

Summer Oncology Nursing Series

A Complimentary NCPD-Accredited Virtual Curriculum

Prostate Cancer

Thursday, July 1, 2021

5:00 PM – 6:00 PM ET

Faculty

Charles J Ryan, MD

Brenda Martone, MSN, NP-BC, AOCNP

Moderator

Neil Love, MD

Faculty



Charles J Ryan, MD
Professor of Medicine
BJ Kennedy Chair in Clinical Medical Oncology
Director, Division of Hematology, Oncology and
Transplantation
University of Minnesota
Minneapolis, Minnesota



Brenda Martone, MSN, NP-BC, AOCNP
Northwestern Medicine
Northwestern Memorial Hospital
Chicago, Illinois

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, 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, 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.

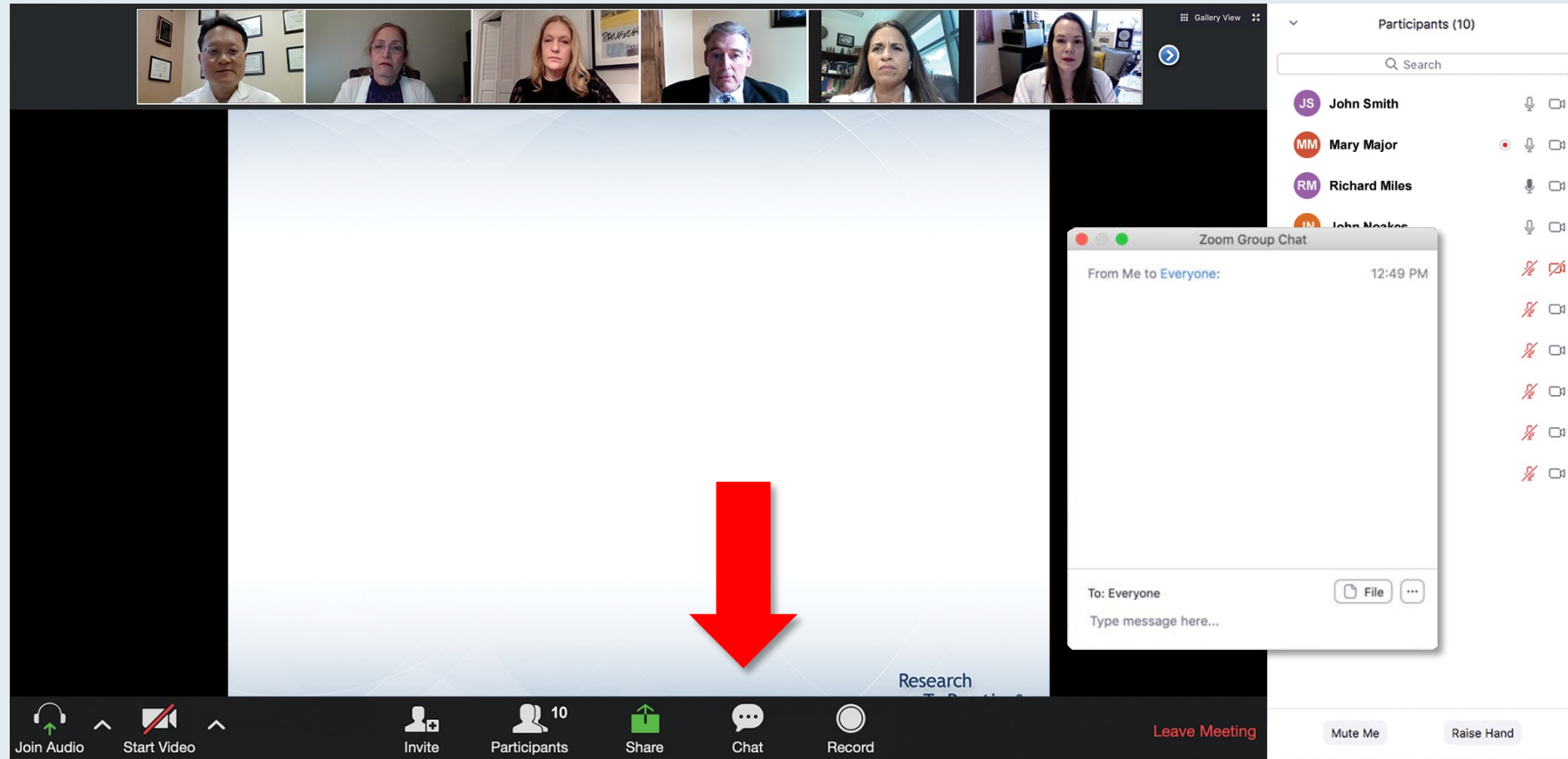
Dr Ryan — Disclosures

No relevant conflicts of interest to disclose

Ms Martone — 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

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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 shows a Zoom meeting interface. At the top, there are video thumbnails for participants: RTP Coordinat..., Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. A 'Recording...' indicator is visible on the left. The main content is a slide titled 'Meet The Professor Program Steering Committee' with six members listed:

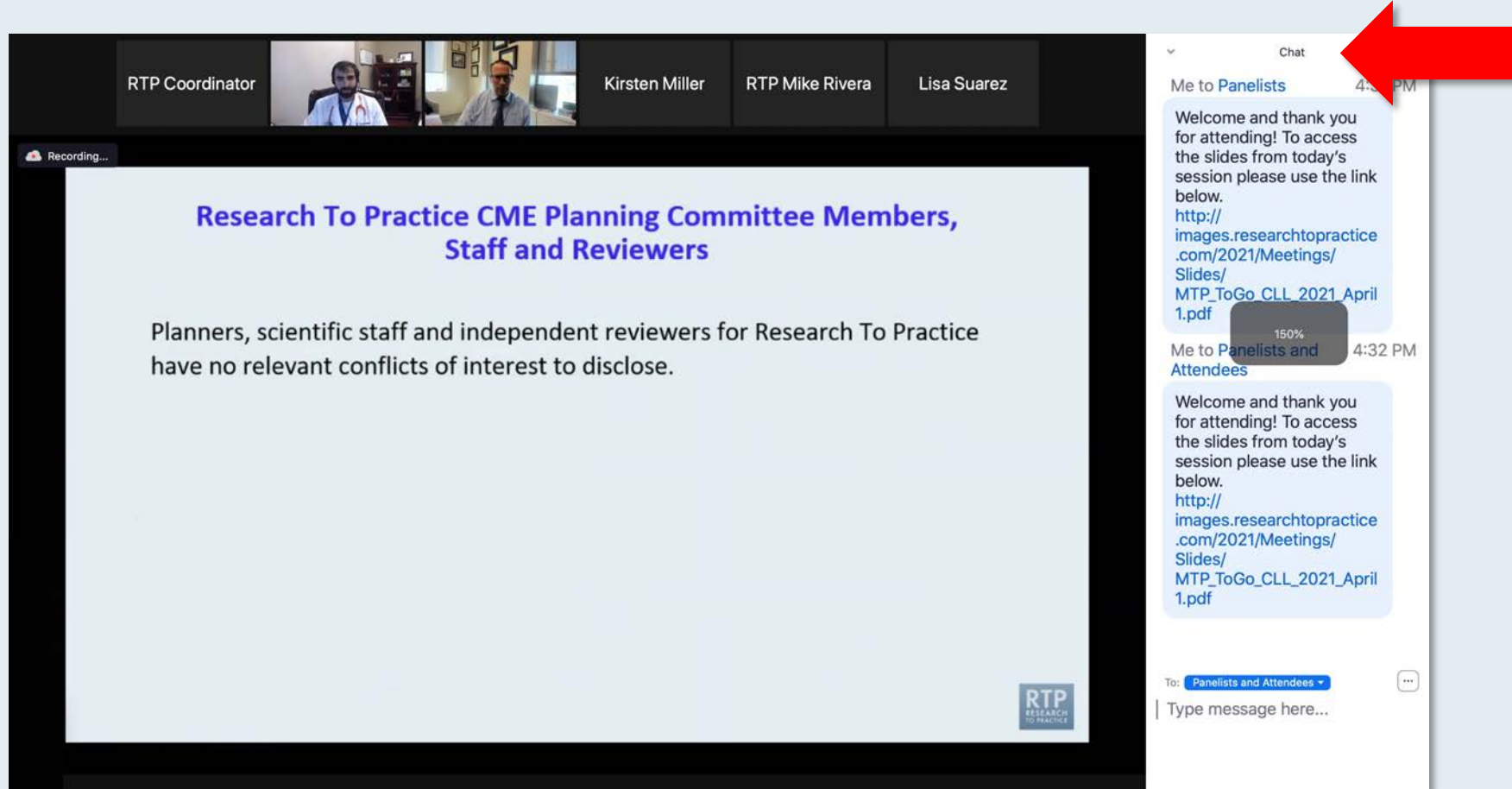
- John N Allan, MD**
Assistant Professor of Medicine
Weill Cornell Medicine
New York, New York
- Ian W Flinn, MD, PhD**
Director of Lymphoma Research Program
Sarah Cannon Research Institute
Tennessee Oncology
Nashville, Tennessee
- Steven Coutre, MD**
Professor of Medicine (Hematology)
Stanford University 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 expanded, showing messages from 'Me to Panelists' and 'Me to Panelists and Attendees'. A red arrow points to the white line above the 'Type message here...' 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



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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.**

ONCOLOGY TODAY

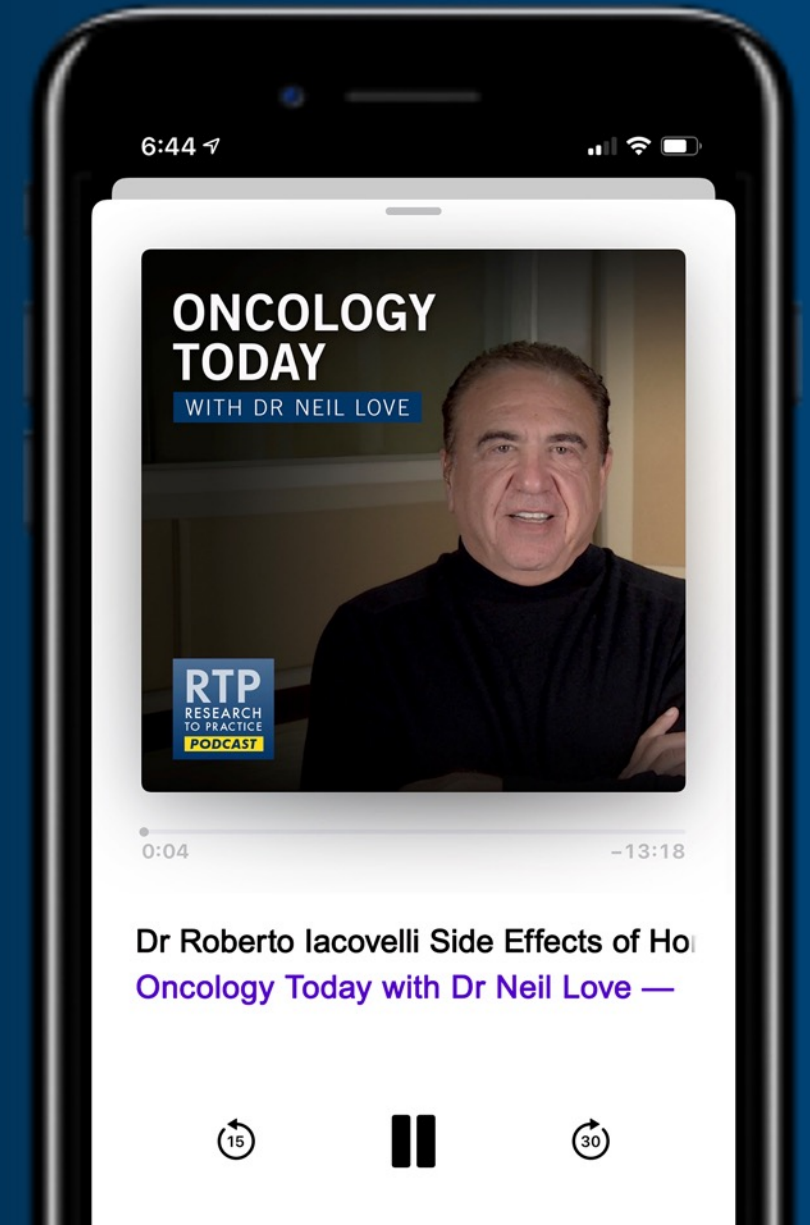
WITH DR NEIL LOVE

Side Effects of Hormonal Therapy in Prostate Cancer



DR ROBERTO IACOVELLI

FONDAZIONE POLICLINICO
UNIVERSITARIO A GEMELLI



Ask the Expert: Clinical Investigators Provide Perspectives on the Management of Renal Cell Carcinoma

In Partnership with Project Echo[®] and Florida Cancer Specialists

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

Faculty

David I Quinn, MBBS, PhD

Moderator

Neil Love, MD

A Conversation with the Investigators: Ovarian Cancer

**Wednesday, July 7, 2021
5:00 PM – 6:00 PM ET**

Faculty

**Michael J Birrer, MD, PhD
Kathleen Moore, MD
Richard T Penson, MD, MRCP**

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Non-Small Cell Lung Cancer

Thursday, July 8, 2021

5:00 PM – 6:00 PM ET

Faculty

Zofia Piotrowska, MD, MHS

Tara Plues, APRN, MSN

Moderator

Neil Love, MD

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

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

A Conversation with the Investigators: Acute Myeloid Leukemia and Myelodysplastic Syndromes

**Wednesday, July 14, 2021
5:00 PM – 6:00 PM ET**

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**Courtney D DiNardo, MD, MSCE
Gail J Roboz, MD
Eytan M Stein, MD**

Moderator

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Summer Oncology Nursing Series

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Gynecologic Cancers

Thursday, July 15, 2021

5:00 PM – 6:00 PM ET

Faculty

Krishnansu S Tewari, MD

Courtney Arn, CNP

Moderator

Neil Love, MD

Thank you for joining us!

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

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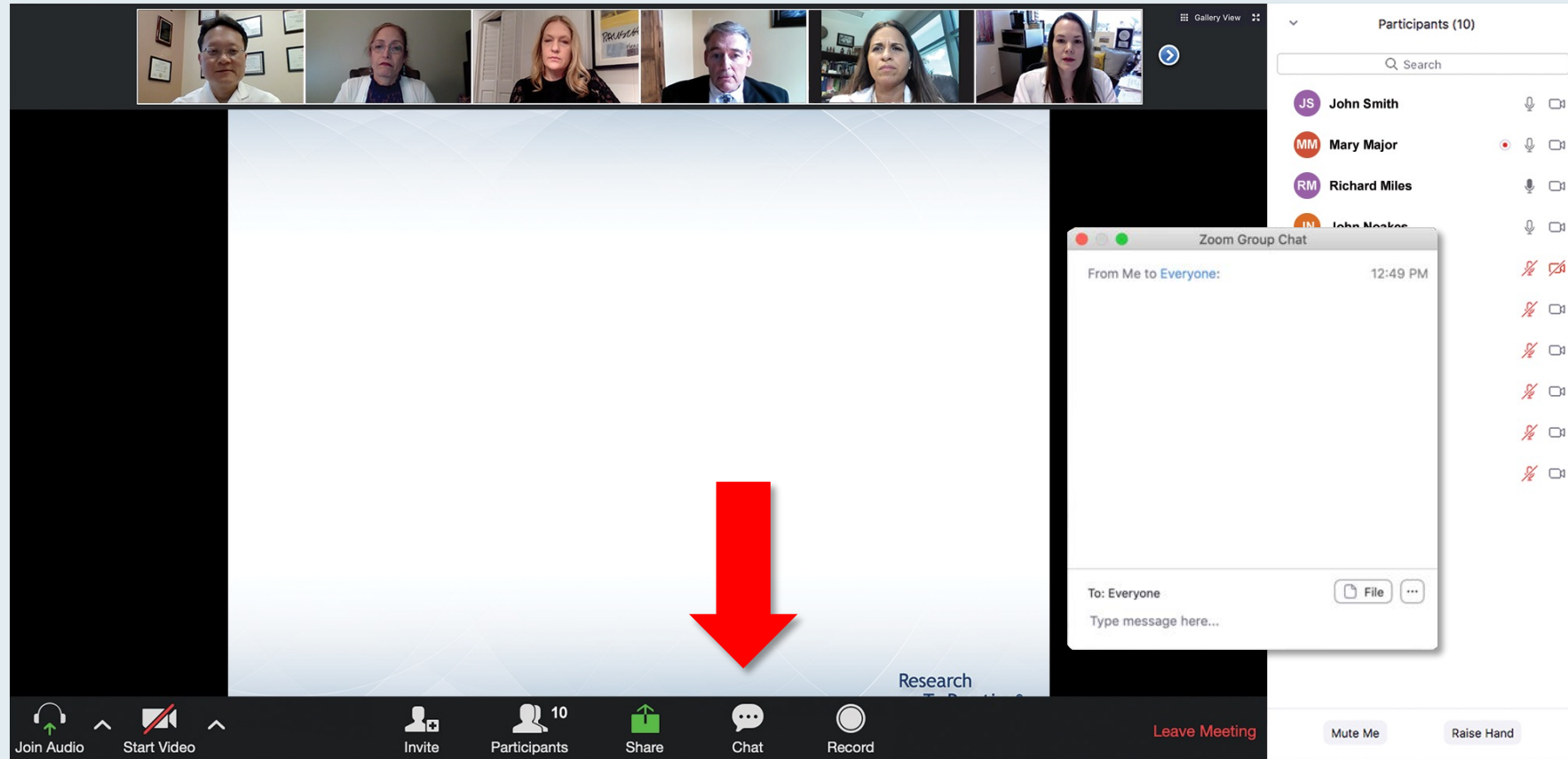


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Oncology Grand Rounds Nursing Webinar Series

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?

Agenda

Case 1: A 69-year-old man with metastatic hormone-sensitive prostate cancer and high-volume disease burden

Case 2: A 72-year-old man with M0 prostate cancer and rising PSA on ADT

Case 3: A 72-year-old man with metastatic castration-resistant prostate cancer (mCRPC) and a somatic BRCA2 mutation

Case 4: A 71-year-old man with mCRPC who enrolled on the CHAARTED2 trial and received abiraterone/prednisone

Case 5: A 65-year-old man with mCRPC

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Case 5: A 65-year-old man with mCRPC

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

Case Presentation – A 69-year-old man with metastatic hormone-sensitive prostate cancer and high-volume disease burden

- PMH: Sarcoidosis and HTN
- Abnormal DRE
- High-volume metastatic prostate cancer to inguinal and retroperitoneal nodes, bone → Leuprolide
- Enzalutamide

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?

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

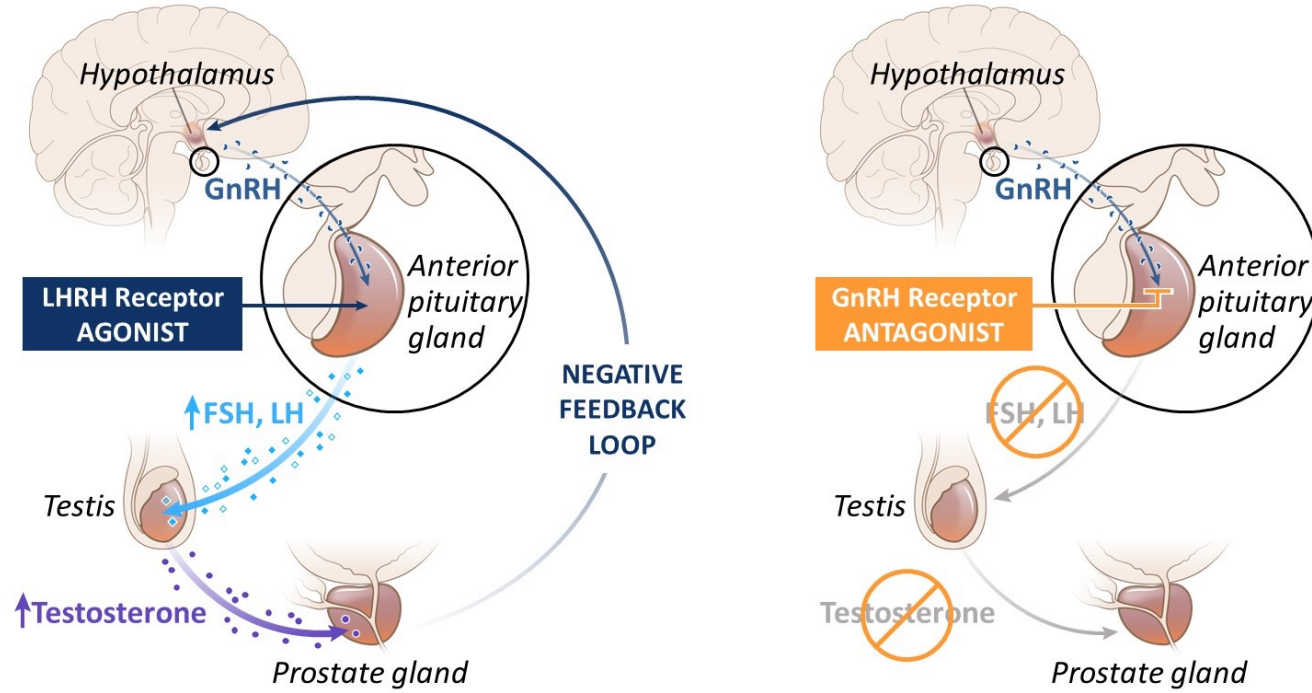
¹ Shore N et al.

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
Slides are the property of the author, permission required for reuse.

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

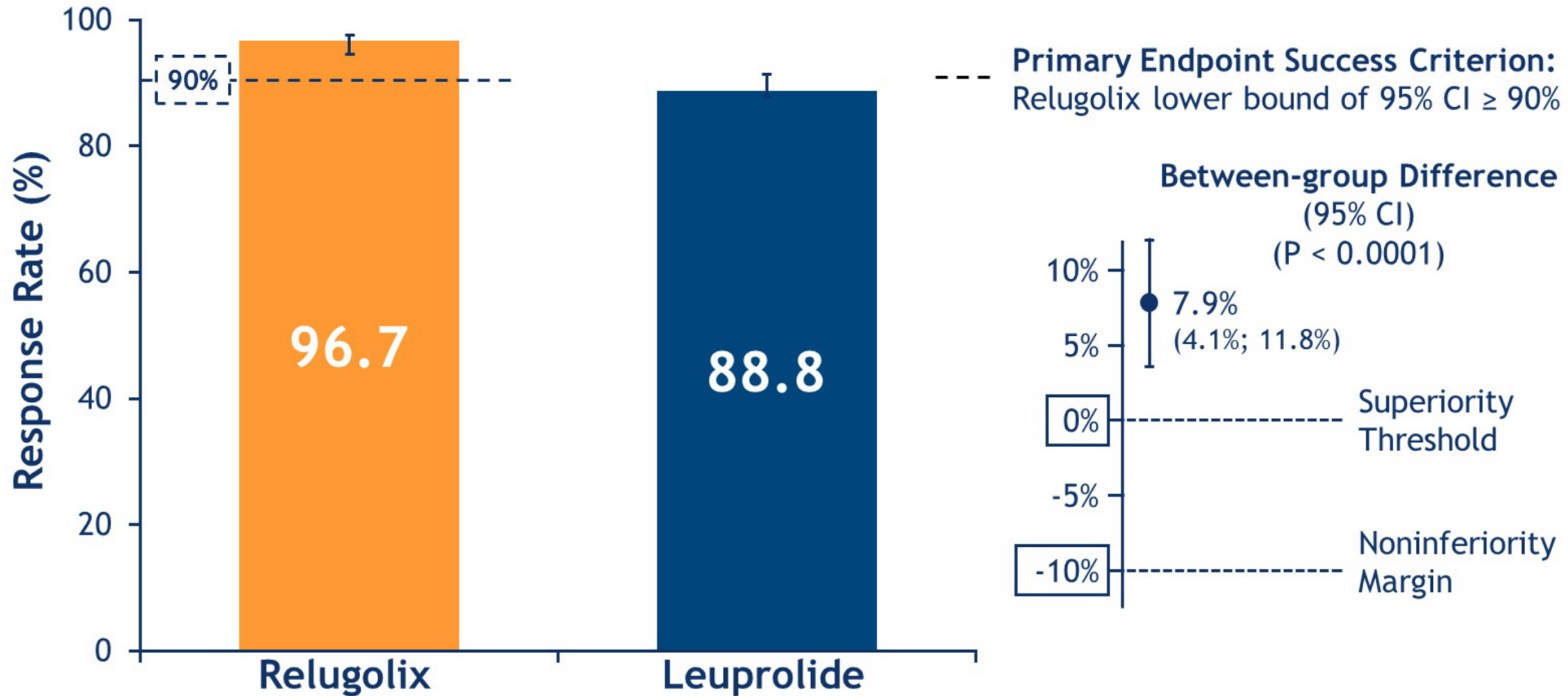
3

	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.

FDA-Approved Next-Generation Antiandrogens in 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

Andrew J. Armstrong, MD, ScM¹; Russell Z. Szmulewitz, MD²; Daniel P. Petrylak, MD³; Jeffrey Holzbeierlein, MD⁴; Arnaud Villers, MD⁵; Arun Azad, MBBS, PhD⁶; Antonio Alcaraz, MD, PhD⁷; Boris Alekseev, MD⁸; Taro Iguchi, MD, PhD⁹; Neal D. Shore, MD¹⁰; Brad Rosbrook, MS¹¹; Jennifer Sugg, MS¹²; Benoit Baron, MS¹³; Lucy Chen, MD¹²; and Arnulf Stenzl, MD¹⁴

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

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JULY 4, 2019

VOL. 381 NO. 1

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., Hirotsugu 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.

Final Analysis Results From TITAN: A Phase 3 Study of Apalutamide vs Placebo in Patients With Metastatic Castration-Sensitive Prostate Cancer Receiving Androgen Deprivation Therapy

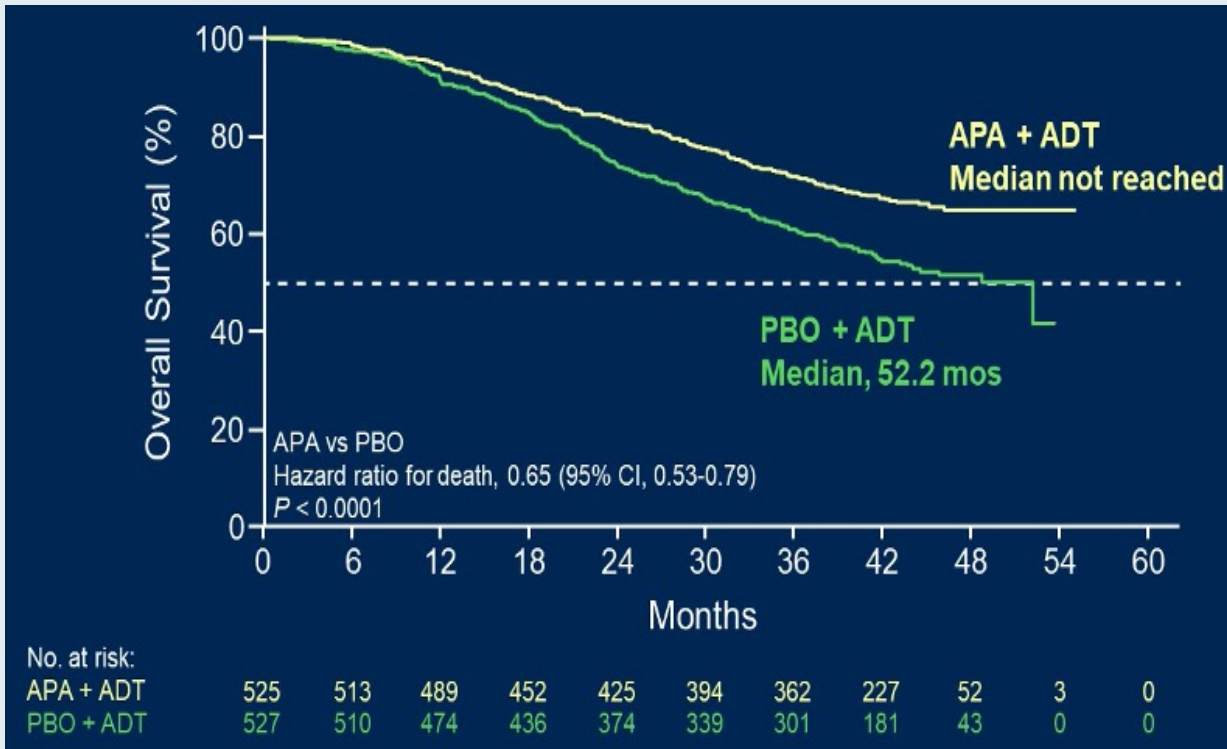
Kim N. Chi,¹ Simon Chowdhury,² Anders Bjartell,³ Byung Ha Chung,⁴ Andrea J. Pereira de Santana Gomes,⁵ Robert Given,⁶ Álvaro Juárez Soto,⁷ Axel S. Merseburger,⁸ Mustafa Özgüroğlu,⁹ Hirotsugu Uemura,¹⁰ Dingwei Ye,¹¹ Spyros Triantos,¹² Sabine Brookman-May,^{12,13} Suneel Mundle,¹⁴ Sharon A. McCarthy,¹⁴ Julie S. Larsen,¹⁵ Weili Sun,¹⁵ Katherine Bevans,¹⁶ Ke Zhang,¹⁷ Nibedita Bandyopadhyay,¹⁴ Neeraj Agarwal,¹⁸ for the TITAN Investigators

¹BC Cancer and Vancouver Prostate Centre, Vancouver, BC, Canada; ²Guy's, King's, and St. Thomas' Hospitals, and Sarah Cannon Research Institute, London, UK; ³Skåne University Hospital, Lund University, Malmö, Sweden; ⁴Yonsei University College of Medicine and Gangnam Severance Hospital, Seoul, South Korea; ⁵Liga Norte Riograndense Contra O Cancer, Natal, Brazil; ⁶Urology of Virginia, Eastern Virginia Medical School, Norfolk, VA; ⁷Hospital Universitario de Jerez de la Frontera, Cadiz, Spain; ⁸University Hospital Schleswig-Holstein, Campus Lübeck, Lübeck, Germany; ⁹Istanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine, Istanbul, Turkey; ¹⁰Kindai University Faculty of Medicine, Osaka, Japan; ¹¹Fudan University Shanghai Cancer Center, Shanghai, China; ¹²Janssen Research & Development, Spring House, PA; ¹³Ludwig-Maximilians-University (LMU), Munich, Germany; ¹⁴Janssen Research & Development, Raritan, NJ; ¹⁵Janssen Research & Development, Los Angeles, CA; ¹⁶Janssen Research & Development, Horsham, PA; ¹⁷Janssen Research & Development, San Diego, CA; ¹⁸Huntsman Cancer Institute, University of Utah, Salt Lake City, UT

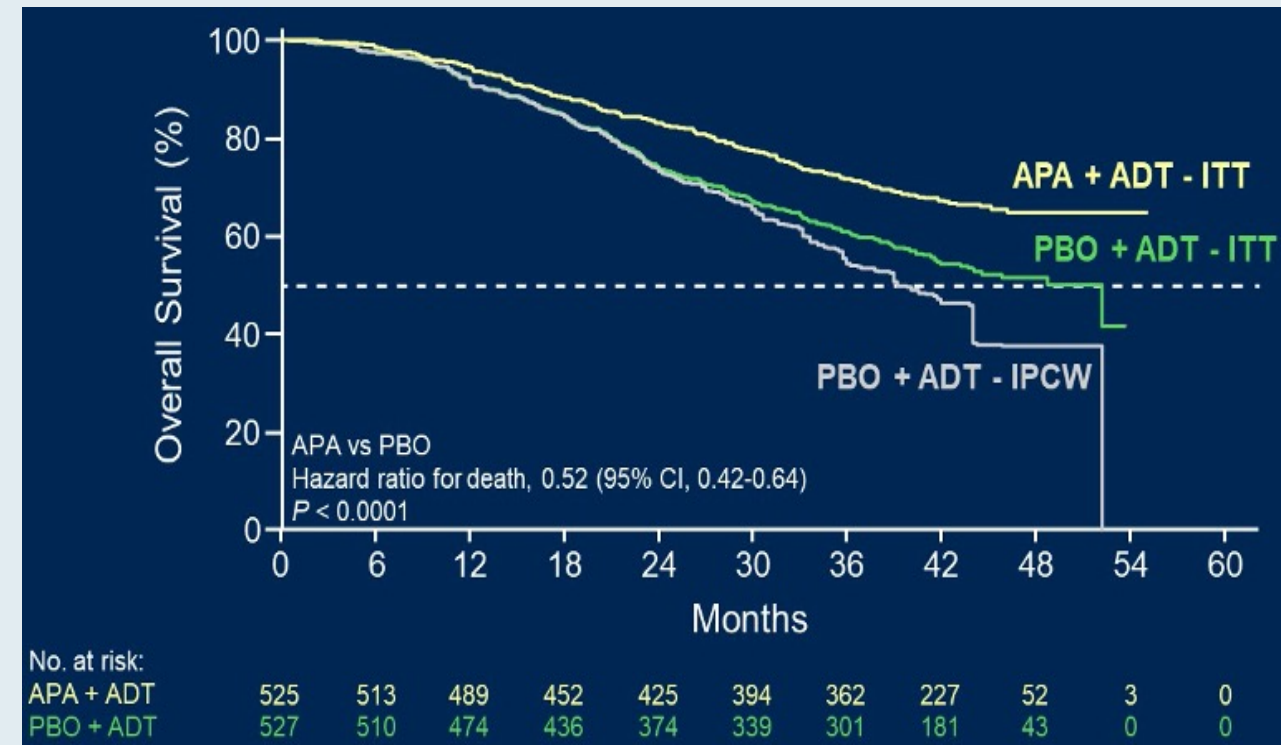


TITAN – Final Analysis: Overall Survival

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



OS with adjustment for ~40%
crossover from PBO



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

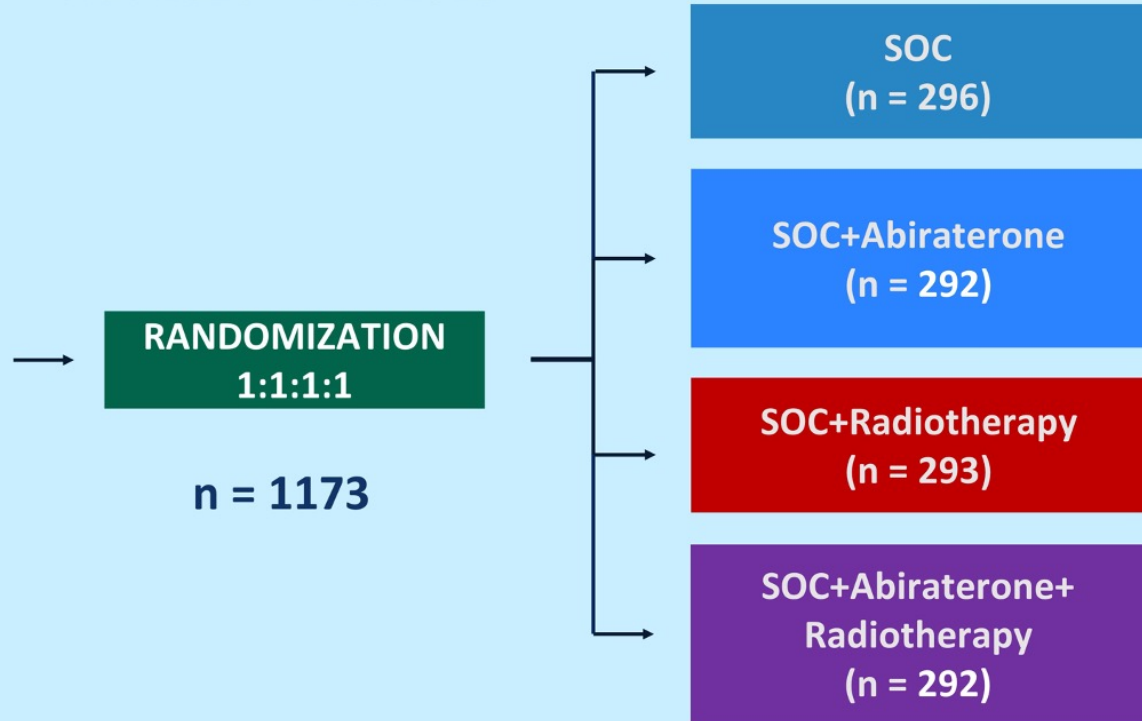
ECOG PS (0 vs 1-2)

Metastatic sites (LN vs bone vs visceral)

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

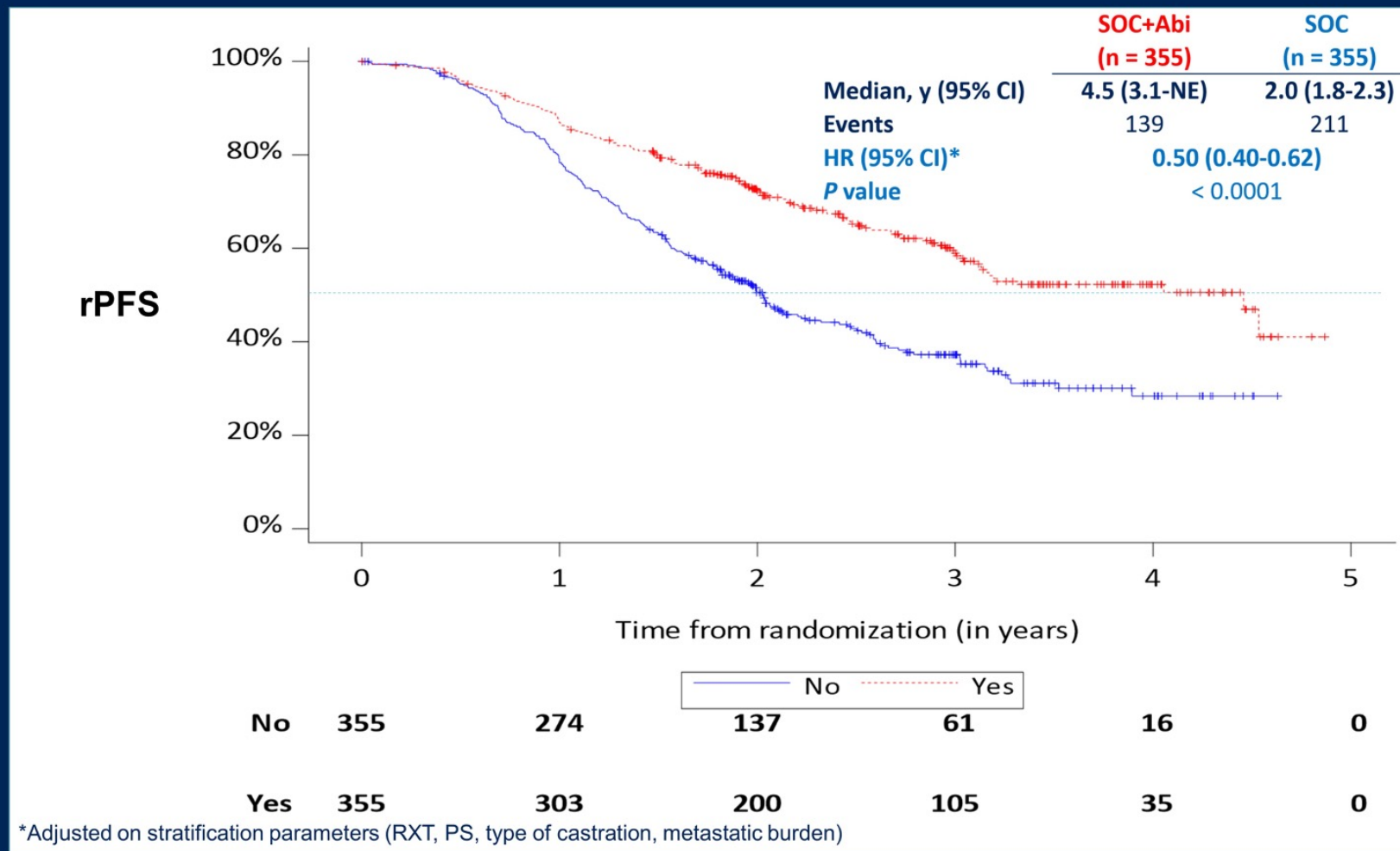
Docetaxel (yes vs no)

Nov 2013 – Dec 2018



ECOG PS, Eastern Cooperative Oncology Group performance status

Radiographic Progression-Free Survival (rPFS) ADT+Docetaxel population: SOC=ADT+Docetaxel (+/- RXT)



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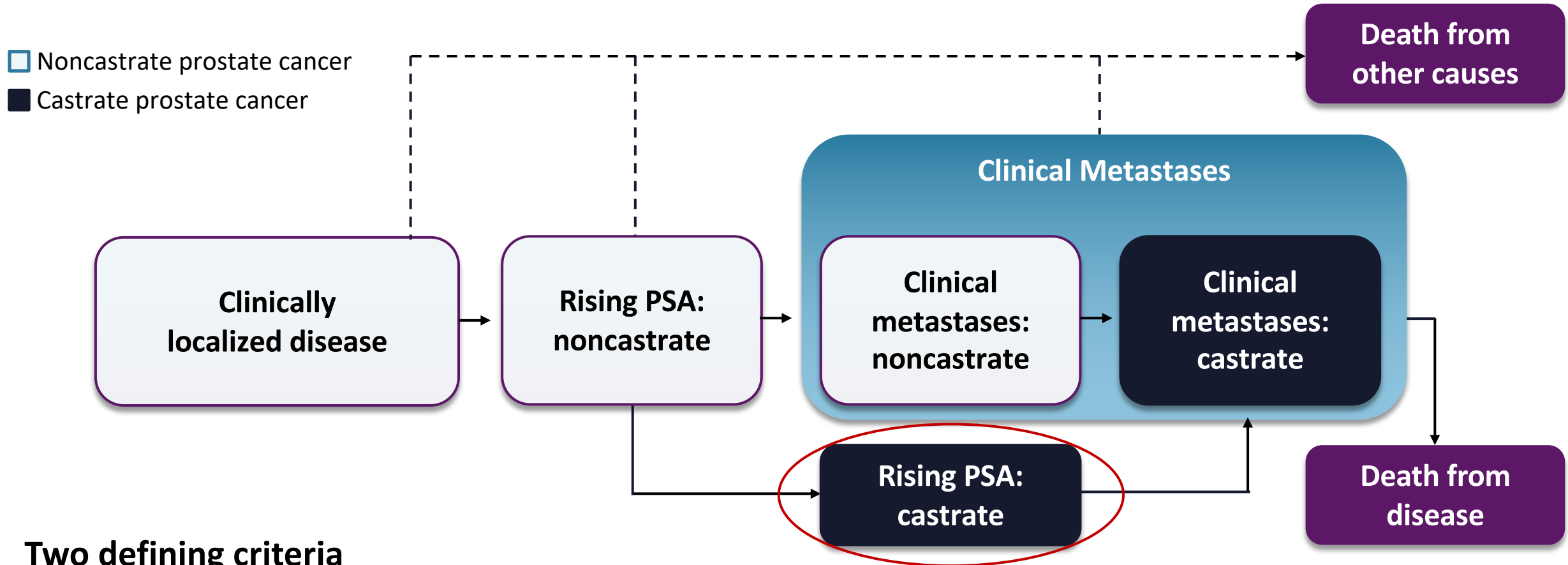
Case 5: A 65-year-old man with mCRPC

Case Presentation – A 72-year-old man with M0 prostate cancer and rising PSA on ADT

- 1998: Diagnosed with prostate cancer and received leuprolide
- PSA recurrence with no evidence of disease
- 2019: Bladder neck recurrence treated with salvage EBRT and apalutamide x 6 months
 - Discontinued due to “out of pocket” cost
- 11/2019: Darolutamide on assistance program and remains NED

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?

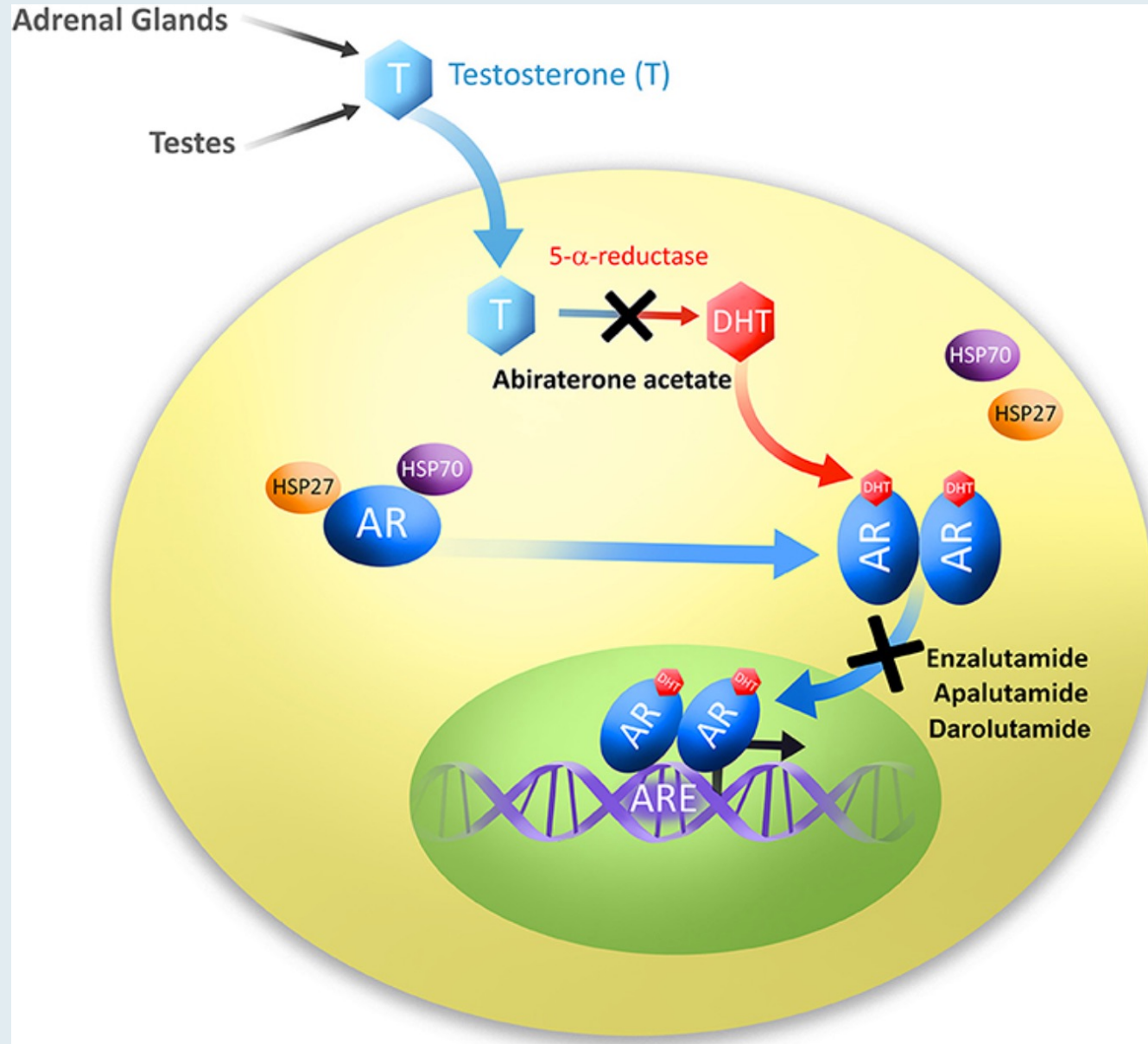
Clinical Disease States Model of Prostate Cancer¹



Two defining criteria

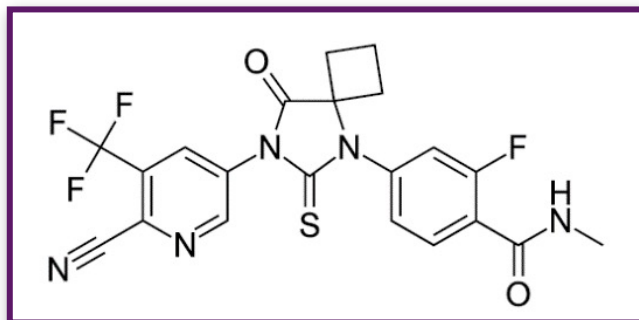
- Rising PSA in the setting of castrate testosterone levels (<50 ng/dL)
- No radiographically identifiable metastasis

Diagram of Androgen Production and Its Targeted Inhibition

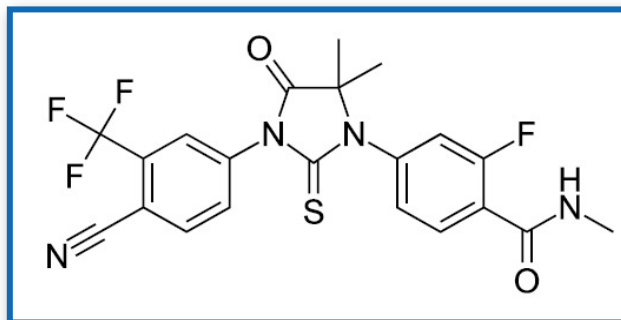


Next-Generation Androgen Receptor Inhibitors^{1,2}

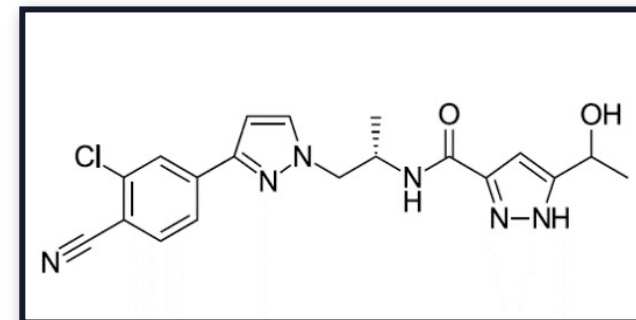
Apalutamide



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*

eau

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.

Agenda

Case 1: A 69-year-old man with metastatic hormone-sensitive prostate cancer and high-volume disease burden

Case 2: A 72-year-old man with M0 prostate cancer and rising PSA on ADT

Case 3: A 72-year-old man with metastatic castration-resistant prostate cancer (mCRPC) and a somatic BRCA2 mutation

Case 4: A 71-year-old man with mCRPC who enrolled on the CHAARTED2 trial and received abiraterone/prednisone

Case 5: A 65-year-old man with mCRPC

Case Presentation – A 72-year-old man with mCRPC and a somatic BRCA2 mutation

- Dentist diagnosed with mCRPC with a somatic BRCA2 mutation
- Olaparib therapy initiated
- Confusion regarding schedule to take oral pills led to underdosing
- Currently at full dose of olaparib and is responding well to treatment

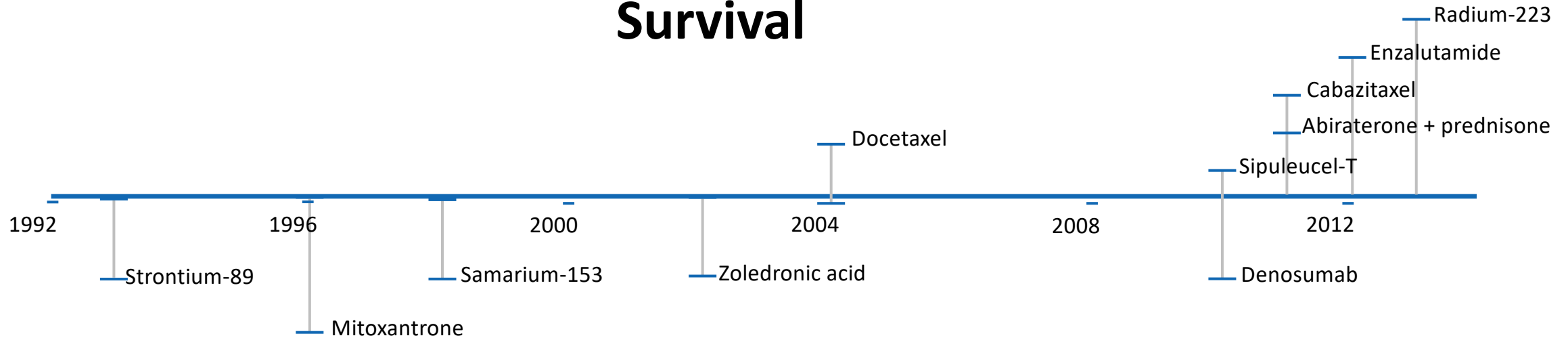
How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

Management of Metastatic Castration-Resistant Prostate Cancer

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

Timeline of FDA Approvals in Metastatic Castration-Resistant Prostate Cancer

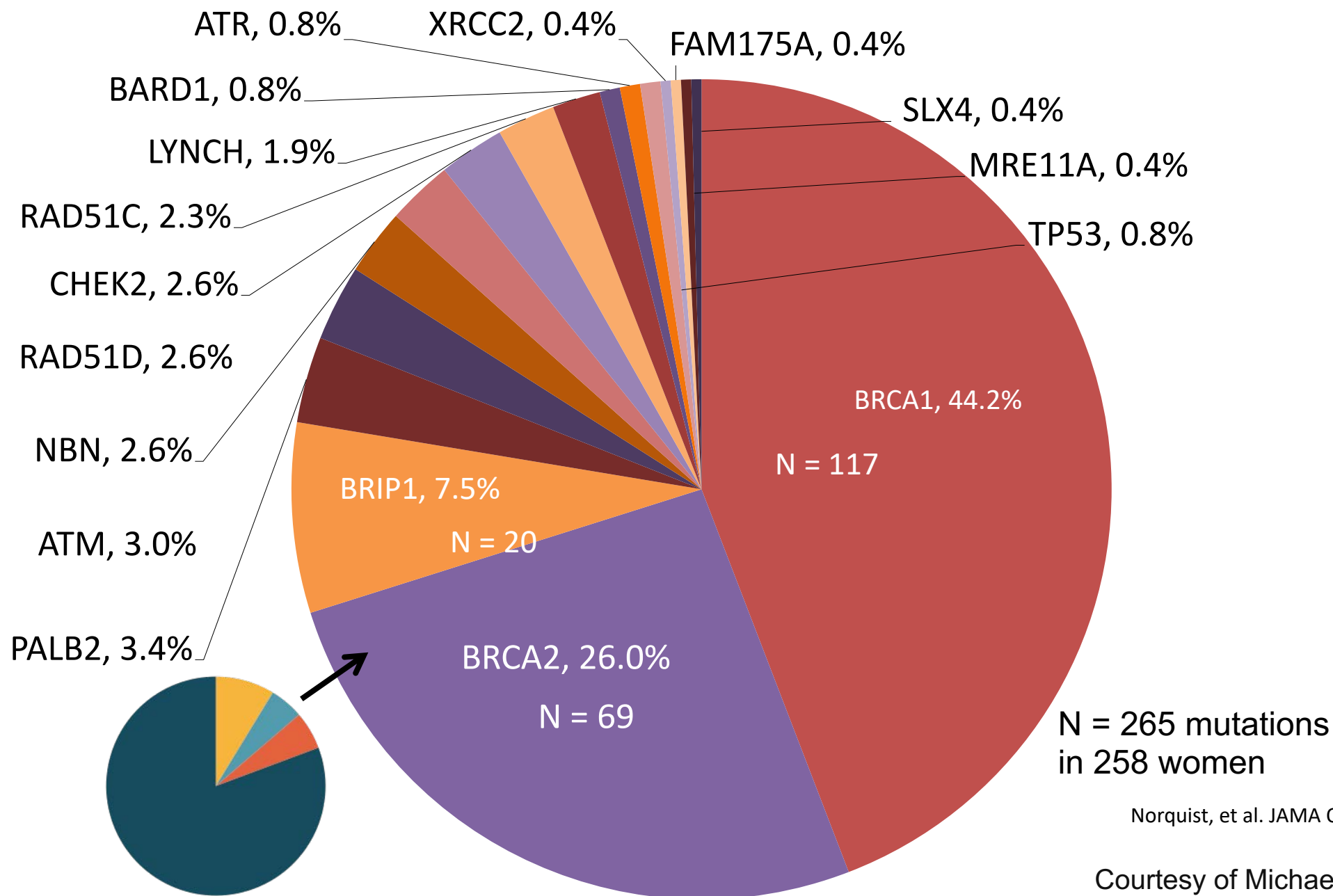
Survival



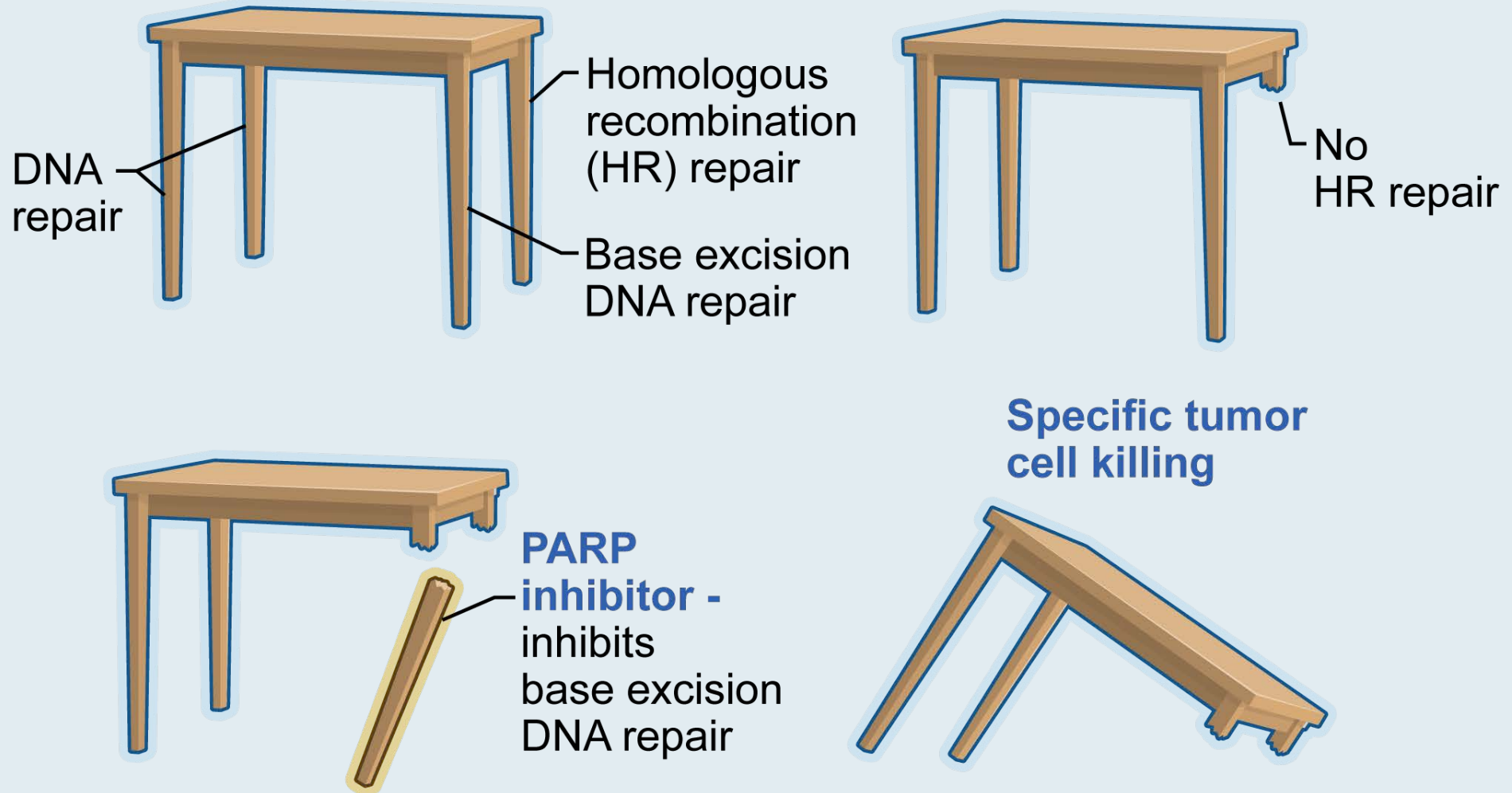
Palliation

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

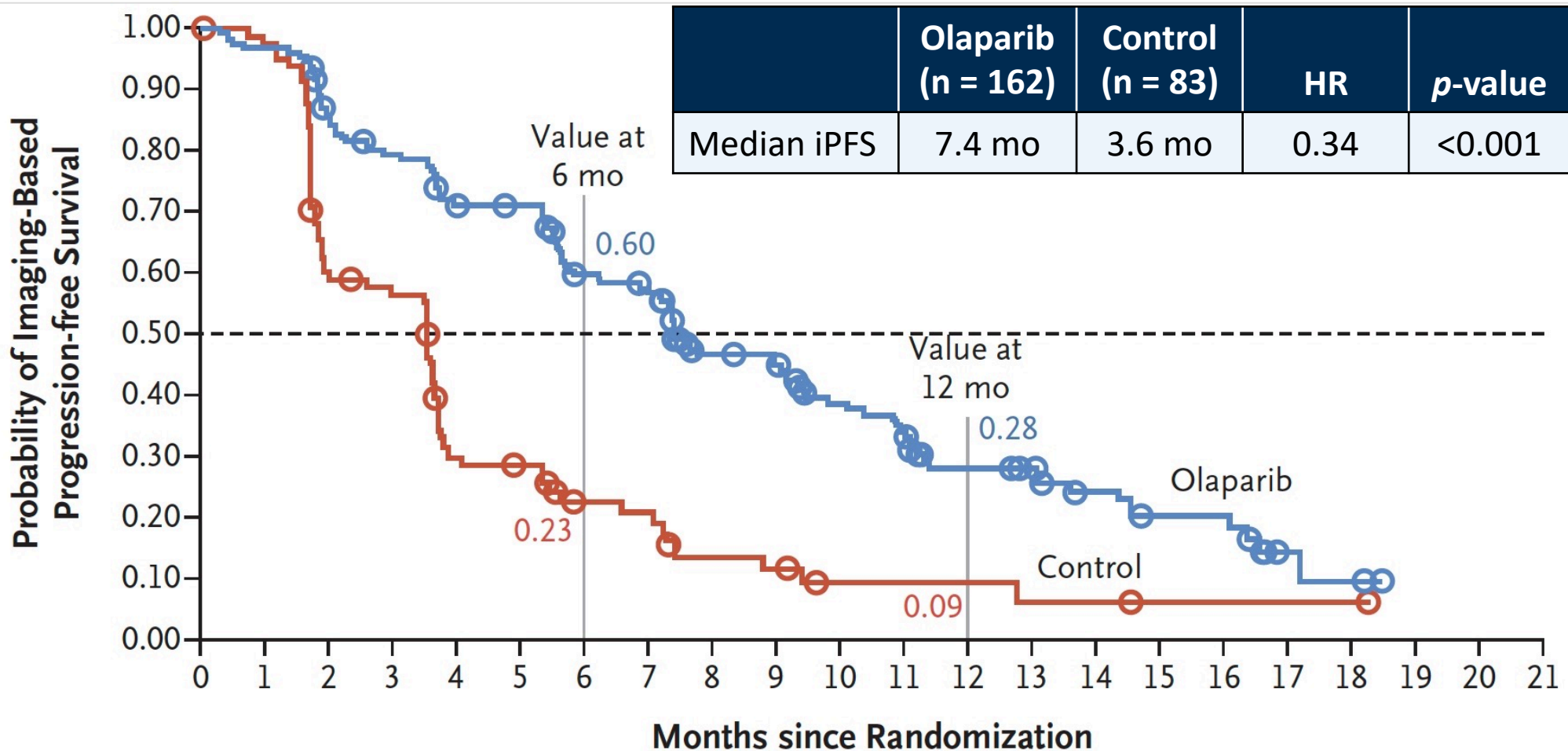
ORIGINAL ARTICLE

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

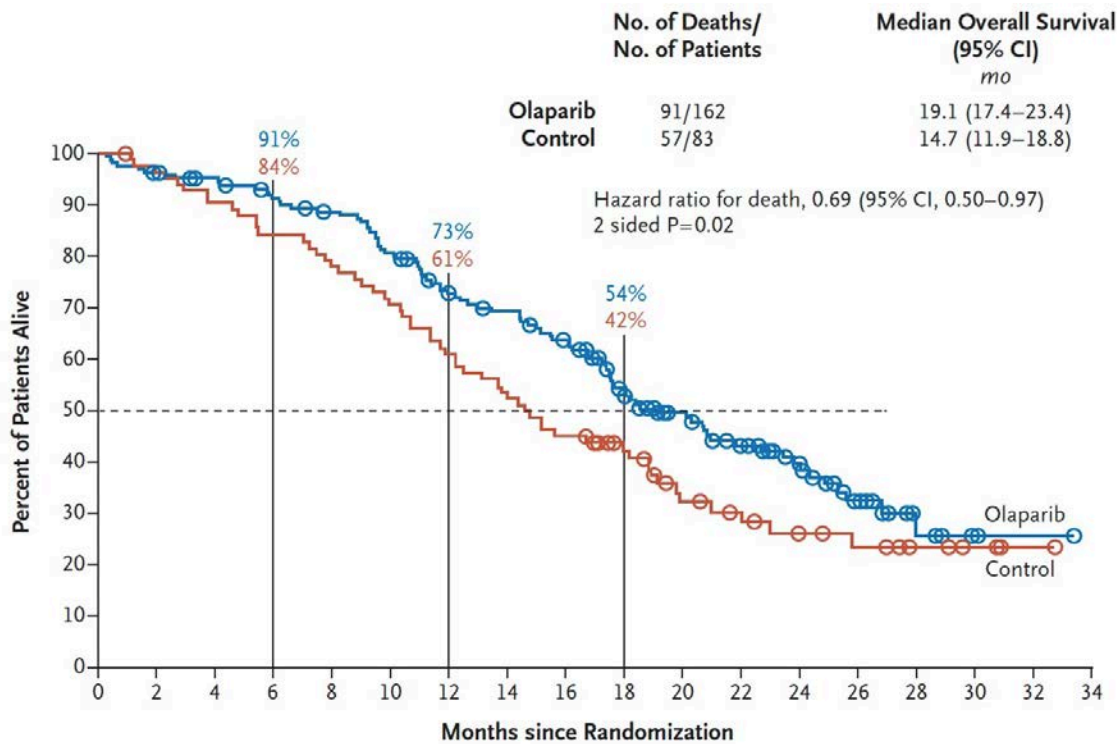
Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

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*

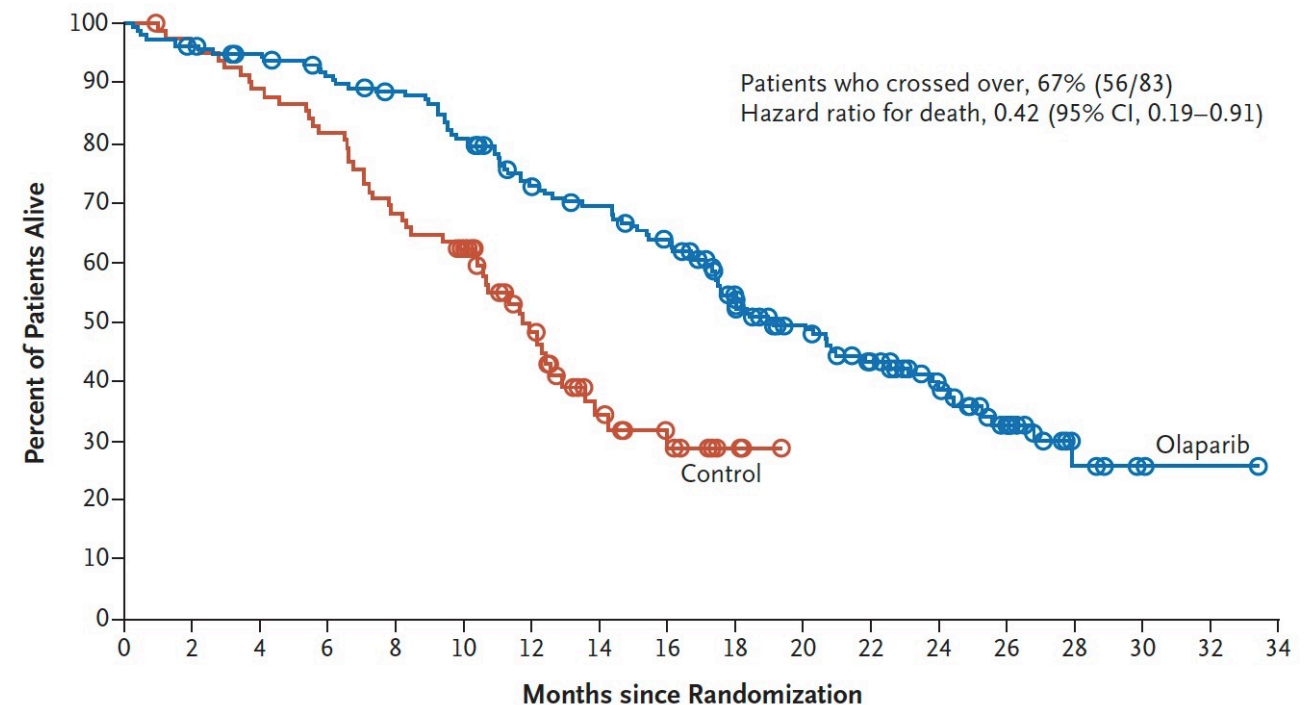
***N Engl J Med* 2020;[Online ahead of print].**

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



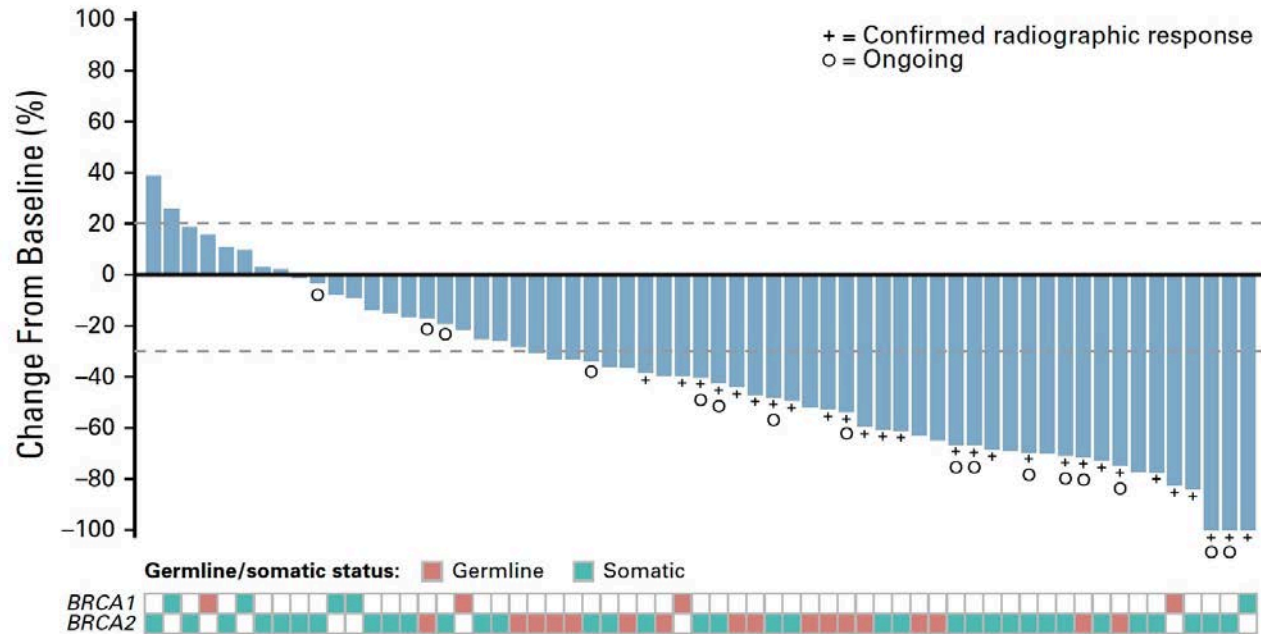
Rucaparib in Men With Metastatic Castration-Resistant Prostate Cancer Harboring a *BRCA1* or *BRCA2* Gene Alteration

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

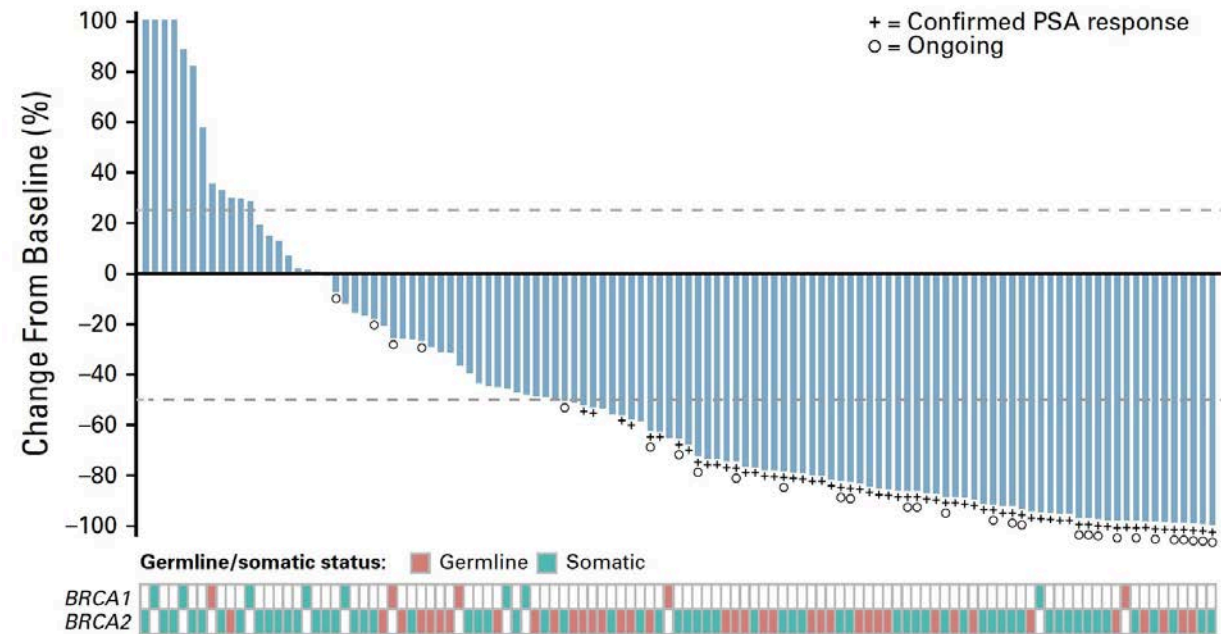
J Clin Oncol 2020;38(32):3763-72.

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.

Agenda

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Case 3: A 72-year-old man with metastatic castration-resistant prostate cancer (mCRPC) and a somatic BRCA2 mutation

Case 4: A 71-year-old man with mCRPC who enrolled on the CHAARTED2 trial and received abiraterone/prednisone

Case 5: A 65-year-old man with mCRPC

Case Presentation – A 71-year-old man with mCRPC who enrolled on the CHAARTED2 trial and received abiraterone/prednisone

- 3/2018: *De novo* high-volume metastatic hormone-sensitive prostate cancer
- 4/2019: Progressive disease → enrolled on CHAARTED2, randomized to abiraterone/prednisone
- 10/2020: Admitted with pneumonia due to COVID-19
 - Residual pulmonary changes after treatment and recovery after 2 months
- Imaging: PD in the bone

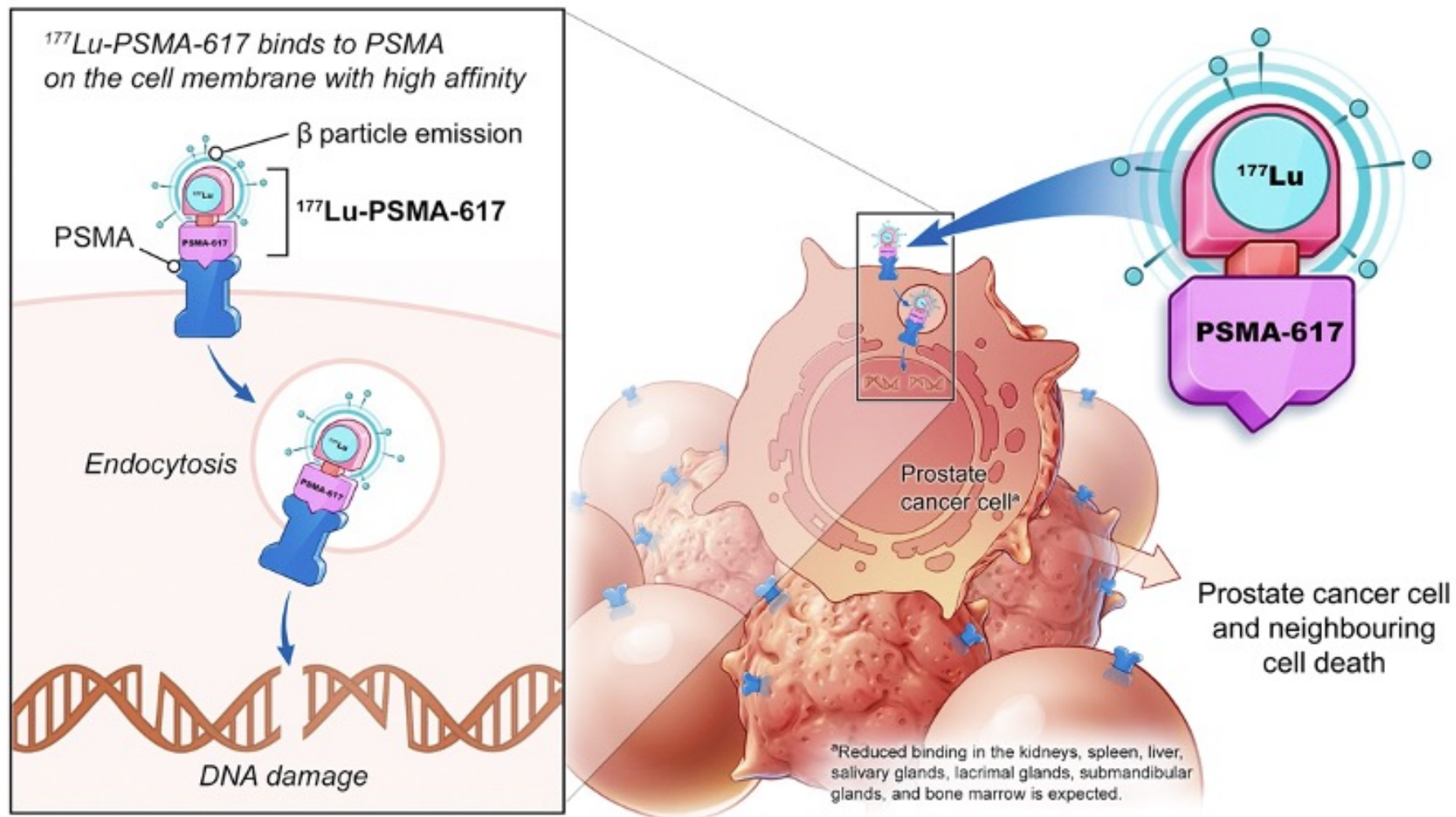
How was it different to take care of this patient versus another patient in the same oncologic setting? What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

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 ± ¹⁷⁷Lu-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 ⁶⁸Ga-PSMA-11

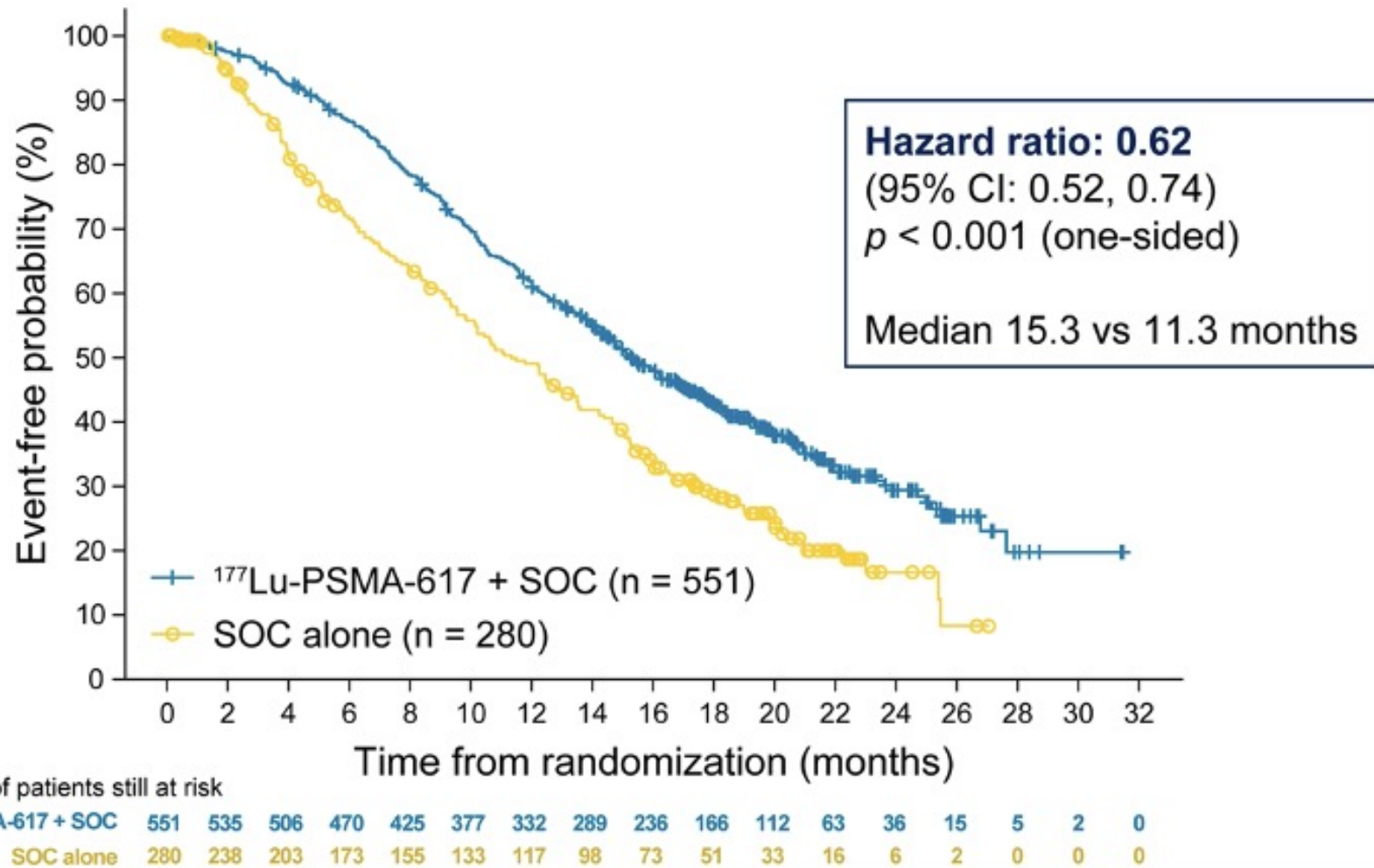


- Randomization stratified by
 - ECOG status (0–1 or 2)
 - LDH (high or low)
 - Liver metastases (yes or no)
 - Androgen receptor pathway inhibitors in SOC (yes or no)
- CT/MRI/bone scans
 - Every 8 weeks (treatment)
 - Every 12 weeks (follow-up)
 - Blinded independent central review

Primary endpoints: ¹⁷⁷Lu-PSMA-617 prolonged OS

Primary analysis

All randomized patients
(N = 831)



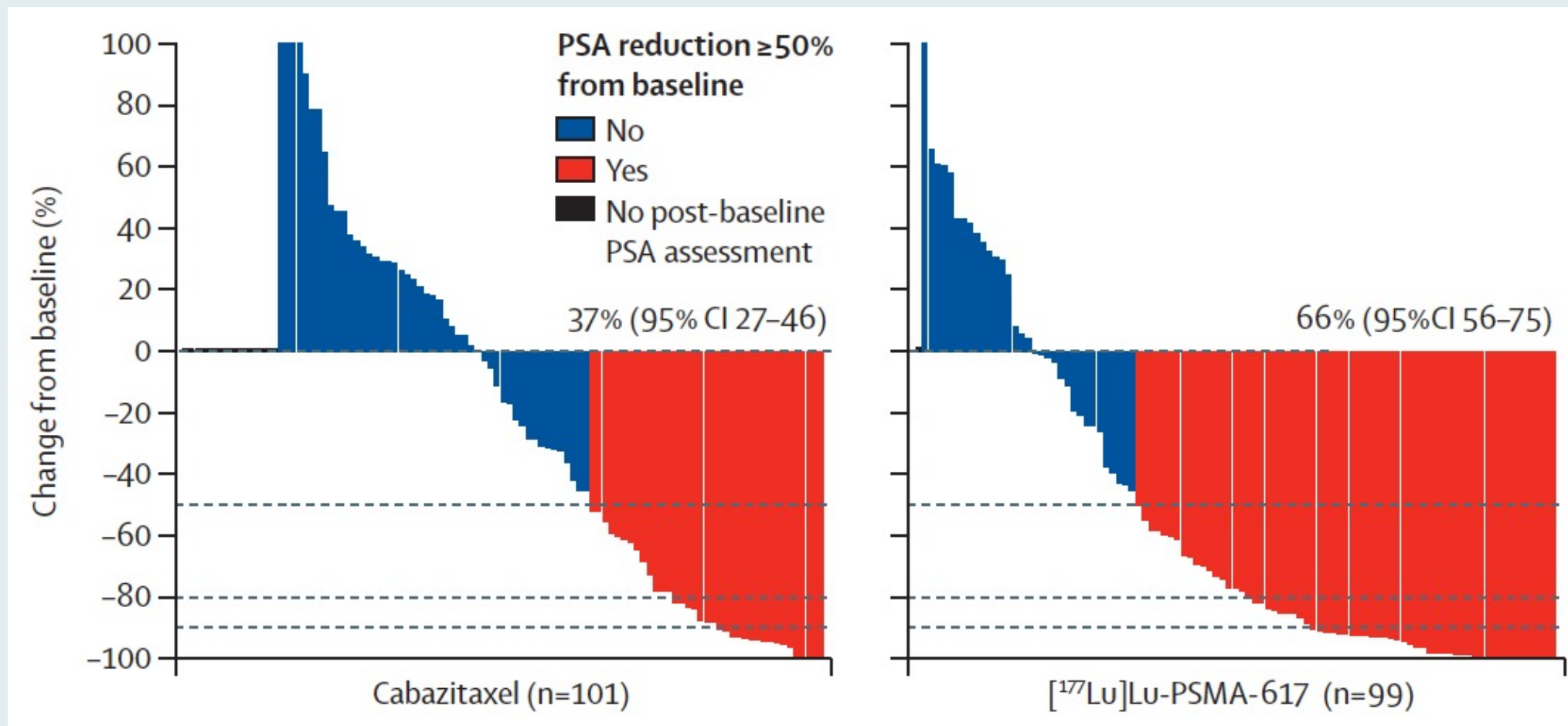
Lancet 2021;397:797-804.

[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 Gedye, 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 McJannett, 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

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Case 5: A 65-year-old man with mCRPC

Case Presentation – A 65-year-old man with metastatic CRPC

- 6/2017: De novo high-volume metastatic prostate cancer
- Docetaxel
- 9/2019: Progressive disease
- Enrolled in CHAARTED2 and received cabazitaxel and abiraterone/prednisone → PD
- Radium-223 delayed until healed from dental extractions

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?

Ask the Expert: Clinical Investigators Provide Perspectives on the Management of Renal Cell Carcinoma

In Partnership with Project Echo® and Florida Cancer Specialists

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

Faculty

David I Quinn, MBBS, PhD

Moderator

Neil Love, MD

Thank you for joining us!

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