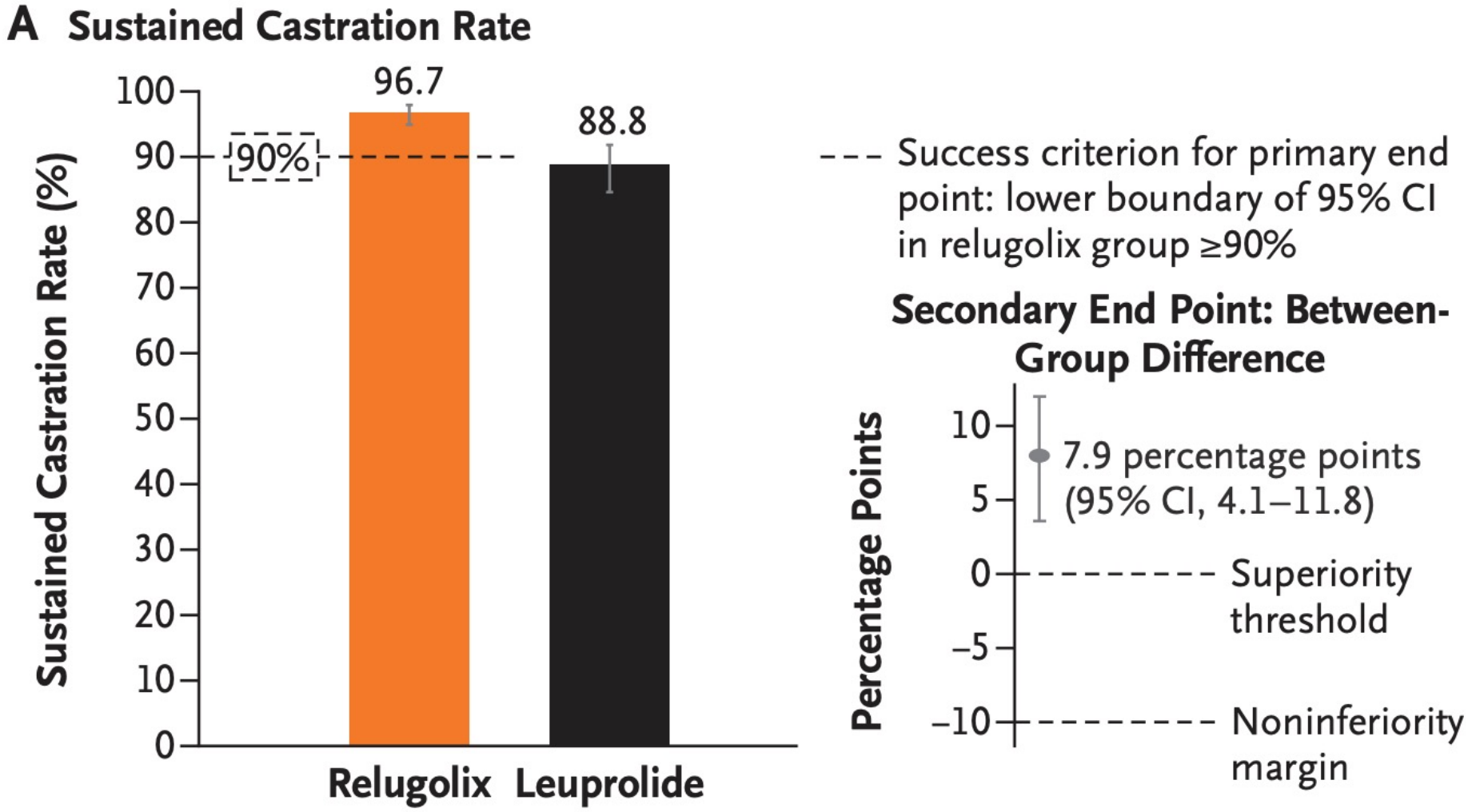
HERO Study: Oral Relugolix vs Leuprolide Acetate for Androgen-Deprivation Therapy



Shore ND et al. *N Engl J Med.* 2020; 382:2187-2196

Courtesy of Matthew R Smith, MD, PhD

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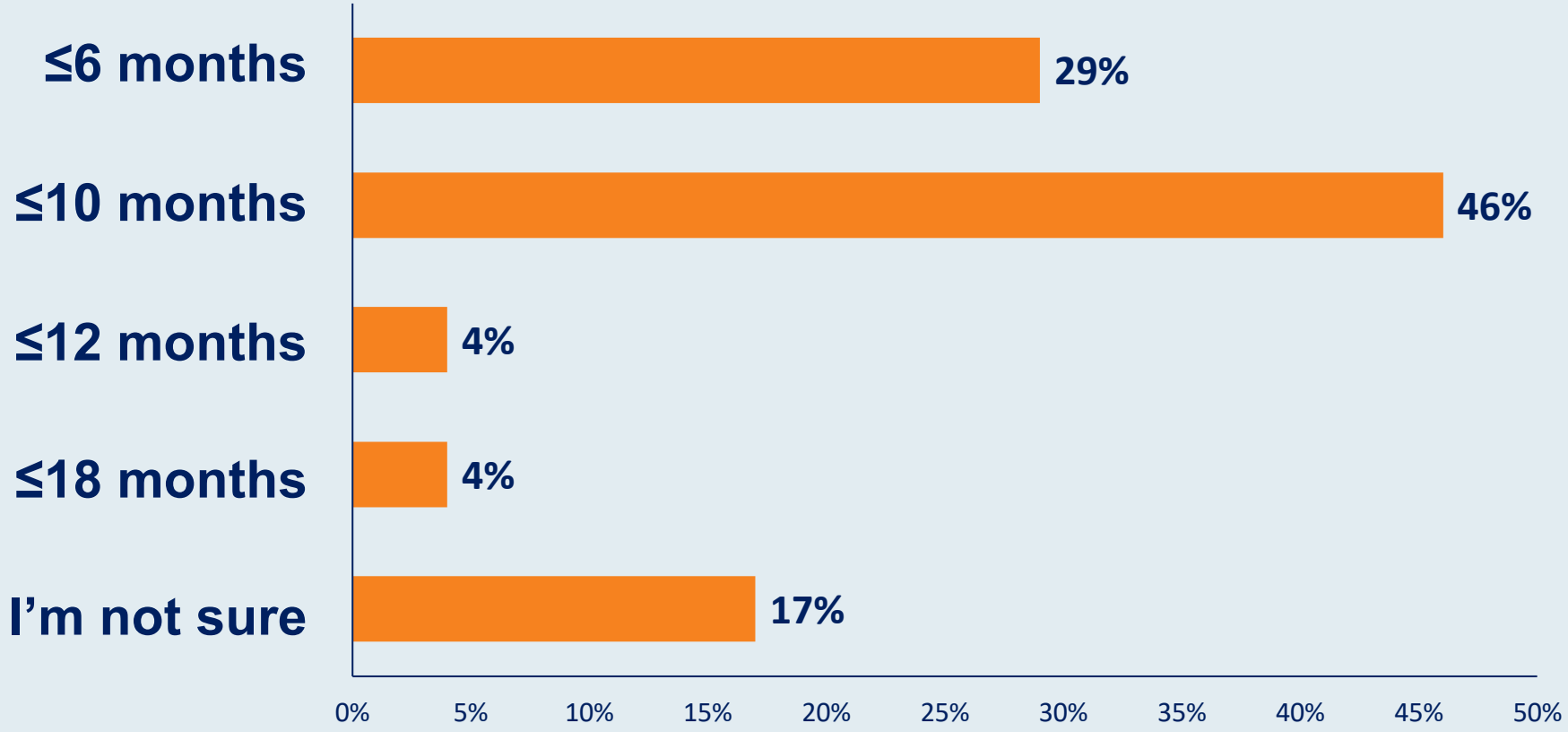
What were the eligibility criteria in terms of PSA doubling time in the Phase III PROSPER, SPARTAN and ARAMIS trials evaluating enzalutamide, apalutamide and darolutamide for patients with nonmetastatic castration-resistant PC (CRPC)?



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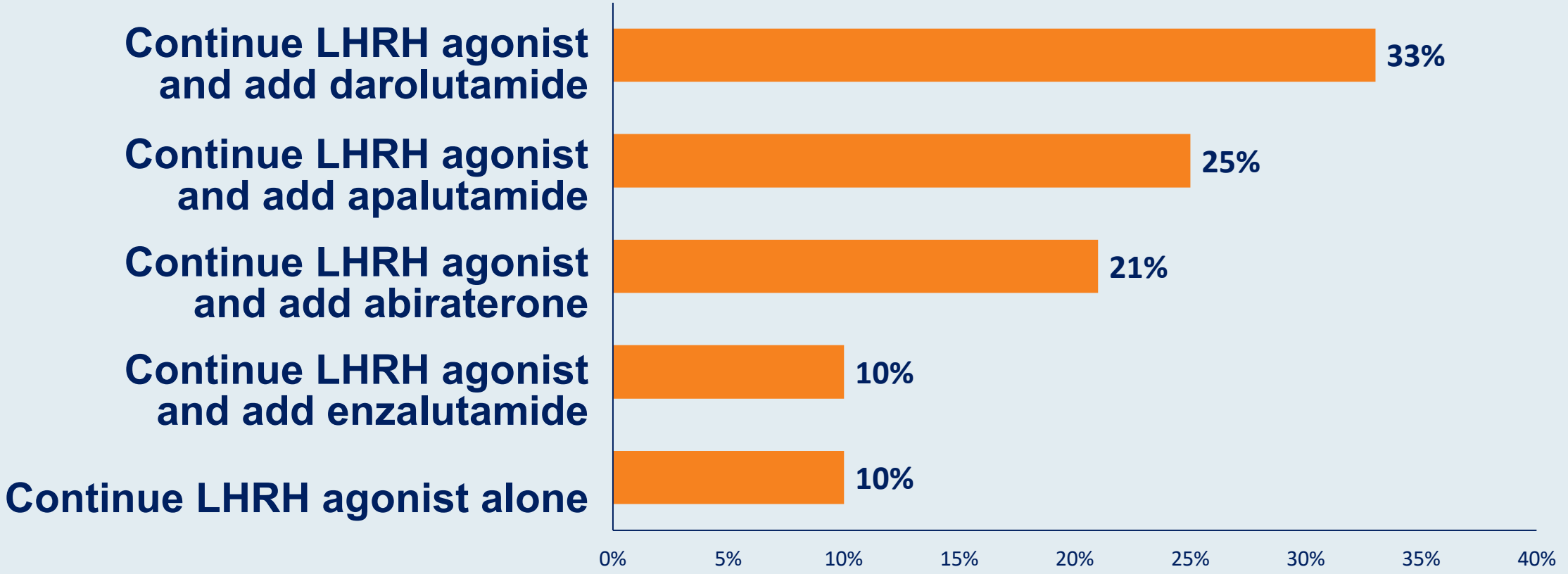
A 65-year-old man s/p radical prostatectomy followed by radiation therapy for PSA-only recurrence (M0) receives an LHRH agonist for further PSA progression. Regulatory and reimbursement issues aside, what would be your most likely treatment recommendation if the patient responded but then experienced PSA progression to a PSA level of 3.4 ng/dL with a doubling time of 6 months?



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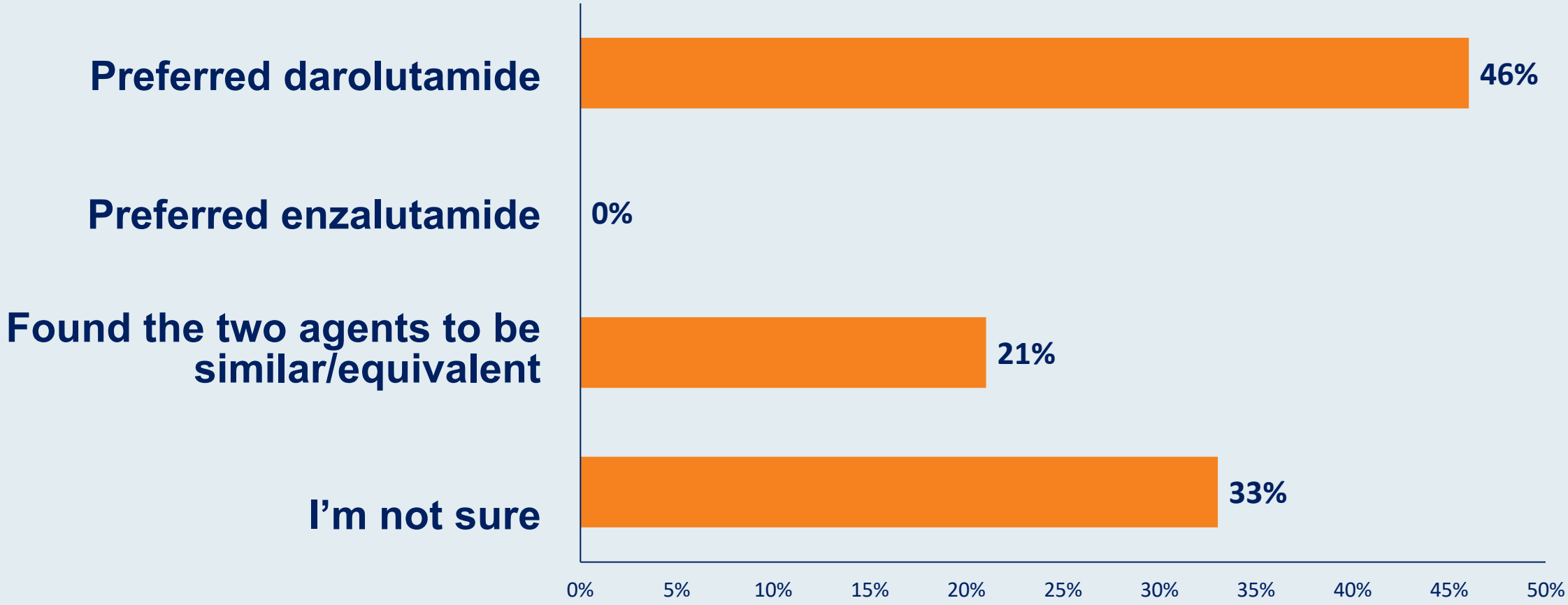
A recent blinded trial that evaluated darolutamide versus enzalutamide in terms of side effects and tolerability found that patients…



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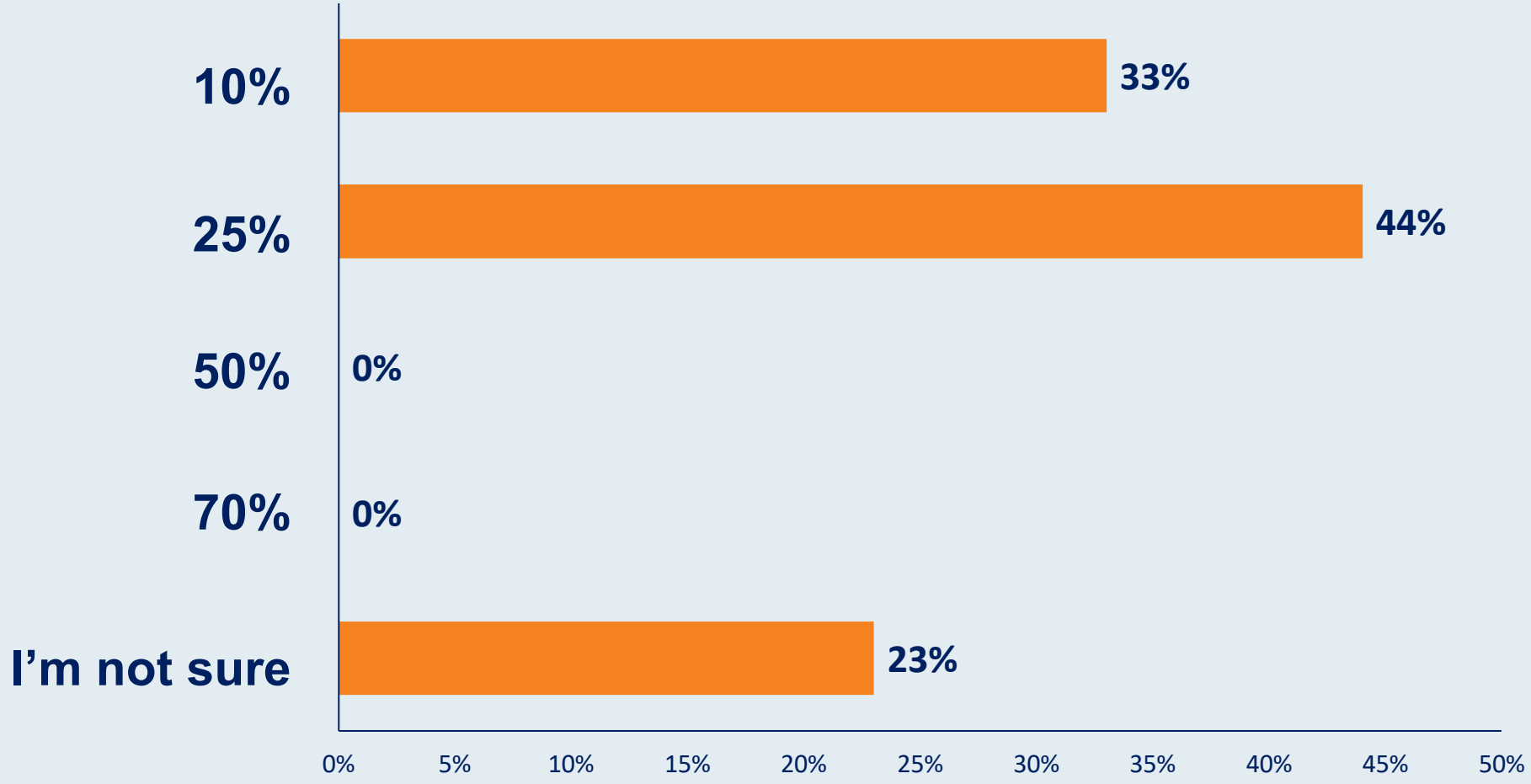
The rash associated with apalutamide occurs in approximately what percent of patients?



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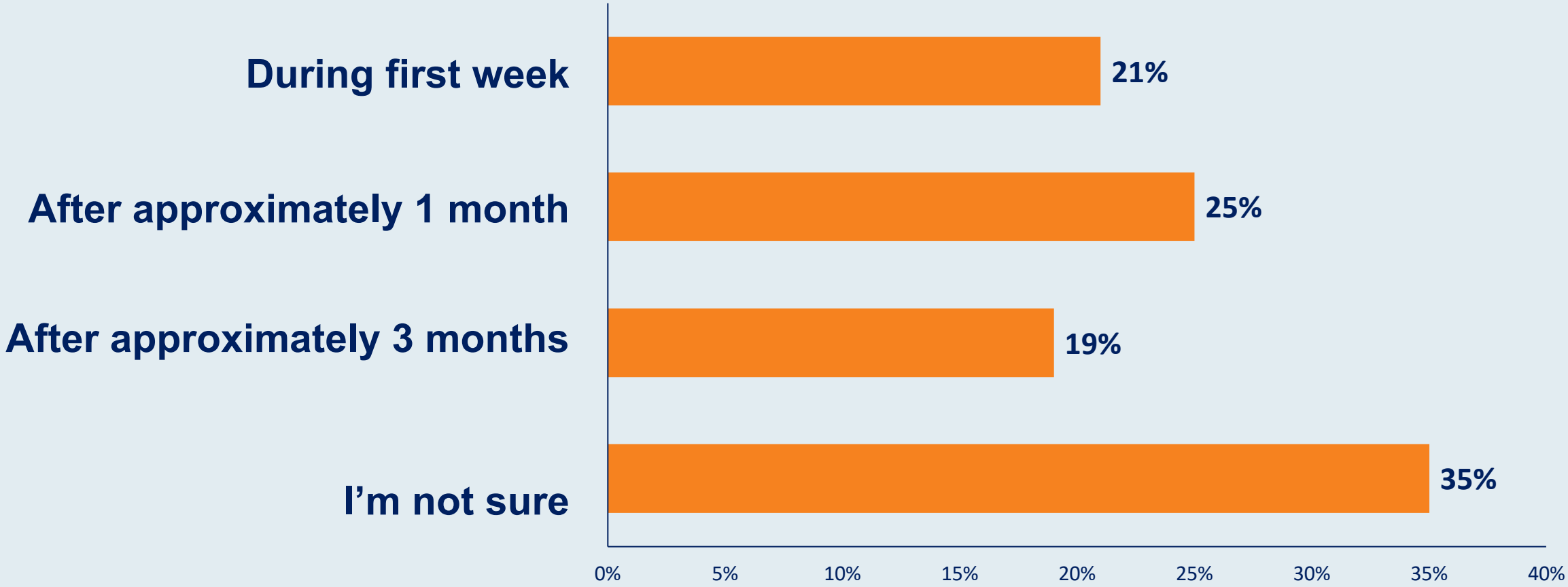
The rash associated with apalutamide typically occurs…



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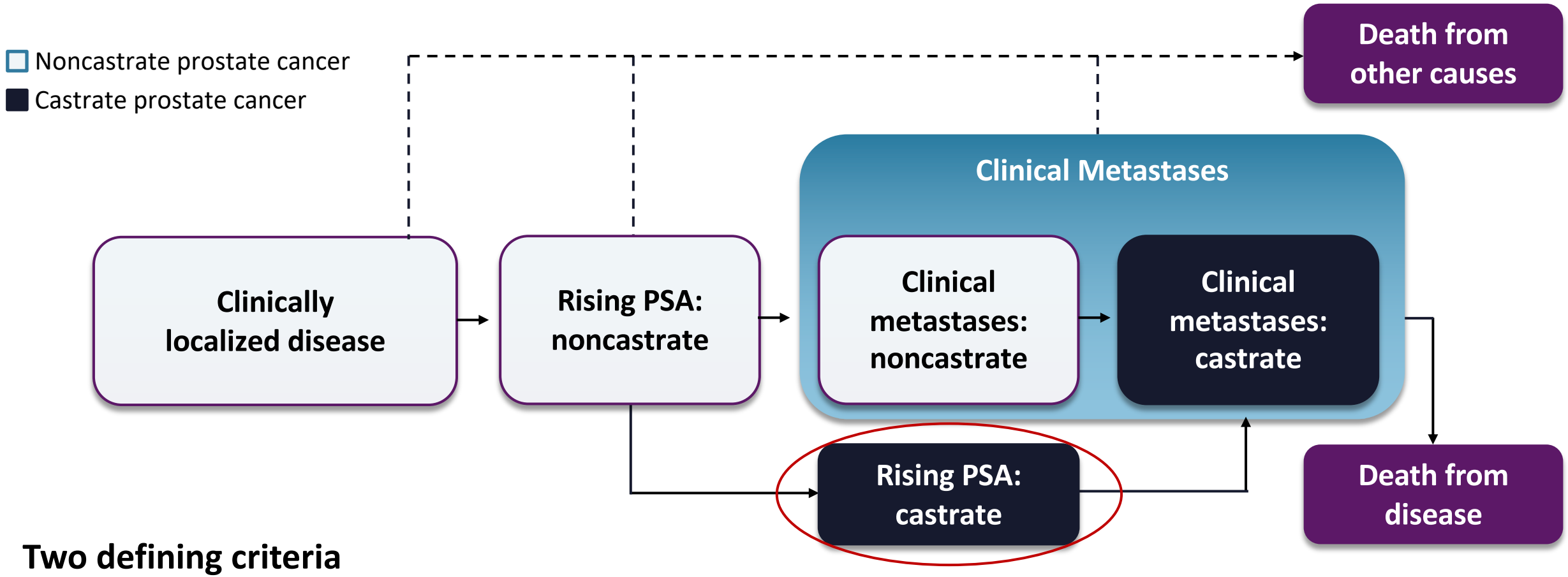
Clinical Disease States Model of Prostate Cancer[1]



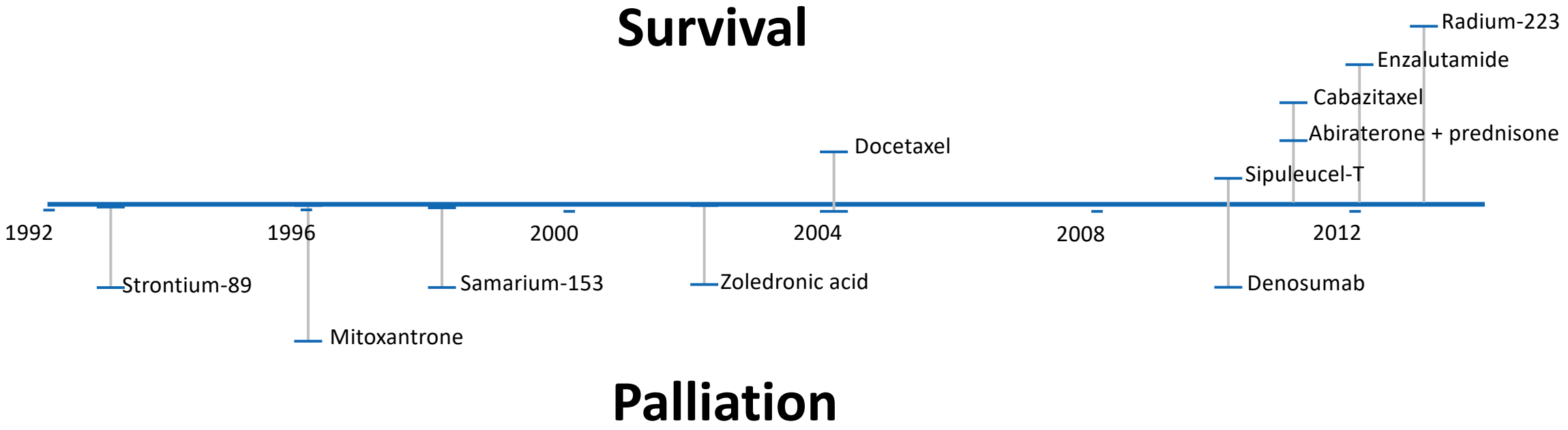
Two defining criteria

- 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.

Courtesy of Matthew R Smith, MD, PhD

Timeline of FDA Approvals in Metastatic Castration-Resistant Prostate Cancer

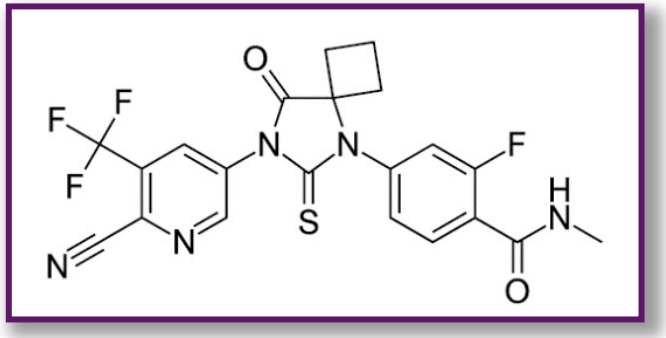


Metastatic disease was defined by conventional imaging (eg, bone scan, CT scans)

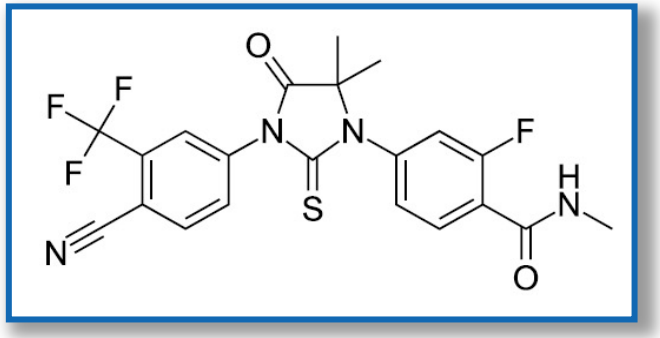
Courtesy of Matthew R Smith, MD, PhD

Next-Generation Androgen Receptor Inhibitors[1,2]

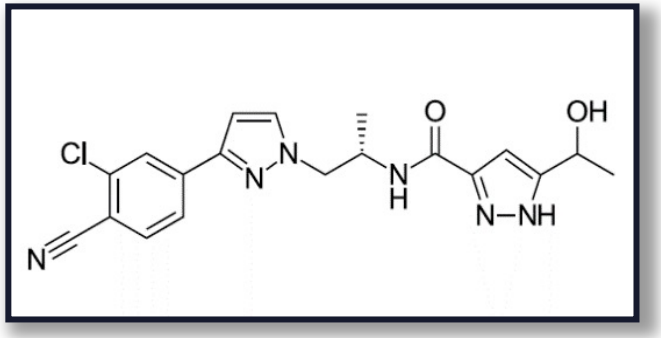
Apalutamide



Enzalutamide



Darolutamide



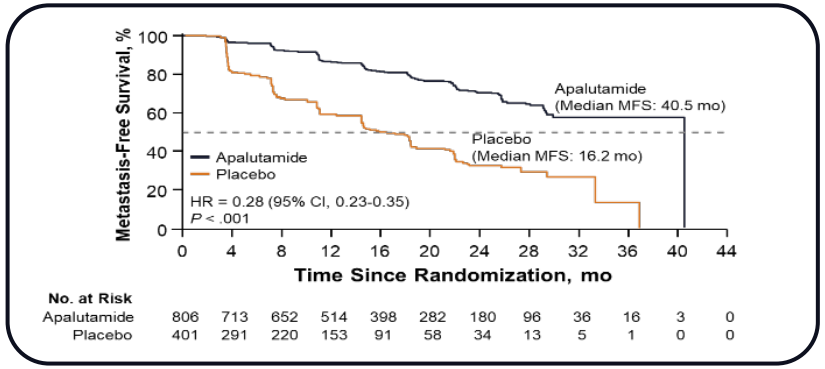
- Apalutamide and enzalutamide have similar structures
- Darolutamide is structurally distinct from apalutamide and enzalutamide, characterized by low blood–brain barrier penetration[1,2,] and may have improved tolerability

Courtesy of Matthew R Smith, MD, PhD

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.

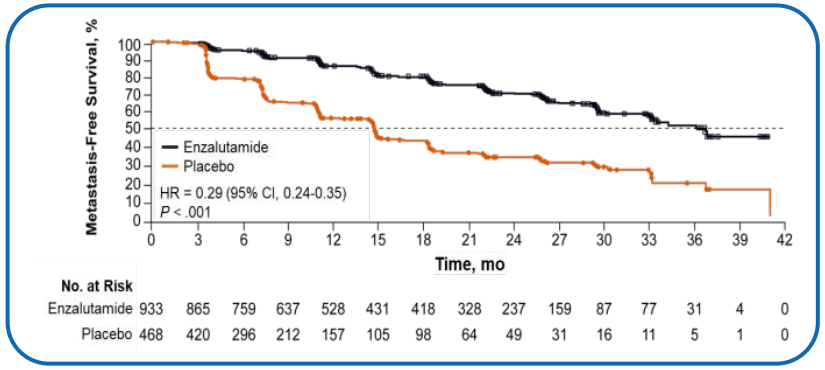
Primary Endpoint: Metastasis-Free Survival

SPARTAN[1]
Apalutamide



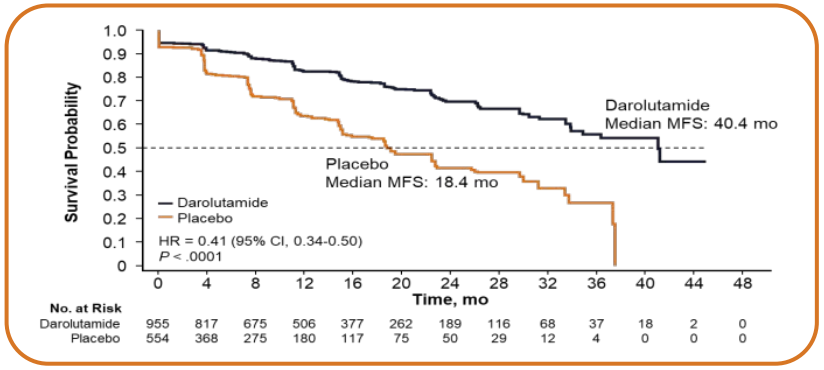
- 72% reduction of distant progression or death
- Median MFS: APA 40.5 vs PBO 16.2 months
- 24-month MFS benefit

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



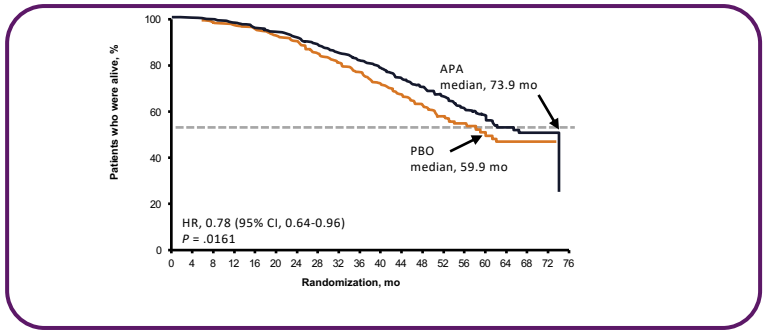
- 59% reduction of distant progression or death
- Median MFS: DARO 40.4 vs PBO 18.4 months
- 22-month MFS benefit

Courtesy of Matthew R Smith, MD, PhD

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

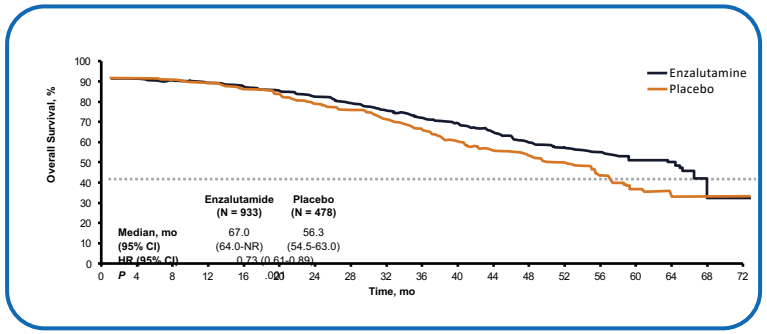
Secondary Endpoint: Overall Survival

SPARTAN1[1]
Apalutamide



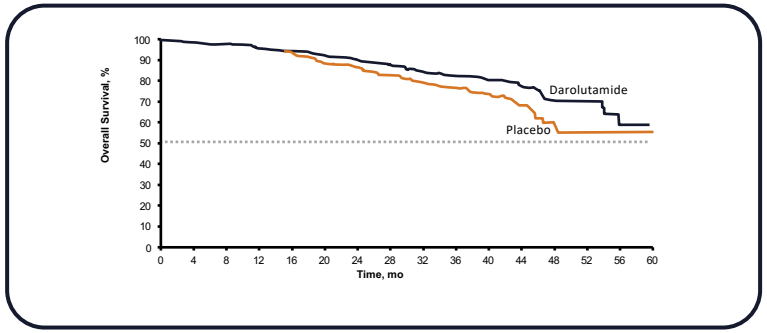
- 22% reduction in risk of death
- Median follow-up of 52.0 mo
- Median OS was significantly longer for apalutamide vs placebo
  - 73.9 mo vs 59.9 mo
  - **HR = 0.78 (95% CI 0.64-0.96); *P* = .016**

PROSPER[2]
Enzalutamide



- 27% reduction in risk of death
- Median follow-up of 48 mo
- Median OS was significantly longer for enzalutamide vs placebo
  - 67.0 mo vs 56.3 mo
  - **HR = 0.73 (95% CI 0.61-0.89); *P* = .001**

ARAMIS[3]
Darolutamide



- 31% reduction in risk of death
- Median follow-up of 29.0 mo
- Median OS was significantly longer for darolutamide vs placebo
  - **HR = 0.69 (95% CI, 0.53-0.88); *P* = .003**

Courtesy of Matthew R Smith, MD, PhD

1. Smith MR et al. *Eur Urol*. 2020;79:150-158. 2. Sternberg CN et al. *NEJM* 2020; 382:2197-2206. 3. Fizazi K et al. *NEJM* 2020;383:1040-1049.

Differential Toxicities of Androgen Receptor Targeted Agents (ARTA)

- Abiraterone
  - Hypertension, lower extremity edema
  - Electrolytes (hyper-aldosterone), liver enzyme elevations
- Apalutamide
  - Rash, Hypothyroid
  - Falls, weight loss
- Darolutamide
  - Very limited increase in toxicity compared to placebo
- Enzalutamide
  - Falls, Weight loss
  - Cognitive/emotional changes

Courtesy of Tanya B Dorff, MD

Differential Toxicities of Androgen Receptor Targeted Agents (ARTA)

- Abiraterone
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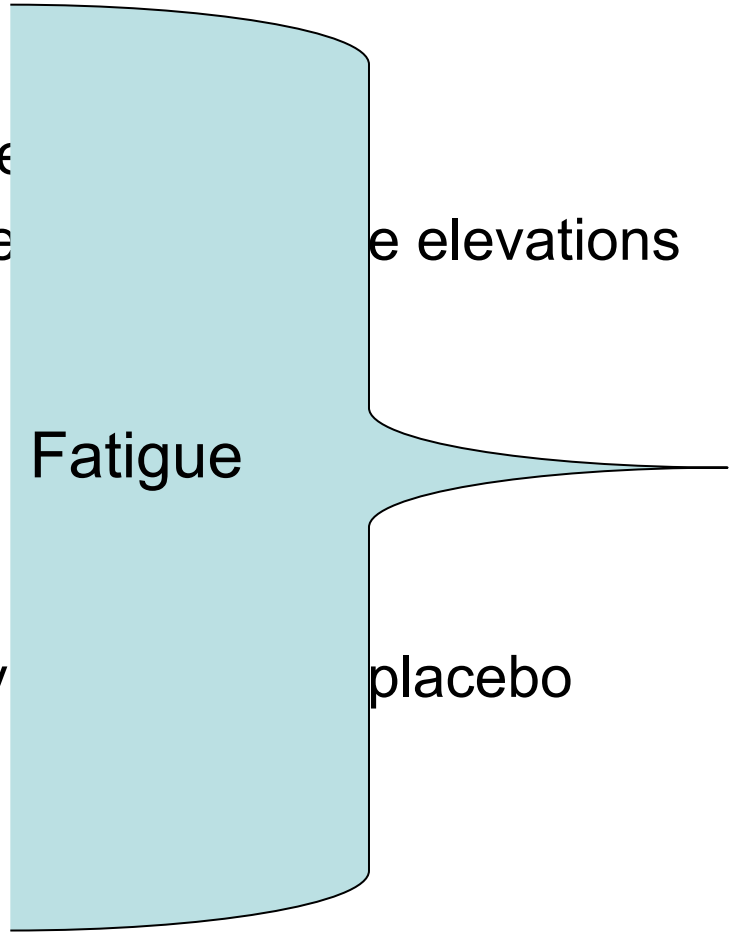

e elevations

placebo

City of Hope

Courtesy of Tanya B Dorff, MD

Which side effects do we really need to focus on?

- **Abiraterone**: arrhythmia potential
  - Avoid if CHF, active arrhythmia

DeBono JS et al. NEJM 2011; 364:1995

	Abiraterone			Placebo		
Fluid retention and edema	241 (31)	16 (2)	2 (<1)	88 (22)	4 (1)	0
Hypokalemia	135 (17)	27 (3)	3 (<1)	33 (8)	3 (1)	0
Cardiac disorder*	106 (13)	26 (3)	7 (1)	42 (11)	7 (2)	2 (<1)
Liver-function test abnormalities	82 (10)	25 (3)	2 (<1)	32 (8)	10 (3)	2 (<1)
Hypertension	77 (10)	10 (1)	0	31 (8)	1 (<1)	0

* Cardiac disorders associated with abiraterone acetate treatment, as defined with the use of the standardized *Medical Dictionary for Regulatory Activities* (version 11.0) queries, included ischemic heart disease, myocardial infarction, supraventricular tachyarrhythmias, ventricular tachyarrhythmias, cardiac failure, and possible arrhythmia-related tests, signs, and symptoms.

James ND et al. NEJM 2017; 377:338-51

Grade 3–5 adverse events — no. (%)		
Endocrine disorders‡	133 (14)	129 (14)
Cardiovascular disorders	41 (4)	92 (10)
Hypertension	13 (1)	44 (5)
Myocardial infarction	9 (1)	10 (1)
Cardiac dysrhythmia	2 (<1)	14 (1)

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Courtesy of Tanya B Dorff, MD

Which side effects do we really need to focus on?

- **Apalutamide**: avoid in elderly/frail
  - Weight loss, falls, fracture

Smith MR et al. NEJM 2018; 387:1408

	Apalutamide		Placebo	
Weight loss	129 (16.1)	9 (1.1)	25 (6.3)	1 (0.3)
Arthralgia	128 (15.9)	0	30 (7.5)	0
Falls‡	125 (15.6)	14 (1.7)	36 (9.0)	3 (0.8)
Other adverse events of interest				
Fracture‡	94 (11.7)	22 (2.7)	26 (6.5)	3 (0.8)
Dizziness	75 (9.3)	5 (0.6)	25 (6.3)	0
Hypothyroidism‡	65 (8.1)	0	8 (2.0)	0
Mental-impairment disorder§	41 (5.1)	0	12 (3.0)	0
Seizure‡	2 (0.2)	0	0	0

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Courtesy of Tanya B Dorff, MD

Which side effects do we really need to focus on?

- **Darolutamide**: no clear AE signal

Fizazi K et al. NEJM 2019; 380:1235

	Darolutamide		Placebo	
Fatigue	115 (12.1)	4 (0.4)	48 (8.7)	5 (0.9)
Back pain	84 (8.8)	4 (0.4)	50 (9.0)	1 (0.2)
Arthralgia	77 (8.1)	3 (0.3)	51 (9.2)	2 (0.4)
Diarrhea	66 (6.9)	0	31 (5.6)	1 (0.2)
Hypertension	63 (6.6)	30 (3.1)	29 (5.2)	12 (2.2)
Bone fracture‡	40 (4.2)	9 (0.9)	20 (3.6)	5 (0.9)
Falls, including accident§	40 (4.2)	8 (0.8)	26 (4.7)	4 (0.7)
Seizure, any event	2 (0.2)	0	1 (0.2)	0
Rash¶	28 (2.9)	1 (0.1)	5 (0.9)	0
Weight decrease, any event	34 (3.6)	0	12 (2.2)	0
Dizziness, including vertigo	43 (4.5)	2 (0.2)	22 (4.0)	1 (0.2)
Cognitive disorder	4 (0.4)	0	1 (0.2)	0
Memory impairment	5 (0.5)	0	7 (1.3)	0
Change in mental status	0	0	1 (0.2)	0

City of Hope

Courtesy of Tanya B Dorff, MD

Which side effects do we really need to focus on?

- **Enzalutamide**: avoid in elderly/frail
  - Weight loss, falls
  - Avoid if prior seizures/risk

Scher HI et al. NEJM 2012;

	Enzalutamide		Placebo	
Cardiac disorder				
Any	49 (6)	7 (1)	30 (8)	8 (2)
Myocardial infarction	2 (<1)	2 (<1)	2 (<1)	2 (<1)
Abnormality on liver-function testing†	8 (1)	3 (<1)	6 (2)	3 (<1)
Seizure	5 (<1)	5 (<1)	0	0
Hypertension‡	114 (12)	43 (5)	25 (5)	11 (2)
Major adverse cardiovascular event§	48 (5)	34 (4)	13 (3)	8 (2)
Mental impairment disorders¶	48 (5)	1 (<1)	9 (2)	0
Fall	106 (11)	12 (1)	19 (4)	3 (1)

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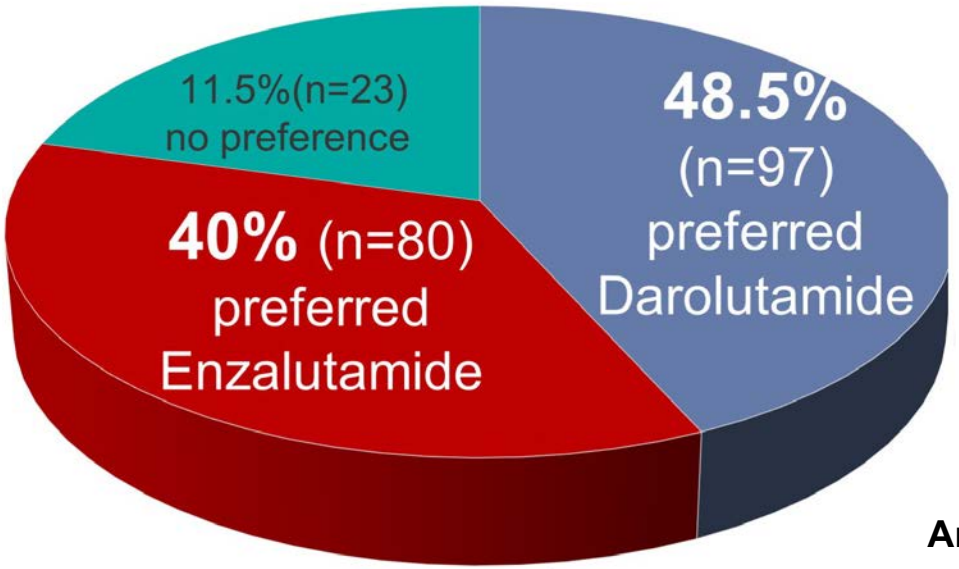
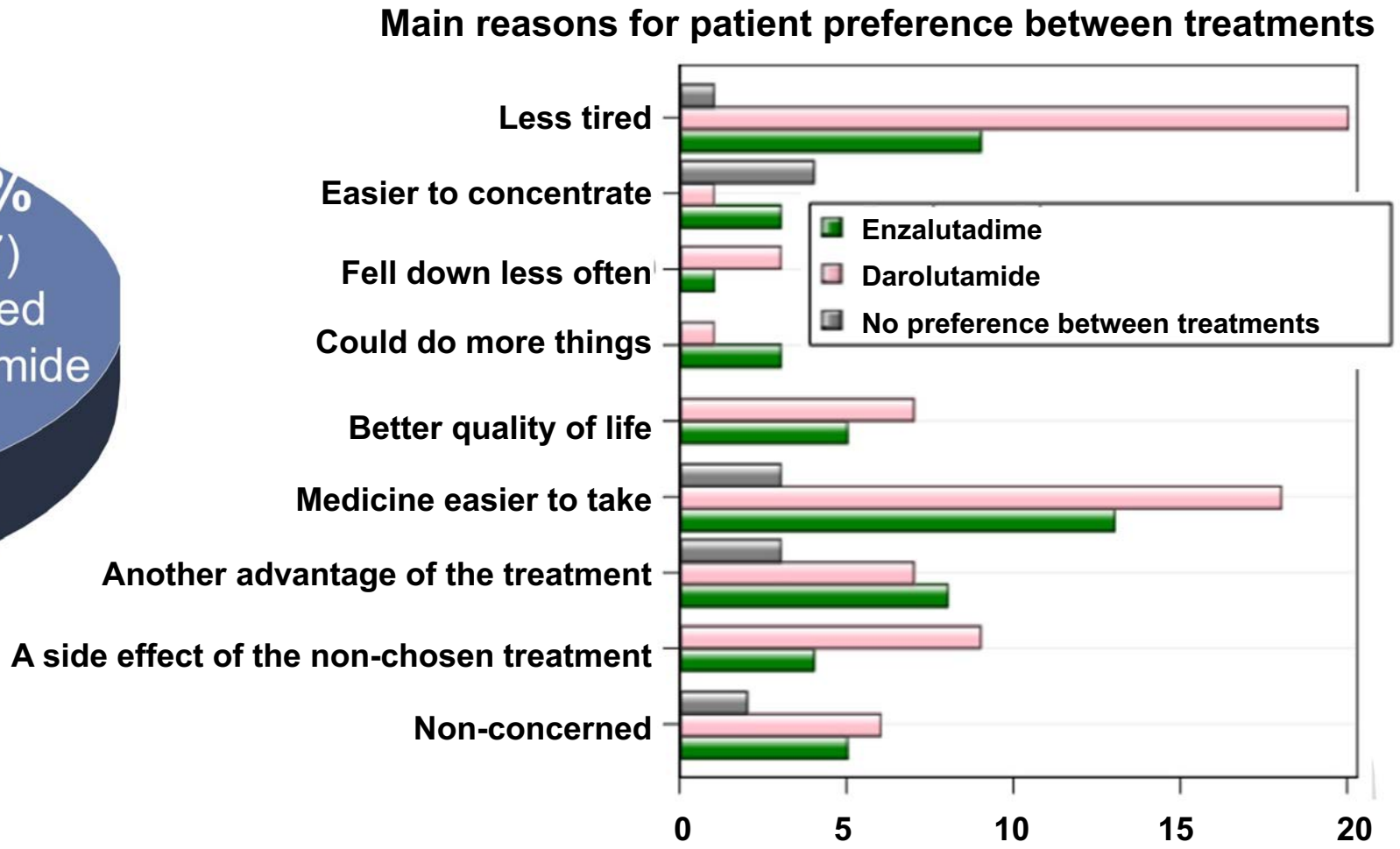
Courtesy of Tanya B Dorff, MD

Hussain M et al. NEJM 2018; 378:2465

Directly comparative data: ODENZA crossover trial





City of Hope

Colomba E et al. abstr 5046 ASCO2021

Practical Points: toxicities of ARTA

- All agents (abiraterone, apalutamide, darolutamide, enzalutamide) are overall very effective and well tolerated
  - In frail elderly, think hard about treating in nmCRPC (weight loss, osteoporosis, cognitive change)
  - Given lower fall/fracture and cognitive impairment, consider darolutamide
- In mHSPC or mCRPC abiraterone seems to be slightly better tolerated
  - Abi preferred in patients with history of seizure or risk factor for seizure, or cognitive impairment/frailty
  - Apa/Enza preferred when cardiovascular comorbidity
- Insurance coverage may dictate choice

Courtesy of Tanya B Dorff, MD

Case Presentation – Dr Smith: A 76-year-old man

- 76-year-old man with nmCRPC
- 6 years ago, he was diagnosed with NCCN unfavorable intermediate prostate cancer
- He received radiation therapy plus short-term ADT. PSA nadir 0.3
- He resumes ADT one year later after PSA was elevated at 8.6
- 4 years after starting salvage ADT, PSA is rising.
  Latest PSA 5.2. Calculated PSA-DT is 6 months
- Pelvic MRI and bone scan report no detectable metastases.
- PMH is notable for distant history of CVA with residual right-sided weakness leg

Courtesy of Matthew R Smith, MD, PhD

Case Presentation – Dr Smith: A 76-year-old man (continued)

- He started darolutamide for nmCRPC.
- He reported mild increase in fatigue.
- PSA nadir <0.10.
- 18 months later, treatment with darolutamide is ongoing. PSA remains undetectable.

Courtesy of Matthew R Smith, MD, PhD

Case Presentation – Dr Smith: A 63-year-old man

- 63-year-old man with pT3bN0 prostate cancer, Gleason 4+4, with positive surgical margins. Postoperative PSA <0.10.
- He receives adjuvant radiation therapy
- About 2 years after prostatectomy, he starts leuprolide depot for "PSA-only" disease recurrence. PSA nadir <0.1
- Three years after starting ADT, PSA is 7.6.
  Calculated PSA-DT is 5 months
- Abdominal-pelvic CT and bone scan report no detectable metastases.

Courtesy of Matthew R Smith, MD, PhD

Case Presentation – Dr Smith: A 63-year-old man (continued)

- He continues leuprolide depot and starts apalutamide.
- He developed a rash over his arms and trunk.
- Following treatment interruption and topical steroids, his rash resolves and he restarts apalutamide
- PSA nadir <0.10.
- 30 months after starting apalutamide, PSA starts to rise.
  Latest PSA 1.1
- Repeat abdominal-pelvic CT and bone scan report no detectable cancer.

Courtesy of Matthew R Smith, MD, PhD

Agenda

Module 1: Choice of Androgen Deprivation Therapy

- HERO study: Oral relugolix versus leuprolide acetate

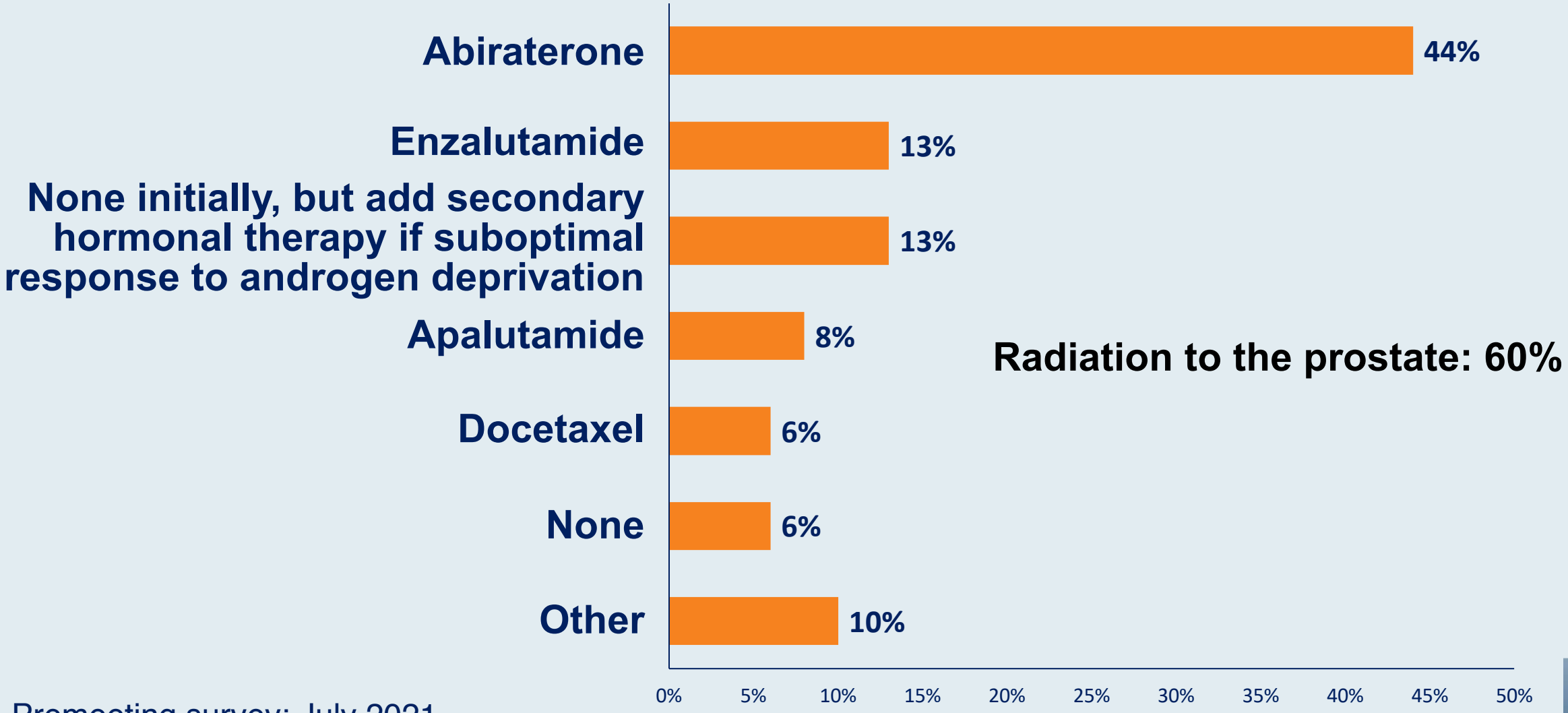
Module 2: Nonmetastatic Castration-Resistant Prostate Cancer (nmCRPC)

- Next-generation androgen receptor inhibitors (ie, apalutamide, darolutamide, enzalutamide)
- Phase III PROSPER, SPARTAN and ARAMIS trials: Long-term efficacy outcomes
- Differential side-effect profiles of abiraterone, enzalutamide, apalutamide and darolutamide
- Incidence of CNS-related adverse events with secondary hormonal therapy

Module 3: Metastatic Hormone-Sensitive PC (mHSPC)

- Real-world treatment patterns in mHSPC
- PEACE-1 study: Abiraterone with prednisone and/or local radiation therapy for men with de novo mHSPC
- ARCHES, ENZAMET and TITAN trials: Long-term results
- Ongoing Phase III trials assessing darolutamide-based therapy for men with mHSPC

Regulatory and reimbursement issues aside, what systemic therapy, if any, would you typically add to androgen deprivation for a 65-year-old patient presenting with Gleason 8 PC and 3 asymptomatic rib metastases?

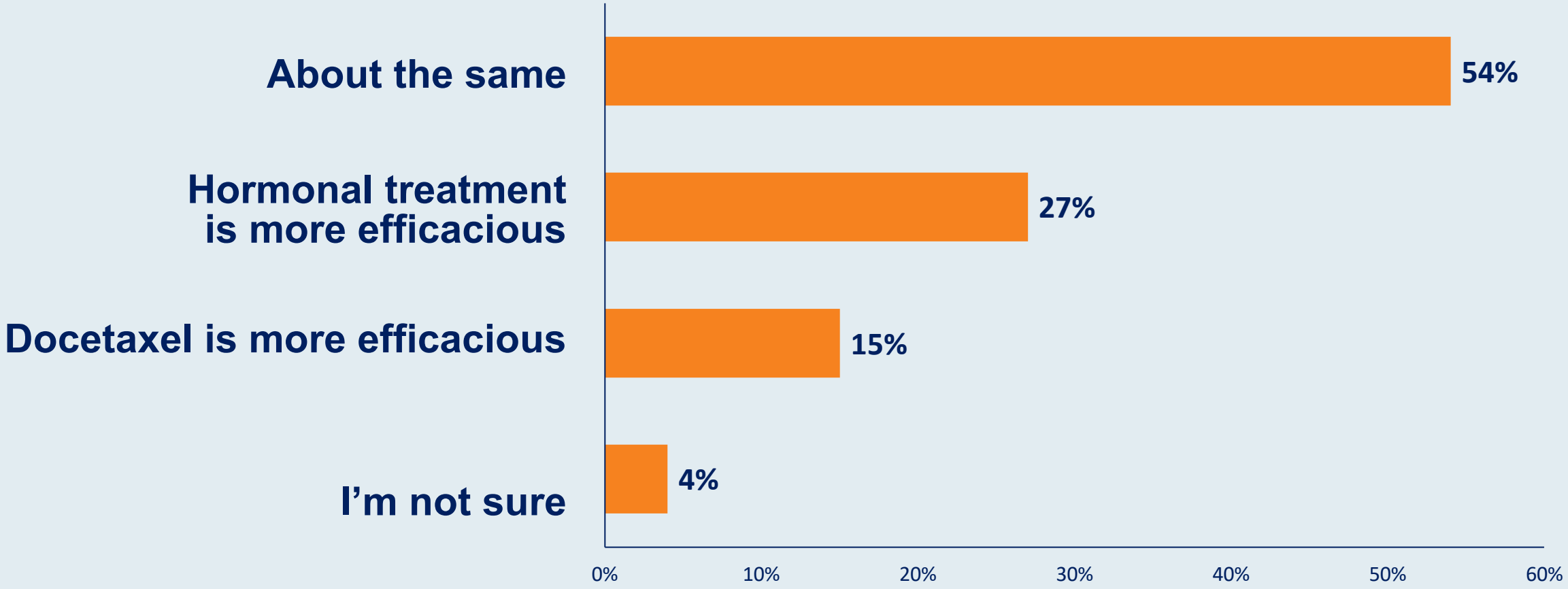


Radiation to the prostate: 60%

Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

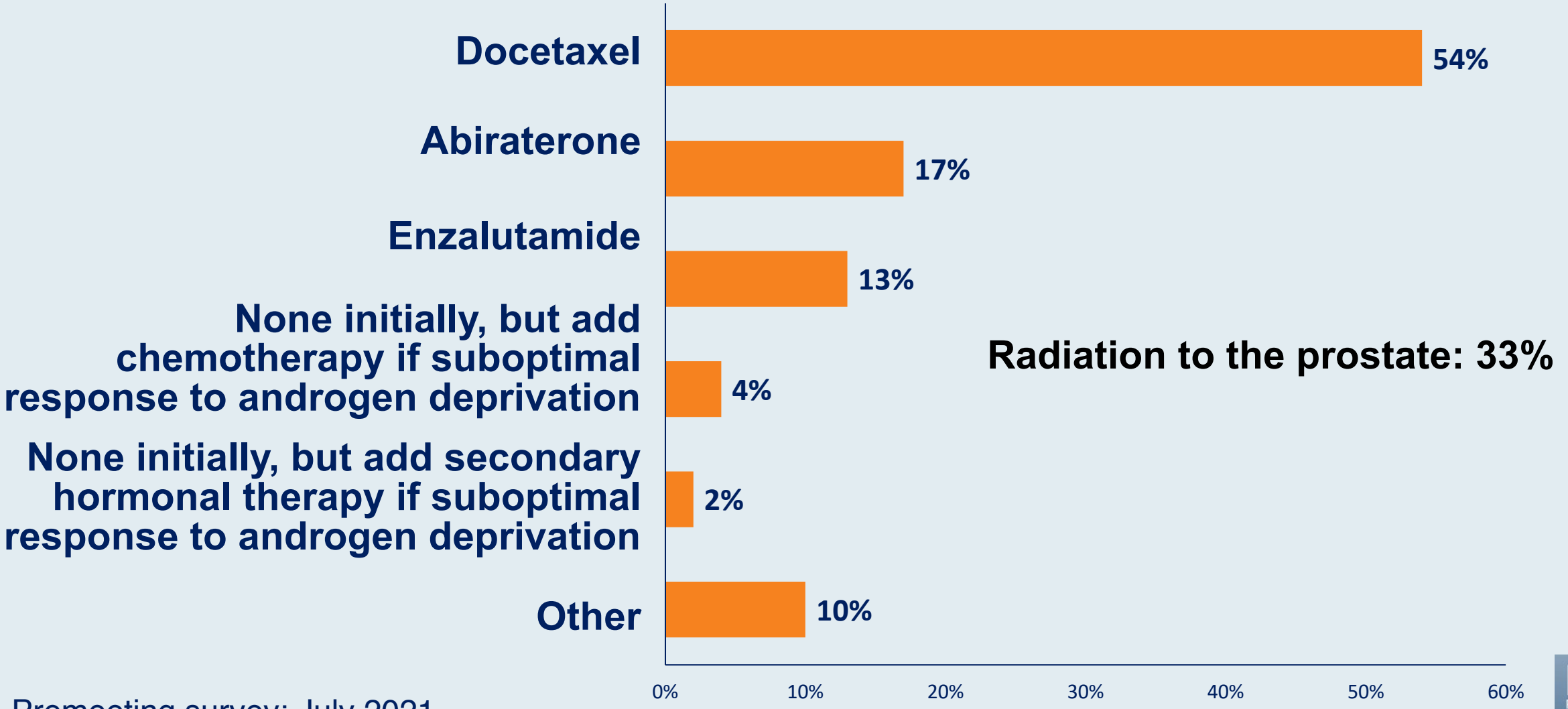
In general, how would you compare the efficacy of ADT with docetaxel versus hormonal treatment for patients with asymptomatic metastatic PC (mPC)?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

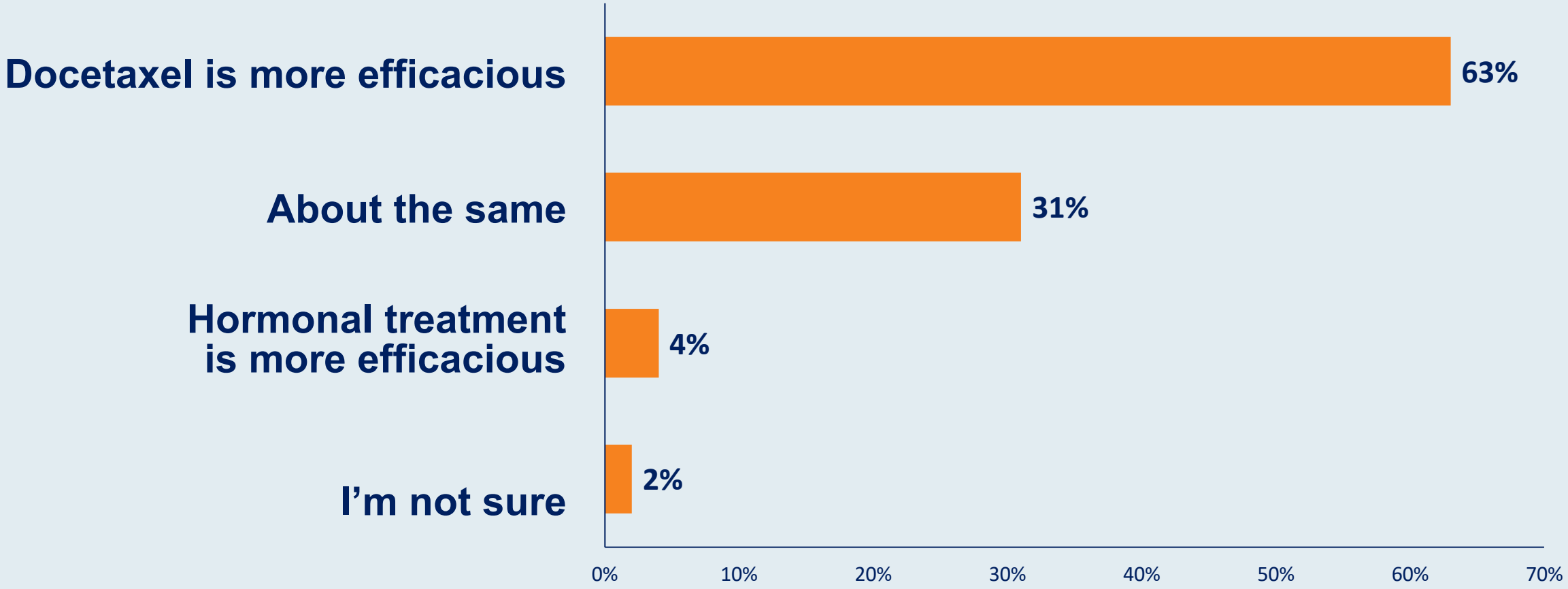
Regulatory and reimbursement issues aside, what systemic therapy, if any, would you typically add to androgen deprivation for a 65-year-old patient presenting with Gleason 8 PC and widespread, moderately symptomatic bone metastases?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

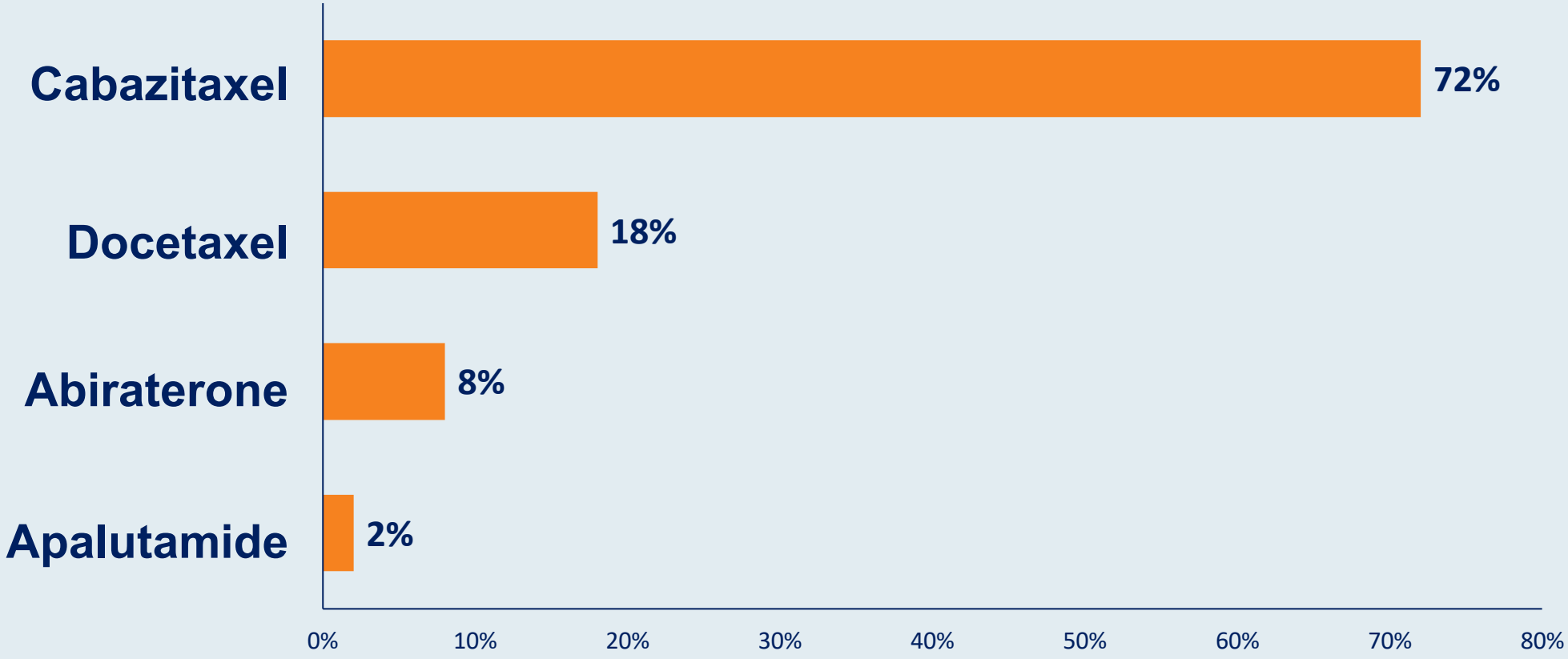
In general, how would you compare the efficacy of ADT with docetaxel versus hormonal treatment for patients with symptomatic mPC?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

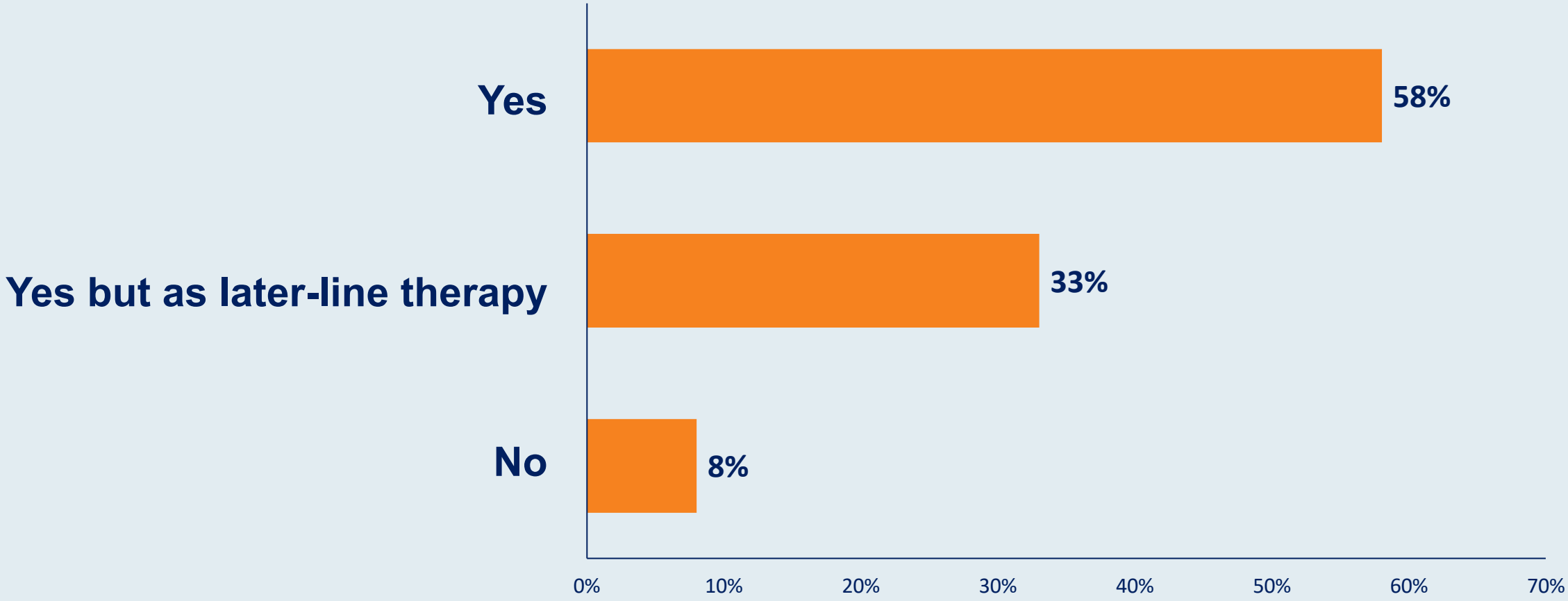
A 75-year-old man presents with PC (BRCA wild type) metastatic to the bone and receives ADT and docetaxel with disease progression 1 year later. He responds to enzalutamide for 9 months, then develops symptomatic progression in the bone along with new lung lesions. What is your most likely treatment?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

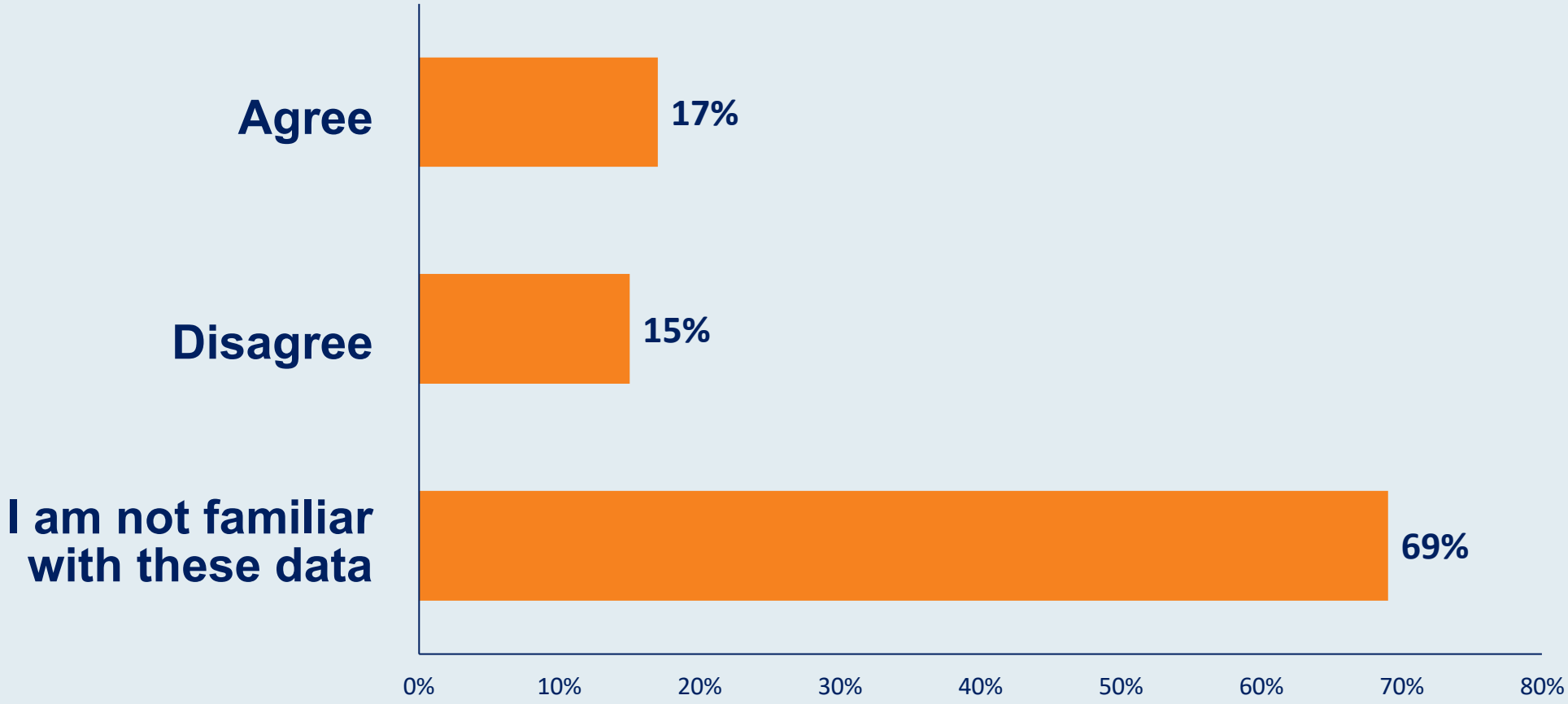
If 77Lu-PSMA-617 were available and this patient was eligible to receive it, would you likely recommend it?



Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Monthly high-dose testosterone appears to be a safe and effective treatment option for mCRPC.



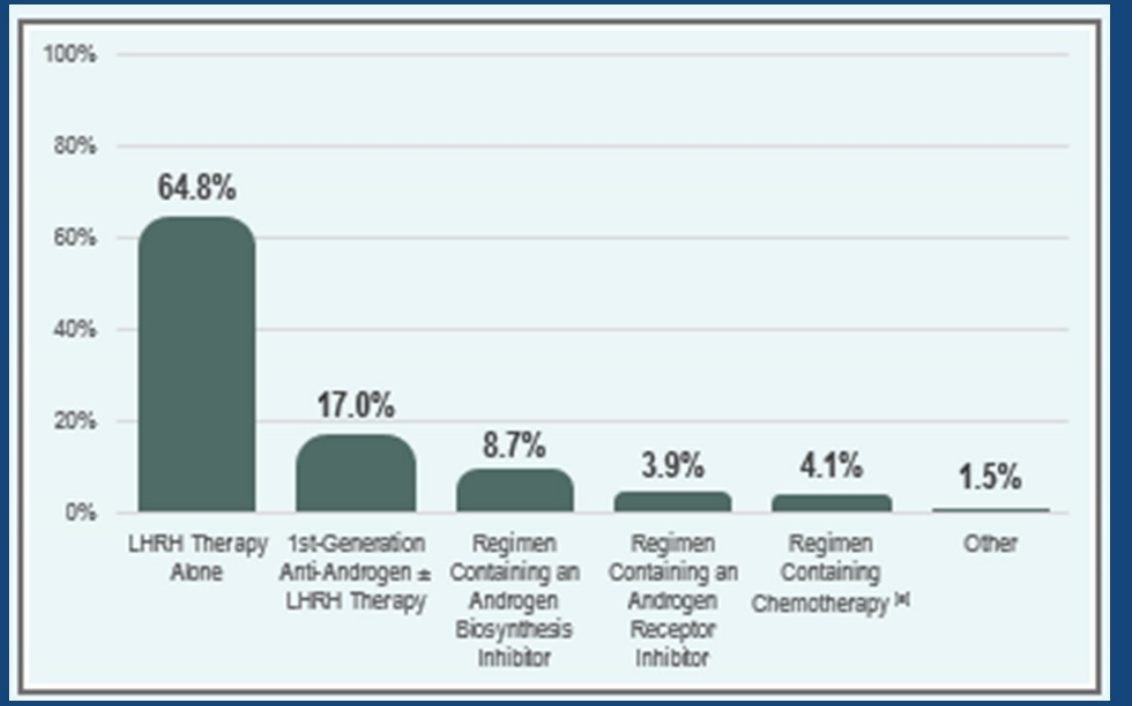
Premeeting survey: July 2021

RTP RESEARCH TO PRACTICE

Real-World Treatment Patterns in mHSPC

- **Most men with mHSPC are treated with LHRH Therapy alone**
  - US, physician-based syndicated patient record tracking study capturing usage of anti-cancer and supportive care agents in PC
    - Data collected online between June 2018 and June 2019
    - 156 physicians reporting on 1360 patients
  - Patients with mHSPC identified with the following query:
    - Prostate, stage IV, not hormone refractory, metastatic line 1 by regimen

Patients Receiving Various Treatment Categories (%)



a. Exlcudes regimens containing an androgen biosynthesis inhibitor or an androgen receptor inhibitor

Ispsos Healthcare US Oncology Monitor (June 2018 to June 2019, 156 physicians reporting on 1360 patients, all data collected online

Poster Number 5074

Real-world treatment patterns among patients diagnosed with metastatic castration-sensitive prostate cancer (mCSPC) in community oncology settings

Daniel J. George, MD[1]; Neeraj Agarwal, MD[2]; Jennifer R. Rider, ScD[3]; Benjamin Li, PhD[4]; Rohan Shirali, MA[3]; Rickard Sandin, PhD[5]; Agnes Hong, PharmD, MS[3]; David Russell, MD[6]; Krishnan Ramaswamy, PhD[4]; Stephen J. Freedland, MD[7]

Courtesy of Simon Chowdhury, MD, PhD

Objective

To investigate the impact of new evidence on treatment selection for patients with mCSPC in real-world US oncology practice settings

Key Finding

Despite an increase in treatment intensification with novel hormonal therapies or docetaxel from 2015 to 2019, more than half of the patients in 2019 did not receive intensified therapy

Context

There is a disconnect between clinical trial evidence and real-world practice in the management of patients with mCSPC in US community oncology practices, but reasons for this underutilization need to be explored

ASCO 2021;Abstract 5074.

Courtesy of Simon Chowdhury, MD, PhD

CONCLUSION

M1 castration-sensitive:

In *de novo* M1 disease, no real reason to believe that low and high burden disease are biologically distinct:

- Docetaxel works (but not fantastically well): HR= 0.76 and 0.81, respectively

- **Abiraterone/Enzalutamide/Apalutamide associated with more profound OS effect.**

Apalutamide has the most robust data for a broad population of mHSPC

Courtesy of Simon Chowdhury, MD, PhD

Overall survival in mHSPC trials

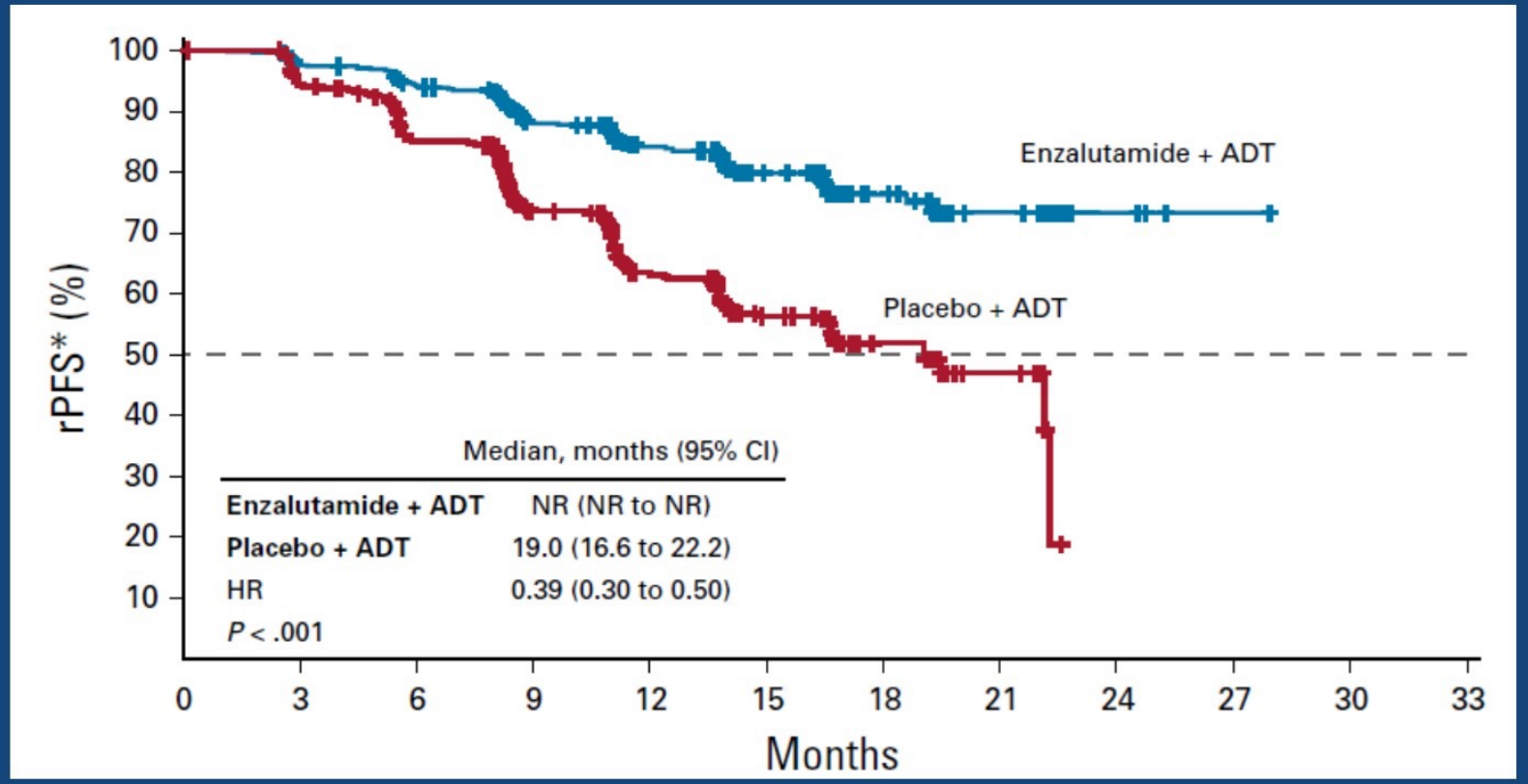
Trial	HR for OS	HR for OS: High volume	HR for OS: Low volume	Follow-up (mo)
STAMPEDE Abi[1]	**0.60 (0.50-0.71)**	0.59 (0.47-0.74)	0.53 (0.38-0.74)	73
TITAN[4]	**0.65 (0.53-0.79)** ***Adjusted 0.52 (0.42−0.64)**	0.70 (0.56-0.88)	0.52 (0.35-0.79)	44
LATITUDE[a,2,3]	**0.66 (0.56-0.78)**	0.62 (0.52-0.74)	0.72 (0.47-1.10)	52
ENZAMET[b,5]	**0.67 (0.52-0.86)**	0.80 (0.59-1.07)	0.43 (0.26-0.72)	34
ARCHES[6]	**0.81 (0.53-1.25)**	-	-	14
CHAARTED[7]	**0.72 (0.59-0.89)**	0.63 (0.50-0.79)	1.04 (0.70-1.55)	54
STAMPEDE Doc[8]	**0.81 (0.69-0.95)**	0.81 (0.64-1.02)	0.76 (0.54-1.07)	78
GETUG-15[9]	**0.88 (0.68-1.14)**	0.78 (0.56-1.09)	1.02 (0.67-1.55)	84

[a] Newly diagnosed, high-risk patients.
[b] 45% of patients received docetaxel.
AA, abiraterone acetate.

1. James ND, et al. N Engl J Med. 2017;377:338-51. 2. Fizazi K, et al. Lancet Oncol. 2019;20:686-700. 3. Fizazi K, et al. N Engl J Med. 2017;377:352-60. 4. Chi KN, et al. Oral presentation at ASCO GU 2021; abstract 11. 5. Davis ID, et al. N Engl J Med. 2019;381:121-31. 6. Armstrong A, et al. J Clin Oncol. 2019;37:2974-86. 7. Kyriakopoulos CE, et al. J Clin Oncol. 2018;36:1080-7. 8. Clarke NW, et al. Ann Oncol. 2019;30:1992-2003. 9. Gravis G, et al. Eur Urol. 2016;70-256-62.

Courtesy of Simon Chowdhury, MD, PhD

ARCHES: Enzalutamide for mHSPC



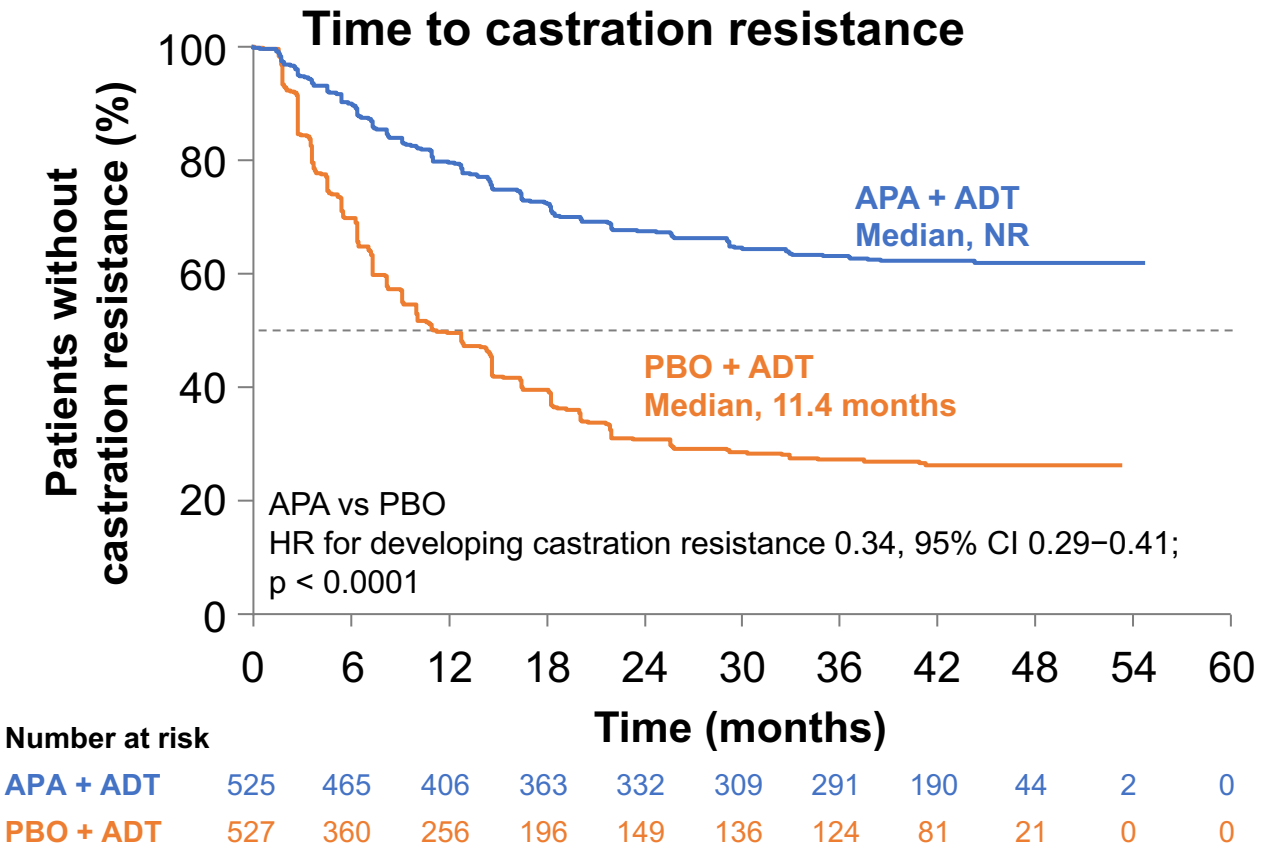
Overall Survival: HR 0.81 (95% CI 0.53, 1.25), P=0.3361 but survival data were immature with only 14.4 months median follow-up and 84 deaths

Armstrong et al (2019) *J Clin Oncol 37:* 2974-2986

Final analysis of results from TITAN: Time to castration resistance

- Other clinically relevant endpoints favoured APA + ADT

Final analysis: Clinical cut-off date 7 September 2020



Number at risk											
APA + ADT	525	465	406	363	332	309	291	190	44	2	0
PBO + ADT	527	360	256	196	149	136	124	81	21	0	0

Castration resistance is defined as time from randomisation to radiographic PD, PSA progression, or symptomatic skeletal event, whichever occurs first.

Chi KN, et al. Oral presentation at ASCO GU 2021; abstract 11.

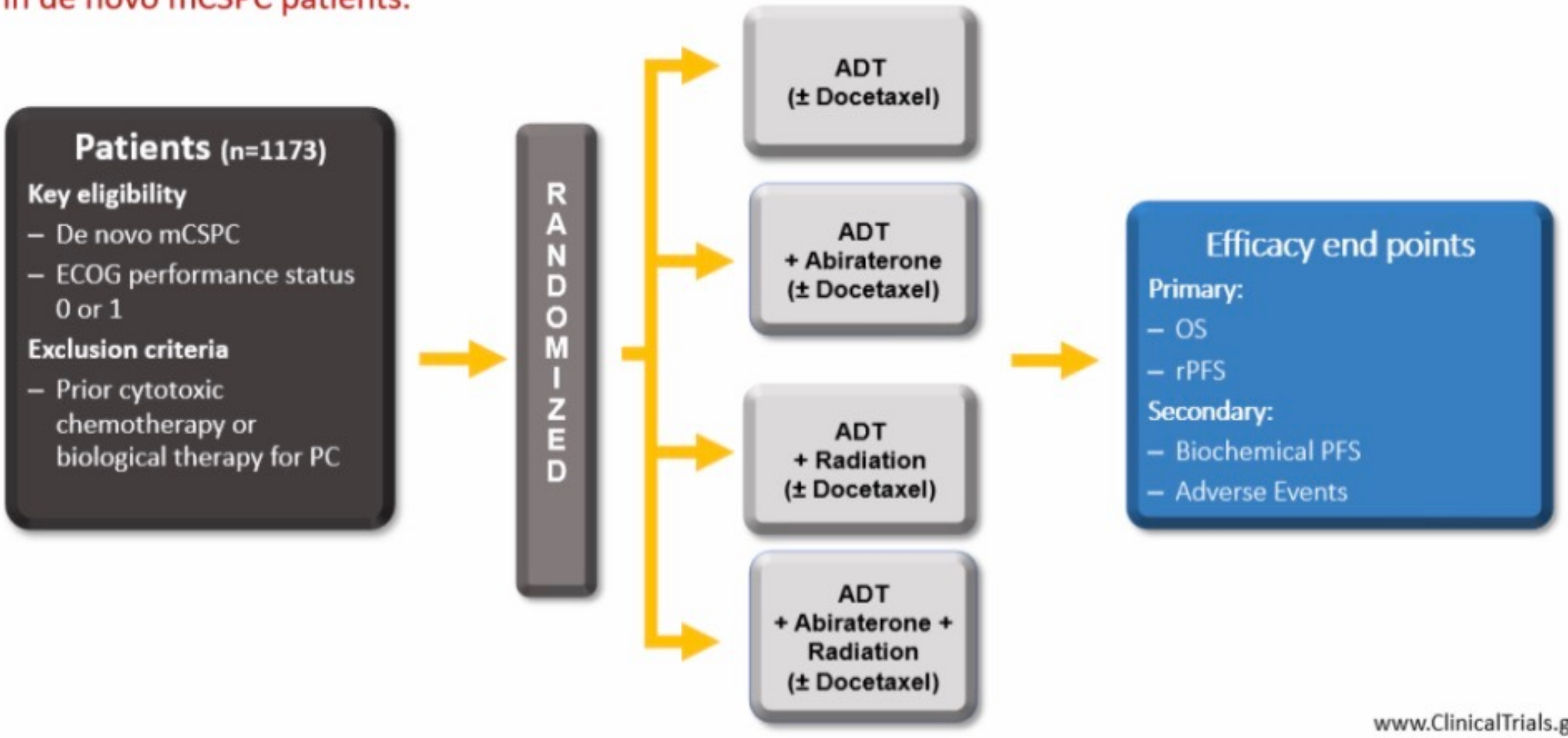
Courtesy of Simon Chowdhury, MD, PhD

ASCO Annual Meeting 2021: Abstract #5000

A phase 3 trial with a 2x2 factorial design of abiraterone acetate plus prednisone and/or local radiotherapy in men with de novo metastatic castration-sensitive prostate cancer (mCSPC): First results of PEACE-1.

Presenting Author: Karim Fizazi

Hypothesis: To investigate the clinical benefit of adding docetaxel, abiraterone acetate or radiation therapy to ADT in de novo mCSPC patients.



www.ClinicalTrials.gov: (NCT02567409)

Courtesy of Simon Chowdhury, MD, PhD

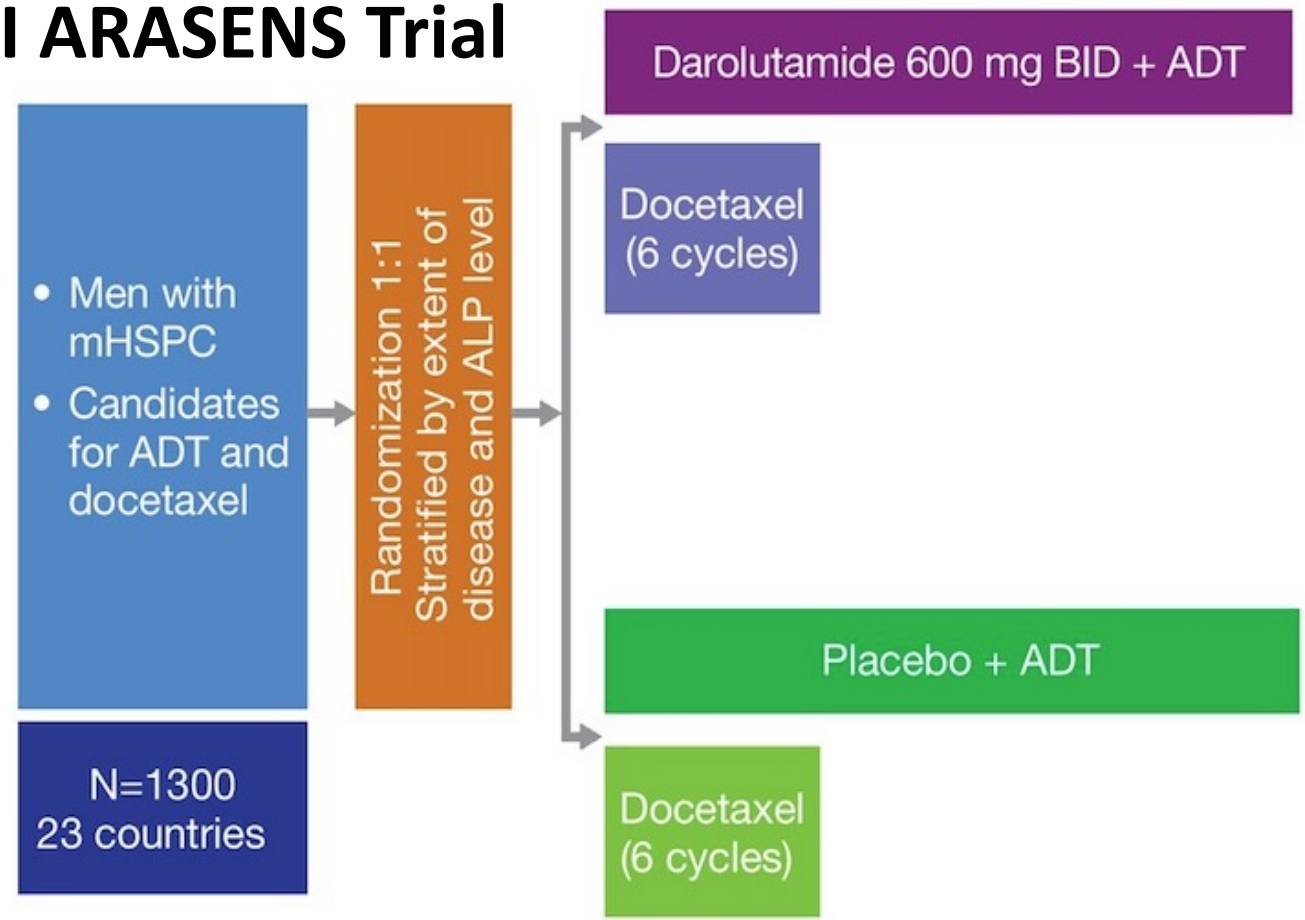
PEACE-1: First Results and Conclusions

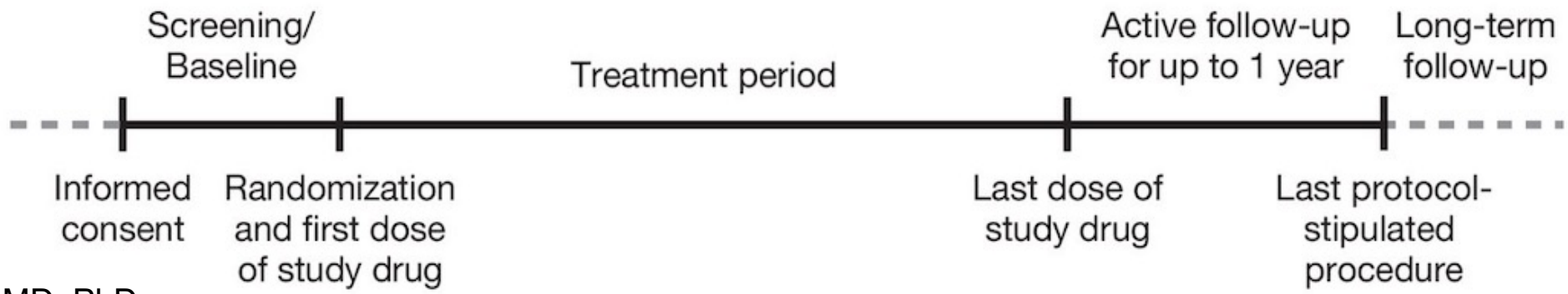
- Median age was 67 years, high volume 57%
- Median follow-up was 3.5 years
- rPFS:
  - significantly improved in the abiraterone arm in the overall population (HR: 0.54 (0.46-0.64), $p < 0.0001$; medians: 2.2 vs 4.5 years)
  - and in the ADT+ docetaxel arms (HR: 0.50 (0.40-0.62), $p < 0.0001$; medians: 2.0 vs 4.5 years)
- Other outcomes favored the abiraterone arm as well as the arms that included docetaxel.
- Safety signals were as expected.

Conclusions: Adding abiraterone to ADT + docetaxel significantly improves rPFS in men with *de novo* metastatic prostate cancer, with about 2.5 years of absolute benefit in medians, and no meaningful additional short-term toxicity.

Courtesy of Simon Chowdhury, MD, PhD

Ongoing Phase III ARASENS Trial



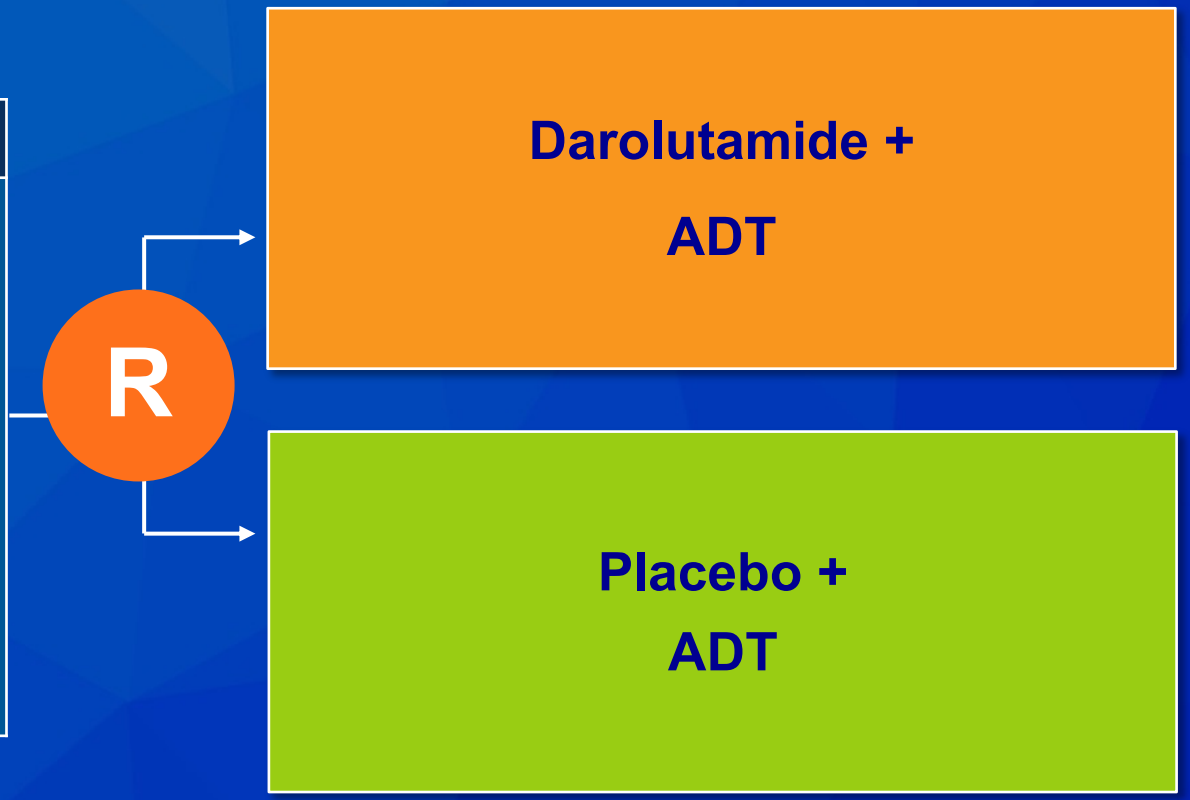


Courtesy of Simon Chowdhury, MD, PhD

ARANOTE: Ongoing Phase III Trial Design

Estimated enrollment (N = 555)

- mHSPC
- ECOG PS 0-2
- No prior treatment with LHRH agonist/antagonist except (neo)adjuvant therapy
- No second-generation AR inhibitors



Primary endpoint: Radiological progression-free survival

Secondary endpoints include OS, time to castration-resistant prostate cancer

www.clinicaltrials.gov. NCT04736199. Accessed July 2021.

Case Presentation – Dr Chowdhury: A 74-year-old man

- Age 74
- mHSPC (T3bN0M1b: R sacrum, T8 and T12 on Bone scan)
- pPSA 89
- Co-morbidity: Smoker 50 pack years, ischemic heart disease (MI)
- June 2016: ADT started
- Sept 2016: TITAN study: Started trial drug
- Feb 2019: Unblinded: On Apalutamide. Minimal SE
- April 2021: PSA <0.03 (for the last 18 months at least). PSMA PET – ve. Continues on Apa

Courtesy of Simon Chowdhury, MD, PhD

Case Presentation – Dr Chowdhury: A 68-year-old man

- Age 68
- mHSPC (Extensive bone and L disease, also anemic at presentation)
- pPSA 208
- May 2019: ADT started. Unfit for Docetaxel.
- **PSA 7.45 falling (Jan 2020)**
- No other co-morbidities. PS 0
- **Is he high risk?**
- Patient too scared to leave house for blood tests…
- June 2020: PSA 52. Progressive bone and LN disease. Cycle 1 Abiraterone.
- April 2021: PSA 10, nadir of 5, planned for repeat imaging…

Courtesy of Simon Chowdhury, MD, PhD

Case Presentation – Dr Dorff: A 74-year-old man

- 74 yo man treated with prostatectomy >10 years ago, T3bN1 Gl 4+3
  - Received adjuvant radiation + short course ADT
- BCR – 4 years later. Intermittent ADT
- Castration resistance after 2 years, imaging showed several osseous metastases
- Enzalutamide added
  - Noted significant cognitive decline
  - Not alleviated with Methylphenidate hydrochloride
- Switched to apalutamide with good cancer control, neurologic toxicity resolved.

Courtesy of Tanya B Dorff, MD

Case Presentation – Dr Dorff: An 81-year-old man

- 81 yo man treated with prostatectomy >10 years ago, bPSA 12, T3aN0 GI 4+3
- BCR – 4 years later, treated with salvage ADT + XRT
- 4 years later with ongoing BCR imaging identified bone and lymph node metastases
  - Started ADT + apalutamide
- After 9 months, patient noticed significant decrease in ability to do yard work
  - He is reluctant to undergo dose reduction
- Progressive decrease in stamina and reported a fall

Courtesy of Tanya B Dorff, MD

Faculty Case Appendix

Case Presentation – Dr Smith: A 71-year-old man

- 71 year-old man with pT3bN1 prostate cancer, Gleason 4+5. Postoperative PSA 1.2.
- He is treated with continuous ADT using goserelin acetate. PSA nadir <0.1
- 29 months after starting ADT, PSA is 6.7. PSA-DT is 3 months.
- Bone scan reports faint uptake in right ischium, left pubic ramus.
- Abdominal-pelvic CT scan reports a small sclerotic lesion in right ischium (bone island versus metastasis) and prominent pelvic nodes (largest 1.1 cm).

Courtesy of Matthew R Smith, MD, PhD

Case Presentation – Dr Smith: A 71-year-old man (continued)

- He is prescribed enzalutamide.
- Treatment was accompanied by increased fatigue.
- PSA nadir <0.10.
- One year after starting enzalutamide, CT scan reports interval decrease in size of pelvic nodes. Bone reports: no interval change.

Courtesy of Matthew R Smith, MD, PhD

Case Presentation – Dr Dorff: A 74-year-old man

- 74 yo man treated with prostatectomy >10 years ago, T3bN1 Gl 4+3
  - Received adjuvant radiation + short course ADT
- BCR – 4 years later. Intermittent ADT
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Courtesy of Tanya B Dorff, MD

Case Presentation – Dr Dorff: A 68-year-old man

- 68 yo man presented with PSA 13, biopsy Gl 3+4, treated with proton beam therapy
- BCR – 8 years after primary treatment imaging revealed bone metastases. Started on ADT
- Castration resistance at 24 months.
  - PMH significant for stroke 1 year ago, no residual sequelae
  - Not on anticoagulation, just aspirin
- Abiraterone + prednisone added
  - PSA decline from 417 to 4.7
- Developed Atrial Fibrillation while traveling

Courtesy of Tanya B Dorff, MD

A Conversation with the Investigators: Chimeric Antigen Receptor T-Cell Therapy in Hematologic Cancers

Tuesday, July 13, 2021
5:00 PM – 6:00 PM ET

Faculty

Caron Jacobson, MD
David G Maloney, MD, PhD
Nikhil C Munshi, MD

Moderator

Neil Love, MD

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Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 2 to 3 business days.

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