Clinical Experience with Lutetium-177 Therapy

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Disclosures

Accuray

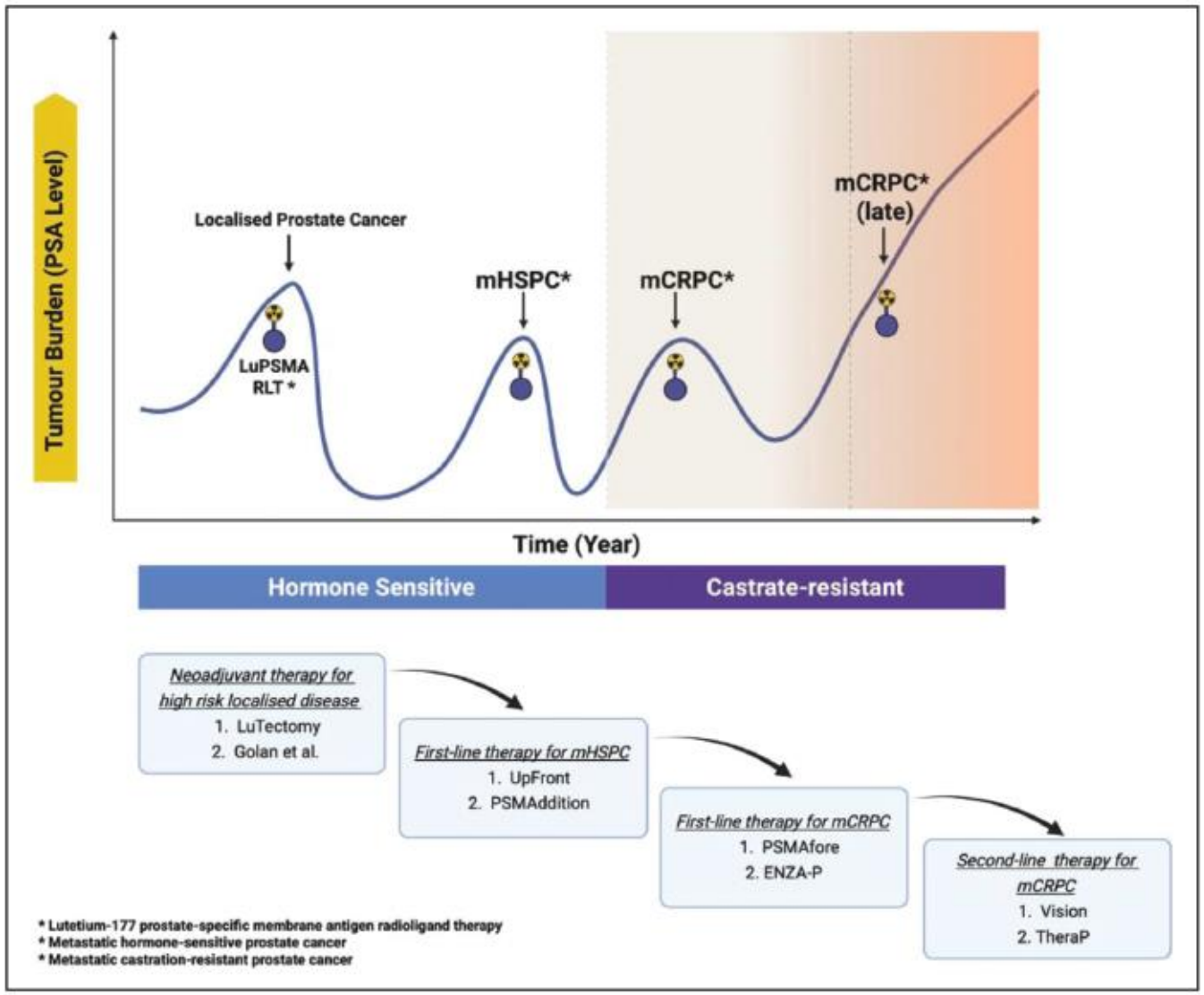
Boston Scientific

Sumitomo/Pfizer

Blue Earth Diagnostics

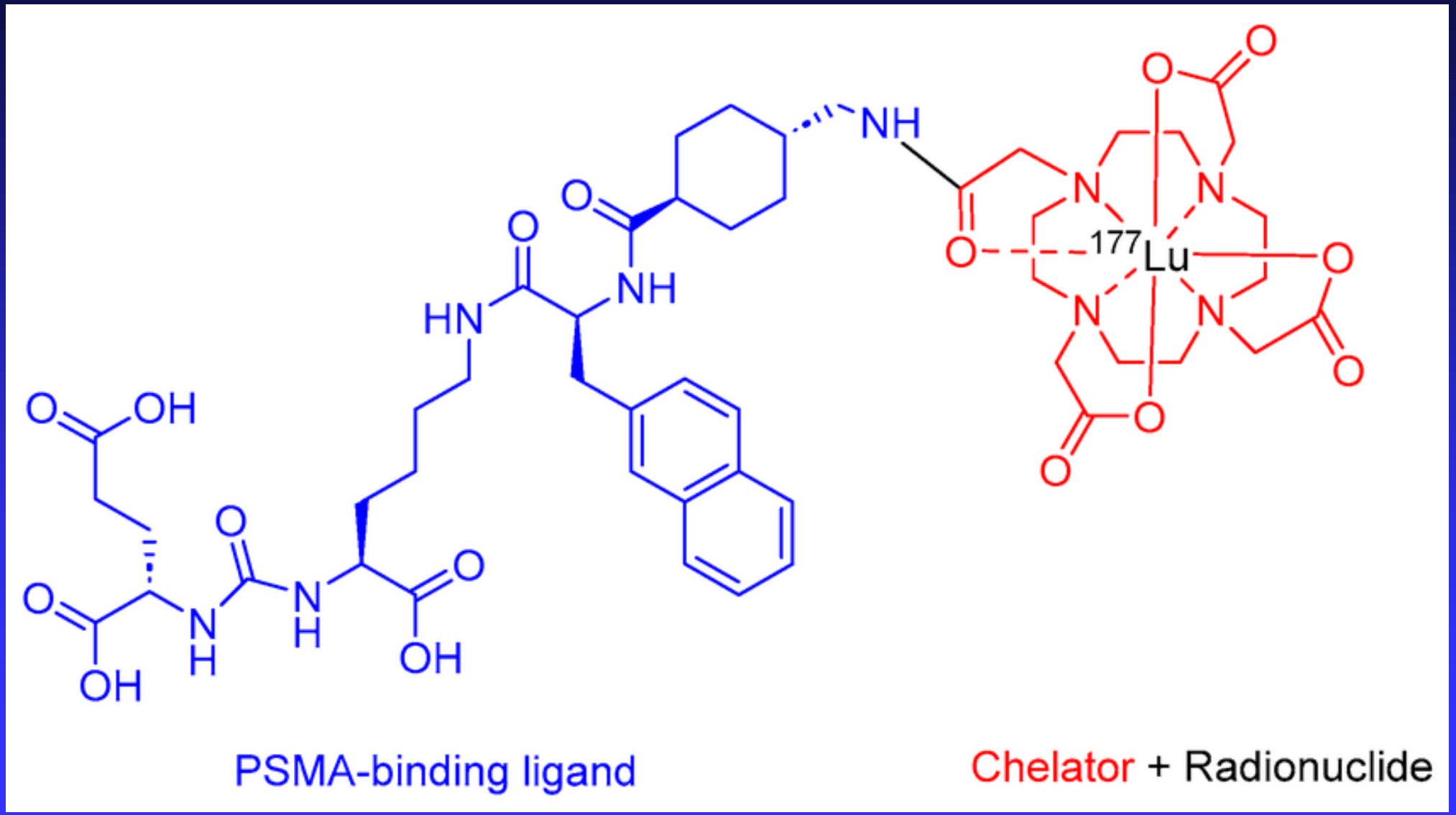
Novartis

Current Treatment Paradigms for LuPSMA



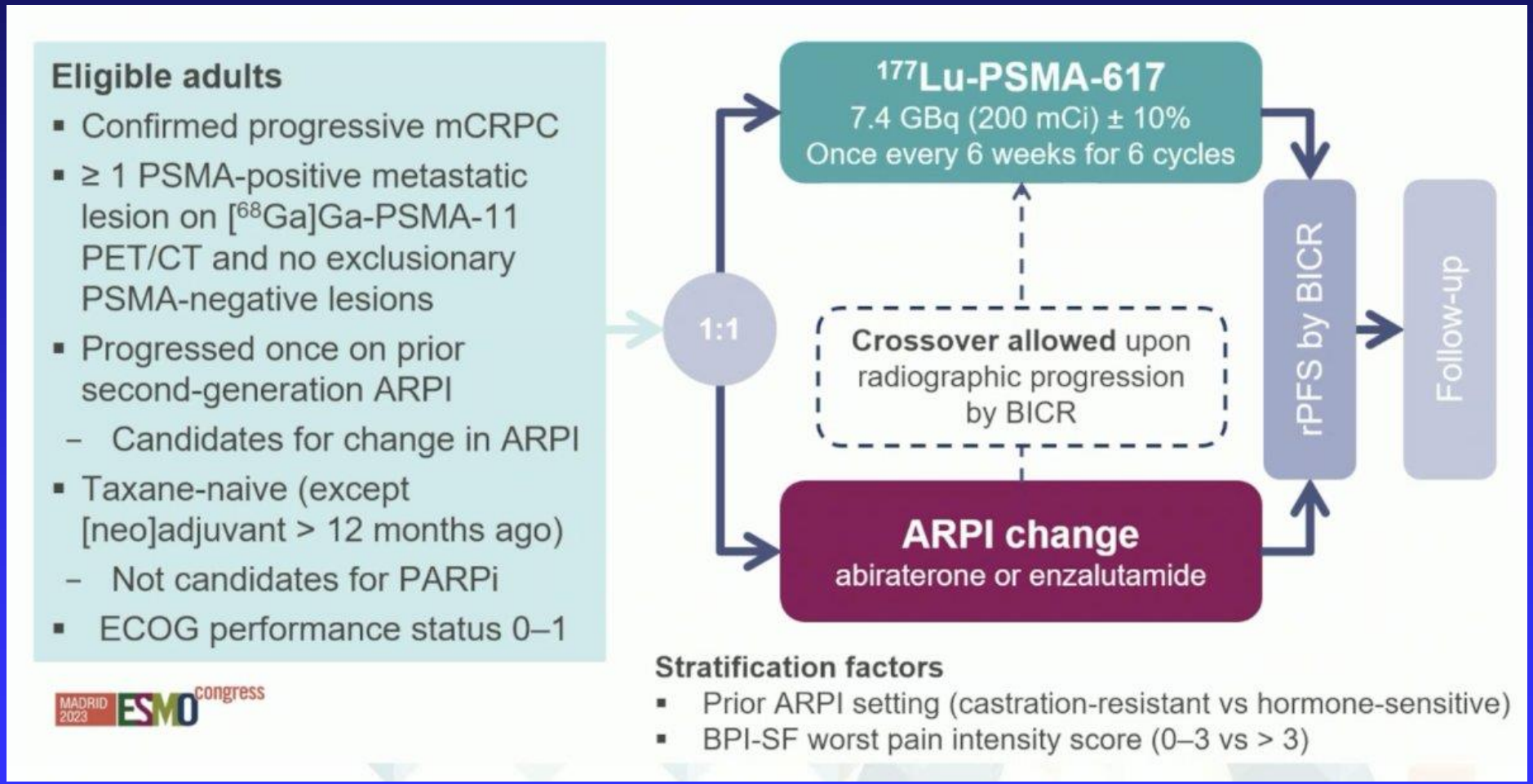
Hennes et al, Curr Opin Urol. 2025

177Lutetium-PSMA-617 (Pluvicto)



177Lu-PSMA-617 in Castrate Resistant Prostate Cancer

PSMAfore Trial Design



UroToday 2024

177Lu-PSMA-617 in Castrate Resistant Prostate Cancer

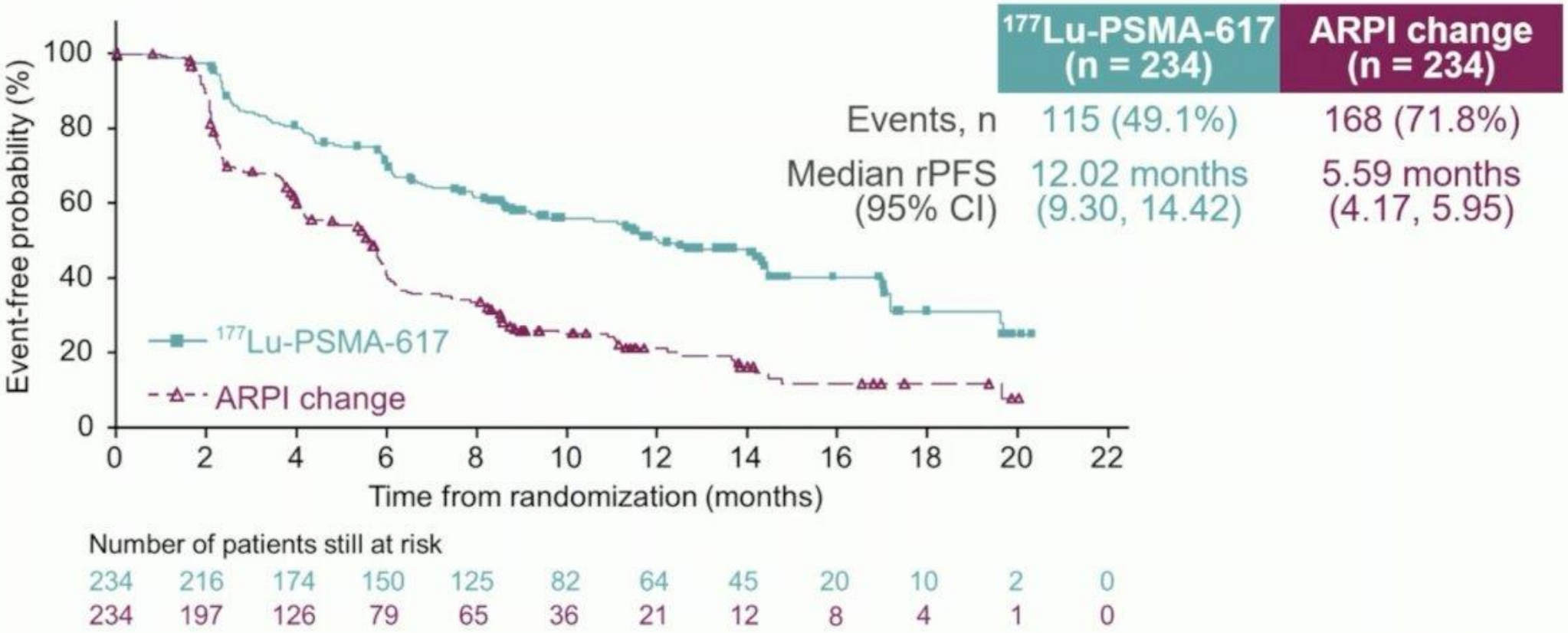
Baseline patient characteristics

OS analysis

	^{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)

177Lu-PSMA-617 in Castrate Resistant Prostate Cancer

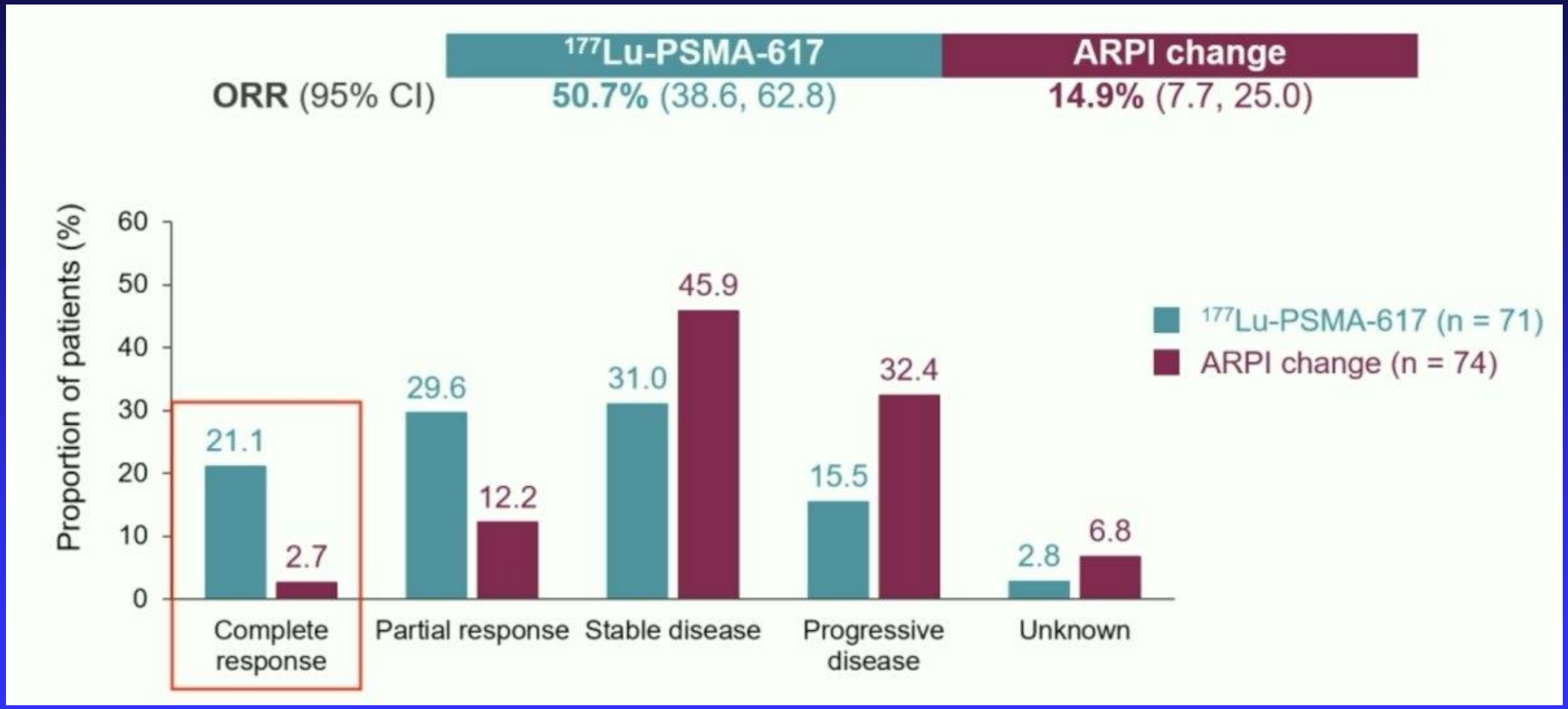
- Primary Endpoint: Radiographic Progression Free Survival



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

- *UroToday 2024*

177Lu-PSMA-617 in Castrate Resistant Prostate Cancer



177Lu-PSMA-617 in Castrate Resistant Prostate Cancer

Time to symptomatic skeletal events – on study treatment

OS a

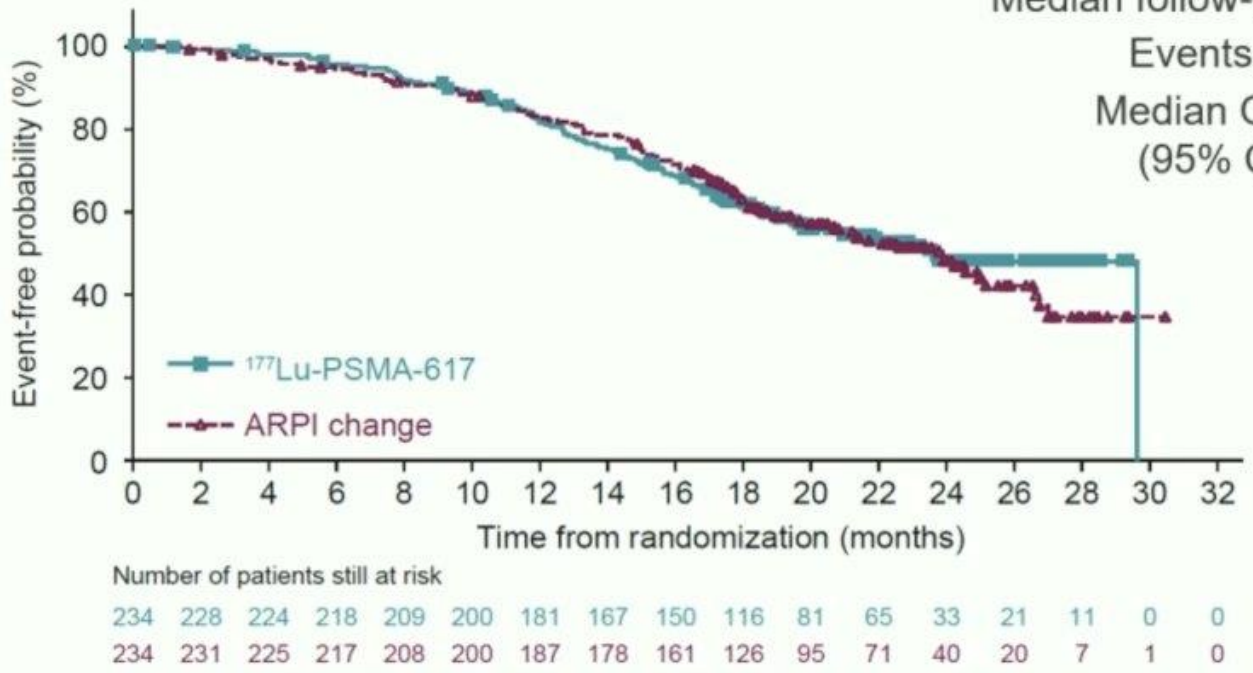
	^{177}Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Events, n (%)	25 (10.7)	59 (25.2)
Symptomatic skeletal event	21 (9.0)	54 (23.1)
Death	4 (1.7)	5 (2.1)
Median, months (95% CI)	NE (NE, NE)	NE (15.61, NE)
HR (95% CI)	**0.35 (0.22, 0.57)**	

177Lu-PSMA-617 in Castrate Resistant Prostate Cancer

OS: HR < 1 at third interim analysis

OS analysis

HR: 0.98 (95% CI: 0.75, 1.28)



	^{177}Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Median follow-up	18.23 months	18.40 months
Events, n	104 (44.4%)	112 (47.9%)
Median OS (95% CI)	23.66 months (19.75, NE)	23.85 months (20.6, 26.55)

Crossover:
134/234 (57.3%) in ARPI change group
134/173 (77.5%) eligible patients

RPSFT crossover-adjusted OS analysis

- HR: 0.98 (95% CI: 0.76, 1.27)
- No difference versus the ITT analysis because the RPSFT model cannot adjust for confounding in the context of overlapping ITT curves

177Lu-PSMA-617 in Castrate Resistant Prostate Cancer

Treatment-emergent adverse events

OS analysis

AEs, n (%)	^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)
Any	223 (98.2)	223 (96.1)
Grade 3–4	77 (33.9)	100 (43.1)
Serious	46 (20.3)	65 (28.0)
Treatment-related	7 (3.1)	5 (2.2)
Fatal[a] (grade 5)	4 (1.8)	5 (2.2)
Treatment-related	0	1 (0.4)
Leading to dose adjustment[b]	8 (3.5)	35 (15.1)
Leading to discontinuation[b]	13 (5.7)	12 (5.2)

[a]Fatal AEs included: COVID-19, cardiac arrest, intestinal ischaemia, sepsis, cerebrovascular accident, coma, dyspnea, multiple organ dysfunction syndrome and treatment-related cerebrovascular accident.
[b]AEs leading to dose adjustment or study treatment discontinuation included: dry mouth, thrombocytopenia, abdominal pain, acute kidney injury, anemia, back pain, neutropenia, platelet count decreased, sepsis, anaphylactic reaction, cerebrovascular accident, coma, dyspnea, fatigue, hepatic cytolysis, hyperaesthesia, spinal cord compression and tremor.

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177Lu-PSMA-617 in Castrate Resistant Prostate Cancer

Treatment-emergent adverse events grouped by safety topics of interest

OS analysis

Safety topic with combined AE incidence ≥ 5%, n (%)	All grades		Grades 3–5	
	^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)	^{177}Lu-PSMA-617 (n = 227)	ARPI change (n = 232)
Dry mouth	131 (57.7)	5 (2.2)	3 (1.3)	0
Myelosuppression[a]	81 (35.7)	49 (21.1)	28 (12.3)	18 (7.8)
Hepatoxicity	29 (12.8)	32 (13.8)	12 (5.3)	12 (5.2)
Renal toxicity	15 (6.6)	17 (7.3)	3 (1.3)	6 (2.6)
Dry eye	14 (6.2)	1 (0.4)	0	0
Fractures	9 (4.0)	13 (5.6)	2 (0.9)	7 (3.0)
QT prolongation	4 (1.8)	5 (2.2)	1 (0.4)	4 (1.7)

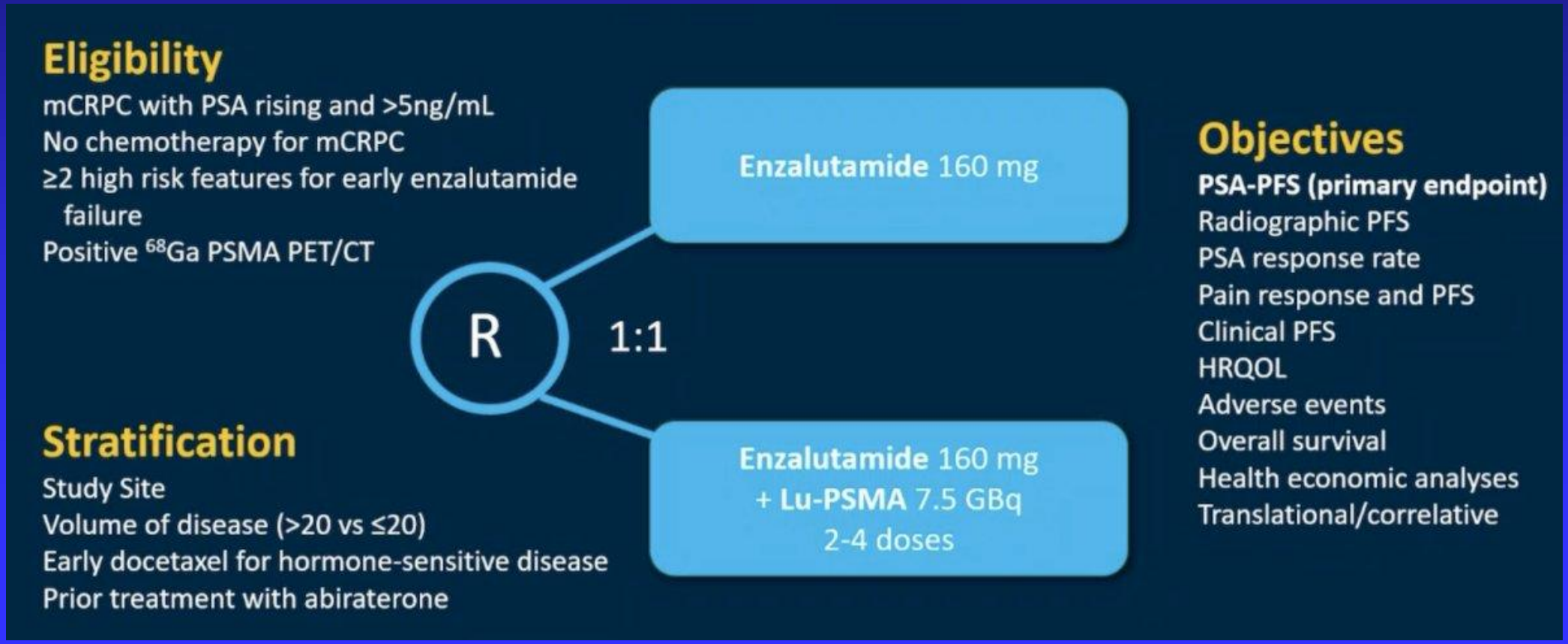
[a]includes anemia, thrombocytopenia and neutropenia

Conclusions

- ^{77}Lu-PSMA-617 treatment prolonged rPFS versus ARPI change in taxane-naïve mCRPC patients.
- Secondary and exploratory endpoints also favored ^{177}Lu-PSMA-617 treatment.
- There was no difference in OS with ^{177}Lu-PSMA-617 versus ARPI change, but results are likely confounded by substantial rate of crossover.
- ^{177}Lu-PSMA-617 had a favorable safety profile and was well-tolerated.

Enzalutamide and 177Lu-PSMA-617 in Poor-Risk Metastatic CRPC, a Randomized, Phase 2 Trial

- Clonal Adjustment Theory
  - Enza Increases Androgen Resistance, Allowing Lu-PSMA to have Increased Activity



ENZA-p: Primary Endpoint

- PSA-PRS (Median)
  - Enza 8 mo
  - Enza + Lu-PSMA 13 mo

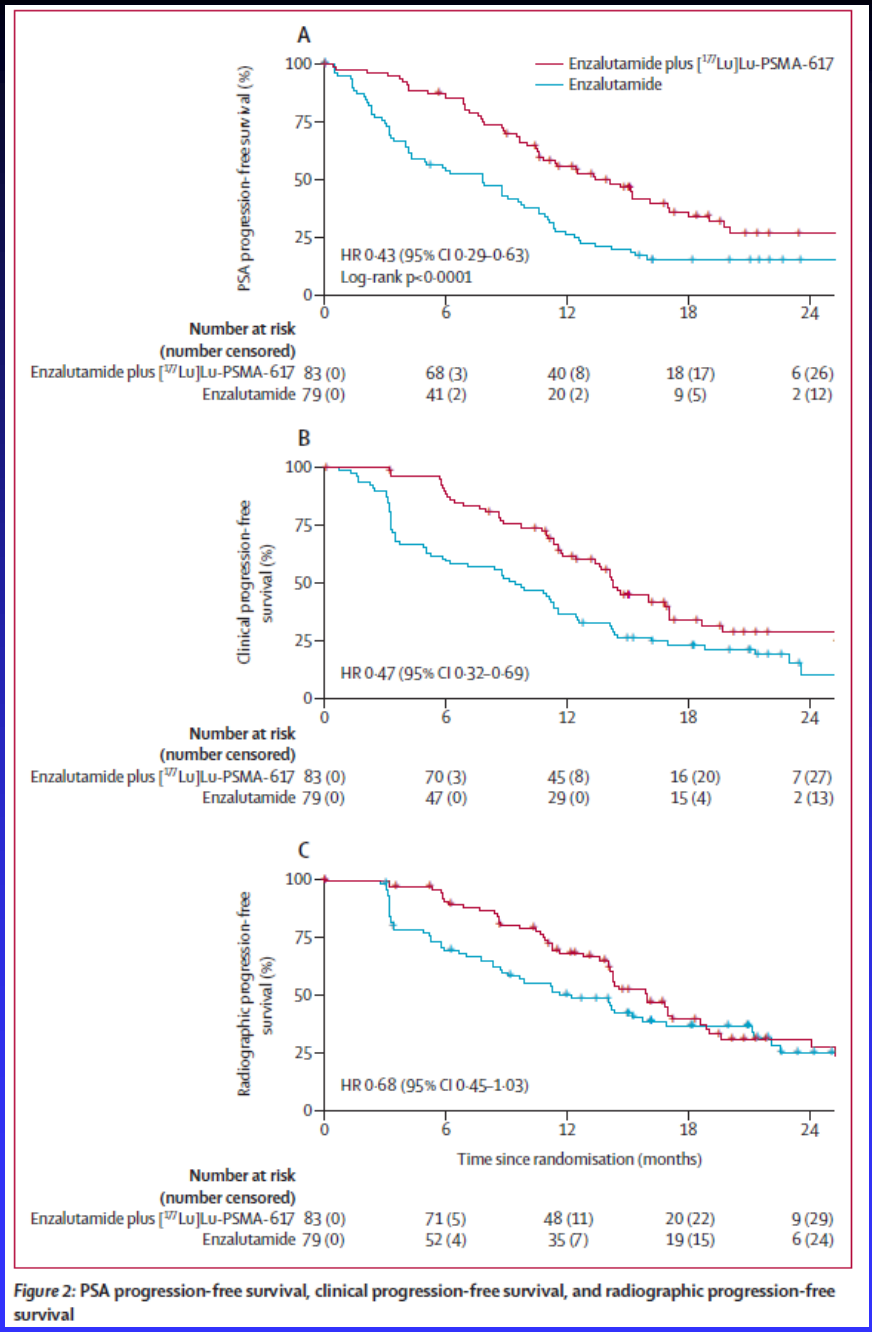


Figure 2: **PSA progression-free survival, clinical progression-free survival, and radiographic progression-free survival**

- ***Emmett et al, Lancet Onc. 2024***

ENZA-p: Overall Survival

- Median Follow-up
  - 34 months
- OS (Median)
  - Enza 26 mo
  - Enza/Lu-PSMA 34 mo

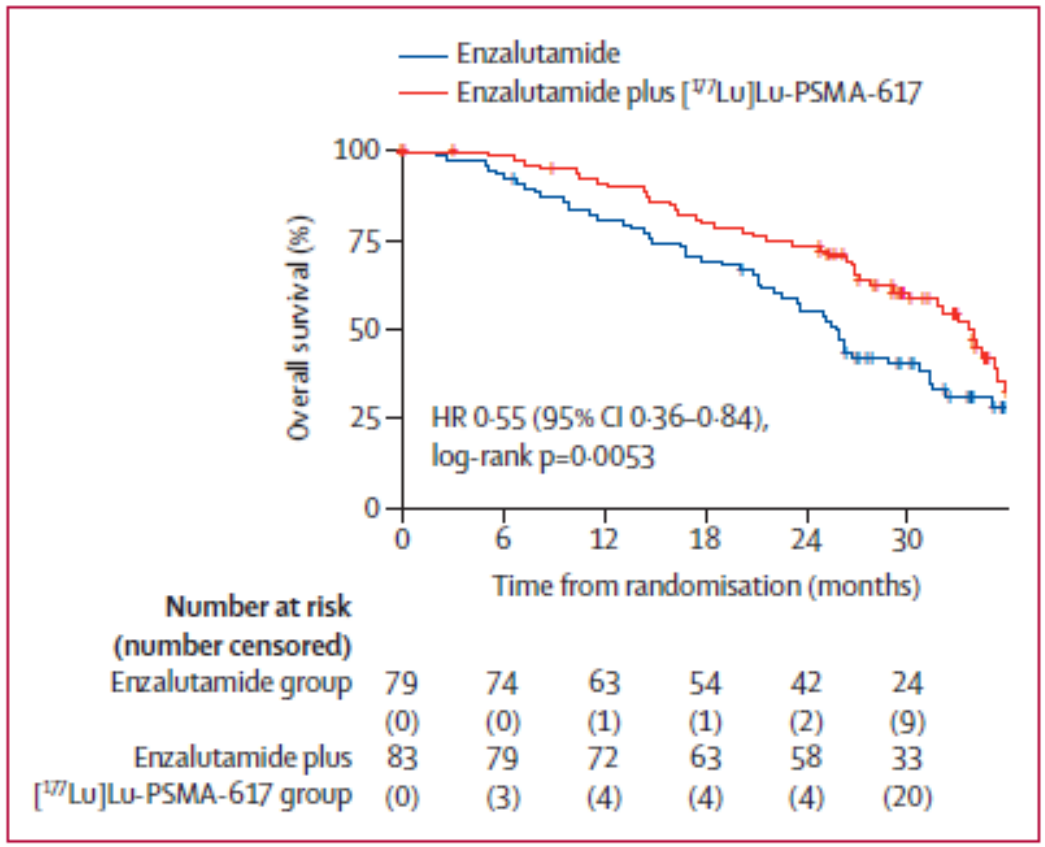


Figure 2: **Overall survival**
^{177}Lu–lutetium-177. HR–hazard ratio.

- ***Emmett et al, Lancet Onc. 2025***

ENZA-p: QOL

- Deterioration-Free Survival (12 mo)
  - EORTC QLQ-C30
  - Physical Function
    - 10.6 mos vs. 3.4 mo
  - Overall Health and QOL
    - 8.7 mos vs. 3.3 mo

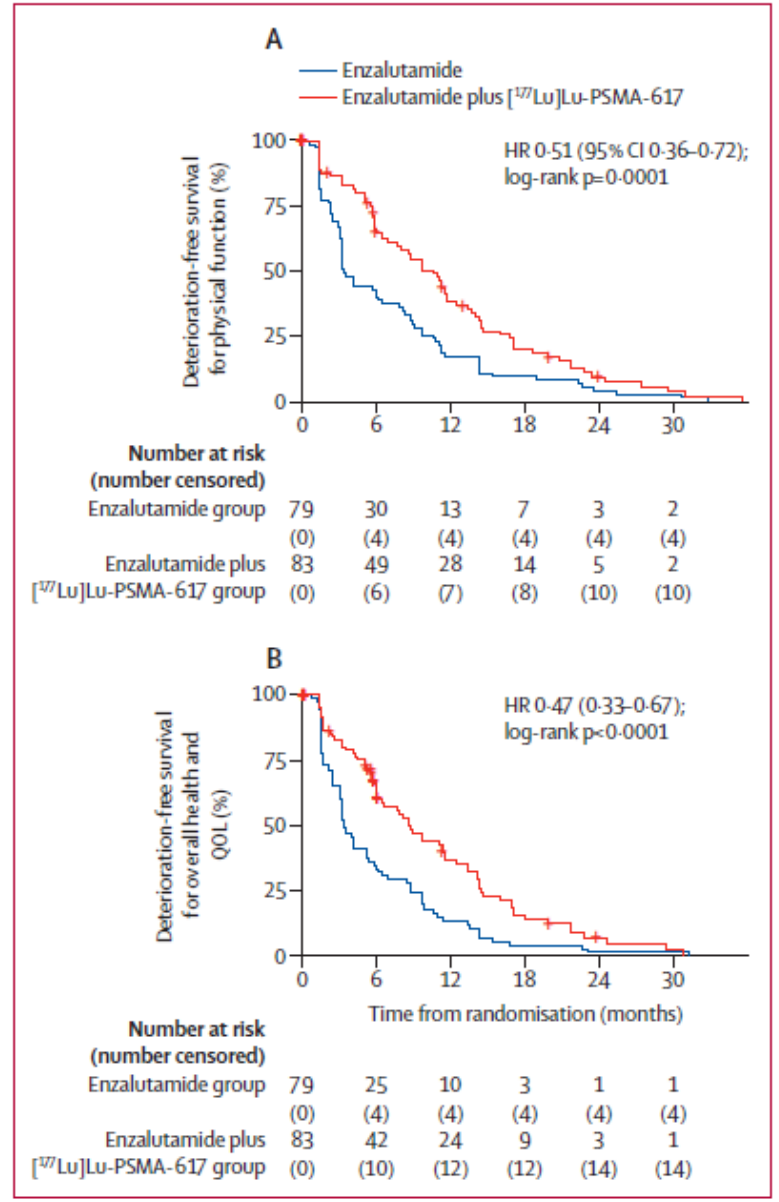


Figure 3: **Deterioration-free survival for physical function (A) and overall health and QOL (B)**

^{177}Lu=lutetium-177. HR=hazard ratio. QOL=quality of life.

- ***Emmett et al, Lancet Onc. 2025***

ENZA-p: QOL

- Mean Scores for Fatigue and Pain Favored Enza/Lu-PSMA

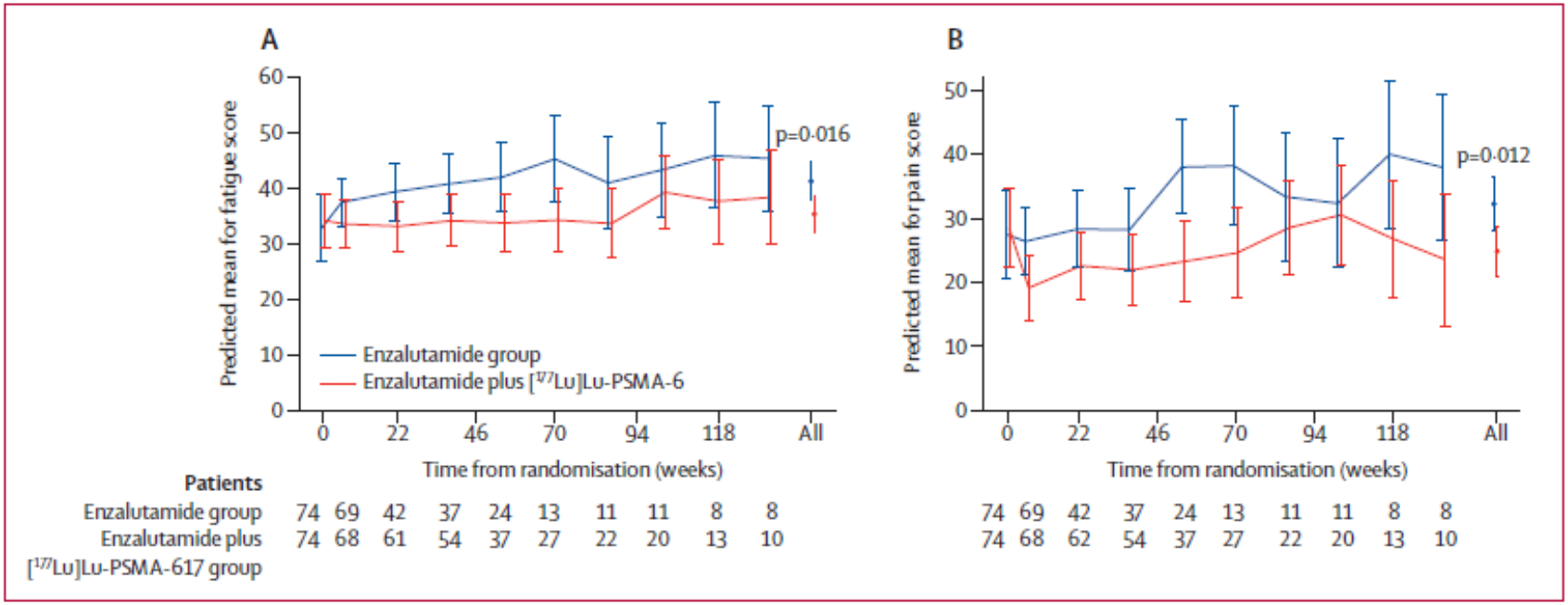


Figure 4: **HRQOL scores over time by randomly assigned treatment for fatigue (A) and pain (B) EORTC QLQ-C30 scales**
Error bars indicate 95% CIs. ^{177}Lu=lutetium-177. EORTC=European Organisation for Research and Treatment of Cancer. HRQOL=health-related quality of life. QLQ-C30=Quality of Life Questionnaire Core 30.

- ***Emmett et al, Lancet Onc. 2025***

ENZA-p: Toxicity

- Increased with Lu-PSMA
  - Anorexia/Nausea
  - Dry Eye/Mouth
  - Fatigue
  - Hematologic
- High Grade Toxicity (Gr 3-5)
  - Enza 44%
  - Enza/Lu-PSMA 46%

	Enzalutamide plus [^{177}Lu]Lu-PSMA-617 group (n=81)		Enzalutamide group (n=79)	
	Grade 1–2	Grade 3	Grade 1–2	Grade 3
Any adverse event	67 (83%)	10 (12%)	64 (81%)	3 (4%)
Anaemia	9 (11%)	3 (4%)	4 (5%)	0
Anorexia	16 (20%)	0	8 (10%)	0
Arthralgia	7 (9%)	2 (2%)	7 (9%)	0
Arthritis	3 (4%)	1 (1%)	0	0
Cognitive disturbance	8 (10%)	1 (1%)	4 (5%)	0
Concentration impairment	2 (2%)	0	1 (1%)	0
Dry eye	10 (12%)	0	2 (3%)	0
Dry mouth	33 (41%)	0	8 (10%)	0
Fatigue	60 (74%)	2 (2%)	53 (67%)	2 (3%)
Generalised muscle weakness	1 (1%)	1 (1%)	2 (3%)	0
Hot flashes	20 (25%)	0	13 (16%)	0
Memory impairment	5 (6%)	0	5 (6%)	0
Nausea	39 (48%)	0	24 (30%)	0
Platelet count decreased	7 (9%)	1 (1%)	0	0
Vomiting	4 (5%)	0	3 (4%)	0
White blood cell count decreased	4 (5%)	1 (1%)	1 (1%)	1 (1%)

Data are n (%). There were no grade 4 or 5 adverse events of interest.

Table 2: **Adverse events of interest**

177Lu-PSMA in CRPC

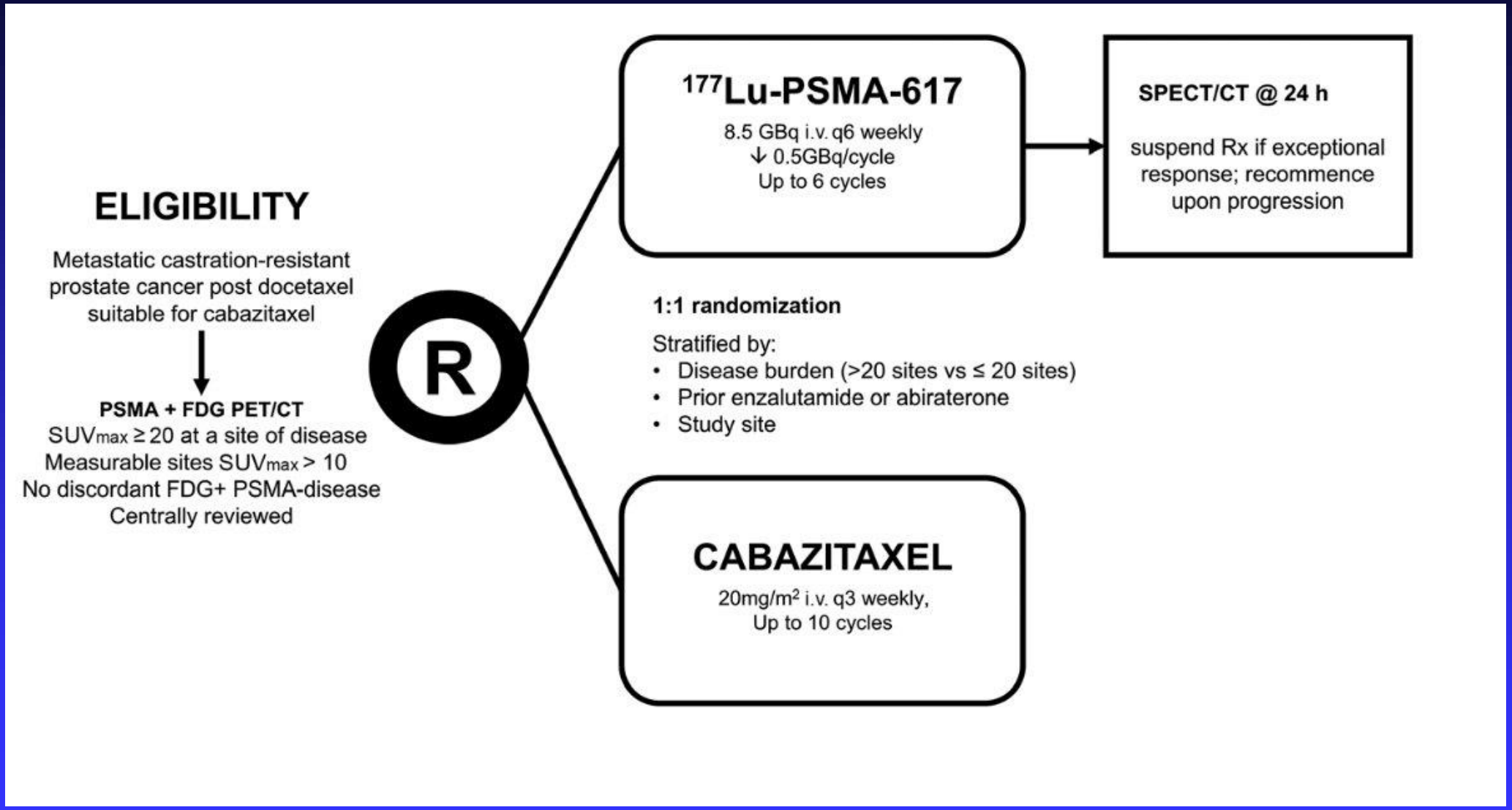
- TheraP Trial

[^{177}Lu]Lu-PSMA-617 versus cabazitaxel in patients with metastatic castration-resistant prostate cancer (TheraP): a randomised, open-label, phase 2 trial

Michael S Hofman, Louise Emmett, Shahneen Sandhu, Amir Iravani, Anthony M Joshua, Jeffrey C Goh, David A Pattison, Thean Hsiang Tan, Ian D Kirkwood, Siobhan Ng, Roslyn J Francis, Craig Gedye, Natalie K Rutherford, Andrew Weickhardt , Andrew M Scott, Sze-Ting Lee, Edmond M Kwan, Arun A Azad, Shakher Ramdave, Andrew D Redfern, William Macdonald, Alex Guminski, Edward Hsiao, Wei Chua, Peter Lin, Alison Y Zhang, Margaret M McJannett, Martin R Stockler, John A Violet, Scott G Williams, Andrew J Martin, Ian D Davis, for the TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group†*

- ***Hofman et al, Lancet. 2021***

177Lu-PSMA in CRPC



177Lu-PSMA in CRPC

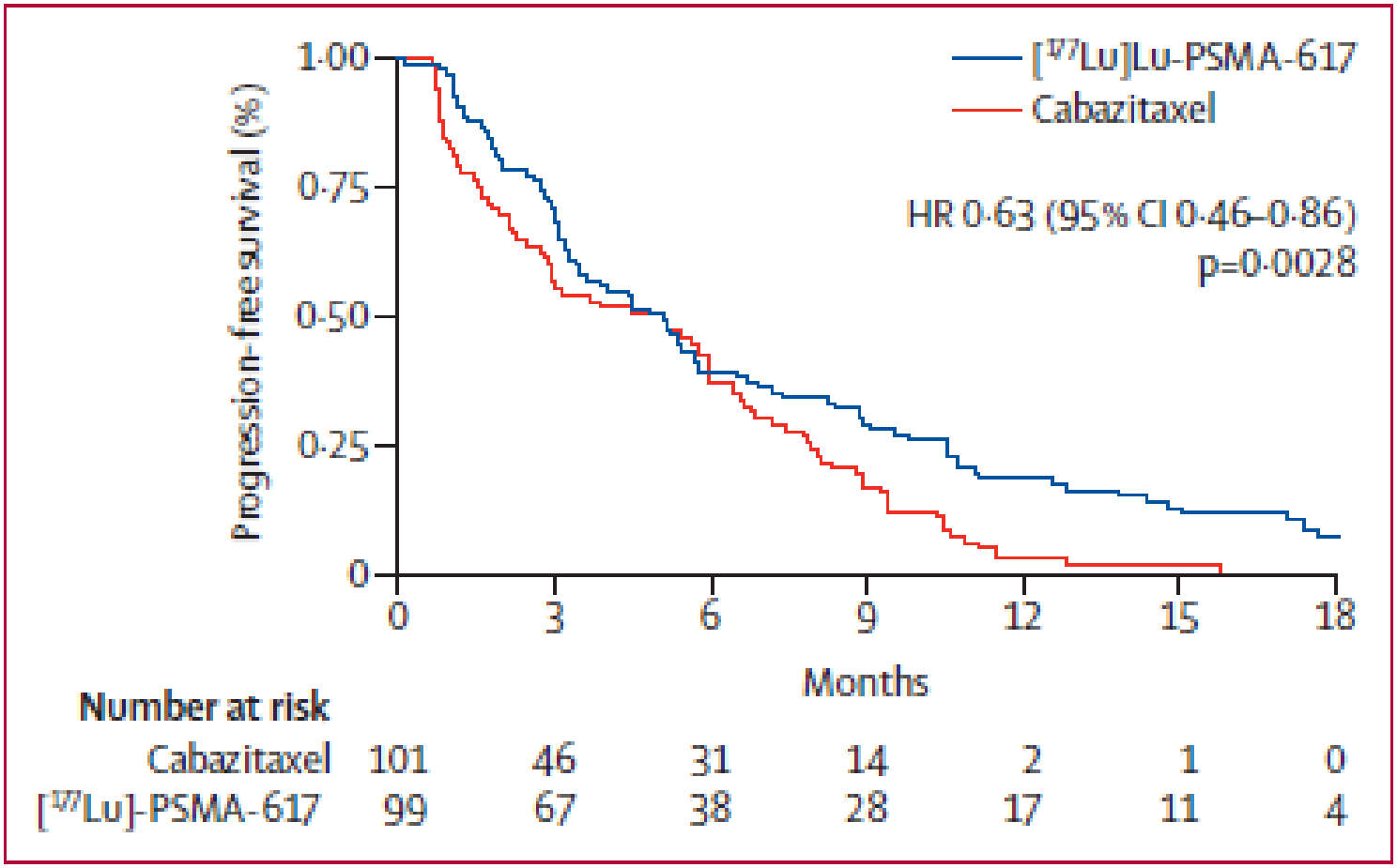
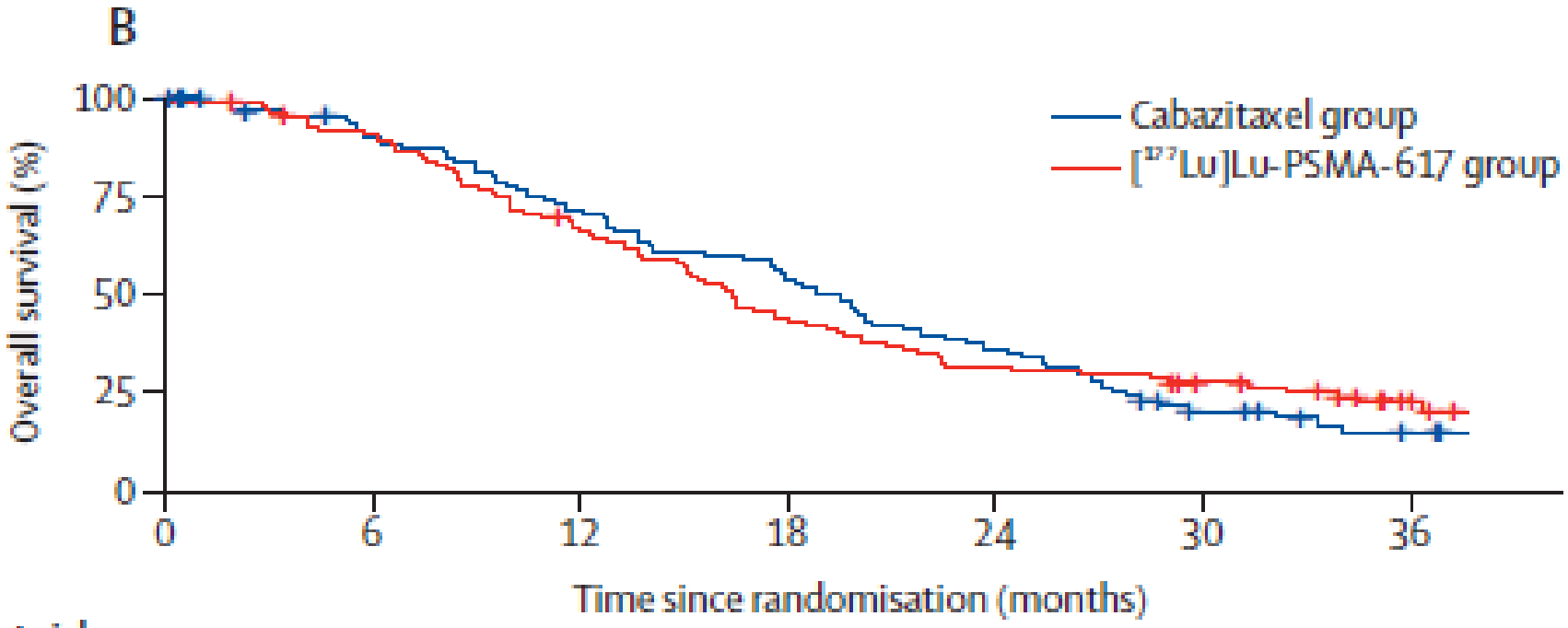


Figure 3: **Radiographic or PSA progression-free survival**
HR=hazard ratio. PSA=prostate-specific antigen. PSMA=prostate-specific membrane antigen. ^{177}Lu=lutetium-177.

Hofman et al, Lancet. 2021

177Lu-PSMA in CRPC



Number at risk (number censored)							
Cabazitaxel group	101	75	60	45	30	14	6
	(0)	(17)	(17)	(17)	(17)	(20)	(25)
[177Lu]Lu-PSMA-617 group	99	88	63	41	30	23	11
	(0)	(2)	(3)	(3)	(3)	(6)	(14)

Hofman et al, Lancet Oncol. 2024

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journal homepage: www.europeanurology.com

European Association of Urology

Platinum Priority – Prostate Cancer

Editorial by Ulrich Krafft, Boris A. Hadaschik, Katharina Lückerath, Ken Herrmann on pp. 227–228 of this issue

Administering [^{177}Lu]Lu-PSMA-617 Prior to Radical Prostatectomy in Men with High-risk Localised Prostate Cancer (LuTectomy): A Single-centre, Single-arm, Phase 1/2 Study

Renu S. Eapen [a,b,c,], James P. Buteau [b,c,d], Price Jackson [c,e], Catherine Mitchell [f], Sheng F. Oon [g], Omar Alghazo [a], Lachlan McIntosh [d], Nattakorn Dhiantravan [d], Mark J. Scalzo [b,d], Jonathan O'Brien [a], Shahneen Sandhu [c,h], Arun A. Azad [c,h], Scott G. Williams [c,i], Gaurav Sharma [b], Mohammad B. Haskali [j], Mathias Bressel [c,k], Kenneth Chen [a], Pocharapong Jenjitranant [a], Aoife McVey [a,b], Daniel Moon [a], Nathan Lawrentschuk [a], Paul J. Neeson [c,l], Declan G. Murphy [a,b,c,†], Michael S. Hofman [b,c,d,†]*

[a] *Division of Cancer Surgery, Peter MacCallum Cancer Centre, Melbourne, Australia;* [b] *Prostate Cancer Theranostics and Imaging Centre of Excellence (ProsTIC), Peter MacCallum Cancer Centre, Melbourne, Australia;* [c] *Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, Australia;* [d] *Department of Molecular Imaging and Therapeutic Nuclear Medicine, Peter MacCallum Cancer Centre, Melbourne, Australia;* [e] *Department of Physical Sciences, Peter MacCallum Cancer Centre, Melbourne, Australia;* [f] *Department of Anatomical Pathology, Peter MacCallum Cancer Centre, Melbourne, Australia;* [g] *Department of Cancer Imaging, Peter MacCallum Cancer Centre, Melbourne, Australia;* [h] *Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia;* [i] *Department of Radiation Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia;* [j] *Radiopharmaceutical Research Laboratory, Peter MacCallum Cancer Centre, Melbourne, Australia;* [k] *Centre for Biostatistics and Clinical Trials, Peter MacCallum Cancer Centre, Melbourne, Australia;* [l] *Cancer Immunology Program, Peter MacCallum Cancer Centre, Melbourne, Australia*

LuTectomy Trial

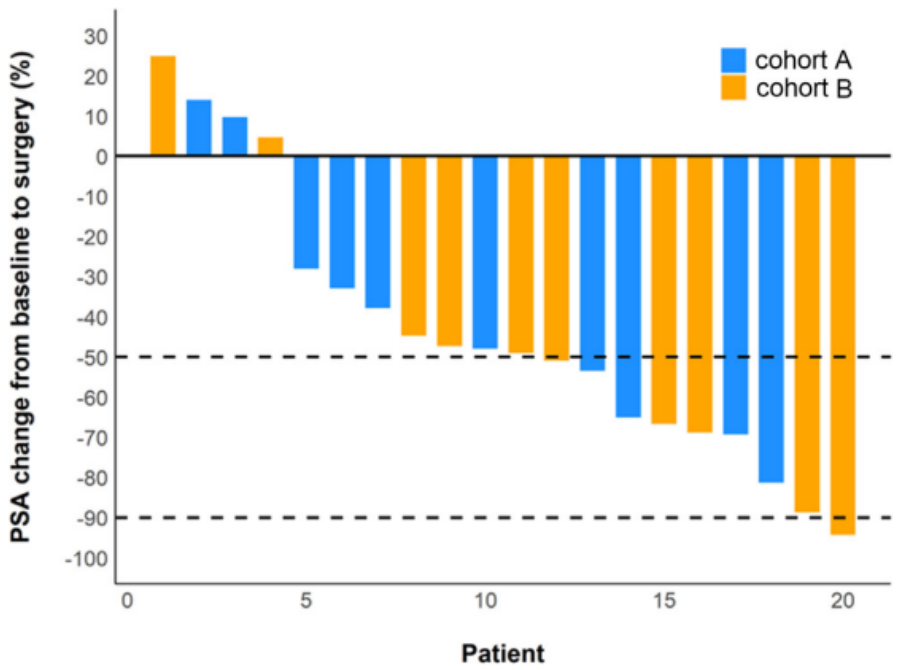


Fig. 2 – PSA reduction from baseline to time of surgery. PSA = prostate-specific antigen.

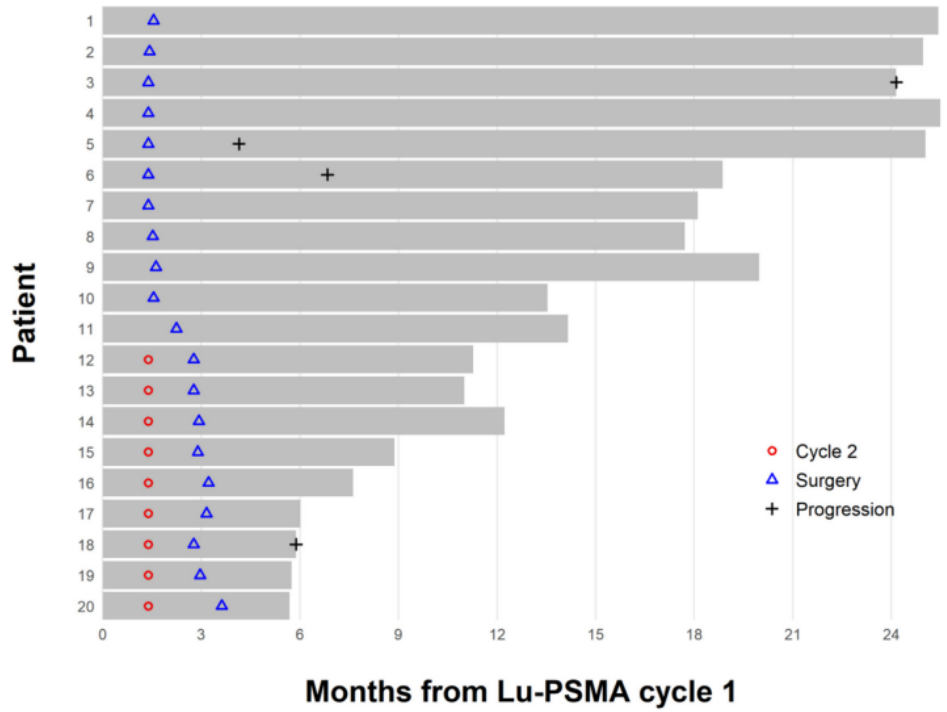


Fig. 4 – Swimmer's plot depicting the timing of events of interest following the first dose of [^{177}Lu]Lu-PSMA-617. No deaths occurred in this study. Progression = biochemical progression. PSMA = prostate-specific membrane antigen.

Eapen et al, Eur Urol. 2024

LuTectomy Trial

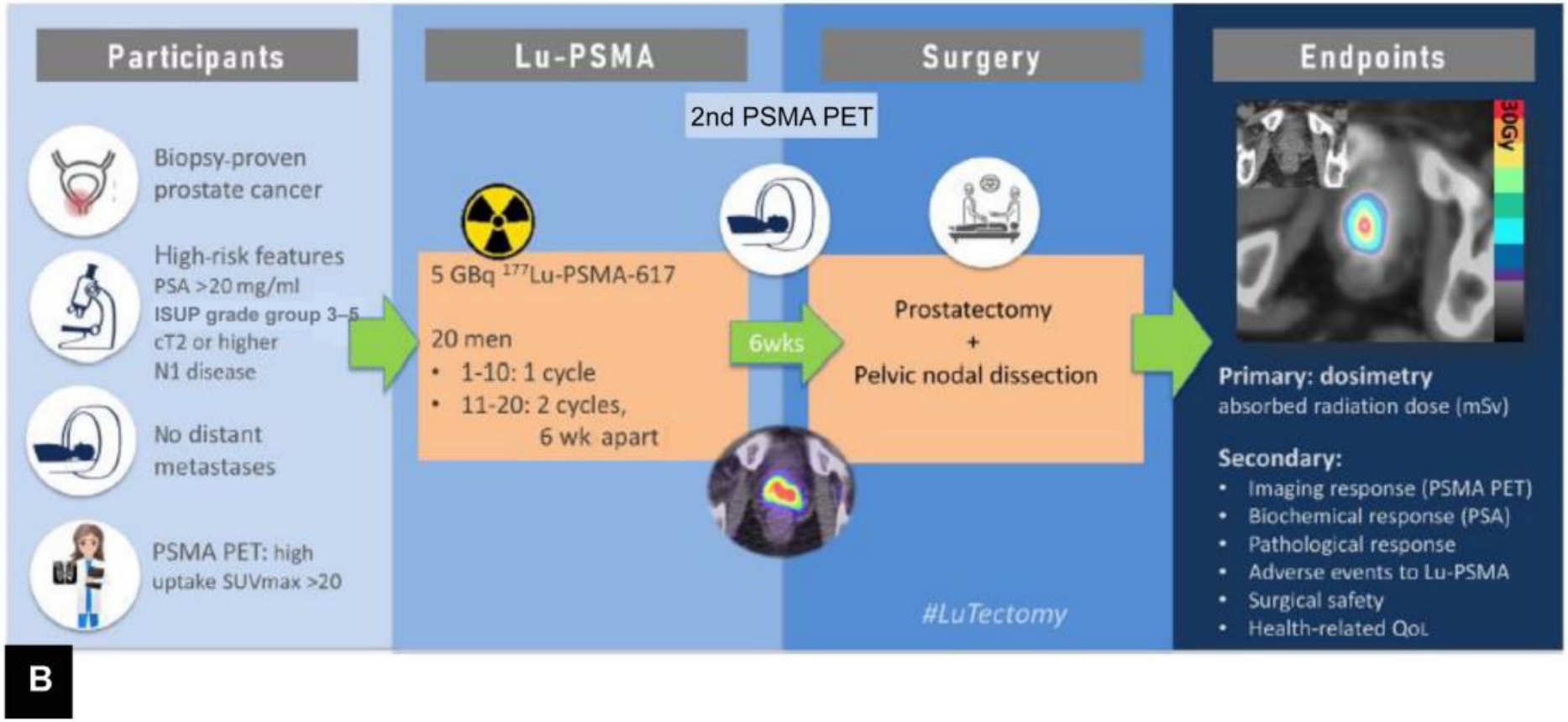
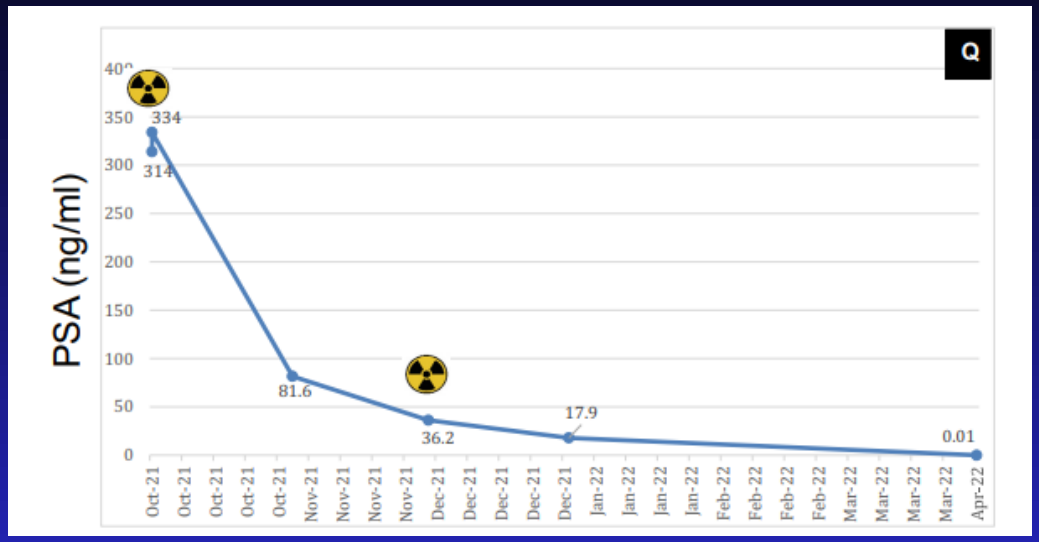
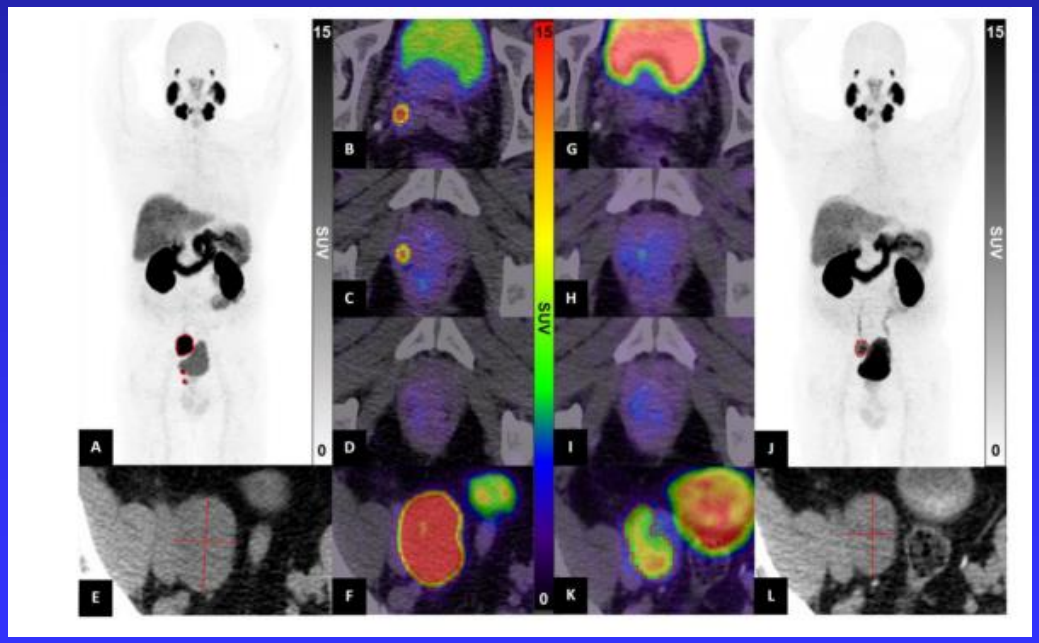


Fig. 1 – Trial schema: (A) patient recruitment and (B) the trial schema are demonstrated. ISUP = International Society of Urological Pathology; PET = positron emission tomography; PSA = prostate-specific antigen; PSMA = prostate-specific membrane antigen; QoL = quality of life; SUVmax = maximum standardised uptake value.

Eapen et al, Eur Urol. 2024

LuTectomy Trial





Eapen et al, Eur Urol. 2024

177Lu-PSMA in Oligorecurrent Prostate Cancer

- LUNAR Trial

^{177}Lu-Prostate-Specific Membrane Antigen Neoadjuvant to Stereotactic Ablative Radiotherapy for Oligorecurrent Prostate Cancer (LUNAR): An Open-Label, Randomized, Controlled, Phase II Study

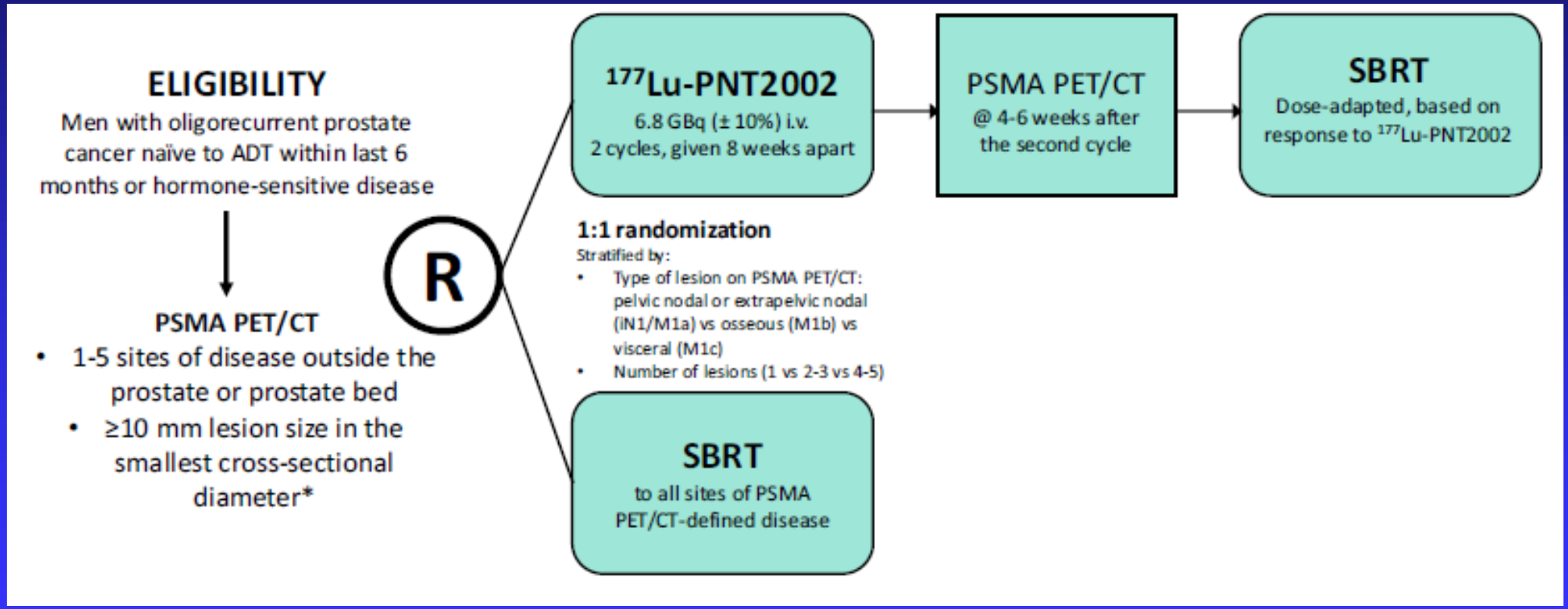
Amar U. Kishan, MD[1,2]; Luca F. Valle, MD[1,3]; Holly Wilhalme, MS[4]; Carol Felix, BS[1]; Rejah Nabong, BS[5]; Jesus E. Juarez-Casillas, MS, BS[1]; Kevin Flores, BS[1]; T. Martin Ma, MD, PhD[6]; Vinicius Ludwig, MD[5]; Mariko Nakayama, MD[5,7]; Zachary Ells, BS[5]; Magnus Dahlbom, PhD[5]; Michael Lauria, PhD[1]; Catherine Meyer, PhD[5]; Minsong Cao, PhD[8]; Joanne B. Weidhaas, MD, PhD[1]; Donatello Telesca, PhD[9]; Kristen McGreevy, PhD[9]; Nicholas G. Nickols, MD, PhD[1,3]; Danielle Karasik, BS[1]; Sophia Parmisano, BS[1]; T. Vincent Basehart, BS[1]; Wayne Brisbane, MD[2]; Leonard Marks, MD[2]; Matthew B. Rettig, MD[3,10]; Robert E. Reiter, MD[2]; Paul C. Boutros, PhD[2,11]; Martin Allen-Auerbach, MD[5]; Johannes Czernin, MD[5]; Michael L. Steinberg, MD[1]; and Jeremie Calais, MD, PhD[5]

DOI https://doi.org/10.1200/JCO-25-01553

- ***Kishan et al, JCO. 2025***

177Lu-PSMA in Oligorecurrent Prostate Cancer

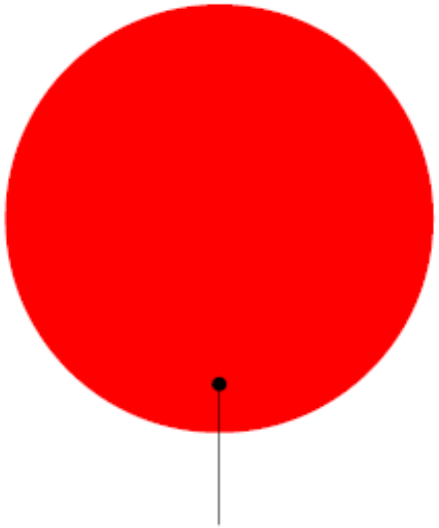
- LUNAR Trial



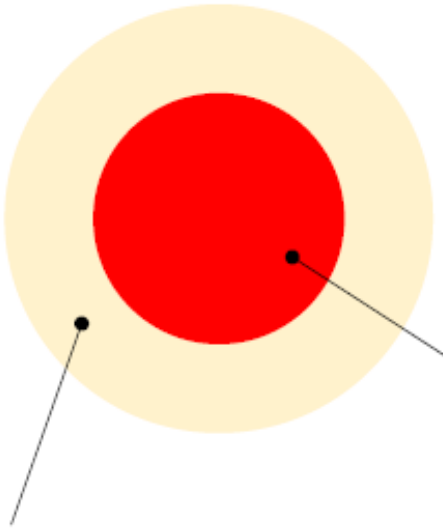
- *Ma et al, BJU Int. 2023*

177Lu-PSMA in Oligorecurrent Prostate Cancer

Before ^{177}Lu-PNT2002



After 2 cycles of ^{177}Lu-PNT2002



Recommended Doses for $PTV_{Baseline}$

No. of Fractions	Dose per Fraction
5 Fractions	6-8 Gy
3 Fractions	9-12 Gy
1 Fraction	16-18 Gy
1 Fraction (spine)	16-20 Gy

Recommended Doses for $PTV_{Adapted}$

No. of Fractions	Dose per Fraction
5 Fractions	5 Gy
3 Fractions	8 Gy
1 Fraction	14 Gy

Recommended Doses for $PTV_{PSMAInterval}$

No. of Fractions	Dose per Fraction
5 Fractions	6-8 Gy
3 Fractions	9-12 Gy
1 Fraction	16-18 Gy
1 Fraction (spine)	16-20 Gy

Ma et al, BJU Int. 2023

177Lu-PSMA in Oligorecurrent Prostate Cancer

Table 3 Study endpoints.

Primary endpoint

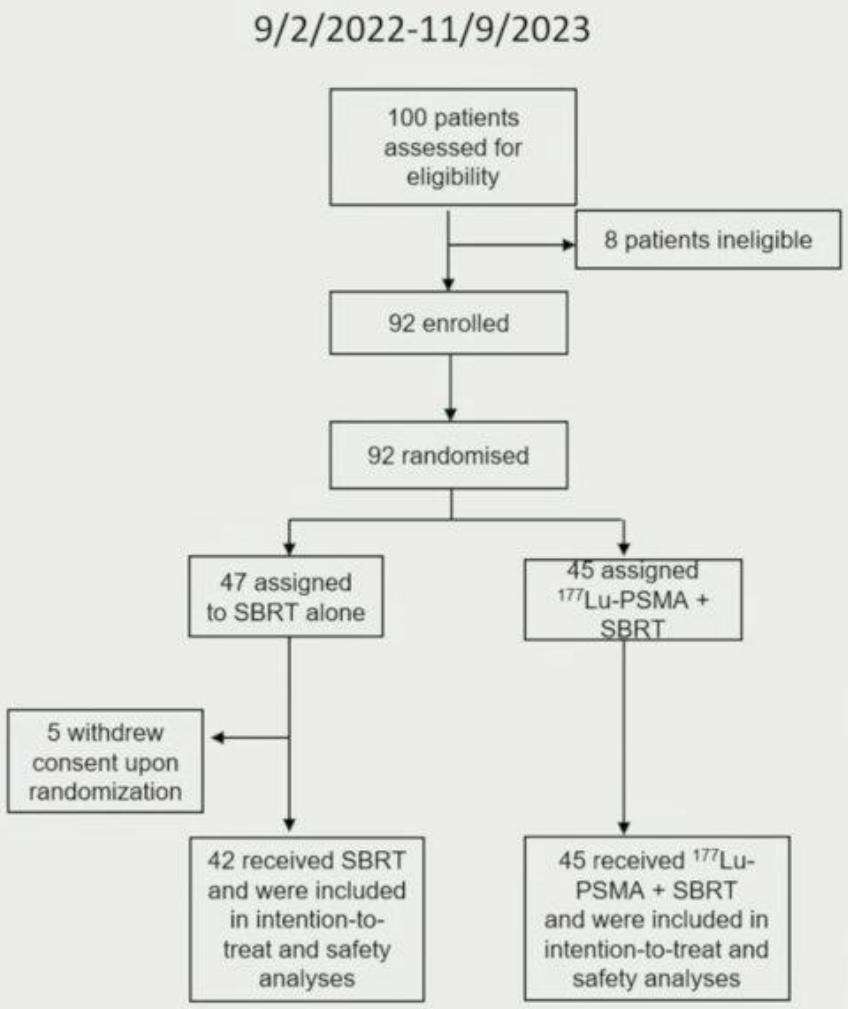
PSMA PET/CT-based progression, defined as either: (i) a new lesion on PSMA PET/CT with or without a serum PSA increase or (ii) local progression on PSMA (>30% increase in lesion SUV or increase of >20% in the sum of the longest dimeter of all target lesions), regardless of new lesions, and a serum PSA increase*

Secondary endpoints

1. Progression as based on a 24-month PSMA PET/CT scan†
2. PSA-based progression*
3. Acute and late physician-scored toxicity (CTCAE version 5.0)
4. Patient-reported quality of life (Brief Pain Inventory scale)
5. ADT-free survival
6. Time to progression: Time from completing SBRT to the time of first documented tumour progression or new lesions by PSMA PET/CT or initiation of ADT
7. Time to local progression and new metastasis: Time from completing SBRT to identification of progression of treated lesions and a new documented tumour metastasis by PSMA PET/CT
8. OS: time from starting treatment until death from any cause
9. Local control and regional control based on by PSMA PET/CT
10. Duration of complete or partial response‡

Ma et al, BJU Int. 2023

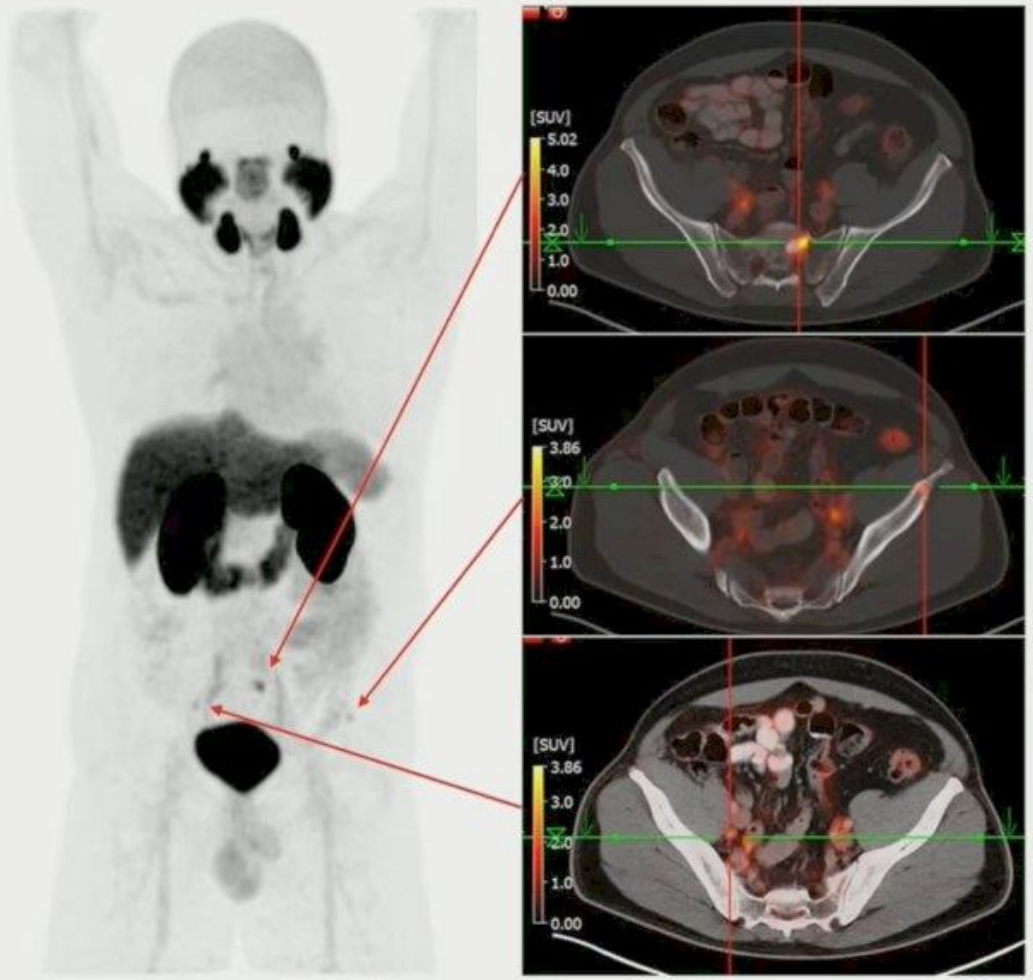
177Lu-PSMA in Oligorecurrent Prostate Cancer



	SBRT only (N=42)	177Lu+SBRT (N=45)
Median Age, years	70.2 (63.5, 77.7)	69.7 (66.2, 76.6)
Race		
White	37 (88.1%)	35 (77.8%)
Black	2 (4.8%)	5 (11.1%)
Other (Hispanic, East Asian)	3 (7.2%)	5 (11.1%)
Type of Prior Definitive Treatment		
Radical Prostatectomy	30 (71.4%)	33 (73.3%)
Radiotherapy	12 (29.3%)	12 (26.7%)
Interval From Definitive Treatment (months)	65.7 (25.3-120.4)	62.1 (37.0-92.8)
PSA at Randomization, ng/mL	1.2 (0.6, 5.5)	1.1 (0.4, 2.0)
Line of Recurrence		
0	1 (2.4%)	1 (2.2%)
1	15 (35.7%)	24 (53.3%)
≥2	26 (61.9%)	20 (44.4%)
Prior Exposure to Androgen Deprivation Therapy		
Yes	16 (38.1%)	25 (55.6%)
Prior Exposure to Androgen Receptor Signaling Inhibitor		
Yes	9 (21.4%)	8 (17.8%)
Prior Exposure to Chemotherapy		
Yes	3 (7.1%)	3 (6.7%)
Prior Exposure to Metastasis-Directed Therapy		
Yes	16 (38.1%)	13 (28.9%)
Concurrent Recurrence in the Prostate or Prostate Fossa		
Yes	9 (21.4%)	5 (11.1%)
Initial ISUP Grade Group		
1	3 (7.1%)	2 (4.4%)
2-3	17 (40.4%)	27 (60.0%)
4-5	22 (52.3%)	16 (35.6%)
Stage by Conventional Imaging		
N0M0	29 (69.0%)	34 (75.6%)
N1M0	2 (4.8%)	1 (2.2%)
N0M1a	2 (4.8%)	1 (2.2%)
N0M1b	9 (21%)	9 (20.0%)

177Lu-PSMA in Oligorecurrent Prostate Cancer

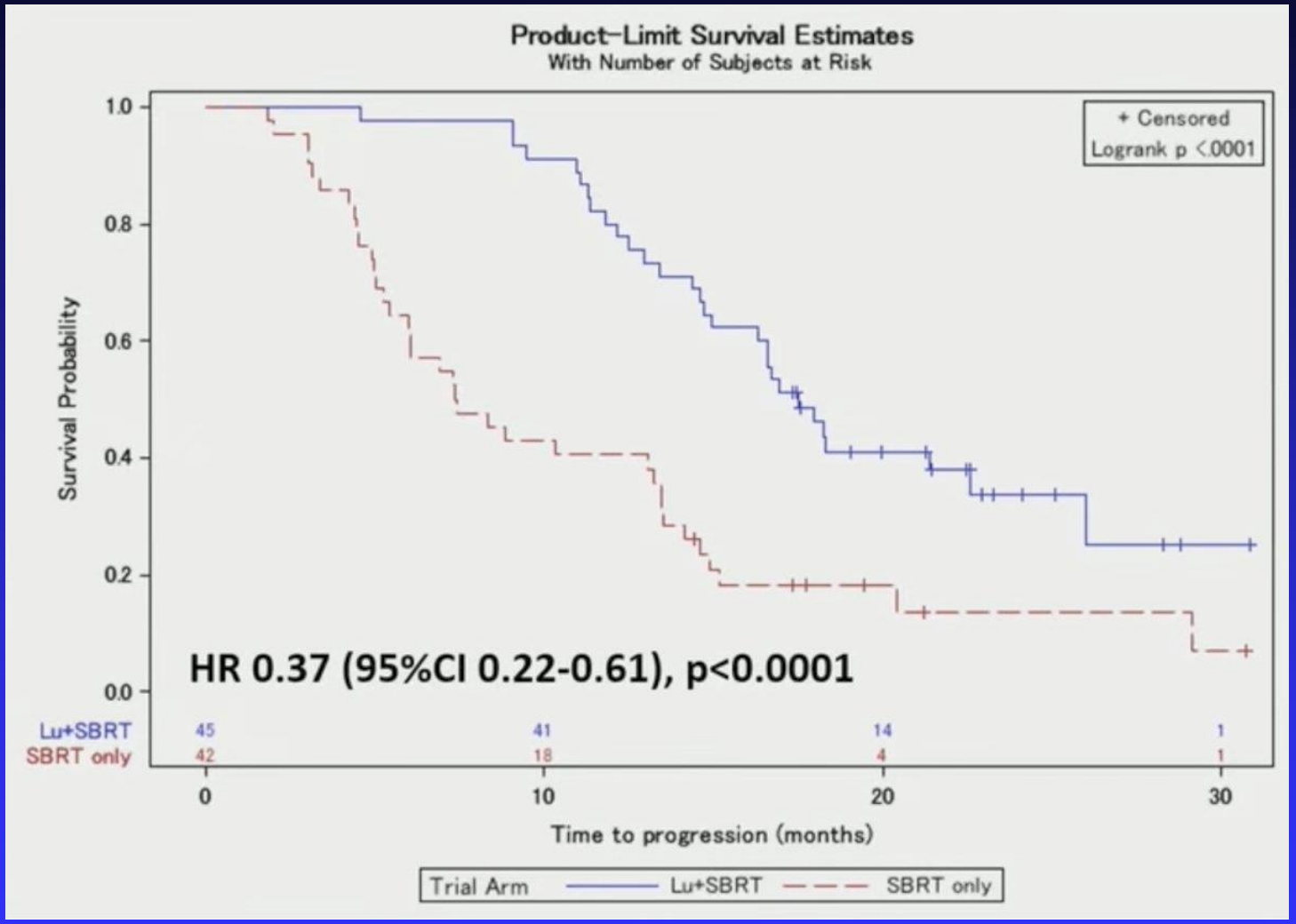
	SBRT only (N=42)	^{177}Lu+SBRT (N=45)
Stage by PSMA		
N1/M1a	16 (38.1%)	17 (37.8%)
M1b	26 (61.9%)	28 (62.2%)
Concurrent Recurrence in the Prostate or Prostate Fossa		
Yes	9 (21.4%)	9 (21.4%)
Lesion Count by PSMA		
1	17 (40.5%)	20 (44.4%)
2-3	18 (42.9%)	18 (40.0%)
4-5	7 (16.7%)	7 (15.6%)
Median Highest SUVmax	6.4 (3.8, 10.9)	4.9 (2.8, 8.0)
PSMA Tracer Used At Screening		
^{68}Ga-PSMA	29 (69%)	25 (55.6%)
^{18}F-piflufolastat	13 (31%)	20 (44.4%)



UroToday. 2025

177Lu-PSMA in Oligorecurrent Prostate Cancer

- Median FU
  - 20 mos
- PFS (Median)
  - SBRT
    - 7.4 mos
  - SBRT/Lu-PSMA
    - 17.6 mo

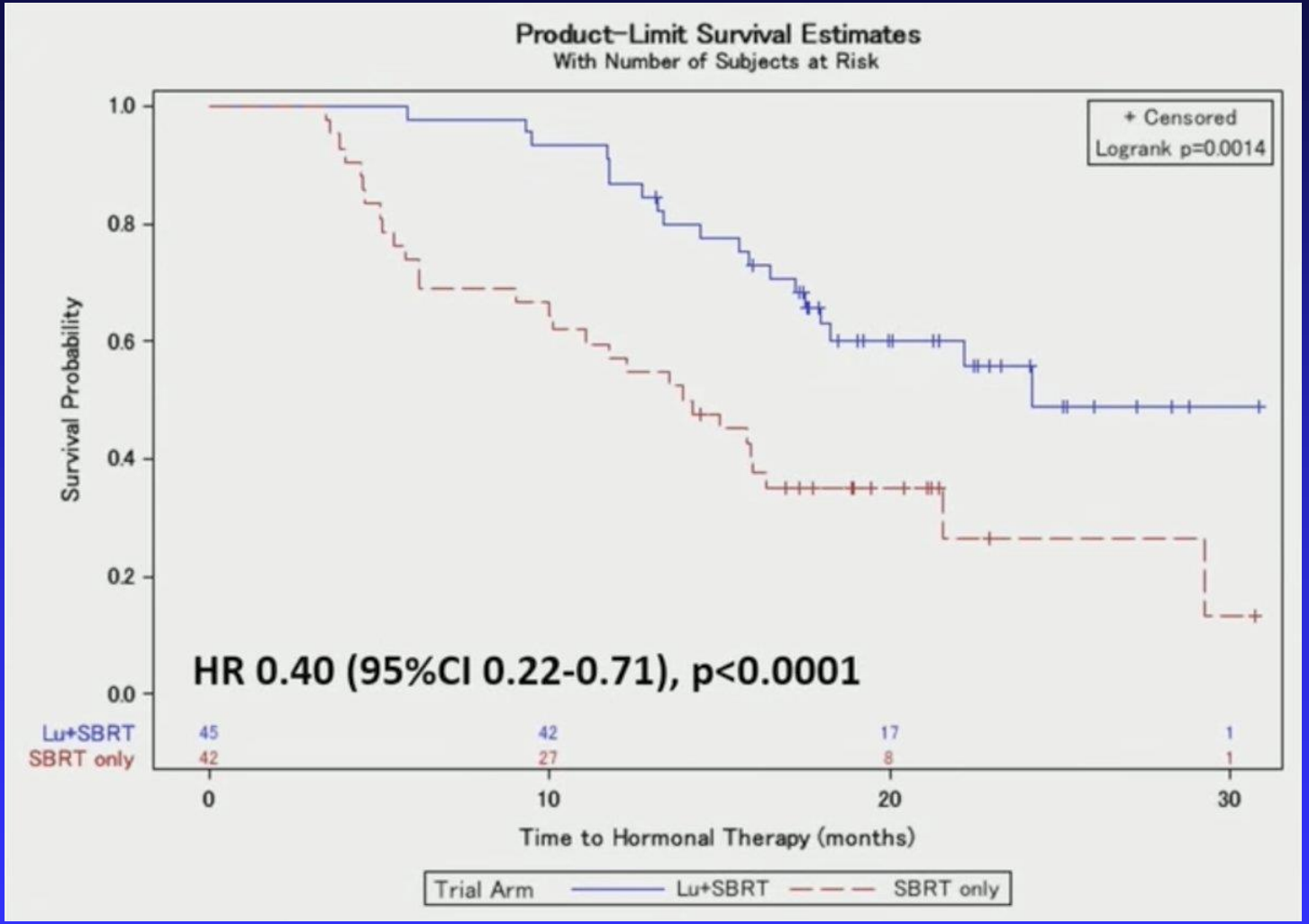


- Vast Majority of Progressions Corresponded to New Lesions!

UroToday. 2025

177Lu-PSMA in Oligorecurrent Prostate Cancer

- HTFS (Median)
  - SBRT
    - 14.1 mos
  - SBRT/Lu-PSMA
    - 24.3 mo



- *UroToday. 2025*

177Lu-PSMA in Oligorecurrent Prostate Cancer

- Lymphopenia (Gr 3)
  - SBRT
    - 5%
  - SBRT/Lu-PSMA
    - 7%

	SBRT only (N=42)	^{177}Lu+SBRT (N=45)	p-value
Anemia			0.3
Grade 1	9 (21.4%)	14 (31.1%)	
Lymphopenia			0.08
Grade 1	6 (14.3%)	14 (31.1%)	
Grade 2	4 (9.5%)	8 (17.8%)	
Grade 3	2 (4.8%)	3 (6.7%)	
Neutropenia			0.4
Grade 1	1 (2.4%)	4 (8.9%)	
Grade 2	0 (0.0%)	1 (2.2%)	
Thrombocytopenia			0.7
Grade 1	4 (9.5%)	6 (13.3%)	
Transaminitis			
Grade 1	1 (2.4%)	0 (0.0%)	0.5
Renal Failure			1.0
Grade 1	0 (0.0%)	0 (0.0%)	
Grade 2	1 (2.4%)	0 (0.0%)	
Fatigue			0.4
Grade 1	26 (76.5%)	27 (64.3%)	
Grade 2	0 (0.0%)	2 (4.8%)	
Dry Mouth			1.0
Grade 1	2 (5.6%)	3 (6.8%)	
Dry Eyes			0.5
Grade 1	0 (0.0%)	2 (4.4%)	
Nausea			
Grade 1	5 (14.3%)	4 (8.9%)	0.4
Grade 2	1 (2.9%)	0 (0%)	0.4

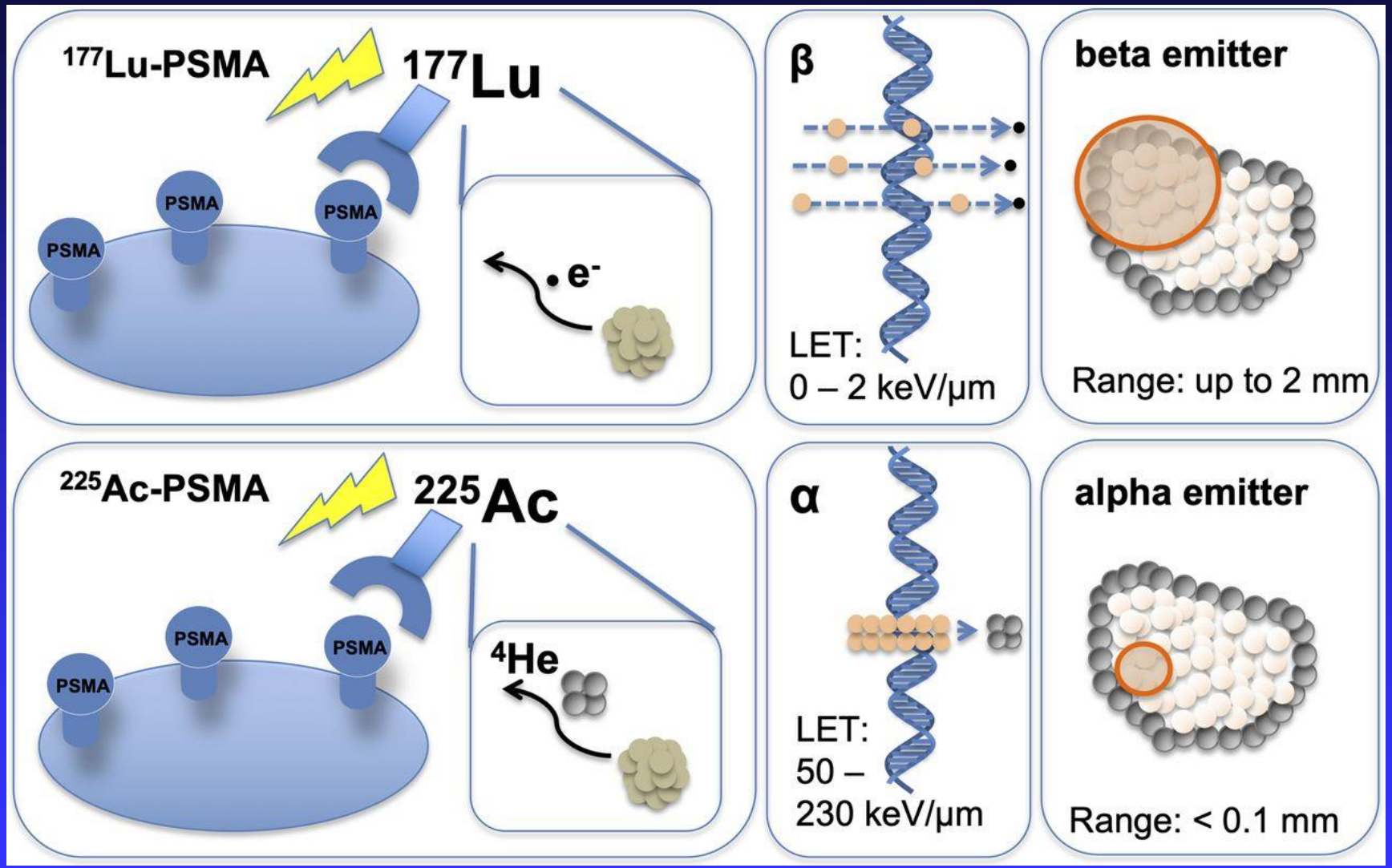
UroToday. 2025

The Future

- Adding two cycles of ^{177}Lu-PSMA to SBRT significantly improved PFS presumably by treating occult metastatic disease, without attendant increase in toxicity

- 64% of patients on the ^{177}Lu-PSMA + SBRT arm still progressed, suggesting that more cycles might have improved benefit

Alpha Therapy



- *Feuerecker et al, J Nucl Med 2023*

Alpha Therapy

- Potential Benefits and Risks
  - Benefit
    - Short Path Length
    - Treat Micro-metastases (- PSMA Scan)
  - Risks
    - Increased Xerostomia/ Marrow Suppression
    - As We Treat Younger/Healthier Patients, Concerns About Late Toxicity Increase

- ***Hennes et al. Curr Opin Urol 2025***

The Future!

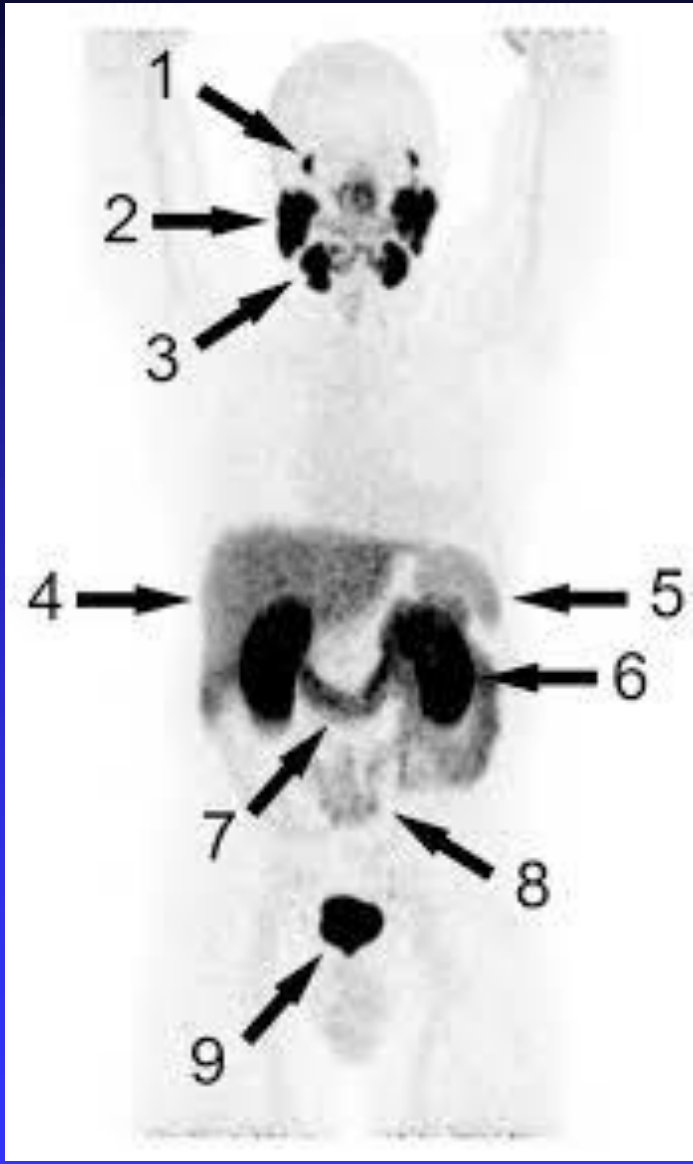
CURRENT OPINION

VISION, TheraP, LuTectomy and beyond – is there a role for lutetium therapy in biochemical recurrence?

David Hennes[a,b,c], Jasmin Weindler[b,d], Christa Babst[a], Marlon L. Perera[a,e,f], Declan G. Murphy[a,f] and Renu S. Eapen[a,e,f]

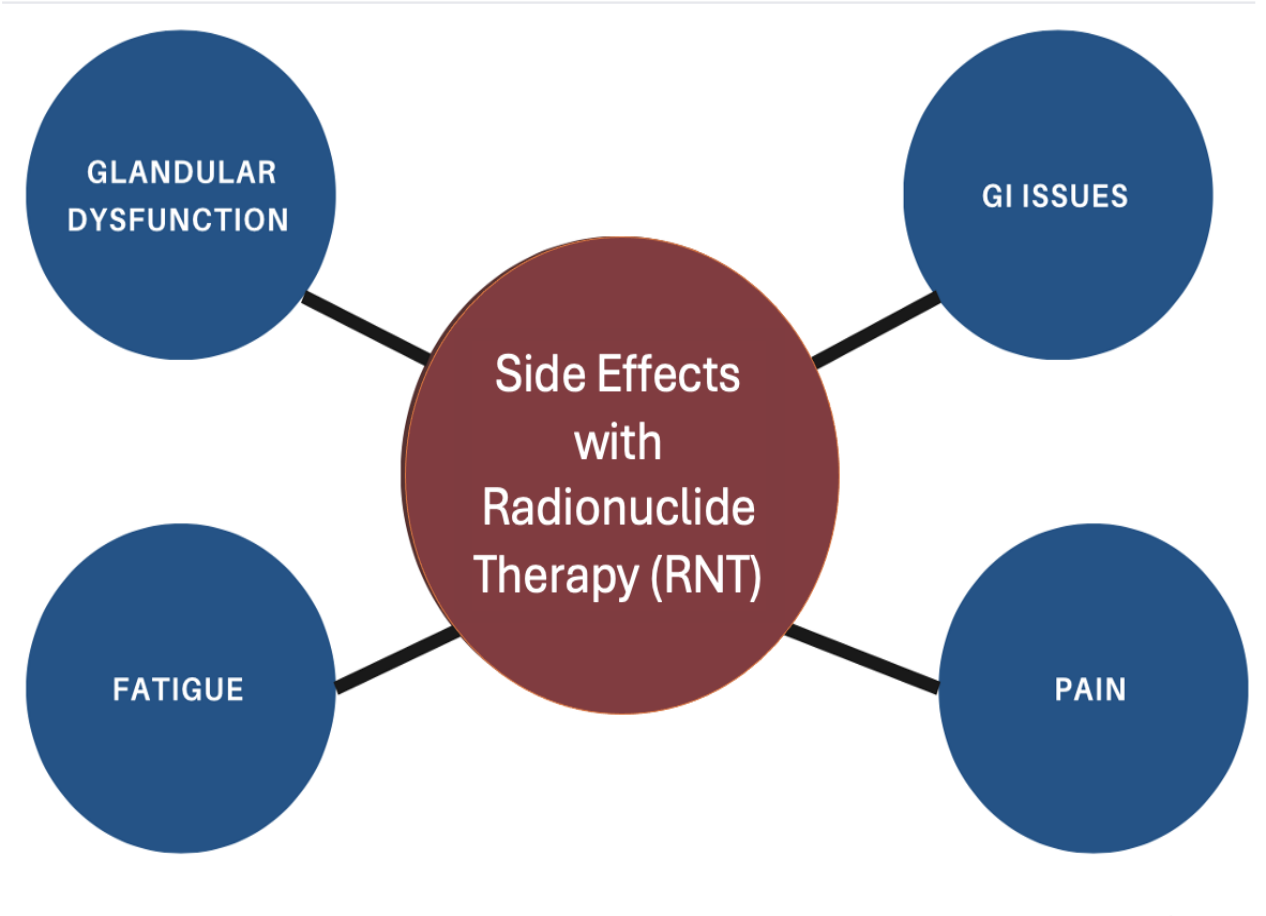
- ***Hennes et al, Curr Opin Urol. 2025***

Physiologic PSMA Uptake



- Lisney et al, Cancers 2022

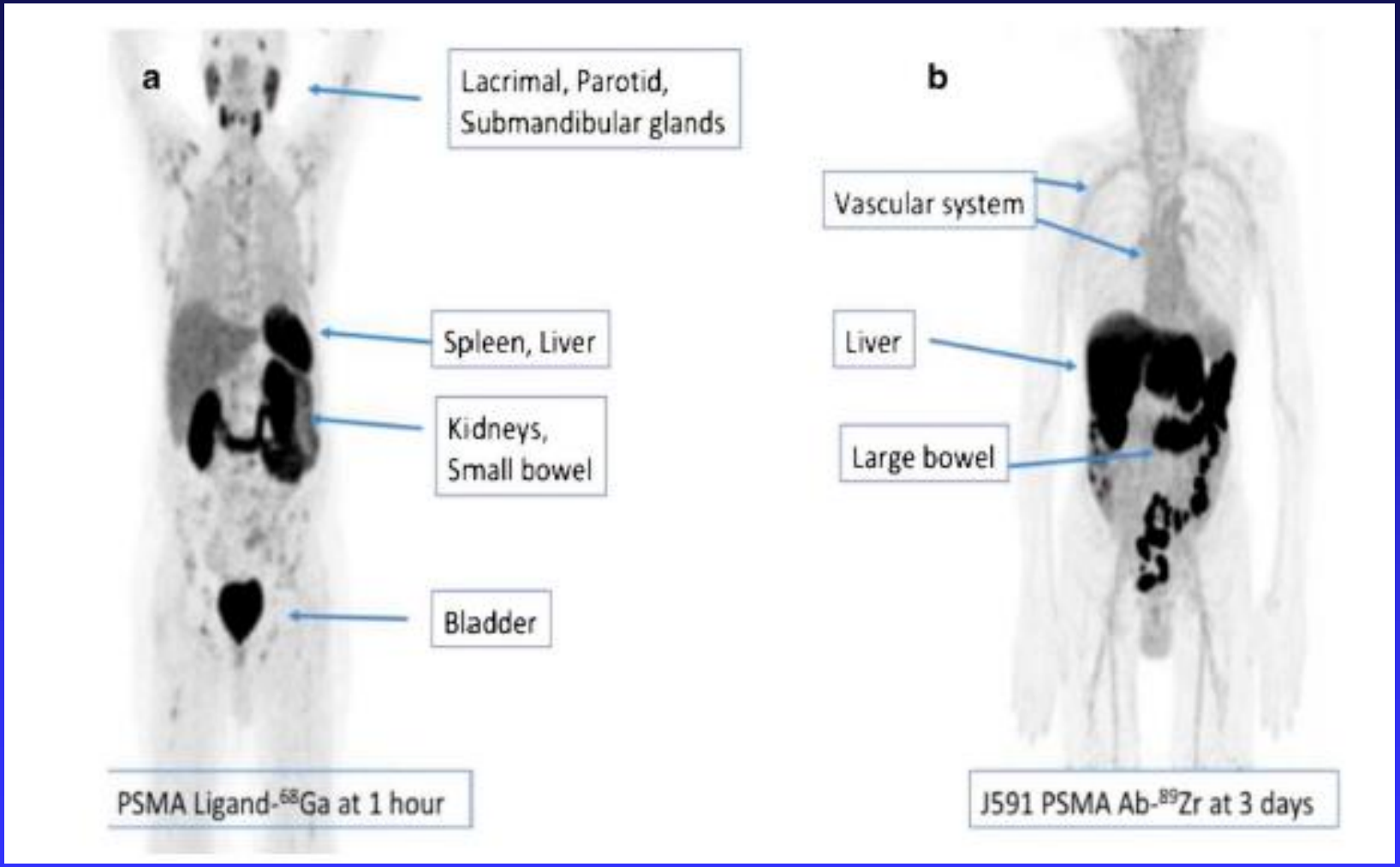
- Quality of Life Variables Assessed by FACT RNT Questionnaire



- Kallam et al, Cureus 2025

Radiolabled Monoclonal Antibodies Targeting PSMA

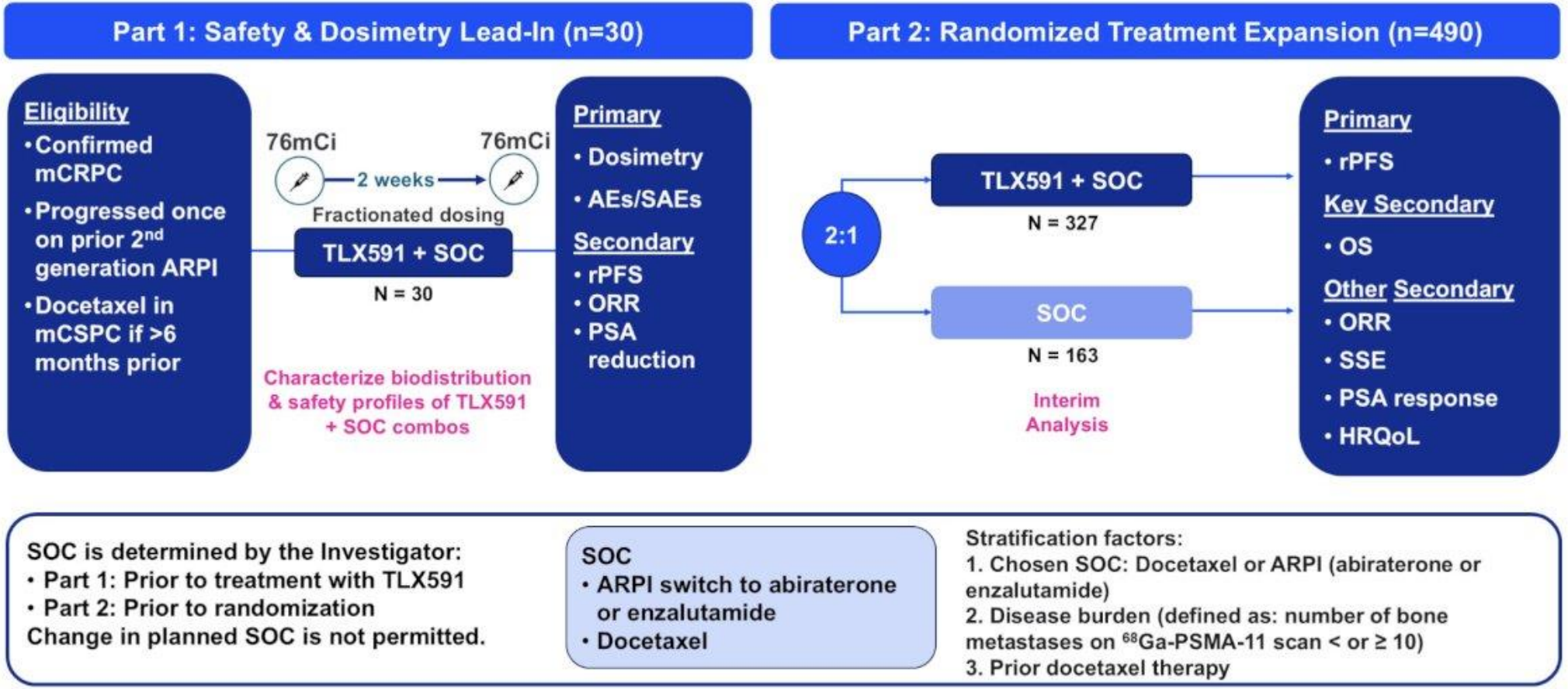
- Variable Physiologic Uptake with Potential Differences in Clinical Efficacy and Toxicity



- ***Abusalem et al. Cancers 2023***

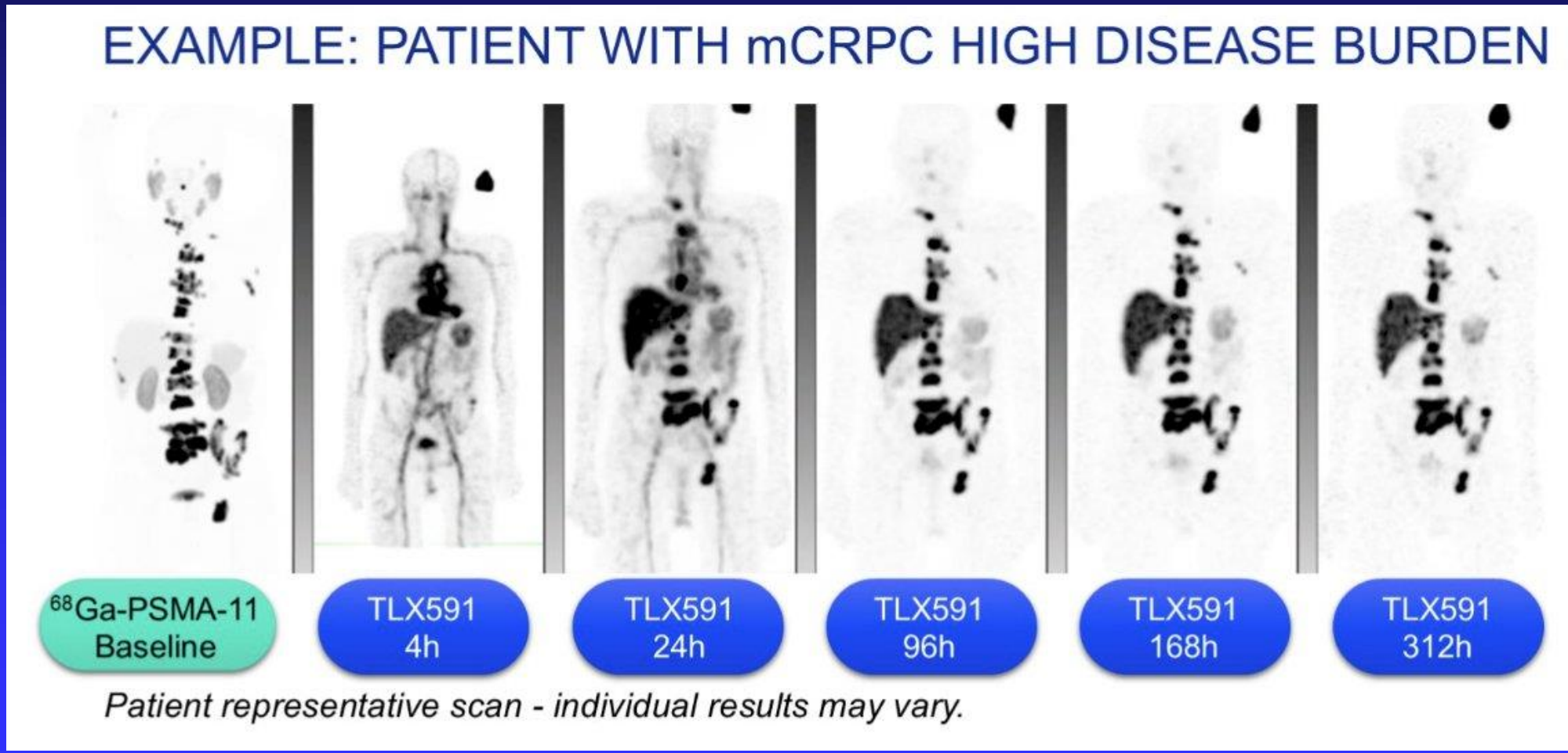
ProstACT GLOBAL: A Phase 3 Study of 177Lu-Rosopatamab (TLX591)

- Presented at ASCO-GU 2025



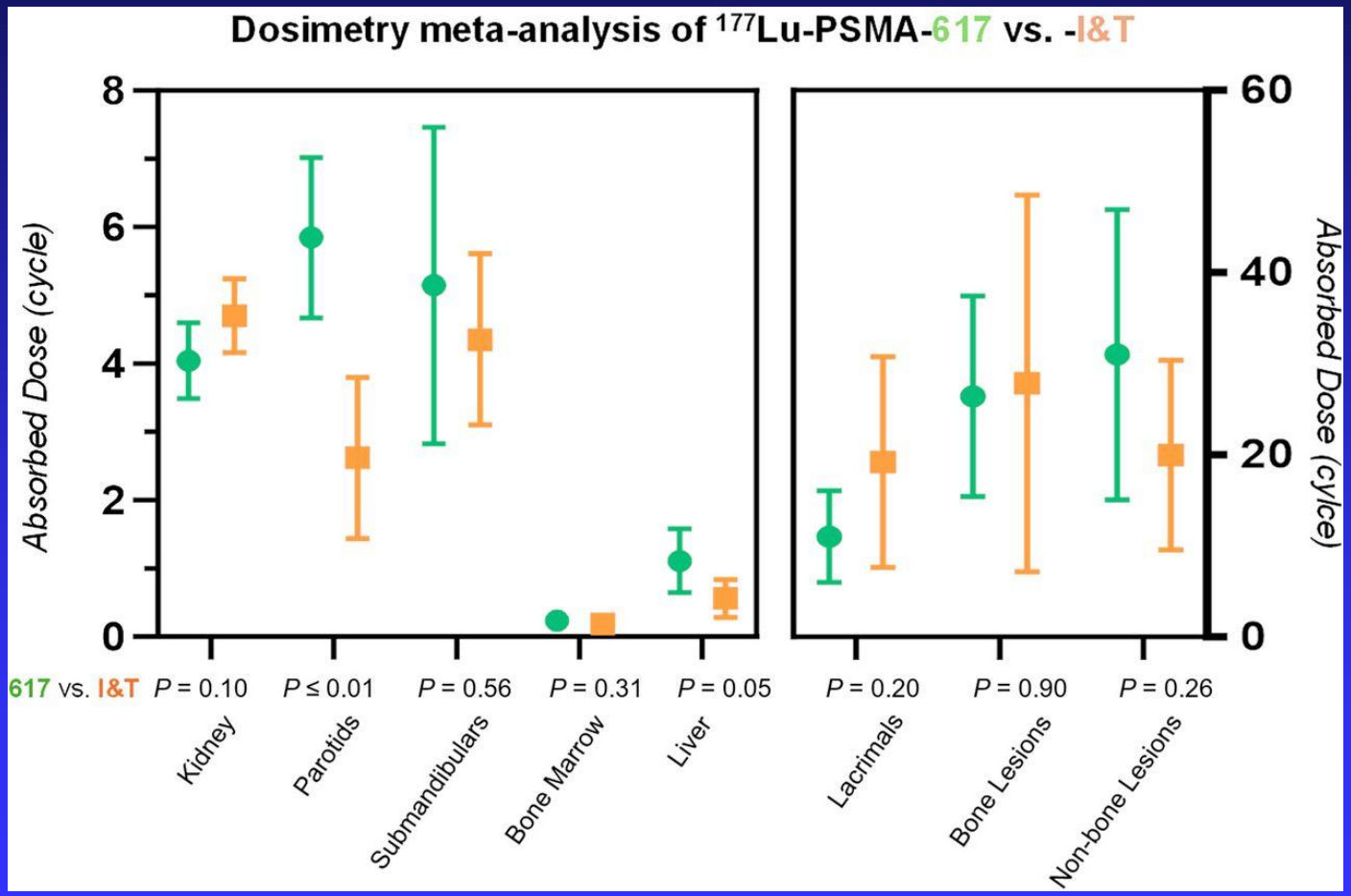
ProstACT GLOBAL: A Phase 3 Study of 177Lu-Rosopatamab (TLX591)

- Presented at ASCO-GU 2025



Comparative Dosimetry

- Will Become More Important as Treatment Moves to More Favorable Disease!



- ***Ells et al. J. Nuc. Med. 2024***

Radiolabled Monoclonal Antibodies Targeting PSMA

- Potential Benefits
  - Significantly Different Targeting and Pharmacology from PSMA Receptor Binding Small Molecules
    - Primary Liver Excretion
    - High Internalization Rate Requiring Lower Radiation Doses
    - Longer Retention Requiring Fewer Injections and Less Radiation Protection Requirements
    - High Tumor Selectivity

- ***Abusalem et al. Cancers 2023***

Thank You for Your Attention!