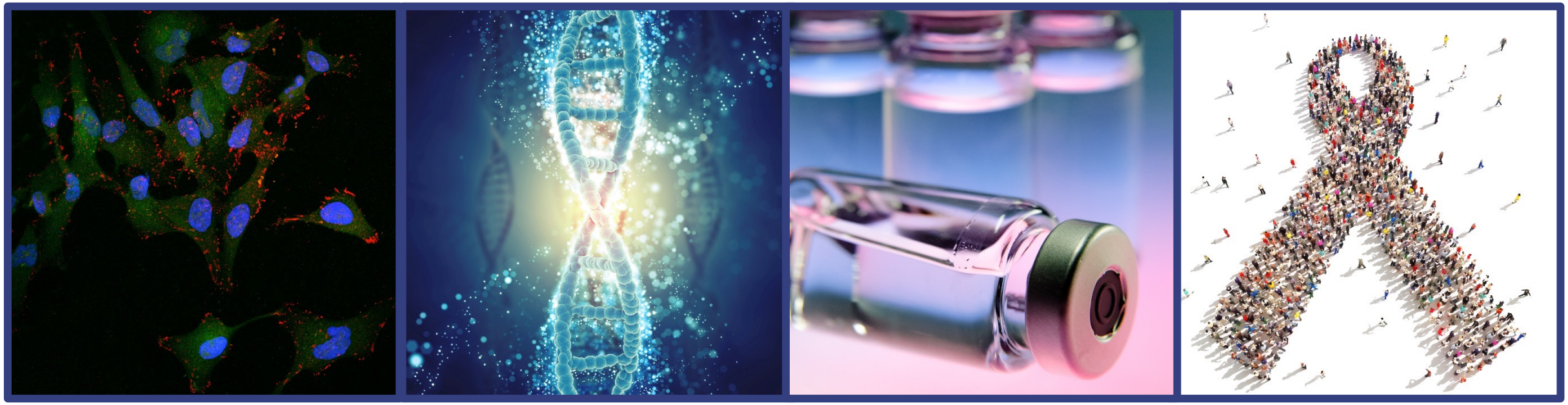

PSMA-Targeted Radioligand Therapy in the Management of Prostate Cancer: A Genitourinary Oncologist's Perspective

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DDHO, July 26 2024

EMORY WINSHIP CANCER INSTITUTE
National Cancer Institute-Designated Comprehensive Cancer Center

Conflict of Interest

- Advisory board: Exelixis, Bayer, BMS, Eisai, Pfizer, AstraZeneca, Janssen, Calithera Biosciences, Genomic Health, Nektar, EMD Serono, SeaGen, and Sanofi

- Research: Xencor, Bayer, Bristol-Myers Squibb, Genentech/Roche, SeaGen, Incyte, Nektar, AstraZeneca, Tricon Pharmaceuticals, Genome & Company, AAA, Peloton Therapeutics, and Pfizer

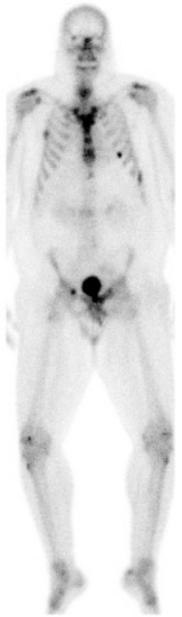
Outline

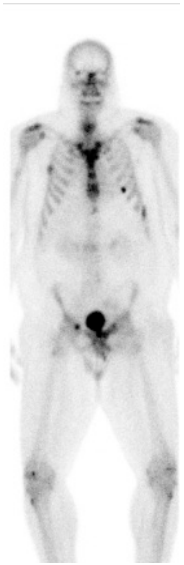
- General overview and treatment updated in mHSPC
- Lu-PSMA
  - VISION
  - TheraP
  - PSMAFore
  - ENZA-P
- Future direction

Therapeutic Options For Advanced Prostate Cancer 2024

CASTRATION SENSITIVE

CASTRATION RESISTANT





ANDROGEN DEPRIVATION

Orchiectomy / GnRH Agonist

GnRH Antagonist

Antiandrogens

Docetaxel

Enzalutamide

Apalutamide

Abiraterone+/- Docetaxel

Daralutamide+ Docetaxel

IMMUNOTHERAPY

Sipuleucel-T

SECONDARY HORMONAL TREATMENTS

Bicalutamide, flutamide, nilutamide

Ketoconazole

DES

Abiraterone

Enzalutamide

M0 CRPC AGENTS

Apalutamide

Enzalutamide

Daralutamide

Radiopharmaceuticals

Radium-223

Lu-177 PSMA

CHEMOTHERAPY

Docetaxel

Cabazitaxel

CRPC with DDR

Olaparib

Rucaparib

PARP combinations

DES = diethylstilbestrol

How do we get here in mCSPC?

- CHAARTED & STAMPEDE (2015-2016):
  - 6 cycles of docetaxel +ADT
  - Improved OS over ADT alone
- LATIDUDE & STAMPEDE (2017):
  - Abiraterone+ADT
  - Improved OS over ADT alone
- ENZAMET &ARCHES (2019):
  - Enzalutamide+ADT
  - Improved OS over ADT alone
- TITAN (2019):
  - Apalutamide+ADT
  - Improved OS over ADT alone

How do we get here in mCSPC?

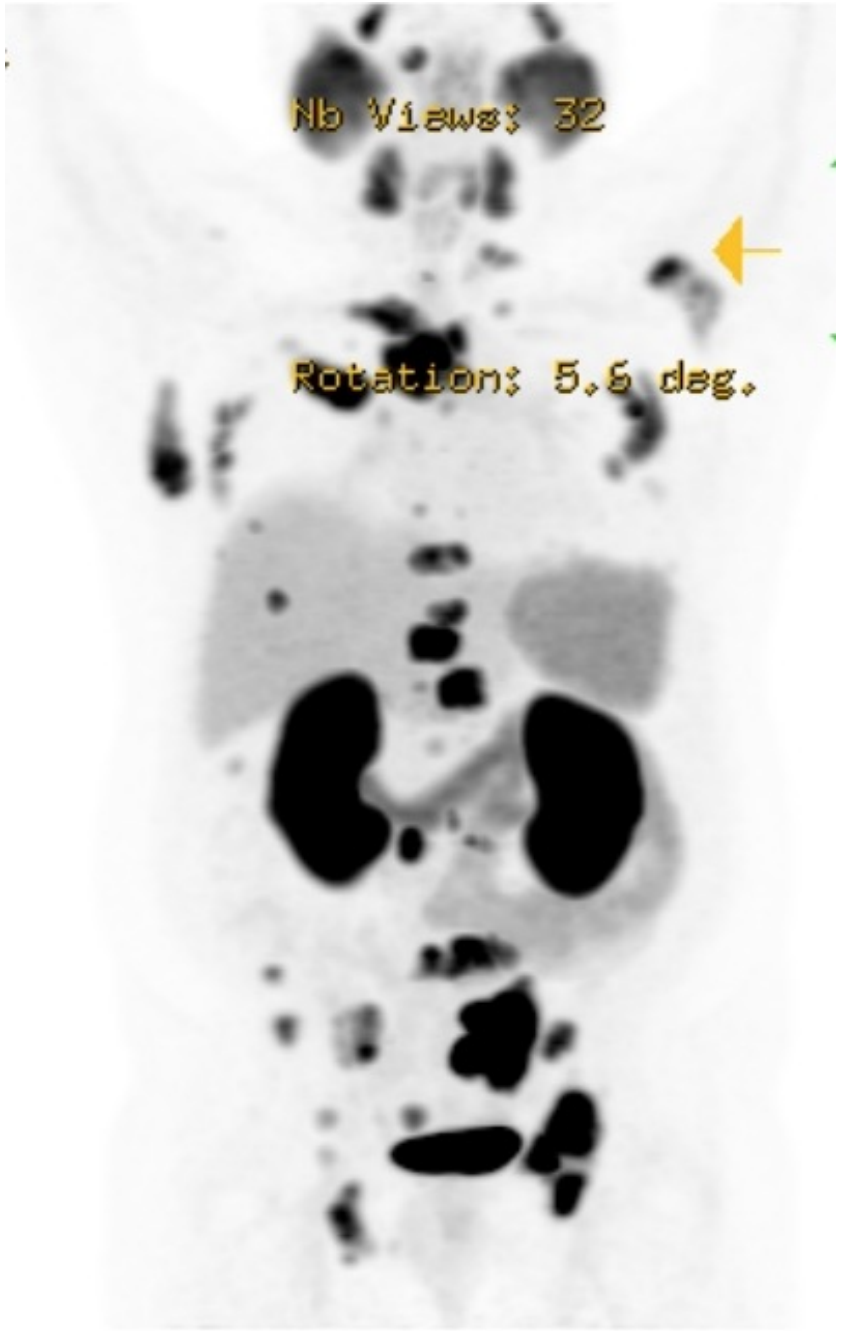
- Triplet treatment (2022)
  - PEACE 1: ADT+Abiraterone+Taxotere
  - ARASENS: ADT+Darolutamide+Taxotere

Mr. JA

- 53 y/o male patient
- Good health with no major issues
- Diagnosed with prostate cancer in 2018, Gleason 4 + 5 = 9
- PSA >1300
- Staging work-up showed >20 bone metastases
- Initially treated with ADT plus abiraterone in castration-sensitive setting

- Became castration resistant in 2021, and found to be BRCA +
- Received olaparib with good response, and then docetaxel
- Most recently have disease progression, with PSA of 495

PSMA PET:

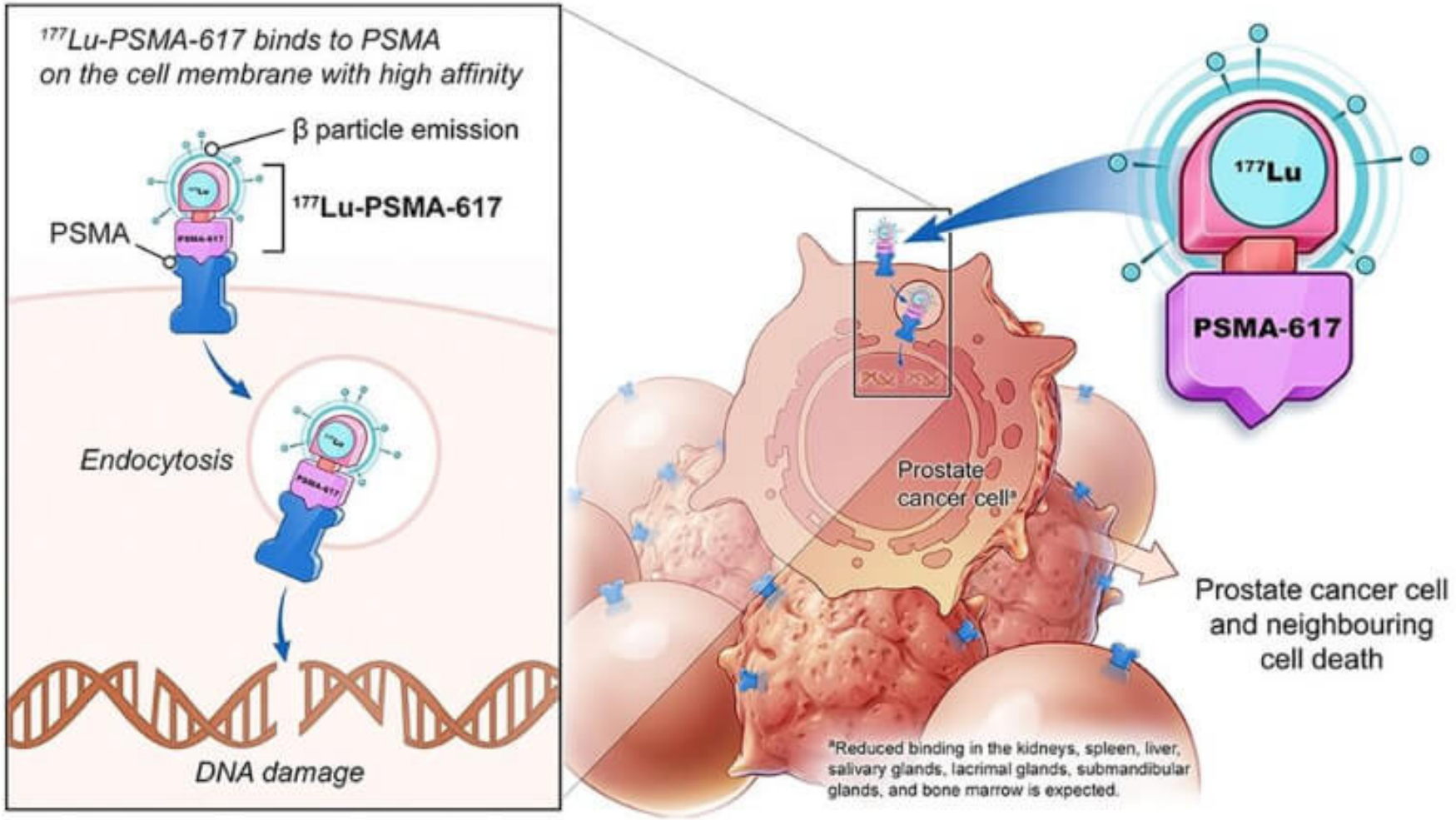


What do you offer him?

SYSTEMIC THERAPY FOR M1 CRPC: ADENOCARCINOMA[nnn,ooo,ppp]

No prior docetaxel/no prior novel hormone therapy[qqq]	Progression on prior novel hormone therapy/no prior docetaxel[qqq]
• Preferred regimens ▸ Abiraterone[y,rrr] (category 1[sss]) ▸ Docetaxel[lll] (category 1) ▸ Enzalutamide[y] (category 1) • Useful in certain circumstances ▸ Niraparib/abiraterone[y,lll,ttt] for *BRCA* mutation (category 1) ▸ Olaparib/abiraterone[y,lll,rrr,uuu] for *BRCA* mutation (category 1) ▸ Pembrolizumab for MSI-high (MSI-H)/dMMR[lll] (category 2B) ▸ Radium-223[u,vvv] for symptomatic bone metastases (category 1) ▸ Sipuleucel-T[lll,www] (category 1) ▸ Talazoparib/enzalutamide for HRR mutation[y,lll,xxx] (category 1) • Other recommended regimens ▸ Other secondary hormone therapy[y]	• Preferred regimens ▸ Docetaxel (category 1)[lll] ▸ Olaparib for *BRCA* mutation[yyy] (category 1) ▸ Rucaparib for *BRCA* mutation[zzz] (category 1) • Useful in certain circumstances ▸ Cabazitaxel/carboplatin[lll,mmm] ▸ Niraparib/abiraterone[y,lll,ttt] for *BRCA* mutation (category 2B) ▸ Olaparib for HRR mutation other than *BRCA1/2*[yyy] ▸ Pembrolizumab for MSI-H/dMMR[lll] (category 2B) ▸ Radium-223[u,vvv] for symptomatic bone metastases (category 1) ▸ Sipuleucel-T[lll,www] ▸ Talazoparib/enzalutamide for HRR mutation[y,lll,xxx] (category 2B) • Other recommended regimens ▸ Other secondary hormone therapy[aaaa]
Progression on prior docetaxel/no prior novel hormone therapy[qqq]	**Progression on prior docetaxel and a novel hormone therapy[qqq]**
• Preferred regimens ▸ Abiraterone[y,rrr] (category 1) ▸ Cabazitaxel[lll] ▸ Enzalutamide[y] (category 1) • Useful in certain circumstances ▸ Cabazitaxel/carboplatin[lll,mmm] ▸ Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[lll] ▸ Niraparib/abiraterone[y,lll,ttt] for *BRCA* mutation ▸ Olaparib/abiraterone[y,lll,rrr,uuu] for *BRCA* mutation ▸ Pembrolizumab for MSI-H/dMMR[lll] (category 2B) ▸ Radium-223[u,vvv] for symptomatic bone metastases (category 1) ▸ Sipuleucel-T[lll,www] ▸ Talazoparib/enzalutamide for HRR mutation[y,lll,xxx] • Other recommended regimens ▸ Other secondary hormone therapy[y]	• Preferred regimens ▸ Cabazitaxel[lll] (category 1) ▸ Docetaxel rechallenge[lll] • Useful in certain circumstances ▸ ~~Cabazitaxel/carboplatin~~[lll,mmm] ▸ Lutetium Lu 177 vipivotide tetraxetan (Lu-177–PSMA-617) for PSMA-positive metastases[bbbb] (category 1) ▸ Mitoxantrone for palliation in symptomatic patients who cannot tolerate other therapies[lll] ▸ Olaparib for HRR mutation[yyy] (category 1) ▸ Pembrolizumab for MSI-H, dMMR, or TMB ≥10 mut/Mb[lll] ▸ Radium-223[u,vvv] for symptomatic bone metastases (category 1) ▸ Rucaparib for *BRCA* mutation[zzz] • Other recommended regimens ▸ Other secondary hormone therapy[aaaa]

Radiopharmaceuticals: Lu-177 PSMA



VISION: Phase 3, Open-Label Study of Protocol-Permitted SOC ± ^{177}Lu-PSMA-617 for PSMA-Positive mCRPC

Eligible patients

- Previous treatment with both
  - ≥ 1 androgen receptor pathway inhibitor
  - 1 or 2 taxane regimens
- Protocol-permitted standard of care (SOC) planned before randomization
  - Excluding chemotherapy immunotherapy, radium-223, investigational drugs
- ECOG performance status 0–2
- Life expectancy > 6 months
- PSMA-positive mCRPC on PET/CT with ^{68}Ga-PSMA-11

2:1

Protocol-permitted SOC + ^{177}Lu-PSMA-617
7.4 GBq (200 mCi) every 6 weeks
4 cycles, increasable to 6

Protocol-permitted SOC alone

Treatment → Follow-up → Final analysis

- Randomization stratified by
  - ECOG status (0–1 or 2)
  - LDH (high or low)
  - Liver metastases (yes or no)
  - Androgen receptor pathway inhibitors in SOC (yes or no)
- CT/MRI/bone scans
  - Every 8 weeks (treatment)
  - Every 12 weeks (follow-up)
  - Blinded independent central review

SOC was investigator determined but excluded cytotoxic chemotherapy and radium-223

Protocol Definitions:

- **PSMA(+) lesions:** ^{68}Ga-PSMA-11 uptake > liver parenchyma in ≥ 1 metastatic lesions of any size in any organ system
- **PSMA(-) lesions:** PSMA uptake ≤ liver parenchyma in any LN w/ short axis of ≥ 2.5 cm, in any metastatic solid-organ lesions w/ short axis ≥ 1.0 cm, or in any metastatic bone lesion with a soft-tissue component of ≥ 1.0 cm in short axis. **Pts w/ any PSMA(-) metastatic lesion meeting these criteria were ineligible**.

Alternate primary endpoints

'Alternate' means the study would be positive if either or both primary endpoints were significant

Radiographic progression-free survival (rPFS) per PCWG3	• 84% power for HR of 0.67 at 364 events in 557 patients • Allocated one-sided α = 0.004 • Stratified log-rank test (plus Cox for HR)
Overall survival (OS)	• 90% power for HR of 0.7306 at 508 deaths in 814 patients • Allocated one-sided α = 0.021 (0.025 if rPFS positive) • Stratified log-rank test (plus Cox for HR)

Key secondary endpoints

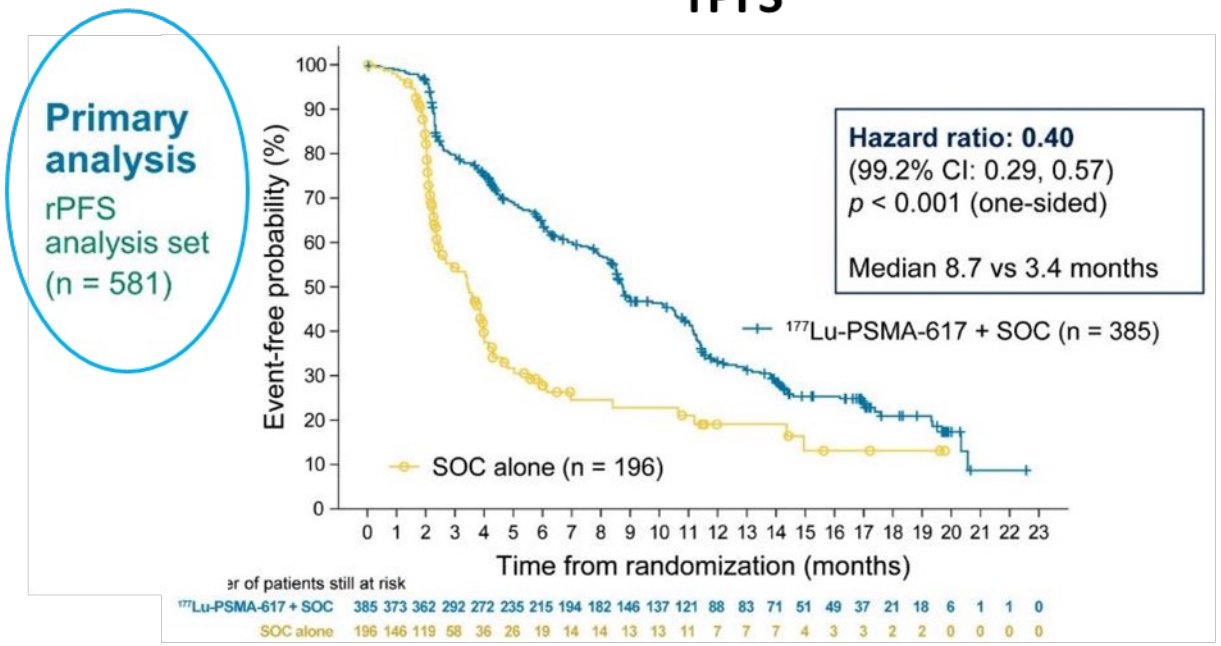
- Time to first symptomatic skeletal event (SSE)
- RECIST v1.1 overall response rate
- RECIST v1.1 disease control rate

NCT03511664

Sartor O, et al. *N Engl J Med*. Jun 23, 2021.
Morris M, et al. ASCO 2021. Abstract LBA4.

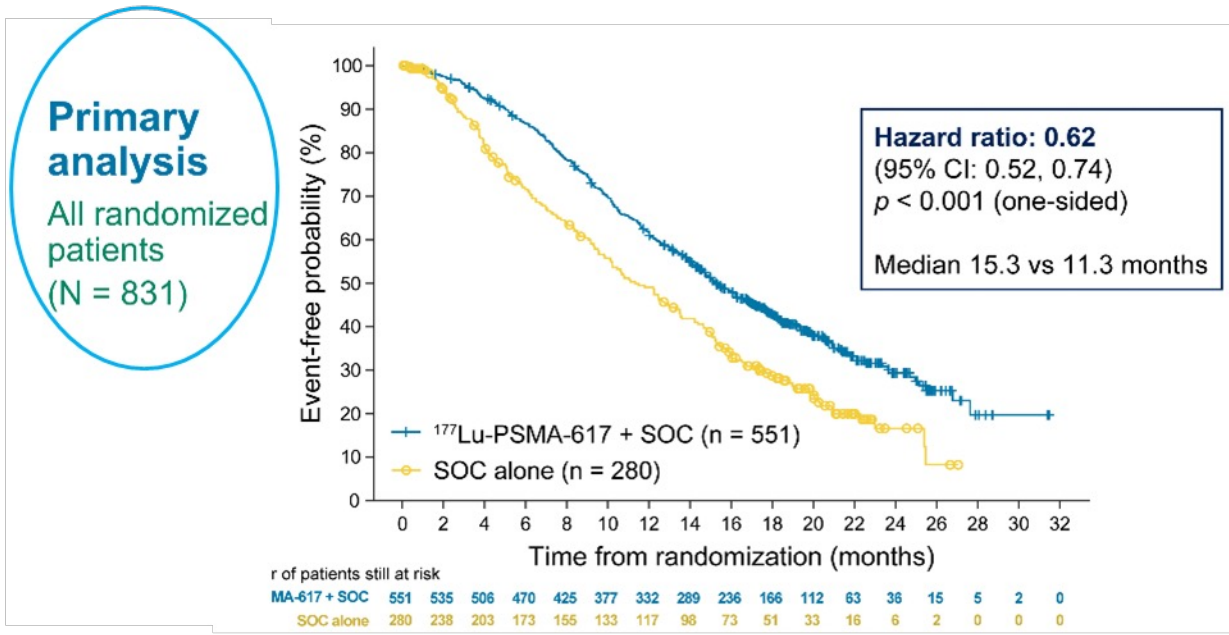
VISION: Co-Primary Endpoints

rPFS



- rPFS benefit observed across most prespecified subgroups

Overall Survival



- OS benefit was observed across most prespecified subgroups

All key secondary end points significantly favored 177Lu-PSMA-617

Median follow-up was 20.9 months

Sartor O, et al. *N Engl J Med*. Jun 23, 2021.

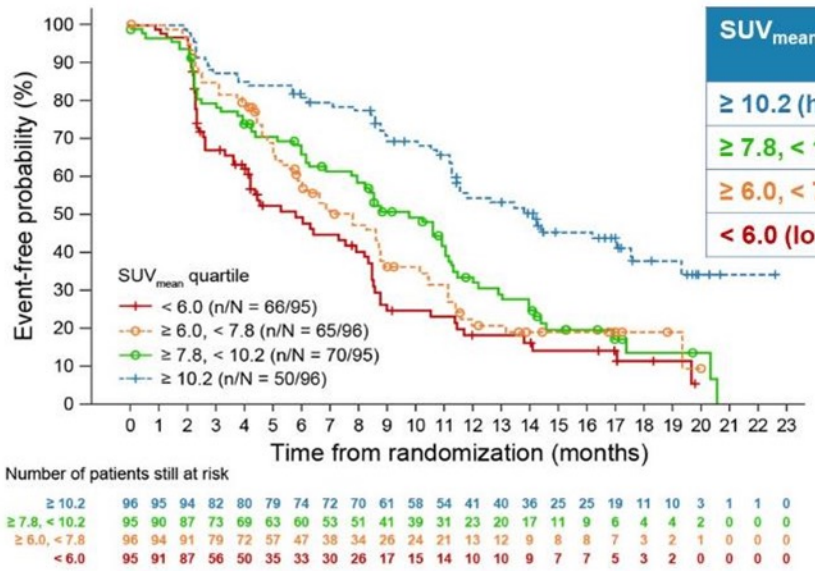
VISION: Efficacy by Whole-Body SUV_{mean}

Higher SUV_{mean} strongly associated with improved outcomes with 177Lu-PSMA-617

15

rPFS by whole-body SUV_{mean} quartiles (PFS-FAS)

- **Higher whole-body SUV_{mean} was associated with prolonged rPFS**



SUV_{mean} quartile	Median rPFS (months)
≥ 10.2 (highest)	14.1
≥ 7.8, < 10.2	9.8
≥ 6.0, < 7.8	7.8
< 6.0 (lowest)	5.8

SUV_{mean}	rPFS HR [95% CI], *p* value
Univariate analysis	**0.88** [0.84, 0.91], < 0.001
Multivariate analysis	**0.86** [0.82, 0.90], < 0.001

CI, confidence interval; HR, hazard ratio; PFS-FAS, progression-free survival-full analysis set; rPFS, radiographic progression-free survival; SUV, standardized uptake value

Median OS

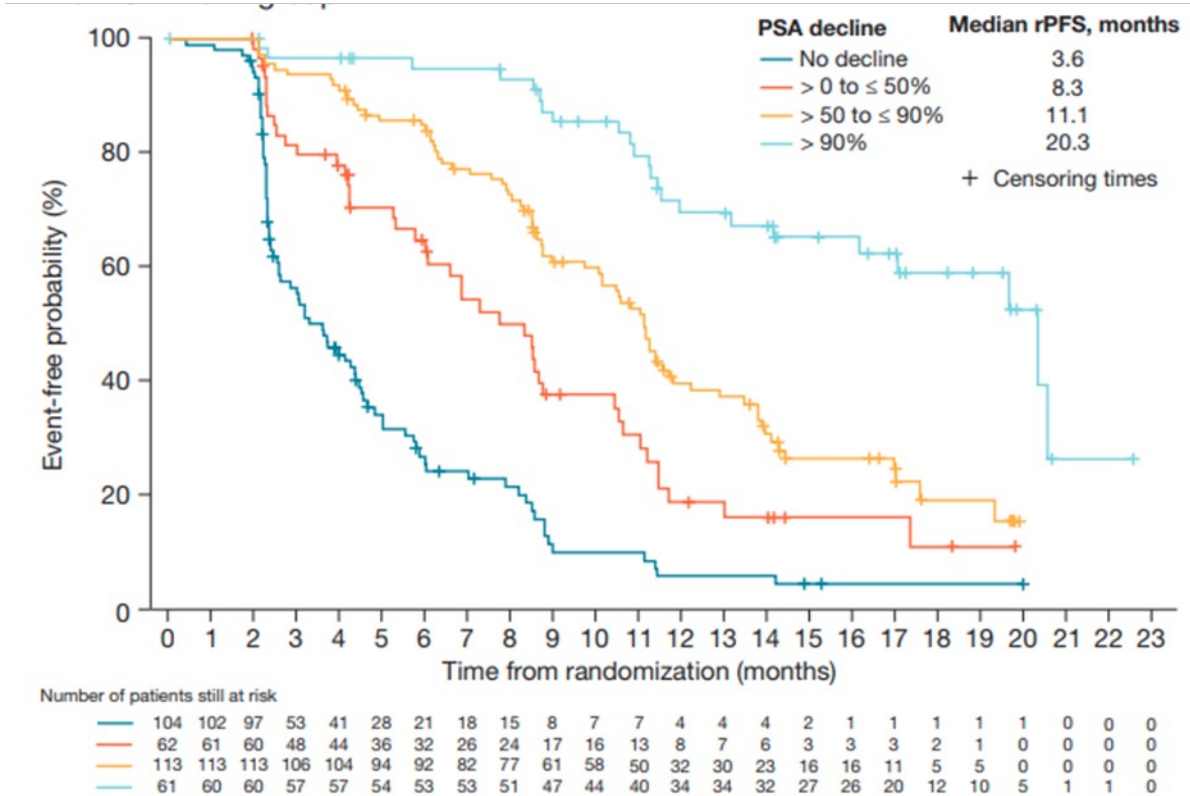
- Highest quartile (SUV_{mean} ≥ 9.9): 21.4 mo
- Lowest quartile (SUV_{mean} < 5.7): 14.5 mo

Absence of PSMA+ lesions in bone, liver, and lymph node, and lower PSMA+ tumor load, were indicators of good prognosis

Armstrong AJ et al. ASCO 2022. Abstract 5002.

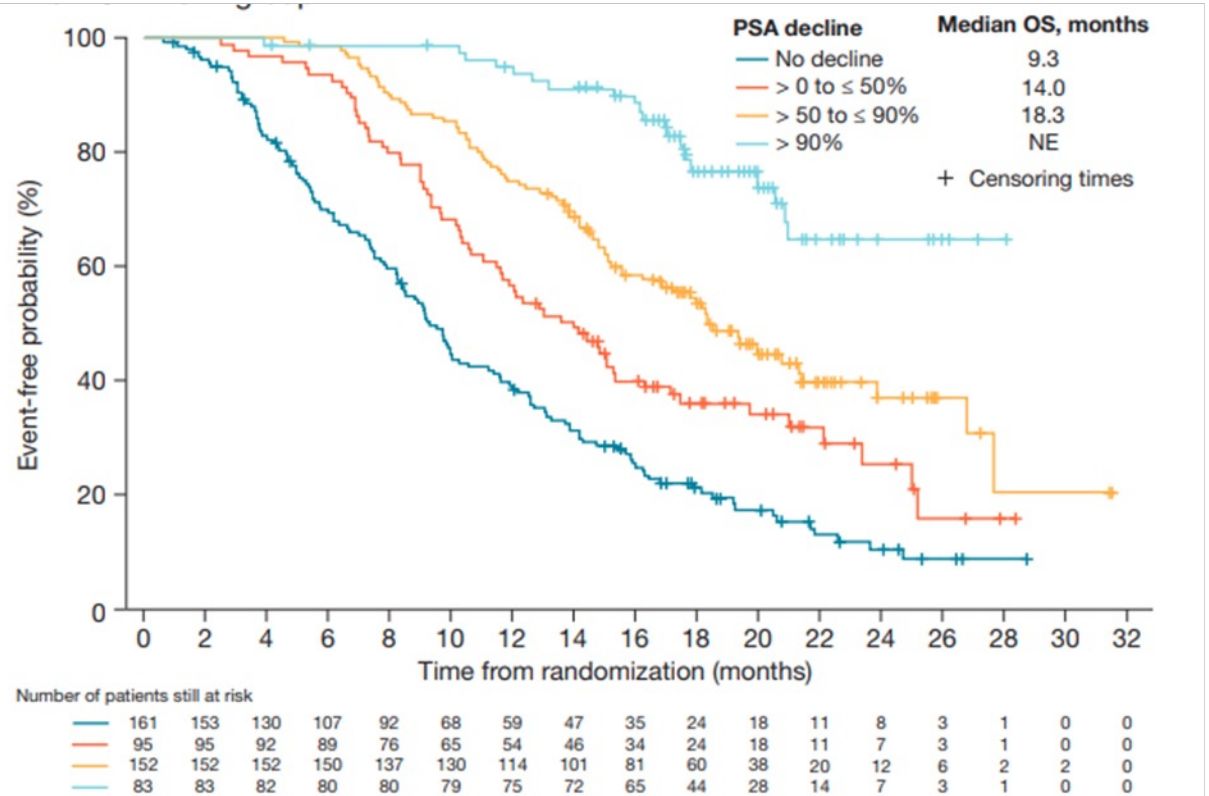
VISION Trial Post Hoc Analysis: Association Between PSA Decline and Clinical Outcomes

rPFS rate by PSA decline up to 12 weeks in the ^{177}Lu-PSMA-617 group (n = 385)



Analyses in patients randomized on or after 5 March 2019 (PFS-FAS).

OS rate by PSA decline up to 12 weeks in the ^{177}Lu-PSMA-617 group (n = 551)



Analyses in all randomized patients (FAS).

Armstrong et al. Abstract 1372P. ESMO 2022, Paris, France.

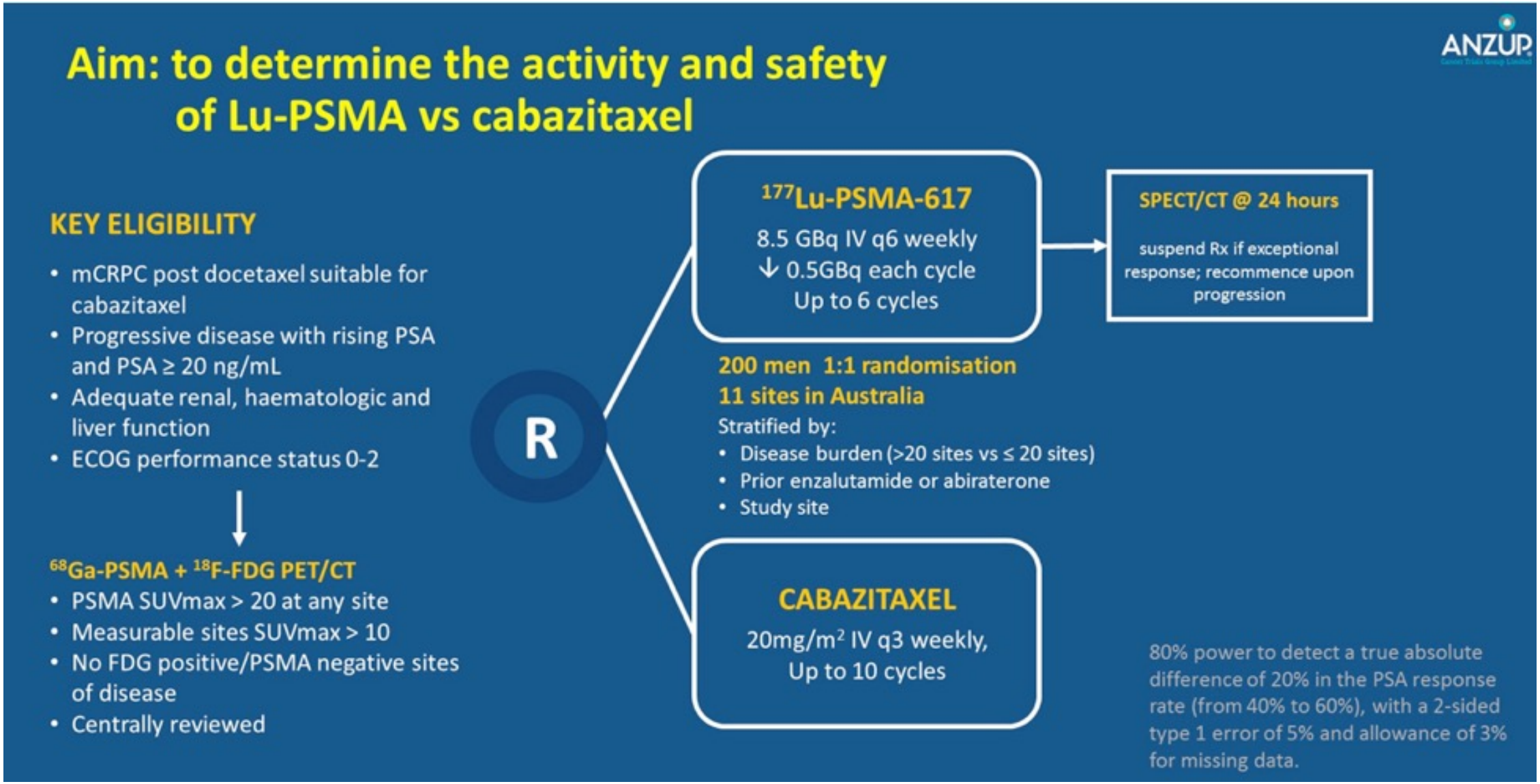
VISION: Treatment-Emergent Adverse Events

Patients, n (%)	All grades		Grade 3–5	
	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)	^{177}Lu-PSMA-617 + SOC (n = 529)	SOC alone (n = 205)
Fatigue	260 (49.1)	60 (29.3)	37 (7.0)	5 (2.4)
Bone marrow suppression	251 (47.4)	36 (17.6)	124 (23.4)	14 (6.8)
Leukopenia	66 (12.5)	4 (2.0)	13 (2.5)	1 (0.5)
Lymphopenia	75 (14.2)	8 (3.9)	41 (7.8)	1 (0.5)
Anemia	168 (31.8)	27 (13.2)	68 (12.9)	10 (4.9)
Thrombocytopenia	91 (17.2)	9 (4.4)	42 (7.9)	2 (1.0)
Dry mouth	208 (39.3)	2 (1.0)	0 (0.0)	0 (0.0)
Nausea and vomiting	208 (39.3)	35 (17.1)	8 (1.5)	1 (0.5)
Renal effects	46 (8.7)	12 (5.9)	18 (3.4)	6 (2.9)
Second primary malignancies	11 (2.1)	2 (1.0)	4 (0.8)	1 (0.5)
Intracranial hemorrhage	7 (1.3)	3 (1.5)	5 (0.9)	2 (1.0)

Median duration of exposure to 177Lu-PSMA-617: 6.9 mo (range, 0.3-10.2); median cycles started: 5 cycles (range, 1-6); median cumulative dose: 37.5 GBq (range, 7.0-48.3).

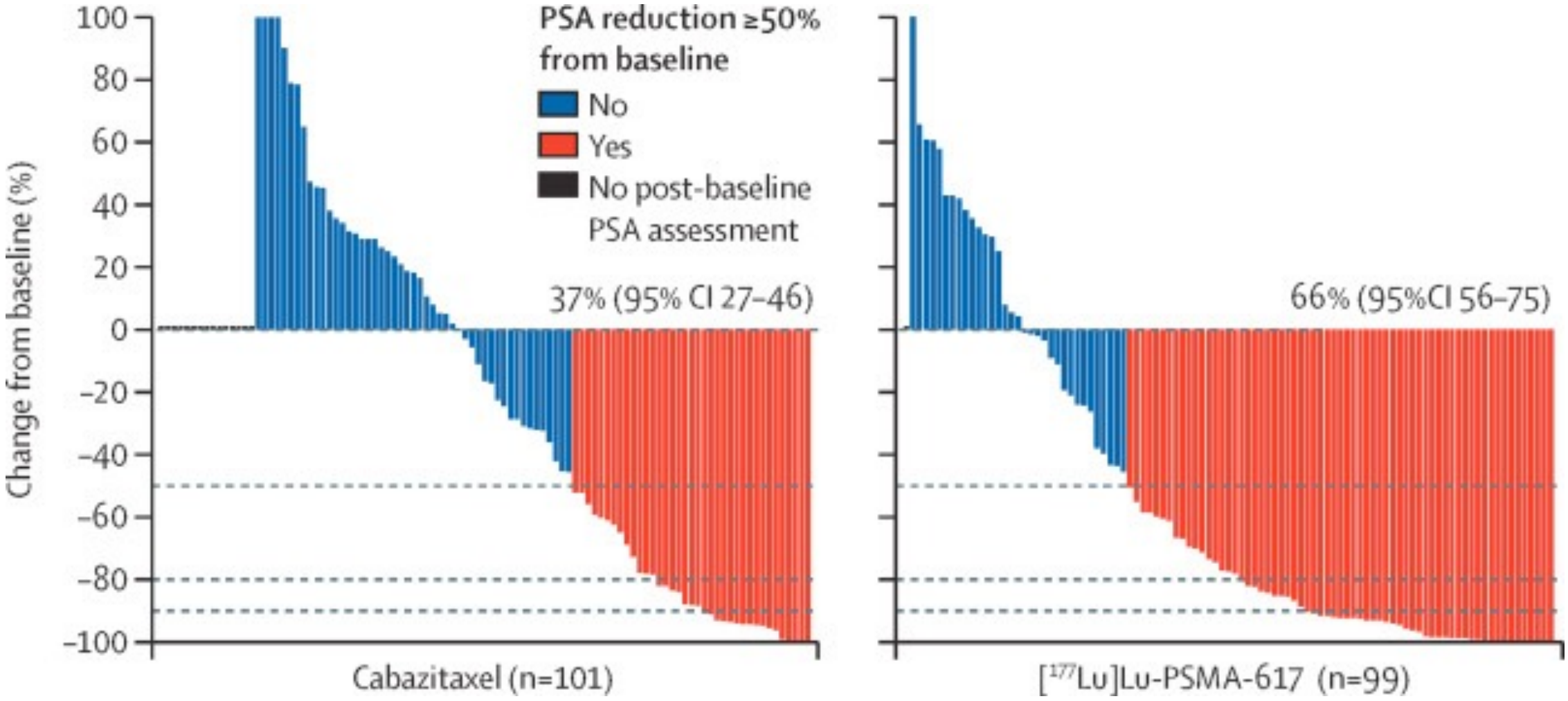
Sartor O, et al. *N Engl J Med*. Jun 23, 2021.
Morris M, et al. ASCO 2021. Abstract LBA4.

TheraP trial: Lu-177 PSMA vs cabazitaxel



Hofman et al. Lancet 2021

TheraP trial: Lu-177 PSMA vs cabazitaxel



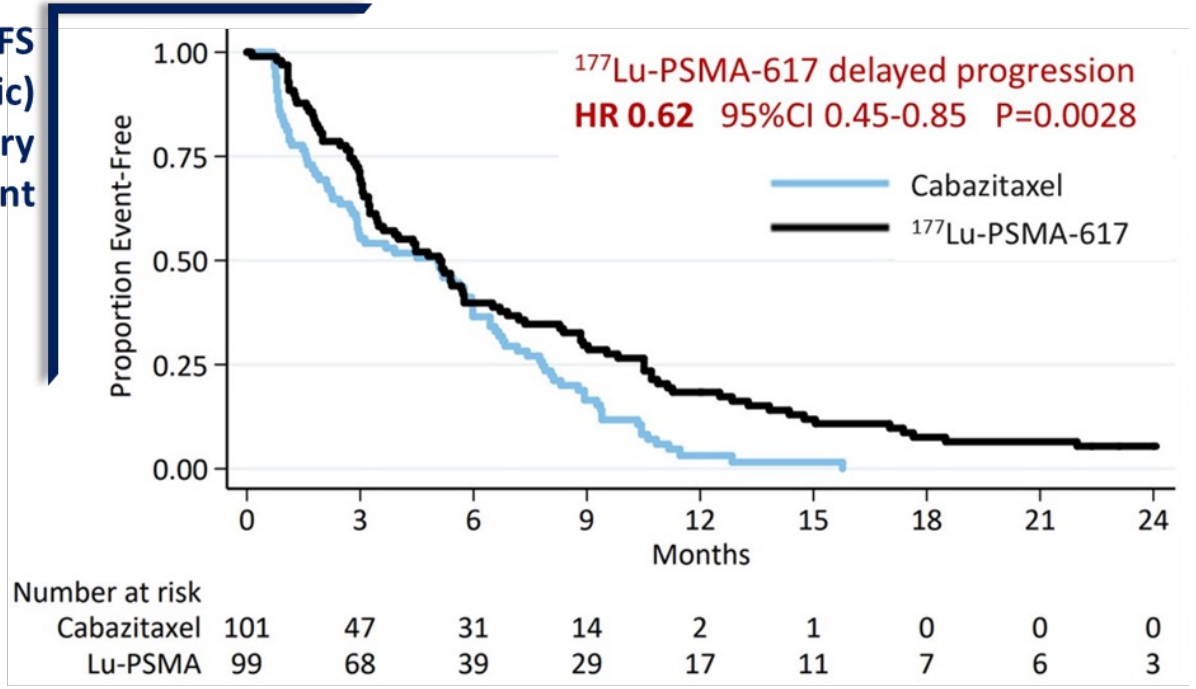
Hofman et al. Lancet 2021

Phase 2 TheraP Trial: Updated Results

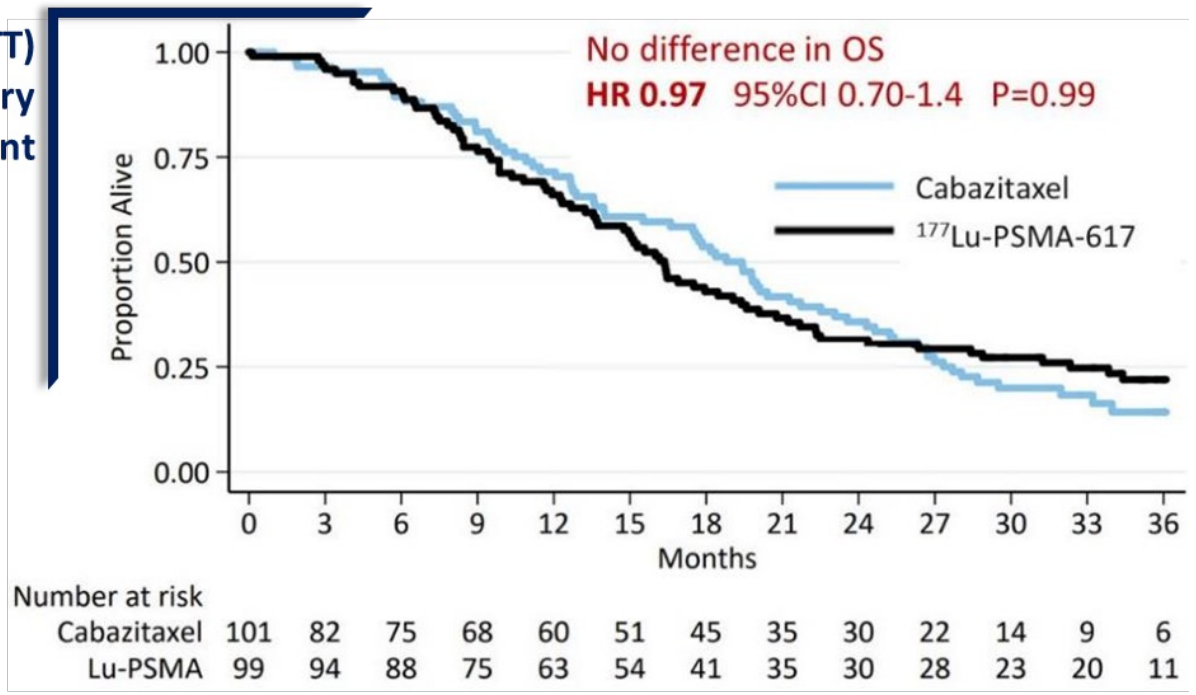
Primary Endpoint	LuPSMA	Cabazitaxel
PSA Reduction ≥ 50% From Baseline	66	37

Secondary Endpoints	LuPSMA	Cabazitaxel
ORR	49	24
AEs Gr 1-2 / 3-4	54 / 33	40 / 43

PFS (PSA + Radiographic) Secondary Endpoint



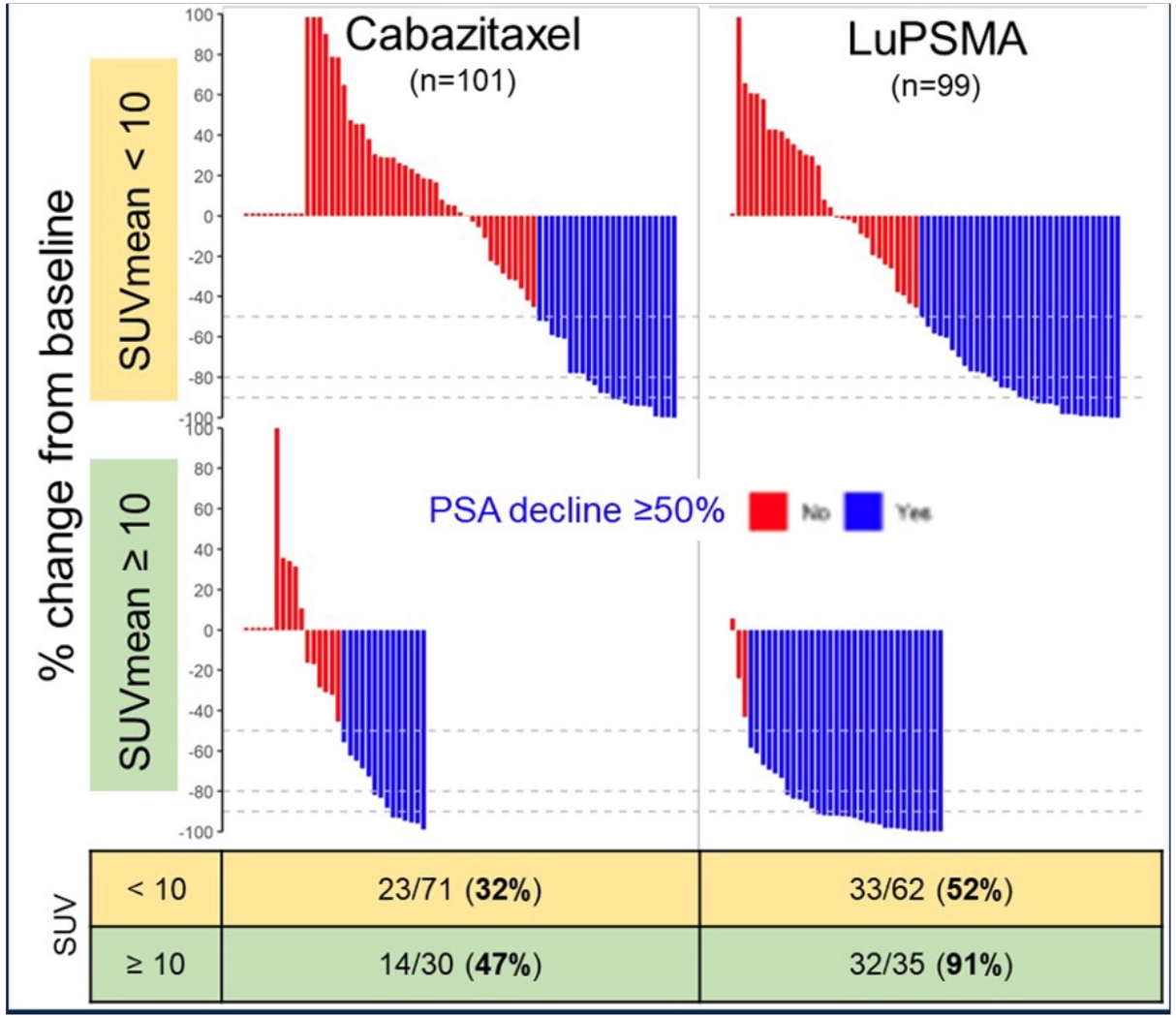
OS (ITT) Secondary Endpoint



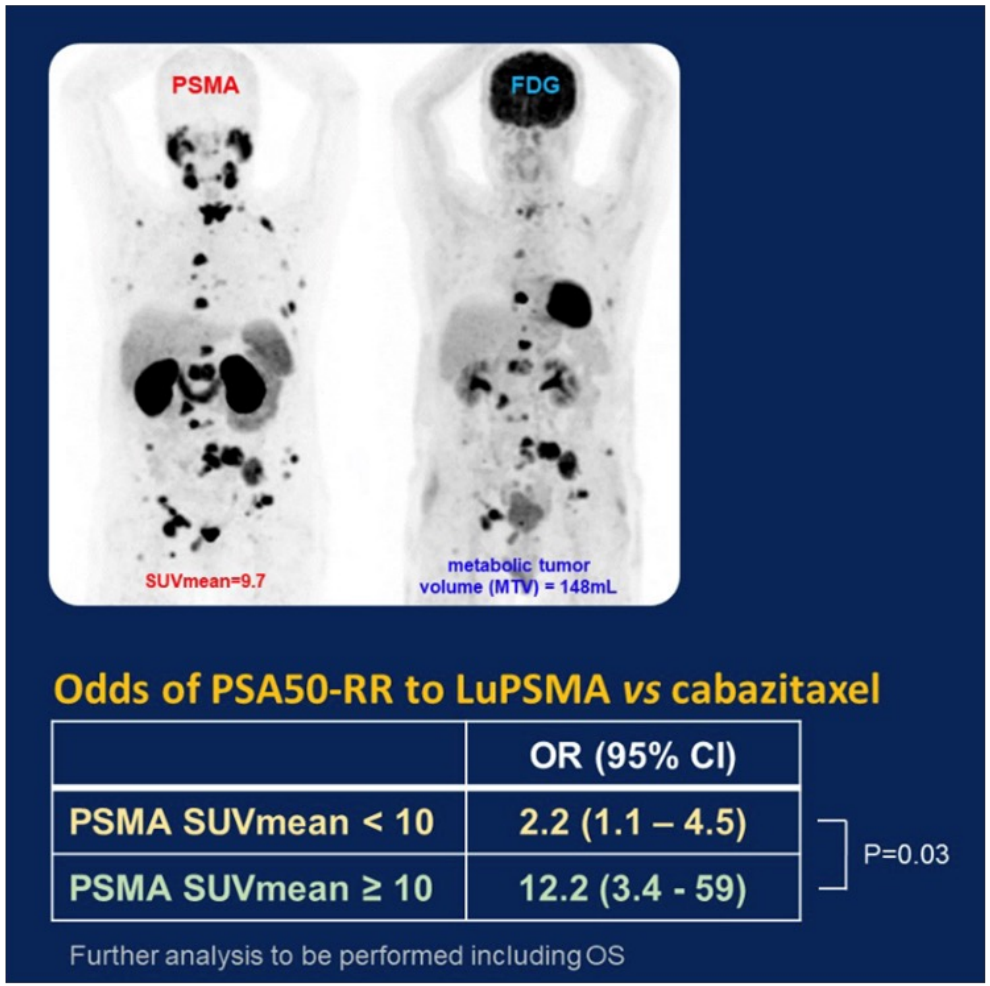
Data cutoff for OS: 31 DEC 2021; median follow-up: 36 mo.

Hofman M, et al. ASCO 2022. Abstract 5000. Hofman M, et al. *Lancet*. 2021;397:797–804.

TheraP PSMA PET As Predictive of Response



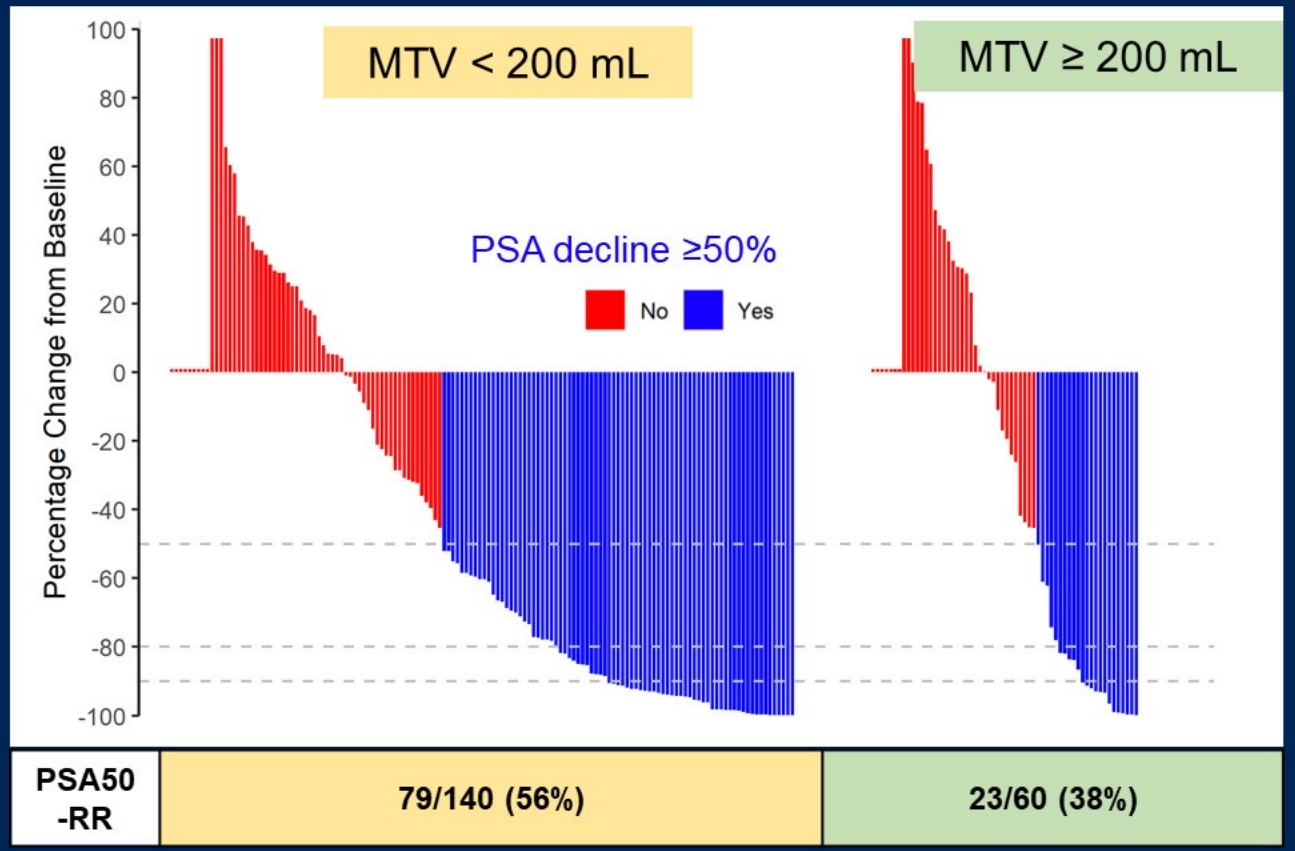
SUV	Cabazitaxel (n=101)	LuPSMA (n=99)
< 10	23/71 (**32%**)	33/62 (**52%**)
≥ 10	14/30 (**47%**)	32/35 (**91%**)



Buteau JP et al, GU ASCO 2022

Buteau JP et al, *Lancet Oncol*, 2022; 23(11): 1389-97.

FDG: prognostic biomarker (PSA50-RR)



PSA50-RR to LuPSMA *vs* cabazitaxel

MTV	Cabazitaxel	LuPSMA
< 200	31/71 (**44%**)	48/69 (**70%**)
≥ 200	6/30 (**20%**)	17/30 (**57%**)

Odds of PSA50-RR lower amongst men with high MTV
OR 0.44; P=0.01

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Radiopharmaceuticals: Lu-177 PSMA

- Lu-PSMA is FDA approved as of March 2022 for patients with PSMA-positive mCRPC who received NHA and taxane-based chemo
- Few eligibility criteria:
  - Ga-68 PSMA scan (initially, later plan to expend PyL PSMA PET scan)
  - Any systemic anti-cancer therapy within 28 days
  - Radionuclide therapy (Strontium-89, Samarium-153, Rhenium-186, Rhenium-188, Radium-223, hemi-body irradiation) within 6 months
  - Unmanageable urinary tract obstruction or hydronephrosis
  - Progressive deterioration of organ function (GFR < 30 mL/min or creatinine > 2-fold upper limit of normal (ULN); liver enzymes > 5-fold ULN)
  - Myelosuppression: (a) Total white cell count less than 2.5 × 109 /L (b) Platelet count less than 75 × 109 /L
- This opens a new era with different combinations, such as IO, and also coming to the front line

MADRID 2023 ESMO congress

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

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

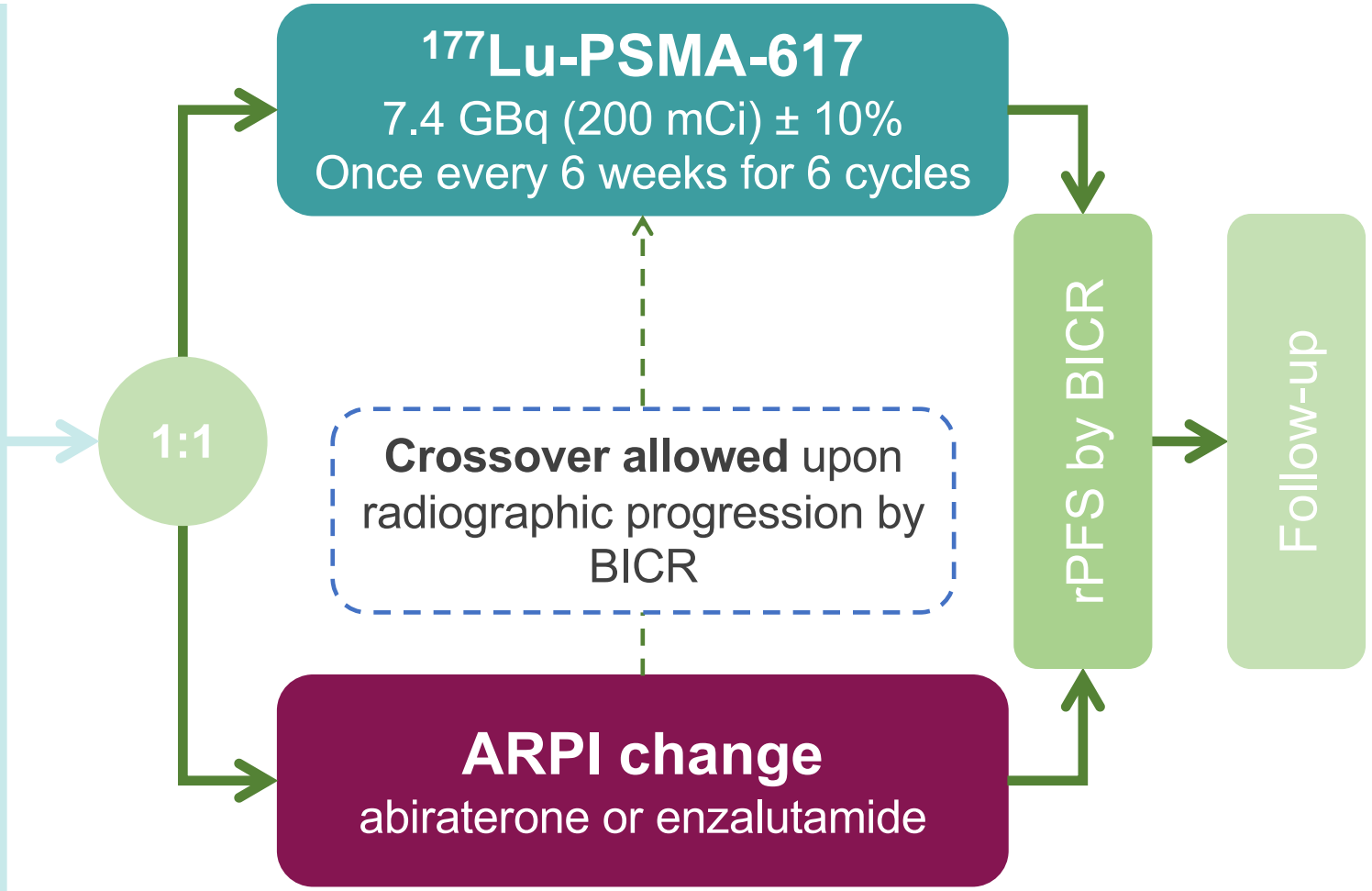
Co-authors: D Castellano, K Herrmann, J de Bono, ND Shore, KN Chi, M Crosby, JM Piulats, A Flechon, XX Wei, H Mahammedi, G Roubaud, H Studentova, S Ghebremariam, E Kpamegan, TN Kreisl, N Delgoshaie, K Lehnhoff, MJ Morris,* K Fizazi,*
on behalf of the PSMAfore investigators

*Contributed equally

PSMAfore: a phase 3, randomized, open-label study

Eligible adults

- Confirmed progressive mCRPC
- ≥ 1 PSMA-positive metastatic lesion on [^{68}Ga]Ga-PSMA-11 PET/CT and no exclusionary PSMA-negative lesions
- Progressed once on prior second-generation ARPI
  - Candidates for change in ARPI
- Taxane-naive (except [neo]adjuvant > 12 months ago)
  - Not candidates for PARPi
- ECOG performance status 0–1



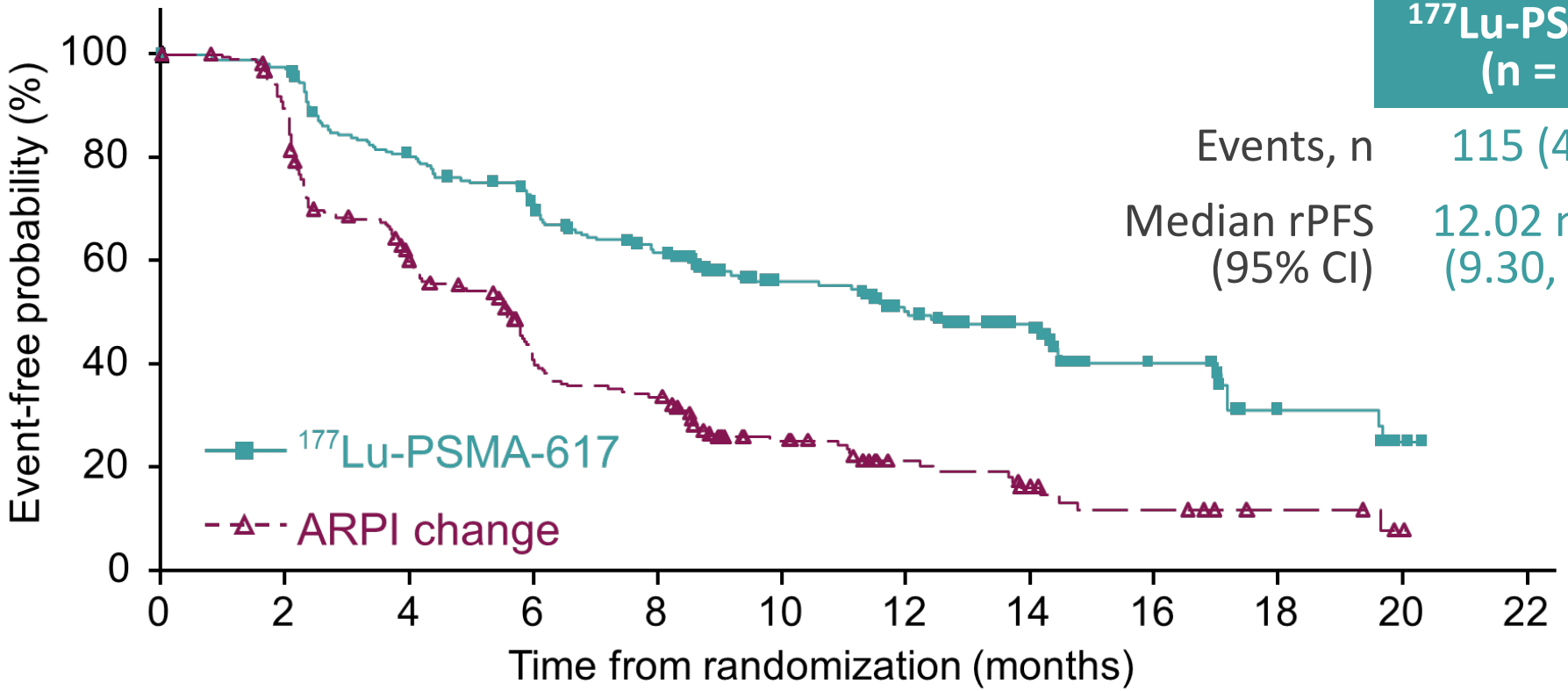
Stratification factors

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

rPFS: primary endpoint was met

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

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



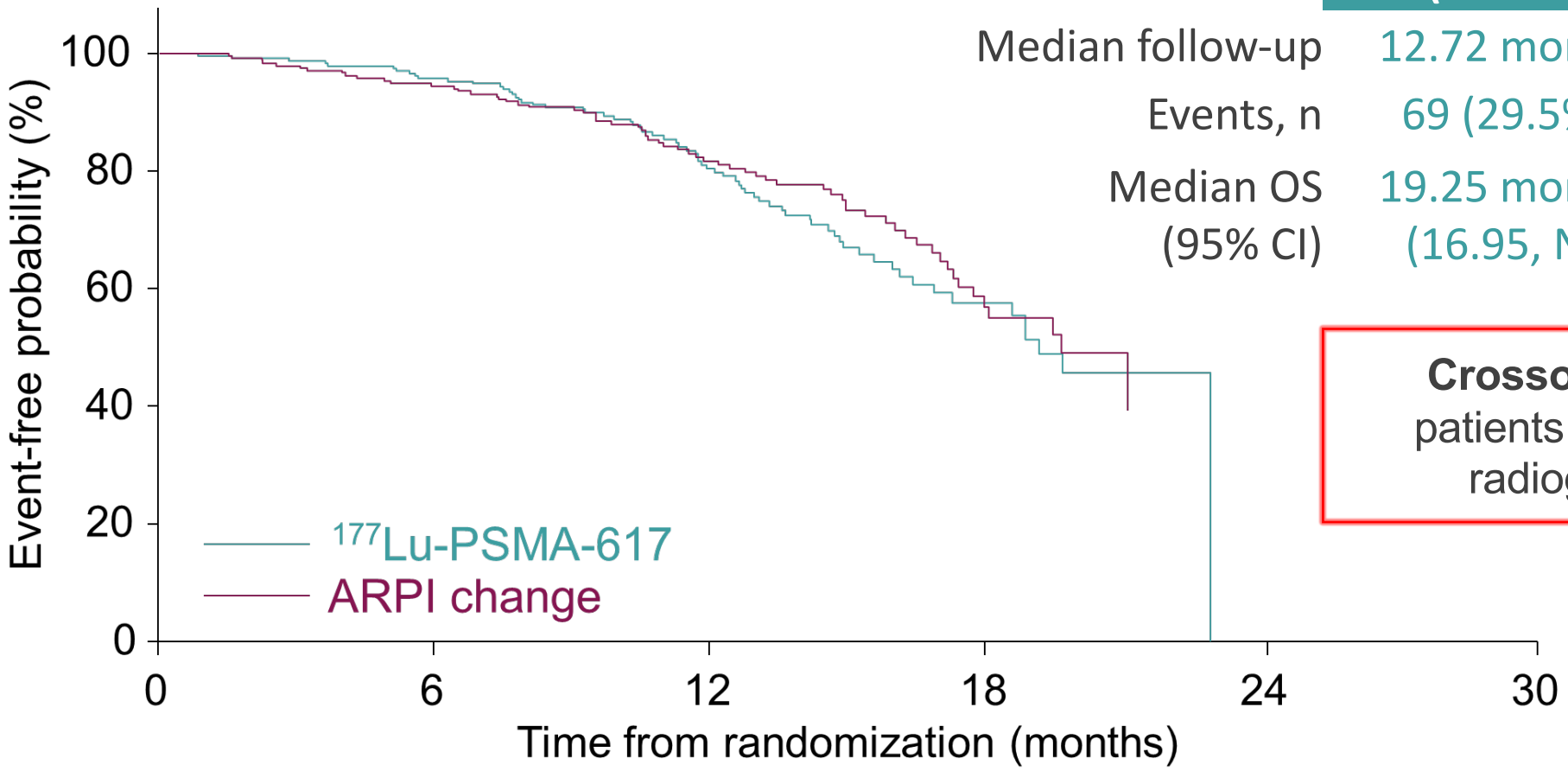
	^{177}Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Events, n	115 (49.1%)	168 (71.8%)
Median rPFS (95% CI)	12.02 months (9.30, 14.42)	5.59 months (4.17, 5.95)

Number of patients still at risk

234	216	174	150	125	82	64	45	20	10	2	0
234	197	126	79	65	36	21	12	8	4	1	0

2nd interim OS: intent-to-treat analysis

HR: 1.16 (95% CI: 0.83, 1.64)

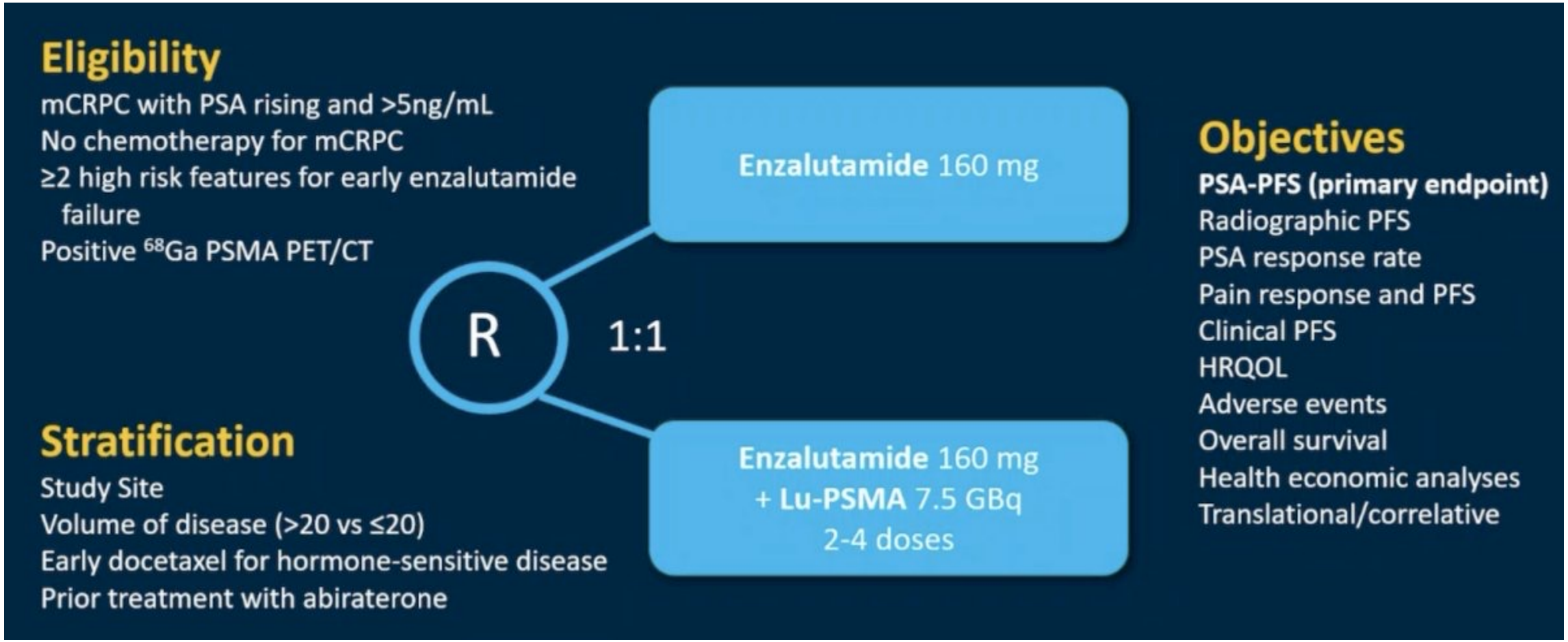


	^{177}Lu-PSMA-617 (n = 234)	ARPI change (n = 234)
Median follow-up	12.72 months	13.08 months
Events, n	69 (29.5%)[a]	65 (27.8%)
Median OS (95% CI)	19.25 months (16.95, NE)	19.71 months (17.81, NE)

Crossover: 123/146 (84.2%) patients who discontinued with radiographic progression

[a]Three patients died before receiving ^{177}Lu-PSMA-617

ENZA-P: Enzalutamide and 177Lu-PSMA-617 in Poor-Risk Metastatic Castration-Resistant Prostate Cancer (mCRPC), a Randomized, Phase 2 Trial

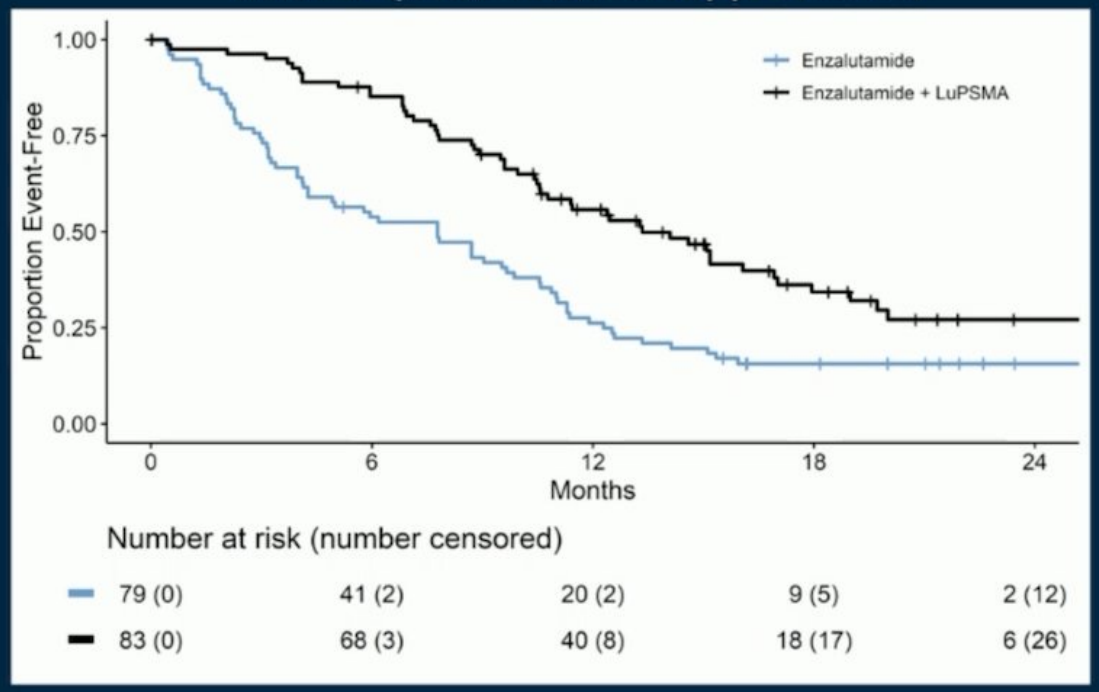


Emmett et al. ESMO 2023

ENZA-P: Enzalutamide and 177Lu-PSMA-617 in Poor-Risk Metastatic Castration-Resistant Prostate Cancer (mCRPC), a Randomized, Phase 2 Trial

PSA-PFS

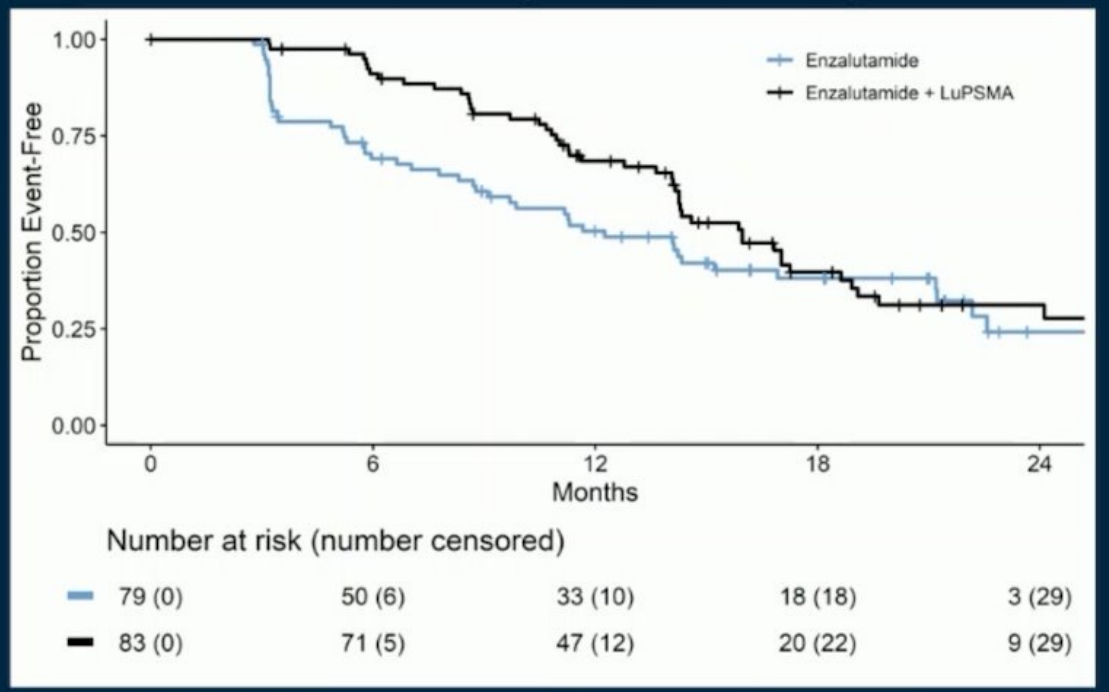
HR 0.43 (95%CI 0.29-0.63) p=0.00001



PSA-PFS	Participants	Events	Censored	Median Months
Enzalutamide	79	65	14	7.8
Enzalutamide + Lu-PSMA	83	52	31	13

R-PFS

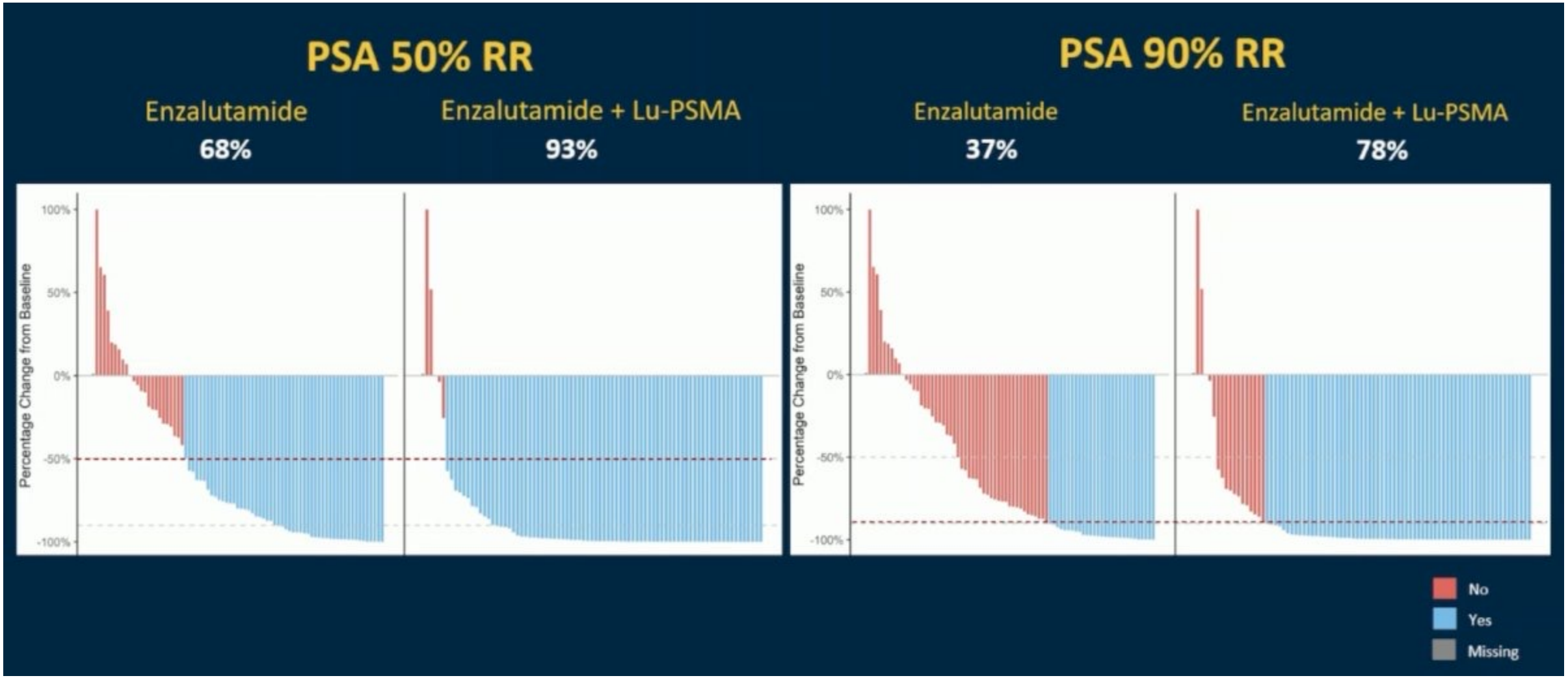
HR 0.67 (95% CI 0.44-1.01)



Radiographic-PFS	Participants	Events	Censored	Median Months
Enzalutamide	79	47	35	12
Enzalutamide + Lu-PSMA	83	48	32	16

Emmett et al. ESMO 2023

ENZA-P: Enzalutamide and 177Lu-PSMA-617 in Poor-Risk Metastatic Castration-Resistant Prostate Cancer (mCRPC), a Randomized, Phase 2 Trial



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Future clinical trials

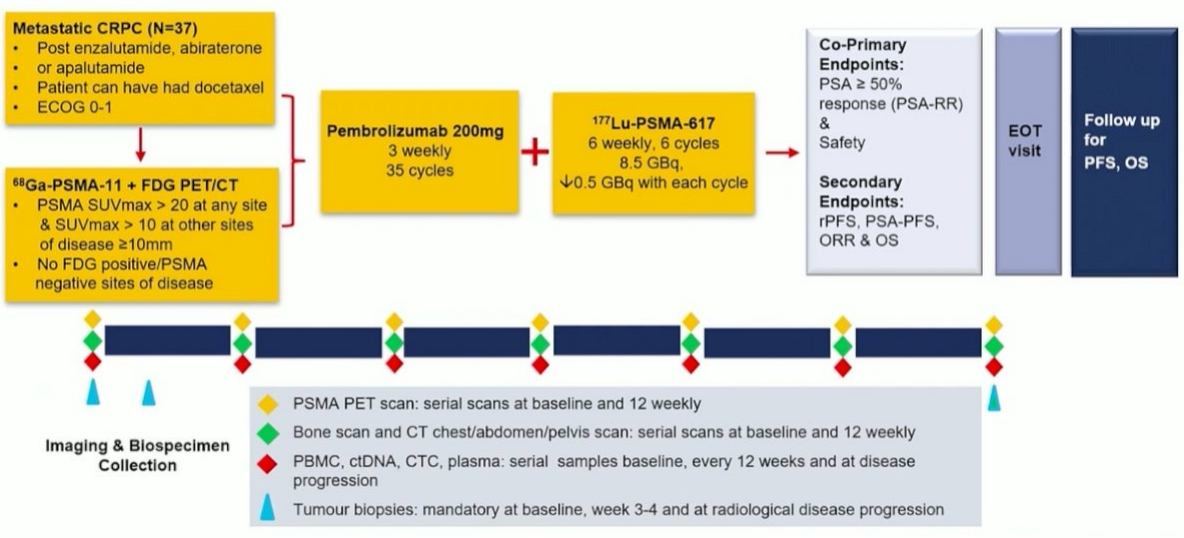
Table 1. Current active and recruiting phase III prostate cancer trials involving PSMA-RLT with lutetium-177. Search performed using clinicaltrials.gov on 15 October 2022 and updated on 21 January 2023.

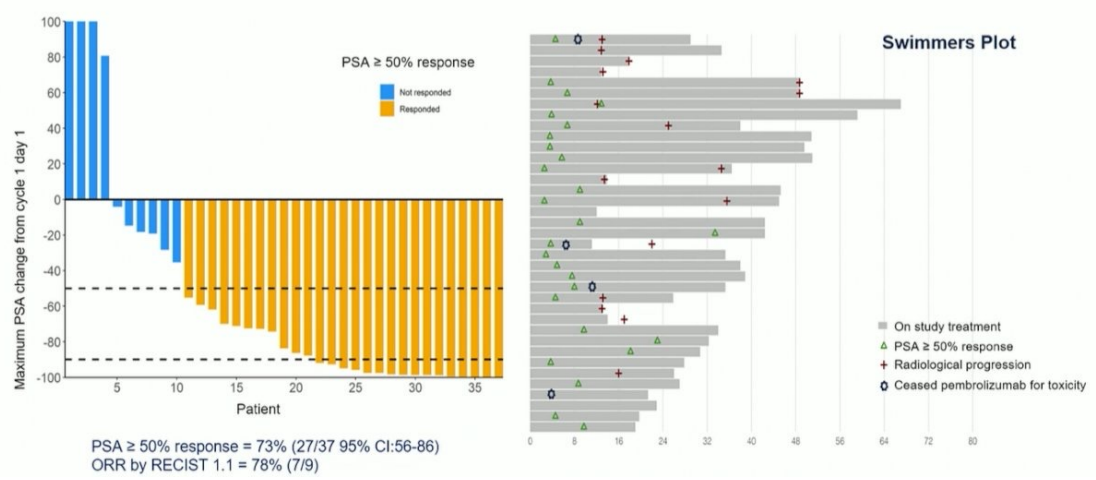
Trial number (name)	Type of prostate cancer	Intervention	Total enrollment	Primary outcome measures
NCT0351164 (VISION)	mCRPC previously treated with ARPI and taxane chemotherapy	^{177}Lu-PSMA-617 with SoC *versus* SoC	831	rPFS and OS
NCT04876651 (PROSTACT)	mCRPC previously treated with ARPI	^{177}Lu-TLX591 with SoC *versus* SoC	387	rPFS
NCT04689828 (PSMAfore)	mCRPC previously treated with ARPI and without prior taxane therapy	^{177}Lu-PSMA-617 *versus* switch of ARPI	450	rPFS
NCT05204927 (ECLIPSE)	mCRPC previously treated with ARPI and without prior taxane therapy	^{177}Lu-PSMA-I&T *versus* abiraterone or enzalutamide	400	rPFS
NCT04647526 (SPLASH)	mCRPC previously treated with second-line ARPI	^{177}Lu-PSMA-I&T *versus* abiraterone or enzalutamide	415	rPFS
NCT04720157 (PSMAddition)	mHSPC	^{177}Lu-PSMA-617 with SoC *versus* SoC alone	1126	rPFS

ARPI, androgen receptor pathway inhibitor; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; OS, overall survival; PSMA-RLT, prostate-specific membrane antigen-radioligand therapy; rPFS, radiographic progression-free survival; SoC, standard of care.

Jang et al, Ther Adv Med Oncol . 2023

PRINCE trial:177Lu-PSMA-617+Pembrolizumab





TRAE term	Grade 1 (%)	Grade 2 (%)	Grade 3 (%)	N=37 (%)
Xerostomia	21 (57%)	7 (19%)	-	28 (76%)
Fatigue	11 (29 %)	3 (8%)	2 (5%)	16 (43%)
Rash	5 (14%)	4 (11%)		9 (25%)
Nausea	8 (21%)	1 (3%)	-	9 (24%)
Pruritis	6 (16%)	1 (3%)	-	7 (19%)
Anorexia	3 (8%)	3 (8%)	-	6 (16%)
Thrombocytopenia	4 (11%)	1(3%)	-	5 (14%)
Bone pain (flare)	4 (11%)	-	-	4 (11%)
Aspartate aminotransferase elevation	2 (5%)	2 (5%)	-	4 (11%)
Dry eye	3 (8%)	-	-	3 (8%)
Dysgeusia	2 (5%)	1 (3%)	-	3 (8%)
Weight loss	2 (5%)	1 (3%)		3 (8%)
Anemia	-	2 (5%)	1(3%)	3 (8%)
Alanine aminotransferase elevation	2 (5%)	1(3%)	-	3 (8%)
Amylase elevation	1 (3%)	1 (3%)	1 (3%)	3 (8%)
Arthralgia	3 (8%)	-	-	3 (8%)
Neutropenia	1 (3%)	-	-	1 (3%)

- PSA50-RR was 73% (27/37 [95% CI: 56-86]).
-9 patients with RECIST measurable disease, 7 (78%) had a partial response

Sandhu et at. ESMO 2021

EVOLUTION: 177Lu-PSMA Therapy Versus 177Lu-PSMA in Combination With Ipilimumab and Nivolumab for Men With mCRPC (ANZUP2001)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT05150236

Recruitment Status : Recruiting
First Posted : December 9, 2021
Last Update Posted : June 10, 2022

See **Contacts and Locations**

View this study on Beta.ClinicalTrials.gov

Sponsor:
Australian and New Zealand Urogenital and Prostate Cancer Trials Group

NIH U.S. National Library of Medicine
ClinicalTrials.gov

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Home > Search Results > Study Record Detail

Save this study

177Lu-PSMA-617 Therapy and Olaparib in Patients With Metastatic Castration Resistant Prostate Cancer (LuPARP)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT03874884

Recruitment Status : Recruiting
First Posted : March 14, 2019
Last Update Posted : November 17, 2022

See **Contacts and Locations**

View this study on Beta.ClinicalTrials.gov

Sponsor:
Peter MacCallum Cancer Centre, Australia

Information provided by (Responsible Party):
Peter MacCallum Cancer Centre, Australia

Future clinical trials

Trial number (name)	Notable characteristics	Intervention	Total enrollment	Primary outcome measures
^{177}Lu monotherapy				
NCT05079698	Hormone sensitive, oligometastatic	^{177}Lu-PSMA-617 with SBRT	6	DLTs
NCT04443062 (BULLSEYE)	Hormone sensitive, oligometastatic	^{177}Lu-PSMA-617 *versus* SoC	58	Disease progression
NCT05114746	mCRPC	^{177}Lu-PSMA-617 with SoC	28	DLTs and ORR
NCT05458544	mCRPC	^{177}Lu-Ludotadipep	26	DLTs and ORR
NCT05579184	mCRPC	^{177}Lu-Ludotadipep	30	PSA response rate
NCT04509557	mCRPC	^{177}Lu-Ludotadipep	30	DLTs
NCT05340374	mCRPC previously treated with docetaxel and ARPI	^{177}Lu-PSMA-617 with cabazitaxel	44	DLTs and MTD
NCT03454750	mCRPC	^{177}Lu-PSMA-617 with radiometabolic therapy	210	DCR, treatment-emergent adverse events
NCT03042468	mCRPC previously treated with ARPI	^{177}Lu-PSMA-617	50	DLTs and MTD
NCT03874884 (LuPARP)	mCRPC previously treated with ARPI	^{177}Lu-PSMA-617 with olaparib	52	DLTs and MTD
NCT04343885 (UpFrontPSMA)	mHSPC	^{177}Lu-PSMA-617 followed by docetaxel *versus* docetaxel	140	Undetectable PSA rate at 12 months
NCT05383079 (AlphaBet)	mCRPC previously treated with ARPI	^{177}Lu-PSMA-I&T with radium-223	36	DLTs, MTD, 50% PSA response rate
NCT04786847 (ProstACTSelect)	mCRPC previously treated with ARPI	^{177}Lu-DOTA-TLX591	50	Treatment-related adverse events
NCT05146973 (ProstACT TARGET)	Biochemically recurrent oligometastatic prostate cancer	^{177}Lu-DOTA-TLX591 with EBRT	50	PSA PFS
NCT03780075	mCRPC	^{177}Lu-EB-PSMA-617	50	PSA change, SUV change
NCT00859781	Biochemically relapsed prostate cancer after local therapy	^{177}Lu-J591 with ketoconazole	55	Proportion of subjects free of radiographically evident metastases
NCT03658447 (PRINCE)	mCRPC previously treated with ARPI	^{177}Lu-PSMA-617 with pembrolizumab	37	PSA response, treatment-related adverse events, tolerability
NCT04430192 (LuTectomy)	High-risk localized prostate cancer	^{177}Lu-PSMA-617	20	Radiation absorbed dose
NCT05547061	mCRPC	^{177}Lu-DGUL	73	ORR
NCT04663997	mCRPC previously treated with ARPI	^{177}Lu-PSMA-617 *versus* docetaxel	200	PFS
NCT05113537 (UPLIFT)	mCRPC previously treated with ARPI	Abemaciclib followed by ^{177}Lu-PSMA-617	30	DLTs and MTD
NCT05230251 (ROADSTER)	Localized prostate cancer with biochemical failure, previously treated with radiation therapy	^{177}Lu-PSMA-I&T with high-dose radiation *versus* high-dose radiation	12	Safety and efficacy
NCT03805594	mCRPC previously treated with ARPI	^{177}Lu-PSMA-617 with pembrolizumab	43	ORR
NCT05162573 (PROQURE-1)	N1M0	^{177}Lu-PSMA-617 with EBRT	18	MTD
NCT05413850	mCRPC	^{177}Lu-rhPSMA-10.1	150	DLTs, treatment-related adverse events, 50% PSA response rate
NCT05496959 (LUNAR)	Oligorecurrent	^{177}Lu-PSMA-I&T before SBRT	100	PSMA-PET/CT-based PFS
NCT03822871	mCRPC previously treated with ARPI	CTT1403	40	DLTs
NCT05150236 (EVOLUTION)	mCRPC previously treated with ARPI	^{177}Lu-PSMA-617 with nivolumab and ipilimumab *versus* ^{177}Lu-PSMA-617	110	PSA-PFS at 1 year
NCT04419402 (ENZA-p)	mCRPC	^{177}Lu-PSMA-617 with enzalutamide *versus* enzalutamide	160	PSA PFS
^{225}Ac monotherapy				
NCT03276572	mCRPC previously treated with ARPI	^{225}Ac-J591	32	DLTs and MTD
NCT04506567	mCRPC previously treated with ARPI	^{225}Ac-J591	105	DLTs and MTD
NCT04946370	mCRPC previously treated with ARPI	^{225}Ac-J591 with pembrolizumab	76	DLTs, optimal dose, response rates
NCT05219500 (TATCIST)	mCRPC previously treated with ARPI	^{225}Ac-PSMA-I&T	100	Efficacy and safety
NCT04597411 (AcTION)	Both prior exposure and naïve to ^{177}Lu acceptable	^{225}Ac-PSMA-517	60	MTD
Combination of ^{177}Lu and ^{225}Ac				
NCT04886986	mCRPC previously treated with ARPI	^{225}Ac-J591 with ^{177}Lu-PSMA-I&T	33	DLTs, MTD, 50% PSA response rate
^{161}Tb				
NCT05521412 (VIOLET)	mCRPC previously treated with ARPI	^{161}Tb-PSMA-I&T	36	DLTs, MTD, treatment-related adverse events
^{227}Th				
NCT03724747	mCRPC previously treated with ARPI	BAY2315497 with or without darolutamide	63	MTD

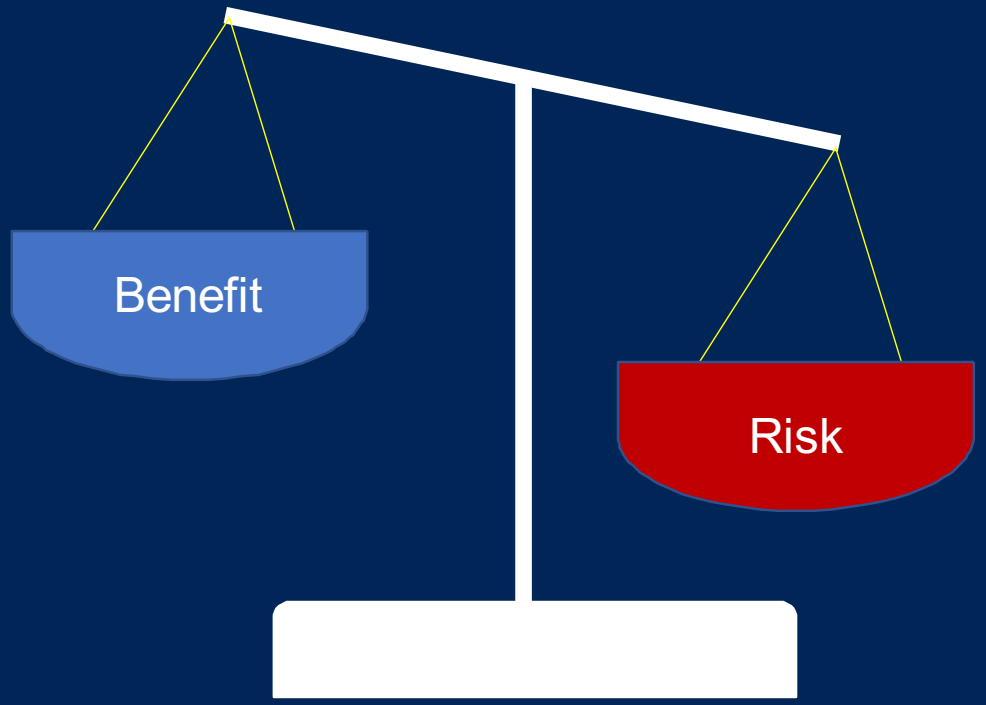
(Continued)

ARPI, androgen receptor pathway inhibitor; DCR, disease control rate; DLTs, dose-limiting toxicities; EBRT, external beam radiation therapy; mCRPC, metastatic castration-resistant prostate cancer; mHSPC, metastatic hormone-sensitive prostate cancer; MTD, maximum tolerated dose; ORR, objective response rate; PSA, prostate-specific antigen; PSMA-RLT, prostate-specific membrane antigen-radioligand therapy; SBRT, stereotactic body radiation therapy; SoC, standard of care.

Jang et al, Ther Adv Med Oncol . 2023

Balancing Outcomes for Selection of Therapy

Improved OS
Improved PFS
Improved response rate
Duration of response
Improved QOL



Toxicity
Risk of Grade 5 event
Primary progression
Worsening QOL
Financial toxicity

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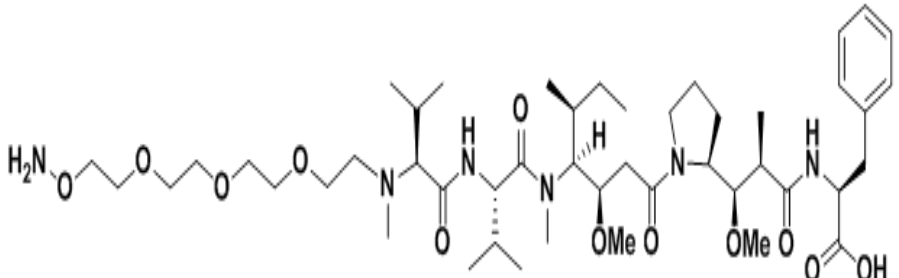
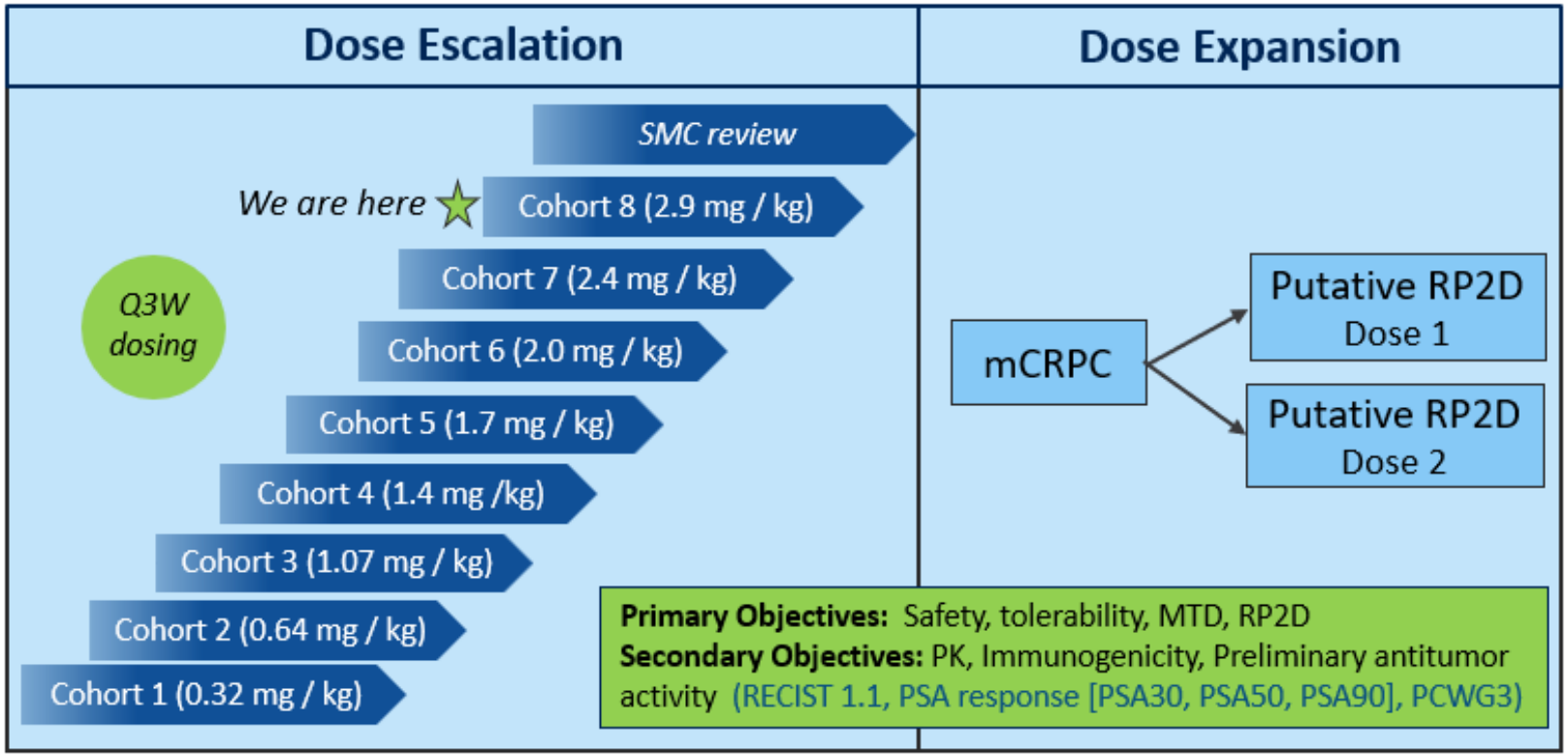
Other novel agents on pipeline for mCRPC

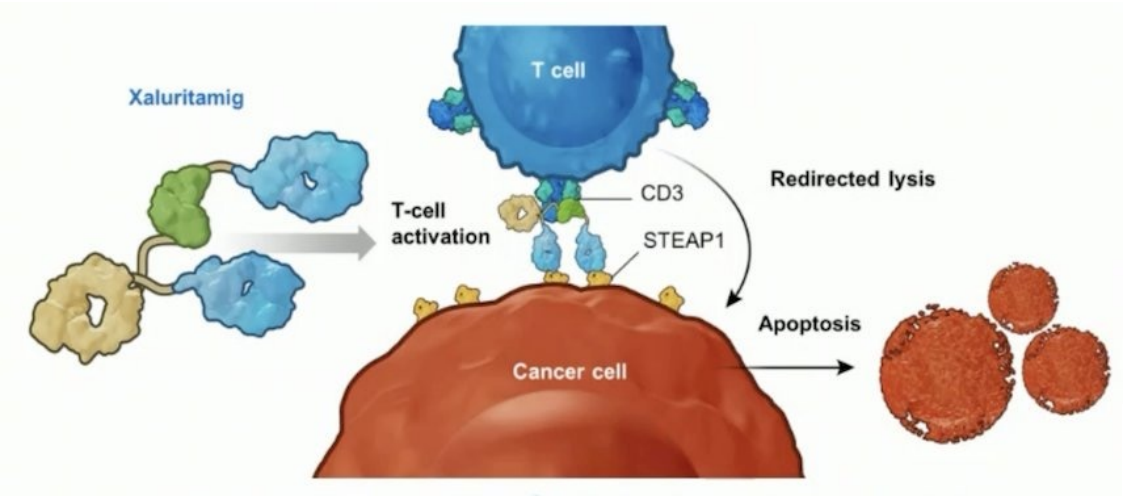
ARX517, an anti-PSMA ADC targeting mCRPC



AS269 Drug-Linker

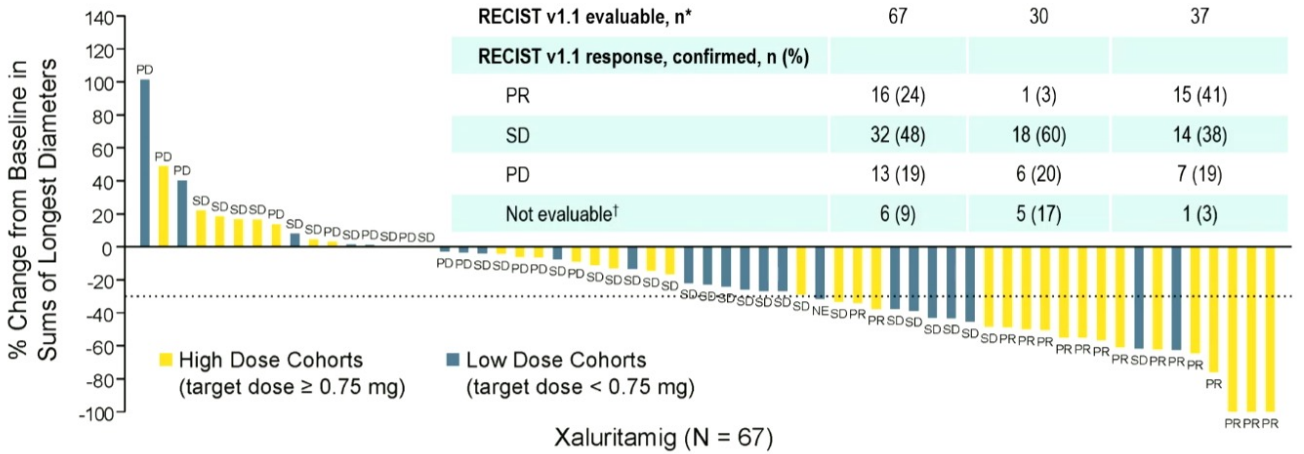


AMG509, STEP 1 BiTE targeting mCRPC



Confirmed RECIST responses occurred more often in high dose cohorts

	All cohorts	Low dose cohorts (1–7a)	High dose cohorts (7b–13)
RECIST v1.1 evaluable, n*	67	30	37
RECIST v1.1 response, confirmed, n (%)			
PR	16 (24)	1 (3)	15 (41)
SD	32 (48)	18 (60)	14 (38)
PD	13 (19)	6 (20)	7 (19)
Not evaluable†	6 (9)	5 (17)	1 (3)



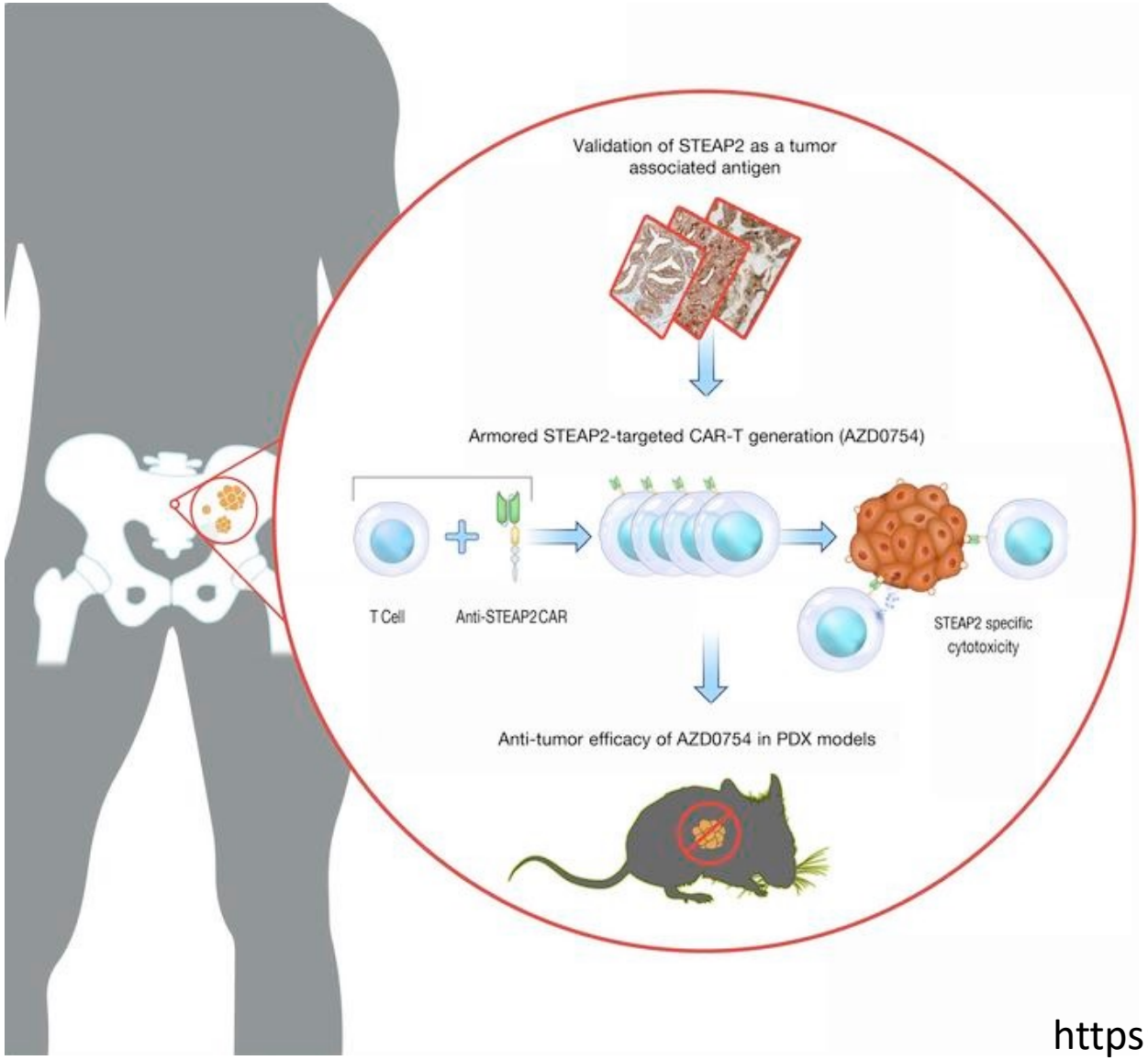
Dashed line indicates 30% reduction in tumor sum of longest diameters from baseline. *Historically, ~40% of mCRPC patients have RECIST measurable disease[1,2]. †BOR of NE includes 5 patients without post-baseline scans and 1 patient without sufficient follow up duration prior to post baseline assessment.

BOR, best overall response; NE, not evaluable; PD, progressive disease; PR, partial response; PSA, prostate specific antigen; RECIST; Response Evaluation Criteria in Solid Tumors; SD, stable disease.

1. Scher HI, et al. *Clin Cancer Res.* 2005;11(14):5223-5232. 2. Lorente D, et al. *Eur Urol Focus.* 2018;4(2):235-244.

AZD0754, TGFβRII-armored, STEAP2-targeted CAR-T cell

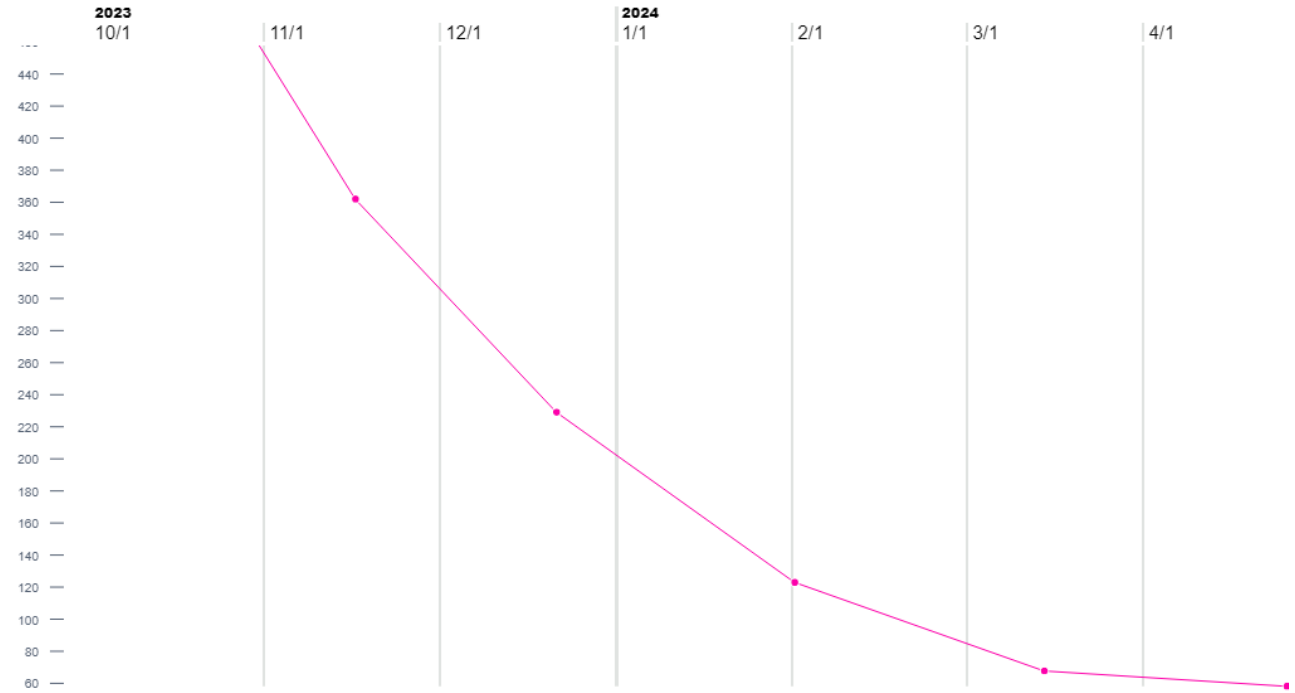
NCT06267729

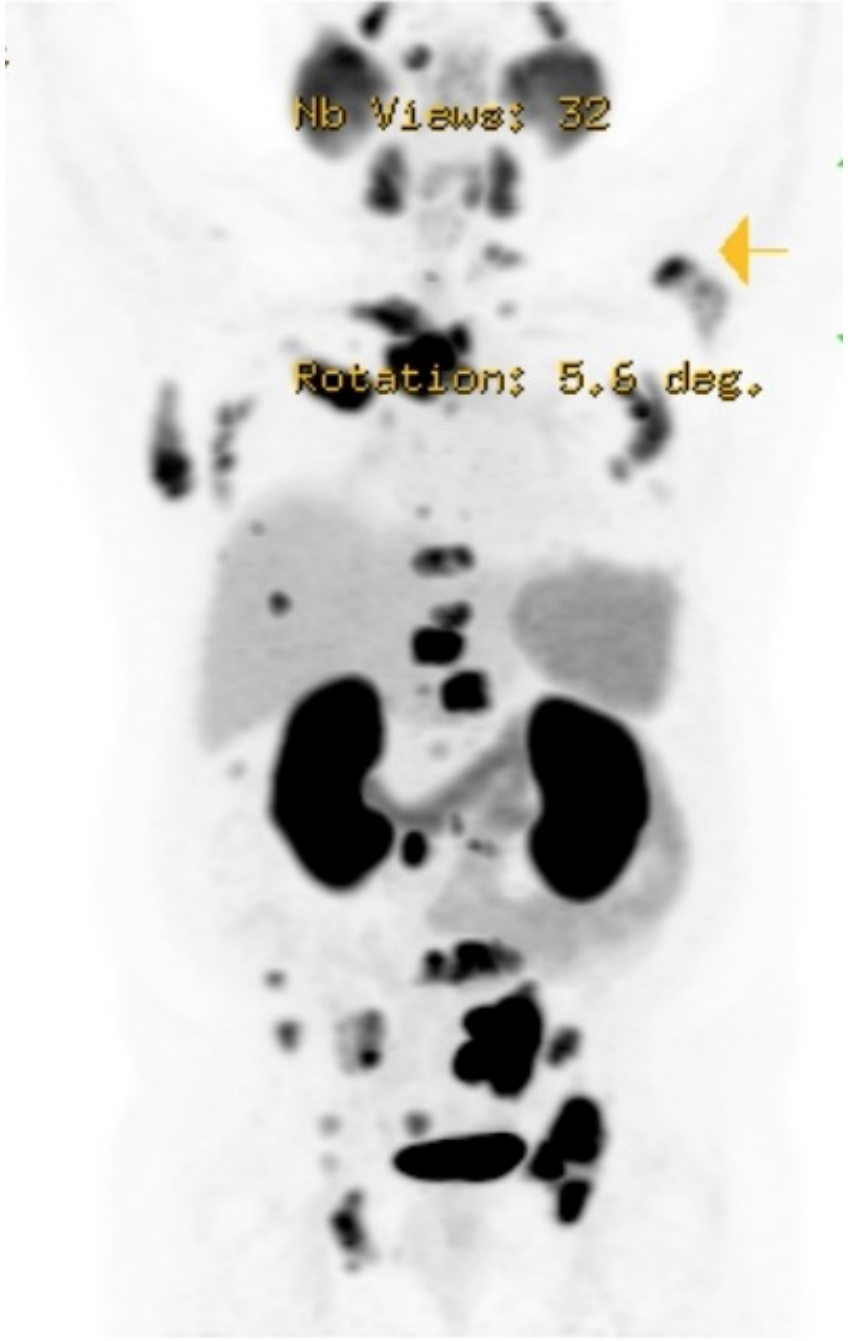


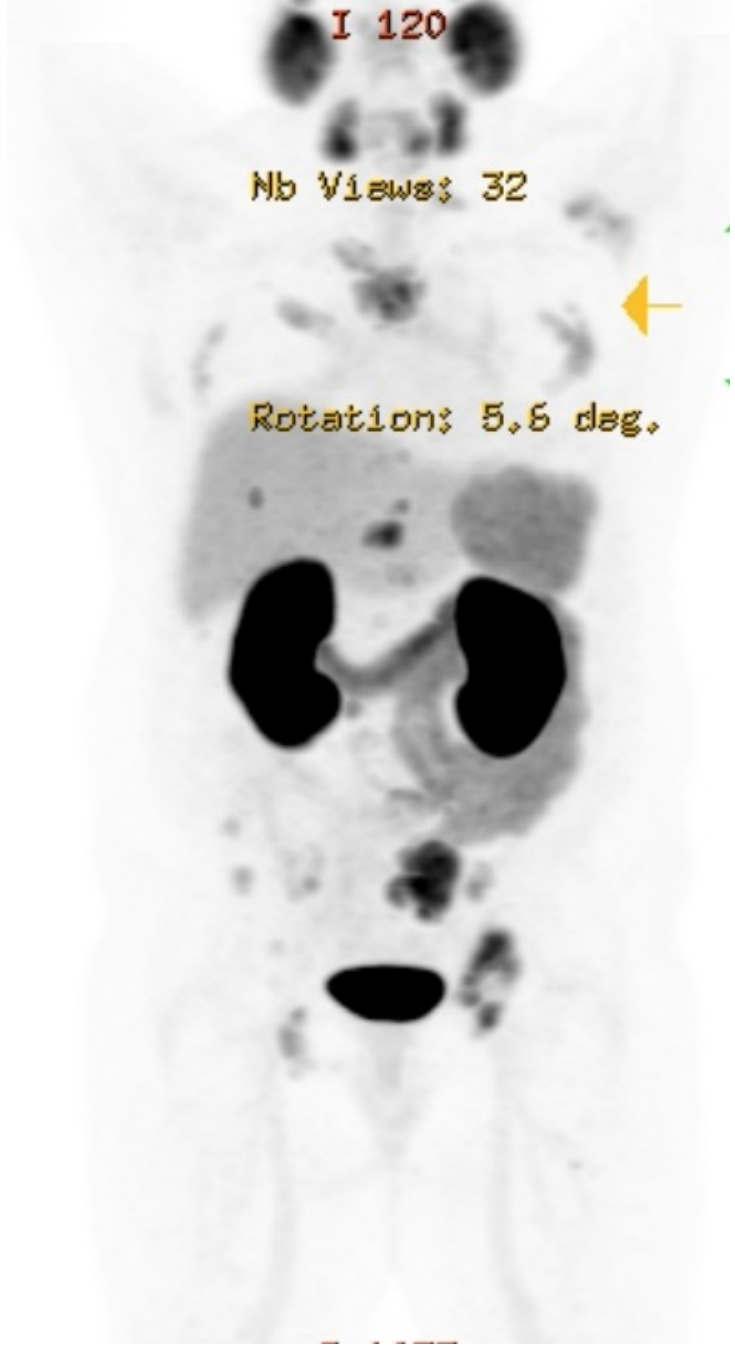
https://www.jci.org/articles/view/169655

Mr. JA treatment update:

- Received Lu-PSMA, completed 6 cycles.
- Tolerated well







Baseline

End of treatment

Summary

- Front-line treatment of prostate cancer evolved by the addition of doublet and triplet combination
- Lu-PSMA-617 is FDA approved for mCRPC post NHA, post taxane
  - PSMAfore and ENZA-P establish the activity of Lu-PSMA-617 post NHA prior to taxane.
- Several trials are testing novel agents, including other PSMA targeted therapies and novel combinations.
- mCRPC treatment will continue to evolve in the near future.

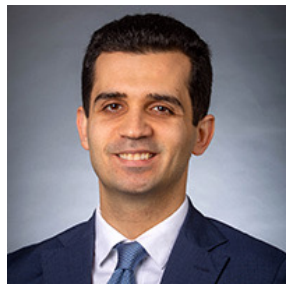
Thank you….

Welcome to our grou
and + 3 new addition

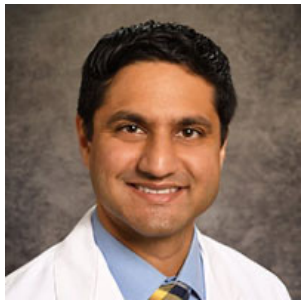
Medical Oncology





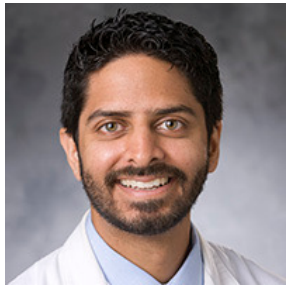



Urologic Oncology




Radiation Oncology

Nuclear Med

Immunology

Epidemiology

GTech