

Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Prostate Cancer

Thursday, August 12, 2021

5:00 PM – 6:00 PM ET

Faculty

A Oliver Sartor, MD

Ronald Stein, JD, MSN, NP-C, AOCNP

Moderator

Neil Love, MD

Faculty



A Oliver Sartor, MD

CE and Bernadine Laborde Professor for
Cancer Research
Medical Director, Tulane Cancer Center
Assistant Dean for Oncology
Tulane Medical School
New Orleans, Louisiana



Ronald Stein, JD, MSN, NP-C, AOCNP

Clinical Instructor of Medicine
USC Norris Comprehensive Cancer Center
Los Angeles, California



Moderator

Neil Love, MD

Research To Practice
Miami, Florida

Commercial Support

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

Dr Love — Disclosures

Dr Love is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, Daiichi Sankyo Inc, Eisai Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, Genentech, a member of the Roche Group, Gilead Sciences Inc, GlaxoSmithKline, Grail Inc, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc and Verastem Inc.

Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

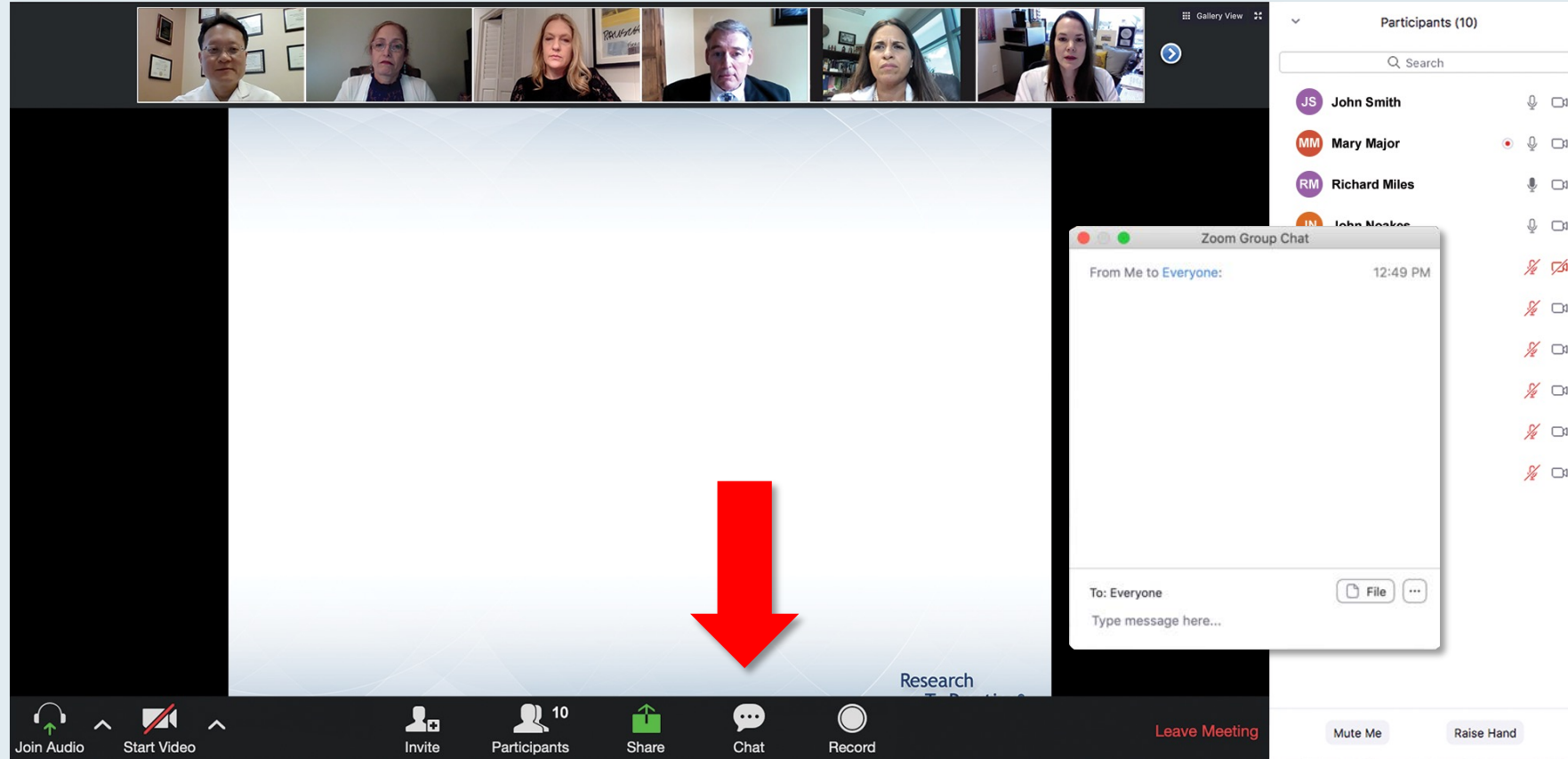
Dr Sartor — Disclosures

Consulting Agreements	Advanced Accelerator Applications, Astellas, AstraZeneca Pharmaceuticals LP, Bavarian Nordic, Bayer HealthCare Pharmaceuticals, Blue Earth Diagnostics, Bristol-Myers Squibb Company, Clarity Pharmaceuticals, Clovis Oncology, Constellation Pharmaceuticals, Dendreon Pharmaceuticals Inc, EMD Serono Inc, Fusion Pharmaceuticals, ITM Isotopen Technologien Muenchen AG, Janssen Biotech Inc, Myovant Sciences, Myriad Genetic Laboratories Inc, Noria Therapeutics Inc, Novartis, Noxopharm, Pfizer Inc, Point Biopharma Inc, Progenics Pharmaceuticals Inc, Sanofi Genzyme, Telix Pharmaceuticals, TeneoBio, Theragnostics
Contracted Research	Advanced Accelerator Applications, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Constellation Pharmaceuticals, Dendreon Pharmaceuticals Inc, Endocyte Inc, Invitae, Janssen Biotech Inc, Merck, Progenics Pharmaceuticals Inc, Sanofi Genzyme, SOTIO LLC

Mr Stein — Disclosures

No relevant conflicts of interest to disclose

We Encourage Clinicians in Practice to Submit Questions



Feel free to submit questions now before the program begins and throughout the program.

Familiarizing Yourself with the Zoom Interface

How to answer poll questions

The screenshot displays a Zoom meeting interface. At the top, a gallery view shows six participants. The main screen displays a poll question: "What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?". Below the question is a list of ten treatment options, each preceded by a number. A "Quick Poll" dialog box is open, showing the same list of options with radio buttons for selection. The bottom of the screen features a toolbar with icons for "Join Audio", "Start Video", "Invite", "Participants" (showing 10), "Share", "Chat", "Record", and a "Leave Meeting" button. On the right side, a "Participants (10)" list is visible, showing names and status icons.

What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?

Quick Poll

- ☐ Carfilzomib +/- dexamethasone
- ☐ Pomalidomide +/- dexamethasone
- ☐ Carfilzomib + pomalidomide +/- dexamethasone
- ☐ Elotuzumab + lenalidomide +/- dexamethasone
- ☐ Elotuzumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + lenalidomide +/- dexamethasone
- ☐ Daratumumab + pomalidomide +/- dexamethasone
- ☐ Daratumumab + bortezomib +/- dexamethasone
- ☐ Ixazomib + Rd
- ☐ Other

Submit

Co-provided by USF Health Research To Practice®

Join Audio Start Video Invite Participants 10 Share Chat Record Leave Meeting Mute Me Raise Hand

Participants (10)

Search

- JS John Smith
- MM Mary Major
- RM Richard Miles
- JN John Noakes
- AS Alice Suarez
- JP Jane Perez
- RS Robert Stiles
- JF Juan Fernandez
- AK Ashok Kumar
- JS Jeremy Smith

When a poll question pops up, click your answer choice from the available options.

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

The screenshot displays a Zoom meeting interface. At the top, a video bar shows participants: RTP Coordinat..., Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. Below the video bar, a 'Recording...' indicator is visible. The main content area shows a presentation slide titled 'Meet The Professor Program Steering Committee'. The slide lists six members of the steering committee, each with a portrait photo and their name and affiliation:

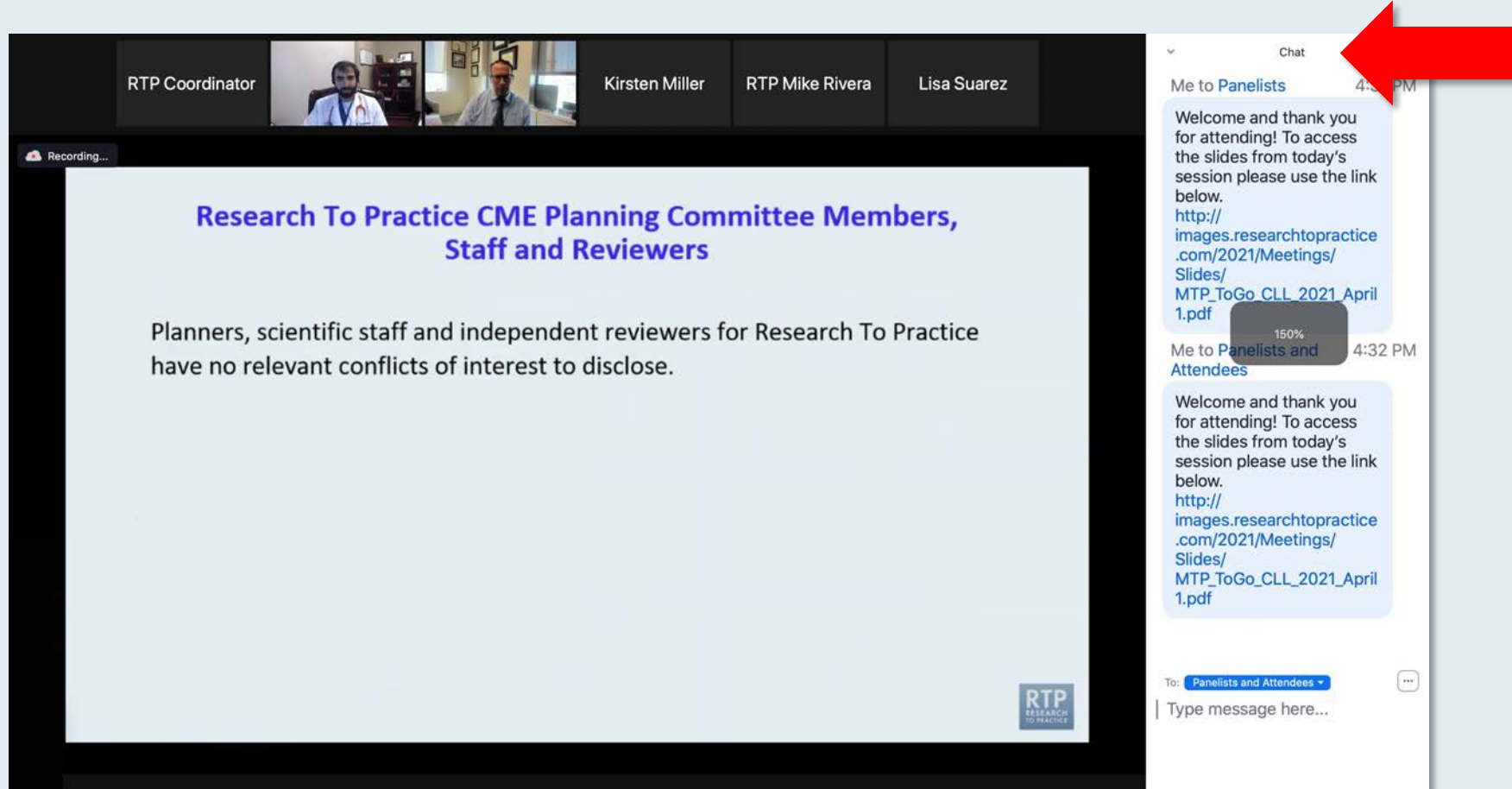
- John N Allan, MD**
Assistant Professor of Medicine
Weill Cornell Medicine
New York, New York
- Ian W Flinn, MD, PhD**
Director of Lymphoma Research Program
Sarah Cannon Research Institute
Tennessee Oncology
Nashville, Tennessee
- Steven Coutre, MD**
Professor of Medicine (Hematology)
Stanford University School of Medicine
Stanford, California
- Prof John G Gribben, MD, DSc, FMedSci**
Chair of Medical Oncology
Barts Cancer Institute
Queen Mary University of London
Charterhouse Square
London, United Kingdom
- Matthew S Davids, MD, MMSc**
Associate Professor of Medicine
Harvard Medical School
Director of Clinical Research
Division of Lymphoma
Dana-Farber Cancer Institute
Boston, Massachusetts
- Brian T Hill, MD, PhD**
Director, Lymphoid Malignancy Program
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio

The chat window on the right is titled 'Chat' and shows two messages from 'Me to Panelists' and 'Me to Panelists and Attendees', both dated 4:31 PM and 4:32 PM respectively. Each message includes a welcome note and a link to a PDF document: http://images.researchtopractice.com/2021/Meetings/Slides/MTP_ToGo_CLL_2021_April1.pdf. At the bottom of the chat window, there is a 'To:' dropdown menu set to 'Panelists and Attendees' and a text input field labeled 'Type message here...'. A large red arrow points to the white line above the text input field, indicating where to drag to expand the box.

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

Familiarizing Yourself with the Zoom Interface

Increase chat font size



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

ONCOLOGY TODAY

WITH DR NEIL LOVE

Side Effects of Hormonal Therapy in Prostate Cancer



DR ROBERTO IACOVELLI

FONDAZIONE POLICLINICO
UNIVERSITARIO A GEMELLI



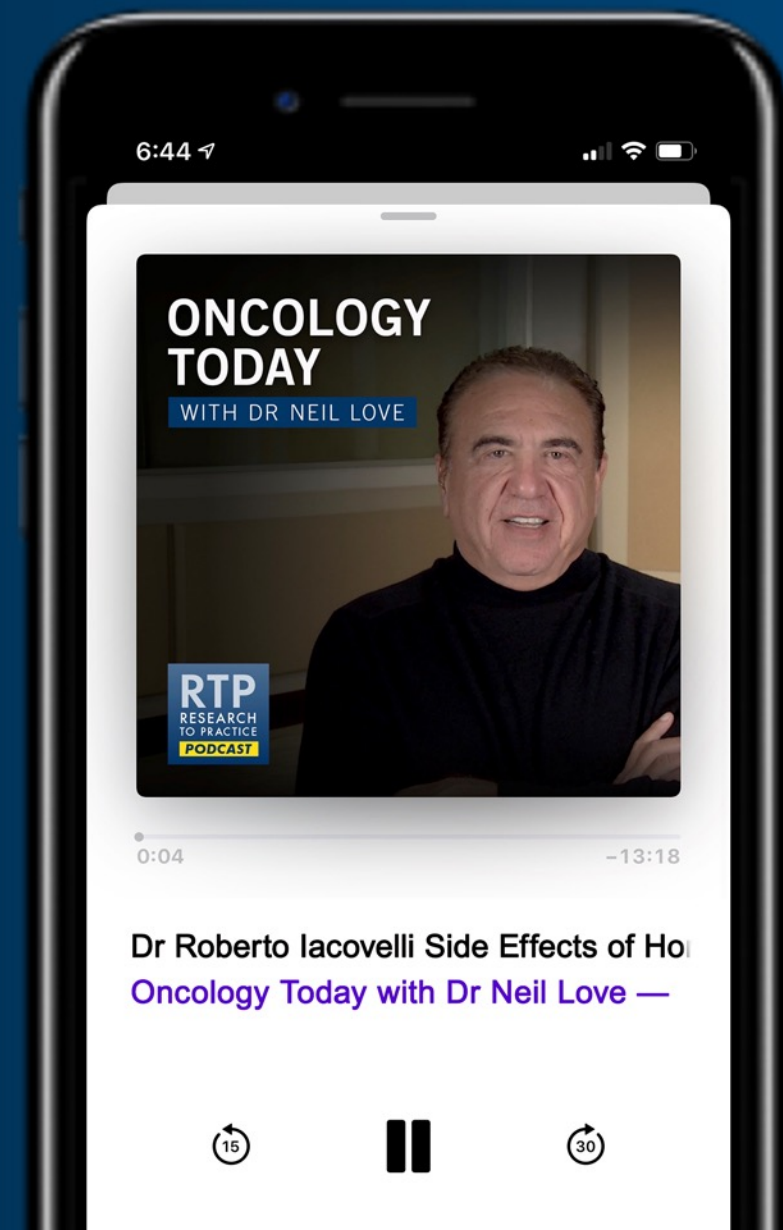
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Cases from the Community — Investigators Discuss Emerging Research and Actual Patients with Multiple Myeloma

Held in Conjunction with the 2021 Pan Pacific Lymphoma Conference

**Thursday, August 12, 2021
7:00 PM – 8:30 PM ET**

Faculty

**Muhamed Baljevic, MD
Joseph Mikhael, MD
Nina Shah, MD**

Moderator

Robert Z Orlowski, MD, PhD

Meet The Professor

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

Monday, August 23, 2021

5:00 PM – 6:00 PM ET

Faculty

Toni K Choueiri, MD

Moderator

Neil Love, MD

Meet The Professor
**Optimizing the Selection and Sequencing
of Therapy for Patients with
Triple-Negative Breast Cancer**

**Tuesday, August 24, 2021
5:00 PM – 6:00 PM ET**

Faculty
Aditya Bardia, MD, MPH

Moderator
Neil Love, MD

Meet The Professor

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

**Wednesday, August 25, 2021
5:00 PM – 6:00 PM ET**

Faculty

Wells A Messersmith, MD

Moderator

Neil Love, MD

Summer Oncology Nursing Series

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Gynecologic Cancers

Thursday, August 26, 2021

5:00 PM – 6:00 PM ET

Faculty

Thomas J Herzog, MD

Kimberly A Spickes, MNSc, RN, APRN, OCN, ACNP-BC

Moderator

Neil Love, MD

Meet The Professor

Immunotherapy and Novel Agents in Gynecologic Cancers

**Wednesday, September 1, 2021
5:00 PM – 6:00 PM ET**

Faculty

Joyce F Liu, MD, MPH

Moderator

Neil Love, MD

Thank you for joining us!

***NCPD credit information will be emailed
to each participant shortly.***

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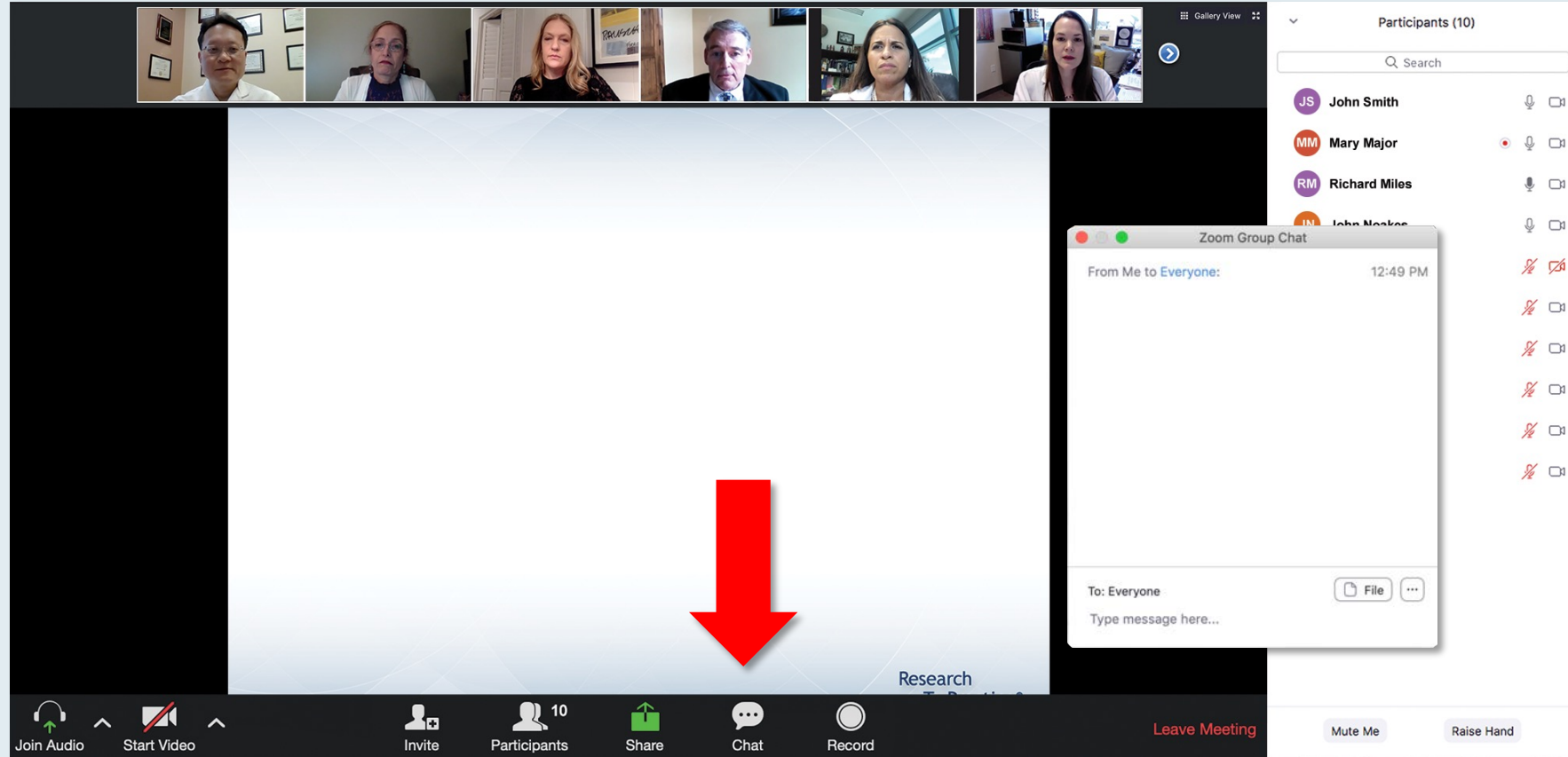
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Quick Poll

What is your usual treatment recommendation for a patient with MM who has been followed by ASCT for 1-5 years who then experiences an asymptomatic relapse?

1. Carfilzomib +/- dexamethasone
2. Pomalidomide +/- dexamethasone
3. Carfilzomib + pomalidomide +/- dexamethasone
4. Elotuzumab + lenalidomide +/- dexamethasone
5. Elotuzumab + pomalidomide +/- dexamethasone
6. Daratumumab + lenalidomide +/- dexamethasone
7. Daratumumab + pomalidomide +/- dexamethasone
8. Daratumumab + bortezomib +/- dexamethasone
9. Ixazomib + Rd
10. Other

Co-provided by USF Health Research To Practice®

Participants (10)

Name	Status
JS John Smith	Microphone On, Video Off
MM Mary Major	Microphone On, Video Off
RM Richard Miles	Microphone On, Video Off
JN John Noakes	Microphone On, Video Off
AS Alice Suarez	Microphone Off, Video Off
JP Jane Perez	Microphone Off, Video Off
RS Robert Stiles	Microphone Off, Video Off
JF Juan Fernandez	Microphone Off, Video Off
AK Ashok Kumar	Microphone Off, Video Off
JS Jeremy Smith	Microphone Off, Video Off

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Oncology Grand Rounds Nursing Webinar Series

April 2021

Monday	Tuesday	Wednesday	Thursday	Friday
19	20	21	22	23
	Breast Ca 8:30 AM <hr/> Lung Ca 5:00 PM	AML 12:00 PM <hr/> CRC and GE Ca 4:45 PM	Prostate Ca 8:30 AM <hr/> Lymphomas 5:00 PM	
26	27	28	29	30
	Multiple Myeloma 8:30 AM <hr/> GYN 5:00 PM	Bladder Ca 12:00 PM	CLL 8:30 AM <hr/> CAR-T 5:00 PM	

13th Annual Oncology Grand Rounds

*A Complimentary NCPD Live Webinar Series
Held During the 46th Annual ONS Congress*

Prostate Cancer

**Thursday, April 22, 2021
8:30 AM – 10:00 AM ET**

Medical Oncologists

**Charles J Ryan, MD
A Oliver Sartor, MD
Mary-Ellen Taplin, MD**

Oncology Nurse Practitioners

**Kathy D Burns, RN, MSN, AGACNP-BC, OCN
Brenda Martone, MSN, NP-BC, AOCNP
Ronald Stein, JD, MSN, NP-C, AOCNP**

Moderator

Neil Love, MD



Kathleen Burns, NP



Brenda Martone MSN NP-BC AOCNP



Ronald Stein, JD, MSN, NP-C, AOCNP

How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

Research To Practice Education Platform

Oncology Nurse Practitioners

Case Presentations

- Key patient-education issues
- Biopsychosocial considerations:
 - Family/loved ones
 - The bond that heals

Clinical Investigators

Oncology Strategy

- New agents and regimens
- Predictive biomarkers
- Ongoing research and implications

Agenda

Introduction: Prostate Cancer Oncology in the Real World

Case 1: A 69-year-old man with metastatic castration-resistant disease, a somatic BRCA1 mutation and loss of heterozygosity

Patient Education: Hormonal Therapy for Prostate Cancer

Case 2: A 59-year-old man with metastatic hormone-sensitive prostate cancer and high-volume disease burden

Agenda

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Case Presentation – A 69-year-old man with metastatic castration-resistant disease, a somatic BRCA1 mutation and loss of heterozygosity

- 2004: Initial diagnosis, underwent prostatectomy for prostate cancer
- 2015: Presents with severe abdominal pain, adrenal mass, retroperitoneal adenopathy, PSA = 240 ng/mL
 - Leuprolide and enzalutamide

Relevant issues

- Patient speaks only Spanish
- Very attentive family
- Extensive use of telemedicine
- Significant comorbidities including diabetes

Agenda

Introduction: Prostate Cancer Oncology in the Real World

Case 1: A 69-year-old man with metastatic castration-resistant disease, a somatic BRCA1 mutation and loss of heterozygosity

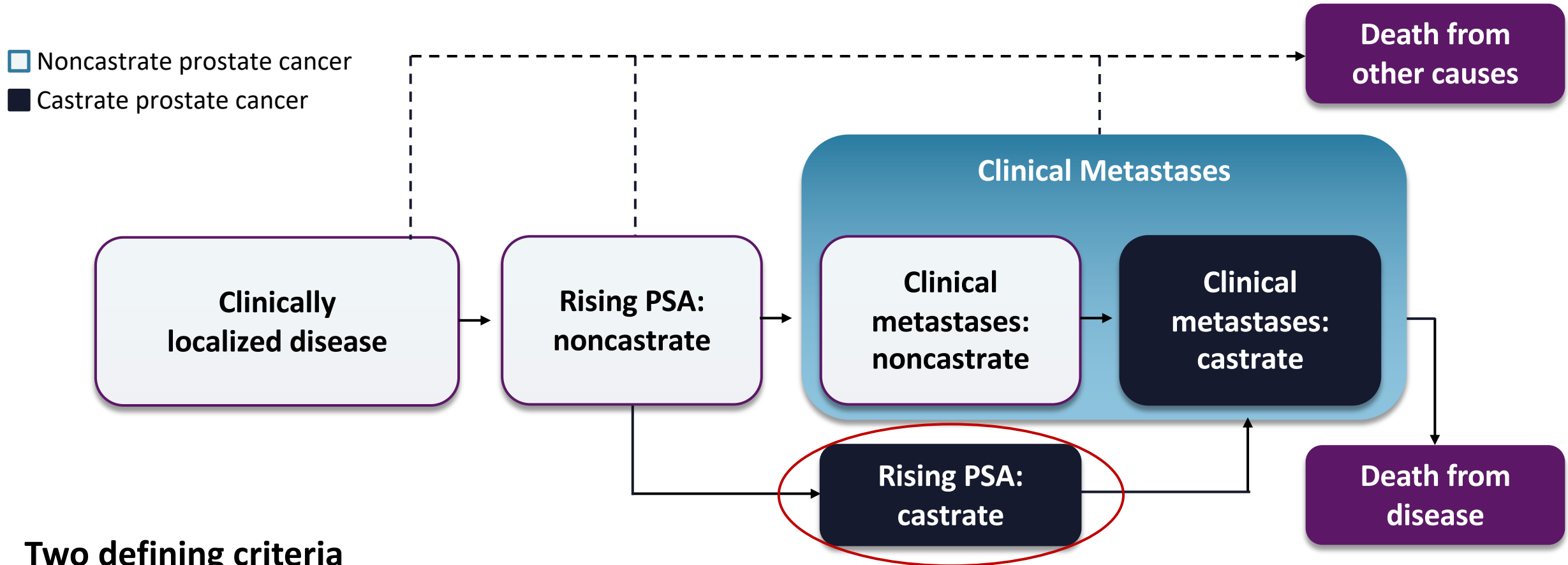
Patient Education: Hormonal Therapy for Prostate Cancer

Case 2: A 59-year-old man with metastatic hormone-sensitive prostate cancer and high-volume disease burden

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

1. Endocrine-based therapy
2. Docetaxel
3. Either endocrine-based therapy or docetaxel — no difference
4. I don't know

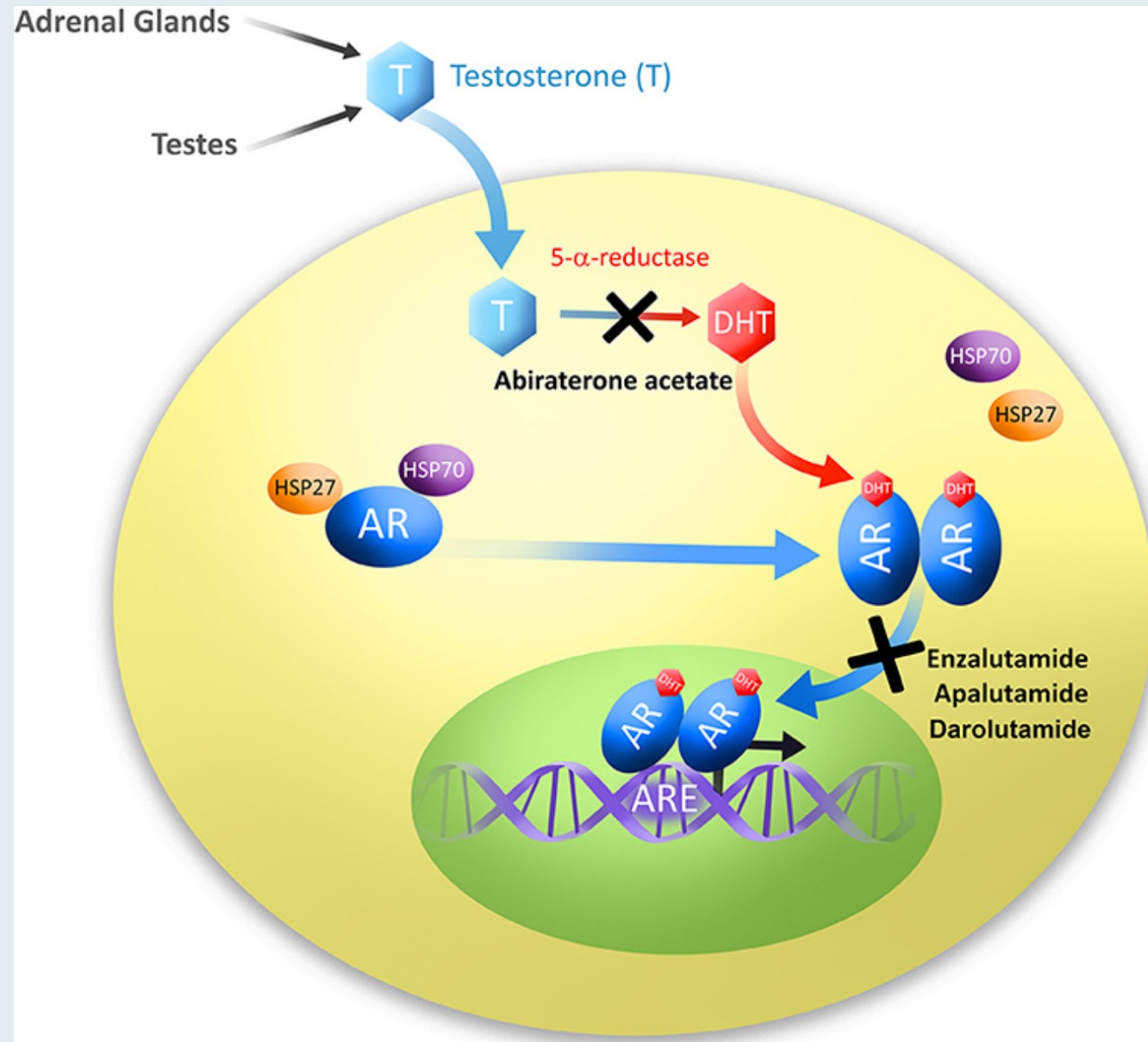
Clinical Disease States Model of Prostate Cancer¹



Two defining criteria

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

Diagram of Androgen Production and Its Targeted Inhibition



FDA Approves Relugolix for Advanced Prostate Cancer

Press Release: December 18, 2020

“On December 18, 2020, the U.S. Food and Drug Administration approved the first oral gonadotropin-releasing hormone (GnRH) receptor antagonist, relugolix, for adult patients with advanced prostate cancer.

Efficacy was evaluated in HERO (NCT03085095), a randomized, open label trial in men requiring at least one year of androgen deprivation therapy with either prostate cancer recurrence following radiation or surgery or newly diagnosed castration-sensitive advanced prostate cancer.

Patients (N=934) were randomized (2:1) to receive relugolix 360 mg oral loading dose on the first day, followed by daily oral doses of 120 mg, or leuprolide acetate 22.5 mg injection subcutaneously every 3 months for 48 weeks.”

HERO Phase III Trial: Results Comparing Relugolix, an Oral GnRH Receptor Antagonist, versus Leuprolide Acetate for Advanced Prostate Cancer¹

Oral Relugolix for Androgen-Deprivation Therapy in Advanced Prostate Cancer²

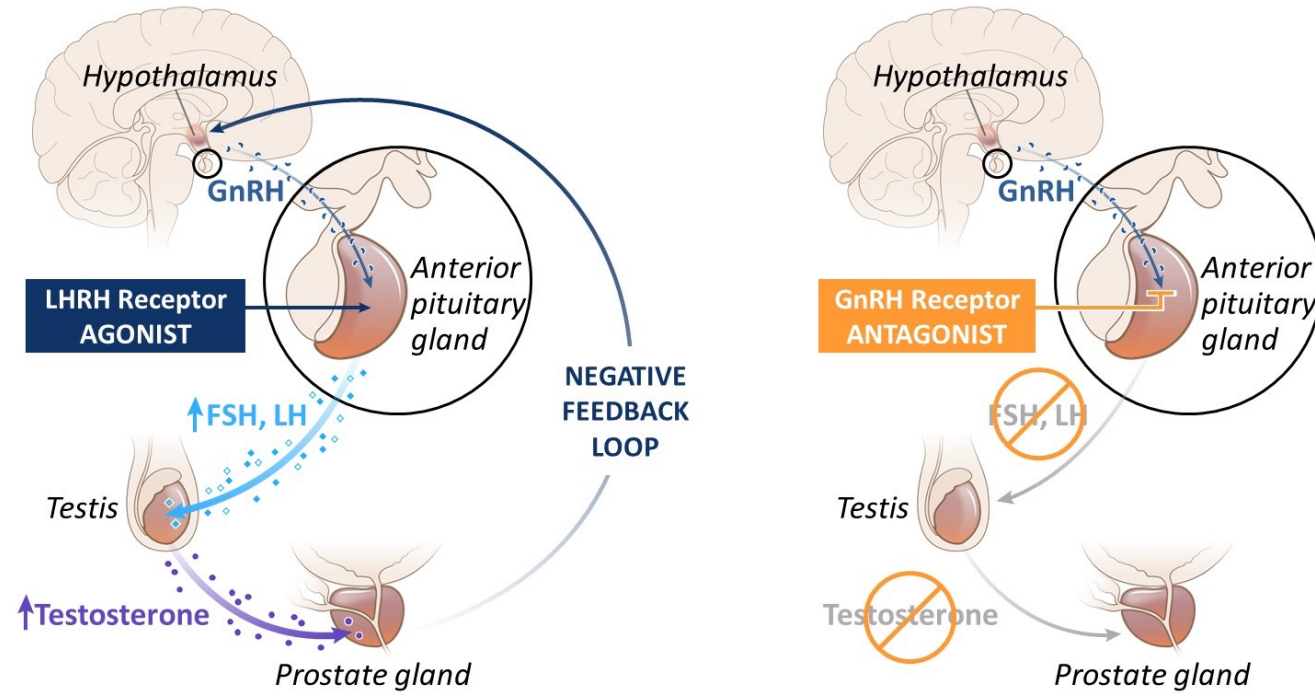
¹ Shore N et al.

ASCO 2020;Abstract 5602.

² Shore ND et al.

N Engl J Med 2020;382(23):2187-96.

LHRH agonist vs antagonist MOA and side effect profile



PRESENTED AT: 2020 ASCO ANNUAL MEETING

#ASCO20
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permission required for reuse.

PRESENTED BY: Neal Shore, MD, FACS
Carolina Urologic Research Center, SC, USA

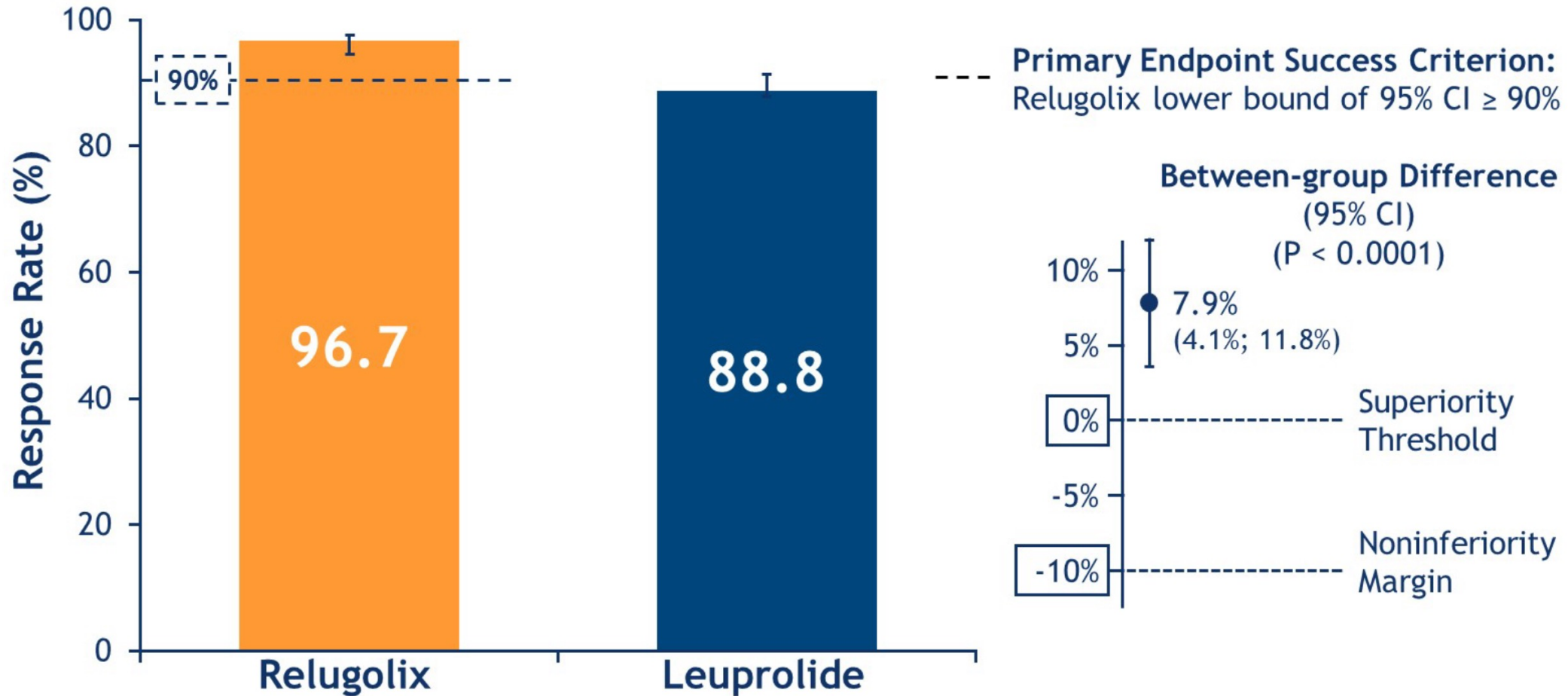
3

	Relugolix (N = 622)	Leuprolide (N = 308)
Hot flush	54.3%	51.6%
Fatigue	21.5%	18.5%
Constipation	12.2%	9.7%
Diarrhea*	12.2%	6.8%
Arthralgia	12.1%	9.1%
Hypertension	7.9%	11.7%

Courtesy of Tanya B Dorff, MD

HERO: Primary Endpoint – Sustained Castration

Key Secondary Endpoint – Noninferiority to Leuprolide



Relugolix: Cardiovascular Safety

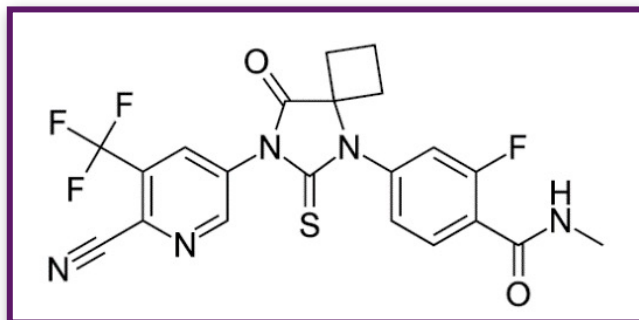
Event	Relugolix (n = 622)		Leuprolide (n = 308)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Major adverse cardiac event (MACE)*	2.9%	1.3%	6.2%	1.3%
In patients <i>without</i> prior history of MACE	2.8%	—	4.2%	—
In patients <i>with</i> prior history of MACE	3.6%	—	17.8%	—

*Nonfatal myocardial infarction, nonfatal stroke and death from any cause

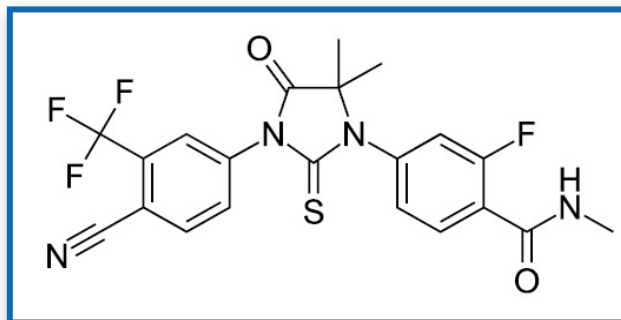
In the subgroup of patients with a reported medical history of MACE, the odds of having an event were 4.8 times as high with leuprolide as with relugolix.

Next-Generation Androgen Receptor Inhibitors^{1,2}

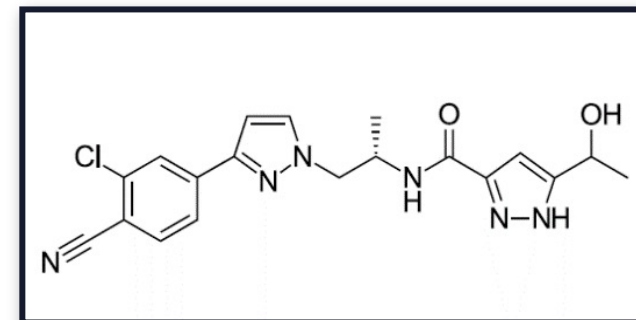
Apalutamide



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.

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2020;383:1040-9.

ORIGINAL ARTICLE

Nonmetastatic, Castration-Resistant Prostate Cancer and Survival with Darolutamide

K. Fizazi, N. Shore, T.L. Tammela, A. Ulys, E. Vjaters, S. Polyakov, M. Jievaltas, M. Luz, B. Alekseev, I. Kuss, M.-A. Le Berre, O. Petrenciuc, A. Snapir, T. Sarapohja, and M.R. Smith, for the ARAMIS Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2020;382(23):2197-206.

ORIGINAL ARTICLE

Enzalutamide and Survival in Nonmetastatic, Castration-Resistant Prostate Cancer

Cora N. Sternberg, M.D., Karim Fizazi, M.D., Ph.D., Fred Saad, M.D., Neal D. Shore, M.D., Ugo De Giorgi, M.D., Ph.D., David F. Penson, M.D., M.P.H., Ubirajara Ferreira, M.D., Ph.D., Eleni Efstathiou, M.D., Ph.D., Katarzyna Madziarska, M.D., Ph.D., Michael P. Kolinsky, M.D., Daniel I. G. Cubero, M.D., Ph.D., Bettina Noerby, M.D., Fabian Zohren, M.D., Ph.D., Xun Lin, Ph.D., Katharina Modelska, M.D., Ph.D., Jennifer Sugg, M.S., Joyce Steinberg, M.D., and Maha Hussain, M.D., for the PROSPER Investigators*



European Association of Urology

Eur J Cancer 2020;[Online ahead of print].

Prostate Cancer

Apalutamide and Overall Survival in Prostate Cancer

Matthew R. Smith^{a,*}, Fred Saad^b, Simon Chowdhury^c, Stéphane Oudard^d, Boris A. Hadaschik^e, Julie N. Graff^f, David Olmos^g, Paul N. Mainwaring^h, Ji Youl Leeⁱ, Hiroji Uemura^j, Peter De Porre^k, Andressa A. Smith^l, Sabine D. Brookman-May^{m,n}, Susan Li^l, Ke Zhang^o, Brendan Rooney^p, Angela Lopez-Gitlitz^m, Eric J. Small^q

Overall Survival: Darolutamide, Enzalutamide, Apalutamide

	ARAMIS ¹	PROSPER ²	SPARTAN ³
Antiandrogen	Darolutamide	Enzalutamide	Apalutamide
Median follow-up	49 mo	47 mo	52 mo
Median OS	Not estimated	57 vs 56 mo	74 vs 60 mo
OS hazard ratio	0.69 ($p = 0.003$)	0.73 ($p = 0.001$)	0.78 ($p = 0.0161$)

¹ Fizazi K et al; ARAMIS Investigators. *N Engl J Med* 2020;383:1040-9.

² Sternberg CN et al; PROSPER Investigators. *N Engl J Med* 2020;382(23):2197-206.

³ Smith MR et al; SPARTAN Investigators. *Eur Urol* 2021;79(1):150-158.

Comparison of Toxicities: Darolutamide, Enzalutamide, Apalutamide

Toxicity	ARAMIS		PROSPER		SPARTAN	
	Darolutamide	Placebo	Enzalutamide	Placebo	Apalutamide	Placebo
Fatigue/asthenia	16%	11%	33%	14%	30%	21%
Falling	4%	5%	11%	4%	16%	9%
Dizziness	5%	4%	10%	4%	9%	6%
Mental impairment	1%	2%	5%	2%	5%	3%

Sternberg CN et al; PROSPER Investigators. *N Engl J Med* 2020;382(23):2197-206.

Fizazi K et al; ARAMIS Investigators. *N Engl J Med* 2020;383:1040-9.

Small EJ et al; SPARTAN Investigators. ASCO 2020;Abstract 5516.

FDA-Approved Next-Generation Antiandrogens for Metastatic Hormone-Sensitive Prostate Cancer

Agent	Approval date	Pivotal study
Enzalutamide	December 16, 2019	ARCHES
Apalutamide	September 17, 2019	TITAN

original report

ARCHES: A Randomized, Phase III Study of Androgen Deprivation Therapy With Enzalutamide or Placebo in Men With Metastatic Hormone-Sensitive Prostate Cancer

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J Clin Oncol 2019;37(32):2974-86.

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Apalutamide for Metastatic, Castration-Sensitive Prostate Cancer

Kim N. Chi, M.D., Neeraj Agarwal, M.D., Anders Bjartell, M.D., Byung Ha Chung, M.D.,
Andrea J. Pereira de Santana Gomes, M.D., Robert Given, M.D., Álvaro Juárez Soto, M.D.,
Axel S. Merseburger, M.D., Mustafa Özgüroğlu, M.D., Hirotugu Uemura, M.D., Dingwei Ye, M.D.,
Kris Deprince, M.D., Vahid Naini, Pharm.D., Jinhui Li, Ph.D., Shinta Cheng, M.D., Margaret K. Yu, M.D.,
Ke Zhang, Ph.D., Julie S. Larsen, Pharm.D., Sharon McCarthy, B.Pharm., and Simon Chowdhury, M.D.,
for the TITAN Investigators*

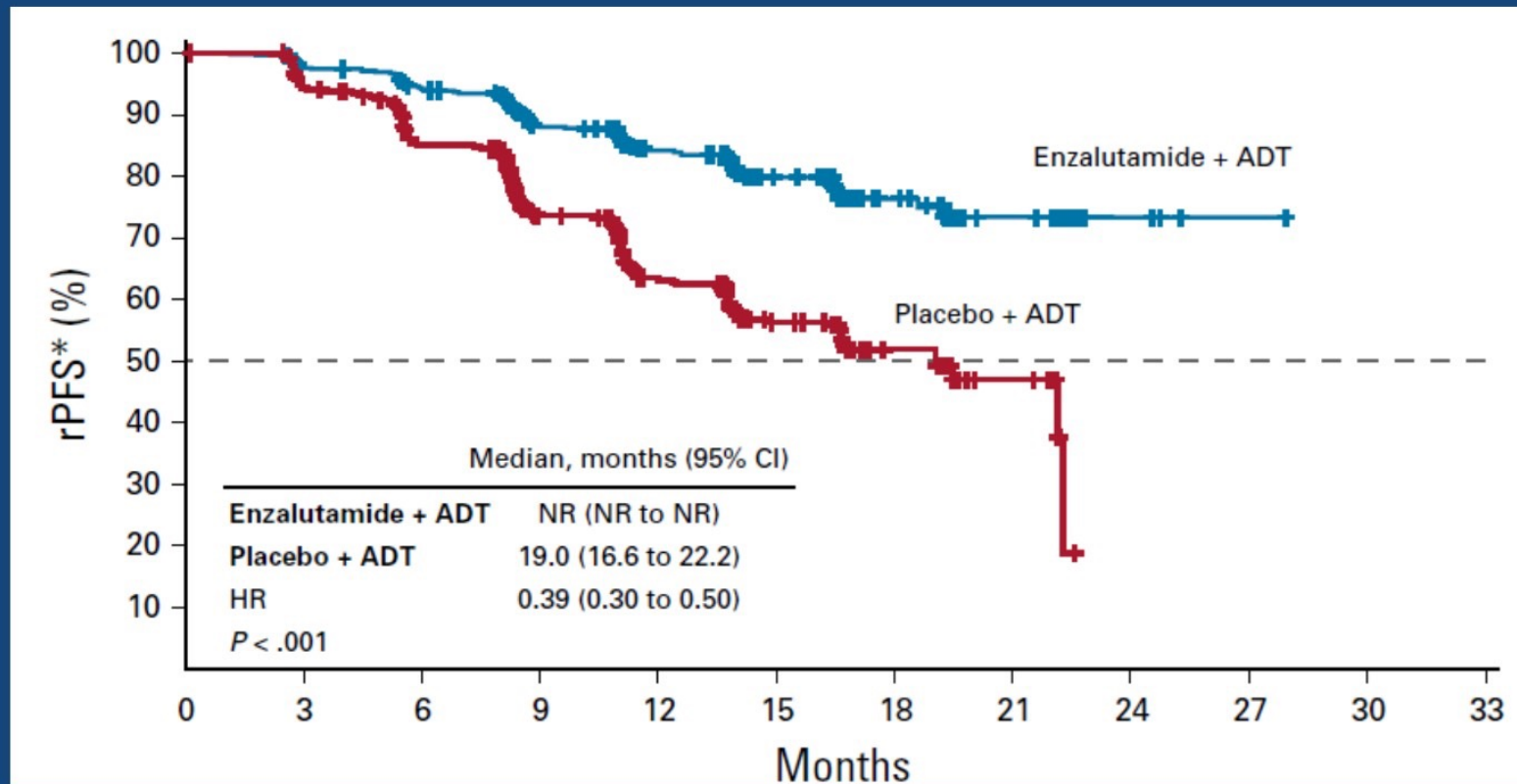
N Engl J Med 2019;381(1):13-24.

Survival Analyses for ARCHES and TITAN: ADT + Enzalutamide or Apalutamide for Metastatic Hormone-Sensitive Prostate Cancer

	ARCHES (N = 1,150)		TITAN (N = 1,052)	
Characteristics	<ul style="list-style-type: none"> 2/3rd high volume 17% prior docetaxel 25% prior RP/XRT 		<ul style="list-style-type: none"> 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 <ul style="list-style-type: none"> HR (prior docetaxel): 0.52 HR (high volume): 0.43 HR (low volume): 0.25 		HR (overall): 0.48 <ul style="list-style-type: none"> 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 <ul style="list-style-type: none"> HR (prior docetaxel): 1.27 HR (high volume): 0.68 HR (low volume): 0.67 	

NR = not reached

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

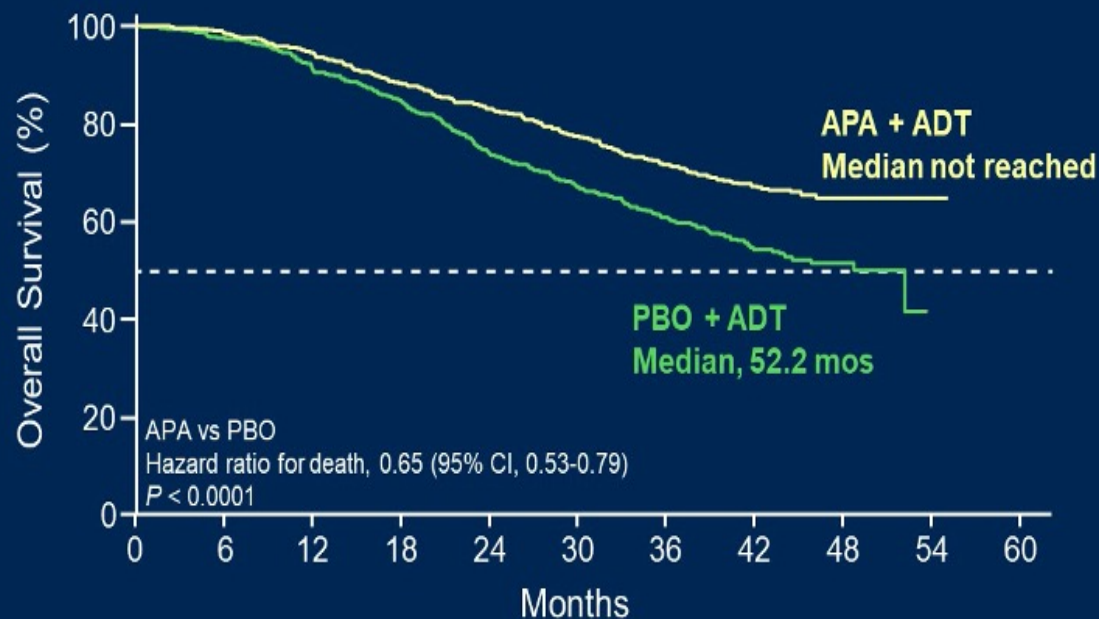
PRESENTED AT: **2020 ASCO**
ANNUAL MEETING

#ASCO20
Slides are the property of the author,
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PRESENTED BY: Neal Shore, MD, FACS

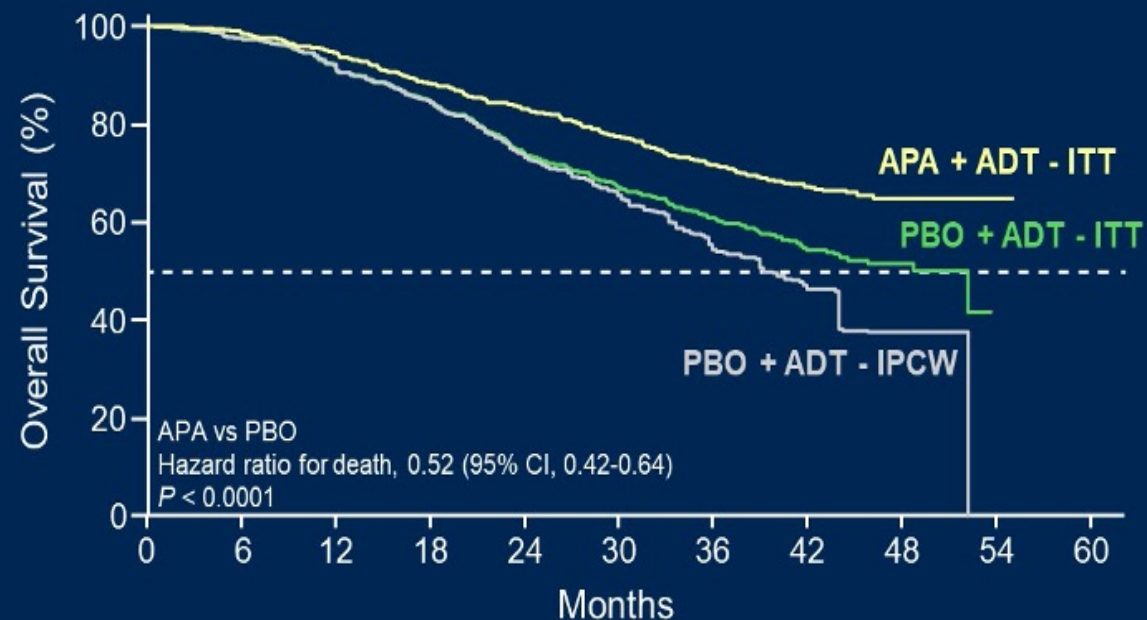
TITAN – Final Analysis: Overall Survival

OS (Co-primary endpoint)
Median follow-up: 44.0 months



No. at risk:											
APA + ADT	525	513	489	452	425	394	362	227	52	3	0
PBO + ADT	527	510	474	436	374	339	301	181	43	0	0

OS with adjustment for ~40%
crossover from PBO



No. at risk:											
APA + ADT	525	513	489	452	425	394	362	227	52	3	0
PBO + ADT	527	510	474	436	374	339	301	181	43	0	0

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

Karim Fizazi, MD, PhD

Institut Gustave Roussy, France

June 8, 2021

Karim Fizazi, Xavier Maldonado, Stéphanie Foulon, Guilhem Roubaud, Ray McDermott, Aude Fléchon, Bertrand Tombal, Stéphane Supiot, Dominik Berthold, Philippe Ronchin, Gabriel Kacsó, Gwenaëlle Gravis, Fabio Calabro, Jean-François Berdah, Ali Hasbini, Marlon Silva, Antoine Thiery-Vuillemin, Isabelle Rieger, Marie-Laure Tanguy, Alberto Bossi

Design of PEACE-1

Key Eligibility Criteria

De novo mCSPC

Distant metastatic disease by ≥ 1 lesion on bone scan and/or CT scan

ECOG PS 0 -2

On-Study Requirement

Continuous ADT

Permitted

ADT ≤ 3 months

Stratification

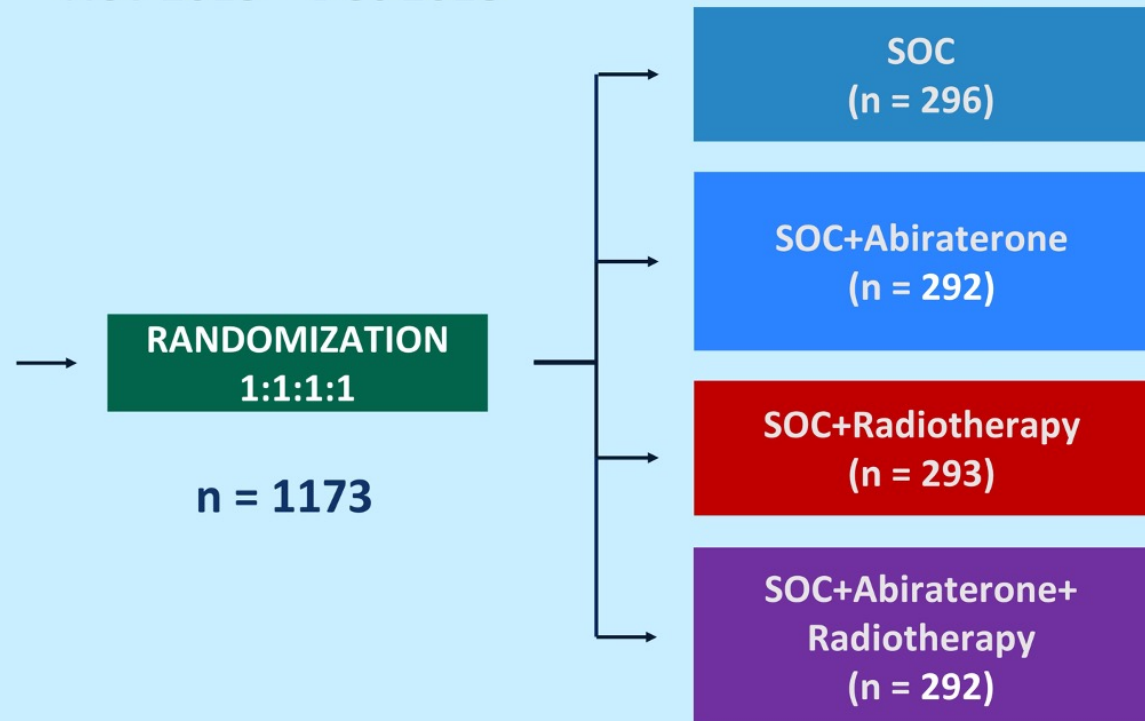
ECOG PS (0 vs 1-2)

Metastatic sites (LN vs bone vs visceral)

Type of castration (orchidectomy vs LHRH agonist vs LHRH antagonist)

Docetaxel (yes vs no)

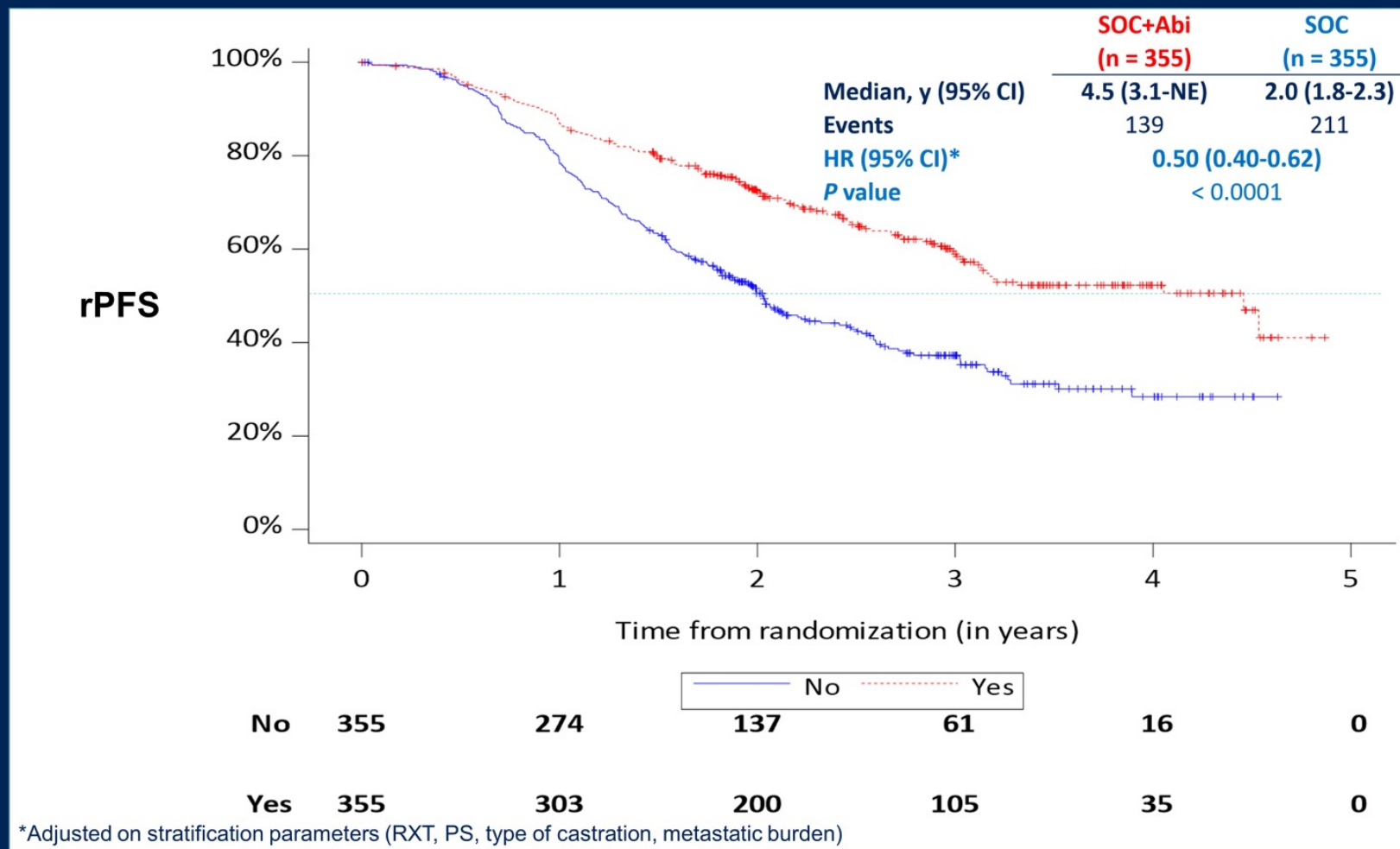
Nov 2013 – Dec 2018



ECOG PS, Eastern Cooperative Oncology Group performance status

Radiographic Progression-Free Survival (rPFS)

ADT+Docetaxel population: SOC=ADT+Docetaxel (+/- RXT)



Case Presentation – A 69-year-old man with metastatic castration-resistant disease, a somatic BRCA1 mutation and loss of heterozygosity

- 2004: Initial diagnosis, underwent prostatectomy for prostate cancer
- 2015: Presents with severe abdominal pain, adrenal mass, retroperitoneal adenopathy, PSA = 240 ng/mL
 - Leuprolide and enzalutamide
- **2016: Bone metastases found on routine scanning**
 - Zoledronic acid and docetaxel
- **2018: Disease progression**
 - Cabazitaxel
- **June 2020: Progression of bone metastases**
 - Radium-223

Case Presentation – A 69-year-old man with metastatic castration-resistant disease, a somatic BRCA1 mutation and loss of heterozygosity (continued)

- **December 2020: “Code spine”; NGS performed – somatic BRCA 1 mutation, HRD positive, germline testing negative**
 - **Started on Olaparib for 1 month, entered hospice care for 2 weeks**

Relevant issues

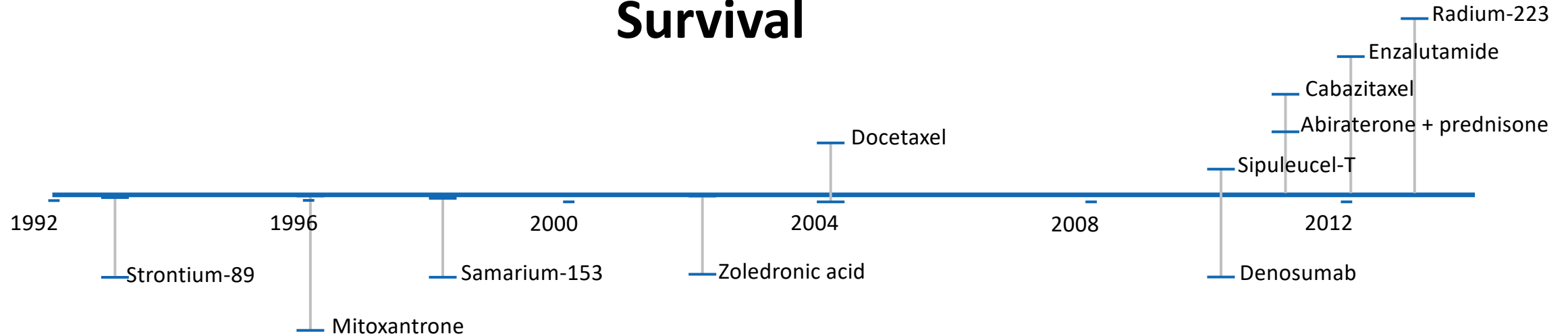
- Patient speaks only Spanish
- Very attentive family
- Extensive use of telemedicine
- Significant comorbidities including diabetes

Management of Metastatic Castration-Resistant Prostate Cancer (mCRPC)

- Enzalutamide
- Abiraterone/prednisone
- Radium-223
- Sipuleucel-T
- Cabazitaxel
- Docetaxel
- PARP inhibitors

Timeline of FDA Approvals in Metastatic Castration-Resistant Prostate Cancer

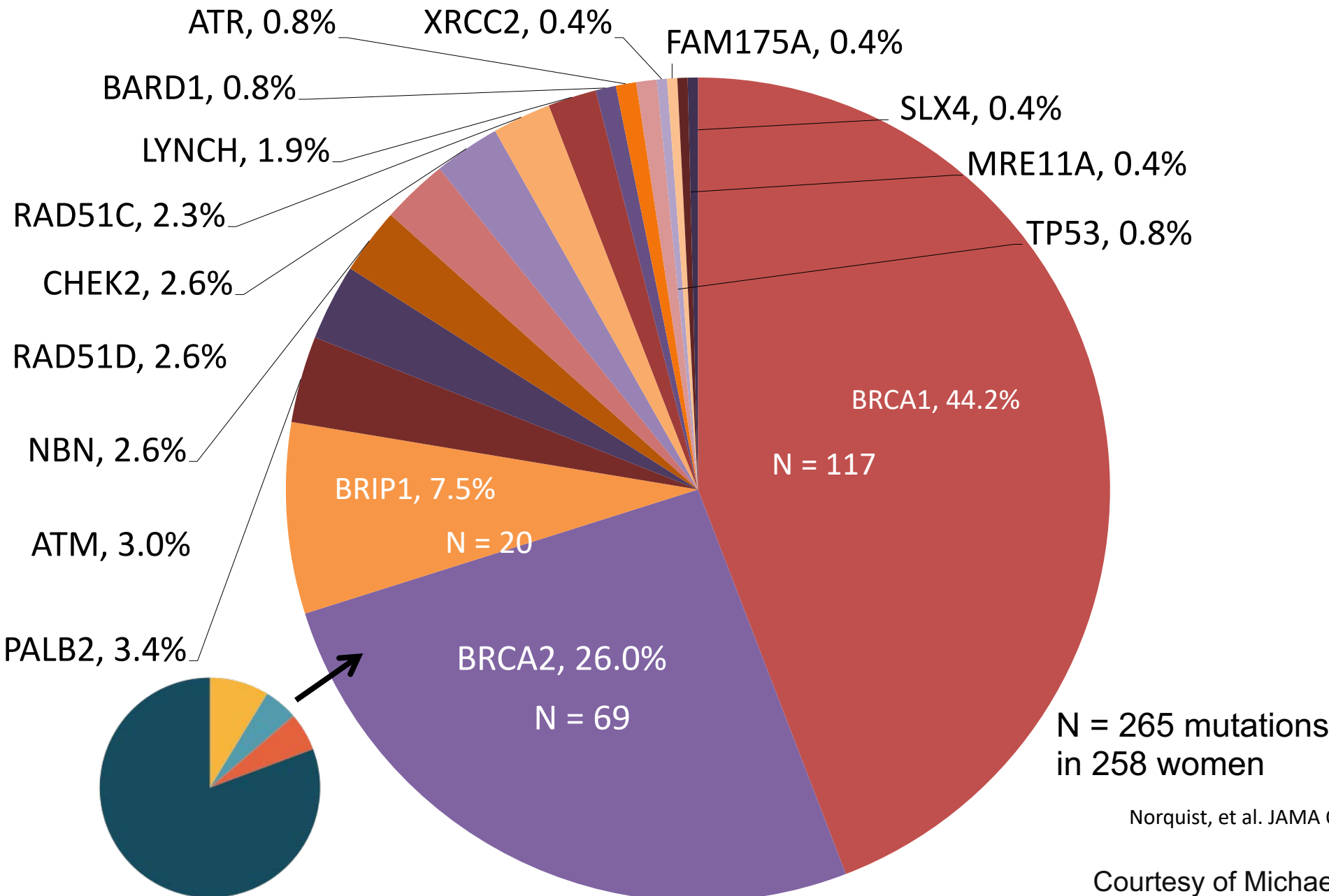
Survival



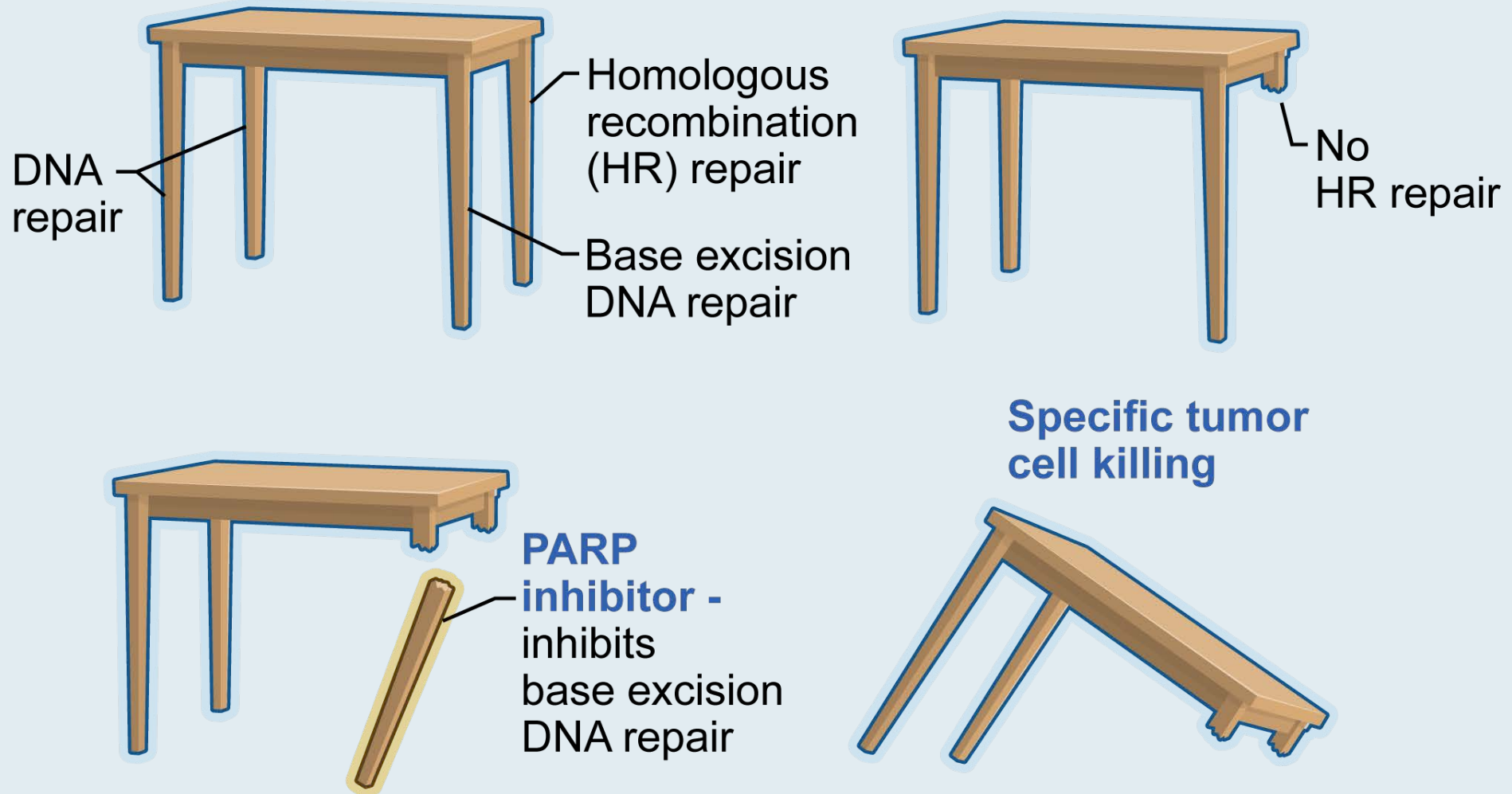
Palliation

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

Summary of Germline Cancer-Associated Mutations: GOG 218 and GOG 262



Mechanism of Cell Death from Synthetic Lethality Induced by PARP Inhibition



Recent FDA Approvals of PARP Inhibitors for mCRPC

PARP inhibitor	Approval date	Pivotal study
Olaparib	May 19, 2020	PROfound
Rucaparib	May 15, 2020	TRITON2

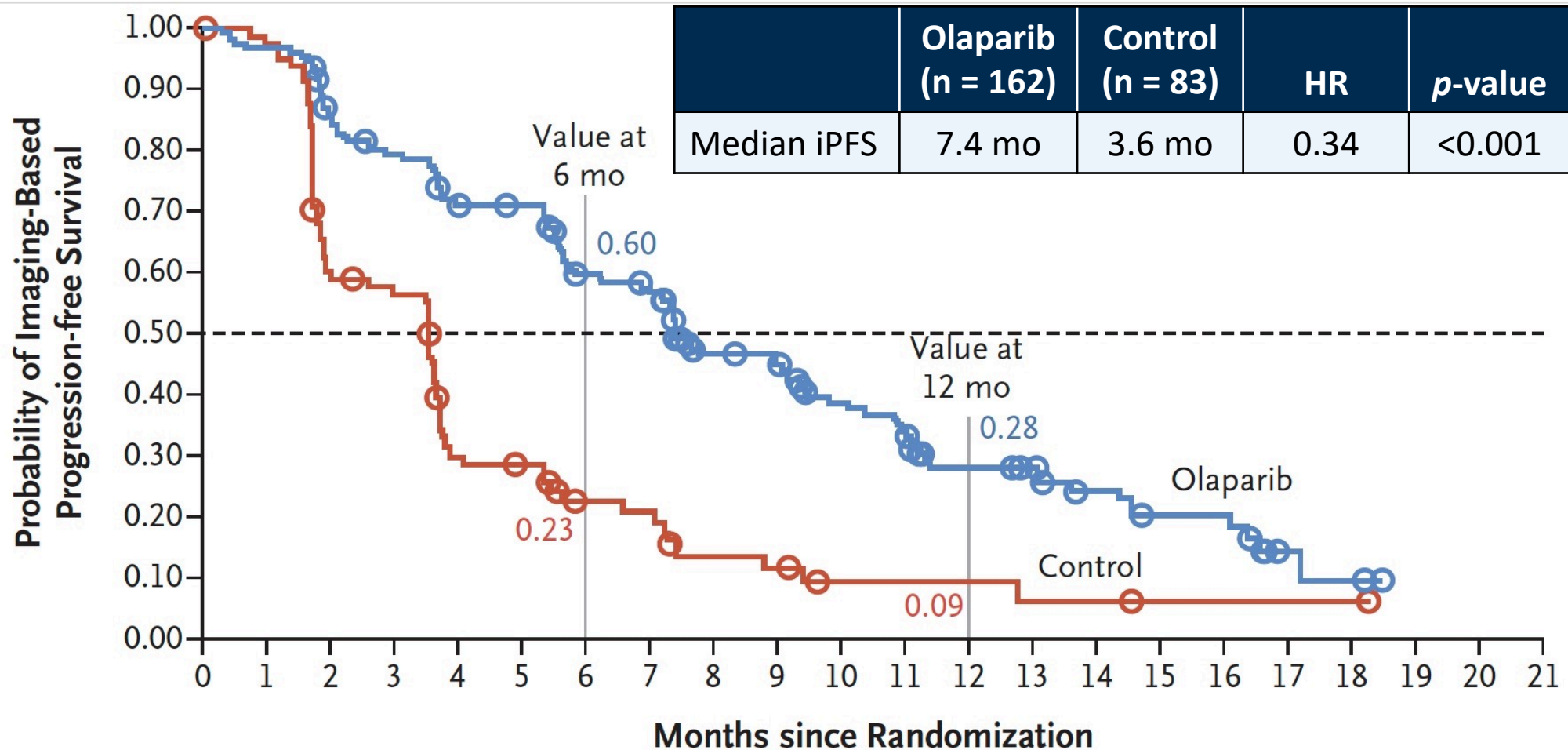
ORIGINAL ARTICLE

Olaparib for Metastatic Castration-Resistant Prostate Cancer

J. de Bono, J. Mateo, K. Fizazi, F. Saad, N. Shore, S. Sandhu, K.N. Chi, O. Sartor, N. Agarwal, D. Olmos, A. Thiery-Vuillemin, P. Twardowski, N. Mehra, C. Goessl, J. Kang, J. Burgents, W. Wu, A. Kohlmann, C.A. Adelman, and M. Hussain

***N Engl J Med* 2020;382:2091-102.**

PROfound Primary Endpoint: Imaging-Based PFS with Olaparib for Patients with mCRPC Who Had at Least 1 Alteration in BRCA1, BRCA2 or ATM (Cohort A)



ORIGINAL ARTICLE

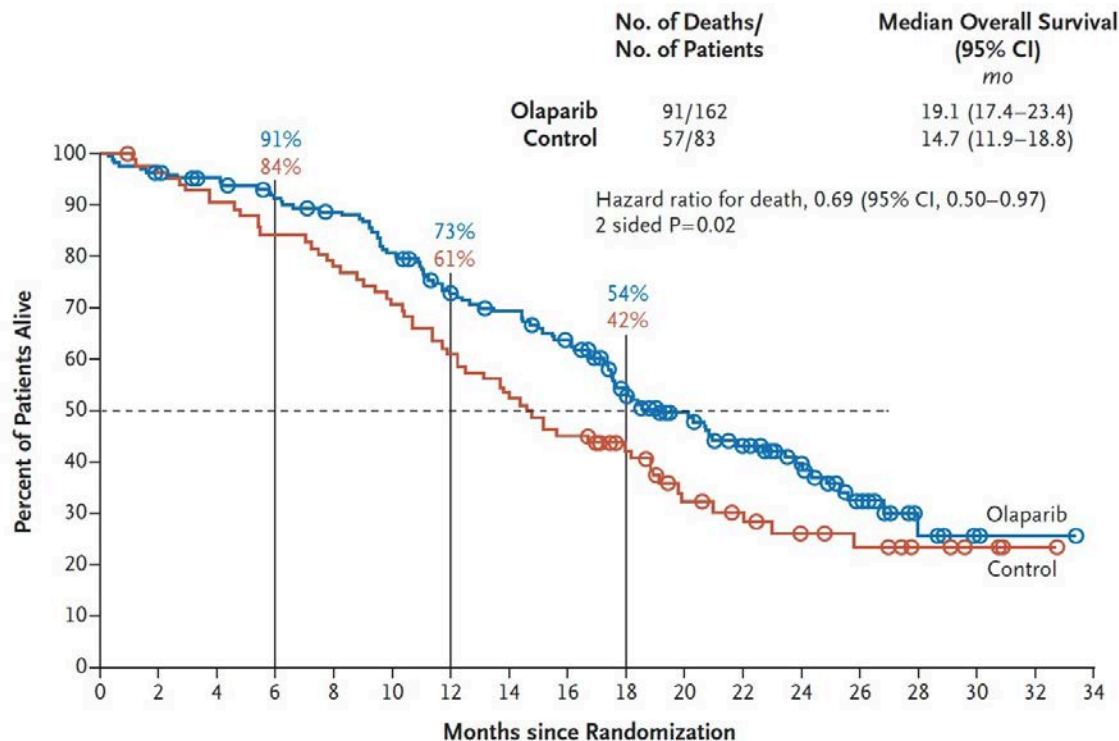
Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

M. Hussain, J. Mateo, K. Fizazi, F. Saad, N. Shore, S. Sandhu, K.N. Chi, O. Sartor,
N. Agarwal, D. Olmos, A. Thiery-Vuillemin, P. Twardowski, G. Roubaud,
M. Özgüroğlu, J. Kang, J. Burgents, C. Gresty, C. Corcoran, C.A. Adelman,
and J. de Bono, for the PROfound Trial Investigators*

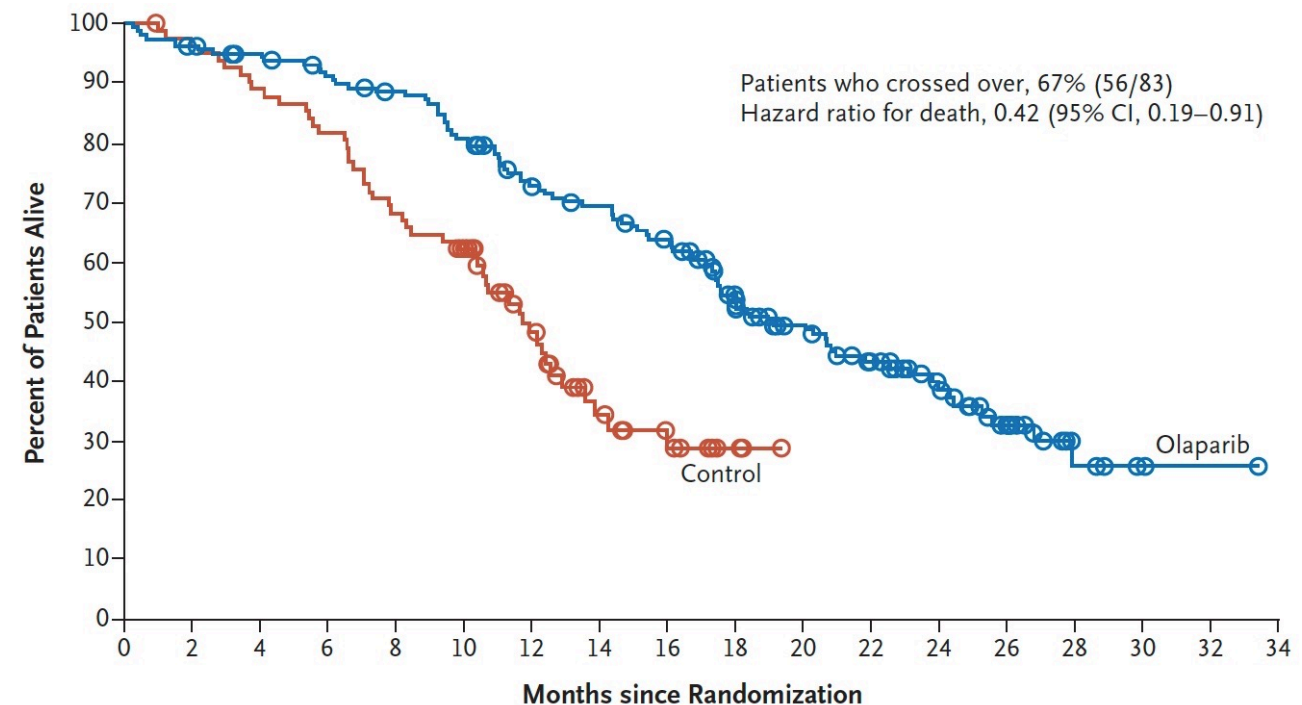
***N Engl J Med* 2020;[Online ahead of print].**

PROfound: Overall Survival with Olaparib for Patients with mCRPC Who Had at Least 1 Alteration in BRCA1, BRCA2 or ATM (Cohort A)

Overall survival



Cross-over adjusted overall survival



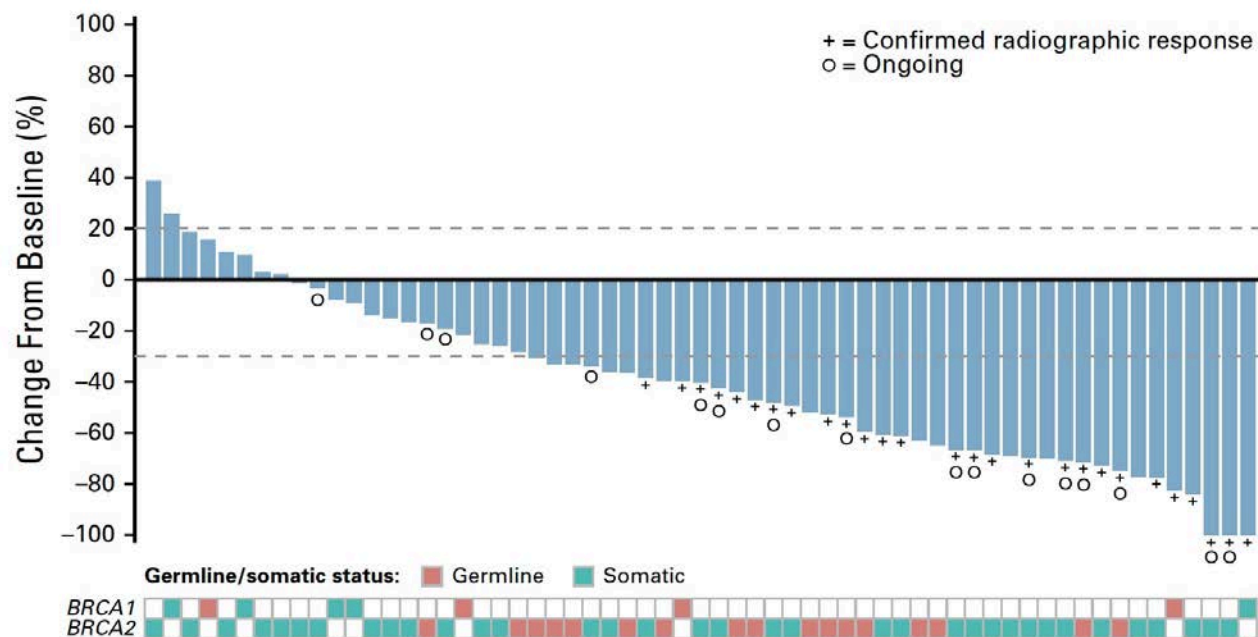
Rucaparib in Men With Metastatic Castration-Resistant Prostate Cancer Harboring a *BRCA1* or *BRCA2* Gene Alteration

Wassim Abida, MD, PhD¹; Akash Patnaik, MD, PhD, MMSc²; David Campbell, MBBS³; Jeremy Shapiro, MBBS⁴; Alan H. Bryce, MD⁵; Ray McDermott, MD, PhD, MBA⁶; Brieuc Sautois, MD, PhD⁷; Nicholas J. Vogelzang, MD⁸; Richard M. Bambury, MD⁹; Eric Voog, MD¹⁰; Jingsong Zhang, MD, PhD¹¹; Josep M. Piulats, MD¹²; Charles J. Ryan, MD¹³; Axel S. Merseburger, PhD¹⁴; Gedske Daugaard, DMSc¹⁵; Axel Heidenreich, MD¹⁶; Karim Fizazi, MD, PhD¹⁷; Celestia S. Higano, MD¹⁸; Laurence E. Krieger, MBChB¹⁹; Cora N. Sternberg, MD²⁰; Simon P. Watkins, PhD²¹; Darrin Despain, MStat²²; Andrew D. Simmons, PhD²³; Andrea Loehr, PhD²³; Melanie Dowson, BA²⁴; Tony Golsorkhi, MD²⁵; and Simon Chowdhury, MD, PhD^{26,27}; on behalf of the TRITON2 investigators

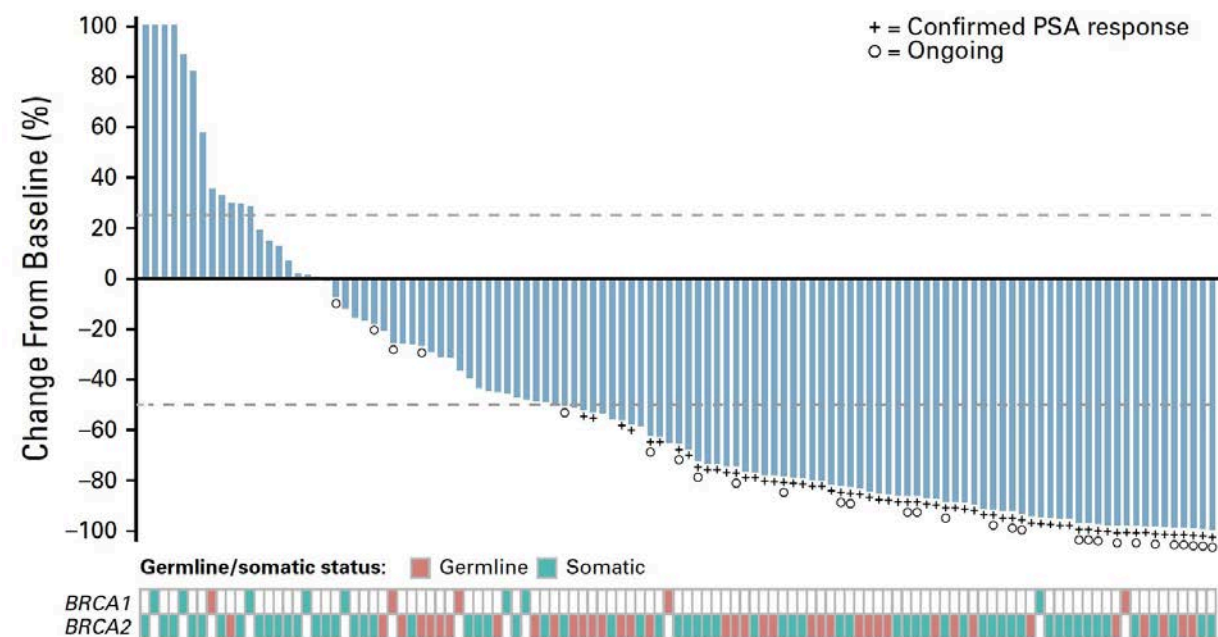
J Clin Oncol 2020;38(32):3763-72.

TRITON2: Response to Rucaparib in Patients with mCRPC Harboring a BRCA1 or BRCA2 Gene Alteration

ORR per independent radiology review: 43.5%



Confirmed PSA response rate: 54.8%

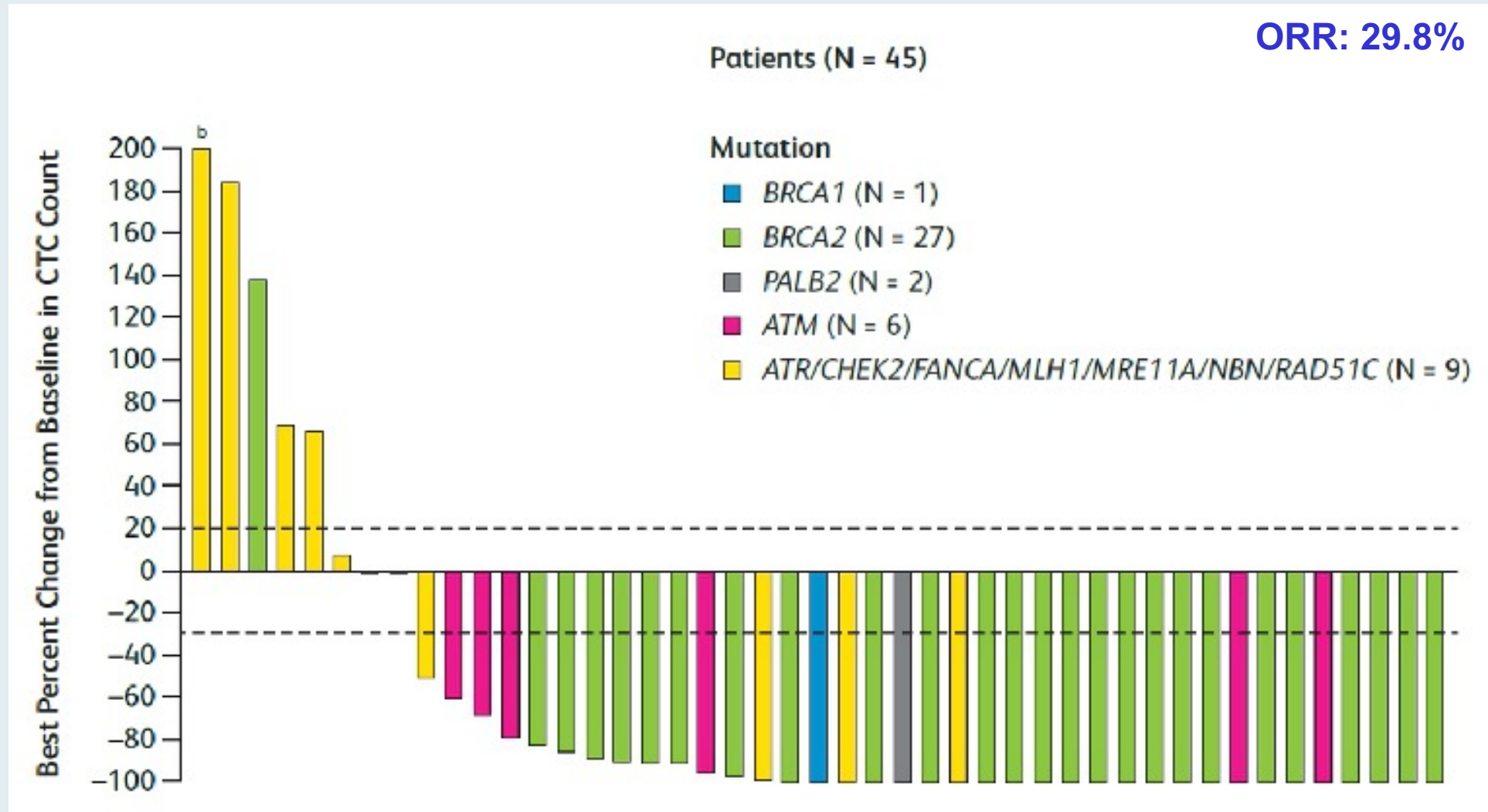


TALAPRO-1: Phase II Study of Talazoparib (TALA) in Patients (pts) with DNA Damage Repair Alterations (DDRm) and Metastatic Castration-Resistant Prostate Cancer (mCRPC)

de Bono JS et al.

Genitourinary Cancers Symposium 2021;Abstract 93.

TALAPRO-1: Best Change from Baseline in Circulating Tumor Cell Count with Talazoparib

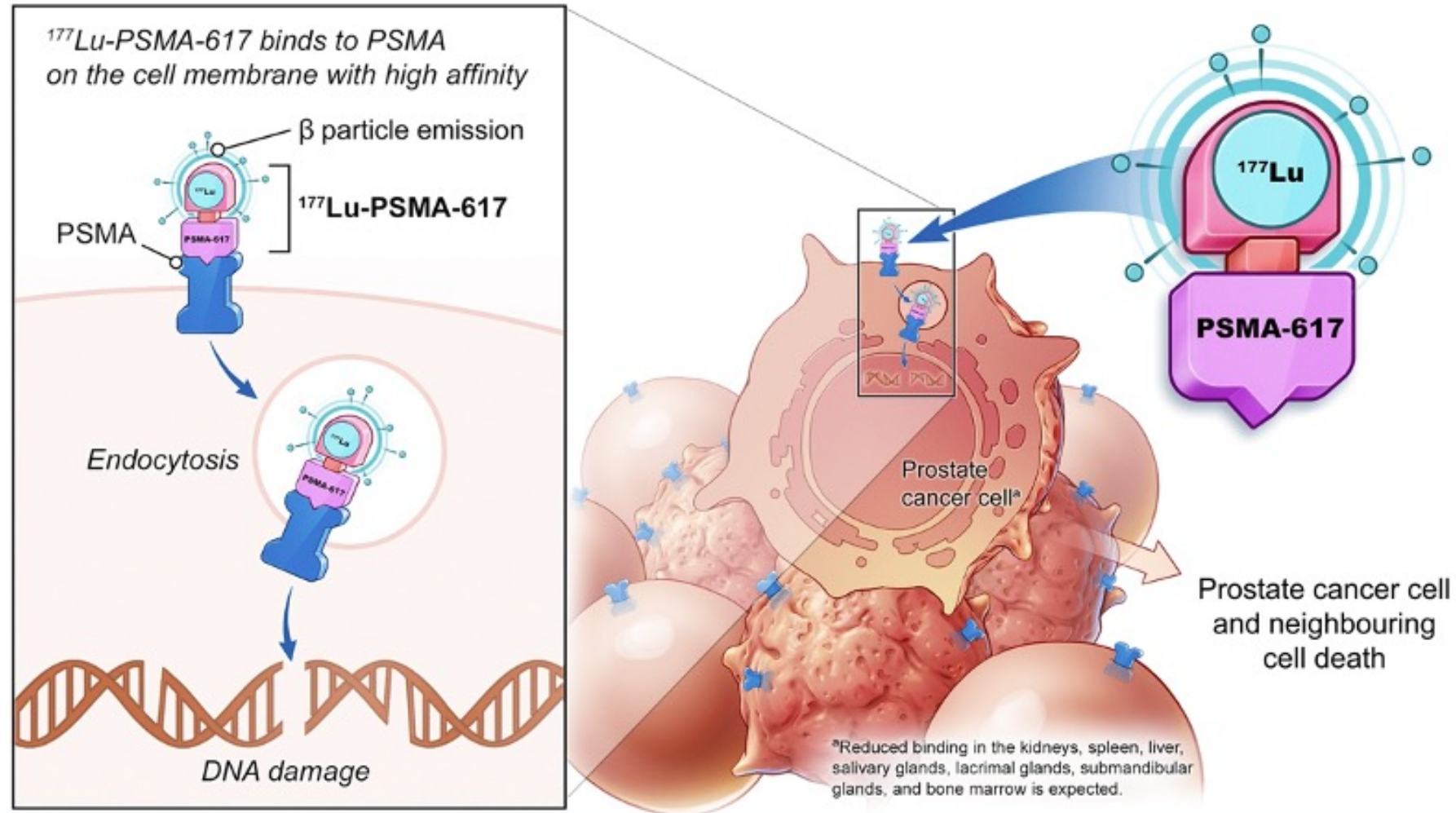


Phase 3 study of ^{177}Lu -PSMA-617 in patients with metastatic castration-resistant prostate cancer (VISION)

Presenter: Michael J. Morris, Memorial Sloan Kettering Cancer Center

Co-authors: J. de Bono, K. N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S. T. Tagawa, L. T. Nordquist, N. Vaishampayan, G. El-Haddad, C. H. Park, T. M. Beer, W. J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R. A. Messmann, B. J. Krause, O. Sartor, for the VISION investigators

^{177}Lu -PSMA-617 targeted radioligand therapy



Open-label study of protocol-permitted standard of care ± ^{177}Lu -PSMA-617 in adults with PSMA-positive mCRPC

Eligible patients

- Previous treatment with both
 - ≥ 1 androgen receptor pathway inhibitor
 - 1 or 2 taxane regimens
- Protocol-permitted standard of care (SOC) planned before randomization
 - Excluding chemotherapy immunotherapy, radium-223, investigational drugs
- ECOG performance status 0–2
- Life expectancy > 6 months
- PSMA-positive mCRPC on PET/CT with ^{68}Ga -PSMA-11

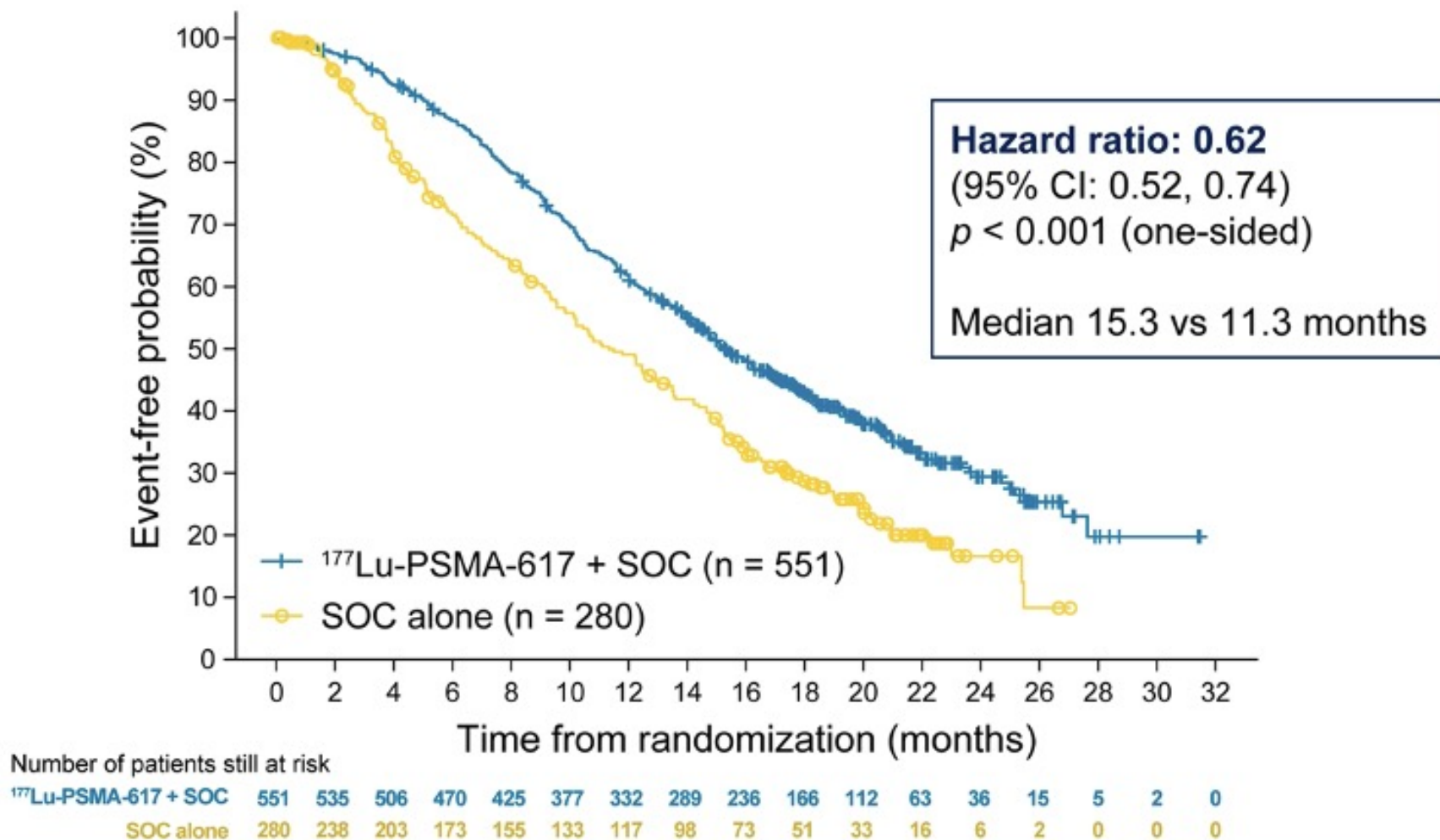


- Randomization stratified by
 - ECOG status (0–1 or 2)
 - LDH (high or low)
 - Liver metastases (yes or no)
 - Androgen receptor pathway inhibitors in SOC (yes or no)
- CT/MRI/bone scans
 - Every 8 weeks (treatment)
 - Every 12 weeks (follow-up)
 - Blinded independent central review

Primary endpoints: ^{177}Lu -PSMA-617 prolonged OS

Primary analysis

All randomized patients
(N = 831)



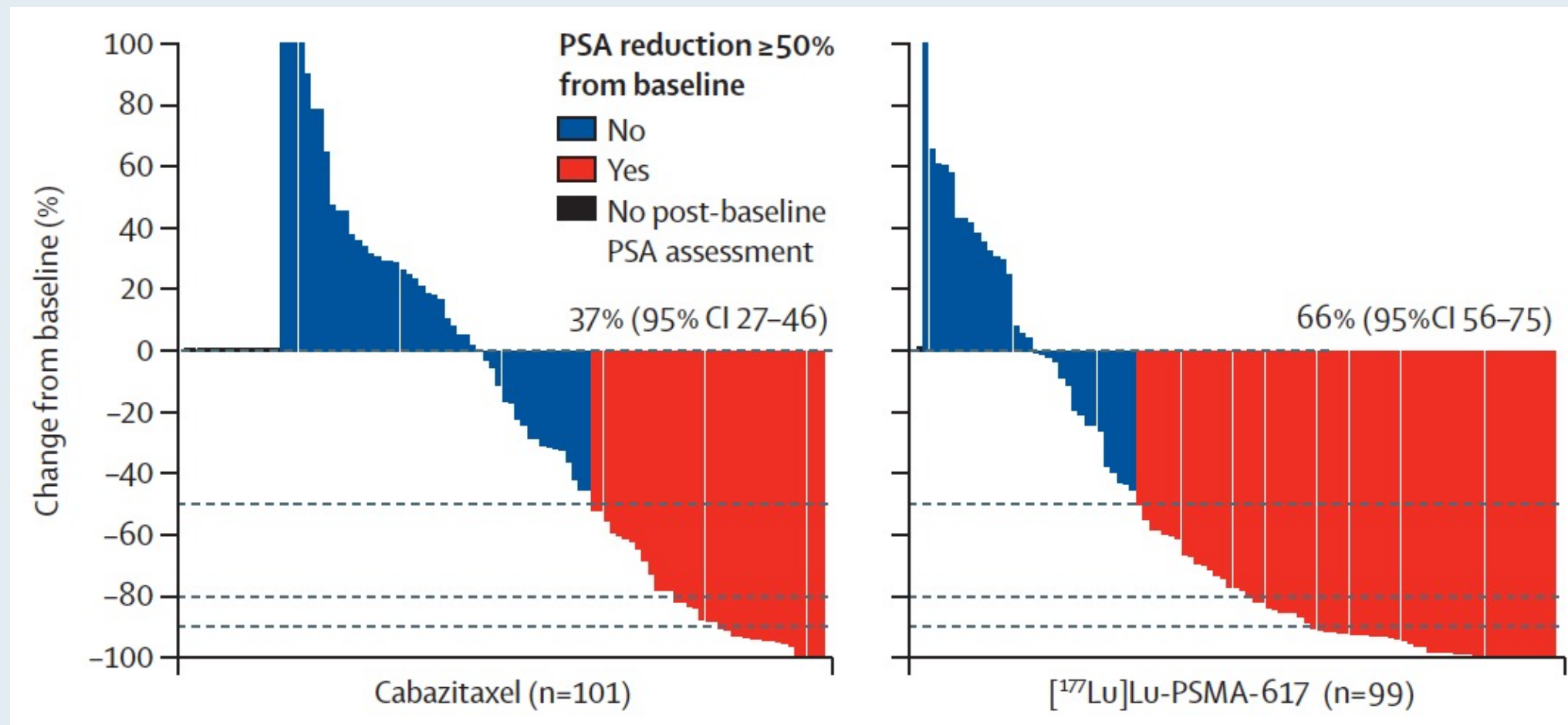
Lancet 2021;397:797-804.

[¹⁷⁷Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial



Michael S Hofman, Louise Emmett, Shahneen Sandhu, Amir Iravani, Anthony M Joshua, Jeffrey C Goh, David A Pattison, Thean Hsiang Tan, Ian D Kirkwood, Siobhan Ng, Roslyn J Francis, Craig Gedy, Natalie K Rutherford, Andrew Weickhardt, Andrew M Scott, Sze-Ting Lee, Edmond M Kwan, Arun A Azad, Shakher Ramdave, Andrew D Redfern, William Macdonald, Alex Guminski, Edward Hsiao, Wei Chua, Peter Lin, Alison Y Zhang, Margaret M McLannett, Martin R Stockler, John A Violet, Scott G Williams, Andrew J Martin, Ian D Davis, for the TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group†*

TheraP: Primary Endpoint — PSA Response $\geq 50\%$



TheraP: Select Adverse Events

Event	¹⁷⁷ Lu-PSMA-617 (n = 98)		Cabazitaxel (n = 85)	
	Grade 1/2	Grade 3/4	Grade 1/2	Grade 3/4
Pain	61%	11%	61%	5%
Thrombocytopenia	18%	11%	5%	0
Anemia	19%	8%	13%	8%
Neutropenia	7%	4%	5%	13%

Agenda

Introduction: Prostate Cancer Oncology in the Real World

Case 1: A 69-year-old man with metastatic castration-resistant disease, a somatic BRCA1 mutation and loss of heterozygosity

Patient Education: Hormonal Therapy for Prostate Cancer

Case 2: A 59-year-old man with metastatic hormone-sensitive prostate cancer and high-volume disease burden

Case Presentation – A 59-year-old man with metastatic hormone-sensitive prostate cancer and high-volume disease burden

- Retired national park ranger living in a rural area presents to local clinic with significant back pain and unable to walk
- Workup reveals vertebral metastases all along spinal column
- PSA 6,400 ng/mL
- Patient receives leuprolide and enzalutamide and is responding well with pronounced improvement in back pain
 - Decrease in PSA to 221 ng/mL, off pain medication
- 6 months ago: “My neck is so swollen, and I’m having trouble breathing.”

Cases from the Community — Investigators Discuss Emerging Research and Actual Patients with Multiple Myeloma

Held in Conjunction with the 2021 Pan Pacific Lymphoma Conference

**Thursday, August 12, 2021
7:00 PM – 8:30 PM ET**

Faculty

**Muhamed Baljevic, MD
Joseph Mikhael, MD
Nina Shah, MD**

Moderator

Robert Z Orlowski, MD, PhD

Thank you for joining us!

***NCPD credit information will be emailed
to each participant shortly.***