Optimal Use of Hormonal Therapy in the Care of Patients with Prostate Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 29, 2026
5:00 PM – 6:00 PM ET

Faculty

William K Oh, MD
Mary-Ellen Taplin, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

William K Oh, MD
Director of Precision Medicine
Yale Cancer Center and Smilow Cancer Hospital
Professor of Medicine, Section of Medical Oncology
Yale School of Medicine
New Haven, Connecticut

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Mary-Ellen Taplin, MD
Professor of Medicine
Harvard School of Medicine
Dana-Farber Cancer Institute
Boston, Massachusetts

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by an educational grant from Johnson & Johnson.

Dr Love — Disclosures

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

RTP
RESEARCH
TO PRACTICE

Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant financial relationships to disclose.

Dr Oh — Disclosures

Advisory Committees	Analysis Group, AstraZeneca Pharmaceuticals LP, Biocartis, Novartis, Pfizer Inc
Stock Options/Stock — Public Companies	GeneDx

Dr Taplin — Disclosures

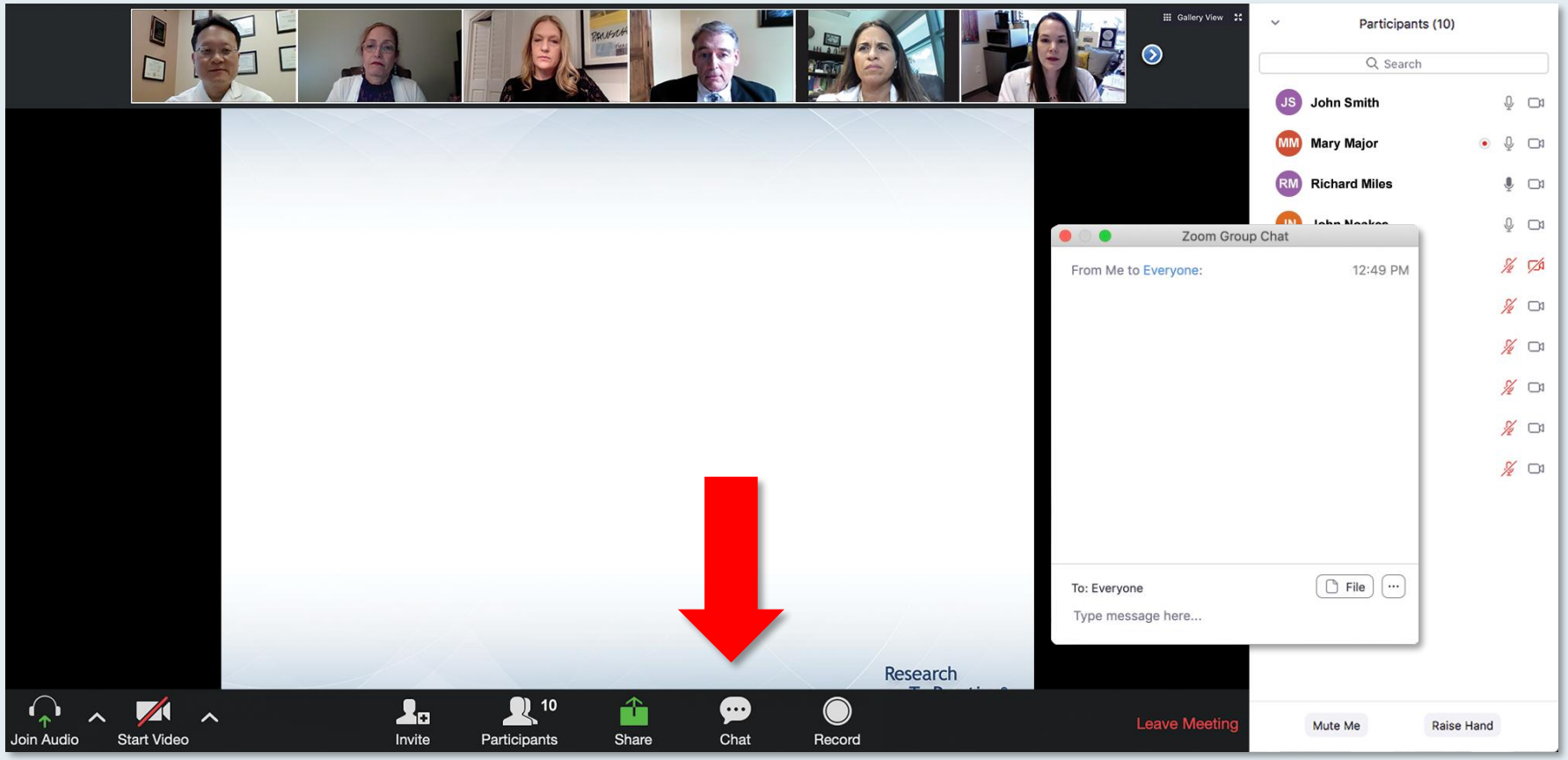
Advisory Committees	AstraZeneca Pharmaceuticals LP, BioNTech SE, Delphia Therapeutics, Flare Therapeutics, GSK, Johnson & Johnson, Novartis
Consulting Agreements	Johnson & Johnson
Data and Safety Monitoring Boards/ Committees	Amgen Inc
Education	Curio Science, DAVA Oncology
Nonrelevant Financial Relationships	AXIS Medical Education Inc, MJH Life Sciences, Reach MD, UpToDate

RTP RESEARCH TO PRACTICE

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

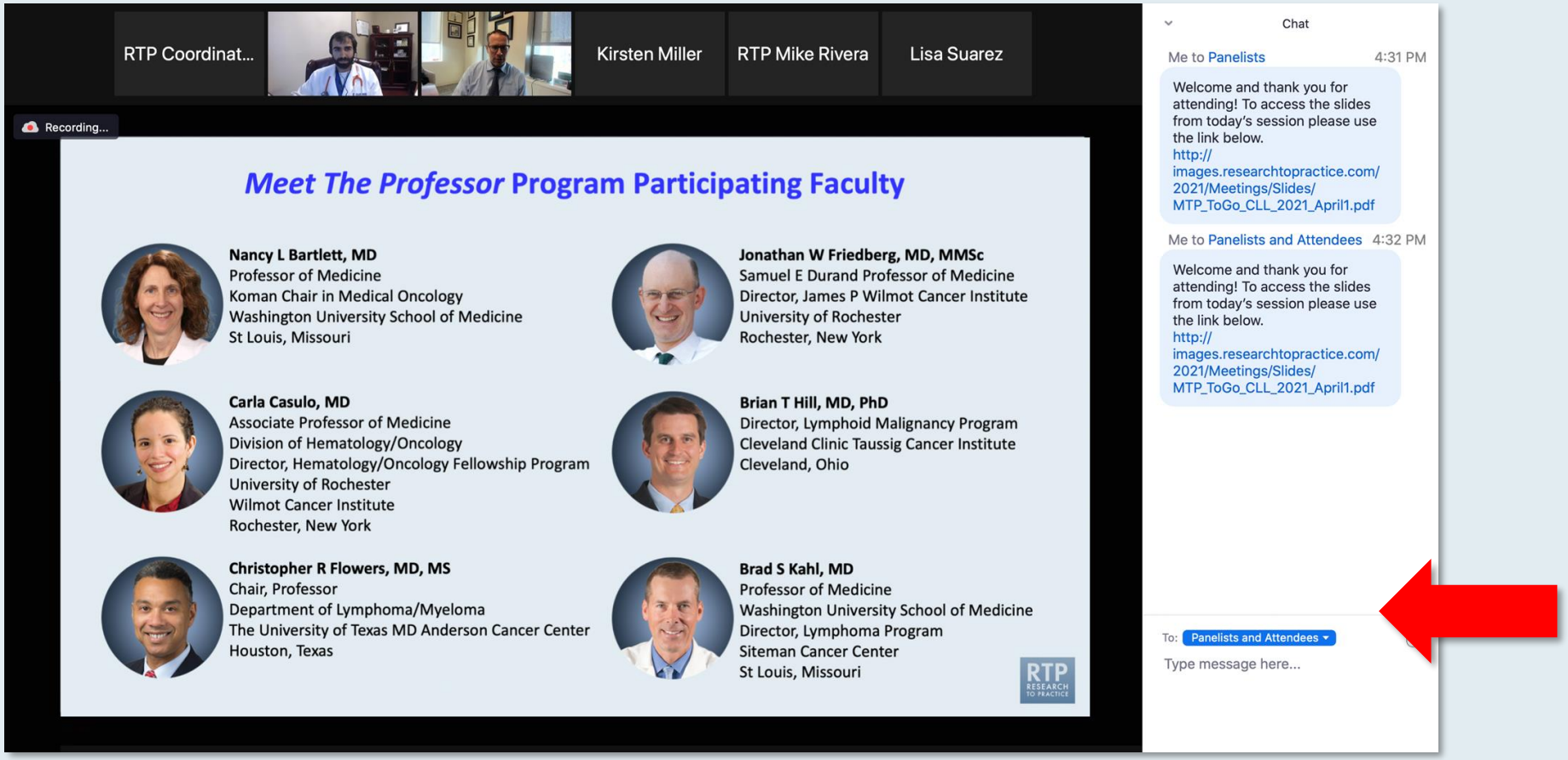


Feel free to submit questions now before the program begins and throughout the program.

RTP RESEARCH TO PRACTICE

Familiarizing Yourself with the Zoom Interface

Expand chat submission box

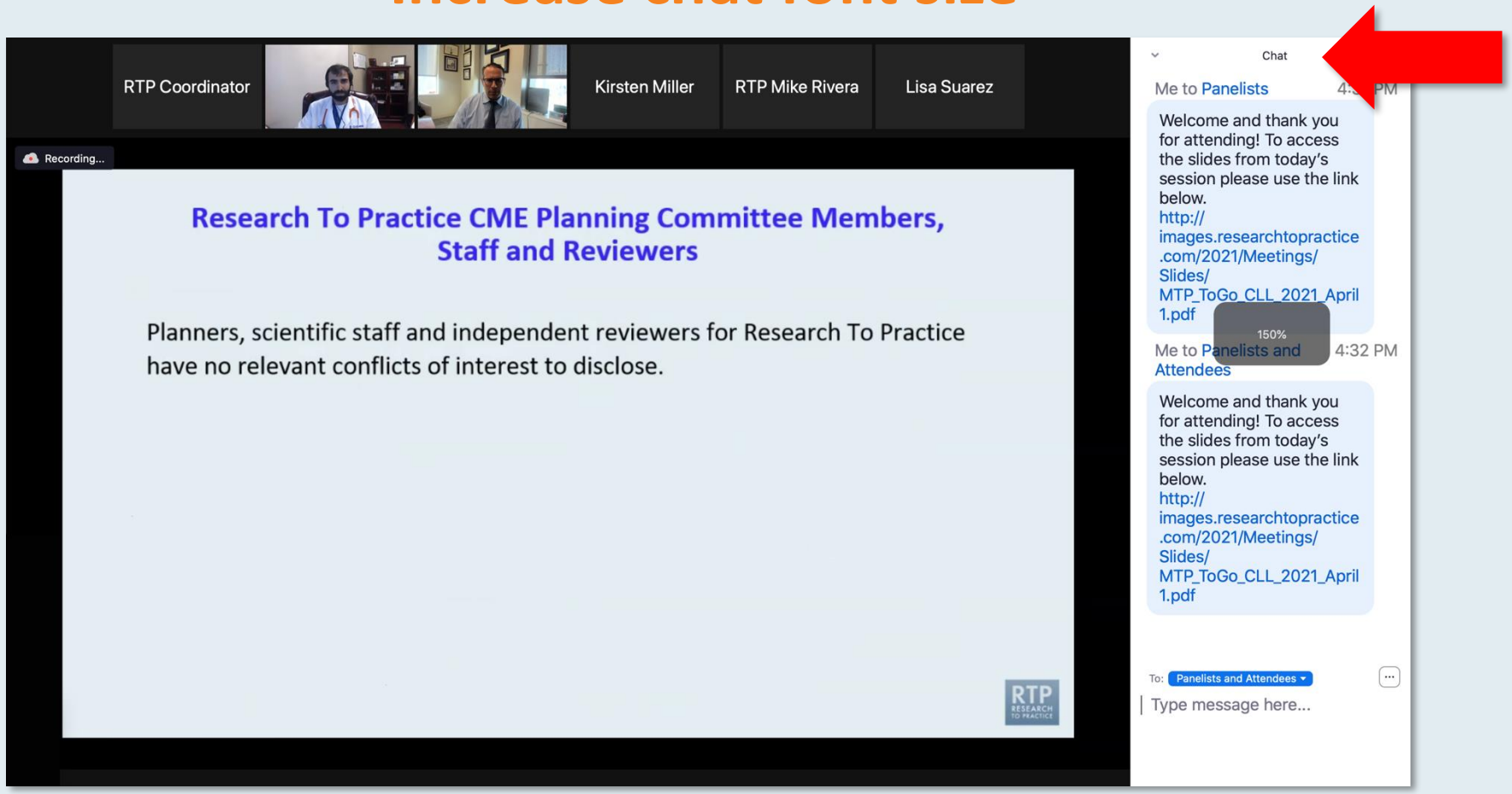


Drag the white line above the submission box up to create more space for your message.

RTP RESEARCH TO PRACTICE

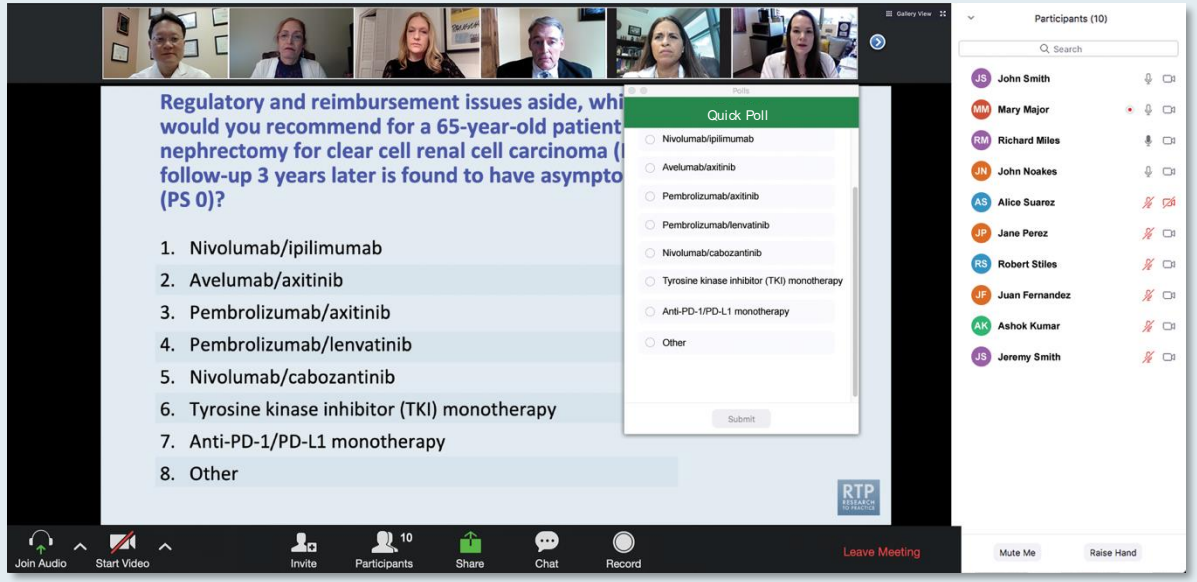
Familiarizing Yourself with the Zoom Interface

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



ONCOLOGY TODAY

WITH DR NEIL LOVE

Androgen Deprivation Therapy for Prostate Cancer — An Interview with Dr Rana R McKay

RANA R MCKAY, MD, FASCO
UC SAN DIEGO MOORES CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

The Implications of Recent Datasets for the Current and Future Management of Breast Cancer — An ASCO 2026 Review

A CME/MOC-Accredited Live Webinar

Thursday, July 30, 2026
5:00 PM – 6:30 PM ET

Faculty

Aditya Bardia, MD, MPH
Kevin Kalinsky, MD, MS, FASCO
Joyce O'Shaughnessy, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Join Us In Person or Virtually

Integrating New Advances into Community Oncology Practice

A Multitumor Symposium Hosted in Conjunction with the American Oncology Network

Saturday, August 22, 2026

JW Marriott Nashville | Nashville, Tennessee

Chronic Lymphocytic Leukemia
9:05 AM – 9:55 AM CT

Gastroesophageal Cancers
9:55 AM – 10:45 AM CT

Gynecologic Cancers
11:00 AM – 11:50 AM CT

Diffuse Large B-Cell Lymphoma
12:40 PM – 1:30 PM CT

Lung Cancer
1:30 PM – 2:20 PM CT

Moderator
Stephen “Fred” Divers, MD

RTP RESEARCH TO PRACTICE

The Implications of Recent Datasets for the Current and Future Management of Gynecologic Cancers — An ASCO 2026 Review

A CME/MOC-Accredited Live Webinar

Wednesday, August 26, 2026
5:00 PM – 6:00 PM ET

Faculty

Faculty to be announced

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Data + Perspectives: Investigators Discuss the Optimal Management of Relapsed/Refractory Multiple Myeloma

A CME-Accredited Satellite Symposium During the Society of Hematologic Oncology 2026 Annual Meeting

Wednesday, September 9, 2026
11:56 AM – 12:56 PM CT

Faculty

Noopur Raje, MD
Paul G Richardson, MD

Moderator

Robert Z Orlowski, MD, PhD

RTP RESEARCH TO PRACTICE

Grand Rounds

CME/MOC-Accredited Interactive Series

Regional Activities

Three Series

Integrating Recent Advances into the Management of Gastroesophageal Cancers

Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

Optimizing Therapy for Patients with Hormone Receptor-Positive Localized Breast Cancer

Host a 1-hour session at your institution:
Email Meetings@ResearchToPractice.com
or call (800) 233-6153

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.

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

RTP
RESEARCH TO PRACTICE

Optimal Use of Hormonal Therapy in the Care of Patients with Prostate Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 29, 2026
5:00 PM – 6:00 PM ET

Faculty

William K Oh, MD
Mary-Ellen Taplin, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Faculty

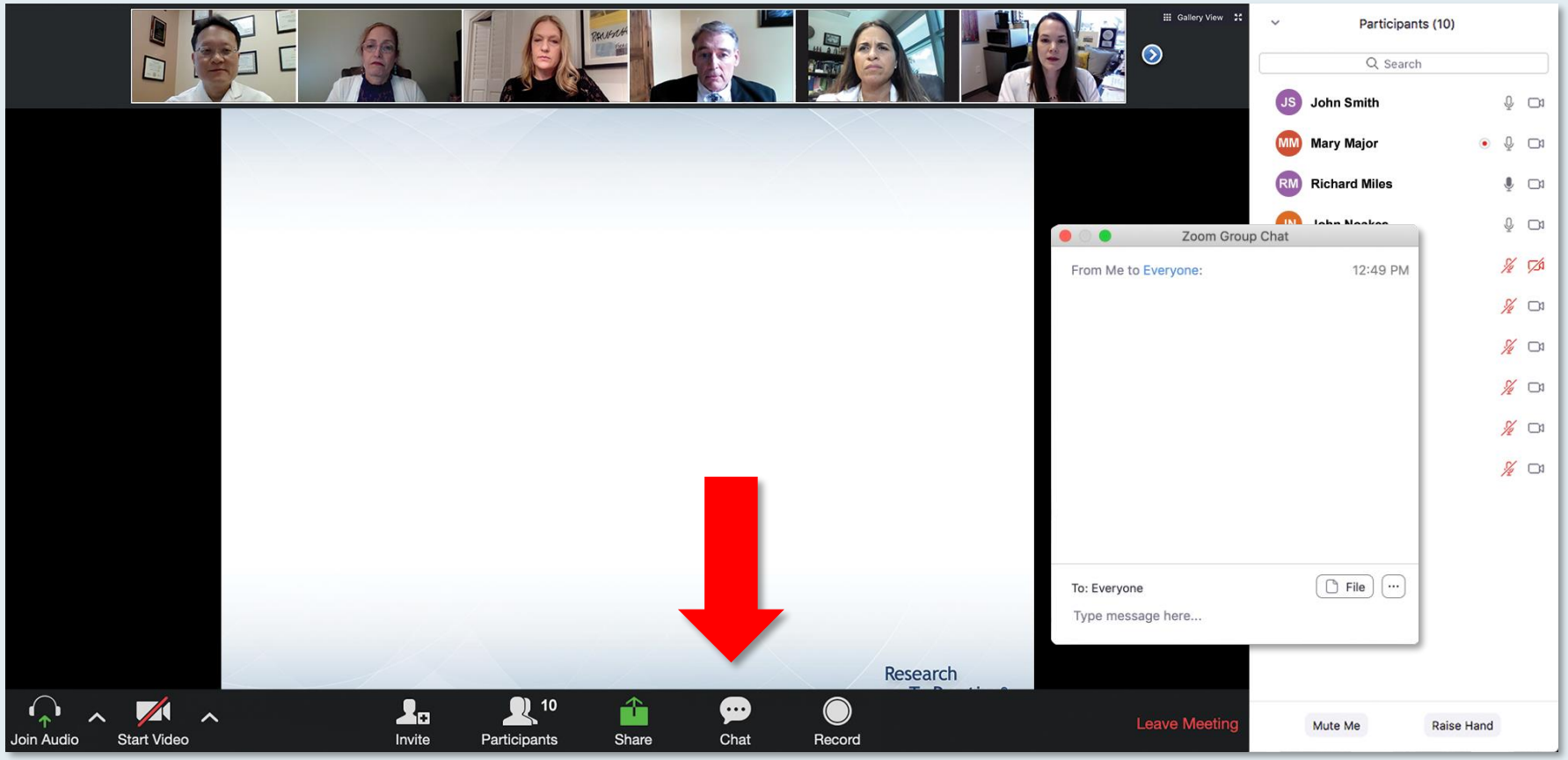
William K Oh, MD
Director of Precision Medicine
Yale Cancer Center and Smilow Cancer Hospital
Professor of Medicine, Section of Medical Oncology
Yale School of Medicine
New Haven, Connecticut

MODERATOR
Neil Love, MD
Research To Practice
Miami, Florida

Mary-Ellen Taplin, MD
Professor of Medicine
Harvard School of Medicine
Dana-Farber Cancer Institute
Boston, Massachusetts

RTP
RESEARCH
TO PRACTICE

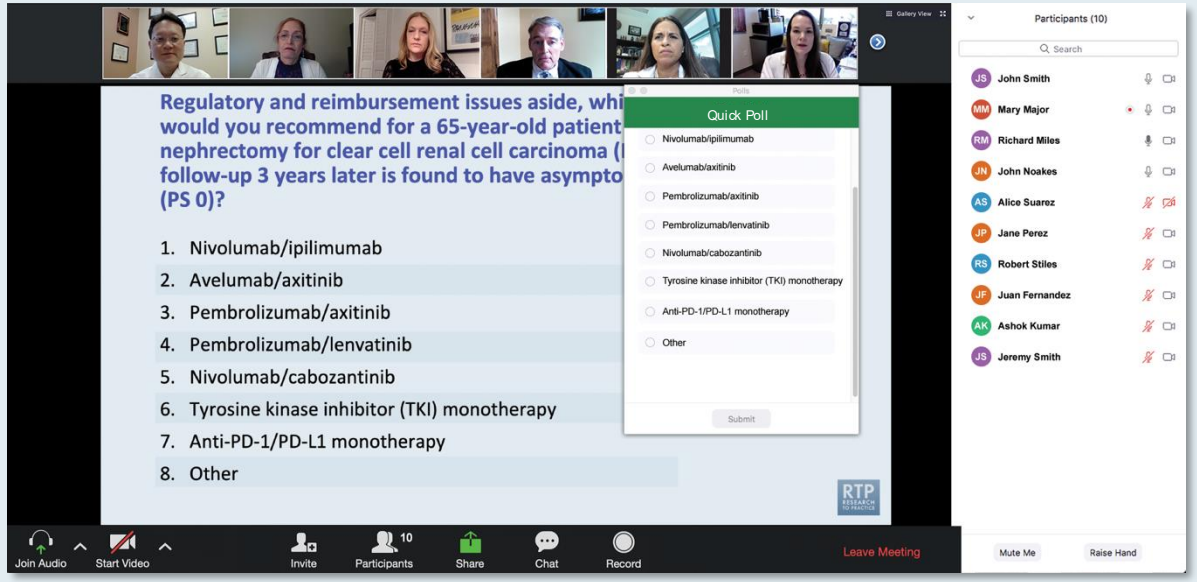
We Encourage Clinicians in Practice to Submit Questions



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



ONCOLOGY TODAY

WITH DR NEIL LOVE

Androgen Deprivation Therapy for Prostate Cancer — An Interview with Dr Rana R McKay

RANA R MCKAY, MD, FASCO
UC SAN DIEGO MOORES CANCER CENTER

Listen on Apple Podcasts

Spotify

Listen on Google Podcasts

The Implications of Recent Datasets for the Current and Future Management of Breast Cancer — An ASCO 2026 Review

A CME/MOC-Accredited Live Webinar

Thursday, July 30, 2026
5:00 PM – 6:30 PM ET

Faculty

Aditya Bardia, MD, MPH
Kevin Kalinsky, MD, MS, FASCO
Joyce O'Shaughnessy, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Join Us In Person or Virtually

Integrating New Advances into Community Oncology Practice

A Multitumor Symposium Hosted in Conjunction with the American Oncology Network

Saturday, August 22, 2026

JW Marriott Nashville | Nashville, Tennessee

Chronic Lymphocytic Leukemia
9:05 AM – 9:55 AM CT

Gastroesophageal Cancers
9:55 AM – 10:45 AM CT

Gynecologic Cancers
11:00 AM – 11:50 AM CT

Diffuse Large B-Cell Lymphoma
12:40 PM – 1:30 PM CT

Lung Cancer
1:30 PM – 2:20 PM CT

Moderator
Stephen “Fred” Divers, MD

RTP RESEARCH TO PRACTICE

The Implications of Recent Datasets for the Current and Future Management of Gynecologic Cancers — An ASCO 2026 Review

A CME/MOC-Accredited Live Webinar

Wednesday, August 26, 2026
5:00 PM – 6:00 PM ET

Faculty

Faculty to be announced

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Data + Perspectives: Investigators Discuss the Optimal Management of Relapsed/Refractory Multiple Myeloma

A CME-Accredited Satellite Symposium During the Society of Hematologic Oncology 2026 Annual Meeting

Wednesday, September 9, 2026
11:56 AM – 12:56 PM CT

Faculty

Noopur Raje, MD
Paul G Richardson, MD

Moderator

Robert Z Orlowski, MD, PhD

RTP RESEARCH TO PRACTICE

Grand Rounds

CME/MOC-Accredited Interactive Series

Regional Activities

Three Series

Integrating Recent Advances into the Management of Gastroesophageal Cancers

Optimizing the Use of Novel Therapies for Patients with Diffuse Large B-Cell Lymphoma

Optimizing Therapy for Patients with Hormone Receptor-Positive Localized Breast Cancer

Host a 1-hour session at your institution:
Email Meetings@ResearchToPractice.com
or call (800) 233-6153

RTP RESEARCH TO PRACTICE

Optimal Use of Hormonal Therapy in the Care of Patients with Prostate Cancer

A CME/MOC-Accredited Live Webinar

Wednesday, July 29, 2026
5:00 PM – 6:00 PM ET

Faculty

William K Oh, MD
Mary-Ellen Taplin, MD

Moderator

Neil Love, MD

RTP RESEARCH TO PRACTICE

Dr Oh — Disclosures

Advisory Committees	Analysis Group, AstraZeneca Pharmaceuticals LP, Biocartis, Novartis, Pfizer Inc
Stock Options/Stock — Public Companies	GeneDx

Dr Taplin — Disclosures

Advisory Committees	AstraZeneca Pharmaceuticals LP, BioNTech SE, Delphia Therapeutics, Flare Therapeutics, GSK, Johnson & Johnson, Novartis
Consulting Agreements	Johnson & Johnson
Data and Safety Monitoring Boards/ Committees	Amgen Inc
Education	Curio Science, DAVA Oncology
Nonrelevant Financial Relationships	AXIS Medical Education Inc, MJH Life Sciences, Reach MD, UpToDate

RTP RESEARCH TO PRACTICE

Dr Love — Disclosures

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

RTP
RESEARCH
TO PRACTICE

Commercial Support

This activity is supported by an educational grant from Johnson & Johnson.

Research To Practice CME Planning Committee Members, Staff and Reviewers

Planners, scientific staff and independent reviewers for Research To Practice have no relevant financial relationships 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: Another Perspective on the Treatment of Localized Prostate Cancer

Module 1: Nonmetastatic Disease

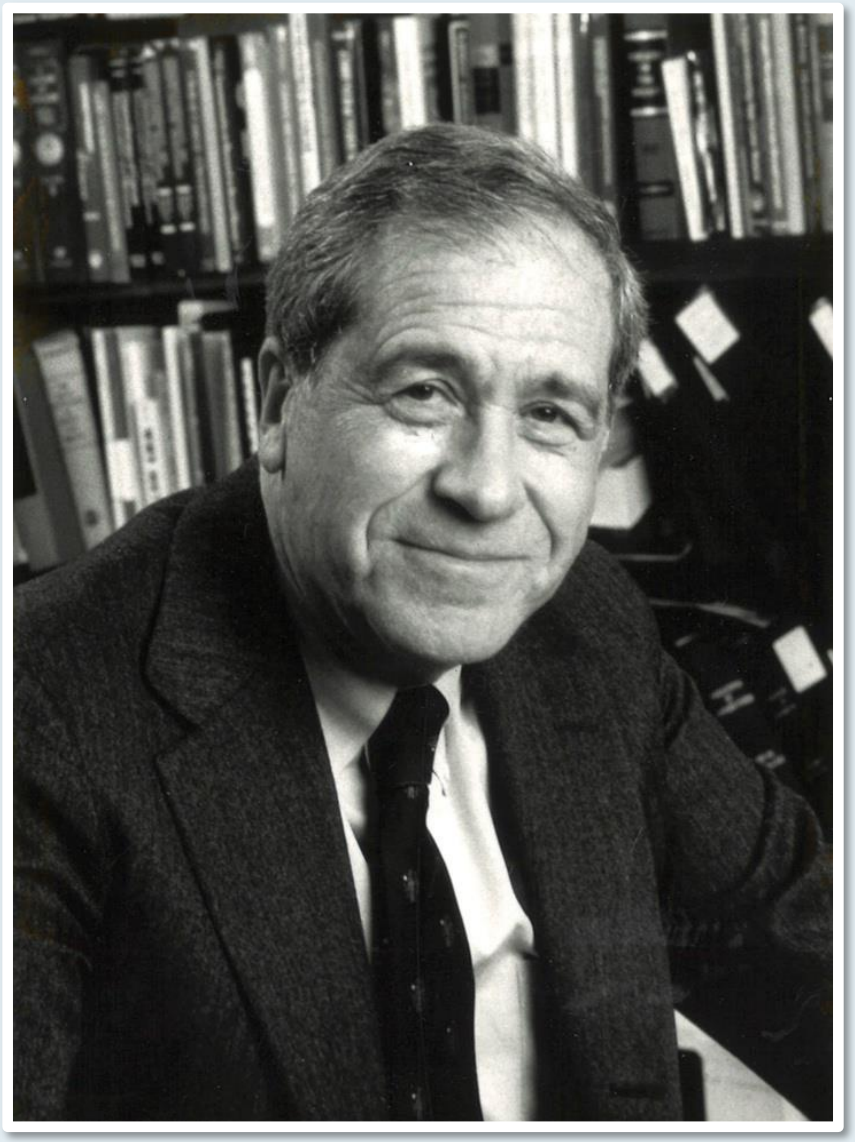
Module 2: Metastatic Androgen Pathway Modulation-Naïve and Androgen Pathway Modulation-Sensitive Disease

Agenda

Introduction: Another Perspective on the Treatment of Localized Prostate Cancer

Module 1: Nonmetastatic Disease

Module 2: Metastatic Androgen Pathway Modulation-Naïve and Androgen Pathway Modulation-Sensitive Disease



Bernard Fisher, MD

RTP
RESEARCH
TO PRACTICE

COMPARISON OF RADICAL MASTECTOMY WITH ALTERNATIVE TREATMENTS FOR PRIMARY BREAST CANCER

A First Report of Results from a Prospective Randomized Clinical Trial

BERNARD FISHER, MD, ELEANOR MONTAGUE, MD, CAROL REDMOND, ScD,
BRUCE BARTON, MS, DONNA BORLAND, RN, EDWIN R. FISHER, MD,
MELVIN DEUTSCH, MD, GEORGE SCHWARZ, MD, RICHARD MARGOLESE, MD.,
WILLIAM DONEGAN, MD, HERBERT VOLK, MD, CARL KONVOLINKA, MD,
BERNARD GARDNER, MD, ISIDORE COHN, JR, MD, GERSON LESNICK, MD,
ANATOLIO B. CRUZ, MD, WALTER LAWRENCE, MD, THOMAS NEALON, MD,
HARVEY BUTCHER, MD, RICHARD LAWTON, MD, (and other NSABP investigators)*

Fisher B et al. *Cancer* 1977;39(6 Suppl):2827-39.

TWENTY-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING TOTAL MASTECTOMY, LUMPECTOMY, AND LUMPECTOMY PLUS IRRADIATION FOR THE TREATMENT OF INVASIVE BREAST CANCER

BERNARD FISHER, M.D., STEWART ANDERSON, PH.D., JOHN BRYANT, PH.D., RICHARD G. MARGOLESE, M.D.,
MELVIN DEUTSCH, M.D., EDWIN R. FISHER, M.D., JONG-HYEON JEONG, PH.D., AND NORMAN WOLMARK, M.D.

Fisher B et al. *N Engl J Med* 2002;347(16):1233-41.

Is there a patient age at which you generally discourage RP?

 Dr Oh	75 years
 Dr Taplin	About 75 years
 Dr Dorff	80 years
 Dr Smith	70 years
 Dr Srinivas	75 years
 Dr Yu	80 years

RTP
RESEARCH
TO PRACTICE

Agenda

Introduction: Another Perspective on the Treatment of Localized Prostate Cancer

Module 1: Nonmetastatic Disease

Module 2: Metastatic Androgen Pathway Modulation-Naïve and Androgen Pathway Modulation-Sensitive Disease

RECENT DATA DEFINING THE OPTIMAL USE OF HORMONAL THERAPY FOR PATIENTS WITH NON-METASTATIC PROSTATE CANCER

MARY-ELLEN TAPLIN, MD

PROFESSOR OF MEDICINE

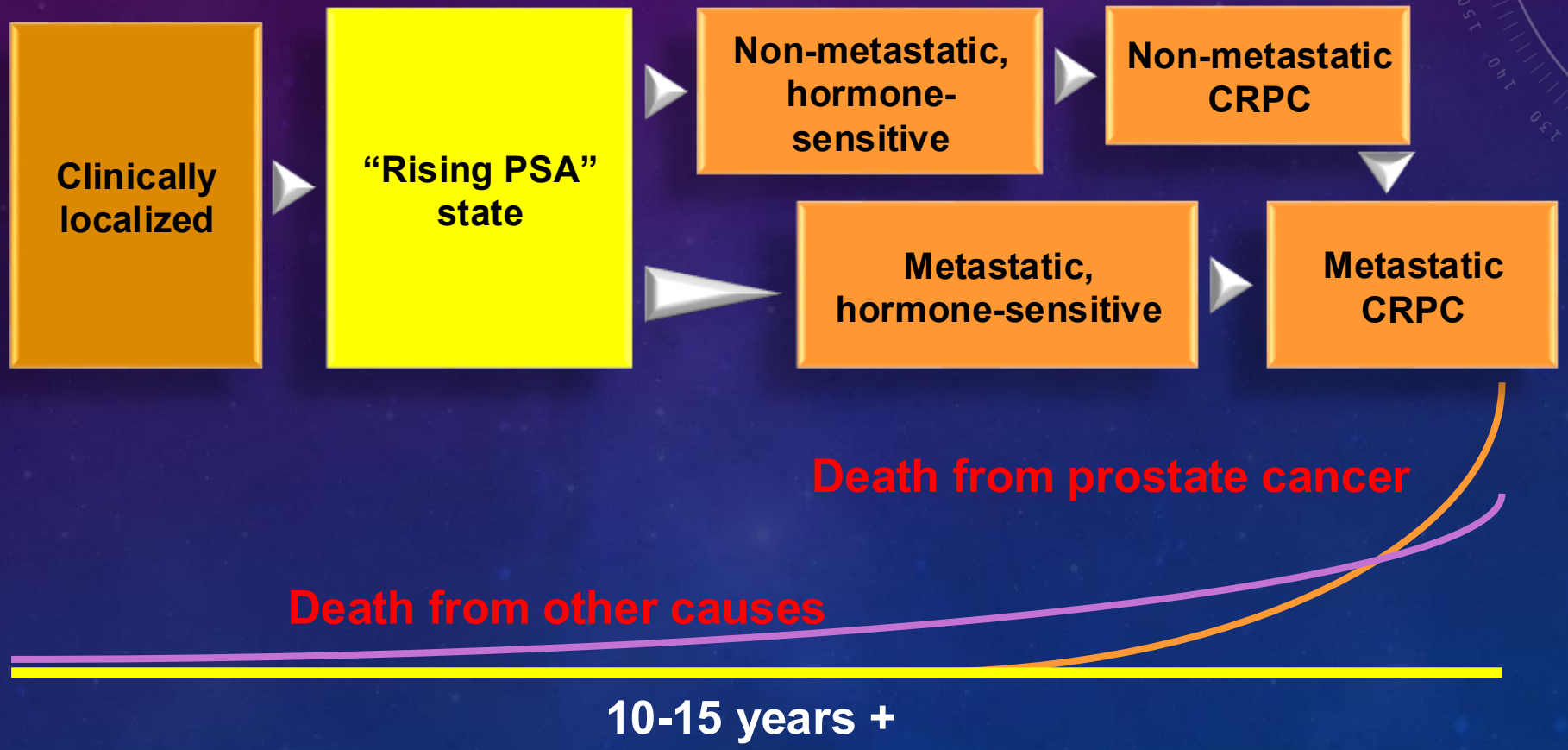
DANA-FARBER CANCER INSTITUTE

BOSTON, MA

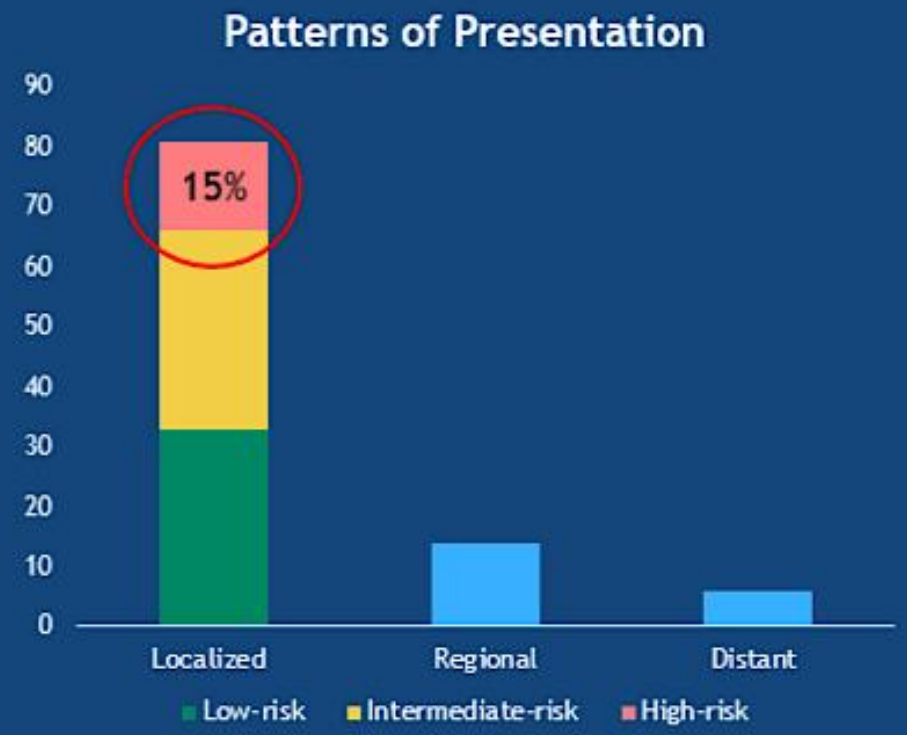
TOPICS

- Risk Stratification and selection of initial therapy for localized high-risk prostate cancer
- Major efficacy and safety results
  - PROTEUS – Apalutamide
  - EMBARK – Enzalutamide
  - PRESTO – abiraterone/apalutamide
- Ongoing phase III trials investigating ARPIs for nmHSPCa
- Cases
  - Localized high-risk candidate for neoadjuvant ADT/Apalutamide
  - nmHSPCa and high-risk biochemical recurrence

CLINICAL STATES OF PROSTATE CANCER



Defining High-Risk Prostate Cancer



Definition	Gleason	PSA	T Stage*
D'Amico/AUA/EAU	8-10	> 20	≥ cT2c
NCCN	8-10	> 20	≥ cT3
RTOG	≥ 7 8-10	20-100 < 100	Any T cT2c
CAPRA	Age, Gleason, PSA, clinical stage, and % of positive biopsy cores		
Kattan	Gleason, PSA, and cT (nomogram)		

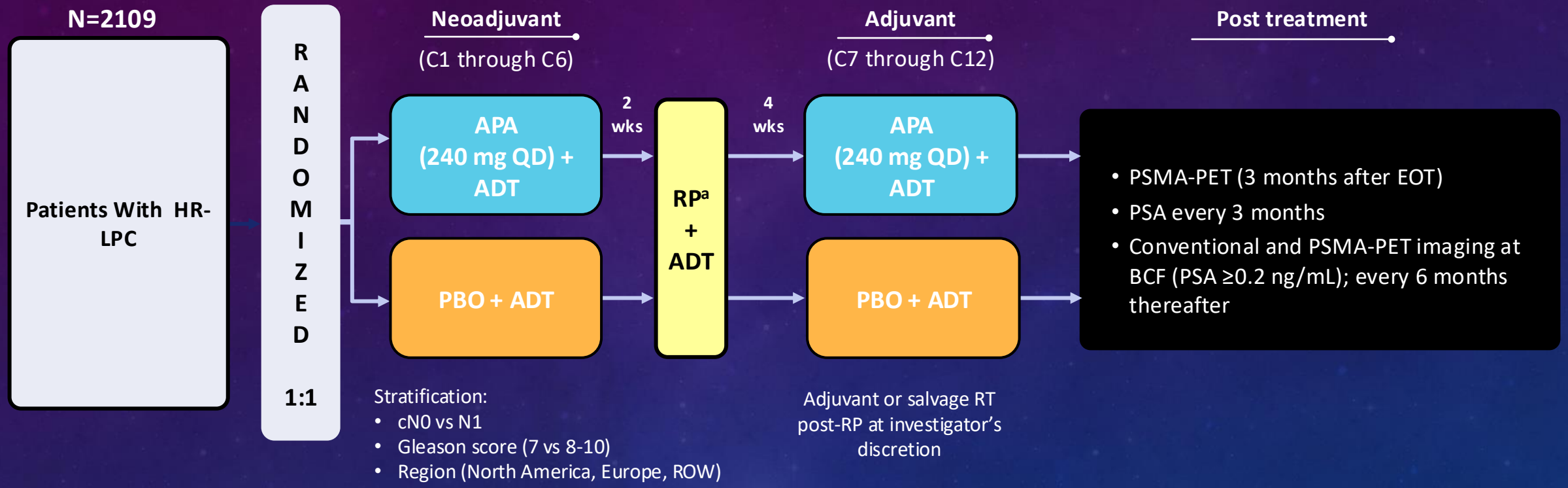
PSA=Prostate specific antigen; AUA=American Urologic Association; EAU=European Association of Urology; NCCN=National Comprehensive Cancer Network; RTOG=Radiation Therapy Oncology Group; CAPRA=Cancer of the Prostate Risk Assessment. *AJCC recognizes utility of multi-parametric MRI of the prostate.

Cooperberg, JCO, 2010
Chang, Nat Rev Clin Oncol, 2014

NCCN – Very High-Risk (at least one): T3b, T4, Primary Gleason pattern 5, 5 or more biopsy cores containing Grade Group 4 or 5, two or three NCCN high-risk features

McKay R et al. ASCO 2020

PROTEUS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 STUDY IN HR-LPC



- To complement these data, a substudy is ongoing to further inform on the role of APA + ADT + RP versus RP alone

Patients randomized from July 15, 2019, to June 30, 2022.
Protocol Amendment 7 for including PSMA-PET into MFS assessment (April 14, 2022).

APA, apalutamide; BCF, biochemical failure; C, cycle; EOT, end of treatment; PBO, placebo; PSA, prostate-specific antigen; PSMA-PET, prostate-specific membrane antigen positron emission tomography; QD, daily; ROW, rest of the world; RT, radiation therapy.
[a]APA/PBO is stopped 2 weeks prior to planned RP and then resumed 4 weeks after RP. Cardiovascular risk prophylaxis and venous thromboembolism prophylaxis given based on risk.

Taplin ME et al. ASCO 2026;Abstract LBA1

END POINTS AND HIERARCHICAL TESTING:

Dual primary, assessed by BICR

- pCR/MRD (ypT0 or ≤ypT2; ≤5 mm tumor)
- MFS (metastasis by conventional or PSMA-PET[a] imaging or histopathology, or death)

Secondary (in hierarchical testing order)

- EFS
- Time to first subsequent therapy
- TTDM by conventional or PSMA-PET imaging
- NED at 4 years
- MFS (by conventional imaging)
- Time to PSA-free survival with testosterone recovery[b]

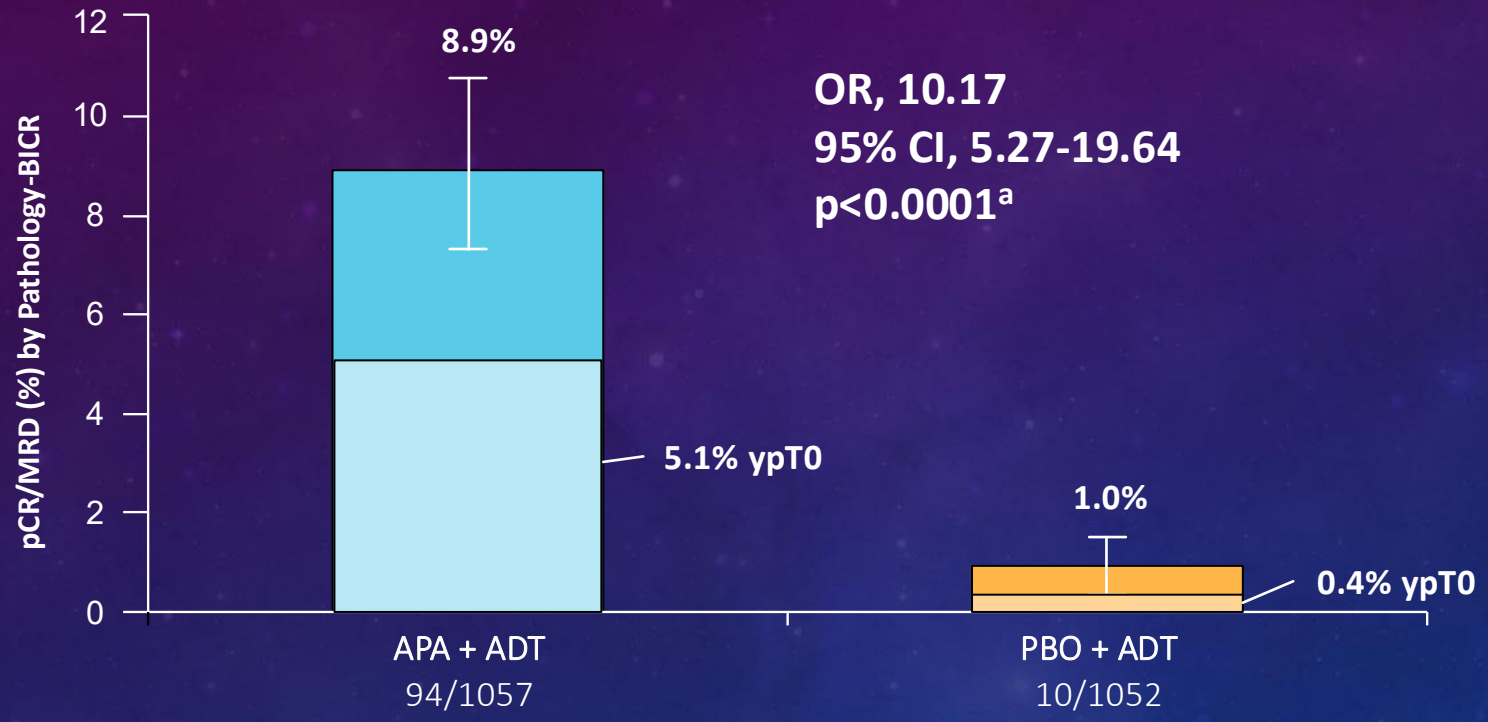
Additionally, exploratory end points included RCB, OS for no detriment of treatment, and testosterone recovery >200 ng/dL

BICR, blinded independent central review; MRD, minimal residual disease; NED, no evidence of disease; pCR, pathological complete response; OS, overall survival; RCB, residual cancer burden; TTDM, time to distant metastasis.

[a]Imaging was assessed by BICR. [b]Not formally tested after MFS by conventional imaging was insignificant.

Taplin ME et al. ASCO 2026;Abstract LBA1

DUAL PRIMARY END POINT MET: PCR/MRD



9-fold improvement in pCR/MRD at RP after 6-cycle neoadjuvant APA + ADT vs PBO + ADT

Exploratory end point of RCB (≤ypT2, N0, ≤0.25 cm^3) corroborates pCR/MRD:

- APA + ADT vs PBO + ADT, 30.6% vs 11.7%
- OR, 3.36; 95% CI, 2.67-4.23; p<0.0001

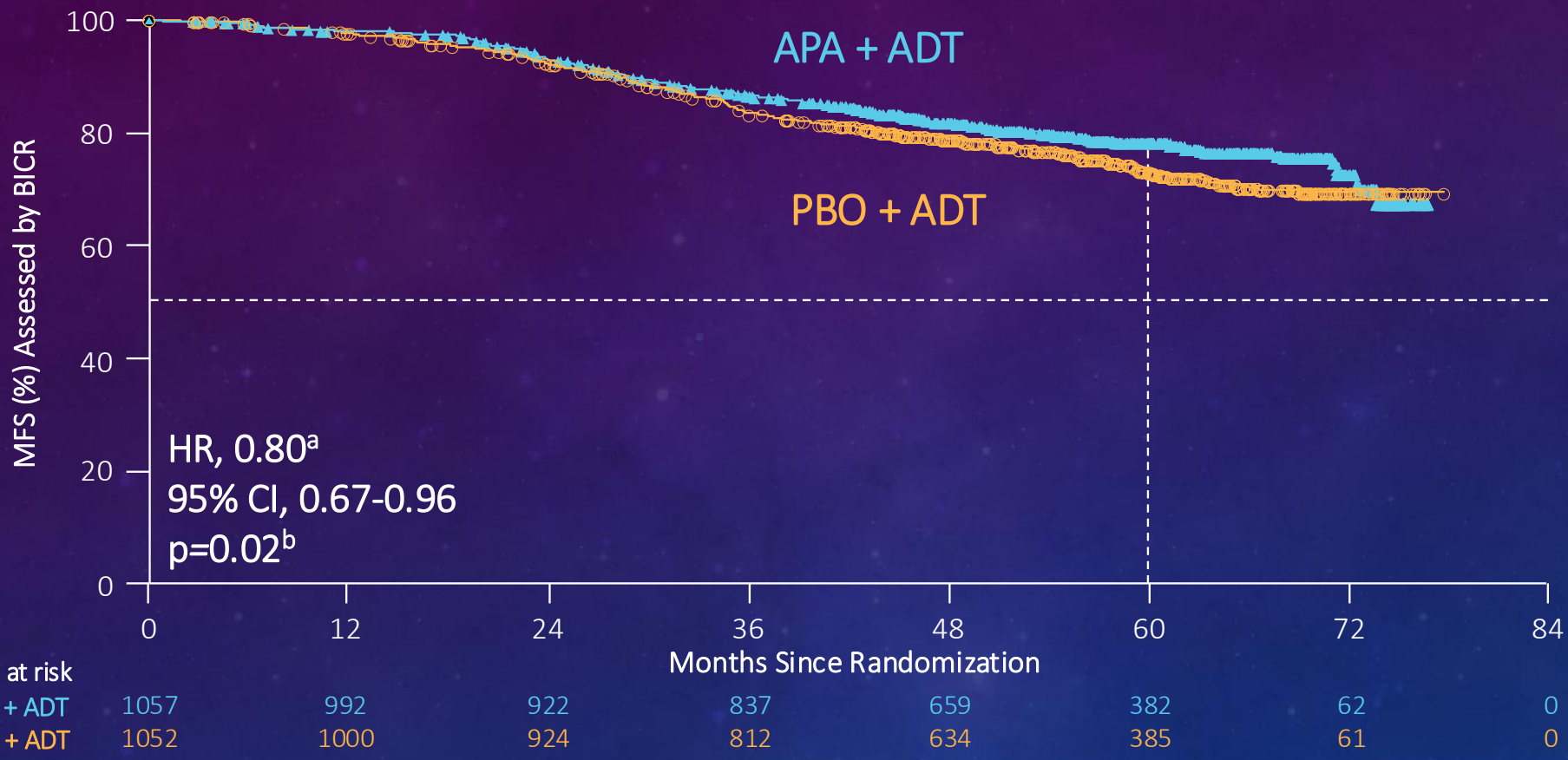
pCR/MRD: Minimal residual tumor ≤5 mm (greatest dimension of largest tumor lesion) in prostate-confined disease (≤ypT2, N0) or no tumor identified (ypT0)
RCB: Residual cancer burden ≤0.25 cm^3 in prostate-confined disease (≤ypT2, N0)

Error bars indicate 95% confidence intervals (CIs). Odds ratio (OR) is from a logistic regression adjusted for stratification factor; OR >1 favors APA + ADT.
[a]p Value is based on Cochran-Mantel-Haenszel test stratified by Gleason score (7, ≥8), nodal status (N0, N1), geographic region (North America, Europe, and rest of the world).

Taplin ME et al. ASCO 2026;Abstract LBA1

PRIMARY END POINT

DUAL PRIMARY END POINT MET: MFS BY CONVENTIONAL OR PSMA-PET IMAGING



No. at risk								
APA + ADT	1057	992	922	837	659	382	62	0
PBO + ADT	1052	1000	924	812	634	385	61	0

20% reduction in the risk of metastasis or death after 1 year of perioperative APA + ADT with RP by BICR

Investigator-assessed MFS was consistent

HR, 0.74;
95% CI, 0.62-0.87;
p=0.0004

MFS: Time to first occurrence of radiographic distant metastasis based on conventional imaging or PSMA-PET imaging, pathologic finding of distant metastasis, or death from any cause

[a]Hazard ratio (HR) is from stratified proportional hazards model. HR <1 favors APA + ADT.
[b]p Value is from a log-rank test stratified by Gleason score (7, ≥8), nodal status (N0, N1), geographic region (North America, Europe, and rest of the world).

Taplin ME et al. ASCO 2026;Abstract LBA1

TREATMENT-EMERGENT ADVERSE EVENTS OF SPECIAL INTEREST

Special Interest Category, n (%)	APA + ADT (n=1050)		PBO + ADT (n=1050)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
≥1 TEAE of special interest	398 (37.9)	90 (8.6)	214 (20.4)	23 (2.2)
Skin rash	346 (33.0)	62 (5.9)	161 (15.3)	3 (0.3)
Fall	34 (3.2)	6 (0.6)	29 (2.8)	5 (0.5)
Ischemic heart disease	25 (2.4)	13 (1.2)	22 (2.1)	9 (0.9)
Nonpathological fracture	22 (2.1)	6 (0.6)	19 (1.8)	5 (0.5)
Cerebrovascular disorders	8 (0.8)	5 (0.5)	13 (1.2)	6 (0.6)
Seizure	2 (0.2)	2 (0.2)	1 (0.1)	0
Fatigue	291 (27.7)	4 (0.4)	281 (26.8)	1 (0.1)

TEAEs are those that occurred on or after the first dose of study drug through the last dose of study treatment plus 30 days or prior to the start of subsequent therapy, whichever is earlier, or any AE that is considered treatment related regardless of the start date of the event. Patients are counted only once for any given event, regardless of the number of times they actually experienced the event. The event with the worst toxicity grade is used. If a patient has all adverse events with missing toxicity grades, the patient is only counted in the total column.

Taplin ME et al. ASCO 2026;Abstract LBA1

CASE 1: LOCALIZED HIGH-RISK CANDIDATE FOR NEOADJUVANT ADT/APALUTAMIDE

- 55 year old man who presents with a PSA 22, prostate MRI with 3 cm PIRAD 5 lesions, Prostate biopsy with Gleason 8 (4+4) in 6 cores and Gleason 7 (4+3) in 2 cores, +PNI, -cribriform, bone scan NED, PSMA-PET/CT with low volume pelvic nodes with SUV slightly over blood pool (indeterminate). Patient had treated hypertension and states that he "wants aggressive treatment".
  - What are the SOC treatment options?
  - What are the pros and cons of the PROTEUS regimen compared to RP (+/- salvage RT/ADT) and RT/ADT
  - If patient chooses RT/ADT, should an ARPI be added to the ADT?
  - Is there a cohort of patients with localized high-risk prostate cancer who should not be considered for ARPI/ADT and RP?

Do you anticipate that the PROTEUS trial strategy of perioperative apalutamide/androgen deprivation therapy (ADT) will receive FDA approval for patients with high-risk localized or locally advanced prostate cancer undergoing RP?

 Dr Oh	Yes
 Dr Taplin	Yes
 Dr Dorff	Yes
 Dr Smith	No
 Dr Srinivas	Yes
 Dr Yu	Yes

RTP RESEARCH TO PRACTICE

For which patients, if any, would you use the PROTEUS strategy?

 Dr Oh	Younger fit patients with NCCN VHR, urinary symptoms, interested in surgery, locally advanced
 Dr Taplin	High risk, high volume, up to N1 nodes by conventional imaging
 Dr Dorff	Younger patients with high-risk disease and patients with a lot of urinary symptoms that might worsen with RT
 Dr Smith	I do not expect to use the 'PROTEUS strategy'. The small effect on an intermediate endpoint of uncertain clinical importance is not compelling
 Dr Srinivas	Young, large prostate, high grade, bulky disease who are contemplating surgery as primary therapy
 Dr Yu	Only for the very high-risk patients who are young (eg.,<65) and who want to be very aggressive

RTP RESEARCH TO PRACTICE

For a patient who received the PROTEUS strategy and attained a pathologic complete response, would you offer the option of forgoing postoperative treatment?

 Dr Oh	No
 Dr Taplin	Yes
 Dr Dorff	No, I'd want at at least a year of postoperative treatment
 Dr Smith	Yes, although from the data, that is a rare outcome
 Dr Srinivas	No
 Dr Yu	Yes

RTP RESEARCH TO PRACTICE

Otherwise healthy patient presents with PSA of 9 ng/mL; Gleason 5 + 4 in 3 out of 20 cores; MRI: Extracapsular extension; clinical T2. Local and systemic therapy?

	55-year-old	70-year-old	80-year-old
 Dr Oh	RP or RT; PROTEUS or ADT/ARPI for 2 years	RP or RT; PROTEUS or ADT/ARPI for 2 years	RT; ADT for 2 years
 Dr Taplin	RP; PROTEUS	RP; PROTEUS	RT; ADT for 18-24 months
 Dr Dorff	RP; PROTEUS	RT; ADT for 18-24 months	RT; ADT for 18-24 months
 Dr Smith	RP or RT; None or long-term ADT	RT; Long-term ADT	RT; Long-term ADT
 Dr Srinivas	RP; PROTEUS	RT; ADT for 18 months	RT; ADT for 18 months
 Dr Yu	RT; ADT/abiraterone for 2 years	RT; ADT/abiraterone for 2 years	RT; ADT/abiraterone for 2 years

RP = radical prostatectomy; RT = radiation therapy; PROTEUS = perioperative apalutamide/androgen deprivation therapy; ADT = androgen deprivation therapy; ARPI = androgen receptor pathway inhibitor

Otherwise healthy patient presents with urinary symptoms; large prostate (100 cm^3); 10 out of 12 cores with Gleason 8 cancer; PSMA PET with suspicious nodes, pelvic nodes. Local and systemic therapy?

	55-year-old	70-year-old	80-year-old
 Dr Oh	RP or RT; PROTEUS or ADT/ARPI for 2 years	RP or RT; PROTEUS or ADT/ARPI for 2 years	RT; ADT for 2 years
 Dr Taplin	RP; PROTEUS	RP; PROTEUS	RT; ADT for 18-24 months
 Dr Dorff	RP; PROTEUS or ADT/abiraterone	RP; PROTEUS or ADT/abiraterone	RT; ADT/abiraterone for 2 years
 Dr Smith	RP or RT; None or ADT/ARPI for 24 months	RT; ADT/ARPI for 24 months	RT; ADT/ARPI for 24 months
 Dr Srinivas	RT; ADT/abiraterone for 18-24 months	RT; ADT/abiraterone for 18-24 months	RT; ADT/darolutamide for 18-24 months
 Dr Yu	RT; ADT/abiraterone for 2 years	RT; ADT/abiraterone for 2 years	RT; ADT/abiraterone for 2 years

Otherwise healthy patient presents with urinary symptoms; prostate 35 cm^3; 10 out of 12 cores with Gleason 8 cancer; PSMA PET with suspicious nodes, pelvic nodes. Local and systemic therapy?

	55-year-old	70-year-old	80-year-old
 Dr Oh	RP or RT; PROTEUS or ADT/ARPI for 2 years	RT; ADT/ARPI for 2 years	RT; ADT for 2 years
 Dr Taplin	RP; PROTEUS	RP; PROTEUS	RT; ADT for 18-24 months
 Dr Dorff	RP; PROTEUS	RT; ADT/abiraterone for 2 years	RT; ADT/abiraterone for 2 years
 Dr Smith	RP or RT; None or ADT/ARPI for 24 months	RT; ADT/ARPI for 24 months	RT; ADT/ARPI for 24 months
 Dr Srinivas	RT; ADT/abiraterone for 18-24 months	RT; ADT/abiraterone for 18-24 months	RT; ADT/darolutamide for 18-24 months
 Dr Yu	RT; ADT/abiraterone for 2 years	RT; ADT/abiraterone for 2 years	RT; ADT/abiraterone for 2 years

Patient is otherwise healthy; Gleason 7 (4 + 3 in multiple cores); negative PSMA PET, but MRI suggests seminal vesicle invasion and extracapsular extension (T3 disease). Local and systemic therapy?

	55-year-old	70-year-old	80-year-old
 Dr Oh	RP or RT; None or ADT for 6-24 months	RP or RT; None or ADT for 6-24 months	RT; ADT for 6-24 months
 Dr Taplin	RP; None	RP; None	RT; ADT for 18-24 months
 Dr Dorff	RP; Neoadjuvant ADT, ARPI doublet for downstaging	RT; ADT for 18-24 months	RT; ADT (duration based on Decipher score)
 Dr Smith	RP or RT; None or long-term ADT	RP or RT; None or long-term ADT	RT; Long-term ADT
 Dr Srinivas	RP; None	RP; None	RT; ADT for 6 months
 Dr Yu	RP; PROTEUS	RT; ADT for 2 years	RT; ADT/abiraterone for 2 years

PSA RECURRENCE AFTER LOCAL THERAPY

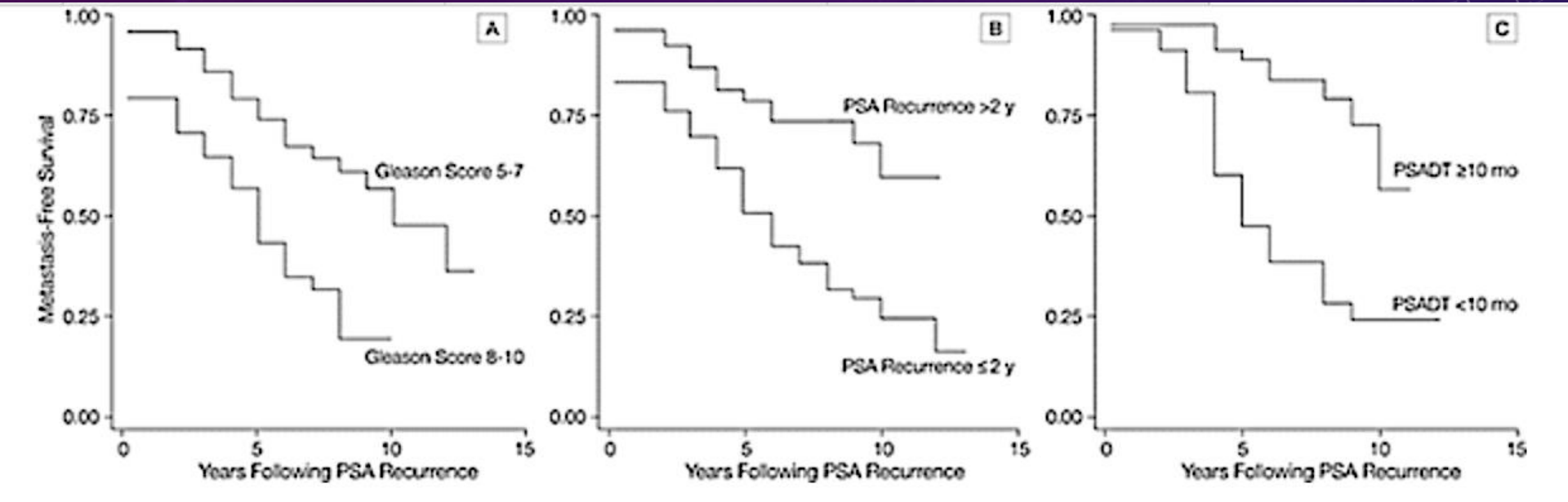
Prostatectomy

- Definition of recurrence = PSA 0.2
- Practical definition of recurrence PSA 0.1-0.2
- Staging with PSMA-PET
- SOC = salvage RT +/- ADT

Primary radiation +/- ADT

- Definition of recurrence = PSA 2.0
- Staging PSMA-PET
- Some consideration of salvage RP or salvage RT (HDR brachytherapy)
- SOC = ADT
  - Timing of ADT per clinical judgment
  - Trials EMBARK, PRESTO

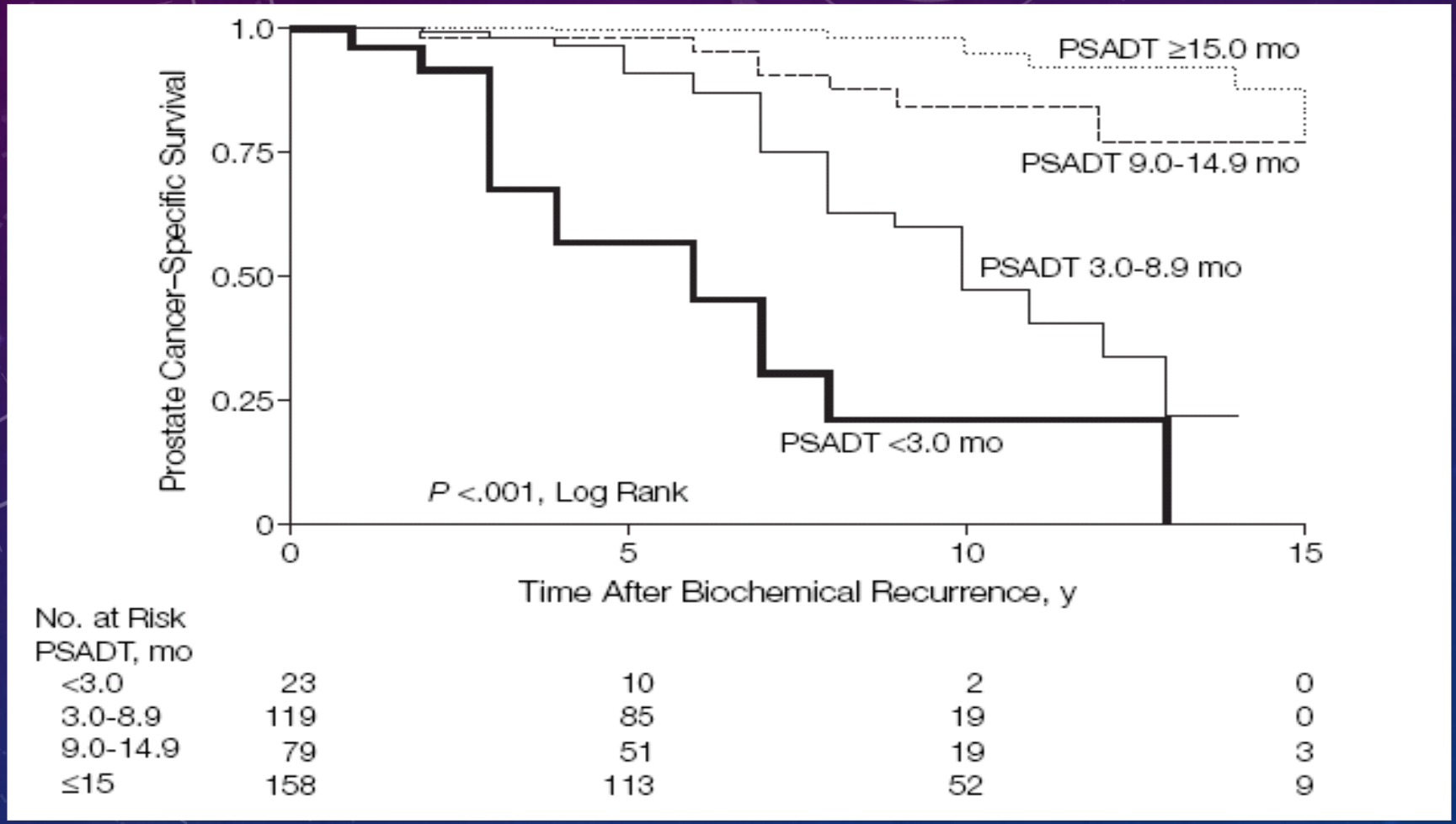
ACTUARIAL LIKELIHOOD OF MFS WITH PSA ELEVATION AFTER RADICAL PROSTATECTOMY



A, Based on Gleason scores in the radical prostatectomy specimen (*P*<.001).
B, Based on years until initial biochemical recurrence (*P*<.001).
C, Based on prostate-specific antigen doubling time (PSADT) (*P*<.001).

Pound CR et al. JAMA. 1999 May 5;281(17):1591-7.

Patients with a Rising PSA-Importance of PSADT



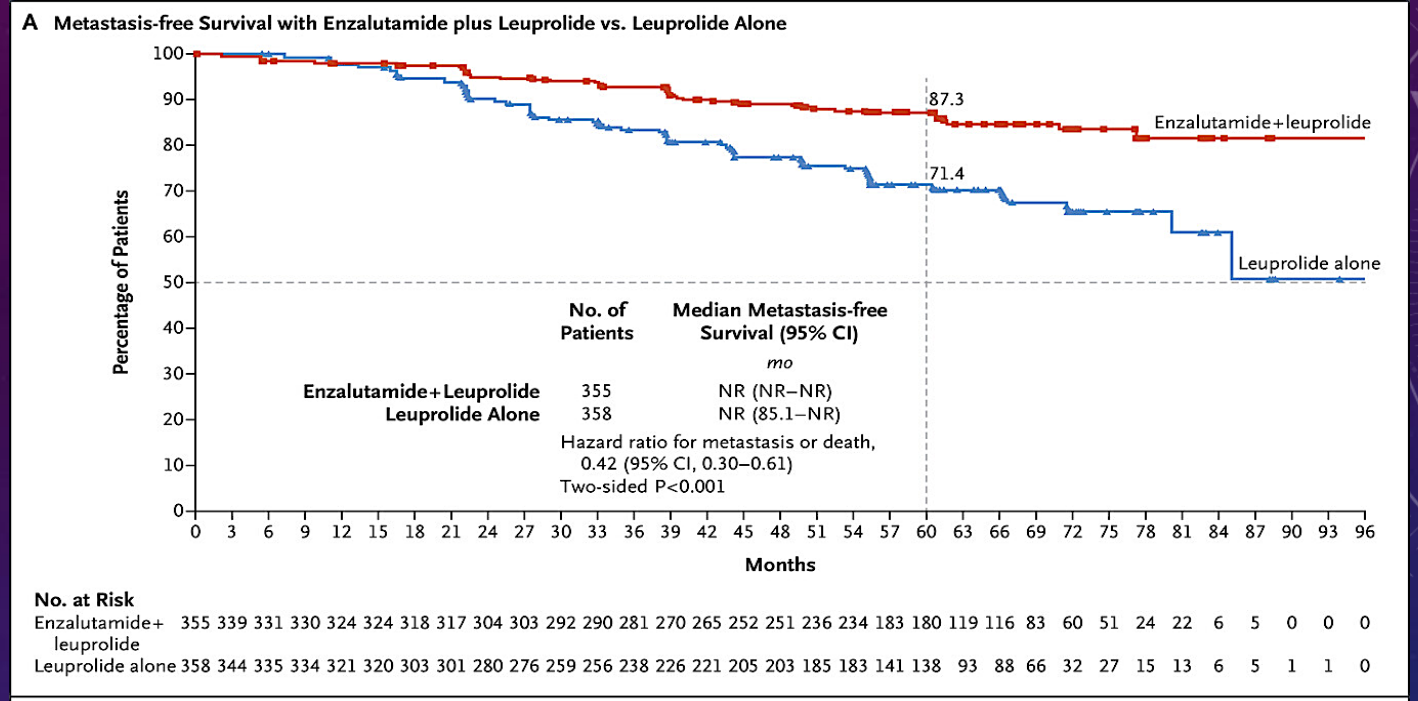
No. at Risk PSADT, mo				
<3.0	23	10	2	0
3.0-8.9	119	85	19	0
9.0-14.9	79	51	19	3
≤15	158	113	52	9

Freedland SJ, et al. JAMA. 2005

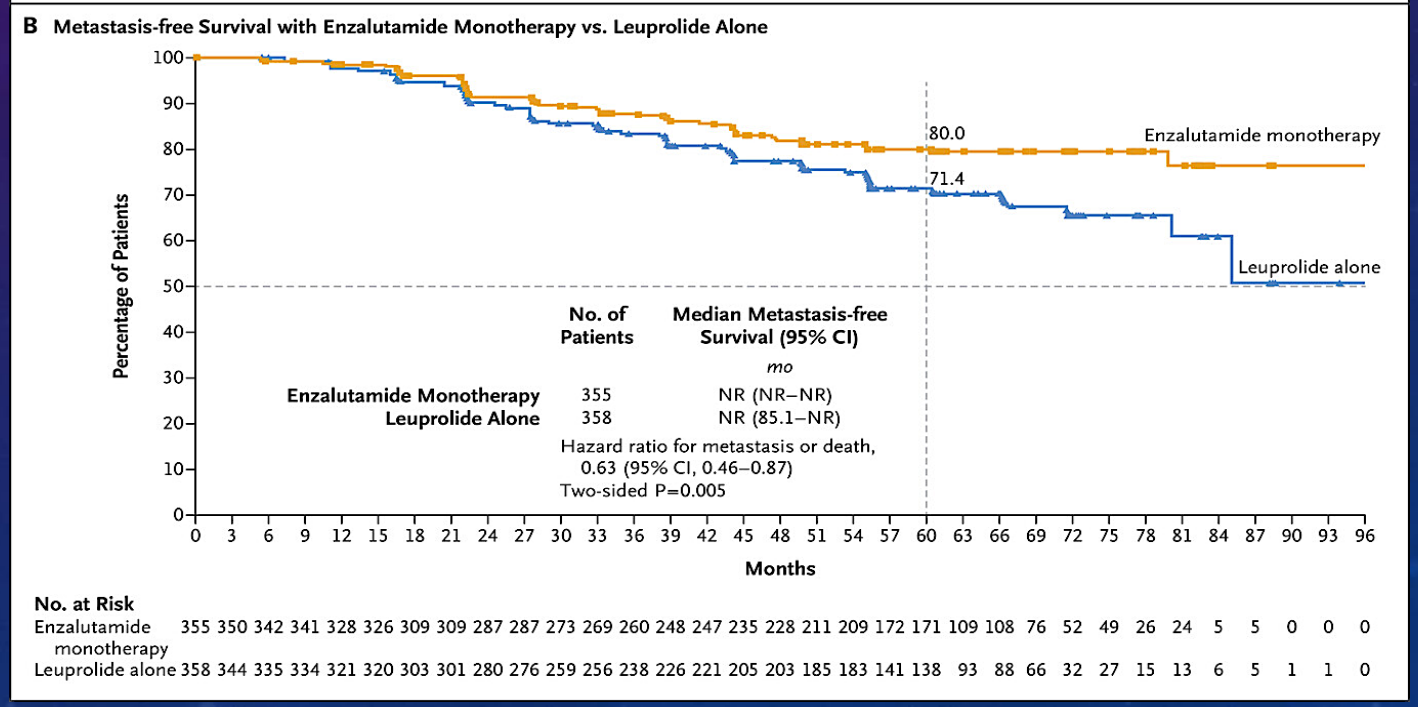
EMBARK trial

ADT vs ADT/ENZA
ADT vs ENZA monotherapy

Med f/u = 5 yr
Med PSAdt 4.9 mo
Med PSA 5.2



HR 0.42



HR 0.63

Freedland SJ et al. N Engl J Med. 2023 Oct 19;389(16):1453-1465.

Table 2. Adverse Events (Safety Population).*

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

Permanent discontinuation
Enza/ADT: 20%
Enza: 18%
ADT: 10%

Gynecomastia
Enza: 45%
Enza/ADT: 8%
ADT: 9%

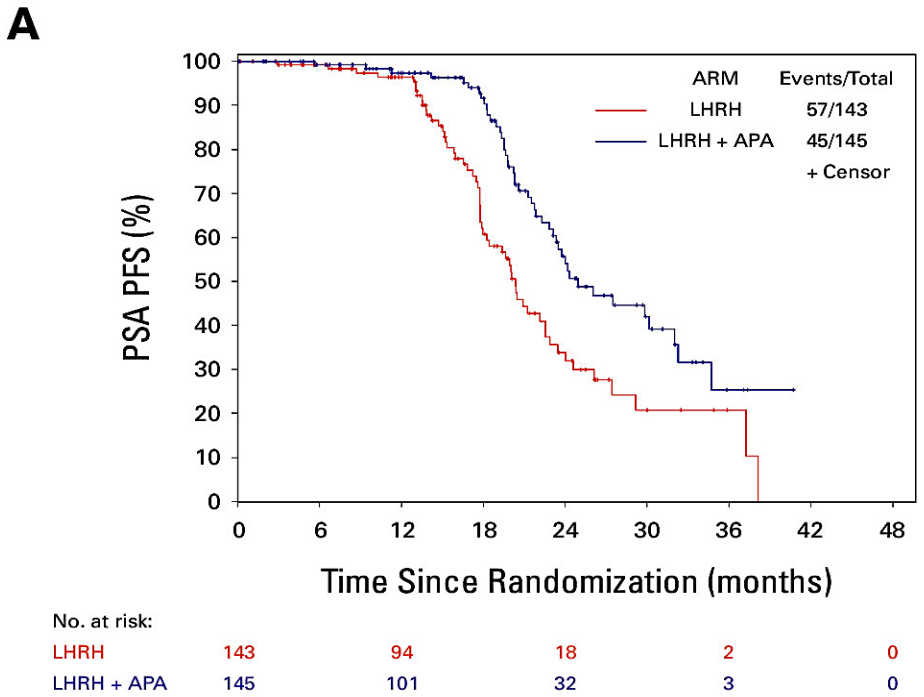
Freedland SJ et al.
N Engl J Med. 2023 Oct 19;389(16):1453-1465.

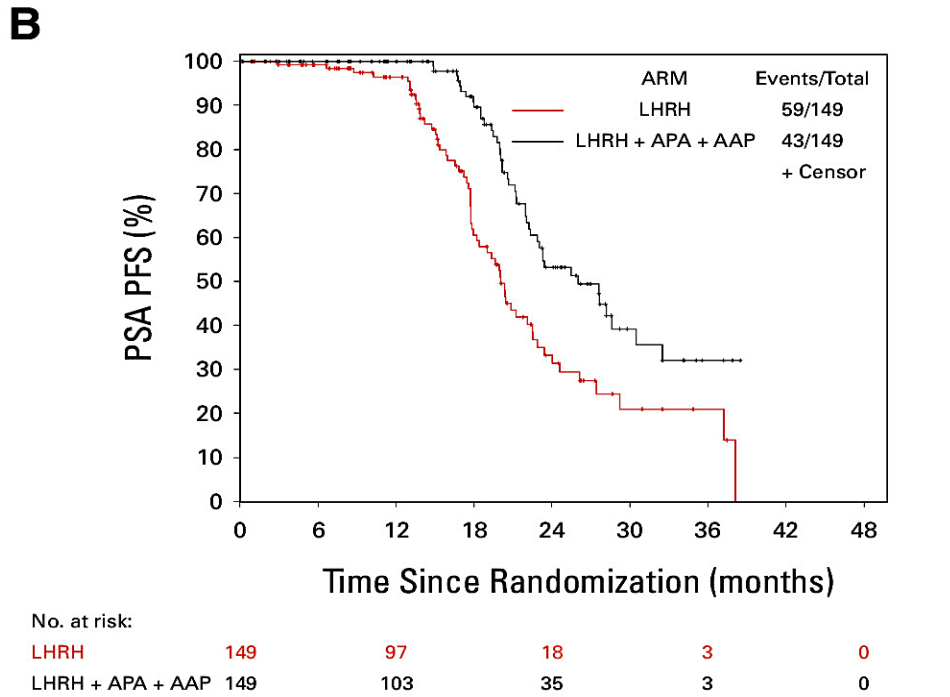
PRESTO trial

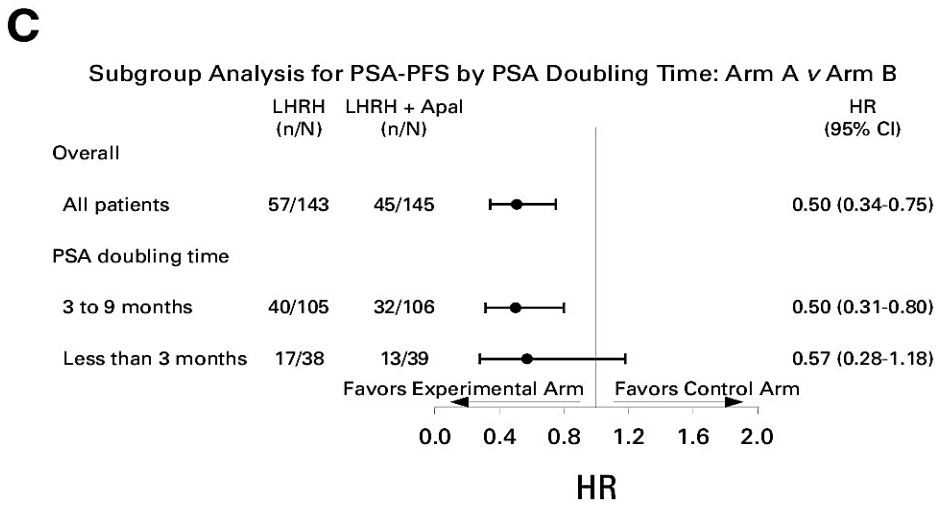
ADT vs ADT/Apa
ADT vs ADT/Apa/ Abi

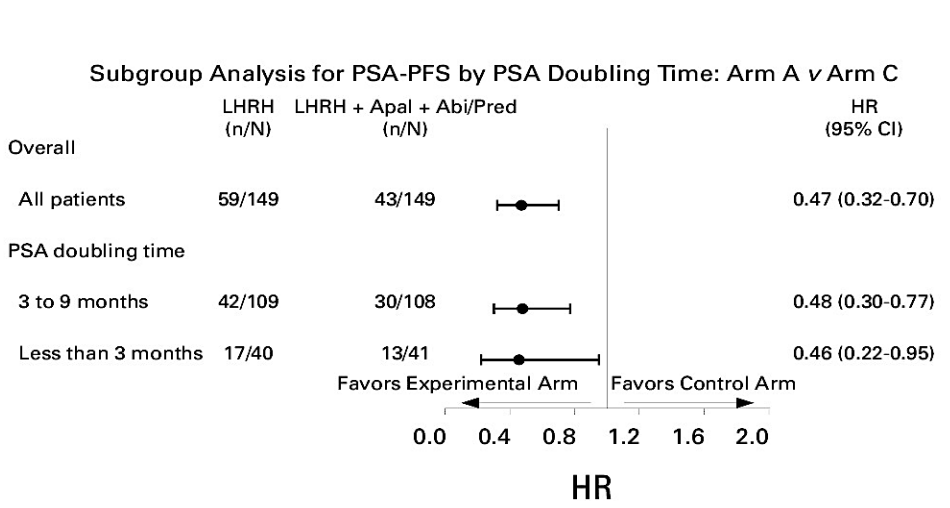
PSAdt ≤ 9 mo

PSA progression-free end point









Aggarwal R et al. J Clin Oncol. 2024 Apr 1;42(10):1114-1123.

PHASE III TRIALS OF ARPI IN NON-METASTATIC PROSTATE CANCER

Trial	Drug	Disease Setting	Local Rx	Key Result
STAMPEDE (g)	Abi +/- Enza	High-risk non-metastatic	RT	Pos OS and MFS, Enza no benefit
ENZARAD	Enzalutamide	High-risk localized	RT	Neg 8-year MFS
EMBARK	Enzalutamide	High-risk biochemical recurrence	Prior RP and/or RT	Pos
PROTEUS	Apalutamide	Localized high-risk/N1	RP	Pos major path response and MFS
ATLAS	Apalutamide	Localized high-risk/N1	RT	Pending
DASL-HiCaP	Darolutamide	Localized very high-risk	RT	MFS, Pending
ARASTEP	Darolutamide	High-risk biochemical recurrence	Prior RP and/or RT	RPFS (PET), Pending
ALADDIN (French)	Darolutamide	Localized, N1 by PET	RT	FFS, Pending

SUMMARY

BENEFIT FOR ARPIS IN LOCALIZED, HIGH-RISK AND BIOCHEMICAL RECURRENCE

ARPIS HAVE KNOWN TOXICITIES

WHEN MAKING TREATMENT DECISIONS NEED CAREFUL ATTENTION TO PATIENTS BASELINE CO-MORBIDITIES, AGE, GOALS

CASE 2: NON-METASTATIC BIOCHEMICAL RECURRENCE

- 72 year old man s/p RP (age 65) and salvage RT/ADT (age 67) who has a PSA of 5 and PSAdt of 7 months. A PSMA-PET/CT = NED. He has baseline treated hypercholesterolemia and is fit. He notes that he wants to be aggressive and live as long as possible.
  - What is the significance of the PSAdt?
  - What treatment options are available?
  - If he chooses treatment with ADT/Enzalutamide per EMBARK, how should he be followed and how long should he be treated?
  - What was the average time off therapy in EMBARK for each cohort – ADT, ADT/ENZA and ENZA monotherapy?

For patients with a rising PSA after primary RT or RP and salvage RT, what factors would lead you to initiate systemic treatment, and which systemic treatment do you generally recommend?

 Dr Oh	PSA doubling time, absolute PSA, initial Gleason and stage — EMBARK regimen: ADT/enzalutamide
 Dr Taplin	PSA doubling time < 10 months — ADT/enzalutamide
 Dr Dorff	Combination of PSA level + kinetics, and PSMA PET findings. If SBRT to oligomet can be done, I use 6 months relugolix. If not, I recommend EMBARK
 Dr Smith	Gleason score, interval from completion of primary treatment to PSA failure, PSA doubling time, and PSMA PET CT findings — ADT alone or ADT/ARPI
 Dr Srinivas	PSMA PET findings, Decipher assay, PSA number, PSA doubling time — ADT alone or ADT/abiraterone
 Dr Yu	Absolute PSA value and PSA doubling time. I prefer to just do intermittent ADT, unless the patient is very high risk with PSA doubling <3 months. Then I would offer ADT plus enzalutamide but I would consider intermittent with breaks, if PSA reaches undetectable

RTP RESEARCH TO PRACTICE

In which situations, if any, are you recommending enzalutamide monotherapy?

 Dr Oh	History of poor tolerance of ADT, frail patients where I may even start lower-dose enzalutamide
 Dr Taplin	Select rising PSA after local therapy per EMBARK
 Dr Dorff	Only the patients who absolutely refuse castration
 Dr Smith	Patients who were intolerant of ADT or refuse ADT
 Dr Srinivas	Patient preference; those who do not like side effects of low testosterone
 Dr Yu	Essentially never

RTP RESEARCH TO PRACTICE

In which situations do you use intermittent endocrine treatment, and how do you generally approach it?

 Dr Oh	BCR frequently is IADT, repeatedly based on PSA and tolerance. Oligomets, esp if only on PSMA PET. Some patients with more mets who are in remission
 Dr Taplin	mHSPC low vol after 2 years of ADT/ARPI if NED by PSA/PET will offer to stop all Rx and non-metastatic rising PSA after local therapy
 Dr Dorff	Generally use for BCR, repeatedly. Discontinue after minimum 6 months, when PSA undetectable ideally. Resume when PSMA PET shows new activity or rapid rising PSA >1-2. For mHSPC I consider treatment holiday but when specific criteria met
 Dr Smith	Patients with lower risk of prostate cancer-specific mortality; treat for 12 months, hard stop, restart at PSA threshold similar to the value that prompted treatment initiation; repeat holiday for those with reasonable treatment holiday
 Dr Srinivas	Patient preference; discontinue after undetectable PSA for 12-18 months; follow the A-DREAM approach rather than EMBARK
 Dr Yu	Biochemical recurrence. I do this repeatedly and restart with PSA level between 5 to 10

RTP RESEARCH TO PRACTICE

In which situations, if any, do you prefer relugolix?

 Dr Oh	Distance, no high copay, patient preference (AEs from degarelix)
 Dr Taplin	Most situations
 Dr Dorff	For intermittent therapy. Also for short course with definitive RT or salvage. For metastatic, I prefer when CV comorbidities are significant
 Dr Smith	Patients who require short-term (6 months) ADT or patients with higher CVD risk
 Dr Srinivas	Patient preference
 Dr Yu	In patients very, very concerned about cardiac risk

AEs = adverse events; CV = cardiovascular; CVD = CV disease

How would you manage mHSPC in a patient with inadequate response to ADT, an ARPI and docetaxel?

	BRCA wild type Not PTEN deficient	BRCA2 mutant Not PTEN deficient	BRCA wild type PTEN deficient
 Dr Oh	Follow closely	Consider PARPi	Consider capivasertib
 Dr Taplin	Restage and consider SBRT or prostate RT	Restage, only add PARPi upon clear PD	Restage, only add new therapy upon clear PD
 Dr Dorff	No change	No change, would not add PARPi until PD	No change
 Dr Smith	Consider cabazitaxel + carboplatin	Consider cabazitaxel + carboplatin	Consider cabazitaxel + carboplatin
 Dr Srinivas	No change	Consider a PARPi	No change
 Dr Yu	No change	Add a PARPi	Consider capivasertib

PD = progressive disease

Agenda

Introduction: Another Perspective on the Treatment of Localized Prostate Cancer

Module 1: Nonmetastatic Disease

Module 2: Metastatic Androgen Pathway Modulation-Naïve and Androgen Pathway Modulation-Sensitive Disease

Updates in Metastatic HSPC

William K. Oh, MD
Director, Precision Medicine
Yale Cancer Center and Smilow Cancer Hospital

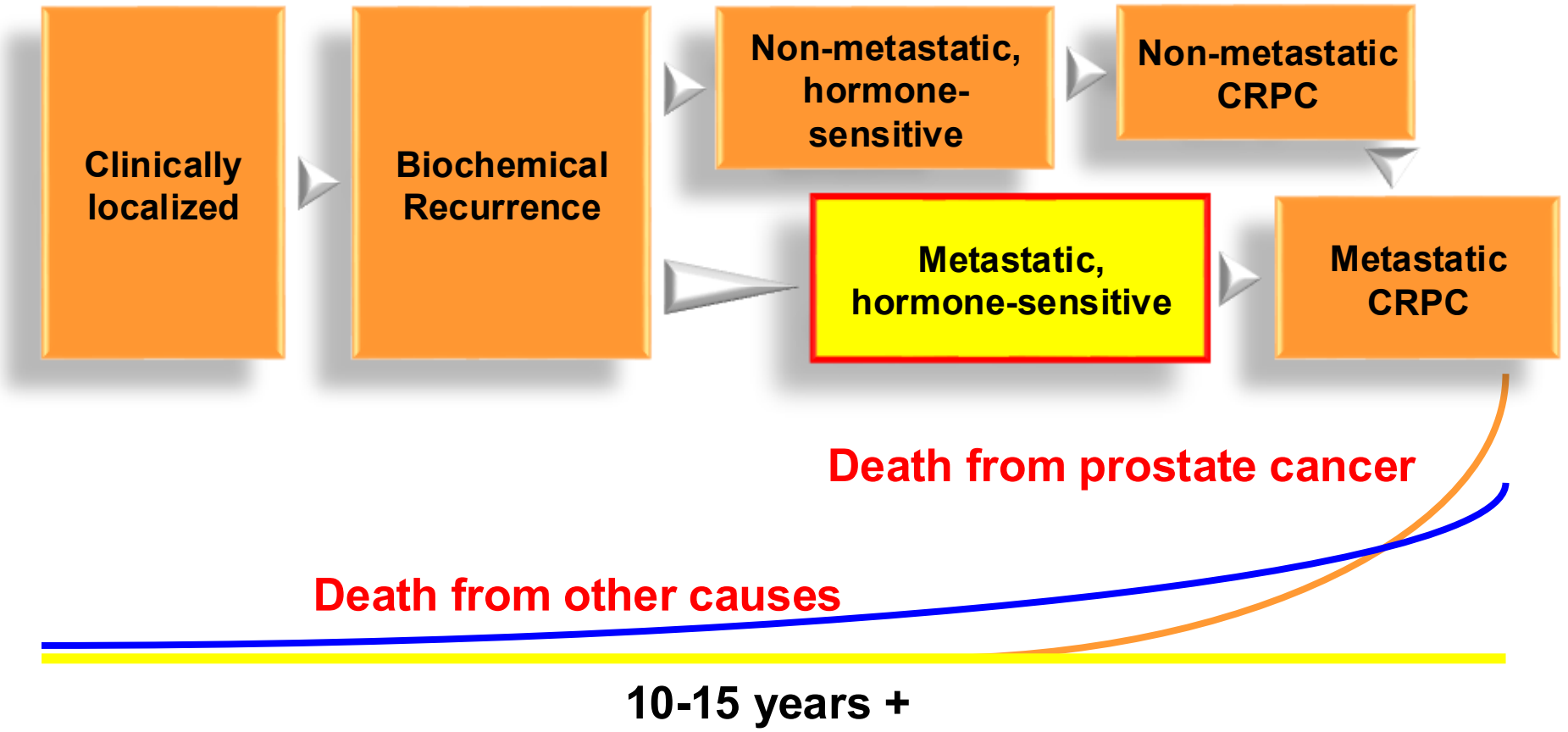
Jean and David W. Wallace Medical Director
Smilow Cancer Hospital at Greenwich Hospital

Chair, National Prostate Cancer Roundtable
American Cancer Society

YaleNewHavenHealth
Smilow Cancer Hospital

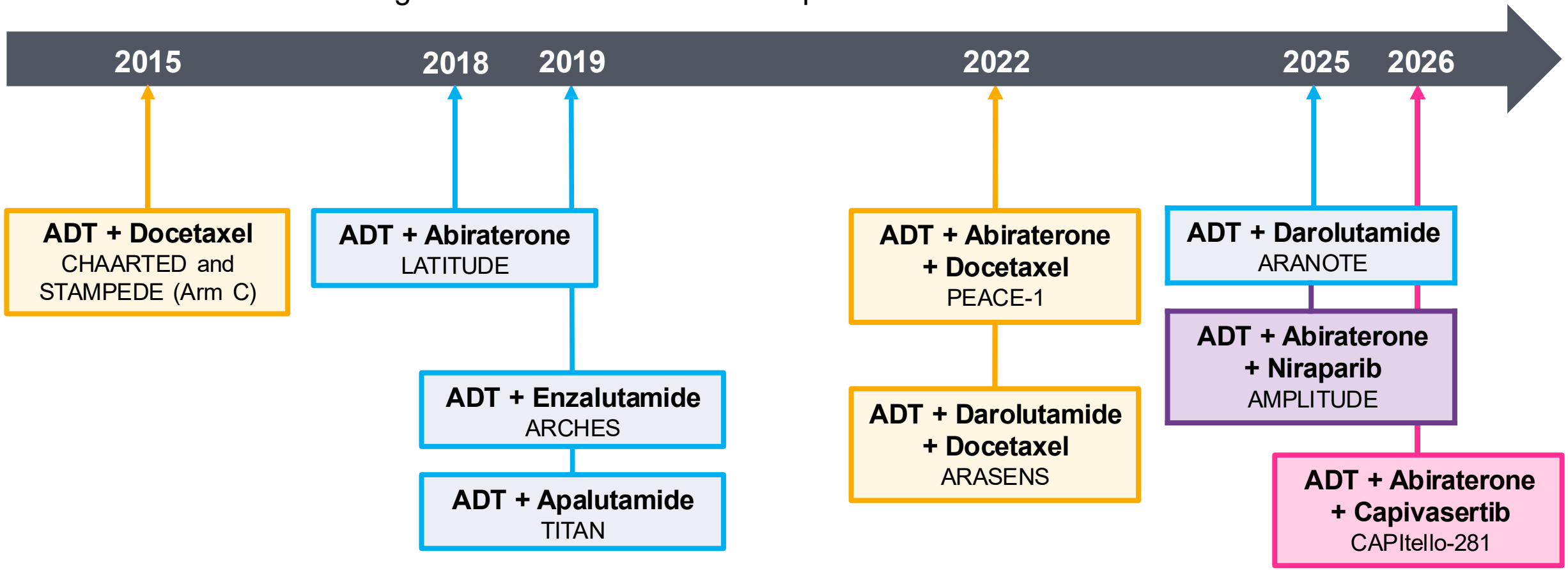
Yale CANCER CENTER
A Comprehensive Cancer Center Designated by the National Cancer Institute

Clinical States of Prostate Cancer



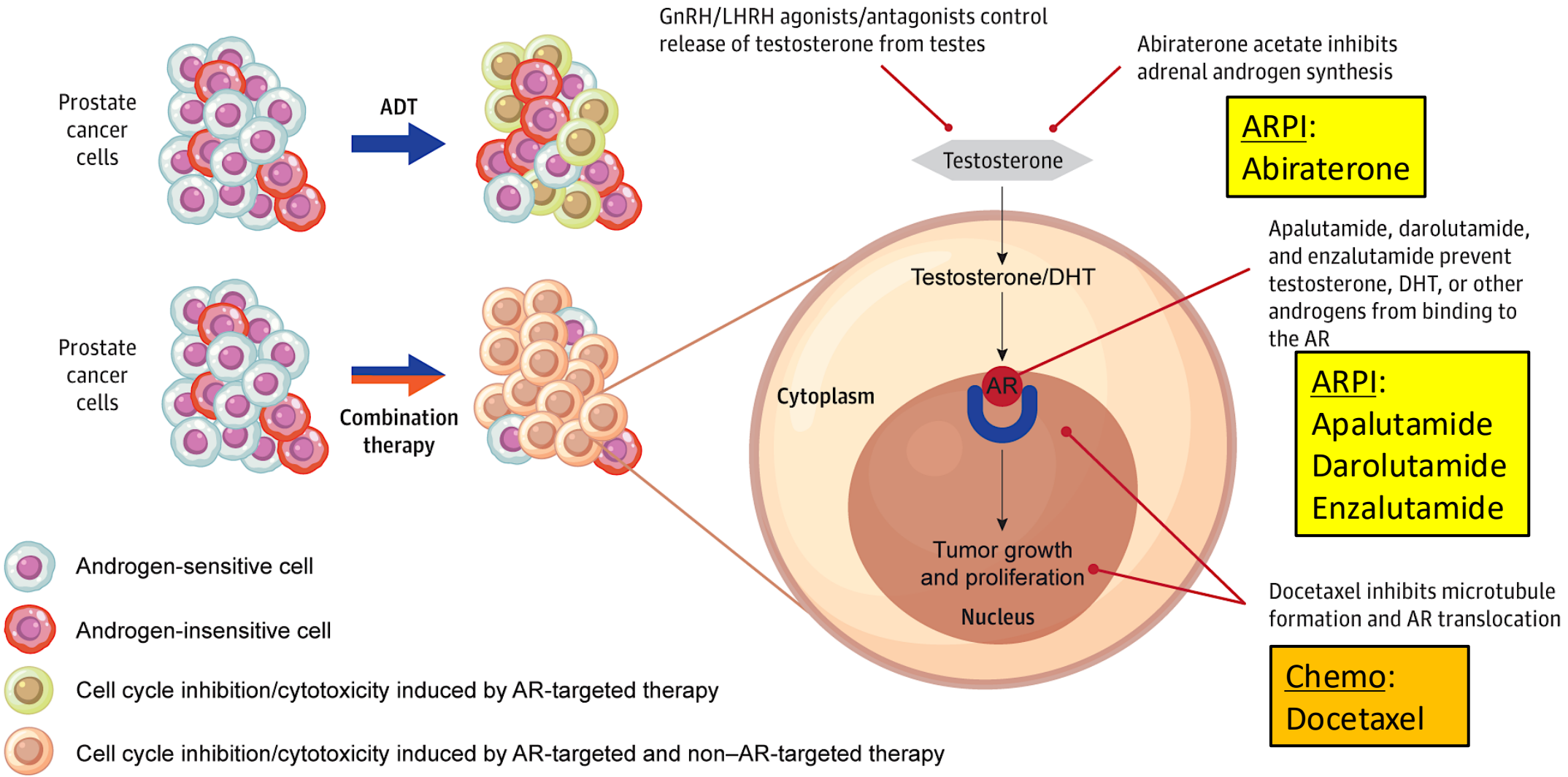
FDA-Approved Treatments in Metastatic HSPC

Multiple ADT + ARPI combinations are approved for mHSPC
allowing tailored treatment based on patient and disease characteristics



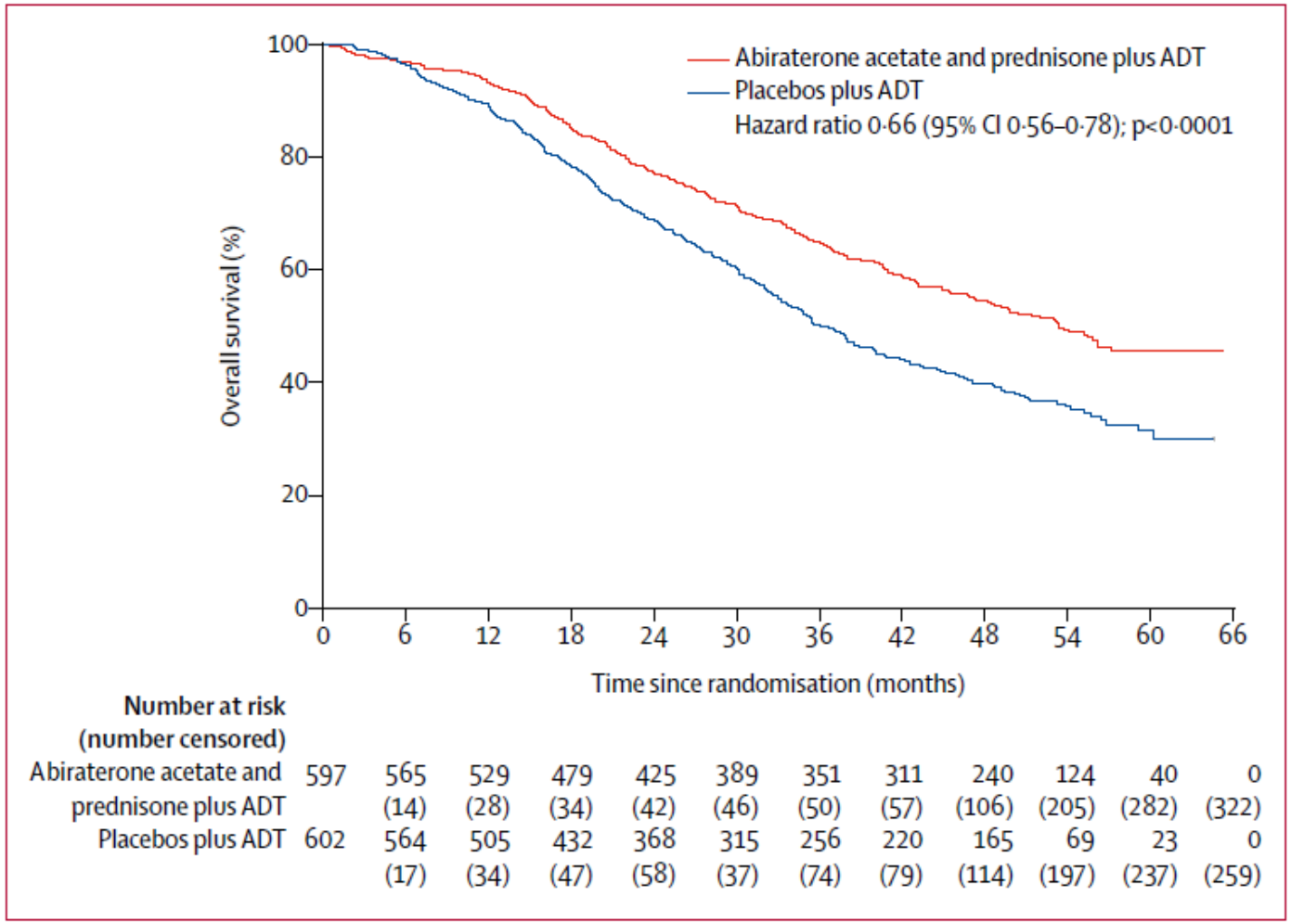
Fizazi K et al. *Lancet Oncology*. 2019; 20(5):686-700.; Fizazi K et al. ESMO 2021.; Chi KN et al. *JCO.* 2021; 39(20):2294-2303.; Andrew Armstrong, ASCO 2025; Smith MR et al. *NEJM*. 2022; 386:1132-1142.; Saad F et al. *J Clin Oncol*. 2024;42(36):4271-4281.; Gerhardt Attard, ASCO 2025; Karim Fizazi,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

Combination Therapy Targets Tumor Heterogeneity in mHSPC



Hussain. JAMA Onc 10:807, 2024

Abiraterone acetate plus prednisone in patients with newly diagnosed high-risk metastatic castration-sensitive prostate cancer (LATITUDE): final overall survival analysis of a randomised, double-blind, phase 3 trial



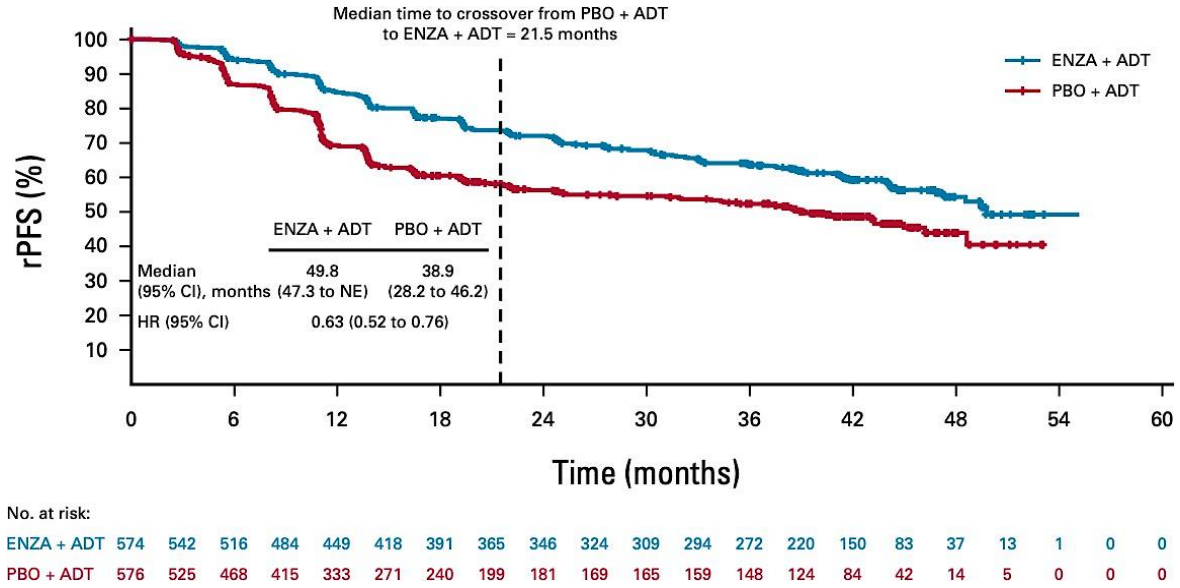
Number at risk (number censored)												
Abiraterone acetate and prednisone plus ADT	597	565 (14)	529 (28)	479 (34)	425 (42)	389 (46)	351 (50)	311 (57)	240 (106)	124 (205)	40 (282)	0 (322)
Placebos plus ADT	602	564 (17)	505 (34)	432 (47)	368 (58)	315 (37)	256 (74)	220 (79)	165 (114)	69 (197)	23 (237)	0 (259)

Figure 2: **Kaplan-Meier curve of overall survival in the intention-to-treat population**
ADT=androgen deprivation therapy.

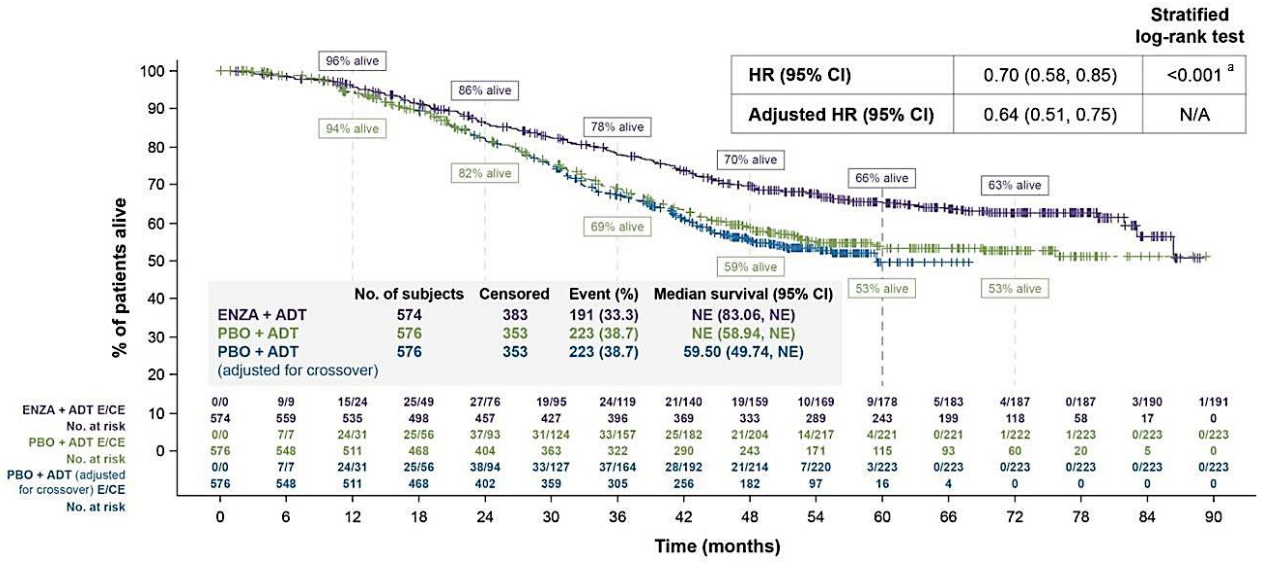
Fizazi K et al. *Lancet Oncol*. 2019 May;20(5):686-700.

ARCHES: Key Endpoints for Enzalutamide in mHSPC

Radiographic Progression Free Survival



5-Year Overall Survival (Adjusted for Crossover)

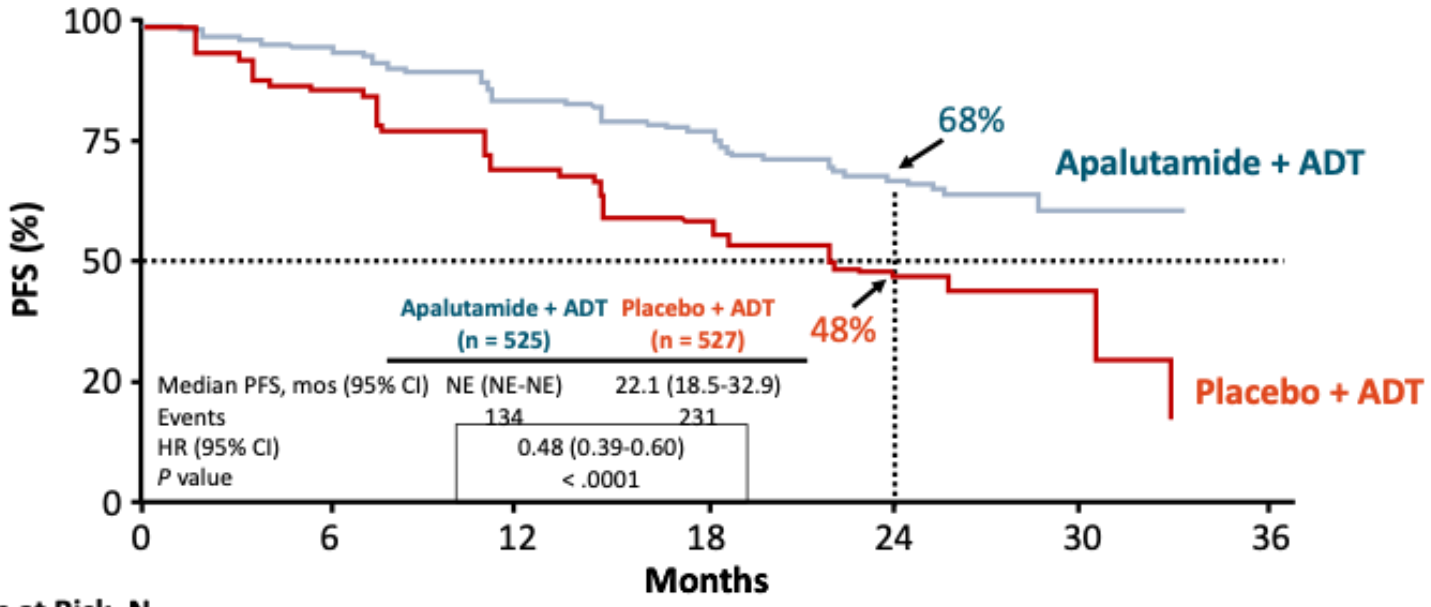


ArmstrongAJ et al. *J Clin Oncol*. 2022; 40:1616-1622.
Armstrong AJ et al. *Eur Urol*. 2026 May;89(5):396-403.

YaleNewHavenHealth Smilow Cancer Hospital | Yale CANCER CENTER A Comprehensive Cancer Center Designated by the National Cancer Institute

TITAN: Key Endpoints for Apalutamide in mHSPC

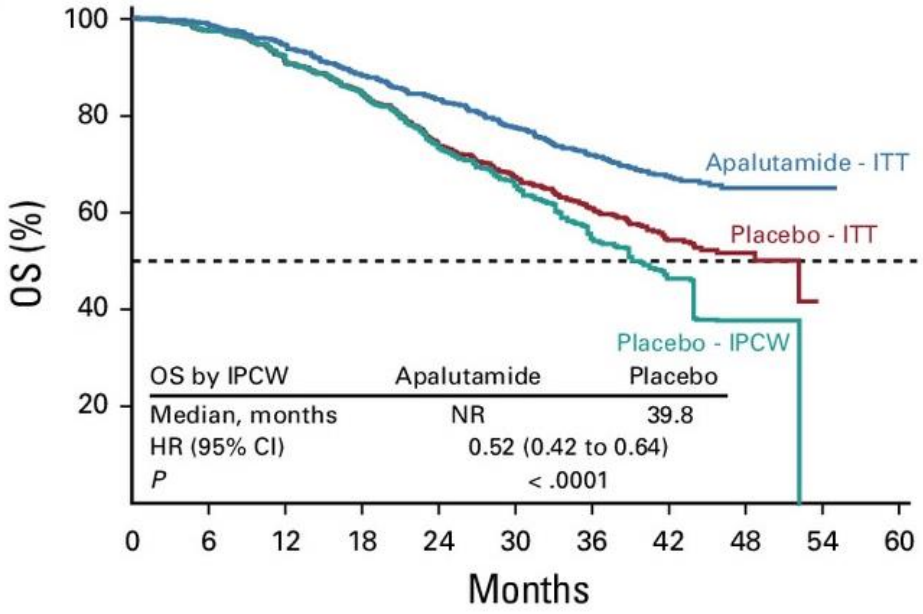
Radiographic Progression Free Survival



Patients at Risk, N

Apalutamide	525	469	389	315	89	2	0
Placebo	527	437	325	229	57	3	0

Overall Survival (Adjusted for Crossover)



No. at risk:

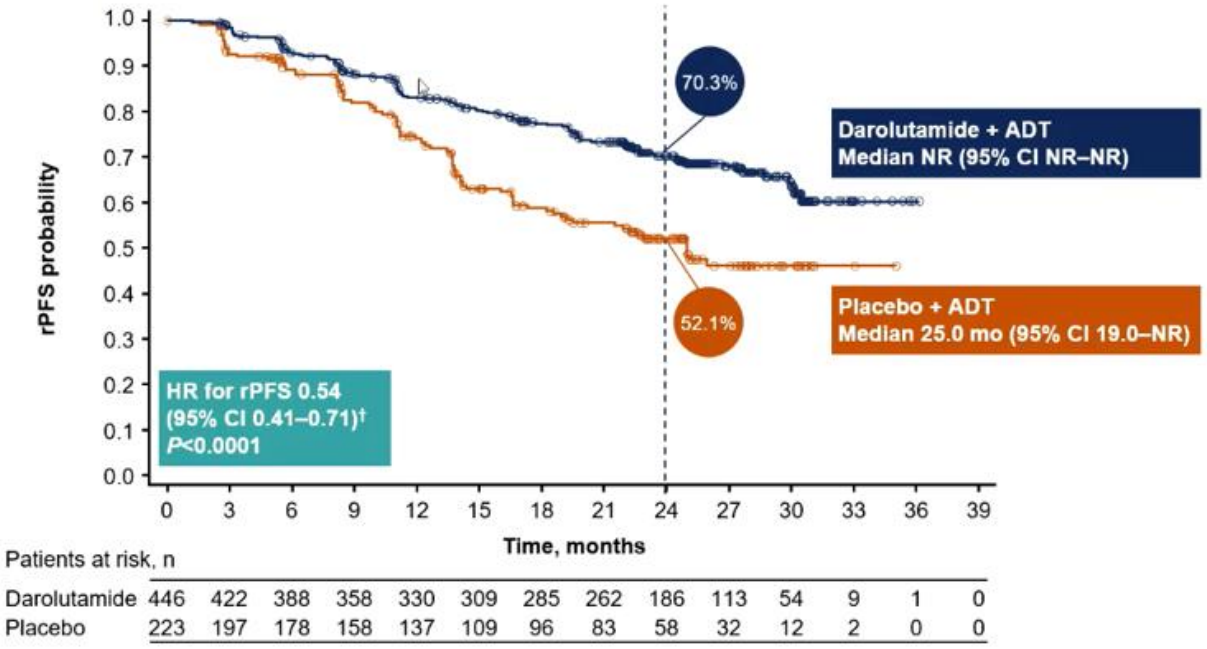
Apalutamide	525	513	489	452	425	394	362	227	52	3	0
Placebo	527	510	474	436	374	339	301	181	43	0	0

Chi KN et al. *JCO.* 2021; 39(20):2294-2303.

YaleNewHavenHealth Smilow Cancer Hospital | Yale CANCER CENTER A Comprehensive Cancer Center Designated by the National Cancer Institute

ARANOTE (Phase 3): Radiological PFS and PSA

Primary endpoint: Radiological PFS

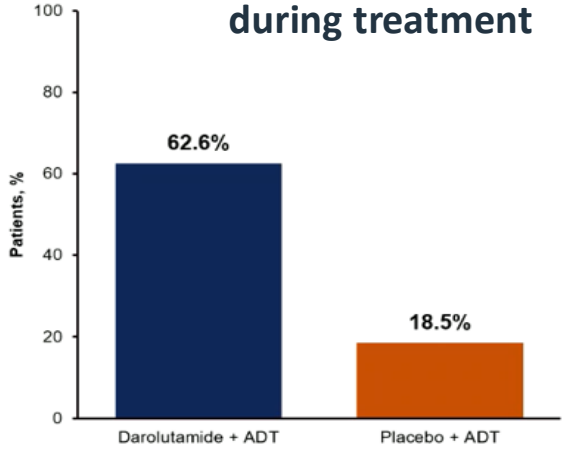


Patients at risk, n

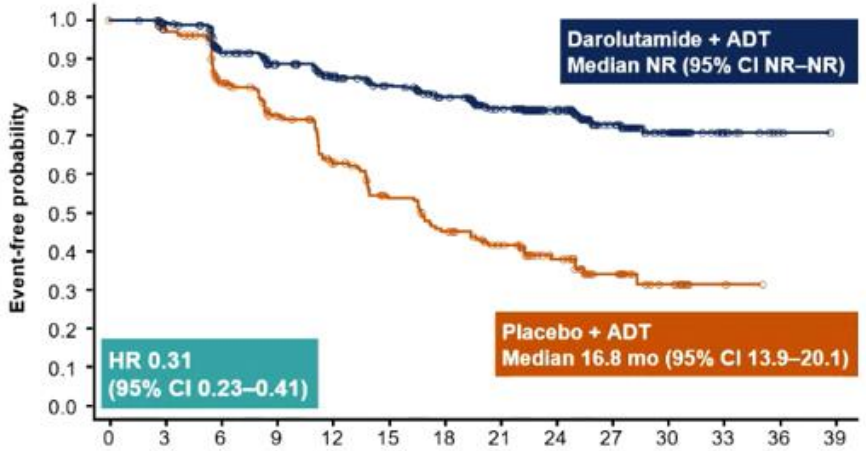
Darolutamide	446	422	388	358	330	309	285	262	186	113	54	9	1	0
Placebo	223	197	178	158	137	109	96	83	58	32	12	2	0	0

- Benefit of darolutamide was consistent across all subgroups

PSA <0.2 ng/mL at any time during treatment



Time to PSA progression



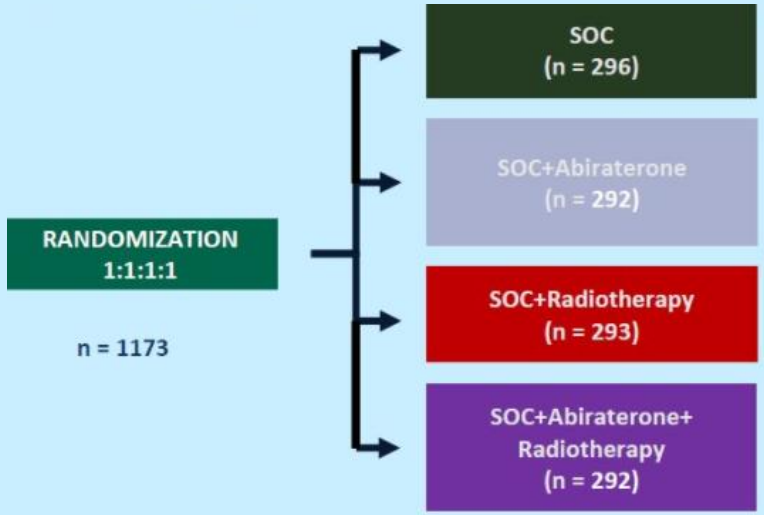
Patients at risk, n

Darolutamide	446	408	357	330	301	280	256	220	158	95	48	12	2	0
Placebo	223	195	158	130	102	81	67	54	36	20	9	2	0	0

ADT, androgen-deprivation therapy.
Saad F, et al. ESMO 2024. Abstract LBA68

Phase 3 PEACE-1 Study (2x2): Abiraterone + ADT + Docetaxel ± RT for mHSPC

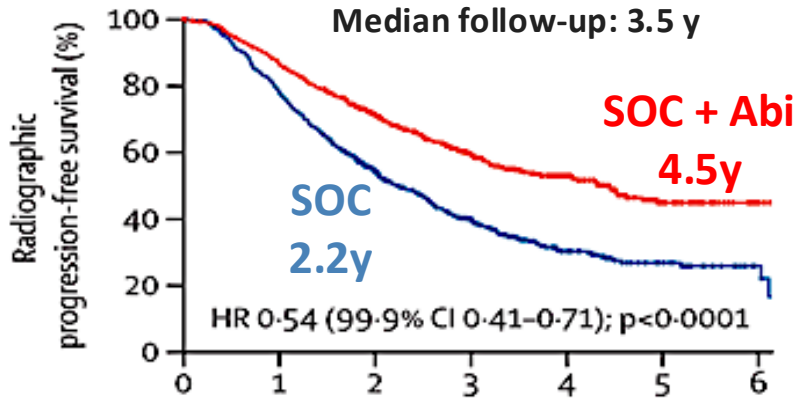
≥ 1 distant lesion on bone and/or CT scan), ECOG PS 0-2



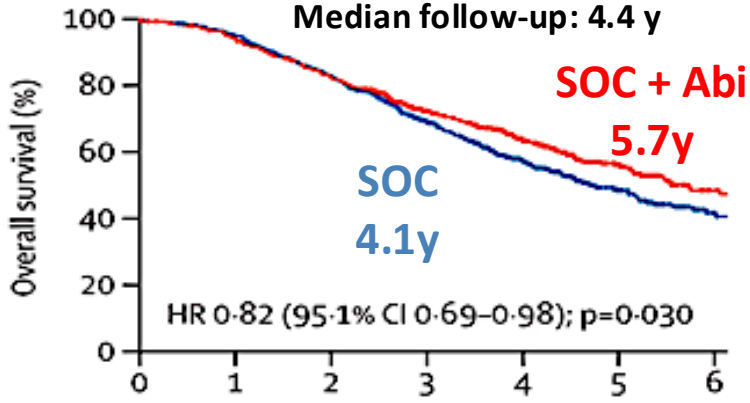
Grade 3-5 AEs (>5%, ABI vs control):
neutropenic fever (5% vs 5%), neutropenia (10% vs 9%), liver toxicity (6% vs 1%) and HTN (21% vs 13%)

Fizazi K, et al. *Lancet*. 2022 Apr 30;399(10336):1695-1707.

Coprimary Endpoints (Overall Population)



Number at risk							
SOC without abiraterone groups	589	453	274	158	72	31	7
SOC plus abiraterone groups	583	495	355	230	119	47	12



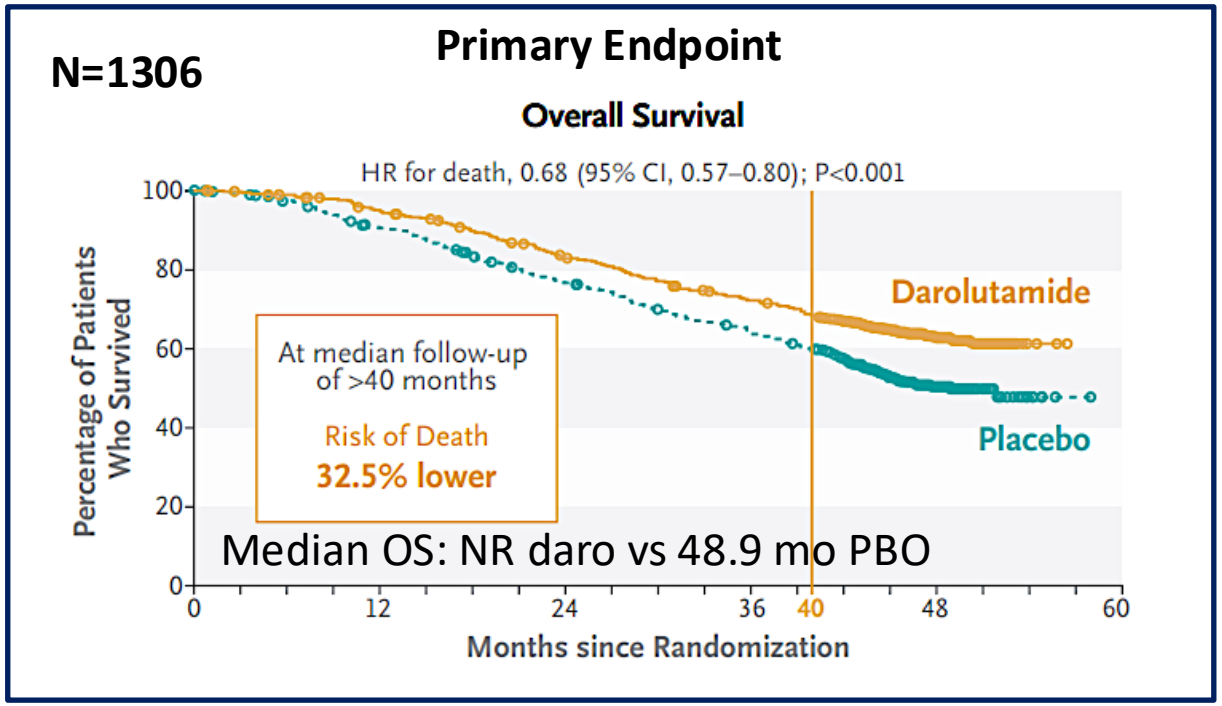
Number at risk							
SOC without abiraterone groups	589	556	480	334	207	101	37
SOC plus abiraterone groups	583	541	470	340	230	111	47

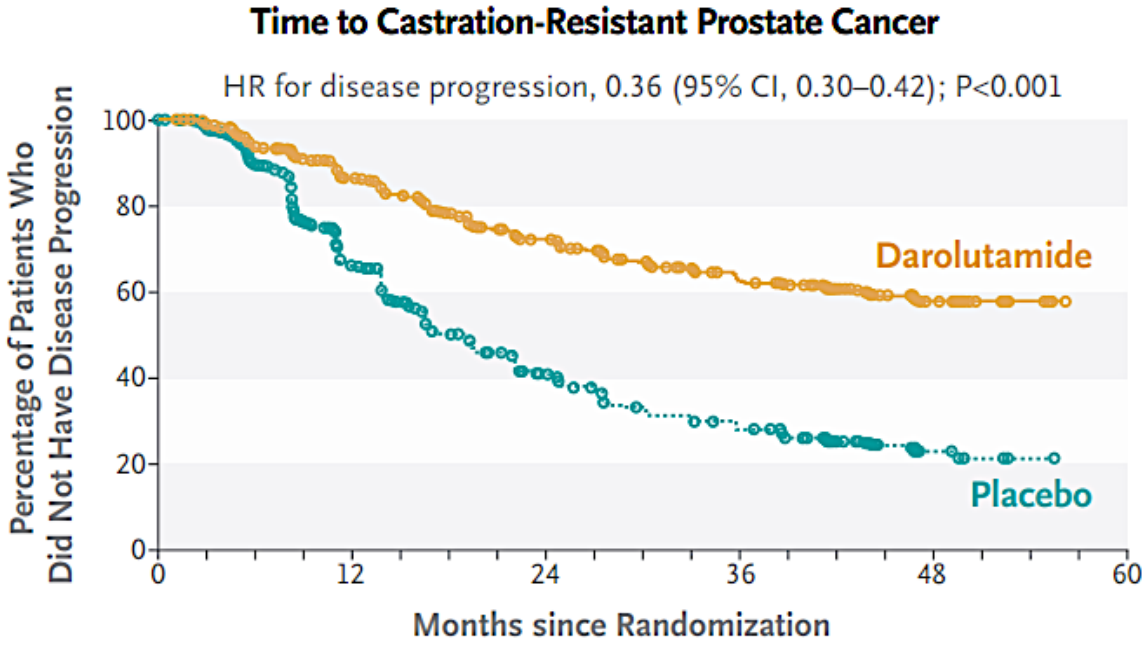
Phase 3 ARASENS Study of Darolutamide + ADT + Docetaxel for Advanced HSPC

- mHSPC, ECOG PS 0-1, candidates for ADT and docetaxel

Safety

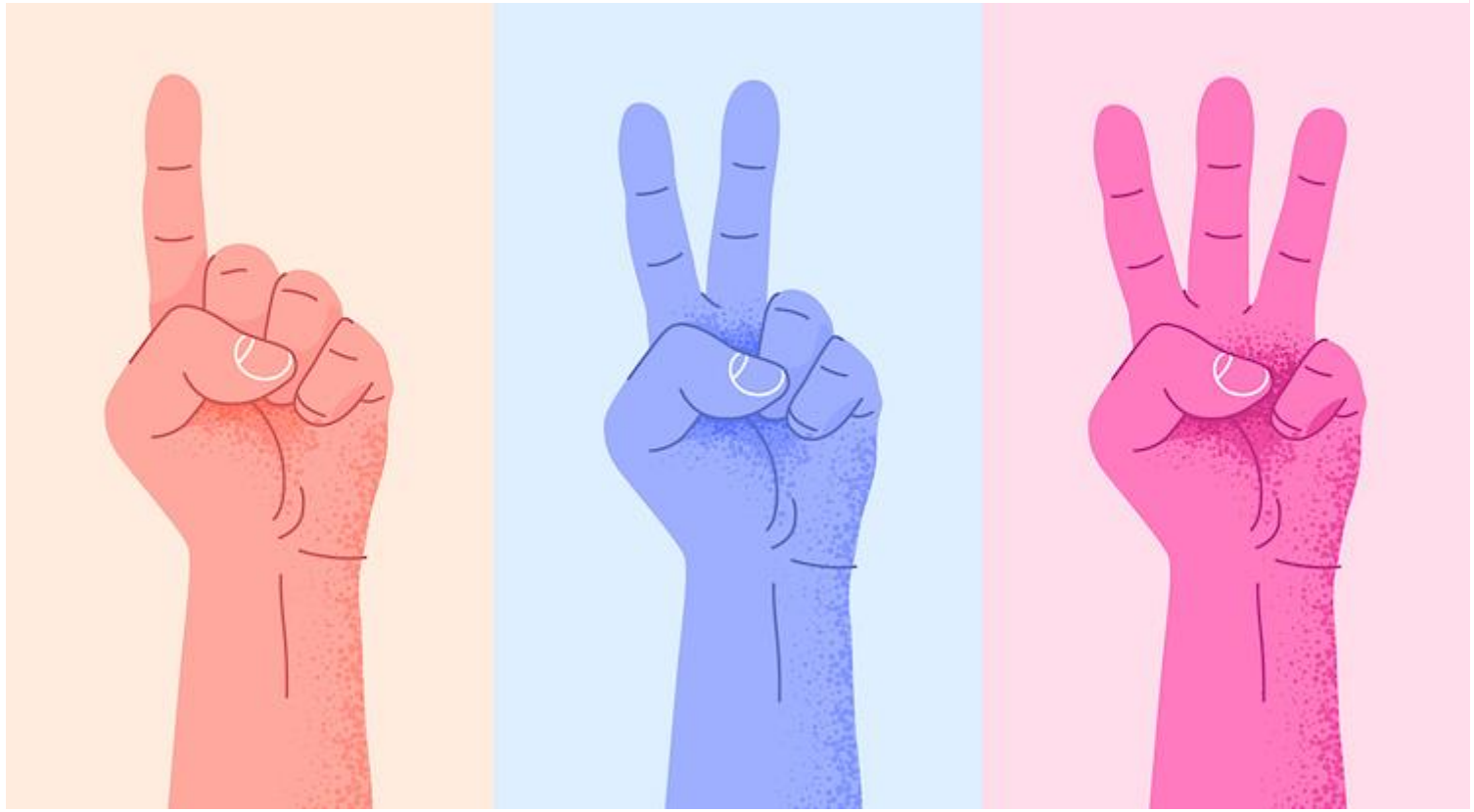
- AE incidence: similar in the 2 groups
- Incidences of most common AEs (≥ 10%) highest during overlapping docetaxel treatment period in both groups
- Grade 3/4 AEs: 66.1% (daro) vs 63.5% (pbo)
  - Neutropenia: 33.7% vs 34.2%
- Serious AEs: 45% vs 42%





Smith MR, et al. *N Engl J Med*. 2022;386:1132-1142.

Metastatic Hormone Sensitive Prostate Cancer



~~AD[illegible]one~~

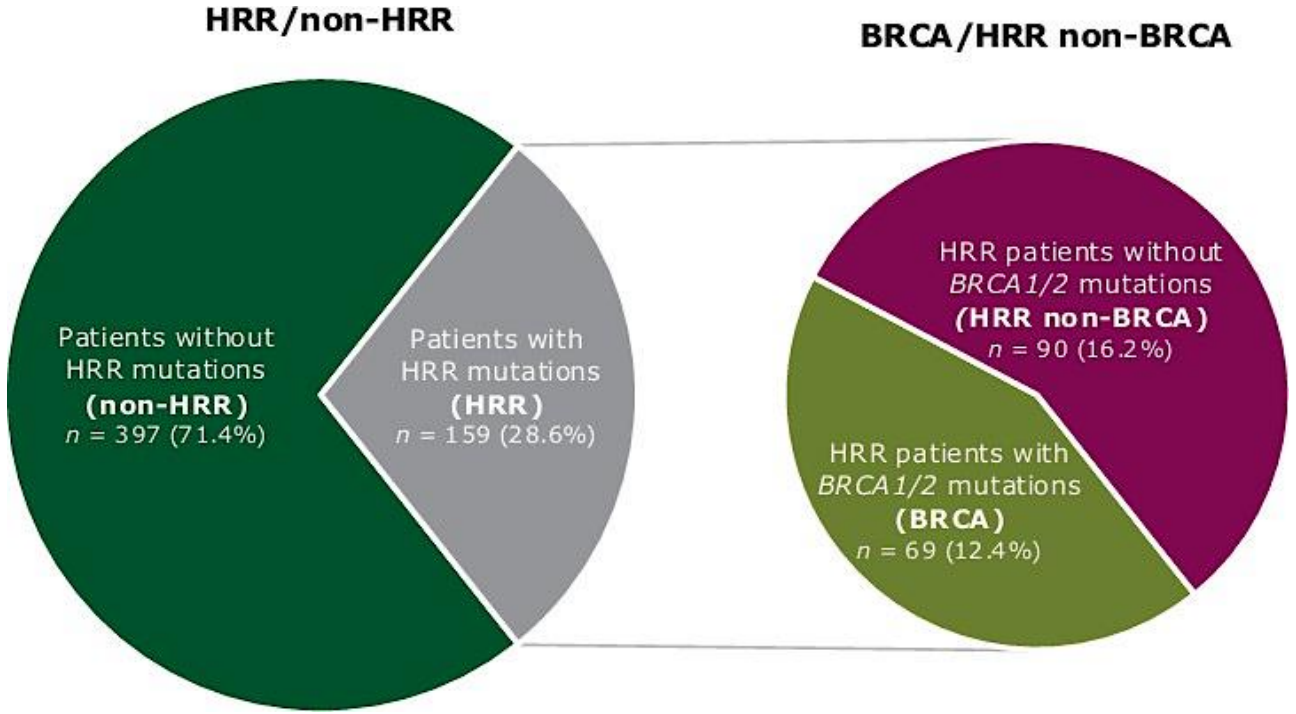
~~ADT + Docetaxel~~

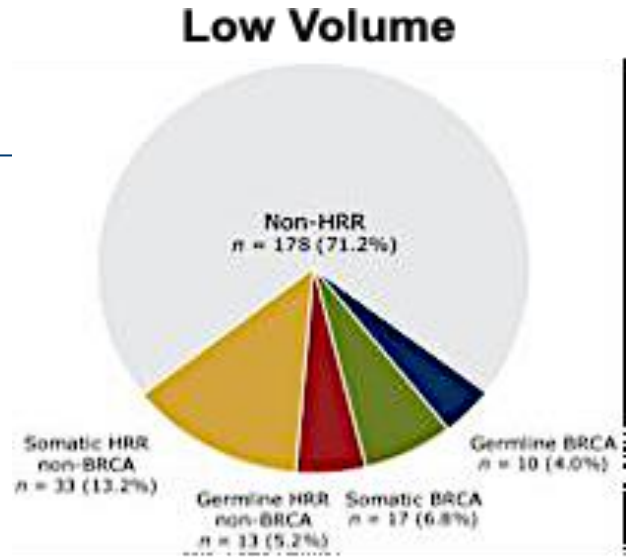
ADT + ARPI

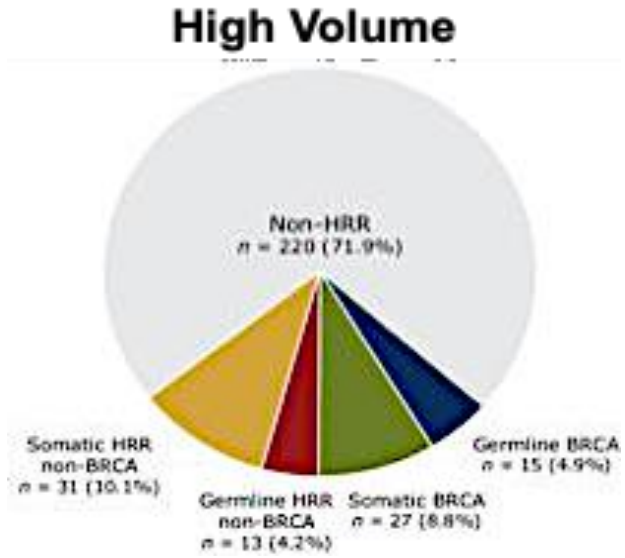
ADT + Docetaxel + Abiraterone

ADT + Docetaxel + Darolutamide

BRCA1/2 and HRR Alterations are Common in the Metastatic Hormone Sensitive Setting





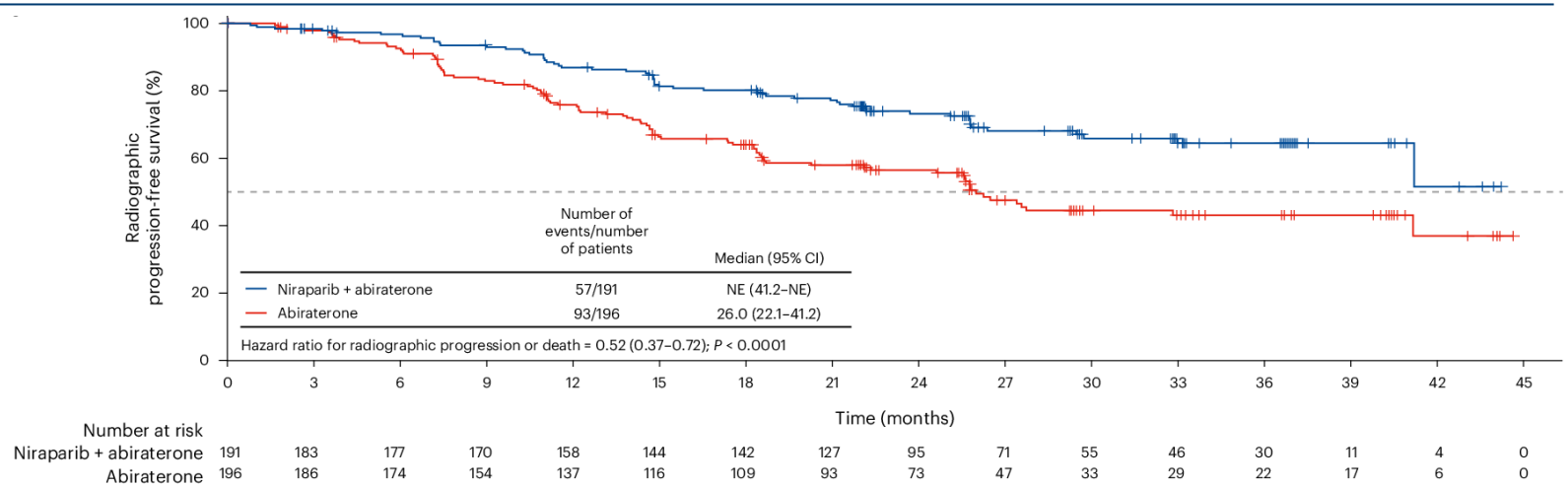


Approximately one-third of mHSPC patients will present with an HRR mutation, with just under half of those patients harboring BRCA mutations; no difference in prevalence is seen in high versus low volume disease, **highlighting the need to test all patients regardless of volume status**

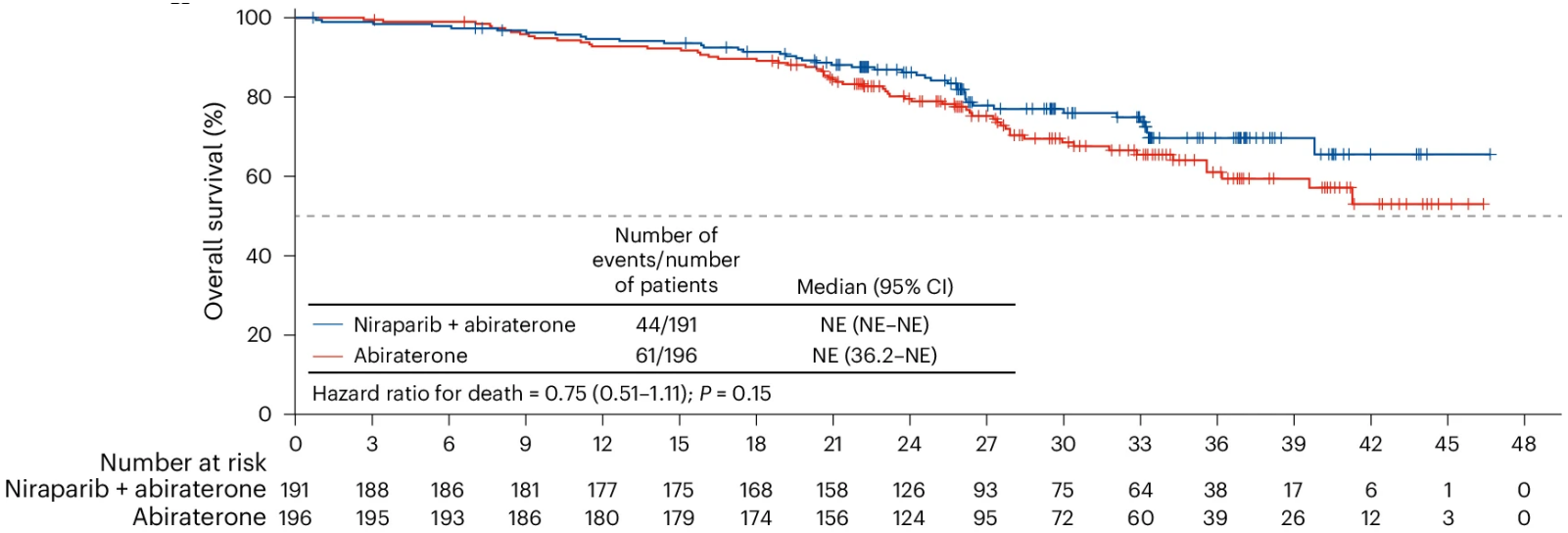
Olmos D et al. *Annals of Oncology*. 2025;36(10):1190-1202.

AMPLITUDE: Abiraterone +/- Niraparib, rPFS and OS in BRCA Subgroup

AMPLITUDE met the primary endpoint: **Nira + AAP significantly reduced the risk of radiographic progression or death by 48% in BRCAm group** (HR 0.52, 95% CI 0.37–0.72)



At the first interim analysis (~50% of total needed events) estimates show **Nira + AAP reduced the risk of death by 25% in the BRCAm subgroup** (HR 0.75, 95% CI 0.51–1.11)



Attard G et al. ASCO 2025; Attard G et al. *Nature*. 2025;31:4109-4118.

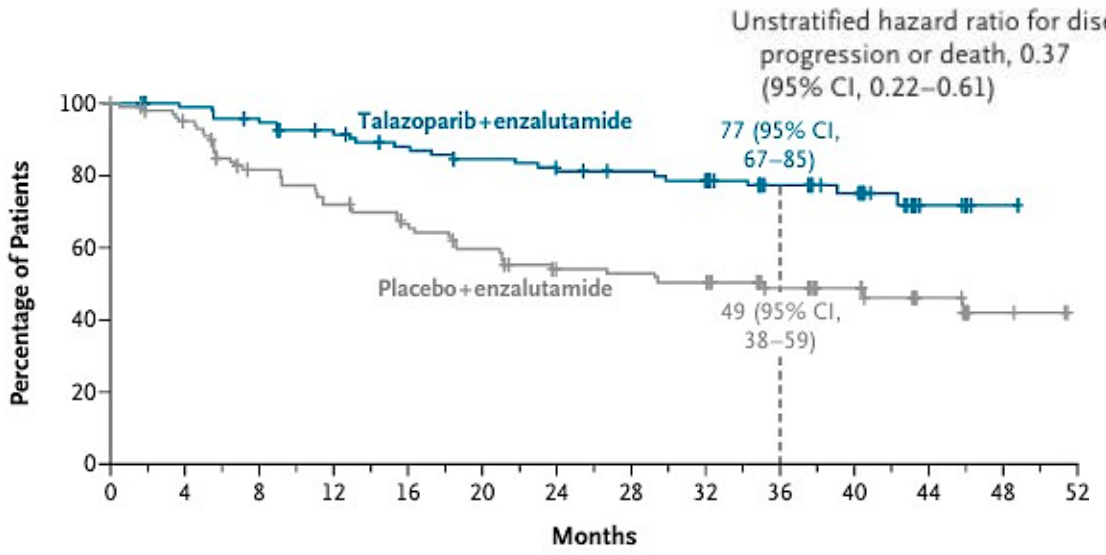
YaleNewHavenHealth Smilow Cancer Hospital | Yale CANCER CENTER A Comprehensive Cancer Center Designated by the National Cancer Institute

TALAPRO-3: rPFS in BRCAm and Interim OS in All Patients

rPFS in Patients with BRCA Mutations

HR 0.37 (95% CI, 0.22–0.61)

	No. of Events/ No. of Patients	Median Imaging-Based Progression-free Survival (95% CI)
		mo
Talazoparib+ Enzalutamide	22/104	NC (NC–NC)
Placebo+ Enzalutamide	49/103	35.1 (18.6–NC)



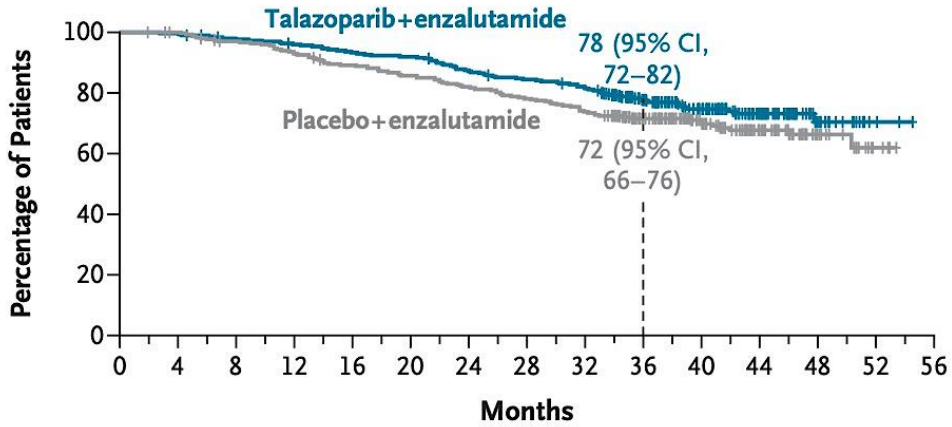
No. at Risk														
Talazoparib+ enzalutamide	104	93	89	82	77	73	69	66	64	46	35	10	4	0
Placebo+ enzalutamide	103	93	76	67	60	53	44	43	41	29	23	12	4	0

Overall Survival in All Patients

HR 0.77 (95% CI, 0.56–1.04)

	No. of Events/ No. of Patients	Median Overall Survival (95% CI)
		mo
Talazoparib+Enzalutamide	74/300	NC (NC–NC)
Placebo+Enzalutamide	91/299	NC (NC–NC)

Stratified hazard ratio for death, 0.77 (95% CI, 0.56–1.04)



No. at Risk															
Talazoparib+enzalutamide	300	299	290	284	276	272	257	248	239	183	121	69	24	3	0
Placebo+enzalutamide	299	297	285	273	260	250	239	228	215	166	113	64	21	5	0

Agarwal N et al. *N Engl J Med*. 2026 May 30;doi:10.1056/NEJMoa2604126

YaleNewHavenHealth Smilow Cancer Hospital | Yale CANCER CENTER A Comprehensive Cancer Center Designated by the National Cancer Institute

CAPItello-281: Trial Design

Patients with PTEN deficient *de novo* mHSPC

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

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

1,012 patients (R 1:1)

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

Primary endpoint

- **Investigator assessed rPFS**

Secondary endpoints

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

Exploratory *post-hoc* PTEN deficiency subgroups

Stratification factors:†

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

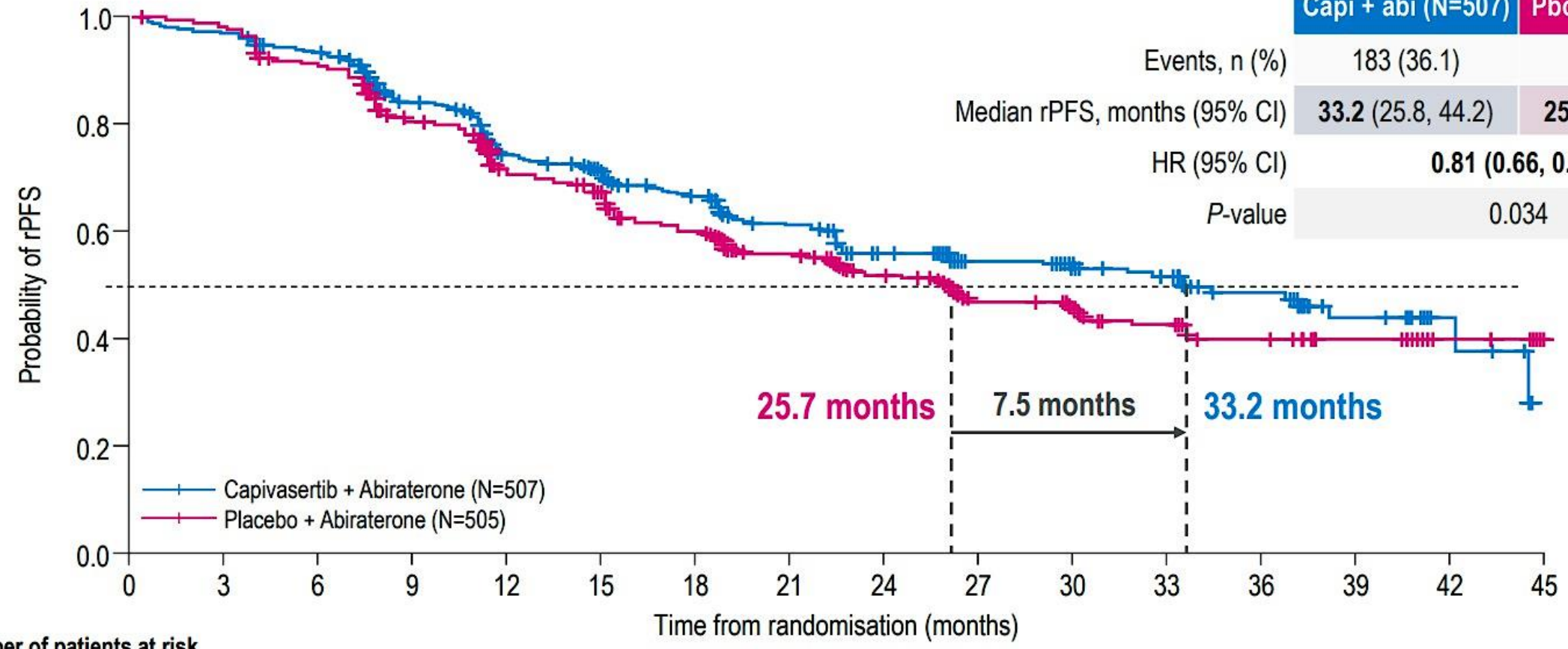
Study timeline

Current analysis

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

Karim Fizazi, ESMO 2025

CAPItello-281: Primary Endpoint rPFS



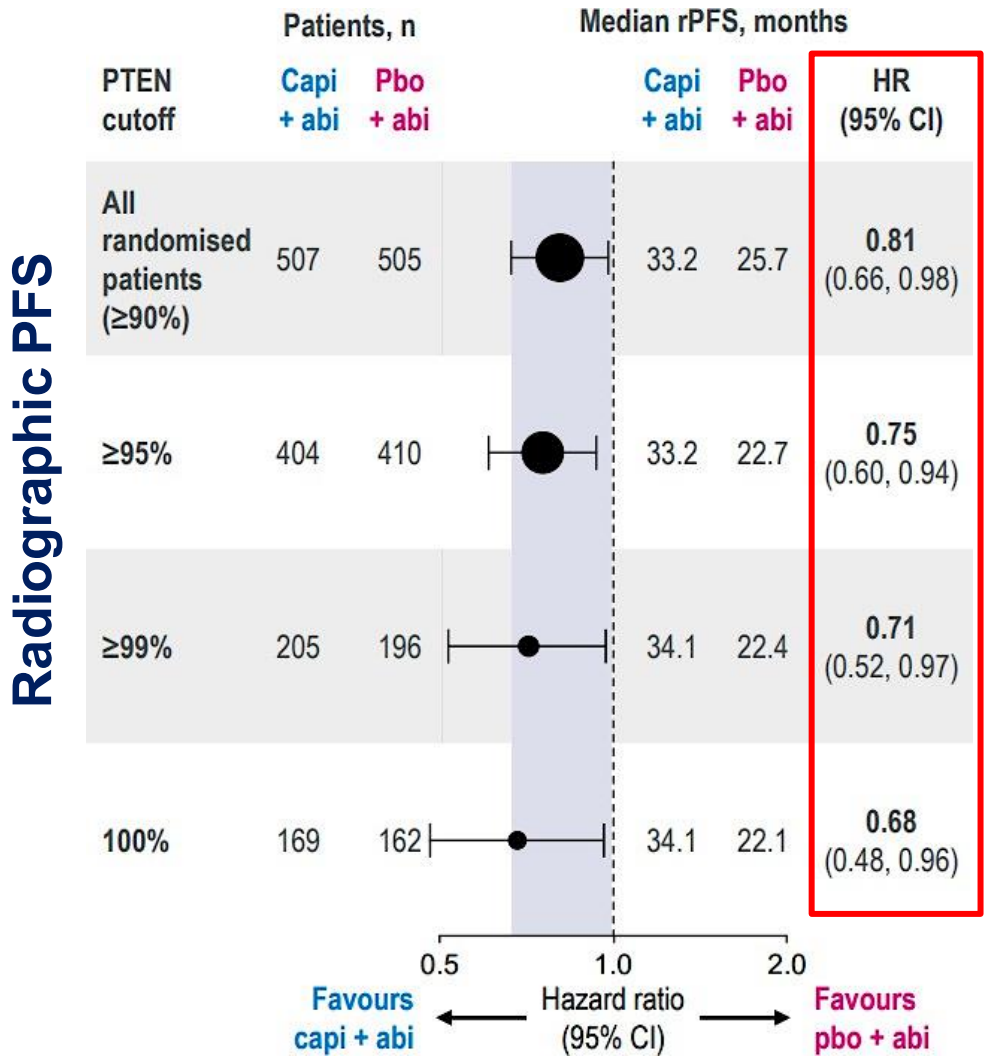
	Capi + abi (N=507)	Pbo + abi (N=505)
Events, n (%)	183 (36.1)	215 (42.6)
Median rPFS, months (95% CI)	**33.2** (25.8, 44.2)	**25.7** (22.0, 29.9)
HR (95% CI)	**0.81 (0.66, 0.98)**	
P-value	0.034	

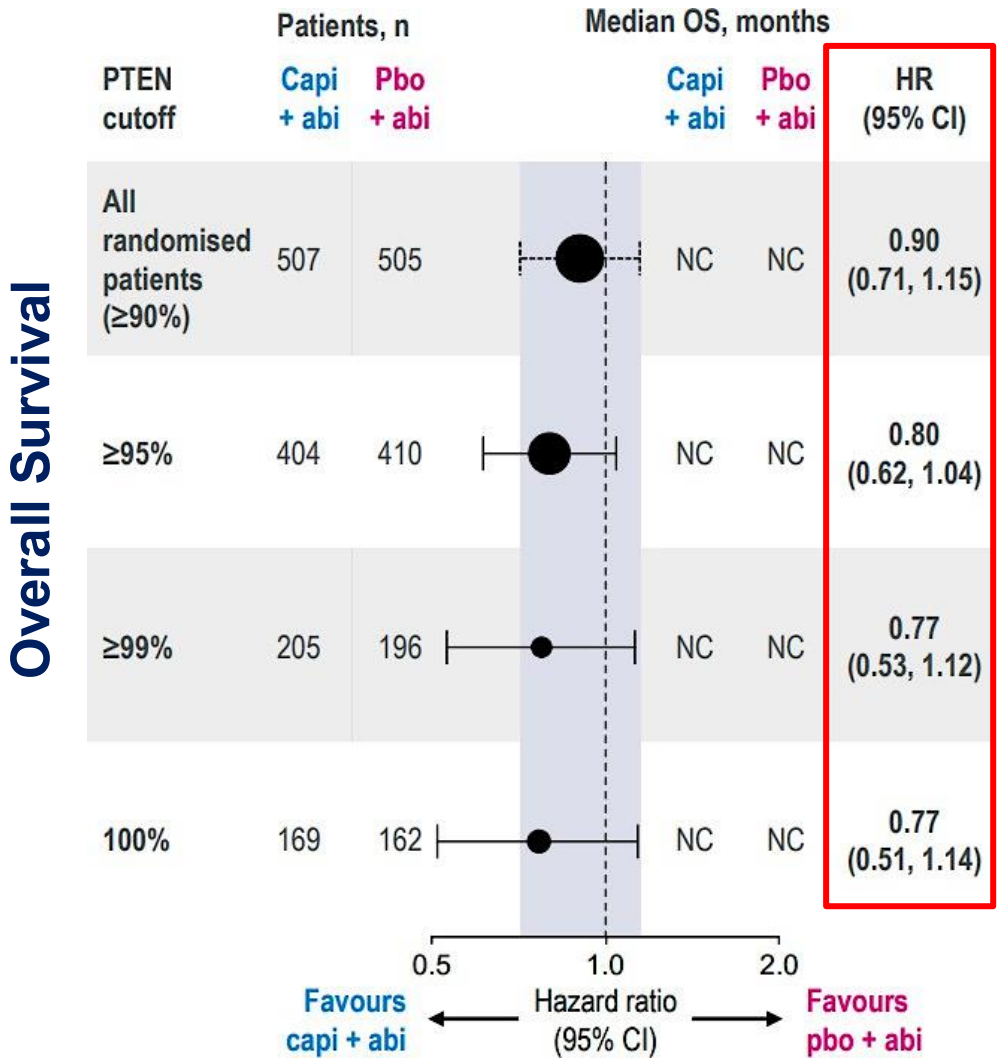
Number of patients at risk

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

Karim Fizazi, ESMO 2025

CAPItello-281: rPFS and OS by PTEN Cutoff

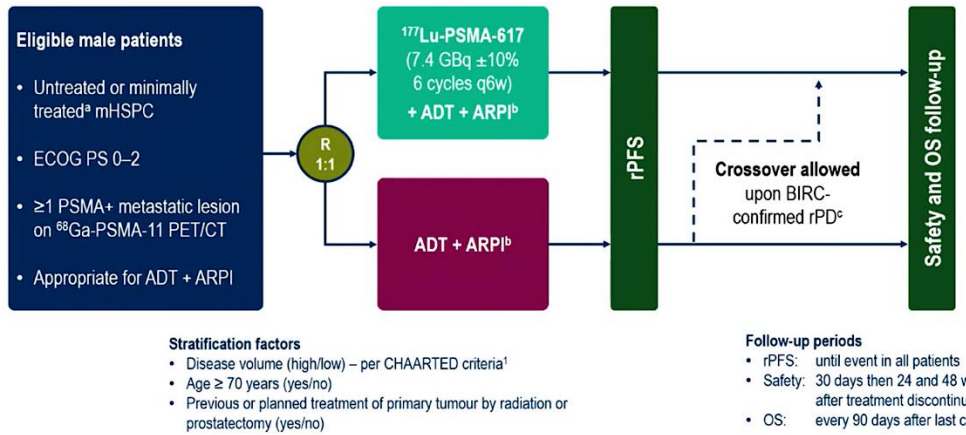




Karim Fizazi, ESMO 2025

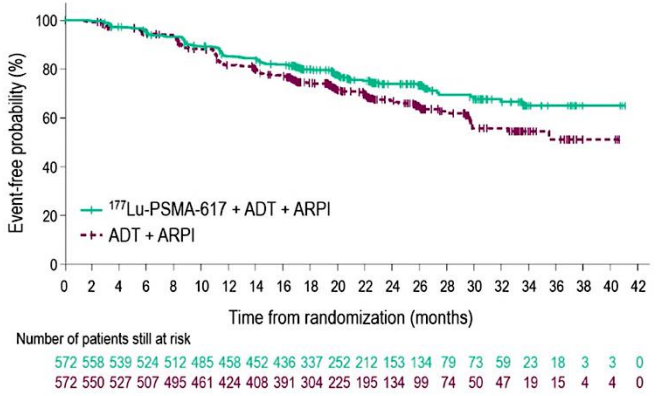
PSMAddition (Phase 3): [177Lu]Lu-PSMA-617 + ADT + ARPI for PSMA-positive metastatic HSPC

PSMAddition: randomized phase 3 trial of ^{177}Lu-PSMA-617 in mHSPC



rPFS by BIRC – the primary endpoint was met

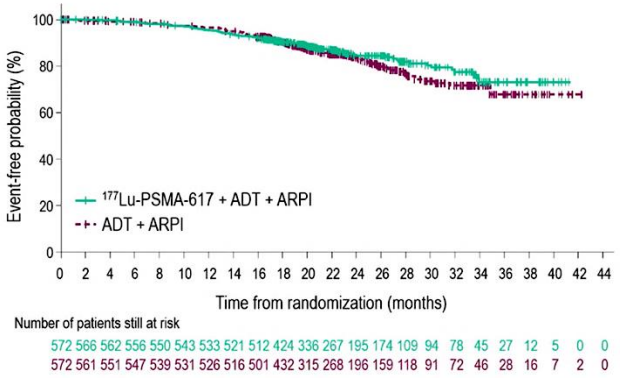
Data cut-off: 13 January 2025



	^{177}Lu-PSMA-617 + ADT + ARPI (N = 572)	ADT + ARPI (N = 572)
Events – n (%) rPD Death without rPD	139 (24.3) 112 (19.6) 27 (4.7)	172 (30.1) 152 (26.6) 20 (3.5)
HR (95% CI)	0.72 (0.58, 0.90)	
p value	0.002[a]	
Median rPFS (95% CI) – months	NR (NE, NE)	NR (29.7, NE)

Interim OS (prespecified intent-to-treat analysis – follow-up continues)

Data cut-off: 13 January 2025



	^{177}Lu-PSMA-617 + ADT + ARPI (N = 572)	ADT + ARPI (N = 572)
Events – n (%)	85 (14.9)	99 (17.3)
Censored – n (%)	487 (85.1)	473 (82.7)
HR (95% CI)	0.84 (0.63, 1.13)	
p value	0.125[a]	
Median OS (95% CI) – months	NR (NE, NE)	NR (NE, NE)

[a] Significance threshold at OS IA1: 0.0011 (one-sided; stratified log-rank test); information fraction, 47.3%

Insights

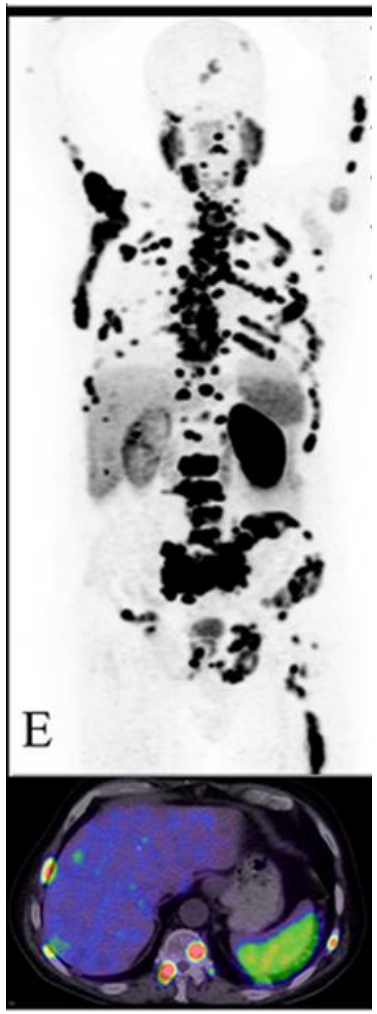
- 6 cycles of Lu177-PSMA in mHSPC had rPFS benefit—met primary endpoint!
- Are 6 cycles too many? PSMA signal is gone
- What are the long-term toxicities?
- Should PSMA PET guide total # cycles?

Tagawa ST, et al. ESMO 2025. Abstract LBA6

Patient 1: A 60 year old Man with Liver Mets

A 60-year-old man presents with urinary retention, fatigue and poor appetite

- Initial PSA 150 ng/mL (none prior)
- TRUS biopsy: adenocarcinoma of the prostate, Gleason score 8
- PSMA PET/CT shows multiple metastatic bone lesions in the pelvis, spine, ribs as well as diffuse liver lesions
- No family history of prostate or other cancers
- Germline and somatic genetic testing is negative
- PMH: HTN



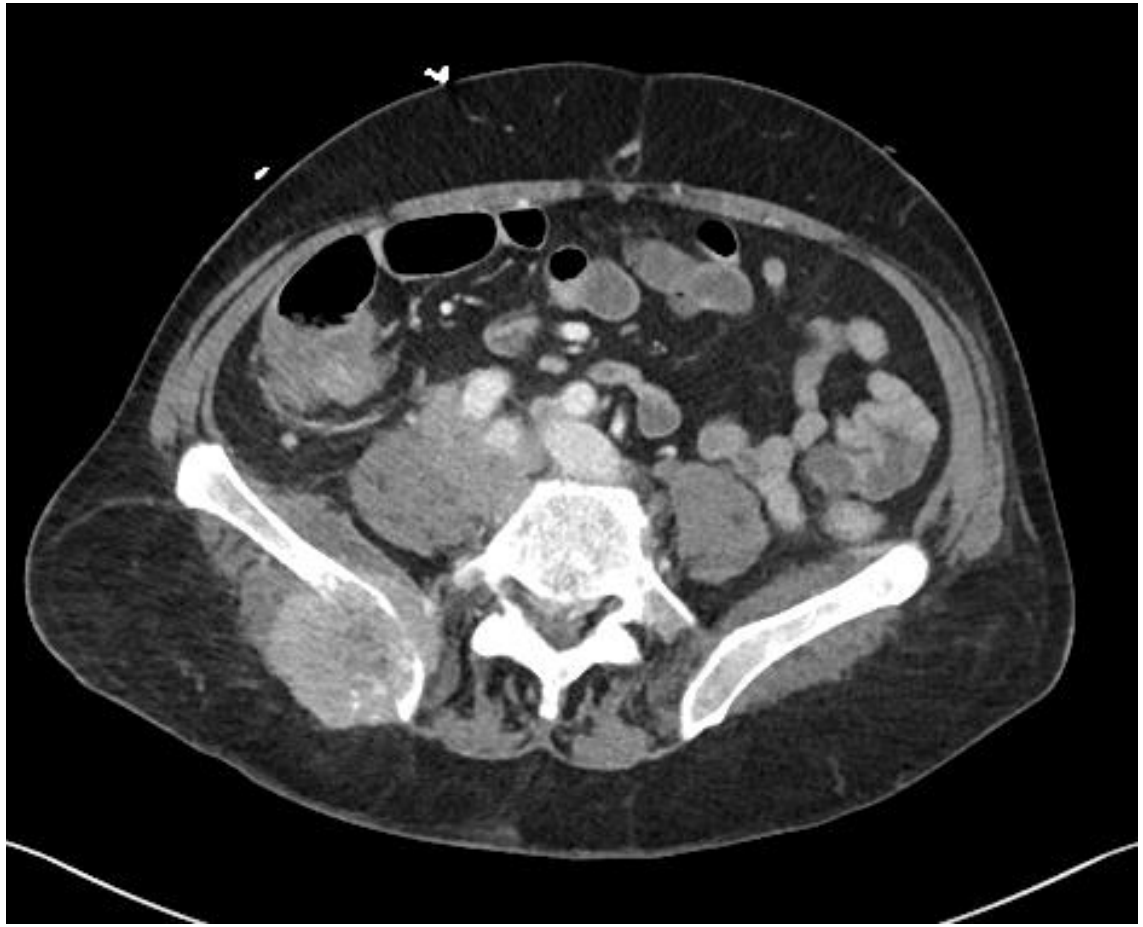
Patient 1

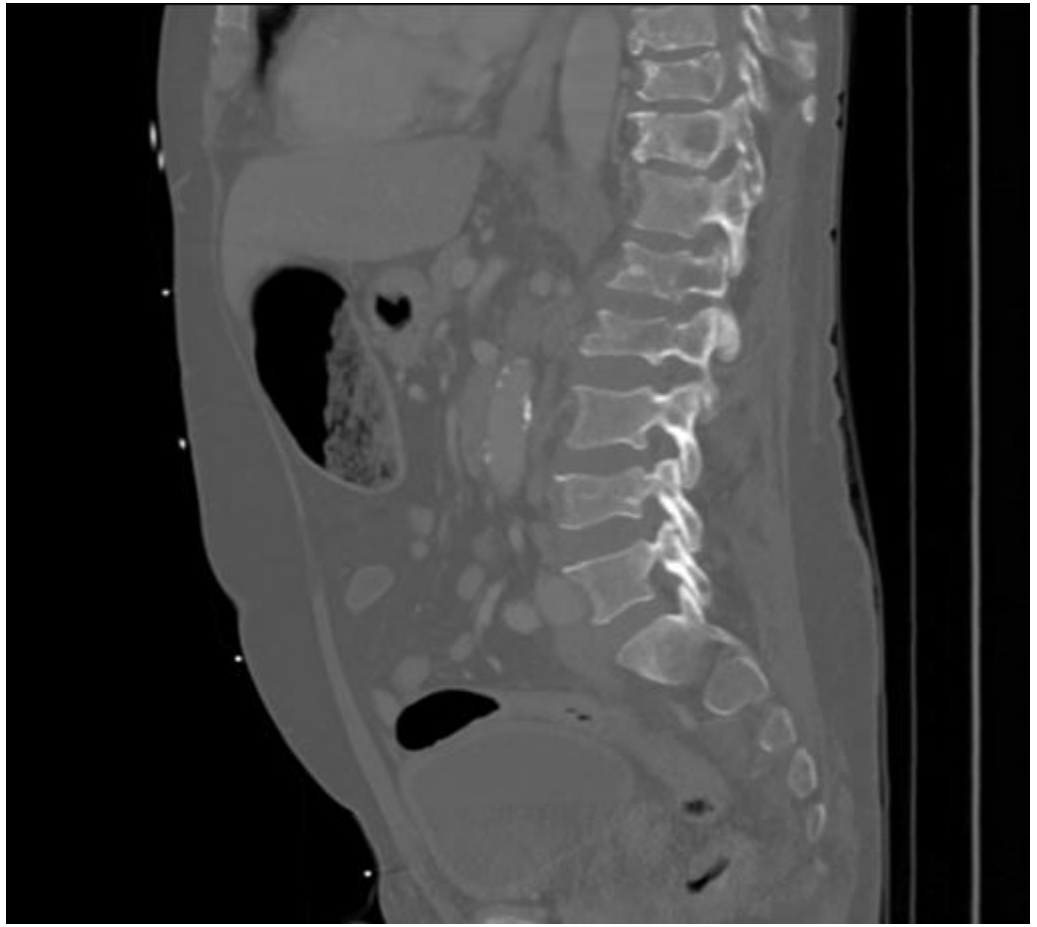
- Therapeutic options available were reviewed with the patient
- ADT was started immediately with leuprolide
- Darolutamide + docetaxel x 6 cycles was recommended given his young age and aggressive recurrence
- Chemotherapy was complicated by fatigue, but he actually gained weight as his tumor regressed
- His PSA responded, dropping to 0.4 after 6 months
- He continues on leuprolide and darolutamide
- PSA, labs and visits are conducted every 3 months

Patient 2: mHSPC in a healthy 82 yo

- 82 yo man presents to the ER with acute back and hip pain: admitted for workup and pain control
- CT CAP with bone metastases but no soft tissue disease
- Bone scan with widespread metastases of the spine, ribs, pelvis, and femur
- No other past medical history
- FH: mother died of ovarian cancer at age 65
- PSA 590 ng/mL

Patient 2





Patient 2

- Biopsy of the iliac mass shows high grade adenocarcinoma, consistent with prostate primary
- PSA (+), synaptophysin and chromogranin A (-)
- Somatic testing shows: SPOP mutation, MSS, TMB low
- Germline testing negative
- He starts ADT and apalutamide and his PSA declines after 1 mo to 25 ng/ml and pain resolves
- He develops an itchy maculopapular rash over arms and back
  - He is prescribed topical steroids and antihistamine and his rash improves over several weeks
- His PSA becomes undetectable within 4 mo and he continues on therapy after 2 years

65-year-old man; Presenting de novo with Gleason 8 prostate cancer; 3 minimally symptomatic bone metastases. What systemic therapy would you recommend?

	BRCA wild type Not PTEN deficient	BRCA2 mutant Not PTEN deficient	BRCA wild type PTEN deficient
 Dr Oh	ADT/ARPI	ADT/ARPI ± PARPi	ADT/ARPI
 Dr Taplin	ADT/ARPI	ADT/ARPI + PARPi	ADT/abiraterone + capivasertib
 Dr Dorff	ADT/ARPI	ADT/enzalutamide + talazoparib	ADT/ARPI
 Dr Smith	ADT/ARPI	ADT/ARPI	ADT/ARPI
 Dr Srinivas	ADT/abiraterone	ADT/abiraterone	ADT/abiraterone + docetaxel
 Dr Yu	ADT/abiraterone	ADT/abiraterone + niraparib	ADT/abiraterone

65-year-old man; Presenting de novo with Gleason 8 prostate cancer; 6 moderately symptomatic bone metastases. What systemic therapy would you recommend?

	BRCA wild type Not PTEN deficient	BRCA2 mutant Not PTEN deficient	BRCA wild type PTEN deficient
 Dr Oh	ADT/ARPI ± docetaxel	ADT/ARPI + PARPi	ADT/ARPI ± capivasertib
 Dr Taplin	ADT/ARPI + docetaxel	ADT/ARPI + PARPi	ADT/abiraterone + capivasertib
 Dr Dorff	ADT/ARPI + docetaxel	ADT/ARPI + PARPi	ADT/abiraterone + capivasertib
 Dr Smith	ADT/ARPI	ADT/ARPI	ADT/ARPI
 Dr Srinivas	ADT/abiraterone	ADT/enzalutamide + talazoparib	ADT/abiraterone
 Dr Yu	ADT/abiraterone	ADT/abiraterone + niraparib	ADT/abiraterone + capivasertib

65-year-old man; Presenting de novo with Gleason 8 prostate cancer; 3 bone and liver metastases. What systemic therapy would you recommend?

	BRCA wild type Not PTEN deficient	BRCA2 mutant Not PTEN deficient	BRCA wild type PTEN deficient
 Dr Oh	ADT/ARPI + docetaxel	ADT/ARPI + docetaxel (consider adding PARPi)	ADT/ARPI + docetaxel (consider adding capi)
 Dr Taplin	ADT/ARPI + docetaxel	ADT/ARPI + docetaxel (consider adding carbo)	ADT/ARPI + docetaxel (consider adding carbo)
 Dr Dorff	ADT/ARPI + docetaxel	ADT/enzalutamide + talazoparib	ADT/abiraterone + (capivasertib or docetaxel)
 Dr Smith	ADT/darolutamide + docetaxel	ADT/darolutamide + docetaxel	ADT/darolutamide + docetaxel
 Dr Srinivas	ADT/abiraterone + docetaxel	ADT/abiraterone + docetaxel	ADT/abiraterone
 Dr Yu	ADT/darolutamide + docetaxel	ADT/abiraterone + niraparib	ADT/darolutamide + docetaxel

How do you manage non-oligometastatic disease observed on PSMA PET only?

 Dr Oh	Treat similar to conventional imaging
 Dr Taplin	SBRT ± ADT or ADT/ARPI
 Dr Dorff	ADT/enzalutamide for 9 months/intermittent (EMBARK)
 Dr Smith	Treat as metastatic disease
 Dr Yu	ADT, preferentially intermittent if there is nothing on conventional imaging

RTP RESEARCH TO PRACTICE

Is there a patient age at which you generally withhold the use of abiraterone?

 Dr Oh	75 years
 Dr Taplin	About 75 years
 Dr Dorff	I prefer AR antagonist for >75 years but will use abiraterone in patients >75 when appropriate
 Dr Smith	I prefer darolutamide (or enzalutamide) for all age groups
 Dr Srinivas	80 years
 Dr Yu	No

RTP RESEARCH TO PRACTICE

In which situations, if any, do you order a bone scan for patients with prostate cancer?

 Dr Oh	Rarely to never
 Dr Taplin	I do not order bone scans outside a clinical trial
 Dr Dorff	When insurance requires, when considering radium-223, or for equivocal PET findings with high suspicion
 Dr Smith	Screening for radium-223, or if required for a clinical trial
 Dr Srinivas	Clinical trials
 Dr Yu	Right now, I'm still doing bone scan most of the time, unless I have a negative PSMA PET. Then it isn't needed

RTP RESEARCH TO PRACTICE

What are your usual criteria for using ADT with docetaxel and darolutamide for patients with metastatic hormone-sensitive prostate cancer (mHSPC)?

 Dr Oh	Fit for chemo, high Gleason, extensive/symptomatic mets, liver mets
 Dr Taplin	High volume, more than 4 metastases
 Dr Dorff	De novo presentation, high volume. Or symptomatic bone mets or high-risk features but not technically high volume
 Dr Smith	De novo metastatic disease with 'high volume' or other criteria (ie tumor suppressor gene loss) consistent with particularly poor expected cancer-specific survival. Also age and comorbidities
 Dr Srinivas	High volume, chemo fit, not an abiraterone candidate
 Dr Yu	De novo and high volume disease by CHAARTED criteria

RTP RESEARCH TO PRACTICE

Do you use the Decipher Prostate genomic classifier assay in deciding when to administer docetaxel for patients with mHSPC?

 Dr Oh	Yes
 Dr Taplin	Not yet, but probably will
 Dr Dorff	No
 Dr Smith	No
 Dr Srinivas	Yes
 Dr Yu	No

RTP RESEARCH TO PRACTICE

The Implications of Recent Datasets for the Current and Future Management of Breast Cancer — An ASCO 2026 Review

A CME/MOC-Accredited Live Webinar

Thursday, July 30, 2026

5:00 PM – 6:30 PM ET

Faculty

Aditya Bardia, MD, MPH

Kevin Kalinsky, MD, MS, FASCO

Joyce O'Shaughnessy, MD

Moderator

Neil Love, 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.

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

RTP
RESEARCH TO PRACTICE