

19^{as} Jornadas HITOS ONCOLÓGICOS: LO MEJOR DE 2024

MADRID 20 - 21 NOVIEMBRE 2024



15:50-16:35

MESA DE CÁNCER GENITOURINARIO II

Modera:

Dr. Javier Cassinello, Hospital Universitario de Guadalajara

15:50-16:05

Cáncer de próstata metastásico sensible a castración

Dr. Álvaro Pinto, Hospital Universitario La Paz, Madrid

16:05-16:20

Cambio de paradigma en el cáncer de próstata: terapia con radioligandos

Dr. José Ángel Arranz, Hospital General Universitario Gregorio Marañón, Madrid

16:20-16:35

DISCUSIÓN

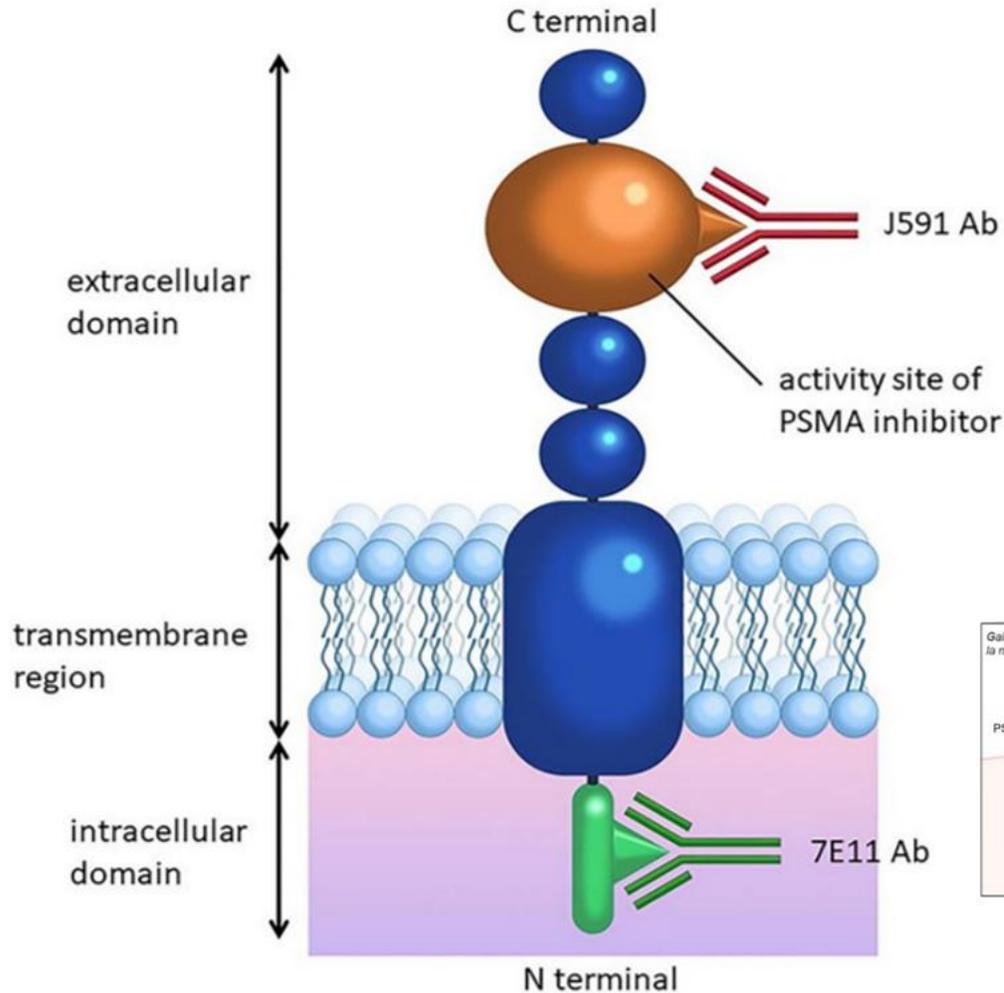
MD Anderson
Cancer Center
Madrid · España



- PSMA “Antígeno prostático específico de membrana”

- Galio⁶⁸-PSMA-11 [PSMA 11: Gozetotida (Locametz®)]

- Lutecio¹⁷⁷-PSMA-617 [Pluvicto®]



PET

⁸⁹Zr-J591

¹²⁴I-J591

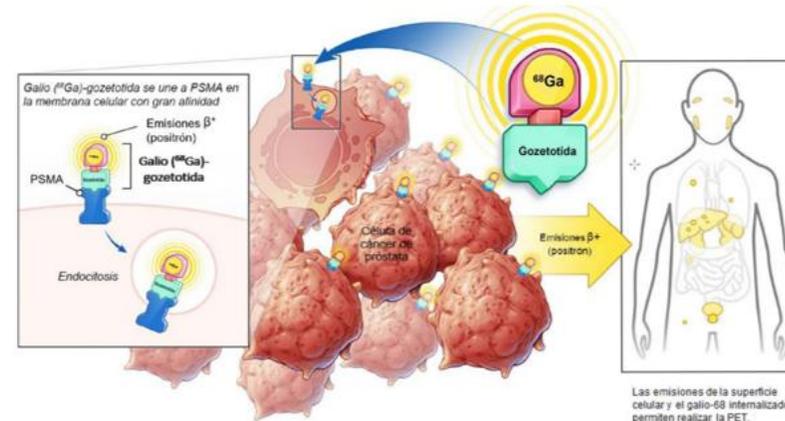
⁶⁸Ga-PSMA-11

¹⁸F-DCFBC

¹⁸F-DCFPyL

¹⁸F-PSMA-1007

¹⁸F-rhPSMA



TERAPIA

¹⁷⁷Lu-J591

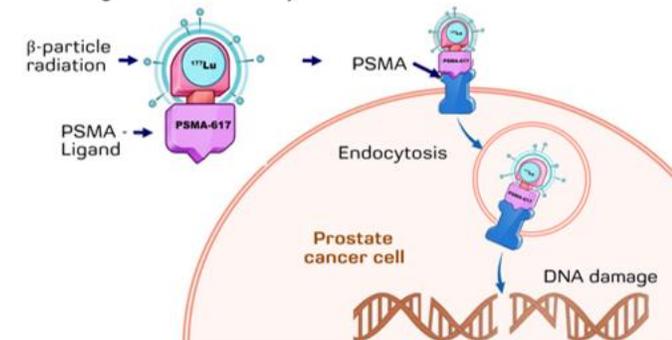
⁹⁰Y-J591

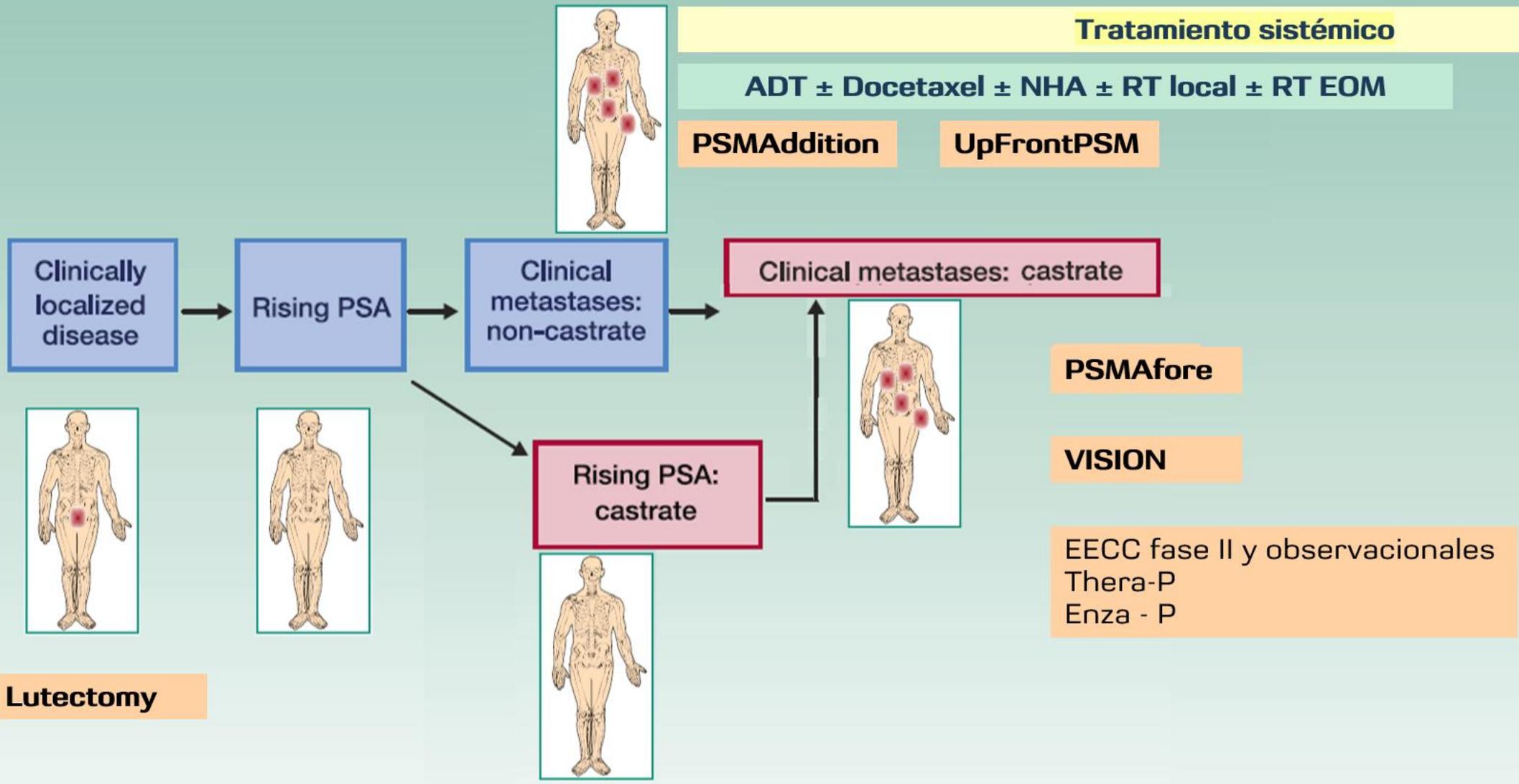
¹⁷⁷Lu-PSMA-I&T

¹⁷⁷Lu-PSMA-617

²²⁵Ac-PSMA-617

¹³¹I-MIP-1095





- 2016 **Series de casos**
- 2017 **Metanálisis de estudios retrospectivos**
- 2018 Hofman **Fase II CPRC**
 - 57% ↓ PSA > 50%

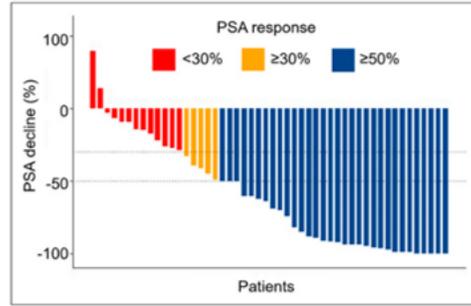
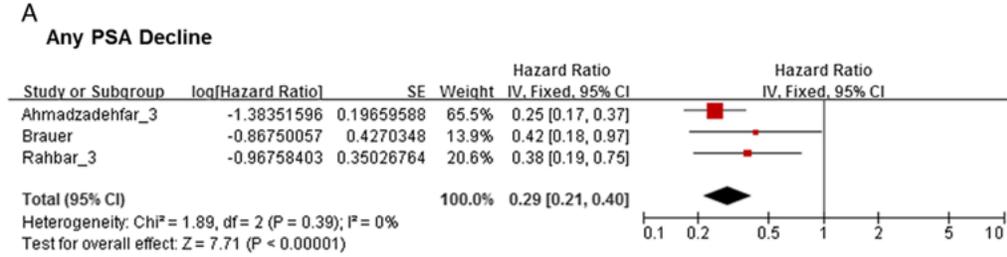


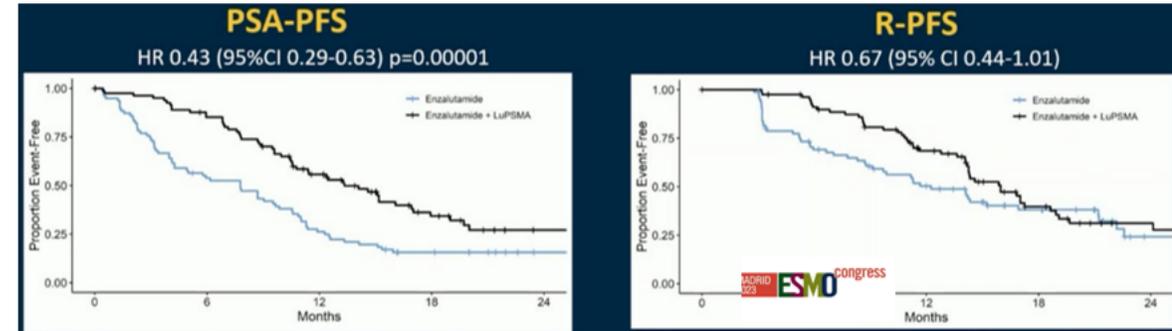
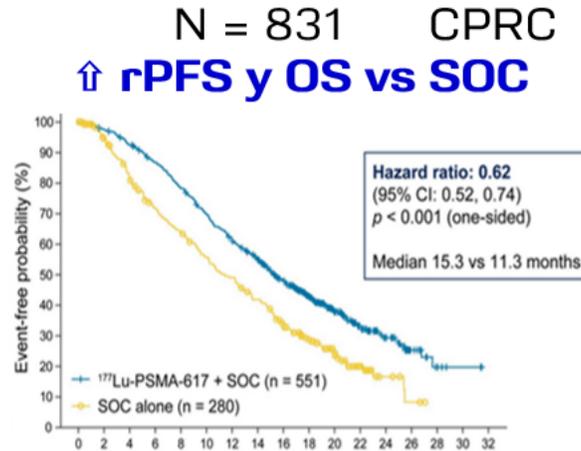
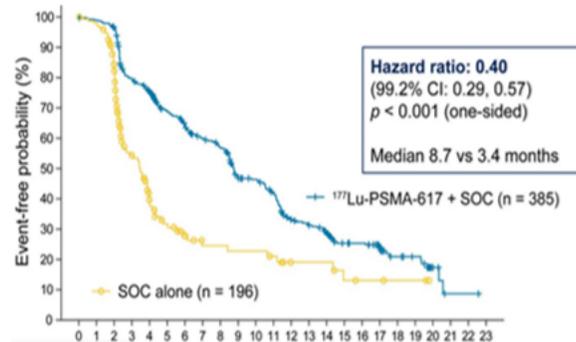
FIGURE 2. Waterfall plot of best PSA decline compared with baseline.

1 - 4 ciclos 30 - 60% ↓ PSA > 50%
 ≥ 1 ciclo 34.5% ↓ PSA > 50%
 Mayor SG si ↓ PSA



- 2021 Hofman Fase IIR CPRC **TheraP ANZUP 1603** N = 200 CPRC
- 2023 Emmet Fase IIR CPRC **EnzaP ANZUP 1901** N = 162 CPRC
- 2021 Morris Fase III CPRC **VISION** Hasta 6 ciclos N = 831 CPRC

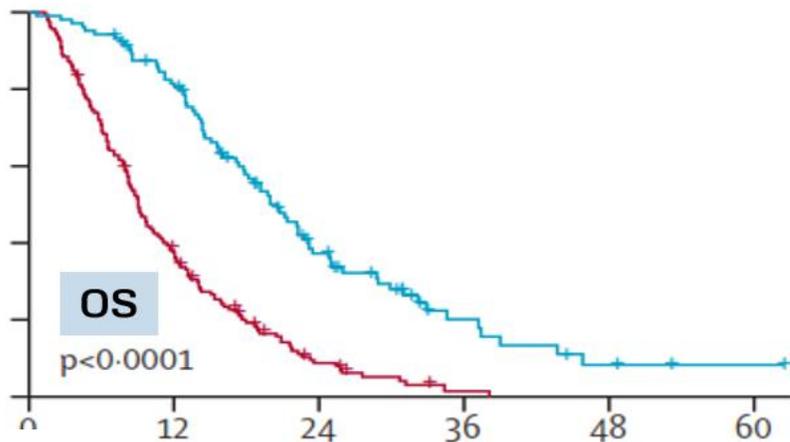
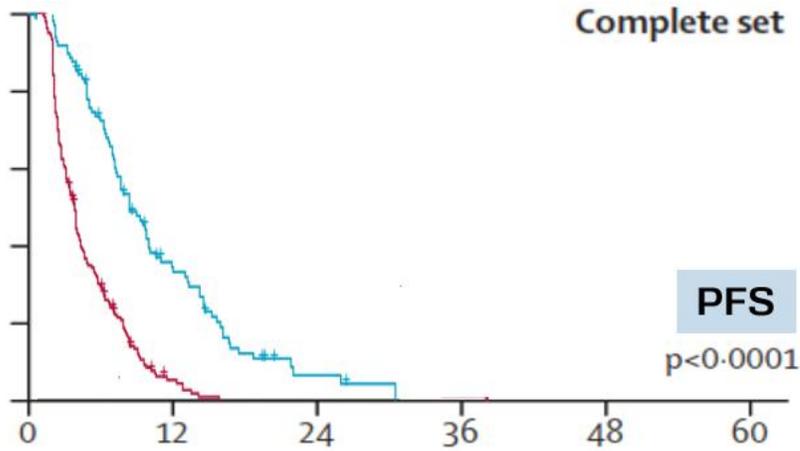
Hasta 6 ciclos ↑ ↓ PSA > 50% vs Cabazitaxel [66% vs 37%]. No ↑ SG
 Hasta 6 ciclos ↑ PSA-PFS vs Enzalutamida [13 vs 7.8 m]



Nomograms to predict outcomes after ¹⁷⁷Lu-PSMA therapy in men with metastatic castration-resistant prostate cancer: an international, multicentre, retrospective study

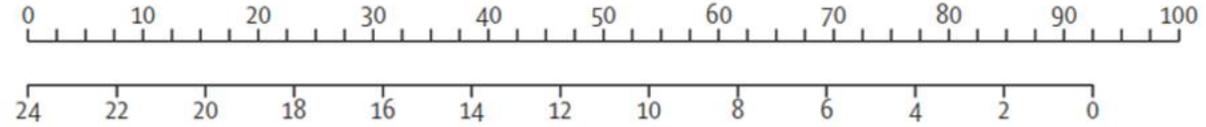
Andrei Gafita, Jeremie Calais, Tristan R Grogan, Boris Hadaschik, Hui Wang, Manuel Weber, Shahneen Sandhu, Clemens Kratochwil, Rouzbeh Esfandiari, Robert Tauber, Anna Zeldin, Hendrik Rathke, Wesley R Armstrong, Andrew Robertson, Pan Thin, Calogero D'Alessandria, Matthew B Rettig, Ebrahim S Delpassand, Uwe Haberkorn, David Elashoff, Ken Herrmann, Johannes Czernin, Michael S Hofman, Wolfgang P Fendler, Matthias Eiber

Lancet Oncol 2021; 22: 1115-25

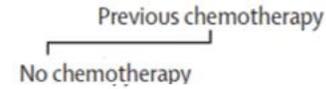


Points

Time since diagnosis (years)



Chemotherapy status



Haemoglobin (g/dL)



Tumour SUV_{mean}



Number of lesions



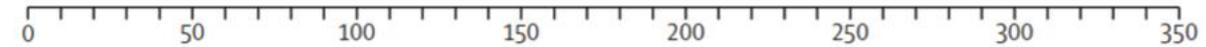
Bone metastases



Liver metastases



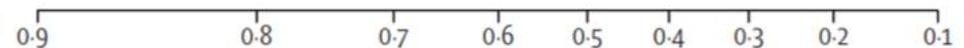
Total points



12-month overall survival probability



18-month overall survival probability



Health-related quality of life and pain outcomes with [¹⁷⁷Lu] Lu-PSMA-617 plus standard of care versus standard of care in patients with metastatic castration-resistant prostate cancer (VISION): a multicentre, open-label, randomised, phase 3 trial

Karim Fizazi, Ken Herrmann, Bernd J Krause, Kambiz Rahbar, Kim N Chi, Michael J Morris, Oliver Sartor, Scott T Tagawa, Ayse T Kendi, Nicholas Vogelzang, Jeremie Calais, James Nagarajah, Xiao X Wei, Vadim S Koshkin, Jean-Mathieu Beaugreard, Brian Chang, Ray Ghossein, Michelle DeSilvio, Richard A Messmann, Johann de Bono

Lancet Oncol 2023; 24: 597-610

	[¹⁷⁷ Lu]Lu-PSMA-617 plus standard of care (n=385)	Standard of care (n=196)	Hazard ratio (95% CI)
Bone-targeted agents			
Symptomatic skeletal event or death	115/175 (66%)	66/96 (69%)	..
Median time to event, months	12.0 (10.0-14.2)	7.2 (5.6-10.2)	0.49 (0.36-0.68)
Median follow-up time, months	17.1 (14.6-17.7)	16.6 (11.0-NE)	..
No bone-targeted agents			
Symptomatic skeletal event or death	141/210 (67%)	71/100 (71%)	..
Median time to event, months	11.5 (9.8-13.7)	5.8 (4.1-9.2)	0.50 (0.37-0.68)
Median follow-up time, months	17.0 (15.6-17.4)	19.8 (11.5-NE)	..
Overall			
Symptomatic skeletal event or death	256/385 (66%)	137/196 (70%)	..
Median time to event, months	11.5 (10.3-13.2)	6.8 (5.2-8.5)	0.50 (0.40-0.62)
Median follow-up time, months	17.0 (15.9-17.3)	16.9 (11.5-NE)	..

Data are n/N (%) or median (95% CI). Stratified by concurrent use of bone-targeted agents as part of standard of care. Hazard ratio based on Cox proportional hazards model stratified for lactate dehydrogenase (≤ 260 IU/L vs >260 IU/L); presence of liver metastases (yes vs no); Eastern Cooperative Oncology Group performance status score (0 or 1 vs 2); and inclusion of androgen receptor pathway inhibitor in best supportive care or standard of care at time of randomisation (yes vs no). Median time to event and median follow-up times estimated from Kaplan-Meier curves censored for event (symptomatic skeletal event or death). Analyses in the 581 patients randomly assigned after measures were implemented on or after March 5, 2019. NE=not estimable. Lu=lutetium. PSMA=prostate-specific membrane antigen.

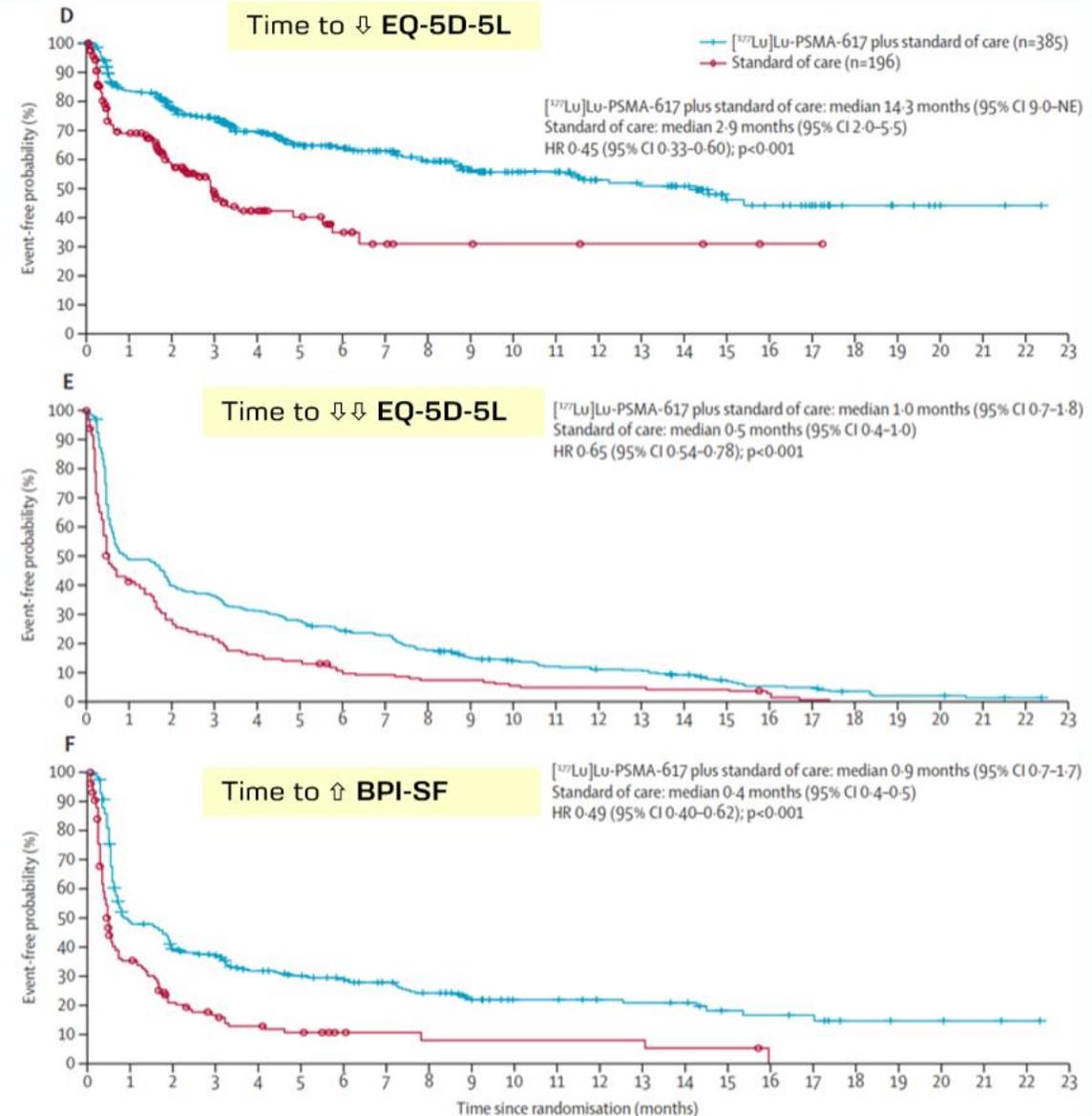
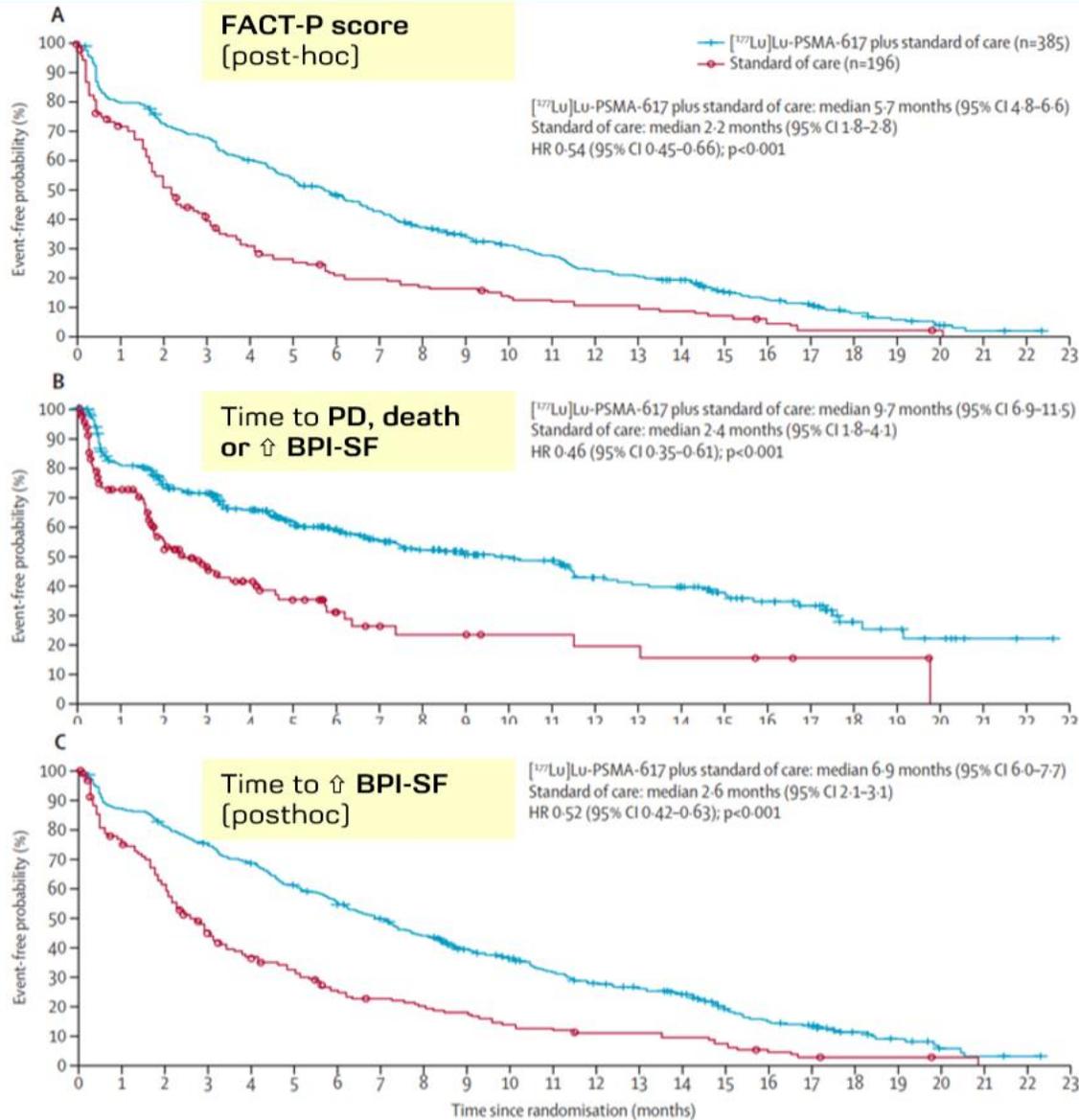
Table 3: Overall and post-hoc subgroup analysis of time to first symptomatic skeletal event or death

Background In VISION, the prostate-specific membrane antigen (PSMA)-targeted radioligand therapy lutetium-177 [¹⁷⁷Lu]Lu-PSMA-617 (vipivotide tetraxetan) improved radiographic progression-free survival and overall survival when added to protocol-permitted standard of care in patients with metastatic castration-resistant prostate cancer. Here, we report additional health-related quality of life (HRQOL), pain, and symptomatic skeletal event results.

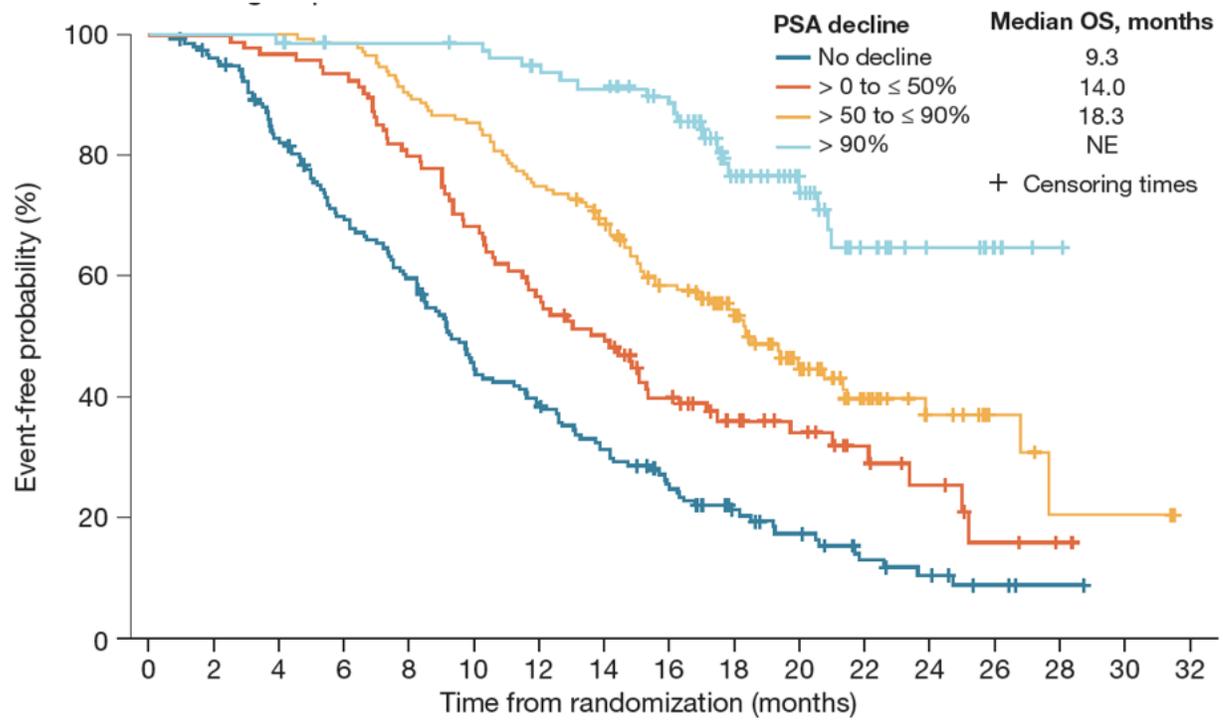
Methods This multicentre, open-label, randomised, phase 3 trial was conducted at 84 cancer centres in nine countries in North America and Europe. Eligible patients were aged 18 years or older; had progressive PSMA-positive metastatic castration-resistant prostate cancer; an Eastern Cooperative Oncology Group (ECOG) performance status score of 0-2; and had previously received of at least one androgen receptor pathway inhibitor and one or two taxane-containing regimens. Patients were randomly assigned (2:1) to receive either [¹⁷⁷Lu]Lu-PSMA-617 plus protocol-permitted standard of care ([¹⁷⁷Lu]Lu-PSMA-617 group) or standard of care alone (control group) using permuted blocks. Randomisation was stratified by baseline lactate dehydrogenase concentration, liver metastases, ECOG performance status, and androgen receptor pathway inhibitor inclusion in standard of care. Patients in the [¹⁷⁷Lu]Lu-PSMA-617 group received intravenous infusions of 7.4 gigabecquerel (GBq; 200 millicurie [mCi]) [¹⁷⁷Lu]Lu-PSMA-617 every 6 weeks for four cycles plus two optional additional cycles. Standard of care included approved hormonal treatments, bisphosphonates, and radiotherapy. The alternate primary endpoints were radiographic progression-free survival and overall survival, which have been reported. Here we report the key secondary endpoint of **time to first symptomatic skeletal event**, and other secondary endpoints of HRQOL assessed with the Functional Assessment of Cancer Therapy-Prostate (FACT-P) and EQ-5D-5L, and pain assessed with the Brief Pain Inventory-Short Form (BPI-SF). Patient-reported outcomes and symptomatic skeletal events were analysed in all patients who were randomly assigned after implementation of measures designed to reduce the dropout rate in the control group (on or after March 5, 2019), and safety was analysed according to treatment received in all patients who received at least one dose of treatment. This trial is registered with ClinicalTrials.gov, NCT03511664, and is active but not recruiting.

Findings Between June 4, 2018, and Oct 23, 2019, 831 patients were enrolled, of whom **581 were randomly assigned to the [¹⁷⁷Lu]Lu-PSMA-617 group (n=385) or control group (n=196) on or after March 5, 2019, and were included in analyses of HRQOL, pain, and time to first symptomatic skeletal event.** The median age of patients was 71 years (IQR 65-75) in the [¹⁷⁷Lu]Lu-PSMA-617 group and 72.0 years (66-76) in the control group. **Median time to first symptomatic skeletal event or death was 11.5 months (95% CI 10.3-13.2) in the [¹⁷⁷Lu]Lu-PSMA-617 group and 6.8 months (5.2-8.5) in the control group (hazard ratio [HR] 0.50, 95% CI 0.40-0.62).** Time to worsening was delayed in the [¹⁷⁷Lu]Lu-PSMA-617 group versus the control group for **FACT-P score (HR 0.54, 0.45-0.66) and subdomains, BPI-SF pain intensity score (0.52, 0.42-0.63), and EQ-5D-5L utility score (0.65, 0.54-0.78).** **Grade 3 or 4 haematological adverse events included decreased haemoglobin (80 [15%] of 529 assessable patients who received [¹⁷⁷Lu]Lu-PSMA-617 plus standard of care vs 13 [6%] of 205 who received standard of care only), lymphocyte concentrations (269 [51%] vs 39 [19%]), and platelet counts (49 [9%] vs five [2%]).** Treatment-related adverse events leading to **death occurred in five (1%) patients who received [¹⁷⁷Lu]Lu-PSMA-617 plus standard of care (pancytopenia [n=2], bone marrow failure [n=1], subdural haematoma [n=1], and intracranial haemorrhage [n=1]) and no patients who received standard of care only.**

Interpretation [¹⁷⁷Lu]Lu-PSMA-617 plus standard of care **delayed time to worsening in HRQOL and time to skeletal events compared with standard of care alone.** These findings support the use of [¹⁷⁷Lu]Lu-PSMA-617 in patients with metastatic castration-resistant prostate cancer who received previous androgen receptor pathway inhibitor and taxane treatment.



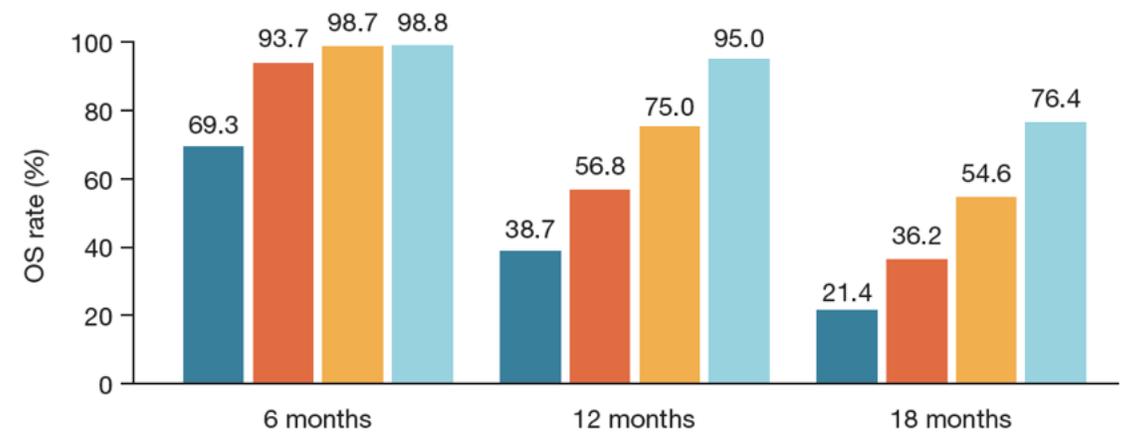
OS by PSA decline up to 12 weeks in the LuPSMA arm



Number of patients still at risk

—	161	153	130	107	92	68	59	47	35	24	18	11	8	3	1	0	0
—	95	95	92	89	76	65	54	46	34	24	18	11	7	3	1	0	0
—	152	152	152	150	137	130	114	101	81	60	38	20	12	6	2	2	0
—	83	83	82	80	80	79	75	72	65	44	28	14	7	3	1	0	0

OS rate by PSA decline up to 12 weeks in the LuPSMA arm



Andrew J Armstrong, et al, ESMO 2022



Dr. Shahneen Sandhu

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Quantitative ⁶⁸Ga-PSMA-11 PET and Clinical Outcomes in Metastatic Castration-resistant Prostate Cancer Following ¹⁷⁷Lu-PSMA-617 (VISION Trial)

Phillip H. Kuo, MD, PhD* • Michael J. Morris, MD* • Jacob Hesterman, PhD • A. Tuba Kendi, MD •

Radiology 2024; 312(2):e233460

Background: Lutetium 177 [¹⁷⁷Lu]Lu-PSMA-617 (¹⁷⁷Lu-PSMA-617) is a prostate-specific membrane antigen (PSMA)-targeted radioligand therapy for metastatic castration-resistant prostate cancer (mCRPC). Quantitative PSMA PET/CT analysis could provide information on ¹⁷⁷Lu-PSMA-617 treatment benefits.

Purpose: To explore the association between quantitative baseline gallium 68 [⁶⁸Ga]Ga-PSMA-11 (⁶⁸Ga-PSMA-11) PET/CT parameters and treatment response and outcomes in the VISION trial.

Materials and Methods: This was an exploratory secondary analysis of the VISION trial. Eligible participants were randomized (June 2018 to October 2019) in a 2:1 ratio to ¹⁷⁷Lu-PSMA-617 therapy (7.4 GBq every 6 weeks for up to six cycles) plus standard of care (SOC) or to SOC only. Baseline ⁶⁸Ga-PSMA-11 PET parameters, including the mean and maximum standardized uptake value (SUV_{mean} and SUV_{max}), PSMA-positive tumor volume, and tumor load, were extracted from five anatomic regions and the whole body. Associations of quantitative PET parameters with radiographic progression-free survival (rPFS), overall survival (OS), objective response rate, and prostate-specific antigen response were investigated using univariable and multivariable analyses (with treatment as the only other covariate). Outcomes were assessed in subgroups based on SUV_{mean} quartiles.

Results: Quantitative PET parameters were well balanced between study arms for the 826 participants included. The median whole-body tumor SUV_{mean} was 7.6 (IQR, 5.8–9.9). Whole-body tumor SUV_{mean} was the best predictor of ¹⁷⁷Lu-PSMA-617 efficacy, with a hazard ratio (HR) range of 0.86–1.43 for all outcomes (all *P* < .001). A 1-unit whole-body tumor SUV_{mean} increase was associated with a 12% and 10% decrease in risk of an rPFS event and death, respectively. ¹⁷⁷Lu-PSMA-617 plus SOC prolonged rPFS and OS in all SUV_{mean} quartiles versus SOC only, with no identifiable optimum among participants receiving ¹⁷⁷Lu-PSMA-617. Higher baseline PSMA-positive tumor volume and tumor load were associated with worse rPFS (HR range, 1.44–1.53 [*P* < .05] and 1.02–1.03 [*P* < .001], respectively) and OS (HR range, 1.36–2.12 [*P* < .006] and 1.04 [*P* < .001], respectively).

Conclusion: Baseline ⁶⁸Ga-PSMA-11 PET/CT whole-body tumor SUV_{mean} was the best predictor of ¹⁷⁷Lu-PSMA-617 efficacy in participants in the VISION trial. Improvements in rPFS and OS with ¹⁷⁷Lu-PSMA-617 plus SOC were greater among participants with higher whole-body tumor SUV_{mean}, with evidence for benefit at all SUV_{mean} levels.

	SUV _{mean} quartile	Events (n/N)		Median (months; 95% CI)		HR (95% CI) ¹⁷⁷ Lu-PSMA-617 + SoC vs SoC only
		¹⁷⁷ Lu-PSMA-617 + SoC	SoC only	¹⁷⁷ Lu-PSMA-617 + SoC	SoC only	
rPFS	<6.0	65/94	19/50	5.8 (4.1, 8.2)	4.0 (2.2, NE)	0.75 (0.45, 1.26)
	≥6.0 – <7.8	65/95	29/49	7.8 (5.8, 8.8)	2.5 (2.1, 3.4)	0.19 (0.11, 0.31)
	≥7.8 – <10.1	70/96	21/48	9.8 (7.8, 11.0)	4.3 (2.4, 7.0)	0.57 (0.35, 0.95)
	≥10.1	51/97	23/47	13.8 (11.3, 17.8)	3.9 (2.1, 5.0)	0.34 (0.20, 0.56)
OS	<5.7	95/139	39/67	14.5 (11.9, 15.9)	11.3 (8.9, 13.5)	0.87 (0.60, 1.27)
	≥5.7 – <7.5	98/141	48/66	12.6 (10.5, 15.0)	9.4 (6.7, 12.3)	0.58 (0.41, 0.83)
	≥7.5 – <9.9	88/132	50/75	14.6 (12.0, 16.9)	12.3 (7.7, 15.2)	0.70 (0.49, 0.99)
	≥9.9	60/136	48/71	21.4 (18.2, NE)	15.0 (9.9, 19.0)	0.47 (0.32, 0.68)

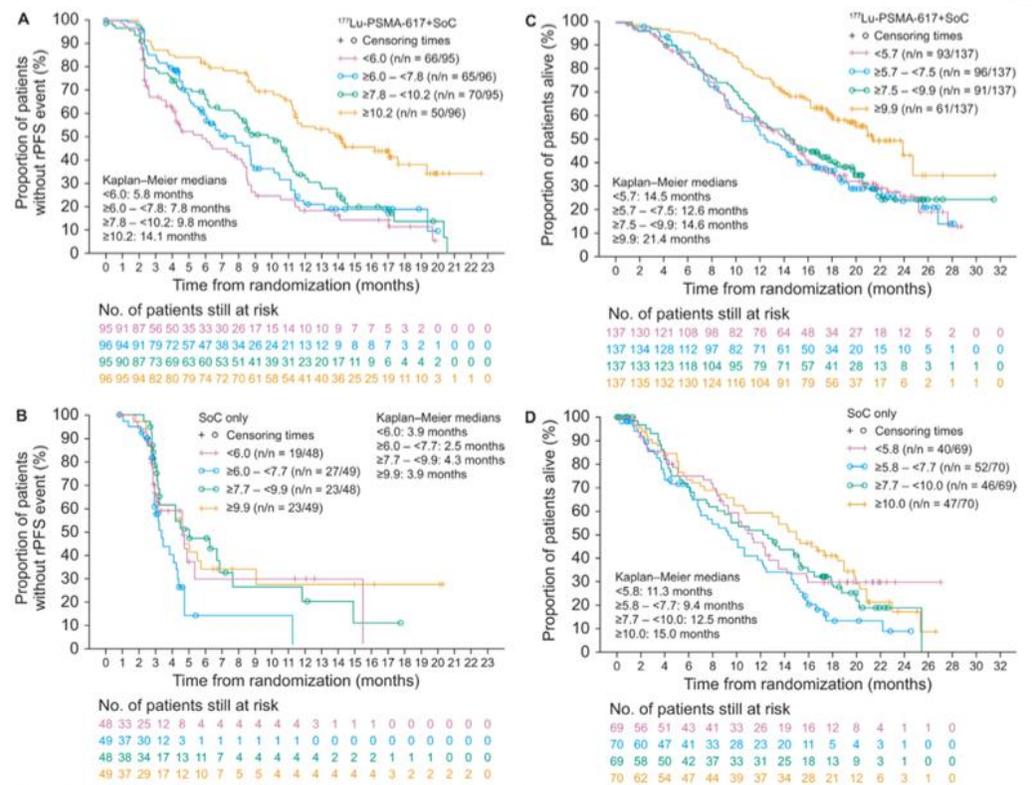


Figure 5: Kaplan-Meier curves show radiographic progression-free survival (rPFS) according to whole-body tumor mean standardized uptake value (SUV_{mean}) quartile for (A) ¹⁷⁷Lu-PSMA-617 plus standard of care (SOC) (n = 382) and (B) SOC only (n = 194) treatment arms (body, progression-free survival, full analysis set). SUV_{mean} quartiles were derived from either the SUV_{mean} of the ¹⁷⁷Lu-PSMA-617 plus SOC arm or the SOC only arm. PSMA = prostate-specific membrane antigen (Fig 5 continues).

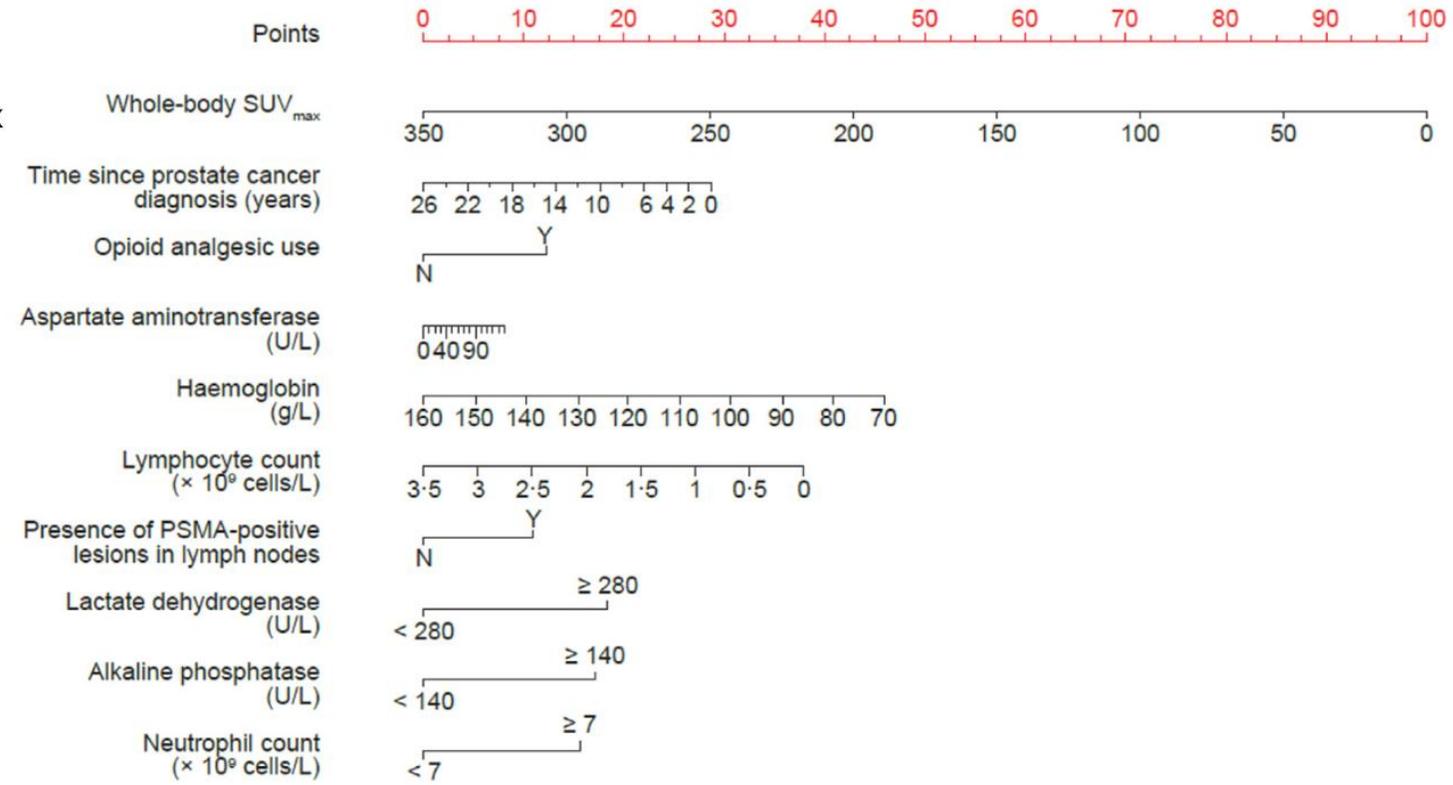
Figure 5 (continued): Kaplan-Meier curves show overall survival according to whole-body tumor mean standardized uptake value (SUV_{mean}) quartile for (C) ¹⁷⁷Lu-PSMA-617 plus standard of care (SOC) (n = 548) and (D) SOC only (n = 278) treatment arms (body, full analysis set). SUV_{mean} quartiles were derived from either the SUV_{mean} of the ¹⁷⁷Lu-PSMA-617 plus SOC arm or the SOC only arm. PSMA = prostate-specific membrane antigen.

Multivariable models of outcomes with [¹⁷⁷Lu]Lu-PSMA-617: analysis of the phase 3 VISION trial

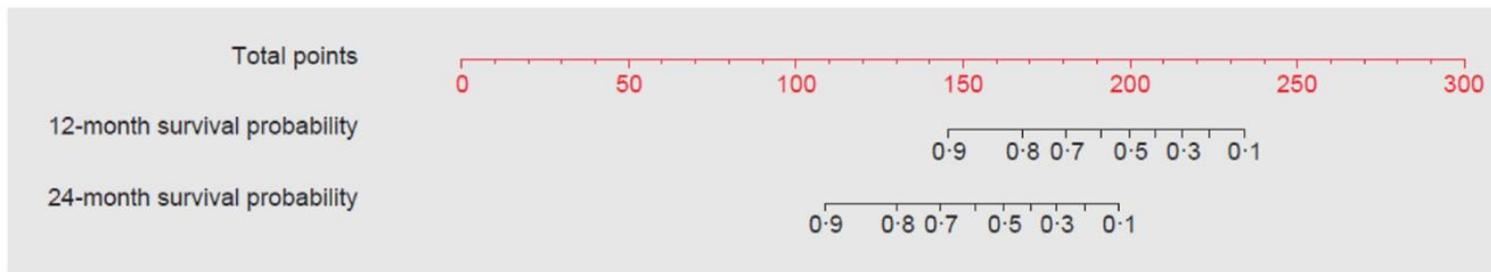
Ken Herrmann,^{a,p,*} Andrei Gafita,^{b,p} Johann S. de Bono,^c Oliver Sartor,^d Kim N. Chi,^e Bernd J. Krause,^f Kambiz Rahbar,^g Scott T. Tagawa,^h Johannes Czernin,ⁱ Ghassan El-Haddad,^j Connie C. Wong,^k Zhaojie Zhang,^k Celine Wilke,^l Osvaldo Mirante,^m Michael J. Morris,^{n,q} and Karim Fizazi^{o,q}

Vol 77 November, 2024

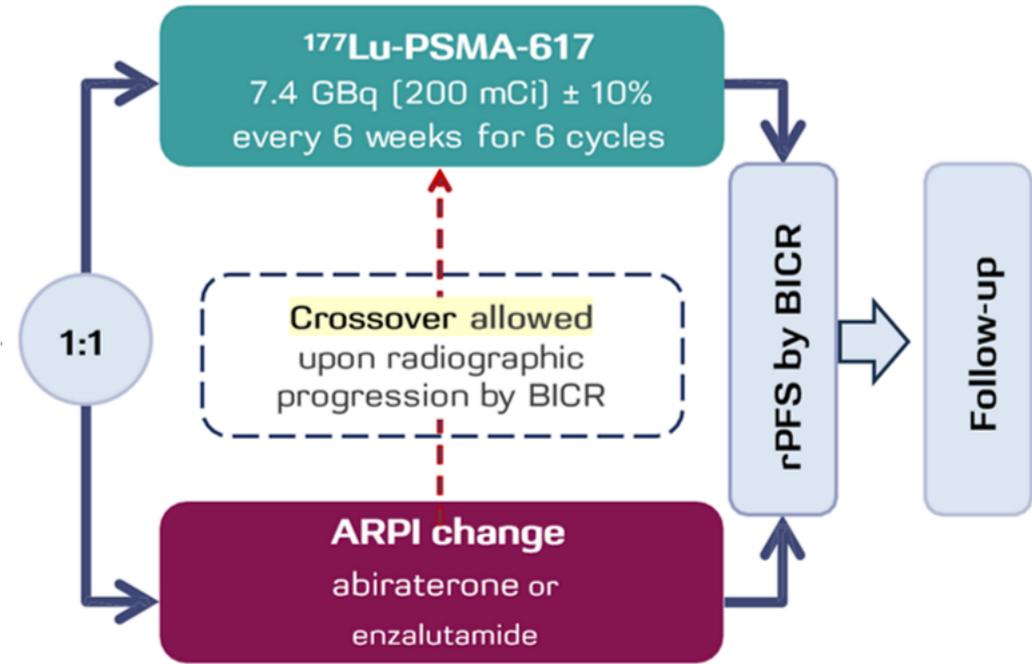
- **Nomograma para OS**
 - ↳ Solo pt tratados con 177-Lu
 - ↳ Incluye Whole-body SUVmax
- **C-index: 0.73**
[95% CI, 0.70-0.76].



The value of each pretreatment parameter [listed on the left] indicates a certain number of points according to the alignment with the points scale at the top of the nomogram. Points for all parameters are summed to provide a total points score [red line in grey box]. The total points score corresponds to respective 12- and 24month OS probabilities.



- Eligible adults**
- Confirmed progressive **mCRPC**
 - **≥ 1 PSMA-positive metastatic lesion on [68Ga]Ga-PSMA-11 PET/CT** and no exclusionary PSMA-negative lesions
 - **Progressed once on prior second-generation ARPI + candidates for change in ARPI**
 - **Taxane-naïve** [except [neo] adjuvant > 12 months ago]
 - **Not candidates for PARPi**
 - **ECOG performance status 0-1**



Primary end point: rPFS
[BICR] PCWG3/ RECIST 1.1

Key secondary end point: OS

OS prespecified for RPSFT crossover-adjusted analysis

Other secondary endpoints

- rPFS2
- PFS, PFS2
- PSA50
- Time to SSE
- Time to soft tissue progression
- Time to chemotherapy
- HRQoL
- Safety and tolerability

Exploratory endpoints

- ORR, DCR, DOR
- Time to PSA progression
- Time to pain progression
- Biomarker associations

Stratification factors

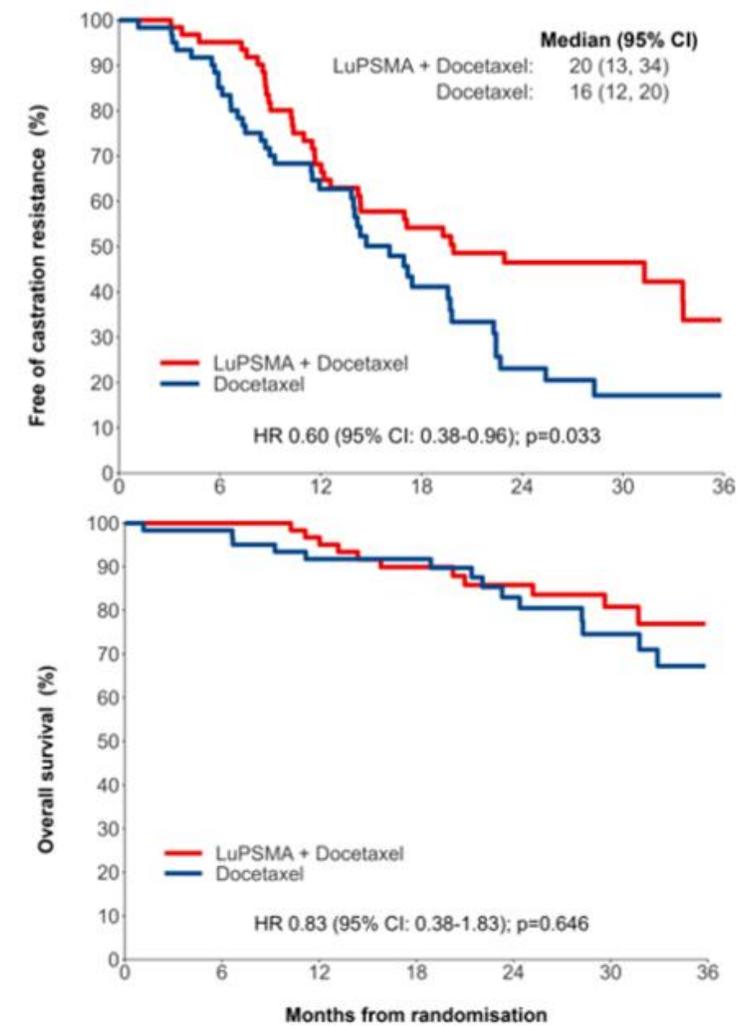
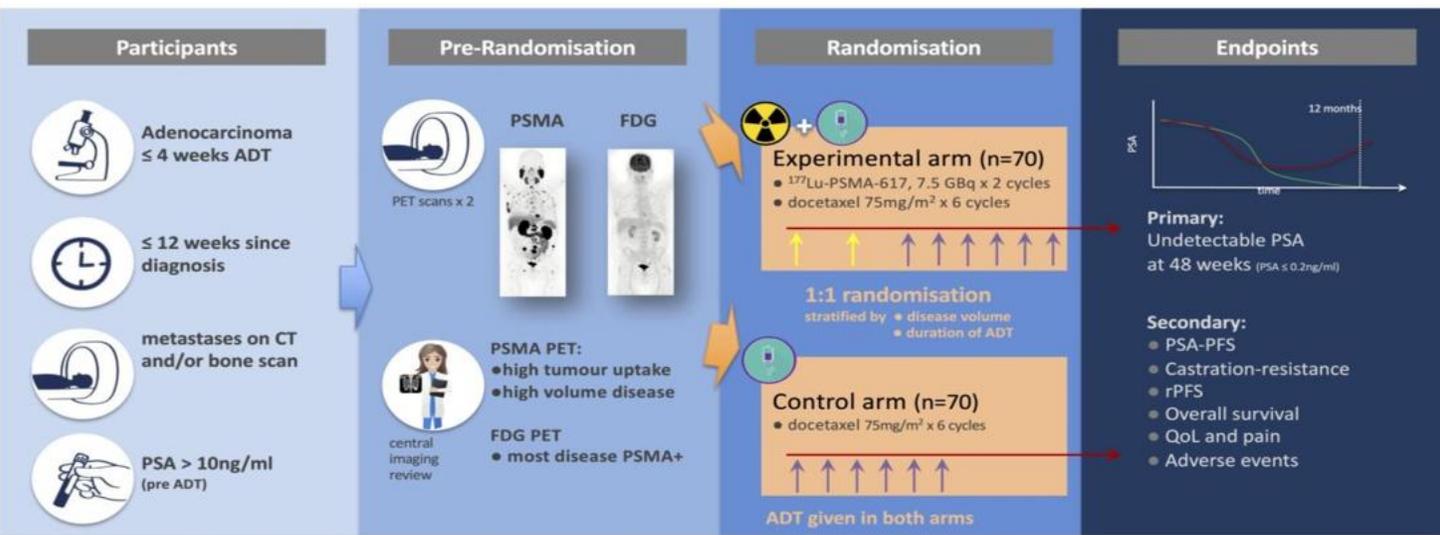
- **Prior ARPI** setting [castration-resistant vs hormone-sensitive]
- **BPI-SF** worst pain intensity score [0-3 vs > 3]



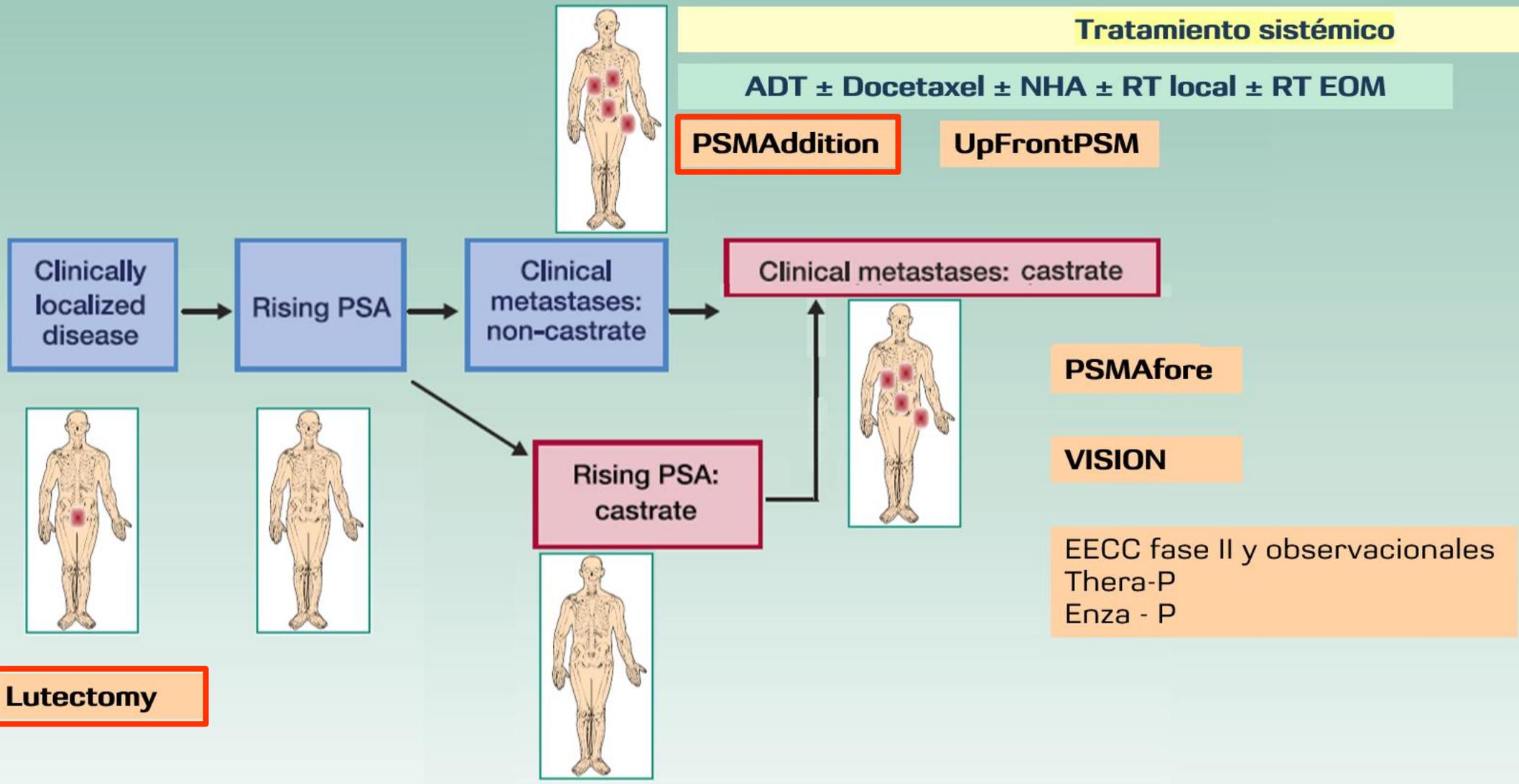
Patient disposition at 2nd IA OS

Screened	585	
68Ga-PSMA-11 PET	547	
	PSMA+: 505	
Randomized	177Lu-PSMA-617: 234	ARPI change: 234
Treated	227 [97.0%]	232 [99.1%]
Discontinued due to Rx progression	51 [21.8%]	146 [62.4%]
	Crossover to 177Lu-PSMA-617: 123/146 [84.2%]	

- ECA FIIR: Análisis final. Objetivo : RC bioquímica.
- Pacientes con CPHSM1 de novo y alto volumen: ADT+ Docetaxel ± 177-Lutecio
- N: 140, Potencia 85% para \hat{u} del 25% al 50% la RC PSA a 6m (CHAARTED 27% a 12m)



Treatment	Lu-PSMA + docetaxel (n=61)*	Docetaxel (n=61)*
Undetectable PSA at week 48, %	41% (95% CI 30-54)	16% (95% CI 9-28)
	OR 3.88 (95% CI 1.61-9.38); p=0.002	
Undetectable PSA at any time point, %	51% (95% CI 39-63)	32% (95% CI 22-45)
	OR 2.14 (95% CI 1.03-4.46); p=0.042	
Undetectable PSA at week 12, %	17% (95% CI 10-29)	18% (95% CI 10-29)
	OR 0.94 (95% CI 0.37-2.36); p=0.895	





15:50-16:35

MESA DE CÁNCER GENITOURINARIO II

Modera:

Dr. Javier Cassinello, Hospital Universitario de Guadalajara

15:50-16:05

Cáncer de próstata metastásico sensible a castración

Dr. Álvaro Pinto, Hospital Universitario La Paz, Madrid

16:05-16:20

Cambio de paradigma en el cáncer de próstata: terapia con radioligandos

Dr. José Ángel Arranz, Hospital General Universitario Gregorio Marañón, Madrid

16:20-16:35

DISCUSIÓN