

Meet The Professor

Optimizing the Management of Metastatic Castration-Resistant Prostate Cancer

Prof Karim Fizazi, MD, PhD

Head of Service and Full Professor

Institut Gustave Roussy

University of Paris Saclay

Villejuif, France

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Exelixis Inc, Merck, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, and Sanofi Genzyme.

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, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Coherus BioSciences, Daiichi Sankyo Inc, Eisai Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Inc, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab, 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, Mersana Therapeutics Inc, Natera Inc, Novartis, Novocure Inc, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seagen Inc, Servier Pharmaceuticals LLC, Sumitomo Dainippon Pharma Oncology Inc, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc and Zymeworks Inc.

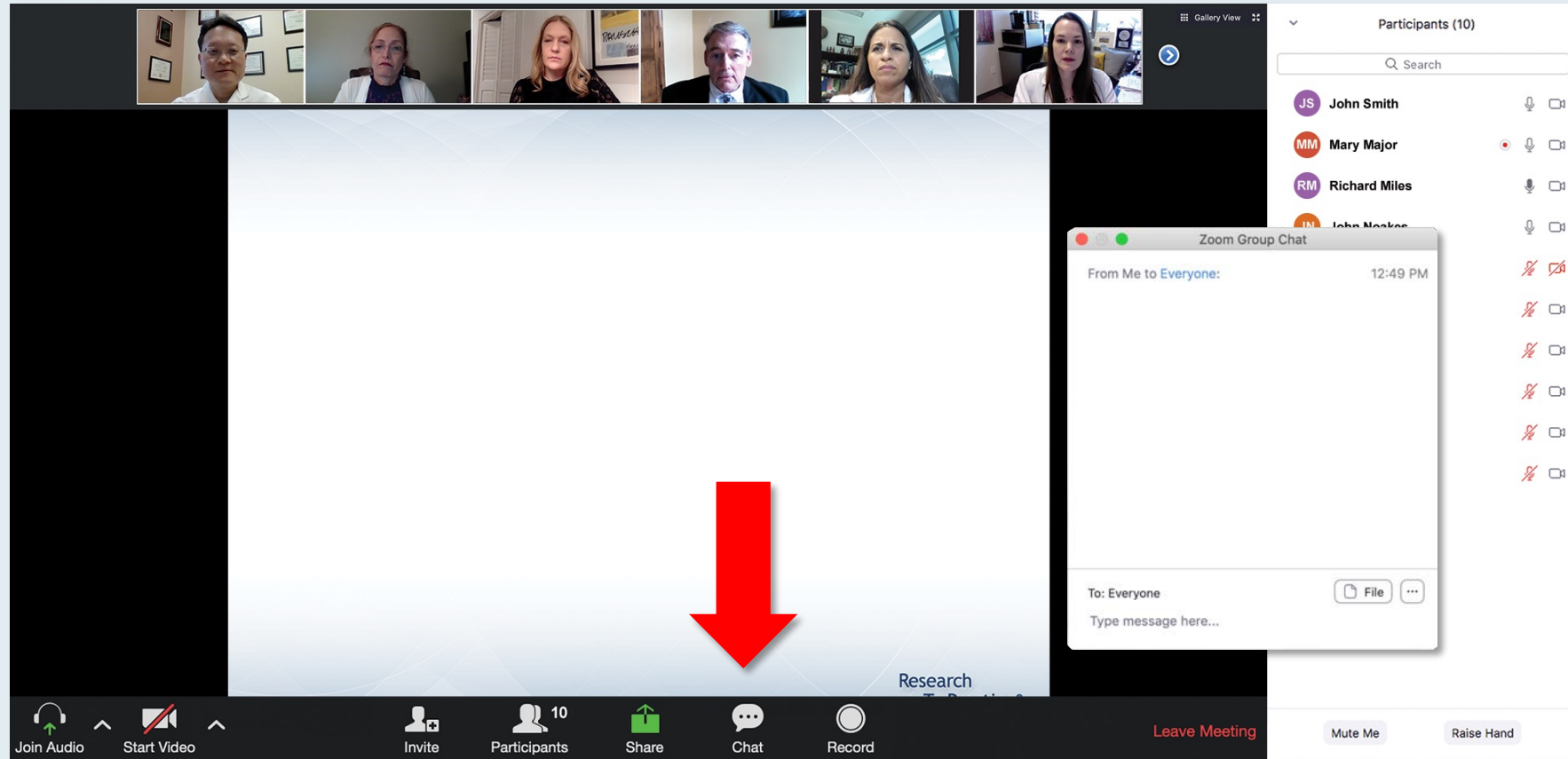
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Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose.

Prof Fizazi— Disclosures

Advisory Committee and Consulting Agreements	Bayer HealthCare Pharmaceuticals, CureVac, Orion Corporation.
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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

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. Below the thumbnails is a slide titled "Meet The Professor Program Steering Committee" with six members listed:

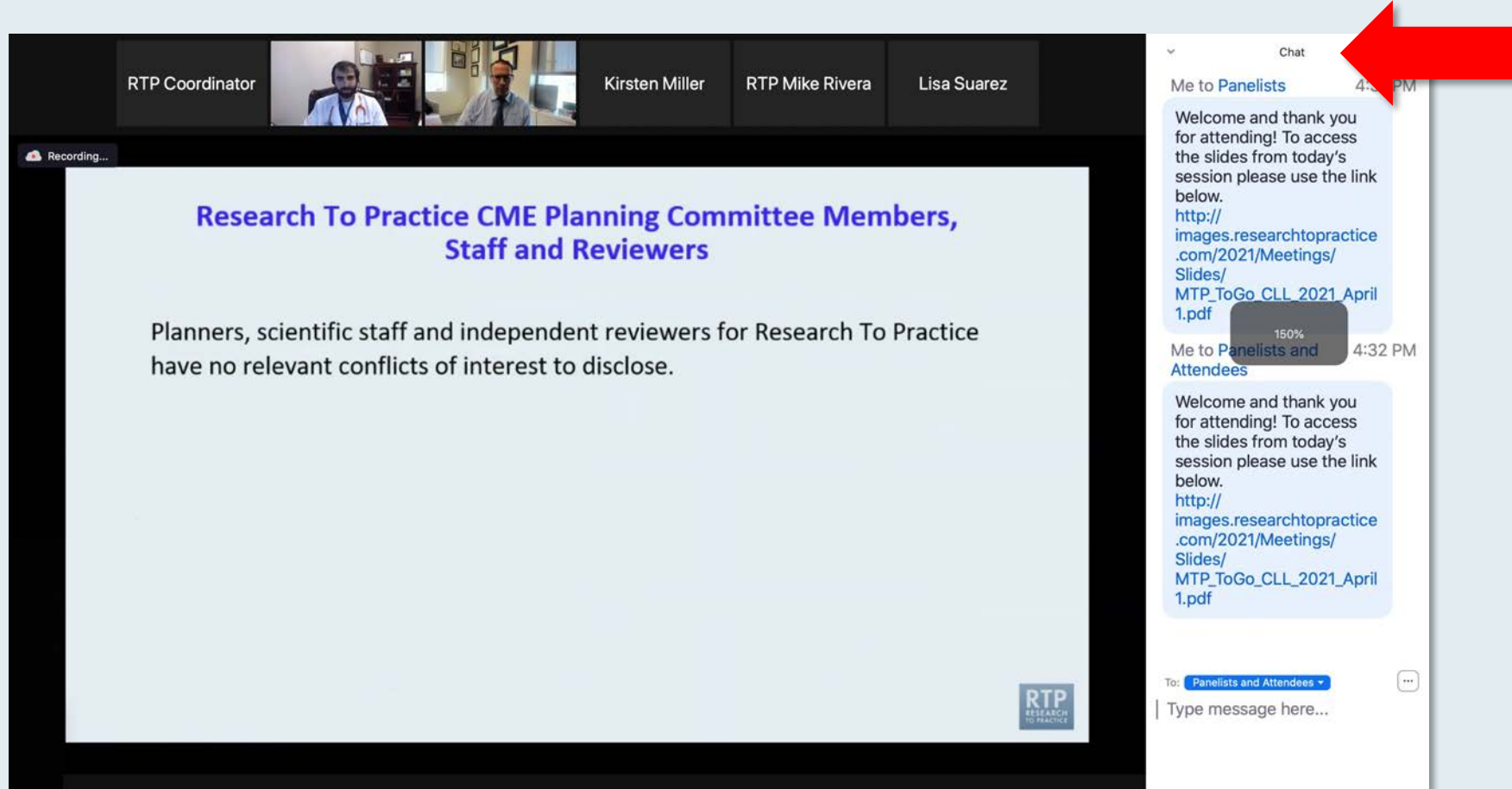
- John N Allan, MD**
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- Ian W Flinn, MD, PhD**
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Tennessee Oncology
Nashville, Tennessee
- Steven Coutre, MD**
Professor of Medicine (Hematology)
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London, United Kingdom
- Matthew S Davids, MD, MMSc**
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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 shows two messages from "Me to Panelists" and "Me to Panelists and Attendees" at 4:31 PM and 4:32 PM respectively. The messages contain a welcome message and a link to a PDF slide: http://images.researchtopractice.com/2021/Meetings/Slides/2021/Meetings/Slides/MTP_ToGo_CLL_2021_April1.pdf. The chat submission box at the bottom right is expanded, showing a red arrow pointing to the white line above the "Type message here..." input field.

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



The screenshot displays a Zoom meeting interface. At the top, there are video thumbnails for participants: RTP Coordinator, Kirsten Miller, RTP Mike Rivera, and Lisa Suarez. Below the thumbnails is a slide titled "Research To Practice CME Planning Committee Members, Staff and Reviewers". The slide content reads: "Planners, scientific staff and independent reviewers for Research To Practice have no relevant conflicts of interest to disclose." A "Recording..." indicator is visible in the top left corner of the slide area. On the right side, the chat window is open, showing a message from "Me to Panelists" at 4:32 PM. The message text is: "Welcome and thank you for attending! To access the slides from today's session please use the link below. http://images.researchtopractice.com/2021/Meetings/Slides/MTP_ToGo_CLL_2021_April 1.pdf". A red arrow points to the chat window, specifically to the font size adjustment icon (a small square with a plus sign) located above the message text. The chat window also shows a "150%" font size indicator and a "Type message here..." input field at the bottom.

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

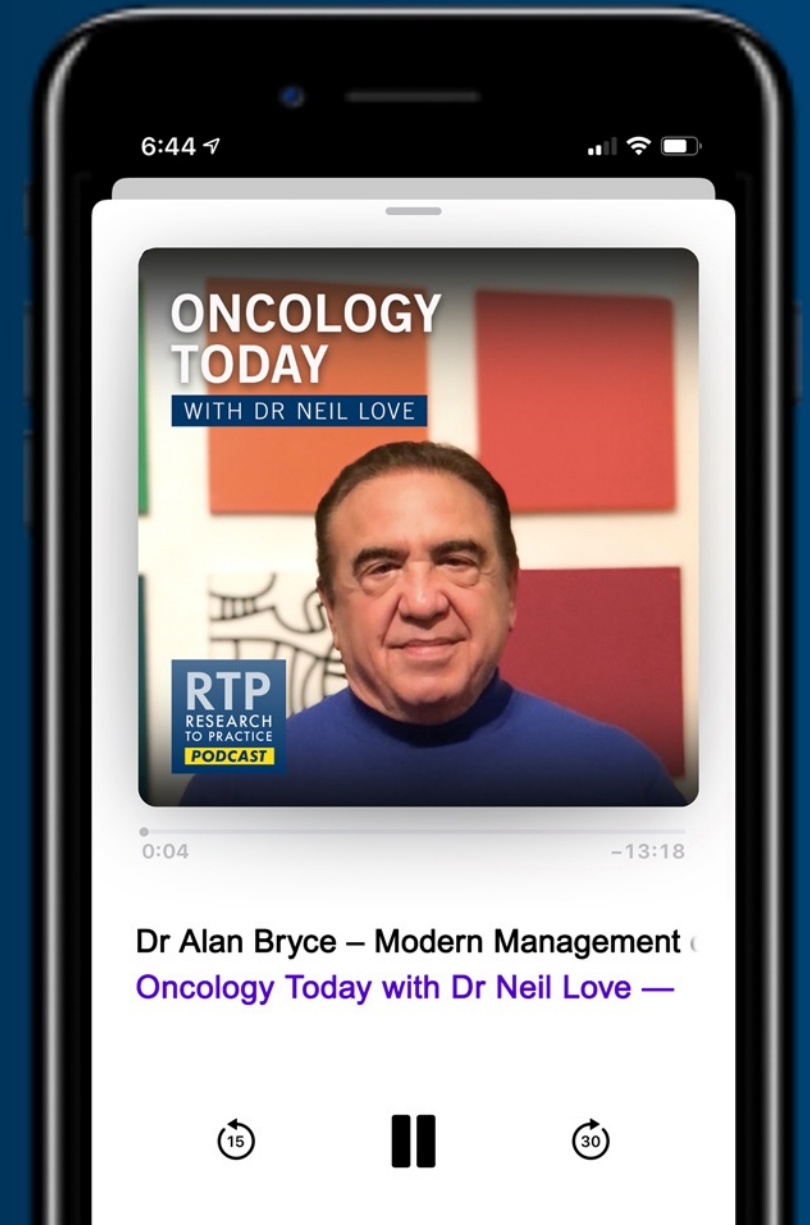
ONCOLOGY TODAY

WITH DR NEIL LOVE

Modern Management of Metastatic Castration-Resistant Prostate Cancer



DR ALAN BRYCE
MAYO CLINIC



**Year in Review: Clinical Investigator
Perspectives on the Most Relevant
New Data Sets and Advances in Oncology
Breast Cancer**

**Thursday, January 6, 2022
5:00 PM – 6:00 PM ET**

Faculty

**Harold J Burstein, MD, PhD
Professor Peter Schmid, FRCP, MD, PhD**

Moderator

Neil Love, MD

**Year in Review: Clinical Investigator Perspectives
on the Most Relevant New Data Sets
and Advances in Oncology
Targeted Therapy for Non-Small
Cell Lung Cancer**

**Tuesday, January 11, 2022
5:00 PM – 6:00 PM ET**

Faculty

**John V Heymach, MD, PhD
Zofia Piotrowska, MD, MHS**

Moderator

Neil Love, MD

Meet The Professor

Optimizing the Selection and Sequencing of Therapy for Patients with HER2-Positive Breast Cancer

Wednesday, January 12, 2022
6:00 PM – 7:00 PM ET

Faculty

Tiffany A Traina, MD

Moderator

Neil Love, MD

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Anne S Tsao, MD, MBA**

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Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Colorectal Cancer (Part 1 of a 3-Part Series)

**Wednesday, January 19, 2022
10:15 PM – 11:45 PM ET**

Faculty

**Cathy Eng, MD
Christopher Lieu, MD
Alan P Venook, MD**

Moderator

Kristen K Ciombor, MD, MSCI

Beyond the Guidelines: Clinical Investigator Perspectives on the Management of Gastroesophageal Cancers (Part 2 of a 3-Part Series)

**Thursday, January 20, 2022
9:15 PM – 10:45 PM ET**

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**Yelena Y Janjigian, MD
Eric Van Cutsem, MD, PhD
Harry H Yoon, MD**

Moderator

Samuel J Klempner, MD

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Robin K Kelley, MD**

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Tanios Bekaii-Saab, MD

Thank you for joining us!

CME and MOC credit information will be emailed to each participant within 5 business days.

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Villejuif, France

Meet The Professor Program Participating Faculty



Andrew J Armstrong, MD, ScM

Professor of Medicine, Surgery, Pharmacology and
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Director of Research

Duke Cancer Institute Center for Prostate and
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Divisions of Medical Oncology and Urology

Duke University

Durham, North Carolina



Simon Chowdhury, MD, PhD

Consultant Medical Oncologist
London, United Kingdom



Alan H Bryce, MD

Chair, Division of Hematology and Medical Oncology

Chair, Genitourinary Disease Group

Mayo Clinic

Phoenix, Arizona



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Head of Service and Full Professor

Institut Gustave Roussy

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Alicia K Morgans, MD, MPH
Genitourinary Medical Oncologist
Medical Director, Survivorship Program
Dana-Farber Cancer Institute
Boston, Massachusetts



Moderator
Neil Love, MD
Research To Practice
Miami, Florida



A Oliver Sartor, MD
Laborde Professor for Cancer Research
Medical Director, Tulane Cancer Center
Assistant Dean for Oncology
Tulane Medical School
New Orleans, Louisiana

We Encourage Clinicians in Practice to Submit Questions

The screenshot displays a Zoom meeting interface. At the top, a gallery view shows six participants. The main area features a presentation slide with the text: "You may submit questions using the Zoom Chat option below". A large red arrow points downwards from this text. On the right side, a "Participants (10)" list is visible, showing names like John Smith, Mary Major, Richard Miles, John Noakes, and Alice Suarez. A "Zoom Group Chat" window is open in the foreground, showing a message from "Me to Everyone" at 12:49 PM. The bottom toolbar includes icons for "Join Audio", "Start Video", "Invite", "Participants", "Share", "Chat", "Record", "Leave Meeting", "Mute Me", and "Raise Hand".

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

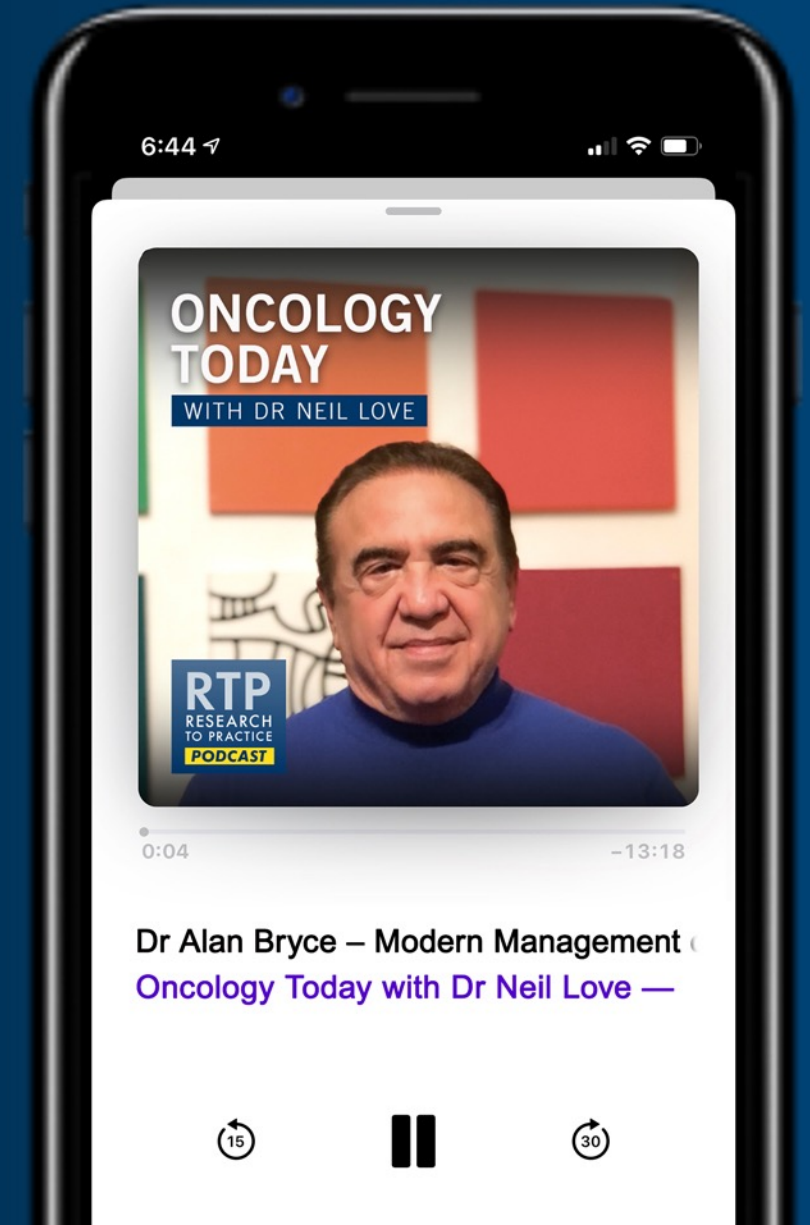
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Rohit Gosain, MD
UPMC Hillman Cancer Center
at UPMC Chautauqua
Jamestown, New York



Nataliya Mar, MD
University of California, Irvine
Irvine, California



Sulfi Ibrahim, MD
Reid Health
Richmond, Indiana



Helen H Moon, MD
Southern California Permanente
Medical Group
Riverside, California



Zanetta S Lamar, MD
Florida Cancer Specialists and
Research Institute
Naples, Florida

Faculty for Second Opinion



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



A Oliver Sartor, MD
Laborde Professor for Cancer Research
Medical Director, Tulane Cancer Center
Assistant Dean for Oncology
Tulane Medical School
New Orleans, Louisiana

A 65-year-old man with MSS prostate cancer metastatic to the bone and a germline BRCA2 mutation who is receiving abiraterone/dexamethasone for hormone-sensitive metastatic disease develops new high-volume symptomatic bone metastases. Which systemic treatment would you most likely recommend?



Dr Armstrong

Olaparib



Prof Fizazi

Olaparib



Dr Bryce

Olaparib



Dr Morgans

Radium-223



Prof Chowdhury

Olaparib



Dr Sartor

Olaparib

Meet The Professor with Prof Fizazi

Introduction

MODULE 1: Journal Club with Prof Fizazi (Part 1)

MODULE 2: Case Presentations and Second Opinion

MODULE 3: Faculty Survey

MODULE 4: Immune Checkpoint Inhibitors in mCRPC

MODULE 5: Journal Club with Prof Fizazi (Part 2)

MODULE 6: Appendix

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MODULE 5: Journal Club with Prof Fizazi (Part 2)

MODULE 6: Appendix

Introduction

Positive Results Announced for the PROpel Phase III Trial of Olaparib with Abiraterone as First-Line Treatment for mCRPC

Press Release: September 24, 2021

“Positive high-level results from the PROpel Phase III trial showed that olaparib in combination with abiraterone demonstrated a statistically significant and clinically meaningful improvement in radiographic progression-free survival (rPFS) versus standard-of-care abiraterone as a 1st-line treatment for men with metastatic castration-resistant prostate cancer (mCRPC) with or without homologous recombination repair (HRR) gene mutations.

At a planned interim analysis, the Independent Data Monitoring Committee concluded that the trial met the primary endpoint of rPFS in men with mCRPC who had not received treatment in the 1st-line setting including with new hormonal agents or chemotherapy.

The data will be presented at an upcoming medical meeting.”

Meet The Professor with Prof Fizazi

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MODULE 6: Appendix



PSMA targeting in metastatic castration-resistant prostate cancer: where are we and where are we going?

Anne-Laure Giraudet , David Kryza, Michael Hofman, Aurélie Moreau, Karim Fizazi, Aude Flechon, Rodney J. Hicks and Ben Tran

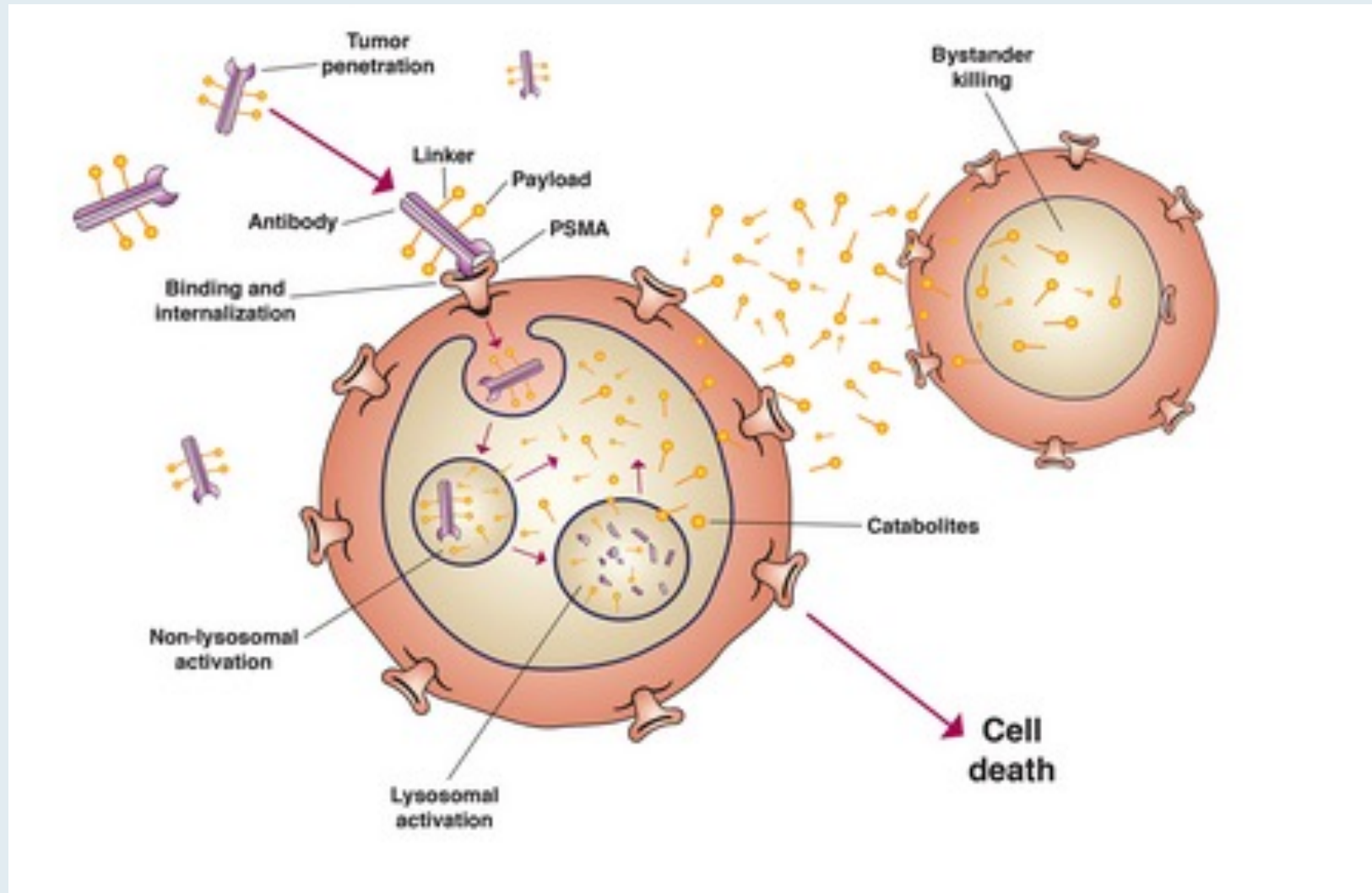
Ther Adv Med Oncol

2021, Vol. 13: 1–14

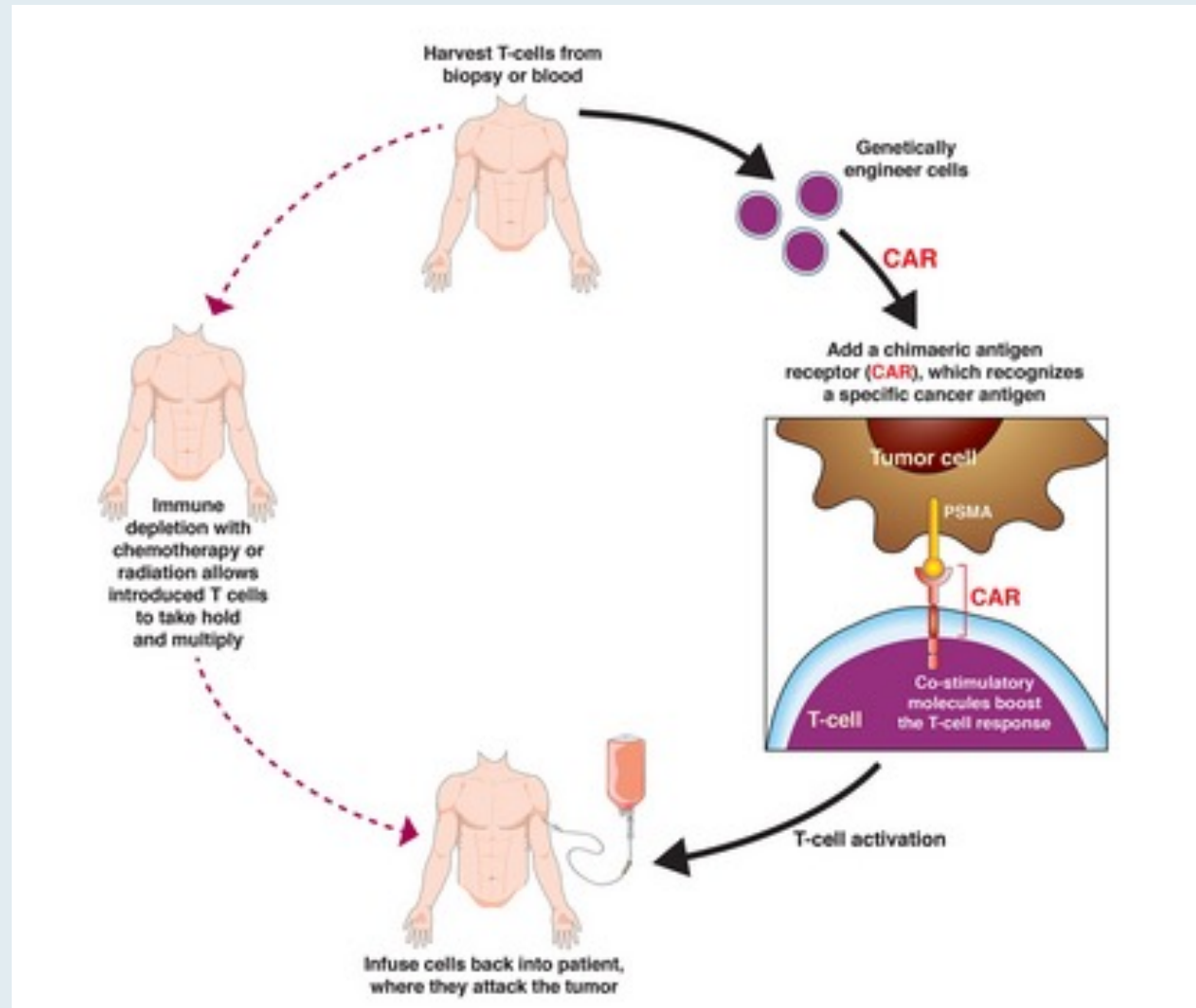
DOI: 10.1177/
17588359211053898

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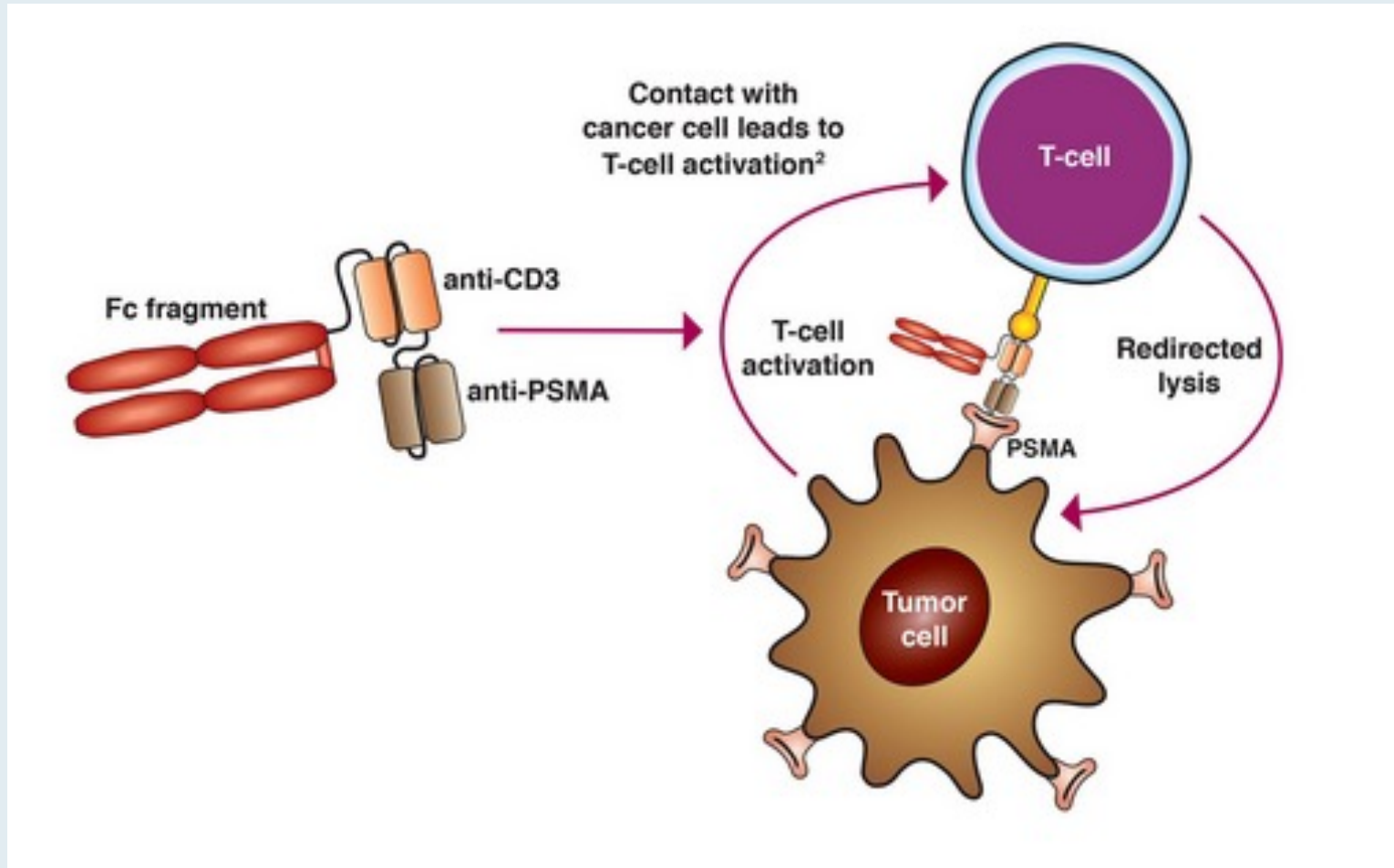
Antibody-Drug Conjugates



PSMA-Targeted CAR T-Cell Therapy



PSMA-Directed Bispecific T-Cell Engager



available at www.sciencedirect.com
journal homepage: www.europeanurology.com



European Association of Urology



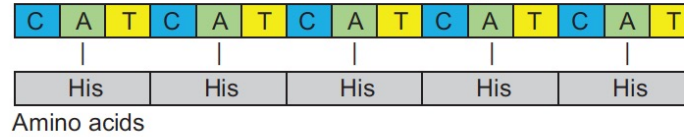
Review – Prostate Cancer

Genomic Testing in Patients with Metastatic Castration-resistant Prostate Cancer: A Pragmatic Guide for Clinicians

Axel S. Merseburger^{a,†,*}, Nick Waldron^{b,†}, Maria J. Ribal^c, Axel Heidenreich^d, Sven Perner^{e,f},
Karim Fizazi^g, Cora N. Sternberg^h, Joaquin Mateoⁱ, Manfred P. Wirth^j, Elena Castro^{k,l},
David Olmos^{k,l}, Daniel P. Petrylak^m, Simon Chowdhury^{b,n}

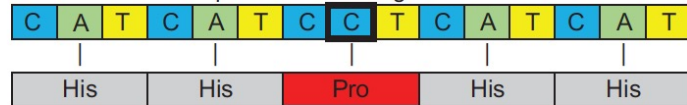
Overview of Common Gene Mutations

Original DNA code for an amino acid sequence



Missense mutation

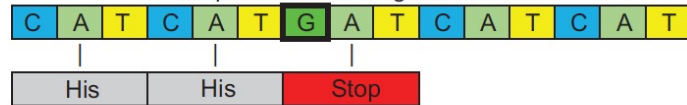
Replacement of single nucleotide



Incorrect amino acid inserted into protein

Nonsense mutation

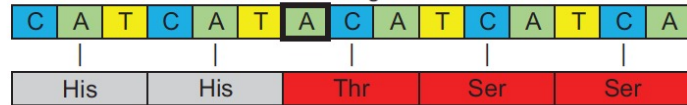
Replacement of single nucleotide



Incorrect sequence causes shortening of protein

Insertion mutation

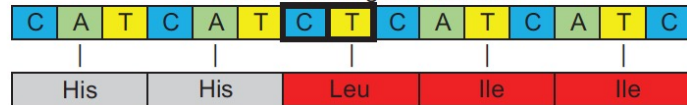
Insertion of single nucleotide



Incorrect amino acid sequence

Deletion mutation

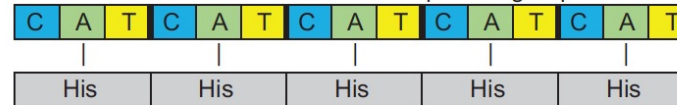
Deletion of single nucleotide



Incorrect amino acid sequence

Frameshift mutation

Normal DNA code for amino acid sequence: groups of three



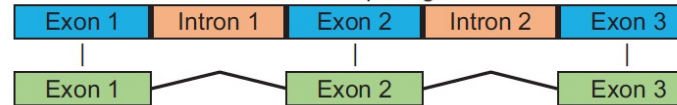
Grouping is shifted along: disrupts order of coding



Incorrect amino acid sequence

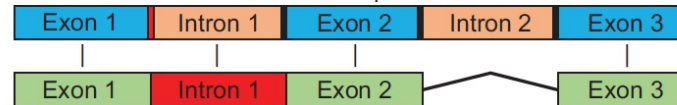
Splice site mutation

Normal splicing



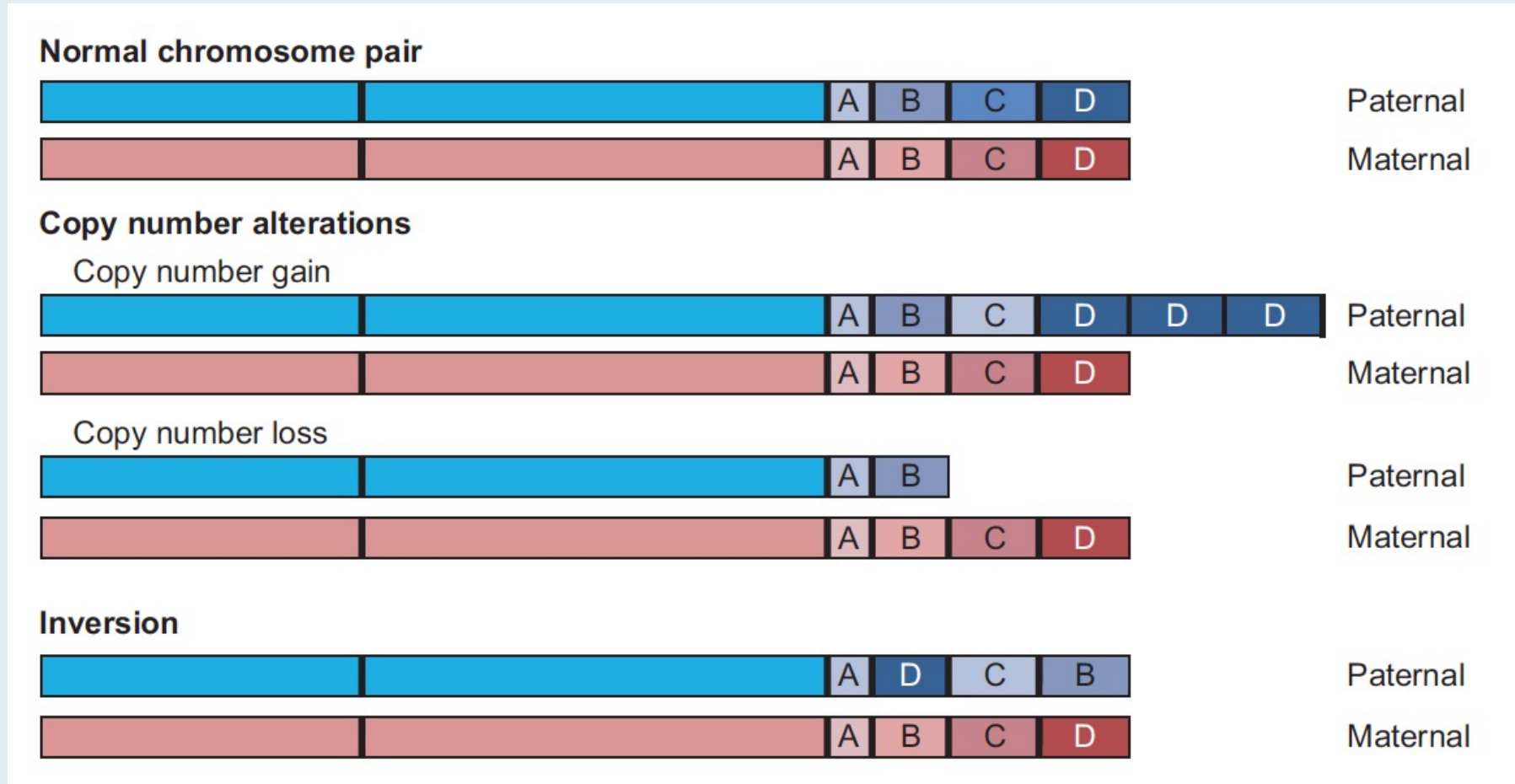
Normal derived mRNA

Mutation in splice site



Mutated mRNA (intron retained)

Overview of Common Large-Scale Alterations



Journal Club with Prof Fizazi – Part 1 (Continued)

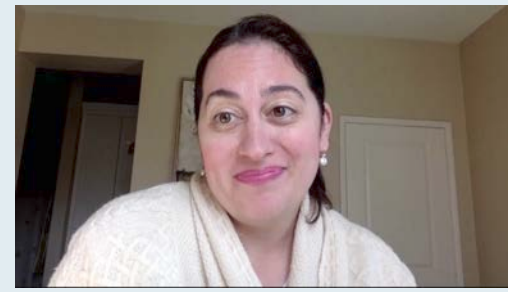
- Tukachinsky H et al. **Genomic analysis of circulating tumor DNA in 3,334 patients with advanced prostate cancer identifies targetable BRCA alterations and AR resistance mechanisms.** *Clin Cancer Res* 2021;27(11):3094-105.
- Petrylak DP et al. **KEYNOTE-921: Phase III study of pembrolizumab plus docetaxel for metastatic castration-resistant prostate cancer.** *Future Oncol* 2021;17(25):3291-9.

Meet The Professor with Prof Fizazi

MODULE 2: Case Presentations and Second Opinion

- Dr Mar: A 68-year-old man with metastatic hormone-sensitive prostate cancer
- Comments on the PEACE-1 Trial by Dr Sartor
- Dr Gosain: A 64-year-old man with mCRPC and a somatic BRCA2 mutation
- *Second Opinion* by Prof Chowdhury: A 67-year-old man with mCRPC and a germline BRCA2 mutation (Dr Lamar)
- Dr Sartor: A 75-year-old man with mCRPC and biallelic BRCA mutations
- Dr Sartor: A 65-year-old man with metastatic small cell prostate cancer
- Comments on the TheraP Trial by Dr Sartor

Case Presentation – Dr Mar: A 68-year-old man with metastatic hormone-sensitive prostate cancer



Dr Nataliya Mar

- Gleason 4 + 3 = 7 prostate cancer with PSA 9.5 ng/mL, s/p radical prostatectomy
- Post-operative PSA undetectable → 0.03 within 6 months → 0.05 → 0.08 ng/mL
- Restaging imaging: No evidence of metastatic disease
- Patient declined salvage RT and/or ADT
- PSA: 3.2 ng/mL within 18 months
- Restaging imaging: Two pulmonary nodules (largest, 1.4 cm), biopsy-proven prostate adenocarcinoma

Questions

- What treatment would you recommend?
- Would you recommend a second-generation antiandrogen, such as abiraterone, enzalutamide or apalutamide?

Comments on the PEACE-1 Trial



Dr A Oliver Sartor



A phase 3 trial with a 2x2 factorial design in men with *de novo* metastatic castration-sensitive prostate cancer (mCSPC): Overall survival with abiraterone acetate plus prednisone in PEACE-1

Karim Fizazi, Joan Carles, 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, Igor Latorzeff, Isabelle Rieger, Alberto Bossi

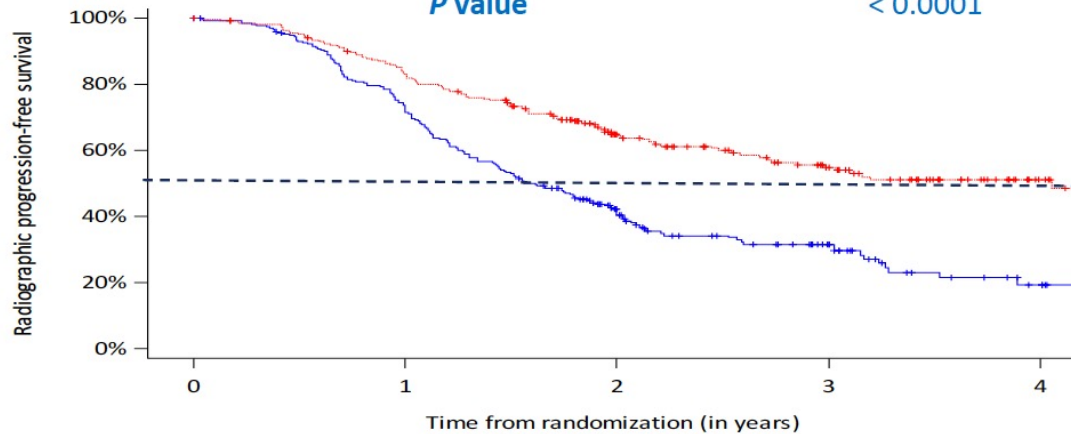
PEACE-1: Radiographic PFS (rPFS) by Metastatic Burden

« High Volume »

SOC+Abi
(n = 225)

SOC
(n = 231)

Median, y (95% CI) 4.1 (2.7-NE) 1.6 (1.4-2.0)
 Events 97 156
 HR (95% CI)* 0.47 (0.36-0.60)
 P value < 0.0001



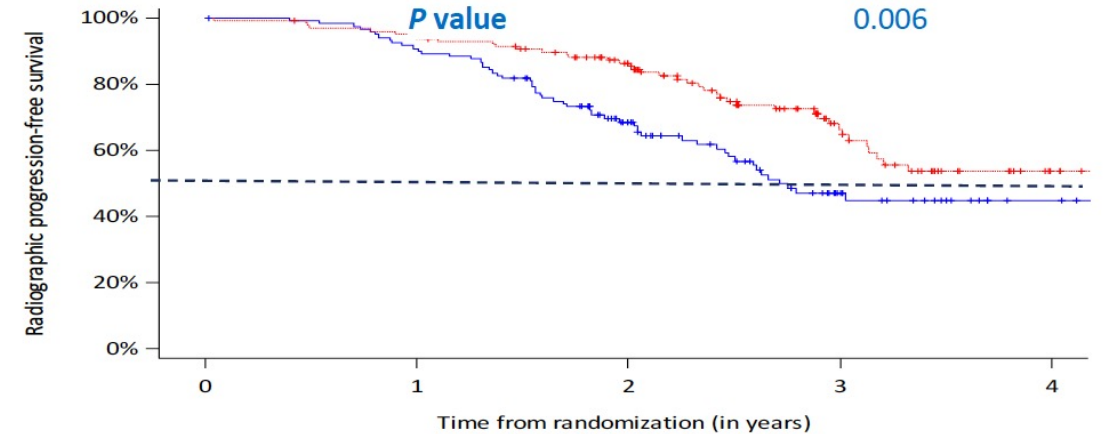
	No	Yes
No	231	162
Yes	225	182

« Low Volume »

SOC+Abi
(n = 129)

SOC
(n = 122)

Median, y (95% CI) NE (3.1-NE) 2.7 (2.5-NE)
 Events 41 55
 HR (95% CI)* 0.58 (0.39-0.87)
 P value 0.006



	No	Yes
No	122	110
Yes	129	120

*Adjusted on stratification parameters (RXT, PS, type of castration, metastatic burden)

PEACE-1: Grade 3-5 Adverse Events (ADT + Docetaxel Safety Population)

Toxicity, n (%)	SOC (+/- RXT) + Abiraterone (n=346)	SOC (+/- RXT) (n=350)
Neutropenia	34 (10)	32 (9)
Febrile neutropenia	18 (5)	19 (5)
Liver	20 (6)	2 (1)
Hypertension	76 (22)	45 (13)
Hypokalemia	11 (3)	1 (0)
Cardiac	6 (2)	5 (1)
Fatigue	10 (3)	15 (4)
Gastro-intestinal	14 (4)	18 (5)
Grade 5	7 (2)	3 (1)

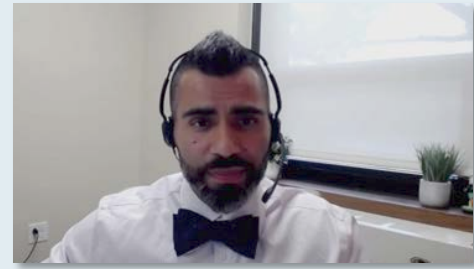
Dr Moon: 2 patients with prostate cancer who received a PARP inhibitor



Dr Helen Moon

- Prostate cancer is one of the solid cancers that right out of the gate we try to subtype – Is it BRCA1 or BRCA2?
- Are they treated differently?
- What about ATM? PTEN?
- Will prostate cancer ever become a disease where precision medicine is the norm?

Case Presentation – Dr Gosain: A 64-year-old man with mCRPC and a somatic BRCA2 mutation



Dr Rohit Gosain

- 2018: Undergoing monitoring for a biochemical recurrence 3 years s/p prostatectomy for Gleason 4 + 4 prostate cancer
- 2019: Leuprolide + abiraterone + prednisone initiated due to PSADT <10 months
- Repeated disease progression noted in the bone, lymph nodes and liver in response to treatment with enzalutamide, docetaxel and cabazitaxel
- NGS testing: Somatic BRCA2 mutation
- Olaparib, with anemia → Dose reduced from 300 mg BID to 200 mg BID to 100 mg BID

Questions

- What is the responsiveness to PARP inhibitors in terms of germline versus somatic mutations? Are PARP inhibitors more responsive to certain mutations?
- What is your approach to dose-reducing PARP inhibitors for patients experiencing anemia? Would you use an alternate schedule instead of dose-reducing?

Second Opinion by Prof Chowdhury: A 67-year-old man with mCRPC and a germline BRCA2 mutation (Dr Lamar)

- Sister died of ovarian cancer; patient and 4 offspring test positive for BRCA2 mutation
- 2005: Prostate cancer s/p prostatectomy, leuprolide/bicalutamide
- 2018: Abiraterone/prednisone
- 2019: Bone metastases
- Olaparib x 9 months → PSA increase
 - Depression
 - Severe fatigue addressed via dose adjustments



Dr Zanetta Lamar



**Prof Simon
Chowdhury**

Case Presentation – Dr Sartor: A 75-year-old man with mCRPC and biallelic BRCA mutations

- Hormone-sensitive metastatic prostate cancer
- Germline BRCA2 mutation and second-hit BRCA mutation (biallelic)
- ADT/abiraterone
- Develops high-volume, symptomatic bone metastases
- Olaparib, alternating between 300 mg BID and QD



Dr Oliver Sartor

Case Presentation – Dr Sartor: A 65-year-old man with metastatic neuroendocrine prostate cancer

- Presents with high-volume, de novo metastatic prostate cancer, PSA 650 ng/mL
- Somatic BRCA2 mutation
- ADT/abiraterone → Recurs with urinary issues
- Biopsy: Small cell recurrence in the neck of the bladder, PSA 0.5 ng/mL
- Carboplatin/VP-16 + atezolizumab



Dr Oliver Sartor

VISION trial of ^{177}Lu -PSMA-617 for mCRPC

- Expected FDA approval of Lutetium-177-PSMA-617 in 2022
- Large magnitude of benefit in the Phase III VISION trial in mCRPC
- Is 6 cycles necessary, or is 3-4 cycles sufficient?
- PSMA expression in salivary and lacrimal glands and the possibility of ^{177}Lu -PSMA-617-associated xerostomia

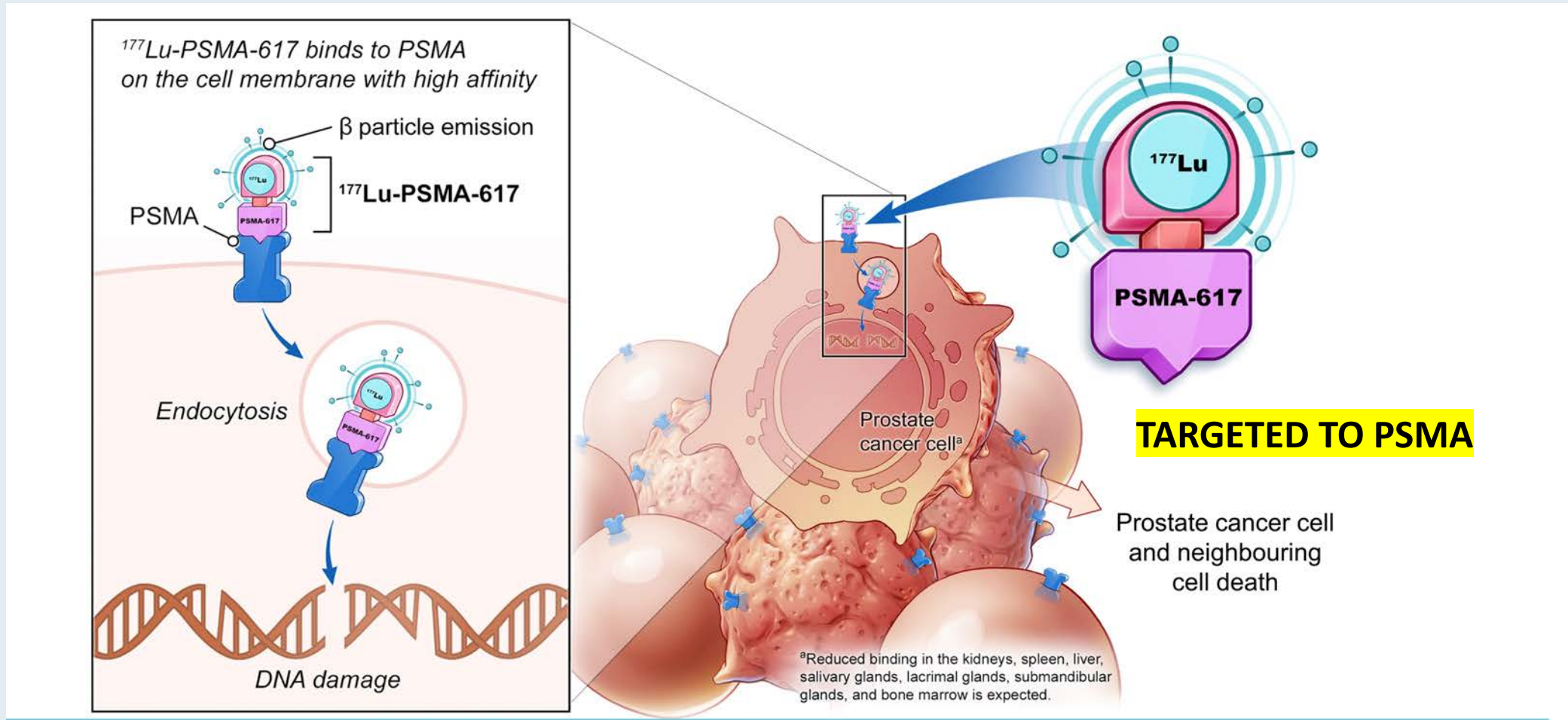


Dr Oliver Sartor



**Prof Simon
Chowdhury**

^{177}Lu -PSMA-617: Mechanism of Action



N Engl J Med 2021;385:1091-103

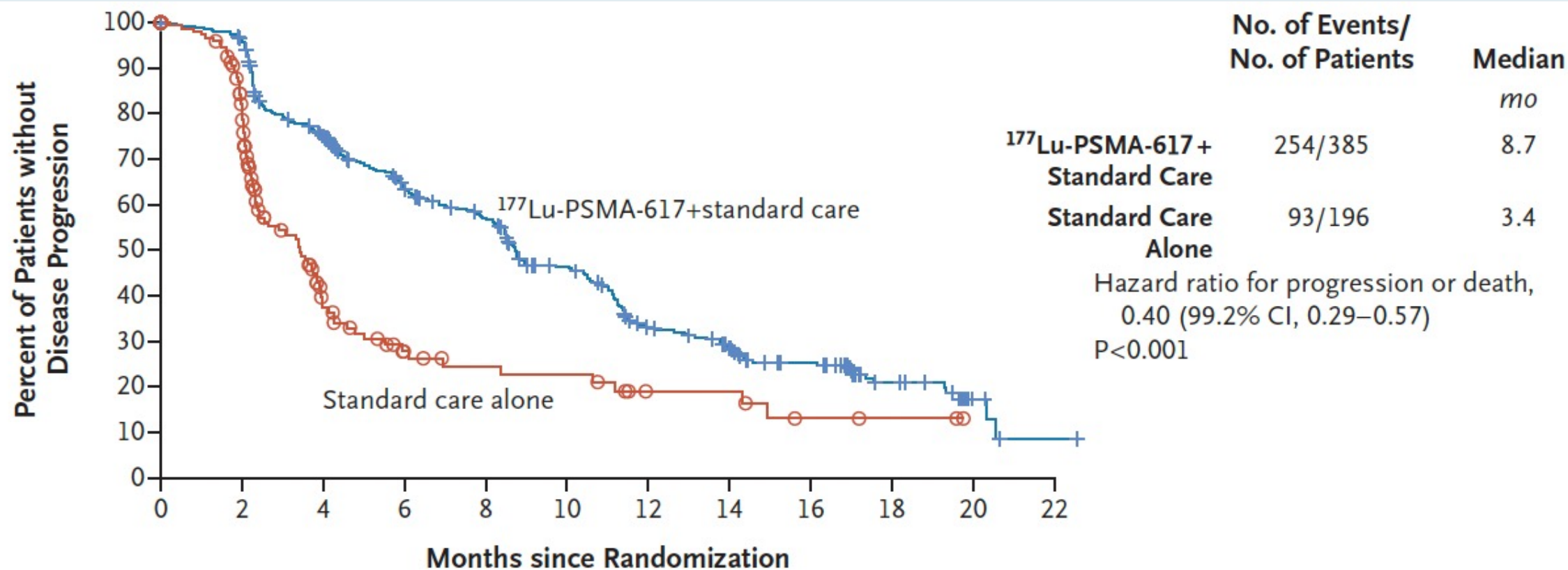
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

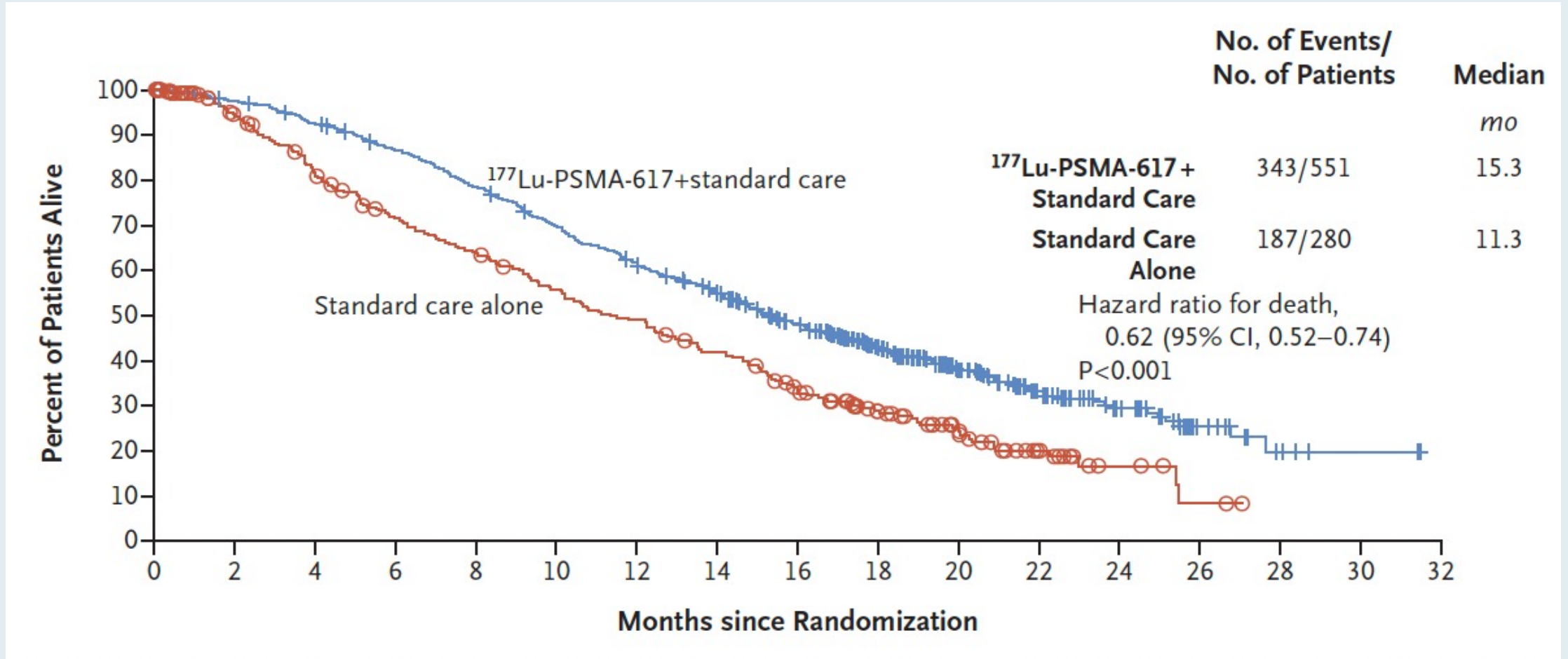
Lutetium-177–PSMA-617 for Metastatic Castration-Resistant Prostate Cancer

O. Sartor, 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, A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION Investigators*

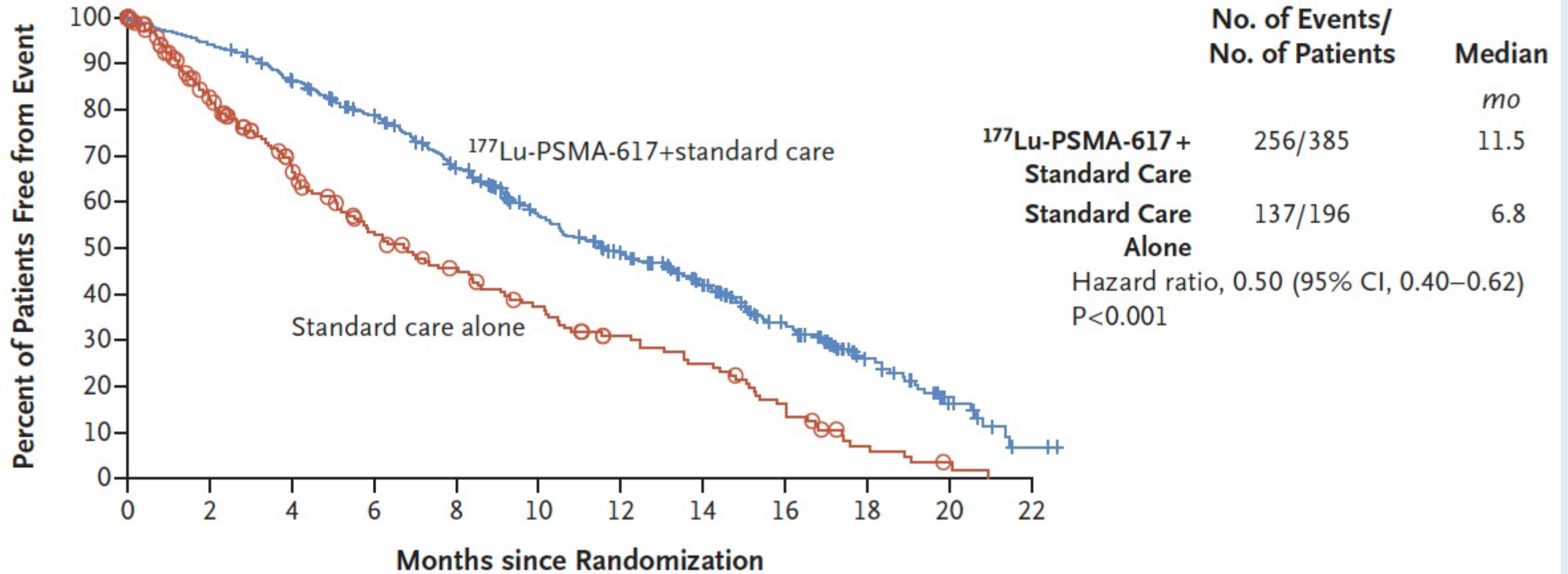
VISION: Imaging-Based Progression-Free Survival



VISION: Overall Survival



VISION: Time to First Symptomatic Skeletal Event



VISION: Selected Adverse Events

Event	¹⁷⁷ Lu-PSMA-617 plus Standard Care (N = 529)		Standard Care Alone (N = 205)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
	<i>number of patients (percent)</i>			
Any adverse event	519 (98.1)	279 (52.7)	170 (82.9)	78 (38.0)
Fatigue	228 (43.1)	31 (5.9)	47 (22.9)	3 (1.5)
Thrombocytopenia	91 (17.2)	42 (7.9)	9 (4.4)	2 (1.0)
Lymphopenia	75 (14.2)	41 (7.8)	8 (3.9)	1 (0.5)
Leukopenia	66 (12.5)	13 (2.5)	4 (2.0)	1 (0.5)
Adverse event that led to reduction in ¹⁷⁷ Lu-PSMA-617 dose	30 (5.7)	10 (1.9)	NA	NA
Adverse event that led to interruption of ¹⁷⁷ Lu-PSMA-617†	85 (16.1)	42 (7.9)	NA	NA
Adverse event that led to discontinuation of ¹⁷⁷ Lu-PSMA-617†	63 (11.9)	37 (7.0)	NA	NA
Adverse event that led to death‡	19 (3.6)	19 (3.6)	6 (2.9)	6 (2.9)

177Lu-PSMA-617 (LuPSMA) versus Cabazitaxel in Metastatic Castration-Resistant Prostate Cancer (mCRPC) Progressing After Docetaxel: Updated Results Including Progression-Free Survival (PFS) and Patient-Reported Outcomes (PROs) (TheraP ANZUP 1603)¹

[¹⁷⁷Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial²

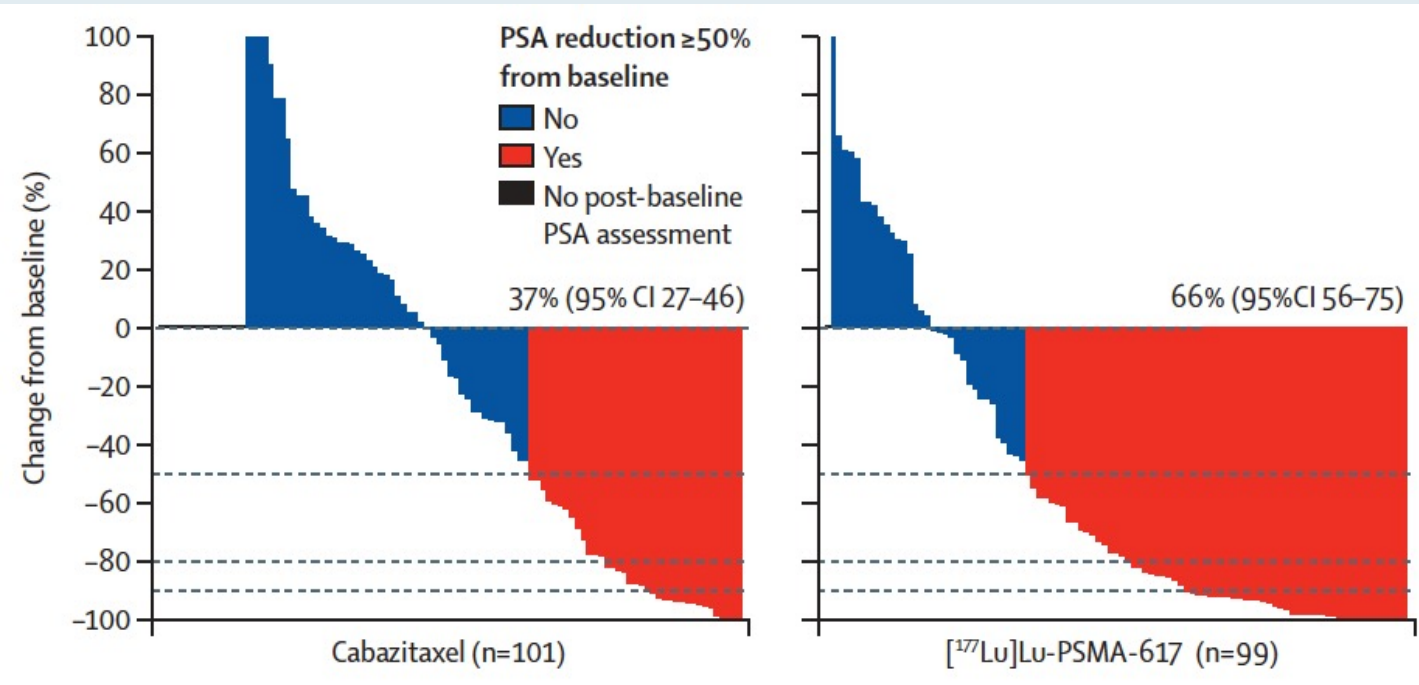
Michael S Hofman, Louise Emmett, Shahneen Sandhu, Amir Iravani, Anthony M Joshua, Jeffrey C Goh, David A Pattison, Thean Hsiang Tan, Ian D Kirkwood, Siobhan Ng, Roslyn J Francis, Craig Gedye, Natalie K Rutherford, Andrew Weickhardt, Andrew M Scott, Sze-Ting Lee, Edmond M Kwan, Arun A Azad, Shakher Ramdave, 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†*

¹ Hofman MS et al. Genitourinary Cancers Symposium 2021;Abstract 6.

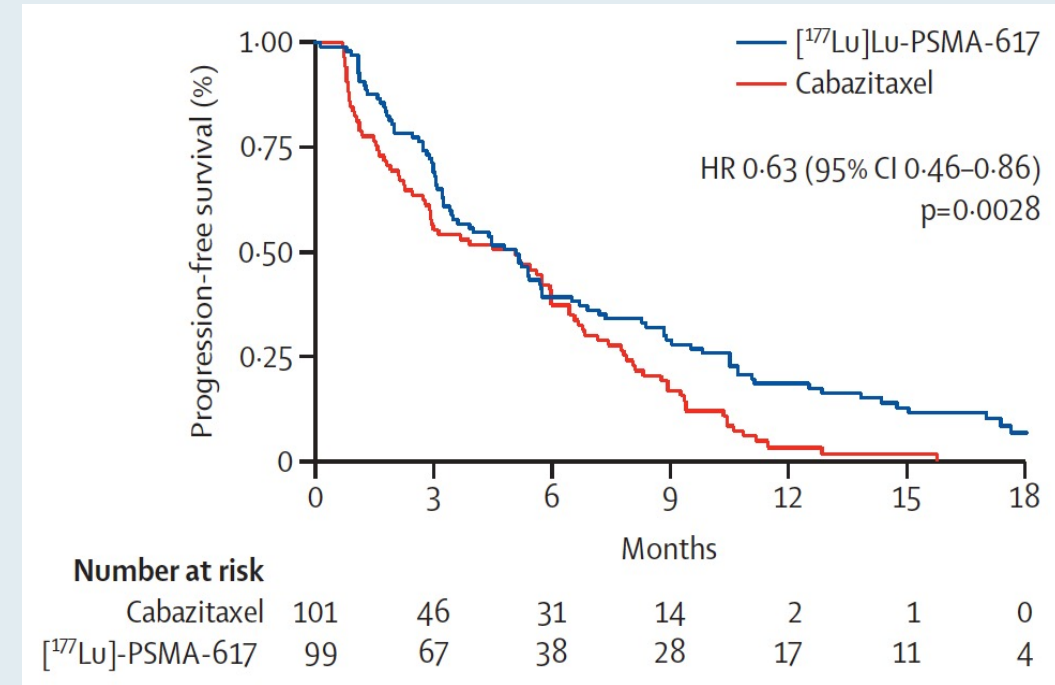
² Hofman MS et al. *Lancet* 2021;397(10276):797-804.

TheraP ANZUP 1603: PSA Response and PFS

PSA response



Radiographic or PSA progression-free survival



TheraP ANZUP 1603: Adverse Events

	^[177Lu] Lu-PSMA-617 (n=98)		Cabazitaxel (n=85)	
	Grade 1-2	Grade 3-4	Grade 1-2	Grade 3-4
Fatigue	69 (70%)	5 (5%)	61 (72%)	3 (4%)
Pain*	60 (61%)	11 (11%)	52 (61%)	4 (5%)
Dry mouth	59 (60%)	0	18 (21%)	0
Diarrhoea	18 (18%)	1 (1%)	44 (52%)	4 (5%)
Nausea	39 (40%)	1 (1%)	29 (34%)	0
Thrombocytopenia	18 (18%)	11 (11%)	4 (5%)	0
Dry eyes	29 (30%)	0	3 (4%)	0
Anaemia	19 (19%)	8 (8%)	11 (13%)	7 (8%)
Neuropathy†	10 (10%)	0	22 (26%)	1 (1%)
Dysgeusia	12 (12%)	0	23 (27%)	0
Haematuria	3 (3%)	1 (1%)	12 (14%)	5 (6%)
Neutropenia‡	7 (7%)	4 (4%)	4 (5%)	11 (13%)
Insomnia	9 (9%)	0	12 (14%)	1 (1%)
Vomiting	12 (12%)	1 (1%)	10 (12%)	2 (2%)
Dizziness	4 (4%)	0	11 (13%)	0
Leukopenia	10 (10%)	1 (1%)	5 (6%)	1 (1%)
Any adverse event	53 (54%)	32 (33%)	34 (40%)	45 (53%)

Comments on the TheraP Trial



Dr Oliver Sartor

Meet The Professor with Prof Fizazi

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MODULE 6: Appendix

A 65-year-old man with BRCA wild-type, MSS prostate cancer metastatic to the bone who is receiving abiraterone/dexamethasone for hormone-sensitive metastatic disease develops new low-volume asymptomatic bone metastases. Which systemic treatment would you most likely recommend?



Dr Armstrong

Sipuleucel-T



Dr Bryce

Docetaxel



Prof Chowdhury

Docetaxel



Prof Fizazi

Docetaxel



Dr Morgans

Sipuleucel-T



Dr Sartor

Docetaxel

A 65-year-old man with MSS prostate cancer metastatic to the bone and a germline BRCA2 mutation who is receiving abiraterone/dexamethasone for hormone-sensitive metastatic disease develops new low-volume asymptomatic bone metastases. Which systemic treatment would you most likely recommend?



Dr Armstrong

Sipuleucel-T followed by olaparib or docetaxel at further progression



Prof Fizazi

Olaparib



Dr Bryce

Olaparib



Dr Morgans

Olaparib



Prof Chowdhury

Olaparib



Dr Sartor

Olaparib

A 65-year-old man with BRCA wild-type, MSS prostate cancer metastatic to the bone who is receiving abiraterone/dexamethasone for hormone-sensitive metastatic disease develops new high-volume symptomatic bone metastases. Which systemic treatment would you most likely recommend?



Dr Armstrong

Docetaxel



Prof Fizazi

Docetaxel



Dr Bryce

Docetaxel



Dr Morgans

Radium-223



Prof Chowdhury

Docetaxel



Dr Sartor

Docetaxel

A 65-year-old man with MSS prostate cancer metastatic to the bone and a germline BRCA2 mutation who is receiving abiraterone/dexamethasone for hormone-sensitive metastatic disease develops new high-volume symptomatic bone metastases. Which systemic treatment would you most likely recommend?



Dr Armstrong

Olaparib



Prof Fizazi

Olaparib



Dr Bryce

Olaparib



Dr Morgans

Radium-223



Prof Chowdhury







Olaparib



Dr Sartor

Olaparib

Which of the following genomic evaluations do you generally order for patients with mCRPC and no specific family history of cancer?

 Dr Armstrong	Germline and somatic panel	 Prof Fizazi	Germline and somatic panel
 Dr Bryce	Germline and somatic panel	 Dr Morgans	BRCA germline and somatic
 Prof Chowdhury	Somatic panel	 Dr Sartor	Germline and somatic panel

At what point, if any, do you generally recommend a PARP inhibitor to a patient with metastatic prostate cancer and a germline BRCA mutation?



Dr Armstrong

After at least 1 line of both hormonal therapy and chemotherapy



Prof Fizazi

After 1 line of hormonal therapy



Dr Bryce

After 1 line of hormonal therapy



Dr Morgans

After 1 line of hormonal therapy



Prof Chowdhury

After 1 line of hormonal therapy



Dr Sartor

After 1 line of hormonal therapy

For a patient with metastatic prostate cancer and a germline BRCA mutation to whom you would administer a PARP inhibitor, which treatment strategy would you likely use?



Dr Armstrong

Olaparib monotherapy



Prof Fizazi

Olaparib monotherapy



Dr Bryce

Olaparib or rucaparib monotherapy



Dr Morgans

Olaparib monotherapy



Prof Chowdhury

Olaparib monotherapy



Dr Sartor

Olaparib monotherapy

Regulatory and reimbursement issues aside, in which line of therapy would you administer 177Lu-PSMA-617 for patients with metastatic prostate cancer?



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Immune Checkpoint Inhibitors in mCRPC

Therapy	Disease State	Disease Response
Pembrolizumab monotherapy ^a	Post-chemotherapy	ORR 9% PSA RR 14%
Pembrolizumab + enzalutamide ^b	Pre-chemotherapy progressing on enzalutamide	ORR 12% PSA RR 14%
Atezolizumab + enzalutamide ^c	Pre- and post-chemotherapy, s/p abiraterone	ORR 14% PSA RR 26%
Atezolizumab + cabozantinib ^d	Pre-chemotherapy s/p enzalutamide or abiraterone	ORR 34% PSA RR 29%

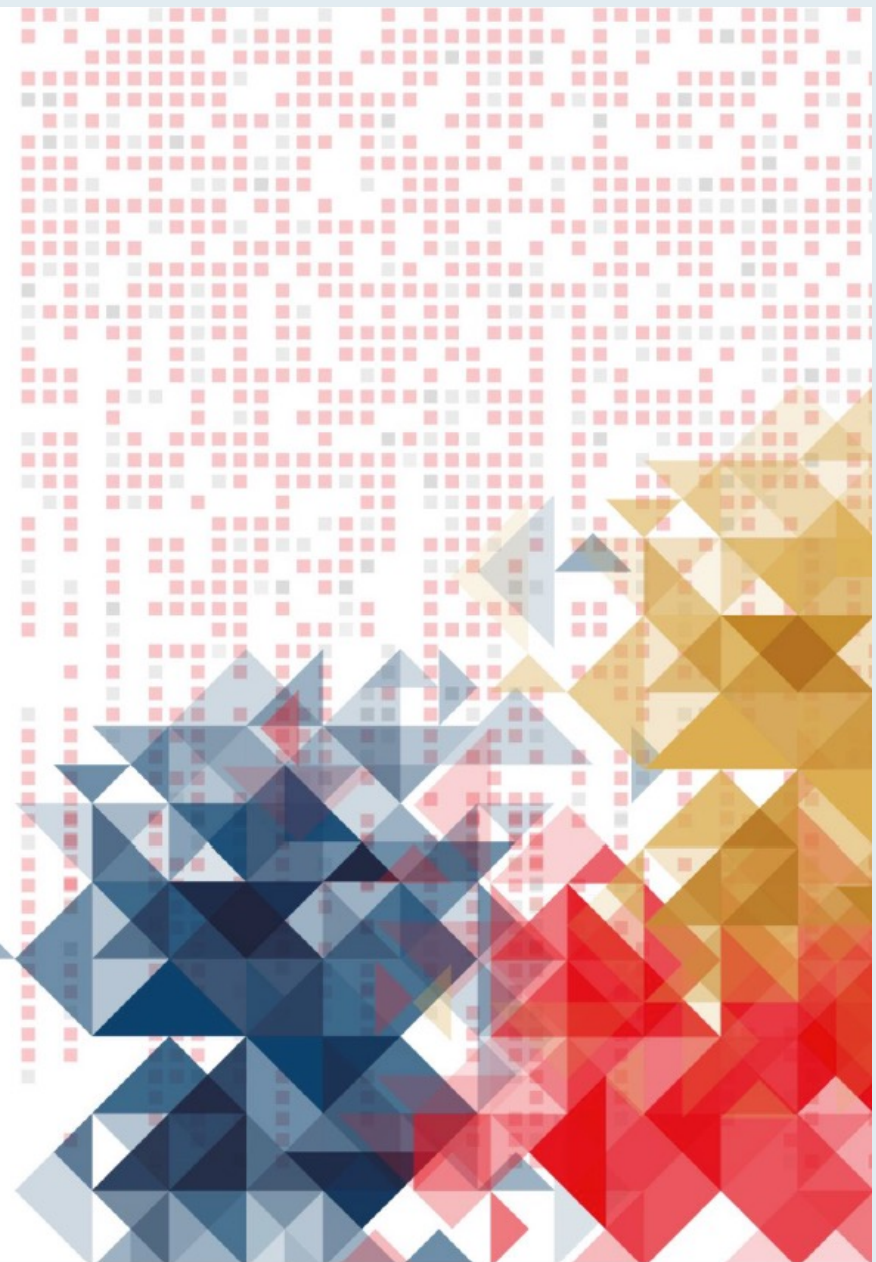
^aJCO 2020: 38(5) 395-405. ^bPresented at the 2021 ASCO Annual Meeting – Virtual; June 4-8, 2021. ^cSweeney C. AACR 2020. IMbassador250. ^dAgarwal ASCO 2020. COSMIC-021

Cabozantinib in combination with atezolizumab in patients with metastatic castration-resistant prostate cancer (mCRPC): results of expanded cohort 6 of the COSMIC-021 Study

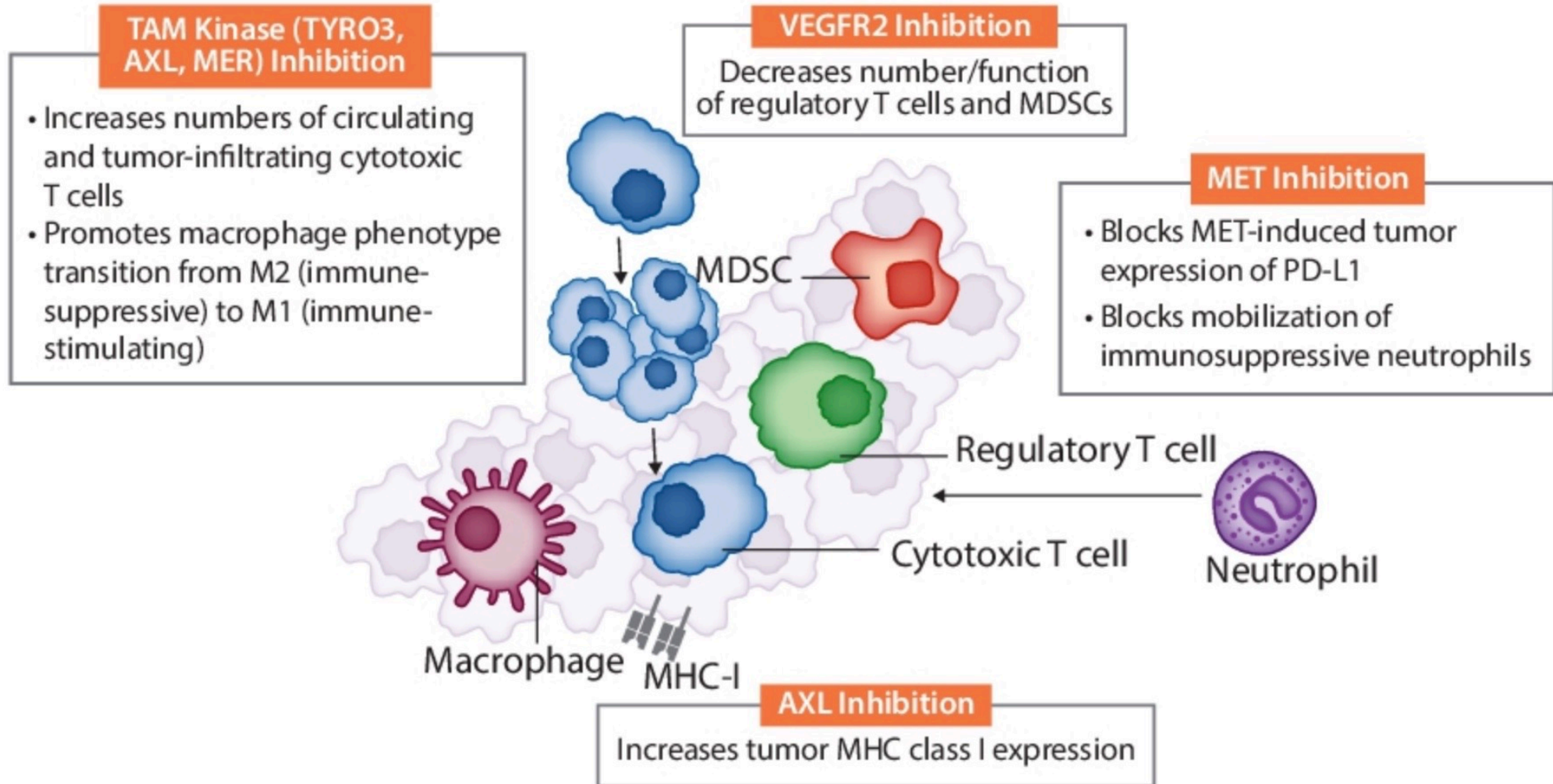
Neeraj Agarwal,¹ Bradley McGregor,² Benjamin L. Maughan,¹ Tanya B. Dorff,³ William Kelly,⁴ Bruno Fang,⁵ Rana R. McKay,⁶ Parminder Singh,⁷ Lance Pagliaro,⁸ Robert Dreicer,⁹ Sandy Srinivas,¹⁰ Yohann Loriot,¹¹ Ulka Vaishampayan,¹² Sanjay Goel,¹³ Dominic Curran,¹⁴ Ashok Panneerselvam,¹⁴ Li-Fen Liu,¹⁴ Toni K. Choueiri,^{2*} Sumanta Pal^{3*}

¹Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA; ²Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA; ³City of Hope Comprehensive Cancer Center, Duarte, CA, USA; ⁴Sidney Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA, USA; ⁵Regional Cancer Care Associates, East Brunswick, NJ, USA; ⁶University of California San Diego, San Diego, CA, USA; ⁷Department of Oncology, Mayo Clinic, Scottsdale, AZ, USA; ⁸Department of Oncology, Mayo Clinic, Rochester, MN, USA; ⁹University of Virginia Cancer Center, Charlottesville, VA, USA; ¹⁰Division of Medical Oncology, Stanford University Medical Center, Stanford, CA, USA; ¹¹Department of Cancer Medicine, Gustave Roussy Institute, INSERM 981, University Paris-Saclay, Villejuif, France; ¹²Karmanos Cancer Center, Wayne State University, Detroit, MI, USA (Current affiliation: Division of Hematology/Oncology, University of Michigan, Ann Arbor, MI, USA); ¹³Department of Medical Oncology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA; ¹⁴Exelixis, Inc., Alameda, CA, USA

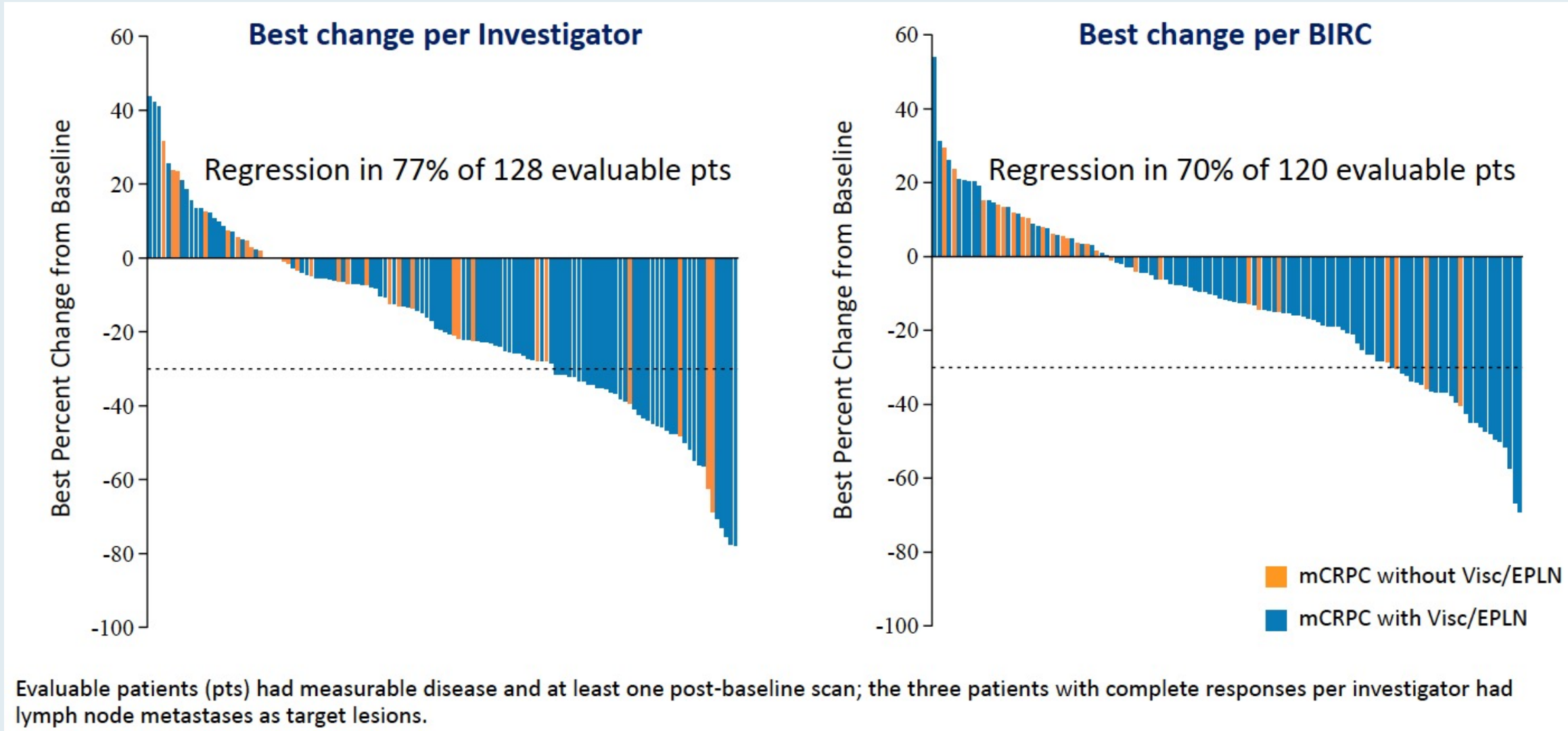
*Co-senior authors



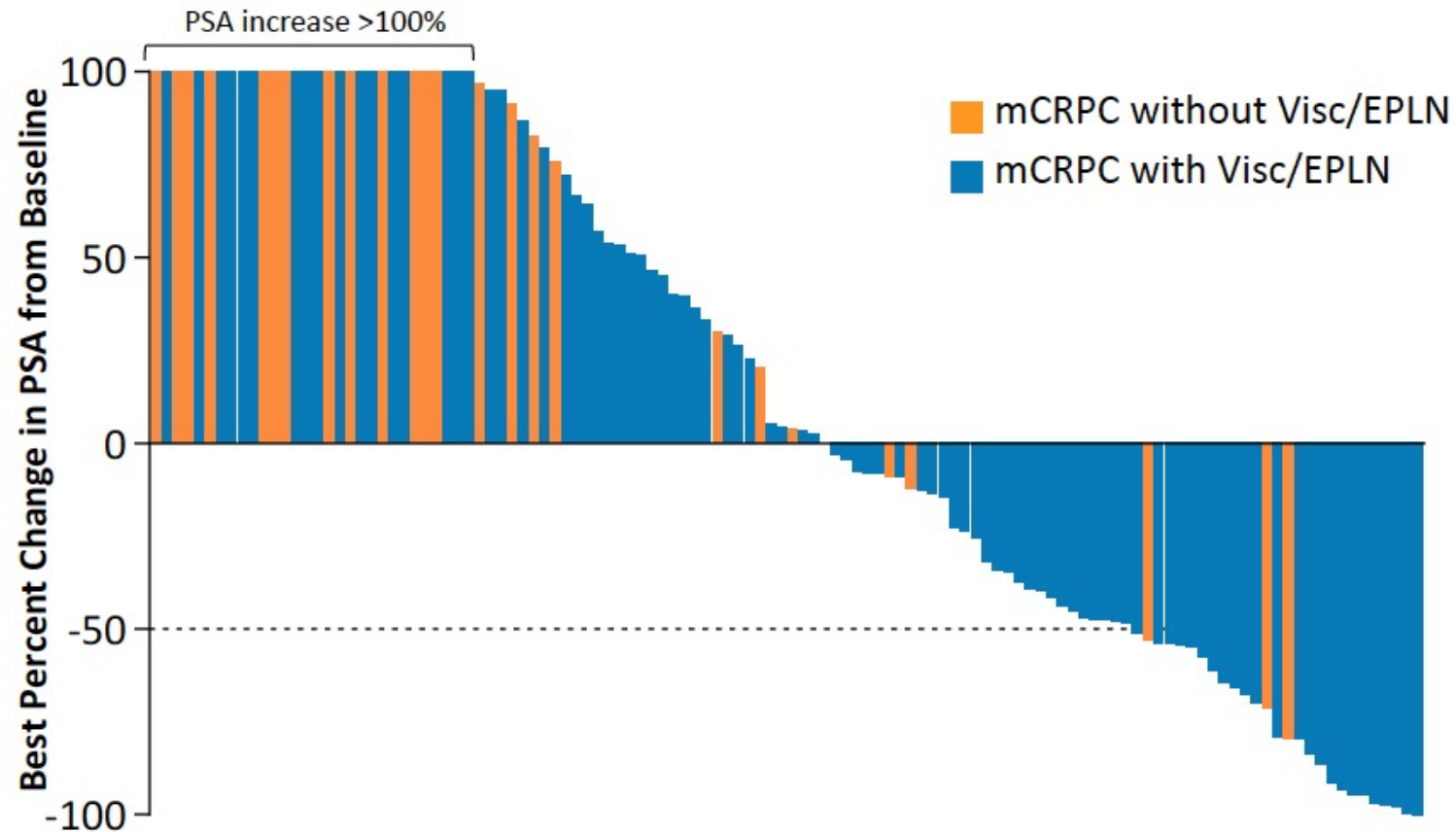
Cabozantinib Targets Pathways Associated with Tumor Immune Suppression



COSMIC-021: Best Change from Baseline in Sum of Target Lesions



COSMIC-021: Best Change in PSA from Baseline

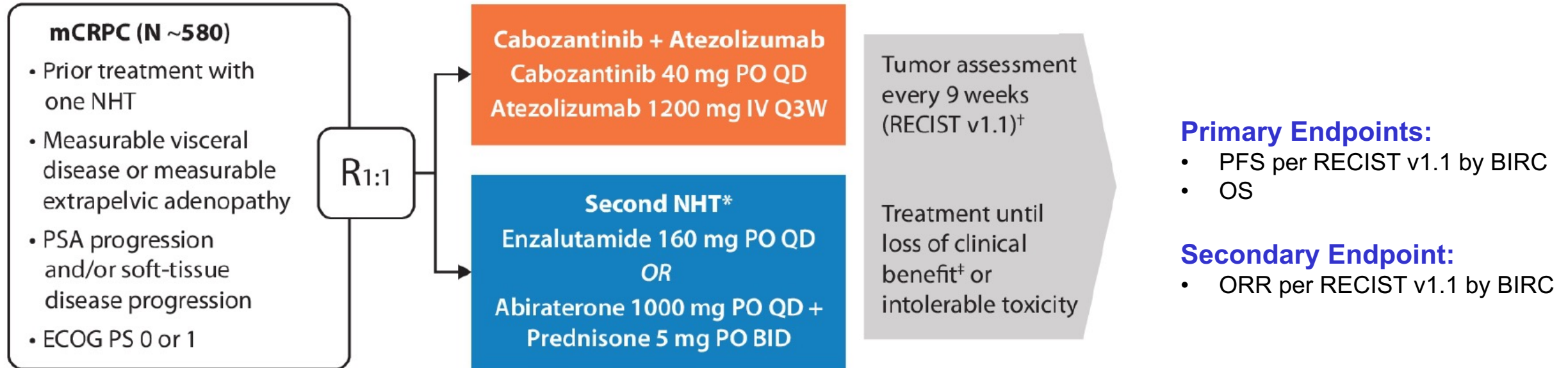


- In 118 patients with post-baseline assessments, 55 (47%) had a decrease in PSA, and 27 (23%) had a decrease $\geq 50\%$
- In 92 patients with Visc/EPLN, 50 (54%) had a decrease in PSA, and 24 (26%) had a decrease $\geq 50\%$

COSMIC-021: Select Treatment-Related Adverse Events

	mCRPC (N=132)	
	Any Grade	Grade 3/4
Any AE, %	95	55
Diarrhea	55	6.8
Fatigue	43	6.8
Nausea	42	0.8
Decreased appetite	34	1.5
Dysgeusia	27	0
Palmar-plantar erythrodysesthesia	25	2.3
Vomiting	23	1.5
Weight decreased	23	1.5
Aspartate aminotransferase increased	20	3.0
Stomatitis	16	0.8
Hypertension	14	6.8
Alanine aminotransferase increased	14	3
Dysphonia	13	0
Hypothyroidism	12	0
Pulmonary embolism	11	8.3

CONTACT-02: Phase III Trial Schema



Stratification

- Liver metastasis (yes, no)
- Prior docetaxel treatment for mCSPC (yes, no)
- Disease stage for which the first NHT was given (mCSPC, M0 CRPC, mCRPC)

*Second NHT must differ from previous NHT taken

[†]Tumor assessment (RECIST v1.1) every 9 weeks for the first 28 weeks then every 12 weeks thereafter

[‡]Patients may be treated beyond progression if there is a clinical benefit in the opinion of the investigator

PRINCE: Interim Analysis of the Phase Ib Study of ^{177}Lu -PSMA-617 in Combination with Pembrolizumab for Metastatic Castration Resistant Prostate Cancer (mCRPC)

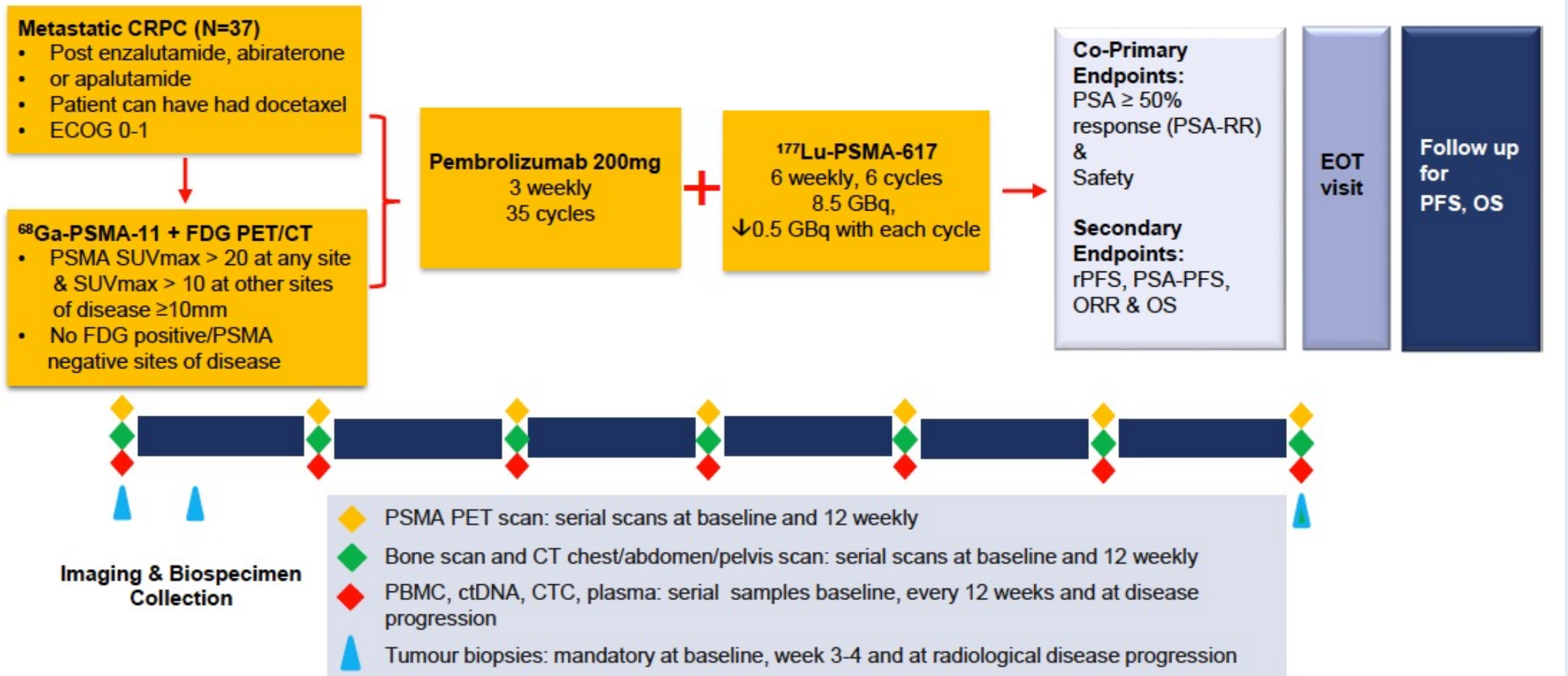
Shahneen Sandhu, Anthony M. Joshua, Louise Emmett, Lavinia Spain, Lisa G. Horvath, Megan Crumbaker, Arsha Anton, Roslyn Wallace, Anupama Pasam, Mathias Bressel, Erin Cassidy, Patricia Banks, Aravind Ravi Kumar, Ramin Alipour, Tim Akhurst, Grace Kong, Ian D. Davis, Scott Williams, Rod Hicks, Michael S. Hofman

Abstract 5770

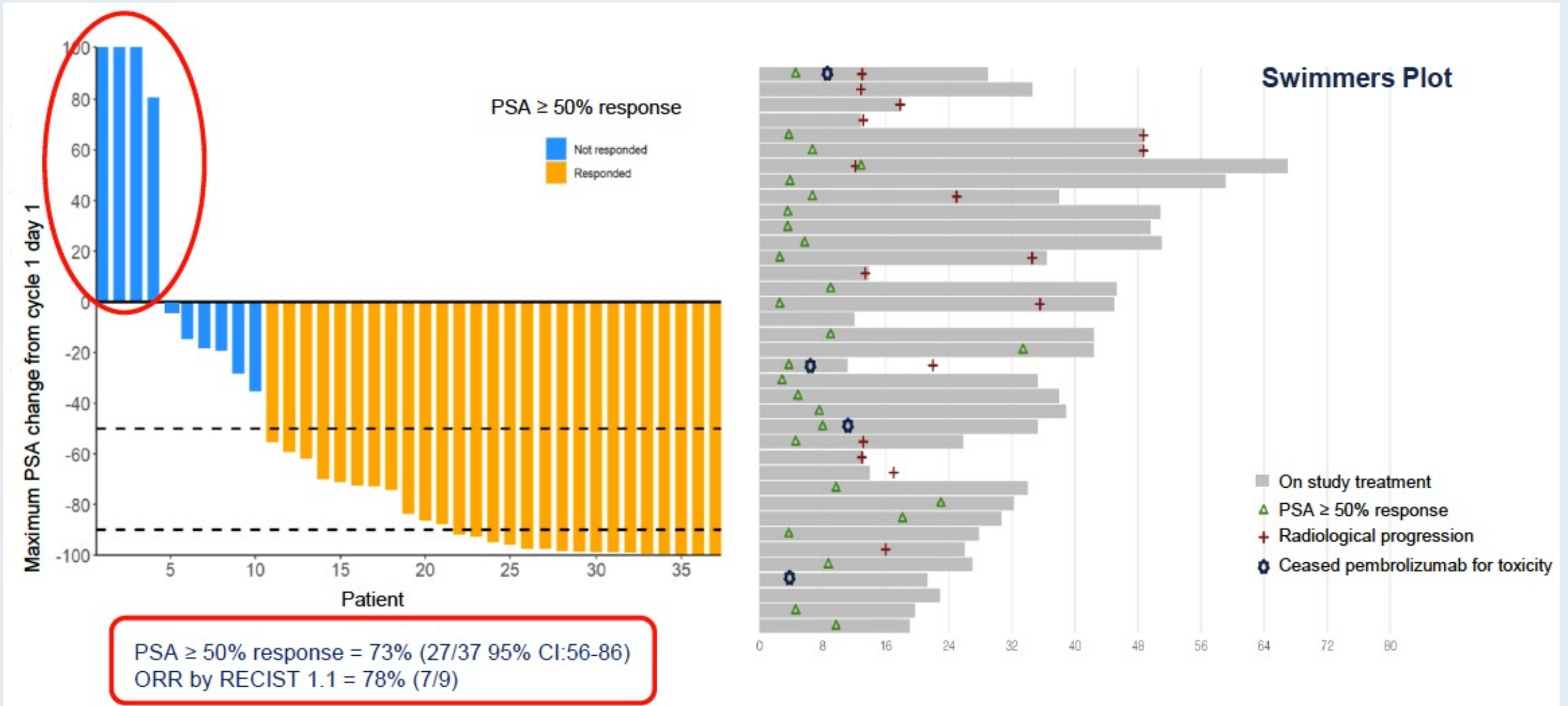


Presented by: Shahneen Sandhu

PSMA-Lutetium Radionuclide Therapy and ImmuNotherapy for Prostate CancEr (PRINCE) Trial Schema



PRINCE: PSA Response Rate (Primary Endpoint)



PRINCE: Treatment-Related Adverse Events

TRAE term	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	N=37 (%)
Xerostomia	21 (57%)	7 (19%)	-	28 (76%)
Fatigue	11 (29 %)	3 (8%)	2 (5%)	16 (43%)
Rash	5 (14%)	4 (11%)	-	9 (25%)
Nausea	8 (21%)	1 (3%)	-	9 (24%)
Pruritis	6 (16%)	1 (3%)	-	7 (19%)
Anorexia	3 (8%)	3 (8%)	-	6 (16%)
Thrombocytopenia	4 (11%)	1(3%)	-	5 (14%)
Bone pain (flare)	4 (11%)	-	-	4 (11%)
Aspartate aminotransferase elevation	2 (5%)	2 (5%)	-	4 (11%)
Dry eye	3 (8%)	-	-	3 (8%)
Dysgeusia	2 (5%)	1 (3%)	-	3 (8%)
Weight loss	2 (5%)	1 (3%)	-	3 (8%)
Anemia	-	2 (5%)	1(3%)	3 (8%)
Alanine aminotransferase elevation	2 (5%)	1(3%)	-	3 (8%)
Amylase elevation	1 (3%)	1 (3%)	1 (3%)	3 (8%)
Arthralgia	3 (8%)	-	-	3 (8%)
Neutropenia	1 (3%)	-	-	1 (3%)

Pembrolizumab cycles: Median (range)	8 (1 - 22)
¹⁷⁷Lu-PSMA-617 cycles: Median (range)	4 (2 - 6)
Discontinuation for toxicity: Pembrolizumab, n (%) ¹⁷⁷ Lu-PSMA-617, n (%)	4 (11%) 0 (0%)

- Treatment related adverse events (TRAEs) in by worst grade affecting > 5% and all hematological toxicity
- There were no grade 4 TRAEs or treatment related deaths

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MODULE 5: Journal Club with Prof Fizazi (Part 2)

MODULE 6: Appendix

Journal Club with Prof Fizazi (Part 2)

- Sternberg CN et al. **Efficacy and safety of cabazitaxel versus abiraterone or enzalutamide in older patients with metastatic castration-resistant prostate cancer in the CARD study.** *Eur Urol* 2021;80(4):497-506.
- Aldea M et al. **Cabazitaxel activity in men with metastatic castration-resistant prostate cancer with and without DNA damage repair defects.** *Eur J Cancer* 2021;159:87-97.
- Baciarello G et al. **Patient preference between cabazitaxel and docetaxel for first-line chemotherapy in metastatic castration-resistant prostate cancer: The CABADOC trial.** *Eur Urol* 2021;[Online ahead of print].
- Fizazi K et al. **Radium-223 (Ra-223) versus novel antihormone therapy (NAH) for progressive metastatic castration-resistant prostate cancer (mCRPC) after 1 line of NAH: RADIANT, an international phase 4, randomized, open-label study.** ASCO 2021;Abstract TPS5093.

Journal Club with Prof Fizazi (Part 2 Continued)

- Agarwal N et al. **TALAPRO-2: A phase 3 randomized study of enzalutamide (ENZA) plus talazoparib (TALA) versus placebo in patients with new metastatic castration-resistant prostate cancer (mCRPC).** ASCO 2021;Abstract TPS5089.
- de Bono JS et al. **Talazoparib monotherapy in metastatic castration-resistant prostate cancer with DNA repair alterations (TALAPRO-1): An open-label, phase 2 trial.** *Lancet Oncol* 2021;22(9):1250-64.
- Loehr A et al. **Response to rucaparib in BRCA-mutant metastatic castration-resistant prostate cancer identified by genomic testing in the TRITON2 study.** *Clin Cancer Res* 2021;27(24):6677-86.

Meet The Professor with Prof Fizazi

Introduction

MODULE 1: Journal Club with Prof Fizazi (Part 1)

MODULE 2: Case Presentations and Second Opinion

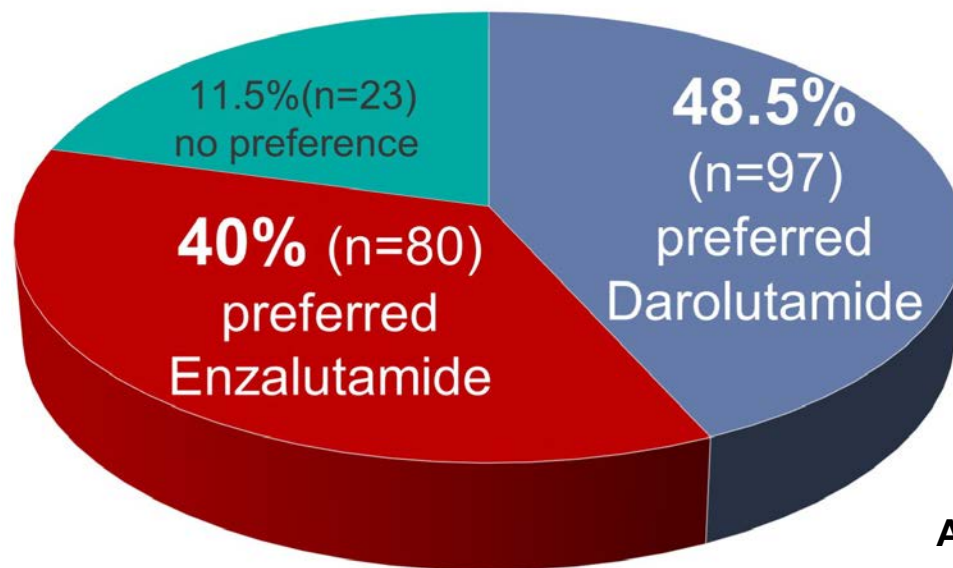
MODULE 3: Faculty Survey

MODULE 4: Immune Checkpoint Inhibitors in mCRPC

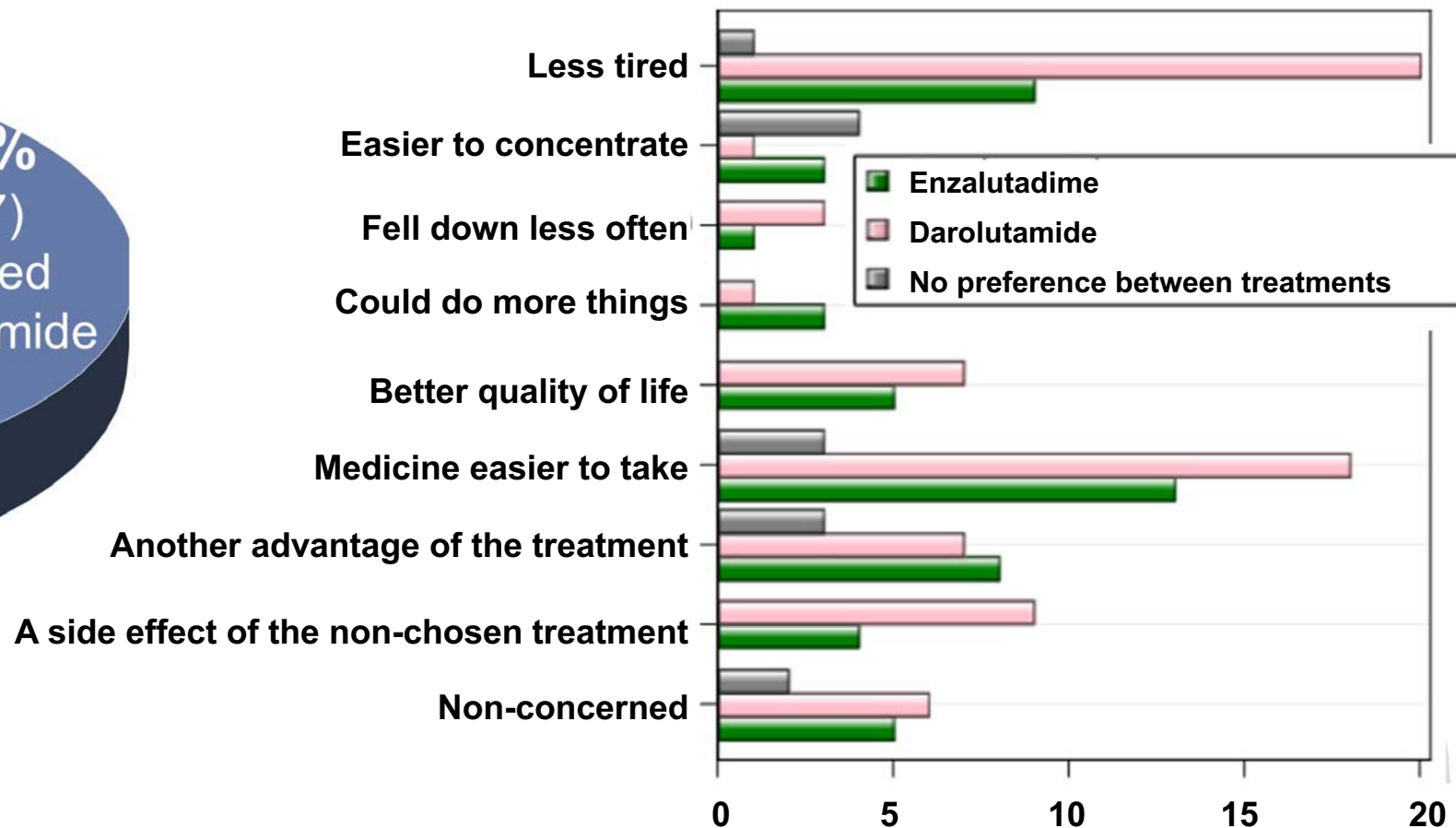
MODULE 5: Journal Club with Prof Fizazi (Part 2)

MODULE 6: Appendix

ODENZA: A Phase II Crossover Trial Evaluating Preference Between Darolutamide and Enzalutamide in Men with Asymptomatic or Mildly Symptomatic mCRPC

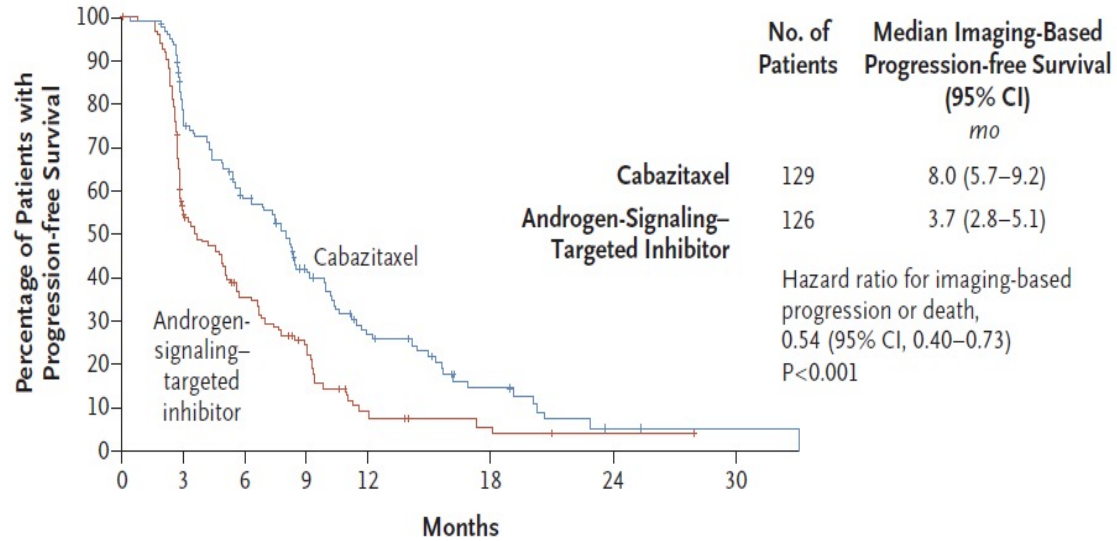


Main reasons for patient preference between treatments



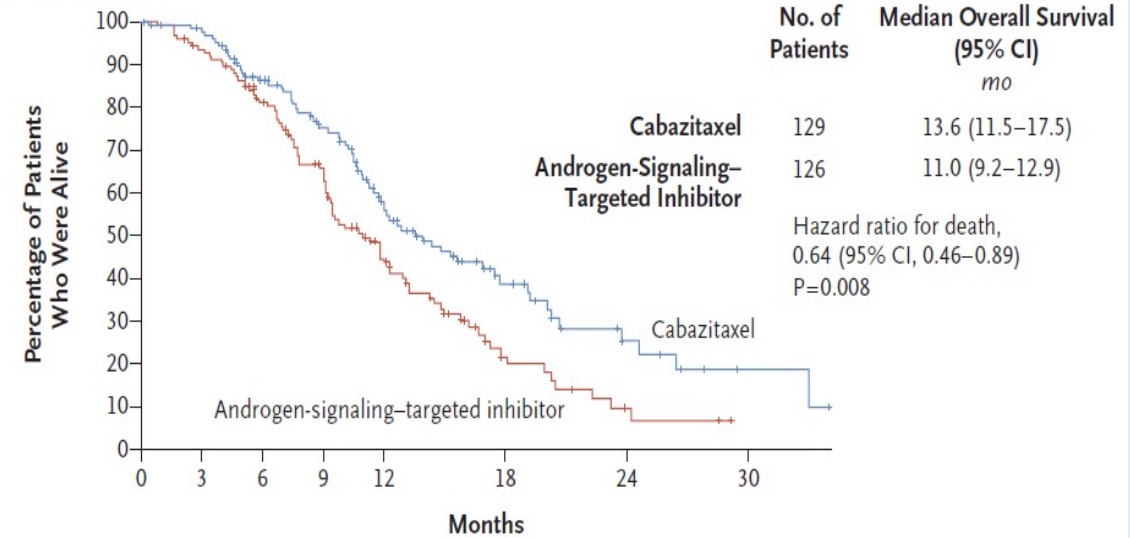
CARD: Imaging-Based PFS and OS with Cabazitaxel versus Abiraterone or Enzalutamide for mCRPC

A Imaging-Based Progression-free Survival



No. at Risk		0	3	6	9	12	18	24	30
Cabazitaxel	129	91	64	41	23	9	2	1	
Androgen-signaling-targeted inhibitor	126	61	36	22	7	3	1	0	

A Overall Survival



No. at Risk		0	3	6	9	12	18	24	30
Cabazitaxel	129	122	96	77	51	21	8	2	
Androgen-signaling-targeted inhibitor	126	116	88	64	39	11	3	0	

CARD: Select Adverse Events

Table 2. Adverse Events (Safety Population).

Event	Cabazitaxel (N=126)		Androgen-Signaling–Targeted Inhibitor (N=124)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any adverse event — no. (%)	124 (98.4)	—	117 (94.4)	—
Any grade ≥3 adverse event — no. (%)	—	71 (56.3)	—	65 (52.4)
Any serious adverse event — no. (%)	49 (38.9)	—	48 (38.7)	—
Any adverse event leading to permanent discontinuation of treatment — no. (%)	25 (19.8)	—	11 (8.9)	—
Any adverse event leading to death — no. (%)*	7 (5.6)	—	14 (11.3)	—
Common adverse events — no. (%)†				
Asthenia or fatigue	67 (53.2)	5 (4.0)	45 (36.3)	3 (2.4)
Diarrhea	50 (39.7)	4 (3.2)	8 (6.5)	0
Infection	40 (31.7)	10 (7.9)	25 (20.2)	9 (7.3)
Musculoskeletal pain or discomfort‡	34 (27.0)	2 (1.6)	49 (39.5)	7 (5.6)
Nausea or vomiting	33 (26.2)	0	29 (23.4)	2 (1.6)
Peripheral neuropathy	25 (19.8)	4 (3.2)	4 (3.2)	0
Constipation	19 (15.1)	0	13 (10.5)	0
Hematuria	19 (15.1)	1 (0.8)	7 (5.6)	2 (1.6)
Laboratory abnormalities — no./total no. (%)††				
Anemia	124/125 (99.2)	10/125 (8.0)	118/124 (95.2)	6/124 (4.8)
Leukopenia	93/125 (74.4)	40/125 (32.0)	39/124 (31.5)	2/124 (1.6)
Neutropenia	81/123 (65.9)	55/123 (44.7)	8/124 (6.5)	4/124 (3.2)
Thrombocytopenia	51/125 (40.8)	4/125 (3.2)	20/124 (16.1)	2/124 (1.6)
Aspartate aminotransferase increased	27/124 (21.8)	4/124 (3.2)	35/124 (28.2)	0/124
Alanine aminotransferase increased	24/124 (19.4)	1/124 (0.8)	11/124 (8.9)	0/124
Hypokalemia	15/125 (12.0)	1/125 (0.8)	19/124 (15.3)	1/124 (0.8)

ORIGINAL RESEARCH

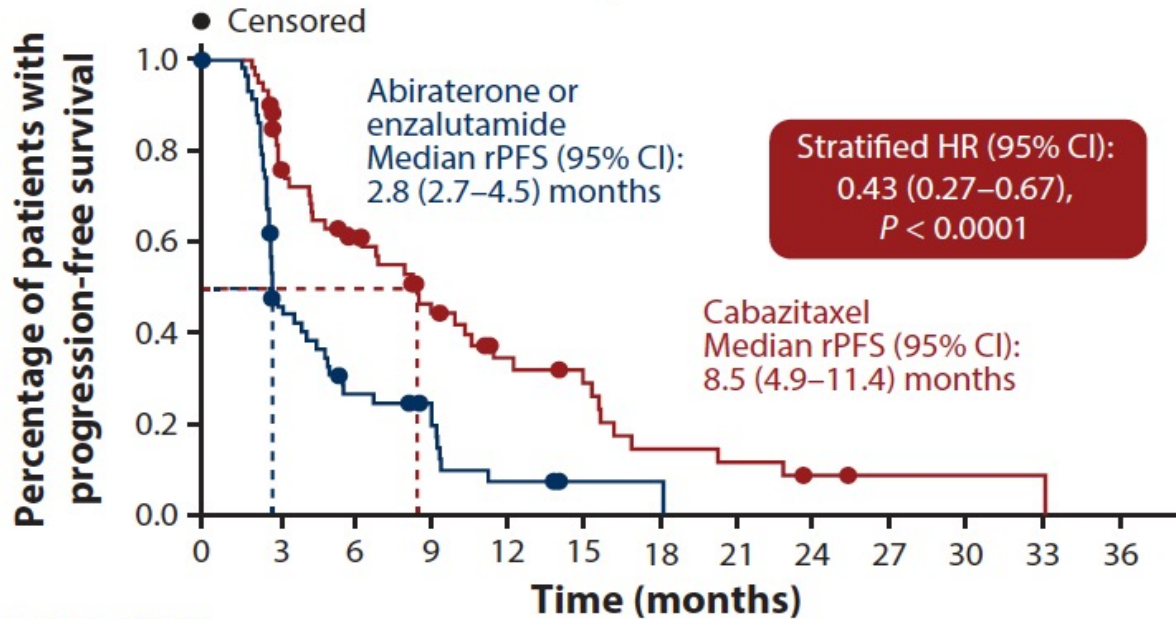
Baseline neutrophil-to-lymphocyte ratio as a predictive and prognostic biomarker in patients with metastatic castration-resistant prostate cancer treated with cabazitaxel versus abiraterone or enzalutamide in the CARD study

R. de Wit^{1*}, C. Wülfing², D. Castellano³, G. Kramer⁴, J.-C. Eymard⁵, C. N. Sternberg⁶, K. Fizazi^{7,8}, B. Tombal⁹, A. Bamias¹⁰, J. Carles¹¹, R. Iacovelli^{12,13}, B. Melichar¹⁴, Á. Sverrisdóttir¹⁵, C. Theodore¹⁶, S. Feyerabend¹⁷, C. Helissey¹⁸, M. C. Foster¹⁹, A. Ozatilgan¹⁹, C. Geffriaud-Ricouard²⁰ & J. de Bono^{21,22}

ESMO Open 2021;[Online ahead of print].

CARD: rPFS by Baseline Neutrophil-to-Lymphocyte Ratio (NLR)

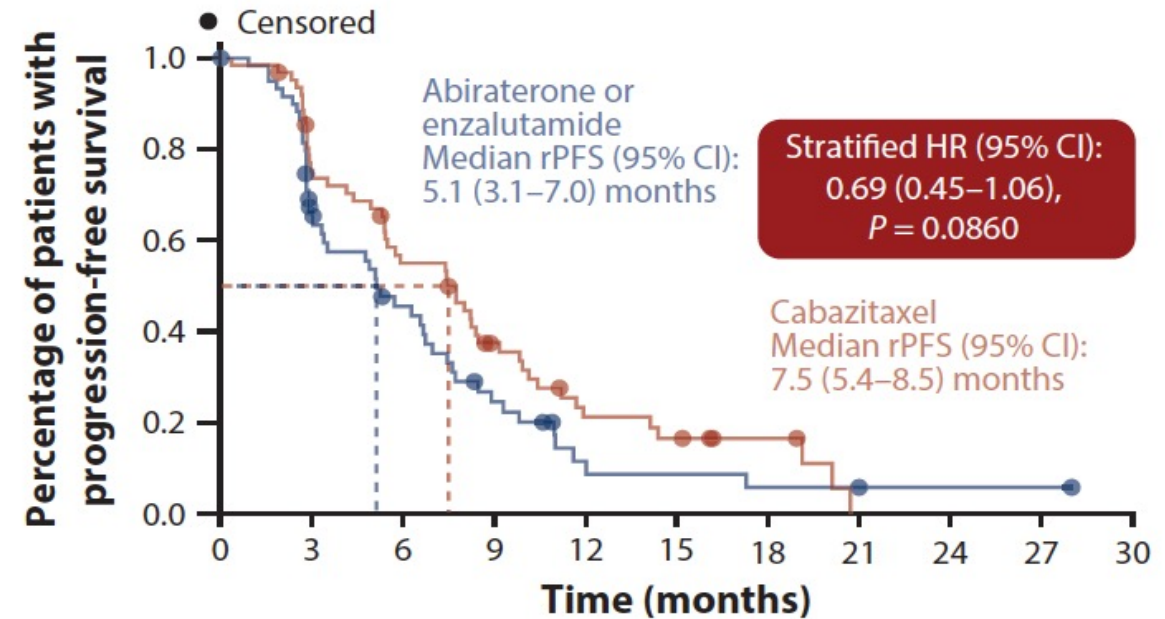
High NLR



Number at risk

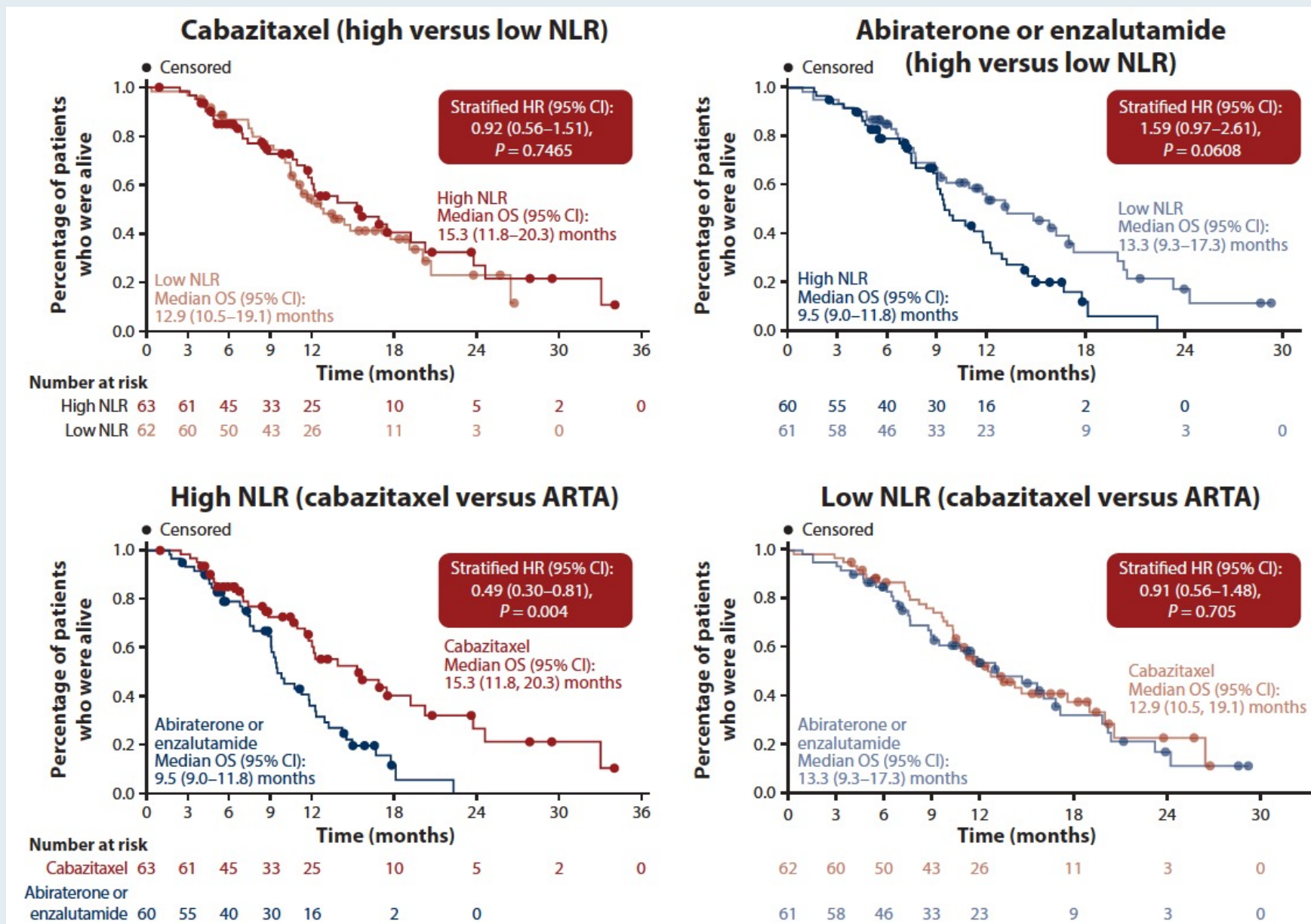
Cabazitaxel	63	45	31	21	13	5	2	1	0
Abiraterone or enzalutamide	60	25	13	10	3	1	0		

Low NLR



Cabazitaxel	62	45	32	19	10	4	0		
Abiraterone or enzalutamide	61	35	22	11	4	2	1	0	

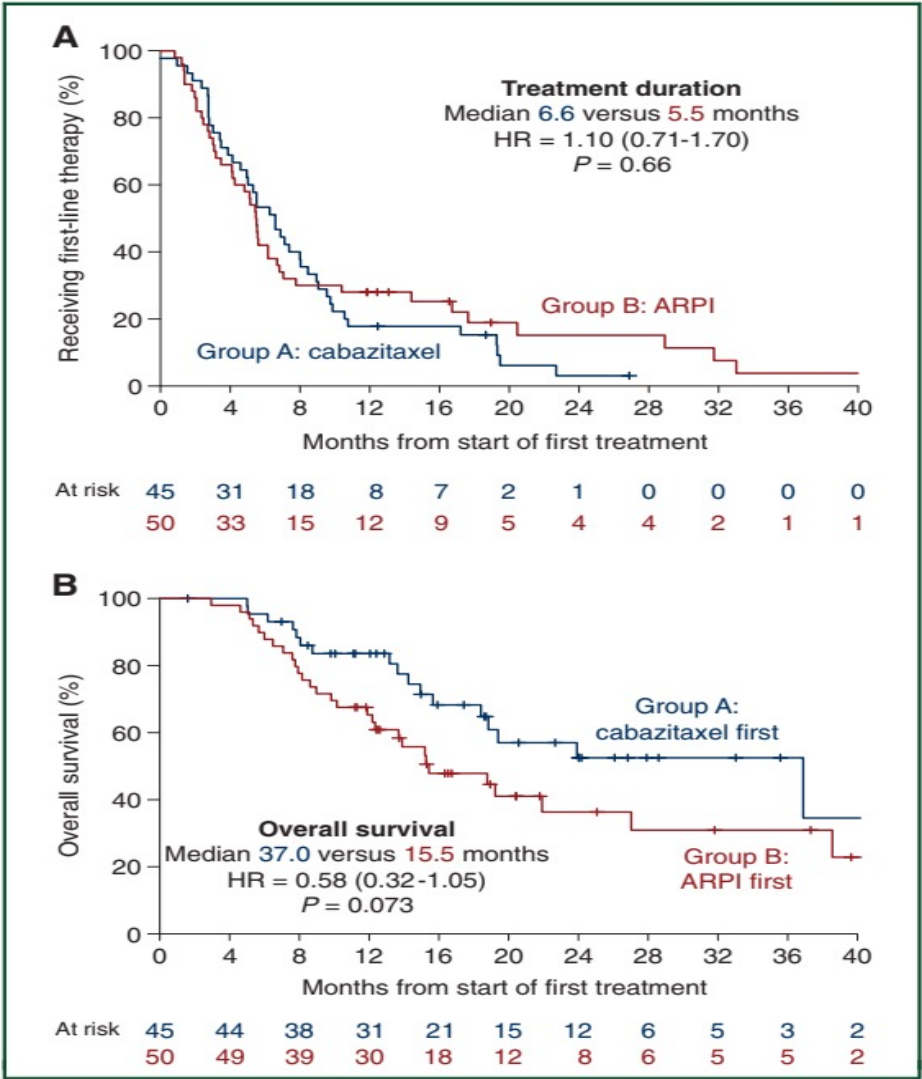
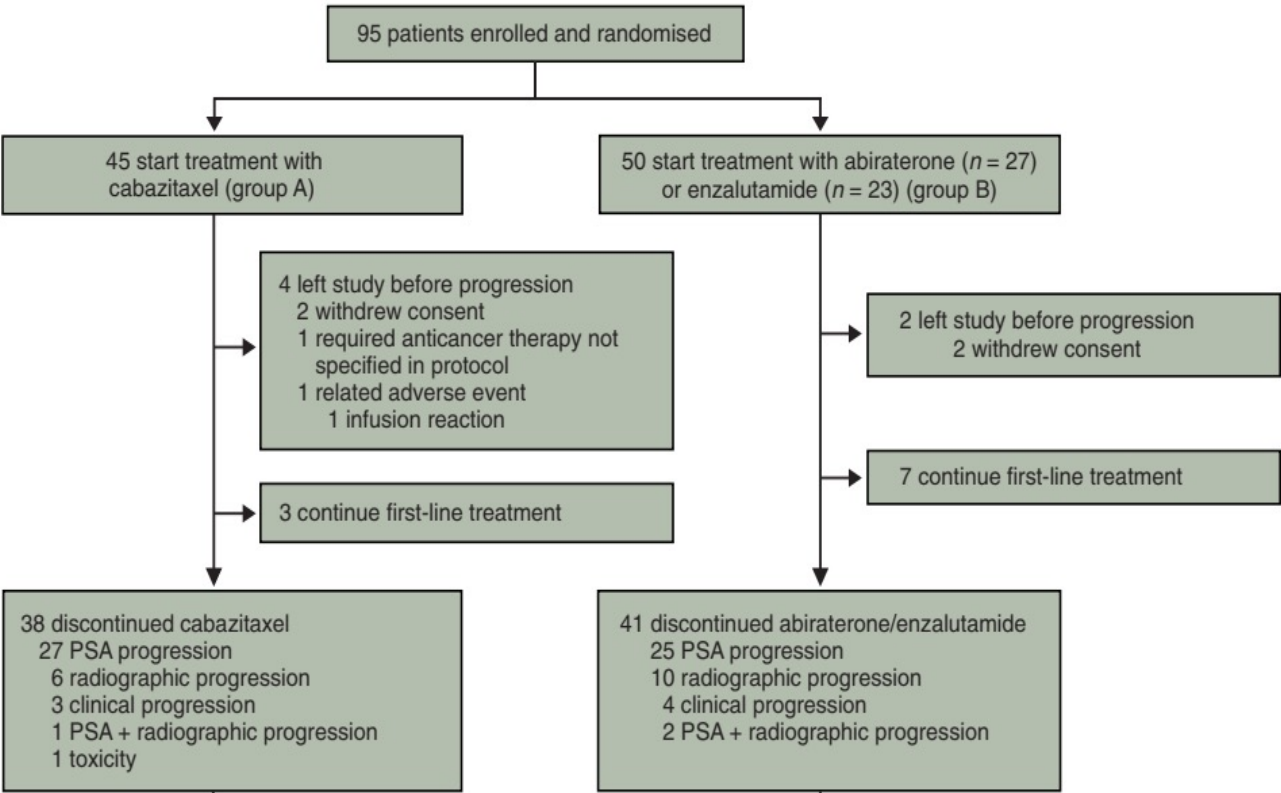
CARD: OS by Baseline NLR



The Canadian Trial (Phase II OZM-054 Trial)

Poor prognosis:

liver mets,
CRPC <12 months,
or >3 of 6 (LDH, ECOG, visceral, albumin, ALP, <36 mo from Dx)



First Results from a Randomized Phase II Study of Cabazitaxel (CBZ) versus an Androgen Receptor Targeted Agent (ARTA) in Patients with Poor-Prognosis Castration-Resistant Prostate Cancer (mCRPC)

van der Zande K et al.

ASCO 2021;Abstract 5059.

The Dutch Trial (Phase II OSTRICH Trial)

Inclusion criteria

- mCRPC
- ECOG PS0-2
- Testosterone <50 ng/dL
- Adequate bone marrow and liver functions
- Prior docetaxel
- Previous ARTA was allowed
- Progressive disease
- Features of poor prognostic disease (≥ 1):
 - ❖ Liver metastasis
 - ❖ Castration resistant <12m
 - ❖ Progressive <6m after docetaxel

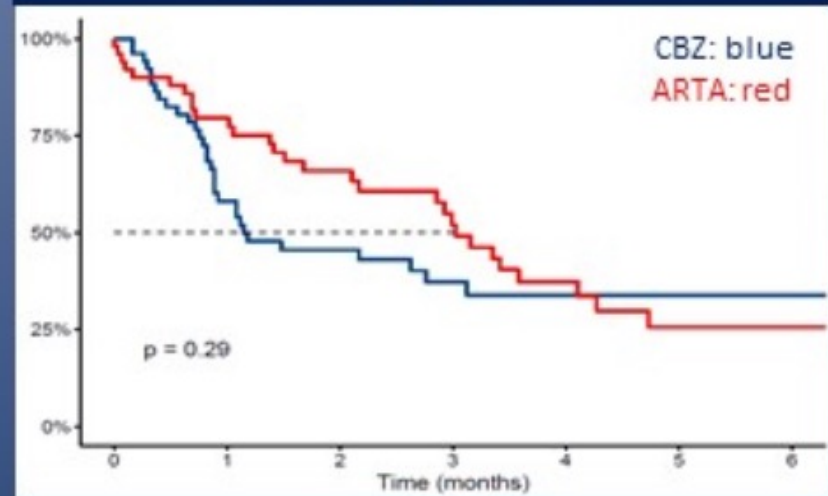
R

Cabazitaxel

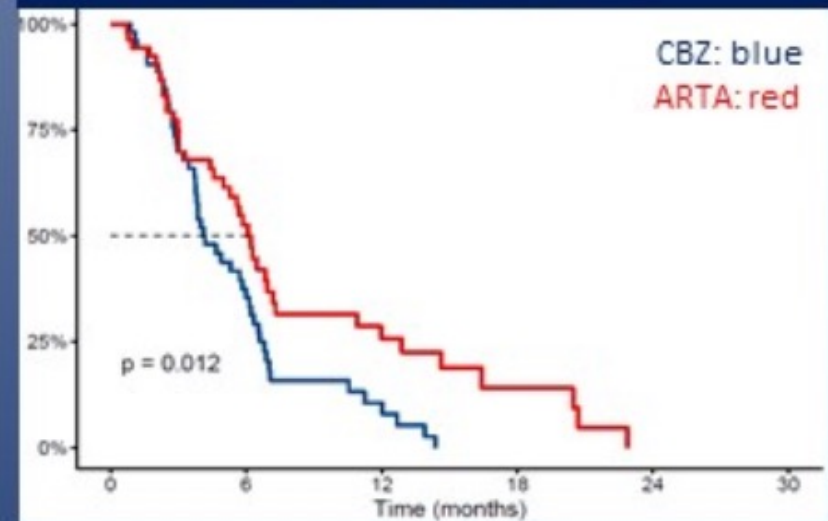
Abiraterone/P
OR enzalutamide



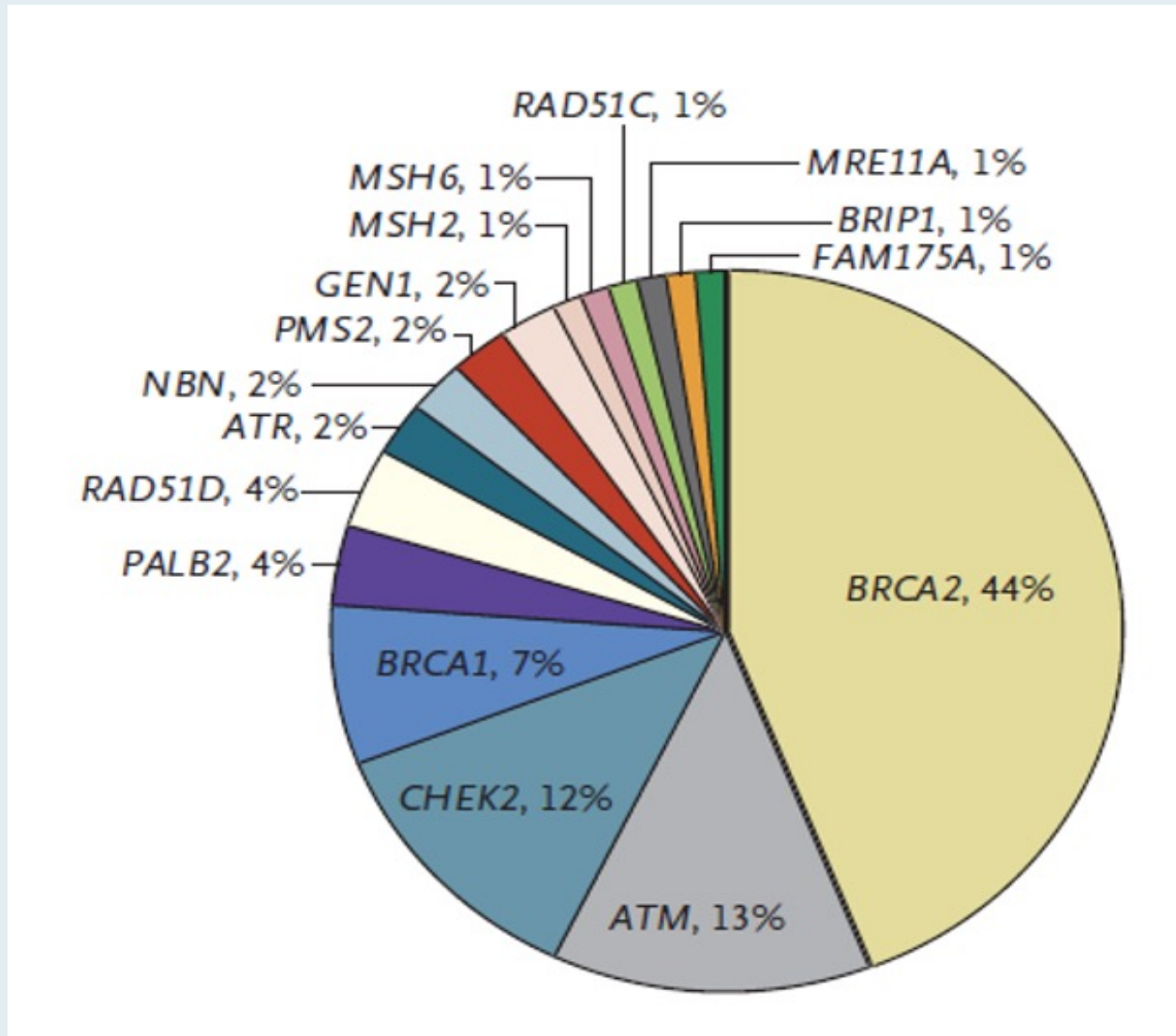
Time to PSA progression



Time to clinical progression



Inherited DNA Repair Gene Mutations in Men with Metastatic Prostate Cancer



- Multicenter study of 692 men
- Deleterious mutations were found in 82 men (11.8%) in 16 genes
- Observed rate exceeded that associated with localized prostate cancer (4.6%) and general population without cancer (2.7%)

Recent FDA Approvals of PARP Inhibitors for mCRPC

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

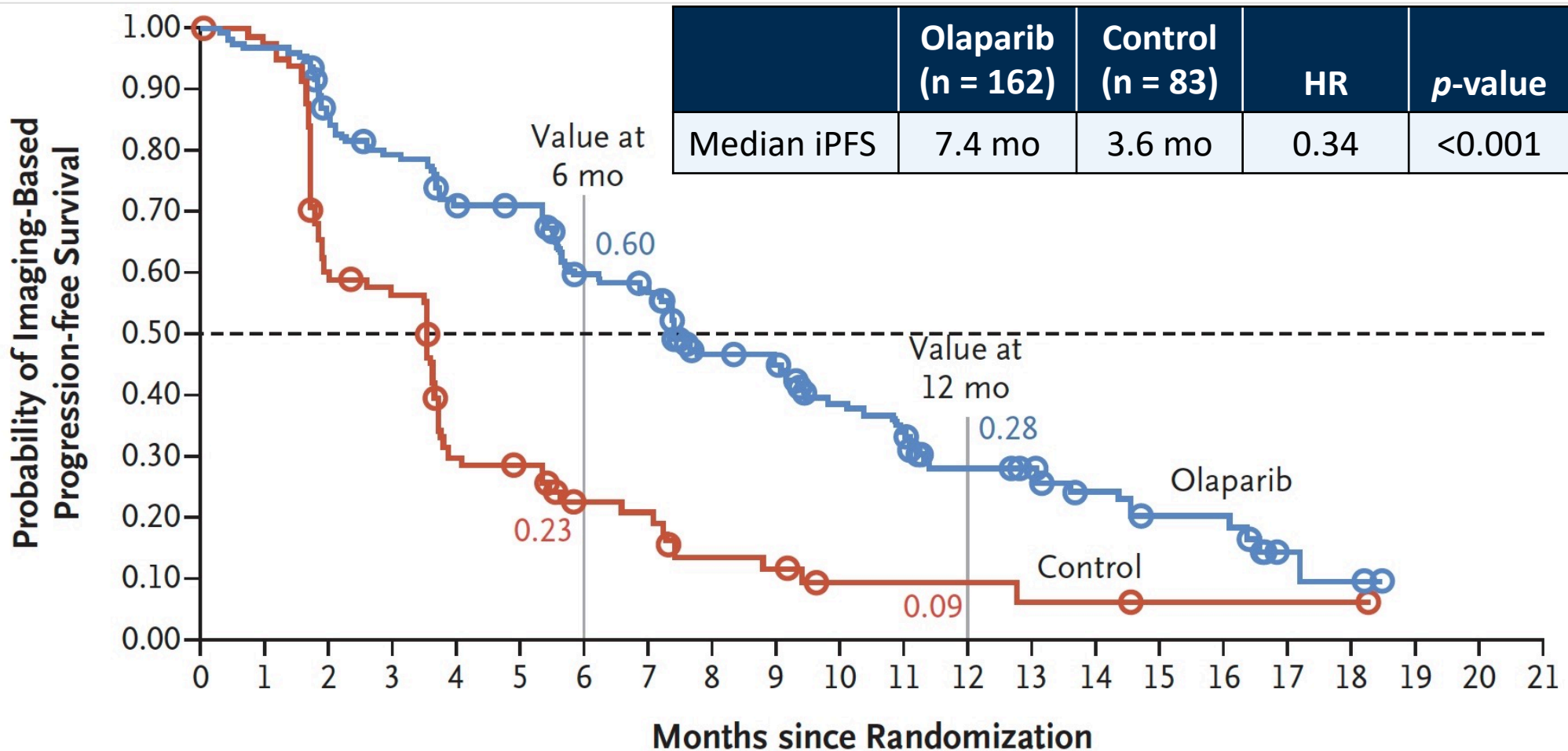
ORIGINAL ARTICLE

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

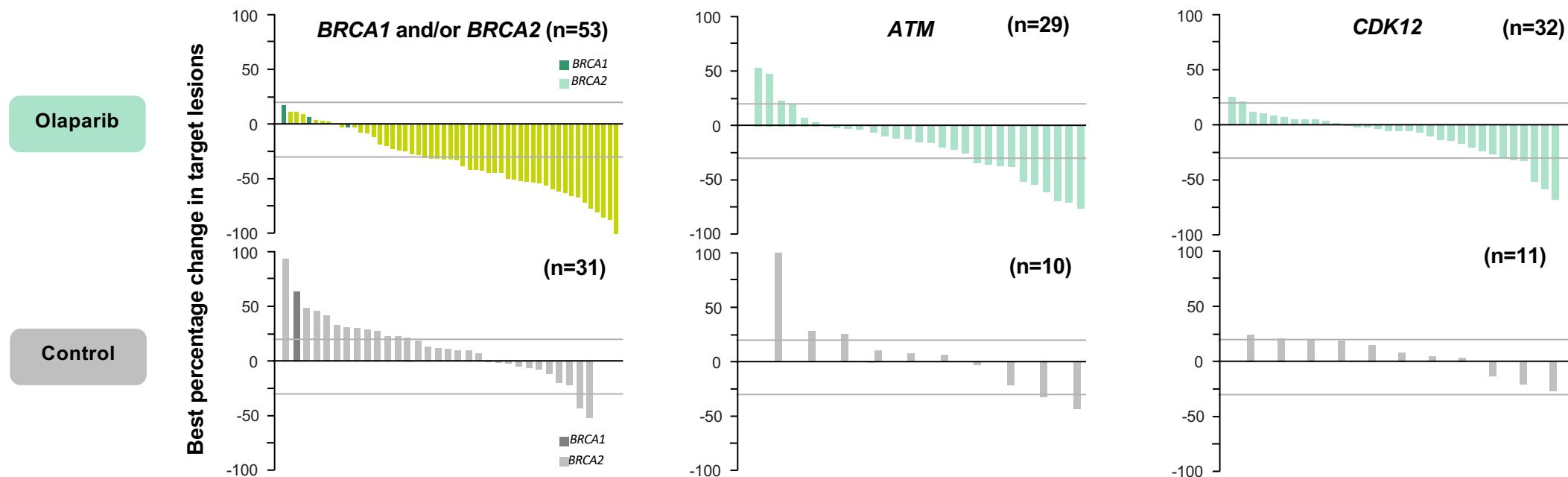
***N Engl J Med* 2020;382:2091-102**

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)



Olaparib Antitumor Activity in PROfound

		Cohort A		Cohorts A+B		BRCA1 and/or BRCA2		ATM		CDK12	
		Olaparib (N=162)	Control (N=83)	Olaparib (N=256)	Control (N=131)	Olaparib (N=102)	Control (N=58)	Olaparib (N=62)	Control (N=24)	Olaparib (N=61)	Control (N=28)
rPFS	Median, months	7.4	3.6	5.8	3.5	9.8	3.0	5.4	4.7	5.1	2.2
	HR (95% CI)	0.34 (0.25–0.47)		0.49 (0.38–0.63)		0.22 (0.15–0.32)		1.04 (0.61–1.87)		0.74 (0.44–1.31)	
OS	Median OS, months	19.1	14.7	17.3	14.0	20.1	14.4	18.0	15.6	14.1	11.5
	HR (95% CI)	0.69 (0.50–0.97)		0.79 (0.61–1.03)		0.63 (0.42–0.95)		0.93 (0.53–1.75)		0.97 (0.57–1.71)	
ORR	Evaluable patients, n	84	43	138	67	57	33	30	10	34	12
	ORR, %	33.3	2.3	21.7	4.5	43.9	0	10.0	10.0	5.9	0
PSA	Evaluable patients, n	153	77	243	123	94	54	61	22	58	27
	Confirmed response, %	43.1	7.8	30.0	9.8	61.7	0	13.1	22.7	5.2	3.7
CTC	Evaluable patients, n	52	22	78	32	29	17	25	3	14	5
	Conversion, %	55.8	22.7	52.6	21.9	69.0	23.5	40.0	33.3	50.0	40.0



ORIGINAL ARTICLE

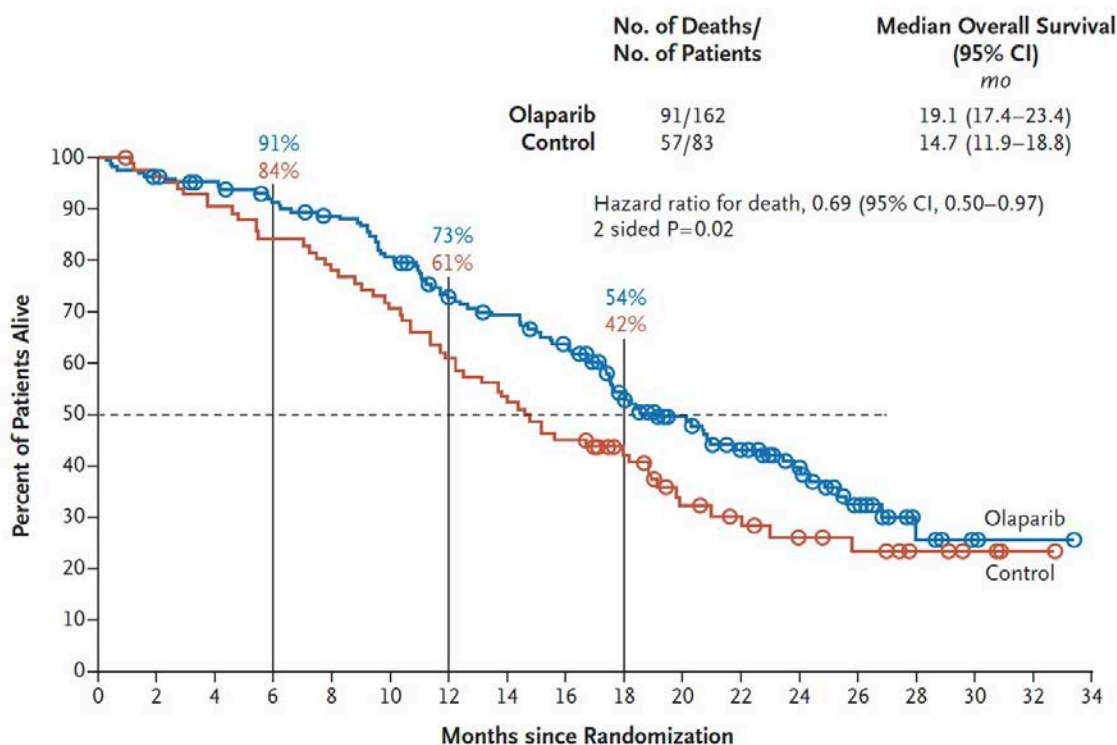
Survival with Olaparib in Metastatic Castration-Resistant Prostate Cancer

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*

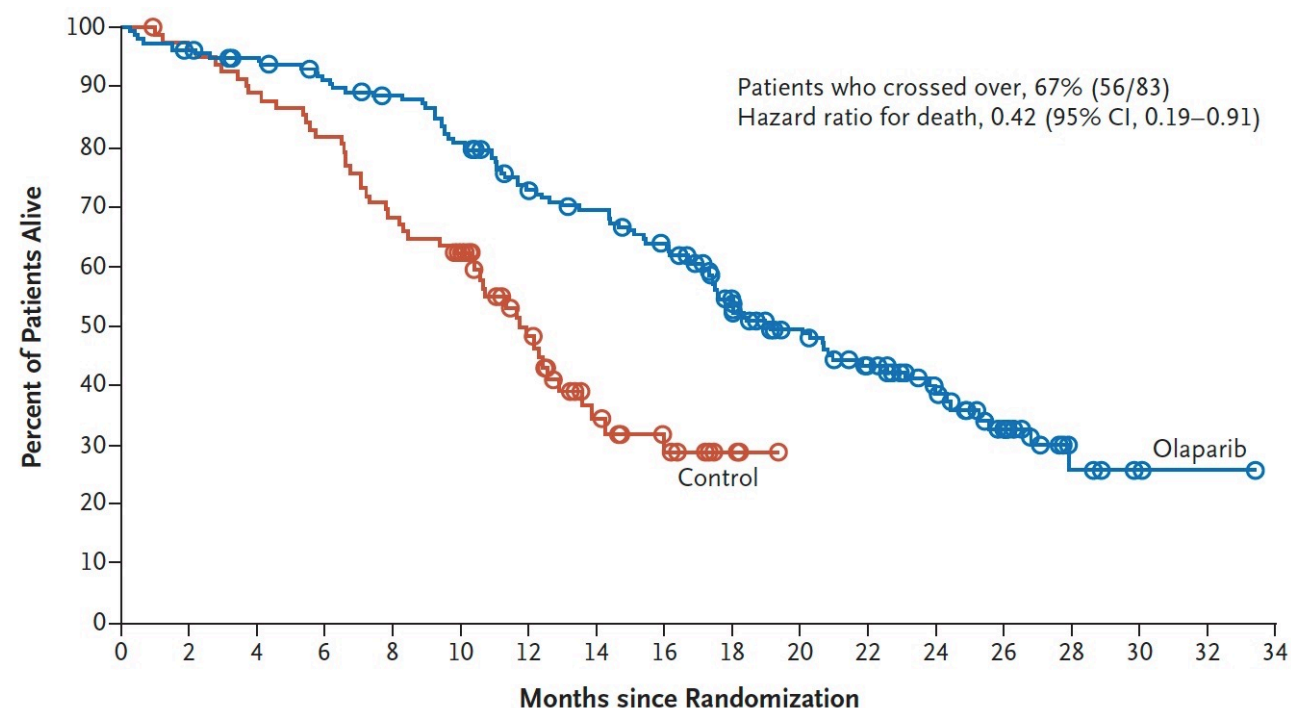
***N Engl J Med* 2020;383(24):2345-57.**

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

Overall survival



Cross-over adjusted overall survival



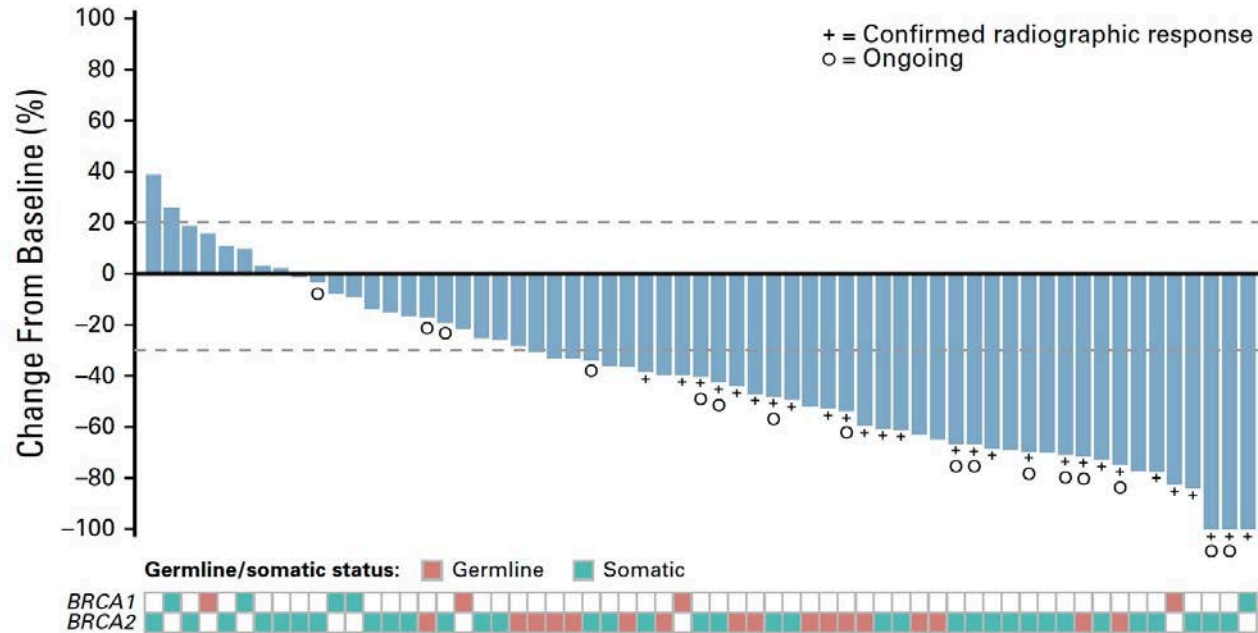
Rucaparib in Men With Metastatic Castration-Resistant Prostate Cancer Harboring a *BRCA1* or *BRCA2* Gene Alteration

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

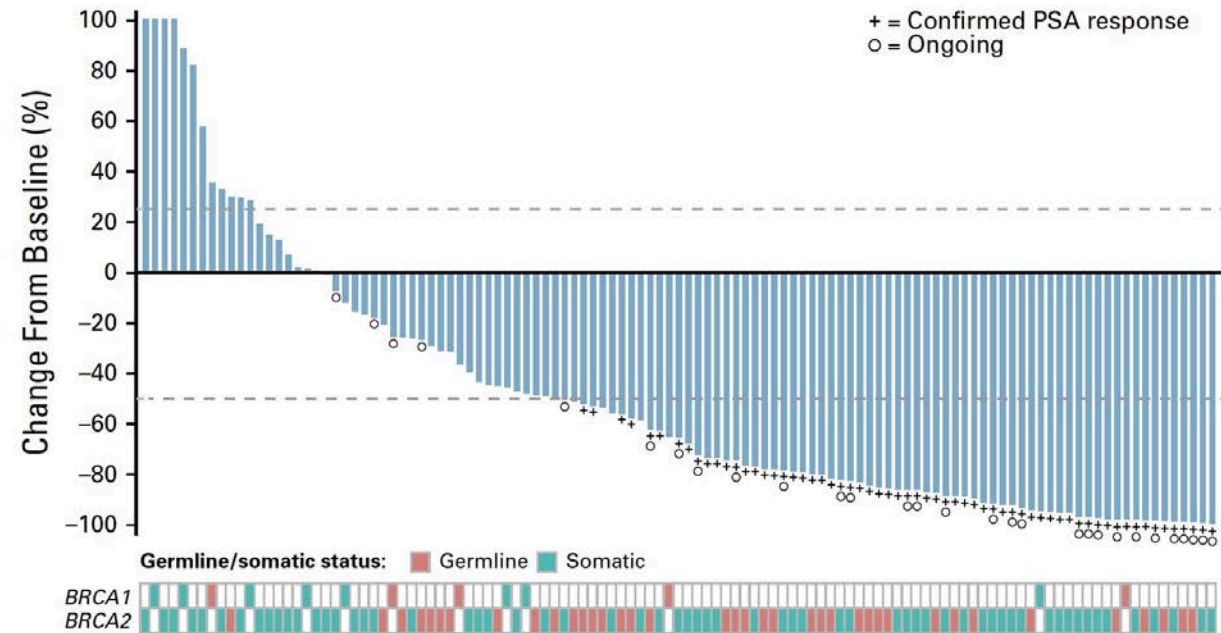
J Clin Oncol 2020;38(22):3763-72.

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%



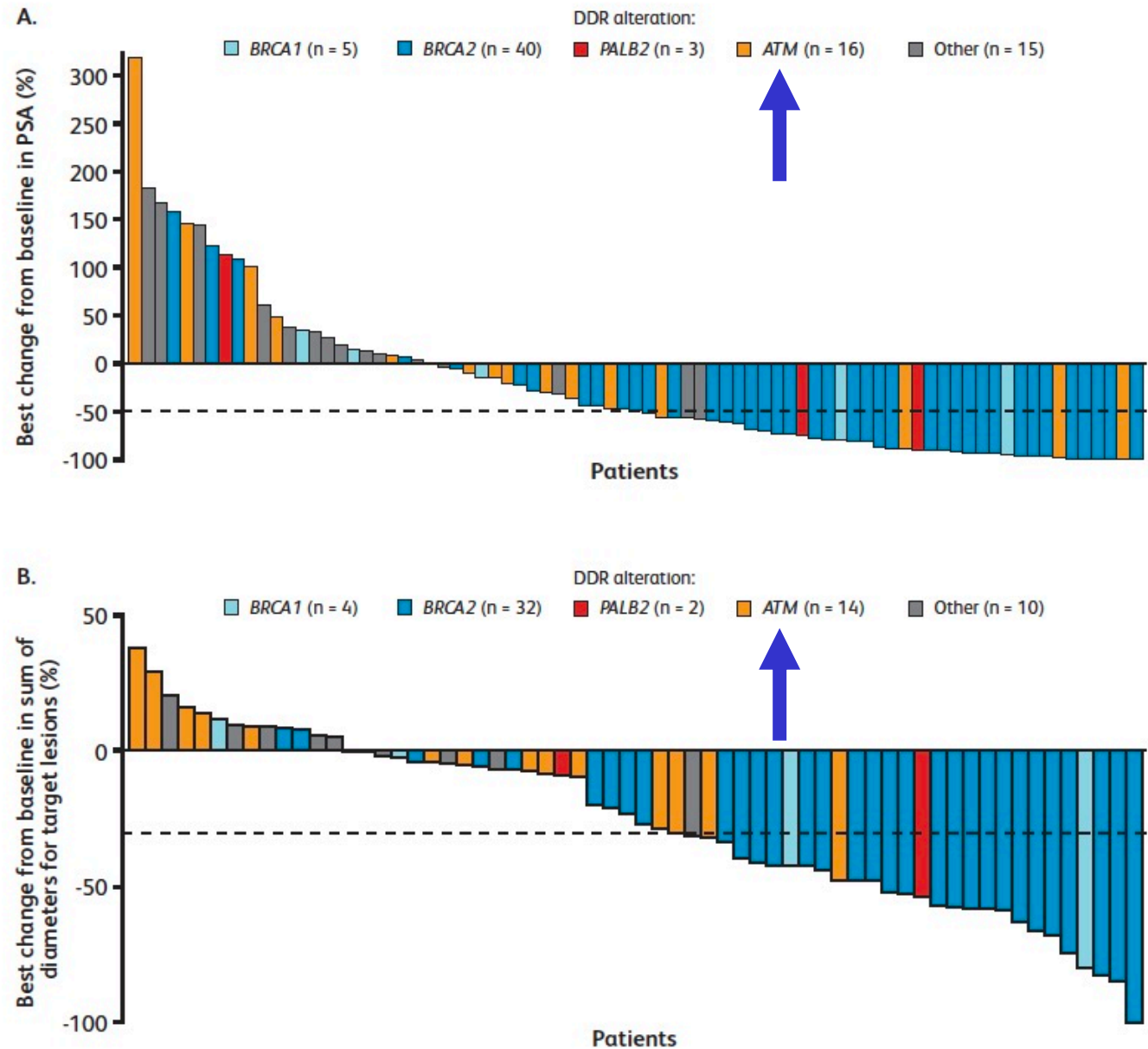
Talazoparib in mCRPC (TALAPRO-1)

BRCA in blue

ATM loss in orange

PALB2 in red

Figure 4. Best Change From Baseline in A. PSA and B. RECIST^a



Abiraterone acetate plus prednisolone with or without enzalutamide added to androgen deprivation therapy compared to ADT alone for men with high-risk nonmetastatic prostate cancer: primary combined analysis from two comparisons in the STAMPEDE platform protocol

Gerhardt Attard, Louise Brown, Noel Clarke, Laura Murphy, William Cross, Rob Jones, Silke Gillessen, J.Martin Russell, Adrian Cook, Jo Bowen, Anna Lydon, Ian Pedley, Omi Parikh, Simon Chowdhury, Zafar Malik, David Matheson, Chris Parker, Matthew Sydes, Mahesh Parmar, Nicholas James **on behalf of the STAMPEDE investigators***

Conducted by Medical Research Council Trials Unit at University College London, U.K.

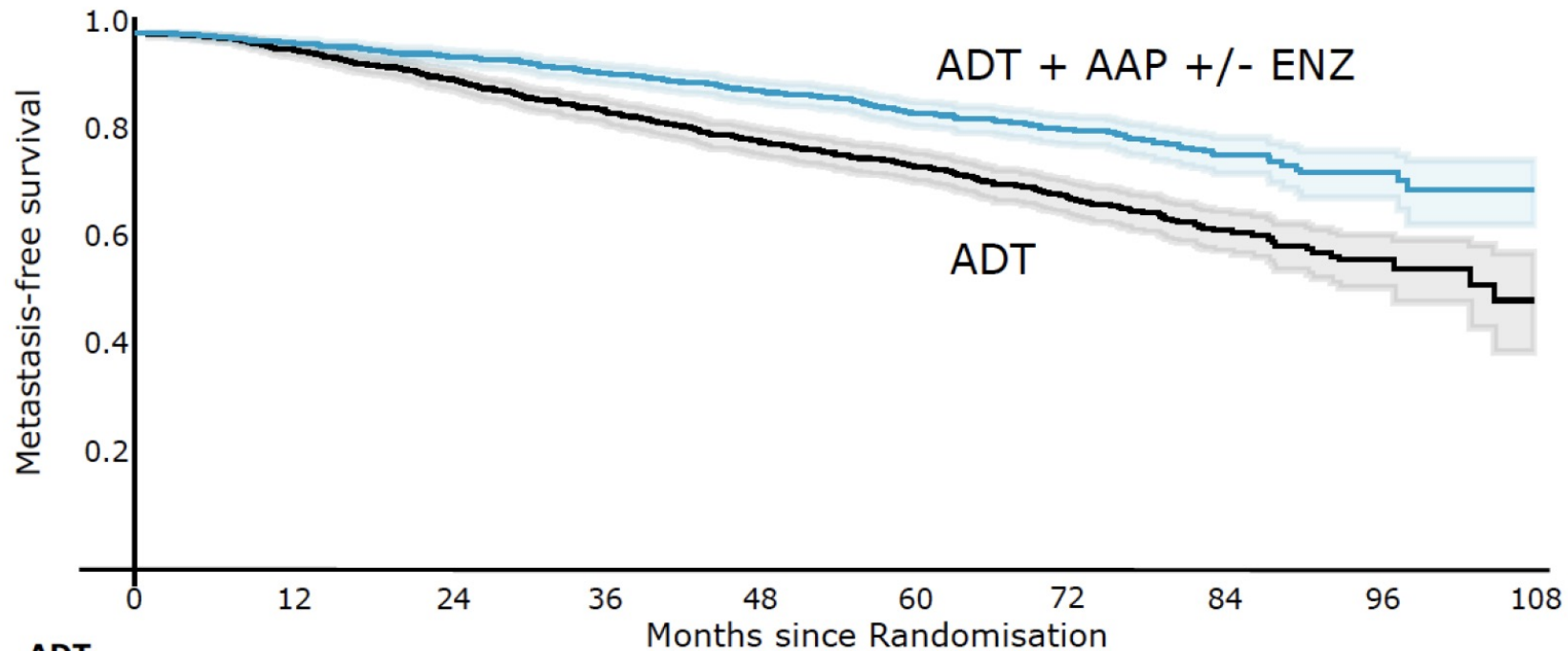
ClinicalTrials.gov number, NCT00268476 & Current Controlled Trials number, ISRCTN78818544

*113 U.K. and Swiss sites: list of investigators and collaborators at www.stampedetrial.org

www.stampedetrial.org



Metastasis-Free Survival with the Addition of Abiraterone Acetate and Prednisolone with or without Enzalutamide to ADT for High-Risk M0 Prostate Cancer



Events
 180 ADT+ AAP +/- ENZ
 306 ADT

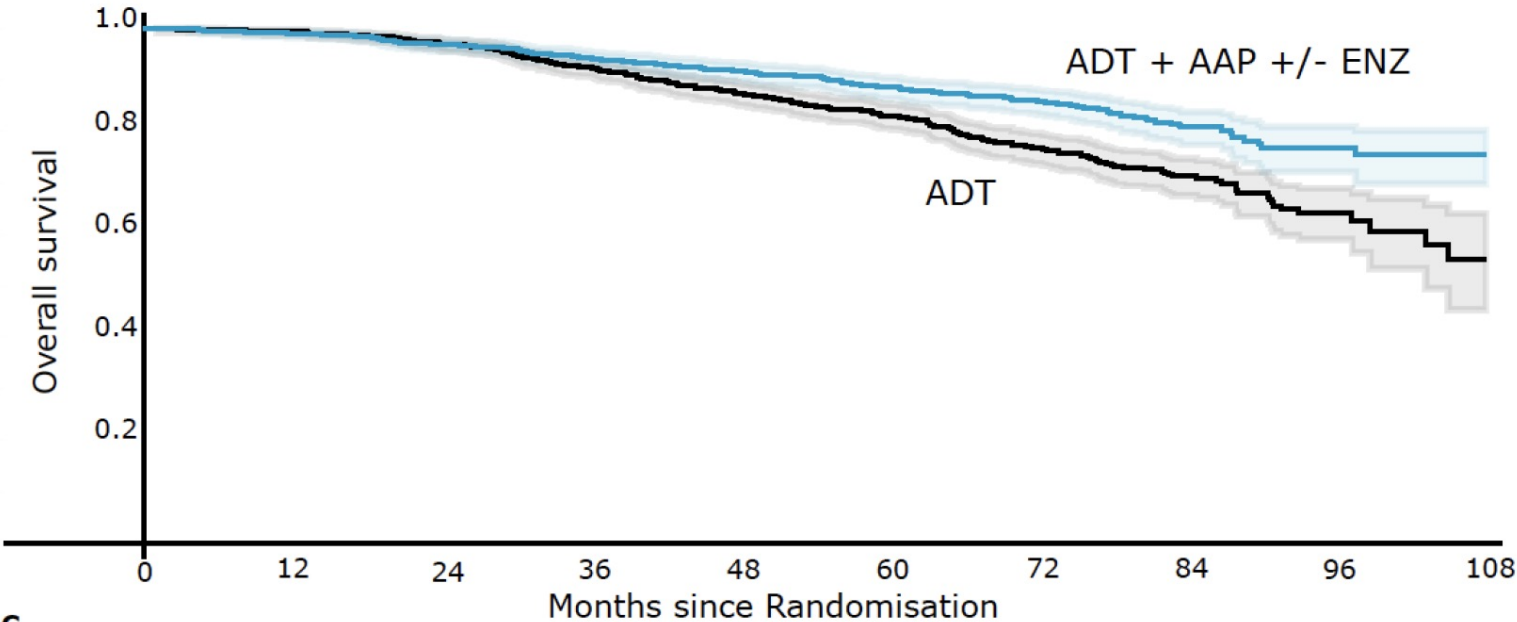
HR: 0.53
 95% CI: 0.44-0.64
 P value 2.9×10^{-11}

6-year MFS improved from 69% to 82%

	0	12	24	36	48	60	72	84	96	108
ADT										
At-risk	988	950	894	836	767	550	329	172	53	9
Censored	0	8	11	14	26	201	387	522	632	673
Event	0	30	83	138	195	237	272	294	303	306
ADT+AAP+/-ENZ										
At-risk	986	948	917	884	839	622	369	198	71	14
Censored	0	21	28	31	45	225	460	615	737	792
Event	0	17	41	71	102	139	157	173	178	180

Overall Survival with the Addition of Abiraterone Acetate and Prednisolone with or without Enzalutamide to ADT for High-Risk M0 Prostate Cancer

Overall survival



Events
 147 ADT+AAP +/- ENZ
 236 ADT

HR: 0.60
 95% CI 0.48 to 0.73
 P value 9.3×10^{-7}

6-year survival improved from 77% to 86%

	0	12	24	36	48	60	72	84	96	108
SOC										
At-risk	988	974	947	901	837	610	368	200	63	10
Censored	0	8	11	14	28	216	421	568	693	742
Event	0	6	30	73	123	162	199	220	232	236
SOC+AAP+/-ENZ										
At-risk	986	956	928	899	861	645	386	205	74	16
Censored	0	21	29	32	46	234	477	641	766	823
Event	0	9	29	55	79	107	123	140	146	147

**Year in Review: Clinical Investigator
Perspectives on the Most Relevant
New Data Sets and Advances in Oncology
Breast Cancer**

**Thursday, January 6, 2022
5:00 PM – 6:00 PM ET**

Faculty

**Harold J Burstein, MD, PhD
Professor Peter Schmid, FRCP, MD, PhD**

Moderator

Neil Love, MD

Thank you for joining us!

***CME and MOC credit information will be emailed
to each participant within 5 business days.***