Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress

Prostate Cancer

Thursday, May 14, 2026

12:15 PM – 1:45 PM

Faculty

Michael Lai, MSN, ARNP, FNP-C
Stacy E Walker, FNP-BC
Evan Y Yu, MD

Moderator

Scott T Tagawa, MD, MS

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Faculty

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Mr Lai — Disclosures

No relevant financial relationships to disclose.

Ms Walker — Disclosures

No relevant financial relationships to disclose.

Dr Yu — Disclosures

Consulting Agreements	Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Johnson & Johnson, Lantheus, Merck, Novartis, Samsung Bioepis, Tolmar
Contracted Research	Bayer HealthCare Pharmaceuticals, Blue Earth Diagnostics, Dendreon Pharmaceuticals Inc, Lantheus, Merck, Pfizer Inc, Tyra Biosciences Inc

Dr Tagawa — Disclosures

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Contracted Research	AIQ Solutions, Bayer HealthCare Pharmaceuticals, Clarity Pharmaceuticals, Gilead Sciences Inc, Janux Therapeutics, Johnson & Johnson, Lilly, Merck, Novartis, Pfizer Inc, Telix Pharmaceuticals Limited
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This educational activity contains discussion of non-FDA-approved uses of agents and regimens. Please refer to official prescribing information for each product for approved indications.

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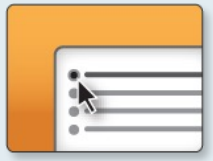
Clinicians in the Meeting Room

Networked iPads are available.

Review Program Slides: Tap the Program Slides button to review speaker presentations and other program content.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Tap Ask a Question to submit a challenging case or question for discussion. We will aim to address as many questions as possible during the program.

For assistance, please raise your hand. Devices will be collected at the conclusion of the activity.

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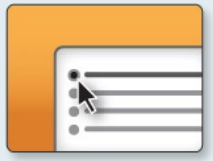
Clinicians Attending via Zoom

Review Program Slides: A link to the program slides will be posted in the chat room at the start of the program.



Answer Survey Questions: Complete the pre- and postmeeting surveys. Survey questions will be discussed throughout the meeting.

Ask a Question: Submit a challenging case or question for discussion using the Zoom chat room.

Get NCPD Credit: An NCPD credit link will be provided in the chat room at the conclusion of the program.

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About the Enduring Program

- The live meeting is being video and audio recorded.
- The proceedings from today will be edited and developed into an enduring web-based program. An email will be sent to all attendees when the activity is available.
- To learn more about our education programs, visit our website, **www.ResearchToPractice.com**

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RTP RESEARCH TO PRACTICE ONCOLOGY NURSING UPDATE WITH NEIL LOVE, MD

NONMELANOMA SKIN CANCERS
Check out our recent program with Dr Nikhil I Khushalni from Moffitt Cancer Center in Tampa, Florida. Published May 7, 2026.

Overview of nonmelanoma skin cancers (12 min)

Systemic therapy for nonmelanoma skin cancers (8 min)

Immune checkpoint inhibitors for special patient populations (12 min)

Hedgehog inhibitors for basal cell carcinoma (6 min)

New developments in therapy for nonmelanoma skin cancers (5 min)

CASE: A man in his early 70s with cutaneous squamous cell carcinoma receives cemiplimab (8 min)

CASE: A man in his mid 70s with a history of basal cell carcinoma presents with disease of the ocular surface and receives immunotherapy (6 min)

CASE: A man in his early 70s with recurrent metastatic basal cell carcinoma receives vismodegib followed by cemiplimab on disease progression (6 min)

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Feedback (Please!)

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“Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse”
Eighteenth Annual RTP-ONS NCPD Symposium Series

Wednesday May 13	**Antibody-Drug Conjugates** 11:15 AM – 12:45 PM CT
	Ovarian Cancer 6:00 PM – 7:30 PM CT
Thursday May 14	**Immunotherapeutic Approaches for Endometrial Cancer** 6:00 AM – 7:30 AM CT
	Prostate Cancer 12:15 PM – 1:45 PM CT
	Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer 6:00 PM – 7:30 PM CT
Friday May 15	**Pancreatic Cancer** 6:00 AM – 7:30 AM CT
	Targeting the PI3K/AKT/mTOR Pathway in HR-Positive Metastatic BC 12:15 PM – 1:45 PM CT
	Non-Hodgkin Lymphoma and Chronic Lymphocytic Leukemia 6:00 PM – 8:00 PM CT
Saturday May 16	**CDK4/6 Inhibitors for HR-Positive Breast Cancer** 6:00 AM – 7:30 AM CT
	Relapsed/Refractory Multiple Myeloma 12:15 PM – 1:45 PM CT
	Oral SERDs for Breast Cancer 6:00 PM – 7:30 PM CT

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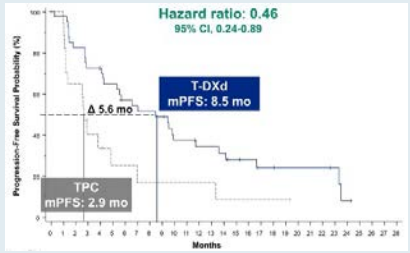
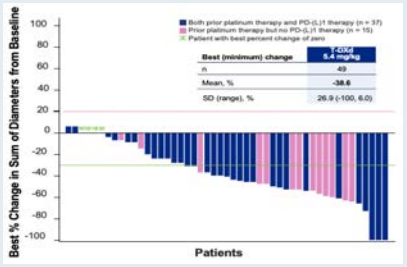
Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

New Agents, Therapies and Regimens

- When should it be used, for whom and why?
- How to prevent and manage side effects: dose holds and reductions
  - Kaplan Meier curves — HR and absolute benefit



  - Waterfall plots



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Agenda

Module 1: Overview of Prostate Cancer

Module 2: Hormonal Therapy for Nonmetastatic and Metastatic Hormone-Sensitive Prostate Cancer (HSPC)

Module 3: Potential Role of Capivasertib in Metastatic HSPC

Module 4: Current and Potential Future Role of PARP Inhibitors in Metastatic PC

Module 5: Current and Future Role of Lutetium Lu 177 Vipivotide Tetraxetan for Patients with Metastatic PC

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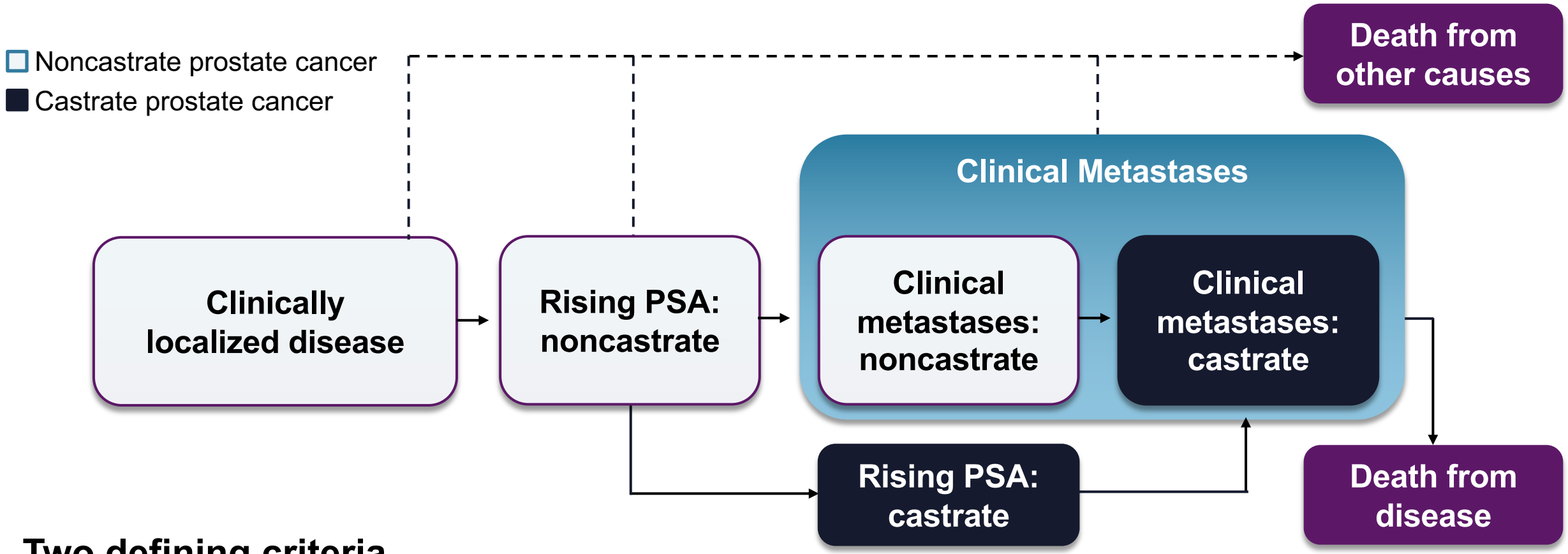
Clinical Disease States Model of Prostate Cancer



Two defining criteria

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

Adapted from Scher HI et al. *J Clin Oncol.* 2008;26:1148-1159.

Agenda

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CANCER CONSORTIUM

Hormonal Therapy for Nonmetastatic and Metastatic Hormone Sensitive Prostate Cancer

Evan Y. Yu, M.D

Section Head, Medical Oncology, Clinical Research Division
Medical Director, Clinical Research Support

Research To Practice at ONS
San Antonio, TX
May 14, 2026

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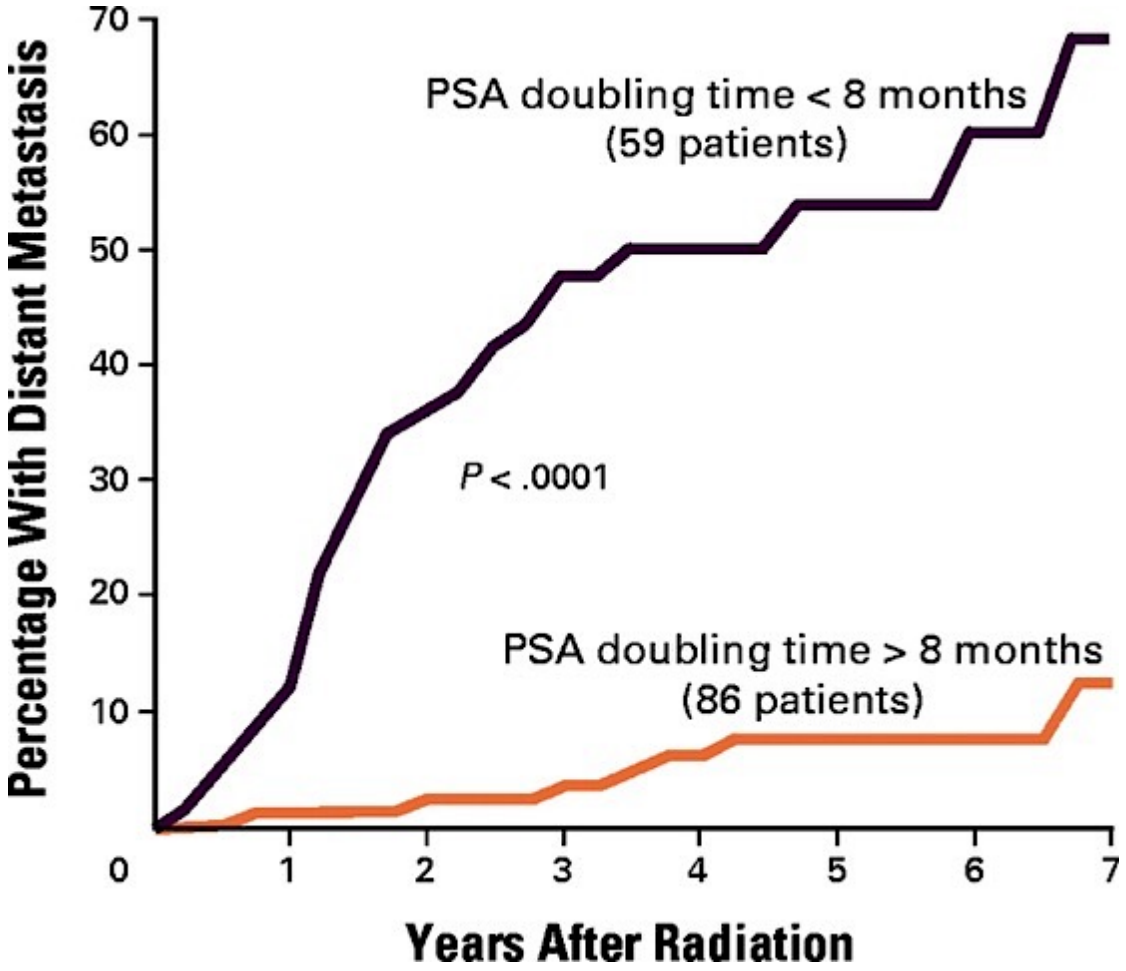
Most Important Prognostic Factor for Biochemical Recurrence: PSA Doubling Time

- Period of time it takes for PSA to double over multiple measurements
  - Most often expressed in terms of months
  - Longer is better!
- After surgery, PSADT >10 months associated with longer time to distant metastasis[1] and survival[2]
- After radiation, PSADT >8 months was better[3]
  - 7 year metastatic disease rates 7% vs. 54%



1. Pound CR et al. JAMA. 1999; 281:1591-7.
2. Freedland SJ et al. JAMA. 2005; 294:433-9.
3. Zagars GK et al. Radiother Oncol. 1997; 44:213-21.

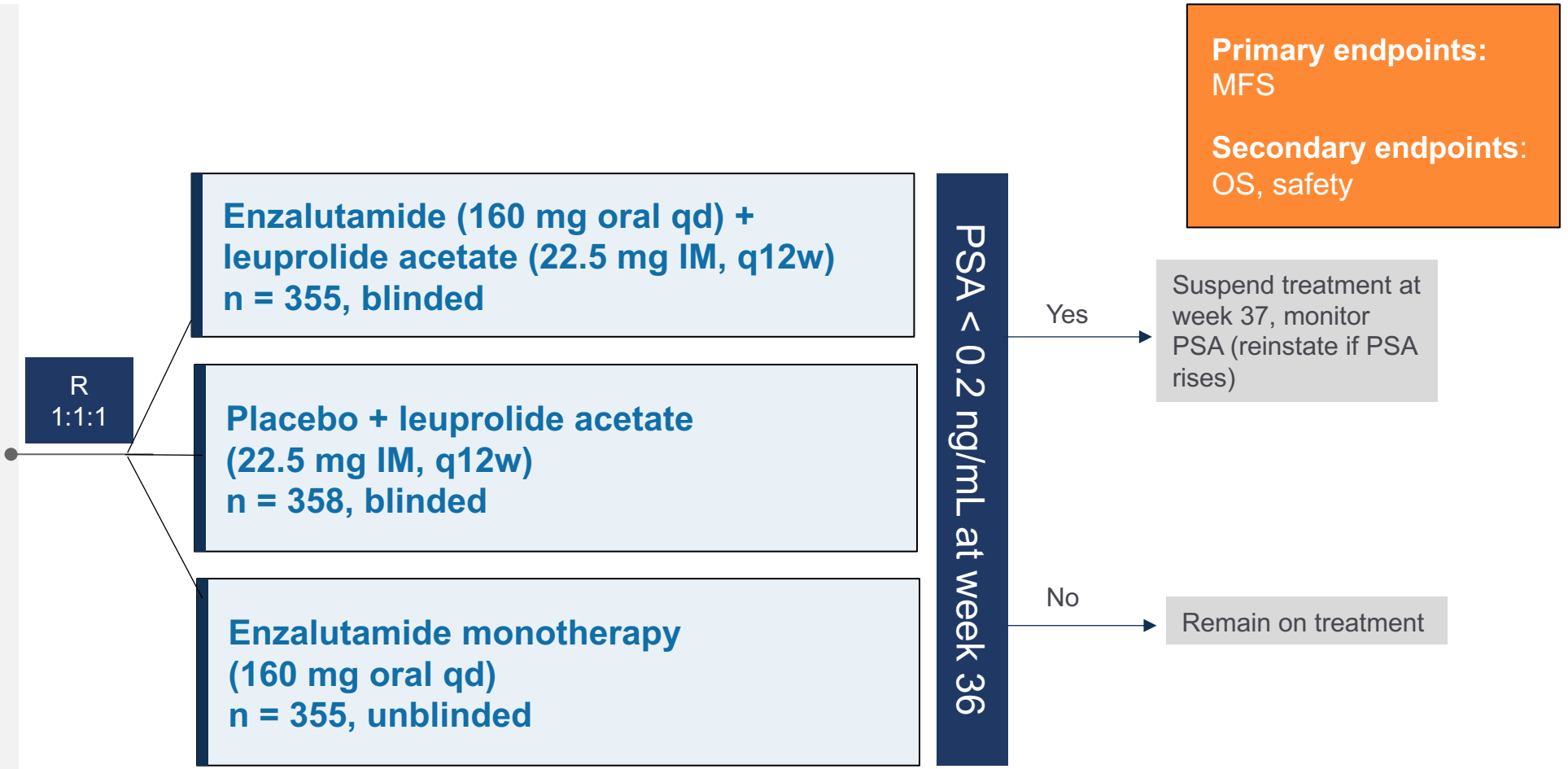
EMBARK Trial for High-Risk Biochemically-Recurrent Prostate Cancer (PSAdt <9 months)

Eligibility criteria

- Screening PSA ≥ 1 ng/mL after RP and at least 2 ng/mL above the nadir for primary EBRT
- No mets on bone scan or CT/MRI
- Testosterone ≥ 150 ng/mL
- Prior hormonal therapy ≥ 9 months prior to randomization (neoadjuvant/adjuvant for ≤ 36 mos or ≤ 6 mos for rising PSA)

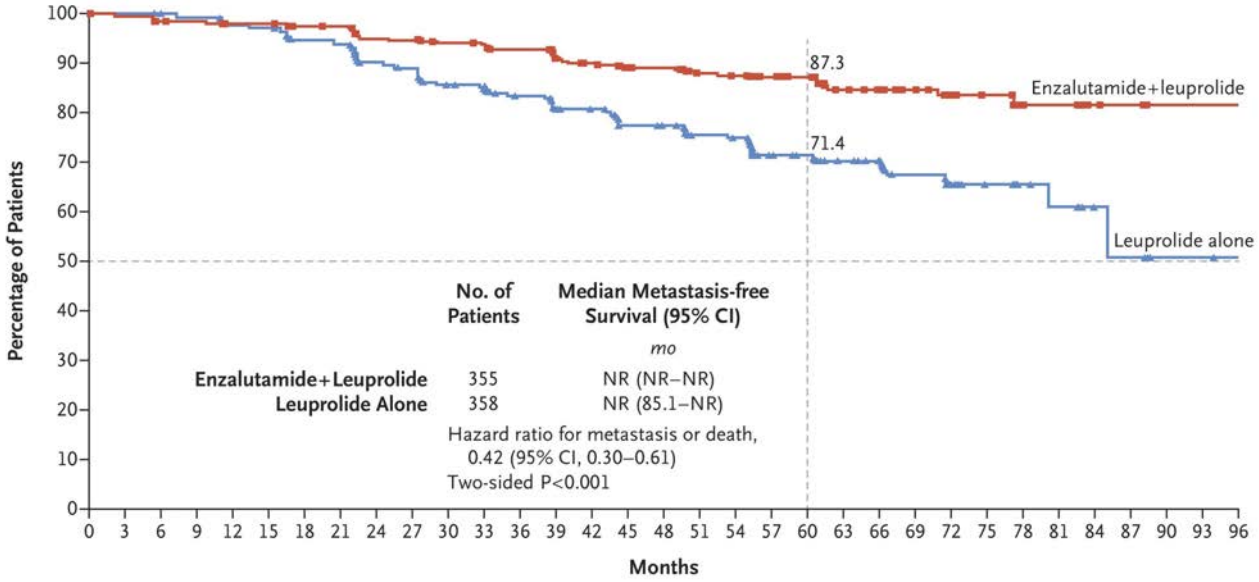
Stratified:

- Screening PSA
- PSADT
- Prior hormonal therapy

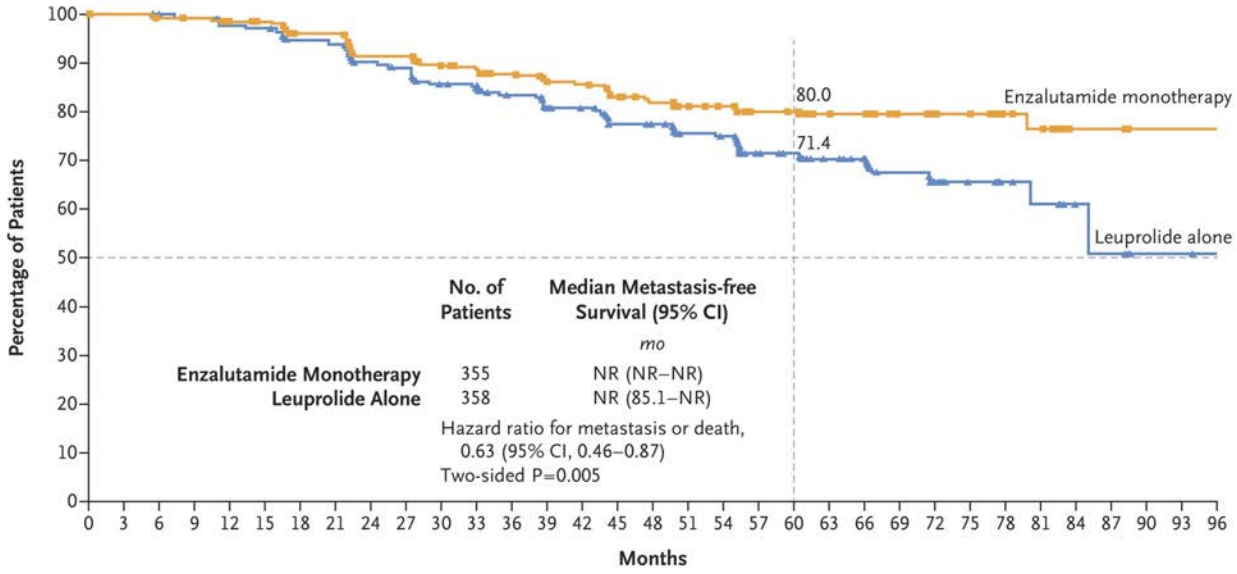


EMBARK Metastasis-Free Survival

MFS for Enzalutamide Combination vs Leuprolide Alone



MFS for Enzalutamide Monotherapy vs Leuprolide Alone



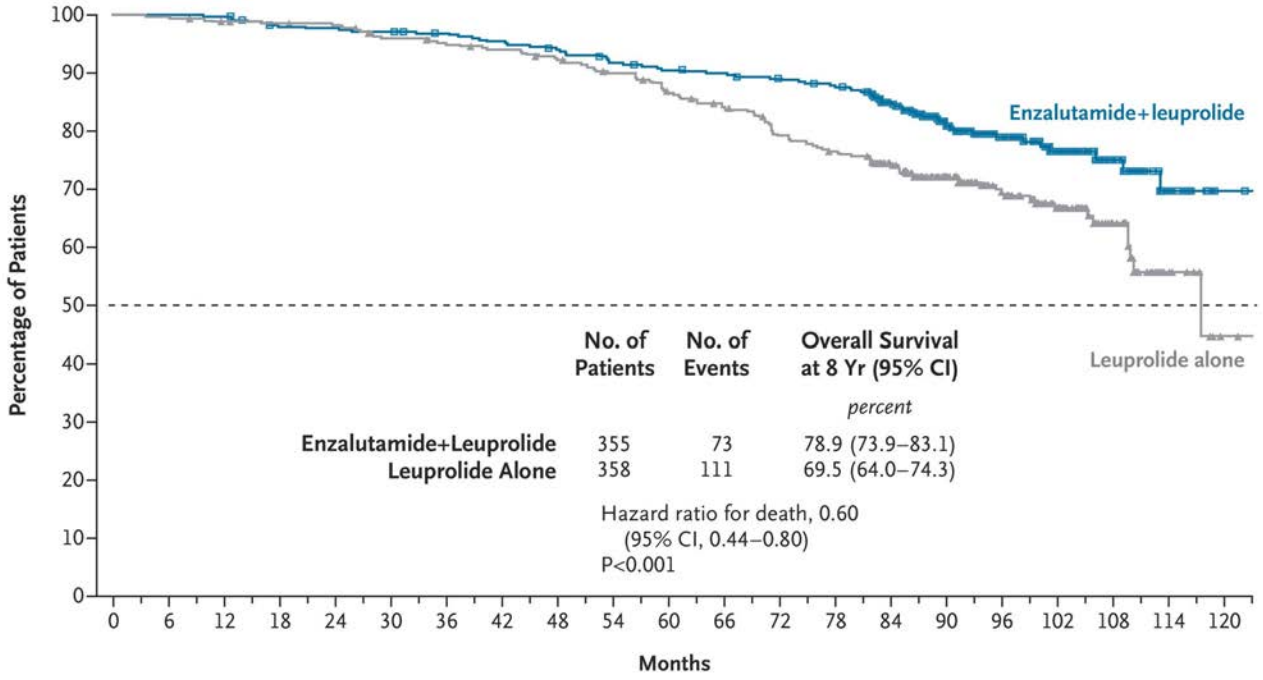
Interim OS trended in favor of enzalutamide + leuprolide alone (HR 0.59; 95% CI: 0.38, 0.91; *P* = .02 [did not cross interim efficacy boundary *P* < .0001]) and enzalutamide monotherapy (HR 0.78; 95% CI: 0.52, 1.17; *P* = .23)

MFS, metastasis free survival; NR, not reported.

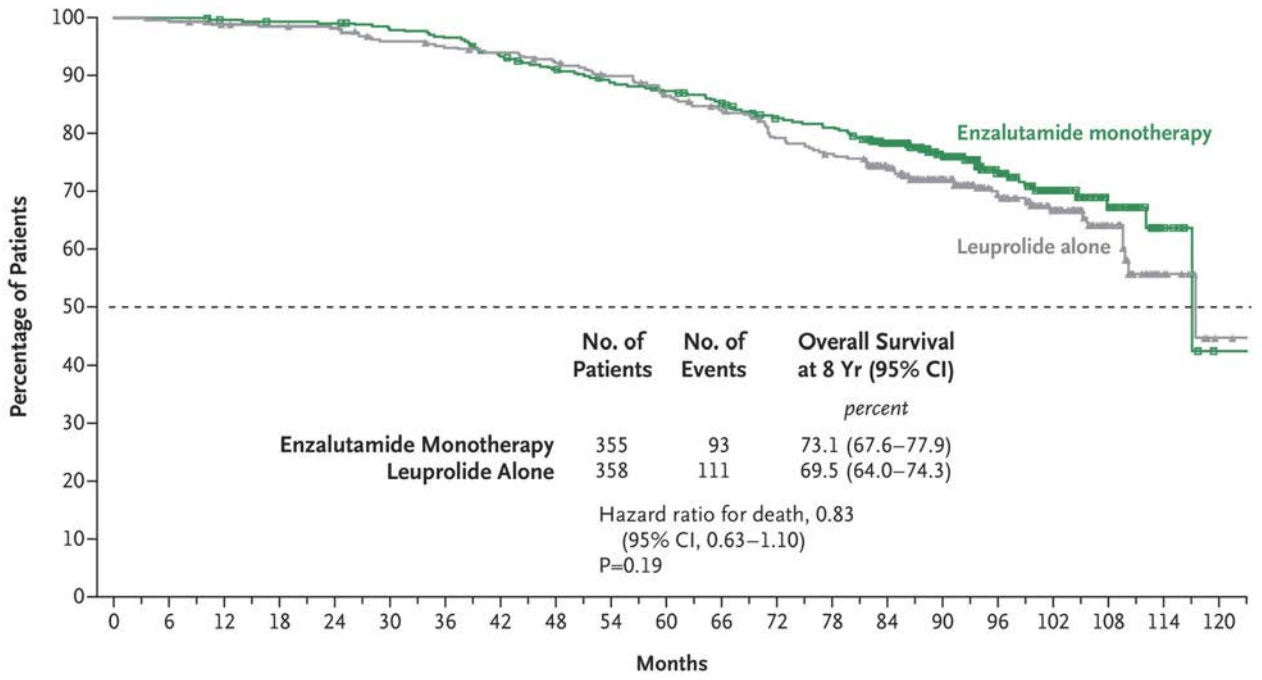
Freedland SJ, et al. N Engl J Med. 2023;389:1453-1465.

EMBARK Overall Survival

Enzalutamide Combination vs Leuprolide Alone



Enzalutamide Monotherapy vs Leuprolide Alone



Shore ND, et al. N Engl J Med. 2026;394:563-575.

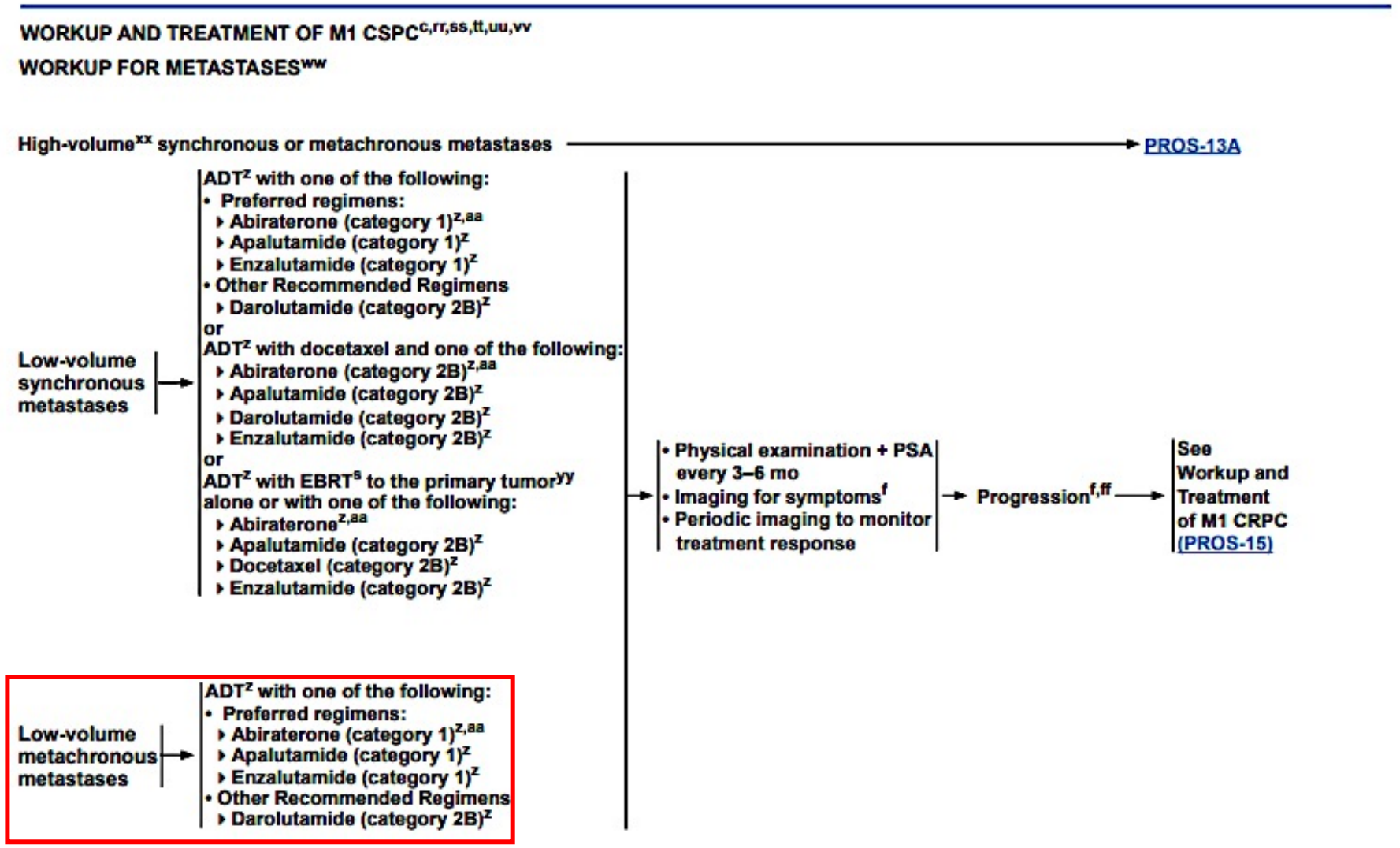
EMBARK Safety Data

- No new safety signals were reported
- Most common AEs (≥ 10%) and TRAEs (≥ 30%) for ENZA + LA were hot flashes and fatigue
- Most common AE for ENZA monotherapy were **gynecomastia**, hot flashes and fatigue
- Sexual activity appears better preserved with ENZA monotherapy than with LA alone

Event	Enzalutamide + Leuprolide (N = 353)		Leuprolide Alone (N = 354)		Enzalutamide Monotherapy (N = 354)	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3	Any Grade	Grade ≥3
	number (percent)					
Any adverse event	343 (97.2)	164 (46.5)	345 (97.5)	151 (42.7)	347 (98.0)	177 (50.0)
Treatment-related adverse event	305 (86.4)	62 (17.6)	283 (79.9)	31 (8.8)	312 (88.1)	57 (16.1)
Serious adverse event	123 (34.8)	110 (31.2)	112 (31.6)	100 (28.2)	131 (37.0)	116 (32.8)
Treatment-related serious adverse event	26 (7.4)	22 (6.2)	8 (2.3)	7 (2.0)	17 (4.8)	17 (4.8)
Adverse event leading to dose reduction	25 (7.1)	11 (3.1)	16 (4.5)	5 (1.4)	56 (15.8)	14 (4.0)
Adverse event leading to permanent discontinuation of treatment	73 (20.7)	31 (8.8)	36 (10.2)	19 (5.4)	63 (17.8)	34 (9.6)
Adverse event leading to death†	6 (1.7)	—	3 (0.8)	—	8 (2.3)	—
Most common adverse events‡						
Hot flash	243 (68.8)§	2 (0.6)	203 (57.3)§	3 (0.8)	77 (21.8)	1 (0.3)
Fatigue	151 (42.8)§	12 (3.4)	116 (32.8)	5 (1.4)	165 (46.6)§	14 (4.0)
Arthralgia	97 (27.5)	7 (2.0)	75 (21.2)	1 (0.3)	81 (22.9)	2 (0.6)
Hypertension	82 (23.2)	24 (6.8)	69 (19.5)	18 (5.1)	67 (18.9)	19 (5.4)
Fall	74 (21.0)	4 (1.1)	51 (14.4)	4 (1.1)	56 (15.8)	7 (2.0)
Back pain	60 (17.0)	3 (0.8)	54 (15.3)	1 (0.3)	62 (17.5)	3 (0.8)
Diarrhea	49 (13.9)	2 (0.6)	31 (8.8)	1 (0.3)	46 (13.0)	1 (0.3)
Constipation	46 (13.0)	1 (0.3)	31 (8.8)	0	34 (9.6)	1 (0.3)
Hematuria	42 (11.9)	8 (2.3)	44 (12.4)	4 (1.1)	45 (12.7)	9 (2.5)
Insomnia	42 (11.9)	2 (0.6)	37 (10.5)	0	25 (7.1)	0
Nausea	42 (11.9)	1 (0.3)	29 (8.2)	1 (0.3)	54 (15.3)	2 (0.6)
Pain in arm or leg	41 (11.6)	3 (0.8)	36 (10.2)	2 (0.6)	40 (11.3)	1 (0.3)
Asthenia	39 (11.0)	2 (0.6)	21 (5.9)	1 (0.3)	39 (11.0)	3 (0.8)
Dizziness	39 (11.0)	2 (0.6)	37 (10.5)	2 (0.6)	41 (11.6)	3 (0.8)
Headache	39 (11.0)	3 (0.8)	32 (9.0)	0	41 (11.6)	1 (0.3)
Urinary incontinence	34 (9.6)	4 (1.1)	28 (7.9)	3 (0.8)	36 (10.2)	6 (1.7)
Gynecomastia	29 (8.2)	0	32 (9.0)	0	159 (44.9)§	3 (0.8)
Coronavirus disease 2019	27 (7.6)	2 (0.6)	36 (10.2)	4 (1.1)	44 (12.4)	2 (0.6)
Peripheral edema	27 (7.6)	1 (0.3)	37 (10.5)	1 (0.3)	31 (8.8)	1 (0.3)
Urinary tract infection	27 (7.6)	1 (0.3)	26 (7.3)	2 (0.6)	37 (10.5)	7 (2.0)
Weight decreased	24 (6.8)	1 (0.3)	12 (3.4)	0	39 (11.0)	1 (0.3)
Nipple pain	11 (3.1)	0	4 (1.1)	0	54 (15.3)	0
Breast tenderness	5 (1.4)	0	4 (1.1)	0	51 (14.4)	0

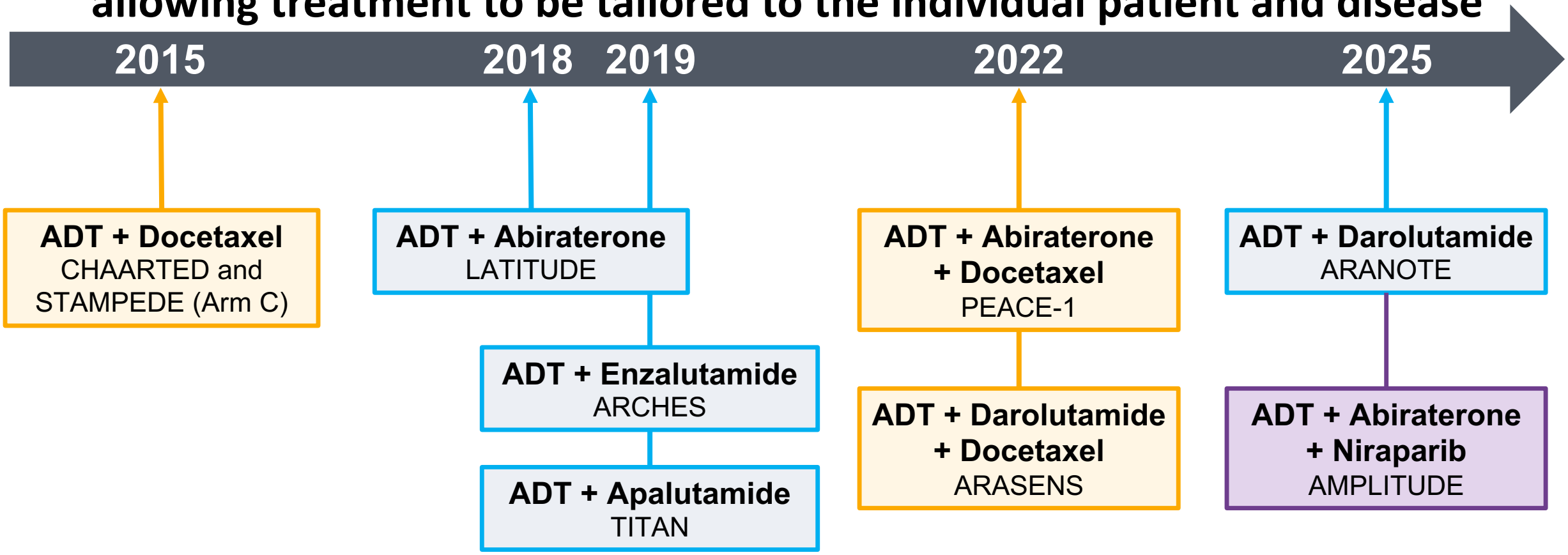
Freedland SJ, et al. N Engl J Med. 2023;389:1453-1465.

NCCN Guidelines for mHSPC



Timeline of FDA Approvals in Metastatic Hormone Sensitive Prostate Cancer

Multiple ADT + ARPI combinations are now approved for mHSPC
allowing treatment to be tailored to the individual patient and disease

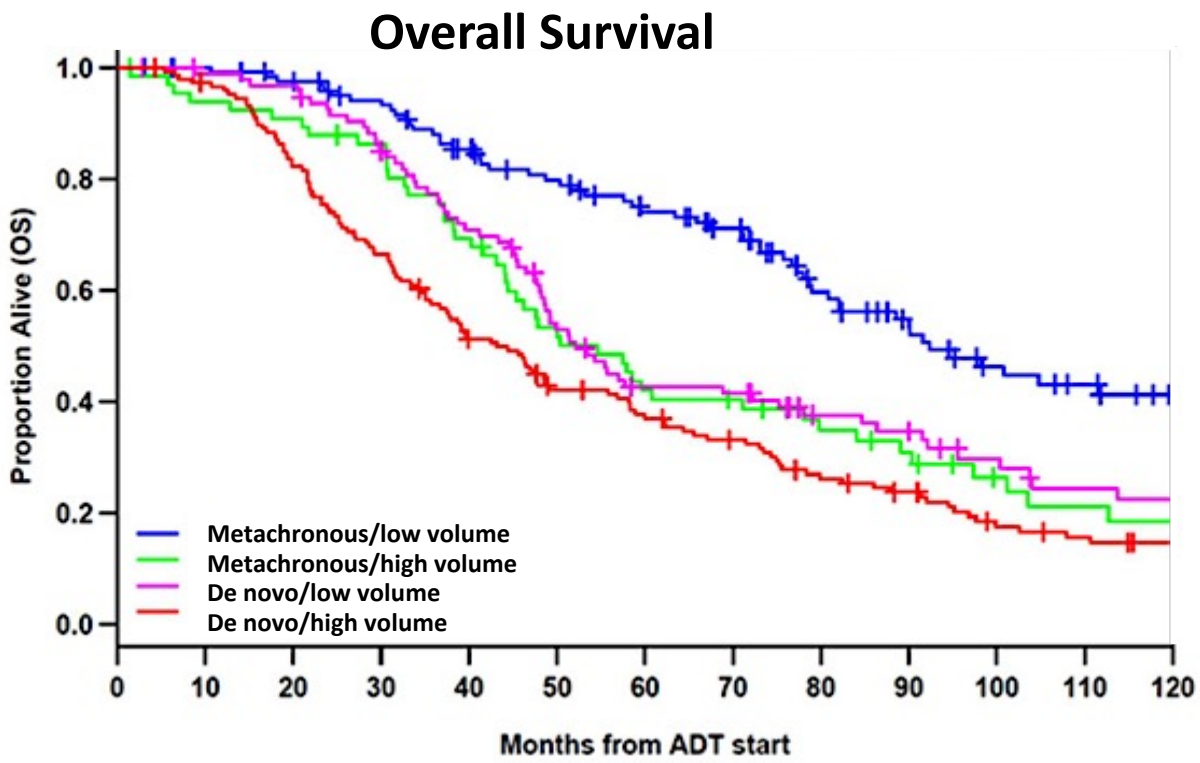


Fizazi K et al. *Lancet Oncology*. 2019; 20(5):686-700.; Fizazi K et al. ESMO 2021.; Chi KN et al. *JCO.* 2021; 39(20):2294-2303.; Andrew Armstrong, ASCO 2025; Smith MR et al. *NEJM*. 2022; 386:1132-1142.; Saad F et al. *J Clin Oncol*. 2024;42(36):4271-4281.; Gerhardt Attard, ASCO 2025

Prognosis by Volume and Presentation at Diagnosis

High-volume de novo metastatic disease is associated with the poorest prognosis

Groups	N (% events)	mOS, years (95% CI)
Metachronous/ low volume	125 (50)	7.7 (6.7-10.6)
Metachronous/ high volume	67 (75)	4.6 (3.7-6.7)
De novo/ low volume	96 (70)	4.3 (4.0-6.5)
De novo/ high volume	148 (84)	3.6 (3.1-4.7)



Francini E, et al. *Prostate*. 2018;78(12):889-895.

Summary

- Enzalutamide with or without ADT is a newer option for patients with high-risk biochemical recurrence
- Short PSA doubling time should help identify patients with high-risk disease who are more likely to benefit from treatment intensification with enzalutamide
- Doublet therapy with ADT and ARPI should be the foundation of treatment for patients with metastatic hormone-sensitive prostate cancer
- For patients fit for docetaxel with metastatic hormone sensitive prostate cancer, consideration should be given to add either darolutamide or abiraterone to ADT + docetaxel, especially for patients with de novo, high-volume prostate cancer

Case Presentation

Case 1 – A Modern Day Scenario

- A 55-year-old gentleman has a history of PSA 12 ng/dL, Grade Group 5, and T3b adenocarcinoma of the prostate
- He is s/p radical prostatectomy 9 months ago
- His PSA nadired to undetectable after surgery, however, 3 months later his PSA was detectable at 0.28 ng/dL
- Every 3 months, he has had his PSA rechecked and it increased to 0.97 and now it is 4.9 ng/dL
- He has no past medical history and is extremely active with ECOG performance status of 0
- He undergoes imaging with CAP CT and bone scan and there is no evidence of metastatic disease
- His goal is to live as long as possible, given his young age and outstanding quality of life

Case – Treatment Options

What treatment(s) should we consider for this patient?

1. PSMA PET to identify oligometastatic disease for potential metastasis directed therapy
2. ADT alone
3. ADT + enzalutamide
4. Enzalutamide alone
5. ADT + enzalutamide + docetaxel

Case – Evan's Thoughts

- This patient has extremely high-risk biochemical recurrence given a PSA doubling time of clearly <3 months
- He is young and wishes for aggressive treatment
- His PSMA PET would highly likely be positive for multiple metastases and likely metastasis directed therapy will not be successful, given the systemic nature of his disease
- ADT + enzalutamide offers overall survival benefit in this setting

Discussion Questions

For which patients with nonmetastatic hormone-sensitive PC (nmHSPC) with high-risk biochemical recurrence after definitive therapy do you employ either enzalutamide alone or combined with leuprolide?

How are the various androgen receptor pathway inhibitors — abiraterone, enzalutamide, apalutamide and darolutamide — similar and how are they different? How do you select which one to use for a patient with mHSPC?

Tolerability of Hormonal Therapy Used in Treatment of Prostate Cancer

Stacy Walker, NP

GnRH Agonists vs Antagonists

Leuprolide, Degarelix, Relugolix

- GnRH antagonists (degarelix, relugolix) may have fewer cardiovascular risks than GnRH agonists (leuprolide)
- HERO trial - 54% lower risk of major adverse cardiovascular events with relugolix compared to leuprolide (2.9% vs 6.2%).
- Risk reduction more pronounced in men with pre-existing conditions (3.6% vs 17.8%)

Zhang KW, Reimers MA, Calaway AC, Fradley MG, Ponsky L, Garcia JA, Cullen J, Baumann BC, Addison D, Campbell CM, Ghosh AK, Lenihan DJ, Desai NR, Weintraub N, Guha A. Cardiovascular Events in Men with Prostate Cancer Receiving Hormone Therapy: An Analysis of the FDA Adverse Event Reporting System (FAERS). J Urol. 2021 Sep;206(3):613-622. doi: 10.1097/JU.0000000000001785. Epub 2021 Apr 19. PMID: 33872049; PMCID: PMC10243352.

CV Toxicity in ARPIs

- Hypertension is most common CV toxicity across all ARPIs
- ARPI therapy doubles risk of grade 3 or higher CV events (with significant agent-level variation)

Agent	Predominant CV Toxicity	Reference
Abiraterone	Hypertension, Heart Failure (r/t mineralocorticoid excess mechanism)	LATITUDE
Enzalutamide	Hypertension, atrial fibrillation, ischemic heart disease	ARCHES
Apalutamide	Myocardial Infarction, Hypertension	TITAN
Darolutamide	Hypertension (modest increase)	ARASENS

Courtesy of Stacy Walker, NP

Cardiovascular Assessment and Management

- Pre-Treatment Assessment
  - Pre-existing and emerging CVD -
    - CAD, PVD, CHF, arrhythmias including a-fib)
  - ASCVD (AtheroSclerotic CardioVascular Disease) risk calculation
    - The 10-year ASCVD risk estimate is used to guide decision-making for many preventive interventions, including lipid and blood pressure management
    - While all individuals should be encouraged to follow a heart-healthy lifestyle, estimating an individual's 10-year absolute ASCVD risk helps guide the intensity of medical management to maximize anticipated benefit and minimize potential harm from overtreatment
    - ASCVD Risk - https://tools.acc.org/ldl/ascvd_risk_estimator/index.html#!/calulate/estimator/
- On Treatment Monitoring
  - Routine monitoring of clinical symptoms - BP, weight, blood sugar
  - Lifestyle management - diet, tobacco, exercise

Managing Cardiovascular Risk - ABCDE

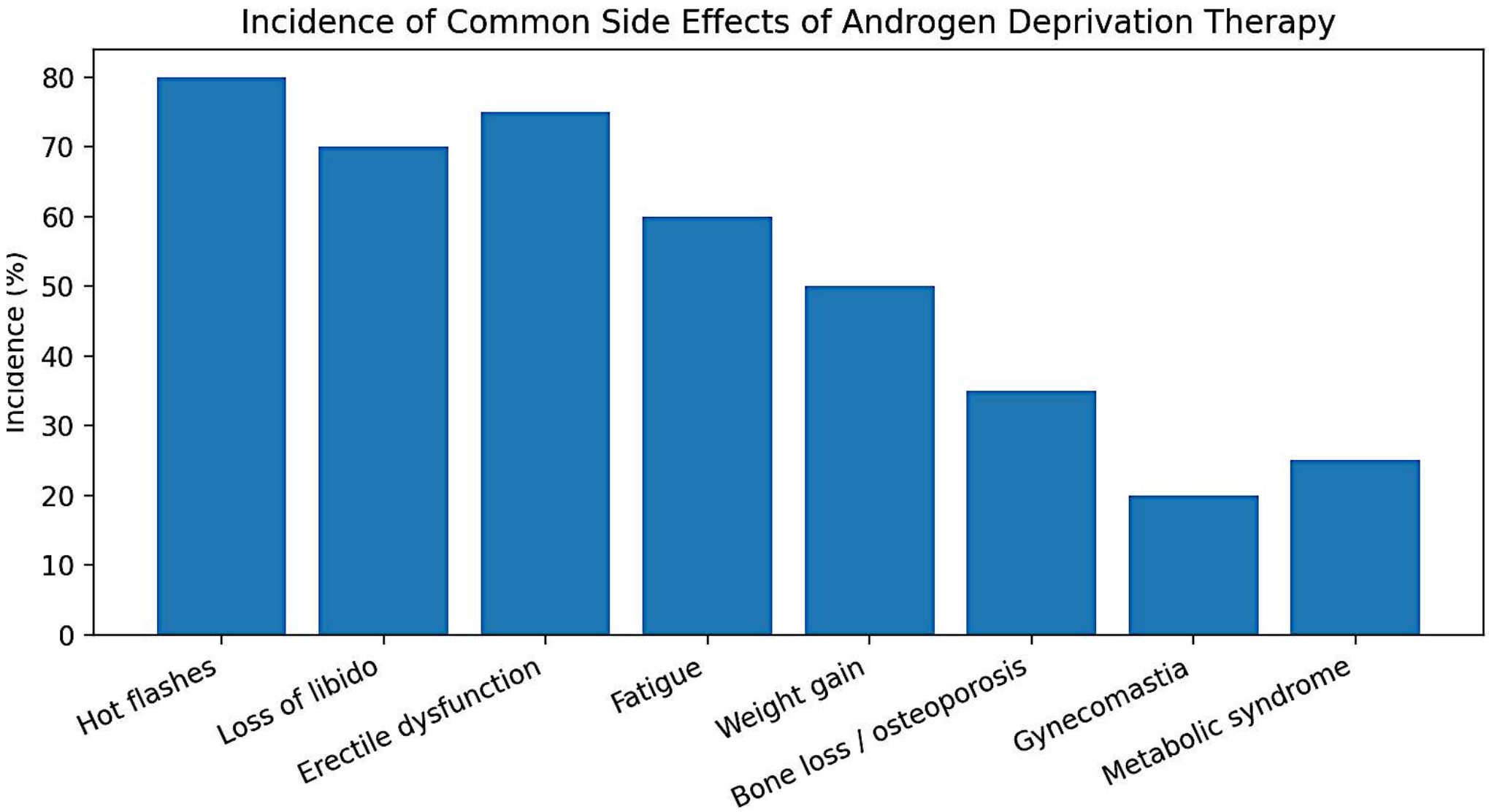
Steps	Risk Modification
A	- Assess cardiovascular risk - Consider aspirin
B	- Blood pressure management
C	- Cholesterol management - Cigarette/tobacco cessation
D	- Diabetes management - Dietary recommendations
E	- Exercise recommendations

- Arnett DK et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2019;140:e596–e646. DOI: 10.1161/CIR.0000000000000678.

CNS Side effects

CNS AE	Enzalutamide	Abiraterone	Apalutamide	Darolutamide
Mental Impairment	✓✓			
Cognitive Impairment	✓✓	✓		
Seizure	✓✓			
Fatigue	✓✓	✓	✓	✓

Matsukawa A, Yanagisawa T, Rajwa P, Fazekas T, Miszczyk M, Tsuboi I, Parizi MK, Laukhtina E, Klemm J, Chiujdea S, Mancon S, Mori K, Kimura S, Karakiewicz PI, Miki J, Kimura T, Shariat SF. Central Nervous System Toxicity in Prostate Cancer Patients Treated with Androgen Receptor Signaling Inhibitors: A Systematic Review, Meta-analysis, and Network Meta-analysis. Clin Genitourin Cancer. 2025 Feb;23(1):102251. doi: 10.1016/j.clgc.2024.102251. Epub 2024 Oct 24. PMID: 39571519.



Courtesy of Stacy Walker, NP

ADT Side Effect Management

Fatigue	Remain active, regular exercise
Hot Flashes	SSRI (venlafaxine commonly), Gabapentin, Oxybutynin, Acupuncture
Gynecomastia/ Breast Tenderness	Weight management, some may consider surgical intervention or radiation
Erectile Dysfunction / Loss of Libido	PDE 5 Inhibitors (Cialis, Viagra), Injections (BiMix), Sexual health counseling
Low Bone Density	DEXA monitoring, Calcium/Vit D supplementation, weight-bearing exercises, bisphosphonates
Depression/ Mood Swings	Antidepressant medication, counseling

Courtesy of Stacy Walker, NP

Discussion Questions

How do you monitor for and manage common ADT-associated toxicities? How, if at all, does this differ based on patient age/performance status and medical history?

What are the most common toxicities observed with enzalutamide monotherapy and in combination with ADT?

What do you tell your patients who are about to start an AR pathway inhibitor about potential toxicities? How does this vary according to the specific agent?

Agenda

Module 1: Overview of Prostate Cancer

Module 2: Hormonal Therapy for Nonmetastatic and Metastatic Hormone-Sensitive Prostate Cancer (HSPC)

Module 3: Potential Role of Capivasertib in Metastatic HSPC

Module 4: Current and Potential Future Role of PARP Inhibitors in Metastatic PC

Module 5: Current and Future Role of Lutetium Lu 177 Vipivotide Tetraxetan for Patients with Metastatic PC

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CANCER CONSORTIUM

Potential Role of Capivasertib in Metastatic Hormone-Sensitive Prostate Cancer

Research To Practice - ONS

Evan Y. Yu, M.D

Section Head, Medical Oncology, Clinical Research Division
Medical Director, Clinical Research Support
Fred Hutchinson Cancer Center
Professor of Medicine, Division of Hematology & Oncology
University of Washington, Seattle, WA

April 26, 2025

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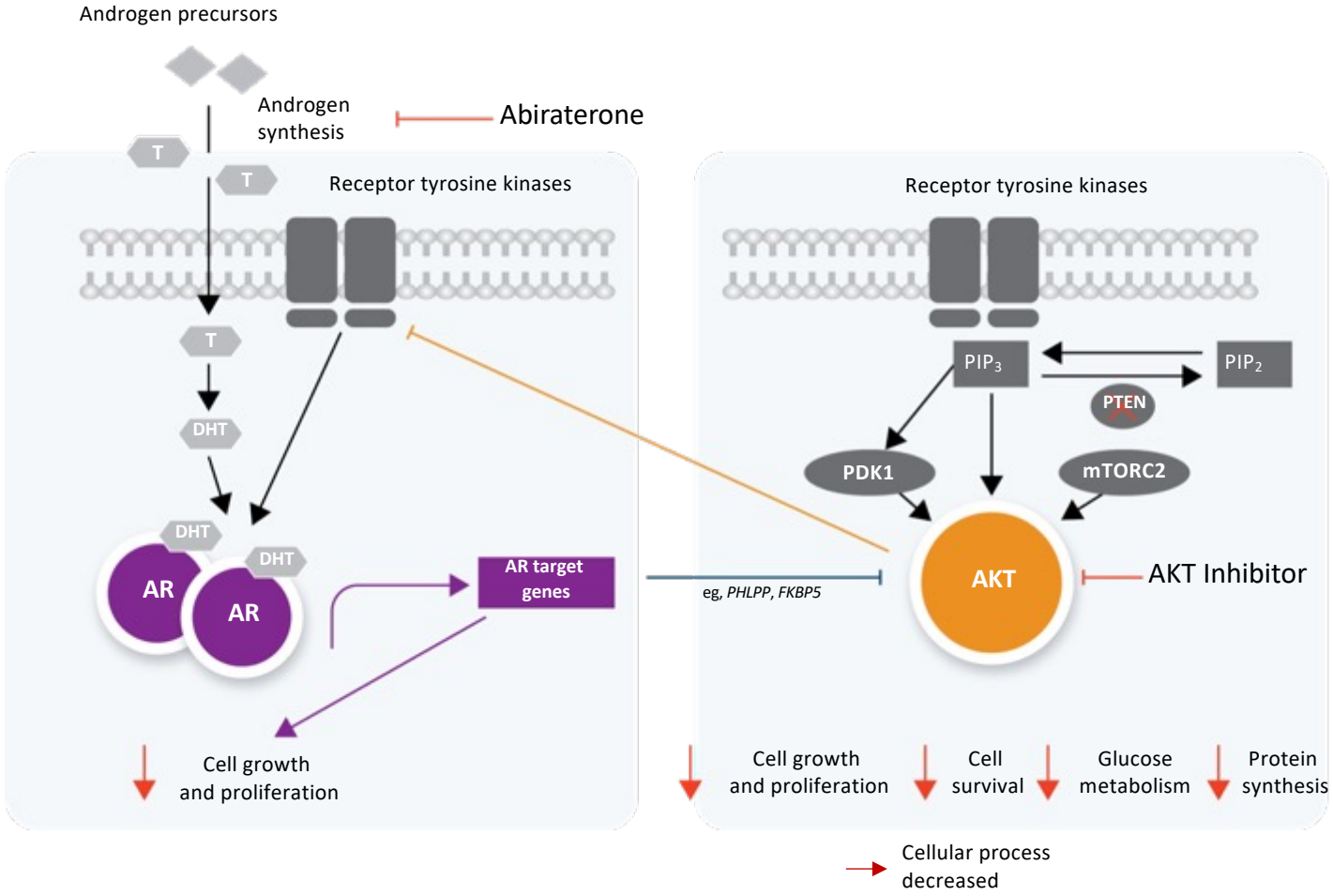
Overview of PTEN-PI3K-AKT and Intersection with AR Pathway

Rationale for Dual Pathway Inhibition



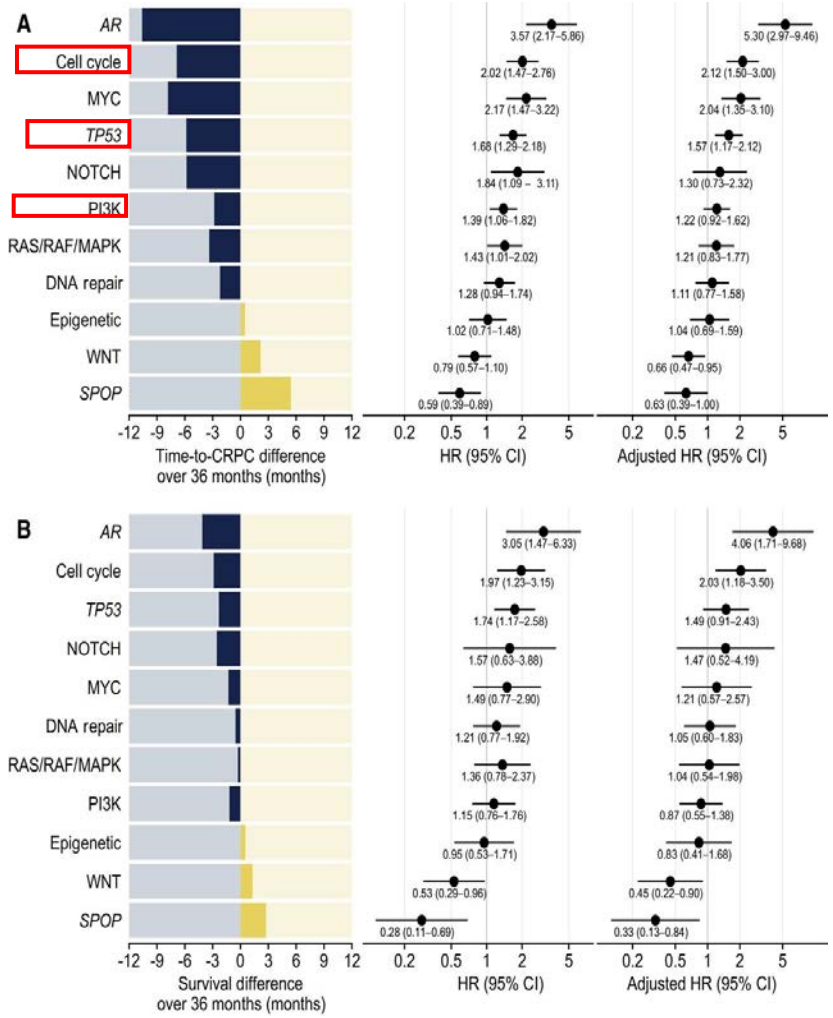
Cross talk between P13K/AKT and AR pathways leads to reciprocal activation when one of the pathways is inhibited, providing an alternative mechanism for tumor growth and survival

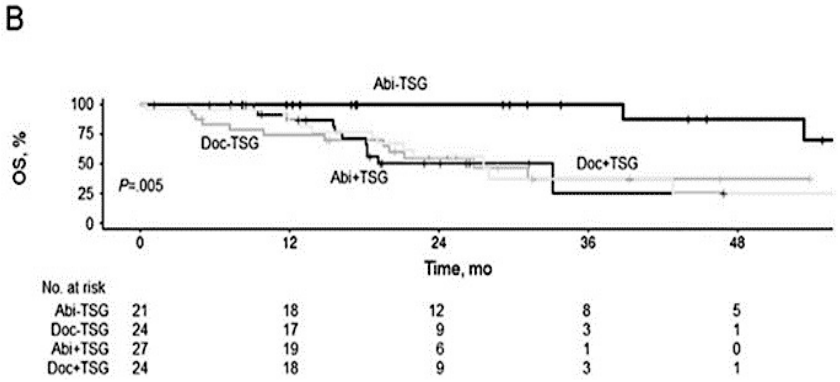
Dual targeting of both pathways may increase antitumor activity

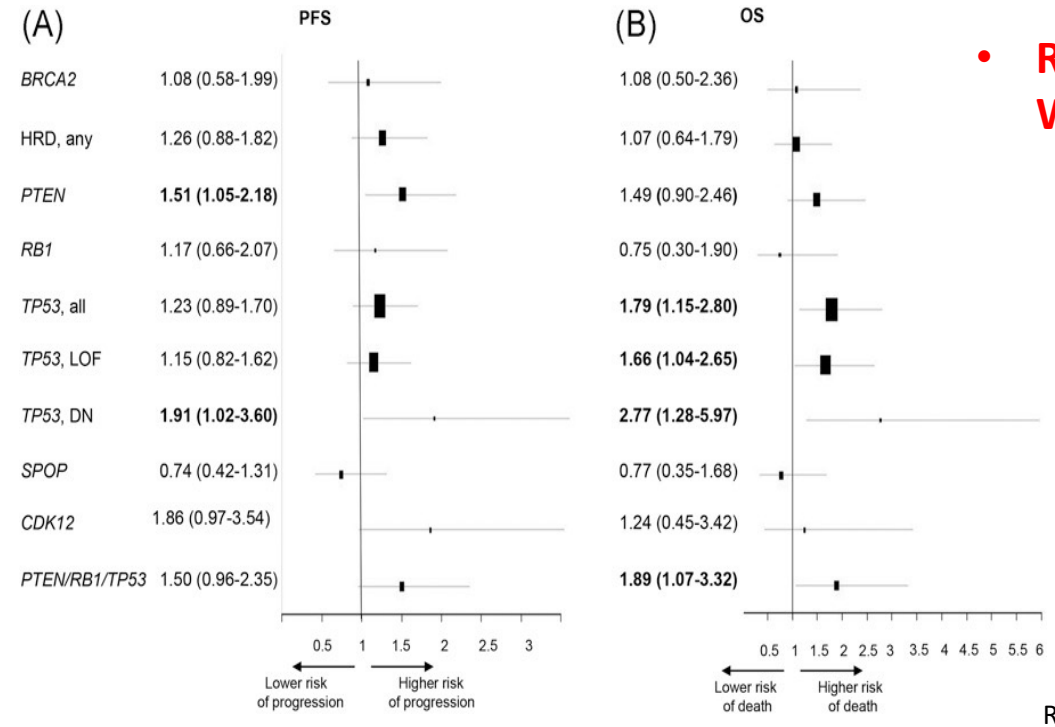
Ipatasertib and Capivasertib are potent AKT Inhibitors

de Bono J et al ESMO 2021;Abstract LBA4.

Outcomes Based on Tumor Suppressor Gene (TSG) Alterations in Metastatic Hormone-Sensitive Prostate Cancer







- **Radiographic PFS and OS Worse with TSG alteration**

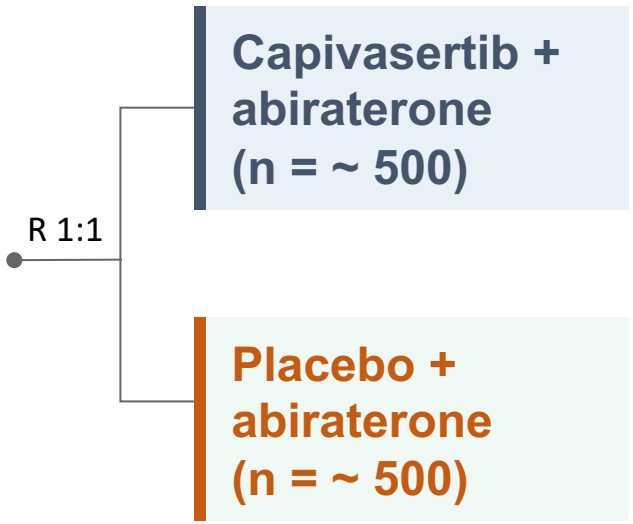
Stopsack et al. CCR 2020.
Ramirez-Velez et al. J Strength Cond Res 2020
Nizialek et al. Prostate 2020.

CAPItello-281: Capivasertib + Abiraterone vs. Placebo + Abiraterone in De Novo Metastatic Hormone Sensitive Prostate Cancer with PTEN Deficiency

Eligible patients:

- Newly diagnosed, previously untreated mHSPC
- IHC-confirmed PTEN deficiency
- ECOG PS 0 or 1

- Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial



All patients to receive continuous ADT

- Primary endpoint: rPFS
- Secondary endpoints: OS, time to start of first subsequent anticancer therapy, SSE-FS, TTPP

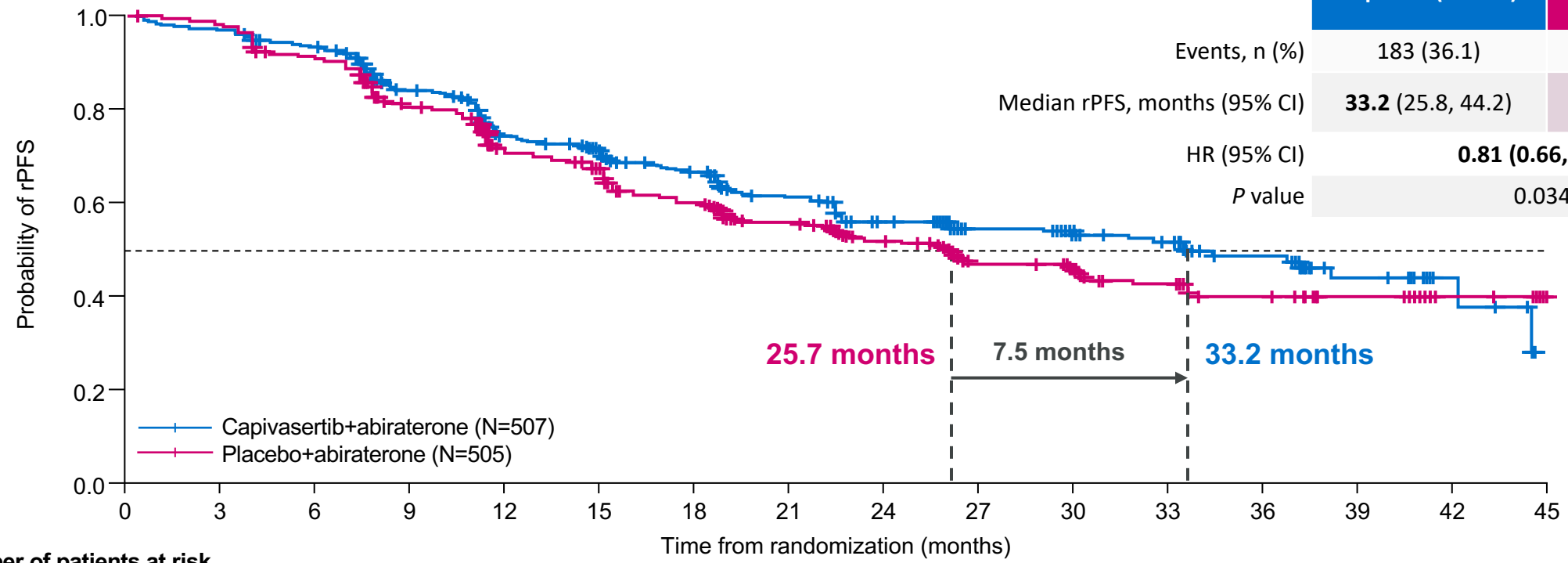
- ECOG, Eastern Cooperative Oncology Group; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PS, performance score; SSE-FS, symptomatic skeletal event-free survival; TTPP, time to pain progression.
- Fizazi K, et al. J Clin Oncol. 2021;39(suppl_6): TPS178; ClinicalTrials.gov. Accessed April 4, 2024. https://clinicaltrials.gov/study/NCT04493853

What is PTEN Deficiency in the Capitello-281 Trial?

- Previous trial with another AKT inhibitor using ≥50% of cells with no viable PTEN IHC staining was positive for rPFS but negative for overall survival
- In Capitello-281, diagnostic cutoff of **≥90%** of viable malignant cells with no specific cytoplasmic staining by IHC
  - Of ~6200 patients submitting tumor tissue, 97% had a valid IHC result and **25%** were PTEN deficient by this above definition

Capitello-281 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	

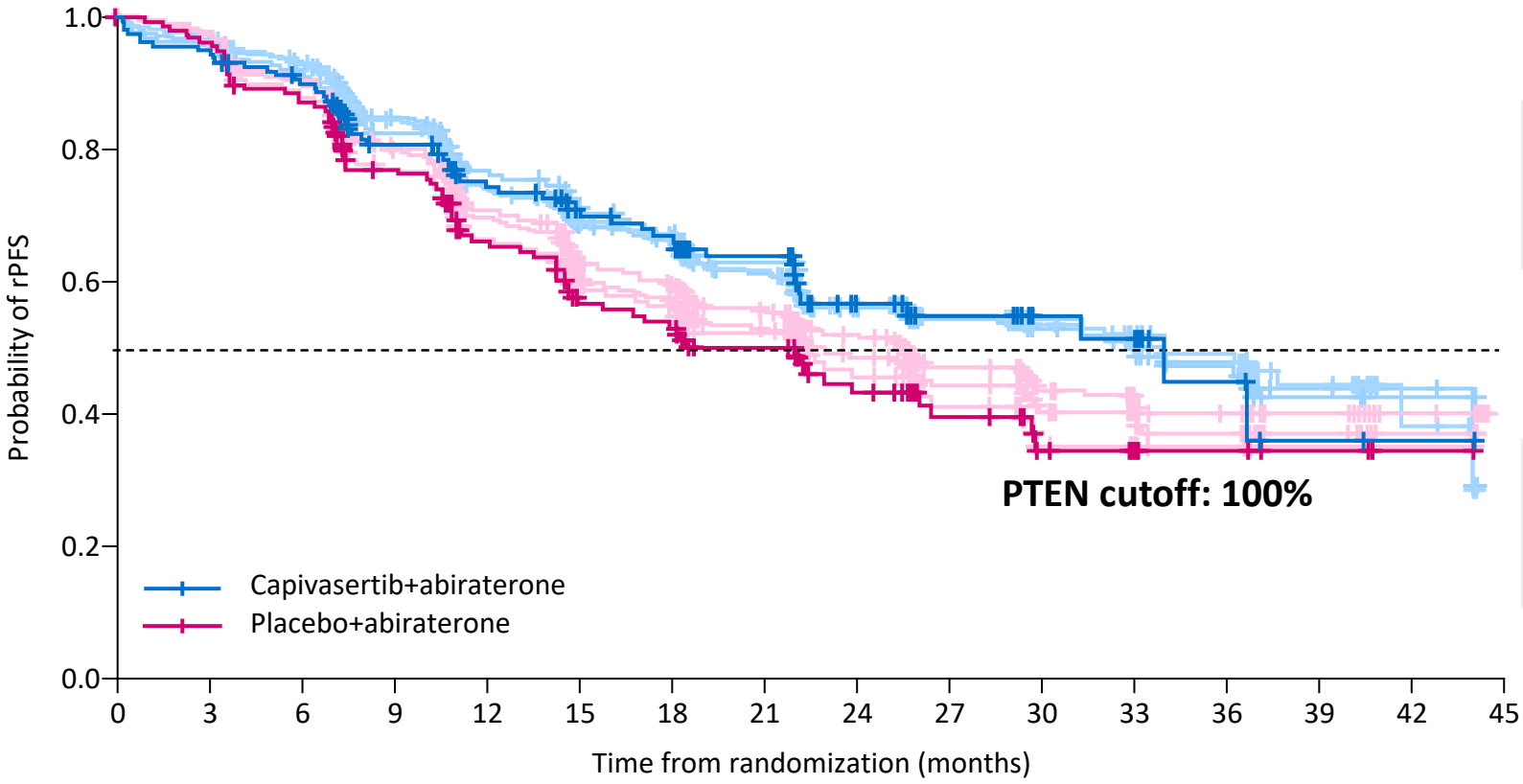


Number of patients at risk

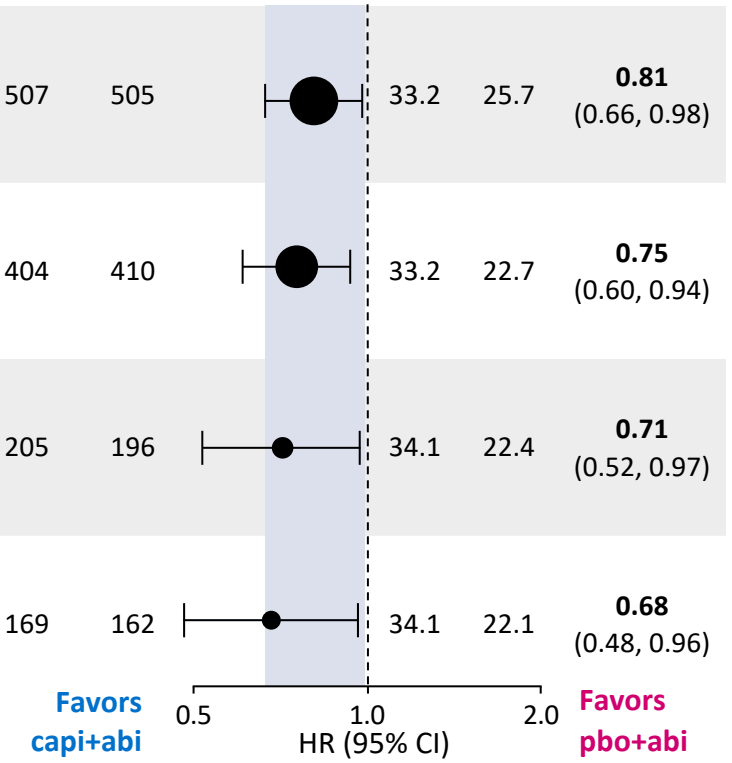
Capi+abi	507	460	435	353	282	233	217	165	123	93	69	62	41	21	6	0
Pbo+abi	505	479	440	359	276	215	198	154	113	83	59	51	37	23	8	0

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
Fizazi K *et al. Ann Oncol* 2026;37:53–68

CAPItello-281 PTEN subgroups: investigator-assessed rPFS



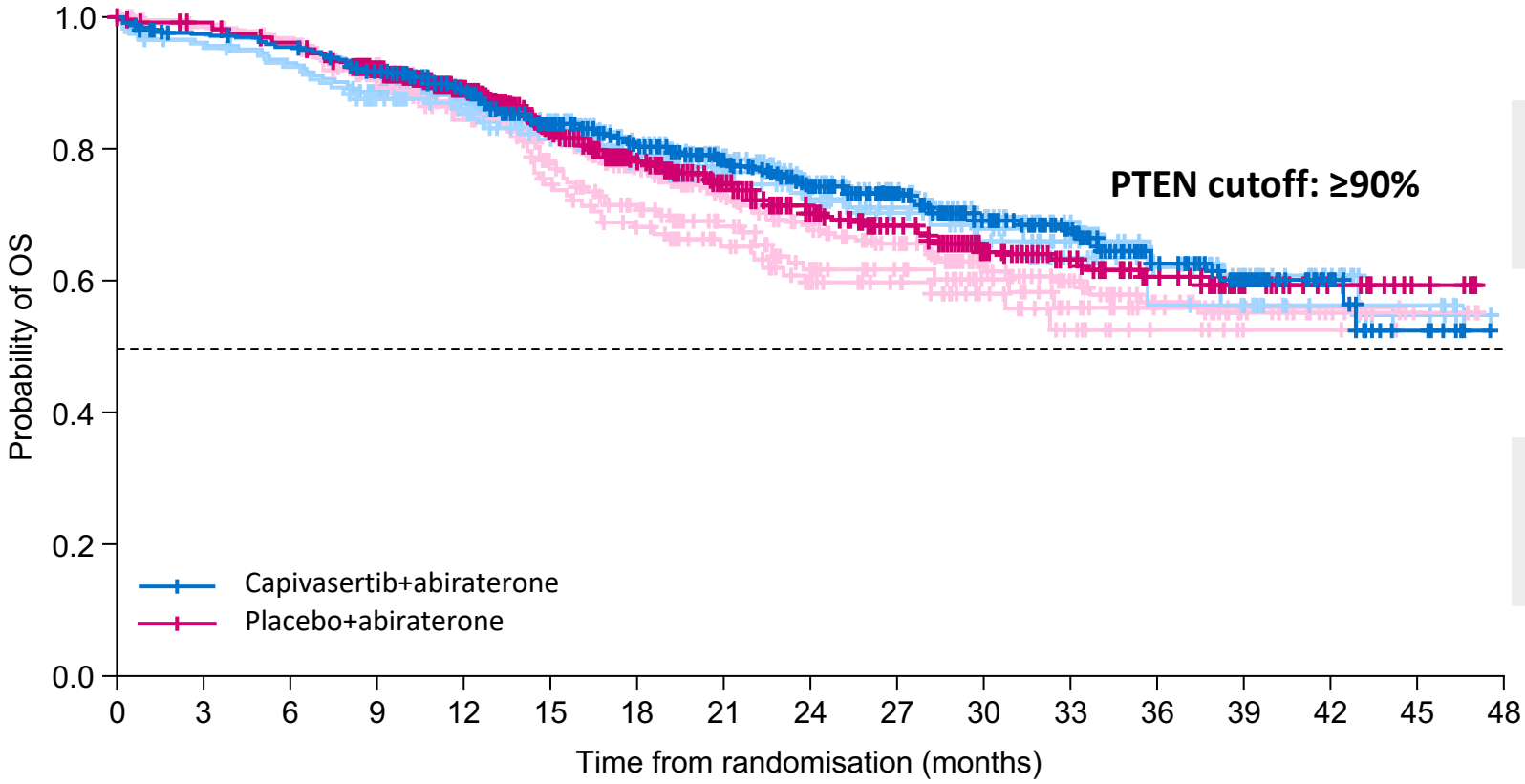
PTEN cutoff	Patients, n: Capi+abi	Patients, n: Pbo+abi	Median rPFS, months: Capi+abi	Median rPFS, months: Pbo+abi	HR (95% CI)
All randomized patients (≥90%)	507	505	33.2	25.7	**0.81** (0.66, 0.98)
≥95%	404	410	33.2	22.7	**0.75** (0.60, 0.94)
≥99%	205	196	34.1	22.4	**0.71** (0.52, 0.97)
100%	169	162	34.1	22.1	**0.68** (0.48, 0.96)



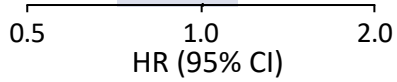
abi, abiraterone; capi, capivasertib; CI, confidence interval; HR, hazard ratio; pbo, placebo; PTEN, phosphatase and tensin homolog; rPFS, radiographic progression-free survival

Fizazi K *et al. Ann Oncol* 2026;37:53–68

CAPItello-281 PTEN subgroups: OS



PTEN cutoff	Patients, n: Capi+abi	Patients, n: Pbo+abi	Median OS, months: Capi+abi	Median OS, months: Pbo+abi	HR (95% CI)
All randomized patients (≥90%)	507	505	NC	NC	**0.90** (0.71, 1.15)
≥95%	404	410	NC	NC	**0.80** (0.62, 1.04)
≥99%	205	196	NC	NC	**0.77** (0.53, 1.12)
100%	169	162	NC	NC	**0.77** (0.51, 1.14)



abi, abiraterone; capi, capivasertib; CI, confidence interval; HR, hazard ratio; pbo, placebo; OS, overall survival; PTEN, phosphatase and tensin homolog

Fizazi K *et al. Ann Oncol* 2026;37:53–68

Summary

- Current treatment for metastatic hormone sensitive prostate cancer includes doublet therapy with ADT + ARPI, at a minimum
- PTEN, p53 and Rb are tumor suppressor genes that confer a poor prognosis
- It is unclear whether PTEN deficiency predisposes to better outcomes with docetaxel
- Capitello-281 with Capivasertib offers rPFS benefit for patients with PTEN deficiency

Case Presentation

Case 2 – A Modern Day Scenario

- A 65-year-old gentleman presents asymptomatically with his initial screening PSA with a new PCP found to be 28 ng/mL
- He has a h/o obesity and hyperlipidemia, but no known cardiac disease
- ECOG performance status is 0
- Labs are all WNL
- CT and bone scan imaging confirm 6 osteoblastic lesions in the thoracic and lumbar spine and 1 in the R femur; PSMA PET is obtained and all lesions are PSMA PET positive with SUVs between 4 and 9
- NGS reveals no alterations in *BRCA1 or 2* or any other homologous recombination repair genes
- PTEN by IHC reveals no tumor cells with PTEN immunostaining

Case – Treatment Options

What treatment(s) should we consider for this patient?

1. ADT alone
2. ADT + abiraterone
3. ADT + abiraterone + capivasertib
4. ADT + docetaxel
5. ADT + darolutamide + docetaxel

Case – Evan's Thoughts

- This patient has de novo, high volume disease (7 total bone metastases with 1 in the appendicular skeleton)
- He has multiple comorbidities that are not ideal for ADT, but none of which preclude him from any of the treatment intensification options
- Although ADT + abiraterone or ADT + docetaxel could be administered, he is a decent candidate for ADT + darolutamide + docetaxel
- Given his PTEN deficiency, ADT + abiraterone + capivasertib is something to watch out for in the future

Discussion Questions

What is the optimal method to assess PTEN status, and when should testing be done?

How, if at all, does PTEN deficiency influence your treatment decision-making today?

If capivasertib were to become available, for which patients with mHSPC and PTEN deficiency would you prioritize its use?

Tolerability Profile of Capivasertib

Research to Practice - ONS

Michael Lai, MSN, ARNP, NP-C

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Teaching Associate
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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

Courtesy of Michael Lai, MSN, ARNP, NP-C.

CAPitello-291: most frequent AEs in the overall population

Table 2. Most Frequent Adverse Events in the Overall Population (Safety Population).*

Event	Capivasertib–Fulvestrant (N=355)					Placebo–Fulvestrant (N=350)				
	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4	Any Grade	Grade 1	Grade 2	Grade 3	Grade 4
	number of patients (percent)									
Any adverse event	343 (96.6)	52 (14.6)	139 (39.2)	139 (39.2)	9 (2.5)	288 (82.3)	115 (32.9)	118 (33.7)	44 (12.6)	10 (2.9)
Diarrhea	257 (72.4)	164 (46.2)	60 (16.9)	33 (9.3)	0	70 (20.0)	60 (17.1)	9 (2.6)	1 (0.3)	0
Rash†	135 (38.0)	57 (16.1)	35 (9.9)	43 (12.1)	0	25 (7.1)	19 (5.4)	5 (1.4)	1 (0.3)	0
Nausea	123 (34.6)	85 (23.9)	35 (9.9)	3 (0.8)	0	54 (15.4)	42 (12.0)	10 (2.9)	2 (0.6)	0
Fatigue	74 (20.8)	49 (13.8)	23 (6.5)	2 (0.6)	0	45 (12.9)	35 (10.0)	8 (2.3)	2 (0.6)	0
Vomiting	73 (20.6)	54 (15.2)	13 (3.7)	6 (1.7)	0	17 (4.9)	10 (2.9)	5 (1.4)	2 (0.6)	0
Headache	60 (16.9)	47 (13.2)	12 (3.4)	1 (0.3)	0	43 (12.3)	33 (9.4)	8 (2.3)	2 (0.6)	0
Decreased appetite	59 (16.6)	37 (10.4)	21 (5.9)	1 (0.3)	0	22 (6.3)	11 (3.1)	9 (2.6)	2 (0.6)	0
Hyperglycemia	58 (16.3)	24 (6.8)	26 (7.3)	7 (2.0)	1 (0.3)	13 (3.7)	8 (2.3)	4 (1.1)	1 (0.3)	0
Stomatitis	52 (14.6)	24 (6.8)	21 (5.9)	7 (2.0)	0	17 (4.9)	15 (4.3)	2 (0.6)	0	0
Asthenia	47 (13.2)	29 (8.2)	14 (3.9)	4 (1.1)	0	36 (10.3)	31 (8.9)	3 (0.9)	2 (0.6)	0
Pruritus	44 (12.4)	32 (9.0)	10 (2.8)	2 (0.6)	0	23 (6.6)	19 (5.4)	4 (1.1)	0	0
Anemia	37 (10.4)	15 (4.2)	15 (4.2)	7 (2.0)	0	17 (4.9)	4 (1.1)	9 (2.6)	4 (1.1)	0
Urinary tract infection	36 (10.1)	8 (2.3)	23 (6.5)	5 (1.4)	0	23 (6.6)	2 (0.6)	21 (6.0)	0	0

* The safety population included all the patients who received at least one dose of capivasertib, fulvestrant, or placebo. The listed events were reported as a single term (or for rash, as a group term) in at least 10% of the patients for any grade in the capivasertib–fulvestrant group. Adverse events are reported regardless of the relationship to capivasertib, fulvestrant, or placebo.

† The group term of rash includes the preferred terms of rash, rash macular, maculopapular rash, rash papular, and rash pruritic.

Turner et al *N Engl J Med* 2023;388: 2058-2070

Capivasertib: Diarrhea management

Dose Level	Capivasertib Dose	Schedule
Starting dose	400 mg twice daily	4 days on, 3 days off
First dose reduction	320 mg twice daily	4 days on, 3 days off
Second dose reduction	200 mg twice daily	4 days on, 3 days off

- **Grade 2:** Withhold until ≤ Grade 1. Resume at same dose or one lower dose if recovery ≤ 28 days; reduce by one level if > 28 days. For recurrence, reduce by one dose level.
- **Grade 3:** Withhold until ≤ Grade 1. Resume at same dose or one lower dose if recovery ≤ 28 days; permanently discontinue if > 28 days.
- **Grade 4:** Permanently discontinue.

Patients should be advised to increase oral fluids and start antidiarrheal treatment (e.g., loperamide) at the first sign of diarrhea.

Consider secondary prophylaxis with loperamide for patients who experienced diarrhea in prior cycles.

Capivasertib. FDA Drug Label.

Capivasertib: Hyperglycemia management

Monitor fasting glucose at frequent intervals (baseline, then weekly during the first cycle is reasonable, regularly during first several cycles). Initiate or intensify oral anti-diabetic therapy (metformin preferred) early when glucose trends upward. HbA1c should be checked at baseline

- **FG > ULN–160 mg/dL (or HbA1c > 7%):** Consider initiation or intensification of oral anti-diabetic treatment; no dose hold required.
- **FG 161–250 mg/dL:** Withhold until FG ≤ 160 mg/dL. Resume at same dose if recovery ≤ 28 days; reduce by one level if > 28 days.
- **FG 251–500 mg/dL:** Withhold until FG ≤ 160 mg/dL. Resume at one lower dose if recovery ≤ 28 days; permanently discontinue if > 28 days.
- **FG > 500 mg/dL or life-threatening sequelae:** Withhold. Permanently discontinue if FG persists ≥ 500 mg/dL after 24 hours or life-threatening sequelae occur. If FG falls to ≤ 500 mg/dL within 24 hours, follow guidance for the relevant grade.

Capivasertib. FDA Drug Label.

Capivasertib: Cutaneous AE management

Monitor closely during the first 2–4 weeks. Initiate antihistamines and/or topical corticosteroids promptly. For severe or widespread rash, systemic corticosteroids may be needed.

- **Grade 2:** Withhold until ≤ Grade 1, then resume at same dose. For persistent or recurrent Grade 2, reduce by one dose level.
- **Grade 3:** Withhold until ≤ Grade 1. Resume at same dose if recovery ≤ 28 days; reduce by one level if > 28 days. Permanently discontinue for recurrent Grade 3.
- **Grade 4:** Permanently discontinue.

Capivasertib. FDA Drug Label.

Capivasertib: Cytopenias monitoring and management

Laboratory Abnormality	Capivasertib + Fulvestrant	Placebo + Fulvestrant
	All Grades (%)	All Grades (%)
Decreased lymphocytes	49	14
Decreased hemoglobin	47	22
Decreased leukocytes	35	23
Decreased neutrophils	25	16
Decreased platelets	12	6

In clinical practice, following the **CAPItello-291 monitoring schedule** (hematologic tests on days 1 and 15 of cycles 1–2, then day 1 of each subsequent cycle) is reasonable and evidence-based. More frequent monitoring may be warranted in patients with baseline cytopenias, heavy prior treatment, or concurrent myelosuppressive therapies

- **Grade 2:** Withhold capivasertib until recovery to ≤ Grade 1, then resume at the same dose.
- **Grade 3:** Withhold until recovery to ≤ Grade 1. Resume at the same dose if recovery occurs within 28 days; reduce by one dose level if recovery takes > 28 days.
- **Grade 4:** Permanently discontinue capivasertib.

Capivasertib. FDA Drug Label.
Turner et al *N Engl J Med* 2023;388: 2058-2070

Case Presentation

Case 1 – A Modern Day Scenario .. Enrolled onto CAPItello-281

- A 60-year-old gentleman presents asymptomatically with an initial screening PSA found to be 21 ng/mL
- He has a h/o obesity, hypertension, and hyperlipidemia, but no known cardiac disease
- ECOG performance status is 0
- Labs are all WNL
- CT and bone scan imaging confirm 4 osteoblastic lesions in the thoracic and lumbar spine and 1 in the R acetabulum
- NGS reveals no alterations in *BRCA* or any other homologous recombination repair genes; however, the patient is labeled as having PTEN loss
  - This is confirmed on IHC with 90% of prostate tumor cells lacking PTEN immunostaining

Case 1 – A Modern Day Scenario .. Enrolled onto CAPItello-281

Enrolled on CAPItello-281 trial, randomized to the experimental arm: capivasertib 400 mg PO BID (4 days on, 3 days off) + abiraterone 1,000 mg QD, prednisone 5 mg QD and ADT with leuprolide.

C1D10 (during his second "on" period of capivasertib): he contacts the clinic reporting 5–6 loose, watery bowel movements/day over the past 2 days, an increase of 4–5 stools above his baseline of 1/day. He reports mild abdominal cramping but no fever, blood in stool, or signs of dehydration. He is tolerating oral fluids. He has not yet started any antidiarrheal medication

Meets CTCAE v5.0 criteria for **Grade 2 diarrhea**: increase of 4–6 stools/day over baseline, not interfering with ADLs but limiting instrumental ADLs. This timing is consistent with the expected onset of capivasertib-associated diarrhea.

Case 1 – A Modern Day Scenario .. Enrolled onto CAPItello-281

Step 1: Withhold capivasertib.

- Per the FDA-approved dose modification table for capivasertib, Grade 2 diarrhea requires withholding capivasertib until recovery to ≤ Grade 1 (≤3 stools above baseline per day).

Step 2: Initiate antidiarrheal therapy.

- **loperamide 4 mg** loading dose, then **2 mg after each loose stool**, max 16 mg/day.
- consider adding **diphenoxylate/atropine 1–2 tablets every 6 hours PRN** (max 8 tablets/day).

Case 1 – A Modern Day Scenario .. Enrolled onto CAPItello-281

Step 3: Supportive care.

- Advise PO fluid intake with electrolyte-containing solutions.
- Recommend dietary modifications: low-fiber, lactose-free diet; BRAT diet
- Assess for signs of dehydration (orthostatic HoTN, decreased UOP, dry mucous membranes). If unable to tolerate PO fluids, arrange IVF.

Step 4: Rule out alternative etiologies.

- Assess for infectious causes. Review concomitant medications

Step 5: Continue abiraterone, prednisone, and ADT.

- Capivasertib is the causative agent

Discussion Questions

In your experience, what is the most common toxicity that affects adherence to capivasertib?

How should clinicians approach prophylaxis and early intervention for diarrhea? At what point do you hold versus dose reduce versus discontinue capivasertib for diarrhea?

Should clinicians assess baseline hemoglobin A1C in all patients before administering capivasertib? How frequently are endocrinology referrals necessary for patients receiving this drug?

Agenda

Module 1: Overview of Prostate Cancer

Module 2: Hormonal Therapy for Nonmetastatic and Metastatic Hormone-Sensitive Prostate Cancer (HSPC)

Module 3: Potential Role of Capivasertib in Metastatic HSPC

Module 4: Current and Potential Future Role of PARP Inhibitors in Metastatic PC

Module 5: Current and Future Role of Lutetium Lu 177 Vipivotide Tetraxetan for Patients with Metastatic PC

Weill Cornell Medicine

NewYork-Presbyterian

Current and potential use of PARP inhibitors for advanced prostate cancer

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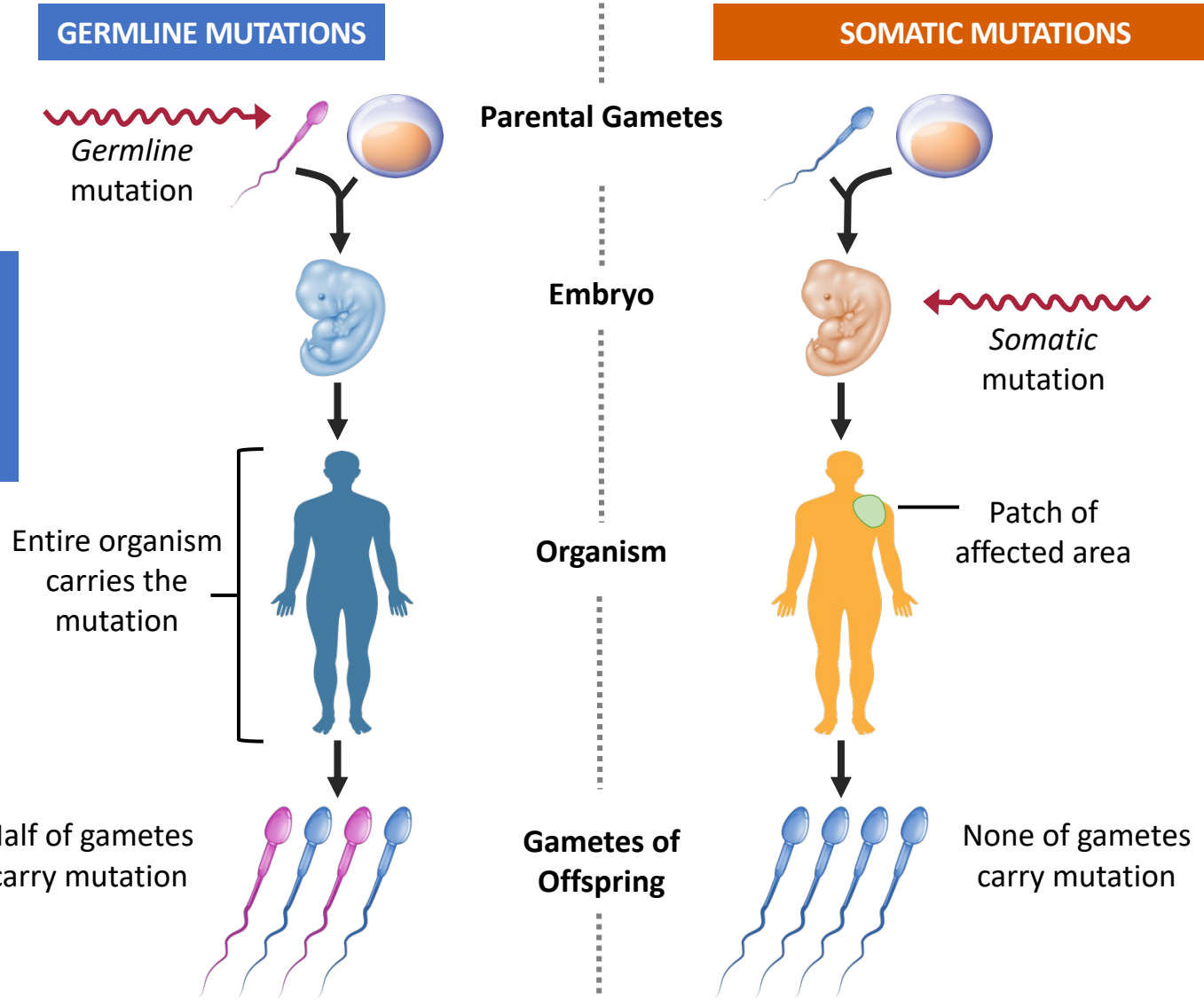
Weill Cornell Medicine
Meyer Cancer Center

Germline vs Somatic Mutations

<u>Inherited</u> mutations can be detected in all cells

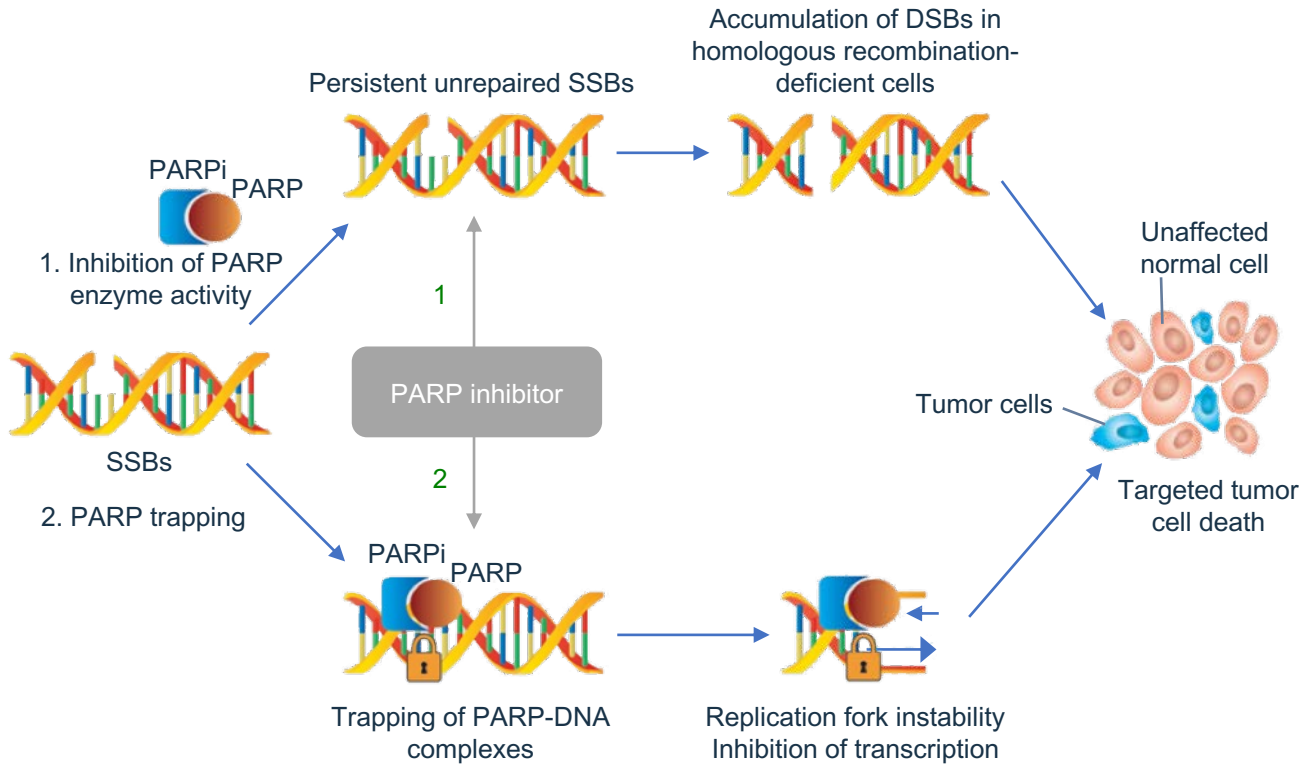


<u>Somatic/acquired</u> mutations can be detected in tumor cells

Bioninja. Accessed August 26, 2024. https://ib.bioninja.com.au/mutation-outcomes/

Rationale for PARP Inhibitors as PC Therapy

- Poly (ADP-ribose) polymerase (PARP) inhibitors block the enzyme PARP in cells
- PARP enzymes help with DNA repair
- Tumor cells that have alterations in homologous recombination repair (HRR) will die when PARP enzyme is blocked (synthetic lethality)
- About 20–25% of patients with mPC have tumor cells with alterations in HRR[1,2]



SSBs, single strand break; DSBs, double strand breaks

1. Robinson. *Cell*, 2015;161(5):1215-1228. 2. Chung. *JCO Precis Oncol*. 2019:3:PO.18.002839. ; 3. Agarwal. *Future Oncol*. 2022;18(4):425-436.

Phase 3 PROfound* in mAPMR With HRR Gene Alterations[1,2]

Olaparib vs Enzalutamide or Abiraterone

Key eligibility criteria

- mAPMR PC with disease progression on prior ARPI; eg, abiraterone or enzalutamide
- Alterations in ≥ 1 of any qualifying gene with a direct or indirect role in HRR*

Stratification factors

- Previous taxane
- Measurable disease

R 2:1 Open-label

N = 387

Cohort A
BRCA1, *BRCA2*, or *ATM*
n = 245

- **Olaparib, 300 mg bid** n = 162
- **Choice Abi/Enza‡** n = 83

Cohort B
Other alterations
n = 142

- **Olaparib, 300 mg bid** n = 94
- **Choice Abi/Enza‡** n = 48

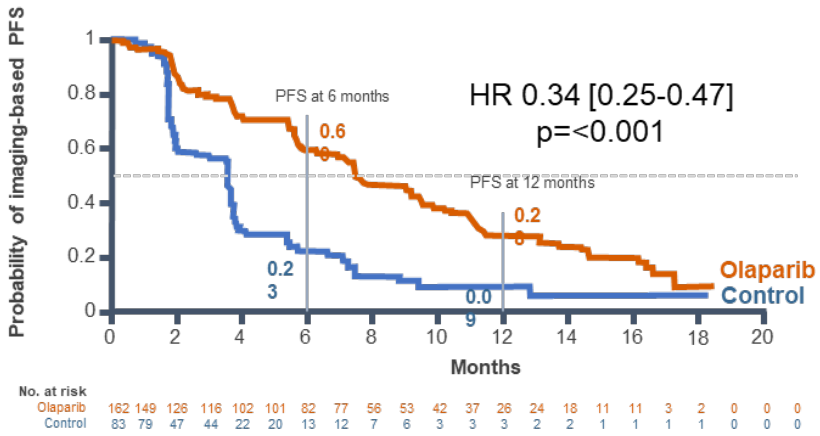
Upon BICR progression, physician's choice patients were allowed to cross over to olaparib

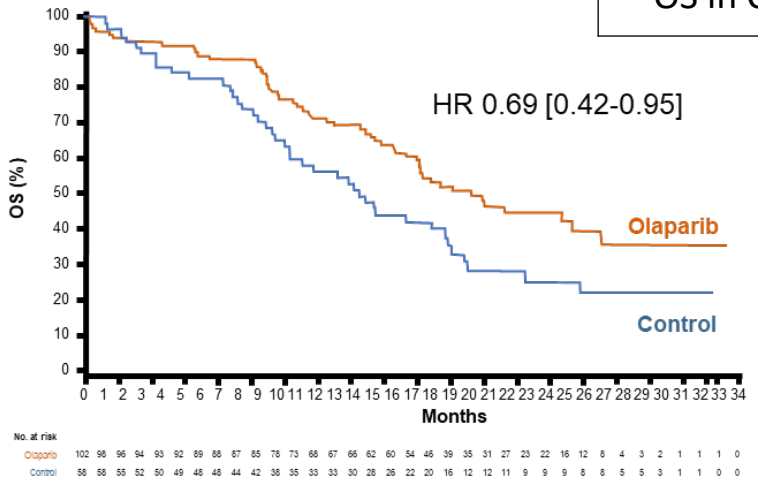
Primary Endpoint

- rPFS in Cohort A (RECIST 1.1 & PCWG3 by BICR)

Key Secondary Endpoints

- rPFS in Cohorts A+B
- Confirmed radiographic objective response rate in Cohort A
- Time to pain progression in Cohort A
- OS in Cohort A





HRR, homologous recombination repair.
‡Physician's choice of either enzalutamide (160 mg qd) or abiraterone (1000 mg qd + prednisone [5 mg bid]); BICR, blinded independent central review

1. Hussain. *N Engl J Med*. 2020; 383:2345-2357. 2. de Bono. *N Engl J Med*. 2020; 382:2091-2102.

Phase 3 TRITON3 Trial mAPMR PC with *BRCA/ATM* Mutation

Rucaparib vs Physician's Choice (abi/enza or docetaxel)

Patient population

- ARPI-resistant mAPMR PC
- *BRCA1/2* or *ATM* mutation
- ECOG 0-1
- No prior chemotherapy

R 2:1

Rucaparib 600 mg BID n = 270

Docetaxel OR abiraterone OR enzalutamide n = 135

Radiographic progression or Tx discontinuation

Optional crossover to rucaparib if progression on comparator

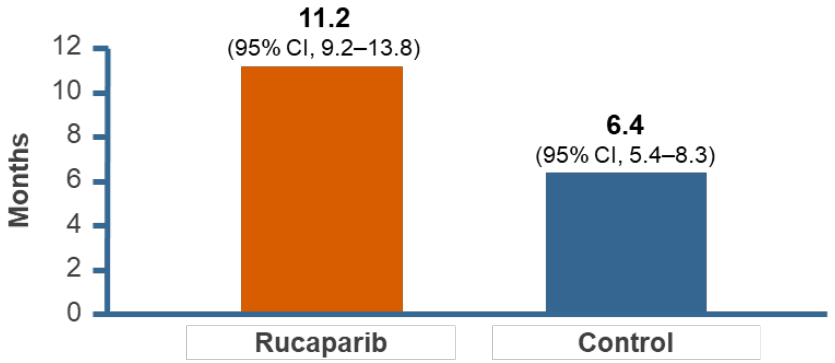
Primary endpoint

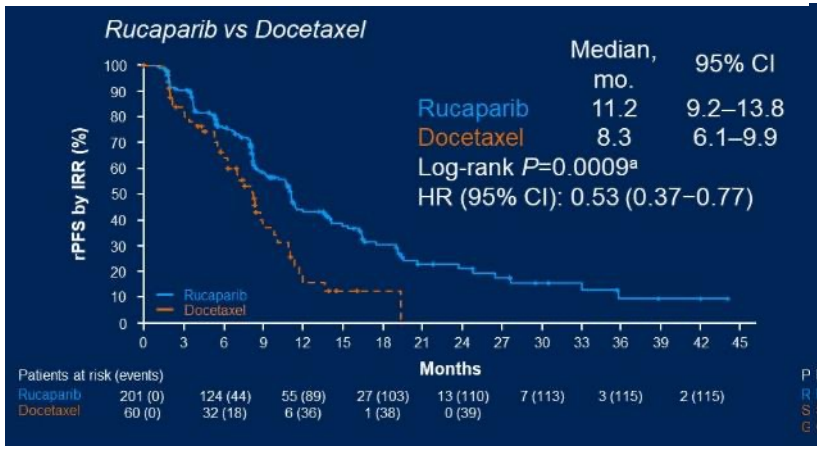
- Radiographic PFS

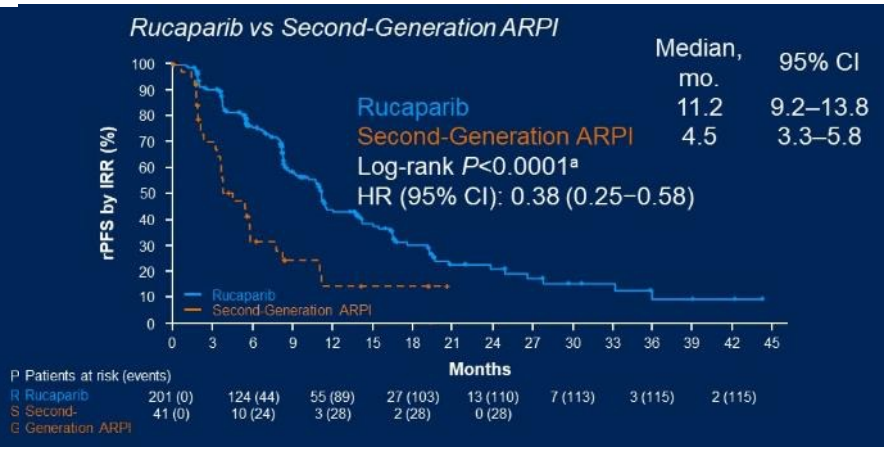
Secondary end points

- ORR and DoR
- OS
- Clinical benefit rate
- PSA response
- Time to PSA progression
- Patient-reported outcome
- Safety/tolerability

	Rucaparib	Control
Median PFS, mo	**11.2**	**6.4**
HR (95%, CI)	**0.50** (0.36–0.69)	
***P* value**	**< 0.001**	







Rucaparib with regular FDA approval for BRCA+ mAPMR PC after ARPI

*ATM included in trial

Fizazi K. *N Engl J Med*. 2023; 388(8):719-732. FDA grants regular approval to rucaparib for metastatic castration-resistant prostate cancer | FDA

Phase 3 TRITON3 Trial in patients with mAPMR PC and BRCA/ATM

Rucaparib vs Physician's Choice: Docetaxel subset

n (%)	Rucaparib (n=270)		Docetaxel (n=71)	
At least 1 any-grade TEAE	270 (100)		71 (100)	
At least 1 grade ≥3 TEAE	161 (60)		43 (61)	
Dose reductions due to TEAEs	104 (39)		21 (30)	
Dose interruptions due to TEAEs	142 (53)		19 (27)	
Discontinuations due to TEAEs	40 (15)		23 (32)	
Death due to TEAEs	5 (2)		0	
Most frequently reported TEAEs	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**
Asthenia/fatigue	165 (61)	19 (7)	48 (68)	7 (10)
Nausea	134 (50)	7 (3)	11 (15)	1 (1)
Anemia/hemoglobin decreased	126 (47)	64 (24)	10 (14)	1 (1)
Neuropathy[a]	25 (9)	0	34 (48)	4 (6)

Fizazi K. *N Engl J Med*. 2023; 388(8):719-732

PARP Inhibitor + AR Pathway Inhibitor

Rationale: Pre-clinical synergy

- PARP is a transcriptional co-activator of AR
- AR induces expression of PARP

Olaparib + AAP[1]

- **First-line therapy** for patients with ARPI-naïve mAPMR PC and known or suspected ***BRCA* alterations**
- Prior **docetaxel** for mCSPC permitted

Niraparib + AAP[2]

- **First-line therapy for** patients with mAPMR PC and ***BRCA* alterations**
- No prior systemic therapy for mAPMR PC, except up to 4 months of AAP and ongoing ADT; Prior **docetaxel** and **ARPIs** received in mAPMN/S PC permitted

Talazoparib + enzalutamide[3]

- **First-line therapy** for patients with ARPI-naïve mAPMR PC and **HRR alterations**

1. US FDA. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-olaparib-abiraterone-and-prednisone-or-prednisolone-brca-mutated-metastatic-castration. 2. US FDA. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-niraparib-and-abiraterone-acetate-plus-prednisone-brca-mutated-metastatic-castration. 3. US FDA. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-talazoparib-enzalutamide-hrr-gene-mutated-metastatic-castration-resistant-prostate.

PARPi + ARPI combinations for mAPMR PC: Data for reference

	Olaparib + AAP[1,2]	Niraparib + AAP[3,4]	Talazoparib + Enzalutamide[5-7]
PC Approvals	***BRCA*-mutated mAPMR PC**	***BRCA*-mutated mAPMR PC**	**HRR-gene mutated mAPMR PC**
Dose	300 mg olaparib BID plus 1,000 mg abiraterone acetate qday with 5mg prednisone BID	200 mg niraparib qday combined with 1,000 mg abiraterone acetate qday with 10 mg of prednisone daily	Talazoparib 0.5 mg qday plus Enzalutamide 160 mg qday
Most frequent AEs (≥ 20%), All Grades	**Anemia (50%)**, fatigue (39%), nausea (31%), Back pain (22%), diarrhea (21%)	**Decreased hemoglobin (67%)**, decreased lymphocytes (55%), decreased white blood cells (48%), musculoskeletal pain (44%), fatigue (43%), decreased platelets (37%), increased alkaline phosphatase (34%), constipation (34%), hypertension (33%), nausea (33%), decreased neutrophils (32%), increased creatinine (30%), increased potassium (25%), decreased potassium (20%) and increased AST (20%)	**Anemia (66%),** neutropenia (36%), fatigue (34%), thrombocytopenia (25%), back pain (22%), leukopenia (22%), decreased appetite (22%), nausea (21%)

Clinical Benefit	• 34% reduced risk for radiographic progression (overall)
	• In exploratory ***BRCA*m mCRPC subgroup**:
	  • **HR for rPFS: 0.24** (95% CI, 0.12–0.45)
	  • **HR for OS: 0.29** (95% CI, 0.14–0.56)
		• In the ***BRCA*1/2 subgroup**:
		  • **HR for rPFS: 0.55** (95% CI, 0.39–0.78); *P* = 0.0007
		  • **HR for OS: 0.788** (95% CI 0.554-1.120); nominal *p* = 0.183
			• HR for rPFS: (HR 0.67; 95% CI 0.55–0.81; *P*<.0001)
			• In the **HRR subgroup**:
			  • **HR for rPFS: 0.46** (0.30–0.70; *P* = 0.0003)
			  • **HR for mOS: 0.55** (0.36–0.83; *P* = 0.0035)
			• In the ***BRCA*1/2 *m*** subgroup
			  • **HR for mOS: 0.497** (0.318-0.776); *P*=0.0017

1. Clarke. *N Eng J Med Evid.* 2022;1(9):EVIDoa2200043. 2. Saad. *Lancet Oncol*. 2023 Oct;24(10):1094-1108. 3. Chi. *Ann Oncol.* 2023;34: 772-782. 4. Chi. *Eur Urol Oncol*. 2025; 8(4):986-998. 5. Agarwal. *Lancet*. 2023;402(10398):291-303. 6. Agarwal. *Lancet*. 2025;406:447.460. 7. Agarwal. ASCO GU 2025, LBA18.

Phase 3 AMPLITUDE Trial in HRRm mAPMN/S PC

Niraparib + AAP +ADT vs placebo + AAP +ADT

1,2

Eligibility Criteria:
- *Prostate adenocarcinoma*
- *HRR gene alteration*
- *ADT started ≤6 mo prior to R and continued through study*
- *Prior doce allowed; up to 45 days abi/pred allowed*
- *No prior PARPi treatment*

1:1 R 696

Niraparib + abiraterone acetate (1,000 mg) + prednisone (5 mg)
Continuous administration, 28-day C
(n = 348)

Placebo + abiraterone acetate (1,000 mg) + prednisone (5 mg)
Continuous administration, 28-day C
(n = 348)

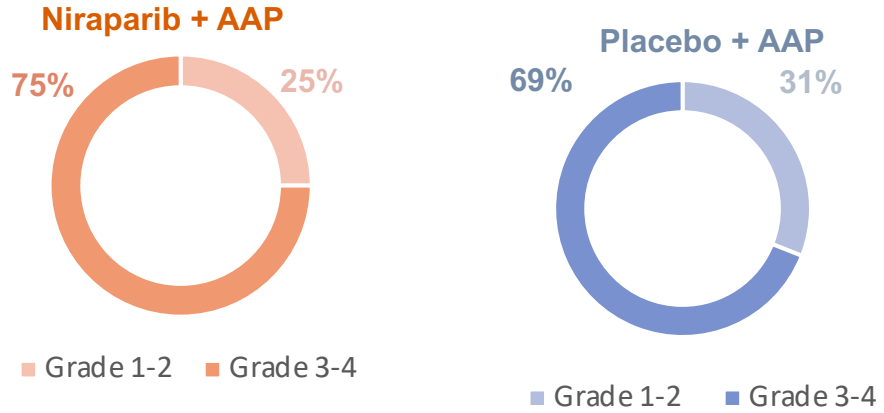
Primary Endpoint
rPFS

Secondary Endpoint
OS

This regimen was FDA-approved December 12, 2025 for those with known or suspected deleterious BRCA2m mAPMN/S PC.

3

Adverse Events



Anemia (25% needed blood transfusion) and hypertension

Endpoints	Nira + AAP vs Placebo + APP (N = 696)	
	Niraparib + AAP (n = 348)	Placebo + AAP (n = 348)
Median rPFS (mos)	NE	29.5
HR (95% CI)	**0.63** (0.49, 0.8)	
P	.0001	
Median OS (mos)	NE	NE
HR (95% CI)	**0.75** (0.51, 1.11)	
P	.15	

BRCA Subgroup Analysis

	Nira + AAP n = 191	Placebo + AAP n = 196
Median rPFS	NR	26 mos

rPFS HR: **0.52**
95% CO: 0.37, 0.72; **P < .0001**

HRR Effector Subgroup Analysis

	Nira + AAP n = 230	Placebo + AAP n = 226
Median rPFS	NR	27.6 mos

rPFS HR: **0.57**
95% CO: 0.42, 0.77; **P < .0003**

AAP, abiraterone acetate + prednisone; ADT, androgen deprivation therapy; BRCA2m, BRCA2-mutated; C, cycles; HRR, homologous recombination repair; mCSPC, metastatic castration-sensitive prostate cancer; NE, not evaluable; Nira, niraparib; rPFS, radiographic progression-free survival.
1. ClinicalTrials.gov. NCT04497844. 2. Food and Drug Administration. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-niraparib-and-abiraterone-acetate-plus-prednisone-brca2-mutated-metastatic-castration. Accessed Feb 19, 2026. 3. Attard. Nat Med. 2025;31(12):4109-4118.

PARP inhibitor summary

- mAPMN/S
  - ADT/Abi/pred + niraparib FDA approved for BRCA2
    - Need longer follow up for other groups
  - *ADT/Enza/talazoparib with positive trial (press release → ASCO 2026)*
- ARPI-naïve mAPMR
  - ARPI + PARPi better than ARPI alone in molecularly selected
    - Abi/pred/olaparib, Abi/pred/niraparib, Enza/talazoparib
- ARPI-resistant mAPMR
  - Rucaparib > doce/ARPI in BRCA2/1
  - Olaparib > ARPI in molecularly selected

- Additional combinations being studied
- PARP1 selective?

Case Presentation

- At age 68, pt presented with PSA 11, Gleason grade group 4, cT3N0 prostate adenocarcinoma
  - Family history of breast and prostate cancer
  - History of diet-controlled hyperlipidemia, no other co-morbidities
- Started ADT and received radiation to prostate and pelvic lymph nodes. PSA declined to 0.5.
  - Complains of fatigue and weakness with occasional stumbling
- Towards the end of year 2 of ADT, PSA begins rising
  - 0.5 → 0.9 → 2.1 (doubling time 2.5 months) without new symptoms
  - Scans c/w multifocal lymph node and bone metastases
  - Biopsy confirms prostate adenocarcinoma
  - Germline assessment = pathogenic BRCA2 alteration
  - Biopsy genomics = BRCA2 and TMPRSS2-Erg fusion
- How would you treat this patient?

Discussion Questions

What is the incidence of BRCA1/2 and other homologous recombination repair abnormalities in PC? Who should be tested for them, when and how?

When do you use PARP inhibitor monotherapy and when do you recommend a PARP inhibitor/AR pathway inhibitor combination for individual patients?

Tolerability of PARP Inhibitors Used in the Treatment of PC

Research to Practice - ONS

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Comparative Toxicity Across PARP Inhibitors

- Class effect toxicities seen across all PARPi
  - GI disturbances
  - Fatigue
  - Anemia
- Care team should be proactive in management of AEs
  - Consider prescribing antiemetics and antidiarrheals prior to first dose
  - Consider initiating treatment at reduced dose based on patient profile
- Close laboratory and clinical monitoring for initial 3 months.
- Other AE considerations
  - Hypertension and cardiovascular events
  - Pneumonitis
  - Myelodysplastic Syndrome / Acute Myeloid Leukemia

Comparative Toxicity Across PARP Inhibitors

Adverse Event	Olaparib (PROfound, n=256)	Rucaparib (TRITON3, n=270)	Niraparib (GALAHAD, n=289)	Talazoparib (TALAPRO-1, n=127)
Anemia (any grade)	50%	49%	54%	49%
Anemia (Grade ≥3)	23%	23%	33%	31%
Neutropenia (any grade)	9%	17%	14%	17%
Neutropenia (Grade ≥3)	4%	9%	10%	8%
Thrombocytopenia (any grade)	12%	14%	24%	19%
Thrombocytopenia (Grade ≥3)	4%	6%	16%	9%
Nausea (any grade)	43%	49%	58%	33%
Fatigue/Asthenia (any grade)	42%	55%	33%	24%/20%
Decreased appetite (any grade)	31%	29%	25%	28%
Discontinuation due to AE	18%	15%	15%	12%

Optimal Monitoring and Management of PARP Inhibitors

At PARP initiation:

- CBC + differential, monitor monthly

For Niraparib:

- FDA label recommends weekly CBC during first month (high incidence thrombocytopenia)
- Then convert to monthly monitoring
  - May be reasonable to apply this principle to all PARPs

La Fargue et al *Lancet Oncol* 2019 Jan; 20(1) e15-e28 Niraparib PI

Optimal Monitoring and Management of PARP Inhibitors

Hematologic toxicities tend to occur early

- PROfound (Olaparib): all 4 most common AEs peaked within first 2 months
  - Managed with dose modifications
- TALAPRO1 (Talazoparib): median time to onset …
  - ≥G3 anemia was first 56 days
  - ≥G3 neutropenia 48 days
  - ≥G3 thrombocytopenia 17 days

For Niraparib:

- FDA label recommends weekly CBC during first month (high incidence thrombocytopenia)
- Then convert to monthly monitoring
  - May be reasonable to apply this principle to all PARPs

Roubaud et al *Eur J Cancer 2022* Jul: 170: 73-84 Mehra et al *J Clin Oncol* 39, 5047 (2021) Niraparib PI

Optimal Monitoring and Management of PARP Inhibitors

Anemia – the most clinically impactful toxicity

- Dose interruptions, dose reductions
- Transfusions
  - TALAPRO1: 34% received this, most when Hgb 7.0-10.0g/dL

Nausea/Vomiting

- Generally G1-2 tends to peak early, then improve with continued tx
- Standard antiemetics

Thrombocytopenia

- Niraparib: decreases occur predominantly during C1, stabilize by C2-3
- Dose modifications, primary strategy

Olaparib PI

Mehra et al *J Clin Oncol* 39, 5047 (2021)

Optimal Monitoring and Management of PARP Inhibitors

VTE

- Routine thromboprophylaxis not currently recommended, but awareness prudent.
- PROpel (Olaparib): most PEs were incidental findings on imaging

MDS/AML surveillance

- If unexplained pancytopenia develops, nutritional deficiencies and viral infections should be excluded
- Persistent issue should prompt bone marrow aspirate to evaluate for dysplasia
- Must discontinue the PARP if MDS/AML confirmed.

Yazgan et al *Crit Rev Oncol Hematol 2024* Jun:98:104376

La Fargue et al *Lancet Oncol* 2019 Jan; 20(1) e15-e28

Combo Therapy Impacts on Tolerability

Three phase III combination trials in 1st line mCRPC

- PROpel (Olaparib + abiraterone)
- TALAPRO2 (Talazoparib + enzalutamide)
- MAGNITUDE (Niraparib + abiraterone)

The rate of ≥G3 AEs is 10-30% higher with PARP inhibitor/ARPI combinations compared to ARPI alone

Table 2. Treatment-Emergent Adverse Events (Safety Analysis Set).*

	Abiraterone and Olaparib (n=398)		Abiraterone and Placebo (n=396)	
Adverse Event	**All Grades**	**Grade ≥3**	**All Grades**	**Grade ≥3**
Any	387 (97.2)	188 (47.2)	376 (94.9)	152 (38.4)
Any serious	135 (33.9)	NA	107 (27.0)	NA
Interruption due to adverse event				
Olaparib or placebo	178 (44.7)	NA	100 (25.3)	NA
Abiraterone	131 (32.9)	NA	87 (22.0)	NA
Dose reduction due to adverse event				
Olaparib or placebo	80 (20.1)	NA	22 (5.6)	NA
Abiraterone	10 (2.5)	NA	17 (4.3)	NA
Discontinuation due to adverse event				
Olaparib or placebo	55 (13.8)	NA	31 (7.8)	NA
Abiraterone	34 (8.5)	NA	35 (8.8)	NA
Death due to adverse event	16 (4.0)	NA	17 (4.3)	NA
Type (in ≥10% of patients in abiraterone and olaparib arm)				
Anemia†	183 (46.0)	60 (15.1)	65 (16.4)	13 (3.3)
Fatigue or asthenia	148 (37.2)	9 (2.3)	112 (28.3)	6 (1.5)
Nausea	112 (28.1)	1 (0.3)	50 (12.6)	1 (0.3)
Diarrhea	69 (17.3)	3 (0.8)	37 (9.3)	1 (0.3)
Constipation	69 (17.3)	0	55 (13.9)	1 (0.3)
Back pain	68 (17.1)	3 (0.8)	73 (18.4)	4 (1.0)
Decreased appetite	58 (14.6)	4 (1.0)	23 (5.8)	0
Vomiting	52 (13.1)	4 (1.0)	36 (9.1)	1 (0.3)
Arthralgia	51 (12.8)	0	70 (17.7)	2 (0.5)
Hypertension	50 (12.6)	14 (3.5)	65 (16.4)	13 (3.3)
Dizziness	43 (10.8)	0	25 (6.3)	0
Peripheral edema	41 (10.3)	0	45 (11.4)	1 (0.3)
Urinary tract infection	41 (10.3)	8 (2.0)	31 (7.8)	4 (1.0)
Other				
Cardiac failure‡	6 (1.5)	4 (1.0)	5 (1.3)	1 (0.3)
Embolic and thrombotic events				
Arterial‡	8 (2.0)	6 (1.5)	10 (2.5)	8 (2.0)
Venous‡	29 (7.3)	27 (6.8)	13 (3.3)	8 (2.0)

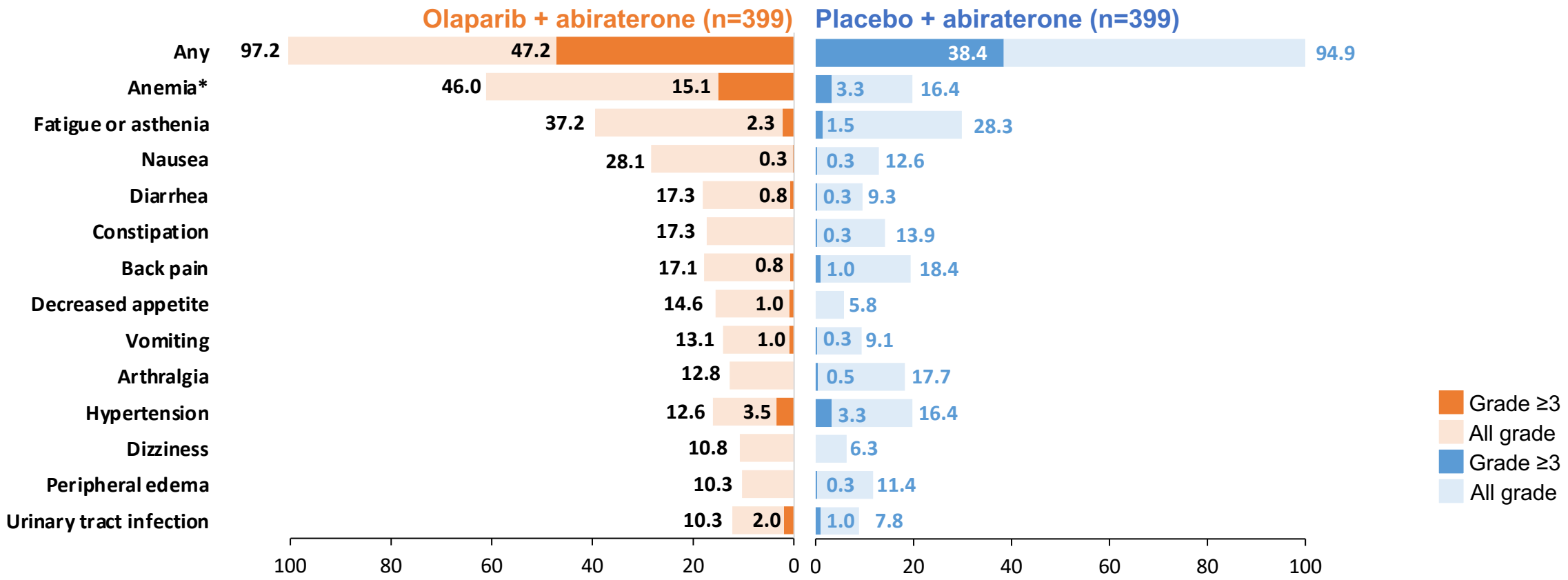
* Patients were counted once for each type of adverse event and are reported regardless of the investigators' assessment of causality. Adverse events with an onset date, or worsening, on or after the date of first dose and up to and including 30 days after discontinuation of randomized treatment were included. Common Terminology Criteria for Adverse Events version 4.03 was used. NA denotes not applicable.

† Anemia included anemia, decreased hemoglobin level, decreased red blood cell count, decreased hematocrit level, erythropenia, macrocytic anemia, normochromic anemia, normochromic normocytic anemia, and normocytic anemia.

‡ Based on standardized MedDRA query.

Clarke et al *NEJM Evid* 2022; 1(9):EVIDoa2200043

PROpel: Most Common Adverse Events



Safety was assessed through the reporting of AEs according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE v4.03) and laboratory assessments.
*Anemia category includes anemia, decreased hemoglobin level, decreased red-cell count, decreased hematocrit level, erythropenia, macrocytic anemia, normochromic anemia, normochromic normocytic anemia, and normocytic anemia.

Saad F, et al. *GU ASCO* 2022.

Case Presentation

Identifying Toxicity Cause in PARP/ARPI Combos – Case Discussion

Toxicities Predominantly Attributable to the PARPi

- **Myelosuppression** In PROpel, Grade ≥3 anemia was 15.1% with olaparib-abiraterone vs. 3.3% with placebo-abiraterone, clearly attributable to olaparib. Similarly, in TALAPRO-2, Grade ≥3 anemia was 43% vs. 2%. ARPIs alone cause minimal myelosuppression.
- **Nausea, vomiting, decreased appetite:** GI toxicities are well-established PARP inhibitor class effects and occur at much lower rates with ARPIs alone.
- **MDS/AML:** Exclusively attributable to PARP inhibition.

Toxicities Predominantly Attributable to the ARPI:

- **Hypertension:** known abiraterone effect (mineralocorticoid excess) and, to a lesser extent, enzalutamide. In PROpel, hypertension rates were similar between arms (12.6% vs. 16.4%), confirming this is an abiraterone-driven effect
- **Hepatotoxicity (elevated transaminases):** Primarily an abiraterone effect (though rucaparib also causes ALT/AST elevations independently)
- **Fatigue:** Shared by both drug classes, making attribution difficult. However, fatigue rates in PROpel were modestly higher with the combination (37.2% vs. 28.3%), suggesting an additive effect
- **Cognitive effects, seizure risk:** Enzalutamide-specific.
- **Peripheral edema, hypokalemia:** Abiraterone-specific (mineralocorticoid pathway)

Clarke et al *NEJM Evid* 2022; 1(9):EVIDoa2200043

Roubaud et al *Eur J Cancer 2022* Jul: 170: 73-84

Fizazi et al *Lancet* 2025 Aug 2; 406 (10502): 461-474

Prostate Cancer. NCCN Guidelines

La Fargue et al *Lancet Oncol* 2019 Jan; 20(1) e15-e28

Identifying Toxicity Cause in PARP/ARPI Combos – Case Discussion

72-year-old man with BRCA2-mutated metastatic castration resistant prostate cancer with bone metastases to the pelvis, lumbar spine, and ribs. PMhx well controlled HTN (on lisinopril 10 mg), T2 DM (on metformin 1000 mg BID), and mild CKD (baseline eGFR 55 mL/min). He was started on first-line Olaparib 300 mg BID + abiraterone 1000 mg QD + prednisone 5 mg BID, with ongoing ADT (leuprolide depot injections). Baseline Hgb 11.8 g/dL, otherwise CBC and CMP largely unremarkable.

At his routine 8-week follow-up, he reports progressive fatigue over past 3 weeks now limiting instrumental ADLs, intermittent nausea (3-4 episodes/week), bilateral ankle swelling, mild dizziness on standing. No chest pain, dyspnea, melena, or hematuria.

Identifying Toxicity Cause in PARP/ARPI Combos – Case Discussion

VS:

- BP 162/96, HR 88 bpm, wt 92 kg (up 3.5 kg)

Labs:

- Hgb 8.4 (down from 11.8)
- MCV 102
- Reticulocyte count 1.8% (inappropriately low)
- K 3.1 (down from normal range)
- AST 78 (~2x ULN)
- ALT 62 (~1.5x ULN)
- Fasting glucose 198 mg/dL

Discussion Questions

How do you counsel patients with germline BRCA and other germline homologous recombination repair abnormalities about the potential utility of genetic testing for children or grandchildren?

What are the common side effects associated with PARP inhibitors? What do you tell your patients about to start one of these agents about potential toxicities? How does this vary according to the specific agent and whether it is used alone or in combination with an AR pathway inhibitor?

How would you alleviate the concern of a patient who expressed fear about the potential development of AML/MDS on a PARP inhibitor?

Agenda

Module 1: Overview of Prostate Cancer

Module 2: Hormonal Therapy for Nonmetastatic and Metastatic Hormone-Sensitive Prostate Cancer (HSPC)

Module 3: Potential Role of Capivasertib in Metastatic HSPC

Module 4: Current and Potential Future Role of PARP Inhibitors in Metastatic PC

Module 5: Current and Future Role of Lutetium Lu 177 Vipivotide Tetraxetan for Patients with Metastatic PC

Weill Cornell Medicine

NewYork-Presbyterian

Current and future role of Lu-177 vipivotide tetraxetan for advanced prostate cancer

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Professor of Medicine & Urology
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@DrScottTagawa

Weill Cornell Medicine
Meyer Cancer Center

Targeted Radionuclide Therapy (TRT)

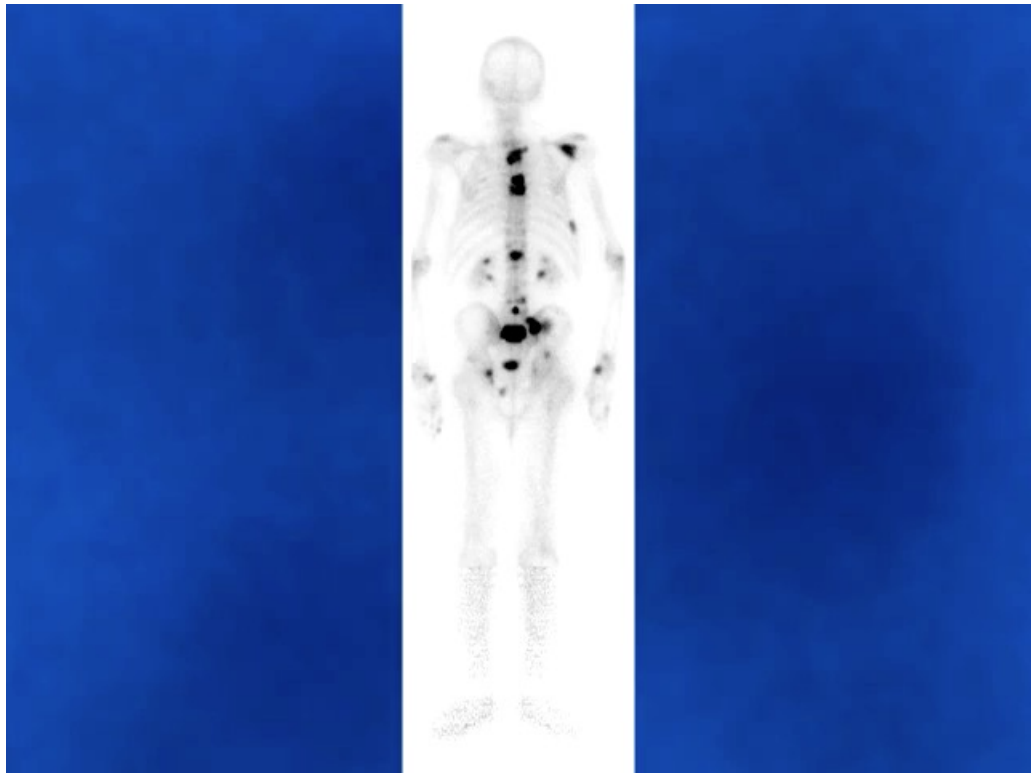
- TRT = preferred term for targeted delivery of therapeutic radionuclide
  - Radiopharmaceutical therapy (RPT)
    - RLT = small molecule ligand; PRRT = peptide; RIT = antibody
- Examples (with typical "**theranostic**" pair), partial list
  - Iodine-131 (^{123}I / ^{131}I)
  - Strontium-89, samarium-153 (^{99Tm}-MDP)
  - Radium-223 dichloride (^{99Tm}-MDP)
  - Lutetium-177 dotatate (^{68}Ga/^{64}Cu-dotatate)
  - Lutetium-177 vipivotide tetraxetan (^{68}Ga-PSMA-11 / ^{18}F-DCFPyL / ^{18}F-PSMA-7.3)

Al-Ibraheem A et al. *J Nucl Med.* 2025;66(5):757-763..

Targeted Diagnostics & Therapeutics

- PSMA = a very specific lock present on most prostate cancers
  also salivary/lacrimal glands, small intestine, proximal renal tubules, solid tumor neovasculature
- We have engineered specific “keys” that only target PSMA “locks”
  and we can attach cancer killers or other molecules to keys that enter via locks

APPLICATIONS



VISION: pre-treated mAPMR PC

N=814
Alternative 1° endpoint:
rPFS **or** OS acceptable with FDA

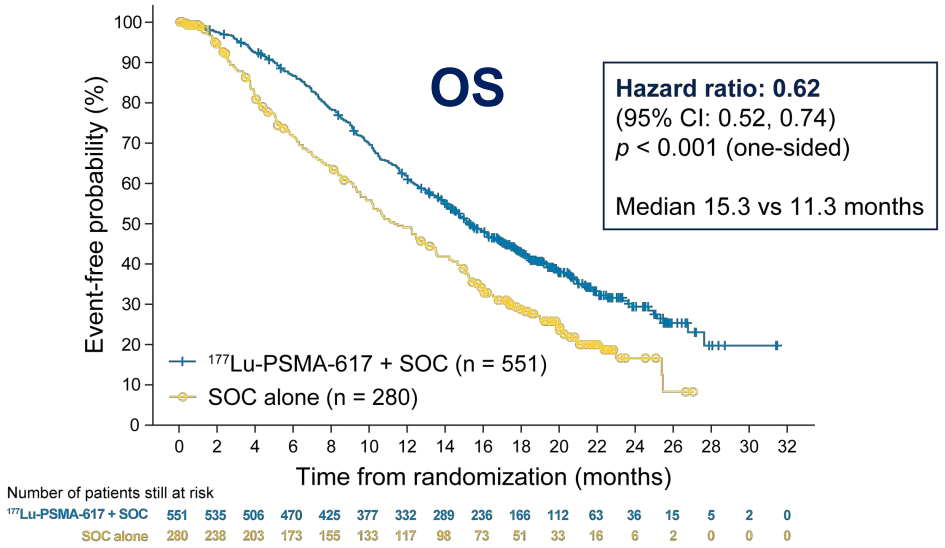
mAPMR PC
- at least 1 prior ARPI
- at least 1 prior taxane
- PS = 0-2
- PSMA PET+

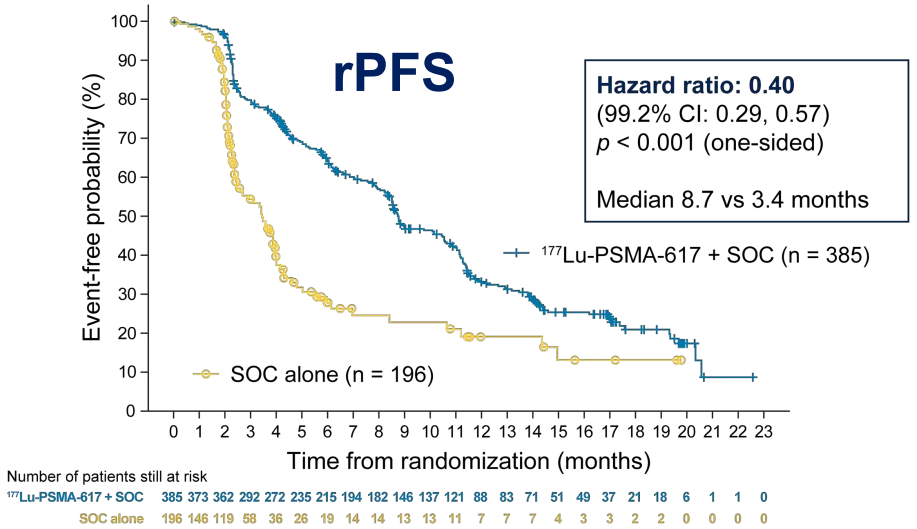
Stratification Factors
- LDH (above/below 260)
- Liver mets (Y/N)
- PS (0-1 vs 2)
- ARPI as BSC (Y/N)

2:1 Randomization

- **Best standard care**
- **^{177}Lu-PSMA-617**
  7.4 GBq q6 wks x4-6

- **Best standard care**





Sartor et al. *N Engl J Med*. 2021; 385:1091-1103.

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

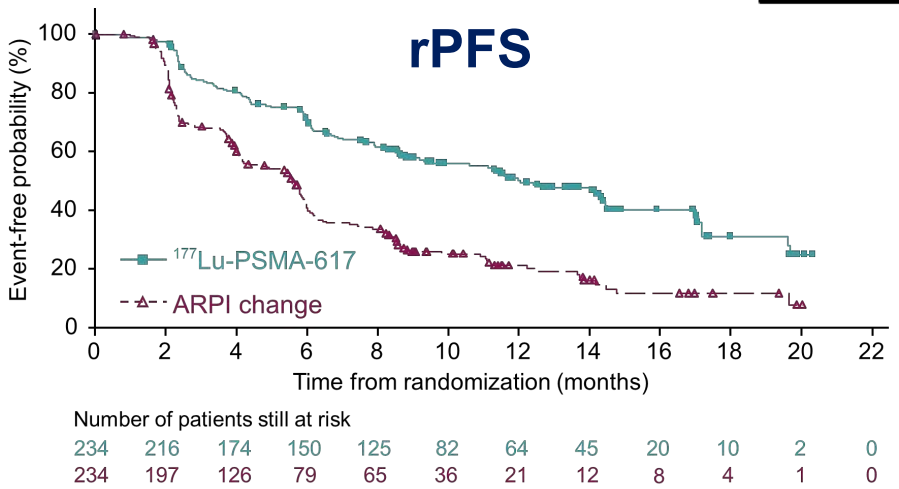
Crossover allowed upon radiographic progression by BICR

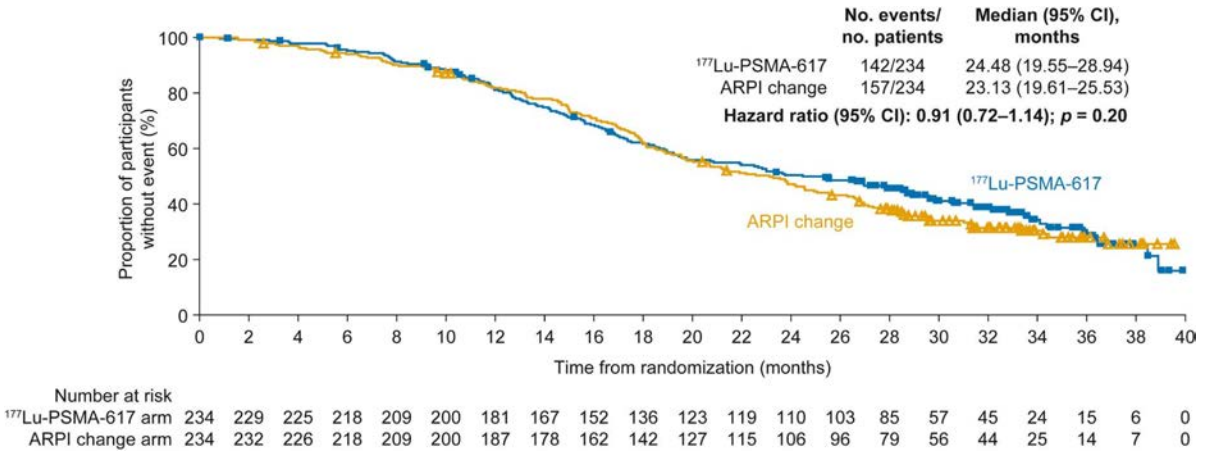
ARPI change
abiraterone or enzalutamide

rPFS by BICR

Follow-up

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





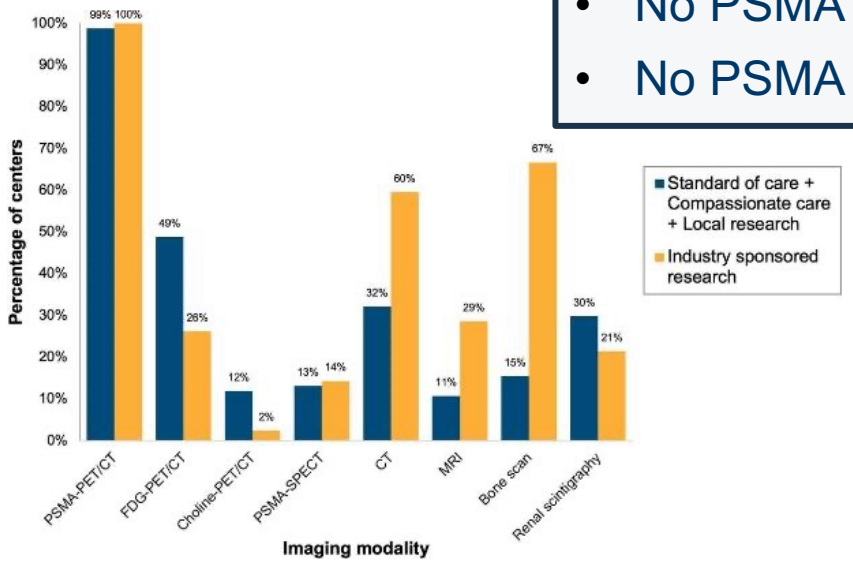
Morris et al. *Lancet.* 2024; 404:1227-1239.
Fizazi et al, Ann Oncol 2025

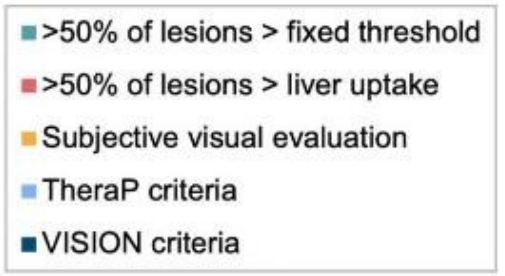
VISION: ^{177}Lu-PSMA-617: Patient Selection With PSMA PET

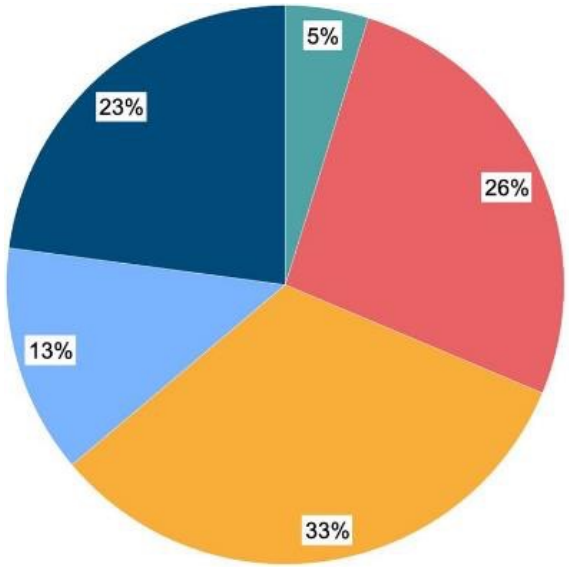
1003 patients received ^{68}Ga-PSMA-11 PET/CT → 869/1003 patients (~87%) met PSMA criteria (95% at least 1 PSMA+ lesion > liver)

Pre-Specified Criteria for PSMA Positivity

- PSMA-positive metastatic lesion
  - PSMA PET positivity defined as visual uptake > liver
- No size criteria for PSMA-positive lesions
- No PSMA < liver visceral or lytic bone lesions ≥ 1 cm
- No PSMA < liver lymph node lesions ≥ 2.5 cm



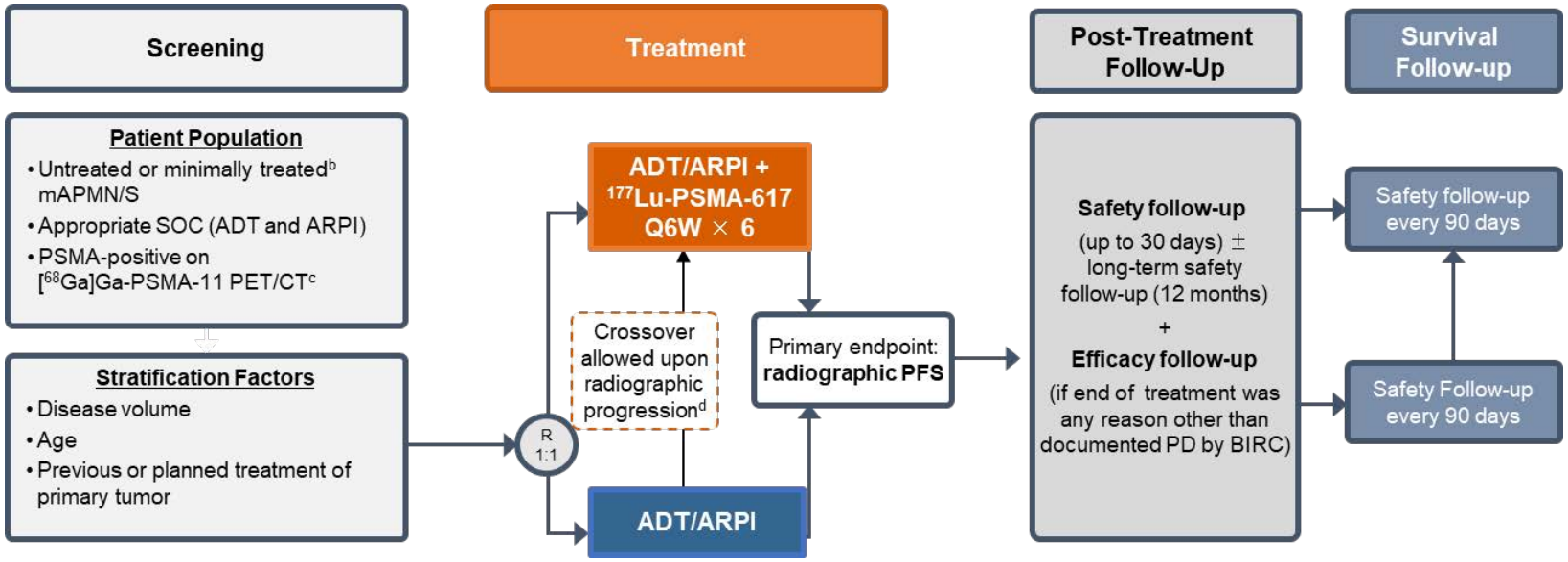


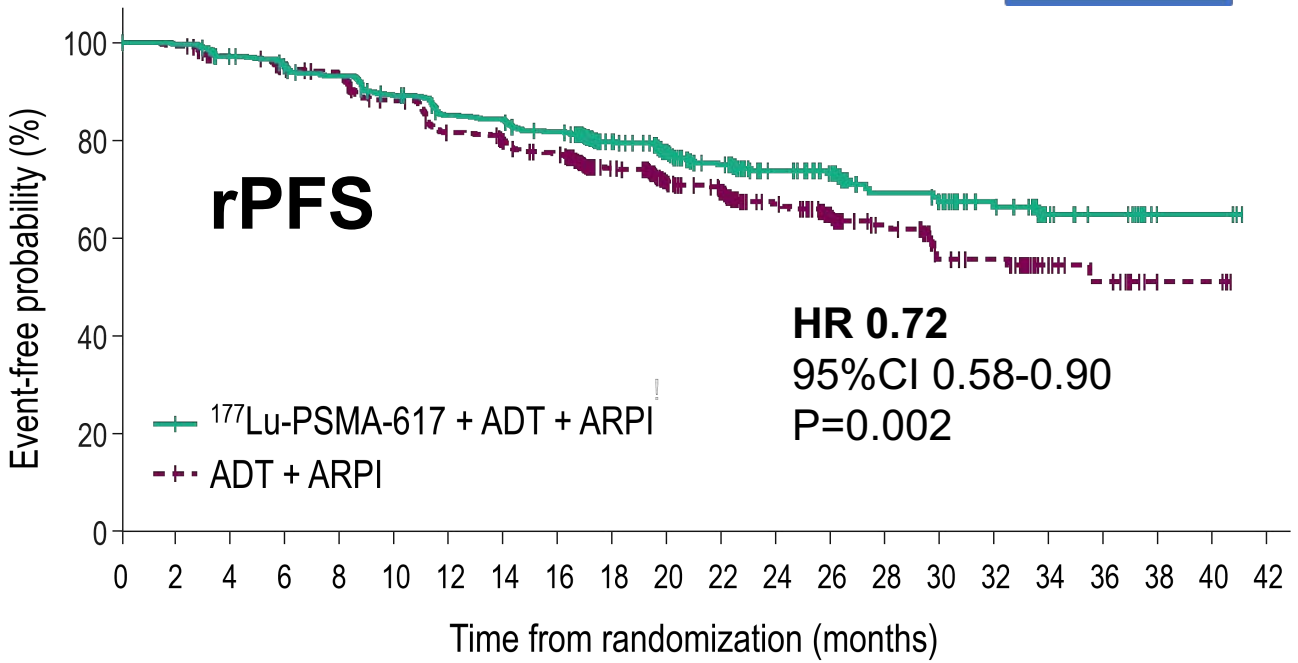


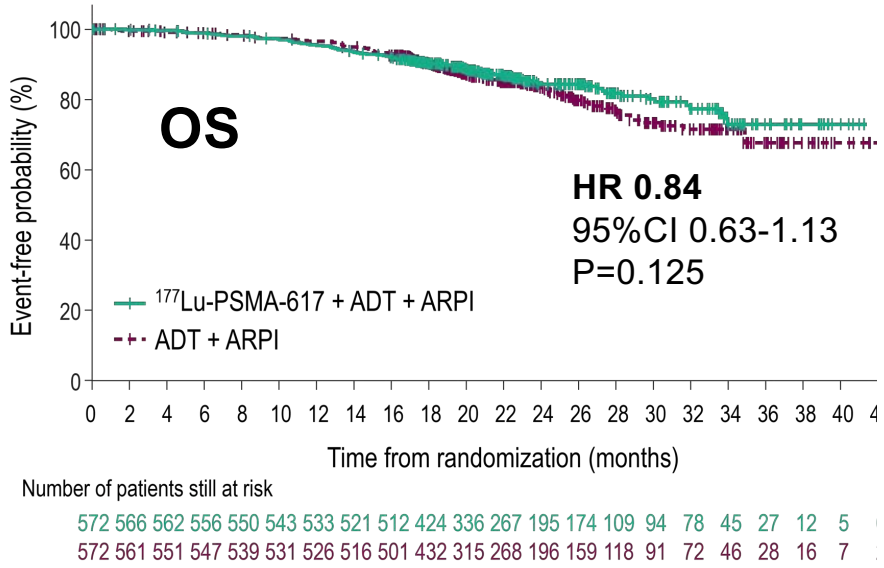
^{68}Ga-PSMA-11 PET/CT, Gallium-68 prostate-specific membrane antigen-11 positron emission tomography/computed tomography; PSMA, prostate-specific membrane antigen

Sartor O et al. *N Engl J Med*. 2021;385:1091-1103. Farolfi A et al. *J Nucl Med.* 2024;65:438-45.

PSMAddition







Other endpoints favoring ^{177}Lu-PSMA-617

- PSA<0.2
- RECIST
- Time to SSE, PSA progression, hormone resistance

Tagawa S et al. ESMO 2025;Abstract LBA6

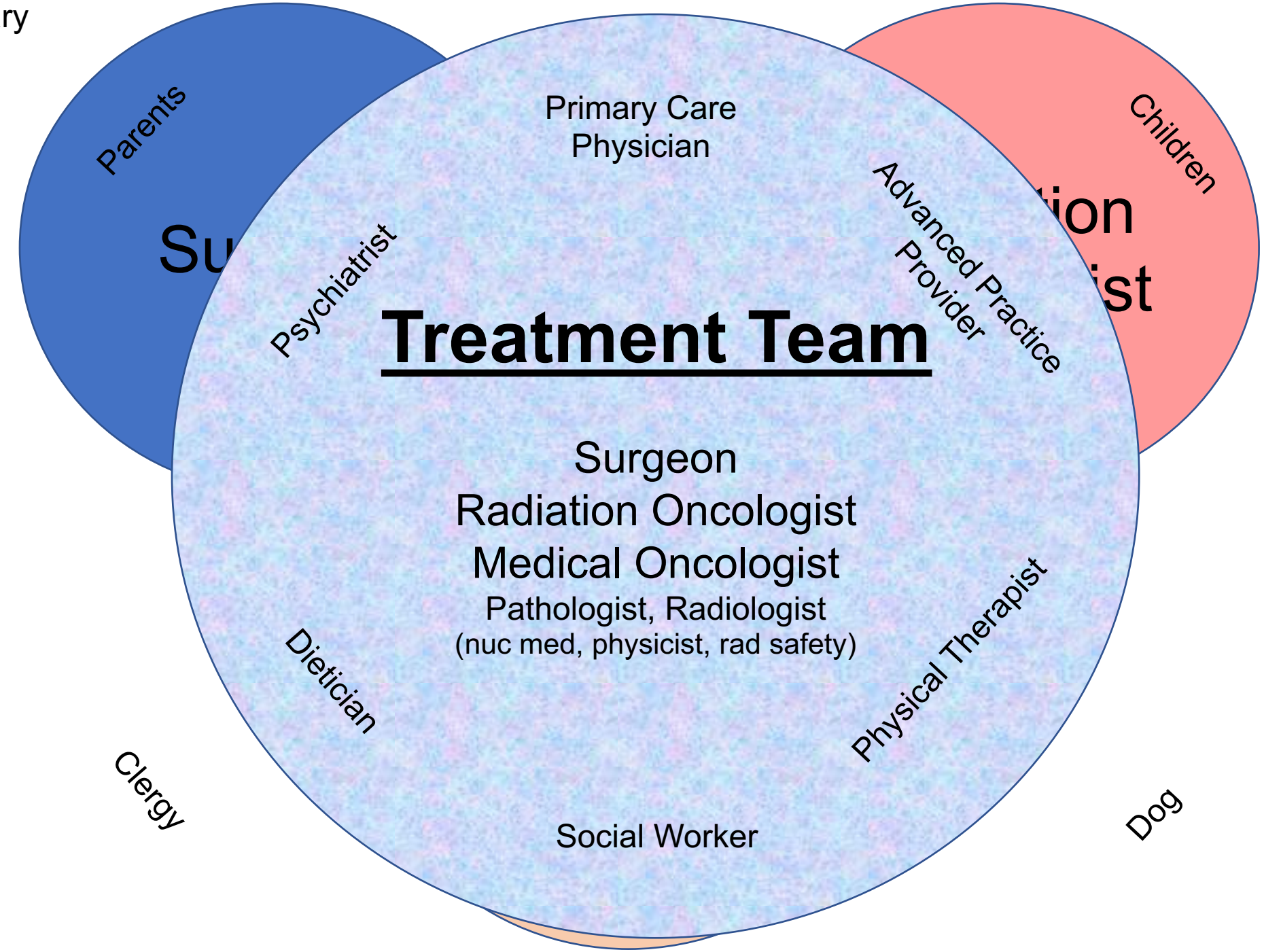
PSMAddition safety findings (ADT/ARPI +/- ^{177}Lu-PSMA-617)

AEs in ≥10% of patients in the ^{177}Lu-PSMA-617 arm – n (%)	^{177}Lu-PSMA-617 + ADT + ARPI (N = 564)		ADT + ARPI (N = 565)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
Dry mouth[a]	258 (45.7)	0	21 (3.7)	0
Fatigue	196 (34.8)	6 (1.1)	158 (28.0)	6 (1.1)
Nausea	193 (34.2)	1 (0.2)	53 (9.4)	0
Hot flush	164 (29.1)	0	205 (36.3)	0
Anaemia	153 (27.1)	28 (5.0)	75 (13.3)	15 (2.7)
Arthralgia	111 (19.7)	5 (0.9)	130 (23.0)	9 (1.6)
Back pain	101 (17.9)	8 (1.4)	110 (19.5)	16 (2.8)
Constipation	101 (17.9)	0	91 (16.1)	0
Asthenia	92 (16.3)	2 (0.4)	73 (12.9)	5 (0.9)
Decreased appetite	81 (14.4)	5 (0.9)	37 (6.5)	1 (0.2)
Vomiting	78 (13.8)	4 (0.7)	21 (3.7)	0
COVID-19	76 (13.5)	5 (0.9)	60 (10.6)	2 (0.4)
Hypertension	76 (13.5)	34 (6.0)	95 (16.8)	35 (6.2)
Diarrhoea	69 (12.2)	1 (0.2)	56 (9.9)	0
Headache	69 (12.2)	0	51 (9.0)	2 (0.4)
Alanine aminotransferase increased	68 (12.1)	19 (3.4)	73 (12.9)	14 (2.5)
Dysgeusia	67 (11.9)	0	23 (4.1)	0
White blood cell count decreased	63 (11.2)	12 (2.1)	18 (3.2)	3 (0.5)
Aspartate aminotransferase increased	61 (10.8)	10 (1.8)	65 (11.5)	11 (1.9)
Lymphocyte count decreased	60 (10.6)	28 (5.0)	21 (3.7)	7 (1.2)

[a] Grade 1 in 231 (41.0%) and grade 2 in 27 (4.8%) in the ^{177}Lu-PSMA-617 + ADT + ARPI arm; grade 1 in 19 (3.4) and grade 2 in 2 (0.4%) in the ADT + ARPI arm

Tagawa S et al.
ESMO 2025;Abstract LBA6

Multidisciplinary Care



SNMMI Consensus Statement on Patient Selection and Appropriate Use of ^{177}Lu-PSMA-617 Radionuclide Therapy

- Pre-existing renal dysfunction
  - Slower renal clearance → monitor closely for marrow toxicity
- Pre-existing low blood counts
  - If due to bone marrow infiltration, treat promptly and monitor
- On-/post- treatment monitoring
  - At least CBC and chemistry following treatment / before next cycle; interim contrast CT
- Supportive care
  - Anti-emetics: not mandatory for prophylaxis in all, but have available prn
  - Pain meds / steroids: not mandatory for pain flare prophylaxis, but be aware of pain flares
  - Blood growth factors: occasionally indicated, involve heme; cautious use of WBC growth factors close to TRT dosing; transfusions prn
- Holding / discontinuing therapy
  - Discuss hold for exceptional responders
  - Discontinue if not tolerated despite adjustments or progression of cancer (esp PSMA low) with additional treatment options

Hope TA et al. *J Nucl Med.* 2023;64(9):1417-1423.

PSMA-TRT (risks) for the PCP*

- Main categories of toxicity
  - Constitutional, myelosuppression, PSMA+ organs
- Dry mouth (and dry eye)
  - Typically mild, reversible (with beta)
  - Dry eye less common, but be mindful
- Myelosuppression
  - Timing different than chemo
- Fatigue, nausea, pain flare
- ? Long-term
  - Most worry about kidney, bone marrow, additional malignancy
  - Baseline organ function appears important
- Radioactivity to others
  - Particularly gamma
  - Early urine; body exposure esp first 2-3 days

*Primary care providers or primary cancer providers (oncologists, urologists, etc.)

Case Presentation

- Pt with controlled DM and HTN presents with multiple bone and lymph node metastases
  - No known family history of cancer
  - Biopsy reveals Gleason grade group 3
  - Germline testing without pathologic alterations
- Treated with ADT and enzalutamide. PSA declines from 45 to 1 and he feels OK.
  - With hot flashes, low libido, erectile dysfunction
  - Enrolls in S1802 and gets radiation to prostate
- After 20 months, PSA begins increasing and continues to increase
  - PSA 4.1, Hgb 11, alk phos 210, LDH 90
- Plasma DNA with low TMB, microsatellite stable, no pathogenic alterations
- Repeat imaging ordered

- ^{68}Ga-PSMA-11 PET/CT
  - SUVmax 81.1; SUVmean 9.3; TTV 161.9
- Wishes to avoid chemo
- Receives 3 cycles of ^{177}Lu-PSMA-617
- PSA 4.1 → <0.02; Hgb 9.8
- Feels OK with mild dry mouth and fatigue
- Repeat PSMA PET with resolution of most lesions; residual bone lesions with SUVmax 2.1 – 2.9 (liver = 5.4)
- Elect to stop / pause treatment

Discussion Questions

How common is PSMA expression in mCRPC, and how do you test for it?

For which patients with PSMA-positive mCRPC do you use lutetium Lu 177 vipivotide tetraxetan? Are you generally using this before chemotherapy?

What other radioligand therapies are available for PC, and how do they compare in terms of their effectiveness?

Tolerability and Other Practical Considerations with the Use of Lutetium Lu 177 Vipivotide Tetraxetan in Prostate Cancer

Stacy Walker, NP

Lutetium - administration and indication

Lu-177 – PSMA-617 (lutetium Lu 177 vipivotide tetraxetan)

- **IV administration Q6 weeks x6 cycles**
  - **If good response and significant decrease in PSMA avidity, can consider pausing and resuming with additional progression**
- **Approved for patients with mCRPC who have progressed with ARPI**
- **Emits gamma radiation and therefore higher risk of radioactive exposure to others than Radium-223 – consideration for patients who are caregivers or require caregivers**

Hygiene and Contact Considerations

Contact Restrictions

- No close contact (less than 3 feet) with people in household for 3 days
- Sleep in separate bed at least 3 feet away for at least 3 days
- No close contact (less than 3 feet) with children less than 10 years of age for at least 7 days
- Stay away from public spaces for 3 days

Hygiene Considerations

- Wash soiled laundry separate from other household laundry (when possible patient should wash their own laundry to minimize exposure)
- Separate toilets encouraged

Lutetium Side effects

- Decreased blood cell counts - consider mid cycle safety checks
- Fatigue
- Dry mouth (salivary glands express PSMA)
  - Moisturizing mouth rinse, xylitol gum, hard candies
- Nausea
- Anorexia
- Joint pain
- Constipation
- Back pain

Lutetium Availability

- Not all oncology locations offer Lutetium -
  - May need to consider referral to another location for duration of treatment
  - us.pluvicto.com/treatment-center-locator
  - Treatment centers may have different eligibility requirements
  - May require management and coordination of care between two different locations

Case Presentation

Case Study - Lutetium

- 49 y/o male with metastatic hormone resistant prostate cancer. Treatment history includes leuprolide + abi/pred, docetaxel x10 cycles.
- After completion of 10 cycles of docetaxel he had 2 consecutive PSA rises, PSMA PET 4/2025 showed new and increasing, now extensive, PSMA avid osseous metastatic lesions compared to November 2024
- PMH: None
- Social History - married, two children ages 6 and 8. Raised in France, works remotely for company in France, parents retired in Portugal

Case Study - Lutetium

- Clinical trial considered, however patient's family opted to spend summer in Portugal near patient's parents.
- To minimize visits - opted for lutetium (Q6 week dosing). Cycle 1 5/2025, PSA 18.86
- PSA with good response
- Mild dry mouth managed with moisturizing mouth rinse and hard candies; Nausea for a few days after treatment each cycle - managed with ondansetron. Mild neutropenia.
- Special considerations given to children in the household (no close contact to his children for 3 days after treatment)
- Carrying card with radioactive explanation for airport travel
- Schedule alterations to support being with his children (ex: delayed dose so not radioactive for Christmas/school break)

Discussion Questions

What do you tell your patients about to start lutetium Lu 177 vipivotide tetraxetan about potential toxicities?

How do you attempt to prevent or ameliorate dry mouth associated with lutetium Lu 177 vipivotide tetraxetan? How bothersome is this toxicity to patients?

How do you educate your patients receiving radiopharmaceuticals regarding radiation risks and appropriate precautions to protect their loved ones?

RTP
RESEARCH
TO PRACTICE

Recent Advances in Cancer Care — New Paradigms, Novel Agents and What It Means for the Oncology Nurse

A Complimentary NCPD Symposium Series Held During the 51st Annual ONS Congress

Non-Muscle-Invasive and Muscle-Invasive Bladder Cancer

Thursday, May 14, 2026

6:00 PM – 7:30 PM

Faculty

Alexandra Drakaki, MD, PhD
Krisztina Emodi, NP-C, MPH, CNS
Margarita Huober, MS, AGNP-C, AOCNP

Moderator

Terence Friedlander, MD

RTP RESEARCH TO PRACTICE

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

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