Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Prostate Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, March 25, 2026
5:00 PM – 6:00 PM ET

Faculty

Andrew J Armstrong, MD, ScM
Scott T Tagawa, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2026

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Andrew J Armstrong, MD, ScM
Professor of Medicine, Surgery, Pharmacology and Cancer Biology
Director of Research
Duke Cancer Institute Center for Prostate and Urologic Cancers
Division of Medical Oncology
Departments of Medicine and Urology
Duke University
Durham, North Carolina

Scott T Tagawa, MD, MS
Professor of Medicine and Urology
Weill Cornell Medicine
Leader, GU Disease Management Team
Meyer Cancer Center
New York, New York

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Commercial Support

This activity is supported by educational grants from AstraZeneca Pharmaceuticals LP, Merck, Novartis, and Sumitomo Pharma America and Pfizer Inc.

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: Aadi Bioscience, AbbVie Inc, ADC Therapeutics, Agendia Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Arvinas, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeOne, Biotheranostics Inc, A Hologic Company, Black Diamond Therapeutics Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celcuity, Clovis Oncology, Coherus BioSciences, Corcept Therapeutics Inc, CTI BioPharma, a Sobi Company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, Exact Sciences Corporation, Exelixis Inc, Genentech, a member of the Roche Group, Genmab US Inc, Geron Corporation, Gilead Sciences Inc, GSK, Helsinn Therapeutics (US) Inc, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Jazz Pharmaceuticals Inc, Johnson & Johnson, Karyopharm Therapeutics, Kite, A Gilead Company, Kura Oncology, Legend Biotech, Lilly, MEI Pharma Inc, Merck, Mersana Therapeutics Inc, Mirati Therapeutics Inc, Mural Oncology Inc, Natera Inc, Novartis, Novartis Pharmaceuticals Corporation on behalf of Advanced Accelerator Applications, Novocure Inc, Nuvalent, Nuvation Bio Inc, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Revolution Medicines Inc, Rigel Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Pharma America, Summit Therapeutics, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, and Tesaro, A GSK Company.

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Dr Tagawa — Disclosures

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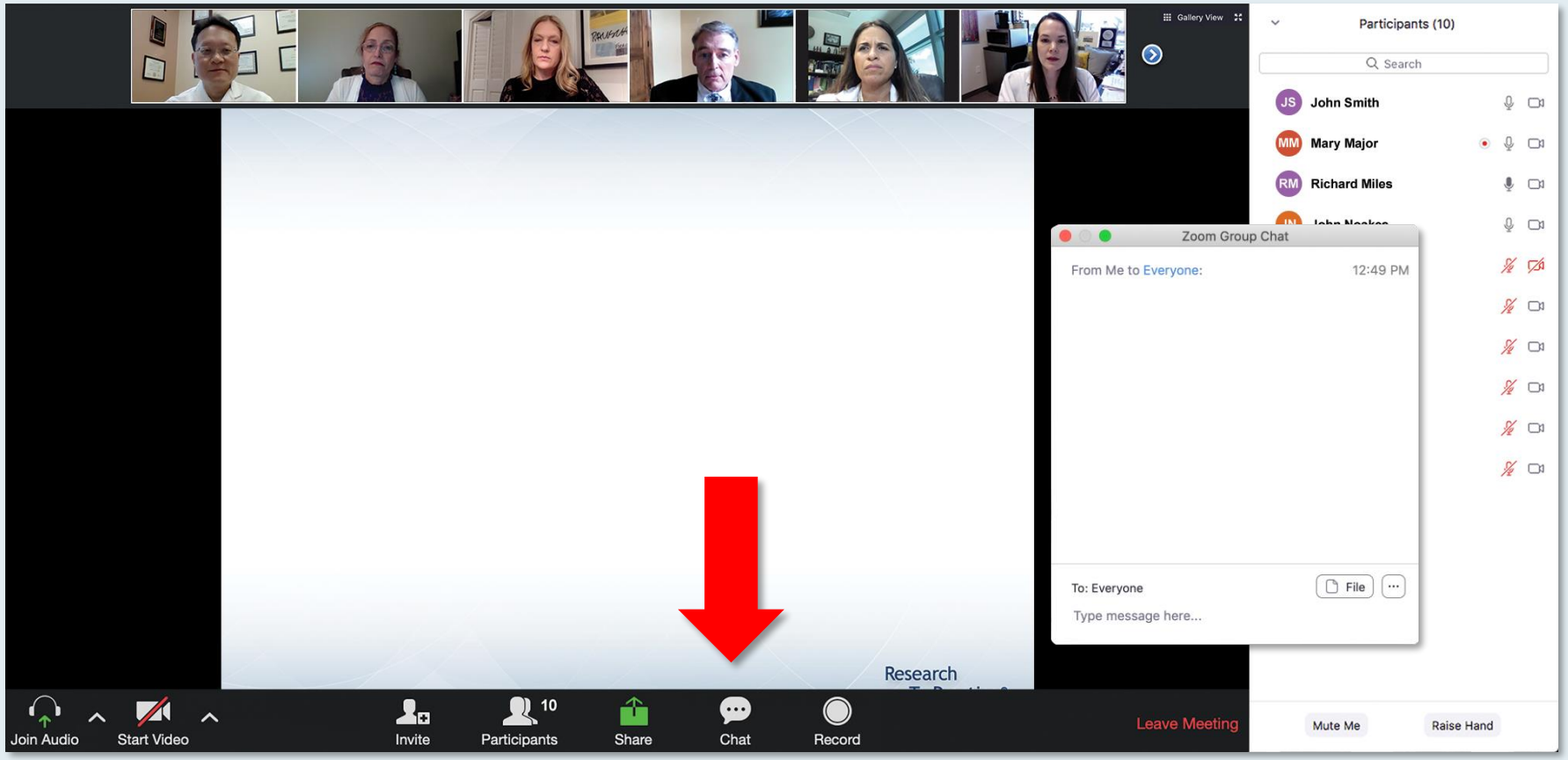

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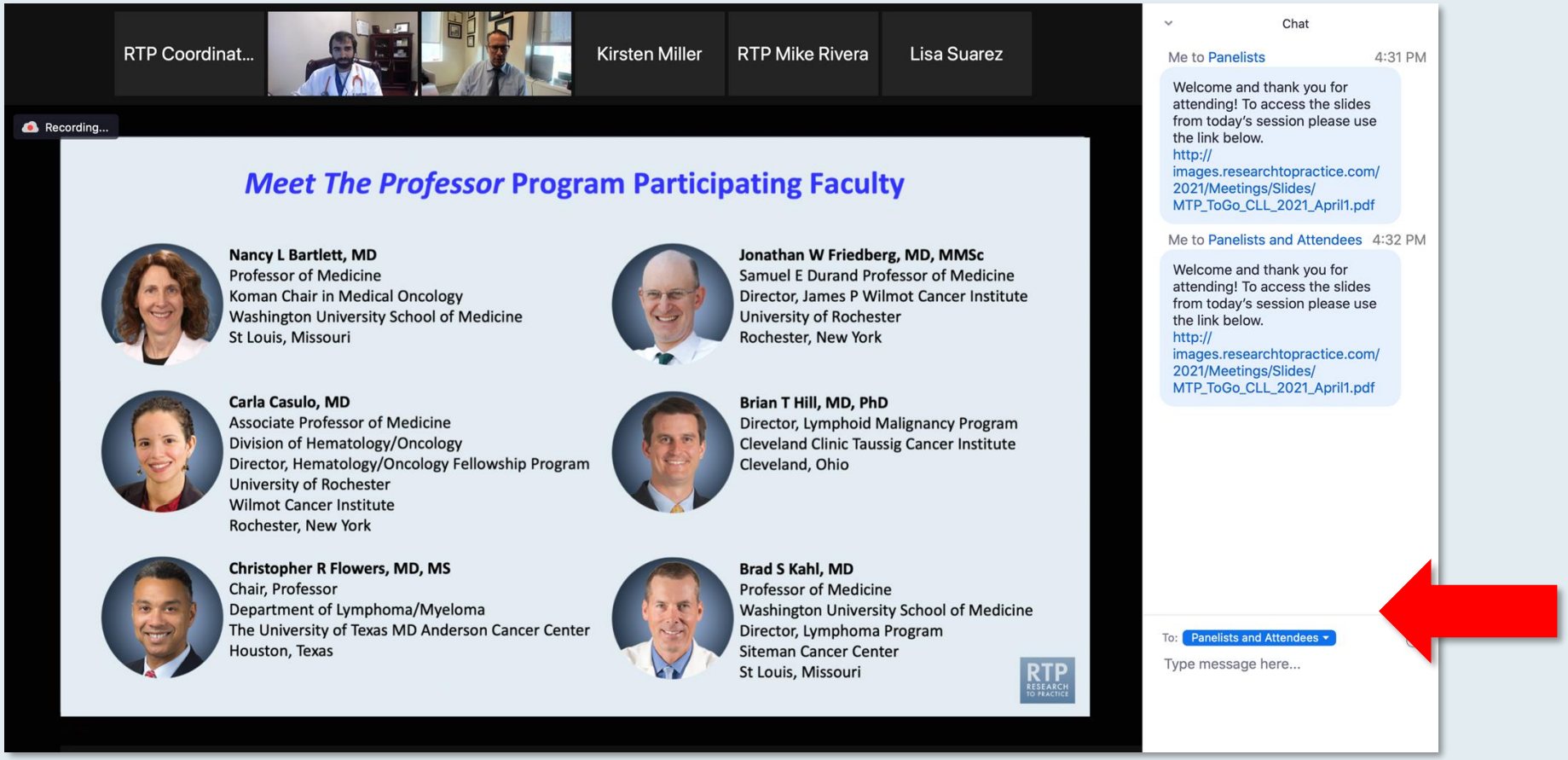

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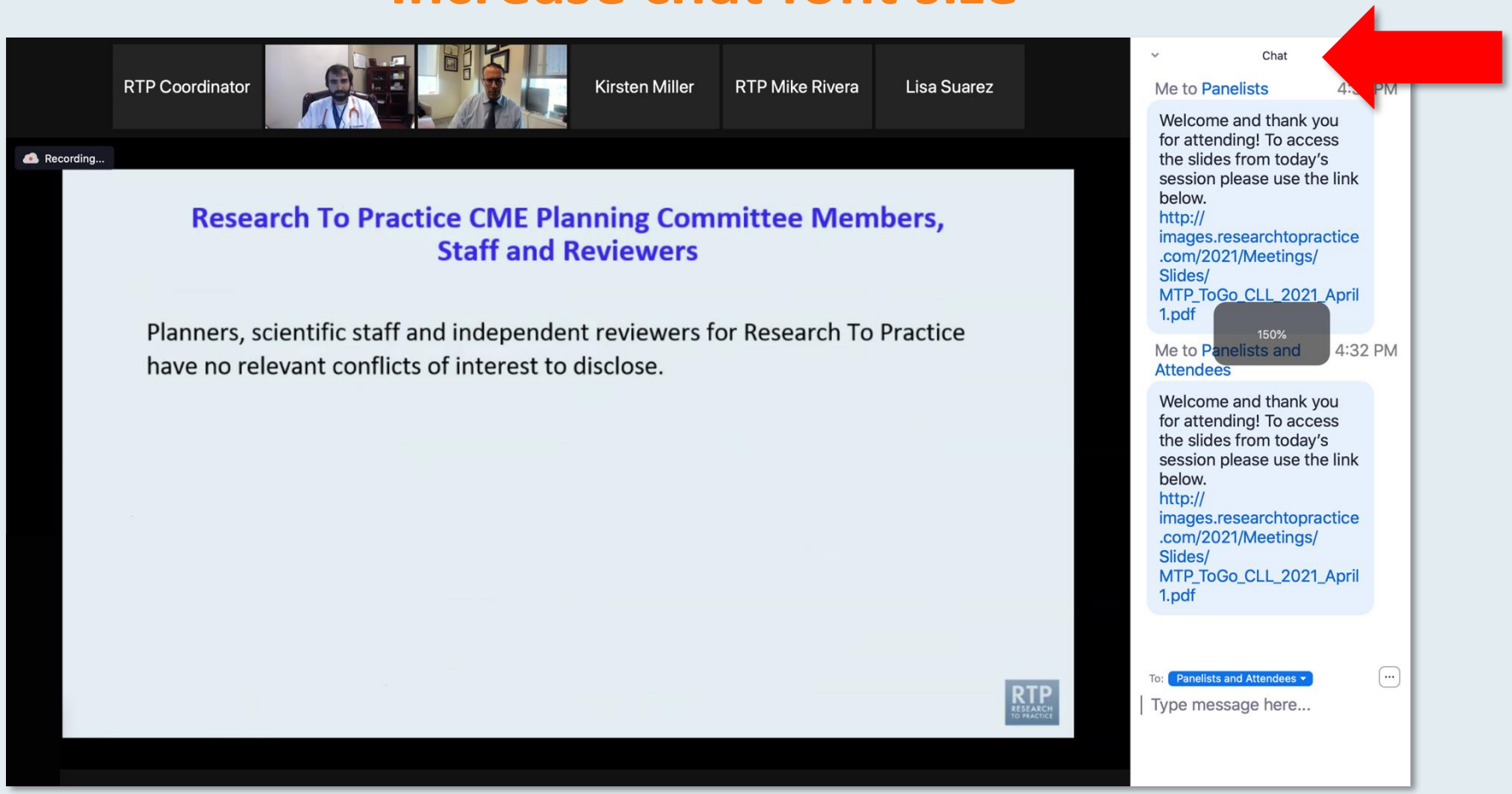

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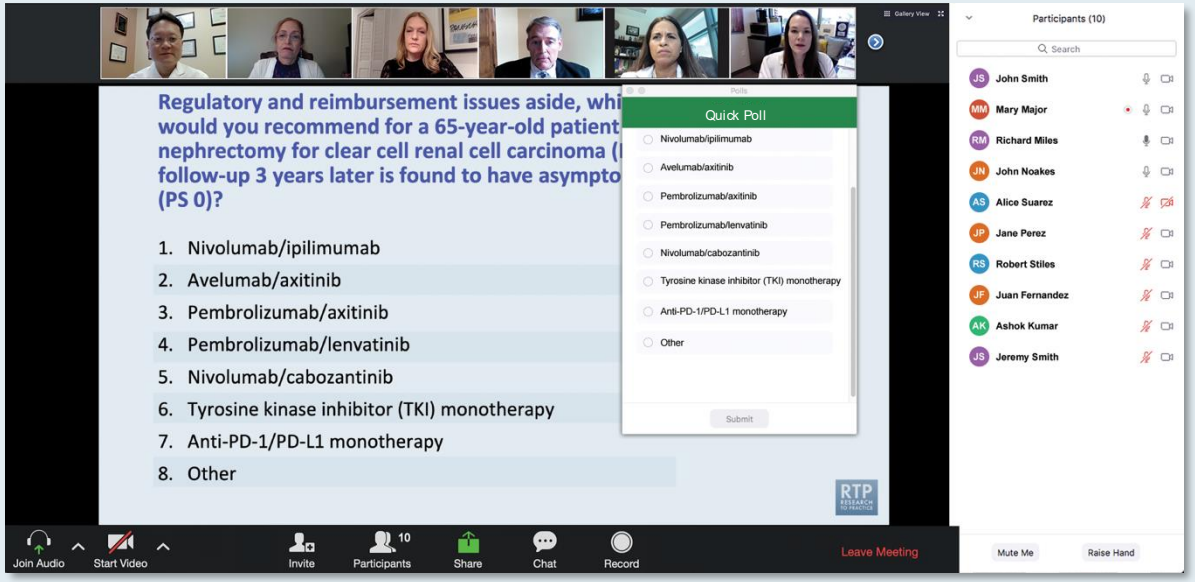

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DR RANA R MCKAY
UC SAN DIEGO MOORES CANCER CENTER

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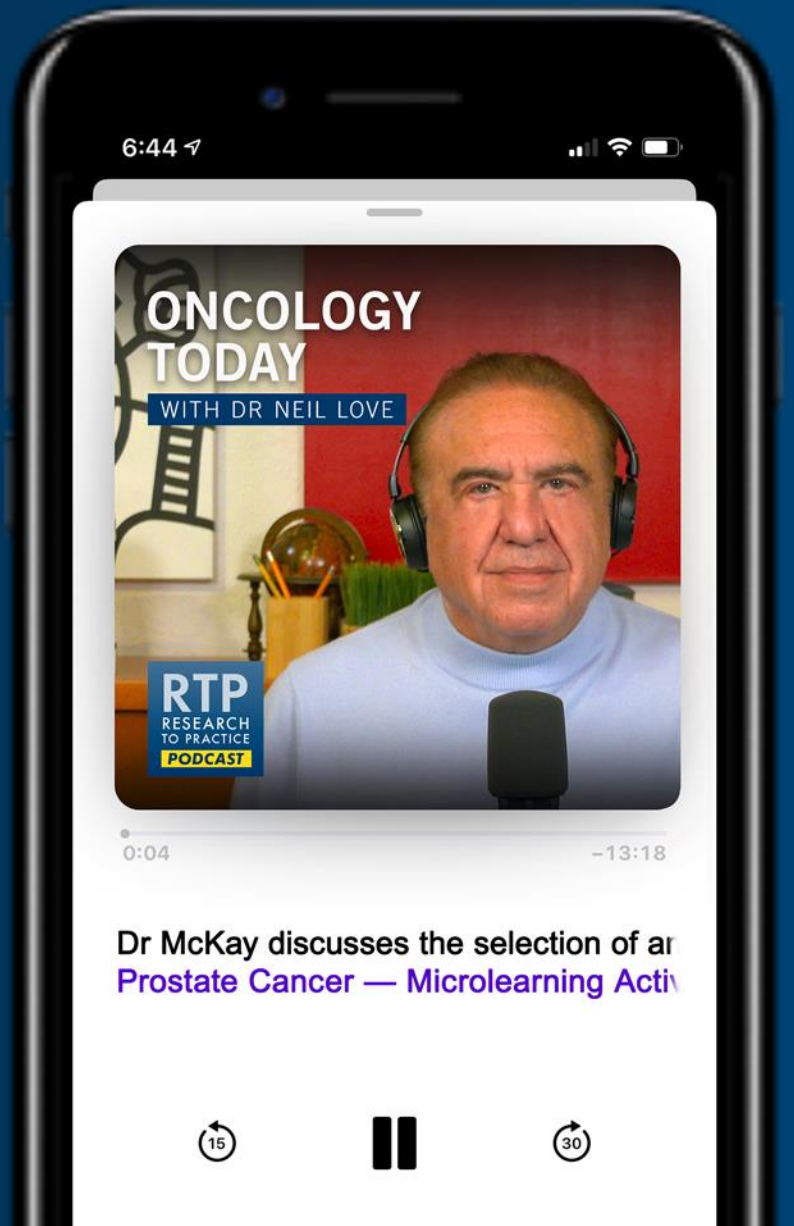

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Helena Yu, MD

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Regional Activities

Three Series

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The Ritz-Carlton Orlando, Grande Lakes | Orlando, Florida

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7:00 PM – 9:00 PM

Keynote Session: Diffuse Large B-Cell Lymphoma and Follicular Lymphoma

Manali Kamdar, MD, MBBS
Krish Patel, MD
Gilles Salles, MD, PhD

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MODULE 1: Hormonal therapy

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MODULE 5: New agents

Thank you for joining us!

Please take a moment to complete the survey currently up on Zoom.
Your feedback is very important to us.

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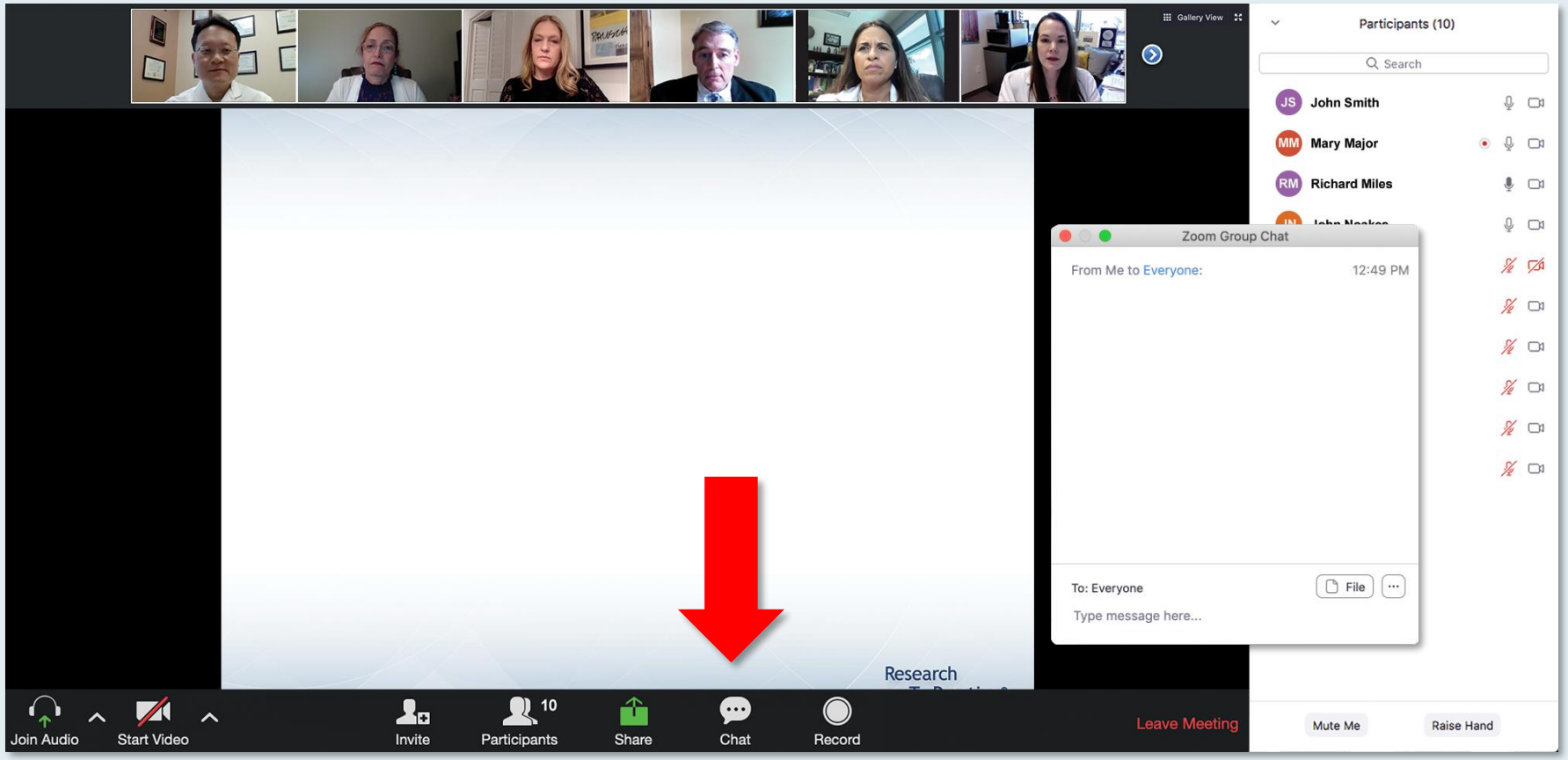

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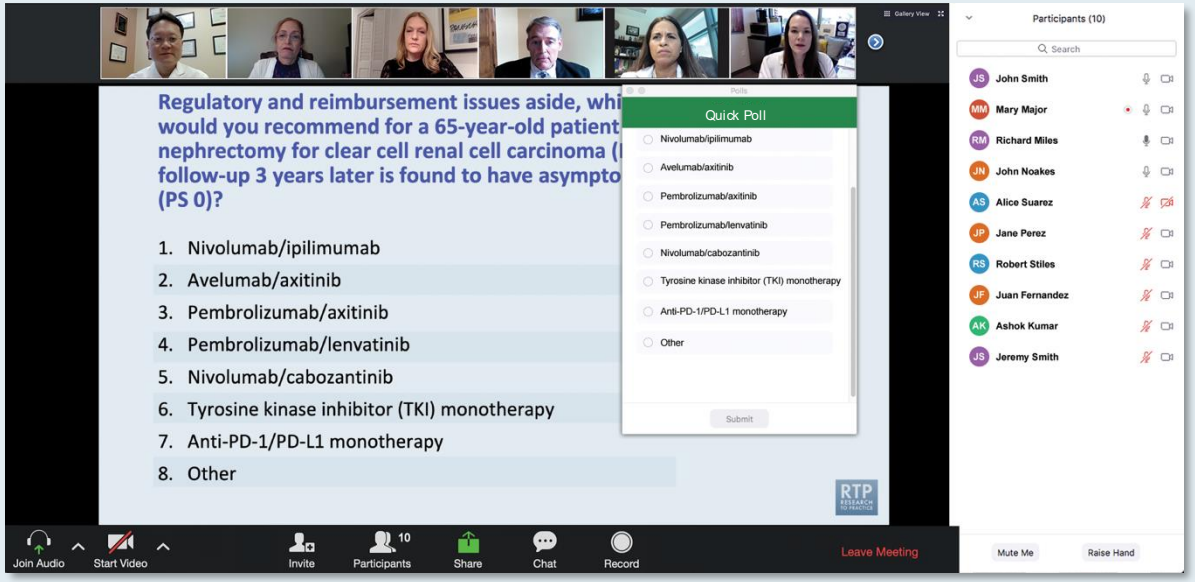

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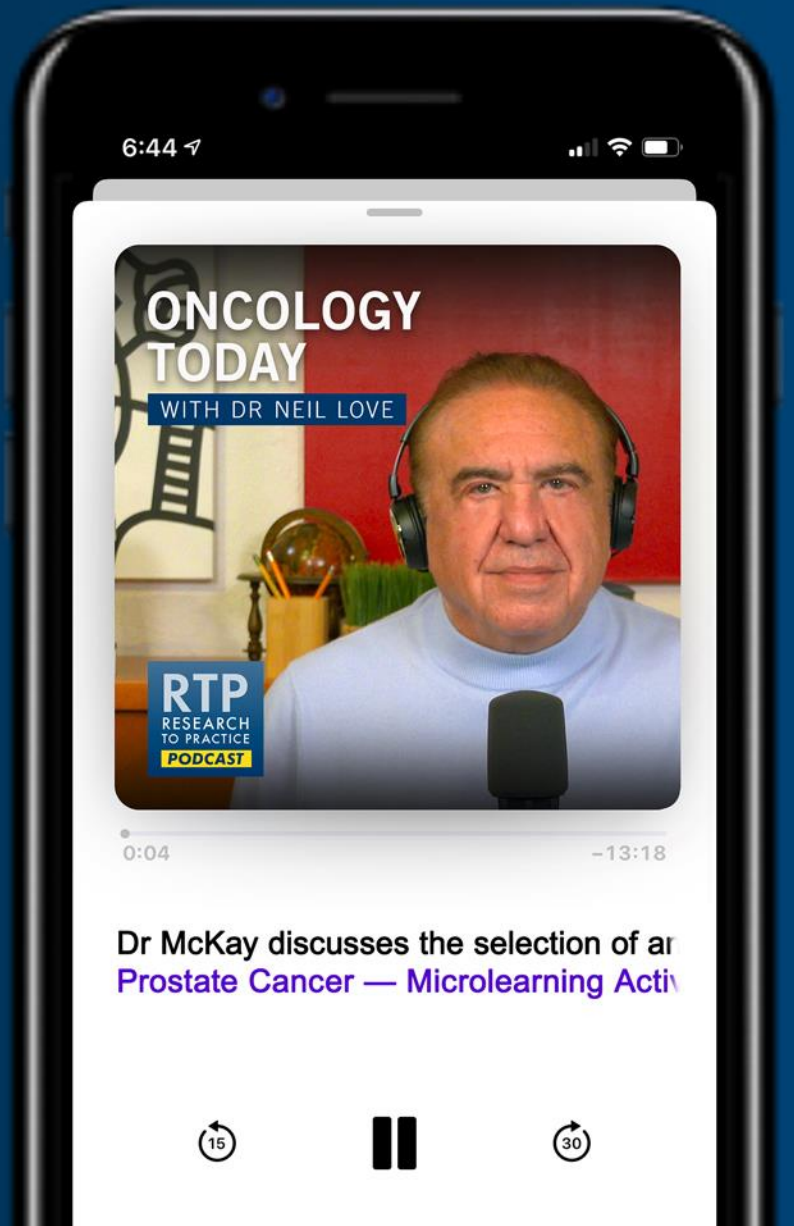

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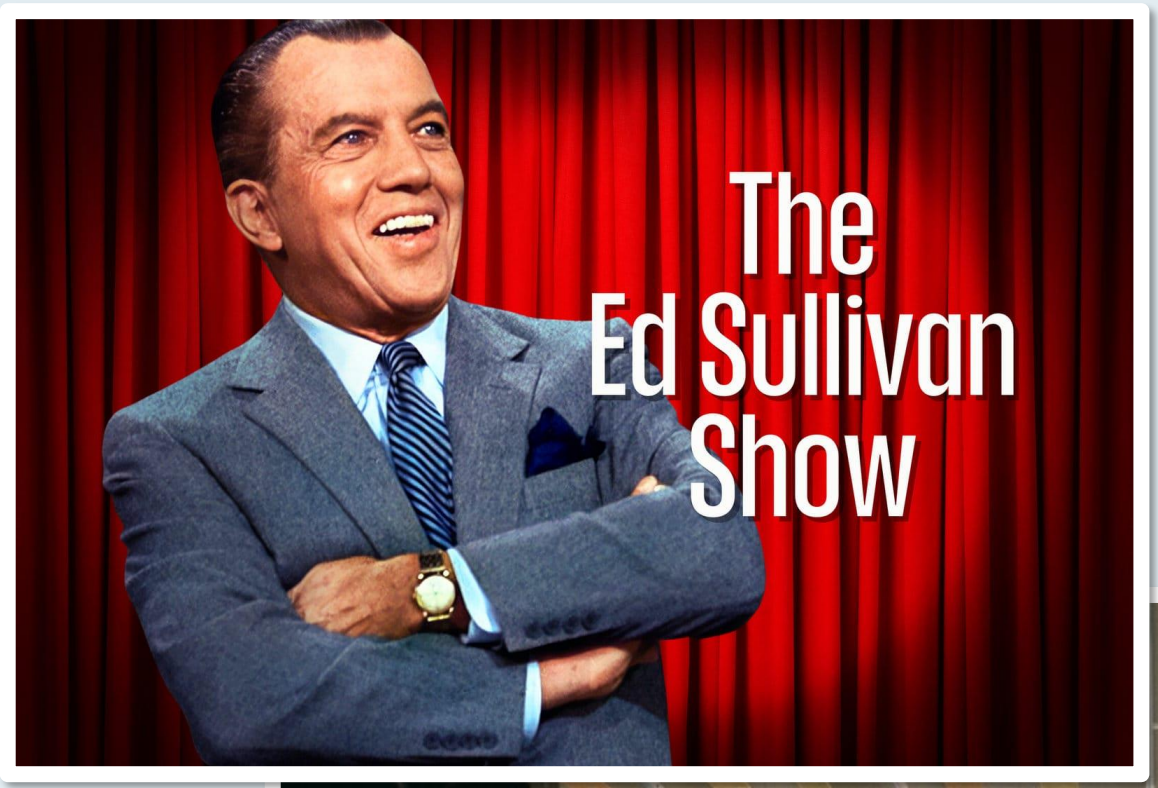
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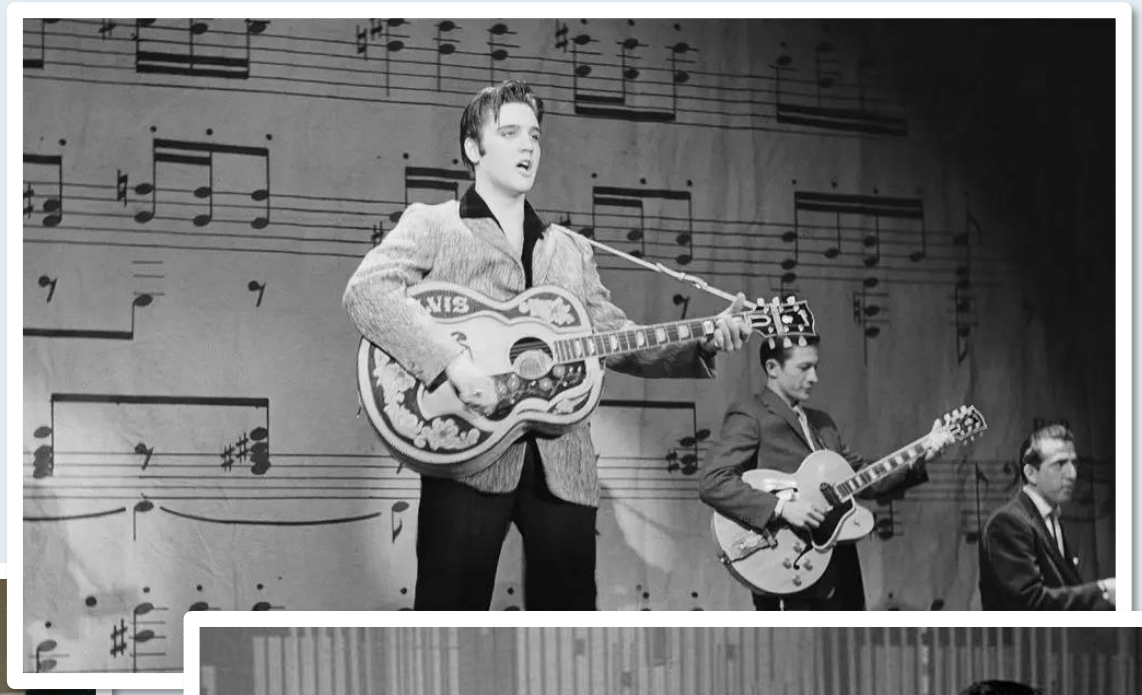
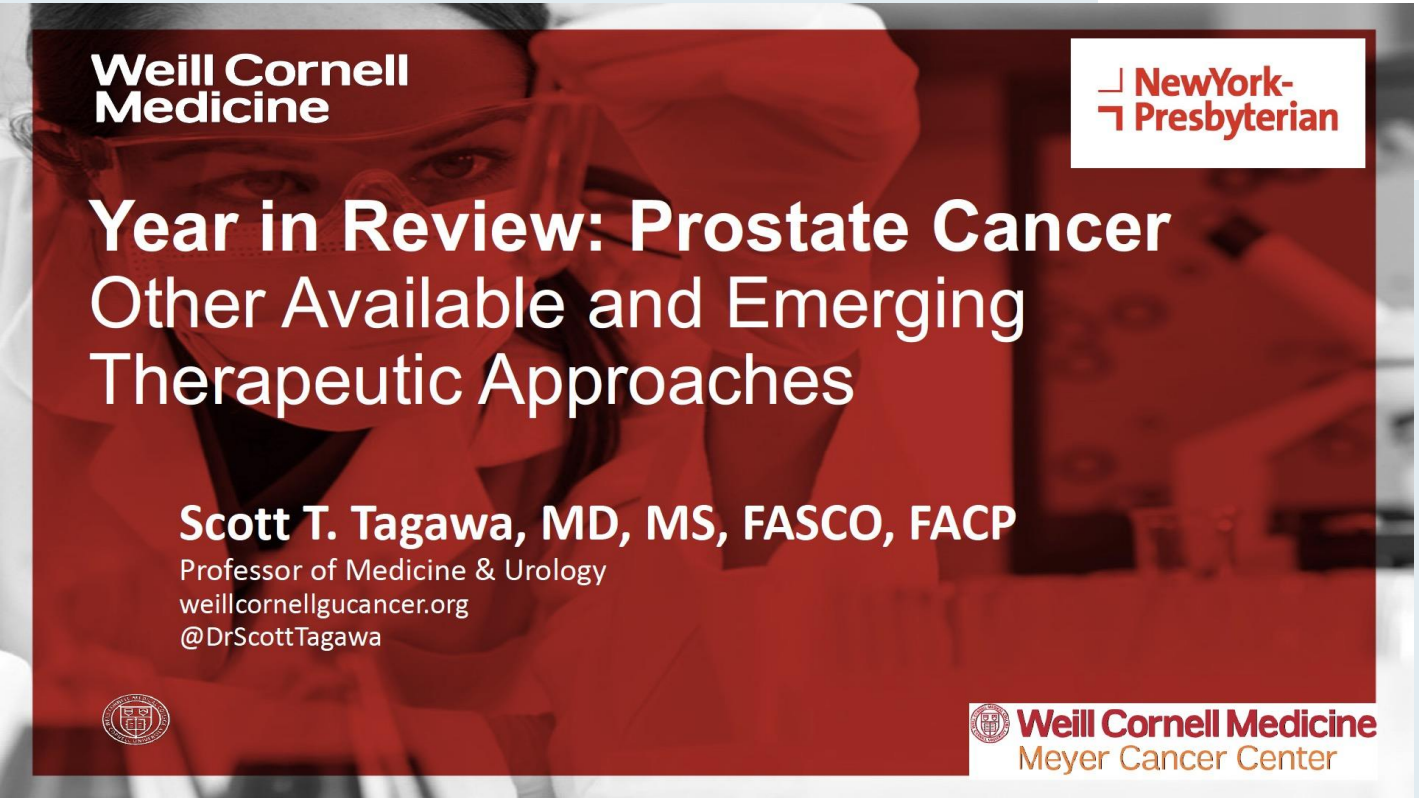


Year in Review: Optimizing the Role of Hormonal Therapy in the Care of Patients with Prostate Cancer

Andrew J Armstrong MD ScM FACP
March 2026
Professor of Medicine, Surgery, Pharmacology and Cancer Biology
Director of Research
Duke Cancer Institute's Center for Prostate and Urologic Cancers

Duke Cancer Institute
Center For Prostate & Urologic Cancers



RTP Year in Review 2026

Key Datasets

Andrew Armstrong, MD, ScM

- De La Cerda J et al. **Safety and tolerability of relugolix in combination with abiraterone or apalutamide** for treatment of patients with **advanced prostate cancer: Data** from a **52-week clinical trial**. *Target Oncol* 2025;20(3):503-17.
- McKay R et al. **Quality of life, adherence, and adverse events** among patients with **advanced prostate cancer** treated with **relugolix: 6-month results** of the **OPTYX multicenter registry**. Genitourinary Cancers Symposium 2026;Abstract 122.
- Francolini G et al. **Ultra-hypofractionated radiotherapy and concomitant oral relugolix** for treatment of **intermediate risk prostate cancer (ULTRA-HERO)**. Genitourinary Cancers Symposium 2026;Abstract TPS411.
- Shore ND et al. **Improved survival with enzalutamide** in **biochemically recurrent prostate cancer**. *N Engl J Med* 2025;[Online ahead of print].
- Freedland SJ et al. **Effects of enzalutamide on the sexual activity** of patients with **biochemically recurrent prostate cancer: A post hoc analysis** of **patient-reported outcomes** in the **EMBARK** study. *Eur Urol* 2025;87(5):507-11.
- Aggarwal R et al. **Final results from PRESTO**: A **phase III open-label** study of **combined androgen blockade** in patients (pts) with **high-risk biochemically relapsed prostate cancer (BRPC) (AFT-19)**. ESMO 2025;Abstract LBA88.

Key Datasets

Andrew Armstrong, MD, ScM (continued)

- Morgans A et al. **Health-related quality of life (HRQoL)** outcomes with **darolutamide** in the **phase 3 ARANOTE** trial. ASCO 2025;Abstract 5004.
- Grimm MO et al. **3-weekly docetaxel 75 mg/m^2** vs 2-weekly docetaxel 50 mg/m^2 in **combination with darolutamide + ADT** in patients with **mHSPC**: **Results** from the **randomised phase III ARASAFE** trial. ESMO 2025;Abstract LBA92.
- Fizazi K et al. **Capivasertib plus abiraterone** in **PTEN-deficient metastatic hormone-sensitive prostate cancer: CAPItello-281 phase III** study. *Ann Oncol* 2026;37(1):53-68.
- George DJ et al. **Patient reported outcomes (PRO) and tolerability** of **capivasertib (capi)** plus abiraterone (abi) versus placebo (pbo) plus abi in patients (pts) with **PTEN-deficient metastatic hormone-sensitive prostate cancer (mHSPC): CAPItello-281**. Genitourinary Cancers Symposium 2026;Abstract 14.
- Fizazi K et al. **OMAHA-004: Phase 3** trial of **CYP11A1 inhibitor opevesostat** versus androgen receptor pathway inhibitor (ARPI) switch in participants with **metastatic castration-resistant prostate cancer (mCRPC) after a prior ARPI**. Genitourinary Cancers Symposium 2026;Abstract TPS299.
- Yu E et al. OMAHA-003: **Phase 3 trial** of **CYP11A1 inhibitor opevesostat** versus androgen receptor pathway inhibitor (ARPI) switch in participants (pts) with **metastatic castration-resistant prostate cancer (mCRPC) after ARPI** and taxane-based chemotherapy. Genitourinary Cancers Symposium 2026;Abstract TPS298.

Key Datasets

Scott Tagawa, MD, MS

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- Chi KN et al. **Niraparib** and abiraterone acetate plus prednisone in **metastatic castration-resistant prostate cancer: Final overall survival analysis** for the **phase 3 MAGNITUDE** trial. *Eur Urol Oncol* 2025;8(4):986-98.
- Agarwal N et al. **Talazoparib plus enzalutamide** in men with **metastatic castration-resistant prostate cancer: Final overall survival results** from the randomised, placebo-controlled, **phase 3 TALAPRO-2** trial. *Lancet* 2025;406(10502):447-60.
- Hussain M et al. **Overall survival** from the **phase 2** trial of **abiraterone, olaparib, or abiraterone + olaparib** in **first-line metastatic castration-resistant prostate cancer (mCRPC) with DNA repair defects (BRCAAway)**. Genitourinary Cancers Symposium 2026;Abstract 16.
- Attard G et al. **Niraparib and abiraterone acetate plus prednisone** for **HRR-deficient metastatic castration-sensitive prostate cancer:** A randomized **phase 3** trial. *Nat Med* 2025;31(12):4109-18.
- Azad AA et al. **First interim efficacy analysis** of the **phase I/II PETRANHA** trial of **saruparib + androgen receptor pathway inhibitors (ARPI)** in patients (pts) with **metastatic prostate cancer (mPC)**. ESMO 2025;Abstract 2384MO.

Key Datasets

Scott Tagawa, MD, MS (continued)

- McKay R et al. **Phase III**, randomized, double-blind, placebo-controlled study of **adjuvant saruparib (AZD5305)** in patients with **BRCAm localized high-risk prostate cancer** who are receiving radiotherapy and androgen deprivation therapy **(EvoPAR-Prostate02)**. Genitourinary Cancers Symposium 2026;Abstract TPS412.
- Gallardo E et al. **Final overall survival results** from the **EORTC 1333/PEACE-3 trial: Enzalutamide with or without radium-223** in **metastatic castration-resistant prostate cancer**. Genitourinary Cancers Symposium 2026;Abstract 15.
- Fizazi K et al. **Final overall survival and safety** analyses of the **phase III PSMAfore** trial of **[(177)Lu]Lu-PSMA-617** versus change of androgen receptor pathway inhibitor in **taxane-naive** patients with **metastatic castration-resistant prostate cancer**. *Ann Oncol* 2025;36(11):1319-30.
- Tagawa ST et al. **Phase III** trial of **[177Lu]Lu-PSMA-617 combined with ADT + ARPI** in patients with **PSMA-positive metastatic hormone-sensitive prostate cancer (PSMAddition)**. ESMO 2025;Abstract LBA6.
- Stein MN et al. **Pasritamig**, a first-in-class, **bispecific T-cell engager targeting human kallikrein 2**, in **metastatic castration-resistant prostate cancer:** A **phase I** study. *J Clin Oncol* 2025;43(22):2515-26.
- De Bono J et al. IDeate-Prostate02: A **phase 1/2,** open-label **umbrella substudy** of **ifinatamab deruxtecan-based treatment combinations or as monotherapy** in participants with **previously treated metastatic castration-resistant prostate cancer**. Genitourinary Cancers Symposium 2026;Abstract TPS297.

Key Datasets

Scott Tagawa, MD, MS (continued)

- McKay R et al. **IDeate-Prostate01:** A **phase 3**, randomized, open-label study of **ifinatamab deruxtecan** versus docetaxel in participants with **previously treated metastatic castration-resistant prostate cancer**. Genitourinary Cancers Symposium 2026;Abstract TPS294.

Agenda
Prostate Cancer

INTRODUCTION: Evolution of the prostate cancer model; PCWG4

MODULE 1: Hormonal therapy

MODULE 2: Chemotherapy (docetaxel)

MODULE 3: PARP inhibition

MODULE 4: Radioligand therapy

MODULE 5: New agents

Special Articles

Trial Design and Objectives for Patients With Prostate Cancer: Recommendations From the Prostate Cancer Working Group 4

Andrew J. Armstrong, MD, ScM, FACP[1]; Michael J. Morris, MD[2]; Wassim Abida, MD, PhD[2]; Rahul R. Aggarwal, MD[3]; Emmanuel S. Antonarakis, MD[4]; Gerhardt Attard, MD, PhD[5]; Himisha Beltran, MD[6]; Alan Bryce, MD[7]; Michael A. Carducci, MD[8]; Heather H. Cheng, MD, PhD[9]; Delphine L. Chen, MD[9]; Kim N. Chi, MD[10]; Daniel S. Childs, MD[11]; William Dahut, MD[12]; Louise Emmett, MD, MBChB, FRACP[13]; Karim Fizazi, MD, PhD[14]; Andrei Ga ta, MD[15]; Daniel J. George, MD[1]; Ken Hermann, MD[16]; Michael S. Hofman, MBBS[17,42]; Thomas Hope, MD[18]; Maha Hussain, MD[19]; W. Kevin Kelly, DO[20]; Elizabeth Kessler, MD[21]; Phillip H. Kuo, MD, PhD[22]; Joshua Lang, MD[23]; Glenn Liu, MD[23]; Catherine H. Marshall, MD, MPH[8]; Alicia K. Morgans, MD, MPH[6]; Rana R. McKay, MD[24]; David Nanus, MD[25,43]; Peter Nelson, MD[26]; Channing Paller, MD[8]; Zachery R. Reichert, MD, PhD[27]; Charles J. Ryan, MD[2]; A. Oliver Sartor, MD[28]; Heiko Schöder, MD, MBA[2]; Lawrence H. Schwartz, MD[2]; Nima Shari , MD[29]; Walter M. Stadler, MD[30]; Mark Stein, MD[31]; Cora N. Sternberg, MD[32,33]; Russell Z. Szmulewitz, MD[34]; Scott T. Tagawa, MD, MS[35]; Alexandra O. Sokolova, MD[36]; Alex W. Wyatt, PhD[37,38]; Kosj Yamoah, MD, PhD[39,40]; Evan Y. Yu, MD[9]; Susan Halabi, PhD[41]; and Howard I. Scher, MD[2]; for the PCWG4 Writing Group

DOI https://doi.org/10.1200/JCO-25-02834

Prostate Cancer Working Group 4 (PCWG4)

"Our objective was to formulate updated criteria based on emerging evidence and clinical trial data in a biomarker context to provide guidance for clinical trial design, eligibility, and end point assessments for patients with advanced prostate cancer."

"PCWG4 redefines terminology around the disease state and previous therapies in a patient-centric context and terminology focused on androgen pathway modulation."

Armstrong AJ et al. *J Clin Oncol* 2026 February 26:JCO2502834.

PCWG4: Updates to Disease State Terminology

PCWG3 Terminology	PCWG4 Terminology
Localized	Localized
Rising PSA noncastrate[a]	Nonmetastatic APMN if no previous APM APMS if responded to previous APM
nmCRPC	Nonmetastatic APMR Metastatic (PET only) APMR
Clinical metastases Noncastrate[b]	Metastatic APMN if no previous APM APMS if responded to previous APM
mCRPC Specify lines of therapy	Metastatic APMR Specify previous therapies

APM = androgen pathway modulator; APMN/S/R = androgen pathway modulator-naïve/sensitive/resistant

Armstrong AJ et al. *J Clin Oncol* 2026 February 26:JCO2502834.

Agenda
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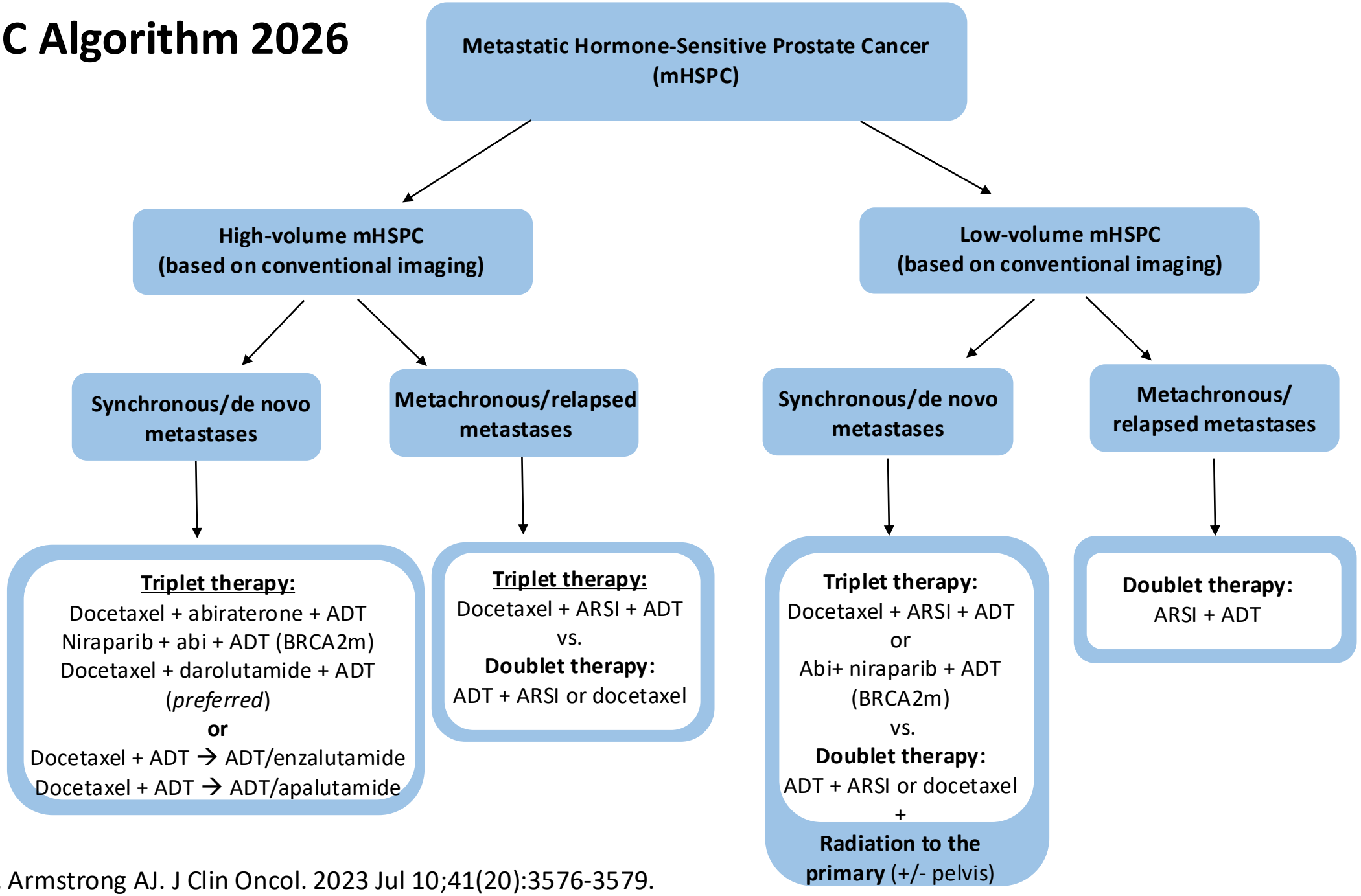
MODULE 5: New agents

2025 – Year of the Androgen Pathway Modulator-Naïve (APMN) Breakthrough

How do you think through the following in the management of APMN prostate cancer?

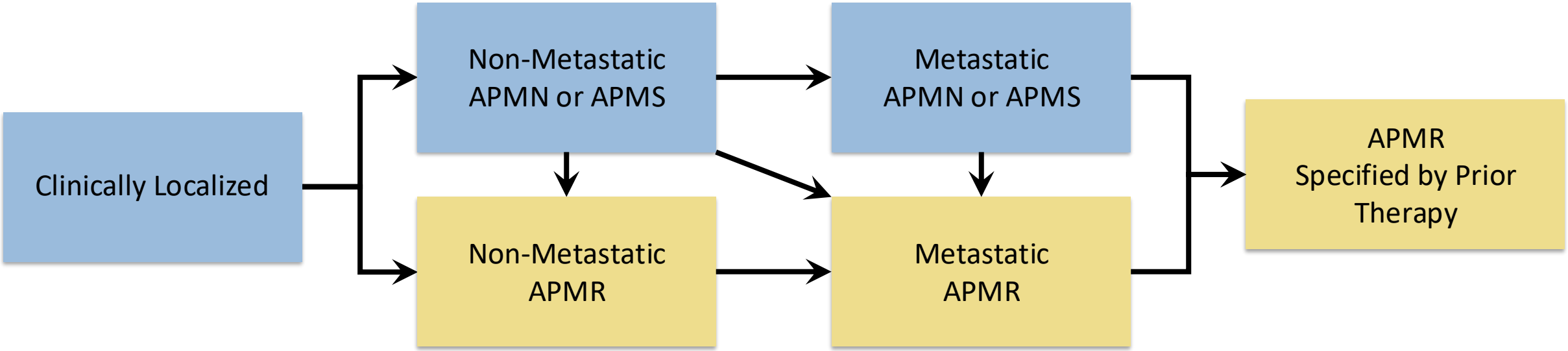
- De novo versus metachronous metastatic disease
- PSMA PET-positive, conventional imaging negative
- Biomarker implications (eg, PTEN, BRCA, HER2, MSI)

mHSPC Algorithm 2026



McManus HD, Armstrong AJ. J Clin Oncol. 2023 Jul 10;41(20):3576-3579.

PCWG4: new indications model and terminology



Androgen Pathway Modulation Sensitive (APMS) or Naïve (APMN)

Androgen Pathway Modulation Resistant (APMR)

Within each state, specify where relevant: 1) genotype (germline, somatic), 2) imaging modality used to define metastasis (PET, CT/MRI/bone scan), 3) disease characteristics and biomarkers critical for risk stratification, and 4) prior therapies.

APMN/S is the preferred term for hormone/castration naïve/sensitive disease (HSPC, CSPC) while APMR is the preferred term for castration/hormone resistant prostate cancer (CRPC/HRPC).

Armstrong AJ, Morris MJ…Scher HI
PCWG4; J Clin Oncol 2026

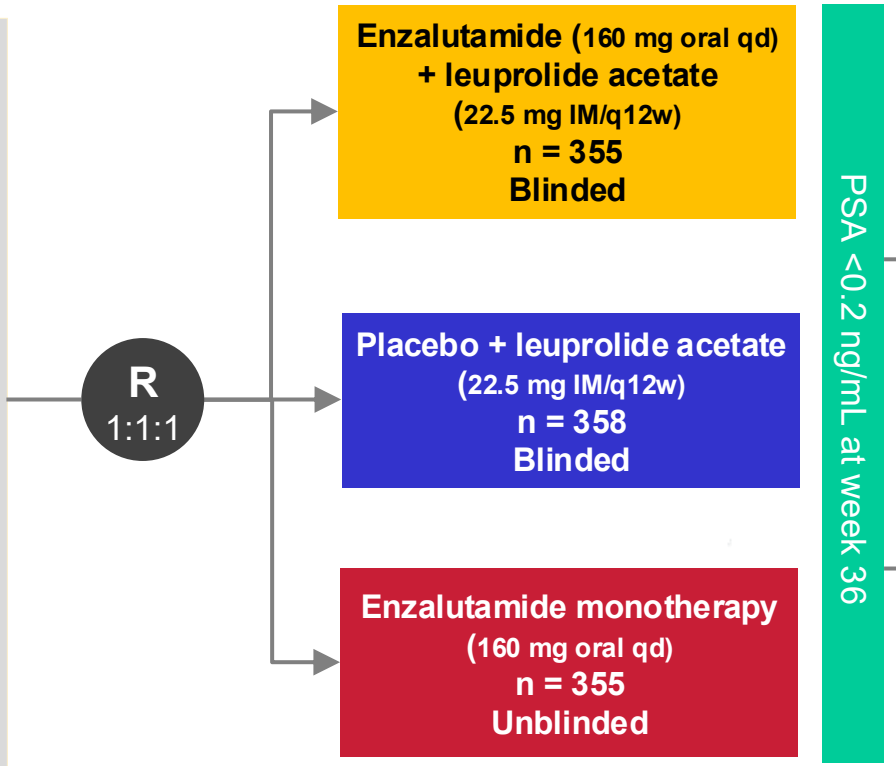
Management of Biomarker-Negative APMN

- When do you utilize intermittent endocrine therapy? Is this related to disease burden?
- What have you observed in terms of relief of treatment-related side effects when intermittent therapy is used? Which side effects are relieved first?
- In which situations, if any, are you offering enzalutamide or any other androgen blocker without ADT? How do you prevent gynecomastia, and what have you observed in terms of quality of life?

EMBARK study design

Patient population:
- Screening PSA ≥1 ng/mL after RP and at least 2 ng/mL above the nadir for primary EBRT
- PSADT ≤9 mo
- No metastases on bone scan or CT/MRI per central read
- Testosterone ≥150 ng/dL
- Prior hormonal therapy ≥9 mo prior to R (neoadjuvant/adjuvant for ≤36 mo OR ≤6 mo for rising PSA)

Stratification factors:
- Screening PSA (≤10 ng/mL vs. >10 ng/mL)
- PSADT (≤3 mo vs. >3 to ≤9 mo)
- Prior hormonal therapy (yes vs. no)



Primary endpoint[b]:
MFS by BICR, enzalutamide + leuprolide acetate vs. leuprolide acetate alone

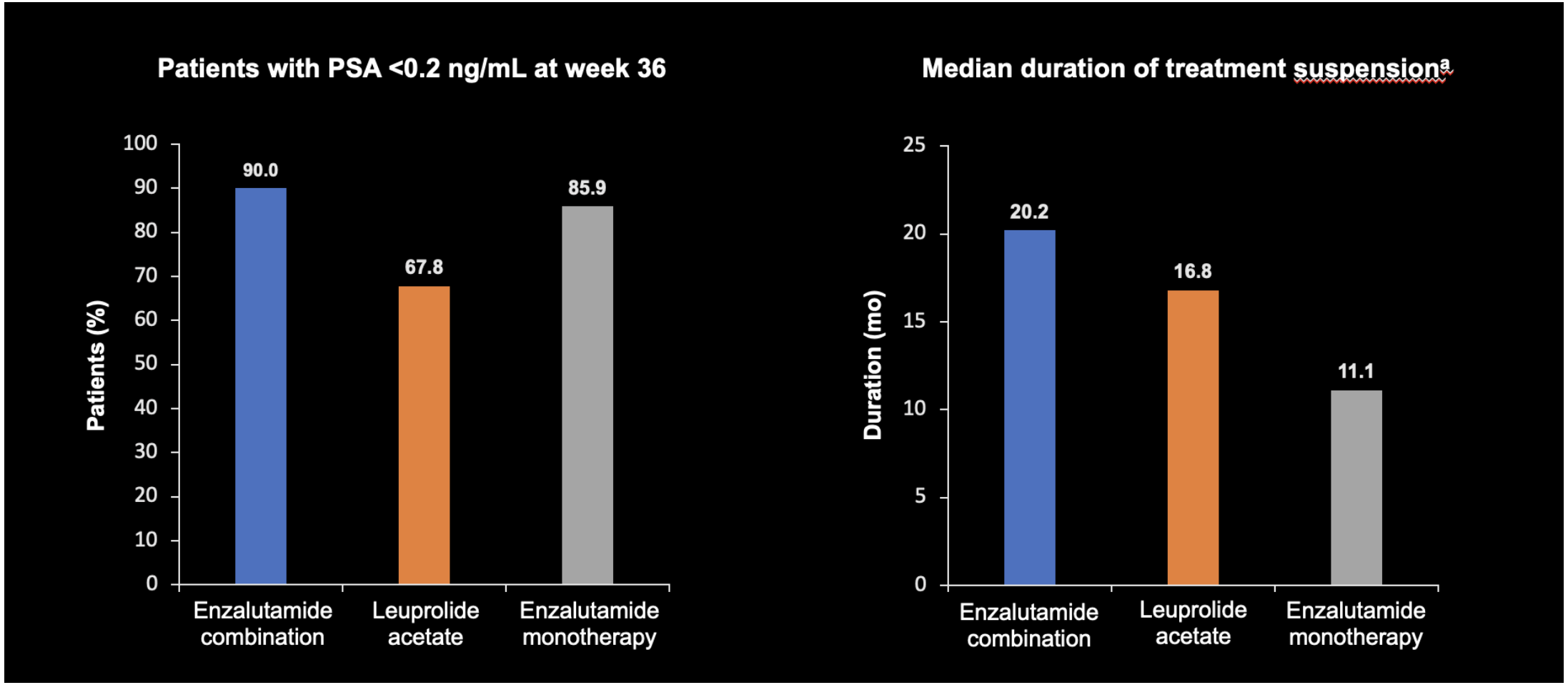
Key secondary endpoints[b,c]:
- MFS by BICR, enzalutamide monotherapy vs. leuprolide acetate alone
- Time to PSA progression
- Time to first use of new antineoplastic therapy
- OS[c]

Other secondary endpoints:
- Safety[d]

[a]Study treatment was suspended once at week 37 if PSA was <0.2 ng/mL and restarted when PSA was ≥5.0 ng/mL (without prior RP) and ≥2 ng/mL (prior RP). [b]Intent-to-treat population. [c]Primary endpoint and key secondary endpoints for enzalutamide combination and enzalutamide monotherapy are alpha-protected. *P*-value to determine significance for OS of combination and monotherapy treatment comparisons was dependent on outcomes of primary endpoint and key secondary endpoints. [d]Safety population. BICR, blinded independent central review; CT, computed tomography; d, day; EBRT, external beam radiotherapy; IM, intramuscular; MFS, metastasis-free survival; mo, month; MRI, magnetic resonance imaging; OS, overall survival; PSA, prostate-specific antigen; PSADT, PSA doubling time; q, every; R, randomization; RP, radical prostatectomy; w, weeks.

Courtesy of Andrew J Armstrong, MD, ScM

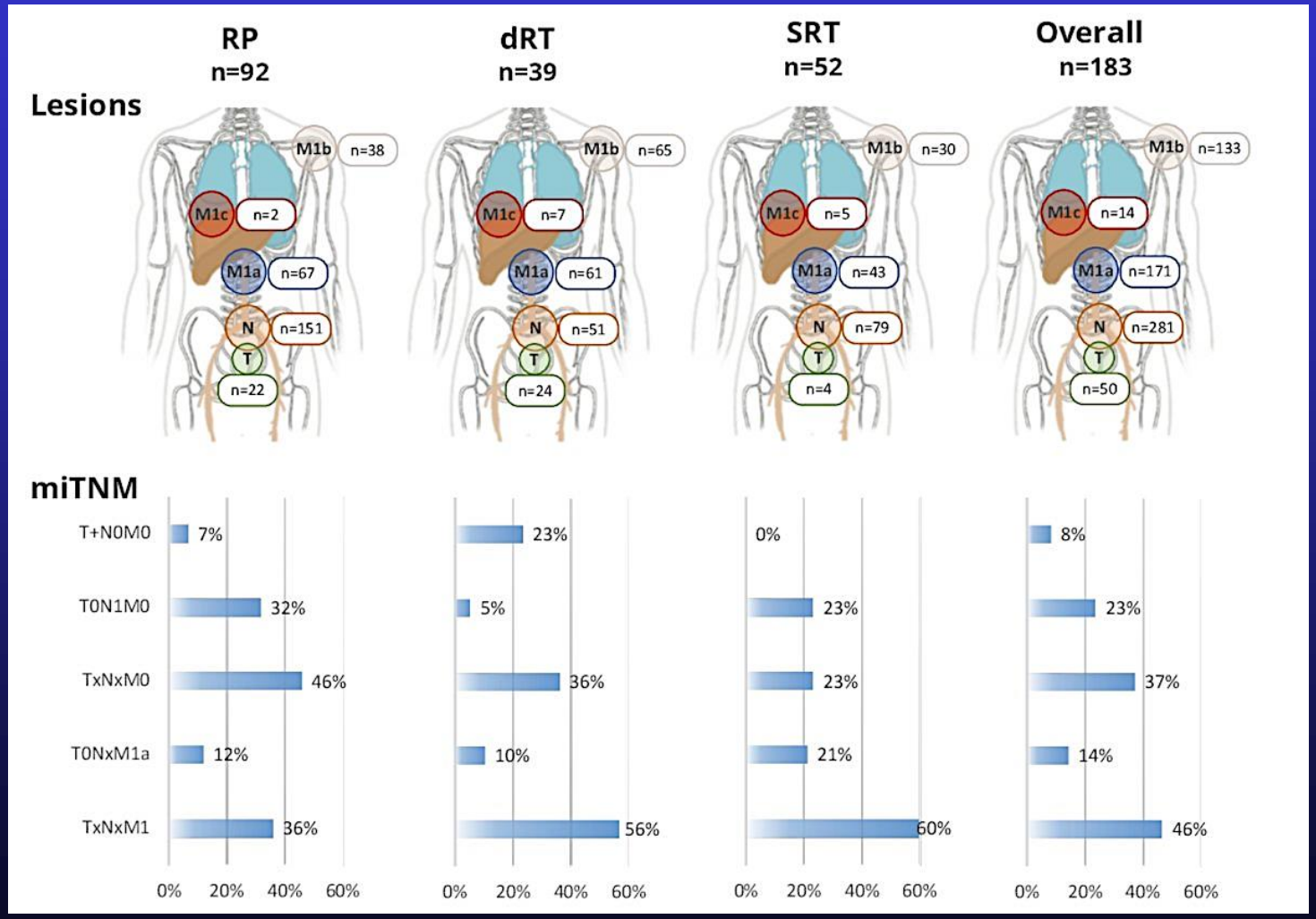
Secondary endpoint
Undetectable PSA and Duration of suspension



Freedland et al. NEJM Oct 2023

CHUM

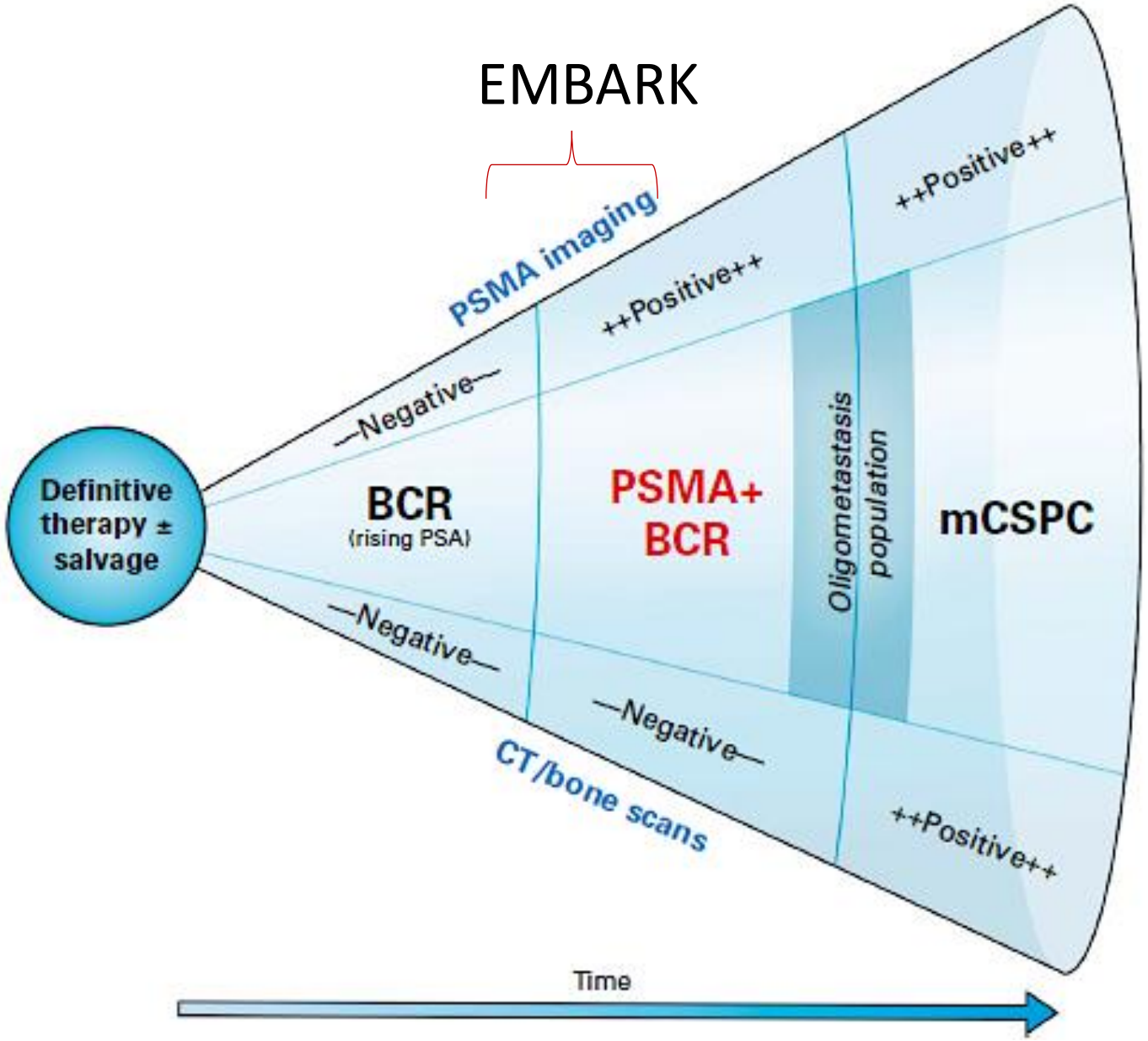
PSMA Imaging in EMBARK-like patients



- In total, 182 patients met EMBARK enrolment criteria
  - Median PSA 2.8 ng/ml
  - Median PSADT 3.6 months
- All had PSMA imaging
- Overall, 84% were PSMA positive
- 46% had distant metastases

Holzgreve et al. *JAMA Network Open*. 2025
Armstrong WR et al. ASCO 2023;Abstract 5091

Who are EMBARK Patients?



Epstein et al J Clin Oncol. 2025 Dec;43(34):3672-3683.

Management of Biomarker-Negative APMN

- **In which situations, if any, are you using relugolix? Does this depend on how long you believe the patient's treatment will be? Do you believe this is a benefit in terms of cardiovascular morbidity?**

Management of Biomarker-Negative APMN

- **If capivasertib were approved, would you discuss or recommend it? Is NGS sufficient or IHC necessary? How would you factor in percent positivity? In addition to improved efficacy with 95% or 100%, is the prognosis worse? How would you decide between a docetaxel triplet and capi triplet?**
- **What HbA1c level would you require to use it? Would you use it for a patient with well controlled Type 2 DM? Would you use preemptive phenformin?**
- **What's next for AKT inhibitors in prostate cancer? Do you anticipate that capivasertib will eventually be used in earlier settings or as a component of other combination strategies? Beyond PTEN deficiency, are there other genomic signatures that may predict benefit from capivasertib?**

Management of Biomarker-Negative APMN

- **What is your approach to the use of local therapy for oligometastatic disease?**

Safety and Tolerability of Relugolix in Combination with Abiraterone or Apalutamide for Treatment of Patients with Advanced Prostate Cancer: Data from a 52-Week Clinical Trial

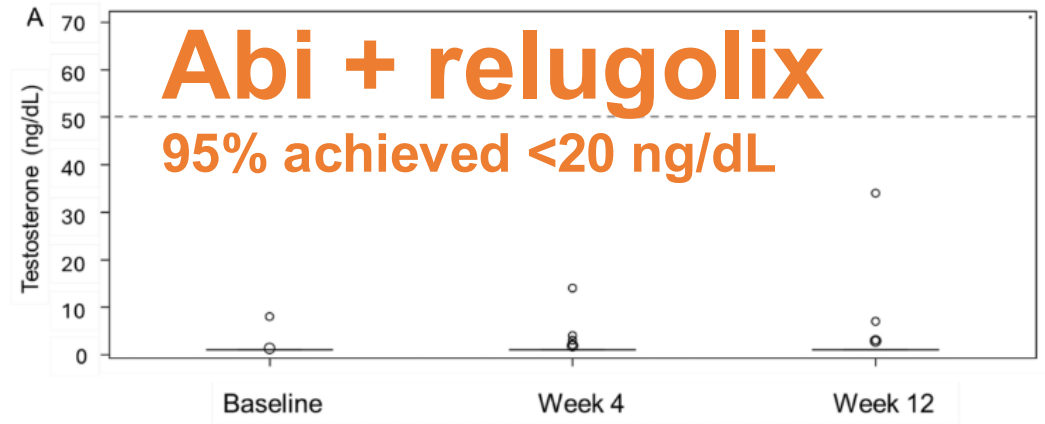
Jose De La Cerda[1] · Laurence Belkoff[2] · Kevin D. Courtney[3] · Elan Diamond[4] · James D'Olimpio[5] · Curtis Dunshee[6] · Lawrence Gervasi[7] · Michael Goodman[8] · Kriti Mittal[9] · David Morris[10] · Paul Sieber[11] · Ronald Tutrone[12] · Michael Ryan[13] · Yi Zhong[14] · Mike Ufer[15] · Neal Shore[16]

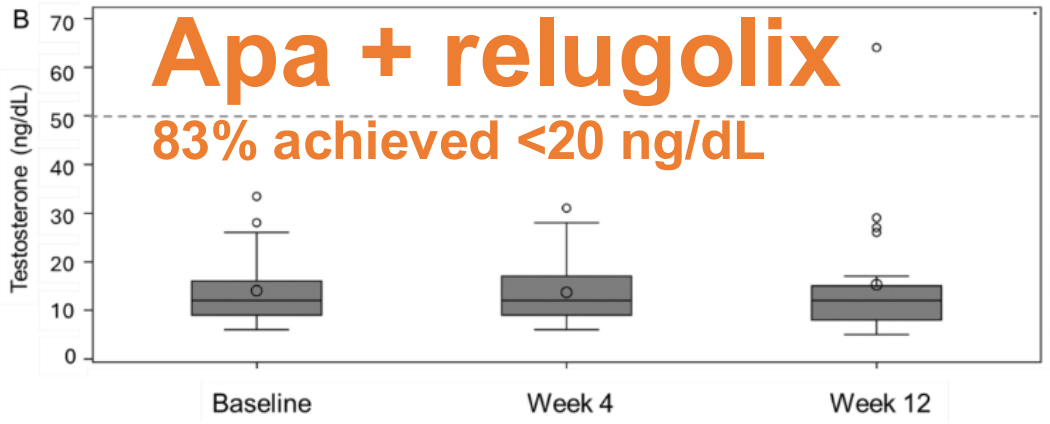
Key take-home point: if you give relugolix with apalutamide, the dose should be 240 mg/d (2x standard dose) due to CYP3A4/2C9/P-gp induction

No adjustments needed for abi (or enza/ darolutamide, not studied here)

Testosterone suppression and PSA decline efficacy was demonstrated

HTN seen with abi (25%) and rash seen with apa (21%)





De La Cerda J et al. Targeted Oncology 2025

McKay R et al. Quality of life, adherence, and adverse events among patients with advanced prostate cancer treated with relugolix: 6-month results of the OPTYX multicenter registry. Genitourinary Cancer Symposium 2026;Abstract 122.

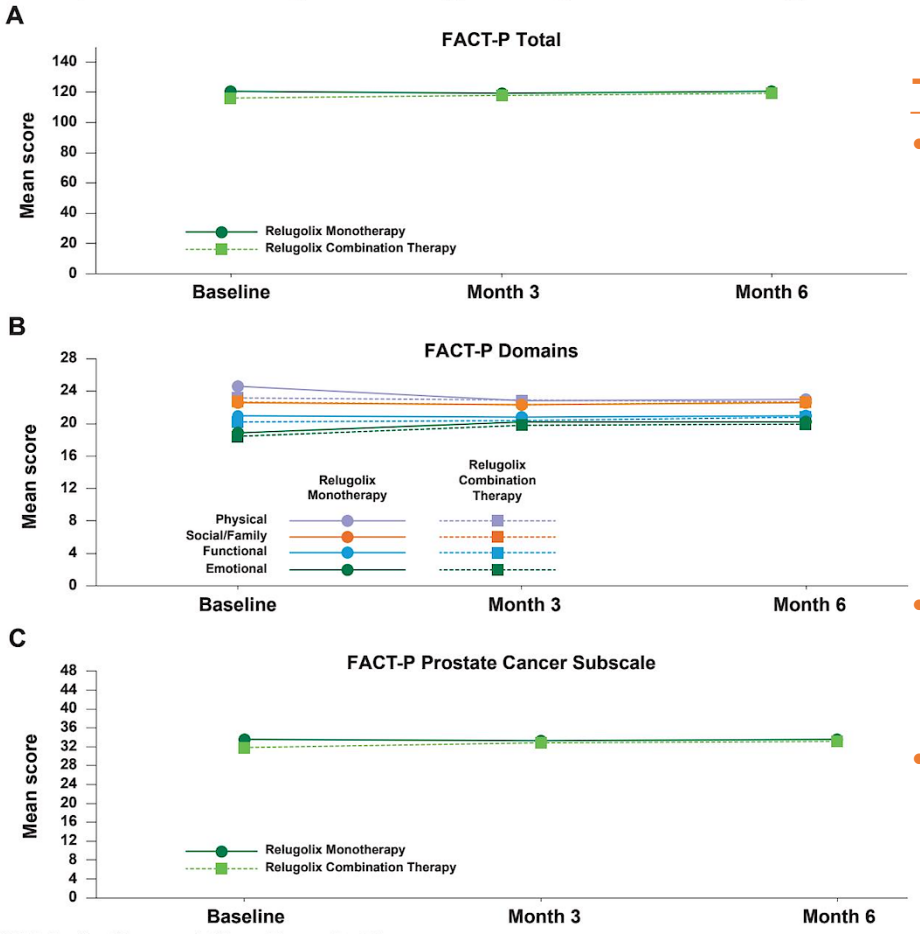
Key Enrollment Criteria	Assessments
• Men ≥18 years old with prostate cancer • Started relugolix treatment ≤1 month before enrollment, and remained on relugolix at the time of enrollment • No participants with relugolix intended treatment plan <4 months	• ***QoL:*** FACT-P • ***Adherence:*** SMAQ • ***Safety:*** SAEs, treatment discontinuation, death

FACT-P, Functional Assessment of Cancer Therapy–Prostate; QoL, quality of life; SAE, serious adverse events; SMAQ, Simplified Medication Adherence Questionnaire.

Patients with AE, n (%)	Relugolix monotherapy[a] (n=844)	Relugolix combination therapy[a,b] (n=155)	Total (N=999)
≥1 SAE	32 (3.8)	7 (4.5)	39 (3.9)
≥1 SAE related to study drug[c]	5 (0.6)	0	5 (0.5)
Discontinuations due to AE	50 (5.9)	11 (7.1)	61 (6.1)
Deaths	2 (0.2)	0	2 (0.1)
SAE occurring in ≥2 patients in either group			
Anemia	3 (0.4)	1 (0.6)	4 (0.4)
Acute myocardial infarction	3 (0.4)	0	3 (0.3)
Cardiac arrest	2 (0.2)	0	2 (0.2)
Chronic obstructive pulmonary disease	2 (0.2)	0	2 (0.2)
Septic shock	2 (0.2)	0	2 (0.2)

AE, adverse event; SAE, serious adverse event.
[a]Assessed at baseline.
[b]Therapies included in combination with relugolix were other systemic therapies for prostate cancer.
[c]SAEs related to relugolix included acute myocardial infarction in 2 patients and acute kidney injury, anemia, asthenia, atrial fibrillation, chest pain, dyspnea, QT prolongation, and hyperkalemia, each in 1 patient.

Figure 3. Mean FACT-P (A) Total, (B) Domain, and (C) Prostate Cancer Subscale Scores at Baseline, 3 Months, and 6 Months for Relugolix Monotherapy and Relugolix Combination Therapy



FACT-P, Functional Assessment of Cancer Therapy–Prostate.

Take Home:

- **Real-world use of relugolix alone or with other systemic therapies was well tolerated with only 6-7% discontinuing due to side effects and 17% reporting a missed dose over 6 mo**
- **CV AEs were very rare during this 6 mo follow up period**
- **Remains unclear if GnRH agonist vs antagonist provides differential CV safety**

CAPItello-281 Study Design

A global, multicentre, randomized, double-blind, Phase 3 study

Patients with PTEN deficient *de novo* mHSPC

- PTEN deficiency: (diagnostic cut-off of **≥90%** of viable malignant cells with **no specific cytoplasmic staining** by IHC)*
  - i.e. <10% of cells expressing PTEN by IHC

Of ~6,200 patients submitting tumour tissue **97%** had a valid IHC result and **25%** were **PTEN deficient**

1,012 patients (R 1:1)

Capivasertib	400 mg BID 4 days on, 3 days off
Abiraterone/pred **+ ADT**	1000 mg/5 mg QD + ADT
Placebo	400 mg BID 4 days on, 3 days off
Abiraterone/pred **+ ADT**	1000 mg/5 mg QD + ADT

Primary endpoint

- **Investigator assessed rPFS**

Secondary endpoints

- Overall survival
- Time to first subsequent therapy
- Symptomatic skeletal-event free survival
- Time to pain progression
- Time to castration resistance
- Time to PSA progression

Exploratory *post-hoc* PTEN deficiency subgroups

Stratification factors:†

- M1 volume (CHAARTED criteria) and visceral mets
- Geography

Study timeline

Current analysis

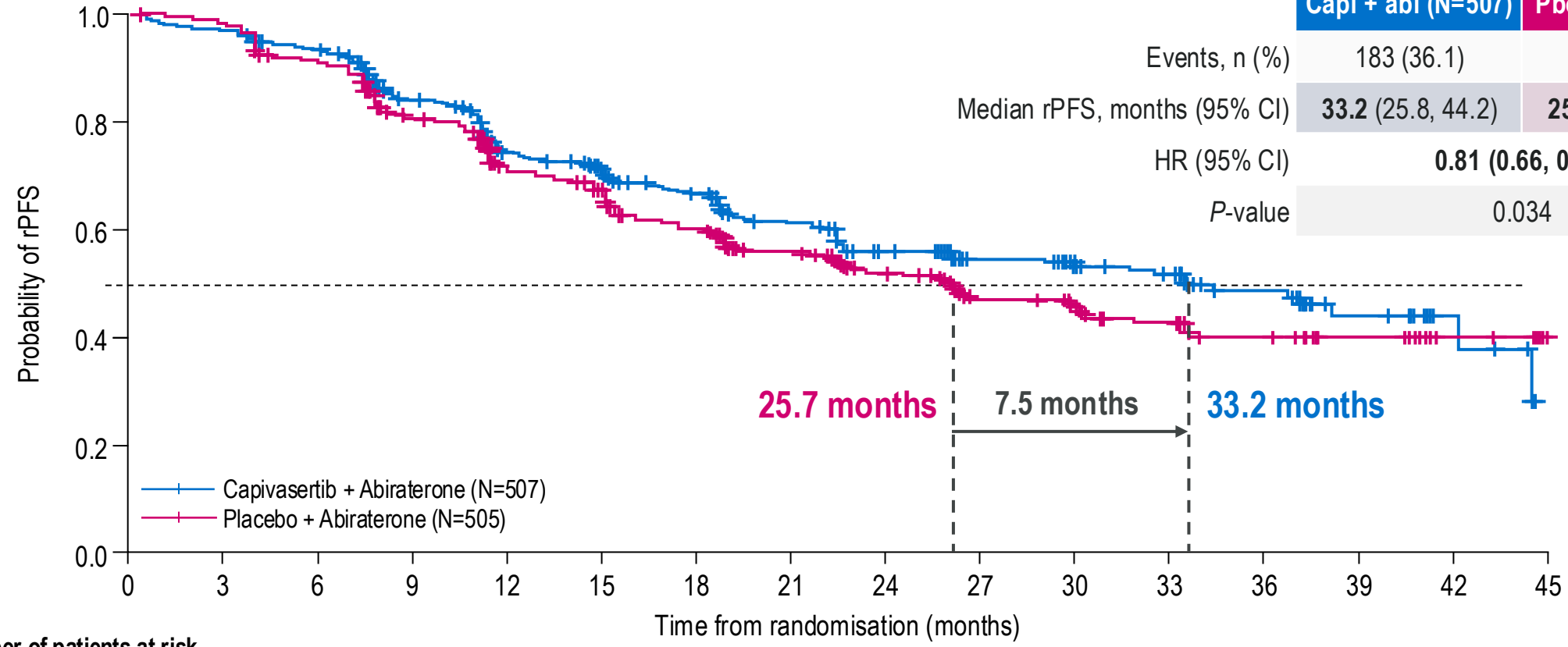
Enrolment period	Primary rPFS DCO	Final OS DCO
13 July 2020–5 Feb 2024	7 Oct 2024 Median rPFS follow-up:‡ ~18 mo	Planned for 522 deaths (52.2% maturity)

NCT04493853. Full eligibility criteria available in the online article. *Determined using investigational antibody for PTEN (SP218) (Roche Diagnostics).
†High-vol. disease with visceral mets, high-vol disease without visceral mets, low-vol. disease; North America; Western Europe and Australia; Latin America and Eastern Europe; Asia. ‡In censored patients.
ADT, androgen deprivation therapy; BID, twice daily; IHC, immunohistochemistry; mHSPC, metastatic hormone-sensitive prostate cancer; pred, prednisone/prednisolone; QD, once daily; rPFS, radiographic progression-free survival

Karim Fizazi MD, PhD
Abstract 2383O

CAPItello-281 Primary endpoint: investigator-assessed rPFS

	Capi + abi (N=507)	Pbo + abi (N=505)
Events, n (%)	183 (36.1)	215 (42.6)
Median rPFS, months (95% CI)	**33.2** (25.8, 44.2)	**25.7** (22.0, 29.9)
HR (95% CI)	**0.81 (0.66, 0.98)**	
P-value	0.034	



Number of patients at risk

Capi + abi	507	460	435	353	282	233	217	165	123	93	69	62	41	21	6	0
Pbo + abi	505	479	440	359	276	215	198	154	113	83	59	51	37	23	8	0

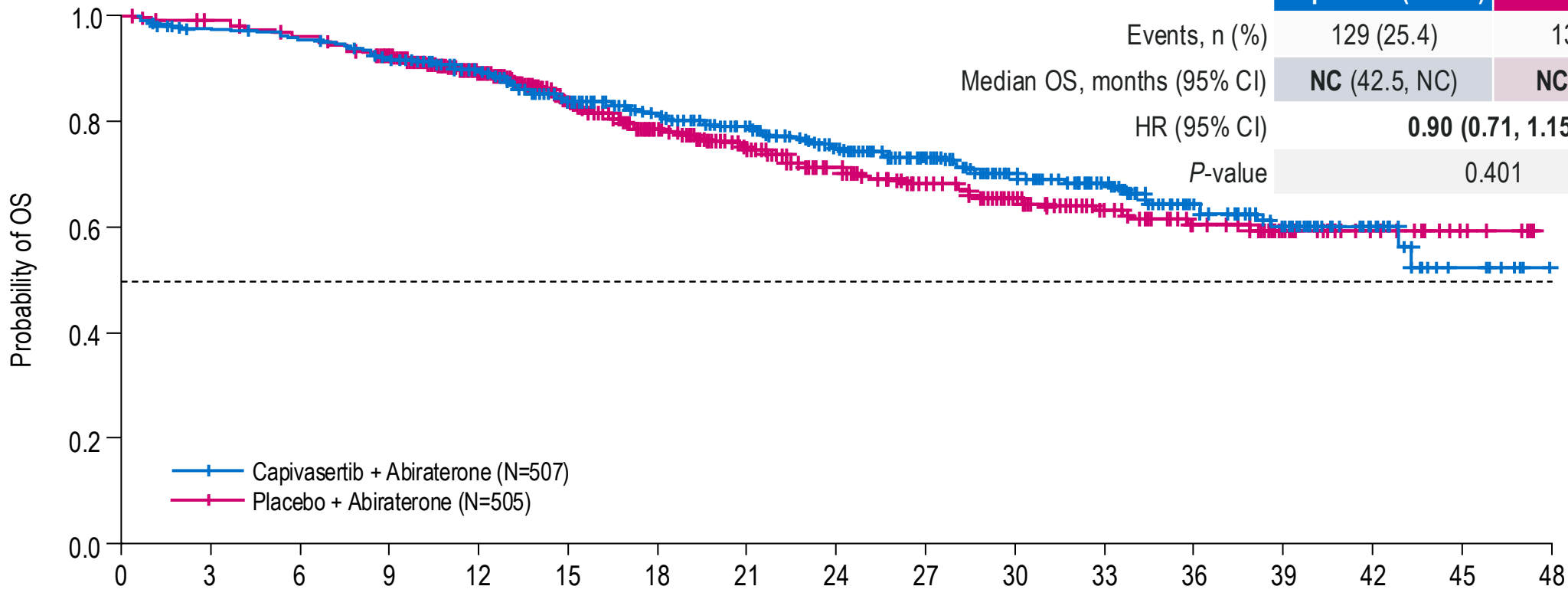
A stratified log-rank test was used to calculate two-sided P values. HRs and 95% CIs were calculated using a stratified Cox proportional-hazards model. Median follow-up: 18.4 months (capi + abi), 18.5 months (pbo + abi)
abi, abiraterone; capi, capivasertib; CI, confidence interval; HR, hazard ratio; pbo, placebo; rPFS, radiographic progression-free survival

Karim Fizazi MD, PhD
Abstract 2383O

CAPItello-281: Interim OS

OS analysis was conducted at 26% maturity, further follow-up is planned

	Capi + abi (N=507)	Pbo + abi (N=505)
Events, n (%)	129 (25.4)	138 (27.3)
Median OS, months (95% CI)	**NC** (42.5, NC)	**NC** (NC, NC)
HR (95% CI)	**0.90 (0.71, 1.15)**	
P-value	0.401	



Number of patients at risk

Capi + abi	507	487	476	447	400	335	286	242	199	164	128	96	60	42	22	7	0
Pbo + abi	505	494	479	449	388	330	273	227	188	153	113	88	56	33	19	7	0

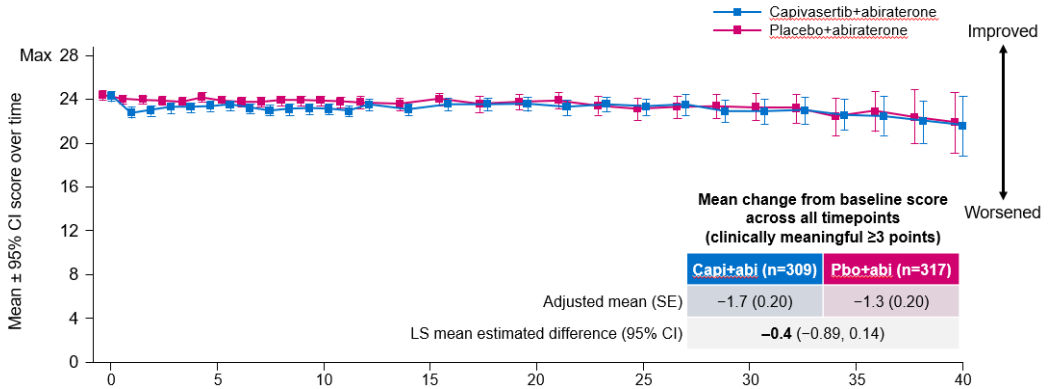
A stratified log-rank test was used to calculate two-sided P values. HRs and 95% CIs were calculated using a stratified Cox proportional-hazards model.
CI, confidence interval; HR, hazard ratio; NC, not calculable; OS, overall survival; pbo, placebo

Karim Fizazi MD, PhD
Abstract 2383O

George DJ et al. Patient reported outcomes (PRO) and tolerability of capivasertib (capi) plus abiraterone (abi) versus placebo (pbo) plus abi in patients (pts) with PTEN-deficient metastatic hormone-sensitive prostate cancer (mHSPC): CAPItello-281. Genitourinary Cancer Symposium 2026;Abstract 14.

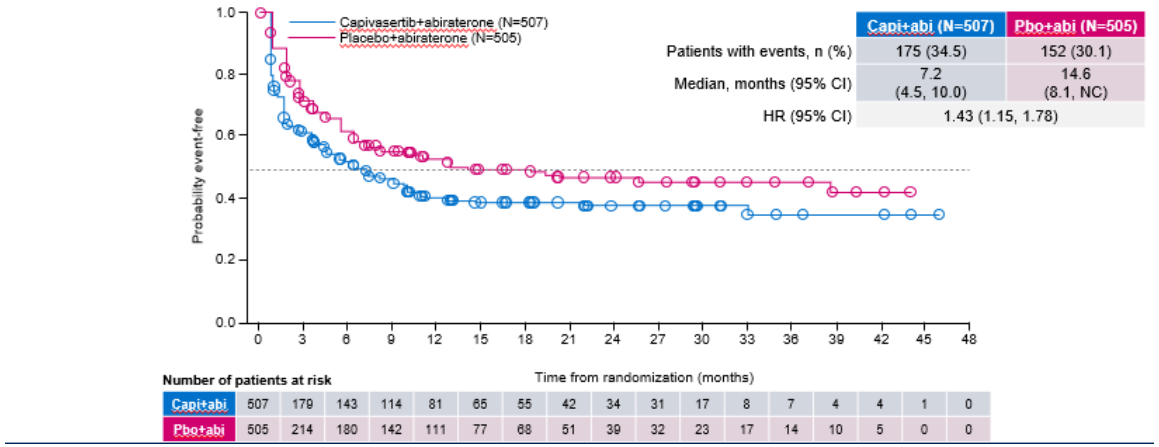
CAPItello-281: FACT–P physical wellbeing (PWB)

PWB includes outcomes such as side effects, energy, nausea and pain



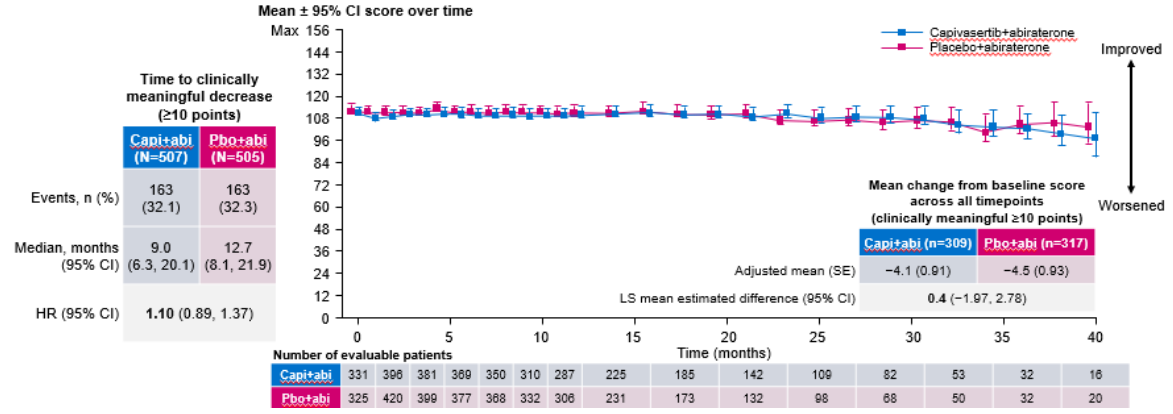
CAPItello-281: time to clinically meaningful decrease in FACT–P physical wellbeing (PWB)

PWB includes outcomes such as side effects, energy, nausea and pain

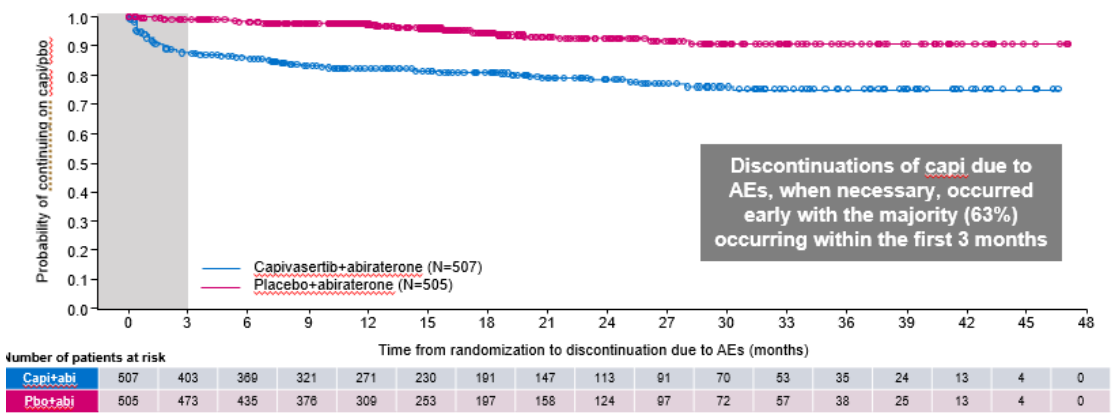


CAPItello-281: FACT–P total score

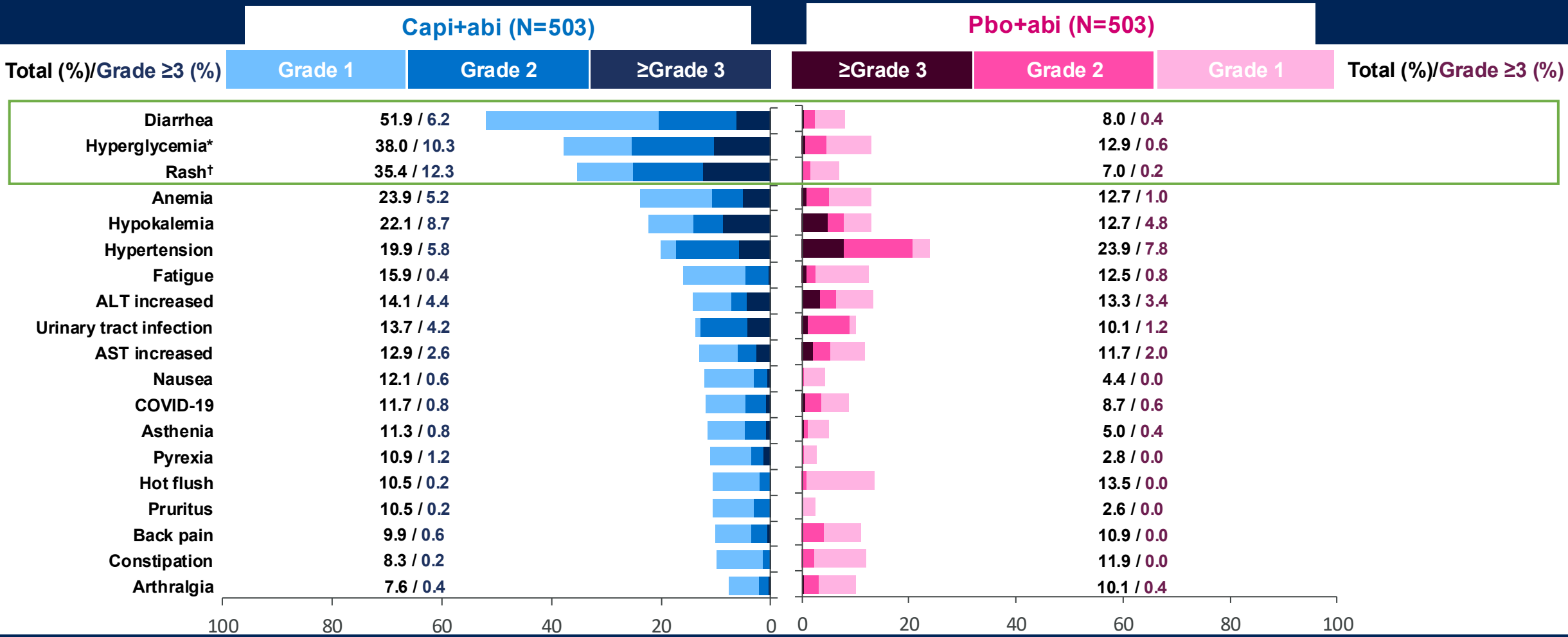
FACT–P total score includes physical, functional and emotional wellbeing, as well as prostate cancer symptoms



CAPItello-281: Discontinuations due to AEs



CAPItello-281: investigator-reported AEs (≥10% of patients)



Diabetic ketoacidosis was reported in six patients (1.2%) in the capi+abi arm and zero patients in the pbo+abi arm

*Grouped term (includes the preferred terms of blood glucose increased, hyperglycemia); †Grouped term (includes the preferred terms of erythema, rash, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pruritic). abi, abiraterone; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase;capi, capivasertib; pbo, placebo; PTEN, phosphatase and tensin homolog

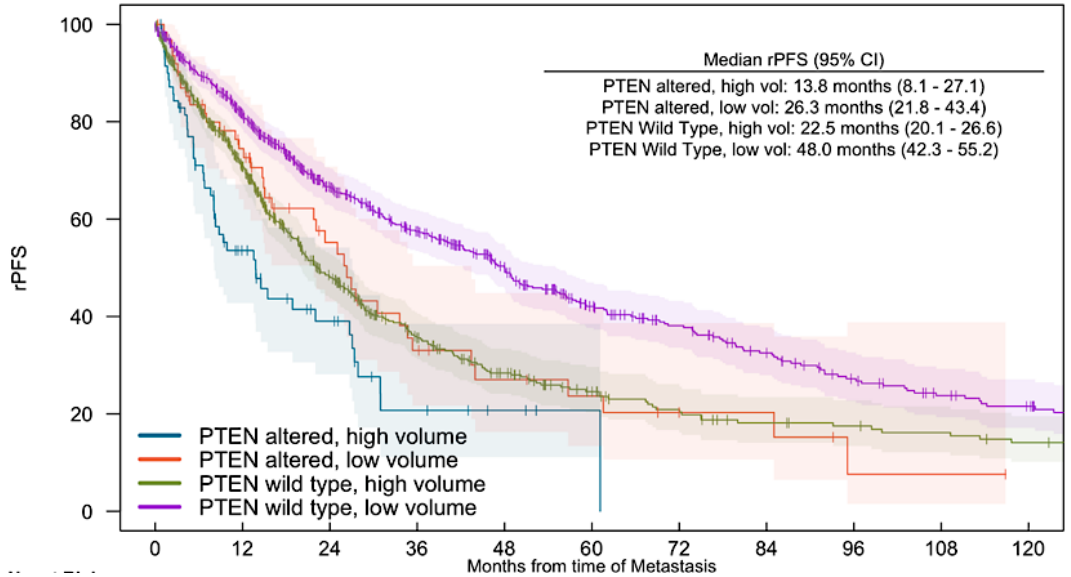
CAPItello-281: common AEs associated with AKT inhibition

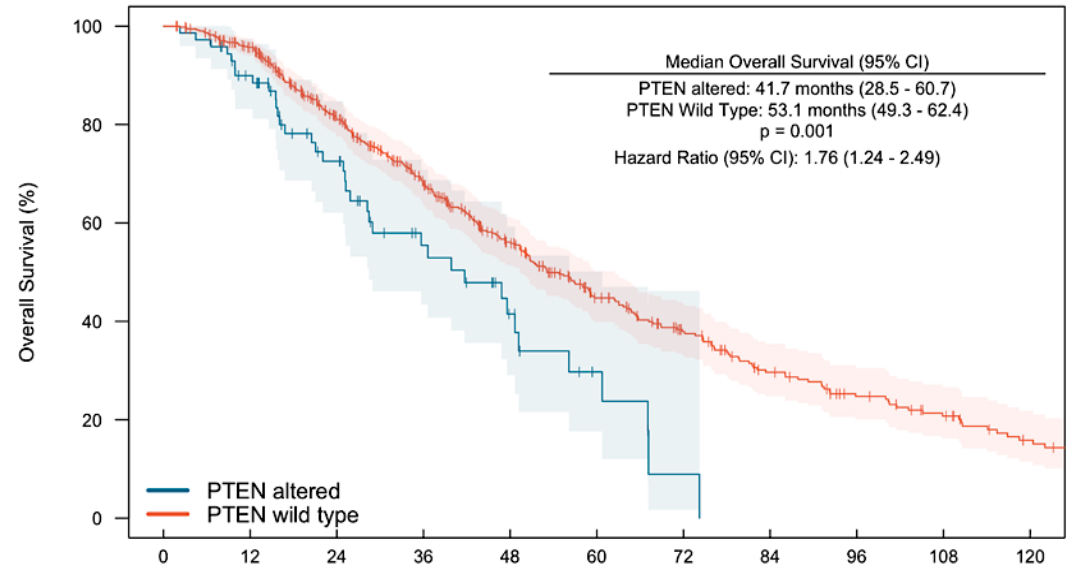
	Rash*		Diarrhea		Hyperglycemia†	
	Capi+abi (N=503)	Pbo+abi (N=503)	Capi+abi (N=503)	Pbo+abi (N=503)	Capi+abi (N=503)	Pbo+abi (N=503)
Any grade AE, n (%)	178 (35.4)	35 (7.0)	261 (51.9)	40 (8.0)	191 (38.0)	65 (12.9)
Grade ≥3 AE,‡ n (%)	62 (12.3)	1 (0.2)	31 (6.2)	2 (0.4)	52 (10.3)	3 (0.6)
Median (IQR) time to onset, days	13 (11–43)	78 (37–195)	12 (3–43)	142 (28–339)	54 (15–114)	114 (71–326)
AE leading to, n (%)						
Interruption of capi/pbo	85 (16.9)	3 (0.6)	63 (12.5)	1 (0.2)	55 (10.9)	4 (0.8)
Reduction of capi/pbo	43 (8.5)	2 (0.4)	22 (4.4)	0	33 (6.6)	1 (0.2)
Discontinuation of capi/pbo	24 (4.8)	0	5 (1.0)	0	5 (1.0)	0
Supportive treatment given, n (%)	146 (29.0)	20 (4.0)	167 (33.2)	19 (3.8)	127 (25.2)	23 (4.6)
Outcome at time of DCO, n (%)						
Recovered/recovering	164 (32.6)	28 (5.6)	238 (47.3)	36 (7.2)	140 (27.8)	43 (8.5)
Not recovered	24 (4.8)	8 (1.6)	45 (8.9)	4 (0.8)	65 (12.9)	25 (5.0)

*Grouped term including the preferred terms of erythema, rash, rash erythematous, rash macular, rash maculopapular, rash papular, rash pruritic. †Grouped term including the preferred terms of blood glucose increased, hyperglycemia. ‡A diarrhea AE of Grade 4 was reported for one patient (0.2%) in the capi+abi arm only, hyperglycemia AEs of Grade 4 and Grade 5 were reported for one patient (0.2%) each in the capi+abi arm only, no Grade 4–5 AEs of rash were reported. No primary prophylaxis interventions were used during the CAPItello-281 trial for prospective AE management. Additional data on supportive treatment received are available via QR code.
abi, abiraterone; AE, adverse event; capi, capivasertib; DCO, data cutoff; IQR, interquartile range; pbo, placebo

My Takeaways: Capitello-281

- PTEN loss is associated with worse rPFS and OS with ADT/ARPI therapy in men with mHSPC. See our data from the PROMISE registry (Thapa and Kilmari, manuscript submitted)
- Similar poor outcomes seen in Capitello-281 (25.7 mo vs LATTITUDE (33.0 mo), with frequent PSA-radiographic discordant progression
- Capi/abi improves rPFS but does not yet improve OS, and is associated with more toxicities, short term worsening of QOL, and treatment discontinuations
- Unclear if this will represent a new standard of care without improved survival





Courtesy of Andrew J Armstrong, MD, ScM

Agenda
Prostate Cancer

INTRODUCTION: Evolution of the prostate cancer model; PCWG4

MODULE 1: Hormonal therapy

MODULE 2: Chemotherapy (docetaxel)

MODULE 3: PARP inhibition

MODULE 4: Radioligand therapy

MODULE 5: New agents

Questions About Chemotherapy

- **In which situations in APMS disease do you use a docetaxel triplet?**
- **For older, more frail patients, do you consider starting ADT with an AP blocker and using delayed docetaxel if the patient doesn't have an optimal response? Would you enter patients on the TRIPLE-SWITCH trial?**
- **In what situations if any do you utilize q2wk docetaxel?**

Can we improve docetaxel tolerability?

BERLIN 2025 ESMO congress

3-Weekly Docetaxel 75 mg/m² vs. 2-Weekly Docetaxel 50 mg/m² in Combination with Darolutamide + ADT in Patients with mHSPC

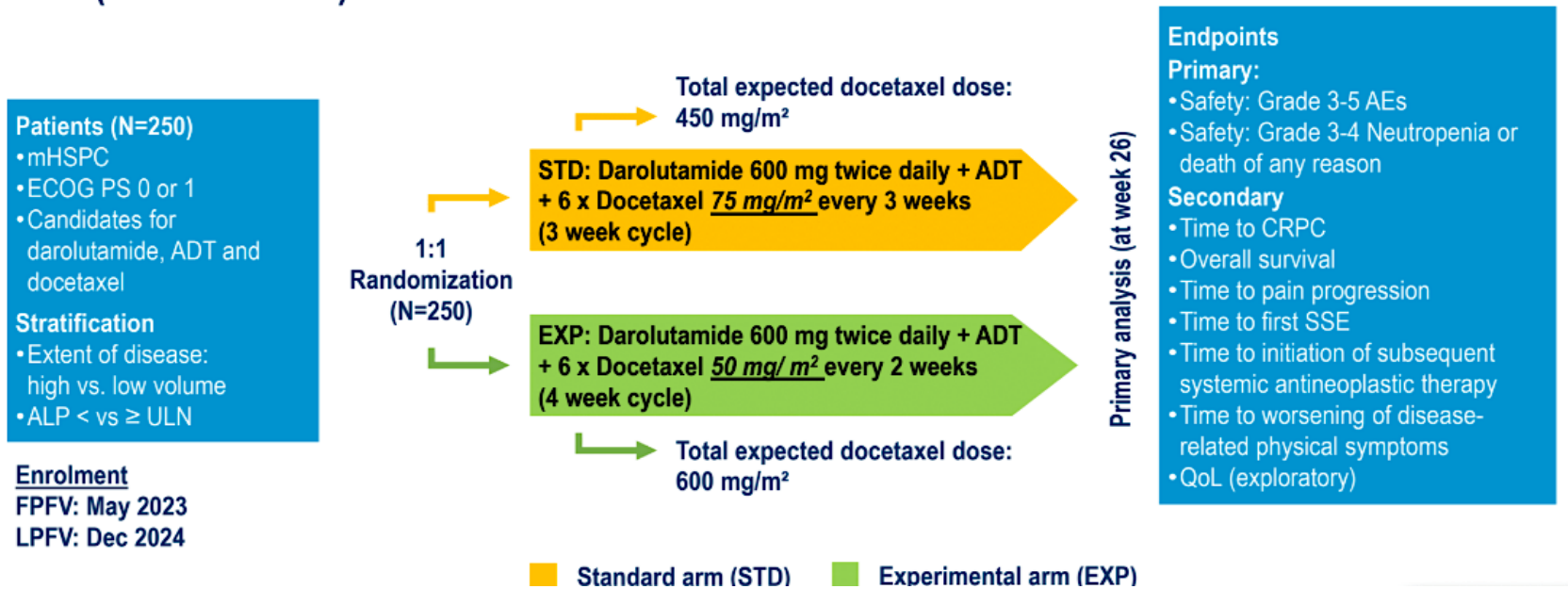
Results from the Randomised, Phase 3 ARASAFE Trial

Primary endpoint: G3-5 AE rates and grade 3-4 neutropenia/death

Study Design and Endpoints

ARASAFE

ARASAFE: randomised, open-label, multicentre phase 3 trial (NCT05676203)



Grimm et al ESMO 2025 LBA92

Q3 vs Q2 week docetaxel in mHSPC patients

Take home: q2 week Rx is safer and similarly effective

Endpoint	Docetaxel 75 mg/m² Q3W, N=128	Docetaxel 50 mg/m² Q2W, N=121	p-value
Grade 3-5 AE rates, % (95% CI)	78.9 (70.8, 85.6)	61.2 (51.9, 69.9)	**0.0024**
Grade 3-4 neutropenia/death, % (95% CI)	64.1 (55.1, 72.3)	24.0 (16.7, 32.6)	**<0.00001**

Adverse Event, n (%)		Docetaxel 75 mg/m² Q3W, N=128	Docetaxel 50 mg/m² Q2W, N=121
Treatment-emergent adverse events	Any grade	128 (100.0)	121 (100.0)
	Grades 3-5	101 (78.9)	74 (61.2)
Worst grade	Grade 1	5 (3.9)	7 (5.8)
	Grade 2	22 (17.2)	40 (33.1)
	Grade 3	52 (40.6)	59 (48.8)
	Grade 4	43 (33.6)	11 (9.1)
	Grade 5	6 (4.7)[1)]	4 (3.3)[2)]
Serious adverse events	All	37 (28.9)	32 (26.4)
	Grades 3-5	30 (23.4)	30 (24.8)
Premature discontinuation of docetaxel due to toxicities		9 (7.0)	12 (9.9)

G3-5 Neutropenia: 56 vs 20%

Febrile neutropenia: 5.5% vs 1.7%

PSA ≤0.2 at week 26: 48.8 vs 41.3%

Courtesy of Andrew J Armstrong, MD, ScM

Agenda
Prostate Cancer

INTRODUCTION: Evolution of the prostate cancer model; PCWG4

MODULE 1: Hormonal therapy

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MODULE 5: New agents

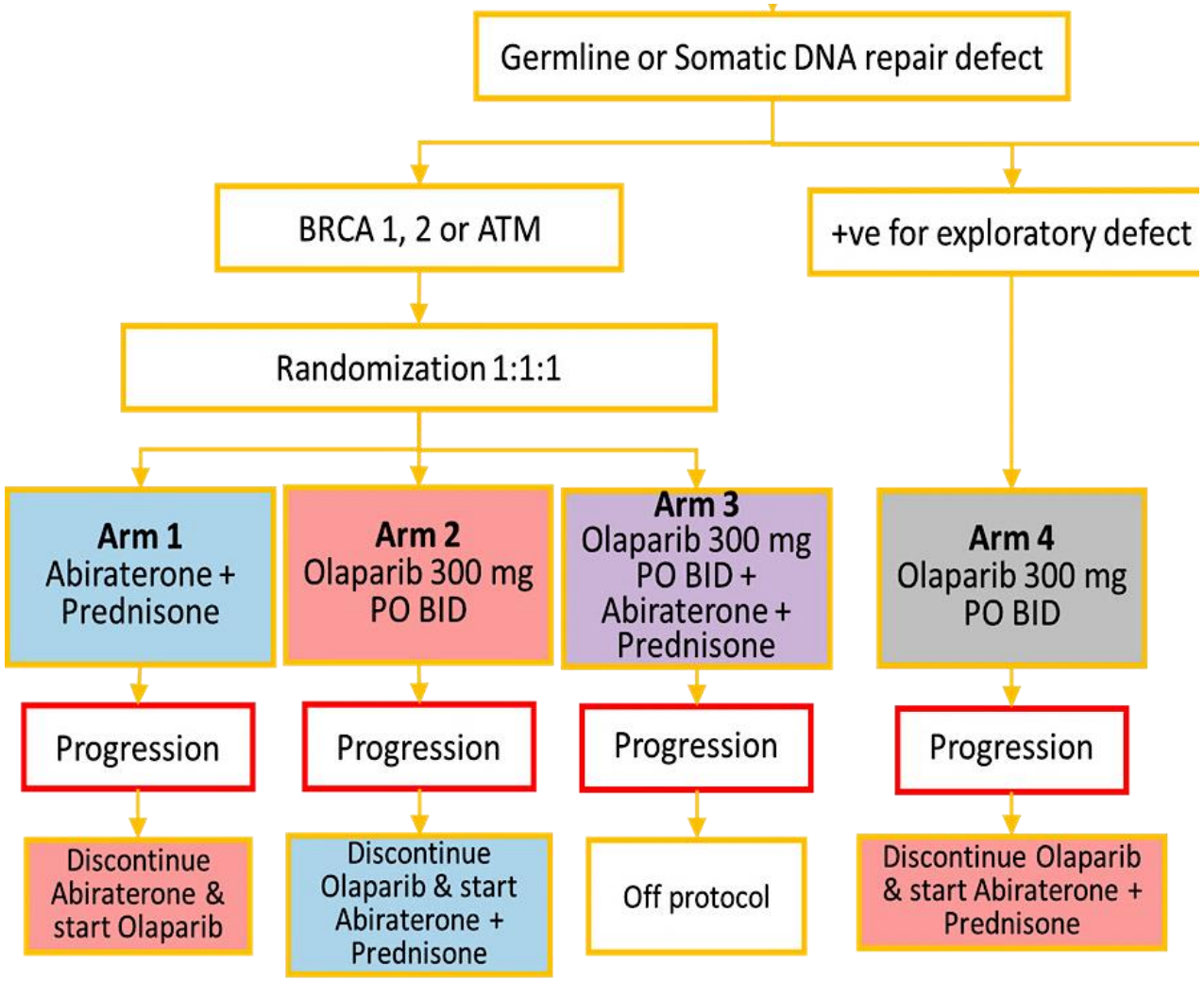
Questions About PARP Inhibitors

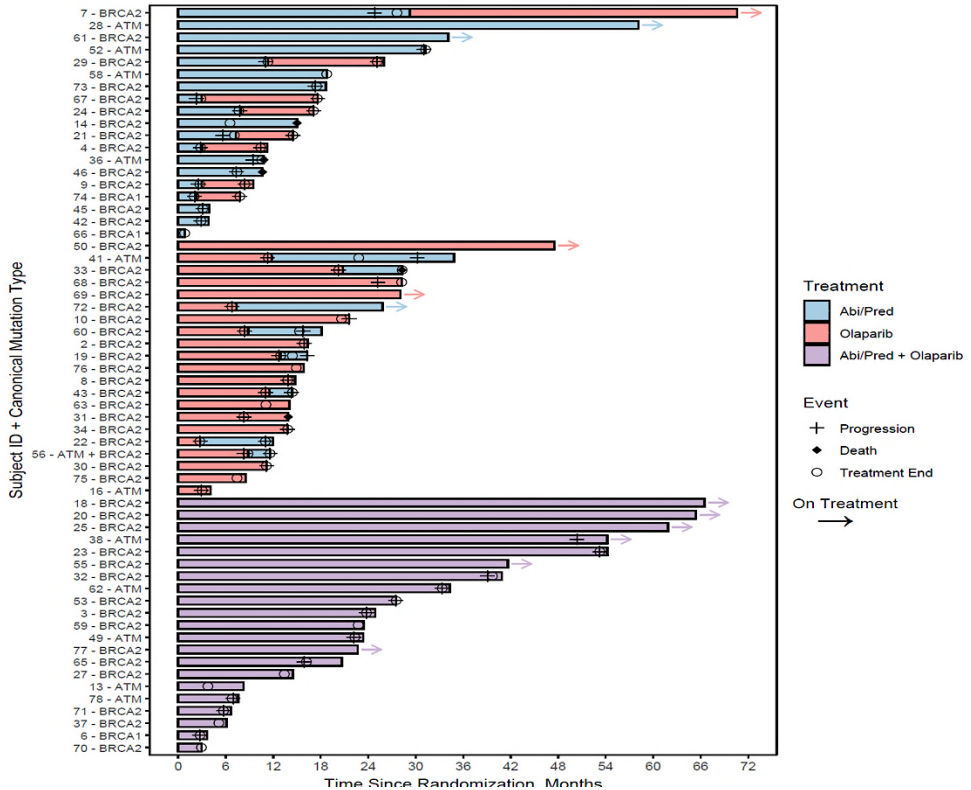
- **In which clinical scenarios do you utilize a PARPi? How often do you evaluate a patient with disease progression on ADT but no prior Api, and what is the typical history? In those patients, for which genomic abnormalities will you use a PARPi, and which one? What are the common tolerability/toxicity issues encountered?**
- **What was your take on the clinical and research implications of the BRCAAway study?**
- **In which clinical scenarios do you utilize a PARPi for patients with APMS disease? Which one? BRCA2 somatic? Would you want to for BRCA1? ATM, CDK12?**

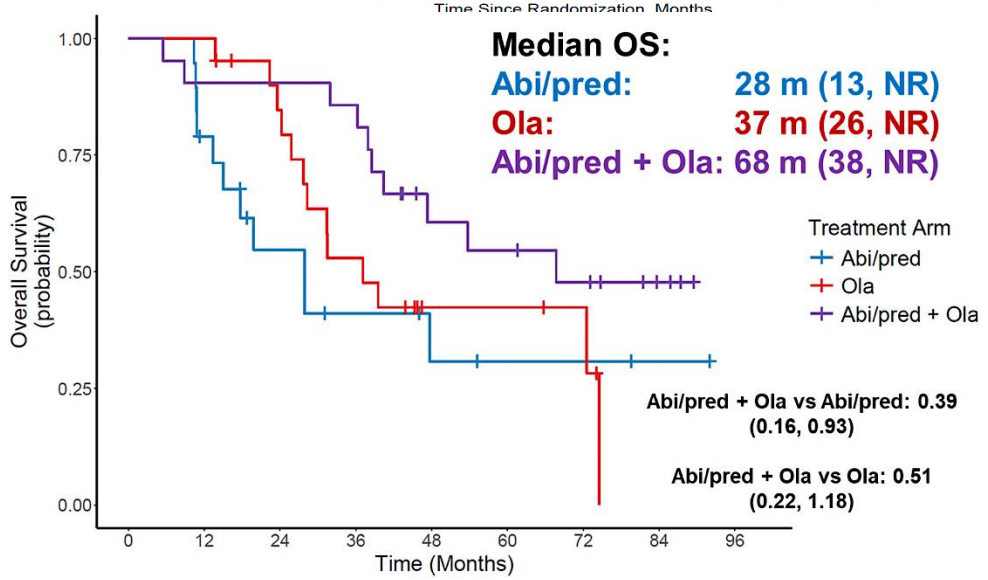
Questions About PARP Inhibitors

- **What is the rationale for the use of saruparib, and what is known about treatment efficacy and tolerability compared to approved agents? What ongoing clinical trials are investigating this agent?**

BRCAAway: Abi, Olaparib, or Abi + Ola for mAPMR PC







Hussain et al, ASCO GU 2026, Abst 16

AMPLITUDE: Abi/pred + niraparib/placebo for mAPMN/S PC

Trial Design

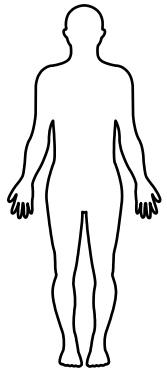
Randomized, double-blind, placebo-controlled, international phase 3 study

Patient Population

- ✓ Insert Patients with **mAPMS**
- ✓ **HRR gene alterations**
- ✓ ADT must have started ≥14d & ≤6mos prior to randomization & was continued during study Tx

Endpoints

- ✓ Primary: rPFS
- ✓ Secondary: OS



	Niraparib + AAP		***Placebo + AAP***
	N = 348		**N = 348**
Median rPFS (ITT)	NE	**HR 0.63** (95% CI: 0.49, 0. 8), P < 0.0001	29.5 mos
Median OS (BRCA) *(immature)*	NE	**HR 0.75** (95% CI: 0.51, 1.11), P = 0.15	NE
Grade 3-4 AEs	**75%**		**69%**

Subgroup Analysis

	Niraparib + AAP	***Placebo + AAP***	
BRCA subgroup (median rPFS)	*(N = 191)* NE	*(N = 196)* 26mo	**rPFS HR**: 0.52 **95% CI**: 0.37, 0.72; *P* < .0001
HRR effector subgroup (median rPFS)	*(N = 230)* NE	*(N = 226)* 27.6mo	**rPFS HR**: 0.57 **95% CI**: 0.42, 0.77; *P* = .0003

BRCA2 exploratory cohort (N = 323):
rPFS: NE vs 26 months, HR: 0.46 (95% CI: 0.32, 0.66)

Attard G, et al. *Nat Med*. 2025;31(12):4109-4118l; U.S. Food and Drug Administration. FDA approves niraparib and abiraterone acetate plus prednisone for BRCA2-mutated metastatic castration-sensitive prostate cancer. Published December 12, 2025. Accessed February 9, 2026.

Talazoparib with Enzalutamide Significantly Improves Radiographic Progression-Free Survival in Metastatic Prostate Cancer
Press Release: March 19, 2026

"[The manufacturer] today announced positive topline results from the Phase 3 TALAPRO-3 study of talazoparib, an oral poly ADP-ribose polymerase (PARP) inhibitor, in combination with enzalutamide, an androgen receptor pathway inhibitor (ARPI), in people with homologous recombination repair (HRR) gene-mutated metastatic castration-sensitive prostate cancer (mCSPC), also known as metastatic hormone-sensitive prostate cancer (mHSPC).

The study met its primary endpoint, with talazoparib plus enzalutamide demonstrating a statistically significant and clinically meaningful improvement in radiographic progression-free survival (rPFS), compared to placebo plus enzalutamide.

At the time of the interim analysis, results showed a strong trend toward improved overall survival (OS), a key secondary endpoint. Benefits were also observed in other secondary endpoints, including overall response rate, duration of response, and time to Prostate-Specific Antigen (PSA) progression. The safety of talazoparib plus enzalutamide was consistent with the known safety profile of each medicine, and no new safety signals were identified.

Talazoparib plus XTANDI in HRR gene-mutated mCSPC is an investigational treatment regimen. **The TALAPRO-3 results will be submitted for presentation at an upcoming medical congress and will be discussed with global health authorities for potential regulatory submissions.**"

https://www.pfizer.com/news/press-release/press-release-detail/talzenna-plus-xtandi-significantly-improves-radiographic

Phase 1/2 PETRANHA trial of saruparib + androgen receptor pathway inhibitors

Part A: Saruparib 60 mg OD + ARPI (N=77)

Patient population

- Adults aged ≥18 years
- Histologically confirmed mPC
- Investigator-assessed mAMPR or de novo/recurrent mAPMN PC
- ECOG PS 0 or 1
- Irrespective of HRRm

Saruparib + Enzalutamide
n=18

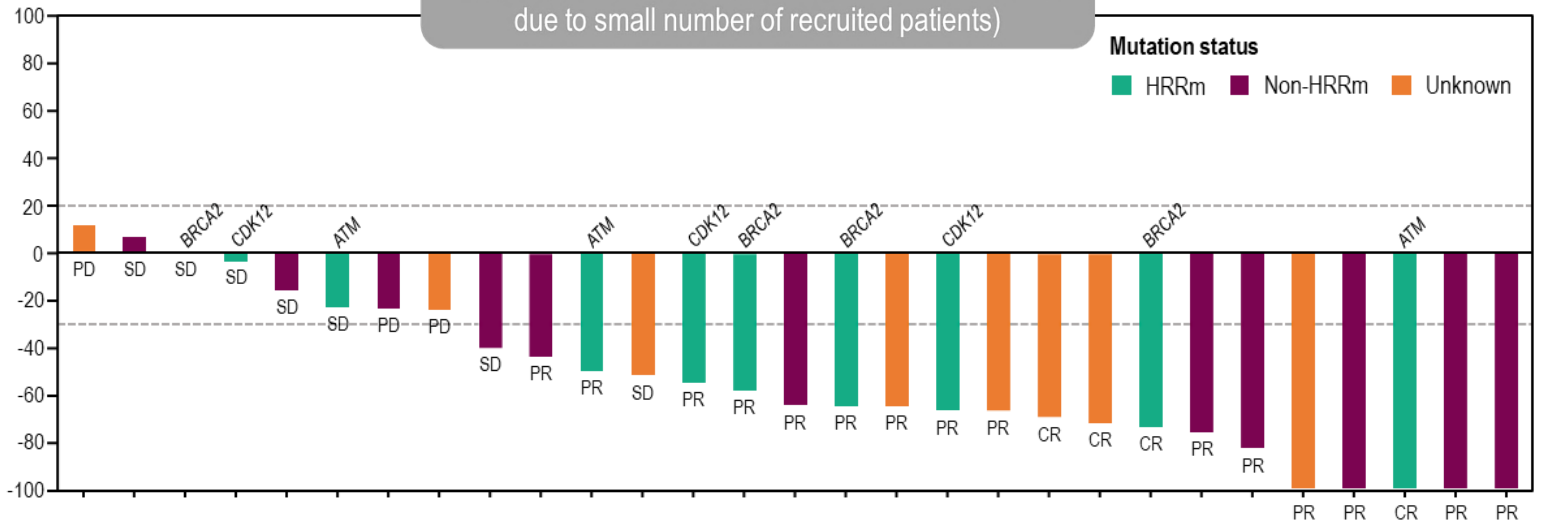
Saruparib + Abiraterone acetate + Prednisone*
n=23†

Saruparib + Darolutamide
n=36†

Saruparib + Apalutamide
Ongoing at data cutoff (not included in this analysis due to small number of recruited patients)

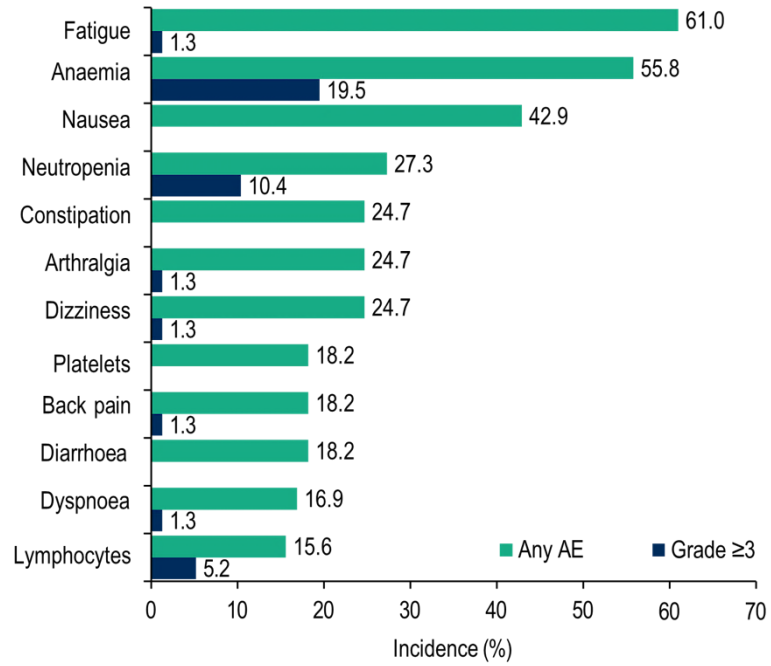
Primary endpoint
- Incidence of AEs

Key secondary endpoints
- ORR
- DoR
- PSA response



Which ARPI	E	A	D	A	D	E	D	D	D	A	E	D	A	A	D	A	A	A	A	D	D	E	A	A	D	E	E	E	D
APM status	R	R	R	R	R	R	R	R	R	S	R	R	R	R	S	R	S	S	R	R	R	R	S	R	R	R	R	R	S
Prior ARPI?	Y	N	Y	Y	Y	N	N	Y	Y	N	N	N	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Most common all cause AEs (≥15%) in all patients (N=77)*



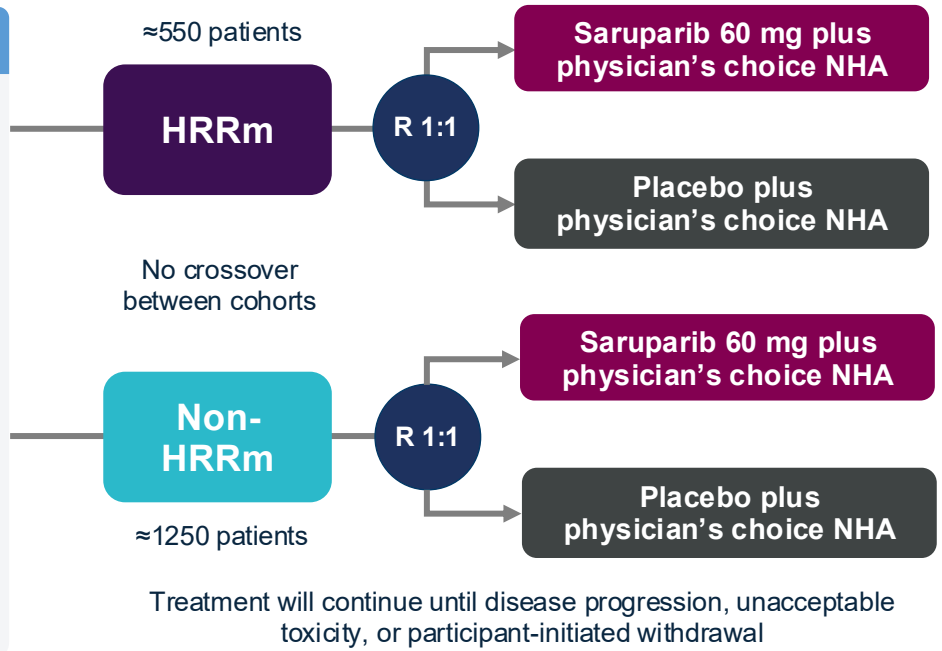
Azad et al, Ann Oncol 2025, Abst 2384MO

EvoPAR-Prostate01: Phase 3 Trial Design (mHSPC)

A Phase III, 2-cohort, 2-arm, randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of saruparib plus physician's choice of NHA (abiraterone, darolutamide, or enzalutamide) versus placebo plus physician's choice of NHA in participants with mCSPC

Eligibility criteria

- Aged ≥18 years
- Histologically confirmed mCSPC (*de novo* or recurrent low- or high-volume disease)
- ECOG PS 0–1
- Prospectively defined HRRm status*
- Must be receiving ADT throughout the study or have undergone bilateral orchiectomy, and must be suitable for treatment with NHAs
- No prior treatment with PARP inhibitors, CT, or NHAs in the metastatic setting†
- No suspected or prior history of myelodysplastic syndrome/acute myeloid leukemia



Treatment will continue until disease progression, unacceptable toxicity, or participant-initiated withdrawal

Select endpoints

HRRm cohort
- rPFS
- OS

Non-HRRm cohort
- rPFS
- OS

Statistical analyses

rPFS and OS will be tested for each cohort separately using a stratified log-rank test

www.clinicaltrials.gov: (NCT06120491)

Agarwal N. *et al*, ***AUA*** 2024

Phase III, randomized, double-blind, placebo-controlled study of adjuvant saruparib (AZD5305) in patients with BRCAm localized high-risk prostate cancer who are receiving radiotherapy and androgen deprivation therapy (EvoPAR-Prostate02)

Rana R. McKay,[1] Wassim Abida,[2] Gerhardt Attard,[3] Boris A. Hadaschik,[4] Takashi Kobayashi,[5] Neal D. Shore,[6] Nianzeng Xing,[7] Mehreteab Aregay,[8] Sarah E. Donegan,[8] Piet Ost[9]

[1]Department of Medicine and Urology, University of California San Diego, La Jolla, CA, USA; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]University College London, London, UK; [4]Department of Urology, University of Duisburg-Essen, Essen, Germany; [5]Department of Urology, Kyoto University Graduate School of Medicine, Kyoto, Japan; [6]START Carolinas/Carolina Urologic Research Center, Myrtle Beach, SC, USA; [7]Department of Urology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [8]Global Medicines Development, Oncology Research and Development, AstraZeneca, Gaithersburg, MD, USA; [9]Department of Radiation Oncology, Iridium Network, Wilrijk, Belgium.

Poster P23 | Abstract number TPS412

Plain language summary

Why are we performing this research?

- Around 15% of early-stage prostate cancers have features that suggest that the cancer will come back after the patient's first treatment. This is known as high-risk prostate cancer
- The currently recommended treatment options for patients with early-stage, high-risk prostate cancer include surgery, radiation therapy (RT), and hormone-blocking agents (androgen deprivation therapy [ADT], with or without abiraterone)
- In many patients, the prostate cancer can come back and get worse after these treatments, and more effective approaches are needed
- PARP inhibitors are drugs that block a protein called PARP1 and kill cancer cells by stopping them from being able to repair their DNA
- PARP inhibitors are currently recommended for patients with metastatic prostate cancer, a type of cancer that has spread from its original site
- Using PARP inhibitors to treat cancer in the early stages of development has shown promising results in patients with other cancer types, such as breast and ovarian cancer
- In patients with some types of cancer, those with mutations in the *BRCA1* and/or *BRCA2* genes (BRCAm) may benefit the most from PARP inhibitor treatments
- Saruparib is a new type of PARP inhibitor currently in development. Early data from clinical trials have shown that patients with some types of prostate cancer can benefit from saruparib
- The EvoPAR-Prostate02 clinical trial will study whether giving saruparib plus hormone-blocking agents to participants with BRCAm high-risk prostate cancer increases the length of time participants live without their prostate cancer growing or spreading

How are we performing this research?

- Approximately 700 adult patients with high-risk and very high-risk BRCAm prostate cancer will be assigned treatment with either saruparib with hormone-blocking agents or placebo (an inactive substance that looks the same and is given in the same way as saruparib) with hormone-blocking agents
- Patients and researchers in this study will not know which treatment has been given
- Every patient will receive treatment for 24 months, or until the participant requests to stop the treatment, the study researcher considers there is evidence that the prostate cancer has progressed, the participant is no longer benefiting from the treatment, or the side effects of the treatment are unacceptable
- Progress of disease will be compared in patients who received saruparib with hormone-blocking agents or placebo with hormone-blocking agents

Who will participate in this study

- Participants in this study must have early-stage high-risk prostate cancer
- BRCA testing will be performed on a piece of tissue from the patient's tumor, and those with BRCAm will be included in the study
- Participants must have received RT and must be eligible to receive hormone-blocking agents during the study

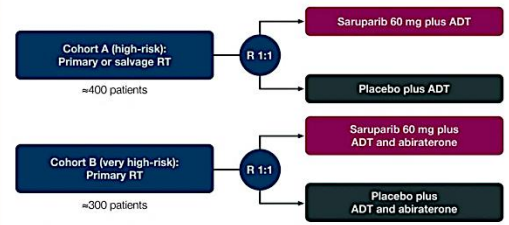
Where can I access more information?

- As this study is ongoing and currently recruiting participants, no results are available yet. More information can be found at: https://www.clinicaltrials.gov/study/NCT06952803
- You may also speak to your doctor about clinical studies

This study is funded by AstraZeneca.

Poster presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU), February 26–28, 2026, San Francisco, CA, USA, by Rana R. McKay.

EvoPAR-Prostate02 (NCT06952803): A phase III, double-blind, placebo-controlled, two-cohort, randomized study of adjuvant saruparib (AZD5305) versus placebo in patients with BRCAm localized high-risk prostate cancer who are receiving RT and ADT



Treatment with saruparib/placebo continues for 24 months or until confirmed disease progression by BICR, unacceptable toxicity, or patient-initiated withdrawal. ADT and abiraterone treatment duration is limited to 24 months, inclusive of the pre-study regimen.

The EvoPAR-Prostate02 study design presented aligns with clinical study protocol v2.0 (April 10, 2025).

Locations participating in EvoPAR-Prostate02

- Recruitment began in July 2025 and is ongoing
- 254 study sites are recruiting or planning to recruit patients from 24 countries, including countries in Europe, Asia, Australasia, North America, and South America

Rationale for treating early-stage high-risk prostate cancer with a PARP1-selective inhibitor

Current standard of care for patients with high-risk prostate cancer

- Approximately 15% of patients with localized prostate cancer have high-risk characteristics[1,2]
- For patients with newly diagnosed high-risk (localized) or very high-risk (locally advanced) prostate cancer, the current standard of care includes surgery, RT, and ADT comprising a gonadotropin-releasing hormone analog[3,4]
  - Clinical guidelines also recommend RT and ADT plus abiraterone/prednisone in patients with very high-risk disease[4,5]
- Patients with high-risk disease have an increased risk of disease recurrence after primary treatment[2]
- BRCAm is associated with aggressive tumor phenotypes and poor survival outcomes in patients with prostate cancer[6,7]

PARP inhibitor therapy for patients with prostate cancer

- The Phase III clinical trials PROfound (NCT02987543) and TRITON3 (NCT02975934) demonstrated that PARP inhibitor therapy improved clinical outcomes in patients with BRCAm and metastatic, castration-resistant prostate cancer[8,9]
- Clinical benefit with combinations of PARP inhibitor plus ARPI was demonstrated in patients with metastatic castration-resistant prostate cancer in the Phase III trials PROpel (NCT03732820) and TALAPRO-2 (NCT03395197), as well as in patients with metastatic hormone-sensitive prostate cancer in the Phase III AMPLITUDE trial (NCT04497844)[10–14]
- Saruparib is a new-generation PARP inhibitor that selectively inhibits and traps PARP1[15,16]
- In the Phase I/IIa PETRA study (NCT04644068), saruparib demonstrated a favorable safety profile at 60 mg QD and meaningful activity (PSA_{50}, objective response) in patients with advanced/metastatic prostate cancer[15]
- The ongoing Phase I/IIa PETRANHA study (NCT05367440) has reported promising efficacy and manageable toxicity with saruparib plus ARPIs for the treatment of metastatic prostate cancer[17,a]
- In other indications, the clinical activity of PARP inhibitors in earlier lines of treatment has demonstrated potential to provide a greater magnitude of benefit and delay disease progression in patients with BRCAm tumors[18,19]

[a]See poster F6 for the latest data from the PETRANHA study. More information here: https://www.asco.org/abstracts-presentations/256435

Key inclusion criteria

- Male and ≥18 years of age
- Newly diagnosed, histologically confirmed, high-risk or very high-risk localized/locally advanced prostate adenocarcinoma, or high-risk biochemical recurrence within 365 days of radical prostatectomy
- ECOG PS 0–1
- Confirmed BRCAm by central tumor tissue testing
- Completed primary or salvage RT with curative intent
- No evidence of distant metastases by CT/MRI and bone scan, or PSMA PET
- Must be receiving ADT with a gonadotropin-releasing hormone analogue throughout the study

Key exclusion criteria

- Prior treatment with PARP inhibitors, chemotherapy, or immunotherapy
- History of myelodysplastic syndrome or acute myeloid leukemia
- Any known predisposition to bleeding
- History of persistent severe cytopenia (>2 weeks)
- Uncontrolled cardiovascular disease, long QT syndrome, or history of arrhythmia

Study endpoints

Primary endpoint

- MFS, defined as the time from randomization to first evidence of distant metastases, excluding pelvic lymph nodes, confirmed by standard clinical imaging (CT/MRI and bone scan) or PSMA PET, as assessed by BICR, or death due to any cause

Secondary endpoints

- OS, defined as the time from randomization until death from any cause
- Progression-free survival 2, defined as radiographic, clinical, or PSA progression after initiation of the first subsequent systemic treatment following the initial investigator-assessed progression, or death
- Time to:
  - biochemical recurrence
  - deterioration in urinary symptoms
  - deterioration in physical function
- Prostate cancer-specific survival
- Pharmacokinetics
- Safety and tolerability

Statistical analyses of MFS and OS will be conducted within each cohort using a stratified log-rank test

Poster

Trial card

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of these materials. Alternatively, please use the link below.

https://bit.ly/4suDfpd

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Abbreviations

ADT, androgen deprivation therapy; ARPI, androgen receptor pathway inhibitor; BICR, blinded independent central review; BRCAm, *BRCA1* and/or *BRCA2* mutation; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; MFS, metastasis-free survival; MRI, magnetic resonance imaging; OS, overall survival; PARP, poly(ADP-ribose) polymerase; PSA, prostate-specific antigen; PSA_{50}, ≥50% drop in PSA levels from baseline; PSMA-PET, prostate-specific membrane antigen-positron emission tomography; QD, once daily; R, randomization; RECIST, Response Evaluation Criteria in Solid Tumors; RT, radiotherapy.

Acknowledgments and disclosures

- We thank the patients and their families who will participate in the EvoPAR-Prostate02 study as well as the investigators, co-investigators, study staff, and Steering Committee.
- This study is supported by AstraZeneca.
- Full author disclosures are available with the published abstract.
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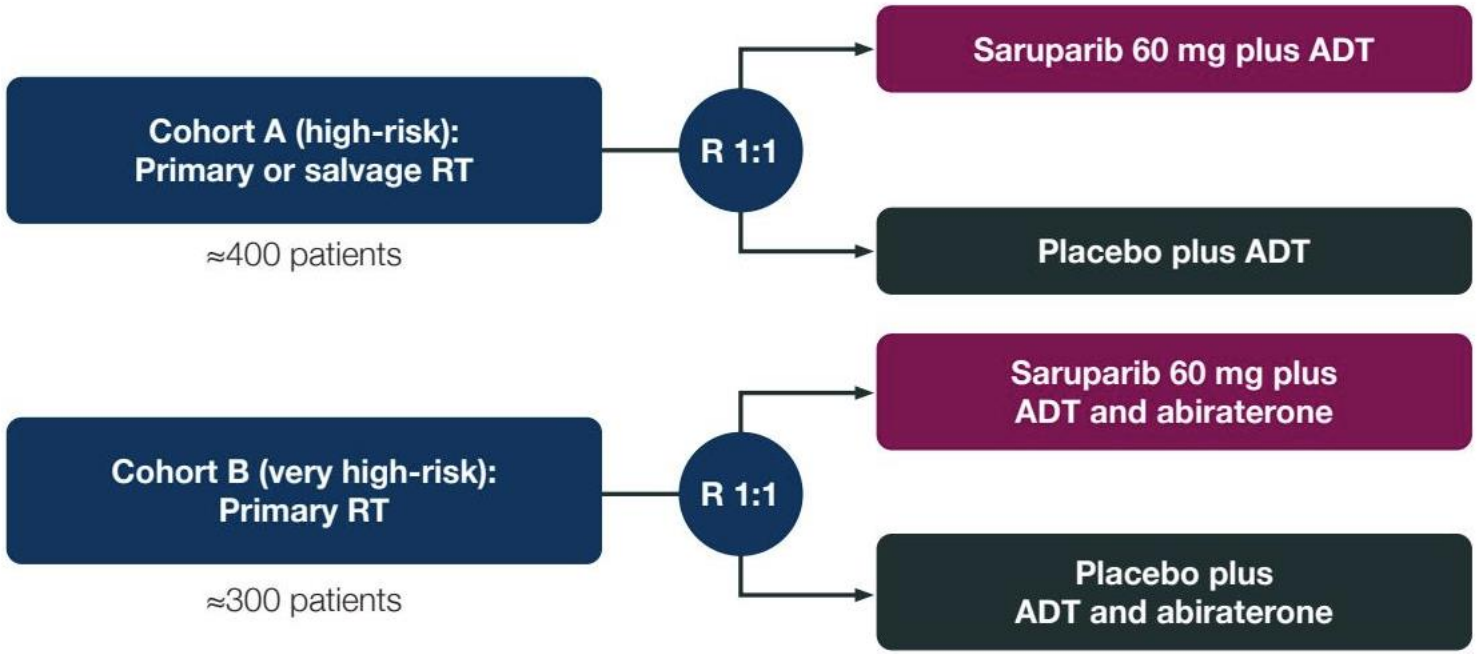
Presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU), February 26–28, 2026, San Francisco, CA, USA. Corresponding author email address: rmckay@health.ucsd.edu

EvoPAR-Prostate02: Phase III Study of Adjuvant Saruparib in Patients with BRCAm Localized High-Risk Prostate Cancer Receiving RT and ADT

Trial Identifier: NCT06952803

Key inclusion criteria

- Male and ≥18 years of age
- Newly diagnosed, histologically confirmed, high-risk or very high-risk localized/locally advanced prostate adenocarcinoma, or high-risk biochemical recurrence within 365 days of radical prostatectomy
- ECOG PS 0–1
- Confirmed BRCAm by central tumor tissue testing
- Completed primary or salvage RT with curative intent
- No evidence of distant metastases by CT/MRI and bone scan, or PSMA PET
- Must be receiving ADT with a gonadotropin-releasing hormone analogue throughout the study



Treatment with saruparib/placebo continues for 24 months or until confirmed disease progression by BICR, unacceptable toxicity, or patient-initiated withdrawal. ADT and abiraterone treatment duration is limited to 24 months, inclusive of the pre-study regimen.

Primary Endpoint: Metastasis-free survival

McKay RR et al. Genitourinary Cancer Symposium 2026;Abstract TPS412.

Agenda
Prostate Cancer

INTRODUCTION: Evolution of the prostate cancer model; PCWG4

MODULE 1: Hormonal therapy

MODULE 2: Chemotherapy (docetaxel)

MODULE 3: PARP inhibition

MODULE 4: Radioligand therapy

MODULE 5: New agents

Questions About Radioligand Therapy

- **What is your perspective on the use of lutetium Lu 177 vipivotide tetraxetan as part of treatment of APMS disease (PSMAddition trial)? If you could access this, in what situations would you utilize it?**
- **What is your perspective on the long-term findings of the hematologic toxicity observed in the PSMAfore trials?**
- **What other toxicities have you observed with lutetium Lu 177 vipivotide tetraxetan and how does this impact both your use of the agent and patient quality of life?**

Questions About Radioligand Therapy

- **Based on recent data, what is your perspective on actinium-225-PSMA? How do you anticipate this radioligand therapy might ultimately be integrated into the treatment algorithm for patients with APMR disease?**

PSMAfore: ARPI-resistant, chemo-naïve mAPMR PC

- Confirmed progressed mAPMR PC
- ≥1 PSMA-positive metastatic lesion on [^{68}Ga]Ga-PSMA-11 PET/CT and no exclusionary PSMA-negative lesions
- Progressed once on prior second-generation ARPI
  - Candidates for change in ARPI
- Taxane-naïve (except [neo]adjuvant >12 months ago)
  - Not candidates for PARPi
- ECOG performance status 0–1

R 1:1

^{177}Lu-PSMA-617
7.4 GBq (200 mCi) ± 10%
Q6W for 6 cycles

Crossover allowed upon radiographic progression by BICR

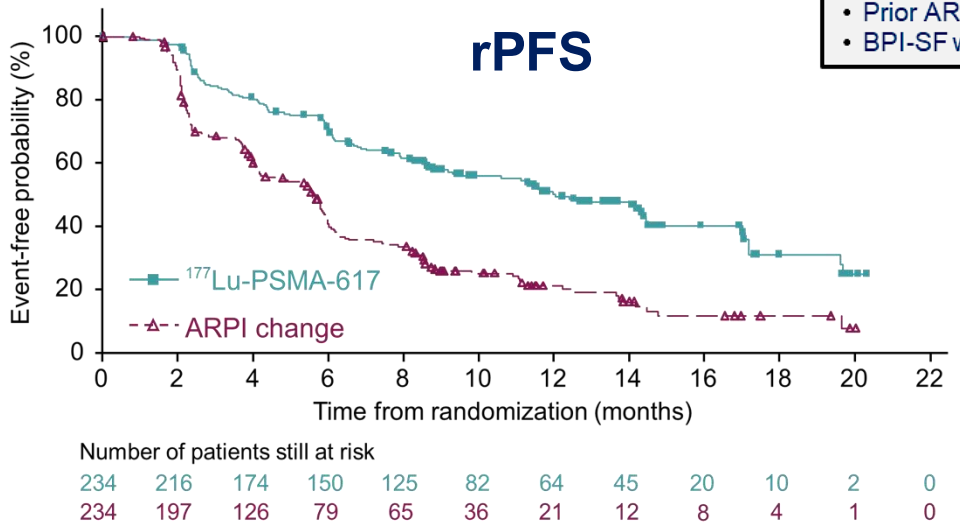
ARPI change
abiraterone or enzalutamide

rPFS by BICR

Follow-up

Strat Factors
- Prior ARPI setting
- BPI-SF worst pain

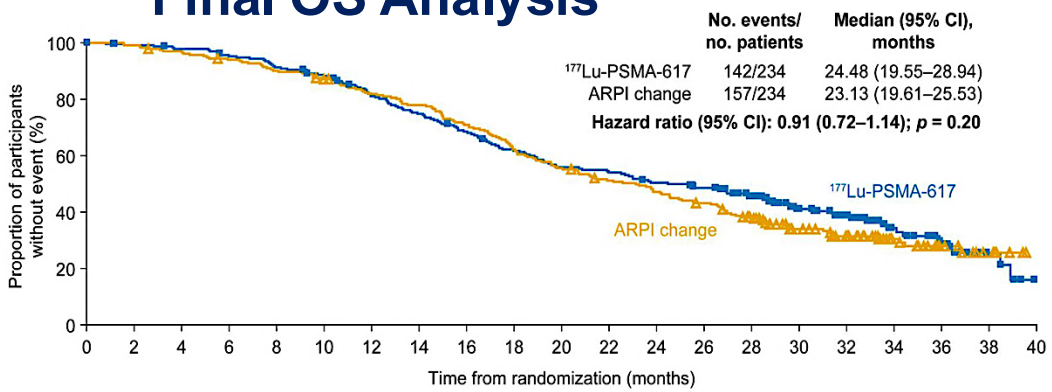
rPFS



Number of patients still at risk

234	216	174	150	125	82	64	45	20	10	2	0
234	197	126	79	65	36	21	12	8	4	1	0

Final OS Analysis

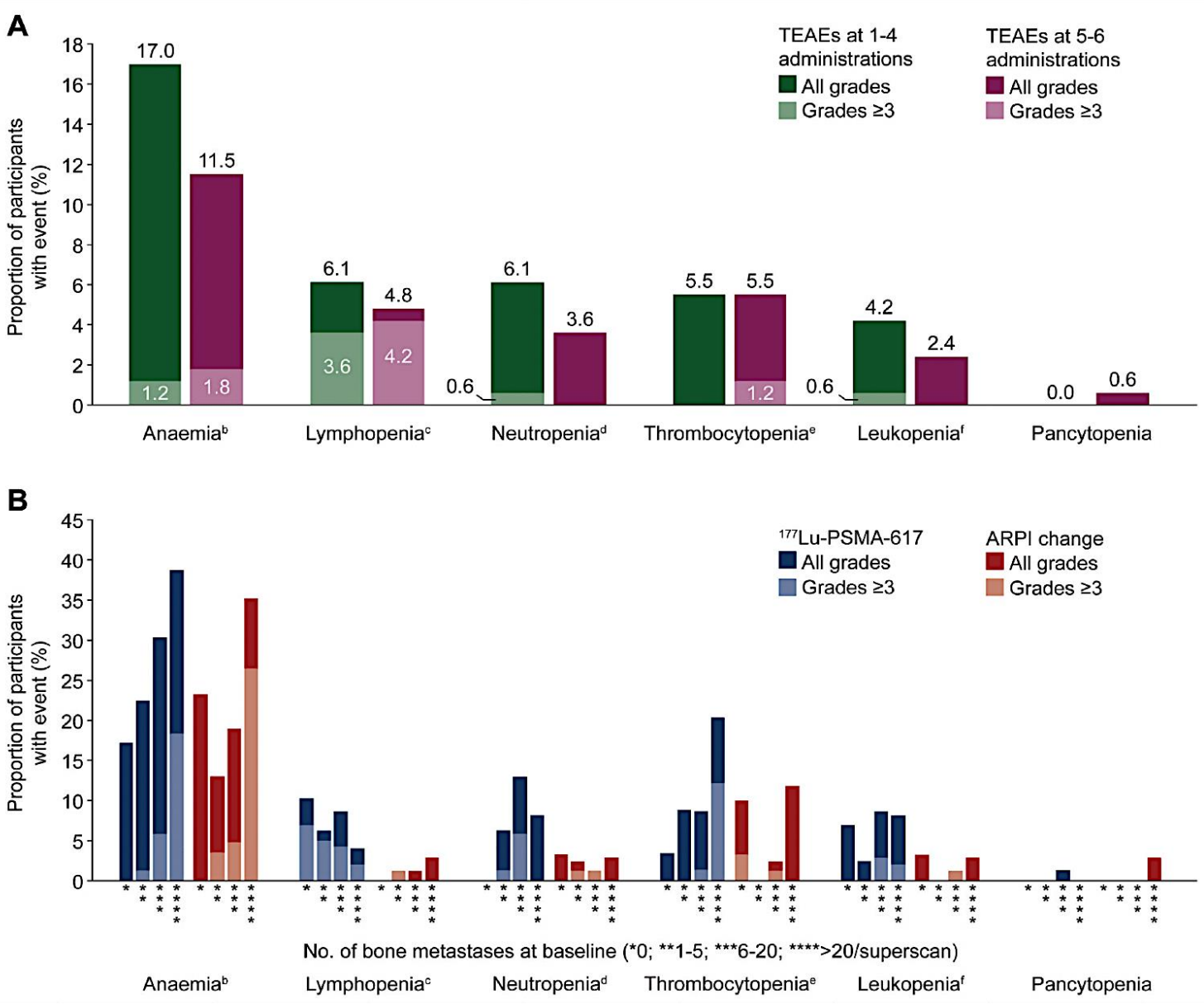


Number at risk

^{177}Lu-PSMA-617 arm	234	229	225	218	209	200	181	167	152	136	123	119	110	103	85	57	45	24	15	6	0
ARPI change arm	234	232	226	218	209	200	187	178	162	142	127	115	106	96	79	56	44	25	14	7	0

Morris et al. *Lancet.* 2024; 404:1227-1239.
Fizazi et al, *Ann Oncol* 2025

PSMAfore: Final Safety Analyses

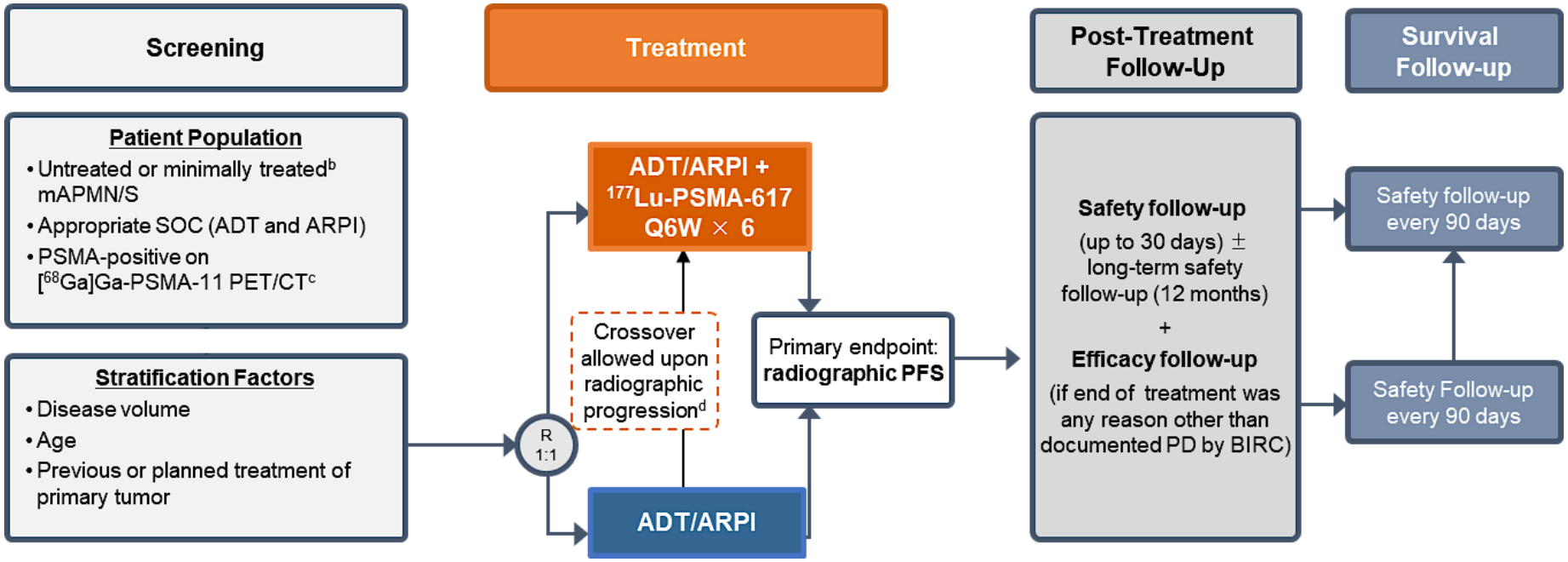


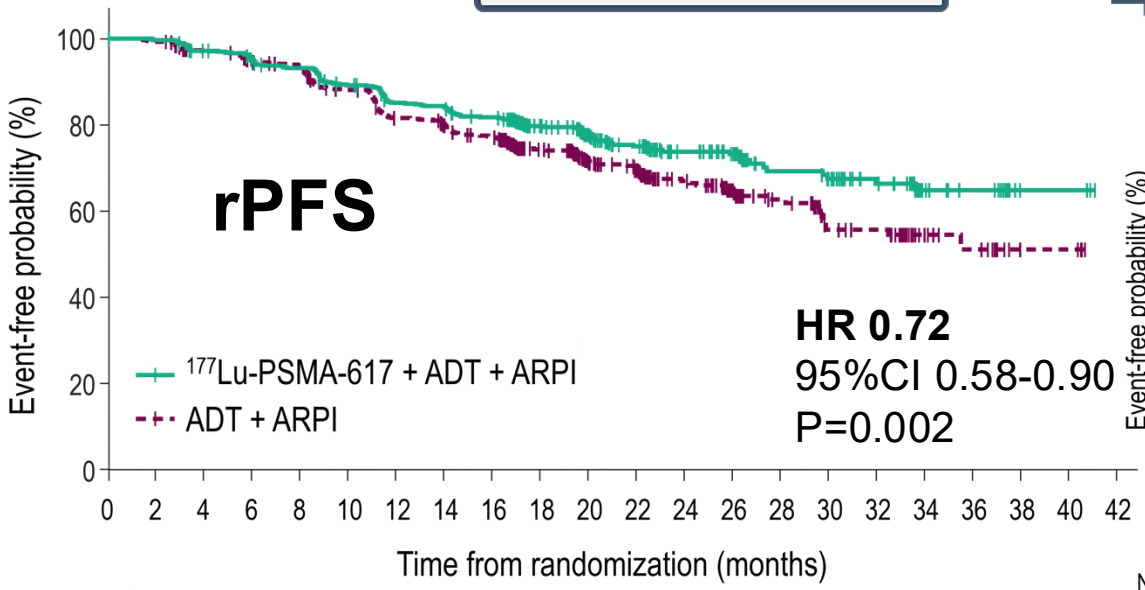
Incidence of haematologic TEAEs by number of 177Lu-PSMA-617 administrations

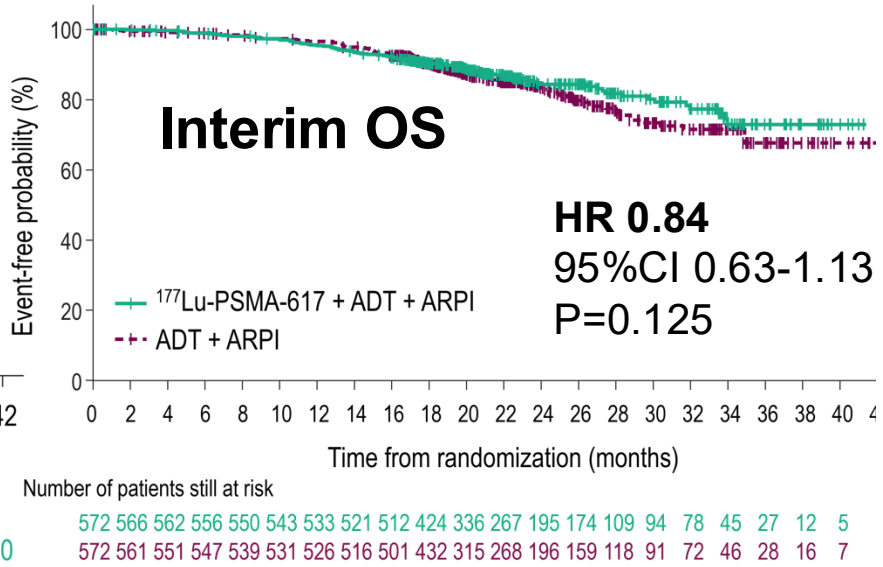
Incidence of haematologic TEAEs by number of bone metastases at baseline

Fizazi et al, *Ann Oncol* 2025

PSMAddition



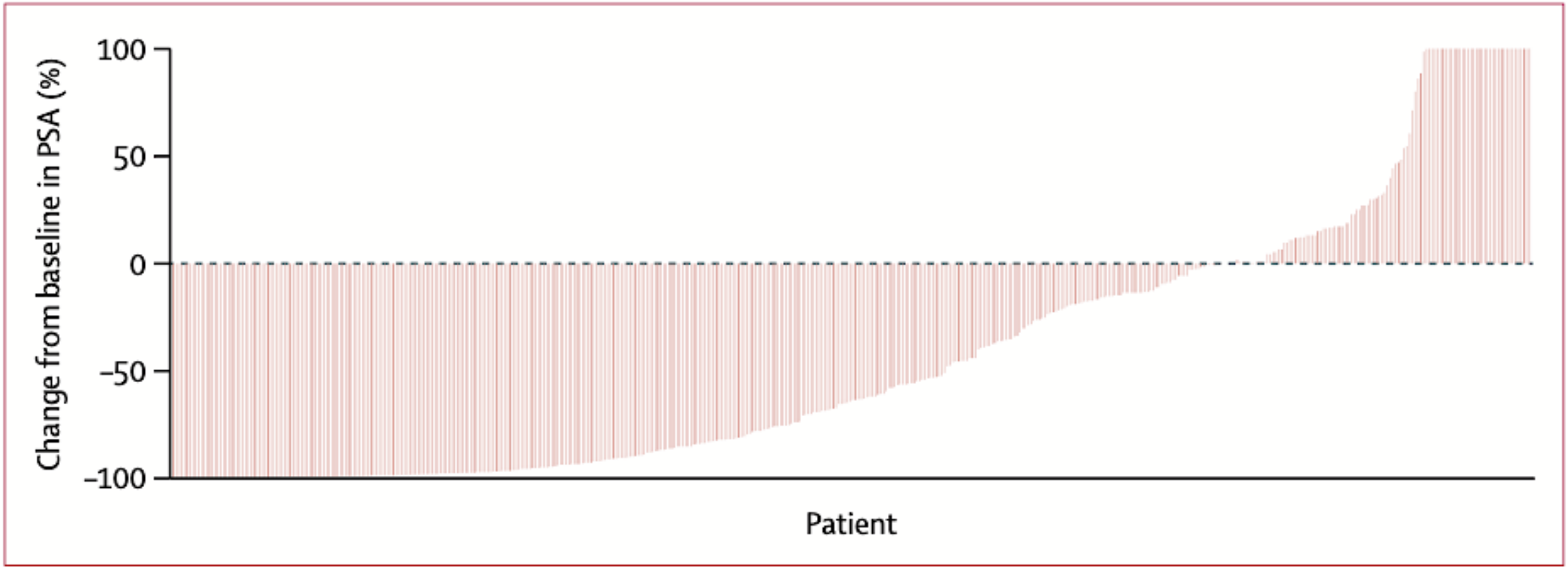




Common TEAEs
- Dry mouth (46%)
- Fatigue (35%)
- Nausea (34%)
- Anemia (28%)
- Neutropenia (15%)
- Thrombocytopenia (11%)

Tagawa T et al. *Annals of Oncology* 36 (2025): S1742-S1743; LBA6.

WARMTH Act: PSA Responses

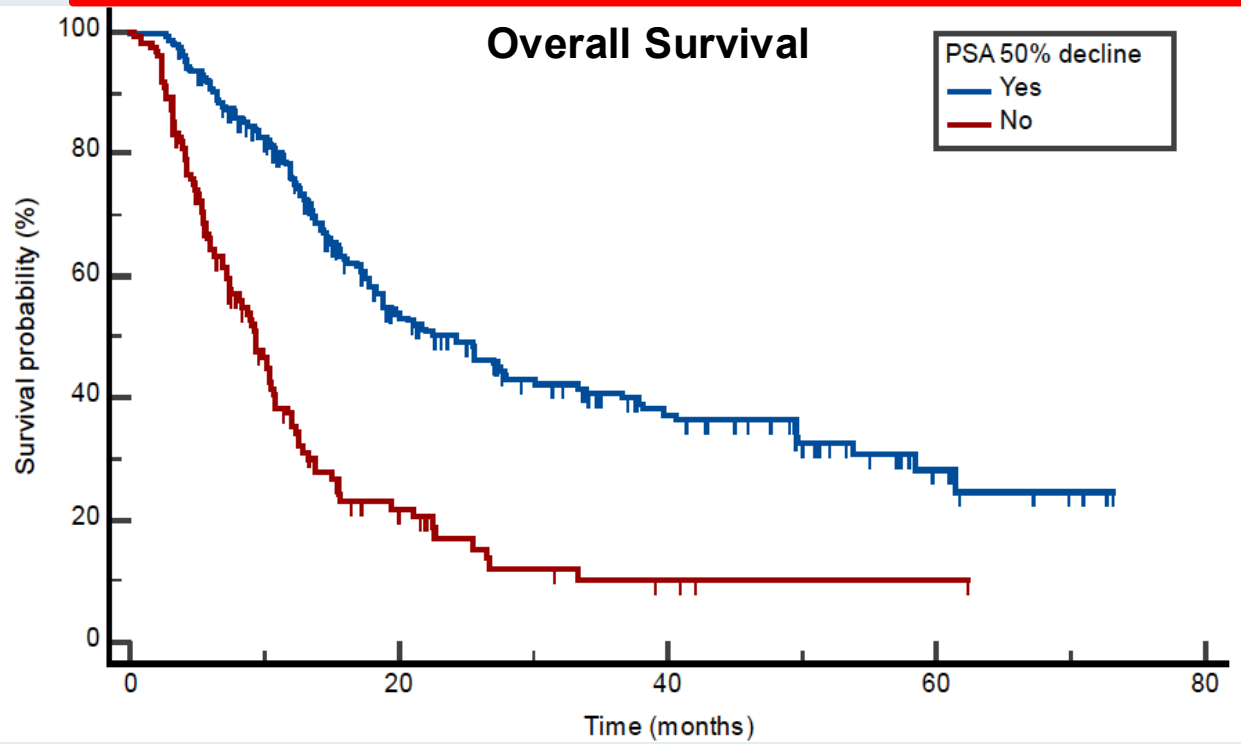


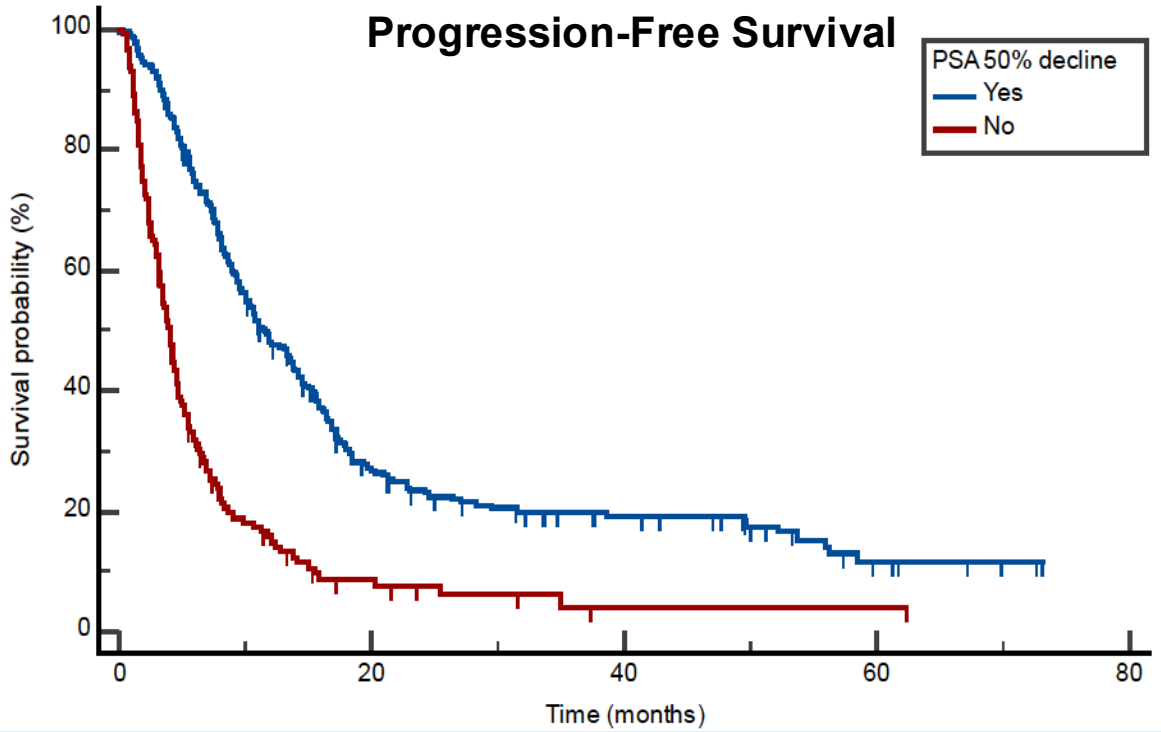
278 patients (57%) had a ≥50% PSA decline. PSA=prostate-specific antigen.

Sathekge MM et al. *Lancet Oncol* 2024 February;25(2):175-83.

WARMTH Act: Survival Benefit with PSA Decline

	Overall survival				Progression-free survival			
	Univariable HR (95% CI)	p value	Multivariable HR (95% CI)	p value	Univariable HR (95% CI)	p value	Multivariable HR (95% CI)	p value
PSA decline of ≥50%	0·348 (0·263–0·460)	<0·0001	0·415 (0·307–0·561)	<0·0001	0·367 (0·291–0·461)	<0·0001	0·431 (0·330–0·565)	<0·0001





Sathekge MM et al. *Lancet Oncol* 2024 February;25(2):175-83.

Actinium-225-PSMA Radioligand Therapy: WARMTH Act Survival Analysis

	Overall survival				Progression-free survival			
	Univariable HR (95% CI)	p value	Multivariable HR (95% CI)	p value	Univariable HR (95% CI)	p value	Multivariable HR (95% CI)	p value
PSA decline of ≥50%	0·348 (0·263–0·460)	<0·0001	0·415 (0·307–0·561)	<0·0001	0·367 (0·291–0·461)	<0·0001	0·431 (0·330–0·565)	<0·0001
Previous docetaxel or cabazitaxel	1·398 (1·062–1·841)	0·017	1·114 (0·772–1·608)	0·56	1·714 (1·360–2·160)	<0·0001	1·370 (1·012–1·853)	0·041
Previous abiraterone or enzalutamide	1·512 (1·170–1·955)	0·0016	1·175 (0·822–1·681)	0·38	1·882 (1·521–2·329)	<0·0001	1·282 (0·966–1·702)	0·085
Treatment with ^{177}Lu-PSMA RLT	1·663 (1·264–2·188)	0·0003	1·213 (0·876–1·680)	0·25	1·693 (1·355–2·116)	<0·0001	1·100 (0·838–1·443)	0·49
Liver metastasis	2·344 (1·597–3·440)	<0·0001	1·895 (1·253–2·867)	0·0025	2·395 (1·712–3·352)	<0·0001	1·878 (1·308–2·696)	0·0006
Peritoneal metastasis	6·728 (3·084–14·676)	<0·0001	5·025 (2·177–11·601)	0·0002	5·115 (2·386–10·966)	<0·0001	4·080 (1·675–9·937)	0·0020
Number of cycles of ^{225}Ac-PSMA RLT	0·861 (0·801–0·927)	0·0001	0·924 (0·850–1·006)	0·067	0·887 (0·834–0·943)	0·0001	0·970 (0·905–1·039)	0·38
Anaemia at baseline	1·886 (1·438–2·473)	<0·0001	1·615 (1·198–2·176)	0·0016	1·450 (1·157–1·817)	0·0012	1·249 (0·965–1·615)	0·091
Platelet count at baseline >300 000/mm^3	0·952 (0·709–1·279)	0·75	NA	NA	0·865 (0·674–1·109)	0·25	NA	NA
Baseline ECOG performance status ≥2	1·223 (0·904–1·653)	0·19	NA	NA	1·452 (1·146–1·839)	0·0020	1·031 (0·7930–1·340)	0·82
Time since diagnosis	1·021 (0·994–1·049)	0·13	NA	NA	1·019 (0·996–1·042)	0·099	NA	NA

^{177}Lu=Lutetium-177. ^{225}Ac=Actinium-225. ECOG=Eastern Cooperative Oncology Group. HR=hazard ratio. NA=not applicable (only variables whose association demonstrated statistical significance with the outcome on univariable analysis are included in the multivariable analysis). PSA=prostate-specific antigen. PSMA=prostate-specific membrane antigen. RLT=radioligand therapy.

Sathekge MM et al. *Lancet Oncol* 2024 February;25(2):175-83.

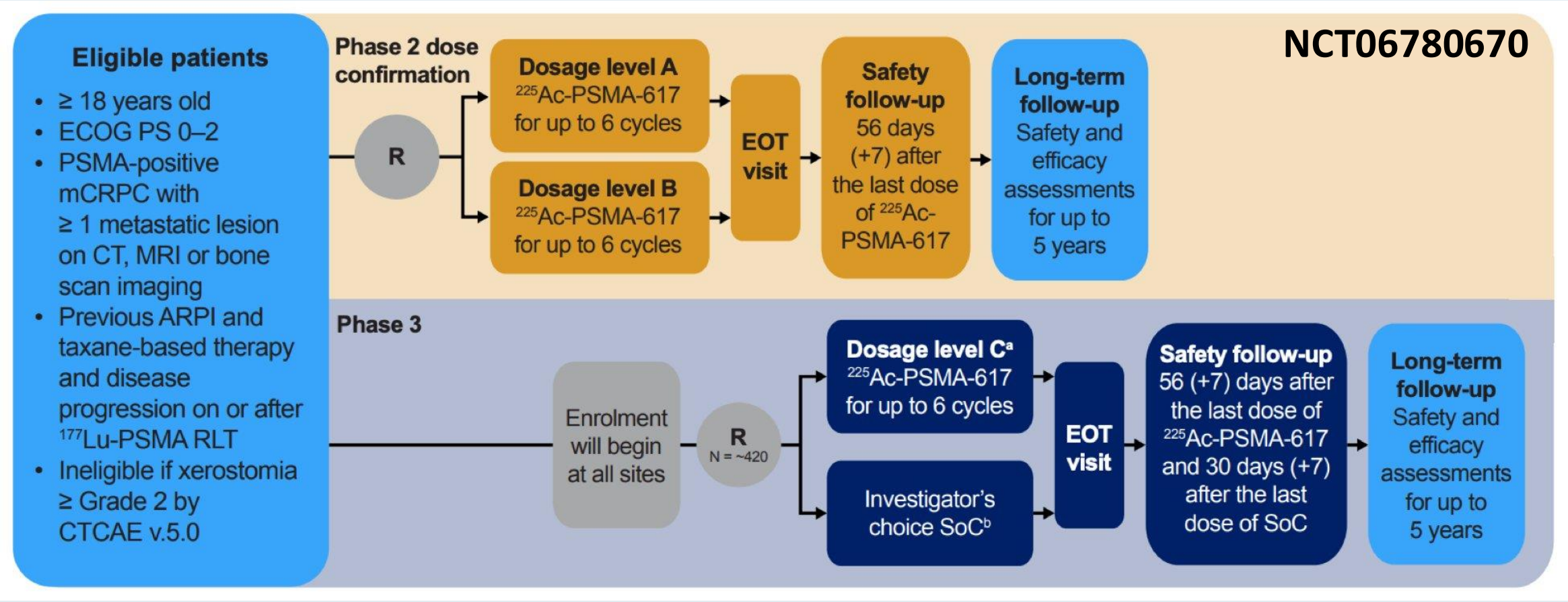
WARMTH Act: Bone Marrow Toxicity, Renal Function Impairment

	Before ^{225}Ac-PSMA RLT (n=488)				After ^{225}Ac-PSMA RLT (n=488)			
	Grade 1–2	Grade 3	Grade 4	Grade 5	Grade 1–2	Grade 3	Grade 4	Grade 5
Anaemia	301 (62%)	23 (5%)	0	0	329 (67%)	64 (13%)	0	0
Leukopenia	85 (17%)	4 (<1%)	0	0	198 (41%)	18 (4%)	1 (<1%)	0
Thrombocytopenia	135 (28%)	5 (1%)	10 (2%)	0	230 (47%)	17 (3%)	15 (3%)	0
Renal function impairment (eGFR)	229 (47%)	11 (2%)	3 (<1%)	0	250 (51%)	17 (3%)	5 (1%)	0

^{225}Ac=Actinium-225. PSMA=prostate-specific membrane antigen. RLT=radioligand therapy. eGFR=estimated glomerular filtration rate.

Sathekge MM et al. *Lancet Oncol* 2024 February;25(2):175-83.

Phase II/III PSMAcTION Study Design



<u>Primary endpoints</u>: Biochemical response rate, safety, tolerability

Secondary endpoints: rPFS, overall response rate

Emmett L et al. ESMO 2025;Abstract 2516TiP.

Agenda
Prostate Cancer

INTRODUCTION: Evolution of the prostate cancer model; PCWG4

MODULE 1: Hormonal therapy

MODULE 2: Chemotherapy (docetaxel)

MODULE 3: PARP inhibition

MODULE 4: Radioligand therapy

MODULE 5: New agents

Questions About New Agents

- **What has been your experience with efficacy and tolerability of B7-H3 ADCs such as ifinatamab deruxtecan? Do you believe these will eventually be used prior to the use of chemotherapy? What about combinations?**
- **What has been your experience in detection of HER2-positive prostate cancer, and what experience if any do you have in the use of T-DXd in terms of efficacy and tolerability? How do you approach the use of preventive antiemetic regimens and screening and management of ILD?**

Questions About New Agents

- **How would you describe the mechanism of action of opevesostat (CYP11A1 inhibitor) to that of abiraterone (CYP17A1 inhibitor)? What impact might this difference have on efficacy and tolerability?**
- **If data with opevesostat are positive, how do you envision this agent being utilized in the clinical setting?**

Questions About New Agents

- **What is the rationale and design of the TulmiSTAR trial? What are tulmimetostat and luxdegalutamide?**

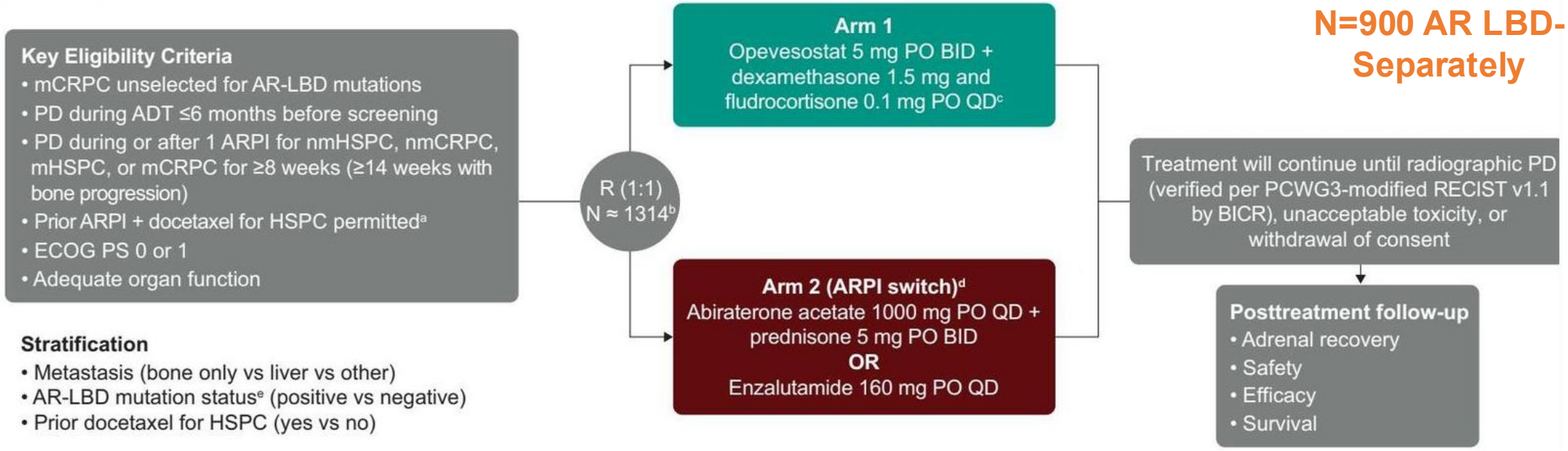
Questions About New Agents

- **What is your experience with the use of CD3 bispecific agents in prostate cancer, such as pasritamig? What have you observed in terms of treatment efficacy and tolerability, including experience with cytokine release syndrome?**
- **What do you see as the future of finger-stick assays for PSA as an initial screening tool and perhaps self-testing?**

Emerging Therapy: Opevesostat (CYP11A1 Upstream Androgen Synthesis Inhibitor)

OMAHA-004

Primary endpoints: rPFS
N=400 AR LBD+
N=900 AR LBD-
Separately



OMAHA-003: Similar but requires 1-2 prior taxanes for mCRPC (n=1310). Primary: OS (separate analysis by AR LBD status)

Fizazi K et al. ASCO GU 2026
Yu E et al. ASCO GU 2026

AbstractsTPS298-9

IDeate-Prostate02: A Phase 1/2, Open-Label Umbrella Substudy of Ifinatamab Deruxtecan-Based Treatment Combinations or as Monotherapy in Participants with Previously Treated Metastatic Castration-Resistant Prostate Cancer

J. de Bono,[1] N. Mehra,[2] M. Tang,[3] S. Wang,[4] F. Jafari,[4] K. Imai,[4] E. Efstathiou[5]

[1]The Institute of Cancer Research and The Royal Marsden Hospital, London, UK; [2]Radboud University Medical Center, Nijmegen, Gelderland, Netherlands; [3]Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [4]Merck & Co., Inc., Rahway, NJ, USA; [5]OHSU Knight Cancer Institute, Portland, OR, USA

Background

- There remains a high unmet need for novel effective therapies to improve outcomes for metastatic castration-resistant prostate cancer (mCRPC)[1]
- B7-H3 (CD276, a type I transmembrane protein) is overexpressed in various types of human cancers, including mCRPC[2,3]
- B7-H3 overexpression is associated with poor prognosis in certain types of cancers, and unresponsiveness to conventional cancer therapies, including immune checkpoint inhibitors[2–5]
- Ifinatamab deruxtecan (I-DXd; MK-2400/DS-7300a) is a B7-H3-directed antibody-drug-conjugate with a plasma-stable, tetrapeptide-based, cleavable linker and the potent topoisomerase I inhibitor payload DXd[6]
- A first-in-human phase 1/2 study of I-DXd demonstrated promising antitumor activity and encouraging duration of response in participants with heavily pretreated mCRPC, with a manageable safety profile[7,8]
- These results merit further clinical investigation of I-DXd-based investigational treatment combinations in mCRPC
- IDeate-Prostate02 is a phase 1/2, multicenter, open-label, umbrella substudy of I-DXd-based treatments (clinical trial registry number: NCT06863272)

Objectives

- Primary and secondary objectives are shown in **Table 1**

Table 1. Primary and secondary objectives

	Efficacy Phase (Arms 1–4)	Combination Safety Lead-In (Arms 3–4)
Primary objectives	To evaluate safety and tolerability To evaluate PSA response rate	To evaluate safety and tolerability To establish the RP2D for the treatment combinations
Secondary objectives	To evaluate: ORR, rPFS, OS, DOR, TFST, time to PSA progression, TTPP	

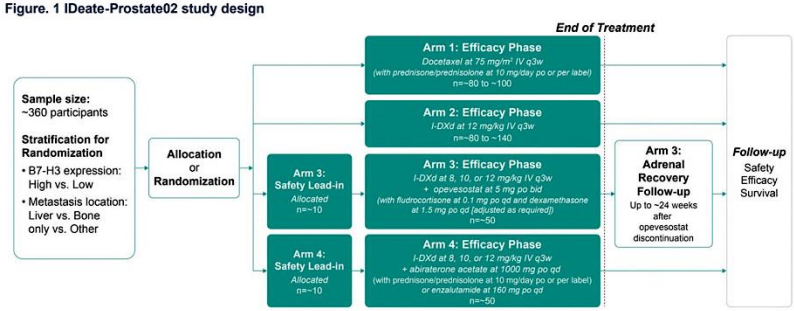
DOR, duration of response; ORR, objective response rate; OS, overall survival; PSA, prostate-specific antigen; RP2D, recommended phase 2 dose; rPFS, radiographic progression-free survival; TFST, time from allocation/randomization to initiation of the first subsequent anticancer therapy; TTPP, time to pain progression.

Methods

Study design, participants, and treatment

- The study design of IDeate-Prostate02 is shown in **Figure 1** and the key eligibility criteria are listed in **Table 2**

Figure. 1 IDeate-Prostate02 study design



B7-H3, CD276; bid, twice daily; I-DXd, ifinatamab deruxtecan; IM, intramuscular; IV, intravenous; n, number of participants; po, per os (by mouth); q3w, once every 3 weeks; qd, once daily.

Assessments

- Primary and secondary endpoints are listed **Table 3**
- Biomarker analysis: B7-H3 expression in tumor samples will be assessed using an analytically validated immunohistochemistry assay, to be used as a stratification factor during randomization

Presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium; San Francisco, CA, USA & Online; February 26-28, 2026

Table 2. Key eligibility criteria

Key Inclusion Criteria	
Demographics	• ≥ 18 years of age
Participant and disease characteristics	• Histologically or cytologically confirmed adenocarcinoma of the prostate without small cell histology • Prostate cancer progression on ADT (or post bilateral orchiectomy) ≤ 6 months prior to screening by ≥ 1 of the following: – Clinical disease progression (per Investigator) and PSA progression – Radiographic disease progression in soft tissue based on RECIST v1.1 criteria with or without PSA progression – Radiographic disease progression in bone based on PCWG3-Modified RECIST v1.1, defined as the appearance of ≥ 2 new bone lesions on bone scan with or without PSA progression • Progression > 4 weeks since last flutamide treatment or > 6 weeks since last bicalutamide or nilutamide treatment, in participants who received first generation ADT prior to enrollment • Metastatic disease documented by either bone lesions on bone scan and/or soft tissue lesions per RECIST v1.1 by CT/MRI • Prior treatment with 1 or 2 ARPI(s) (eg, abiraterone acetate, enzalutamide, apalutamide, or darolutamide) for nonmetastatic HSPC, mHSPC, nonmetastatic CRPC, or mCRPC and progressed during or after ≥ 8 weeks of treatment • Ongoing androgen deprivation with serum testosterone < 50 ng/dL (< 1.7 nM) • Prior treatment with PARPi if indicated by local approved regimen or were deemed ineligible to receive PARPi by the Investigator
Additional criteria	• Evaluable B7-H3 expression prior to allocation/randomization determined from testing of: – Core or excisional biopsy from soft tissue (not previously irradiated and obtained after disease progression on the most recent prior therapy) in participants with soft-tissue disease or – Archival soft-tissue tumor sample in participants with bone-only disease • ECOG performance status ≤ 1 • Adequate organ function
Key Exclusion Criteria	
Medical conditions	• Gastrointestinal disorder affecting absorption, or unable to swallow tablets/capsules • History of ILD/pneumonitis, irrespective of prior steroid use, current ILD, ILD that cannot be ruled out at screening, or suspected ILD • Clinically severe pulmonary compromise resulting from intercurrent pulmonary illnesses • CTCAE grade ≥ 3 peripheral neuropathy, except when due to trauma • Uncontrolled or significant cardiovascular disease
Prior/ Concomitant therapy	• Prior treatment with a taxane-based chemotherapy agent for mCRPC – Docetaxel for HSPC is allowed provided there was no radiographic disease progression ≤ 1 year after the last dose of docetaxel • Prior treatment with orlotamab, enoblituzumab, or other B7-H3-targeted agents, including I-DXd • Prior discontinuation of an ADC that consists of an exatecan derivative due to treatment-related toxicities • Chronic steroid treatment (dose of > 10 mg daily prednisone equivalent)

ADC, anti-drug conjugate; ADT, androgen-deprivation therapy; ARPI, androgen-receptor pathway inhibitor; B7-H3, CD276; CRPC, castration-resistant prostate cancer; CT, computed tomography; CTCAE, Common Terminology Criteria for Adverse Events; ECOG, Eastern Cooperative Oncology Group; HSPC, hormone-sensitive prostate cancer; I-DXd, ifinatamab deruxtecan; ILD, interstitial lung disease; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; MRI, magnetic resonance imaging; PARPi, poly-ADP-ribose polymerase inhibitor; PCWG3, Prostate Cancer Working Group 3; PSA, prostate-specific antigen; RECIST, Response Evaluation Criteria In Solid Tumors..

- Efficacy: Tumor imaging (computed tomography/magnetic resonance imaging) of the chest/abdomen/pelvis will be performed at screening, every 6 weeks from allocation/randomization until week 48, then every 12 weeks to monitor for radiographic disease progression
- Safety: Adverse events and serious adverse events will be monitored from allocation/randomization through to the following days after cessation treatment: 40 days for I-DXd, docetaxel and opevesostat, 14 days for abiraterone acetate and prednisone/prednisolone, and 32 days for enzalutamide

Disclosures

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Contact information

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Table 3. Primary and secondary endpoints

Primary Endpoints
• Efficacy phase – ≥ 50% reduction PSA response
• Efficacy phase and safety lead-in phase: DLT, AE, serious AE, study discontinuation due to AE
Secondary Endpoints
• ORR: CR or PR per PCWG-modified RECIST v1.1 as assessed by BICR
• rPFS: Time from allocation/randomization to the first documented disease progression per PCWG-modified RECIST v1.1 as assessed by BICR, or death from any cause, whichever occurs first
• OS: Time from allocation/randomization to death due to any cause
• DOR: Time from first documented evidence of CR or PR until disease progression or death due to any cause, whichever occurs first
• TFST: Time from allocation/randomization to initiation of the first subsequent anticancer therapy or death, whichever occurs first
• PSA progression: Time from allocation/randomization to PSA progression
• TTPP: Time from allocation/randomization to pain progression as determined by Item 3 of the BPI-SF and AQA score

AE, adverse event; AQA, Analgesic Quantification Algorithm; BICR, blinded independent central review; BPI-SF, brief pain inventory-short form; CR, complete response; DLT, dose-limiting toxicity; DOR, duration of response; ORR, objective response rate; OS, overall survival; PCWG, Prostate Cancer Working Group; PR, partial response; PSA, prostate-specific antigen; RECIST, Response Evaluation Criteria In Solid Tumors; rPFS, radiographic progression-free survival; TFST, time from allocation/randomization to initiation of the first subsequent anticancer therapy; TTPP, time to pain progression.

Analyses

- The intent-to-treat population will be used for the primary efficacy analyses in the efficacy phase; all randomized participants will be included in this population
- The all-participants-as-treated population will be used for the safety data, consisting of all allocated participants in the safety lead-in phase who received ≥ 1 dose of study intervention and all randomized participants in the efficacy phase who received ≥ 1 dose of study intervention
- Participants within the same investigational treatment arm at the same dose level/frequency in the safety lead-in phase and efficacy phase will be pooled in the safety analysis

Current status

- The IDeate-Prostate01 study began on July 03, 2025, and enrollment is currently ongoing globally (**Figure 2**)

Figure 2. Map of IDeate-Prostate02 currently enrolling study sites (since July 2025)

Locations with currently enrolling investigative sites	
Argentina	Netherlands
Australia	New Zealand
Brazil	Poland
Canada	South Korea
Chile	Spain
France	Taiwan
Germany	Turkey
Ireland	UK
Israel	USA
Italy	

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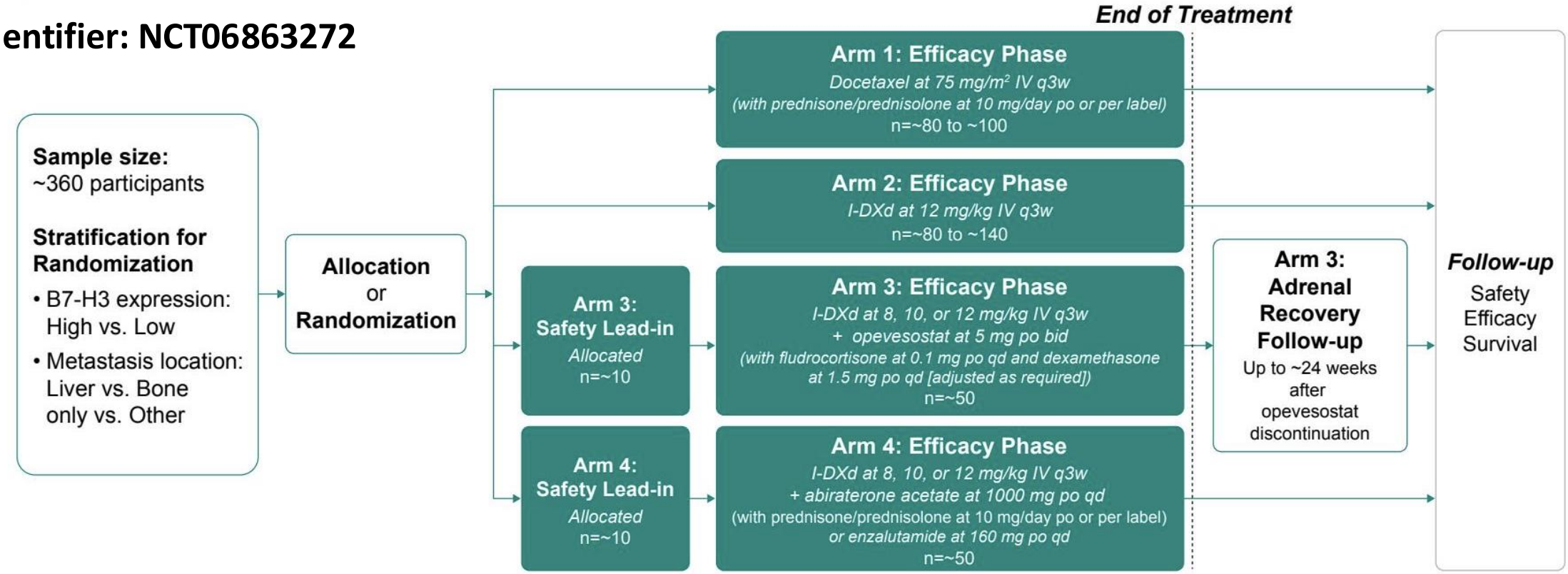
1. EAU - EANM - ESTRO - ESUR - ISUP - SIOG Guidelines on Prostate Cancer. Available from: https://d56bochluxqnz.cloudfront.net/documents/ full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2025_2025-03-24-120144_rma.pdf. Accessed July 07, 2025. 2. Getu AA, et al. *Mol Cancer.* 2023;22:43. 3. Shen Q, et al. *Discov Oncol.* 2024;15:822. 4. Zhao B, et al. *J Hematol Oncol.* 2022;15:153. 5. Lin W, et al. *Front Immunol.* 2021;5;12:757047. 6. Yamato M, et al. *Mol Cancer Ther.* 2022;21:635–46. 7. Patel MR, et al. *Ann Oncol.* 2023;34:S481–S482. 8. Patel MR, et al. *J Clin Oncol.* 2022;40(Suppl 6):Abstract 87.

Acknowledgments

The authors thank the participants and their families and all investigators and site personnel participating in this study. The authors also acknowledge contributions from Jelena Todoric and Christian Poehlein (at the time of study conduct) from Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. Christian Hosius from MSD Sharp & Dohme GmbH, Munich, Germany; and Caleb Lee from Daiichi Sankyo, Inc, Basking Ridge, NJ, USA. This study was funded by Daiichi Sankyo Company, Limited and Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. Medical writing assistance was provided by Jo Fetterman, PhD, and Nicolisha Narainpersad, PhD, Parexel International. This assistance was funded by Daiichi Sankyo Company, Limited and Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

IDeate-Prostate02: Phase I/II Umbrella Substudy of Ifinatamab Deruxtecan-Based Treatment Combinations or as Monotherapy in Previously Treated mCRPC

Trial Identifier: NCT06863272



	Efficacy Phase (Arms 1–4)	Combination Safety Lead-In (Arms 3–4)
Primary objectives	To evaluate safety and tolerability To evaluate PSA response rate	To evaluate safety and tolerability To establish the RP2D for the treatment combinations
Secondary objectives	To evaluate: ORR, rPFS, OS, DOR, TFST, time to PSA progression, TTPP	

DeBono J et al. Genitourinary Cancer Symposium 2026;Abstract TPS297.

IDeate-Prostate01: A Phase 3, Randomized, Open-Label Study of Ifinatamab Deruxtecan versus Docetaxel in Participants with Previously Treated Metastatic Castration-Resistant Prostate Cancer

R. R. McKay,[1] M. Tang,[2] J. Zhang,[3] J. Todoric,[3] K. Imai,[3] A. A. Azad[4]
[1]Moores Cancer Center, University of California San Diego Health, CA, USA; [2]Daiichi Sankyo, Inc., Basking Ridge, NJ, USA; [3]Merck & Co., Inc., Rahway, NJ, USA; [4]Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia

Background

- Standard treatments for metastatic castration-resistant prostate cancer (mCRPC) include androgen-deprivation therapy (ADT) plus systemic androgen-receptor pathway inhibitors (ARPIs), taxanes, radiopharmaceuticals, or targeted therapies[1–3]
- Despite multiple available therapies with diverse mechanisms of action, eventual disease progression is highly likely following each treatment[3]
- There remains a critical and urgent unmet medical need for novel treatments that improve outcomes and delay disease progression with a manageable safety profile
- B7-H3 (CD276), a type I transmembrane protein, is part of the B7 family of immune-regulatory ligands that is overexpressed in various cancers, including mCRPC[4–6]
- B7-H3 overexpression is associated with poor prognosis and unresponsiveness to conventional cancer therapies, including immune checkpoint inhibitors[4–8]
- Ifinatamab deruxtecan (I-DXd; MK-2400/DS-7300a) is a B7-H3-directed antibody-drug-conjugate with a plasma-stable tetrapeptide-based cleavable linker and the potent topoisomerase I inhibitor payload DXd[9–11]
- Preliminary results from the first-in-human phase 1/2 IDeate-PanTumor01 study of I-DXd demonstrated antitumor activity and manageable safety in multiple solid tumors, including heavily pretreated mCRPC[10,11]
- IDeate-Prostate01 (NCT06925737) is a phase 3, randomized, open-label study designed to evaluate the efficacy and safety of I-DXd versus docetaxel in participants with mCRPC previously treated with 1 or 2 ARPIs

Objectives

Dual Primary

- To compare overall survival (OS) with I-DXd versus docetaxel in participants with mCRPC
- To compare radiographic progression-free survival (rPFS) with I-DXd versus docetaxel in participants with mCRPC

Secondary

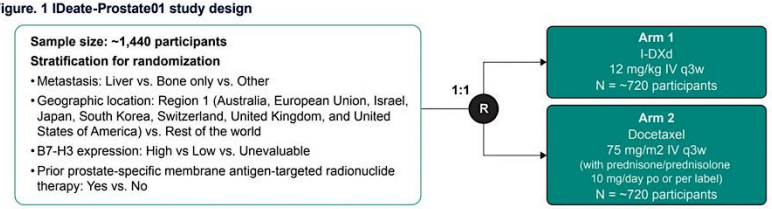
- To evaluate time to first subsequent therapy, objective response, duration of response, time to pain progression, time to prostate-specific antigen (PSA) progression, PSA response, and time to first symptomatic skeletal-related events, and safety

Methods

Study design, participants, and treatment

- The study design of IDeate-Prostate01 is shown in **Figure 1** and the key eligibility criteria are listed in **Table 1**

Figure. 1 IDeate-Prostate01 study design



B7-H3, CD276; I-DXd, ifinatamab deruxtecan; IV, intravenous; po, per oral; q3w, every 3 weeks; R, randomization.
Treatment may continue until radiographically documented and verified disease progression, unacceptable adverse events, intercurrent illness that prevents further administration of study intervention, Investigator's decision to discontinue the participant, withdrawal of consent, or administrative reasons requiring cessation of treatment.

Assessments

- The primary and secondary endpoints of the IDeate-Prostate01 study are shown in **Table 2**
- Assessments for efficacy:
  - Treatment response will be assessed using Prostate Cancer Working Group-modified Response Evaluation Criteria In Solid Tumors v1.1: soft tissue lesions per soft tissue rules (maximum 5 target soft tissue lesions, 2 per organ), and bone lesions per bone lesion rules
    - Soft tissue and bone responses will be integrated to determine overall radiographic response
  - Tumor imaging (computed tomography/magnetic resonance imaging) of the chest/abdomen/pelvis along with whole-body Tc99m bone scan will be performed at screening, every 6 weeks from randomization until week 48, then every 12 weeks to monitor for radiographic disease progression
    - Bone disease progression will be confirmed by a follow-up bone scan ≥ 6 weeks after initial radiographic evidence of disease progression

Table 1. Key eligibility criteria

Key Inclusion Criteria	
Demographics	• ≥ 18 years at the time of providing informed consent
Participant and disease characteristics	• Histologically or cytologically confirmed adenocarcinoma of the prostate without small cell histology • Prostate cancer progression on ADT (or post bilateral orchiectomy) ≤ 6 months prior to screening by means of ≥ 1 of the following: – Clinical disease progression (per Investigator) and PSA progression – Radiographic disease progression in soft tissue based on RECIST v1.1 criteria – Radiographic disease progression in bone based on PCWG3, defined as the appearance of ≥ 2 new bone lesions on bone scan • Evidence of progression > 4 weeks since last flutamide treatment or > 6 weeks since last bicalutamide or nilutamide treatment, in participants who received first-generation ADT prior to enrollment • Current evidence of metastatic disease documented by either bone lesions on bone scan and/or soft tissue disease by CT/MRI • Received prior treatment with 1 or 2 ARPI(s) (eg, abiraterone acetate, enzalutamide, apalutamide, or darolutamide) for nonmetastatic HSPC, mHSPC, nonmetastatic CRPC, or mCRPC and progressed during or after at least 8 weeks of treatment • Ongoing androgen deprivation with serum testosterone < 50 ng/dL (< 1.7 nM) • Prior treatment with PARPi if indicated by local approved regimen or deemed ineligible to receive PARPi treatment by the Investigator
Additional criteria	• ECOG performance status ≤ 1 • Provided tumor tissue from a core or excisional biopsy from soft tissue not previously irradiated and obtained after disease progression on the most recent prior therapy • Adequate organ function
Key Exclusion Criteria	
Medical conditions	• History of (noninfectious) ILD/pneumonitis that required steroids or current ILD/pneumonitis and/or suspected ILD/pneumonitis that cannot be ruled out by standard diagnostic assessments at screening • CTCAE v5.0 grade ≥ 3 peripheral neuropathy, except when due to trauma • Uncontrolled or significant cardiovascular disease
Prior/ Concomitant therapy	• Received prior treatment with a taxane-based chemotherapy agent for mCRPC – Docetaxel for HSPC is allowed provided there was no radiographic disease progression ≤ 1 year after the last dose of docetaxel • Prior treatment with orlotamab, enoblituzumab, or other B7-H3-targeted agents, including I-DXd • Prior discontinuation of an ADC that consists of an exatecan derivative due to treatment-related toxicities • Chronic steroid treatment

ADC, antibody drug conjugate; ADT, androgen-deprivation therapy, ARPI, androgen-receptor pathway inhibitor; B7-H3, CD276; CRPC, castration-resistant prostate cancer; CT, computer tomography; CTCAE, Common Terminology Criteria for Adverse Events; ECOG, Eastern Cooperative Oncology Group; HSPC, hormone-sensitive prostate cancer; I-DXd, ifinatamab deruxtecan; ILD, interstitial lung disease; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; MRI, magnetic resonance imaging; PARPi, poly(adenosine diphosphate-ribose) polymerase inhibitor; PCWG3, Prostate Cancer Working Group 3; PSA, prostate-specific antigen; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

- Assessments for safety will include monitoring of adverse events (including infusion-related reactions), serious adverse events from randomization through 40 days after cessation of study intervention, and followed until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up

Analyses

- The dual primary endpoints (rPFS and OS) will be assessed for the intent-to-treat population, which will include all randomized participants
- Objective response will be assessed in all randomized participants with measurable disease at baseline
- The safety analysis population will include participants who received at least 1 dose of study intervention
- The study would be considered positive if either 1 or both of the dual primary endpoints are met

Acknowledgments
The authors thank the participants and their families and all investigators and site personnel participating in this study. The authors also acknowledge contributions from Caleb Lee from Daiichi Sankyo, Inc. Basking Ridge, NJ, USA, and Christian Poehlein (at the time of study conduct) and Aiying Chen from Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. This study was funded by Daiichi Sankyo Company, Limited and Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA. Medical writing assistance was provided by Nicolisha Narainpersad, PhD, of Parexel. This assistance was funded by Daiichi Sankyo Company, Limited and Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Disclosures
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Table 2. Primary and secondary endpoints criteria

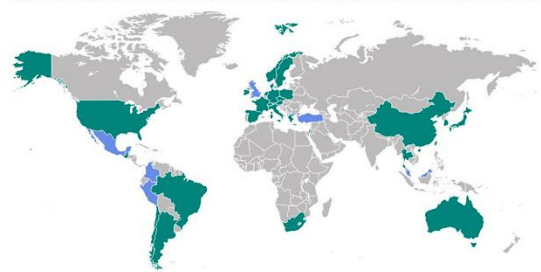
Dual Primary Endpoints
OS: Time from randomization to death due to any cause
rPFS: Time from randomization to radiographic progression per PCWG-modified RECIST v1.1[12] by BICR or death due to any cause, whichever occurs first
Secondary Endpoints
• TFST: Time from randomization to initiation of the first subsequent anticancer therapy or death, whichever occurs first
• OR: Confirmed CR or PR
• DOR: Time from the earliest date of first documented evidence of confirmed CR or PR until the earliest date of disease progression or death from any cause, whichever comes first
• TTPP: Time from randomization to pain progression as determined by brief pain inventory-short form item 3 "worst pain in 24 hours" and analgesic quantification algorithm score
• Time to PSA progression: Time from randomization to PSA progression per PCWG3 criteria[12]
• PSA response: Having a postbaseline PSA reduction ≥ 50% from baseline with a consecutive confirmation assessment at least 3 weeks later per PCWG3 criteria[12]
• Time to first SSRE: Time from randomization to the first occurrence of any of the following symptomatic skeletal related events: 1. Use of external beam radiation therapy to prevent or relieve skeletal symptoms 2. New symptomatic pathologic bone fracture (vertebral or nonvertebral) 3. Spinal cord compression 4. Tumor-related orthopedic surgical intervention
• Safety (AEs; study intervention discontinuation due to AEs)

AE, adverse event; BICR, blinded independent central review; CR, complete response; DOR, duration of response; OR, objective response; OS, overall survival; PCWG, Prostate Cancer Working Group; PCWG3, Prostate Cancer Working Group 3; PR, partial response; PSA, prostate-specific antigen; RECIST v1.1, Response Evaluation Criteria In Solid Tumors version 1.1; rPFS, radiographic progression-free survival; SSRE, symptomatic skeletal-related event; TFST, time to initiation of the first subsequent anticancer therapy; TTPP, time to pain progression.

Current status

- The IDeate-Prostate01 study began on May 13, 2025, and enrollment is currently ongoing globally (**Figure 2**)

Figure 2. Map of IDeate-Prostate01 currently enrolling (since May 2025) and planned study sites



Locations with currently enrolling investigative sites		
Argentina	Greece	Singapore
Australia	Guatemala	South Africa
Austria	Hong Kong	South Korea
Brazil	Ireland	Spain
Chile	Israel	Sweden
China	Italy	Switzerland
Czechia	Japan	Taiwan
Denmark	Netherlands	Thailand
France	Norway	USA
Germany	Poland	

Locations with planned investigative sites		
Columbia	Mexico	Turkey
Malaysia	Peru	UK

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1. Gillette CM, et al. *Cancers (Basel)*. 2023;15:2552. 2. Lowrance W, et al. *J Urol*. 2023;209:1082–90. 3. EAU - EANM - ESTRO - ESUR - ISUP - SIOG Guidelines on Prostate Cancer. Available from: https://d56bochluxqnz.cloudfront.net/documents/full-guideline/EAU-EANM-ESTRO-ESUR-ISUP-SIOG-Guidelines-on-Prostate-Cancer-2025_2025-03-24-120144_rinw.pdf. Accessed September 26, 2025. 4. Ju Y, et al. *Drug Resist Updat*. 2025;79:101207. 5. Getu AA, et al. *Mol Cancer*. 2023;22:43. 6. Shen Q, et al. *Discov Oncol*. 2024;15:822. 7. Zhao B, et al. *J Hematol Oncol*. 2022;15:153. 8. Lin W, et al. *Front Immunol*. 2021; 5:12:757047. 9. Yamato M, et al. *Mol Cancer Ther*. 2022;21: 635–46. 10. Patel MR, et al. *Ann Oncol*. 2023;34:S481–S482. 11. Patel MR, et al. *J Clin Oncol*. 2022;40(Suppl 6):Abstract 87. 12. Schwartz LH, et al. *Eur J Cancer*. 2016;62:138–45.

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Presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium; San Francisco, CA, USA & Online; February 26-28, 2026

IDeate-Prostate01: Phase III Study of Ifinatamab Deruxtecan Versus Docetaxel in Previously Treated mCRPC

Trial Identifier: NCT06925737

Sample size: ~1,440 participants

Stratification for randomization

- Metastasis: Liver vs. Bone only vs. Other
- Geographic location: Region 1 (Australia, European Union, Israel, Japan, South Korea, Switzerland, United Kingdom, and United States of America) vs. Rest of the world
- B7-H3 expression: High vs Low vs. Unevaluable
- Prior prostate-specific membrane antigen-targeted radionuclide therapy: Yes vs. No

1:1 R

Arm 1
I-DXd
12 mg/kg IV q3w
N = ~720 participants

Arm 2
Docetaxel
75 mg/m2 IV q3w
(with prednisone/prednisolone 10 mg/day po or per label)
N = ~720 participants

Dual Primary Endpoints
OS: Time from randomization to death due to any cause
rPFS: Time from randomization to radiographic progression per PCWG-modified RECIST v1.1[12] by BICR or death due to any cause, whichever occurs first

McKay RR et al. Genitourinary Cancer Symposium 2026;Abstract TPS294.

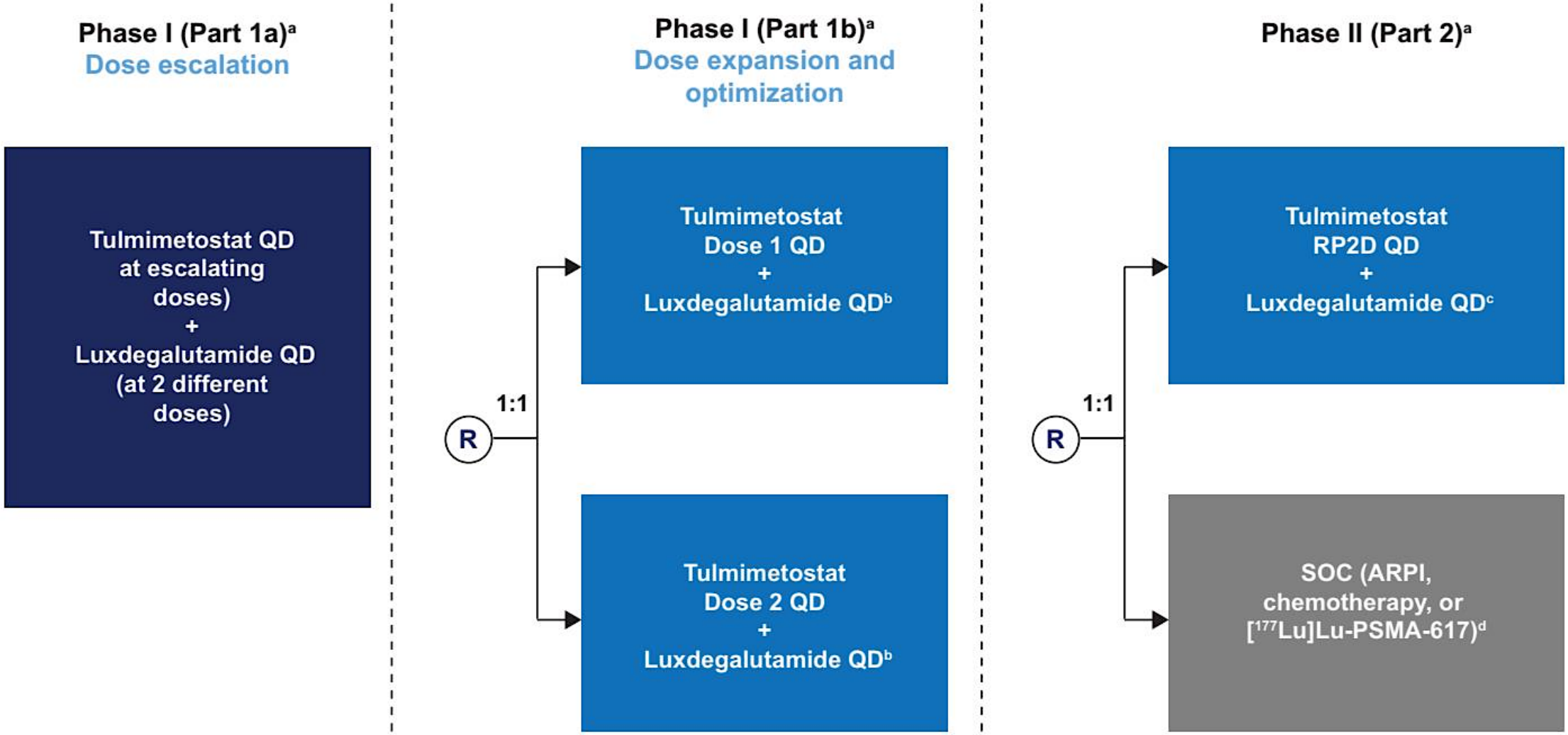
#TPS301

✉ Andrew J. Armstrong | andrew.armstrong@duke.edu

TulmiSTAR-01: A phase I/II dose optimization study of tulmimetostat in combination with luxdegalutamide versus standard of care in patients with progressive metastatic castrate-resistant prostate cancer

Armstrong A et al. ASCO GU 2026

TulmiSTAR01: Study Design



[a]Patients are required to continue ADT and the GnRH analog/antagonist or undergo orchiectomy to achieve castrate levels of testosterone (<50 ng/dL or <1.7 nmol/L); [b]The dose of luxdegalutamide (100 mg or 300 mg) will be determined based on the totality of data from Part 1a, and this may differ in the 2 arms; [c]The dose of luxdegalutamide will be selected dose from Part 1b; [d]Randomization will be stratified by the investigator's choice of SOC and the choice of SOC is at the discretion of the investigator and based on local regulations/regional access.

Armstrong A et al. ASCO GU 2026

TulmiSTAR01: Key Points

- TulmiSTAR-01 (NCT07206056) is a phase I/II, open-label, global, multicenter study assessing the safety and efficacy of the combination of tulmimetostat and luxdegalutamide versus SOC in patients with progressive mCRPC.
- Phase I consists of dose-escalation component (Part 1a), followed by dose-expansion and dose-optimization (Part 1b). Phase II (randomized design) aims to compare the combination of tulmimetostat plus luxdegalutamide with SOC in taxane-naïve patients with mCRPC.
- Primary endpoints include the evaluation of recommended dose(s), pharmacokinetics, safety, and tolerability of the tulmimetostat plus luxdegalutamide combination in phase I and PSA50 response at 6 months compared to SOC in taxane-naïve patients with mCRPC in phase II.
- The secondary efficacy endpoints include PSA50 response at 3, 9, and 12 months, rPFS, OS, ORR, BOR, DOR, and TTSSE.

Tulmimetostat is also being investigated in mHSPC (TulmiSTAR-02, NCT07190300). Please refer to the poster below, which is also being presented at ASCO GU 2026:

TPS302: TulmiSTAR-02: A phase I/II open-label study of dose escalation and expansion of tulmimetostat in combination with darolutamide versus darolutamide, and tulmimetostat with abiraterone in patients with metastatic hormone-sensitive prostate cancer.

Armstrong A et al. ASCO GU 2026

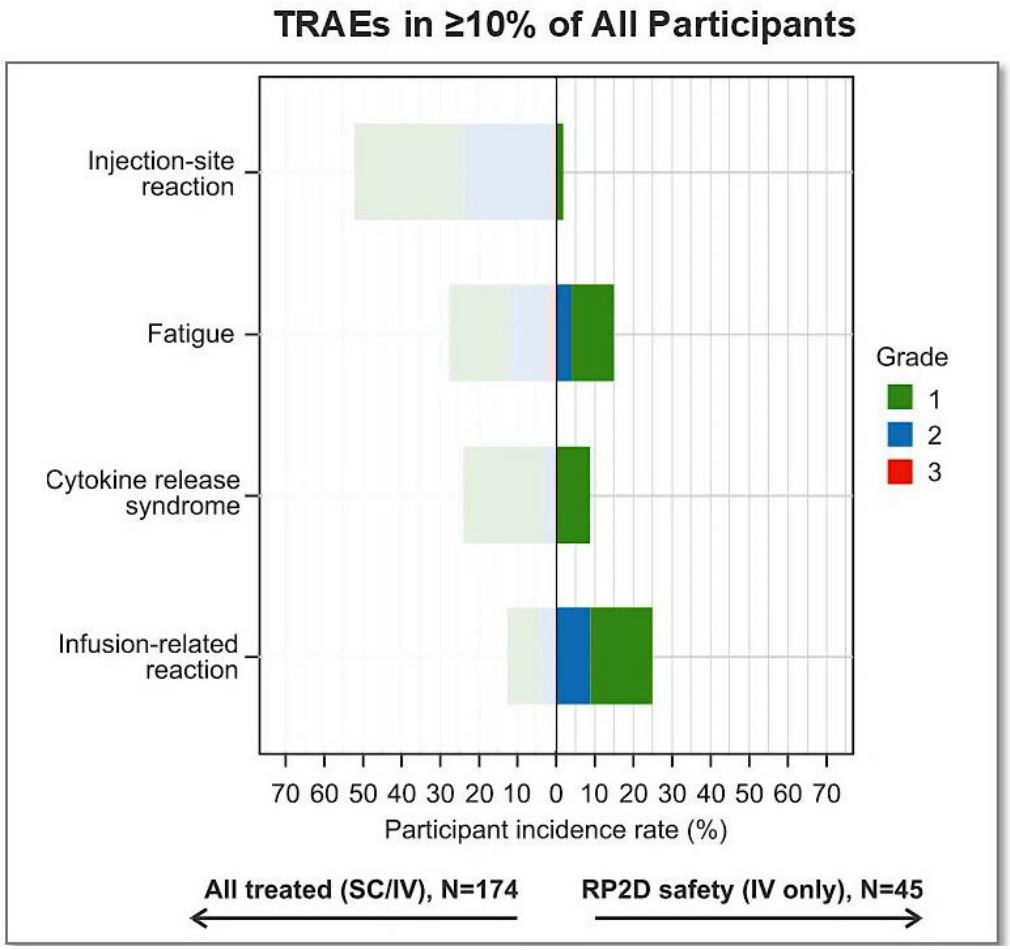
Phase 1 trial of pasritamig for mAPMR PC – Baseline Patient Characteristics

	All-Treated Population (SC/IV)	RP2D Safety Population (IV Only)[a]
	Total N=174	Total N=45[a]
Age, years, median (range)	69.0 (36, 89)	70.0 (36, 89)
ECOG PS, n (%)		
0	88 (50.6)	25 (55.6)
1	86 (49.4)	20 (44.4)
Baseline PSA, ng/mL (range)	74.8 (0.0, 2612.0)	58.4 (0.1, 2117.6)
Disease location,[b] n (%)		
Bone	153 (88.4)	40 (90.9)
Lymph node	81 (46.8)	17 (38.6)
Visceral	42 (24.3)	5 (11.4)
Liver	18 (10.4)	1 (2.3)

	All-Treated Population (SC/IV)	RP2D Safety Population (IV Only)[a]
	Total N=174	Total N=45[a]
Lines of prior systemic therapy, median (range)	**4.0 (1.0, 13.0)**	**4.0 (1.0, 10.0)**
Prior therapy, n (%)		
ARPI	173 (99.4)	45 (100.0)
Taxane chemotherapy[c]	136 (78.2)	34 (75.6)
1 regimen	46 (26.4)	14 (31.1)
>1 regimen	90 (51.7)	20 (44.4)
Lu-177 PSMA RLT	31 (17.8)	17 (37.8)

Stein MN et al, J Clin Oncol 2025; 43: 2516-26.

Phase 1 trial of pasritamig for mAPMR PC – Safety and RP2D



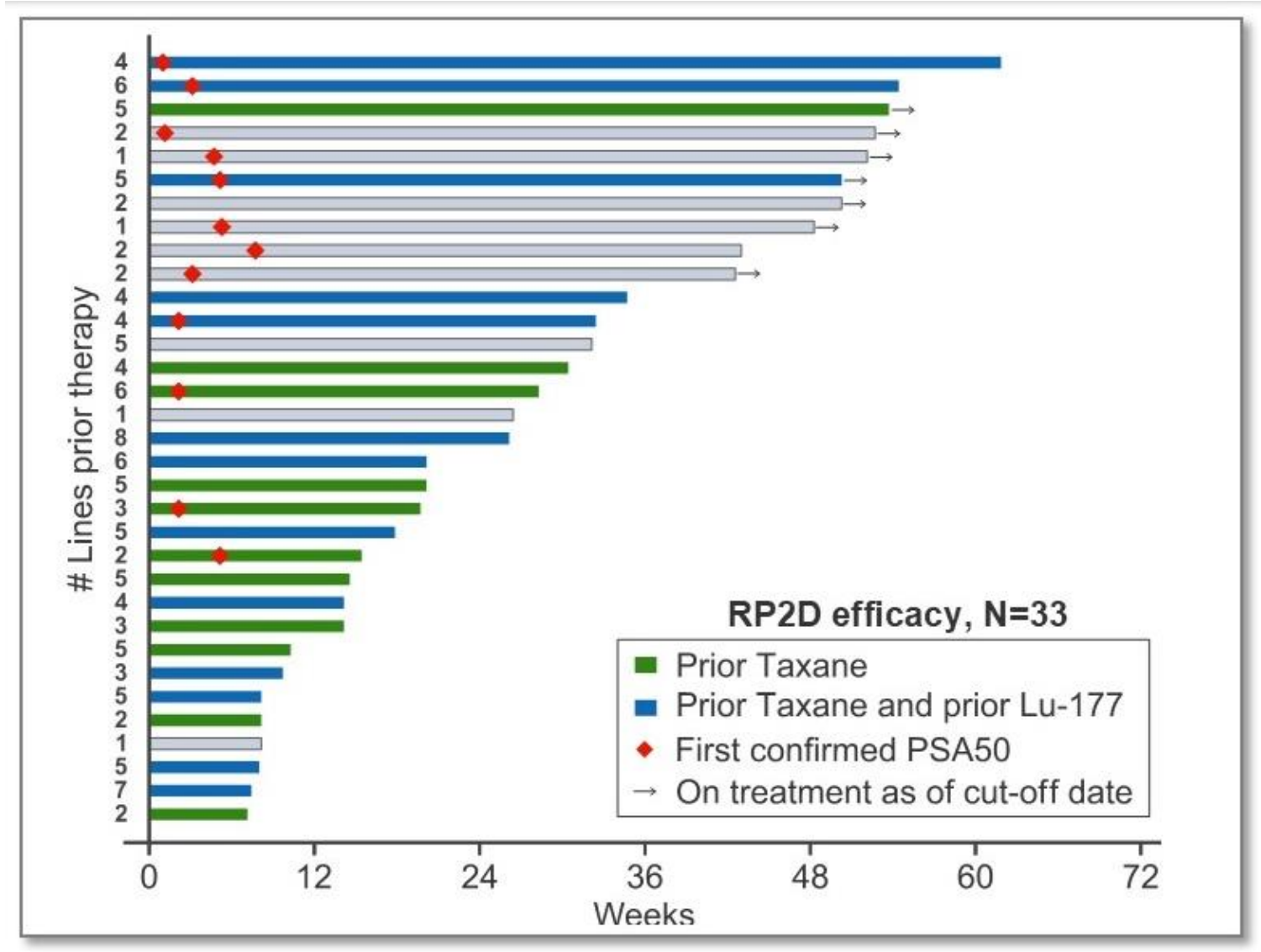
	All-Treated Population (SC/IV)	RP2D Safety Population (IV Only)
	N=174	N=45
Participants with ≥1 TRAE, n (%)	144 (82.8)	27 (60.0)
Serious TRAEs, n (%)	12 (6.9)	2 (4.4)[a]
Grade ≥3 TRAEs, n (%)	17 (9.8)	2 (4.4)
TRAEs leading to treatment discontinuation, n (%)	1 (0.6)	0

RP2D safety population (IV 3.5 mg D1, 18 mg D8, 300 mg D15 then Q3W/Q6W):

- **CRS** occurred in 4 pts (8.9%), **all Grade 1** (fever only) and **did not** require tocilizumab – *no TRAEs reported in 40% of patients*
- **IRRs** were seen **in 24.4%** of participants
  - Management was limited to mostly antipyretics; no steroid or epinephrine was given
- **No** TRAEs led to treatment **discontinuation, dose reduction, ICANS, or death**
- The **only Grade 3** TRAEs were **transient** AST/ALT increases and neutropenia
- **No DLTs**[b]

Stein MN et al, J Clin Oncol 2025; 43: 2516-26.

Phase 1 trial of pasritamig for mAPMR PC – RP2D Efficacy



Stein MN et al, J Clin Oncol 2025; 43: 2516-26.

Year in Review: Clinical Investigator Perspectives on the Most Relevant New Datasets and Advances in Oncology

Menin Inhibitors in Acute Myeloid Leukemia

A CME/MOC-Accredited Live Webinar

Thursday, March 26, 2026
5:00 PM – 6:00 PM ET

Faculty

Amir Fathi, MD
Eunice S Wang, MD

Moderator

Neil Love, MD

RTP Year in Review 2026

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Please take a moment to complete the survey currently up on Zoom. Your feedback is very important to us. The survey will remain open for 5 minutes after the meeting ends.

Information on how to obtain CME, ABIM MOC and ABS credit is provided in the Zoom chat room. Attendees will also receive an email in 1 to 3 business days with these instructions.

RTP Year in Review 2026