What I Tell My Patients: Integrating New Research Information into Current Clinical Care

Prostate Cancer

A Complimentary NCPD Webinar in Partnership with the Oncology Nursing Society

Wednesday, May 1, 2024
7:00 PM – 8:00 PM ET

Faculty

Andrew J Armstrong, MD, ScM
Brenda Martone, MSN, NP-BC, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Commercial Support

This activity is supported by an educational grant from Novartis.

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/NCPD activities from the following companies: AbbVie Inc, Adaptive Biotechnologies Corporation, ADC Therapeutics, Agios Pharmaceuticals Inc, Alexion Pharmaceuticals, Amgen Inc, Array BioPharma Inc, a subsidiary of Pfizer Inc, Astellas, AstraZeneca Pharmaceuticals LP, Aveo Pharmaceuticals, Bayer HealthCare Pharmaceuticals, BeiGene Ltd, BeyondSpring Pharmaceuticals Inc, Blueprint Medicines, Boehringer Ingelheim Pharmaceuticals Inc, Bristol Myers Squibb, Celgene Corporation, Clovis Oncology, Coherus BioSciences, CTI Biopharma, a Sobi company, Daiichi Sankyo Inc, Eisai Inc, Elevation Oncology Inc, EMD Serono Inc, Epizyme Inc, Exact Sciences Corporation, Exelixis Inc, Five Prime Therapeutics Inc, Foundation Medicine, G1 Therapeutics Inc, Genentech, a member of the Roche Group, Genmab US Inc, Gilead Sciences Inc, Grail Inc, GSK, Halozyme Inc, Helsinn Healthcare SA, ImmunoGen Inc, Incyte Corporation, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Karyopharm Therapeutics, Kite, A Gilead Company, Kronos Bio Inc, Legend Biotech, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, 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, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, R-Pharm US, Sanofi, Seagen Inc, Servier Pharmaceuticals LLC, SpringWorks Therapeutics Inc, Stemline Therapeutics Inc, Sumitomo Dainippon Pharma Oncology Inc, Syndax Pharmaceuticals, Taiho Oncology Inc, Takeda Pharmaceuticals USA Inc, TerSera Therapeutics LLC, Tesaro, A GSK Company, TG Therapeutics Inc, Turning Point Therapeutics Inc, Verastem Inc, and Zymeworks Inc.

RTP
RESEARCH
TO PRACTICE

Research To Practice NCPD Planning Committee Members, Staff and Reviewers

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

Dr Armstrong — Disclosures

Advisory Committees	AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Clovis Oncology, Exelixis Inc, GoodRx, Merck, Myovant Sciences, Novartis, Pfizer Inc, Z-Alpha
Consulting Agreements	Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Celgene Corporation, Clovis Oncology, Dendreon Pharmaceuticals Inc, Epic Sciences, Exact Sciences Corporation, Exelixis Inc, Forma Therapeutics, GoodRx, Janssen Biotech Inc, Merck, Myovant Sciences, Novartis, Pfizer Inc, Z-Alpha
Contracted Research	Amgen Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Celgene Corporation, Dendreon Pharmaceuticals Inc, Forma Therapeutics, Janssen Biotech Inc, Merck, Novartis, Pfizer Inc
Nonrelevant Financial Relationships	National Cancer Institute, National Institutes of Health, Prostate Cancer Foundation/Movember, US Department of Defense

RTP
RESEARCH
TO PRACTICE

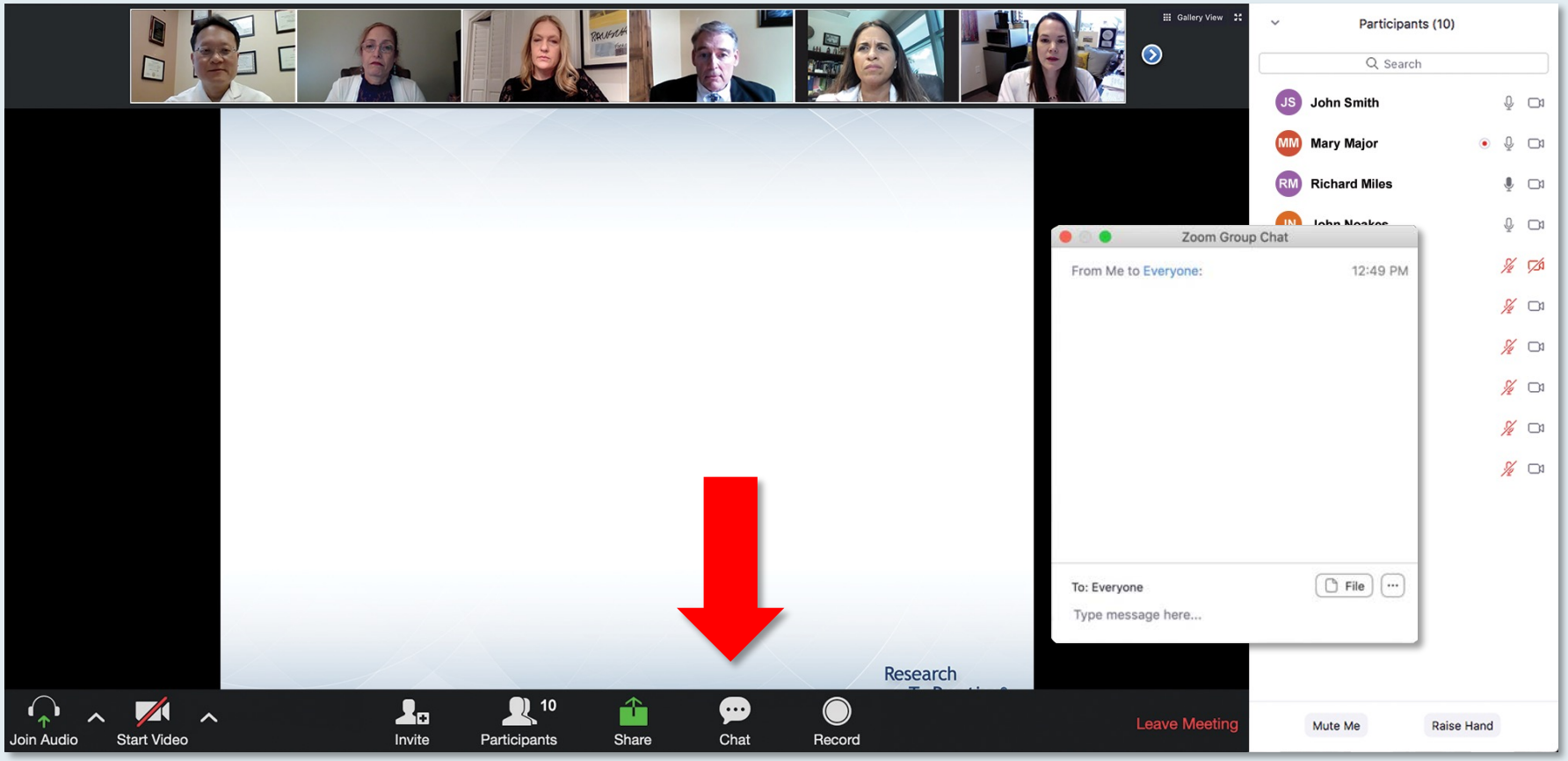
Dr Martone — Disclosures

No relevant conflicts of interest to disclose

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.

RTP
RESEARCH
TO PRACTICE

We Encourage Clinicians in Practice to Submit Questions

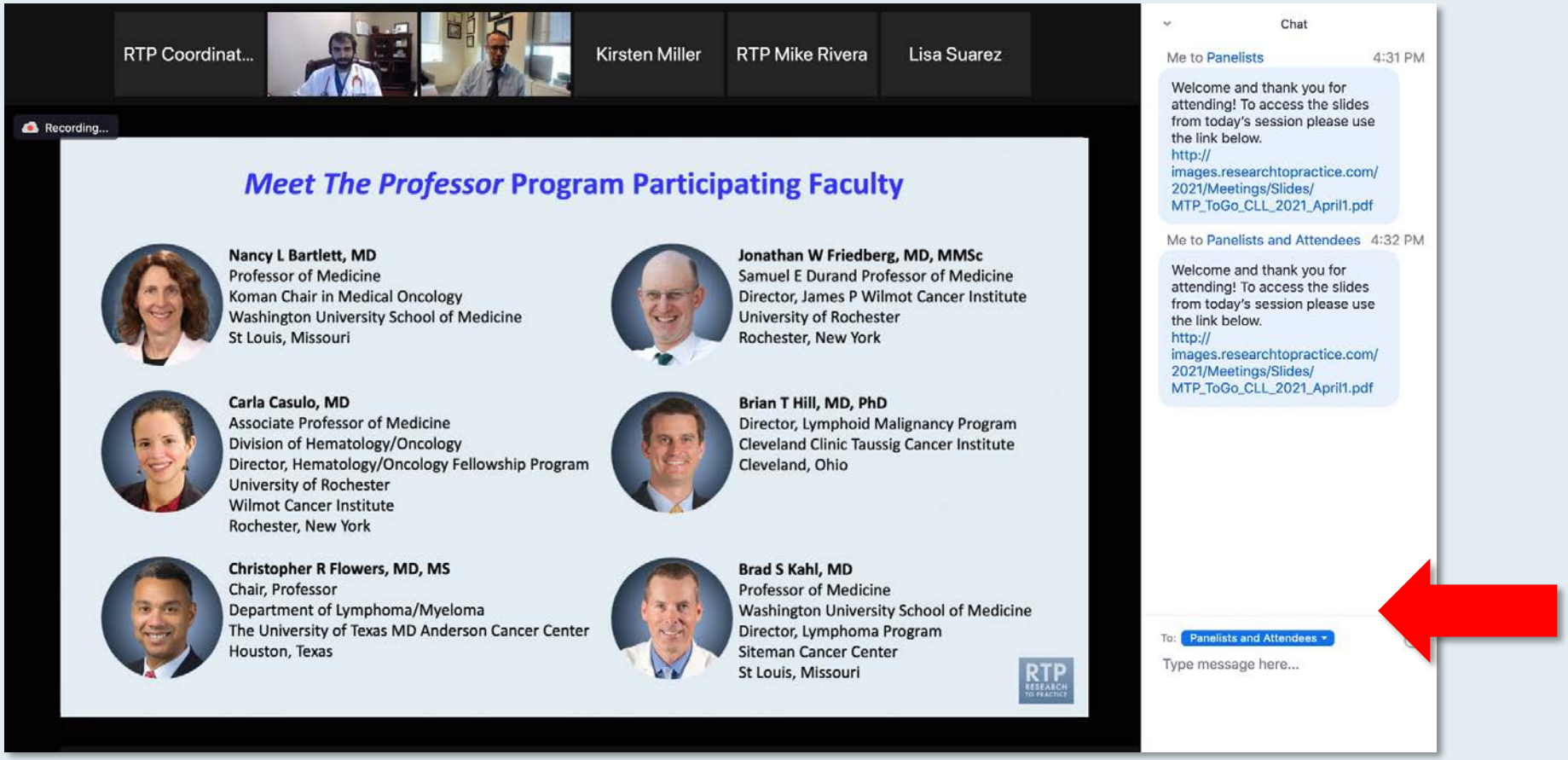


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

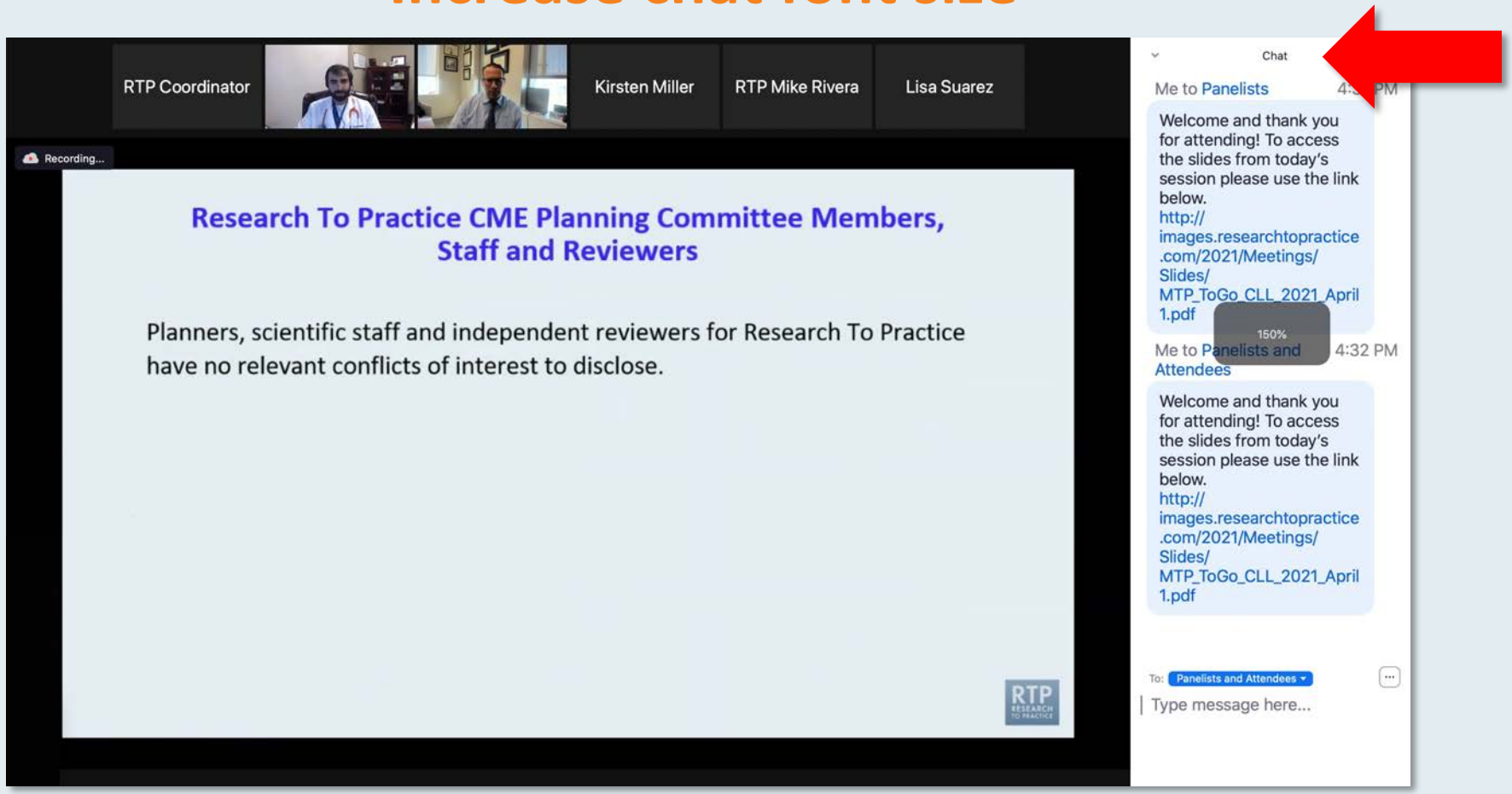


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

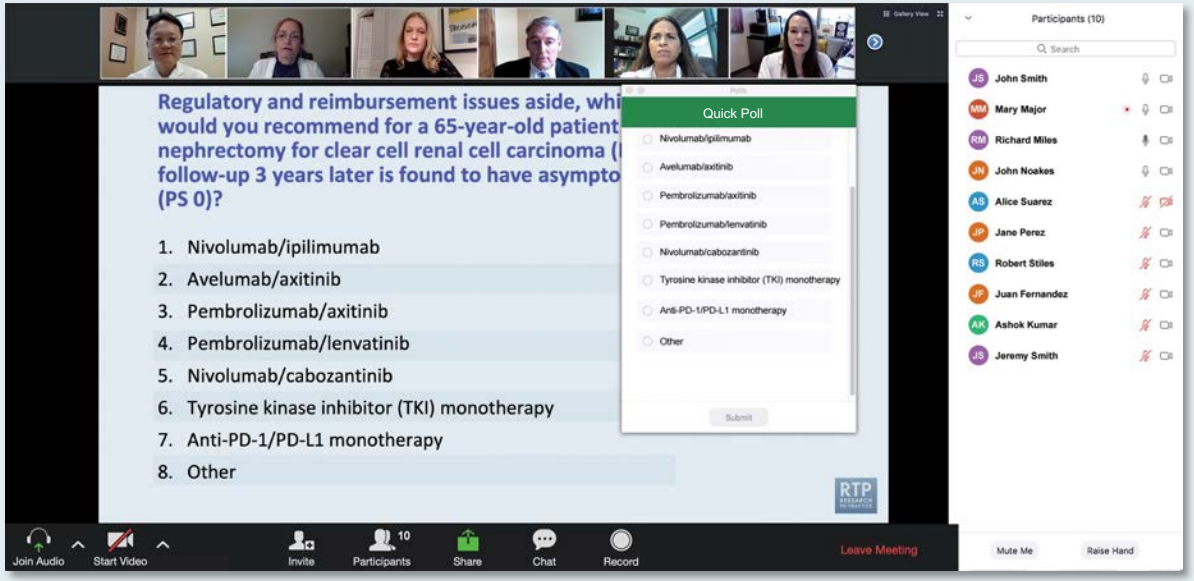
Familiarizing Yourself with the Zoom Interface

Increase chat font size



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

Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys



RTP RESEARCH TO PRACTICE

ONCOLOGY TODAY

WITH DR NEIL LOVE

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

DR ANDREW J ARMSTRONG
DUKE CANCER INSTITUTE

DR MAHA HUSSAIN
ROBERT H LURIE COMPREHENSIVE CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Second Opinion: Urologic Oncology Investigators Discuss How They Apply Clinical Research in the Care of Patients with Prostate Cancer

A CME Satellite Symposium Held in Conjunction with the American Urological Association Annual Meeting 2024 (AUA2024)

Friday, May 3, 2024

8:00 AM – 10:00 AM CT (9:00 AM – 11:00 AM ET)

Faculty

Rahul Aggarwal, MD
Adam S Kibel, MD
Laurence Klotz, CM, MD
Sandy Srinivas, MD

Moderator

Elisabeth I Heath, MD

RTP
RESEARCH TO PRACTICE

Second Opinion: Urologic Oncology Investigators Discuss How They Apply Clinical Research in the Care of Patients with Urothelial Bladder Cancer

A CME-Accredited Virtual Event

Monday, May 6, 2024
5:00 PM – 6:00 PM ET

Faculty

Matthew D Galsky, MD
Ashish M Kamat, MD, MBBS

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Year in Review:
Targeted Therapy for Non-Small Cell Lung Cancer

A Multitumor CME/MOC-Accredited Live Webinar

Wednesday, May 8, 2024
5:00 PM – 6:00 PM ET

Faculty

Justin F Gainor, MD
Karen Reckamp, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

Thank you for joining us!

NCPD credit information will be emailed to each participant within 5 business days.

What I Tell My Patients: Integrating New Research Information into Current Clinical Care

Prostate Cancer

A Complimentary NCPD Webinar in Partnership with the Oncology Nursing Society

Wednesday, May 1, 2024
7:00 PM – 8:00 PM ET

Faculty

Andrew J Armstrong, MD, ScM
Brenda Martone, MSN, NP-BC, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

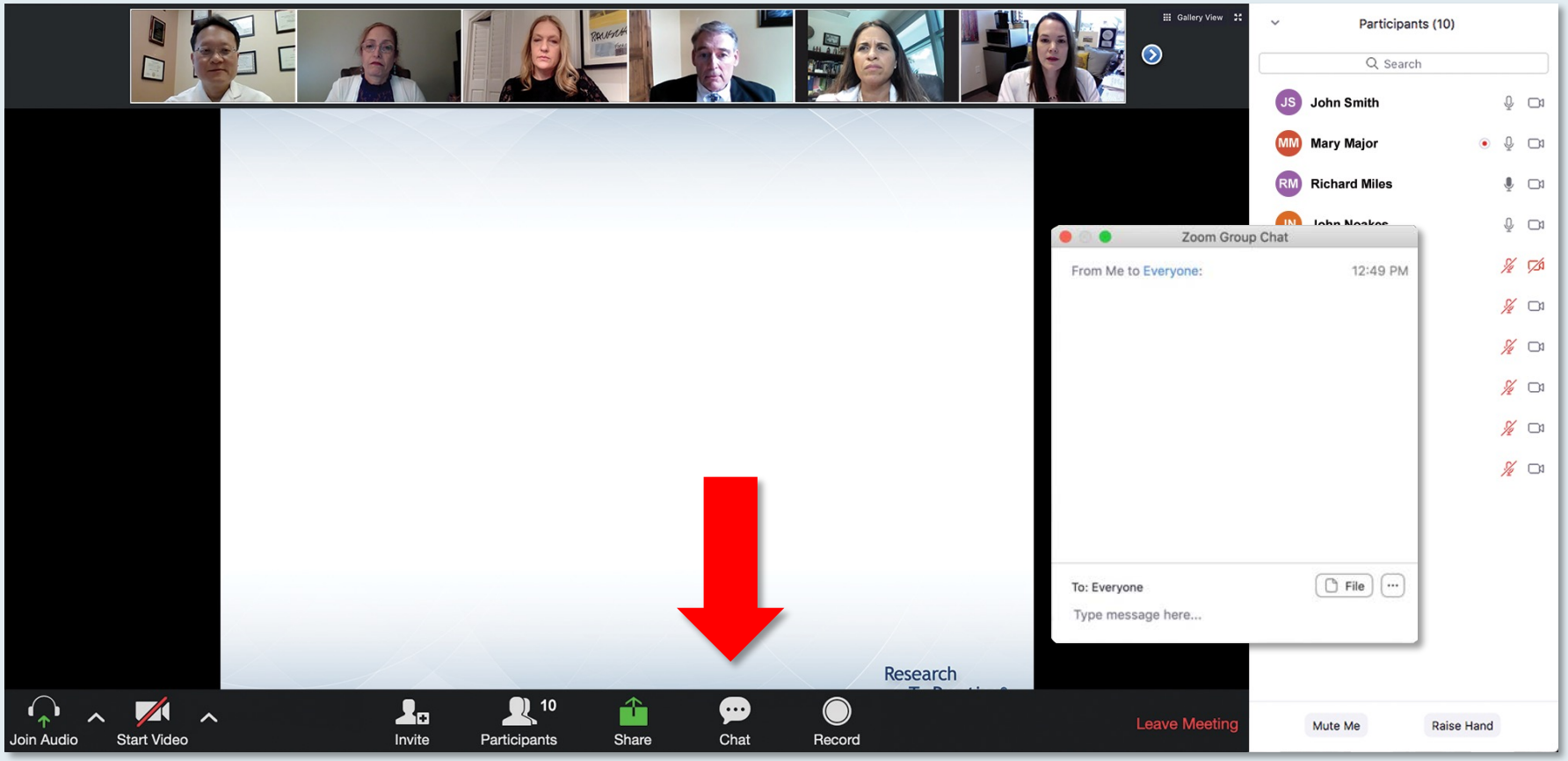
Andrew J Armstrong, MD, ScM
Professor of Medicine, Surgery
Pharmacology and Cancer Biology
Director of Research
Duke Cancer Institute Center for Prostate and Urologic Cancers
Divisions of Medical Oncology and Urology
Duke University
Durham, North Carolina

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

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

RTP
RESEARCH
TO PRACTICE

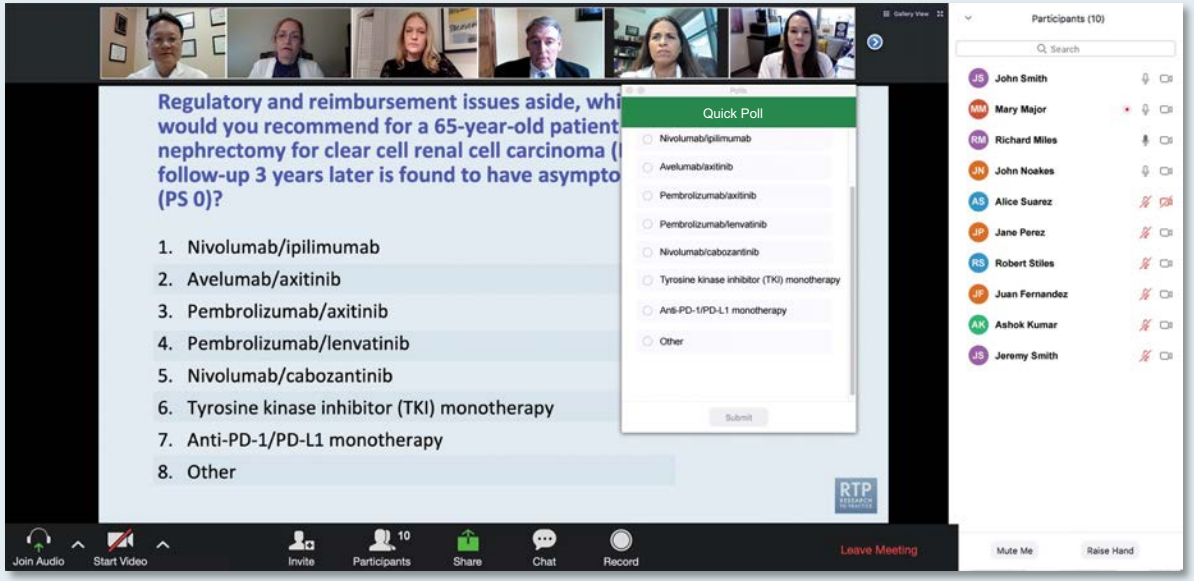
We Encourage Clinicians in Practice to Submit Questions



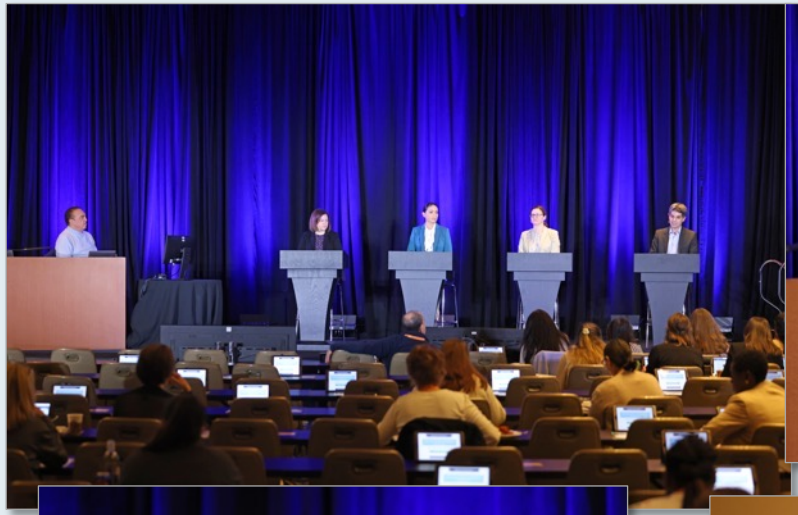
Feel free to submit questions now before the program begins and throughout the program.

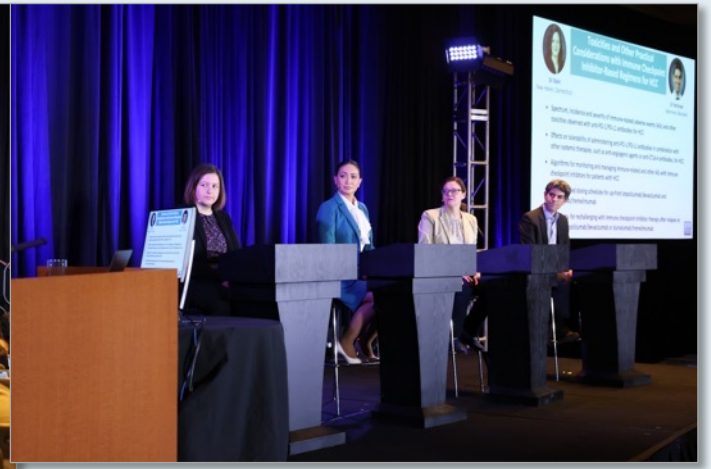
RTP RESEARCH TO PRACTICE

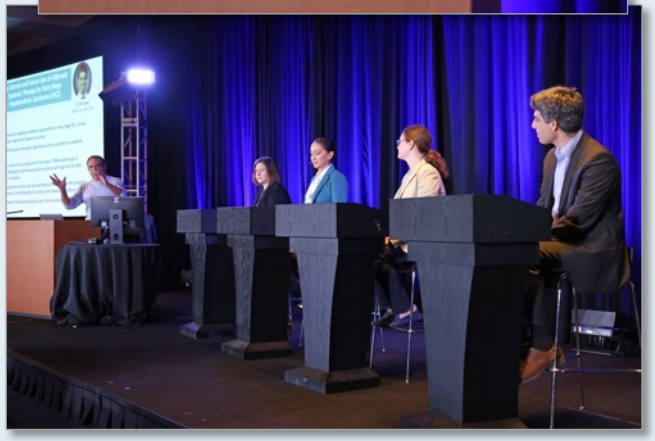
Clinicians in the Audience, Please Complete the Pre- and Postmeeting Surveys

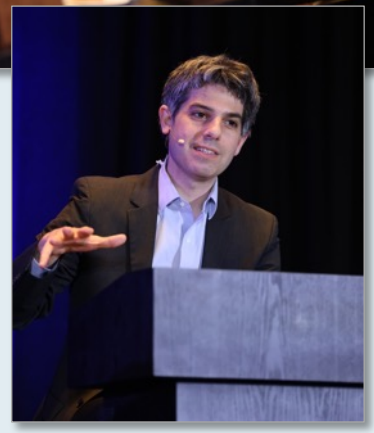


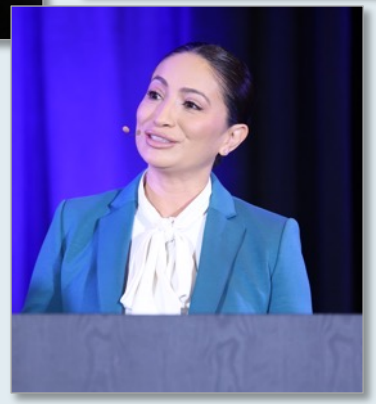
RTP RESEARCH TO PRACTICE

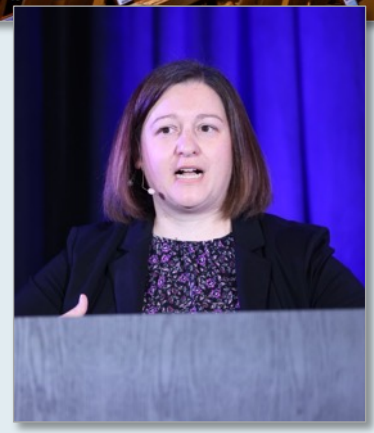






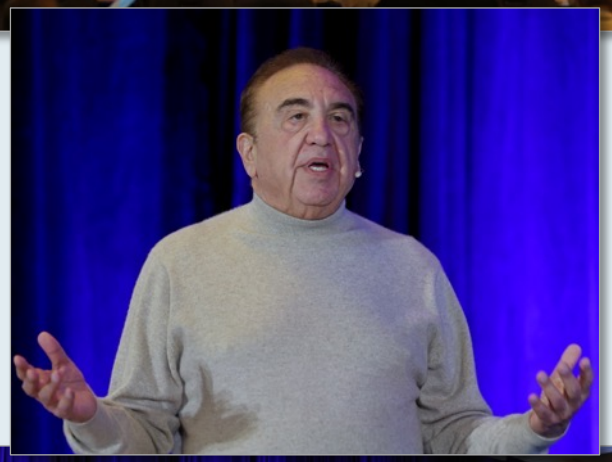


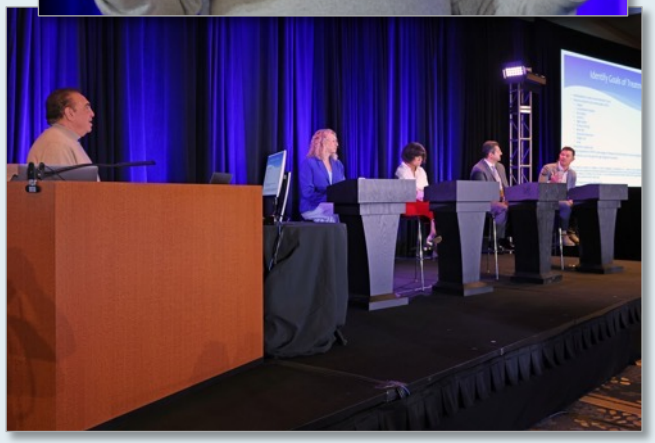


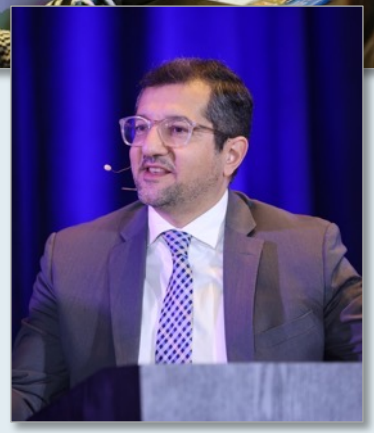


RTP
RESEARCH
TO PRACTICE



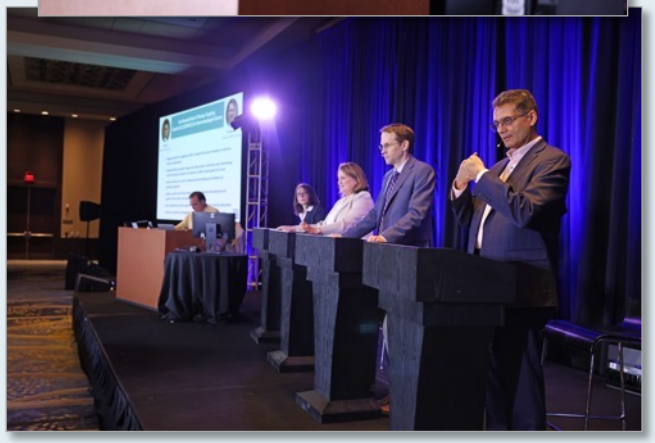


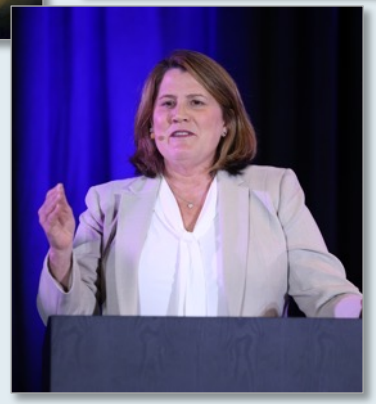
RTP
RESEARCH
TO PRACTICE










Second Opinion: Urologic Oncology Investigators Discuss How They Apply Clinical Research in the Care of Patients with Prostate Cancer

A CME Satellite Symposium Held in Conjunction with the American Urological Association Annual Meeting 2024 (AUA2024)

Friday, May 3, 2024

8:00 AM – 10:00 AM CT (9:00 AM – 11:00 AM ET)

Faculty

Rahul Aggarwal, MD
Adam S Kibel, MD
Laurence Klotz, CM, MD
Sandy Srinivas, MD

Moderator

Elisabeth I Heath, MD

RTP
RESEARCH TO PRACTICE

Second Opinion: Urologic Oncology Investigators Discuss How They Apply Clinical Research in the Care of Patients with Urothelial Bladder Cancer

A CME-Accredited Virtual Event

Monday, May 6, 2024
5:00 PM – 6:00 PM ET

Faculty

Matthew D Galsky, MD
Ashish M Kamat, MD, MBBS

Moderator

Neil Love, MD

RTP
RESEARCH
TO PRACTICE

Year in Review:
Targeted Therapy for Non-Small Cell Lung Cancer

A Multitumor CME/MOC-Accredited Live Webinar

Wednesday, May 8, 2024
5:00 PM – 6:00 PM ET

Faculty

Justin F Gainor, MD
Karen Reckamp, MD, MS

Moderator

Neil Love, MD

RTP Year in Review 2024

ONCOLOGY TODAY

WITH DR NEIL LOVE

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

DR ANDREW J ARMSTRONG
DUKE CANCER INSTITUTE

DR MAHA HUSSAIN
ROBERT H LURIE COMPREHENSIVE CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

Consulting Nurse Faculty

Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Kathleen D Burns, RN, MSN, AGACNP-BC, OCN
City of Hope Comprehensive Cancer Center
Duarte, California

Sonia Glennie, ARNP, MSN, OCN
Swedish Cancer Institute Center for Blood Disorders
Seattle, Washington

Amy Goodrich, CRNP
The Sidney Kimmel Comprehensive Cancer Center
Baltimore, Maryland

Jessica Mitchell, APRN, CNP, MPH
Mayo Clinic College of Medicine and Science
Rochester, Minnesota

Tiffany A Richards, PhD, ANP-BC, AOCNP
The University of Texas
MD Anderson Cancer Center
Houston, Texas

Kimberly A Spickes, MNSc, RN, APRN, OCN, ACNP-BC
University of Arkansas for Medical Sciences
Little Rock, Arkansas

Ronald Stein, JD, MSN, NP-C, AOCNP
USC Norris Comprehensive Cancer Center
Los Angeles, California

https://www.ResearchToPractice.com/ONS2024Clips

RTP RESEARCH TO PRACTICE

How was it different to take care of this patient versus another patient in the same oncologic setting?

What unique biopsychosocial factors (eg, attitude, comorbidities, social support) were considered in the overall management of this case?

What I Tell My Patients: Integrating New Research Information into Current Clinical Care

Prostate Cancer

A Complimentary NCPD Webinar in Partnership with the Oncology Nursing Society

Wednesday, May 1, 2024
7:00 PM – 8:00 PM ET

Faculty

Andrew J Armstrong, MD, ScM
Brenda Martone, MSN, NP-BC, AOCNP

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Dr Armstrong — Disclosures

Advisory Committees	AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Clovis Oncology, Exelixis Inc, GoodRx, Merck, Myovant Sciences, Novartis, Pfizer Inc, Z-Alpha
Consulting Agreements	Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Celgene Corporation, Clovis Oncology, Dendreon Pharmaceuticals Inc, Epic Sciences, Exact Sciences Corporation, Exelixis Inc, Forma Therapeutics, GoodRx, Janssen Biotech Inc, Merck, Myovant Sciences, Novartis, Pfizer Inc, Z-Alpha
Contracted Research	Amgen Inc, Astellas, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Bristol Myers Squibb, Celgene Corporation, Dendreon Pharmaceuticals Inc, Forma Therapeutics, Janssen Biotech Inc, Merck, Novartis, Pfizer Inc
Nonrelevant Financial Relationships	National Cancer Institute, National Institutes of Health, Prostate Cancer Foundation/Movember, US Department of Defense

RTP
RESEARCH
TO PRACTICE

Ms Martone — Disclosures

No relevant conflicts of interest to disclose

Commercial Support

This activity is supported by an educational grant from Novartis.

Research To Practice NCPD Planning Committee Members, Staff and Reviewers

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

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.

RTP
RESEARCH
TO PRACTICE

Agenda

INTRODUCTION: Overview of Prostate Cancer; Hormonal Therapy

MODULE 1: Radiopharmaceuticals for the Management of Metastatic Castration-Resistant Prostate Cancer (mCRPC)

MODULE 2: Biomarker Testing for mCRPC; PARP Inhibitors for mCRPC

RTP
RESEARCH
TO PRACTICE

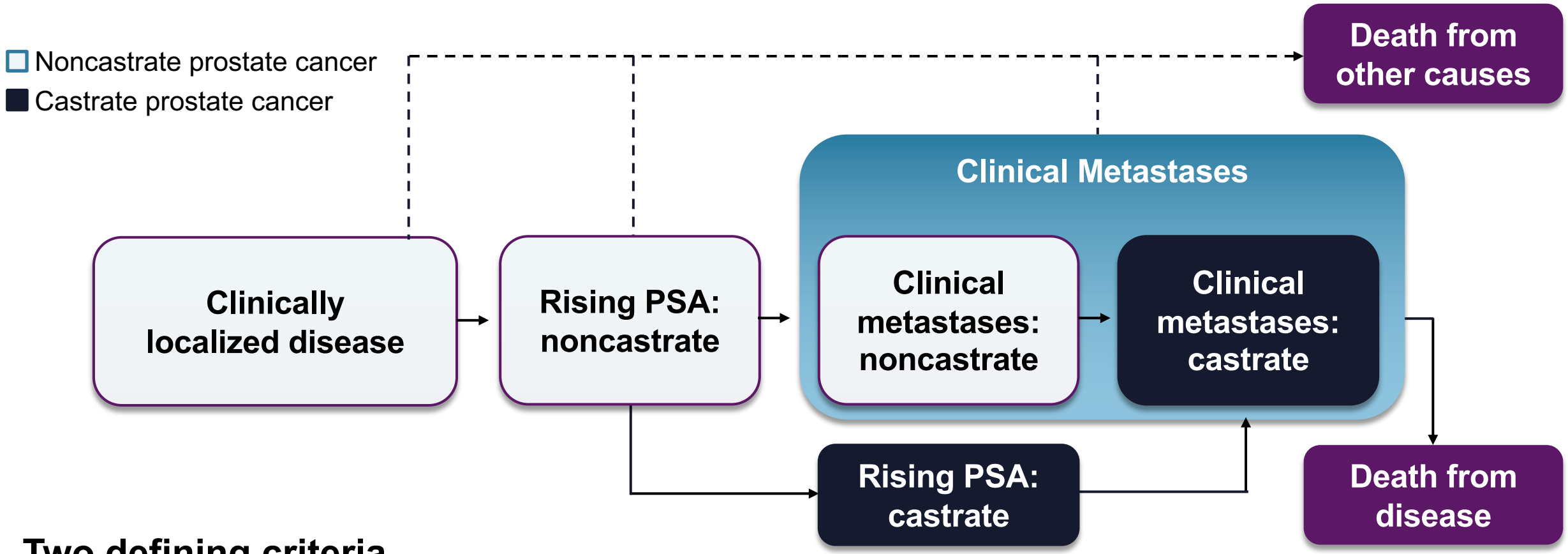
Agenda

INTRODUCTION: Overview of Prostate Cancer; Hormonal Therapy

MODULE 1: Radiopharmaceuticals for the Management of Metastatic Castration-Resistant Prostate Cancer (mCRPC)

MODULE 2: Biomarker Testing for mCRPC; PARP Inhibitors for mCRPC

Clinical Disease States Model of Prostate Cancer

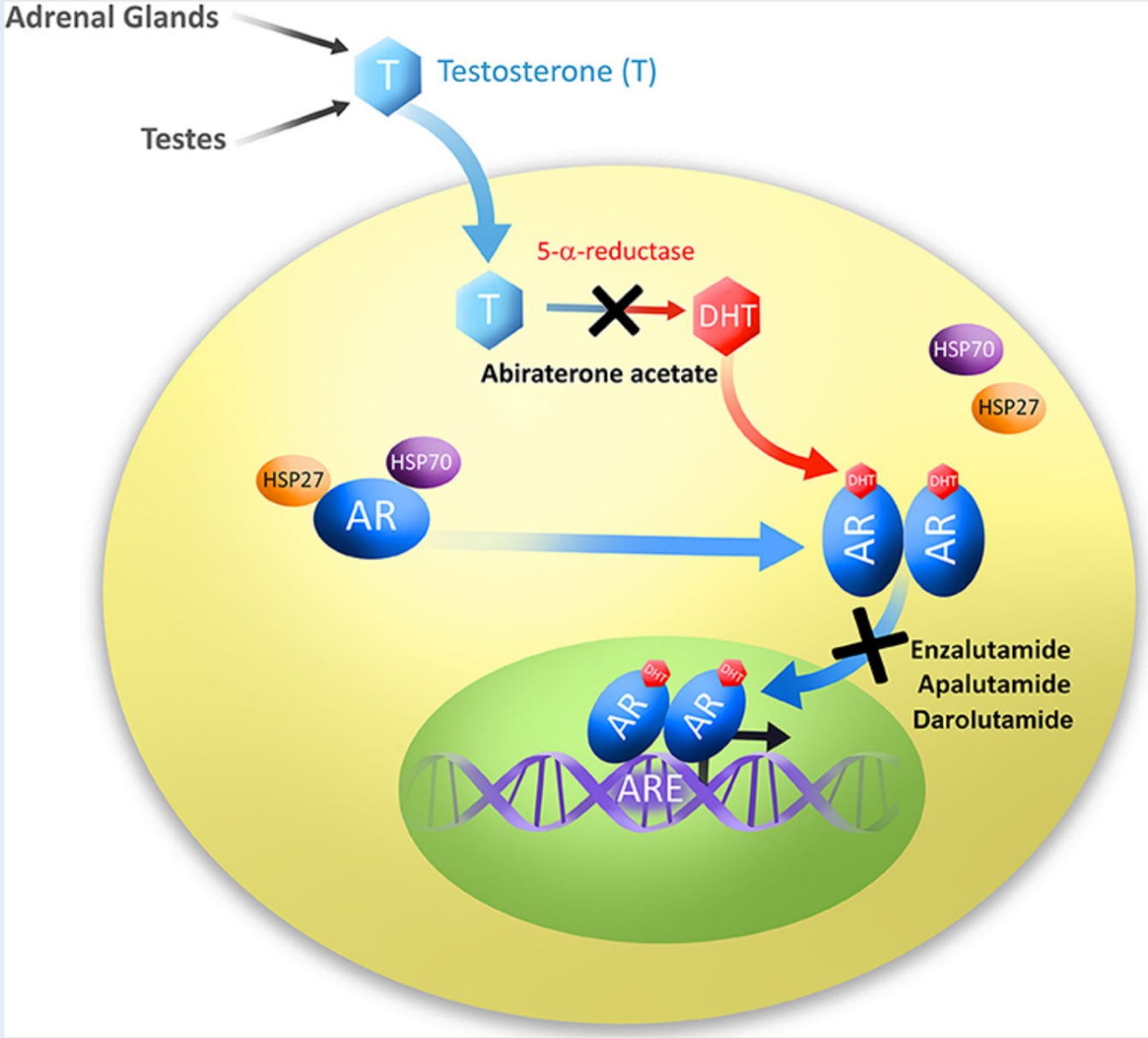


Two defining criteria

- 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.

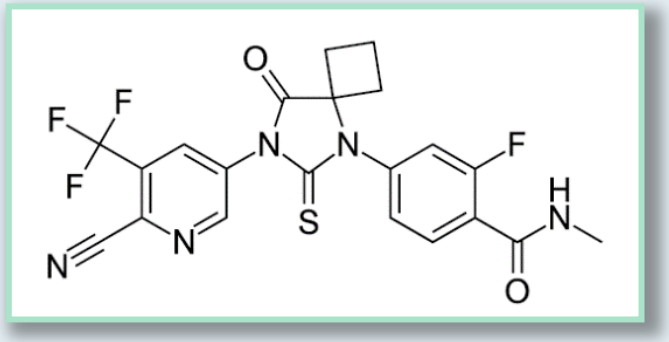
Diagram of Androgen Production and Its Targeted Inhibition



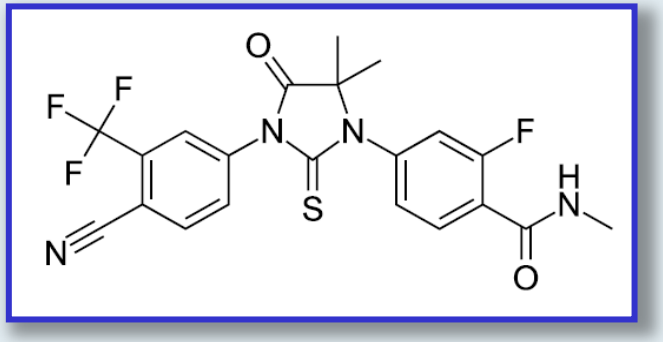
Rice MA et al. *Front Oncol* 2019;9:801.

Next-Generation Androgen Receptor Pathway Inhibitors (ARPIs)[1,2]

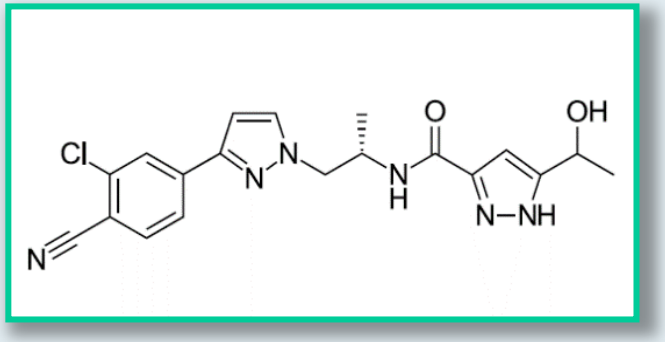
Apalutamide



Enzalutamide



Darolutamide

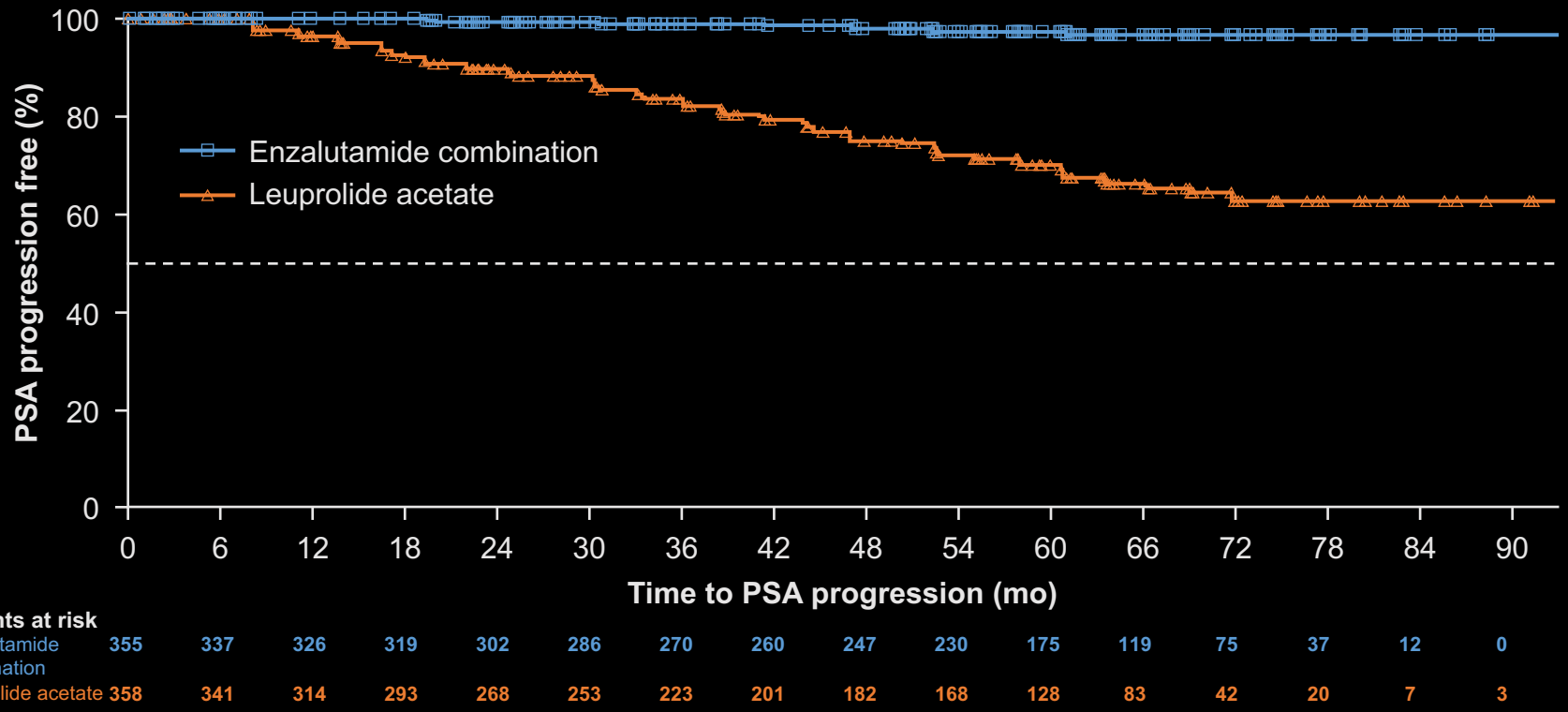


- Apalutamide and enzalutamide have similar structures
- Darolutamide is structurally distinct from apalutamide and enzalutamide, characterized by low blood–brain barrier penetration[1,2] and may have improved tolerability

1. Zurth C et al. Genitourinary Cancers Symposium 2018;Abstract 345.
2. Sandmann S et al. Genitourinary Cancers Symposium 2019;Abstract 156.

AUA 2023
CHICAGO ✶ APR 28-MAY 1

Key secondary endpoint — Time to PSA progression for enzalutamide combination vs. leuprolide acetate



Patients at risk

Enzalutamide combination	355	337	326	319	302	286	270	260	247	230	175	119	75	37	12	0
Leuprolide acetate	358	341	314	293	268	253	223	201	182	168	128	83	42	20	7	3

	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	8 (2)	93 (26)
Median time to PSA progression (95% CI), mo	NR (NR)	NR (NR)

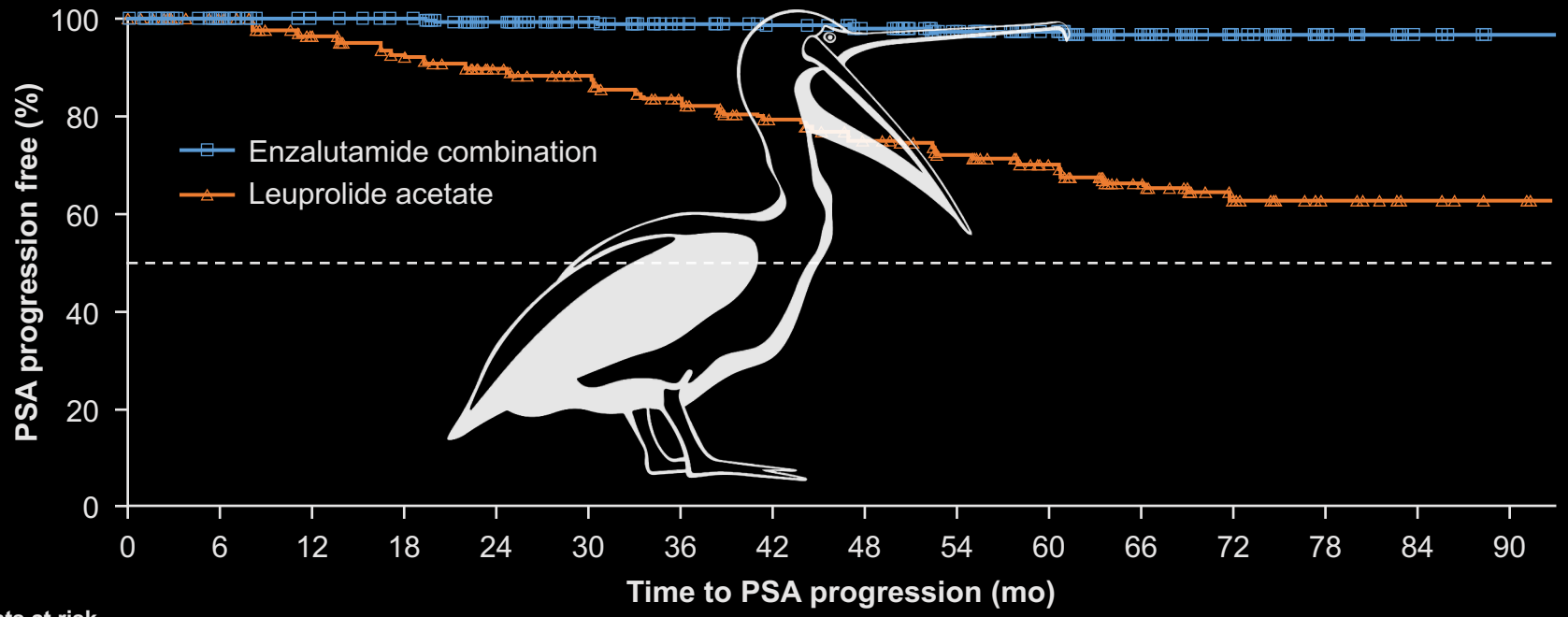
HR (95% CI): 0.07 (0.03–0.14); *P*<0.0001[a]

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]The HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide combination; the two-sided *P*-value is based on a stratified log-rank test.

Shore N et al. AUA 2023;Abstract LBA02-09.

AUA 2023
CHICAGO ✶ APR 28-MAY 1

Key secondary endpoint — Time to PSA progression for enzalutamide combination vs. leuprolide acetate



Patients at risk

Enzalutamide combination	355	337	326	319	302	286	270	260	247	230	175	119	75	37	12	0
Leuprolide acetate	358	341	314	293	268	253	223	201	182	168	128	83	42	20	7	3

	Enzalutamide combination (n = 355)	Leuprolide acetate (n = 358)
Events, n (%)	8 (2)	93 (26)
Median time to PSA progression (95% CI), mo	NR (NR)	NR (NR)

HR (95% CI): 0.07 (0.03–0.14); *P*<0.0001[a]

Data cutoff: January 31, 2023. Symbols indicate censored data. [a]The HR was based on a Cox regression model with treatment as the only covariate stratified by screening PSA, PSADT, and prior hormonal therapy as reported in the IWRS; relative to leuprolide acetate <1 favoring enzalutamide combination; the two-sided *P*-value is based on a stratified log-rank test.

Shore N et al. AUA 2023;Abstract LBA02-09.

Consulting Nursing Faculty Comments

Androgen deprivation therapy for prostate cancer

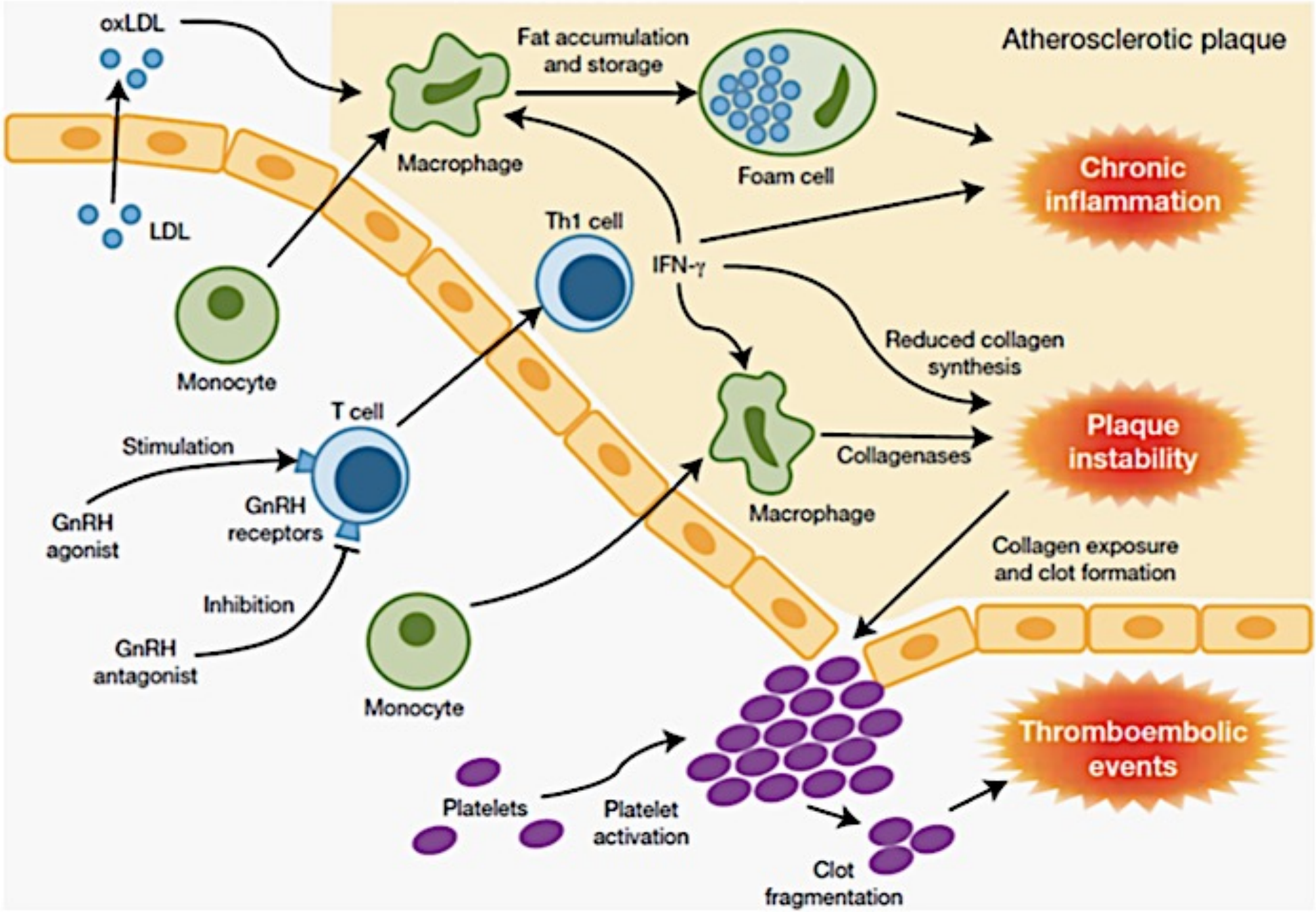
Kathleen D Burns, RN, MSN, AGACNP-BC, OCN

RTP
RESEARCH
TO PRACTICE

Major side effects associated with ADT

Courtesy of Laurence Klotz, CM, MD

Symptom	Comments
Hot flushes	**Very common.** Can be mitigated by use of medications such as venlafaxine or gabapentin. Additionally, acupuncture has a potential role in alleviating symptoms.
Osteoporosis	**Very common.** Estimated 1%–3% fracture risk per year. Men should be given calcium/vitamin D supplements. There is a clear role for osteoclast inhibitors (either zoledronic acid or denosumab) in men with metastatic castration-resistant prostate cancer with bone metastases in preventing skeletal-related events. In men with metastatic castration-sensitive prostate cancer, bisphosphonates have not been shown to be beneficial.
Fatigue	**Very common.** Seen in most men receiving ADT and independent of anemia or depression. Regular exercise can be beneficial in these patients.
Depression	**Common.** Seen frequently in men treated with ADT and should be explored at multiple visits. May be amenable to treatment with SSRI (or SNRI if concurrent with hot flushes).
Gynecomastia	**Common.** Can be a major quality of life issue, although tamoxifen and radiotherapy can be potential treatment options.
Erectile dysfunction	**Common.** Both erectile dysfunction and decreased libido are seen in men receiving ADT and remain major quality-of-life issues. Referral to sexual health counseling may be of benefit.
Metabolic syndrome	**Common.** Weight gain is commonly seen within 1 year of starting ADT. Additionally, insulin resistance, dyslipidemia, and sarcopenic obesity are reported.
Dementia	**Controversial.** Multiple studies have explored this issue, with mixed and conflicting findings. This remains an active area of clinical research.
Thromboembolic disease	**Controversial.** Several meta-analyses have shown an association between VTE and ongoing ADT use, though many have not controlled for ongoing tobacco use and acute hospitalizations, both of which increase thrombotic risk.
Cardiovascular disease	**Controversial.** Several meta-analyses have found conflicting results on risk of cardiovascular disease from ADT. Primary and secondary prevention for cardiovascular disease should be pursued.



Courtesy of Laurence Klotz, CM, MD

Tivesten Å et al. *Urol Oncol* 2015;33(11):464-75.

Unanswered questions:

- Timing of ADT in PSA only recurrence
- Are oligomets on PSMA only = pre-PSMA PSA only recurrence or to N/M positive disease on conventional imaging.
- Can the EMBARK data be extrapolated to the other ARPIs?
- When and how to use intensified AR targeted therapy intermittently? What is the induction period and optimal threshold for re-treatment?
- Once intensified, always intensified?
- Role of ARPI monotherapy—should it be more widely used?
- What about lower risk PSA only recurrence—also a role forADT + ARPI combination?
- Will biomarkers allow for personalized approach (HRR/PARPs, etc.)

Courtesy of Laurence Klotz, CM, MD


MARQUEE
STEVE DANIEL
PROSTATE CANCER WARRIOR

Agenda

INTRODUCTION: Overview of Prostate Cancer; Hormonal Therapy

MODULE 1: Radiopharmaceuticals for the Management of Metastatic Castration-Resistant Prostate Cancer (mCRPC)

MODULE 2: Biomarker Testing for mCRPC; PARP Inhibitors for mCRPC

RTP RESEARCH TO PRACTICE

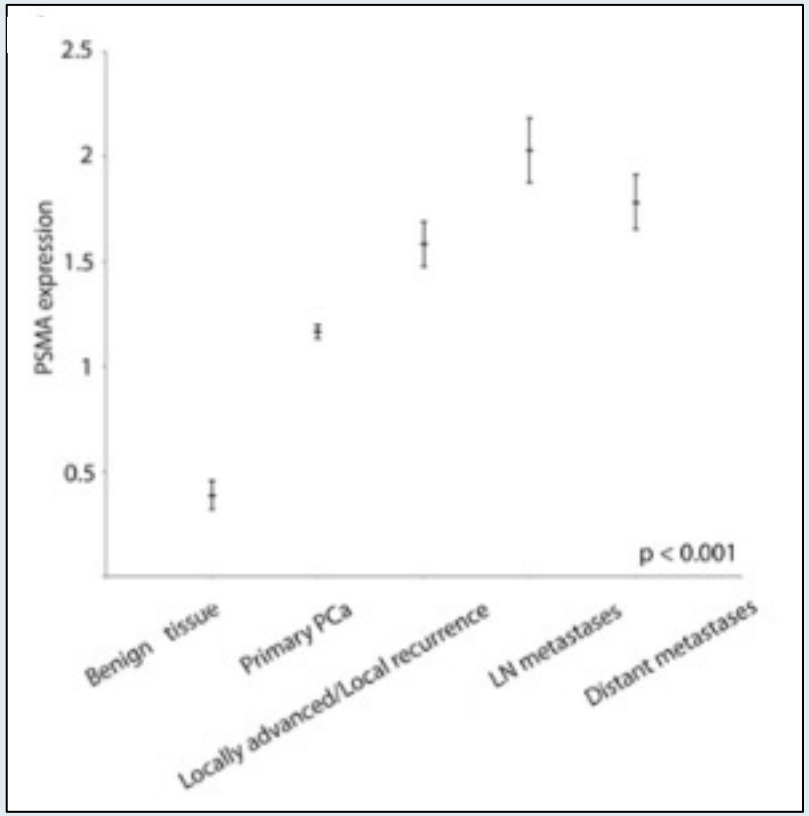
Dr Armstrong
Durham, North Carolina

Lutetium Lu 177 Vipivotide Tetraxetan for mCRPC

- **Mechanism of action of lutetium Lu 177 vipivotide tetraxetan**
- **Published Phase III data sets with lutetium Lu 177 vipivotide tetraxetan for patients with PSMA-positive mCRPC**
- **Implications of recently presented data for the sequencing of lutetium Lu 177 vipivotide tetraxetan; optimal integration into current mCRPC treatment algorithms**
- **Early data with and ongoing evaluation of lutetium Lu 177 vipivotide tetraxetan in combination with other systemic therapies (eg, pembrolizumab, olaparib) or in earlier settings**

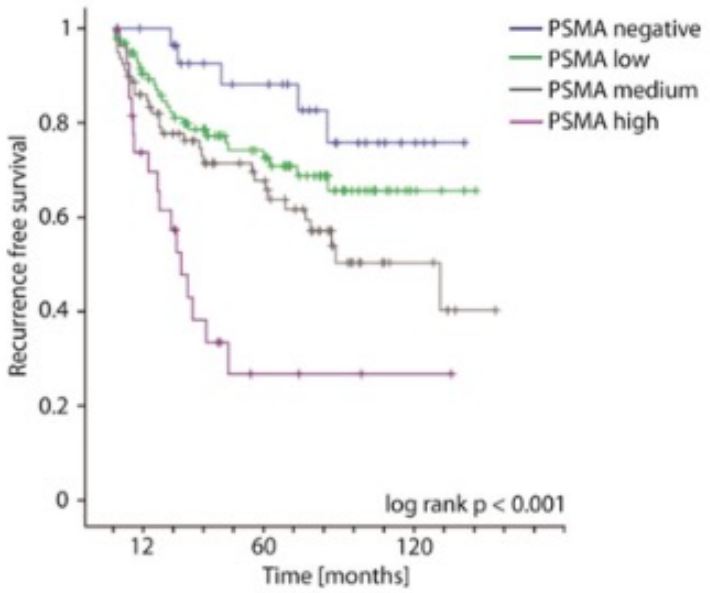
Prostate-Specific Membrane Antigen (PSMA)

PSMA expression increases during prostate cancer progression

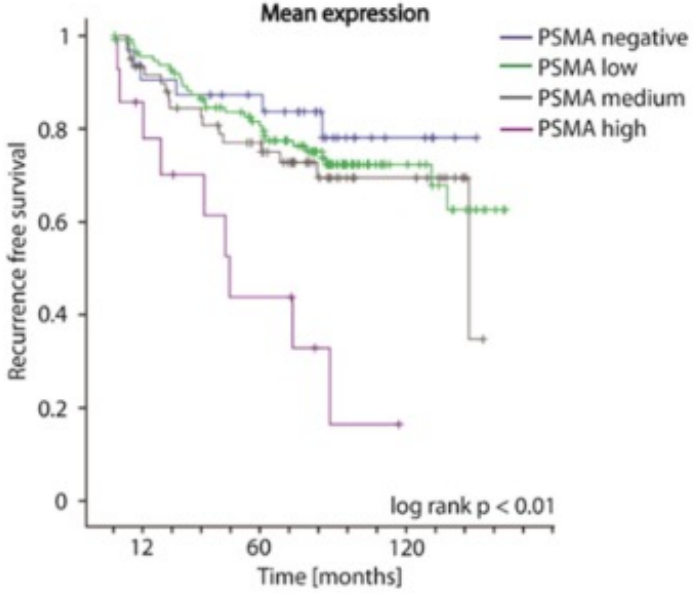


High PSMA expression on both biopsy and radical prostatectomy (RPE) specimens significantly associates with a higher risk of disease recurrence following curative surgery

RFS following RPE stratified by PSMA expression on biopsies



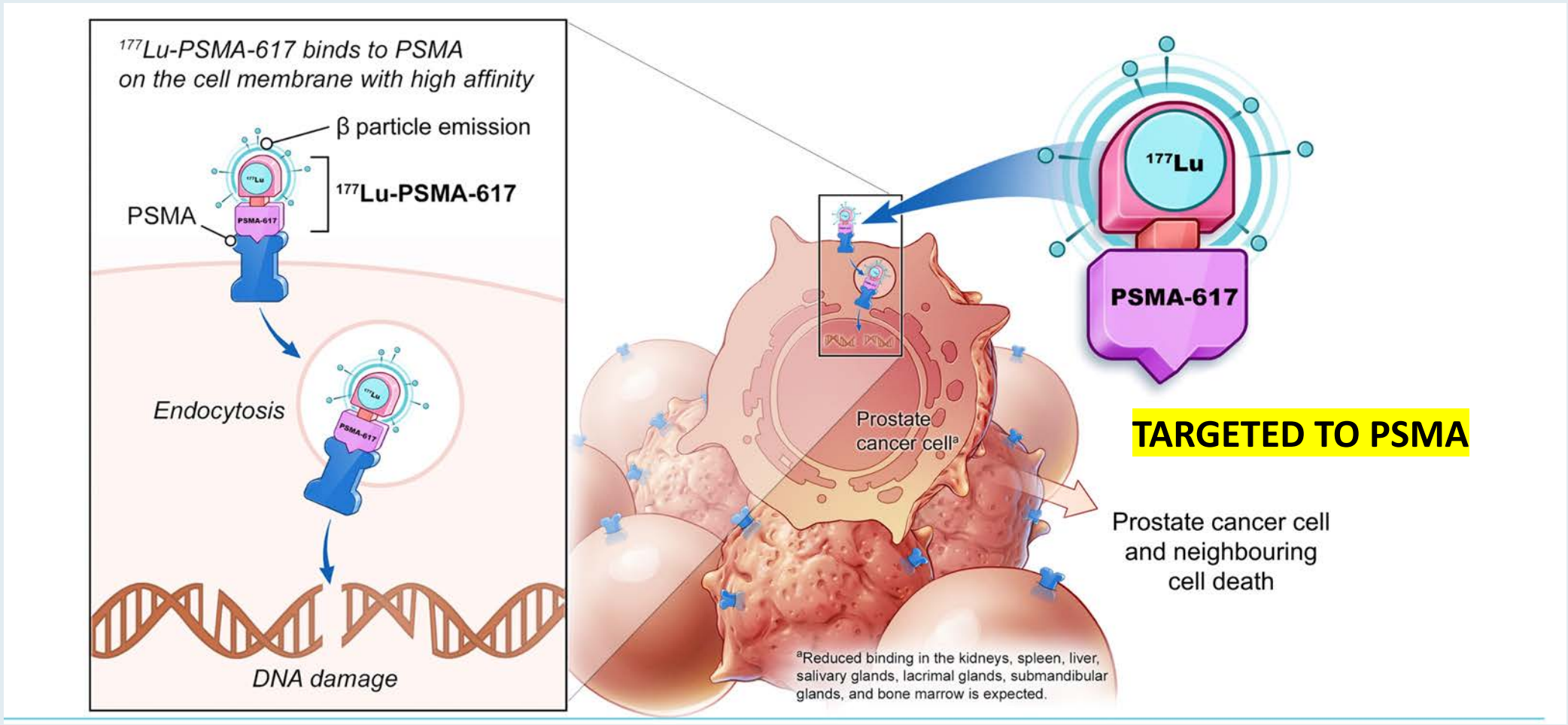
RFS following RPE stratified by PSMA expression on RPE specimens



Hupe MC et al. *Front Oncol* 2018;8:263.

RTP RESEARCH TO PRACTICE

Lutetium Lu 177 Vipivotide Tetraxetan (Formerly ^{177}Lu-PSMA-617): Mechanism of Action



Morris MJ et al. ASCO 2021;Abstract LBA4.

Lutetium Lu 177 Vipivotide Tetraxetan

Mechanism of action

- **Targeted radioligand**

Indication

- **For adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have received androgen receptor (AR) pathway inhibition and taxane-based chemotherapy**

Recommended dose

- **7.4 GBq (200 mCi) every 6 weeks for up to 6 doses**

Lutetium Lu 177 vipivotide tetraxetan package insert, 10/2022.

RTP RESEARCH TO PRACTICE

Brenda Martone, MSN, NP-BC, AOCNP

What I tell my patients with PSMA-positive mCRPC who are about to begin treatment with lutetium Lu 177 vipivotide tetraxetan about how it works and what to expect

RTP
RESEARCH
TO PRACTICE

Prostate Cancer – Editor's Choice

Safety Analyses of the Phase 3 VISION Trial of [^{177}Lu]Lu-PSMA-617 in Patients with Metastatic Castration-resistant Prostate Cancer

Kim N. Chi[a,*], *Andrew J. Armstrong*[b], *Bernd J. Krause*[c], *Ken Herrmann*[d,e], *Kambiz Rahbar*[f], *Johann S. de Bono*[g], *Nabil Adra*[h], *Rohan Garje*[i], *Jeff M. Michalski*[j], *Mette M. Kempel*[k], *Karim Fizazi*[l], *Michael J. Morris*[m], *Oliver Sartor*[n], *Marcia Brackman*[o], *Michelle DeSilvio*[p], *Celine Wilke*[q], *Geoffrey Holder*[q], *Scott T. Tagawa*[r]

Eur Urol **2024 April;85(4):382-91**

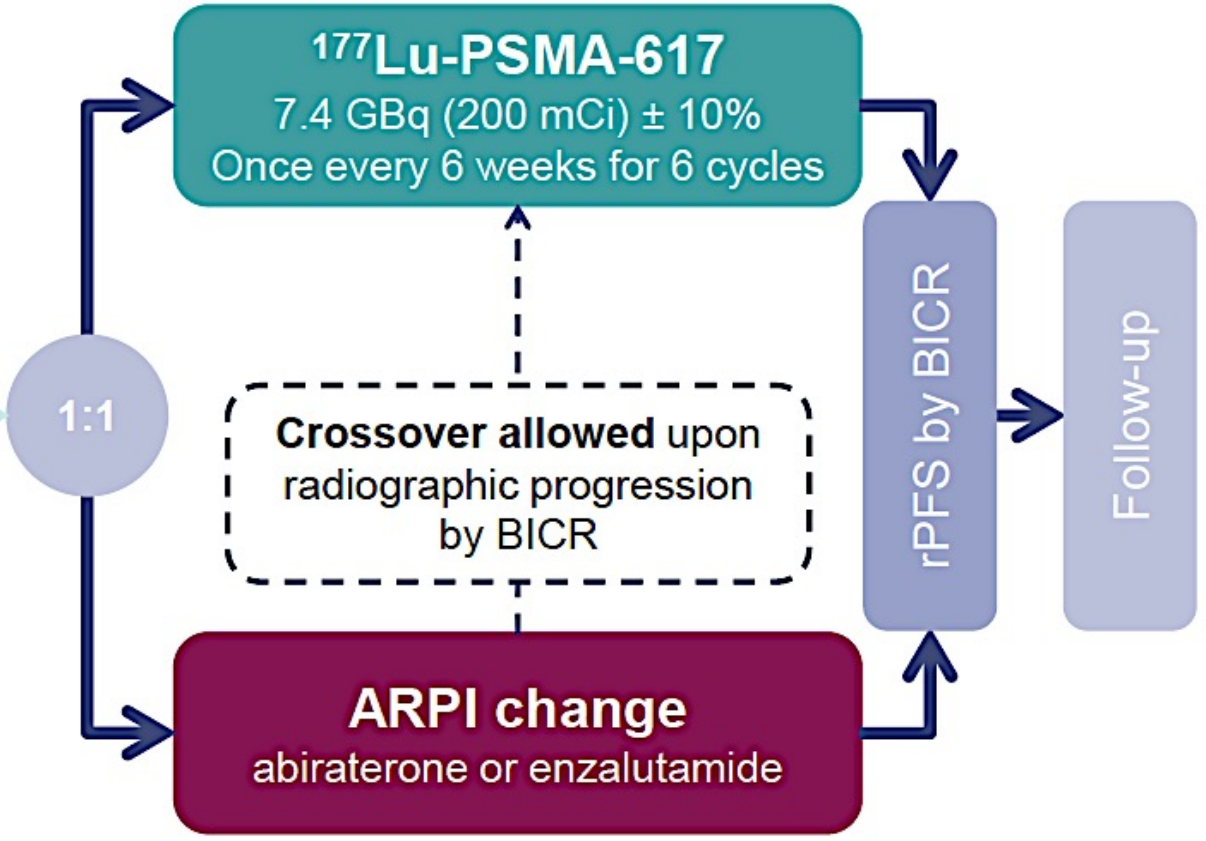
Author Conclusions: *Overall, these safety analyses support a favorable benefit risk profile of up to 6 cycles of ^{177}Lu-PSMA-617 plus SoC in heavily pretreated patients with PSMA-positive mCRPC. The results provide important information for health care providers supporting the use of a further 2 cycles of ^{177}Lu-PSMA-617 in patients who are clinically benefiting and tolerating the therapy after 4 cycles. The analyses also emphasize that differences in treatment exposure and safety observation time between treatment groups are an important consideration when evaluating safety data in clinical studies. Ongoing phase 3 trials are investigating whether radioligand therapy with ^{177}Lu-PSMA-617 has a good safety profile and therapeutic benefit earlier in the treatment sequence for mCRPC.*

RTP RESEARCH TO PRACTICE

PSMAfore Trial: Phase III Study Design

Eligible adults

- Confirmed progressive mCRPC
- ≥ 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-naive (except [neo]adjuvant > 12 months ago)
  - Not candidates for PARPi
- ECOG performance status 0–1



Stratification factors

- Prior ARPI setting (castration-resistant vs hormone-sensitive)
- BPI-SF worst pain intensity score (0–3 vs > 3)

MADRID 2023 ESMO congress

ARPI = androgen receptor pathway inhibitor

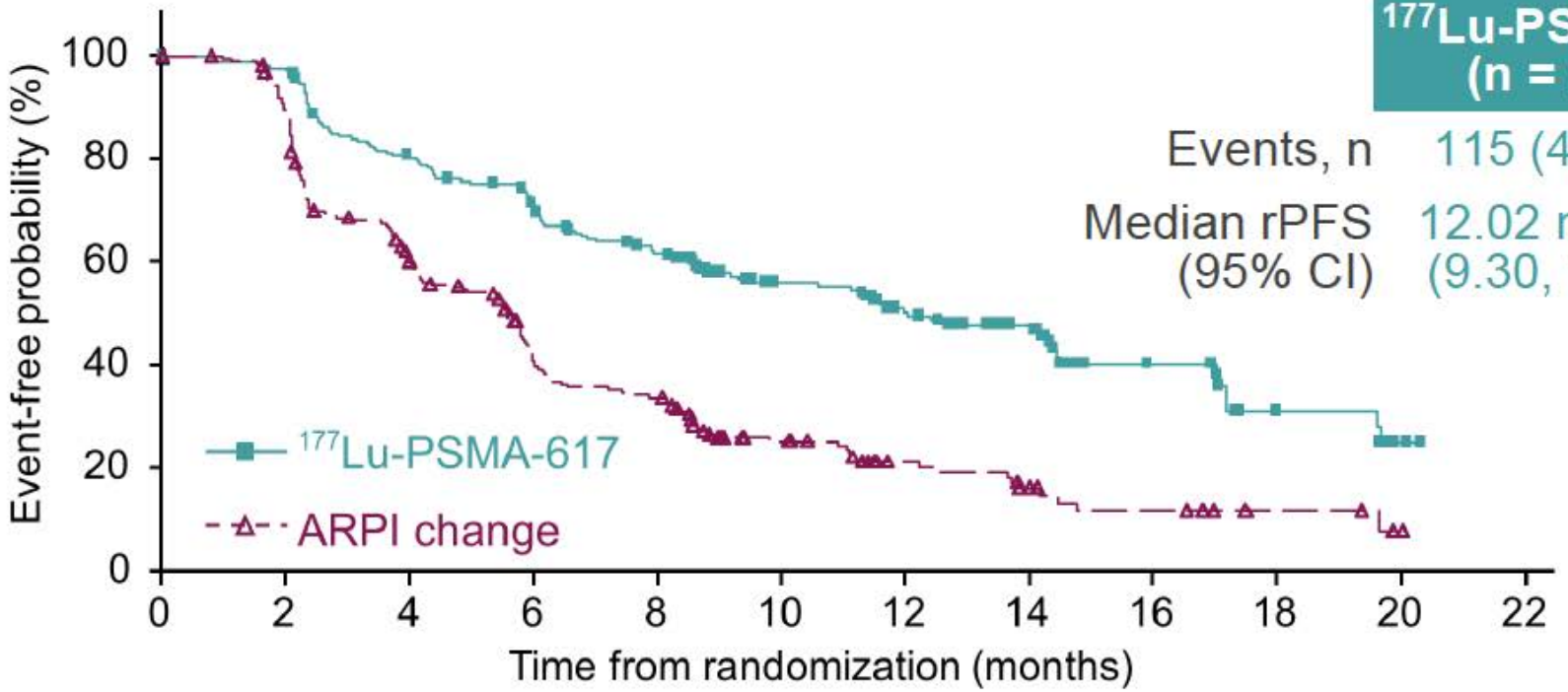
Sartor O et al. ESMO 2023;Abstract LBA13.

RTP RESEARCH TO PRACTICE

PSMAfore: Primary Endpoint Radiographic Progression-Free Survival (rPFS)

Primary HR: 0.41 (95% CI: 0.29, 0.56); $p < 0.0001$

Updated HR: 0.43 (95% CI: 0.33, 0.54)



	^{177}Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Events, n	115 (49.1%)	168 (71.8%)
Median rPFS (95% CI)	12.02 months (9.30, 14.42)	5.59 months (4.17, 5.95)

Sartor O et al. ESMO 2023;Abstract LBA13.

RTP RESEARCH TO PRACTICE

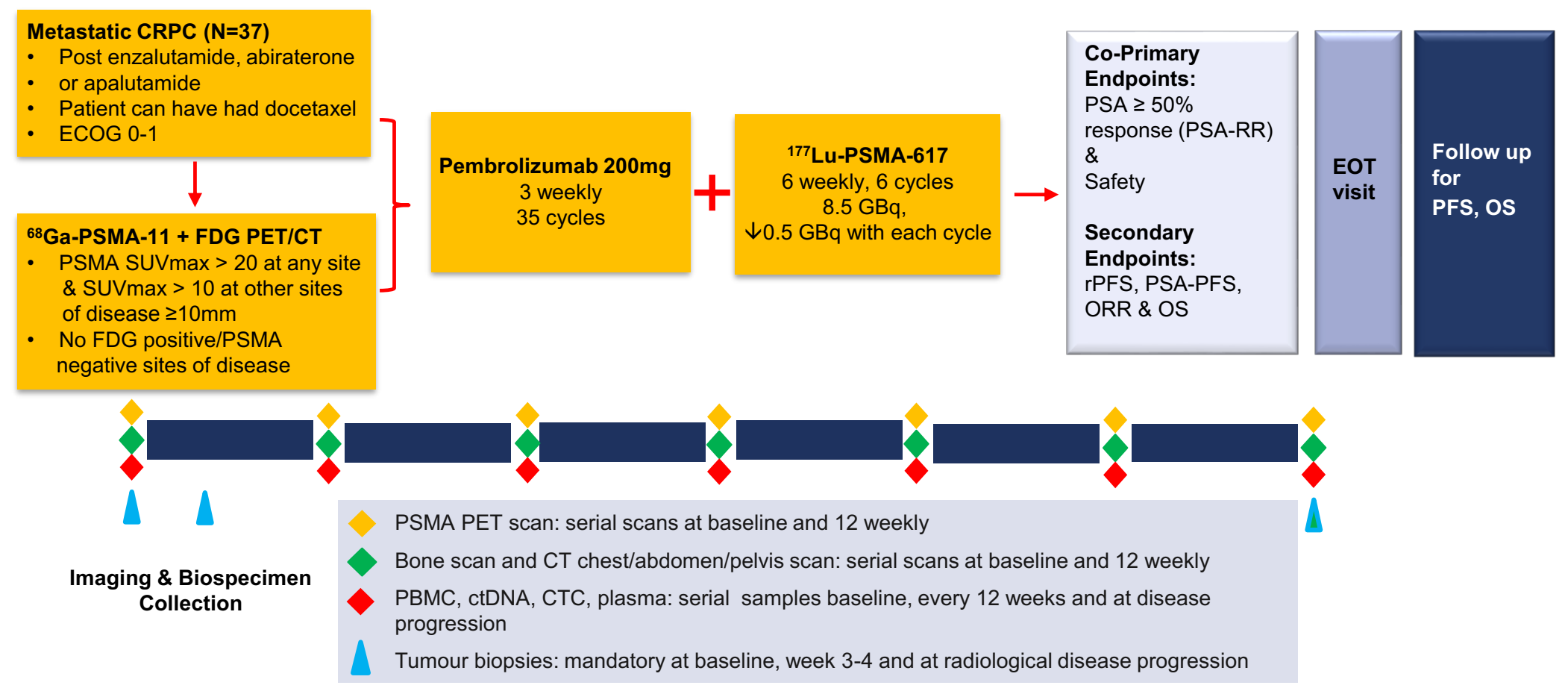
PSMAfore: Treatment-Emergent Adverse Events

AEs, n (%)	All grades		Grades 3–5	
	^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)	^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)
Dry mouth	130 (57.3)	5 (2.2)	3 (1.3)	0
Asthenia	72 (31.7)	67 (28.9)	1 (0.4)	8 (3.4)
Nausea	71 (31.3)	28 (12.1)	0	1 (0.4)
Anaemia	55 (24.2)	39 (16.8)	14 (6.2)	14 (6.0)
Fatigue	52 (22.9)	59 (25.4)	0	4 (1.7)
Constipation	50 (22.0)	31 (13.4)	1 (0.4)	0
Decreased appetite	48 (21.1)	42 (18.1)	0	1 (0.4)
Arthralgia	43 (18.9)	48 (20.7)	0	1 (0.4)
COVID-19	37 (16.3)	26 (11.2)	1 (0.4)	1 (0.4)
Diarrhoea	37 (16.3)	20 (8.6)	0	1 (0.4)
Back pain	28 (12.3)	38 (16.4)	2 (0.9)	5 (2.2)
Vomiting	26 (11.5)	11 (4.7)	0	0
Peripheral oedema	19 (8.4)	26 (11.2)	0	0
Weight loss	15 (6.6)	28 (12.1)	2 (0.9)	5 (2.2)

AEs = adverse events

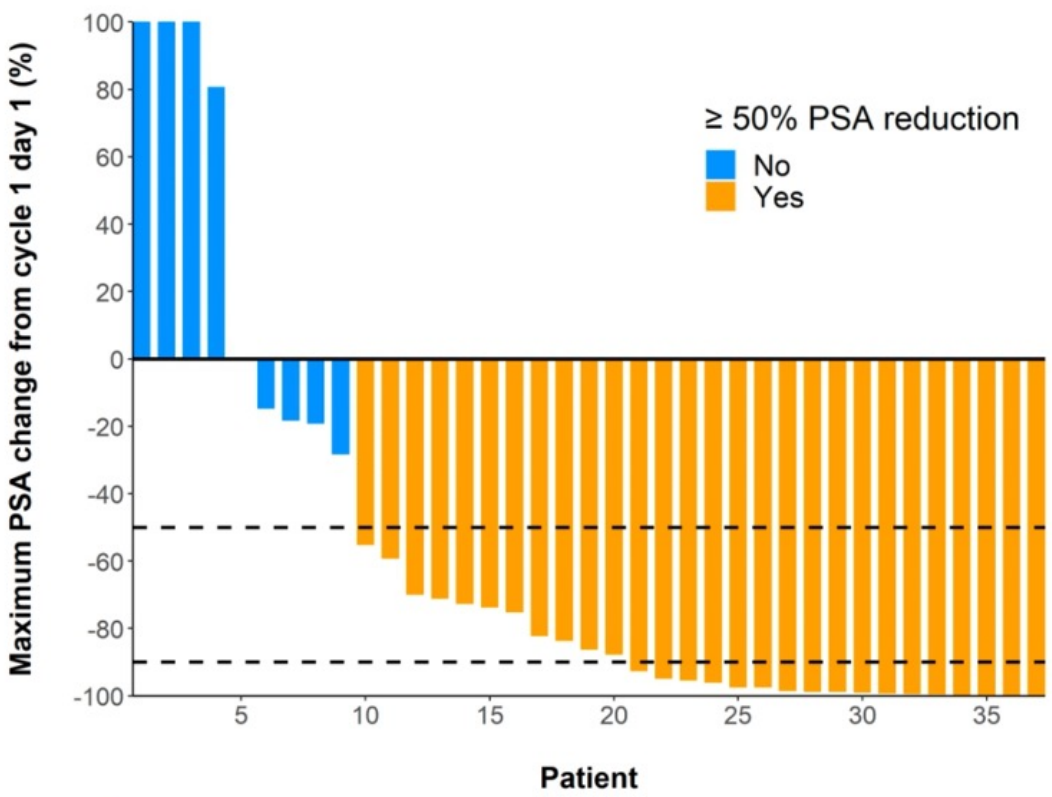
Sartor O et al. ESMO 2023;Abstract LBA13.

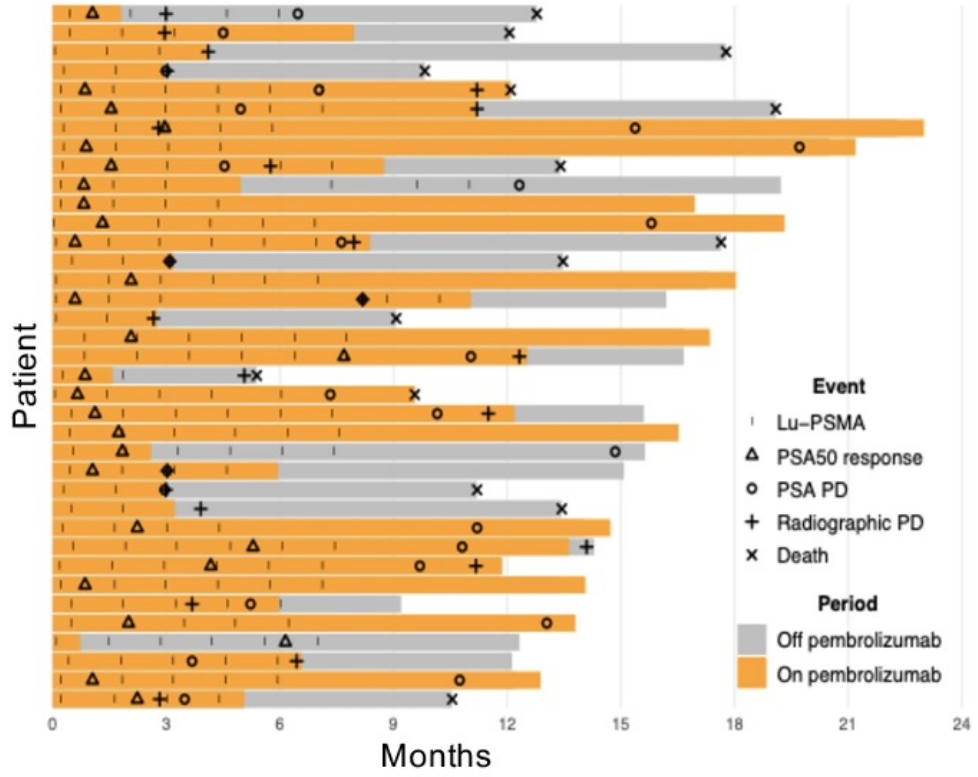
PRINCE: A Phase Ib Study of Pembrolizumab with Lutetium Lu 177 Vipivotide Tetraxetan for mCRPC



Sandhu S et al. ESMO 2021;Abstract 577O.

PRINCE Primary Endpoint: PSA Response Rate



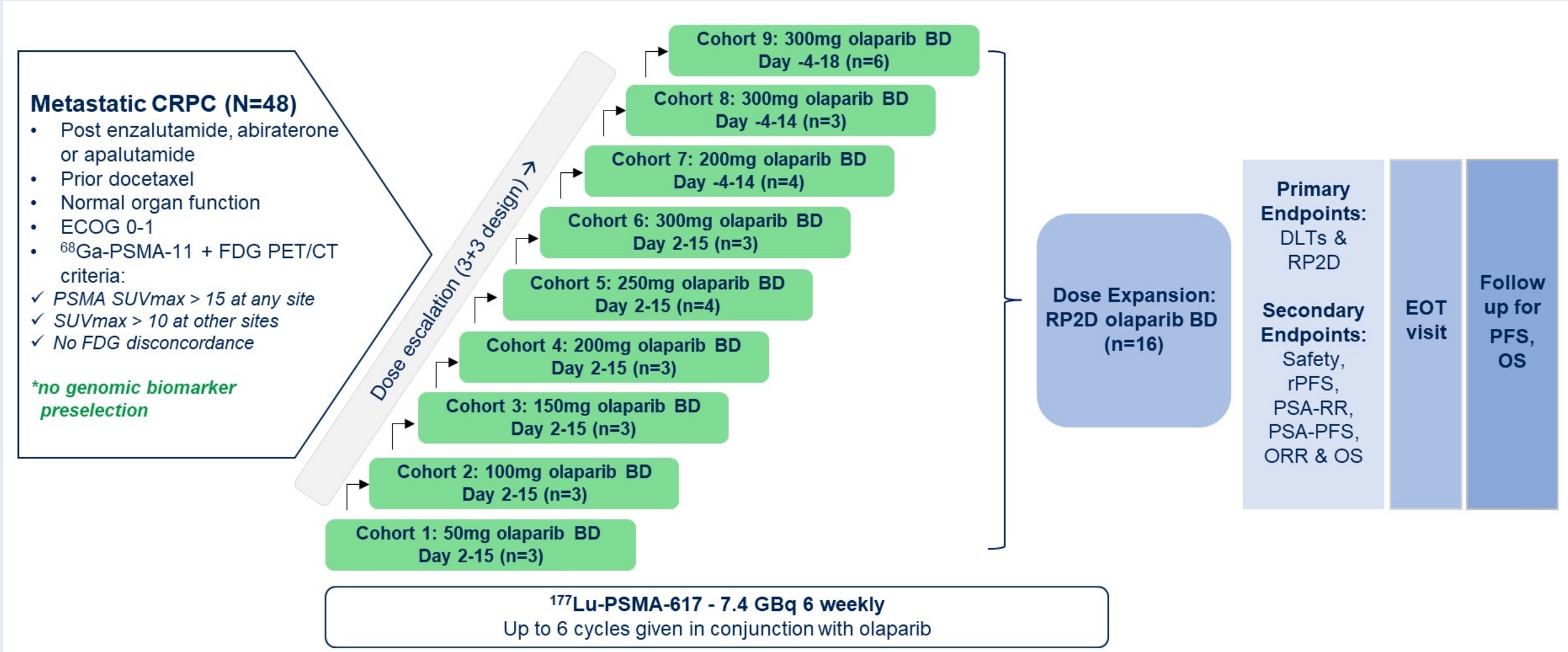


PSA ≥ 50% response = 76% (28/37 95% CI:59-88)
ORR by RECIST 1.1 = 78% (7/9)

median follow up: 16 months at data cut off

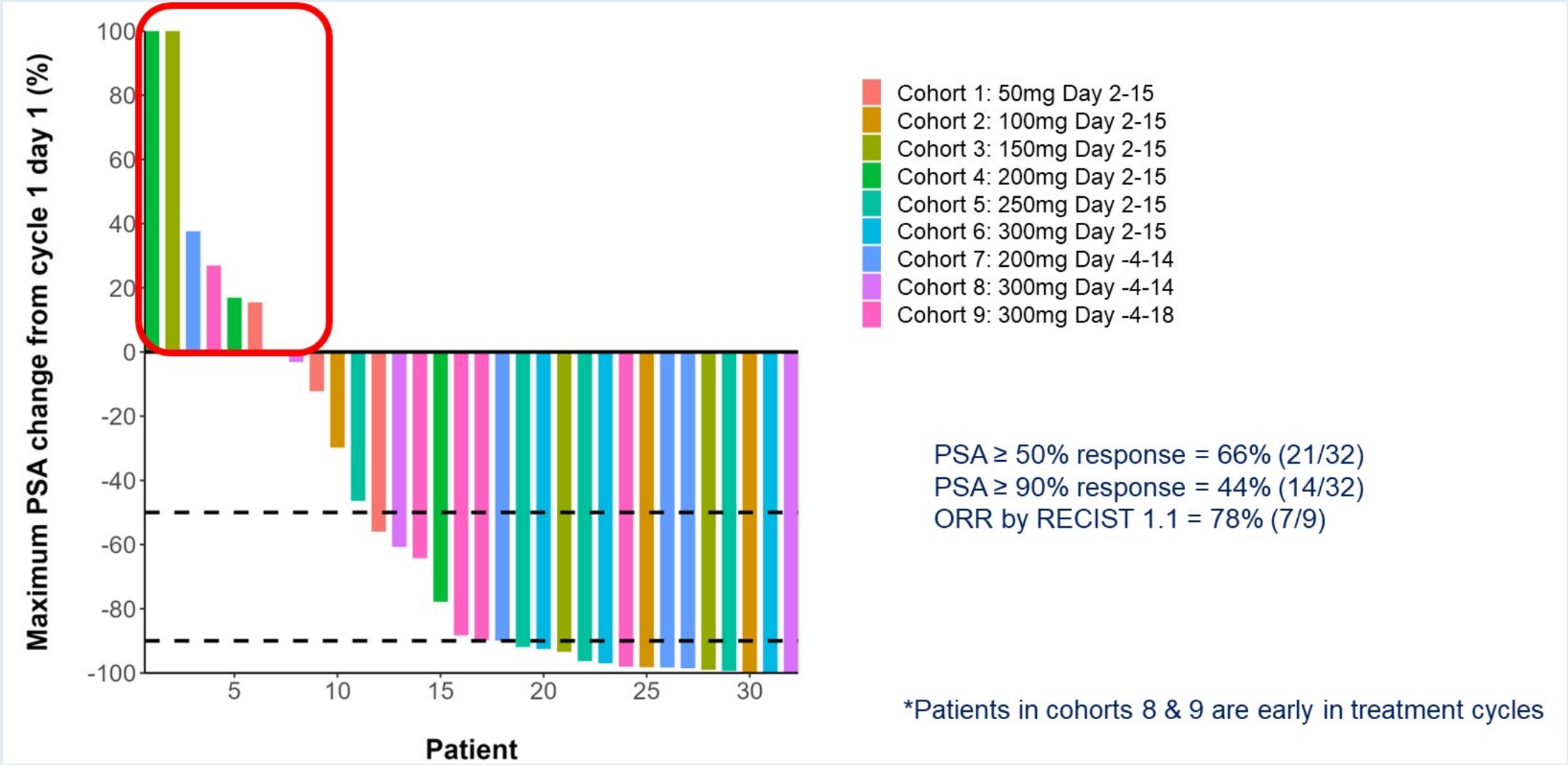
Sandhu S et al. ASCO 2022;Abstract 5017.

LuPARP: A Phase I Trial of Olaparib with Lutetium Lu 177 Vipivotide Tetraxetan for mCRPC



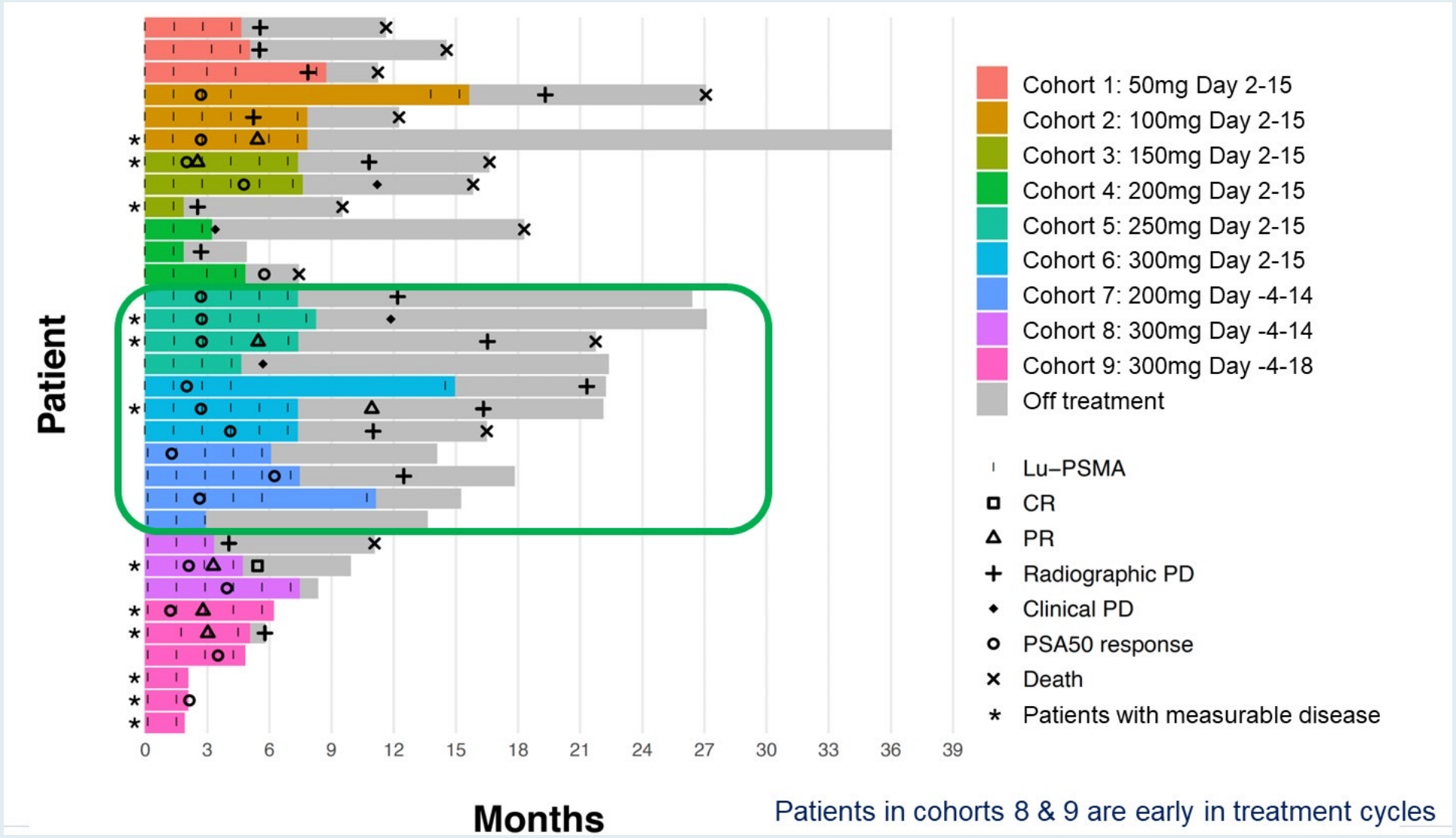
Sandhu S et al. ASCO 2023;Abstract 5005.

LuPARP: PSA Responses



Sandhu S et al. ASCO 2023;Abstract 5005.

LuPARP: Swimmer Plots



Sandhu S et al. ASCO 2023;Abstract 5005.

LuPARP: Common Adverse Events in ≥5%

	N=3 Cohort 1 ^{177}Lu-PSMA & 50mg olaparib BD Day 2-15			N=3 Cohort 2 ^{177}Lu-PSMA & 100mg olaparib BD Day 2-15			N=3 Cohort 3 ^{177}Lu-PSMA & 150 olaparib BD Day 2-15			N=3 Cohort 4 ^{177}Lu-PSMA & 200mg olaparib BD Day 2-15			N=4 Cohort 5 ^{177}Lu-PSMA & 250mg olaparib BD Day 2-15			N=3 Cohort 6 ^{177}Lu-PSMA & 300 olaparib BD Day 2-15			N=4 Cohort 7 ^{177}Lu-PSMA & 200mg olaparib BD Day -4-14			N=3 Cohort 8 ^{177}Lu-PSMA & 300mg olaparib BD Day -4-14			N=6 Cohort 9 ^{177}Lu-PSMA & 300mg olaparib BD Day -4-18			Total (n=32)		
No. cycles of treatment Median (range)	4 (4-5)			6 (5-6)			6 (2-6)			3 (2-4)			6 (4-6)			6 (5-6)			5.5 (3-6)			4 (3-6)			3 (2-5)			5 (2-6)		
Adverse Event (AE) Grade (G)	***G1***	***G2***	***G3***	***G1***	***G2***	***G3***	***G1***	***G2***	***G3***	***G1***	***G2***	***G3***	***G1***	***G2***	***G3***	***G1***	***G2***	***G3***	***G1***	***G2***	***G3***	***G1***	***G2***	***G3***	***G1***	***G2***	***G3***	***G1***	***G2***	***G3***
Anemia	1	-	-	2	1	-	-	-	-	-	-	-	1	1	1	-	-	1	1	-	-	-	-	-	-	1	-	5	3	2
Neutropenia	-	-	-	1	-	-	-	-	-	-	-	-	-	-	1*	-	-	1	-	-	-	-	-	-	-	-	-	1	-	2
Thrombocytopenia	-	1	-	1	-	-	1	-	-	1	-	-	1	-	1	-	1	-	-	-	-	-	-	-	1	-	-	5	2	1
Nausea	1	2	-	3	-	-	1	1	-	2	-	-	1	1	-	1	1	-	2	1	-	-	-	-	2	-	-	13	6	-
Dry Mouth	3	-	-	3	-	-	3	-	-	2	-	-	3	1	-	2	1	-	1	1	-	2	-	-	3	-	-	22	3	-
Constipation	-	-	-	-	-	-	-	1	-	2	-	-	-	-	-	1	-	-	1	1	-	1	-	-	2	-	-	7	2	-
Vomiting	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	1	-	1	-	-	1	-	-	3	1	-
Gastroesophageal Reflux	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	1	-	-	-	-	-	-	-	1	-	-	2	1	-
Diarrhea	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	1	-	-	1	-	-	-	-	-	-	-	-	3	-	-
Weight Loss	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	1	-	-	-	-	-	-	-	-	-	-	-	1	1	-
Anorexia	1	-	-	2	-	-	1	-	-	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-	1	-	-	6	-	-
Dry Eye	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-	1	-	-	2	-	-
Fatigue	-	-	-	1	-	-	1	-	-	2	-	-	1	-	-	2	-	-	1	-	-	1	-	-	6	-	-	15	-	-

Sandhu S et al. ASCO 2023;Abstract 5005.

RTP RESEARCH TO PRACTICE

Dr Armstrong
Durham, North Carolina

Radium-223 for mCRPC

- **Mechanism of antitumor activity of radium-223**
- **Rationale for the activity of radium-223 in bone metastases but not in other organs**
- **Available data with and ongoing research studies of radium-223 for mCRPC**
- **Patient selection for and optimal integration of radium-223 into current mCRPC treatment algorithms**

Radium-223 Chloride

Mechanism of action

- **Alpha particle-emitting radioactive therapeutic agent**

Indication

- **For patients with castration-resistant prostate cancer, symptomatic bone metastases and no known visceral metastatic disease**

Recommended dose

- **55 kBq (1.49 microcurie) per kg of body weight, administered at 4-week intervals for 6 injections**

Radium-223 package insert, 12/2019.

Brenda Martone, MSN, NP-BC, AOCNP

What I tell my patients with mCRPC about to receive radium-223 about how it works and what to expect from treatment, and educating patients regarding appropriate precautions when receiving a radiopharmaceutical

RTP
RESEARCH
TO PRACTICE

Practical Considerations with the Use of Novel Radiopharmaceuticals for Prostate Cancer

Dr Armstrong
Durham, North Carolina

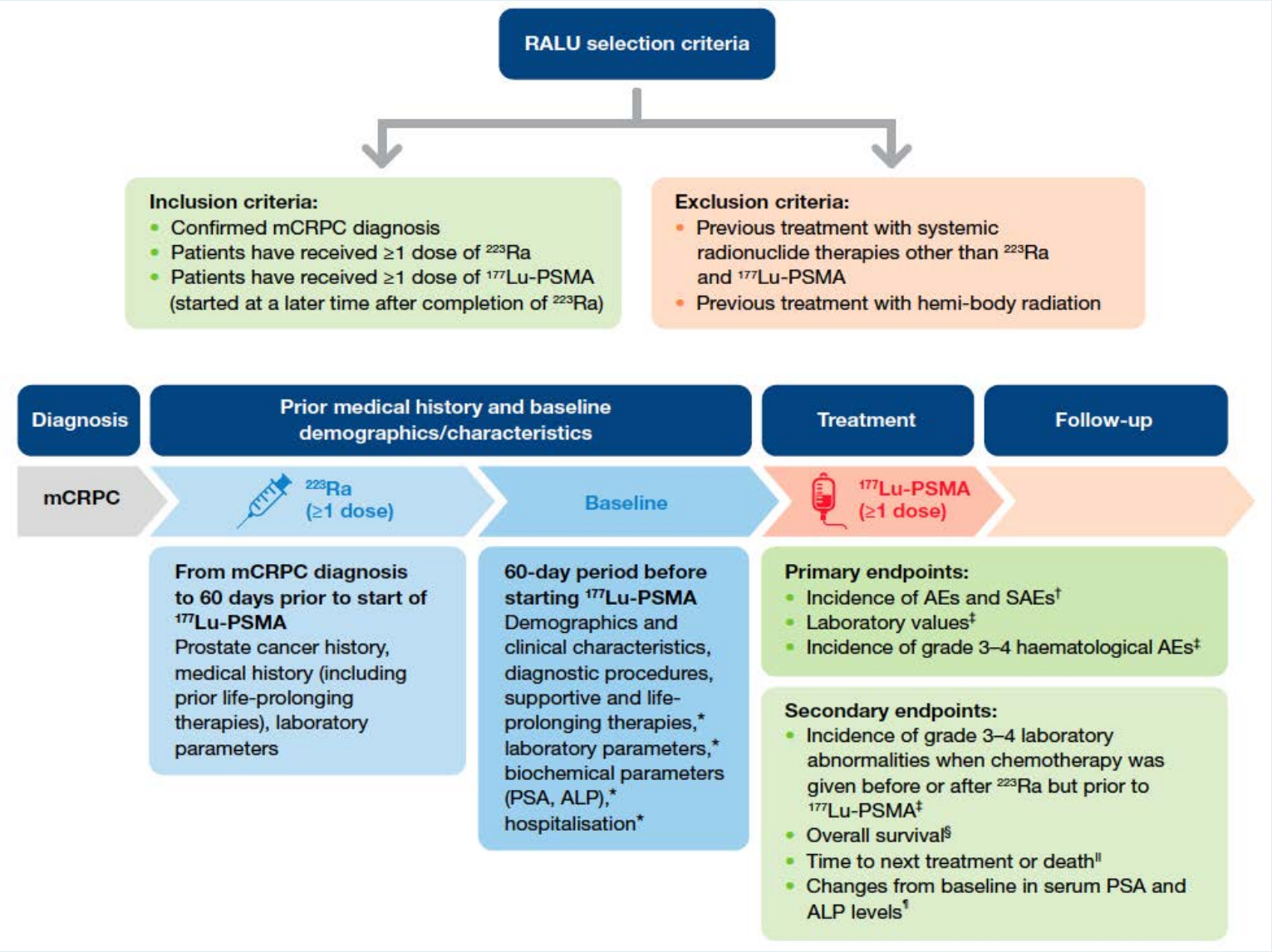
- **Appropriate monitoring of complete blood counts, kidney function and other laboratory values during treatment with lutetium Lu 177 vipivotide tetraxetan**
- **Recommended algorithms for the management of common AEs observed in patients receiving lutetium Lu 177 vipivotide tetraxetan (eg, fatigue, dry mouth, gastrointestinal toxicity, cytopenias)**
- **Incidence, severity and management of commonly occurring AEs with radium-223 (eg, cytopenias, gastrointestinal toxicity, peripheral edema)**
- **Educating patients receiving lutetium Lu 177 vipivotide tetraxetan and radium-223 regarding appropriate radiation protection precautions**

^{177}Lu-Prostate-Specific Membrane Antigen Therapy in Patients with Metastatic Castration-Resistant Prostate Cancer and Prior ^{223}Ra (RALU Study)

Kambiz Rahbar[1], Markus Essler[2], Matthias Eiber[3], Christian la Fougère[4], Vikas Prasad[5], Wolfgang P. Fendler[6], Philipp Rassek[1], Ergela Hasa[3], Helmut Dittmann[4], Ralph A. Bundschuh[2], Kim M. Pabst[6], Milena Kurtinecz[7], Anja Schmall[8], Frank Verholen[8], and Oliver Sartor[9]

J Nucl Med 2023 December 1;64(12):1925-31

RALU Study: Retrospective Analysis Selection Criteria



Rahbar K et al. *J Nucl Med* 2023 December 1;64(12):1925-31.

RTP RESEARCH TO PRACTICE

RALU: Key Points

QUESTION

- Can ^{177}Lu-PSMA be safely given to patients with mCRPC if they have previously received radium-223, and is safety impacted depending on where radium-223 is positioned in the treatment sequence?

PERTINENT FINDINGS

- In this real-world setting, ^{177}Lu-PSMA had an acceptable safety profile for patients who had previously received radium-223, with low rates of hematologic and overall adverse events.
- Median OS from the first dose of ^{177}Lu-PSMA was 13.2 months and was similar irrespective of whether patients had received taxane-based chemotherapy before or after radium-223 or if the time between radium-223 and ^{177}Lu-PSMA was less than 6 months versus 6 months or more.

IMPLICATIONS FOR PATIENT CARE

- For patients with mCRPC and prior radium-223 therapy, ^{177}Lu-PSMA had an acceptable safety profile and an effectiveness comparable to that seen in the VISION trial, irrespective of when patients had received prior radium-223.

Rahbar K et al. *J Nucl Med* 2023 December 1;64(12):1925-31.

Consulting Nursing Faculty Comments

Listening to patients and involving them in their medical care

Jacqueline Broadway-Duren, PhD, DNP, APRN, FNP-BC

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

RTP RESEARCH TO PRACTICE

Agenda

INTRODUCTION: Overview of Prostate Cancer; Hormonal Therapy

MODULE 1: Radiopharmaceuticals for the Management of Metastatic Castration-Resistant Prostate Cancer (mCRPC)

MODULE 2: Biomarker Testing for mCRPC; PARP Inhibitors for mCRPC

Dr Armstrong
Durham, North Carolina

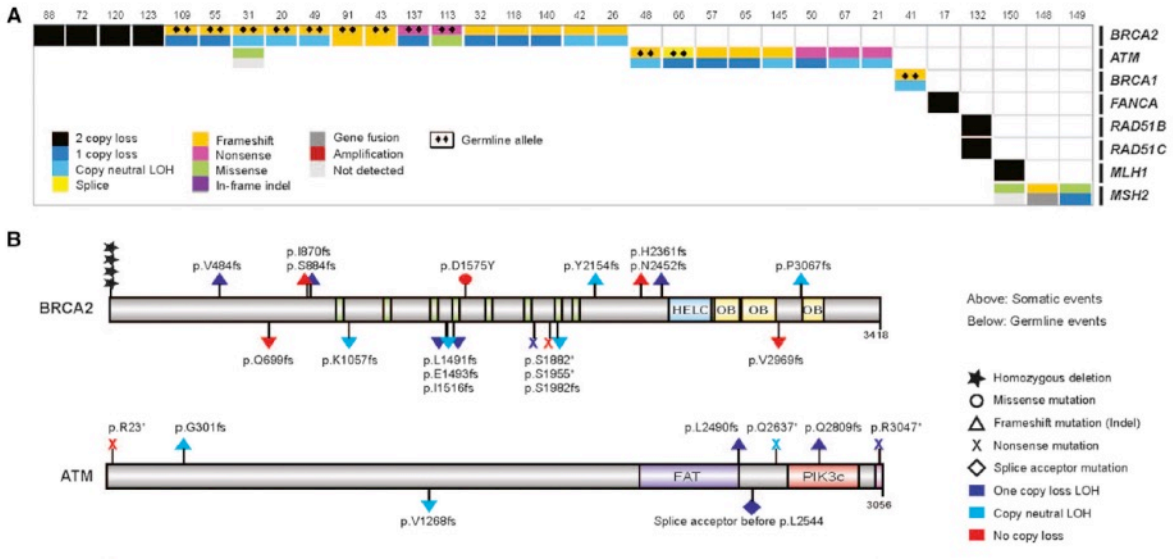
Biomarker Testing in Metastatic Castration-Resistant Prostate Cancer (mCRPC)

- **Spectrum and frequency of BRCA1/2 and other homologous recombination repair (HRR) abnormalities in prostate cancer**
- **Indications for, optimal timing of and practical implementation of genetic testing**
- **Clinical relevance of PSMA expression in prostate cancer; indications for, timing of, and practical implementation of PSMA detection**
- **Clinical and biological factors in the selection and sequencing of therapy for patients with mCRPC without an HRR abnormality; implications of prior therapeutic exposure**

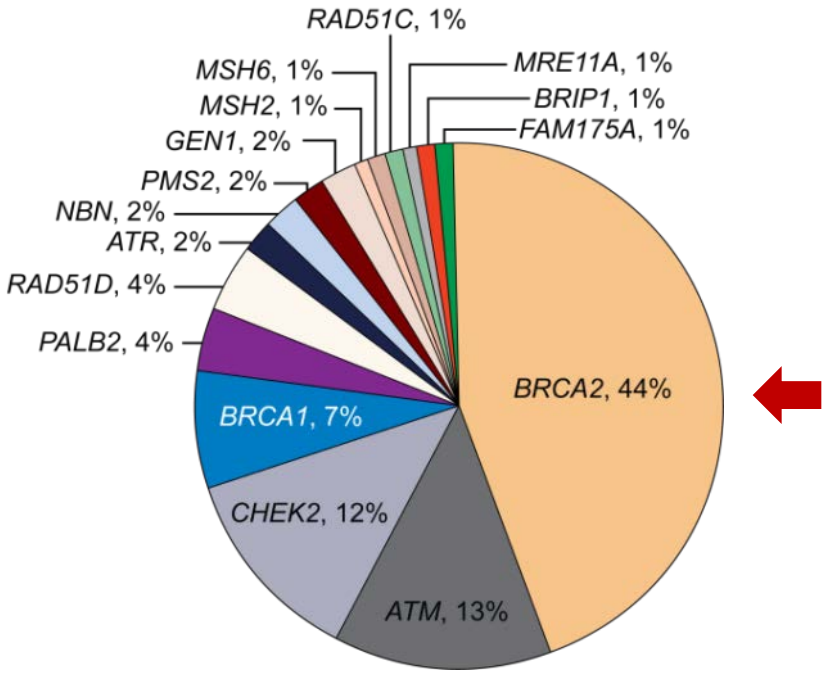
HRR Genes and Metastatic Prostate Cancer

Somatic

- **23%** of metastatic castration-resistant prostate cancers harbor DNA repair alterations
- The frequency of DNA repair alterations **increases in metastatic disease vs. localized disease**



Germline



- **12%** of men with metastatic prostate cancer have a germline DNA repair defect

1. Robinson D, et al. Cell. 2015;161:1215-28. **2.** Pritchard CC, et al. N Engl J Med. 2016;375:443-53.

Courtesy of Emmanuel S Antonarakis, MD

What are the relevant HRR Genes?

"First Tier"	"Second Tier"	"Third Tier"
BRCA2 (6–8%)	***CDK12*** (5–7%)	***ATM*** (5–7%)
BRCA1 (1–2%)	***BARD1*** (1%)	***CHEK2*** (2–3%)
PALB2 (1–2%)	***BRIP1*** (1–2%)	***CHEK1*** (1%)
RAD51B (1%)	***RAD51C*** (1%)	***FANCL*** (1–2%)
RAD54L (1%)	***RAD51D*** (1%)	

Courtesy of Emmanuel S Antonarakis, MD

NCCN Guidelines: Testing Criteria for Prostate Cancer Susceptibility Genes (Specifically ATM, BRCA1, BRCA2, CHEK2 and HOXB13)

Germline testing

<u>Personal history of prostate cancer with specific features:</u>

- By tumor characteristics (any age)
  - Metastatic
  - Histology
    - high- or very-high-risk group
- By family history and ancestry
  - ≥1 close blood relative with:
    - breast cancer at age ≤50 y
    - triple-negative breast cancer at any age
    - male breast cancer at any age
    - ovarian cancer at any age
    - pancreatic cancer at any age
    - metastatic, high-, or very-high-risk group at any age
  - ≥3 close blood relatives with prostate cancer (any grade) and/or breast cancer on the same side of the family including the patient with prostate cancer
  - Ashkenazi Jewish ancestry

<u>Family history of cancer</u>

- An affected (not meeting testing criteria listed above) or unaffected individual with a first-degree blood relative meeting any of the criteria listed above (except unaffected individuals whose relatives meet criteria only for systemic therapy decision-making)

<u>Testing may be considered in the following scenario:</u>

- Personal history of prostate cancer with intermediate-risk prostate cancer with intraductal/cribriform histology at any age

Somatic tumor testing

Somatic testing for alterations in DNA damage response:

- Multigene tumor testing for alterations in HRR genes, including but not limited to BRCA1, BRCA2, ATM, PALB2, FANCA, RAD51D, CHEK2, and CDK12, is recommended in patients with metastatic prostate cancer. This testing can be considered in patients with regional prostate cancer
- Tumor testing for MSI-H or dMMR is recommended in patients with mCRPC and may be considered in patients with regional or castration-sensitive metastatic prostate cancer
- TMB testing may be considered in patients with mCRPC

MSI-H = high miscrosatellite instability; dMMR = mismatch repair deficient; TMB = tumor mutational burden

National Comprehensive Cancer Network (NCCN®). **NCCN clinical practice guidelines in oncology. Prostate cancer — Version 3.2024. NCCN clinical practice guidelines in oncology. Genetic/familiar high-risk assessment: Breast, ovarian, and pancreatic cancer — Version 3.2024**.

RTP RESEARCH TO PRACTICE

Dr Armstrong
Durham, North Carolina

PARP Inhibitors for mCRPC

- **Published findings with olaparib/abiraterone, niraparib/abiraterone and talazoparib/enzalutamide as first-line therapy for patients with mCRPC; outcomes observed in patients with and without HRR gene mutations**
- **FDA-approved indications for olaparib/abiraterone, niraparib/abiraterone and talazoparib/enzalutamide for mCRPC; optimal patient selection for these approaches**
- **Long-term findings with and indications for PARP inhibitor monotherapy for patients with mCRPC**
- **Incidence, timing and severity of common class- and agent-specific toxicities associated with PARP inhibitors alone and in combination with hormonal therapy**

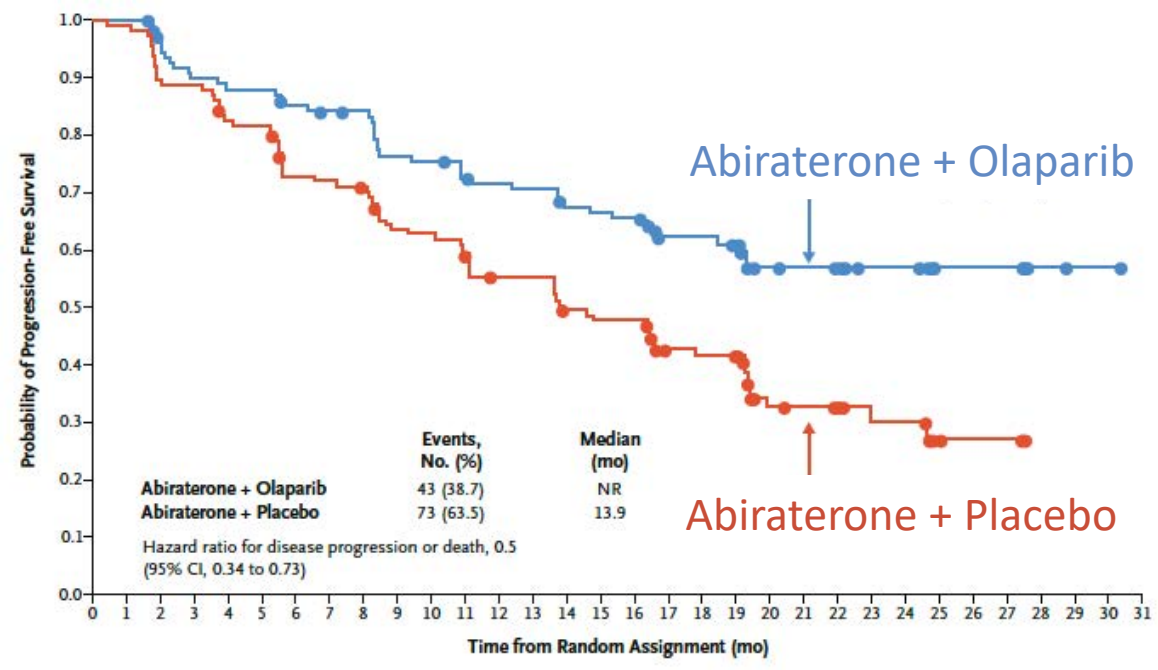
Brenda Martone, MSN, NP-BC, AOCNP

What I tell my patients with mCRPC who are about to begin treatment with a PARP inhibitor alone or in combination with hormonal therapy about the importance of BRCA/HRR testing

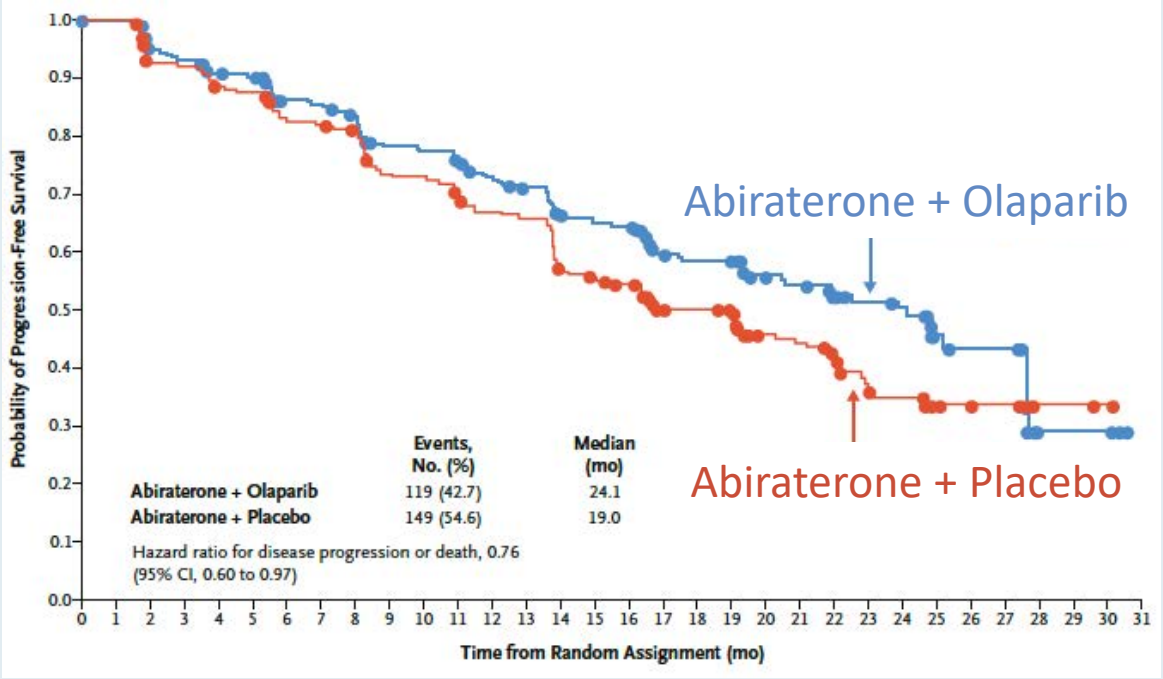
RTP
RESEARCH
TO PRACTICE

PROpel: Primary Radiographic Progression-Free Survival

HRRm subgroup



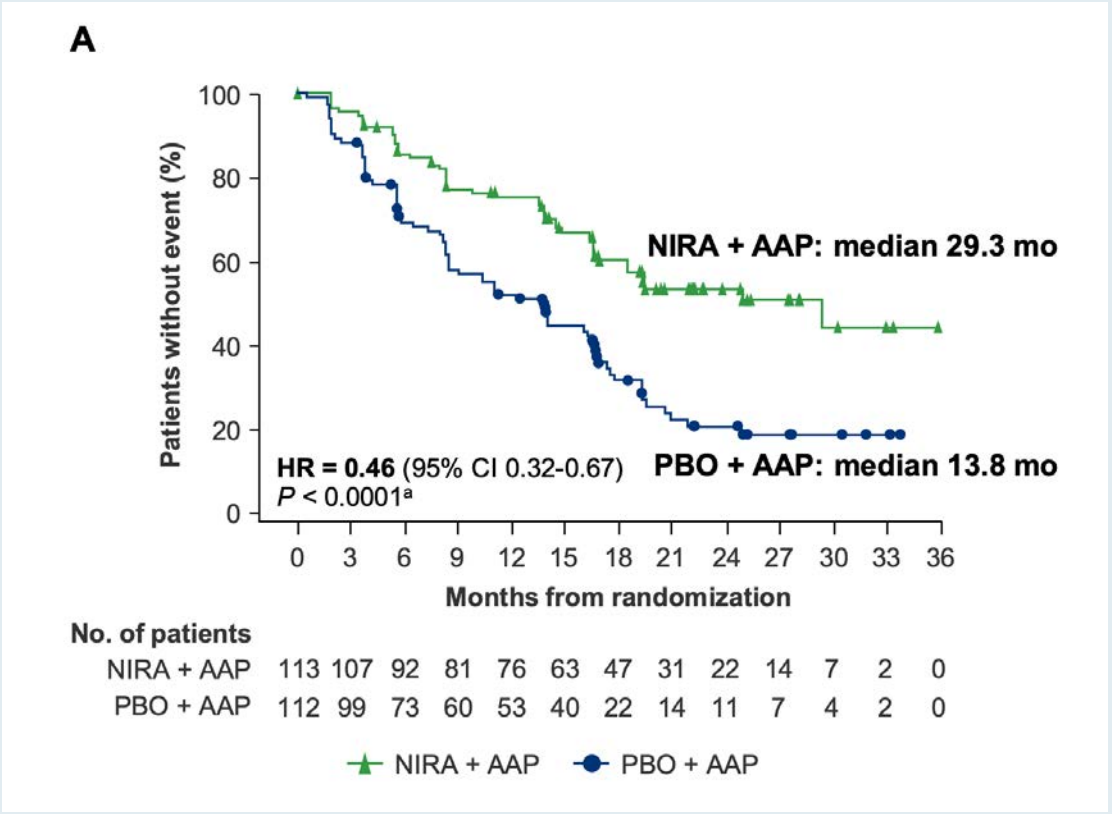
Non-HRRm subgroup



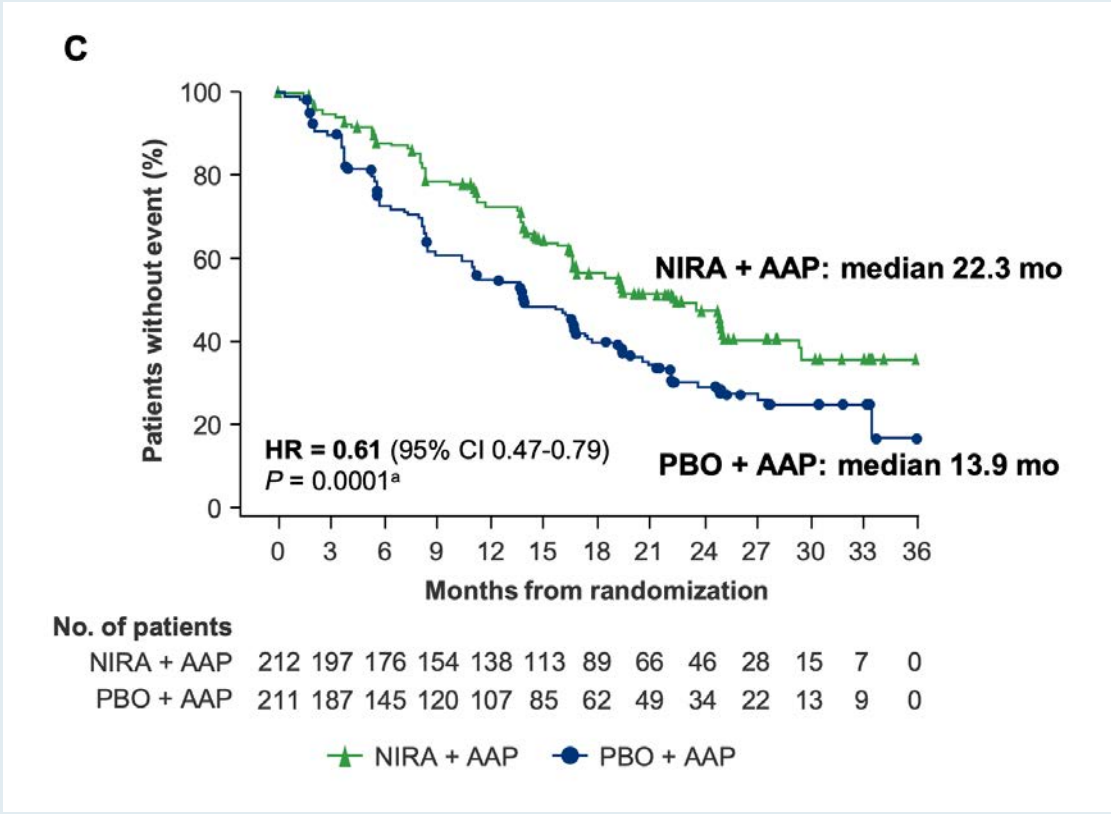
Clarke NW et al. *NEJM Evid* 2022;1(9):EVIDoa2200043.

MAGNITUDE Trial: Radiographic Progression-Free Survival at Second Interim Analysis

BRCA1/2 subgroup



HRR mutation subgroup

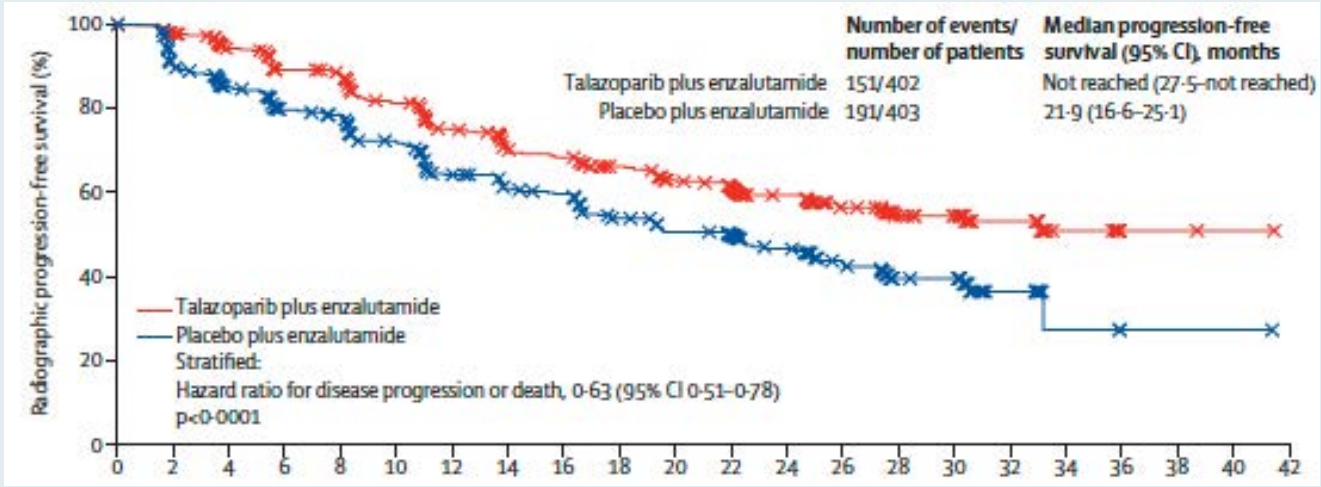


Chi KN et al. *Ann Oncol* 2023;34(9):772-82.

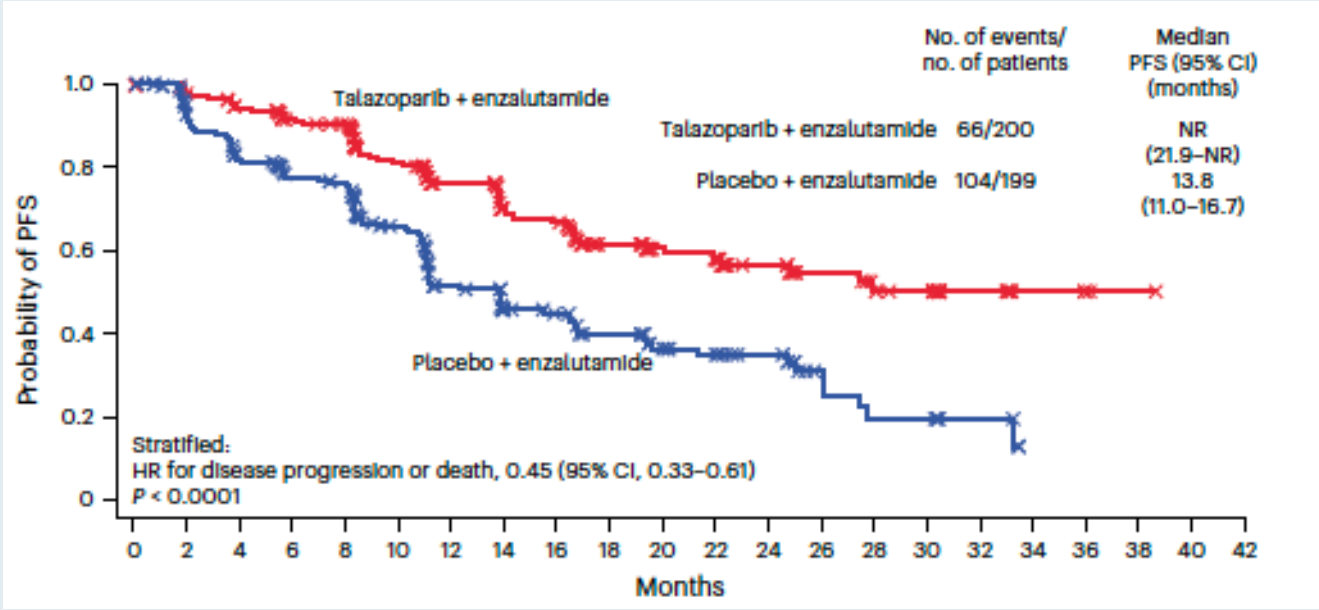
RTP RESEARCH TO PRACTICE

TALAPRO-2 Trial: Radiographic Progression-Free Survival

All patients



HRR-deficient subgroup



Agarwal N et al. *Lancet Oncol* 2023;402(10398):291-303. Fizazi K et al. *Nature Med* 2024;30(1):257-64.

Appendix

FDA Approves Lutetium Lu 177 Vipivotide Tetraxetan for the Treatment of mHRPC

Press Release: March 23, 2022

"On March 23, 2022, the Food and Drug Administration approved [the radioligand therapy lutetium Lu 177 vipivotide tetraxetan] for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy.

On the same day, the FDA approved gallium Ga 68 gozetotide, a radioactive diagnostic agent for positron emission tomography (PET) of PSMA-positive lesions, including selection of patients with metastatic prostate cancer for whom lutetium Lu 177 vipivotide tetraxetan PSMA-directed therapy is indicated. Gallium Ga 68 gozetotide is the first radioactive diagnostic agent approved for patient selection in the use of a radioligand therapeutic agent.

Efficacy was evaluated in [the Phase III VISION trial, which] demonstrated a statistically significant improvement in the primary endpoints OS and rPFS. Hazard ratio (HR) for OS was 0.62 (95% CI: 0.52, 0.74; $p < 0.001$) for the comparison of lutetium Lu 177 vipivotide tetraxetan plus BSoC versus BSoC. Median OS was 15.3 months (95% CI: 14.2, 16.9) in the lutetium Lu 177 vipivotide tetraxetan plus BSoC arm and 11.3 months (95% CI: 9.8, 13.5) in the BSoC arm, respectively."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pluvicto-metastatic-castration-resistant-prostate-cancer

2021;385(12):1091-103

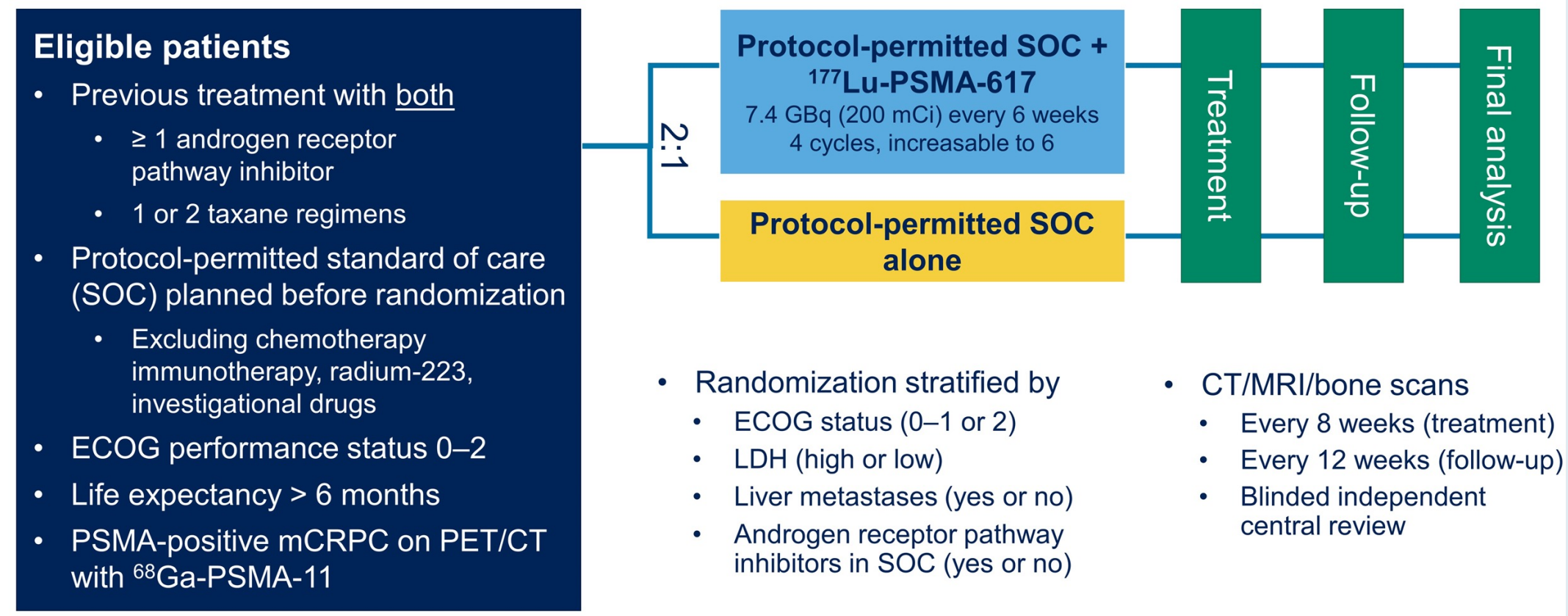
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

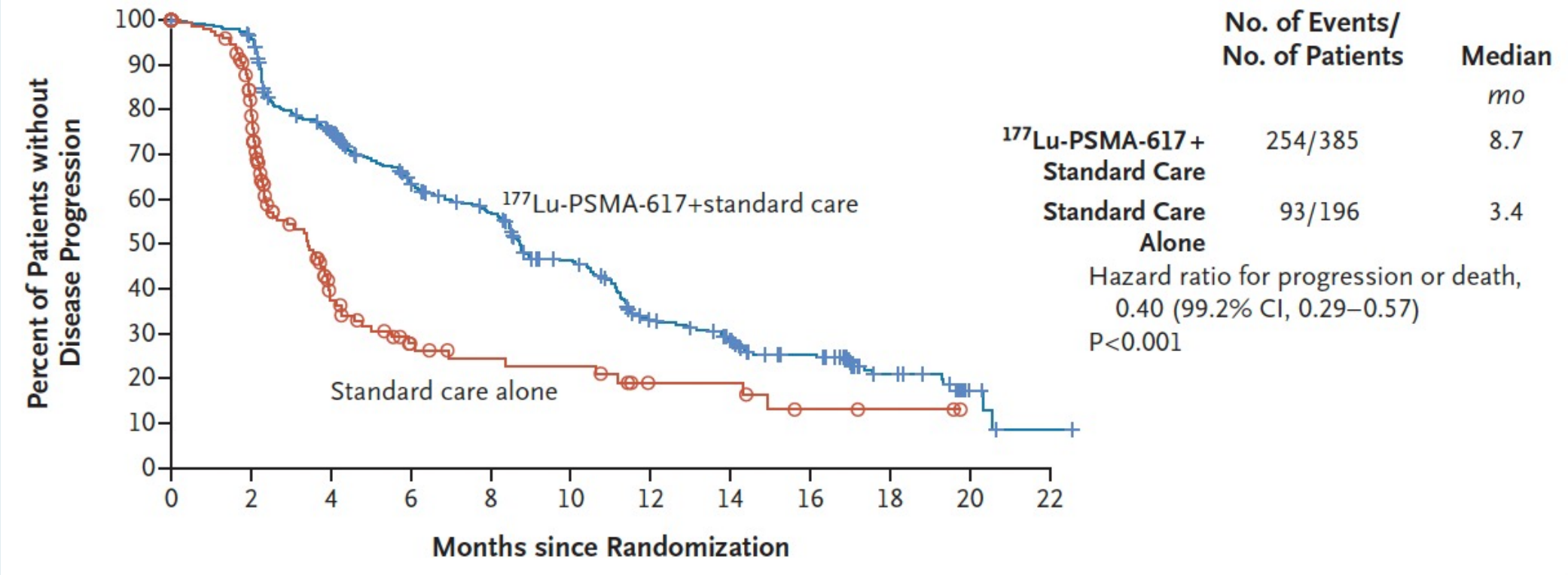
O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S.T. Tagawa, L.T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park, T.M. Beer, A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION Investigators*

VISION: A Pivotal Phase III Trial of Lutetium Lu 177 Vipivotide Tetraxetan for mHRPC



Morris MJ et al. ASCO 2021;Abstract LBA4. Sartor O et al. *N Engl J Med* 2021;385(12):1091-103.

VISION: Imaging-Based Progression-Free Survival by Independent Central Review

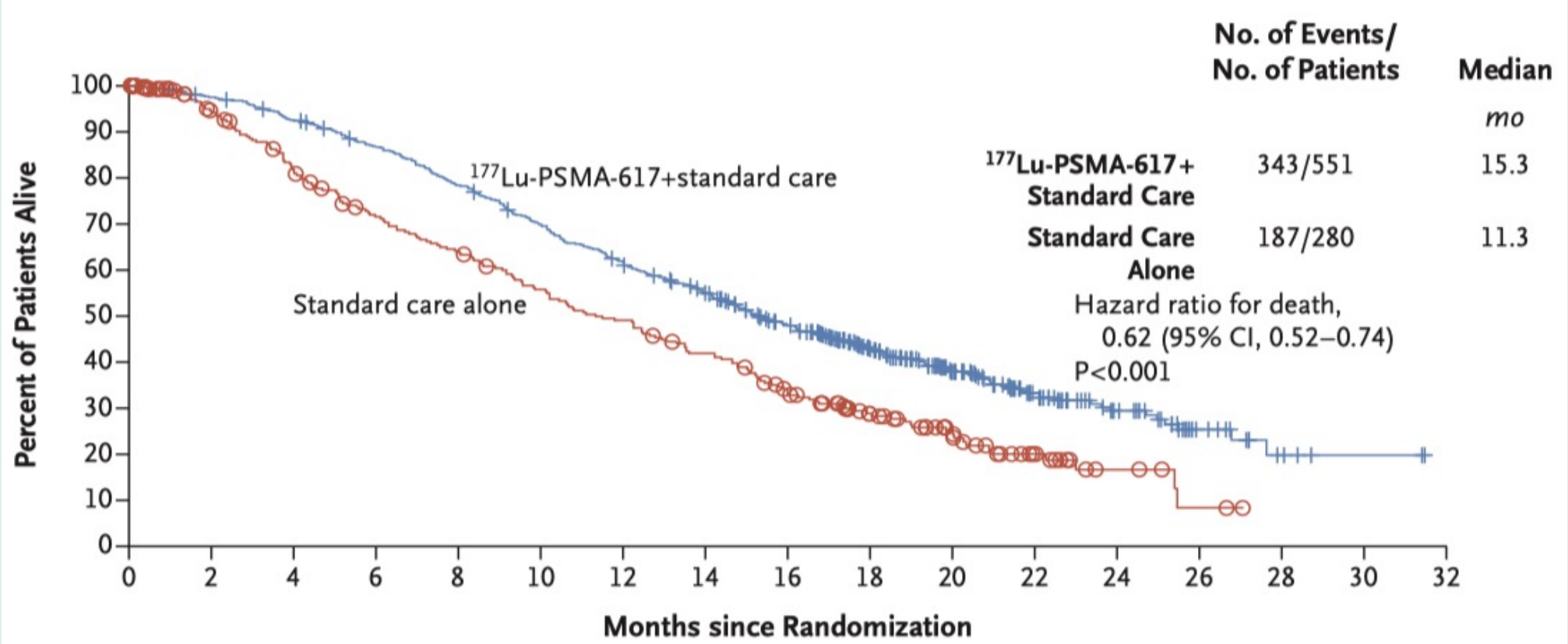


- Median OS (lutetium Lu 177 vipivotide tetraxetan versus standard therapy): 15.3 months versus 11.3 months (HR 0.62, $p < 0.001$)
- Time to first symptomatic skeletal event or death (lutetium Lu 177 vipivotide tetraxetan versus standard therapy): 11.5 months versus 6.8 months (HR 0.50, $p < 0.001$)

Sartor O et al. *N Engl J Med* 2021;385(12):1091-103.

RTP RESEARCH TO PRACTICE

VISION: Overall Survival



Sartor O et al. *N Engl J Med* 2021;385(12):1091-103.

RTP RESEARCH TO PRACTICE

VISION: Selected Adverse Events

Event	^{177}Lu-PSMA-617 plus Standard Care (N = 529)		Standard Care Alone (N = 205)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
	number of patients (percent)			
Any adverse event	519 (98.1)	279 (52.7)	170 (82.9)	78 (38.0)
Adverse event that occurred in >12% of patients				
Fatigue	228 (43.1)	31 (5.9)	47 (22.9)	3 (1.5)
Dry mouth	205 (38.8)	0	1 (0.5)	0
Thrombocytopenia	91 (17.2)	42 (7.9)	9 (4.4)	2 (1.0)
Lymphopenia	75 (14.2)	41 (7.8)	8 (3.9)	1 (0.5)
Leukopenia	66 (12.5)	13 (2.5)	4 (2.0)	1 (0.5)
Adverse event that led to reduction in ^{177}Lu-PSMA-617 dose	30 (5.7)	10 (1.9)	NA	NA
Adverse event that led to interruption of ^{177}Lu-PSMA-617†	85 (16.1)	42 (7.9)	NA	NA
Adverse event that led to discontinuation of ^{177}Lu-PSMA-617†	63 (11.9)	37 (7.0)	NA	NA
Adverse event that led to death‡	19 (3.6)	19 (3.6)	6 (2.9)	6 (2.9)

Sartor O et al. *N Engl J Med* 2021;385(12):1091-103.

RTP RESEARCH TO PRACTICE

MADRID 2023 ESMO congress

Abstract LBA13

Phase 3 trial of [^{177}Lu]Lu-PSMA-617 in taxane-naive patients with metastatic castration-resistant prostate cancer (PSMAfore)

Presenter: Oliver Sartor,*
Mayo Clinic, Rochester, MN, USA

Co-authors: D Castellano, K Herrmann, J de Bono, ND Shore, KN Chi, M Crosby, JM Piulats, A Flechon, XX Wei, H Mahammedi, G Roubaud, H Studentova, S Ghebremariam, E Kpamegan, TN Kreisl, N Delgoshaie, K Lehnhoff, MJ Morris,* K Fizazi,*
on behalf of the PSMAfore investigators

*Contributed equally

RTP RESEARCH TO PRACTICE

PSMAfore: Author Conclusions

- ^{177}Lu-PSMA-617 prolonged rPFS versus ARPI change
- Secondary and exploratory endpoints also favoured ^{177}Lu-PSMA-617
  - PSA response
  - Objective response rate
  - Time to symptomatic skeletal events
  - Time to worsening in HRQoL and pain
- Prespecified crossover-adjusted OS trended favourably
  - The 84.2% crossover rate may have confounded ITT analysis
  - OS data collection continues
- ^{177}Lu-PSMA-617 had a manageable safety profile and was well tolerated

HRQoL = health-related quality of life

Sartor O et al. ESMO 2023;Abstract LBA13.

Safety and effectiveness of the radium-223–taxane treatment sequence in patients with metastatic castration-resistant prostate cancer in a global observational study (REASSURE)

Celestia S. Higano MD[1] | Sabina Dizdarevic MD, PhD, FRCP[2] | John Logue MB[3] | Timothy Richardson MD[4] | Saby George MD[5] | Igle de Jong MD, PhD[6] | Jeffrey J. Tomaszewski MD[7] | Fred Saad MD[8] | Kurt Miller MD[9] | Jeffrey Meltzer EdD[10] | Per Sandström MD, PhD[11] | Frank Verholen MD[12] | Bertrand Tombal MD, PhD[13] | Oliver Sartor MD[14]

Cancer **2024 February 10;[Online ahead of print]**

2023 ASCO ANNUAL MEETING

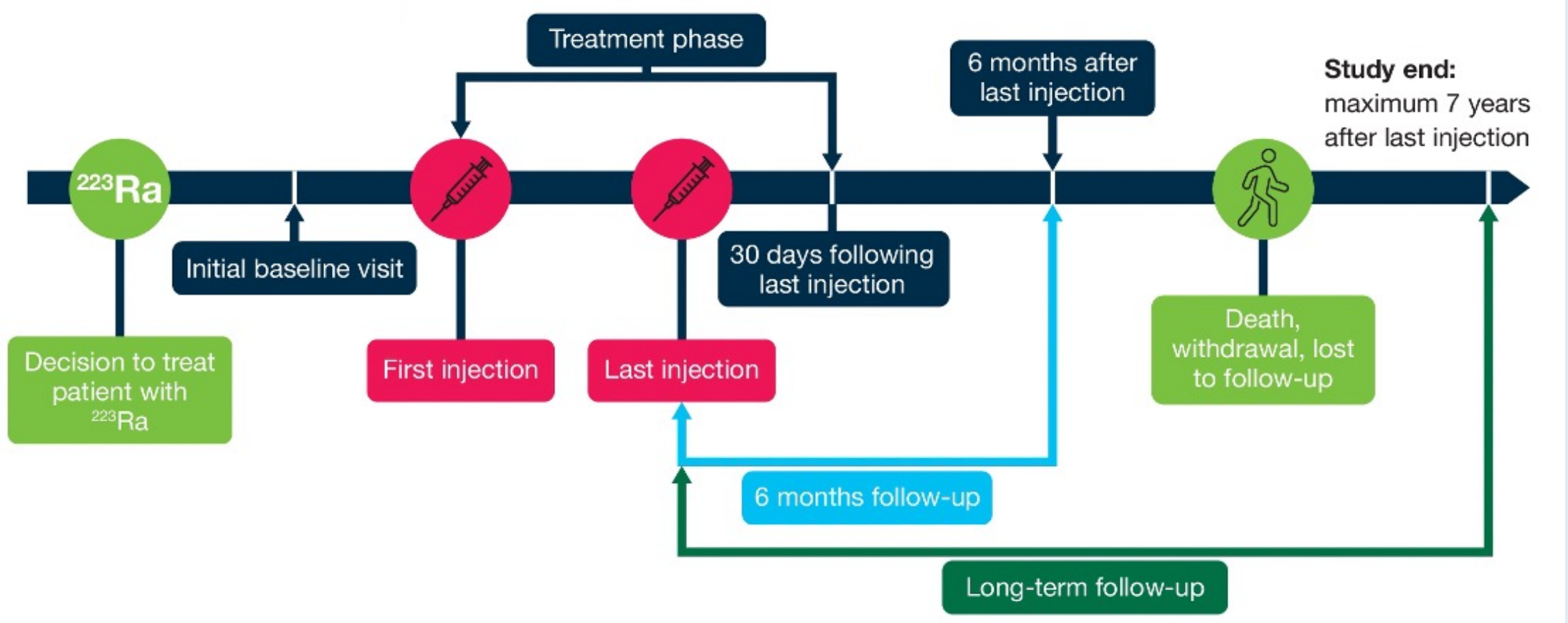
Abstract 5050

Real-world safety and effectiveness of radium-223 (^{223}Ra) in patients with metastatic castration-resistant prostate cancer (mCRPC) treated in the US: the non-interventional REASSURE study

Daniel Y. Song,[1] Saby George,[2] Shawn Zimberg,[3] Luke Nordquist,[4] Jeffrey Tomaszewski,[5] Peter S. Conti,[6] Jeff Meltzer,[7] Frank Verholen,[8] Anja Schmall,[8] Celestia Higano,[9] and Oliver Sartor[10]

RTP RESEARCH TO PRACTICE

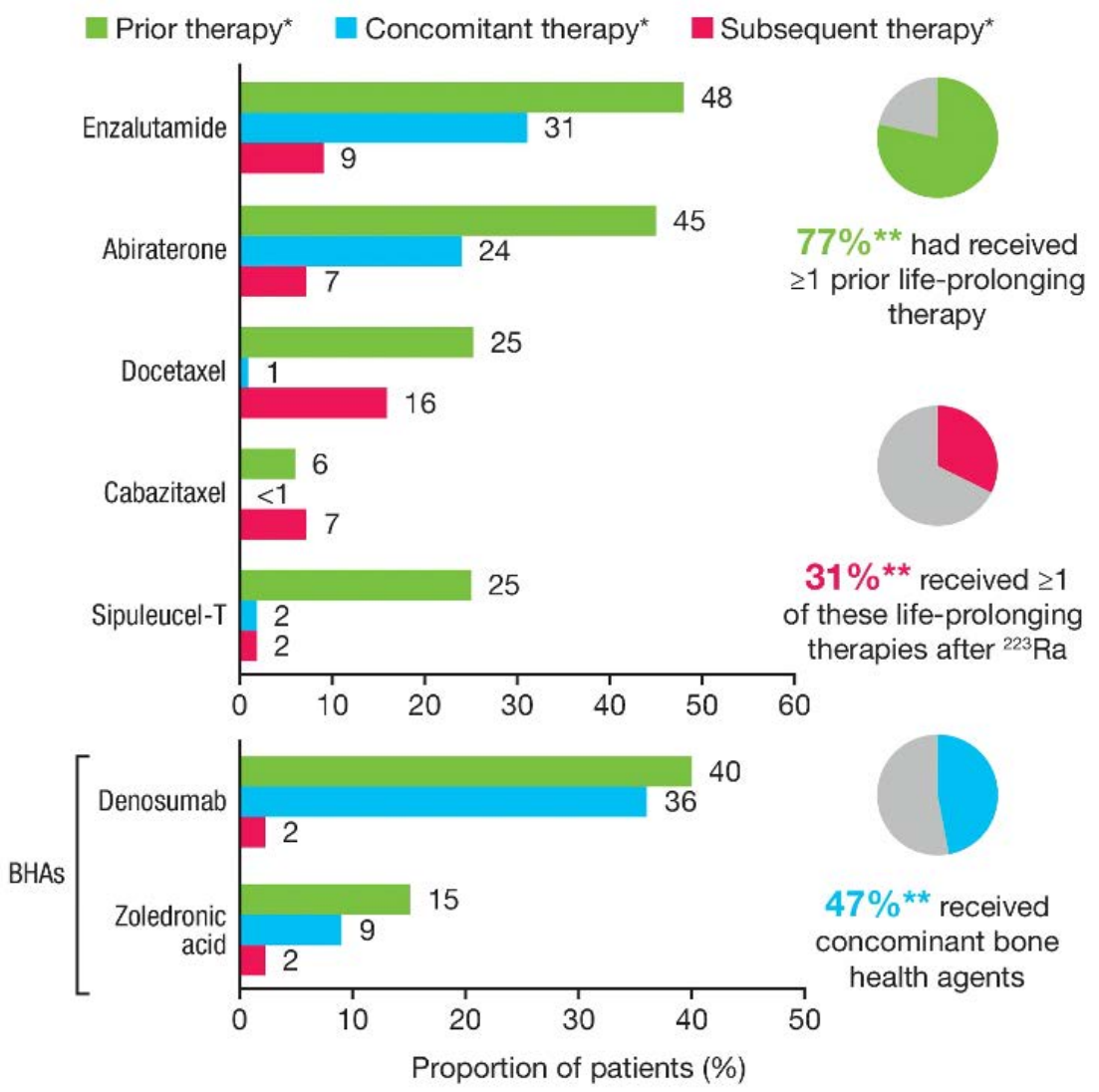
REASSURE: Study Design and Objective



- As practice patterns, drug availability and the treatment landscape are different in the US than in other parts of the world, this analysis aimed to evaluate the safety and effectiveness of ^{223}Ra based on data from the second planned interim analysis of REASSURE for patients treated in the US (N = 498)

Higano CS et al. *Cancer* 2024 February 10;[Online ahead of print]; Song DY et al. ASCO 2023;Abstract 5050.

REASSURE: Life-Prolonging Therapies, Bone Health Agents (BHAs) and Safety



Adverse events, %	N = 498
Any treatment-emergent drug related AE, treatment-emergent SAE or drug-related SAE	44
Treatment-emergent drug-related AE	32
Grade ≥ 3	10
Resulting in ^{223}Ra discontinuation	4
Treatment-emergent SAEs	21
Drug-related SAE	6
Drug-related SAE resulting in death	<1
Most common (>5% of patients) any-grade drug–related TEAEs	
Diarrhea	10
Fatigue	9
Anemia	8
Nausea	7
Any post-treatment grade 3-4 hematological AEs based on bone marrow suppression	12
Leukopenia	1
Neutropenia	1
Pancytopenia	≤1
Thrombocytopenia	4
Anemia	9

SAE = serious adverse event

Song DY et al. ASCO 2023;Abstract 5050.

RTP RESEARCH TO PRACTICE

REASSURE: Author Conclusions and Summary

RESULTS SUMMARY

- Half (51%) of patients received ^{223}Ra in combination with another life-prolonging therapy, with ^{223}Ra and enzalutamide being the most frequent combination
- The safety profile of ^{223}Ra in these patients was consistent with that of the phase 3 ALSYMPCA study.[1,2] No new safety signals were seen
- In routine clinical practice in the US, median OS after ^{223}Ra treatment was close to 18 months

CONCLUSIONS

- In real world clinical practice in the US, ^{223}Ra was safe and effective. Treatment with ^{223}Ra did not preclude patients from receiving subsequent therapies, including chemotherapy. Our observations show that ^{223}Ra can easily be integrated into the treatment sequence for patients with mCRPC

Song DY et al. ASCO 2023;Abstract 5050.

RTP RESEARCH TO PRACTICE

PRINCE: Phase I trial of ^{177}Lu-PSMA-617 in combination with pembrolizumab in patients with metastatic castration-resistant prostate cancer (mCRPC)

Authors: Shahneen Sandhu[1,2], Anthony M. Joshua[3], Louise Emmett[3], Lavinia Spain[1,4], Lisa G. Horvath[5], Megan Crumbaker[3], Arsha Anton[4], Roslyn Wallace[1], Anupama Pasam[1], Mathias Bressel[1,2], Erin Cassidy[1], Patricia Banks[1], Nattakorn Dhiantravan[1], Timothy J. Akhurst[1], Aravind Ravi Kumar[1], Ramin Alipour[1], Mark Scalzo[1], Scott Williams[1,2], Rod J. Hicks[6], Michael S. Hofman[1,2]

[1]Peter MacCallum Cancer Centre, Melbourne; [2]Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne; [3]St Vincent's Hospital, Sydney; [4]Eastern Health, Melbourne; [5]Chris O'Brien Lifehouse, Sydney; [6]St Vincent's Medical School, University of Melbourne, Melbourne

ASCO 2022;Abstract 5017

RTP RESEARCH TO PRACTICE

PRINCE: Treatment-Related Adverse Events (TRAEs)

Table 1: TRAE	Any grade n (%)	Grade 3, n (%)
Xerostomia	29 (78%)	
Fatigue	16 (43%)	2 (5%)
Rash	9 (24%)	
Nausea	10 (27%)	
Pruritis	10 (27%)	
Anorexia	6 (16%)	
Thrombocytopenia	6 (16%)	
Diarrhea	5 (14%)	
Bone pain (flare)	4 (11%)	
Alanine aminotransferase elevation	4 (11%)	
Dry eye	3 (8%)	
Dysgeusia	3 (8%)	
Weight loss	3 (8%)	
Anemia	3 (8%)	1(3%)
Aspartate aminotransferase elevation	3 (8%)	
Amylase elevation	3 (8%)	1 (3%)
Arthralgia	4 (11%)	
Myalgia	3 (8%)	
Neutropenia	1 (3%)	

Table 2: Immune Related Adverse Events (irAEs)	Grade 2 n (%)	Grade 3 n (%)
Fatigue	2 (5%)	2 (5%)
Amylase elevation	-	1 (3%)
Colitis *	-	2 (5%)
Pancreatitis	-	1(3%)
Nephritis	-	1(3%)
Type I Diabetes	-	1 (3%)
Mucosal Pemphigus #	-	1 (3%)
Ocular Myasthenia Gravis *	-	1 (3%)
Optic Neuritis #	1 (3%)	-
Myocarditis *		1 (3%)
Pneumonitis	1 (3%)	1(3%)

Discontinuation for toxicity:
Pembrolizumab, n (%): 5 (19%)
^{177}Lu-PSMA-617, n (%): 0 (0%)

Sandhu S et al. ASCO 2022;Abstract 5017.

Positive Top-Line Results Announced from the Pivotal Phase III SPLASH Trial of ^{177}Lu-PNT2002 for mCRPC

Press Release – December 18, 2023

"[The manufacturers] today announced statistically significant topline results from the pivotal phase 3 SPLASH study evaluating the efficacy and safety of ^{177}Lu-PNT2002, a prostate-specific membrane antigen (PSMA)-targeted radioligand therapy (RLT), in patients with metastatic castration-resistant prostate cancer (mCRPC) after progression on an androgen receptor pathway inhibitor (ARPI).

The SPLASH trial met its primary endpoint, demonstrating a median radiographic progression-free survival (rPFS) per blinded independent central review of 9.5 months for patients treated with ^{177}Lu-PNT2002, compared to 6.0 months for patients treated with ARPI in the control arm, a statistically significant 29% reduction in the risk of radiographic progression or death (hazard ratio [HR] 0.71; p = 0.0088). At the time of the analysis, interim overall survival (OS) results were immature (46% of protocol-specified target OS events reached), the HR was 1.11. The companies expect additional, follow-up data in 2024 prior to the potential submission of a New Drug Application (NDA)."

https://www.globenewswire.com/news-release/2023/12/18/2797730/0/en/Lantheus-and-POINT-Biopharma-Announce-Positive-Topline-Results-from-Pivotal-SPLASH-Trial-in-Metastatic-Castration-Resistant-Prostate-Cancer.html

RTP RESEARCH TO PRACTICE

PARP Monotherapy
Overall survival

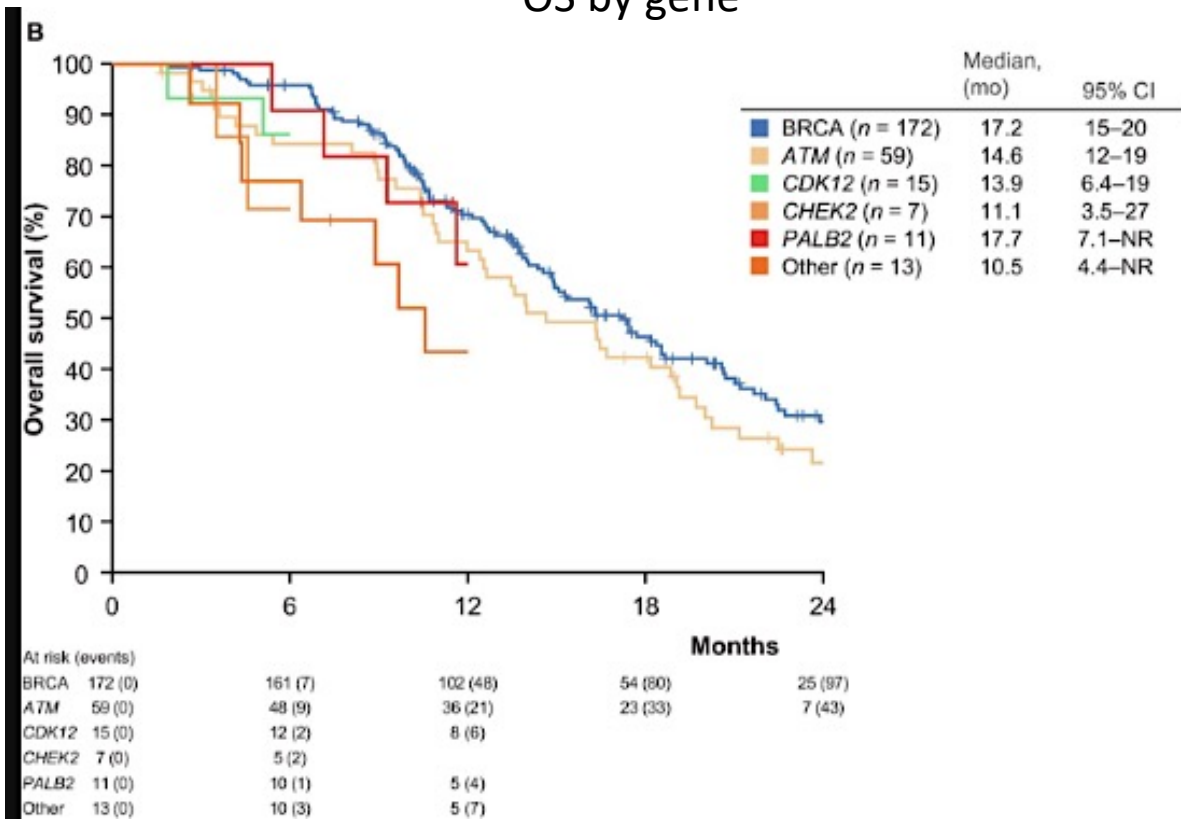
PROFOUND: Olaparib post ARPi, versus ARPi
Cohort A: *BRCA1, BRCA2, or ATM*

Table: 610O

	Cohort A		Overall population	
	Olaparib n=162	Control n=83	Olaparib n=256	Control n=131
Events, n (%)	91 (56)	57 (69)	160 (63)	88 (67)
Median (95% CI) OS (months)	**19.1 (17.4, 23.4)**	**14.7 (11.9, 18.8)**	**17.3 (15.5, 18.6)**	**14.0 (11.5, 17.1)**
HR (95% CI)	**0.69 (0.50, 0.97)**		**0.79 (0.61, 1.03)**	
***P* value (2-sided)**	**0.0175***		**0.0515†**	
OS rate (%)				
12-month	73	61	67	56
18-month	54	42	47	39
Median follow-up (months)‡	21.9	21.0	20.7	20.5

*0.047 alpha spent at final OS analysis; †Nominal; ‡Censored pts. CI, confidence interval; HR, hazard ratio; OS overall survival

Triton 2: Rucaparib post ARPi and Docetaxel
OS by gene



Courtesy of Alan H Bryce, MD.

FDA Approves Olaparib with Abiraterone and Prednisone (or Prednisolone) for mCRPC with a BRCA Mutation

Press Release – May 31, 2023

"… the Food and Drug Administration approved olaparib with abiraterone and prednisone (or prednisolone) for adult patients with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC), as determined by an FDA-approved companion diagnostic test.

Efficacy was evaluated in the PROpel trial (NCT03732820) that enrolled 796 patients with mCRPC, Patients were randomized (1:1) to receive either olaparib with abiraterone or placebo with abiraterone and also received prednisone or prednisolone. The major efficacy outcome measure was investigator-assessed radiological progression-free survival (rPFS) per RECIST version 1.1 for soft tissue and Prostate Cancer Working Group criteria for bone lesions. Overall survival (OS) was an additional endpoint.

The recommended olaparib dose is 300 mg taken orally twice daily with or without food. The recommended abiraterone dose is 1000 mg taken orally once daily. Abiraterone should be administered with prednisone or prednisolone 5 mg orally twice daily. Patients should also receive a GnRH analog concurrently or should have had a prior bilateral orchiectomy."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-olaparib-abiraterone-and-prednisone-or-prednisolone-brca-mutated-metastatic-castration

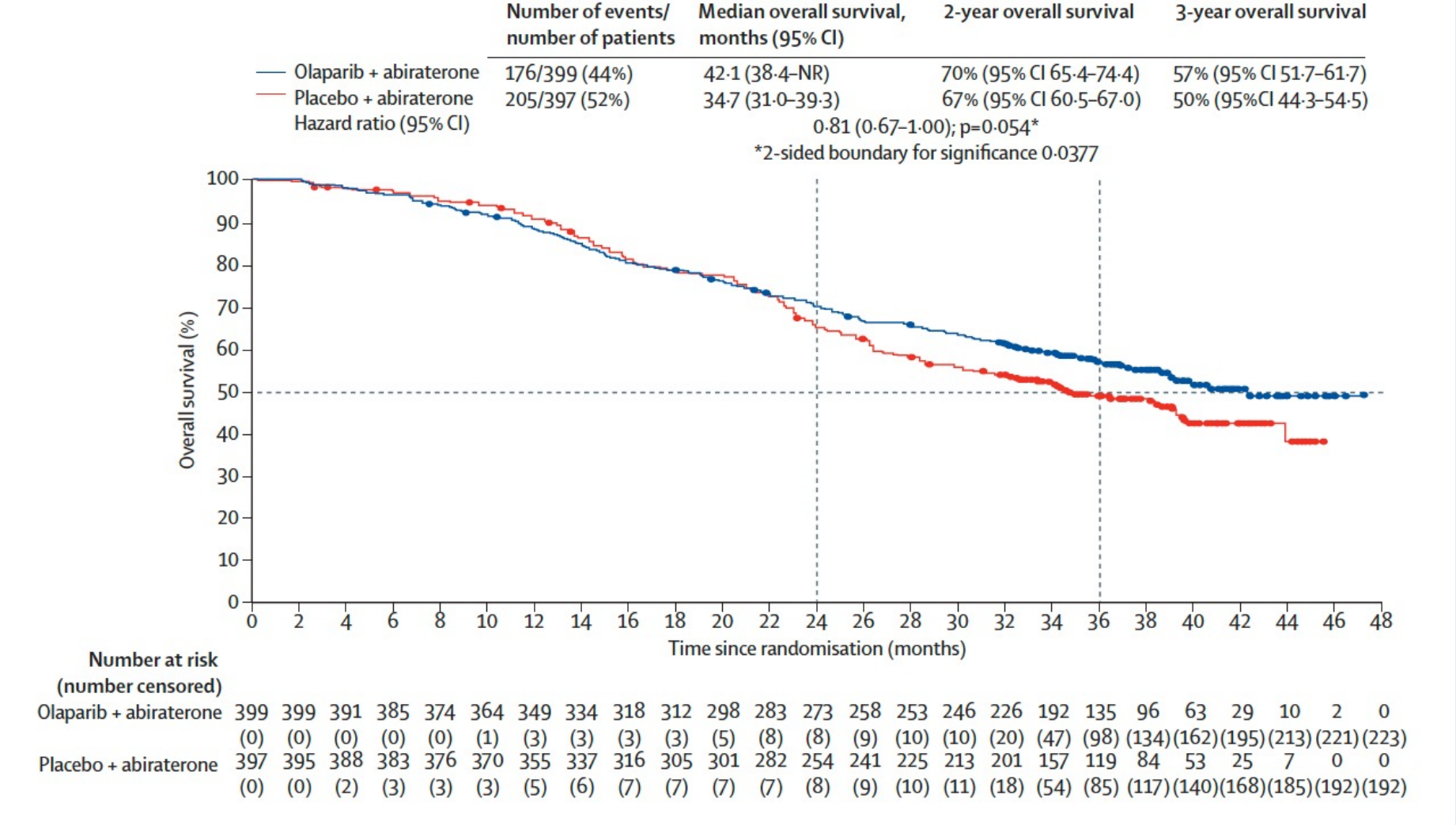
Lancet Oncol 2023;24(10):1094-108

Articles

Olaparib plus abiraterone versus placebo plus abiraterone in metastatic castration-resistant prostate cancer (PROpel): final prespecified overall survival results of a randomised, double-blind, phase 3 trial

Fred Saad, Noel W Clarke, Mototsugu Oya, Neal Shore , Giuseppe Procopio, João Daniel Guedes, Cagatay Arslan, Niven Mehra, Francis Parnis, Emma Brown, Friederike Schlürmann, Jae Young Joung, Mikio Sugimoto, Oliver Sartor, Yu-Zhen Liu, Christian Poehlein, Laura Barker, Paula Michelle del Rosario, Andrew J Armstrong

PROpel Trial: Final Prespecified Overall Survival Results in Intent-to-Treat Population

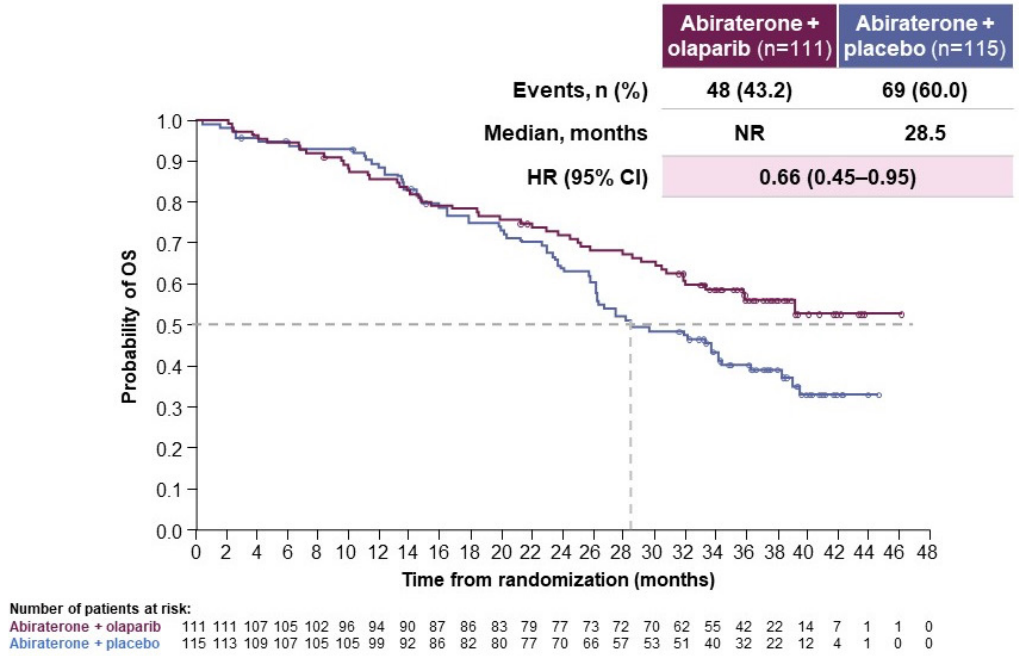


Saad F et al. *Lancet Oncol* 2023;24(10):1094-108.

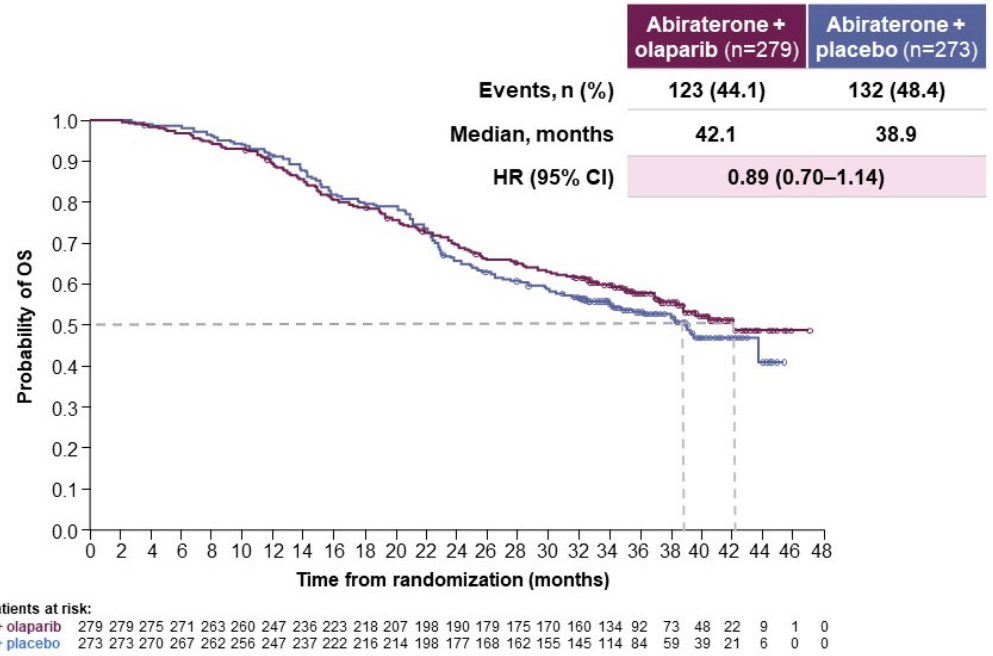
PROpel: Overall Survival (OS) in HRRm and Non-HRRm Subgroups (DCO3)

A trend towards OS benefit was observed across HRRm and non-HRRm subgroups

HRRm (28.4% of ITT population)



Non-HRRm (69.3% of ITT population)



DCO3: 12 October 2022.
The preplanned tumor tissue and plasma ctDNA testing was conducted after randomization and before primary analysis. Results from tumor tissue and plasma ctDNA were combined to determine patients HRRm status (see supplement for more details). 18 patients had unknown HRRm status.

HRRm = homologous recombination repair mutation

Clarke N et al. Genitourinary Cancers Symposium 2023;Abstract LBA16.

FDA Approves Niraparib and Abiraterone Acetate with Prednisone for mCRPC with a BRCA Mutation

Press Release – August 11, 2023

"... the Food and Drug Administration approved the fixed dose combination of niraparib and abiraterone acetate, with prednisone, for adult patients with deleterious or suspected deleterious BRCA-mutated castration-resistant prostate cancer (mCRPC), as determined by an FDA-approved test.

Efficacy was evaluated in Cohort 1 of MAGNITUDE (NCT03748641), a randomized, double-blind, placebo-controlled trial enrolling 423 patients with homologous recombination repair (HRR) gene-mutated mCRPC. Patients were randomized (1:1) to receive niraparib 200 mg and abiraterone acetate 1,000 mg plus prednisone 10 mg daily or placebo and abiraterone acetate plus prednisone daily. The major efficacy outcome measure was radiographic progression-free survival (rPFS) per RECIST version 1.1 for soft tissue and Prostate Cancer Working Group 3 criteria for bone, assessed by blinded independent central review. Overall survival (OS) was an additional endpoint.

The recommended dose is 200 mg niraparib and 1,000 mg abiraterone acetate taken orally once daily in combination with 10 mg of prednisone daily until disease progression or unacceptable toxicity. Patients receiving niraparib and abiraterone acetate plus prednisone should also receive a GnRH analog concurrently or should have had bilateral orchiectomy."

https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-niraparib-and-abiraterone-acetate-plus-prednisone-brca-mutated-metastatic-castration

RTP RESEARCH TO PRACTICE

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY
driving innovation in oncology

ORIGINAL ARTICLE

Niraparib plus abiraterone acetate with prednisone in patients with metastatic castration-resistant prostate cancer and homologous recombination repair gene alterations: second interim analysis of the randomized phase III MAGNITUDE trial☆

K. N. Chi[1*], S. Sandhu[2,3], M. R. Smith[4,5], G. Attard[6,7], M. Saad[8], D. Olmos[9], E. Castro[10], G. Roubaud[11], A. J. Pereira de Santana Gomes[12], E. J. Small[13], D. E. Rathkopf[14,15], H. Gurney[16], W. Jung[17], G. E. Mason[18], S. Dibaj[19], D. Wu[20], B. Diorio[21], K. Urtishak[18], A. del Corral[22], P. Francis[23], W. Kim[20] & E. Efstathiou[24]

2023;34(9):772-82

FDA Approves Talazoparib with Enzalutamide for mCRPC with an HRR Gene Mutation

Press Release – June 20, 2023

"… the Food and Drug Administration approved talazoparib with enzalutamide for homologous recombination repair (HRR) gene-mutated metastatic castration-resistant prostate cancer (mCRPC).

Efficacy was evaluated in TALAPRO-2 (NCT03395197), a randomized, double-blind, placebo-controlled, multi-cohort trial enrolling 399 patients with HRR gene-mutated mCRPC. Patients were randomized (1:1) to receive enzalutamide 160 mg daily plus either talazoparib 0.5 mg or placebo daily. The major efficacy outcome measure was radiographic progression-free survival (rPFS) per RECIST version 1.1 for soft tissue and Prostate Cancer Working Group 3 criteria for bone, assessed by blinded independent central review.

The recommended talazoparib dose is 0.5 mg taken orally once daily in combination with enzalutamide until disease progression or unacceptable toxicity. The recommended enzalutamide dose is 160 mg taken orally once daily. Patients receiving talazoparib and enzalutamide should also receive a GnRH analog concurrently or should have had bilateral orchiectomy."

https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-talazoparib-enzalutamide-hrr-gene-mutated-metastatic-castration-resistant-prostate

Lancet Oncol 2023;402(10398):291-303

Articles

Talazoparib plus enzalutamide in men with first-line metastatic castration-resistant prostate cancer (TALAPRO-2): a randomised, placebo-controlled, phase 3 trial

Neeraj Agarwal, Arun A Azad, Joan Carles, Andre P Fay, Nobuaki M*
Peter C C Fong, Eric Voog, Robert J Jones, Neal D Shore, Curtis Dunsh
*Nicola Di Santo, Fabian Zohren, Karim Fizazi**

2024;30(1):257-64

nature medicine

Article

https://doi.org/10.1038/s41591-023-02704-x

First-line talazoparib with enzalutamide in HRR-deficient metastatic castration-resistant prostate cancer: the phase 3 TALAPRO-2 trial

RTP RESEARCH TO PRACTICE

Safety Summary

	PROPEL Olaparib + Abiraterone	MAGNITUDE Niraparib + Abiraterone	TALAPRO-2 Talazoparib + Enzaluatmide
Select G3-4 Toxicities % (all grades %)			
Anemia ---Transfusion Rate	16.3 (50) 18%	30.1 (50.0) 27.4%	46 (66) 39%
Fatigue	2.5 (39.0)	3.3 (29.7)	4 (34)
Nausea	0.3 (31.0)	0.5 (24.5)	<1 (21)
Hypertension	3.8 (15.0)	33 (15.6)	5 (14)
Pulmonary Embolism	7.3%	1.9%	2.5%
Outcomes			
PARP interruption	49%	49.1%	62.0%
PARP dose reduction	22.6%	20.3%	53.0%
PARP discontinuation	17.3%	15.1%	19.0%

- Toxicities are largely a class effect of PARPi's. Myelosuppression and GI toxicity are most prominent.
- AE's of special interest include MDS/AML and PE.

Courtesy of Alan H Bryce, MD.

Clarke. NEJM Evid. 2022;1. Chi. J Clin Oncol. 2023; JCO2201649. Fizazi. Lancet. 2023;402

Second Opinion: Urologic Oncology Investigators Discuss How They Apply Clinical Research in the Care of Patients with Prostate Cancer

A CME Satellite Symposium Held in Conjunction with the American Urological Association Annual Meeting 2024 (AUA2024)

Friday, May 3, 2024

8:00 AM – 10:00 AM CT (9:00 AM – 11:00 AM ET)

Faculty

Rahul Aggarwal, MD
Adam S Kibel, MD
Laurence Klotz, CM, MD
Sandy Srinivas, MD

Moderator

Elisabeth I Heath, 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 for 5 minutes after the meeting ends.

NCPD credit information will be emailed to each participant within 5 business days.

RTP
RESEARCH
TO PRACTICE