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Multidisciplinary Approaches to Cancer Symposium

Systemic Therapy Updates for Prostate Cancer

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Disclosures

- Consultant for Johnson & Johnson and Dendreon Pharmaceuticals
- Honorarium from MJH Associates

This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

- *Genomic differences between racial groups in patients with prostate cancer*
- *Access to care barriers with emerging prostate cancer therapeutics*

Outline

- **Very high-risk prostate cancer**
  - Multimodal artificial intelligence in STAMPEDE high-risk prostate cancer
- **Metastatic hormone-sensitive prostate cancer (mHSPC)**
  - Health-related quality of life with darolutamide (ARANOTE study)
  - Prognostic value of PSA >0.2 at 6-12 months in mHSPC (IRONMAN registry)
- **Metastatic castration-resistant prostate cancer (mCRPC)**
  - PSMAfore: 177-PSMA-617 in taxane-naïve mCRPC
  - Phase 1 results of pasritamig in mCRPC

Tomorrow (Friday) at 2pm: PARP inhibitors in prostate cancer with Dr. Tanya Dorff

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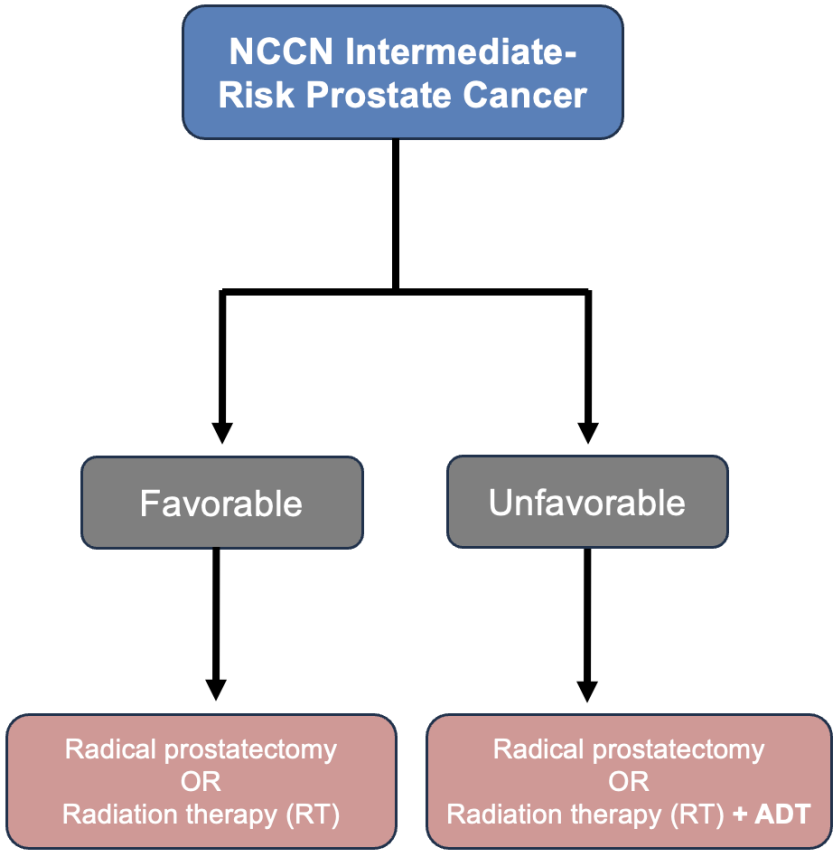
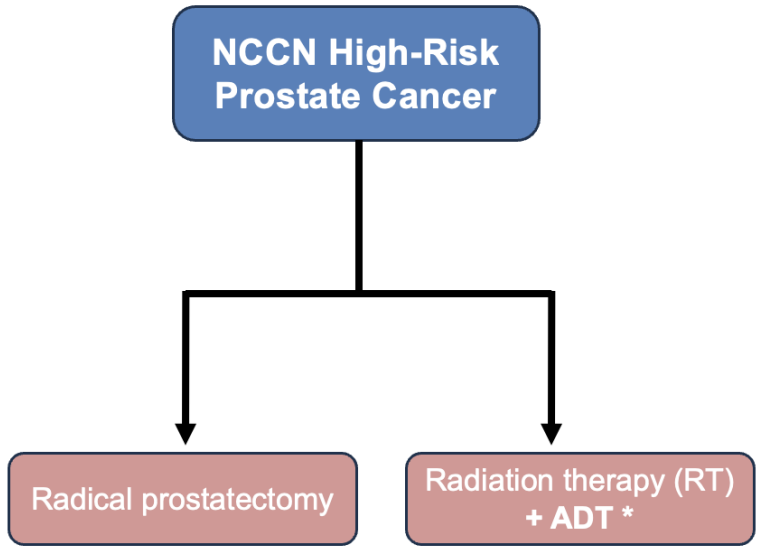
Approach to localized prostate cancer



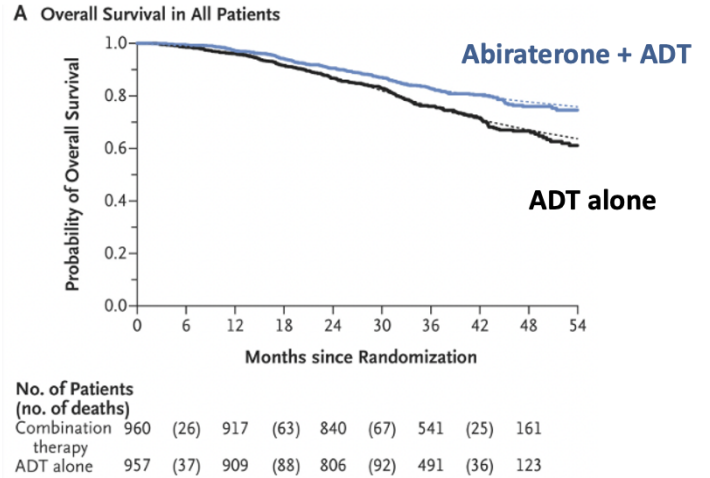


***Add abiraterone if:**
- Node-positive
- NCCN very high-risk

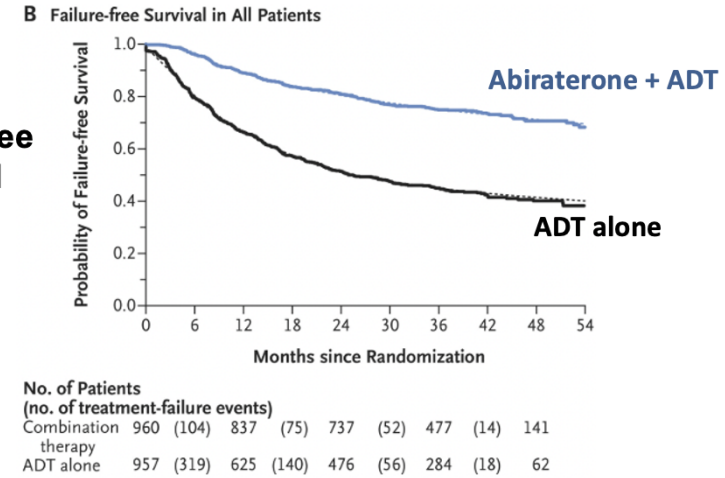
Abiraterone for N+ or NCCN very high risk PC

- **STAMPEDE study**
- Node-positive or
- > 2 of the following
  - T3-T4
  - Gleason 8-10
  - PSA > 40
- Improved outcomes with addition of abiraterone (2-years) to ADT → standard of care
- Increased rates of AEs and Grade 3+ toxicities with combination
- **Can we better select patients for adding abiraterone and other ARPIs?**

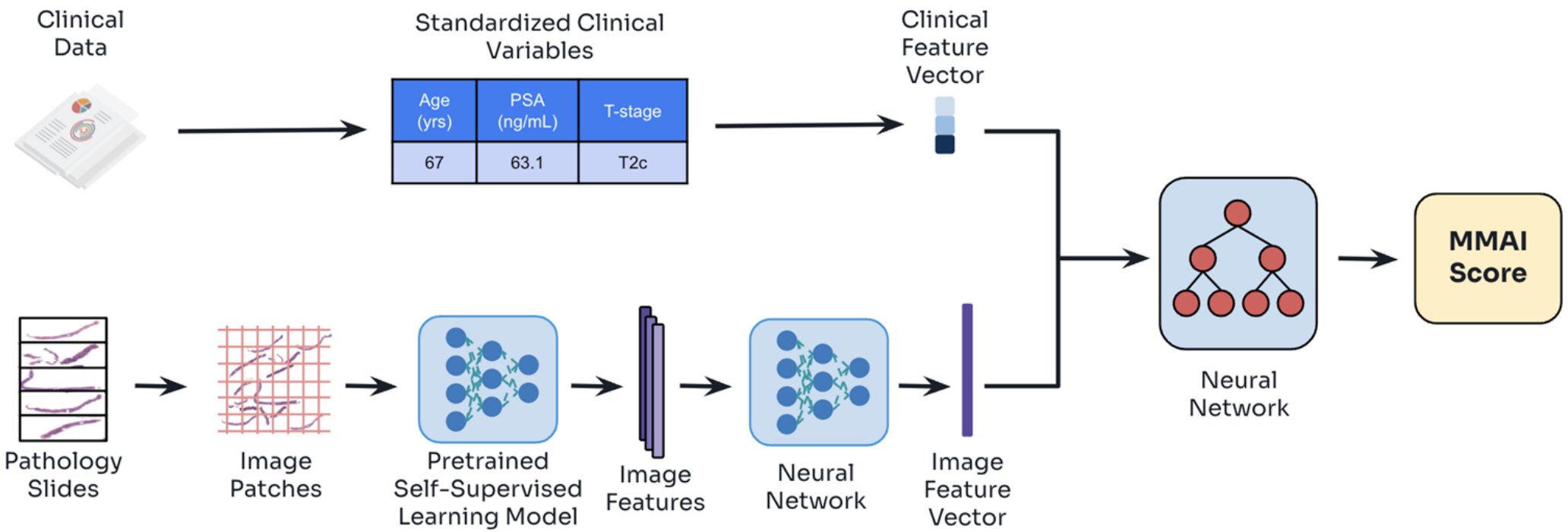
Overall Survival



Failure-Free Survival



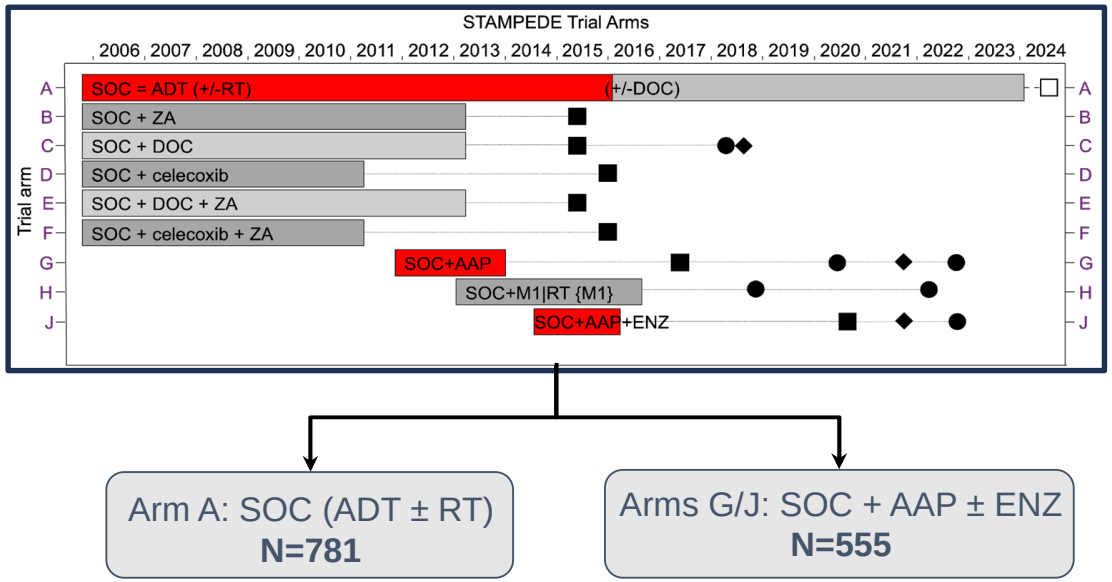
Multimodal artificial intelligence (MMAI) - ArteraAI



James et al. Presented at ASCO 2025

MMAI validation in STAMPEDE

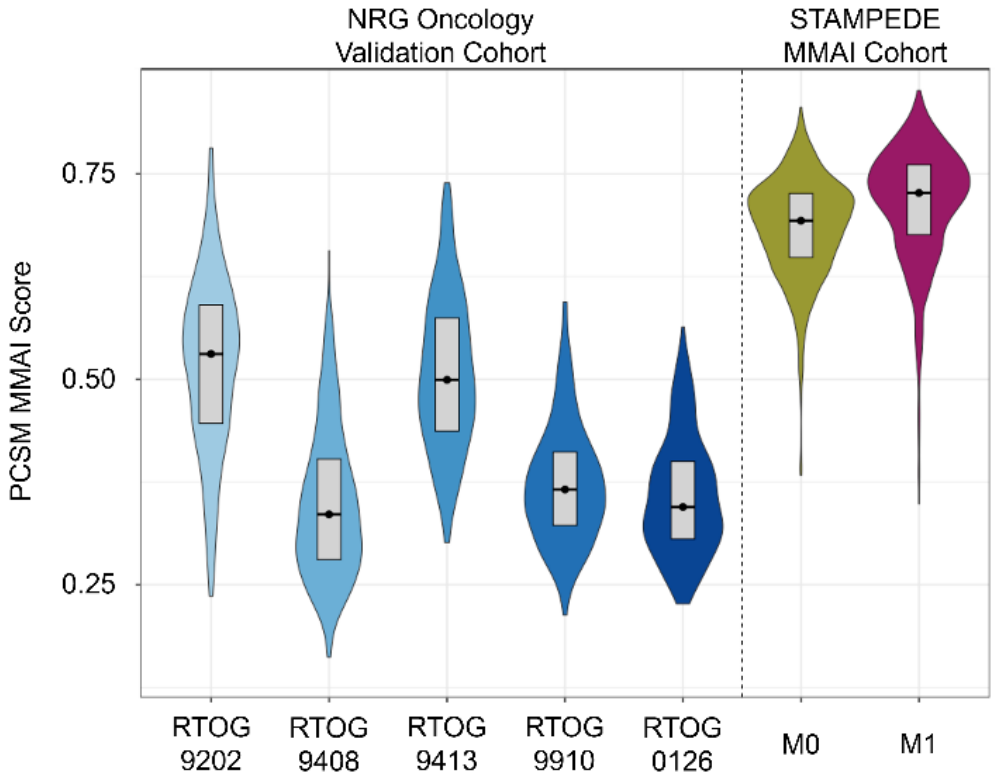
- **Objective:** explore whether MMAI can identify a subset of high-risk patients who are more likely to benefit from the addition of abiraterone
- Post-hoc analysis of STAMPEDE multi-arm studies of ADT + **abiraterone** (+/- enzalutamide)
- Evaluate the association between MMAI scores and clinical outcomes
  - Metastasis-free survival
  - Distant metastasis
  - Prostate cancer-specific mortality



James et al. Presented at ASCO 2025

MMAI validation in STAMPEDE

- MMAI (ArteraAI) was first developed and validated using NRG oncology cohorts of early stage/lower risk prostate cancer
- In STAMPEDE cohort (higher risk) → MMAI scores are overall higher



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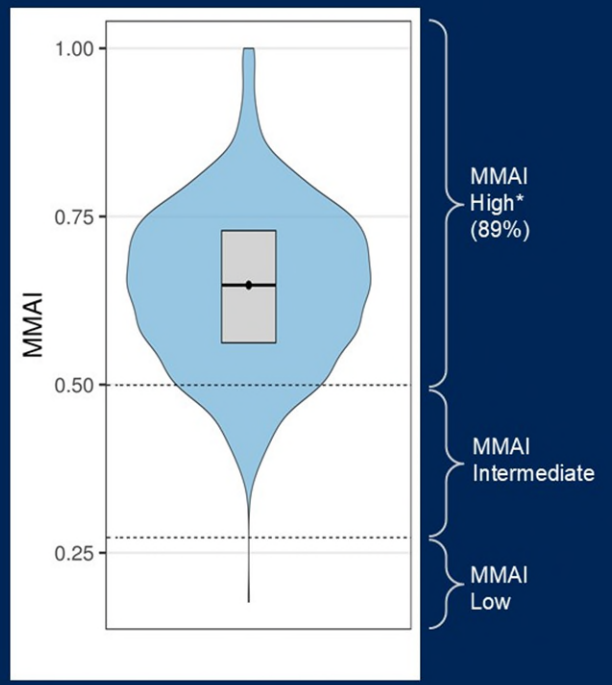
MMAI is prognostic in high-risk disease (STAMPEDE)

Subgroup	Endpoint	(s)/HR (95% CI)	P value
M0	MFS	1.42 (1.29-1.56)	<0.001
	PCSM	1.65 (1.43-1.90)	<0.001
	DM	1.54 (1.36-1.74)	<0.001
N0M0	MFS	1.51 (1.31-1.74)	<0.001
	PCSM	1.95 (1.47-2.60)	<0.001
	DM	1.61 (1.32-1.96)	<0.001
N1M0	MFS	1.26 (1.10-1.43)	<0.001
	PCSM	1.38 (1.18-1.62)	<0.001
	DM	1.38 (1.18-1.63)	<0.001

Continuous MMAI score (per 1 SD increase)



*Using clinically-established prognostic cut-offs, 89% (N=1,189) of M0 patients were MMAI High**

**As per ArteraAI Prostate Test cut-offs*

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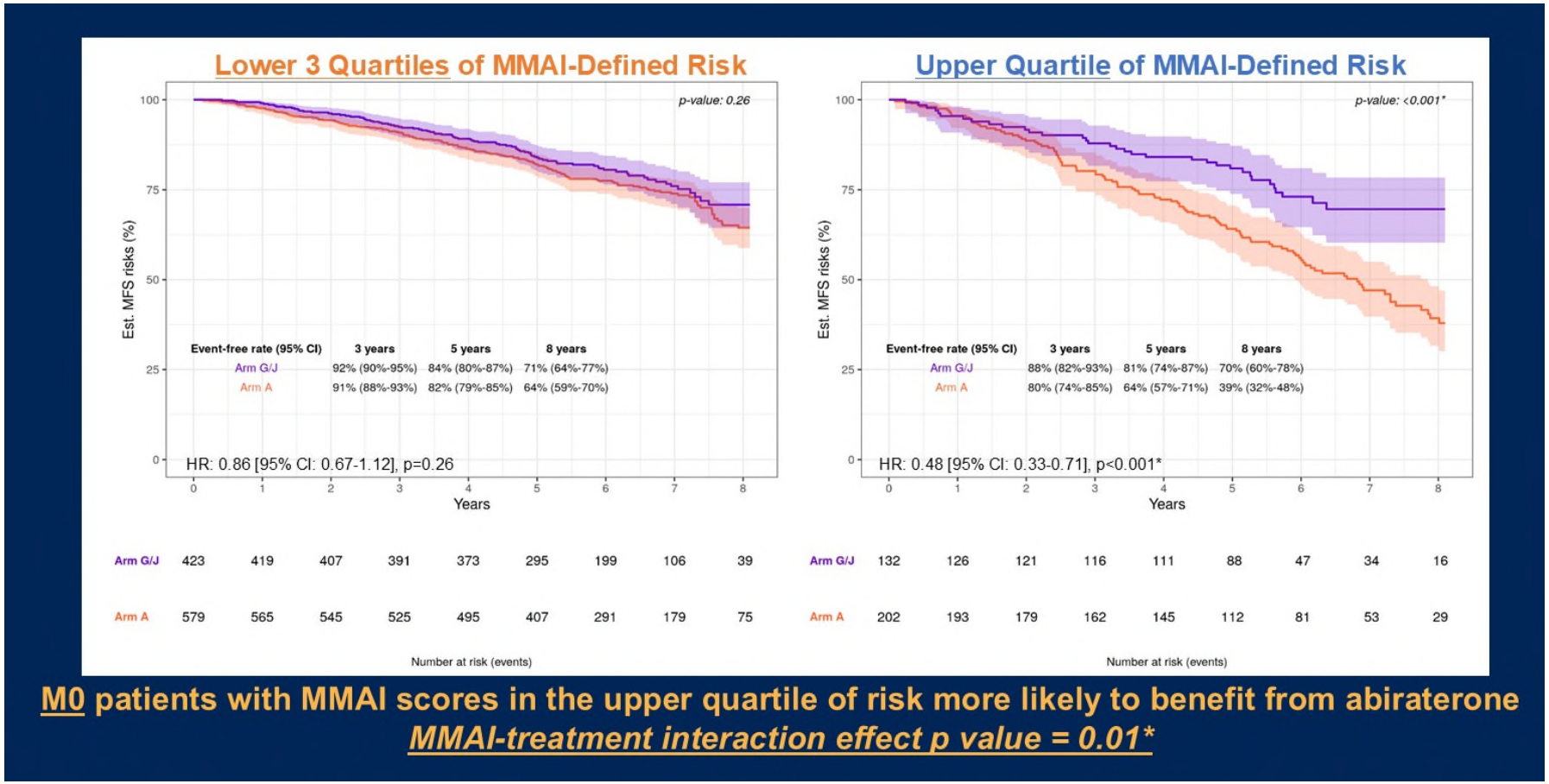
Patients with upper quartile MMAI scores derive greatest benefit from abiraterone



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Patients with upper quartile MMAI scores derive greatest benefit from abiraterone

Endpoint*	Group	SOC	SOC+AAP	Absolute Difference in Risk	Interaction p-value
MFS	**Upper Quartile**	**64% (57%-71%)**	**81% (74%-87%)**	**17%**	0.01*
	Lower 3 Quartiles	82% (79%-85%)	84% (81%-87%)	2%	
PCSM	**Upper Quartile**	**17% (12%-23%)**	**9% (5%-15%)**	**8%**	0.04*
	Lower 3 Quartiles	7% (5%-9%)	4% (3%-7%)	3%	
DM	**Upper Quartile**	**22% (16%-28%)**	**10% (6%-16%)**	**12%**	0.40
	Lower 3 Quartiles	13% (10%-15%)	8% (5%-11%)	5%	

*Estimated 5-year risk

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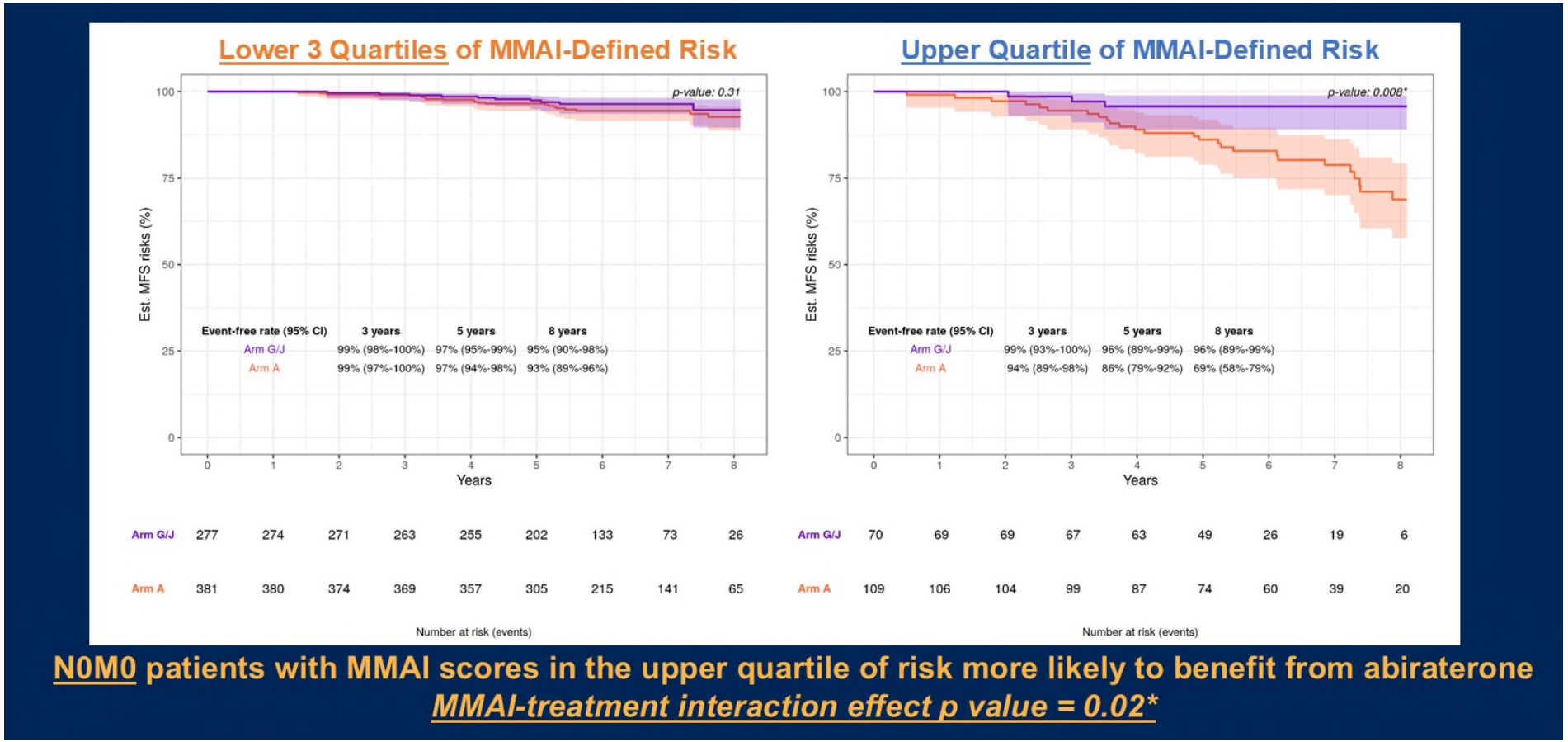
MMAI in node-negative subgroups



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MMAI in STAMPEDE: key takeaways

- Addition of abiraterone (2-years) to ADT is standard of care for patients with node-positive or NCCN very-high risk disease → potential toxicities
- In this post-hoc analysis of STAMPEDE, **MMAI upper quartile scores** are **prognostic** and **may identify** patients who derive the greatest benefit from abiraterone
- Limitations:
  - Cut-point derived retrospectively
  - Needs further validation in other datasets including with other ARPIs and disease stages (e.g., metastatic)
- Supports future integration of digital pathology in prostate cancer treatment decision making and biomarker-guided prospective studies

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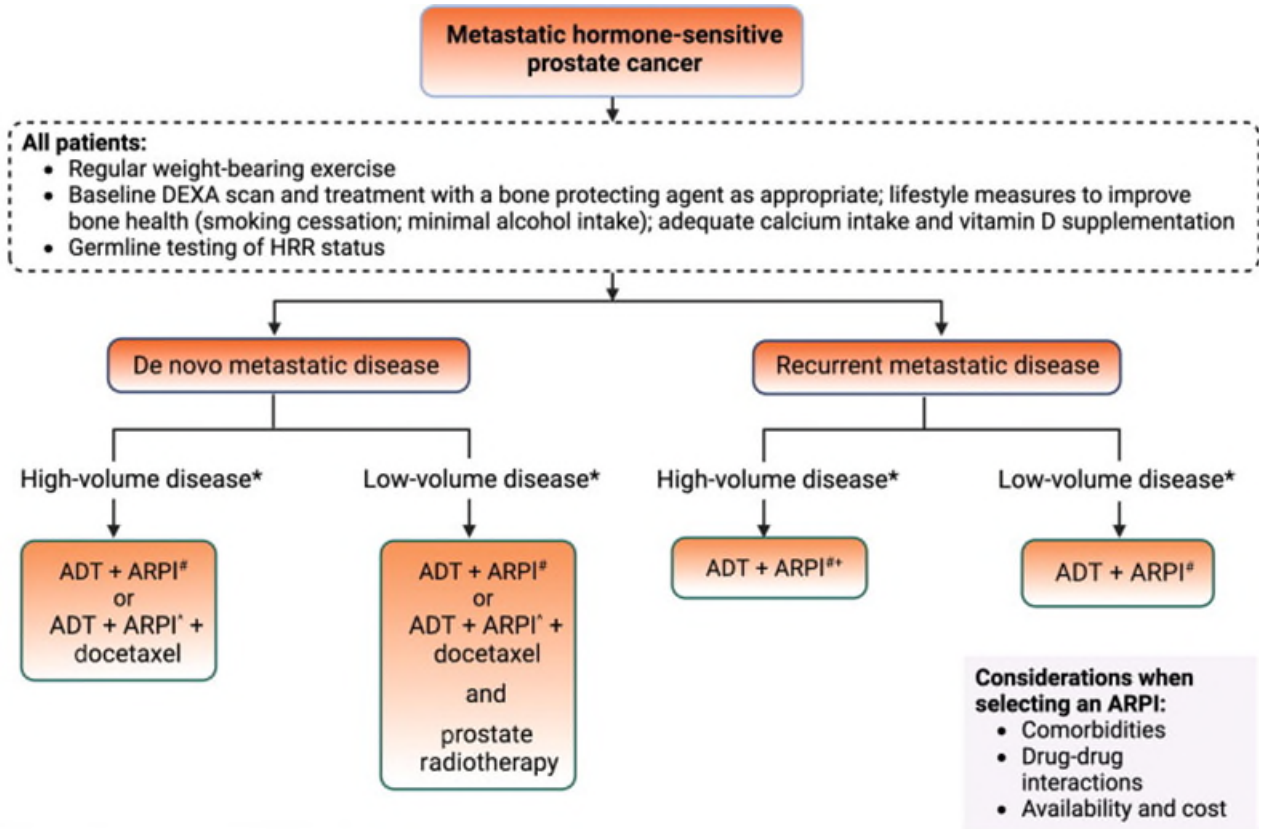
Metastatic hormone-sensitive prostate cancer (mHSPC)

- Current treatment approach relies on disease factors
  - Disease **timing**: de novo versus recurrent disease
  - Disease **volume:** high-volume versus low volume (per CHAARTED criteria)
- *Most* patients are treated with ADT + ARPI doublet
- Triplet therapy with docetaxel if high-volume disease (particularly if *de novo*)
- ARPI options
  - Abiraterone
  - Enzalutamide
  - Apalutamide
  - Darolutamide (ARANOTE and ARASENS)



Azad et al. Eur Urol 2025

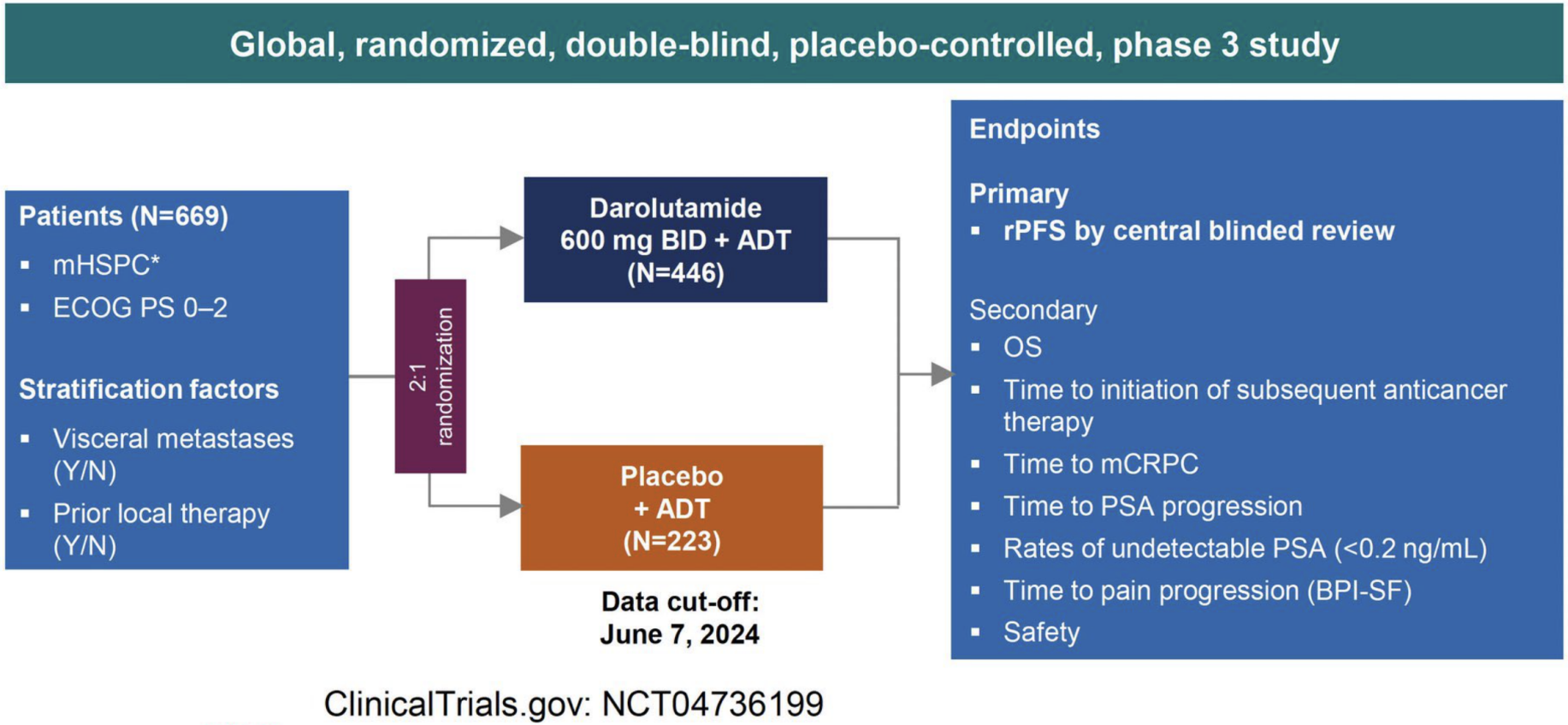
Health-related quality of life (HRQoL) outcomes with darolutamide in the phase 3 ARANOTE trial

Alicia K. Morgans[1], Kunhi Parambath Haresh[2], Mindaugas Jievaltas[3], David Olmos[4], Neal D. Shore[5], Egils Vjaters[6], Nianzeng Xing[7], Ateesha F. Mohamed[8], Natasha Littleton[9], Shankar Srinivasan[8], Frank Verholen[10], and Fred Saad[11]

[1]Dana-Farber Cancer Institute, Boston, MA; [2]All India Institute of Medical Sciences, New Delhi, India; [3]Lithuanian University of Health Sciences, Medical Academy, Kaunas, Lithuania; [4]Hospital Universitario 12 de Octubre, Instituto de Investigación Sanitaria Hospital 12 de Octubre (Imas 12), Madrid, Spain; [5]Carolina Urologic Research Center and AUC Urology Specialists, Myrtle Beach, SC; [6]P. Stradiņs Clinical University Hospital, Riga, Latvia; [7]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [8]Bayer HealthCare Pharmaceuticals, Inc., Whippany, NJ; [9]Bayer Ltd, Dublin, Ireland; [10]Bayer Consumer Care AG, Basel, Switzerland; [11]Department of Surgery/Urology, Centre Hospitalier de l'Université de Montréal, University of Montreal, Montreal, QC, Canada

Morgans et al. Presented at ASCO 2025

ARANOTE: ADT + darolutamide



Saad et al. Presented at ESMO 2024

ARANOTE: ADT + darolutamide

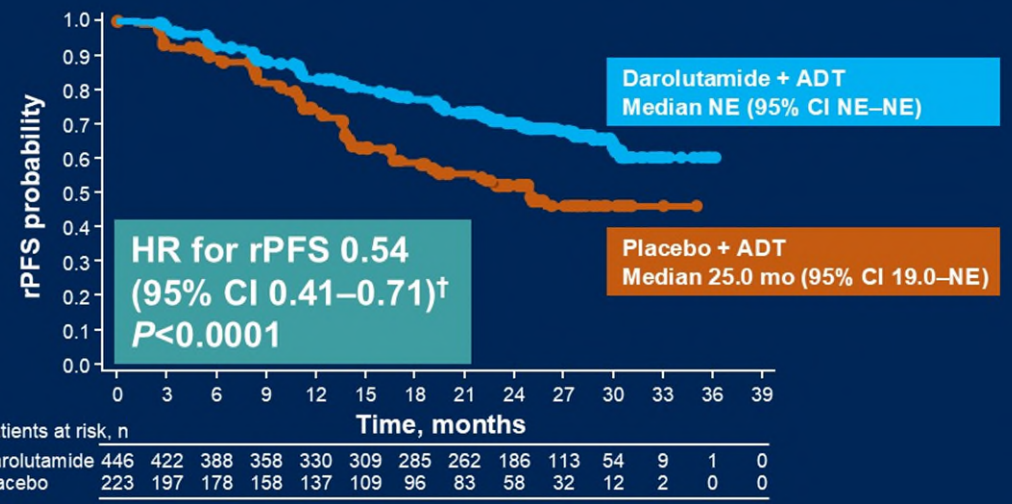
Baseline characteristic		Darolutamide + ADT (n=446)	Placebo + ADT (n=223)
Age, years	Median (range)	70 (43–93)	70 (45–91)
Region, %	Asia	31.6	28.3
	Latin America	26.7	32.3
	Europe/Rest of World	41.7	39.5
ECOG PS, %	0	52.7	43.9
	1–2	47.3	56.1
Gleason score at initial diagnosis, %	≥8	69.7	65.5
Serum PSA, ng/mL	Median (range)	21 (0.02–15,915)	21 (0.02–8,533)
Metastases at initial diagnosis, %	Yes (*de novo*)	71.1	75.3
Disease volume (CHAARTED criteria), %	High	70.6	70.4
Visceral metastases, %	Yes	11.9	12.1
Prior local therapy, %	Yes	17.9	17.9

1. Saad F, et al. *J Clin Oncol* 2024;42:4271–4281. ADT, androgen-deprivation therapy; ECOG PS, Eastern Cooperative Oncology Group performance status; PSA, prostate-specific antigen.

Morgans et al. Presented at ASCO 2025

ARANOTE: ADT + darolutamide

rPFS (primary endpoint)*



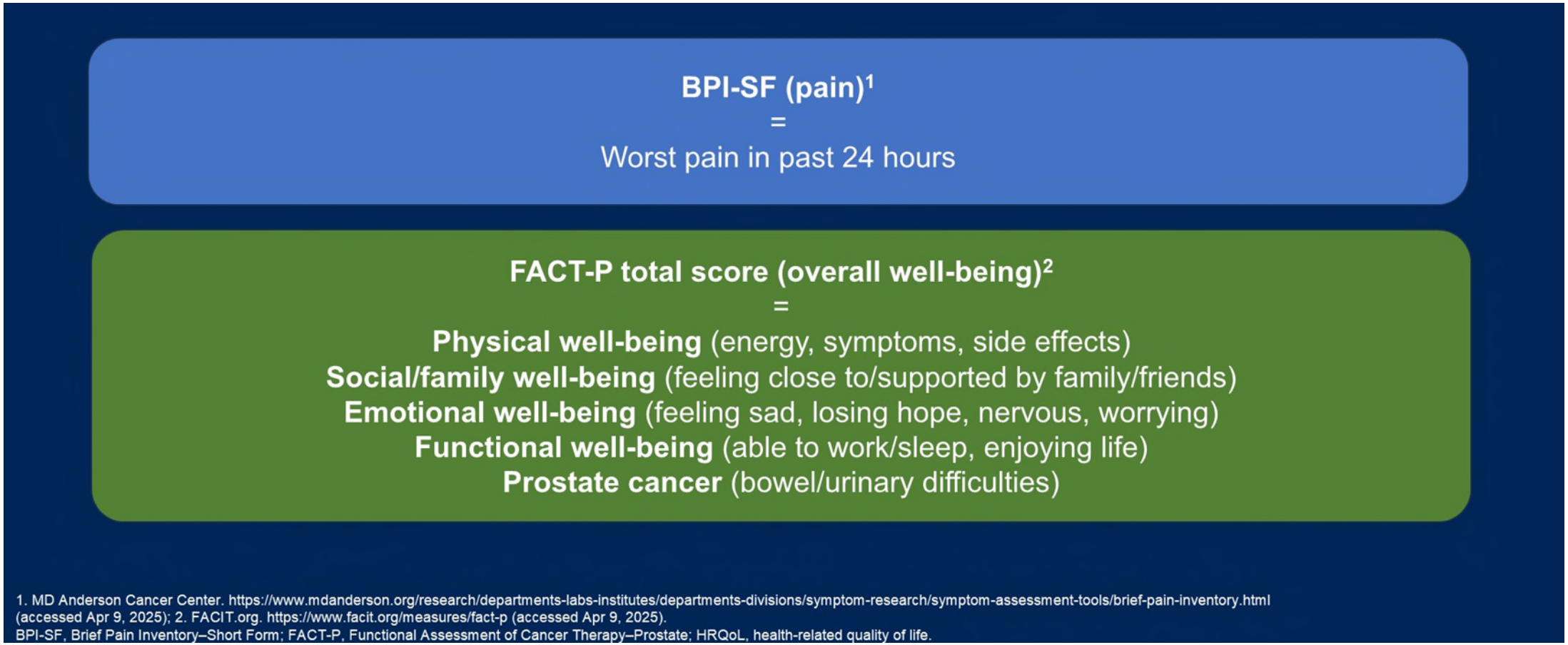
Treatment-emergent adverse events

TEAEs, %	Darolutamide + ADT (n=445‡)	Placebo + ADT (n=221‡)
Any	91.0	90.0
Worst grade		
Grade 3 or 4	30.8	30.3
Grade 5	4.7	5.4
Serious	23.6	23.5
TEAEs leading to permanent discontinuation of study drug	6.1	9.0

1. Saad F, et al. *J Clin Oncol* 2024;42:4271–4281.
Median follow-up: darolutamide group 25.3 months; placebo group 25.0 months; median treatment duration: darolutamide group 24.2 months; placebo group 17.3 months.
*Primary analysis occurred after 222 events (darolutamide 128; placebo 94). †HR and 95% CI were calculated using the Cox model stratified on visceral metastases and prior therapy.
‡Two patients who were randomized to the placebo group but received darolutamide are analyzed in the darolutamide group for the safety analysis set.
ADT, androgen-deprivation therapy; CI, confidence interval; HR, hazard ratio; NE, not estimable; rPFS, radiological progression-free survival; TEAE, treatment-emergent adverse event

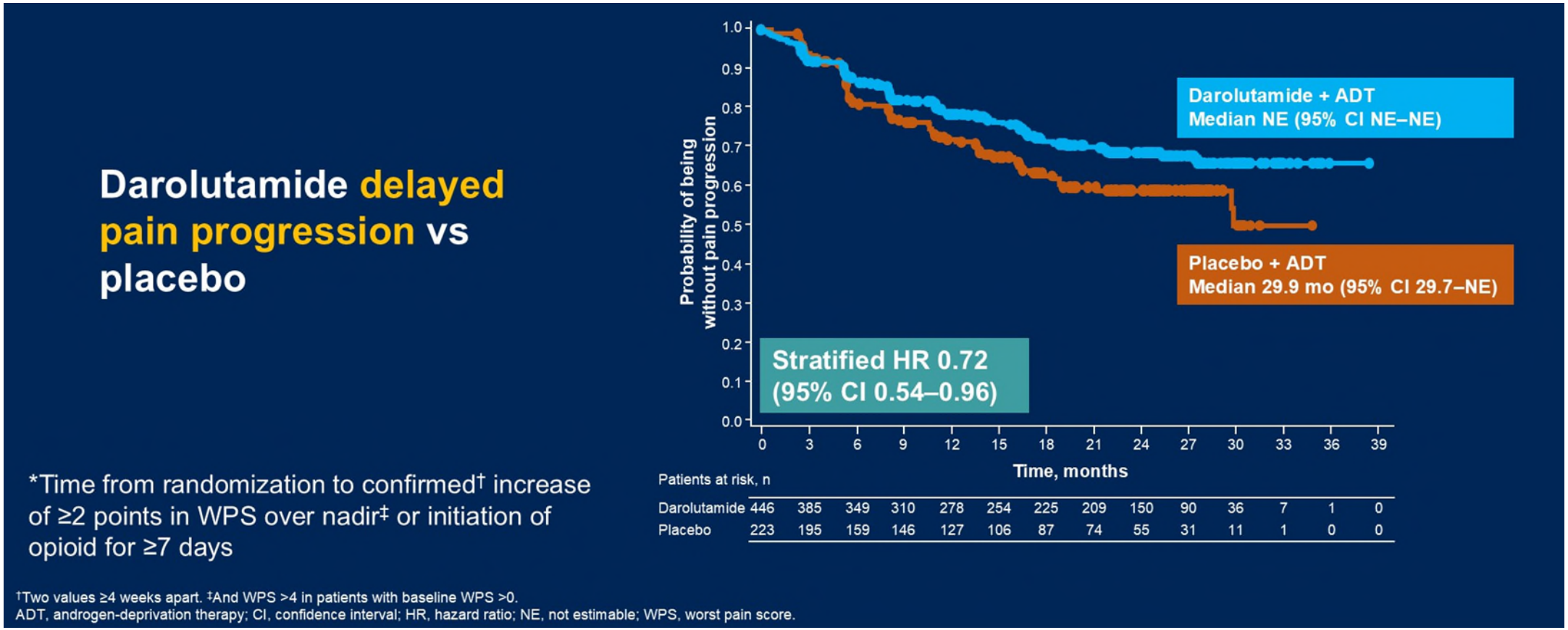
Morgans et al. Presented at ASCO 2025

Assessing pain and HRQoL in ARANOTE



Morgans et al. Presented at ASCO 2025

ARANOTE: time to progression



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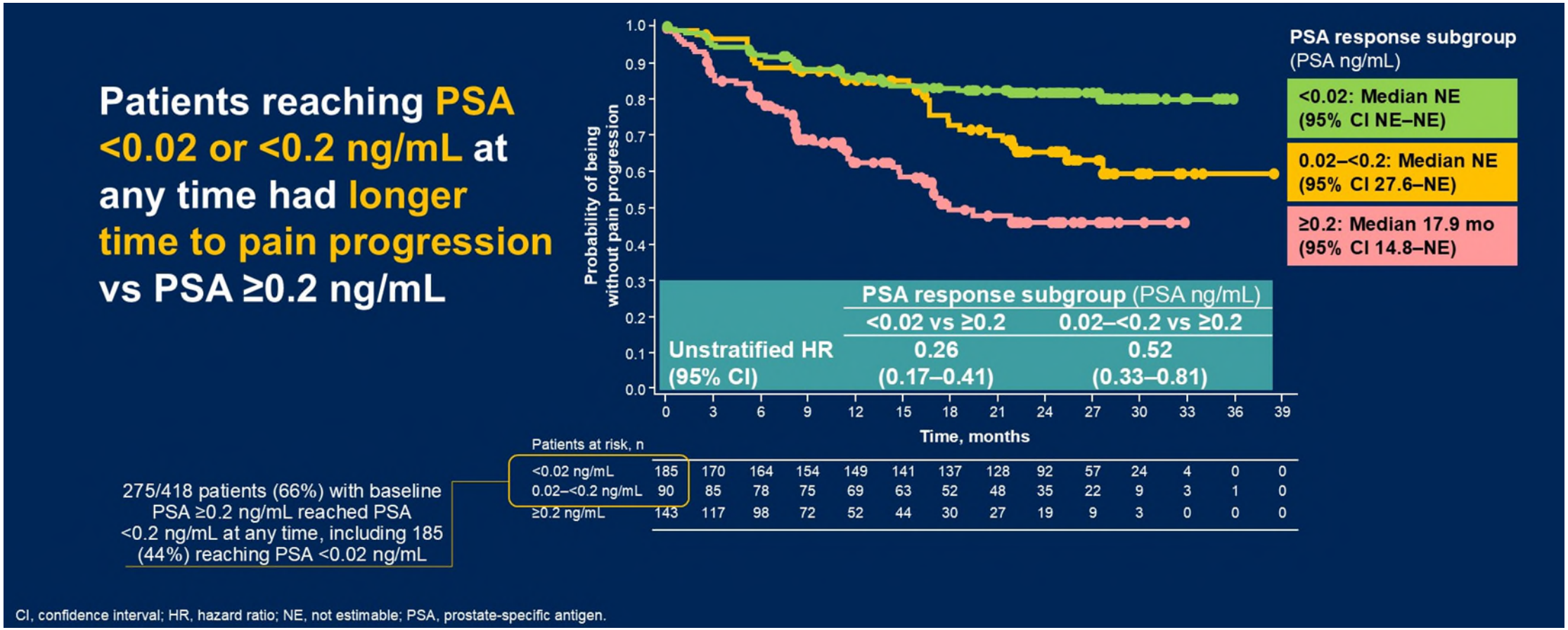
ARANOTE: time to progression by PSA response



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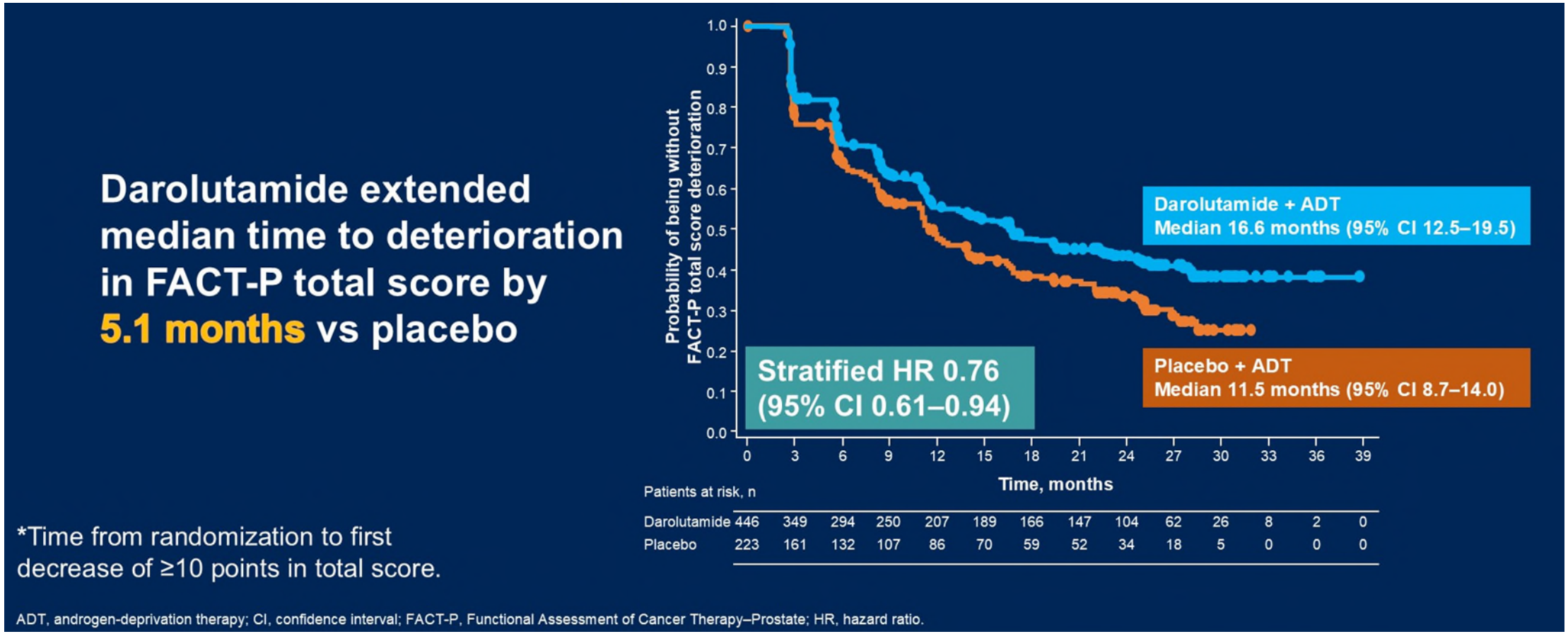
ARANOTE: time to deterioration



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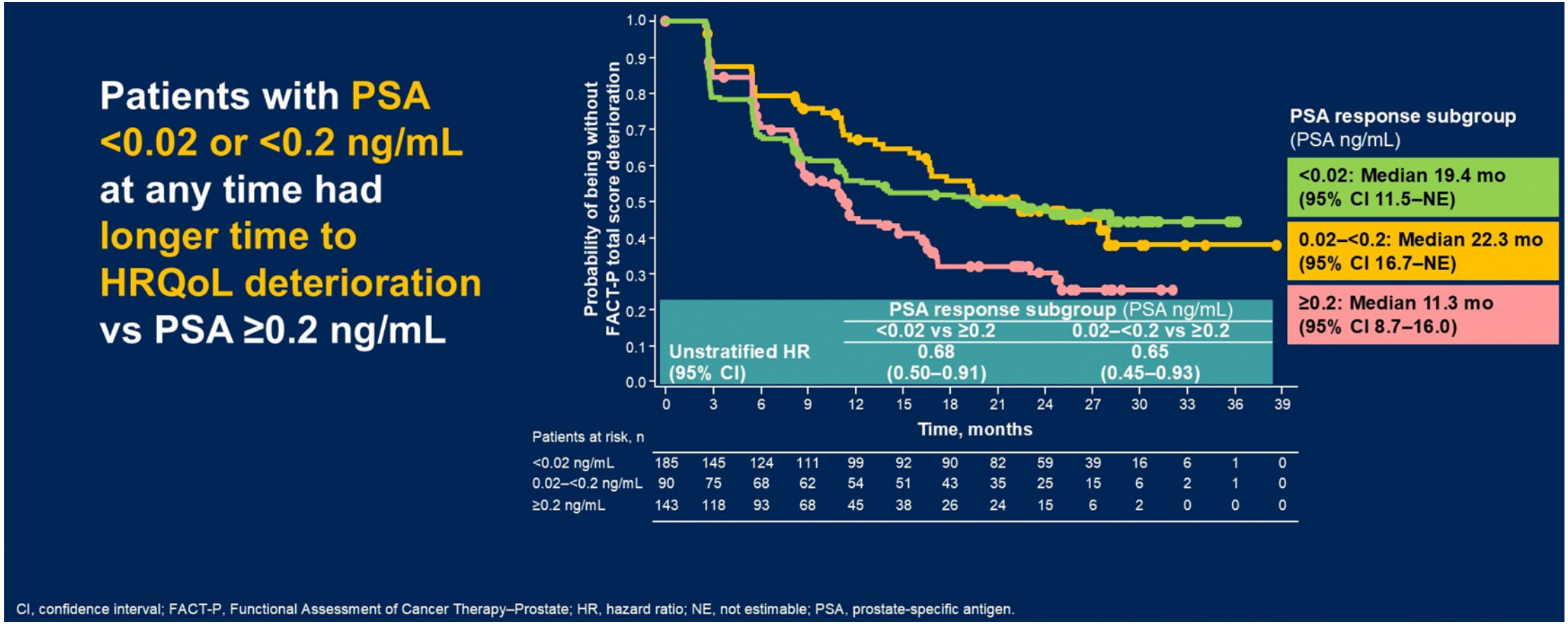
ARANOTE: time to deterioration by PSA response (darolutamide subgroup)



CI, confidence interval; FACT-P, Functional Assessment of Cancer Therapy–Prostate; HR, hazard ratio; NE, not estimable; PSA, prostate-specific antigen.

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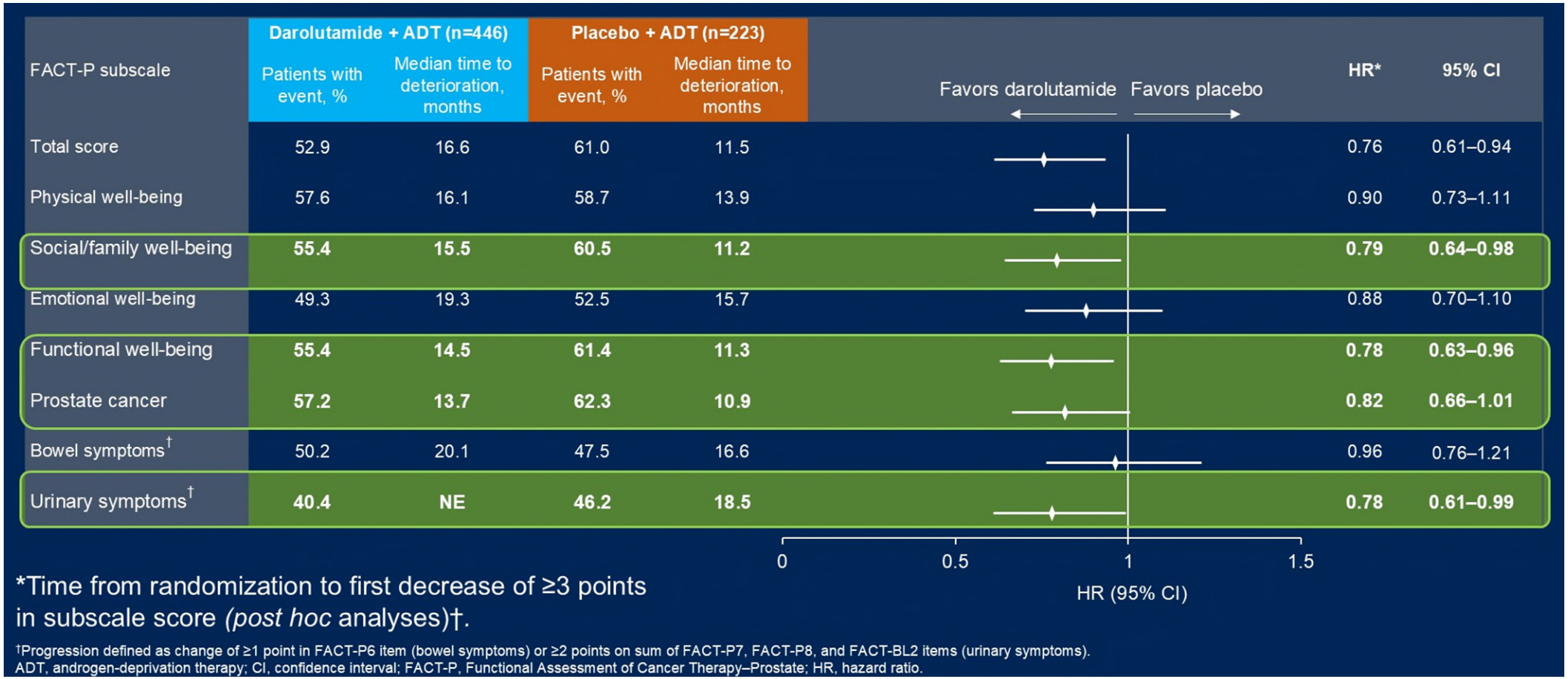
ARANOTE: FACT-P domains



FACT-P subscale	Darolutamide + ADT (n=446)		Placebo + ADT (n=223)		HR*	95% CI
	Patients with event, %	Median time to deterioration, months	Patients with event, %	Median time to deterioration, months		
Total score	52.9	16.6	61.0	11.5	0.76	0.61–0.94
Physical well-being	57.6	16.1	58.7	13.9	0.90	0.73–1.11
Social/family well-being	**55.4**	**15.5**	**60.5**	**11.2**	**0.79**	**0.64–0.98**
Emotional well-being	49.3	19.3	52.5	15.7	0.88	0.70–1.10
Functional well-being	**55.4**	**14.5**	**61.4**	**11.3**	**0.78**	**0.63–0.96**
Prostate cancer	**57.2**	**13.7**	**62.3**	**10.9**	**0.82**	**0.66–1.01**
Bowel symptoms†	50.2	20.1	47.5	16.6	0.96	0.76–1.21
Urinary symptoms†	**40.4**	**NE**	**46.2**	**18.5**	**0.78**	**0.61–0.99**

*Time from randomization to first decrease of ≥3 points in subscale score *(post hoc* analyses)†.

†Progression defined as change of ≥1 point in FACT-P6 item (bowel symptoms) or ≥2 points on sum of FACT-P7, FACT-P8, and FACT-BL2 items (urinary symptoms).
ADT, androgen-deprivation therapy; CI, confidence interval; FACT-P, Functional Assessment of Cancer Therapy–Prostate; HR, hazard ratio.

Morgans et al. Presented at ASCO 2025

ARANOTE HRQoL analyses: key takeaways

- Darolutamide confers a positive impact on several QOL domains
  - Delays in symptomatic pain progression
  - Delays deterioration in overall well-being
- QOL benefits greatest in darolutamide-treated patients who achieved **ultra-low PSA responses (≤ 0.2 and ≤ 0.02 ng/mL)**

Prognostic significance of PSA>0.2 after 6-12 months treatment for metastatic hormone-sensitive prostate cancer (mHSPC) intensified by androgen-receptor pathway inhibitors (ARPI): A multinational real-world analysis of the IRONMAN registry

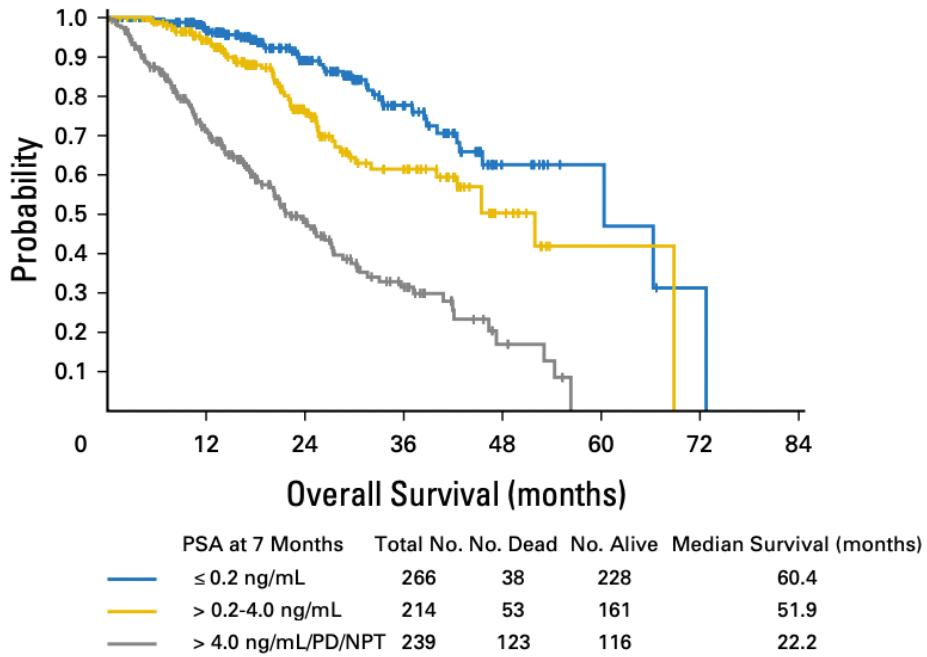
Michael Ong, Soumyajit Roy, Kim N. Chi, Tanya B. Dorff, Sebastien J. Hotte, Alexander W. Wyatt, Lauren Howard, Karen A. Autio, Deborah Enting, Aurelius G. Omlin, Joaquin Mateo, Raymond S. McDermott, Ian D. Davis, Anders Bjartell, Laurel Cannon, Alyssa Chan-Cuzydlo, Philip W. Kantoff, Lorelei A. Mucci, and Daniel J. George
***on behalf of the* IRONMAN investigators**

Michael Ong, MD BSc (Hons) FRCPC
Associate Professor, Medical Oncologist, Ottawa Hospital Research Institute, Canada

Ong et al. Presented at ASCO 2025

Low absolute PSA values on-treatment are prognostic

- **PSA < 0.2 ng/mL at 3-7 months** has favorable prognosis
  - ADT alone (SWOG 9346)
  - ADT + docetaxel (CHAARTED)
  - ADT + ARPIs (LATITUDE, TITAN, ARCHES, ENZAMET)
- **PSA < 0.02 ng/mL at 3-12** months has even better prognosis
  - ADT + ARPIs (TITAN and ARANOTE)
- **Real world** datasets are limited



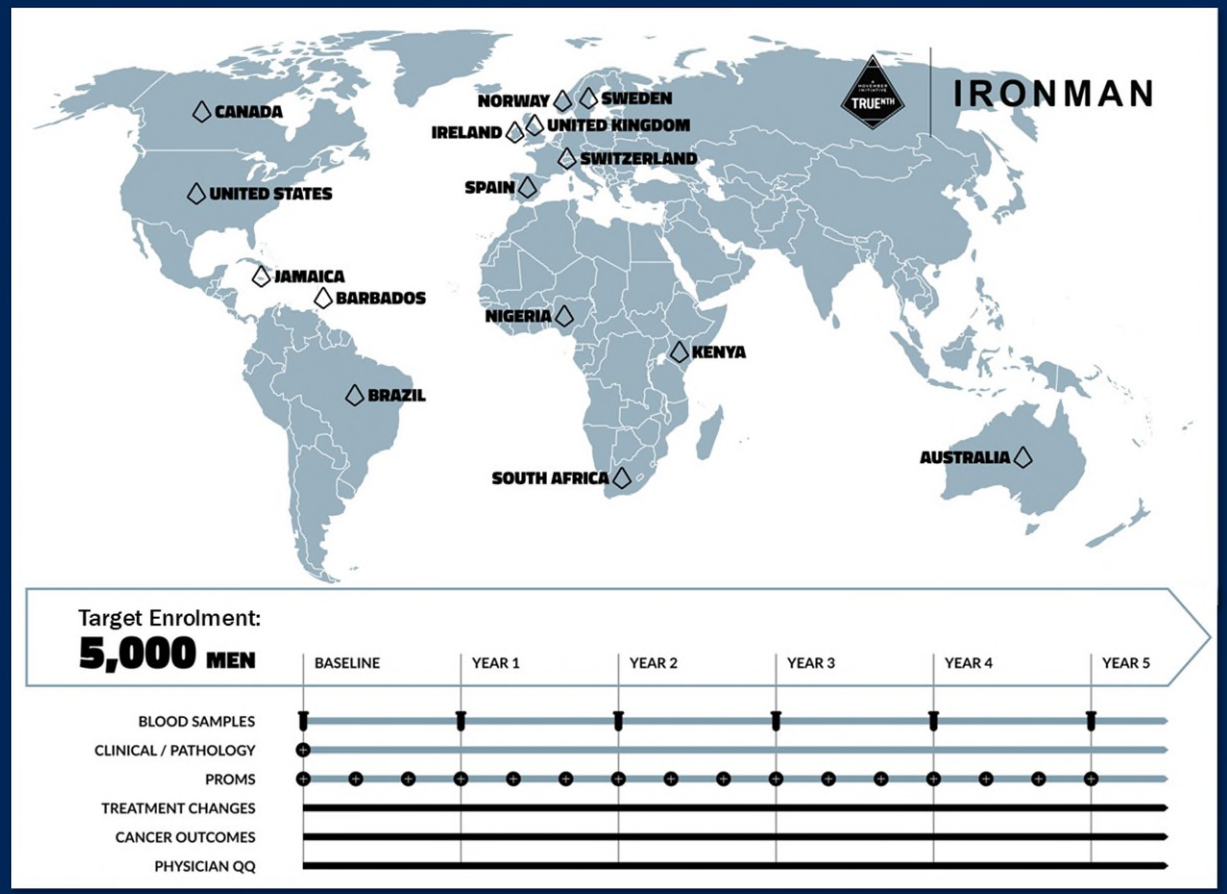
Harshman et al. JCO 2018

IRONMAN Registry

IRONMAN Registry

- Prospective international cohort >4600 patients with mHSPC and CRPC*
- 123 active sites
- 15 countries
- Sources of data:
  - Demographics
  - Blood samples
  - Outcomes data
  - Questionnaires (Patient / MD)

*Castration-resistant prostate cancer



Ong et al. Presented at ASCO 2025

IRONMAN analysis

Methods

Selected patients from the IRONMAN Registry

- mHSPC on ADT and ARPI +/- docetaxel
- PSA data ≥12 months

3 PSA strata were defined at 6 and 12 mo after ADT start

- PSA <0.1 | PSA 0.10-0.19 | PSA ≥0.2

Conducted 12-mo (primary outcome) and 6-mo landmark survival analyses

- **Conditional survival**
  Time from 6- or 12-month landmark → death or censor (months)
- **Conditional progression-free survival (PFS)**
  Time from 6- or 12-month landmark → any biochemical, radiographic or clinical progression or death or censor (months)

Multivariable Cox proportional hazard regression models

- For conditional survival based on 12-month PSA strata adjusted for confounders

Ong et al. Presented at ASCO 2025

IRONMAN: cohort characteristics

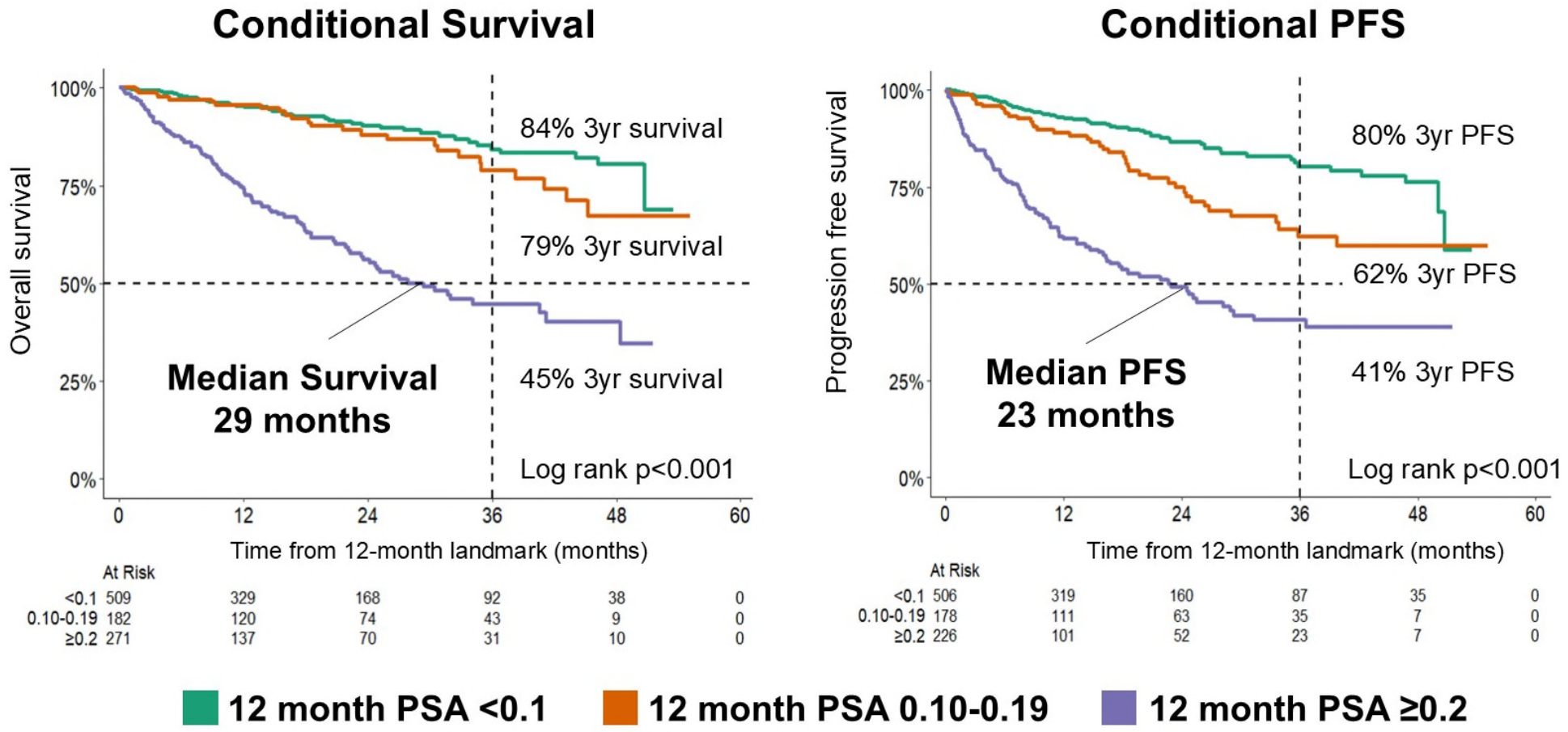
Characteristic	n (%)
Median Age (IQR)	70 (64-76)
Race	
White	900 (74)
Black	96 (8)
Asian	21 (2)
Not listed/unknown	202 (16)
Gleason 8-10*	711 (58)
De novo* mHSPC	916 (75)
Prostatectomy or Radiation to Primary*	329 (27)
Site of Metastases	
Lymph node only	86 (7)
Bone	571 (46)
Lung	109 (9)
Liver	55 (5)
Unknown	398 (33)

*missing/unknown data not displayed

Characteristic	n (%)
PSA at ADT start*	
≤20 ng/mL	188 (15)
>20 ng/mL	555 (46)
Alkaline Phosphatase at ADT start*	
≤150 IU/L	514 (42)
>150 IU/L	247 (20)
Orchiectomy	3 (0.2)
LHRH analogue	1216 (99.8)
Treatment regimen	
ADT + ARPI	1073 (88)
ADT + ARPI + docetaxel	146 (12)
(42 abiraterone, 100 darolutamide, 3 other)	
ARPI drug	
Abiraterone Acetate + Prednisone	536 (44)
Apalutamide	258 (21)
Enzalutamide	266 (22)
Darolutamide	156 (13)

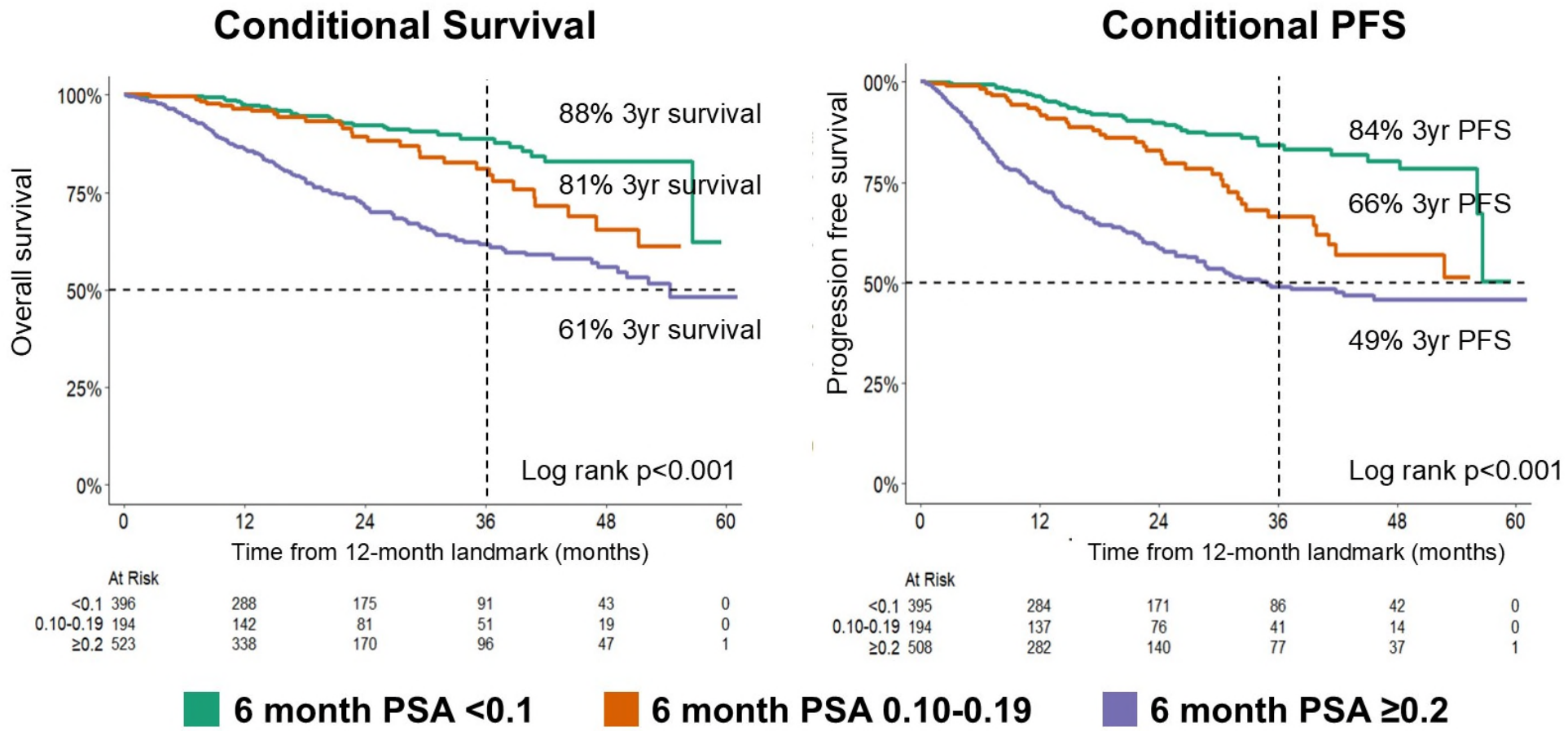
Ong et al. Presented at ASCO 2025

12-month landmark events



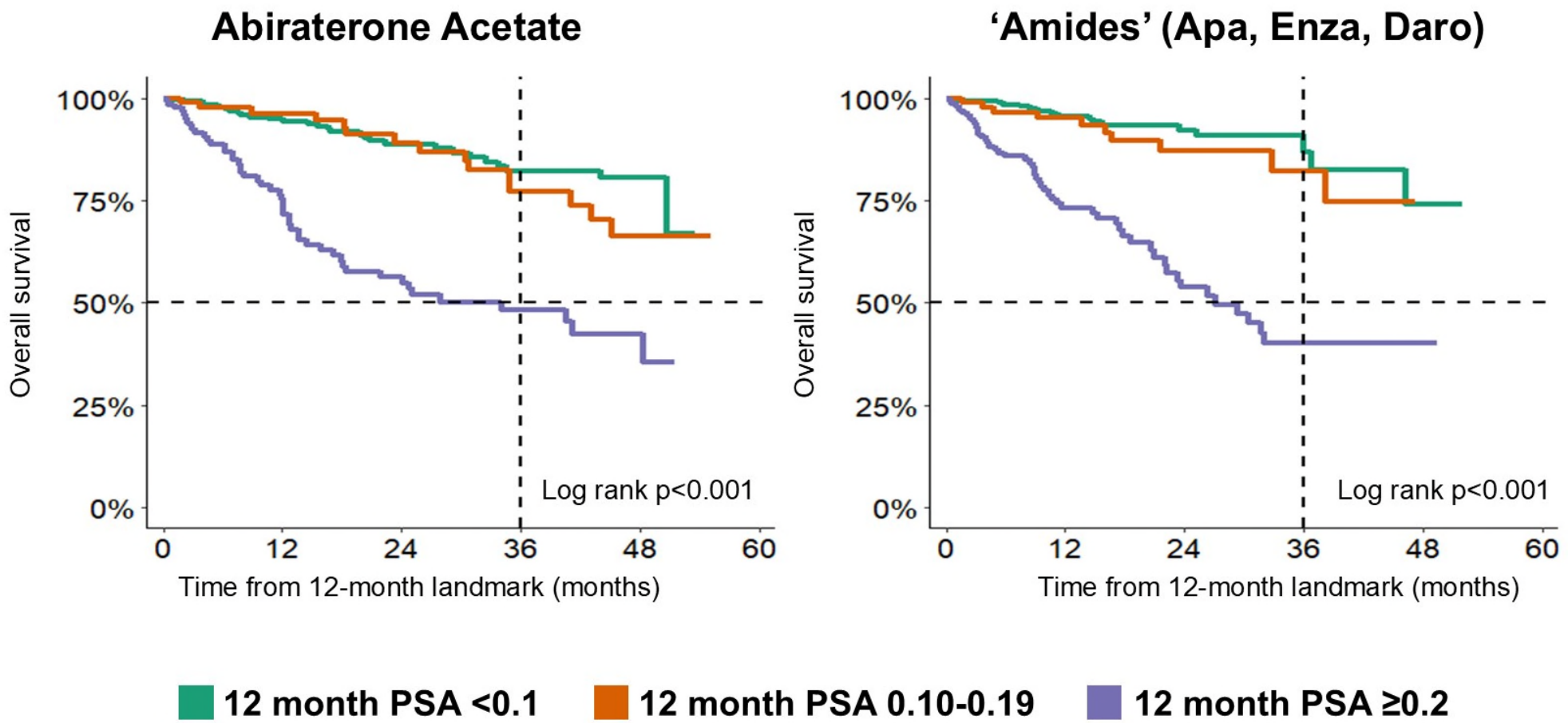
Ong et al. Presented at ASCO 2025

6-month landmark events



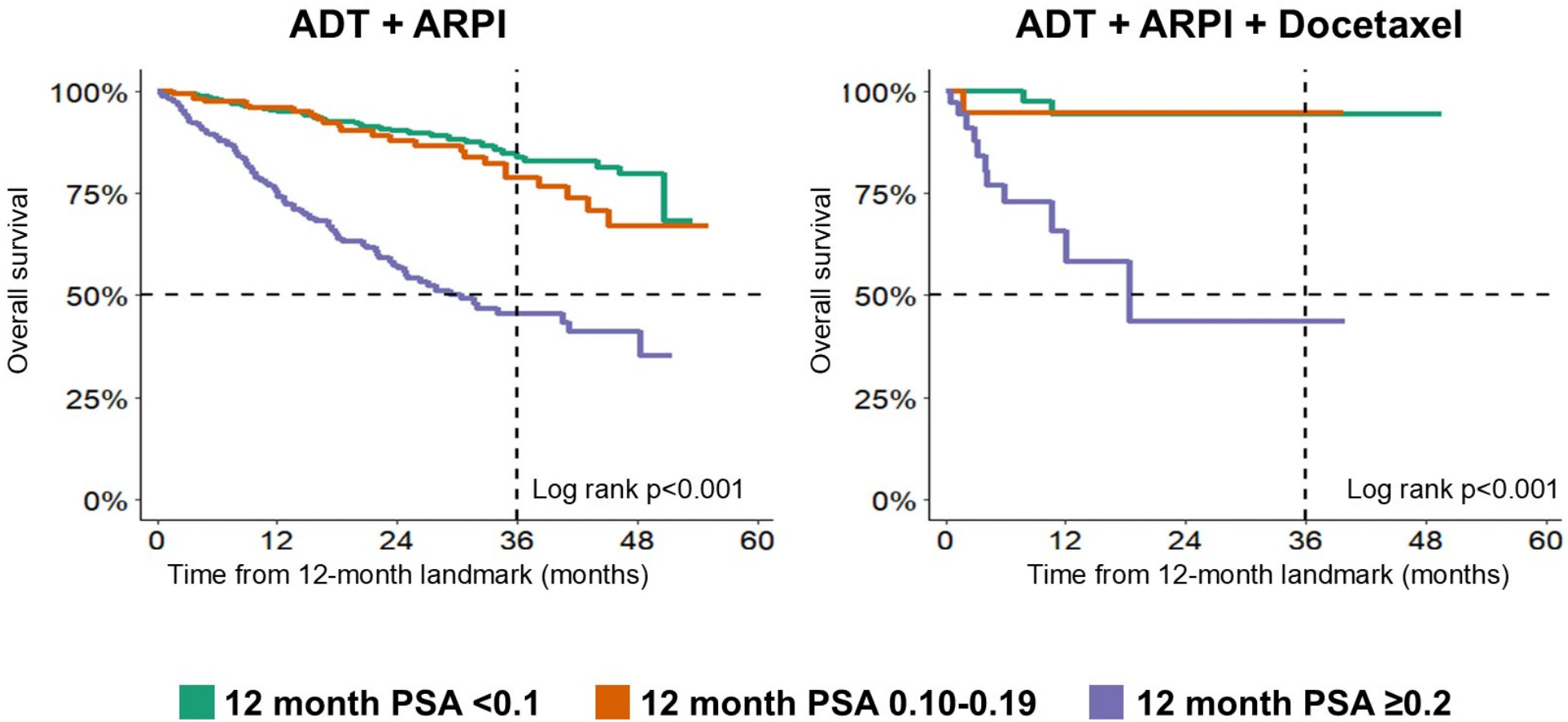
Ong et al. Presented at ASCO 2025

Absolute PSA is prognostic regardless of ARPI



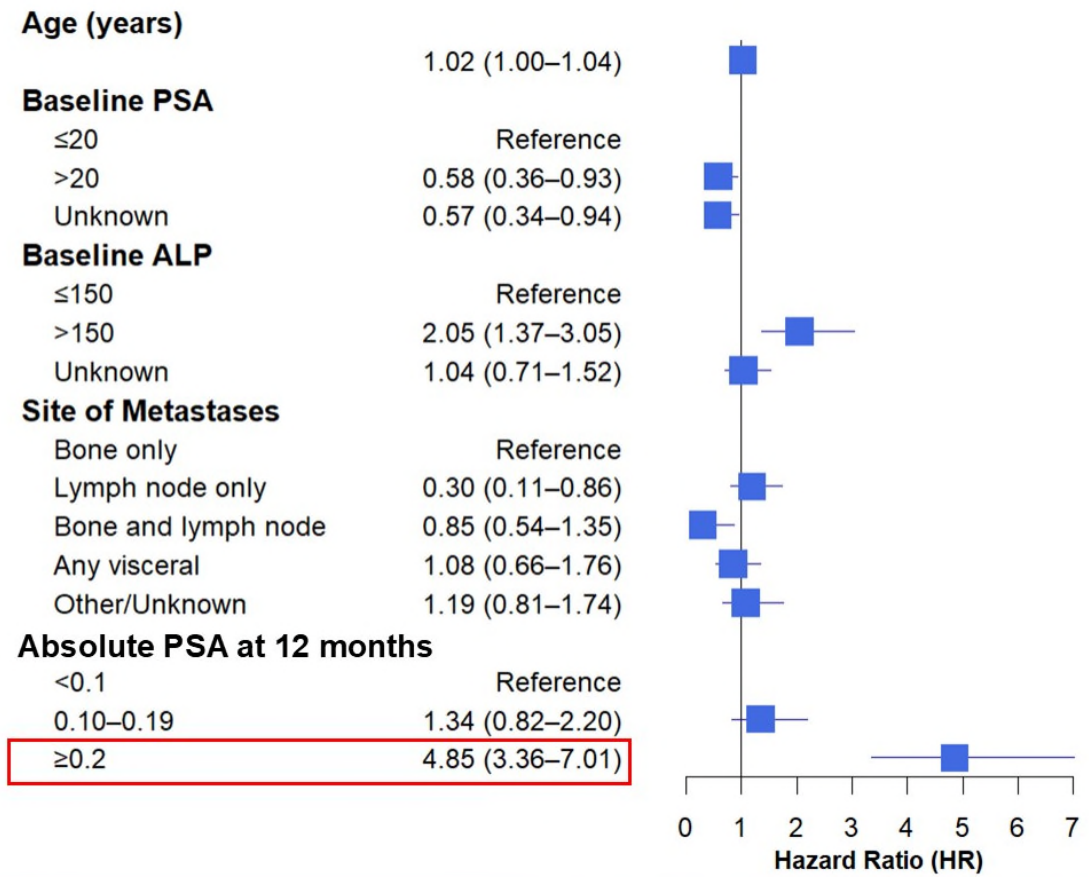
Ong et al. Presented at ASCO 2025

Absolute PSA is prognostic regardless of chemotherapy



Ong et al. Presented at ASCO 2025

PSA ≥0.2 at 6-12 months has poor prognosis



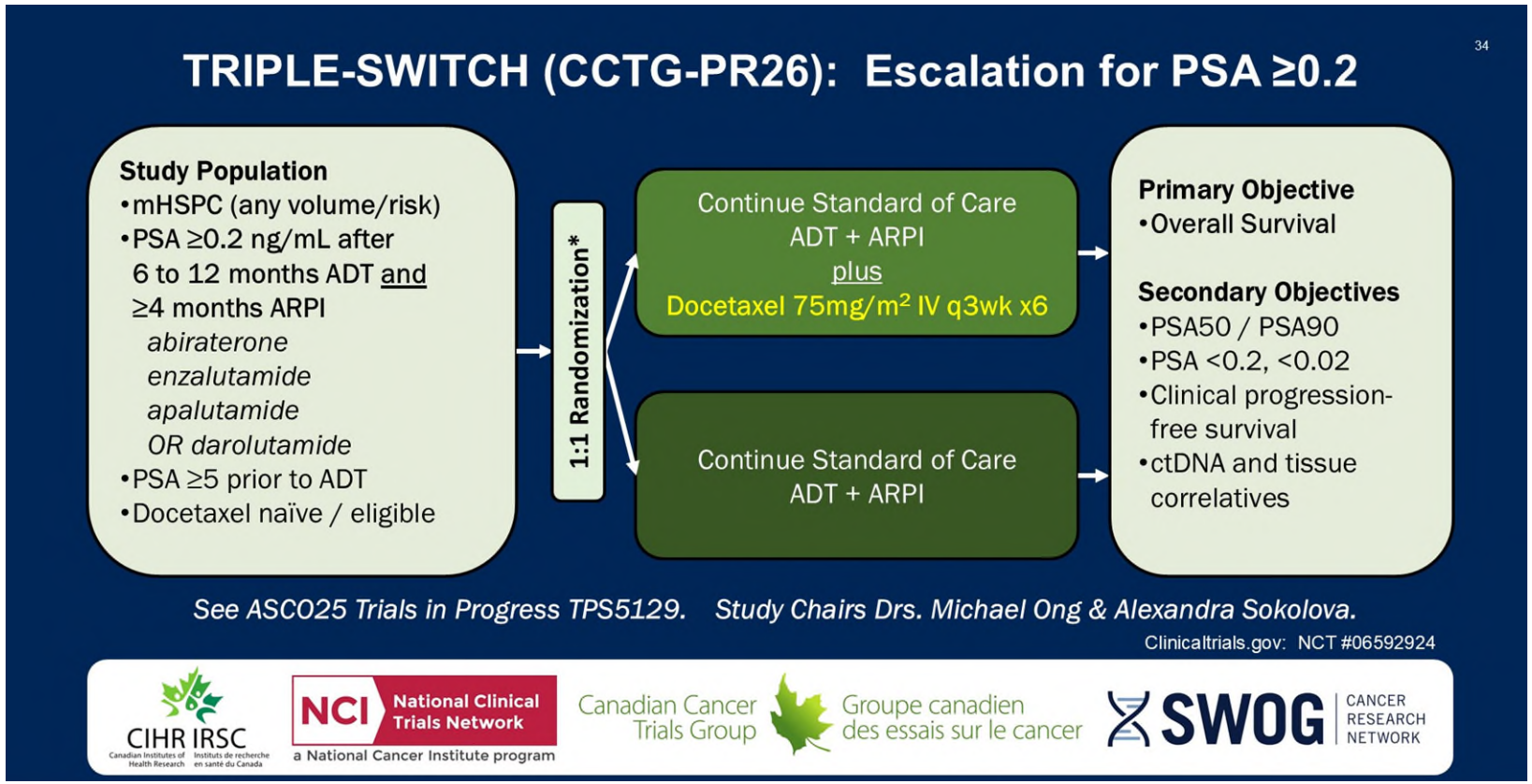
Associated with 5-fold increased risk of death

Ong et al. Presented at ASCO 2025

IRONMAN: key takeaways

- This real-world subset analysis demonstrated the prognostic value of absolute PSA values at 6-12 months after starting therapy, which is consistent with prior datasets
- **PSA < 0.2** at 6-12 months has **good prognosis** (especially if PSA < 0.1)
- PSA $\geq$ 0.2 at 6-12 months has poor prognosis
- Key limitation: variable PSA assays used and sensitivities across institutions and countries
- **Supports potentially using absolute 6-12 month PSA values for treatment intensification and de-escalation in prospective studies**

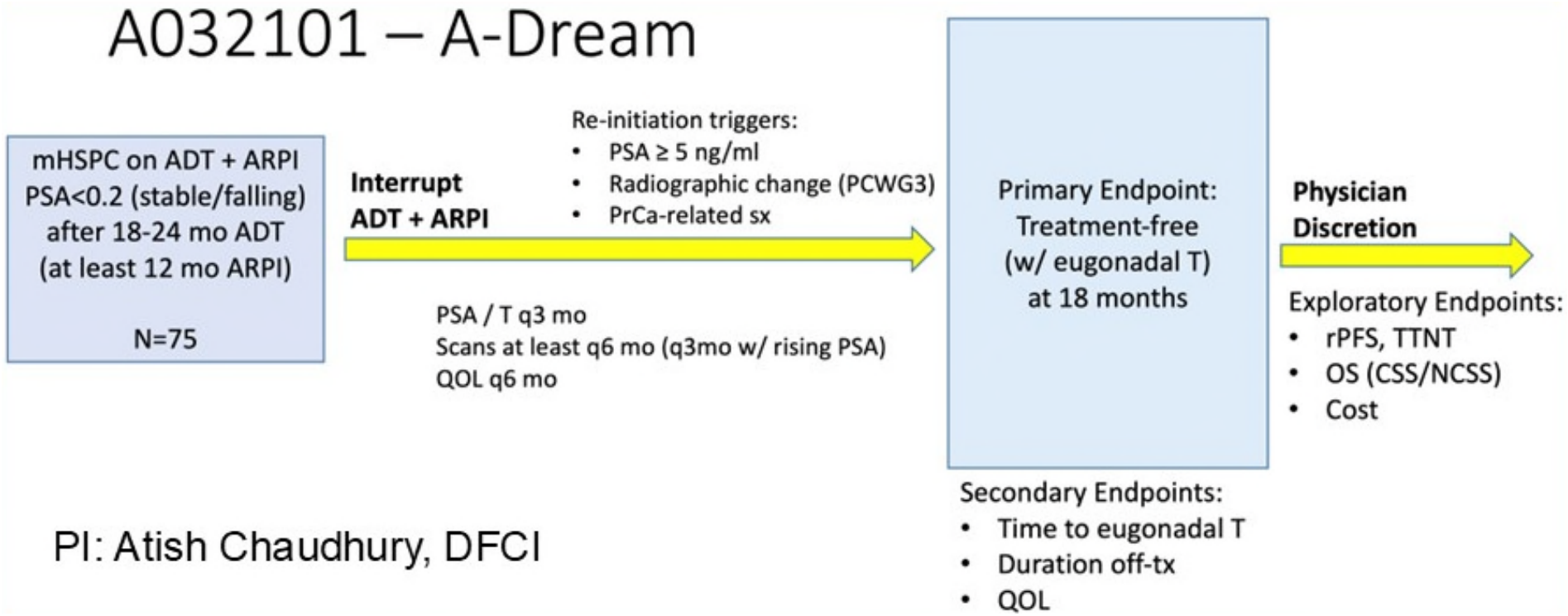
Ongoing studies using PSA nadir to guide therapy



Enrolling at COH!

- Duarte
- OC Lennar
- Long Beach
- Antelope Valley
- South Bay
- South Pasadena
- Upland

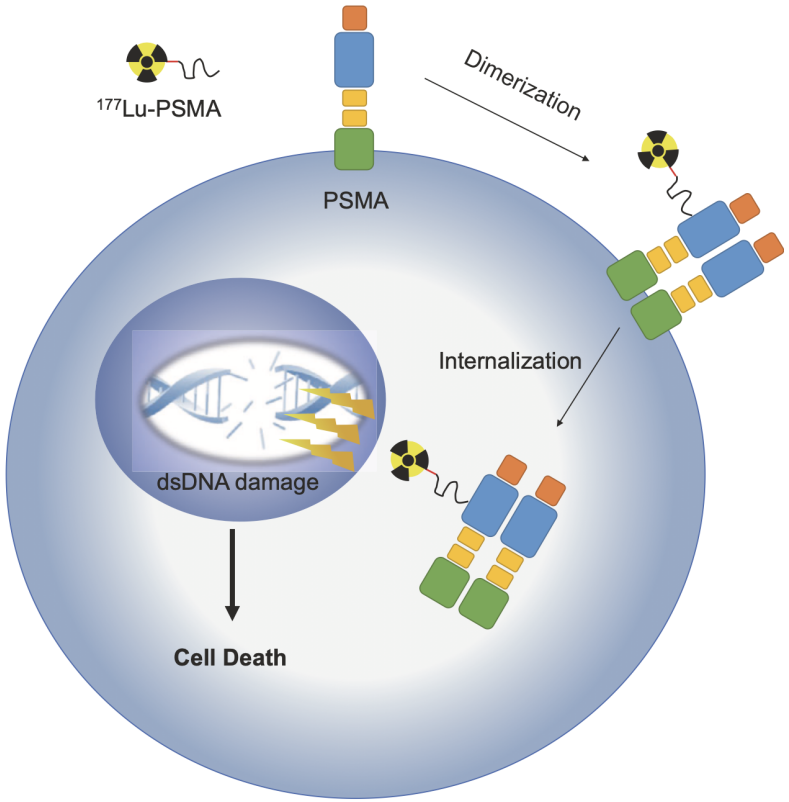
Ongoing studies using PSA nadir to guide therapy

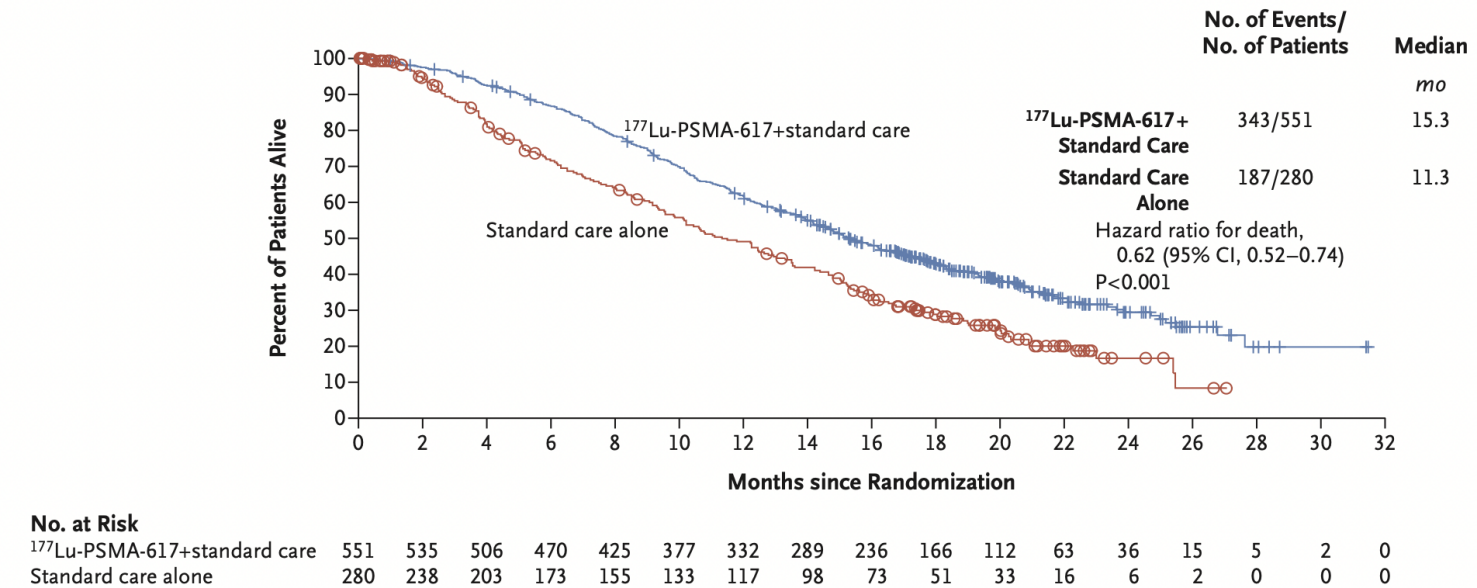


Outline

- **Very high-risk prostate cancer**
  - Multimodal artificial intelligence in STAMPEDE high-risk prostate cancer
- **Metastatic hormone-sensitive prostate cancer (mHSPC)**
  - Health-related quality of life with darolutamide (ARANOTE study)
  - Prognostic value of PSA >0.2 at 6-12 months in mHSPC (IRONMAN registry)
- **Metastatic castration-resistant prostate cancer (mCRPC)**
  - PSMAfore: 177-Lu-PSMA-617 in taxane-naïve mCRPC
  - Phase 1 results of pasritamig in mCRPC

177-Lu-PSMA-617 in mCRPC



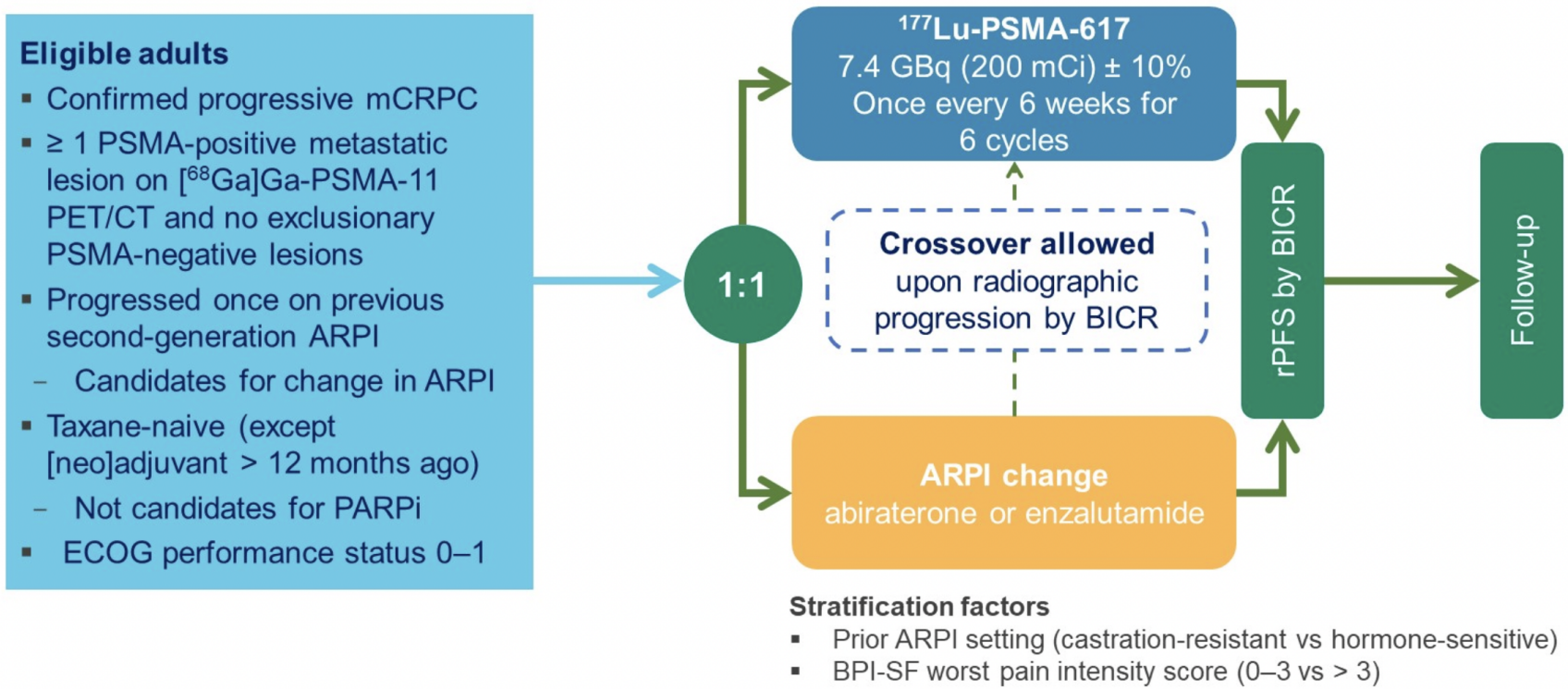


177-Lu-PSMA-617 initially approved for mCRPC post-ARPI and taxane in 2022

Jia et al. Prostate Cancer Prostatic Dis 2023

Sartor et al. NEJM 2021

PSMAfore: 177-Lu-PSMA-617 in taxane-naïve mCRPC



Primary endpoint: rPFS

Secondary endpoints: OS, PSA50 response, safety, and biomarkers

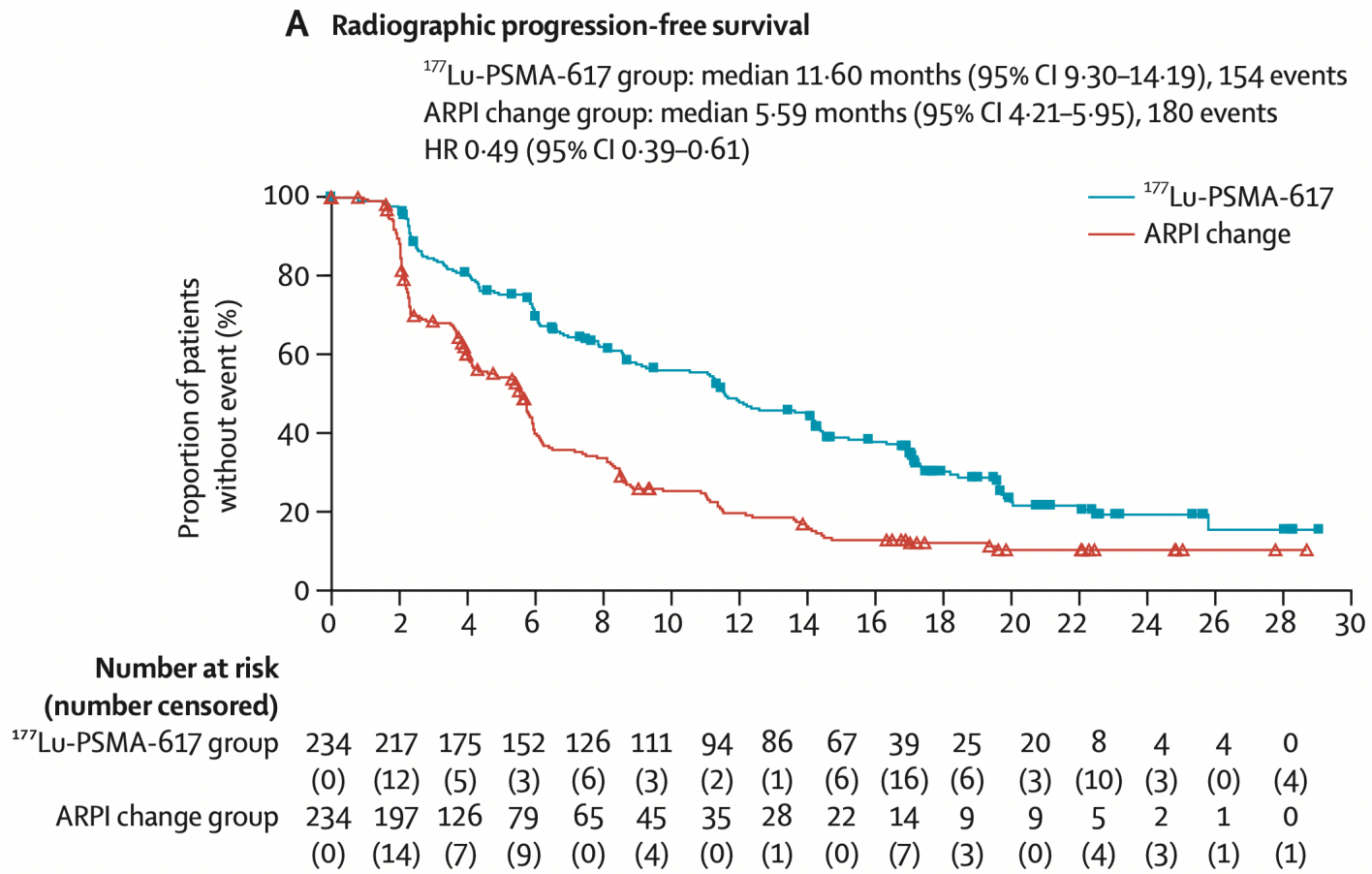
Fizazi et al. Presented at ASCO 2024

PSMAfore: patient characteristics

	^{177}Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Age, median (range), years	71 (43–94)	72 (53–91)
White, n (%)	211 (90.2)	214 (91.5)
ECOG performance status, n (%)		
0	146 (62.4)	115 (49.1)
1	86 (36.8)	114 (48.7)
Gleason score 8–10, n (%)	136 (58.1)	107 (45.7)
PSA, median (range), µg/L	18.4 (0–1197)	14.9 (0–4224)
Hemoglobin, median (range), g/L	128.0 (88–155)	129.0 (88–156)
Alkaline phosphatase, median (range), IU/L	100.0 (36–1727)	103.5 (28–1319)
Site of disease, n (%)		
Liver	13 (5.6)	7 (3.0)
Lymph node	76 (32.5)	74 (31.6)
Bone	205 (87.6)	203 (86.8)
Prior ARPI, n (%)		
Abiraterone	119 (50.9)	130 (55.6)
Enzalutamide	94 (40.2)	84 (35.9)
Other	21 (9.0)	20 (8.5)

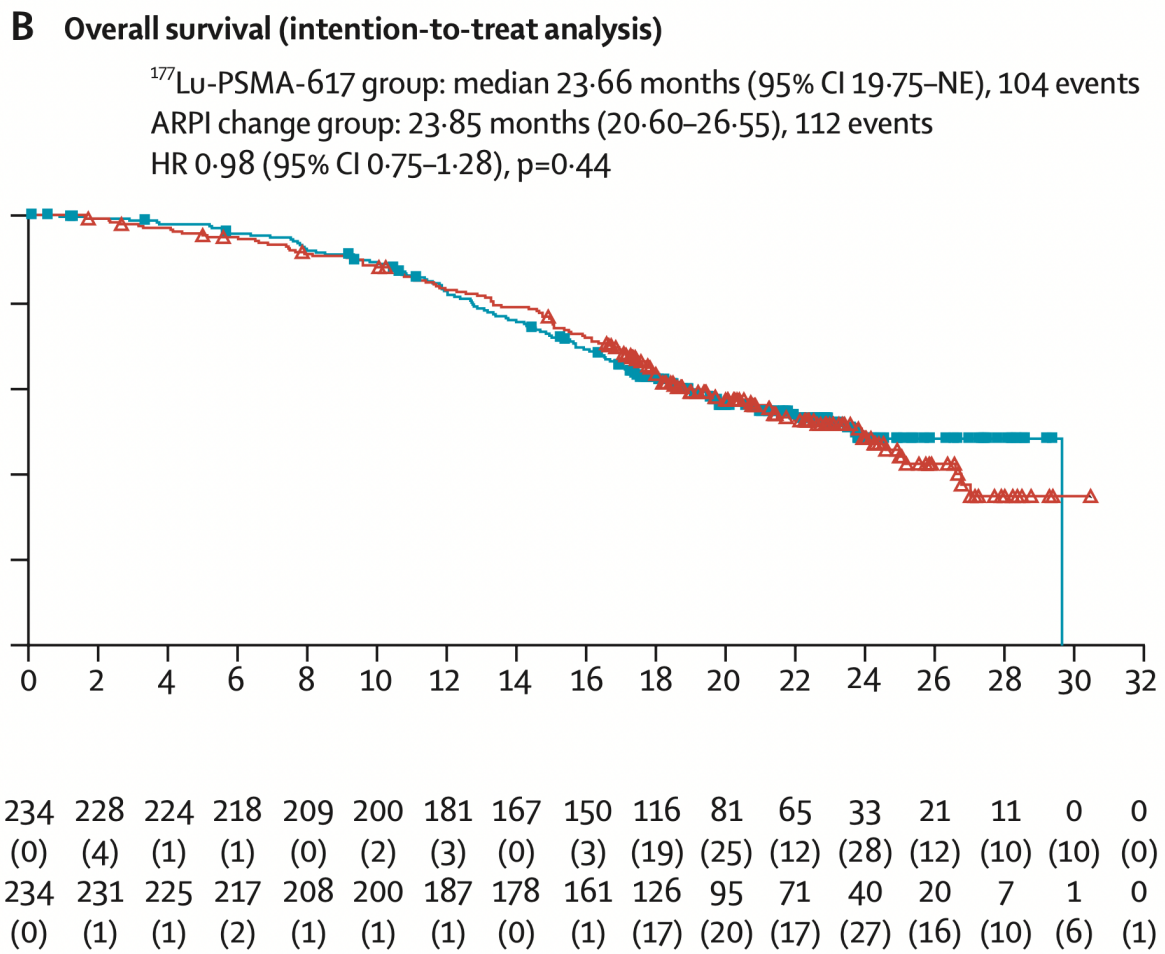
Fizazi et al. Presented at ASCO 2024

Primary endpoint: rPFS



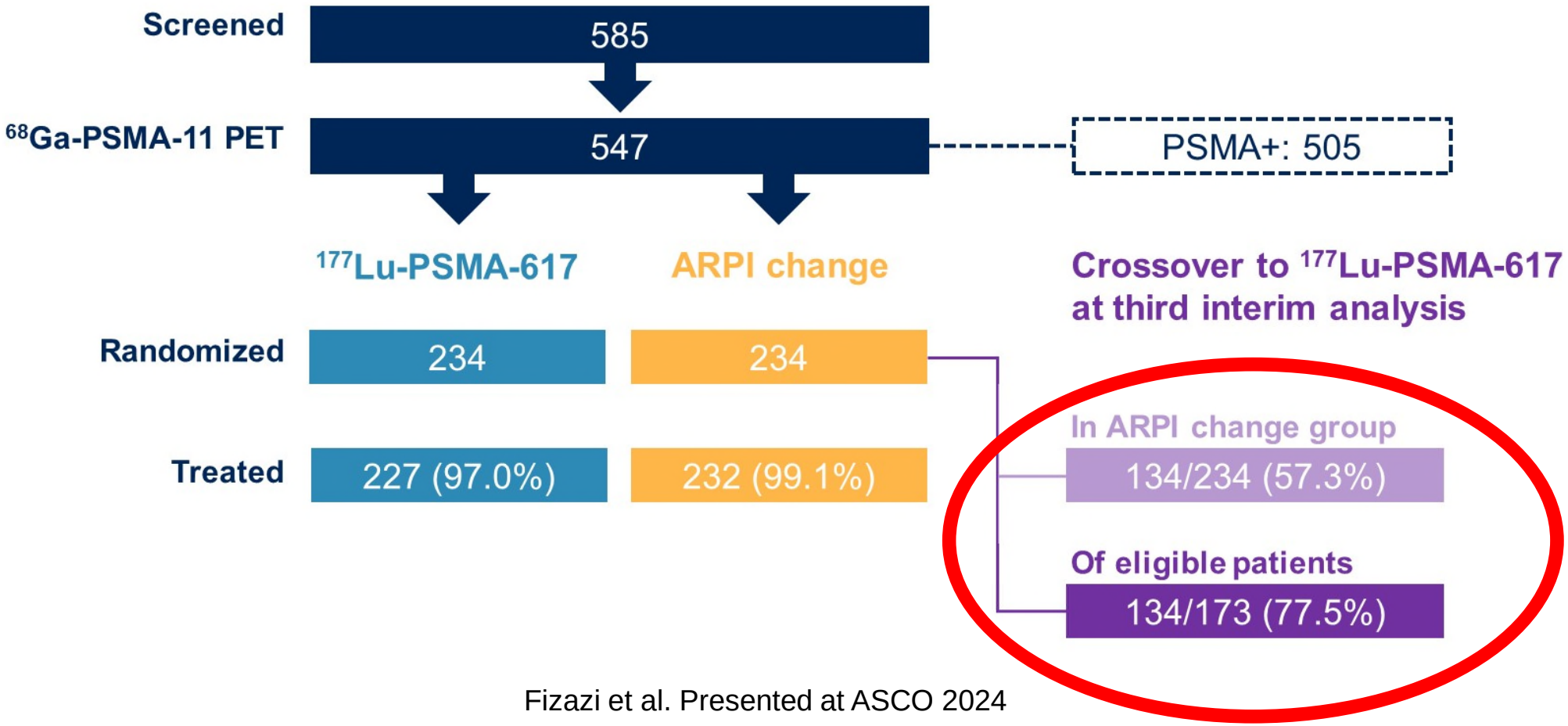
Morris et al. Lancet 2024

Secondary endpoint: overall survival



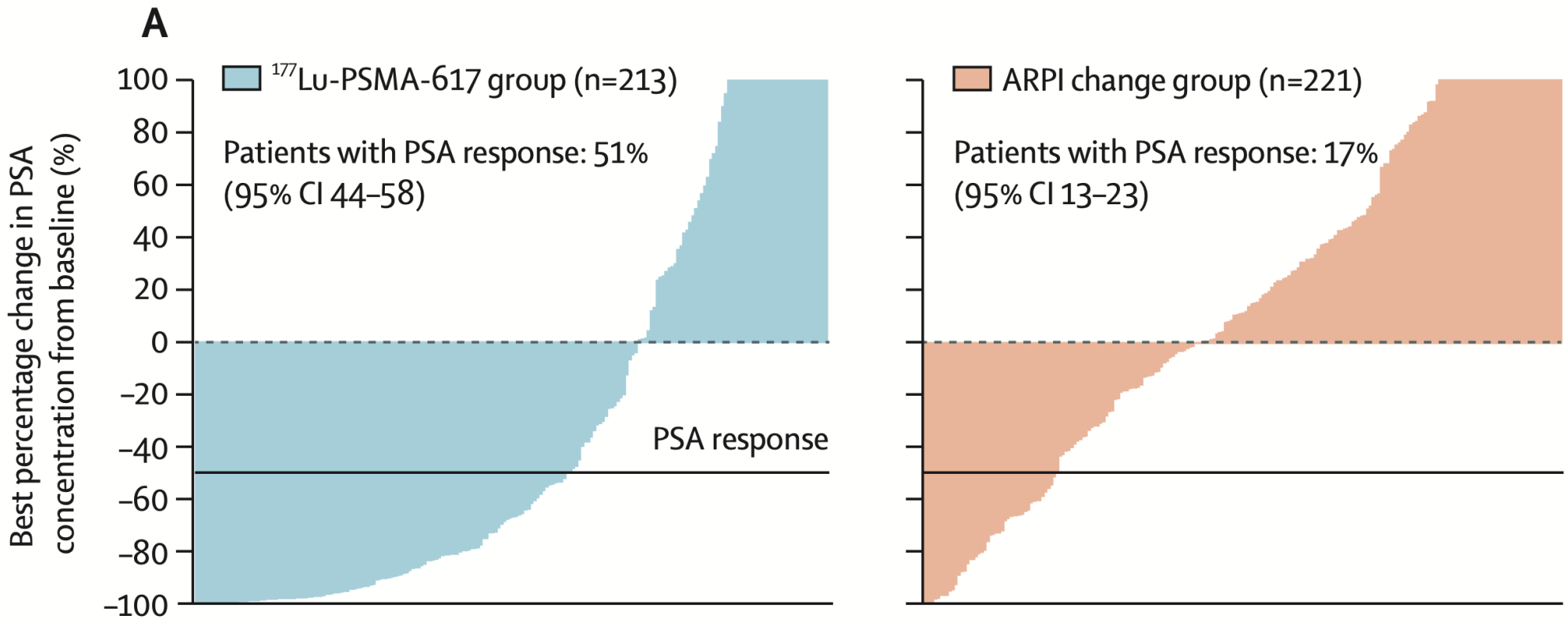
Morris et al. Lancet 2024

High crossover in PSMAfore



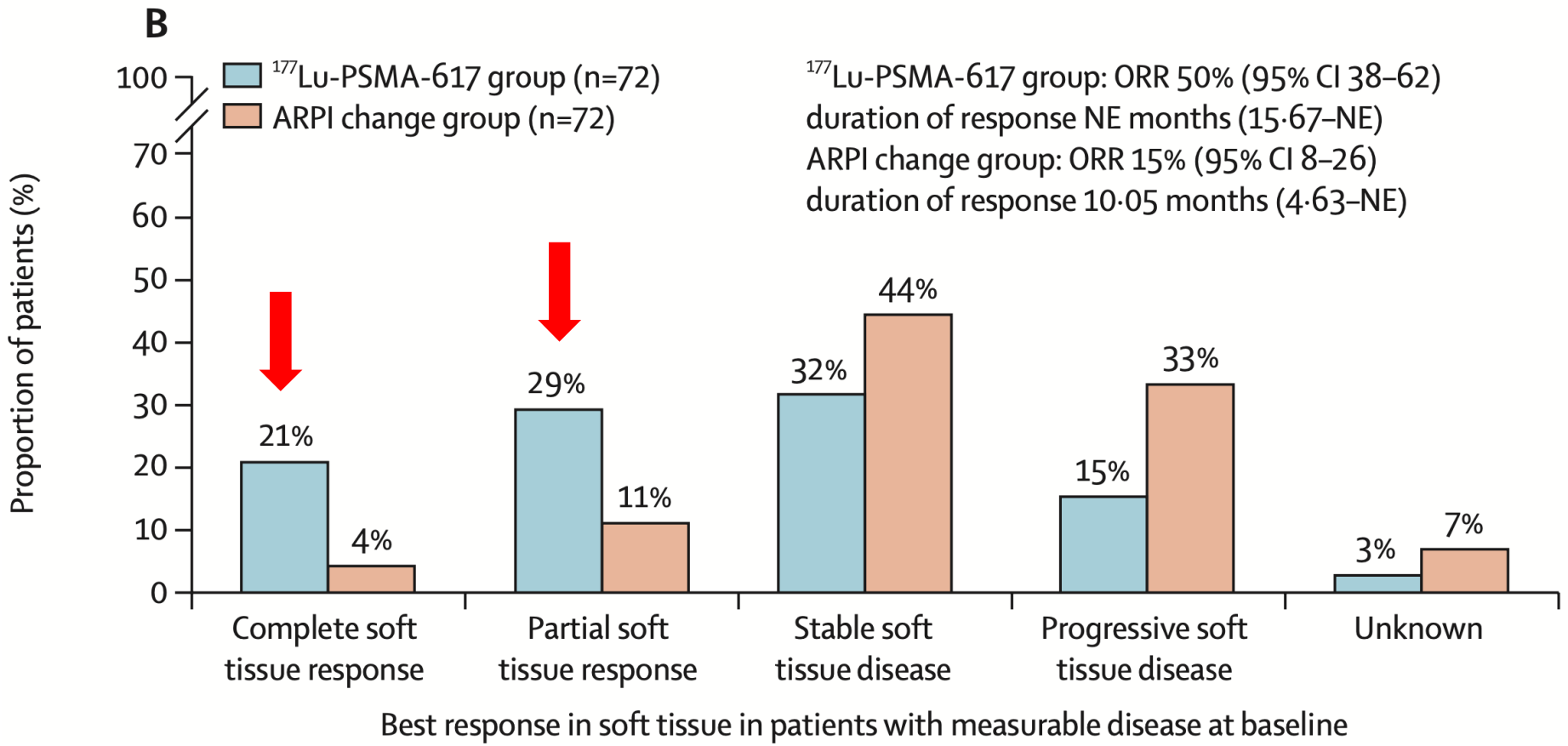
Fizazi et al. Presented at ASCO 2024

Secondary endpoint: PSA responses



Morris et al. Lancet 2024

Secondary endpoint: objective responses



Morris et al. Lancet 2024

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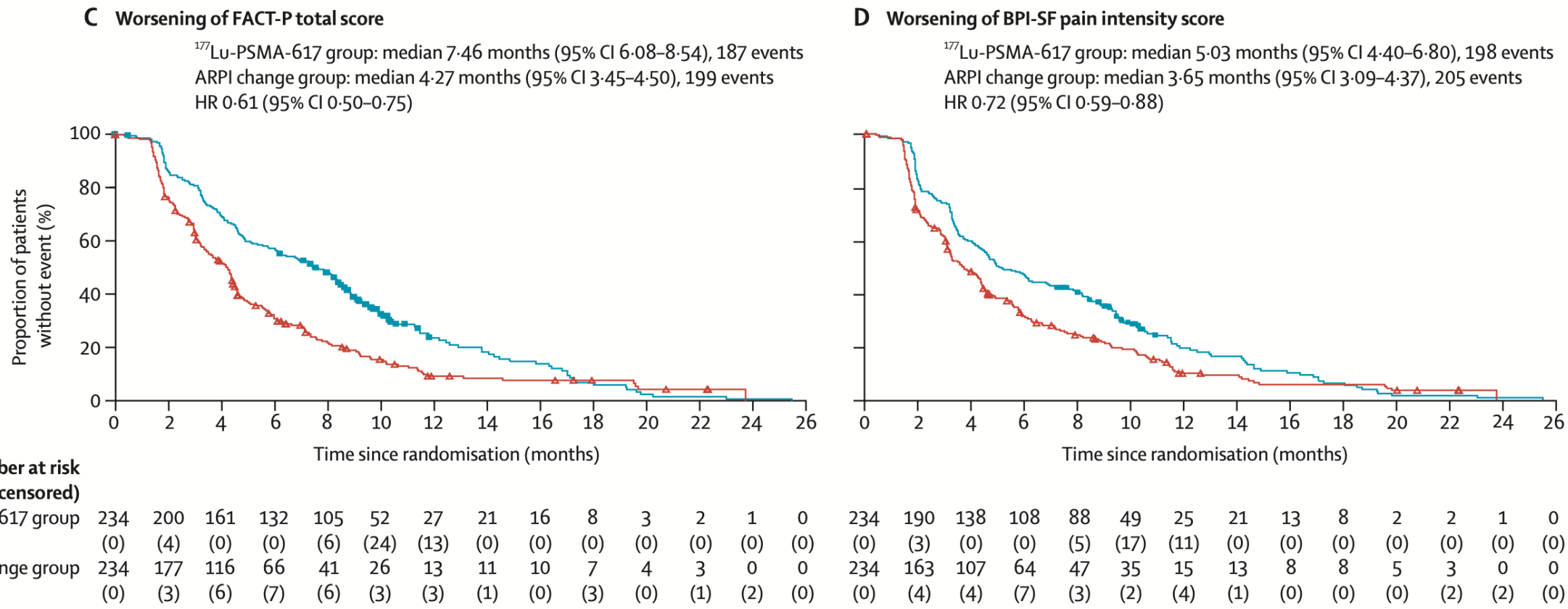


Morris et al. Lancet 2024

PSMAfore: adverse events

- Most frequent all-grade AE with 177-Lu-PSMA-617 compared to control:
    - Dry mouth (58% vs 3%)
    - Asthenia (33% vs 29%)
    - Nausea (32% vs 12%)
    - Anemia (27% vs 19%)
- Grade 3+ AEs
    - Overall lower with 177-Lu-PSMA-617 than control

PSMAfore: key takeaways

- Study demonstrated that 177-Lu-PSMA-617 is active in mCRPC (pre-docetaxel) → FDA approved for pre-docetaxel setting in March 2025
- Key limitations:
    - Control arm utilized ARPI switch (commonly done in real-world practice); how would it compare against docetaxel?
    - High crossover rates in control arm → impacted lack of OS benefit
- Supports a broader role of 177-Lu-PSMA-617 in the mCRPC continuum and potentially earlier in the disease course
    - Move up to metastatic hormone-sensitive (mHSPC) setting?
    - PSMAddition study (mHSPC) results to be presented at upcoming ESMO 2025 (October)
- Future questions:
    - How to best sequence 177-Lu-PSMA-617 in mCRPC
    - Long term toxicities (e.g., cytopenias) and implications on future therapies

Challenges of immunotherapy in prostate cancer

- Immune checkpoint inhibitors (ICIs) have revolutionized the treatment landscape for solid tumors → potential for deep and durable responses
- However, ICIs have had marginal responses in metastatic prostate cancer
- ICIs are currently **only approved** for mCRPC with **dMMR/MSI-H** or **TMB ≥ 10 muts/Mb**
- Potential reasons for poor responses to immunotherapy in mCRPC
    - Decreased populations of CD8+ tumor infiltrating lymphocytes
    - Enrichment in tumor-associated macrophages and myeloid-derived suppressor cells
    - Immunosuppressive bone tumor microenvironment
- **Novel immunotherapeutic agents are promising in prostate cancer**
    - CAR-T
    - **Bispecific T-cell engagers (BiTE antibodies)**

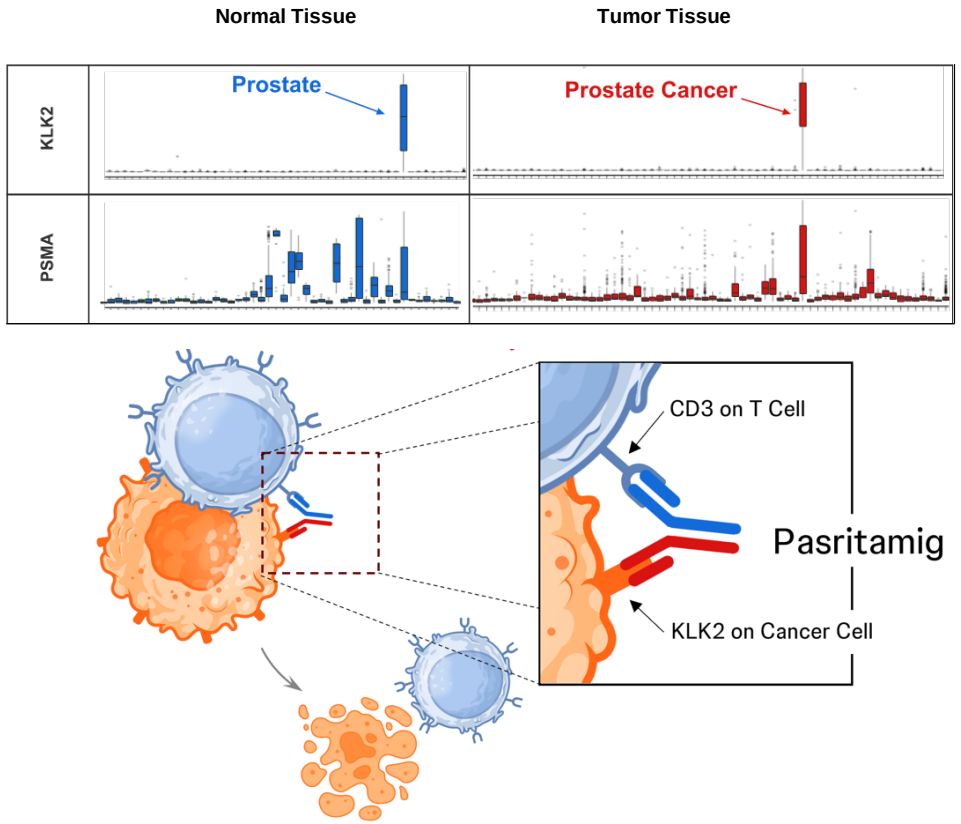
Phase 1 Study Results of Pasritamig (JNJ-78278343) in Metastatic Castration-Resistant Prostate Cancer

Capucine Baldini[1], Armelle Vinceneux[2], Debbie Robbrecht[3], Bernard Doger[4], Karen A. Autio[5], Michael T. Schweizer,[6] Emiliano Calvo[7], Laura Medina[8], Marloes Van Dongen[9], Jean-Laurent Deville[10], Alice Bernard-Tessier[11], Debopriya Ghosh[12], Kristin Shotts[13], Pharavee Jaiprasart[13], Leanne Cartee[13], Daria Gaut[14], Josh Lauring[13], Sherry C. Wang[15], Victor M. Villalobos[13], Mark N. Stein[16]

Baldini et al. Presented at ASCO 2025

Phase 1 study results of JNJ-78278343 (pasritamig) in mCRPC

- **Human kallikrein 2** (encoded by KLK2 gene)
  - Novel cell surface target that is highly expressed on prostate cancer cells with limited expression in normal tissues
- **Pasritamig** (JNJ-78278343) simultaneously binds **KLK2** on prostate cancer cells and **CD3 receptor** complexes on T cells → leading to T-cell activation and cytotoxic activity



Baldini et al. Presented at ASCO 2025

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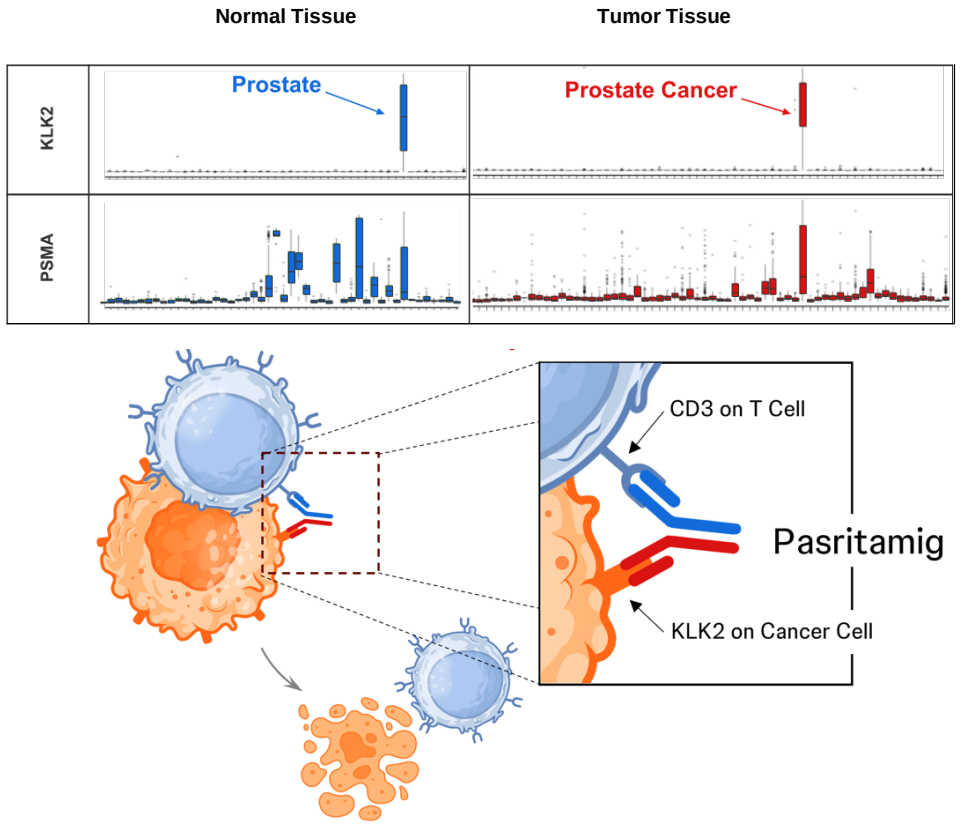

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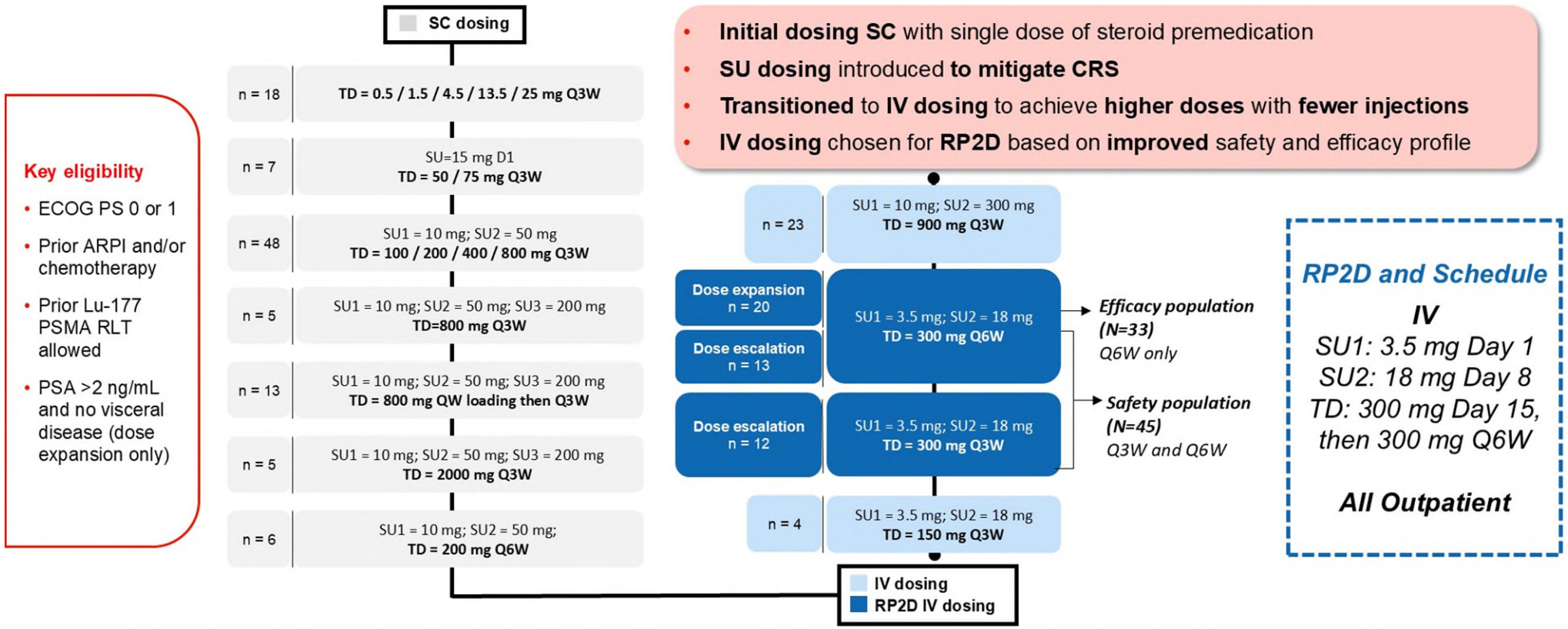

ARPI, androgen receptor pathway inhibitor; CRS, cytokine release syndrome; ECOG; Eastern Cooperative Oncology Group; IV, intravenous; Lu-177 PSMA RLT, lutetium Lu 177 vipivotide tetraxetan prostate-specific membrane antigen radioligand therapy; mCRPC, metastatic castration-resistant prostate cancer; PS, performance status; PSA, prostate-specific antigen; QW, once weekly; Q3/6W, every 3/6 weeks; RP2D, recommended phase 2 dose; SC, subcutaneous; SU, step-up dose; TD, treatment dose.

Baldini et al. Presented at ASCO 2025

Baseline characteristics

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

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

Data cut-off March 7, 2025. [a]RP2D safety population consists of participants in the all-treated population who received IV 3.5 mg D1, 18 mg D8, 300 mg D15, then 300 mg Q3W (Cohort 19) or Q6W (Cohorts 20 and 22). [b]n=173 (total), n=71 (IV), and n=44 (RP2D safety population). [c]All participants with >1 taxane regimen had both docetaxel and cabazitaxel, except 3 who had only docetaxel. AR, androgen receptor pathway inhibitor; D, Day; ECOG, Eastern Cooperative Oncology Group; IV, intravenous; Lu-177 PSMA RLT, lutetium Lu 177 vipivotide tetraxetan prostate-specific membrane antigen radioligand therapy; PS, performance status; PSA, prostate-specific antigen; Q3/6W; every 3/6 weeks; RP2D, recommended phase 2 dose; SC, subcutaneous.

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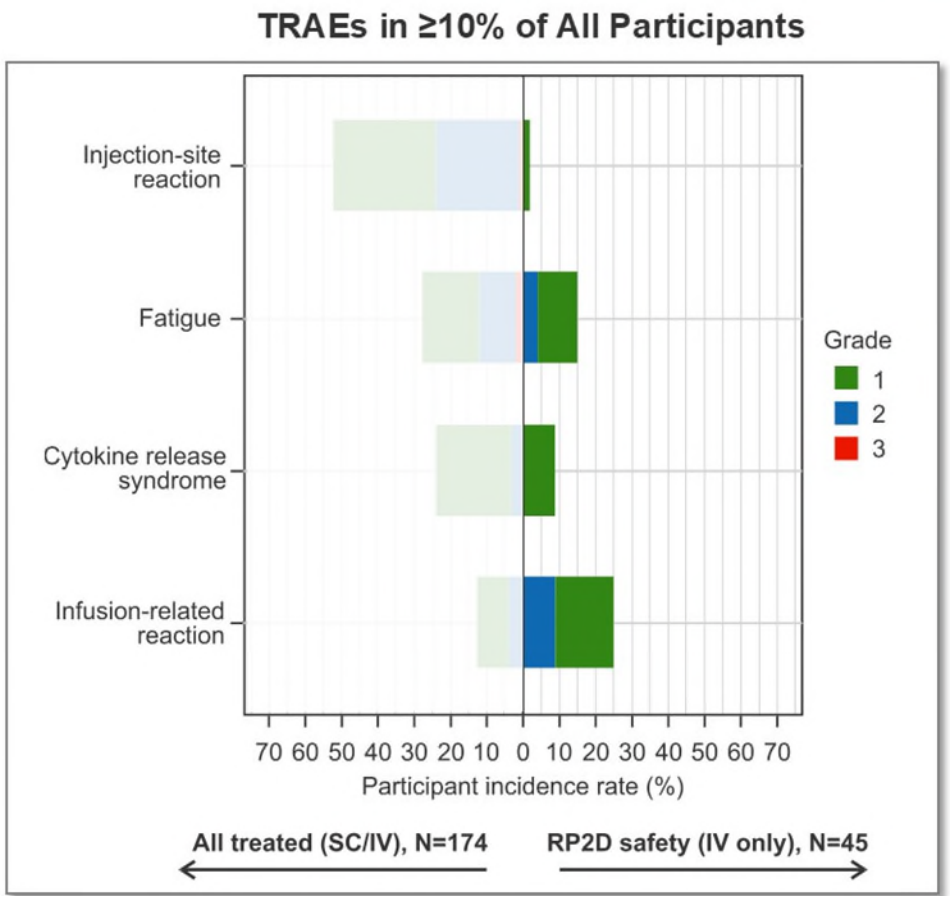
Safety profile and CRS rates



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

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

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

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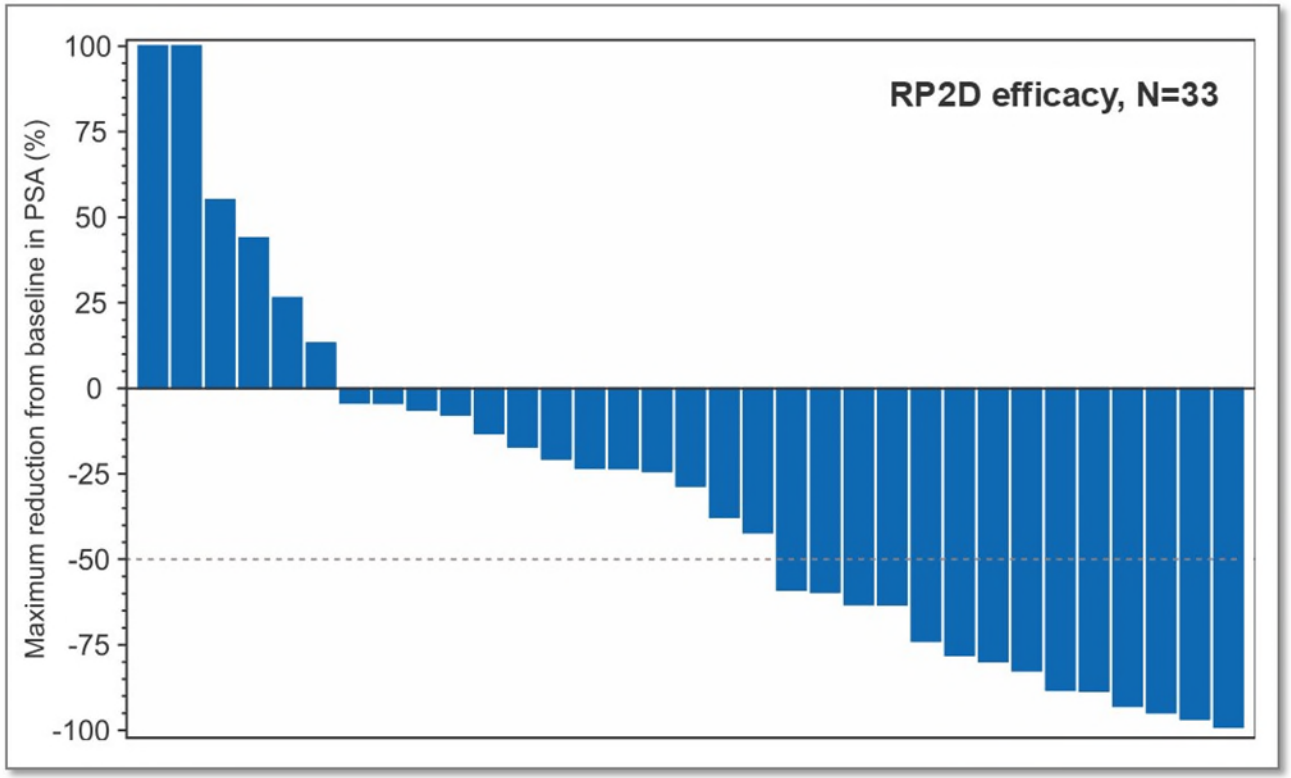
PSA responses to pasritamig



RP2D efficacy population (IV 3.5 mg D1, 18 mg D8, then 300 mg Q6W):

- **PSA decreases** were noted as early as initial step-up doses
- **14/33 (42.4%)** participants achieved **PSA50** at any time
  - **12/33 (36.4%)** participants achieved **confirmed PSA50**

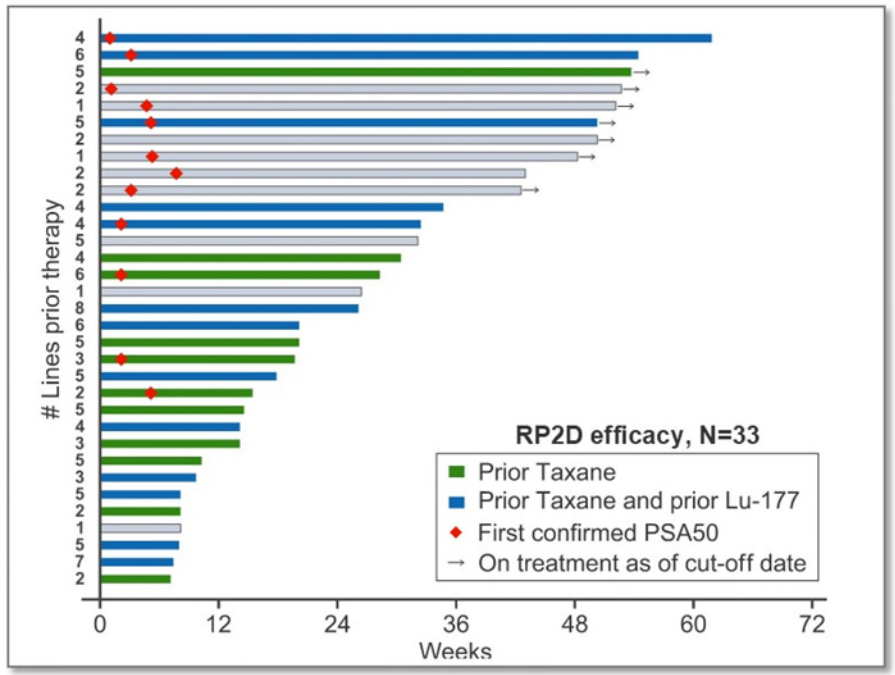
In the **all-treated population** with measurable disease at baseline (n=84/174), **ORR** was **8.3%** (7/84), not including **1 participant with a CR** who had non-measurable disease at baseline

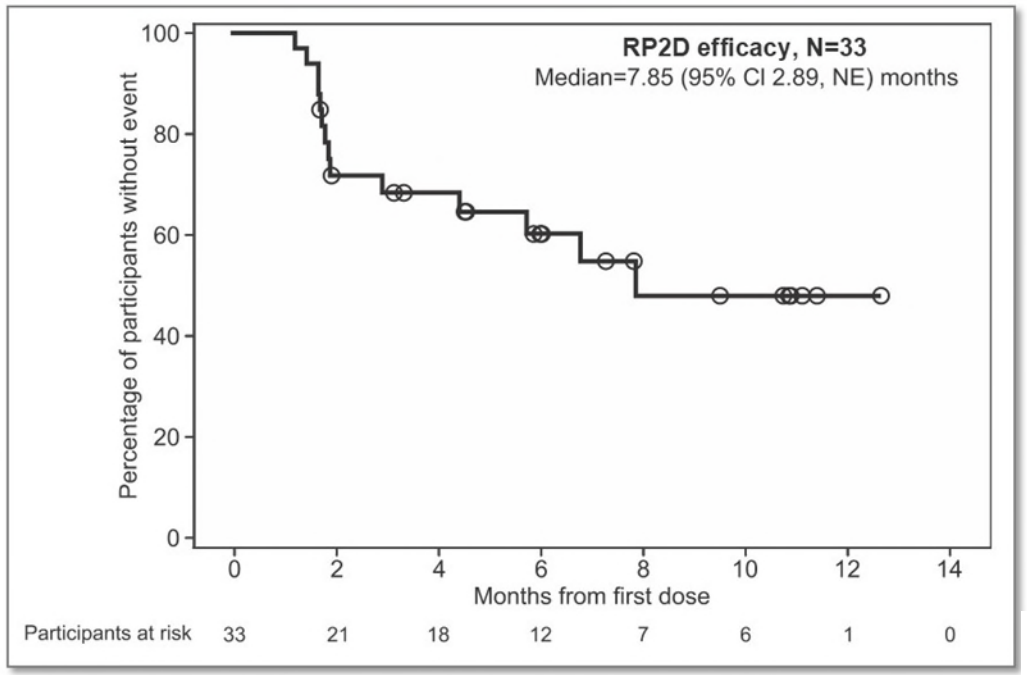
- Median **DOR** was **8.9** (95% CI, 3.6, NE) **months**

Baldini et al. Presented at ASCO 2025

Other clinical responses to pasritamig

- In the **RP2D efficacy population**, median (95% CI) **rPFS** was **7.9** (2.9, NE) **months**
  - **7/33 (21.2%)** participants were on treatment as of data cut-off
  - **PSA50 responses** and **durable disease control** were observed **irrespective of prior treatment** with taxanes or PSMA-targeted radioligand therapy





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Pasritamig: key takeaways

- Pasritamig is novel bispecific T cell engager (BiTE) antibody (KLK2 x CD3)
    - Notably low rates of adverse events and CRS (only grade 1) without tocilizumab use
    - Promising activity in heavily pretreated mCRPC
    - Outpatient dosing and safety profile highlights potential utilization in an outpatient community oncology setting
- **Novel immunotherapeutic agents in prostate cancer are promising → please consider clinical trial referrals for patients!**

Outline

- **Very high-risk prostate cancer**
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Thank you

2nd Annual City of Hope Genitourinary (GU) Oncology Retreat
7/25/2025