

**¿Dónde ubicamos el tratamiento con radioligandos en el espectro
del cáncer de próstata avanzado?**

**Where do we place radioligand treatment in the spectrum of
advanced prostate cancer?**



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Servicio de Medicina Nuclear
Hospital Universitario 12 de Octubre

DISCLOSURES

Scientific Advisory Board and/or speaker:

Adacap, Novartis, Astellas, Bayer, Johnson & Johnson Innovative Medicine Spain, GE HealthCare, MSD, Pharmalex, Luzan5.

Research grants: None

Co-founder: None

Board Member: SEMNim

Shareholder: None

Where? or Whom?

- La RLT con ligandos PSMA en el cáncer de próstata se ha posicionado al final del resto de tratamientos... (CPRCm tras ADT-ARPI-Taxanos).
- La **teragnosis** es un concepto nuevo, donde **imagen y tratamiento van de la mano**.
- El **PET PSMA** es **disruptivo**...
- La **medicina** de precisión y **personalizada**, no encaja bien con las clasificaciones tradicionales para una población.
- *“Dos planteamientos diferentes que confundirse”*



¿Qué **pacientes** se **benefician** de **^{177}Lu -PSMA** (indicación)?
¿Cuales son los **mejores respondedores**?

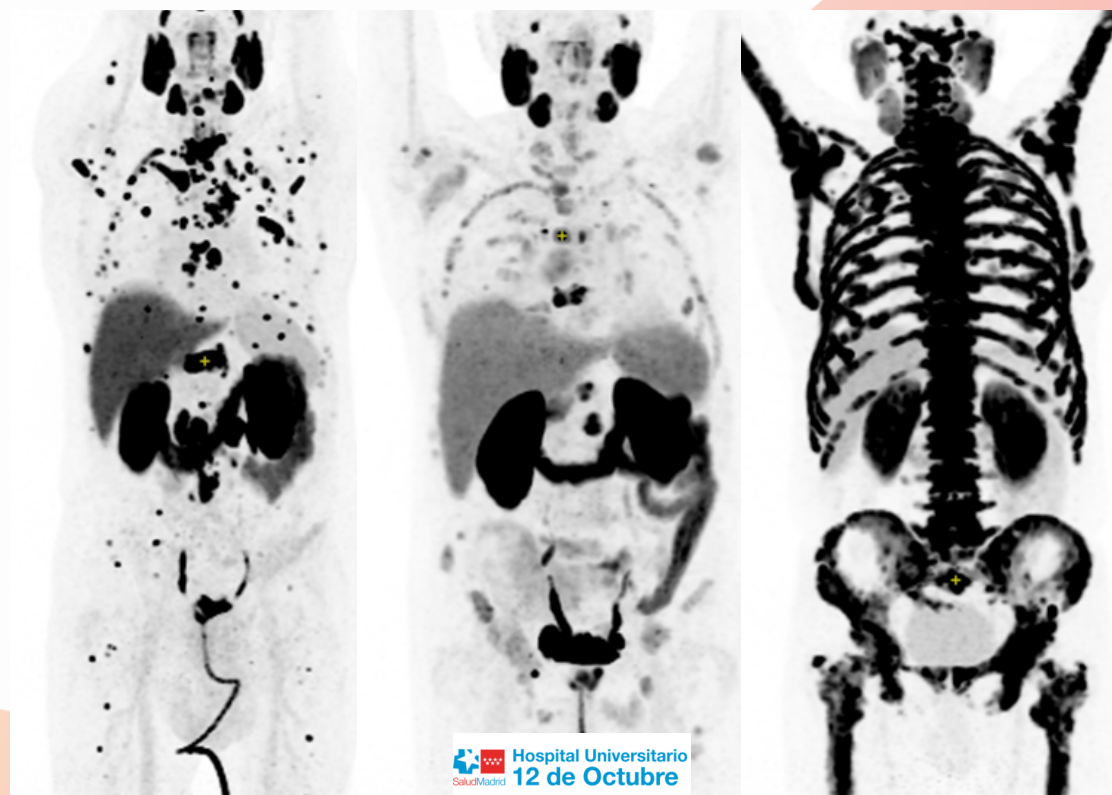
Where?

1. Pacientes con indicación de **^{177}Lu -PSMA.**

Whom?

1. Criterio selección por PET PSMA
2. Selección de mejores respondedores.

CPRCm progresados a ADT-ARPI-Taxanos PET PSMA+



¿Son inguales?
¿Se benefician de ^{177}Lu -PSMA?
¿Responderán igual al ^{177}Lu -PSMA?

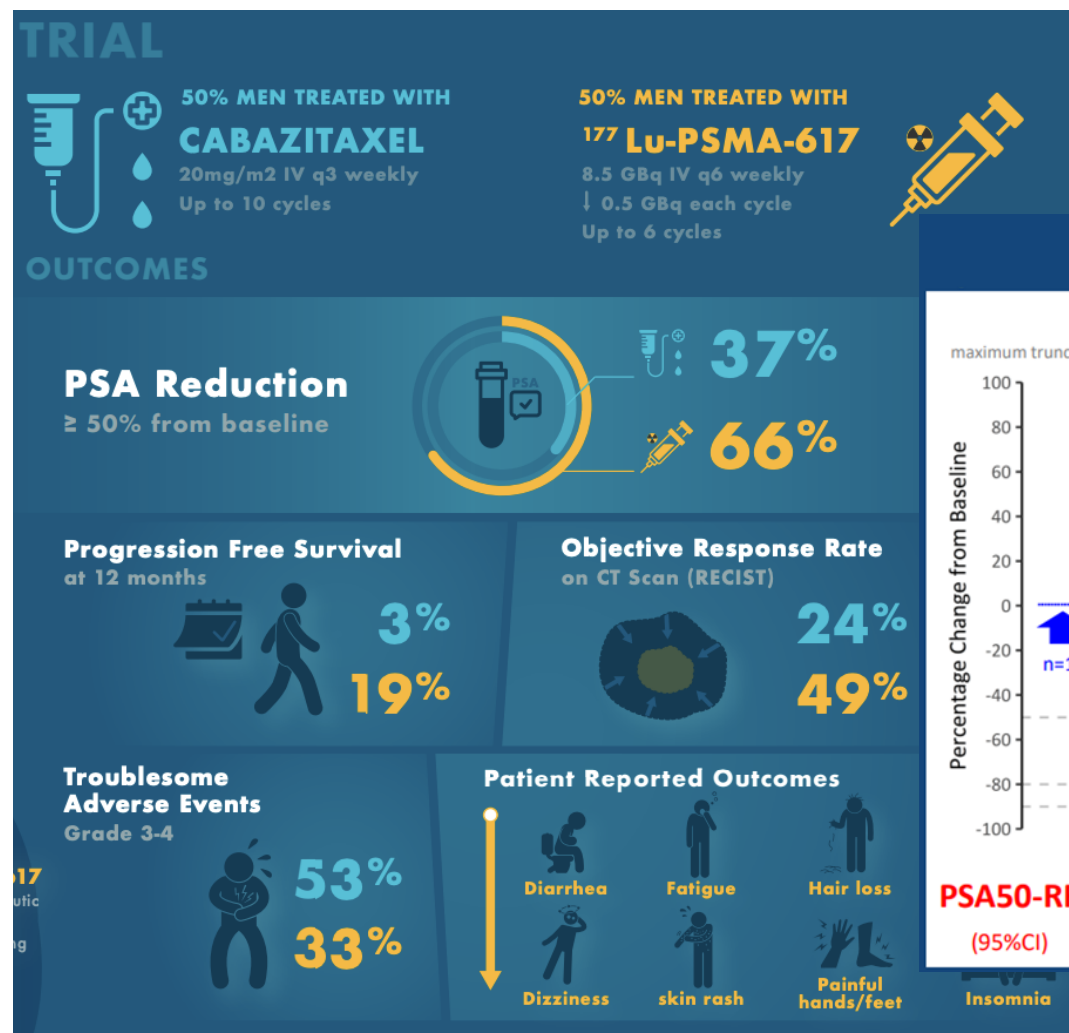
177Lu-PSMA-617 vs Cabazitaxel en CPRCm

TheraP

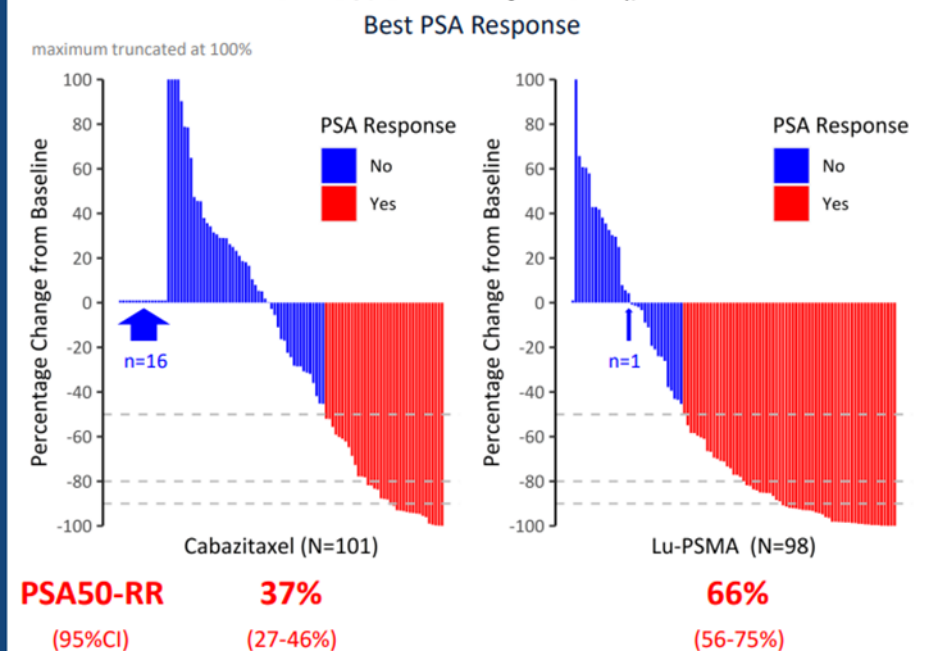
Hofman et al. TheraP:
Fase 2, randomizado
177 Lu-PSMA-617 vs
cabazitaxel in progressive
metastatic castration-
resistant

200p Randomizados

- 99 (98) Lu177 PSMA
- 101 (85) Cabazitaxel



PSA ≥ 50% response (PSA50-RR)



^{177}Lu -PSMA-617-SoC vs SoC en CPRCm

VISION

RESEARCH SUMMARY

Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer

Sartor O et al. DOI: 10.1056/NEJMoa2107322

Fase 3, multicéntrico, aleatorizado. pCPRCm, (PET PSMA+) en progresión después:

- Terapia IRA
- 1L o 2L taxanos

R 2:1
n 813
84 Hosp
9 Países
EEUU y EU

Tuvo dos criterios de valoración principales:
SG y SSP radiográfica

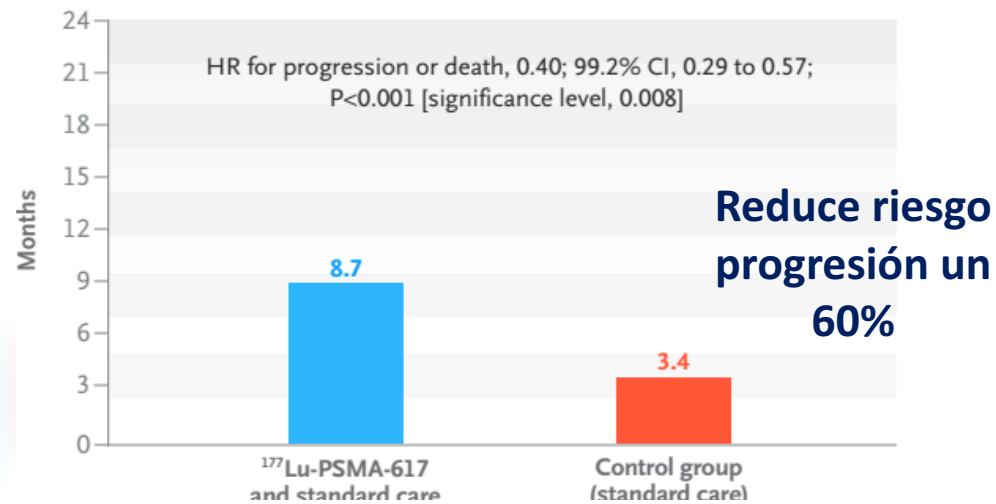
Standard Care
with Infusions of
 ^{177}Lu -PSMA-617



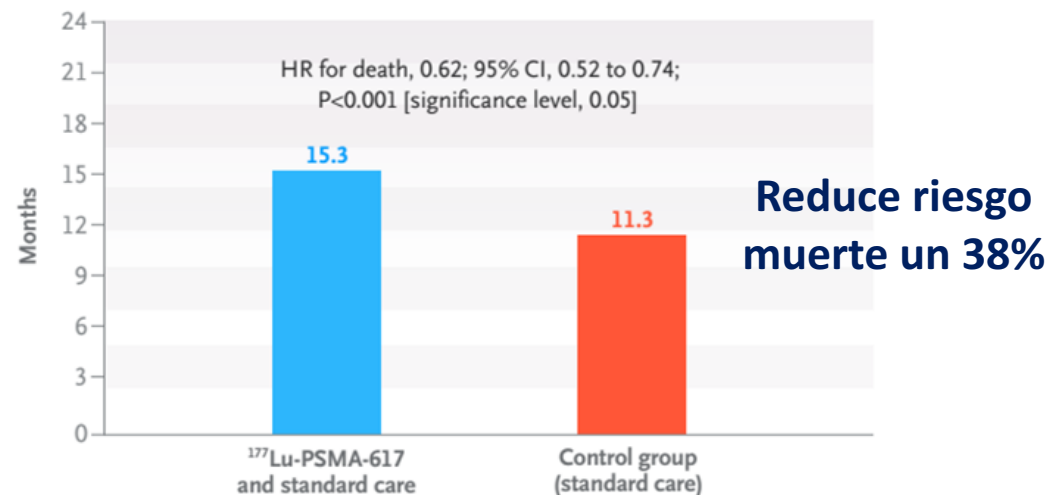
Standard Care



Imaging-Based Progression-free Survival



Overall Survival

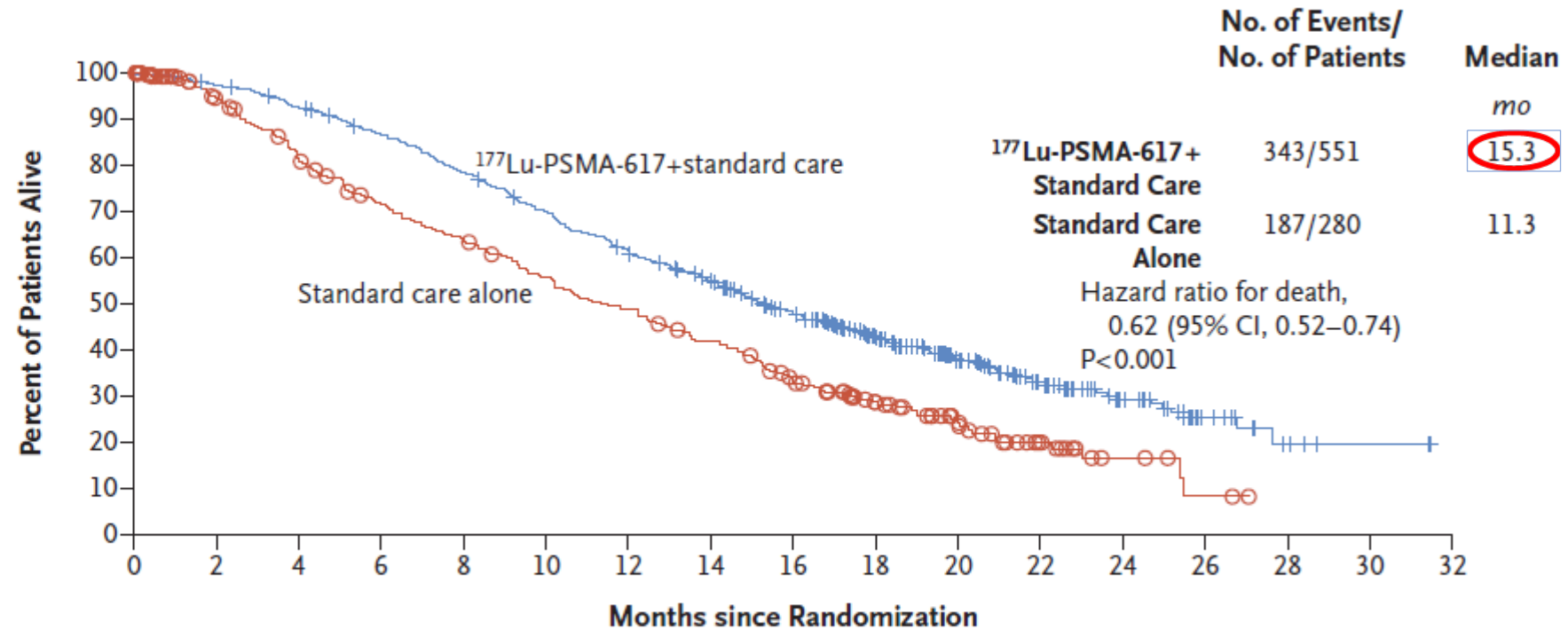


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Lutetium-177-PSMA-617 for Metastatic Castration-Resistant Prostate Cancer

Sartor O et al. DOI: 10.1056/NEJMoa2107322

B Overall Survival



No. at Risk

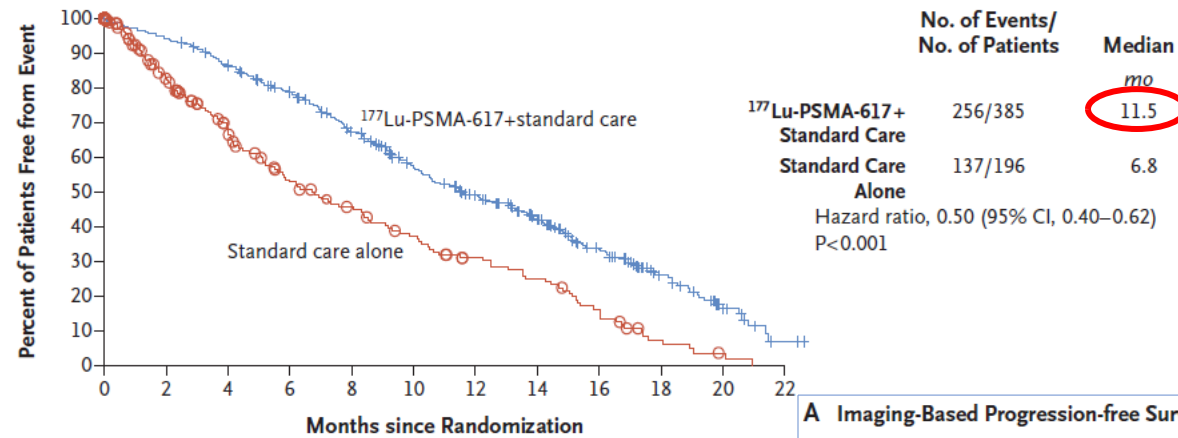
#c	177Lu-PSMA-617+standard care	551	535	506	470	425	377	332	289	236	166	112	63	36	15	5	2	0
X	Standard care alone	280	238	203	173	155	133	117	98	73	51	33	16	6	2	0	0	0

VISION

Lutetium-177-PSMA-617 for Metastatic
Castration-Resistant Prostate Cancer

Sartor O et al. DOI: 10.1056/NEJMoa2107322

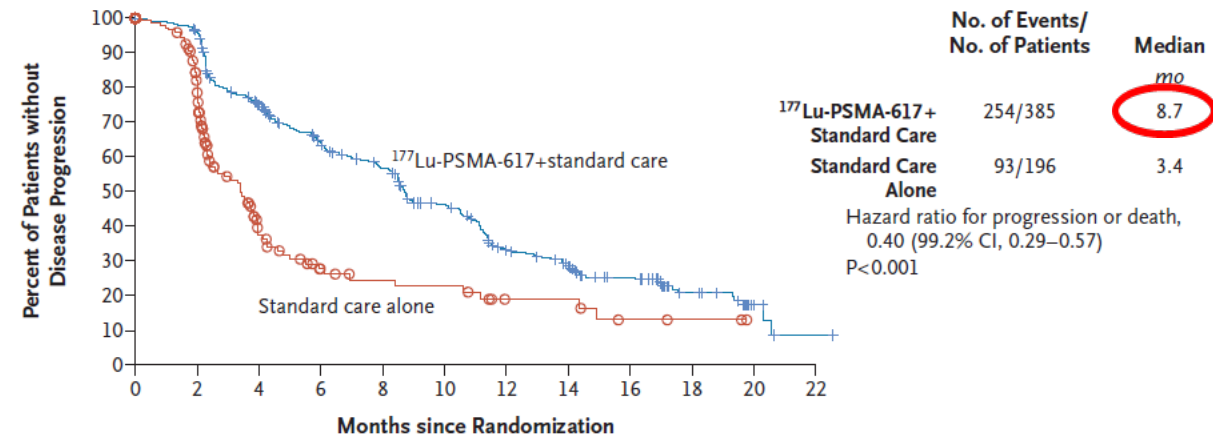
C Time to First Symptomatic Skeletal Event



No. at Risk

¹⁷⁷ Lu-PSMA-617+standard care	385	363	329	290	240	189	153	117	73	34	12	2
Standard care alone	196	141	104	75	61	48	36	29	15	6	2	0

A Imaging-Based Progression-free Survival



No. at Risk

¹⁷⁷ Lu-PSMA-617+standard care	385	362	272	215	182	137	88	71	49	21	6	1
Standard care alone	196	119	36	19	14	13	7	7	3	2	0	0

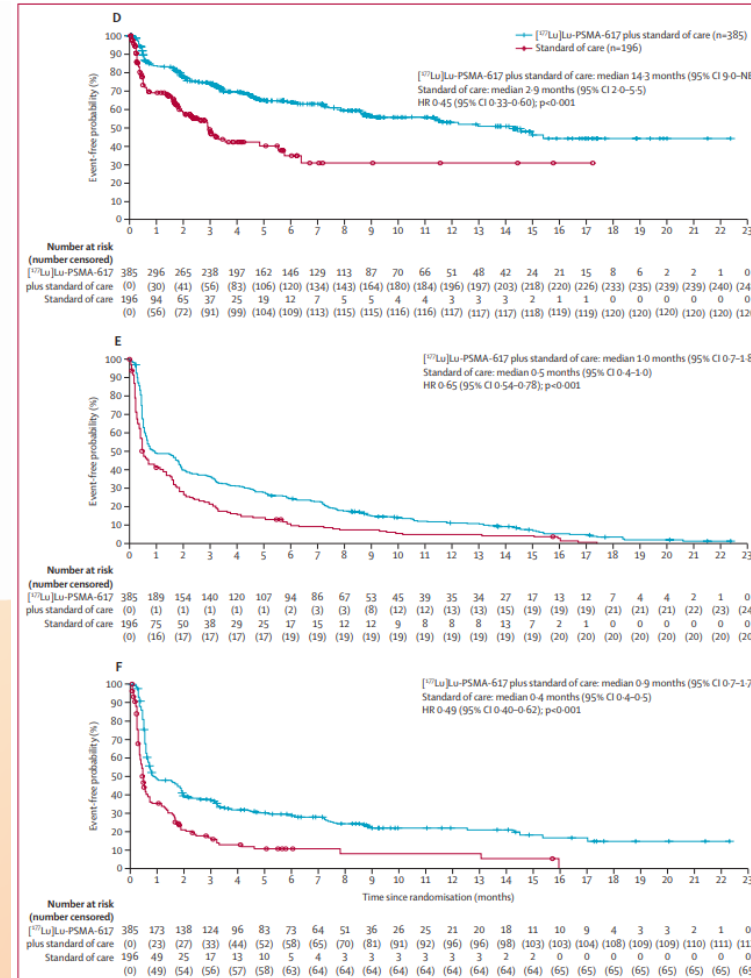
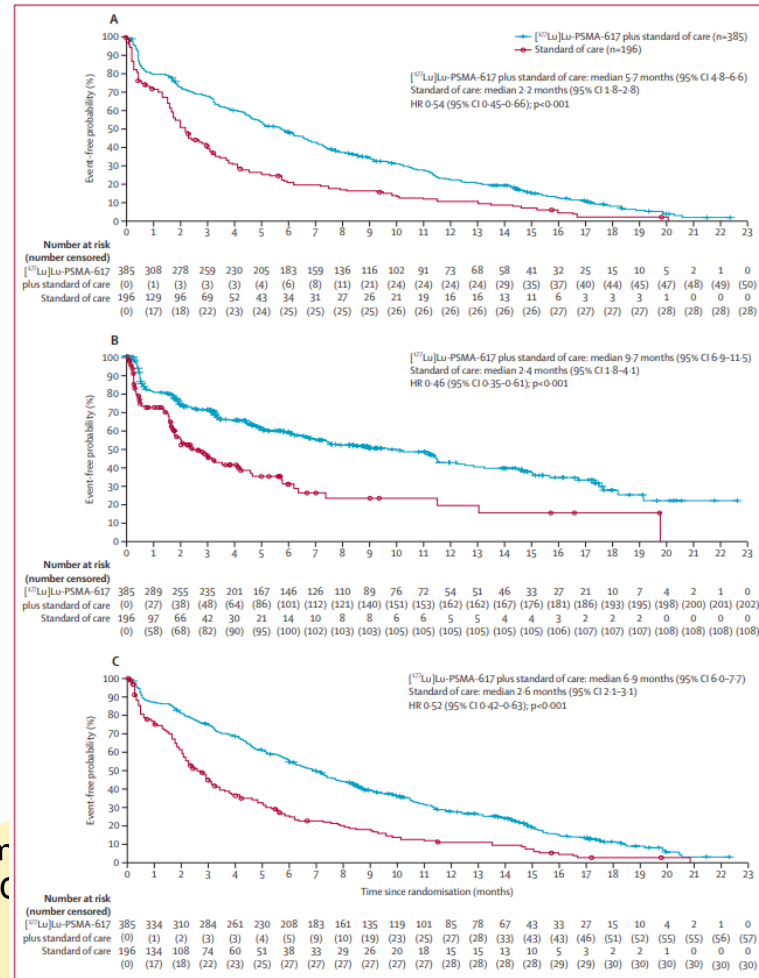
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Health-related quality of life and pain outcomes with [¹⁷⁷Lu] Lu-PSMA-617 plus standard of care versus standard of care in patients with metastatic castration-resistant prostate cancer (VISION): a multicentre, open-label, randomised, phase 3 trial



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 Beaugregard, Brian Chang, Ray Ghouse, Michelle DeSilvio, Richard A Messmann, Johann de Bono



Mejoría en la calidad de vida relacionada con la salud (CVRS), mejoría del dolor y los eventos esqueléticos sintomáticos

^{177}Lu -PSMA-617 en CPRCm

Además de VISION y TheraP

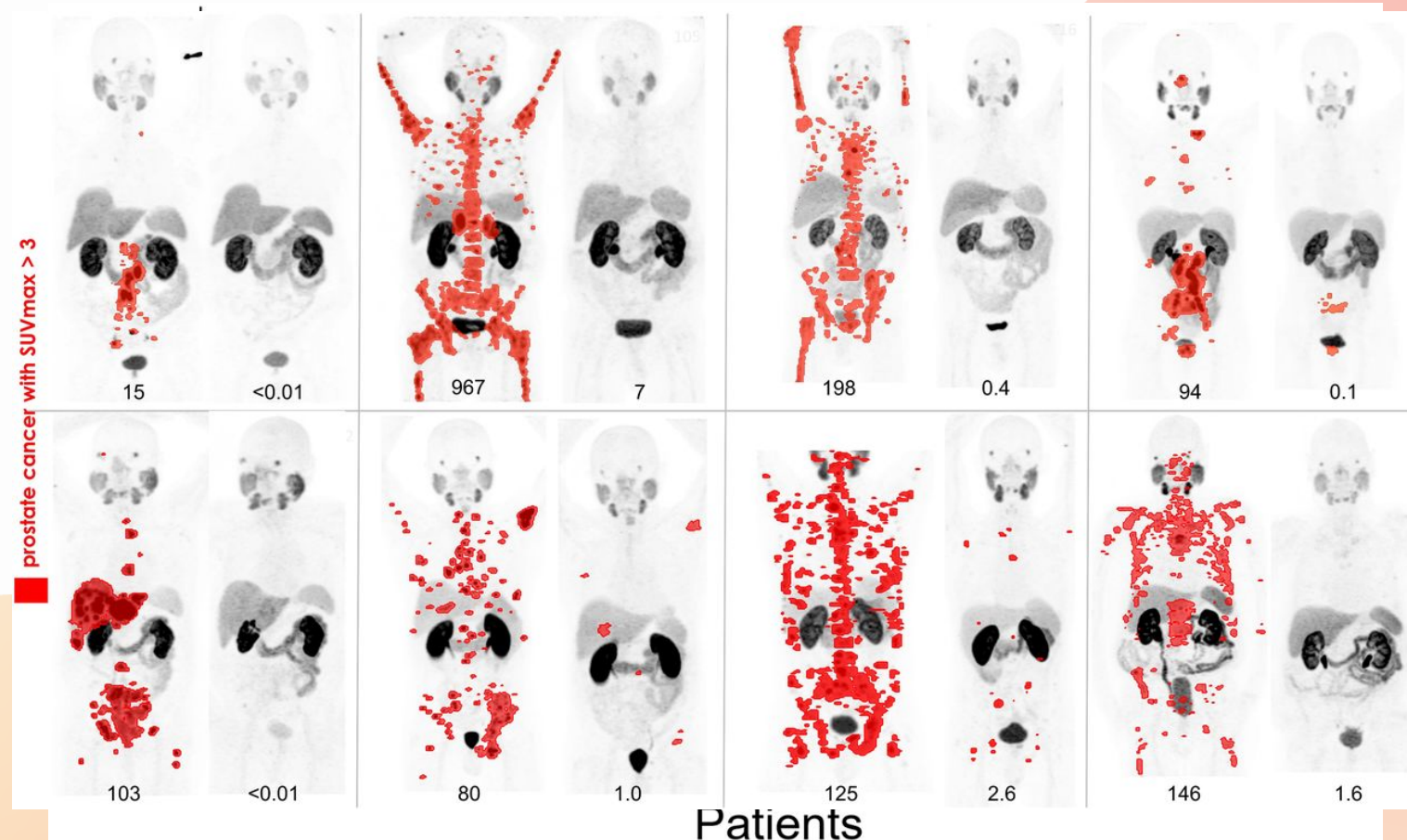
Otros dos estudios:

- cohorte 50p Peter MacCallum

demostró un **PSA50** en el **64 %** de los pacientes.

- el estudio RESIST-PC, 64 p UCLA

el **28%** de los pacientes presentó una **respuesta de PSA50** tras **2 ciclos**.

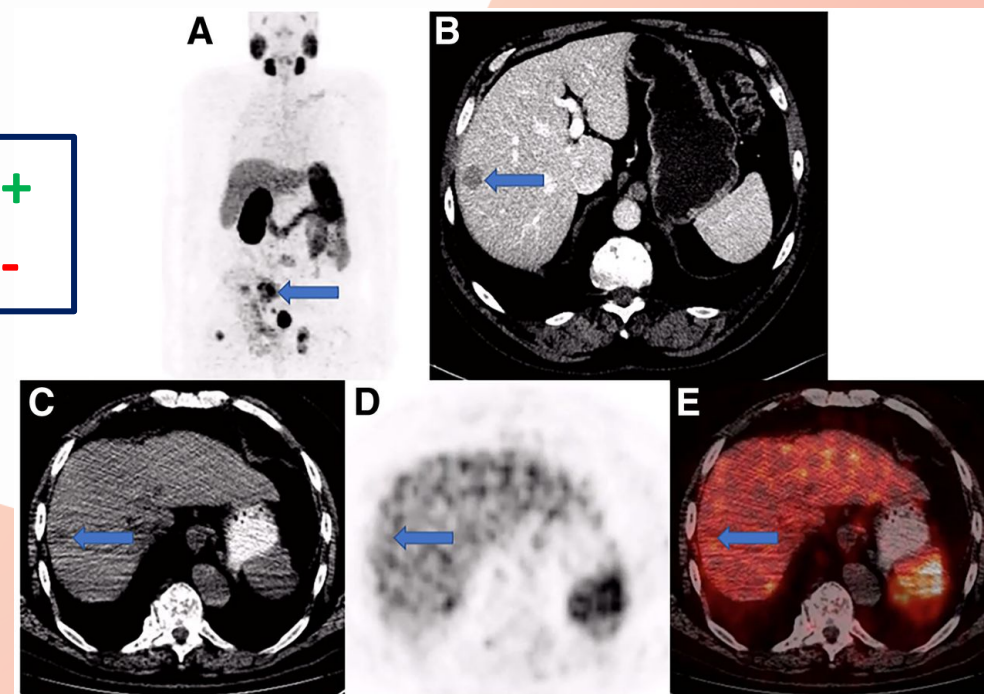
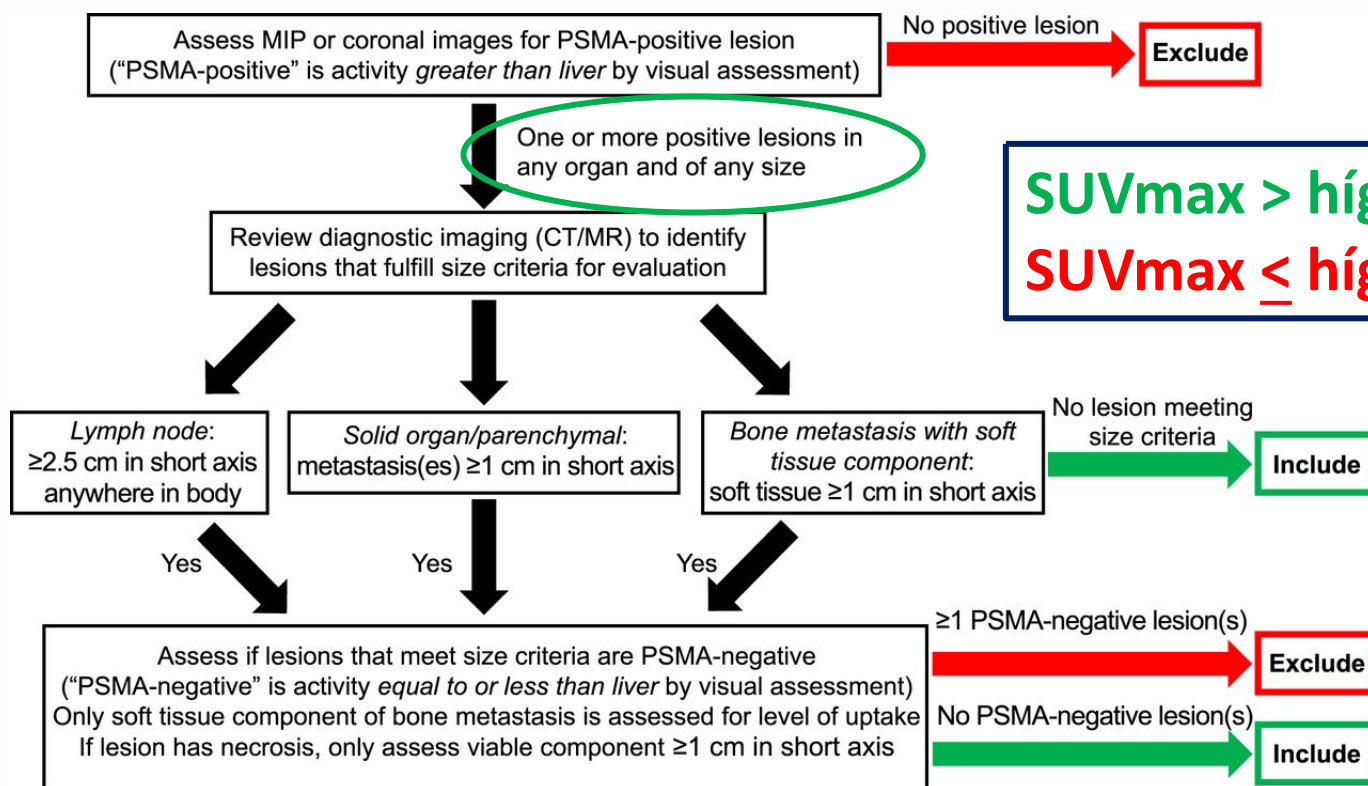


Crterios de seleccin VISION

Why We Did What We Did: PSMA PET/CT Selection Criteria for the VISION Trial

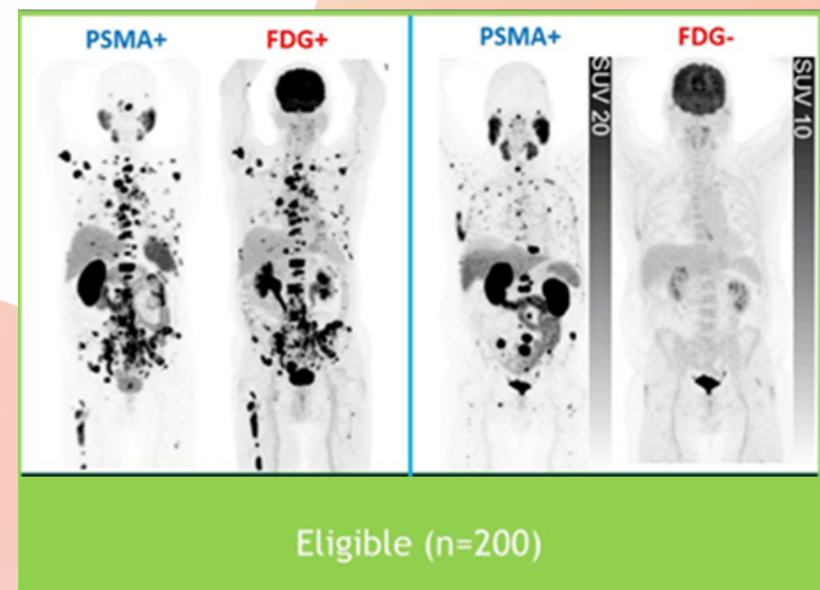
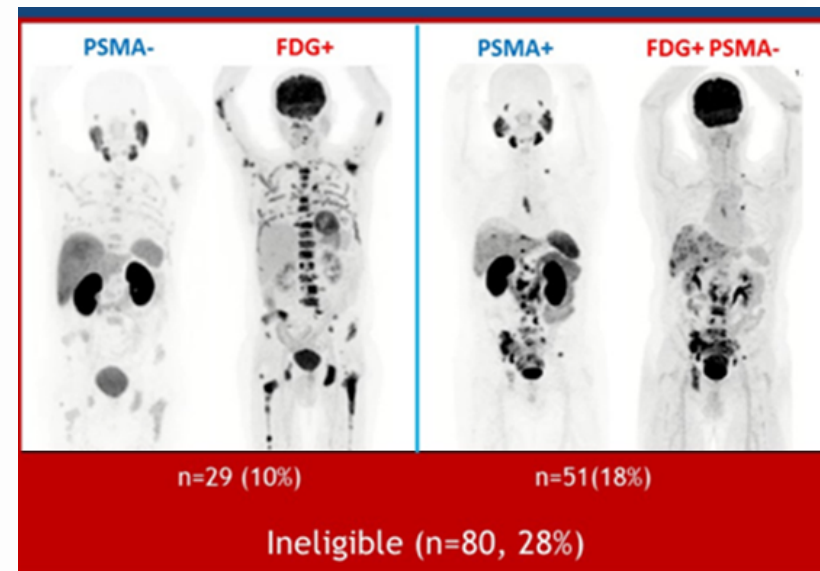
Phillip H. Kuo, Taylor Benson, Richard Messmann and Michael Groaning

Journal of Nuclear Medicine June 2022, 63 (6) 816-818; DOI: <https://doi.org/10.2967/jnumed.121.263638>



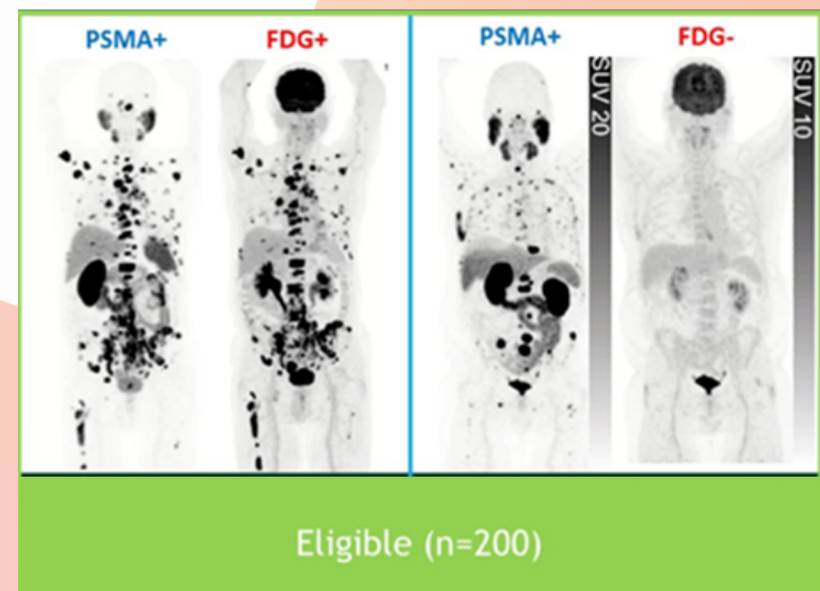
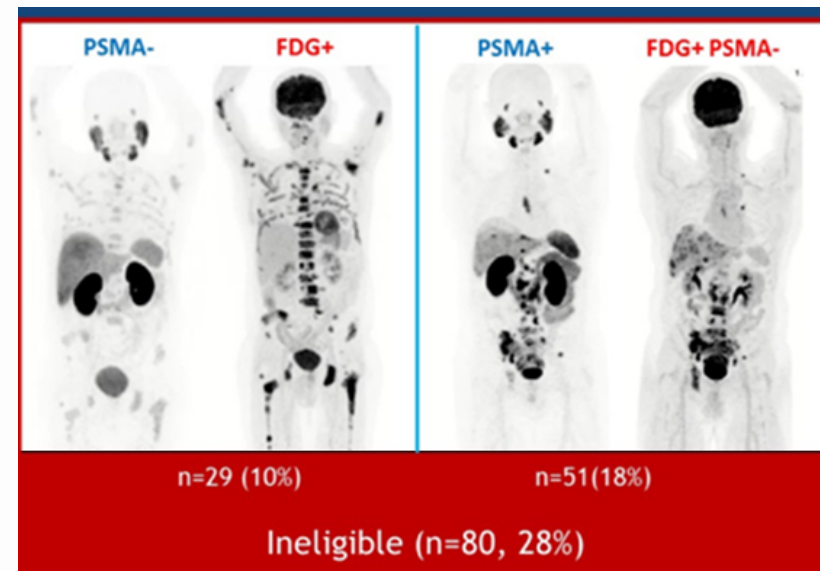
Criterios de selección TheraP vs VISION

Nivel de captación	Visual	Valor SUVmax
Lesiones + o -	PET PSMA / TC	PET FDG
	VISION	TheraP
PET PSMA +	1 lesión con SUVmax > hígado	1 les SUVmax > 20 o todas SUVmax > 10
PET PSMA -	1 lesión RECIST 1.1 en TC con SUVmax ≤ hígado	PSMA - / FDG + PSMA+ / FDG+PSMA-



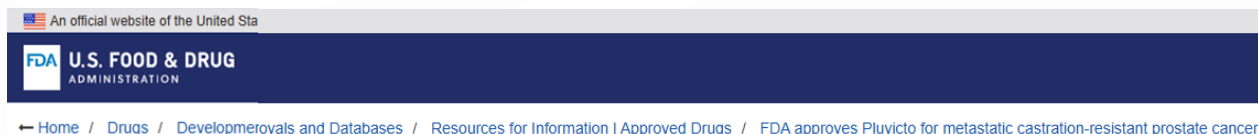
Criterios de selección TheraP vs VISION

	VISION	TheraP
Number patients	830	201
Additional SOC	YES	NO
Imaging threshold	Liver (SUV max 2-8)	SUV max 20 + FDG
Imaging screen failure	13%	28%
Dose	7.5 Gbq X 6	8.5 Gbq X 6 decrease
PSA RR	46%	66%
rPFS	8.7	8.5
OS	15.3	15.1



177Lu-PSMA aprobado para PET PSMA +

En práctica clínica debemos basarnos en VISION, criterio visual por PET PSMA +



FDA approves Pluvicto for metastatic castration-resistant prostate cancer



On March 23, 2022, the Food and Drug Administration approved Pluvicto (lutetium Lu 177 vipivotide tetraxetan, Advanced Accelerator Applications USA, Inc., a Novartis company) for the treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy.

radiopharmaceuticals.

2.2 Patient Selection

Select patients with previously treated mCRPC for treatment with PLUVICTO using LOCAMETZ or another approved PSMA-11 imaging agent based on PSMA expression in tumors. Additional selection criteria were used in the VISION study [see Clinical Studies (14)].

Refer to the prescribing information for the PSMA imaging agent.

2.3 Recommended Dosage

The recommended PLUVICTO dosage is 7.4 GBq (200 mCi) intravenously every 6 weeks for up to 6 doses, or until disease progression, or unacceptable toxicity.

2.4 Dosage Modifications for Adverse Reactions

Recommended dosage modifications of PLUVICTO for adverse reactions are provided in Table 1. Management of adverse reactions may require temporary dose interruption (extending the dosing interval from every 6 weeks up to every



EMA/837969/2022
EMA/H/C/005483

Pluvicto (lutetium (¹⁷⁷Lu) vipivotide tetraxetan)

An overview of Pluvicto and why it is authorised in the EU



What is Pluvicto and what is it used for?

Pluvicto is a medicine used to treat cancer of the prostate (a gland of the male reproductive system). It is used when the cancer is metastatic (spreading to other parts of the body), progressive, castration-resistant (worsens despite treatment to lower levels of the male sex hormone testosterone), and the cancer cells have a protein called prostate-specific membrane antigen (PSMA) on their surface (PSMA-positive prostate cancer).

Pluvicto is used together with androgen deprivation therapy (treatment to lower male sex hormones) in adults previously treated with androgen receptor pathway inhibitors (medicines for prostate cancer), and a medicine of the group of cancer medicines known as taxanes. Androgen receptor pathway inhibitors may also be added to Pluvicto and androgen deprivation therapy.

Pluvicto is a radiopharmaceutical (a medicine that gives off a small amount of radioactivity) that contains the active substance lutetium (¹⁷⁷Lu) vipivotide tetraxetan.

How is Pluvicto used?

Because Pluvicto gives off some radioactivity, it is only used in special controlled areas and must be given to patients by healthcare professionals qualified and authorised to use radiopharmaceuticals.

Before starting treatment, the doctor will check that the patient's tumours have PSMA on their cell surfaces with a positron emission tomography (PET) scan.

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<https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-pluvicto-metastatic-castration-resistant-prostate-cancer>

https://www.ema.europa.eu/en/documents/overview/pluvicto-epar-medicine-overview_en.pdf

RD
CONSORTIUM

RLT previo a taxanos

Home > Oncology News

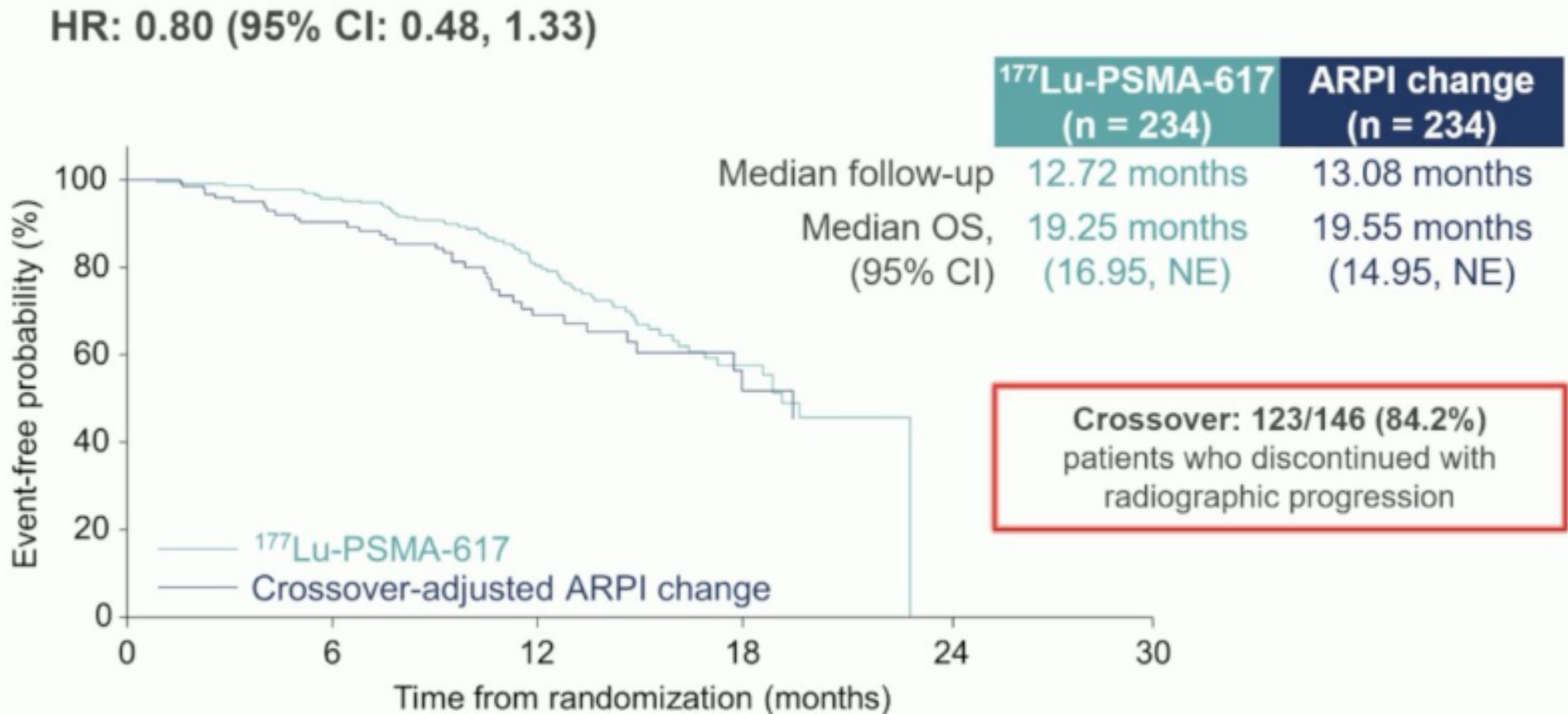
¹⁷⁷Lu-PSMA-617 Prolongs rPFS Relative to Androgen Receptor Pathway Inhibitor Change, with a Favourable Safety Profile in Patients with PSMA-positive mCRPC



Date: 23 Sep 2024

Topics: Endocrine Thera

Tumor Sites: Genitourin



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FDA expands Pluvicto's metastatic castration-resistant prostate cancer indication

On March 28, 2025, the Food and Drug Administration expanded the indication for lutetium Lu 177 vipivotide tetraxetan (Pluvicto, Novartis Pharmaceuticals Corporation) to include adults with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor pathway inhibitor (ARPI) therapy and are considered appropriate for androgen deprivation therapy (ADT) and androgen receptor pathway inhibitor (ARPI)-based chemotherapy.

Patients with previously treated mCRPC should be selected for Pluvicto (active ingredient gallium Ga 68 gozetotide) or another approved PET product based on PSMA expression in tumors.

Full prescribing information for Pluvicto will be posted on [Drugs@FDA](#).



La FDA aprueba la terapia con radioligando Pluvicto® de Novartis para su uso precoz antes de la quimioterapia en el cáncer de próstata metastásico resistente a la castración con PSMA positivo.

28 De Marzo De 2025

Anuncio ad hoc de conformidad con el art. 53 LR

- La nueva indicación aproximadamente triplica la población de pacientes elegibles, lo que permite utilizar Pluvicto® después de un inhibidor de la vía del receptor de andrógenos (ARPI) y ahora antes de la quimioterapia.
- Pluvicto redujo significativamente el riesgo de progresión o muerte en un 59% y más que duplicó la mediana de supervivencia libre de progresión radiográfica (rPFS) frente al cambio en ARPI en el ensayo de fase III PSMAfore*
- Aproximadamente la mitad de los pacientes no viven lo suficiente para recibir un segundo tratamiento para el mCRPC, lo que resalta la necesidad de un uso más temprano de terapias efectivas con tolerabilidad demostrada¹
- Varias instalaciones de fabricación de RLT en EE. UU. satisfacen plenamente las necesidades de suministro para una indicación ampliada, con una infraestructura líder en la industria para acelerar la entrega de RLT a los pacientes.

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Seleccionar mejores respondedores

Estudio terciario, valor predictivo y pronóstico del PET PSMA y PET FDG en los pacientes de TheraP

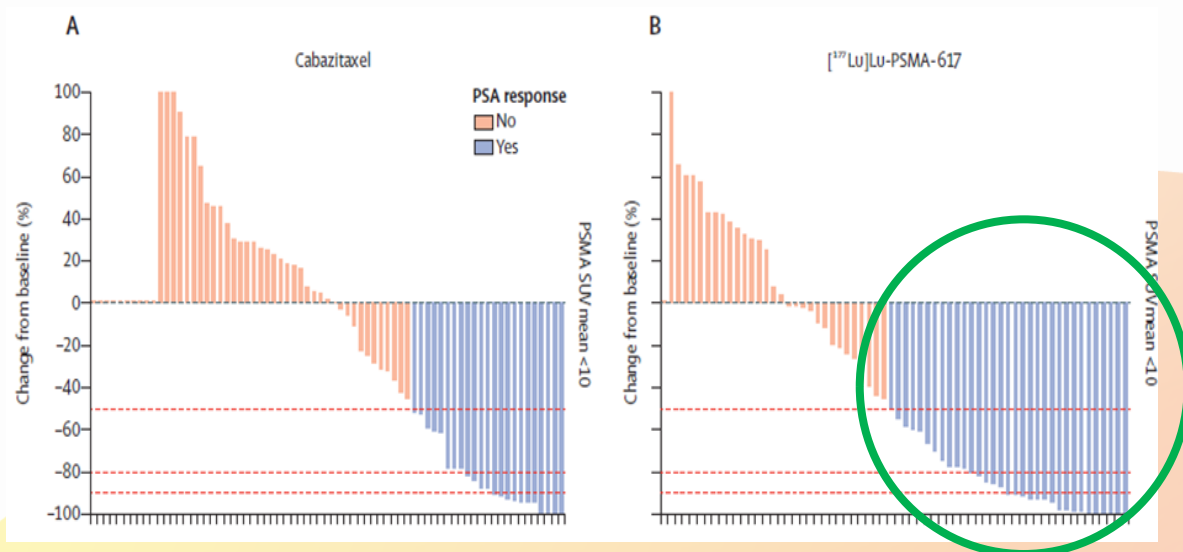
ARTICLES | VOLUME 23, ISSUE 11, P1389-1397, NOVEMBER 2022

THE LANCET
Oncology

PSMA and FDG-PET as predictive and prognostic biomarkers in patients given [^{177}Lu]Lu-PSMA-617 versus cabazitaxel for metastatic castration-resistant prostate cancer (TheraP): a biomarker analysis from a randomised, open-label, phase 2 trial

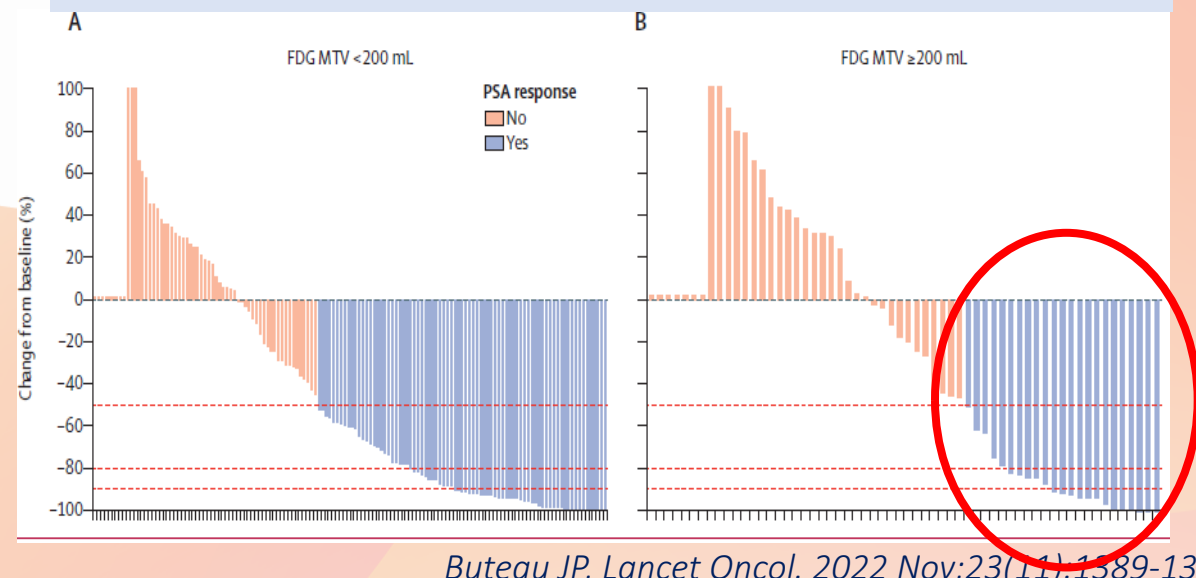
PSMA (SUVmean) predictor of response to Lu-PSMA

PSMA (lesiones SUV>3) SUVmean > 10



FDG prognostic value of response to both therapies

FDG, MTV > 200ml (SUV > liver +2SD)



Seleccionar mejores respondedores

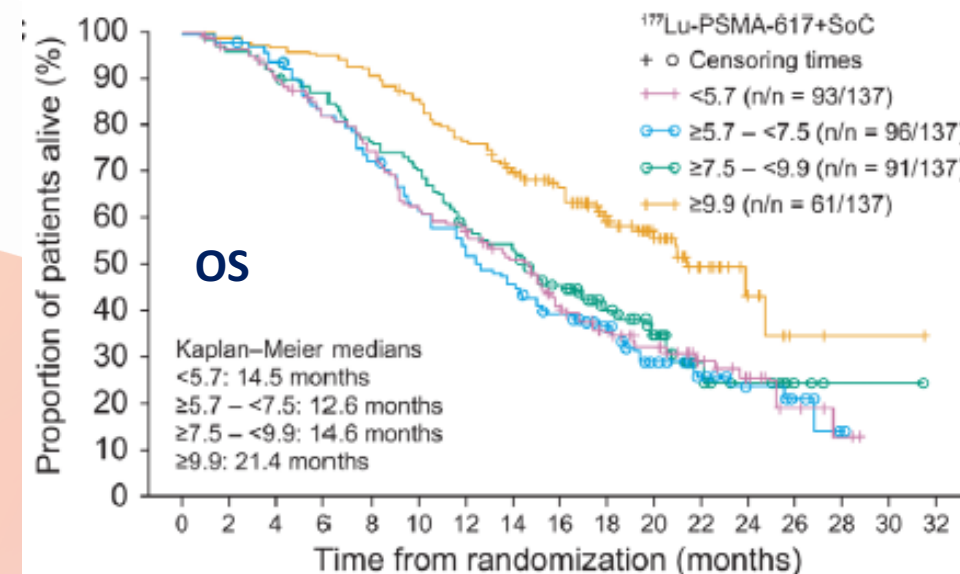
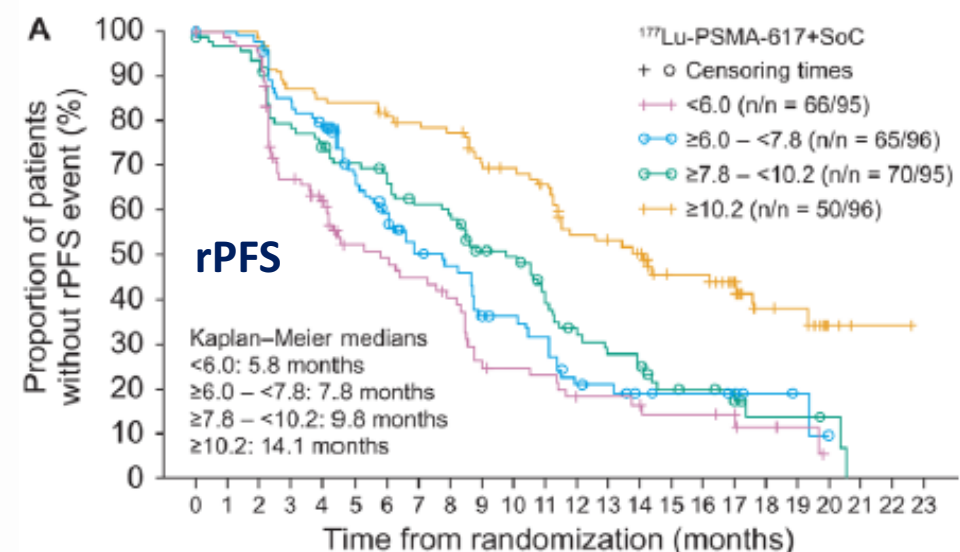
SUVmean PSMA

Radiology

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

Análisis secundario exploratorio del ensayo VISION (n826)

- Mayor **SUVmean** PET ^{68}Ga -PSMA-11 se asoció con **mejores resultados** a la terapia con ^{177}Lu -PSMA-617.
- Un **aumento** de 1 unidad del **SUVmean** se asoció con disminución 12 % riesgo PFSr o 10 % riesgo de muerte, respectivamente.
- A **mayor volumen tumoral de PSMA**, **peor OS**.



Correlación entre SUV y dosis absorbida

Sabemos que:

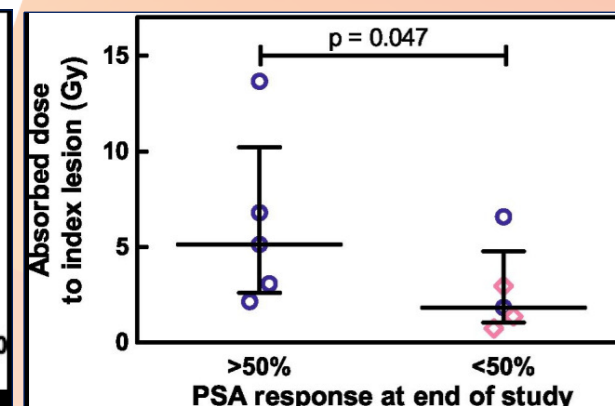
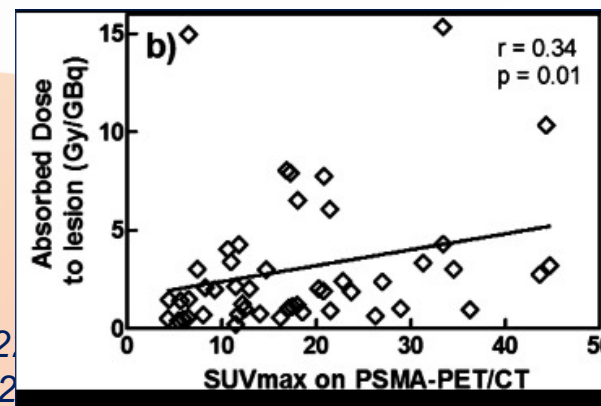
- > MTV FDG, peor pronóstico.
 - > MTV PSMA, peor pronóstico.
 - > Captación en PET-PSMA, mejor respuesta
-
- Correlación entre SUV y dosis absorbida
 - Correlación entre SUV y descenso de PSA

► Eur J Nucl Med Mol Imaging. 2021 Oct 8;49(4):1101–1112. doi: [10.1007/s00259-021-05538-2](https://doi.org/10.1007/s00259-021-05538-2)

[⁶⁸Ga]Ga-PSMA-11 PET imaging as a predictor for absorbed doses in organs at risk and small lesions in [¹⁷⁷Lu]Lu-PSMA-617 treatment

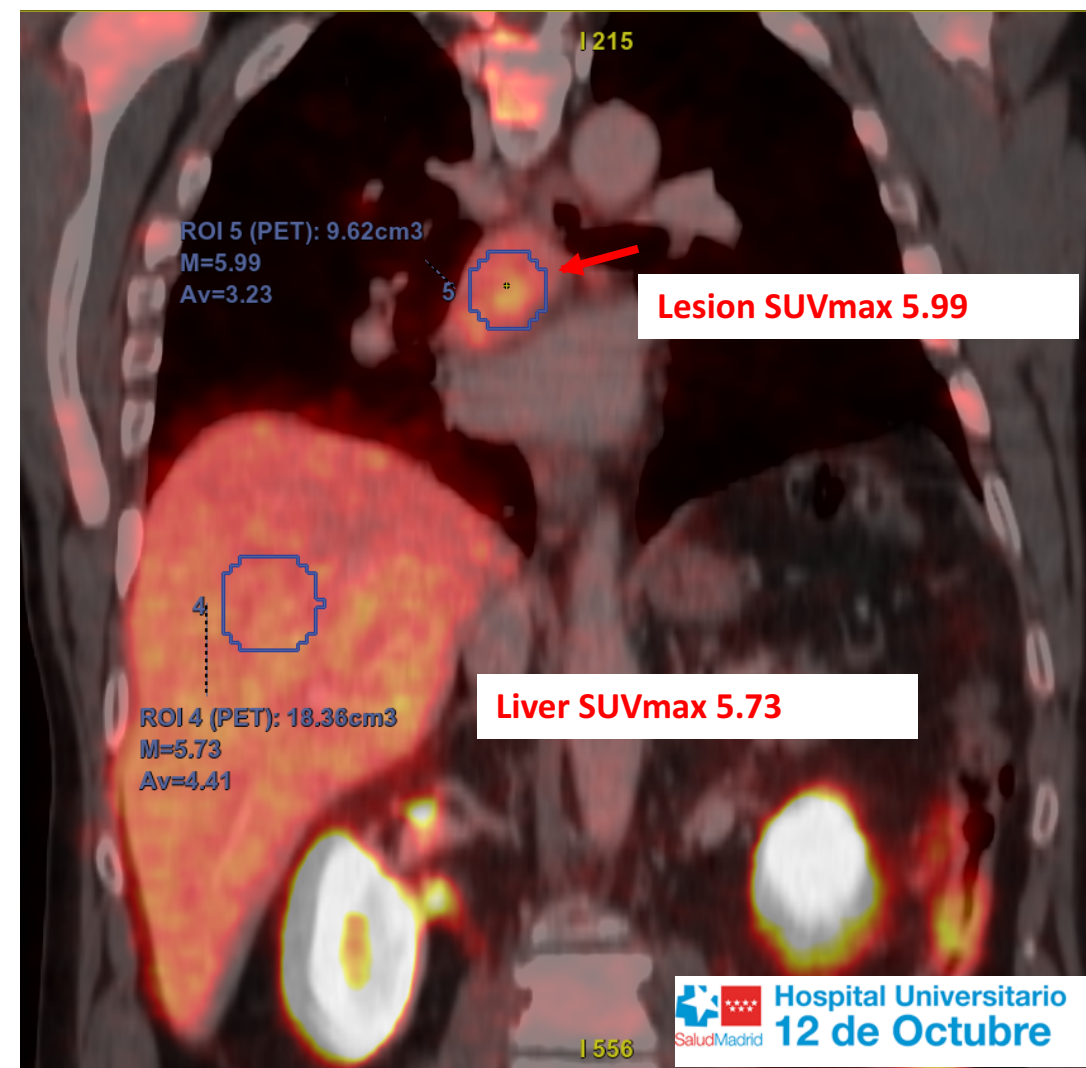
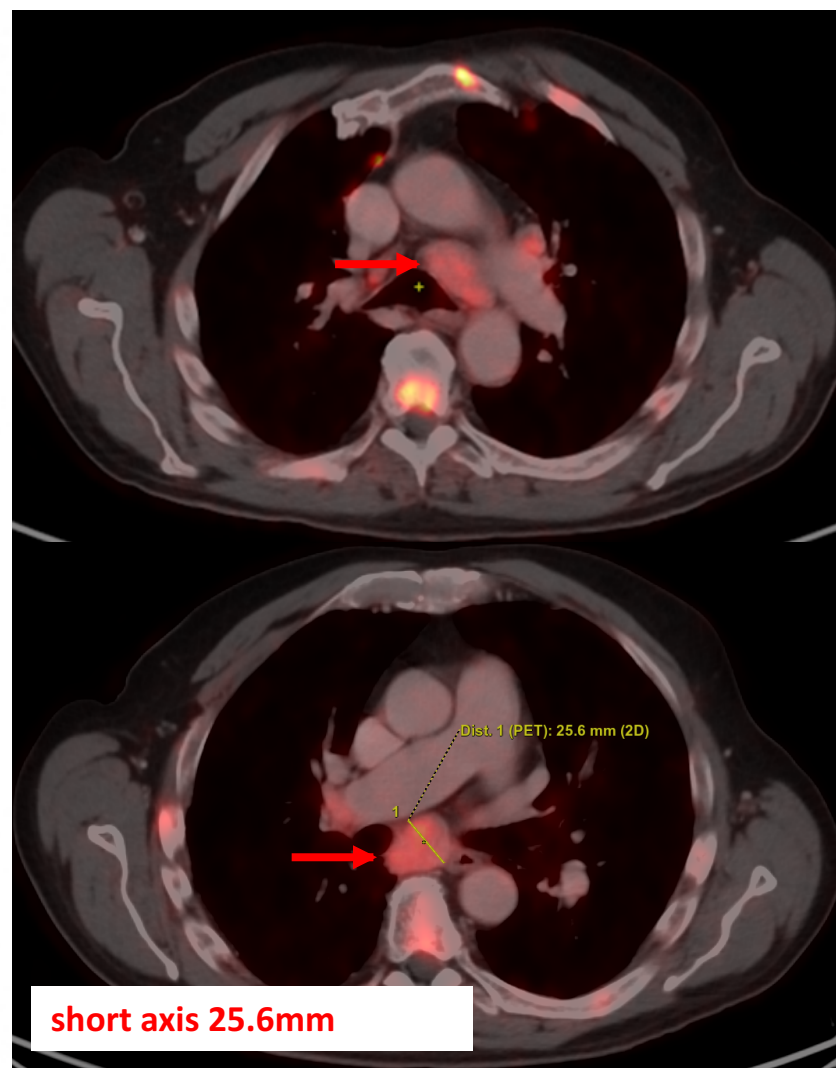
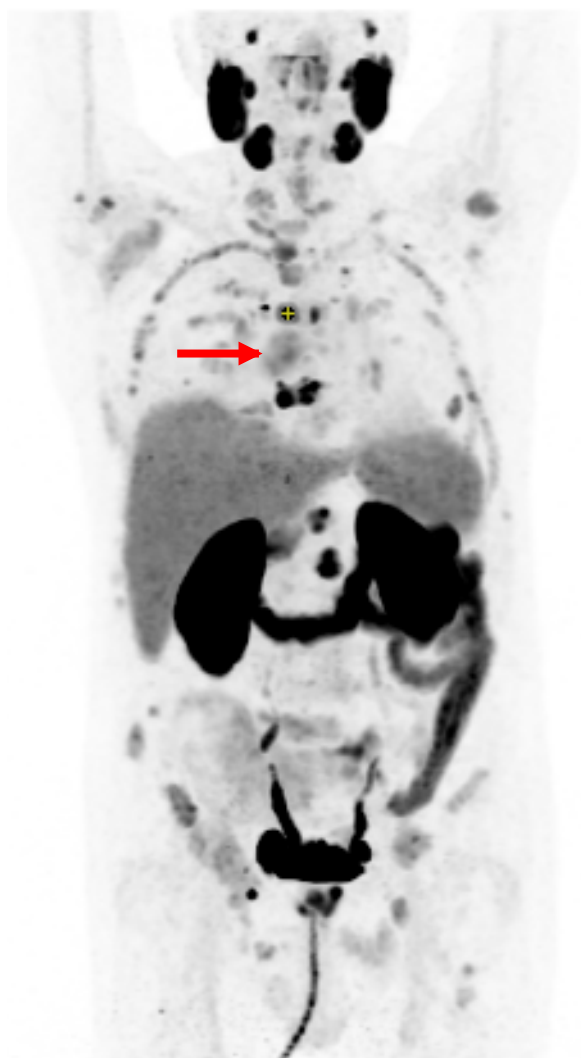
► Eur J Nucl Med Mol Imaging. Enero de 2022;49(2):460–469. doi: 10.1007/s00259-021-05471-4. Epub 4 de julio de 2021.

Dosimetría intraterapéutica de [¹⁷⁷Lu]Lu-PSMA-617 en pacientes con cáncer de próstata metastásico sensible a hormonas de bajo volumen y correlación con el resultado del tratamiento



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Peters SMB, Hofferber R, Privé BM, et al. Eur J Nucl Med Mol Imaging. 2021.
Peters SMB, Privé BM, de Bakker M, et al. Eur J Nucl Med Mol Imaging. 2022.
Ells Z, et al. J Nucl Med. 2024



POSITIVE OR NEGATIVE?

Seleccionar mejores respondedores

¿Qué pasaría si aplicamos criterios TheraP a los pacientes VISION?

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

Resumen de la reunión: Simposio sobre cánceres genitourinarios de la ASCO 2024

ACCESO LIBRE | Cáncer de próstata avanzado | 29 de enero de 2024



Asociación entre la elegibilidad para TheraP basada en PET y los resultados de ^{177}Lu -PSMA-617 (LuPSMA) en pacientes elegibles para VISION con cáncer de próstata metastásico resistente a la castración (mCRPC).

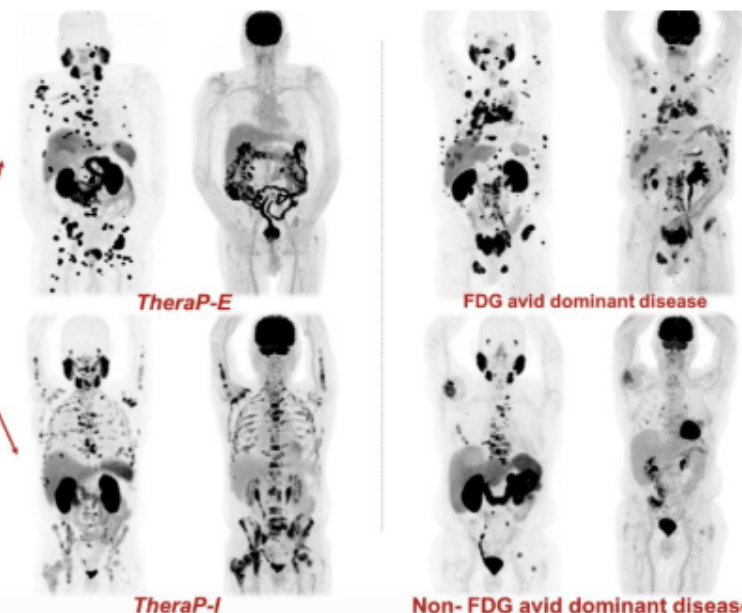
Autores: [Ridvan Arda Demirci](#), [Roman Gulati](#), [Alireza Ghodsi](#), [Peter Nelson](#), [Heather H. Cheng](#), [Jessica E. Hawley](#), [Todd Yezefski](#), ... [MOSTRAR TODOS](#) ...
y [Amir Iravani](#). | [INFORMACIÓN Y AFILIACIONES DE LOS AUTORES](#)

VISION PET-based eligibility

- ≥ 1 PSMA positive lesion (greater than liver parenchyma) of any size in any organ
- And
- No PSMA negative (equal or lower than liver parenchyma)
- > 2.5 cm lymph nodes
- > 1 cm solid organs
- > 1 cm in soft tissue components of bone lesions

TheraP PET-based eligibility

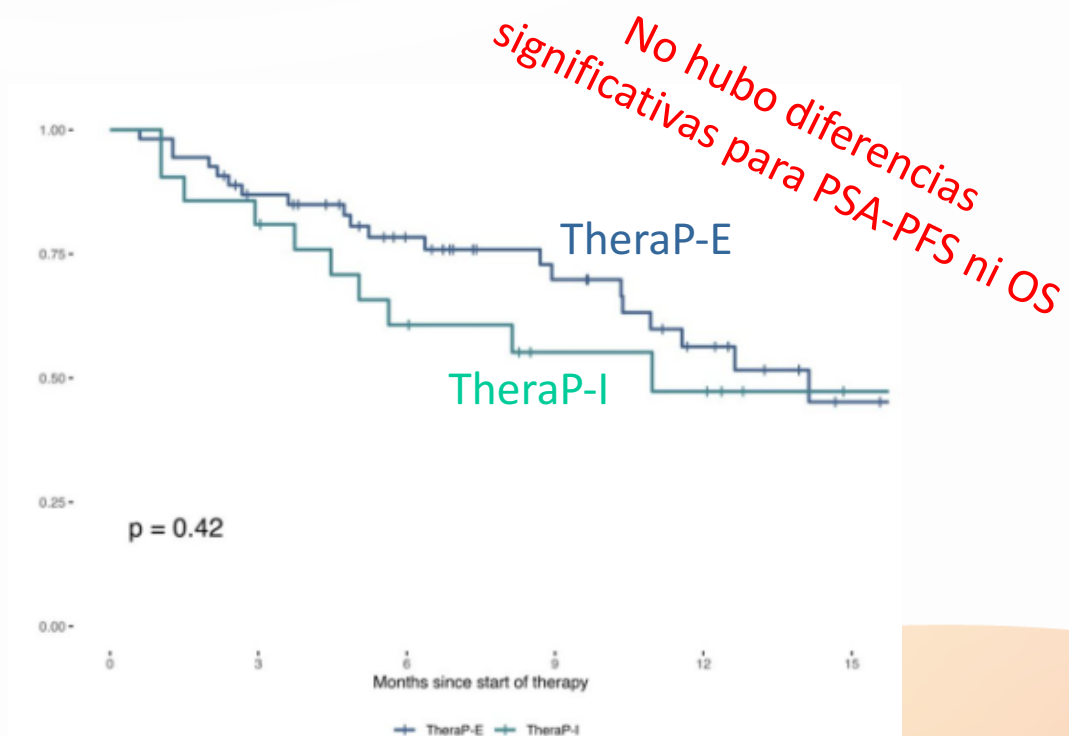
- At least one lesion with PSMA SUVmax ≥ 20
- And
- All measurable sites with PSMA SUVmax ≥ 10 SUV
- And
- No FDG-avid/non-PSMA avid discordant lesion



En general, el 28 % (21/75) de los pacientes fueron evaluados como no elegibles para TheraP (SUVmean y SUVmax de PSMA-PET < elegibles para TheraP)

Seleccionar mejores respondedores

FDG + peor pronóstico



FDG-Non- Avid

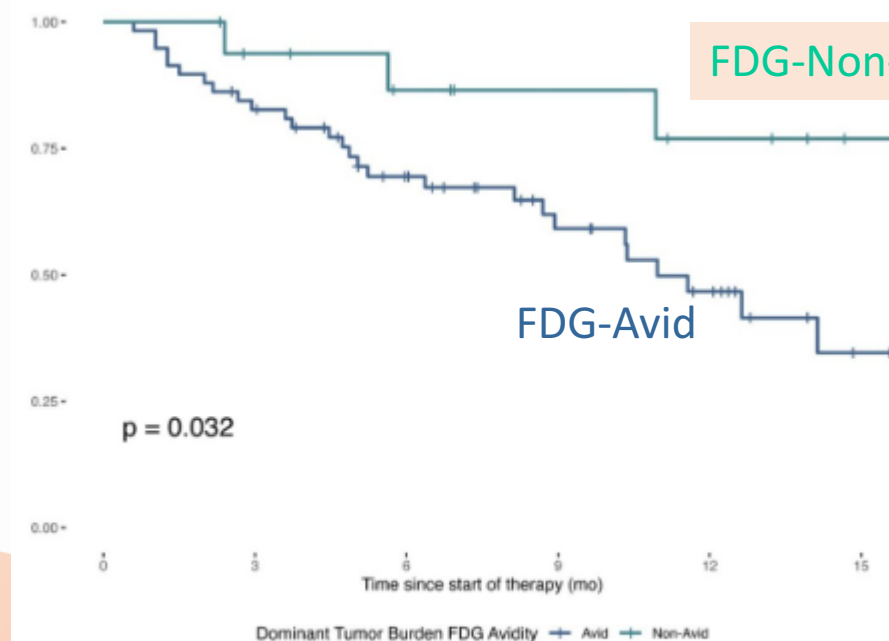


Figure 1 : KM survival curve stratified by PET-based TheraP eligibility

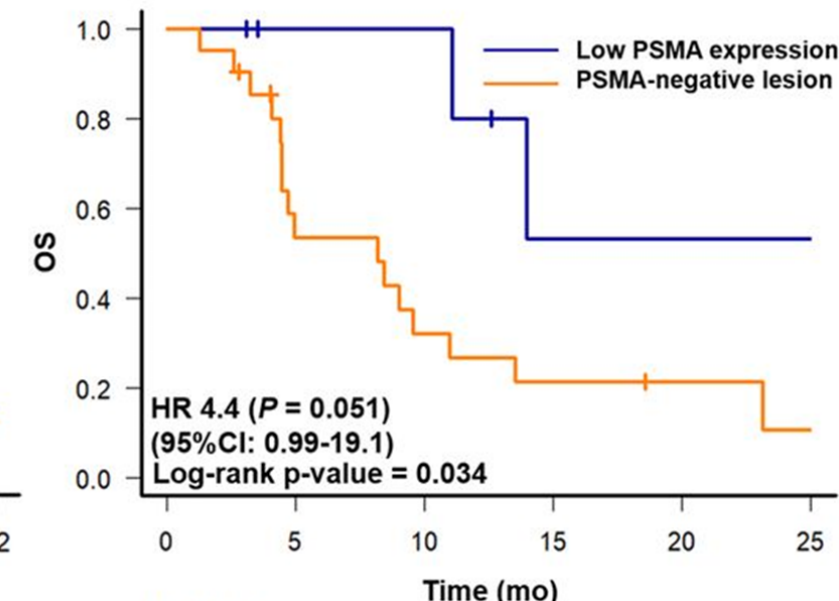
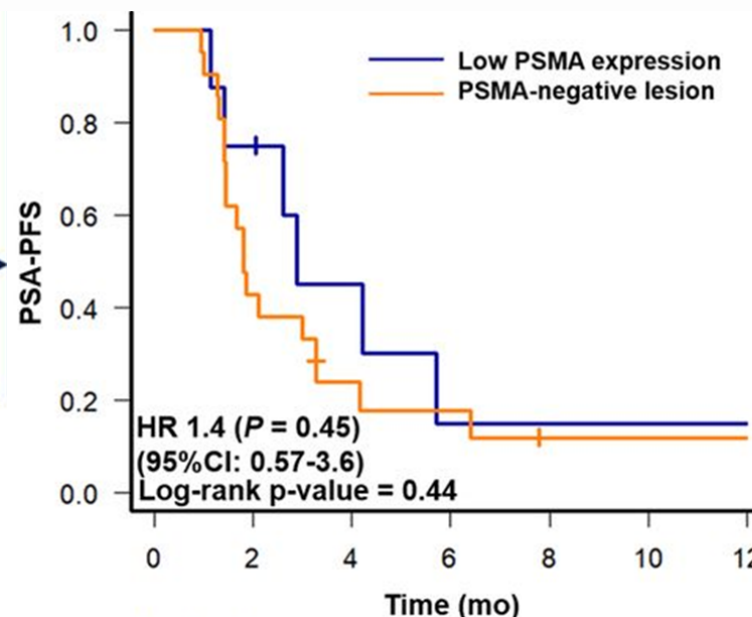
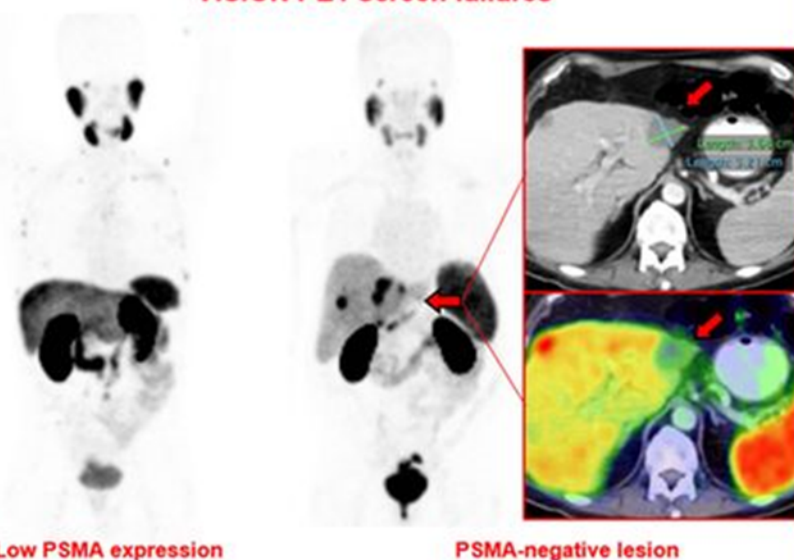
Figure 2 : KM survival curve stratified by FDG avidity of dominant tumor burden.

Seleccionar mejores respondedores

Lesiones PSMA negativas?? Vs Lesiones PSMA + con baja captación?

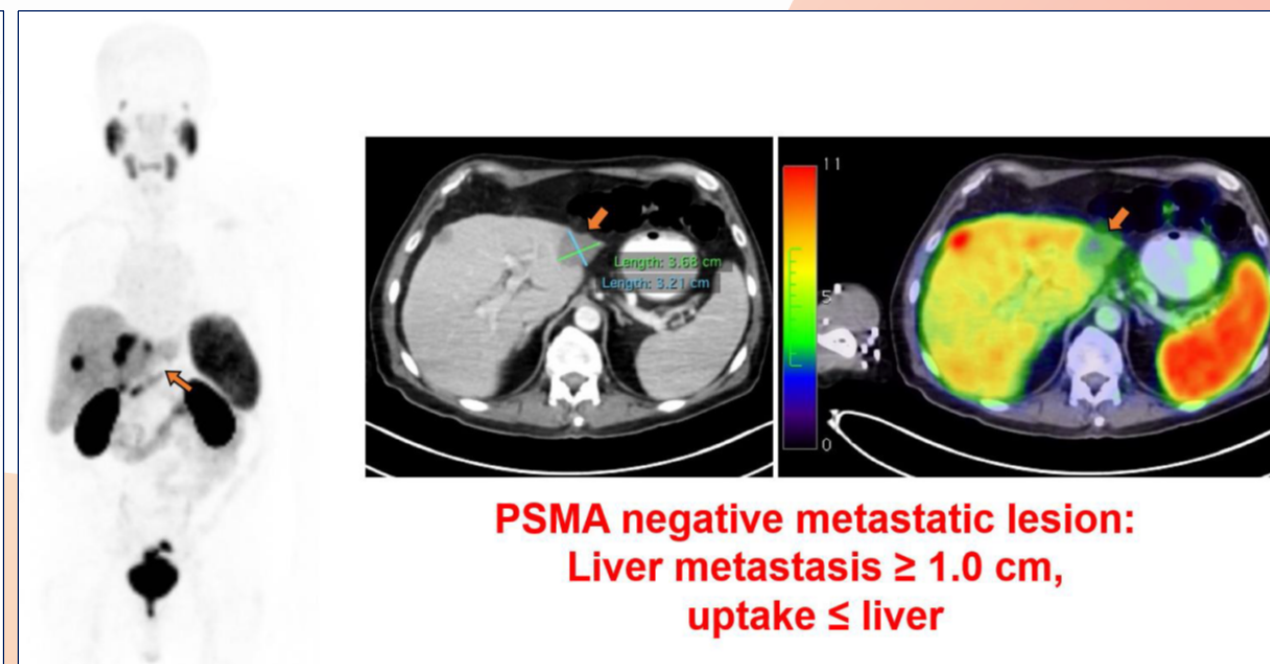
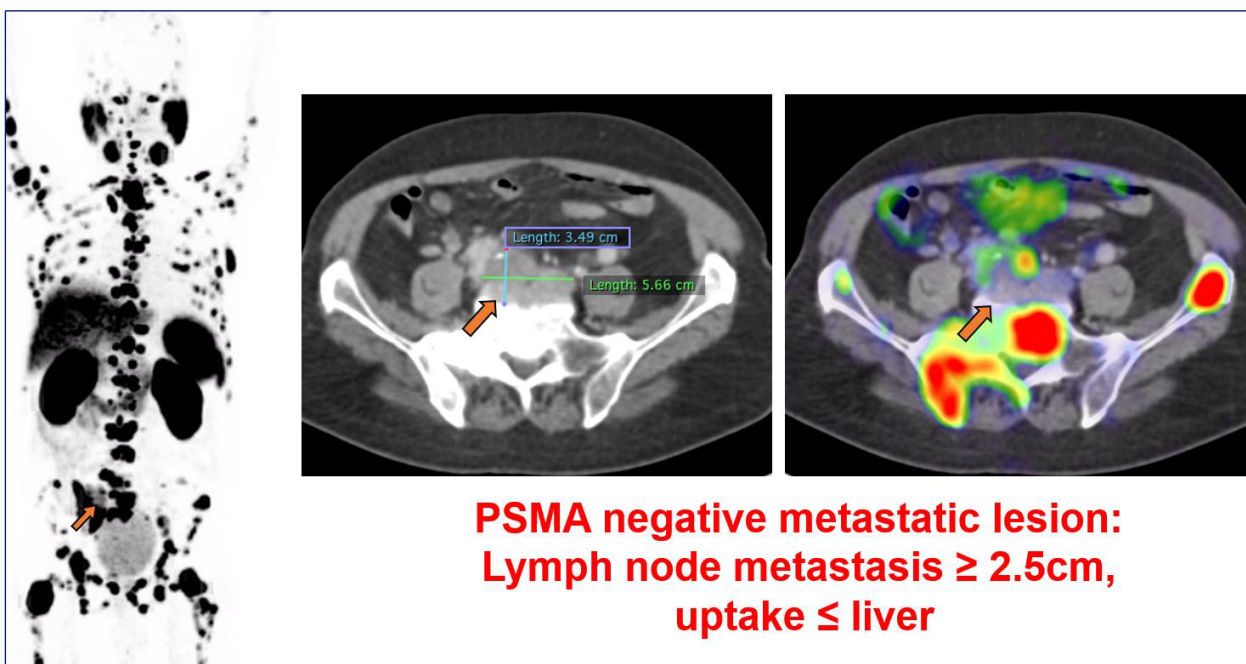
Outcome of Patients with PSMA PET/CT Screen Failure by VISION Criteria and Treated with ^{177}Lu -PSMA Therapy: A Multicenter Retrospective Analysis

VISION PET screen failures

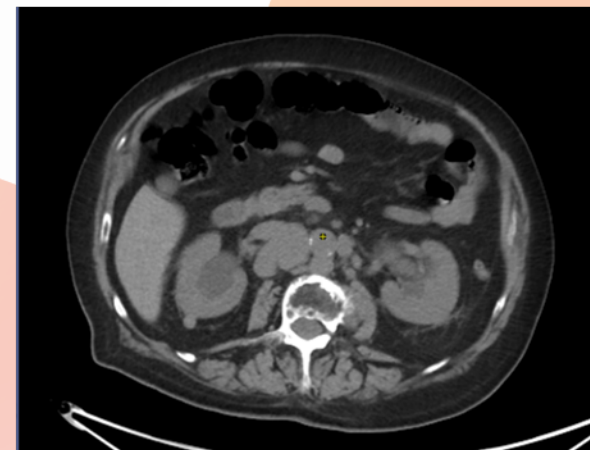
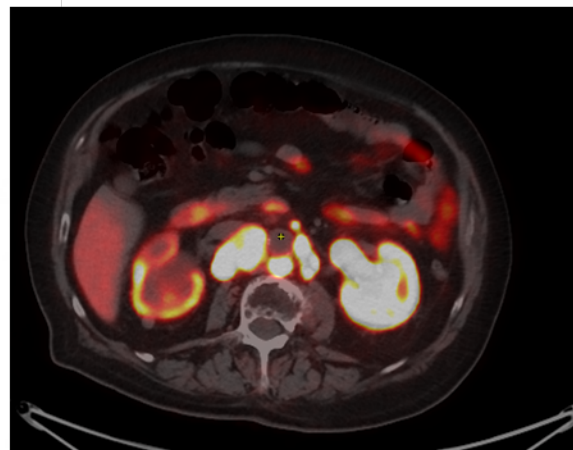
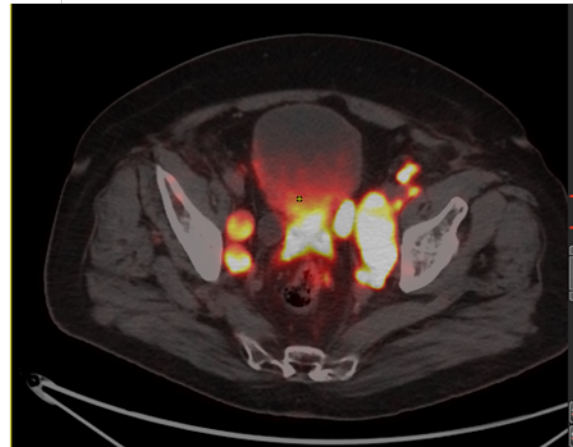
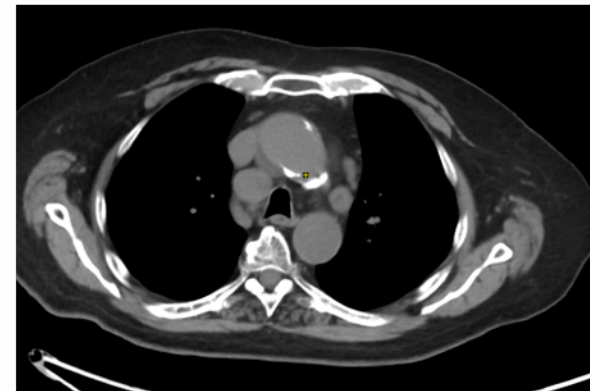
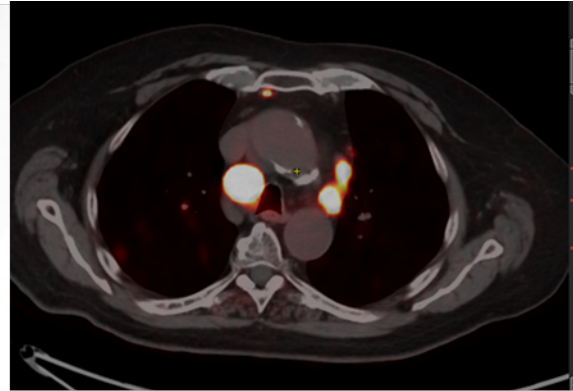


Seleccionar mejores respondedores

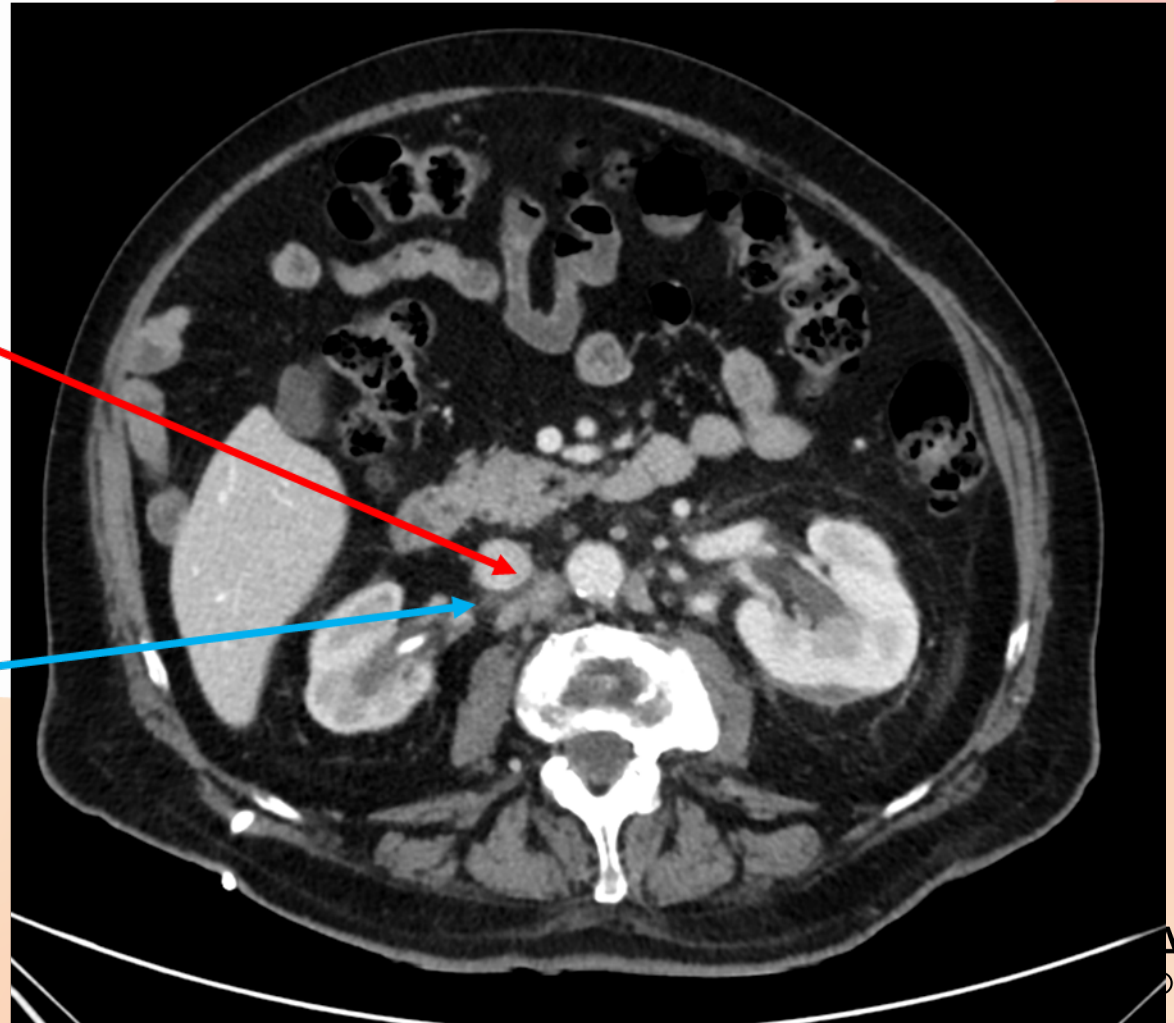
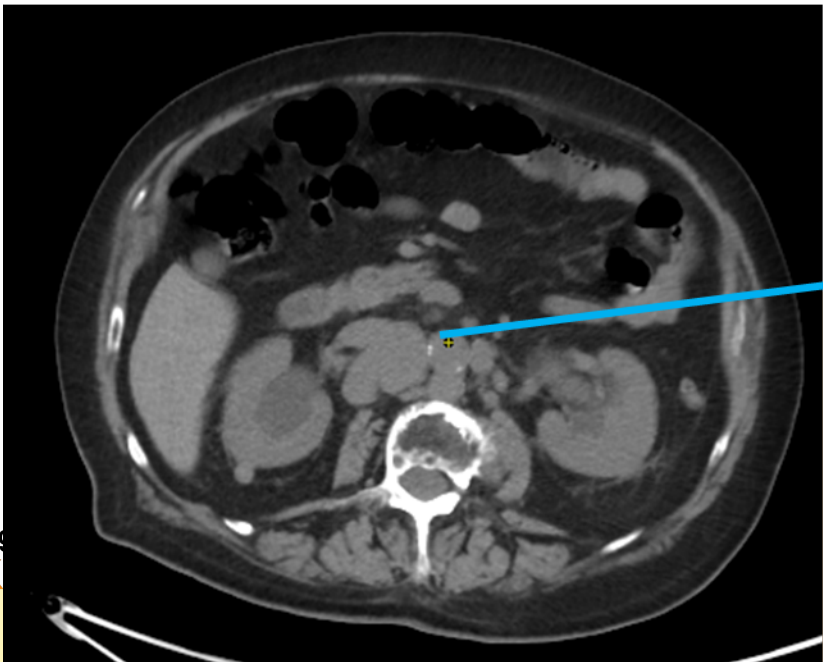
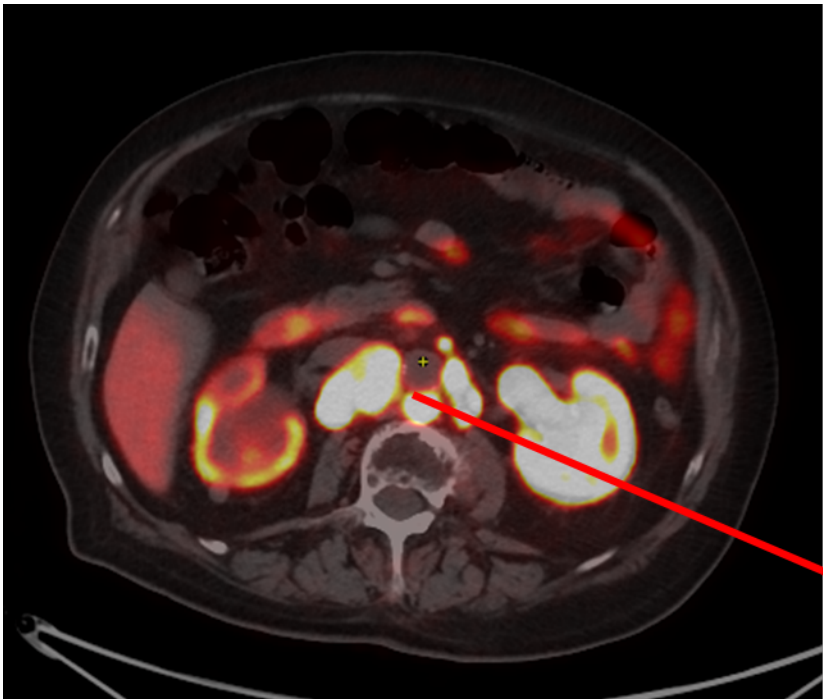
Lesiones PSMA negativas?? Vs Lesiones PSMA + con baja captación?



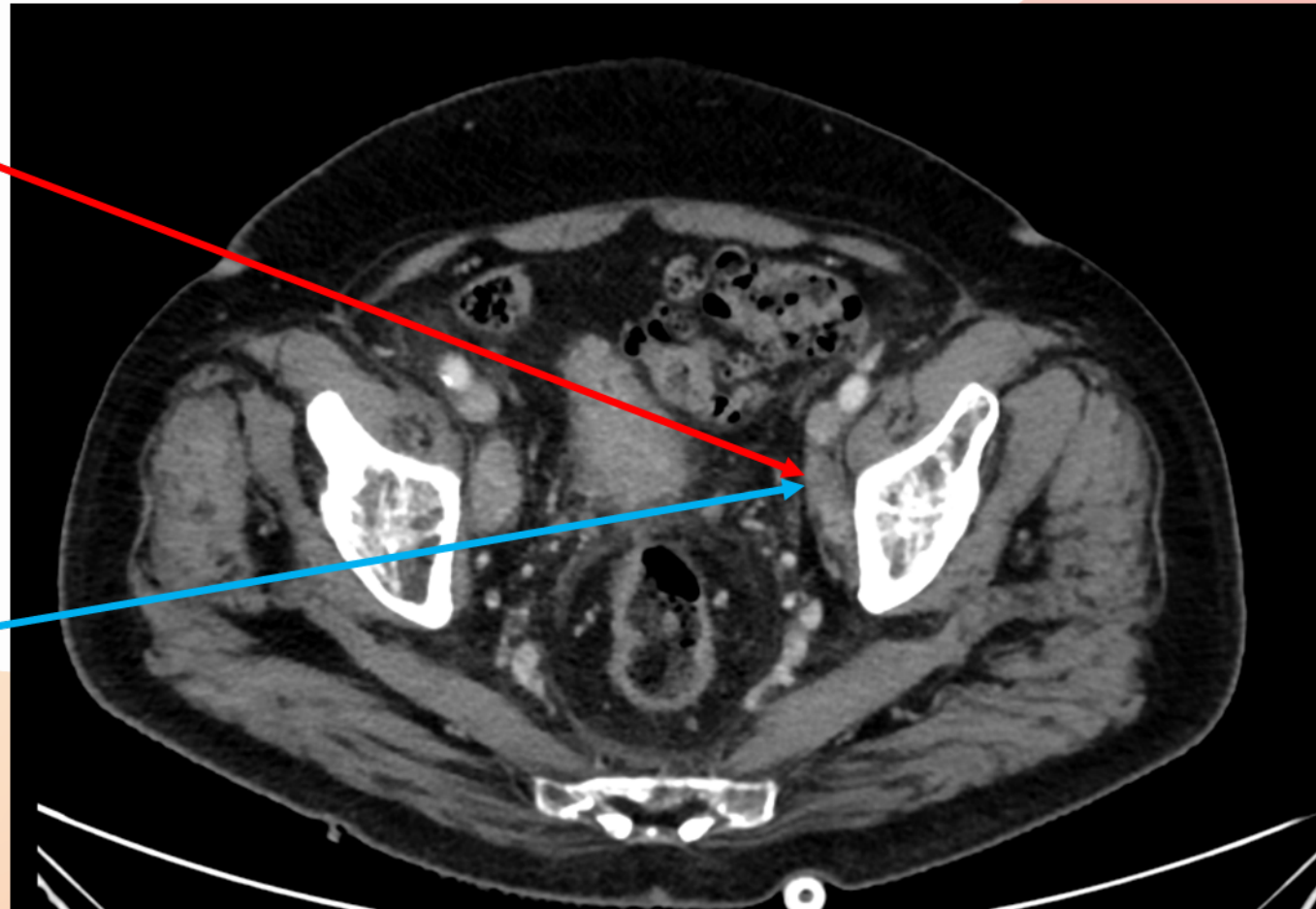
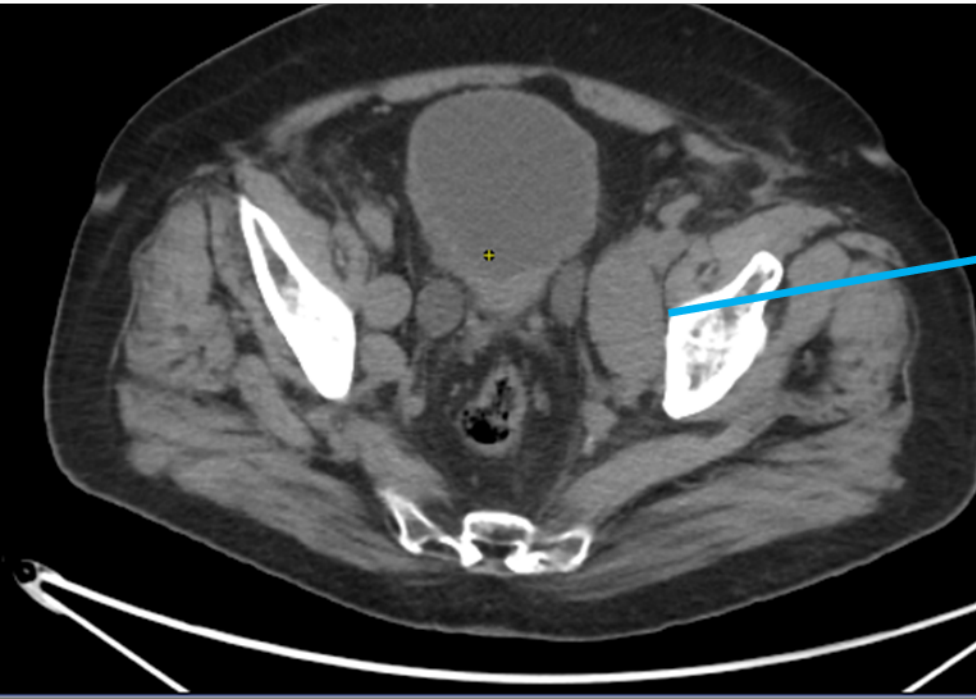
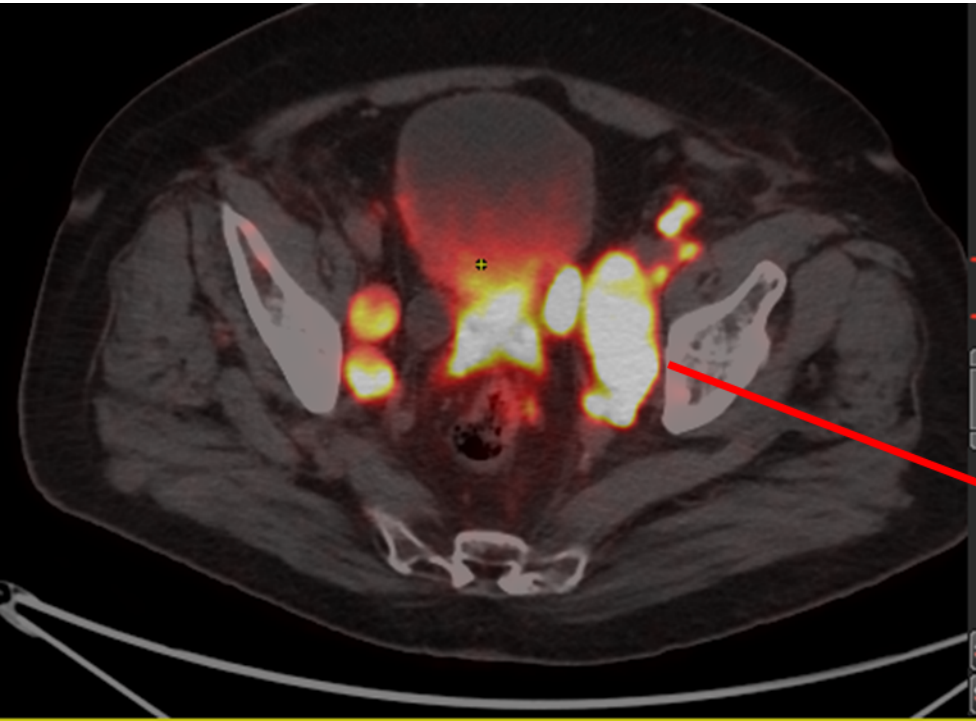
SUVmax 78



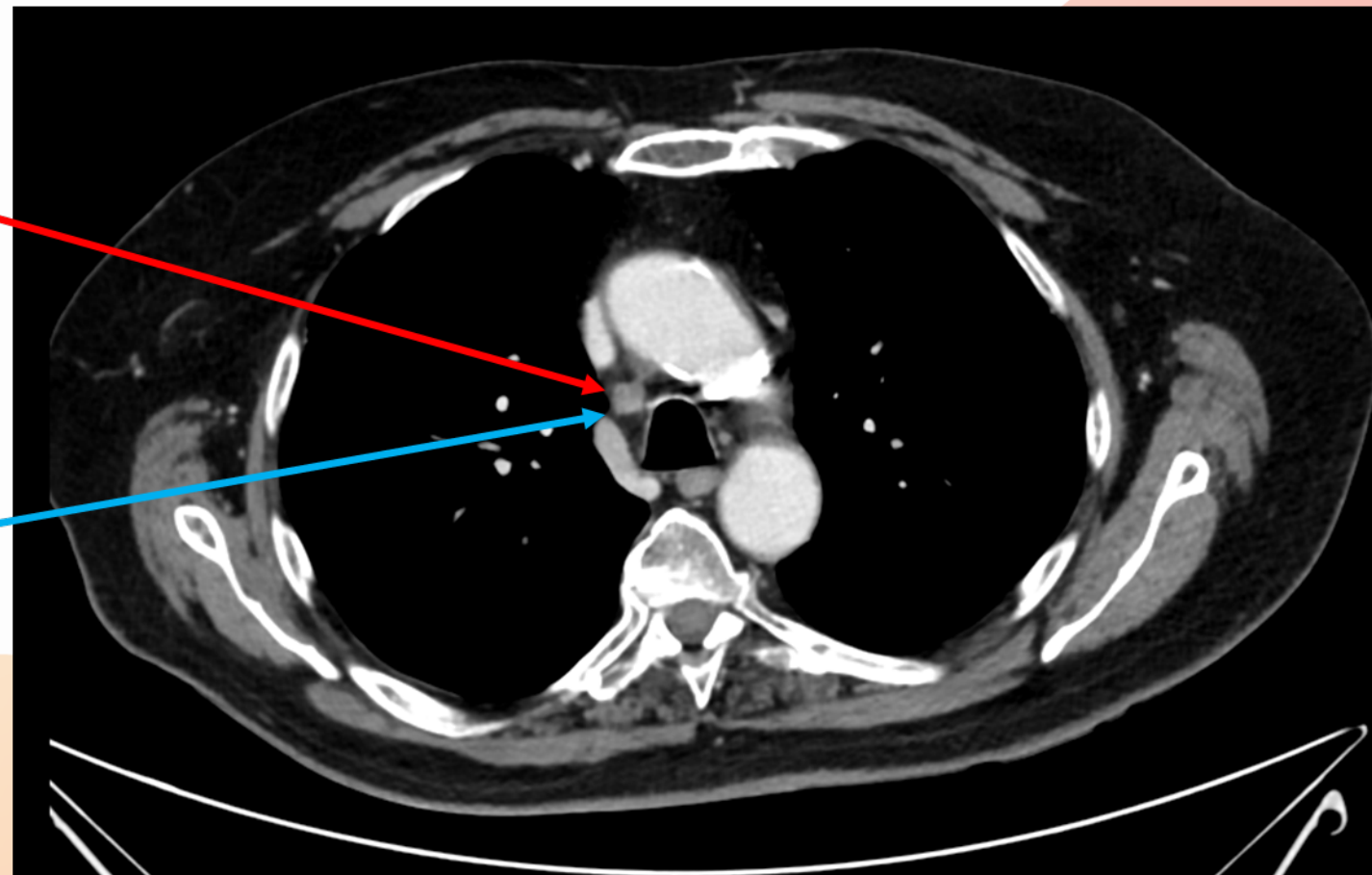
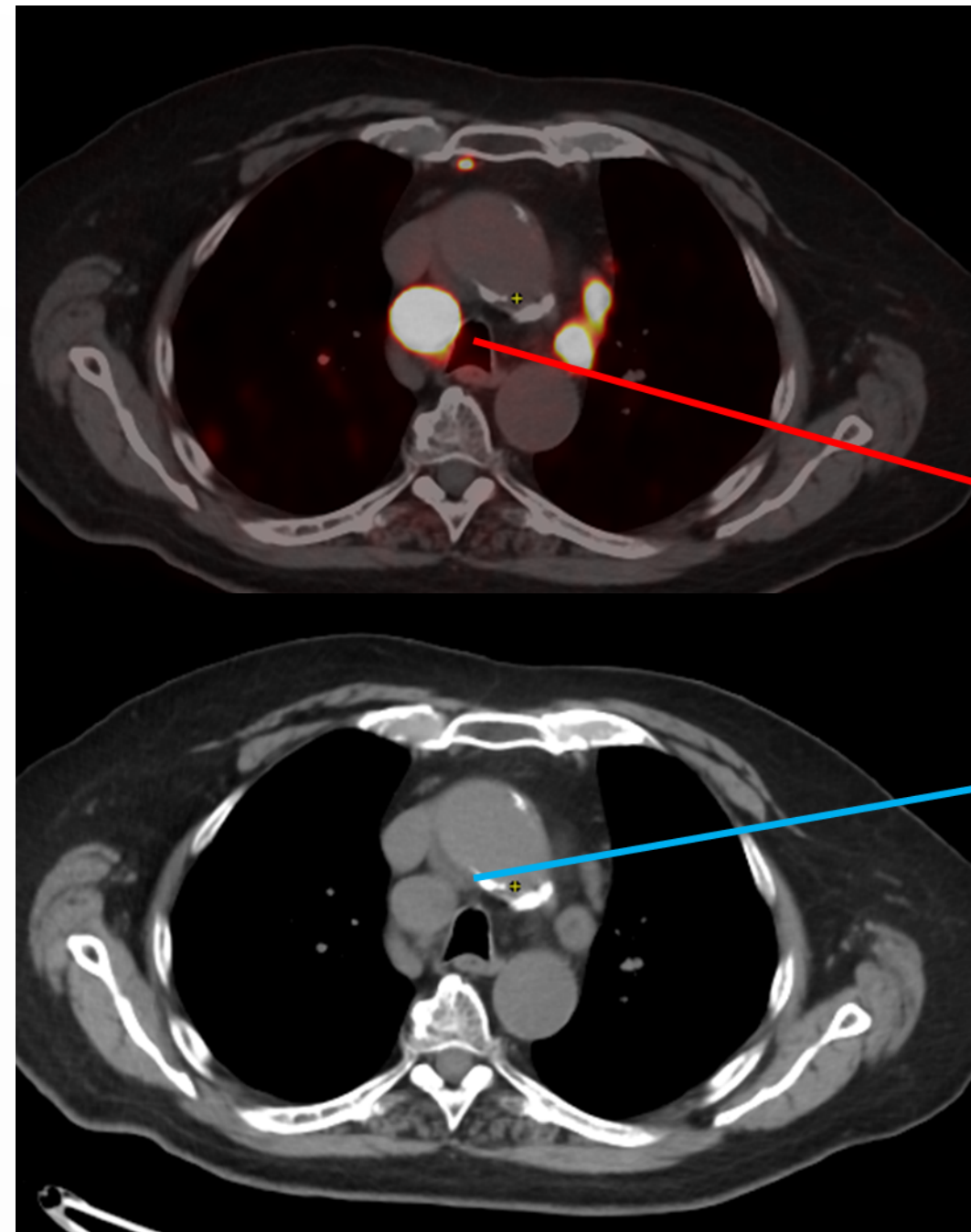
Tras 5c 177Lu-PSMA-617



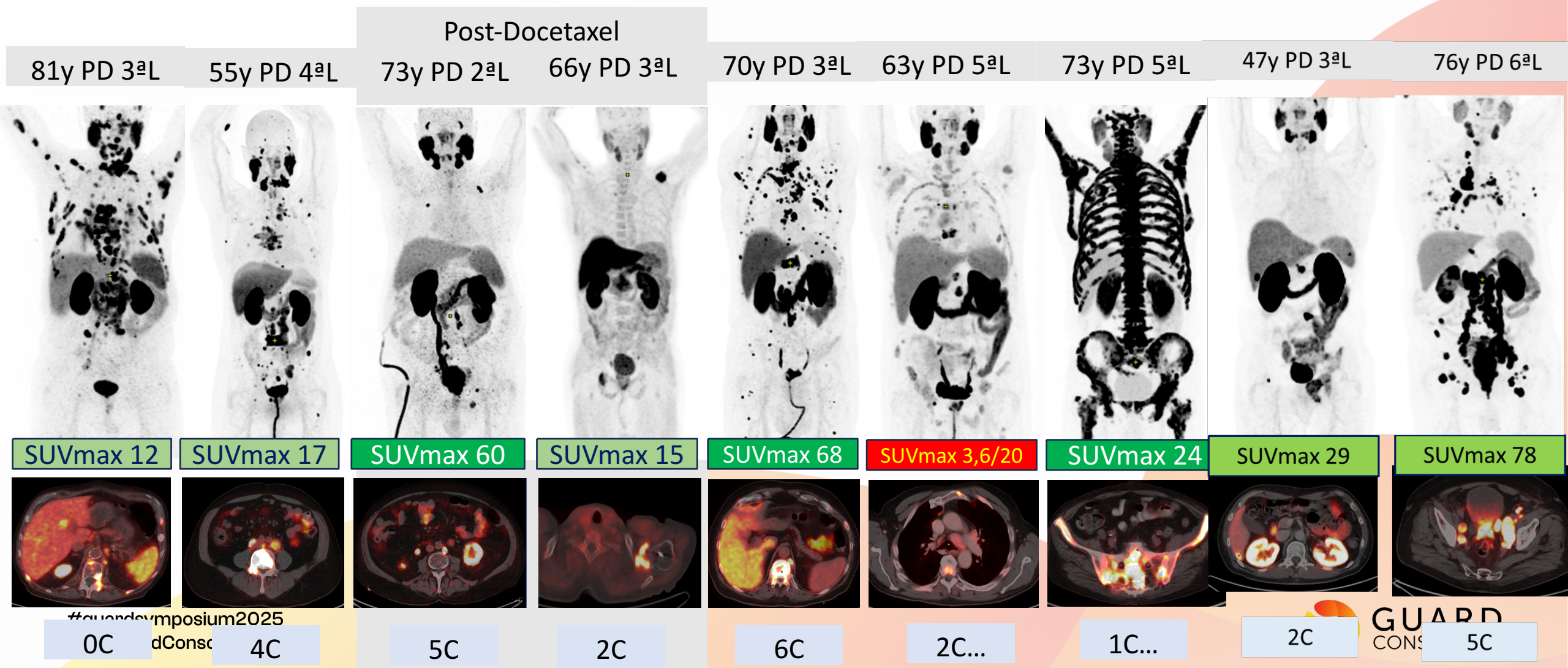
Tras 5c 177Lu-PSMA-617



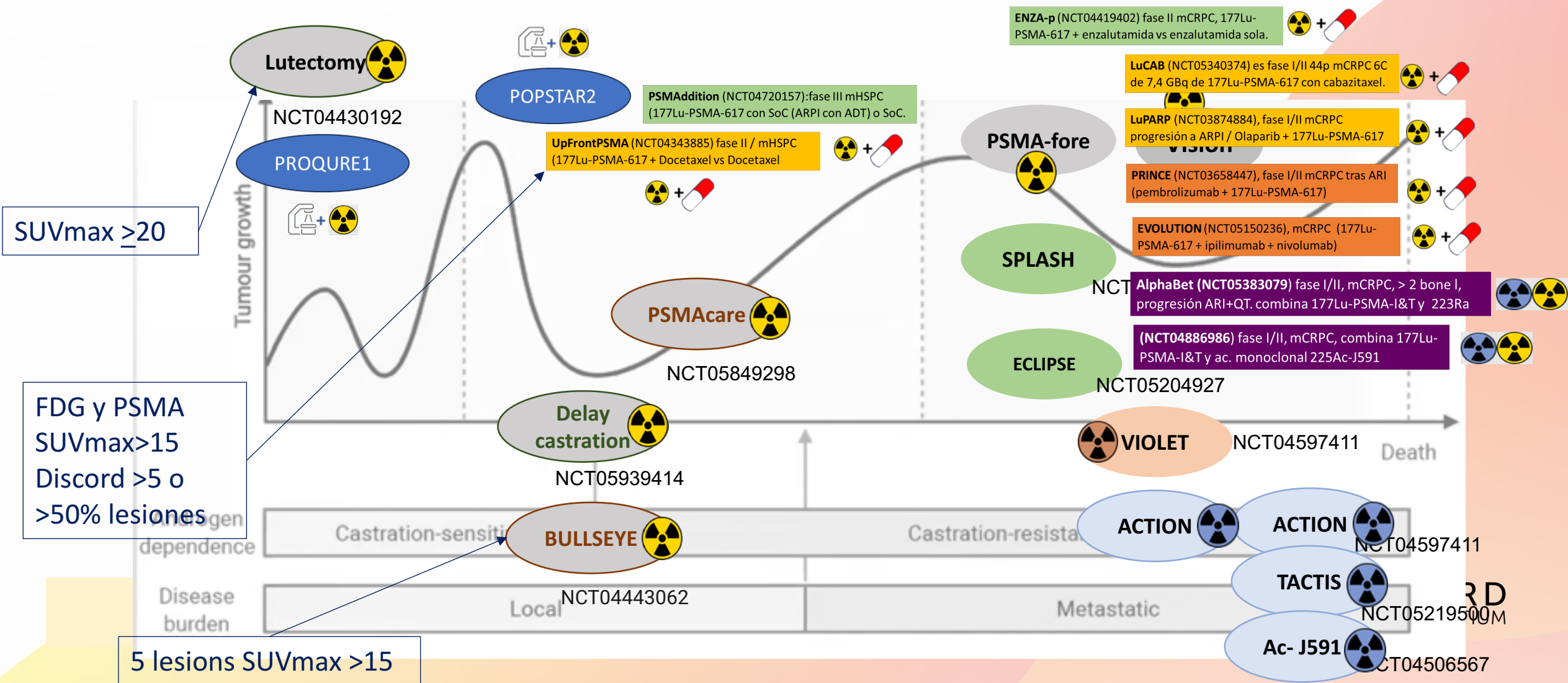
Tras 5c 177Lu-PSMA-617



Experiencia usos compasivos...



Where do we place radioligand treatment in the spectrum of advanced prostate cancer?



Resumen

Aprobado en CPRCm progresado al menos a 1 línea de taxanos.

Tendremos que empezar a seleccionar pacientes mejor respondedores, basándonos en la imagen.

Tendremos que posicionar ^{177}Lu -PSMA antes o después de Cabacitaxel. Criterios basados en imagen nos pueden ayudar a tomar esta decisión o a justificar TRL antes de Cabacitaxel.

En aprobaciones futuras como el escenario Fore o Adittion, tendremos que justificar más aún aquellos pacientes mejores candidatos.

Los EC de TRL adelantan la indicación de ^{177}Lu -PSMA, en monoterapia, en combinación con otros agentes, con otros RL y con RT externa.



¡Gracias!

