XXI Congreso Colombiano de Cáncer

Teragnóstico en Ca de próstata.

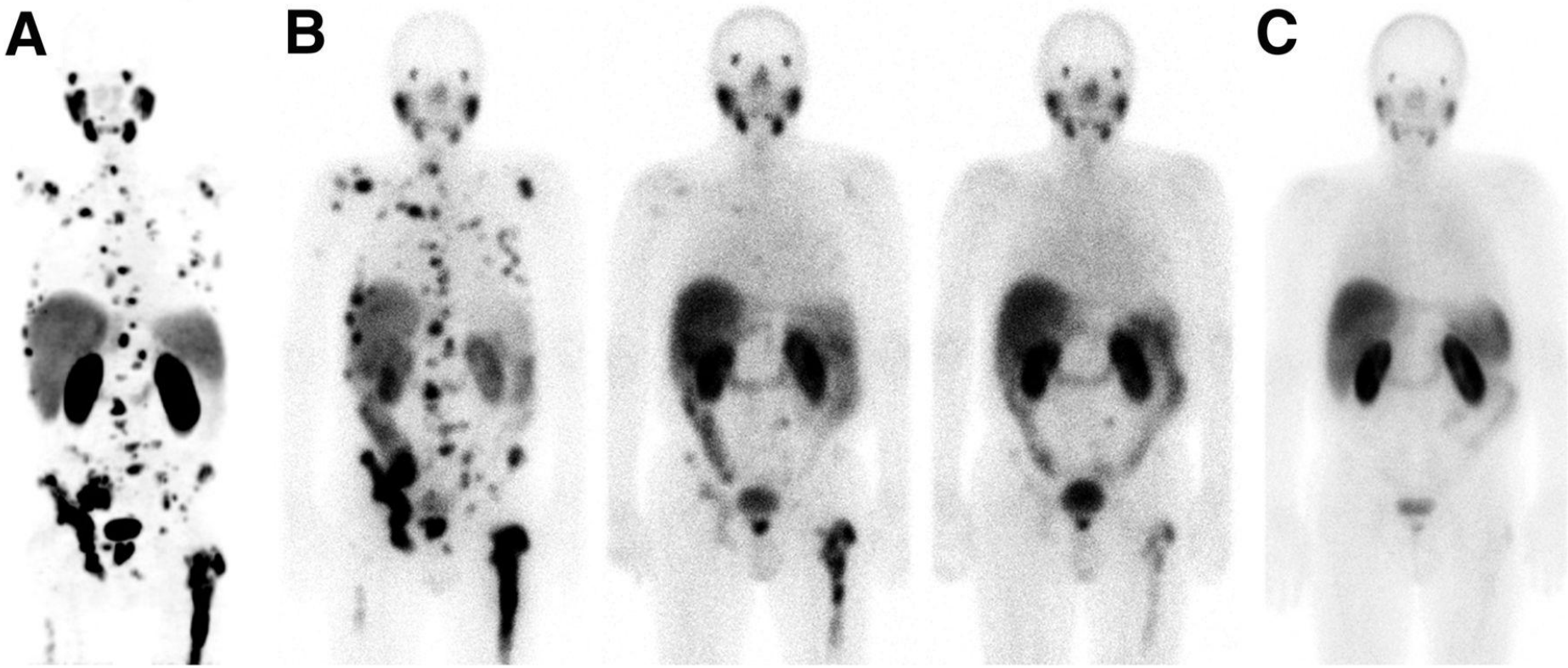
Carlos Eduardo Granados Gómez.

Medellín, 12 de agosto de 2022.

CTIC

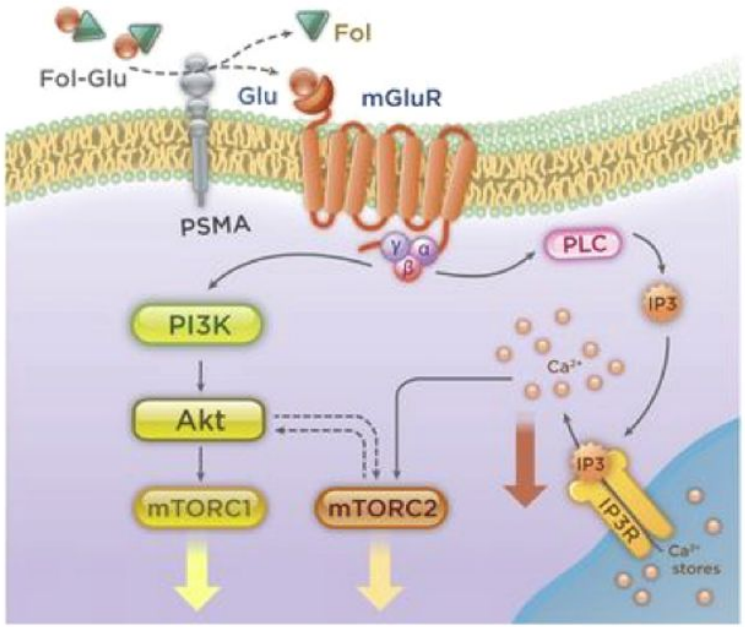
HOSPITAL UNIVERSITARIO SAN IGNACIO
CIENCIA Y TECNOLOGIA CON PROYECCION SOCIAL

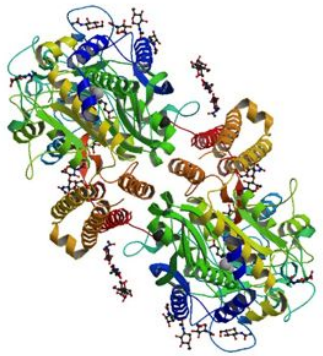
ASOPROCÁNCER
Asociación Pro Congreso de Cancerología



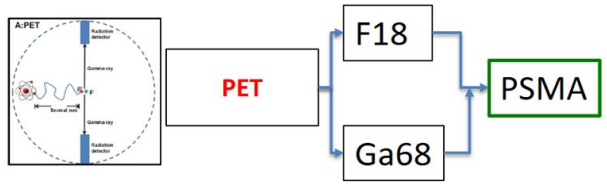
A	B	B	B	C
12/2014 PSA 387.06 ng/mL	12/2014 PSA 387.06 ng/mL	02/2015 PSA 9.21 ng/mL	04/2015 PSA 1.98 ng/mL	06/2015 PSA 1.08 ng/mL
150 MBq ^{68}Ga-PSMA11 PET/CT (MIP) 1 h p.i.	6 GBq ^{177}Lu-PSMA617 Planar scan (GM) 20 h p.i.	6 GBq ^{177}Lu-PSMA617 Planar scan (GM) 20 h p.i.	6 GBq ^{177}Lu-PSMA617 Planar scan (GM) 20 h p.i.	700 MBq ^{99m}Tc-MIP1427 Planar scan (GM) 3 h p.i.

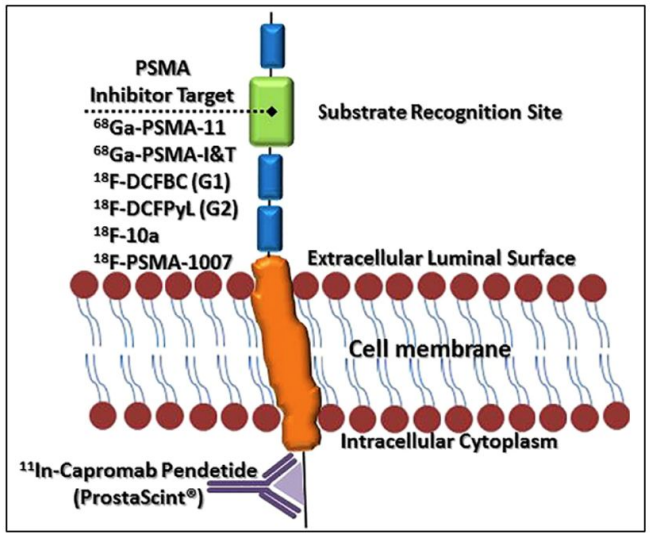
Journal of Nuclear Medicine August 2016, 57 (8) 1170-1176;





Cromosoma 11

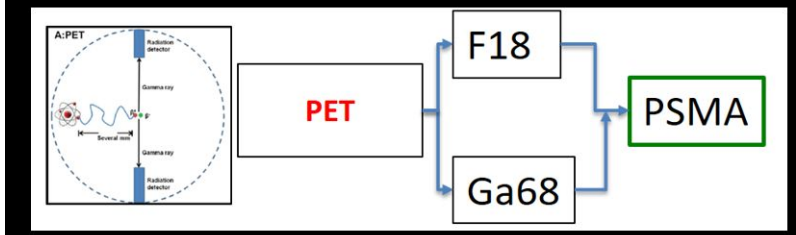


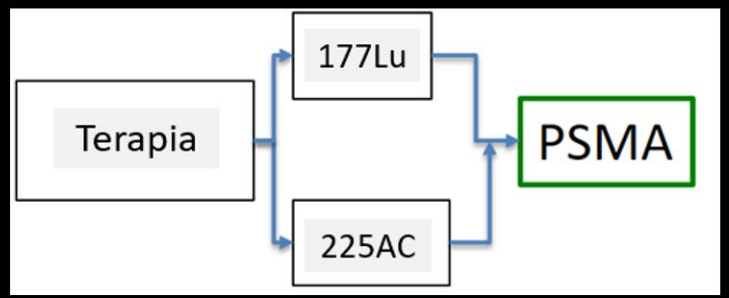


Glucoproteína transmembrana

Practical Radiation Oncology (2018) **8**, 28-39

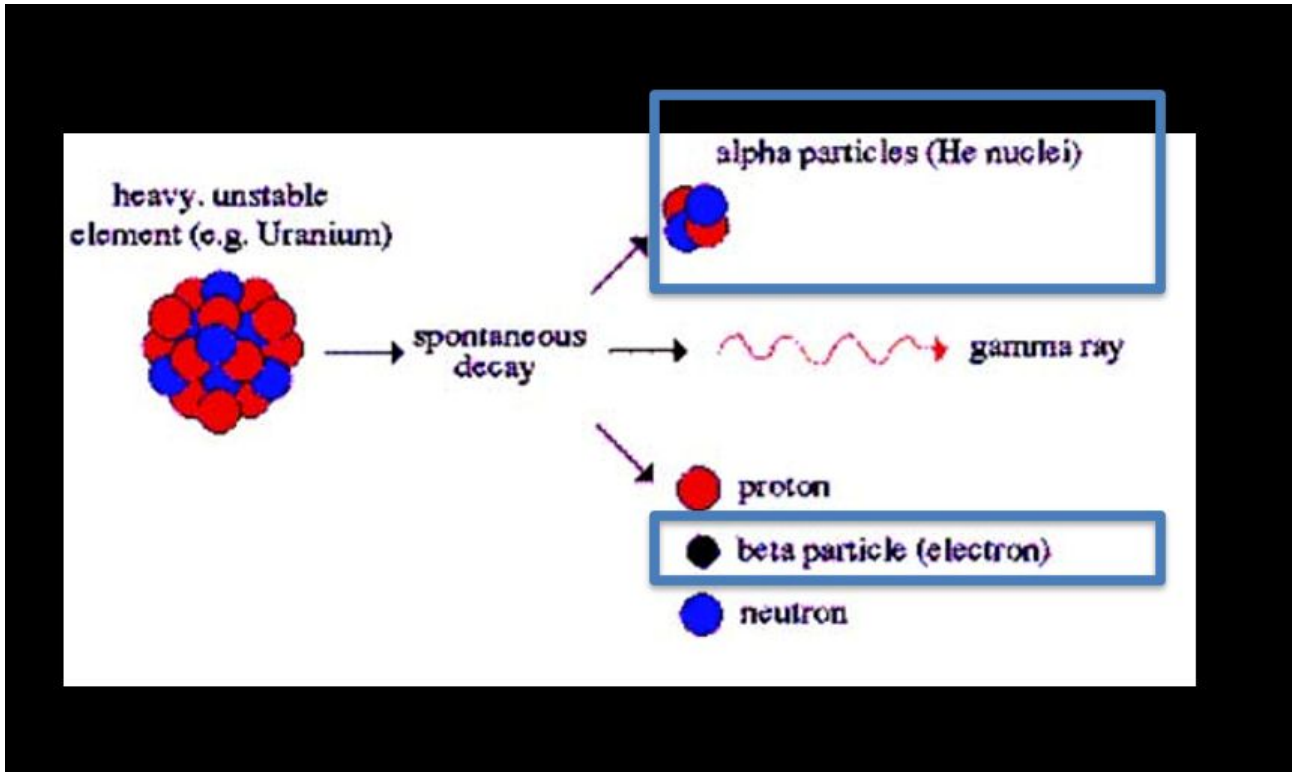
Del Dx al Tx: Teragnóstico





Energía γ = Imagen

Energía β y α = Terapia



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

O. Sartor, J. de Bono, K.N. Chi, K. Fizazi, K. Herrmann, K. Rahbar, S.T. Tagawa, L.T. Nordquist, N. Vaishampayan, G. El-Haddad, C.H. Park, T.M. Beer, A. Armour, W.J. Pérez-Contreras, M. DeSilvio, E. Kpamegan, G. Gericke, R.A. Messmann, M.J. Morris, and B.J. Krause, for the VISION Investigators*

This article was published on June 23, 2021, at NEJM.org.

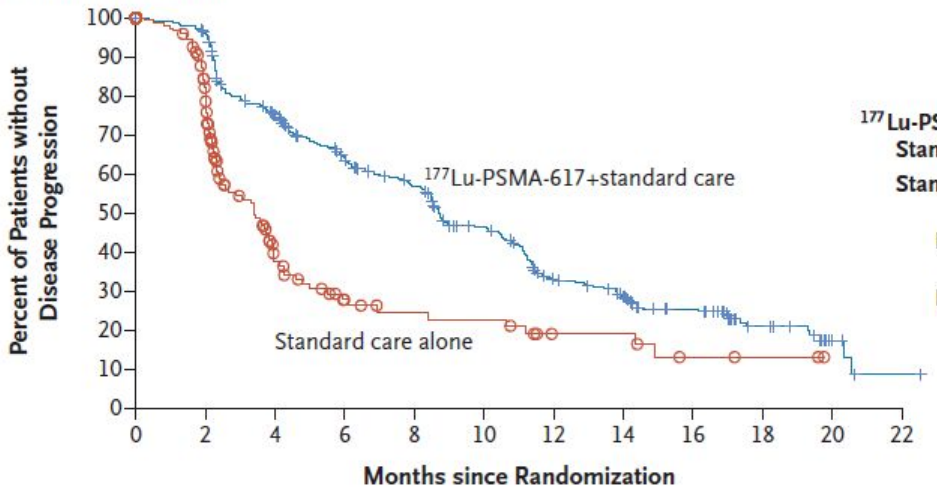
Elegibles

- mCRPC
- Al menos una lesión positivo en Ga68-PSMA(11) (sin lesiones negativas).
- ABI/ENZ previa
- ECOG 0 a 2
- Expectativa de vida de al menos 6 meses.

Intervenciones

- 2:1 (831 pacientes)
- Lu-PSMA-617 (200 x 4 (6) - (6sem)) + BSC vs BSC
- BSC:
  - No citotóxico, no inmunoterapia, no Ra223, no investigación.
  - Terapia hormonal, glucocorticoides, denosumab, bifosfonatos, RT.
- Se deben mantener niveles de castración.

A Imaging-Based Progression-free Survival



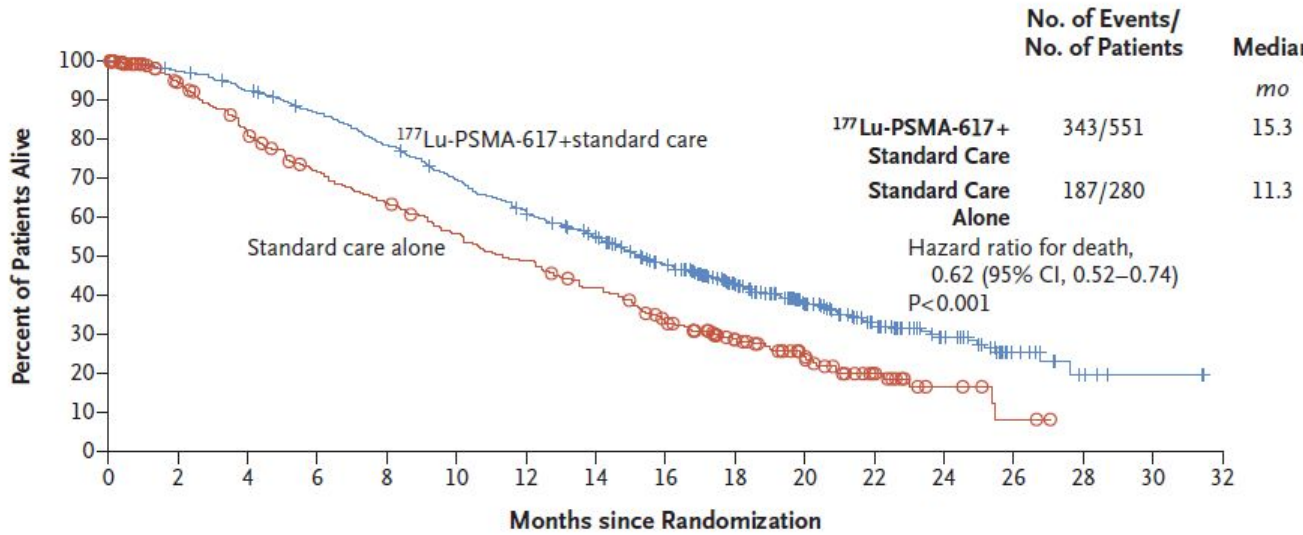
	No. of Events/ No. of Patients	Median *mo*
^{177}Lu-PSMA-617+ Standard Care	254/385	8.7
Standard Care Alone	93/196	3.4

Hazard ratio for progression or death, 0.40 (99.2% CI, 0.29–0.57)
P<0.001

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

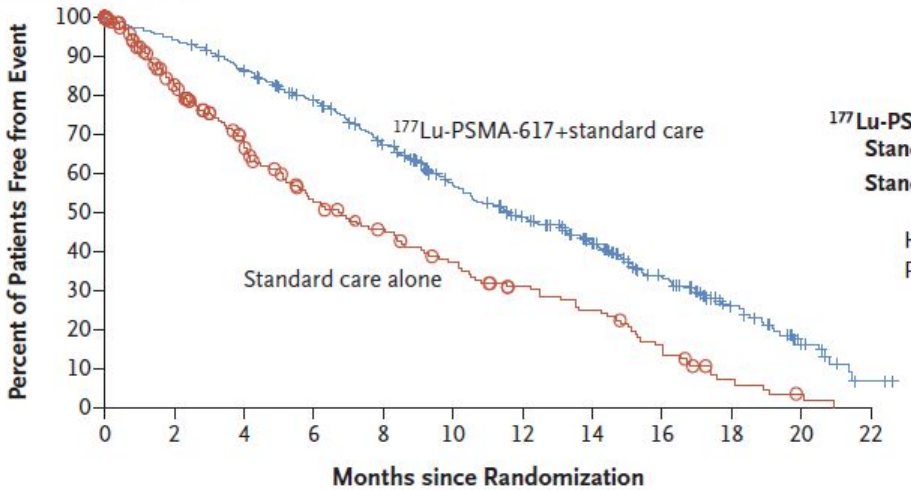
B **Overall Survival**



No. at Risk

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

C Time to First Symptomatic Skeletal Event



	No. of Events/ No. of Patients	Median
		mo
^{177}Lu-PSMA-617+ Standard Care	256/385	11.5
Standard Care Alone	137/196	6.8

Hazard ratio, 0.50 (95% CI, 0.40–0.62)
P<0.001

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

Table 2. Adverse Events.*

Event	^{177}Lu-PSMA-617 plus Standard Care (N=529)		Standard Care Alone (N=205)	
	All Grades	Grade ≥3	All Grades	Grade ≥3
	number of patients (percent)			
Any adverse event	519 (98.1)	279 (52.7)	170 (82.9)	78 (38.0)
Adverse event that occurred in >12% of patients				
Fatigue	228 (43.1)	31 (5.9)	47 (22.9)	3 (1.5)
Dry mouth	205 (38.8)	0	1 (0.5)	0
Nausea	187 (35.3)	7 (1.3)	34 (16.6)	1 (0.5)
Anemia	168 (31.8)	68 (12.9)	27 (13.2)	10 (4.9)
Back pain	124 (23.4)	17 (3.2)	30 (14.6)	7 (3.4)
Arthralgia	118 (22.3)	6 (1.1)	26 (12.7)	1 (0.5)
Decreased appetite	112 (21.2)	10 (1.9)	30 (14.6)	1 (0.5)
Constipation	107 (20.2)	6 (1.1)	23 (11.2)	1 (0.5)
Diarrhea	100 (18.9)	4 (0.8)	6 (2.9)	1 (0.5)
Vomiting	100 (18.9)	5 (0.9)	13 (6.3)	1 (0.5)
Thrombocytopenia	91 (17.2)	42 (7.9)	9 (4.4)	2 (1.0)
Lymphopenia	75 (14.2)	41 (7.8)	8 (3.9)	1 (0.5)
Leukopenia	66 (12.5)	13 (2.5)	4 (2.0)	1 (0.5)
Adverse event that led to reduction in ^{177}Lu-PSMA-617 dose	30 (5.7)	10 (1.9)	NA	NA
Adverse event that led to interruption of ^{177}Lu-PSMA-617†	85 (16.1)	42 (7.9)	NA	NA
Adverse event that led to discontinuation of ^{177}Lu-PSMA-617†	63 (11.9)	37 (7.0)	NA	NA
Adverse event that led to death‡	19 (3.6)	19 (3.6)	6 (2.9)	6 (2.9)

XXI CONGRESO COLOMBIANO DE CÁNCER

[^{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†*

www.thelancet.com **Published online February 11, 2021** **https://doi.org/10.1016/S0140-6736(21)00237-3**

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Elegibles

- mCRPC en progresión (PCWG3).
- Positivo en Ga68-PSMA(11): SUVmax 20 en próstata o al menos de 10 en enfermedad metastásica (lesiones medibles). Y sin lesiones discordantes en el PET FDG.
- ABI/ENZ permitido
- ECOG 0 a 2
- Expectativa de vida de al menos 6 meses.

Intervenciones

- 1:1 (200 pacientes)
- Lu-PSMA-617 (230 mCi x 6 - (6sem)) vs Cabazitaxel 20 (10 – 3 sem).

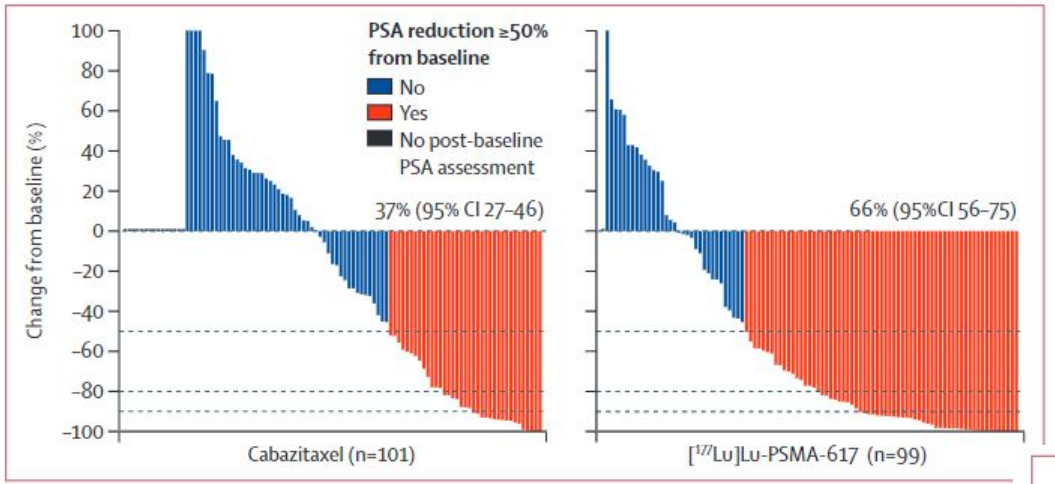


Figure 2: **PSA response**
PSA=prostate-specific antigen. ^{177}Lu=lutetium-177.

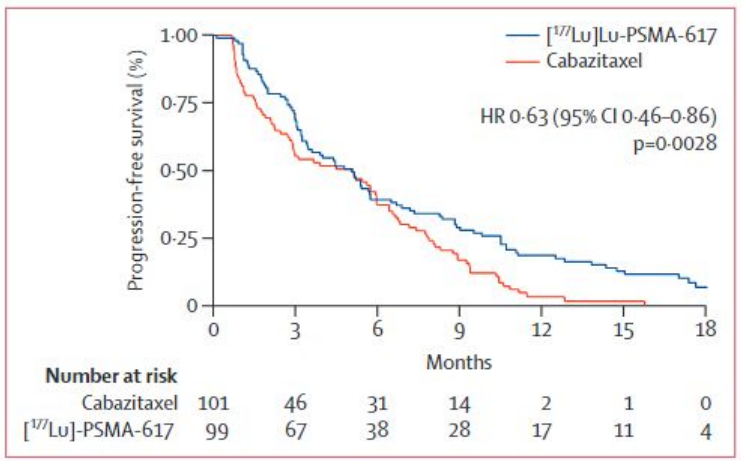


Figure 3: **Radiographic or PSA progression-free survival**
HR=hazard ratio. PSA=prostate-specific antigen. PSMA=prostate-specific membrane antigen. ^{177}Lu=lutetium-177.

	[^{177}Lu]Lu-PSMA-617 (n=98)		Cabazitaxel (n=85)	
	Grade 1–2	Grade 3–4	Grade 1–2	Grade 3–4
Fatigue	69 (70%)	5 (5%)	61 (72%)	3 (4%)
Pain*	60 (61%)	11 (11%)	52 (61%)	4 (5%)
Dry mouth	59 (60%)	0	18 (21%)	0
Diarrhoea	18 (18%)	1 (1%)	44 (52%)	4 (5%)
Nausea	39 (40%)	1 (1%)	29 (34%)	0
Thrombocytopenia	18 (18%)	11 (11%)	4 (5%)	0
Dry eyes	29 (30%)	0	3 (4%)	0
Anaemia	19 (19%)	8 (8%)	11 (13%)	7 (8%)
Neuropathy†	10 (10%)	0	22 (26%)	1 (1%)
Dysgeusia	12 (12%)	0	23 (27%)	0
Haematuria	3 (3%)	1 (1%)	12 (14%)	5 (6%)
Neutropenia‡	7 (7%)	4 (4%)	4 (5%)	11 (13%)
Insomnia	9 (9%)	0	12 (14%)	1 (1%)
Vomiting	12 (12%)	1 (1%)	10 (12%)	2 (2%)
Dizziness	4 (4%)	0	11 (13%)	0
Leukopenia	10 (10%)	1 (1%)	5 (6%)	1 (1%)
Any adverse event	53 (54%)	32 (33%)	34 (40%)	45 (53%)

Data are n (%). Events that occurred in at least 10% of participants are shown. ^{177}Lu=Lutetium-177. PSMA=prostate-specific membrane antigen. *Including bone, buttock, chest wall, flank, neck, extremity, tumour pain, or pelvic pain. †Motor or sensory. ‡Febrile neutropenia.

Table 2: **Adverse events**

Abstract #5000, #ASCO22, Hofman et. al.

Results and Conclusions:

- In this PSMA +ve mCRPC pt population, **overall survival was similar** in those patients randomly assigned to **LuPSMA versus cabazitaxel** (restricted mean survival time to 36 months was 19.1 vs. 19.6 months, difference -0.5, 95% CI -3.7 to + 2.7).
- No additional safety signals were identified with longer follow-up.
- Subsequent treatments among those assigned cabazitaxel included cabazitaxel in 21, and LuPSMA in 20; and among those assigned LuPSMA included additional LuPSMA in 5, and cabazitaxel in 32 .

@neerajaiims

biomedicines

MDPI

Systematic Review

^{177}Lu-PSMA Radioligand Therapy Is Favorable as Third-Line Treatment of Patients with Metastatic Castration-Resistant Prostate Cancer. A Systematic Review and Network Meta-Analysis of Randomized Controlled Trials

Finn E. von Eyben [1,*], Kalevi Kairemo [2,3], Channing Paller [4], Manuela Andrea Hoffmann [5,6], Giovanni Paganelli [7], Irene Virgolini [8] and Giandomenico Roviello [9]

Biomedicines **2021**, *9*, 1042. https://doi.org/10.3390/biomedicines9081042

Table 3. Ranking of treatments regarding PSA response.

Treatment	IXA	MITO	ABI/ENZA	CABA20	CABA25	PRLT	BSC
Best treatment	0.1	0.0	0.0	0.0	2.3	97.6	0.0
Worst treatment	0.0	0.0	59.1	0.0	0.0	0.0	33.1

Abbreviations as in Tables 1 and 2.

Table 4. Ranking of treatments regarding radiographic progression-free survival.

Treatment	CABA20	PRLT	BSC
Best treatment	18.5	81.5	0.0
Worst treatment	0.0	0.0	100

Abbreviations as in Tables 1 and 2.

XXI Congreso Colombiano de Cáncer

Nomograms to predict outcomes after ^{177}Lu-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

ASOPROCÁNCER
Asociación Pro Congreso de Cancerología

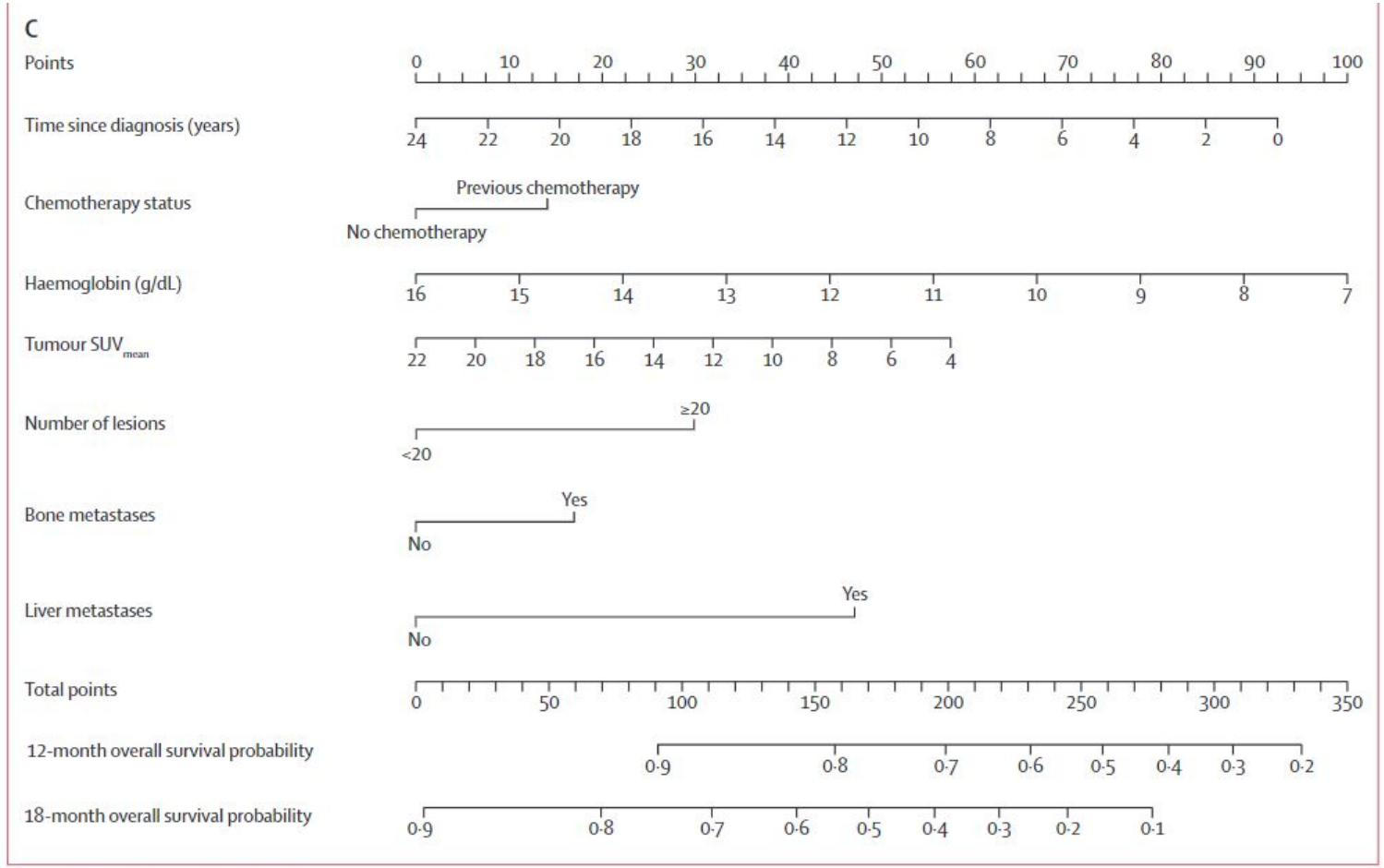


Figure 2: **Overall survival probabilities**

European Journal of Nuclear Medicine and Molecular Imaging (2019) 46:2536–2544
https://doi.org/10.1007/s00259-019-04485-3

GUIDELINES

Check for updates

EANM procedure guidelines for radionuclide therapy with ^{177}Lu-labelled PSMA-ligands (^{177}Lu-PSMA-RLT)

Clemens Kratochwil[1] · Wolfgang Peter Fendler[2] · Matthias Eiber[3] · Richard Baum[4] · Murat Fani Bozkurt[5] · Johannes Czernin[6] · Roberto C. Delgado Bolton[7] · Samer Ezziddin[8] · Flavio Forrer[9] · Rodney J. Hicks[10] · Thomas A. Hope[11] · Levant Kabasakal[12] · Mark Konijnenberg[13] · Klaus Kopka[1] · Michael Lassmann[14] · Felix M. Mottaghy[15] · Wim Oyen[16,17,18] · Kambiz Rahbar[19] · Heiko Schöder[20] · Irene Virgolini[21] · Hans-Jürgen Wester[22] · Lisa Bodei[20] · Stefano Fanti[23] · Uwe Haberkorn[1] · Ken Herrmann[2]

Contraindications

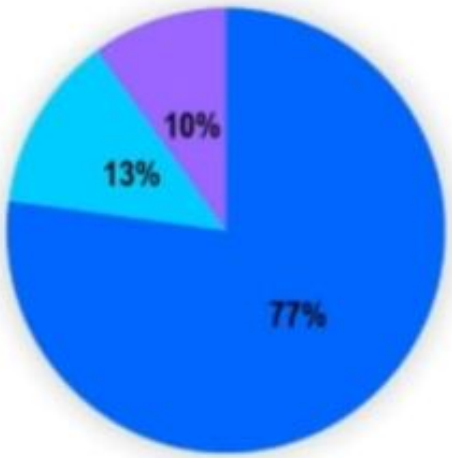
1. Life expectancy is less than 6 months (ECOG performance status > 2); unless the main objective is alleviating suffering from disease-related symptoms.
2. Unacceptable medical or radiation safety risk for isolation on a nuclear medicine therapy unit (if required by national regulations).
3. Unmanageable urinary tract obstruction or hydronephrosis; in patients with diagnosed or who are at high risk of urinary retention, ^{99m}Tc-MAG3 or ^{99m}Tc-DTPA renal scintigraphy should be considered as a baseline exam.
4. Progressive deterioration of organ function (GFR < 30 mL/min or creatinine > 2-fold upper limit of normal (ULN); liver enzymes > 5-fold ULN).
5. Myelosuppression:
   a. Total white cell count less than 2.5×10^9/L
   b. Platelet count less than 75×10^9/L
6. Conditions which require timely interventions (radiation therapy, surgery), e.g. spinal cord compression and unstable fractures, PSMA-RLT might be performed afterwards upon patient's condition. Borderline cases should be evaluated within the multidisciplinary tumour board for the individual benefit-to-risk ratio.

PSMA Questions

APCCC Advanced Prostate Cancer Consensus Conference www.apccc.org

63. For chemotherapy fit patients with PSMA imaging-positive mCRPC who meet any relevant criteria for Lutetium-PSMA therapy, who have received at least one line of AR pathway inhibitor and one line of taxane-based chemotherapy, what is your preferred treatment option for the majority of patients assuming treatments are readily available and there is no molecular alteration with approved therapy?

1. Lutetium-PSMA therapy
2. Cabazitaxel
3. Radium-223 if relevant criteria for treatment are met
4. Abstain



Option	Votes
Option 1	54
Option 2	9
Option 3	7
Abstain	4
Total votes	74

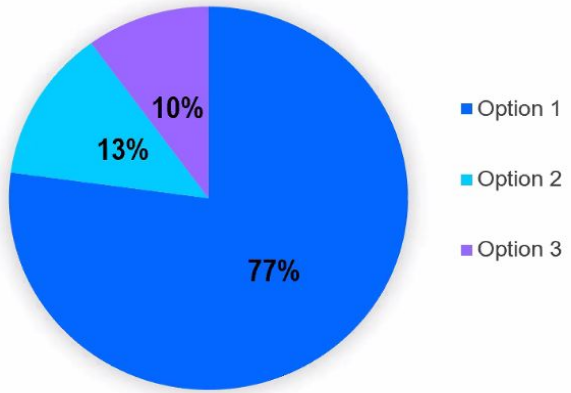
Preliminary results. For interpretation of results please refer to publication, which will follow shortly after APCCC 2021

Lu-PSMA: In which indication

APCCC ADVANCED PROSTATE CANCER CONSENSUS CONFERENCE www.apccc.org

For chemotherapy fit patients with PSMA imaging-positive mCRPC who meet any relevant criteria for Lutetium-PSMA therapy, who have received at least one line of AR pathway inhibitor and one line of taxane-based chemotherapy, what is your preferred treatment option for the majority of patients assuming treatments are readily available and there is no molecular alteration with approved therapy?

1. Lutetium-PSMA therapy
2. Cabazitaxel
3. Radium-223 if relevant criteria for treatment are met

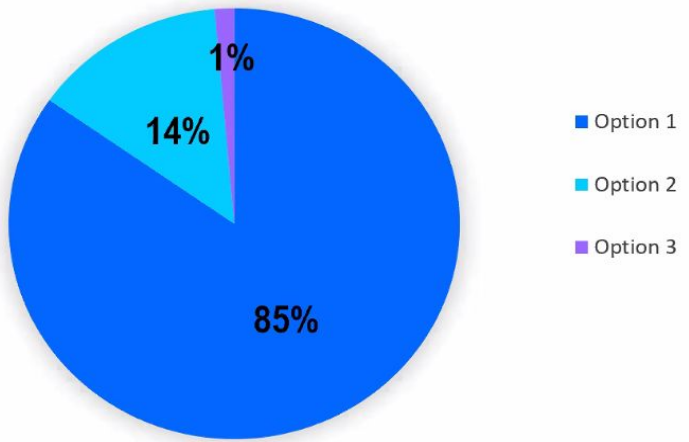


Gillessen S et al; 2022 Eur Urol

Lu-PSMA: In which indication

For chemotherapy fit patients with PSMA imaging-positive mCRPC who meet any relevant criteria for Lutetium-PSMA therapy, who have received at least one line of AR pathway inhibitor but no chemotherapy, what is your preferred treatment option for the majority of patients assuming treatments are readily available and there is no molecular alteration with approved therapy?

1. Docetaxel
2. Lutetium-PSMA therapy
3. Radium-223 if relevant criteria for treatment are met



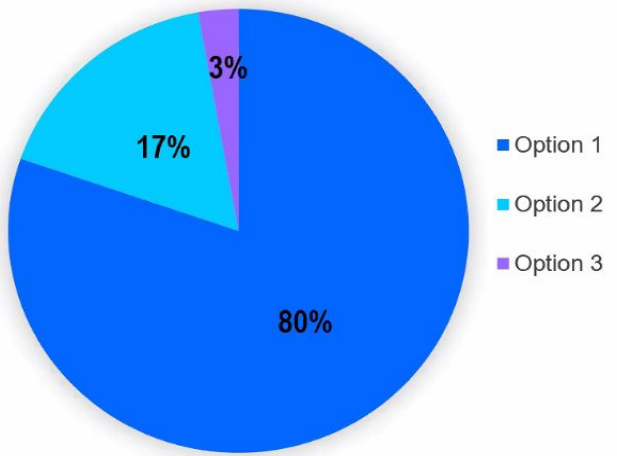
Gillessen S et al; 2022 Eur Urol

Lu-PSMA: In which indication

APCCC Advanced Prostate Cancer Consensus Conference www.apccc.org

For chemotherapy unfit patients with PSMA imaging-positive mCRPC who meet any relevant criteria for Lutetium-PSMA therapy progressing after at least one line of AR pathway inhibitor who cannot enrol in a clinical trial and if there is no molecular alteration with approved therapy, do you recommend Lutetium-PSMA therapy?

1. Yes
2. Yes, but only if the patient does not meet the criteria for treatment with radium-223
3. No

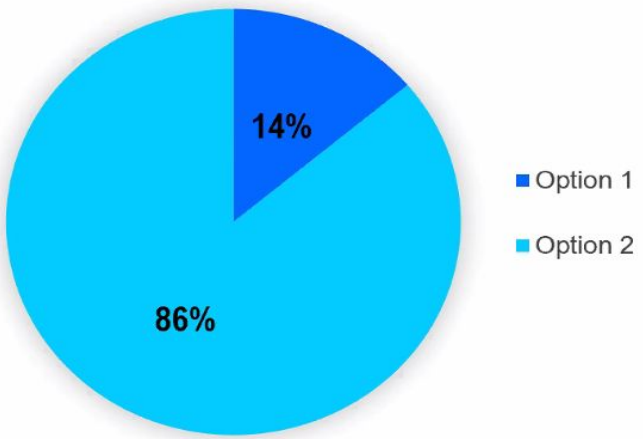


Gillessen S et al; 2022 Eur Urol

Lu-PSMA: In which indication

Is it appropriate to recommend Lutetium-PSMA therapy in patients with mHSPC outside of a clinical trial?

1. Yes
2. No

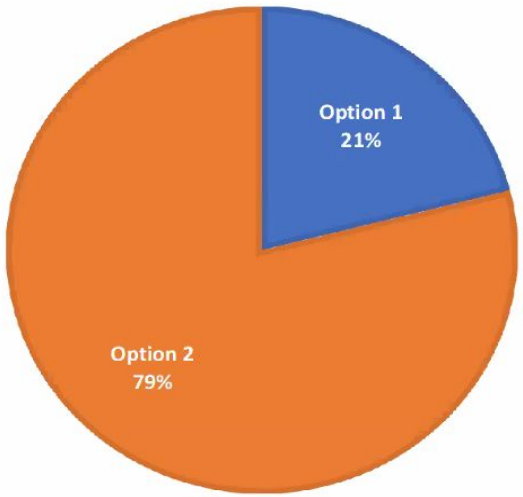


CRPC: Sequencing of therapies

APCCC Advanced Prostate Cancer Consensus Conference www.apccc.org

In the majority of patients with symptomatic mCRPC meeting criteria for both treatment with Radium-223 and ^{177}Lu-PSMA, which treatment do you recommend?

1. Radium-223
2. **^{177}Lu-PSMA**
3. Abstain/unqualified to answer



Preliminary results. For interpretation of results please refer to publication, which will follow shortly after APCCC 2022

Lu-PSMA: In which indication

Summary:

Consenus for
mCRPC:

- In chemotherapy-fit patients after ARPI **and** docetaxel
- In chemotherapy-unfit patients after ARPI
- If criteria fulfilled consensus for using Lu-PSMA over Rad-223

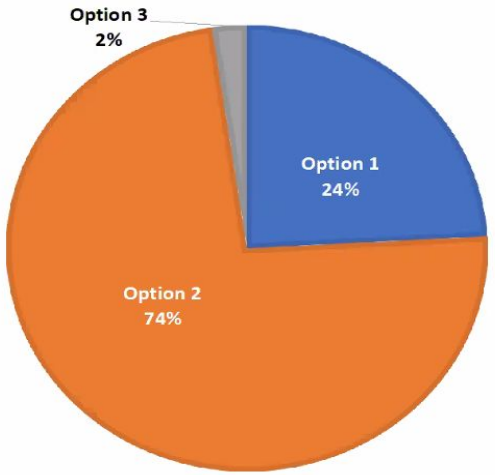
NOT in hormone-sensitive settings (outside of clinical trials)

How to select patients for Lu-PSMA

APCCC ADVANCED PROSTATE CANCER CONSENSUS CONFERENCE www.apccc.org

159. Based on PSMA PET, what threshold of uptake do you recommend for ^{177}Lu-PSMA therapy?

1. According to TheraP criteria (At least one metastatic lesion with PSMA-uptake SUVmax > 20)
2. According to VISION criteria (At least one metastatic lesion with PSMA-uptake > liver)
3. A PSMA PET is not needed for treatment selection
4. Abstain/unqualified to answer



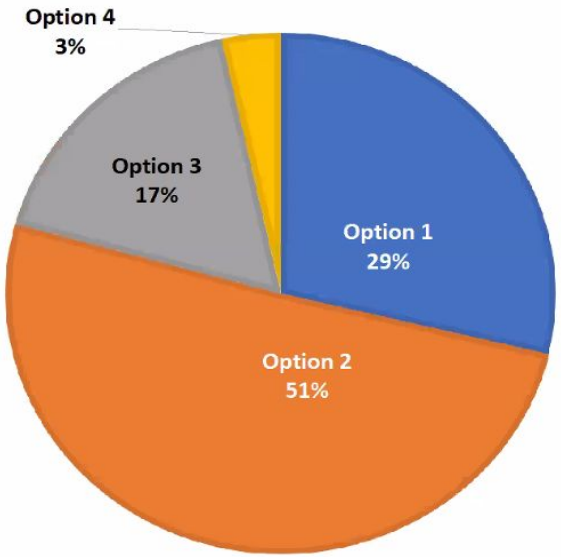
Option	Votes
Option 1	21
Option 2	64
Option 3	2
Option 4	17
Total votes	104

Preliminary results. For interpretation of results please refer to publication, which will follow shortly after APCCC 2022

How to select patients for Lu-PSMA

160. In the workup for ^{177}Lu-PSMA therapy, how do you identify PSMA-negative sites of disease in the majority of patients?

1. Correlate PSMA PET/CT with FDG PET/CT (like in the TheraP study)
2. Correlate PSMA PET/CT with contrast-enhanced CT (like in the VISION study)
3. Use FDG PET/CT selectively, if the correlation with contrast-enhanced CT provides equivocal results
4. Identification of PSMA-negative lesions is not needed
5. Abstain/unqualified to answer



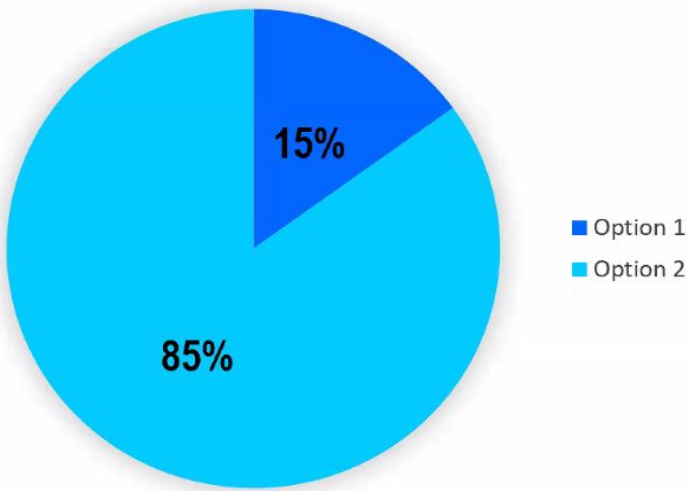
Option	Votes
Option 1	25
Option 2	44
Option 3	15
Option 4	3
Option 5	17
Total votes	104

Preliminary results. For interpretation of results please refer to publication, which will follow shortly after APCCC 2022

Patient selection

Is it safe to recommend initiating treatment with Lutetium-PSMA in a patient with mCRPC and relevant impaired bone marrow function (e.g. outside of the permitted VISION inclusion criteria: haemoglobin <9 g/l and/or neutrophils <1.5 G/l and/or platelets <100 G/l)

1. Yes
2. No



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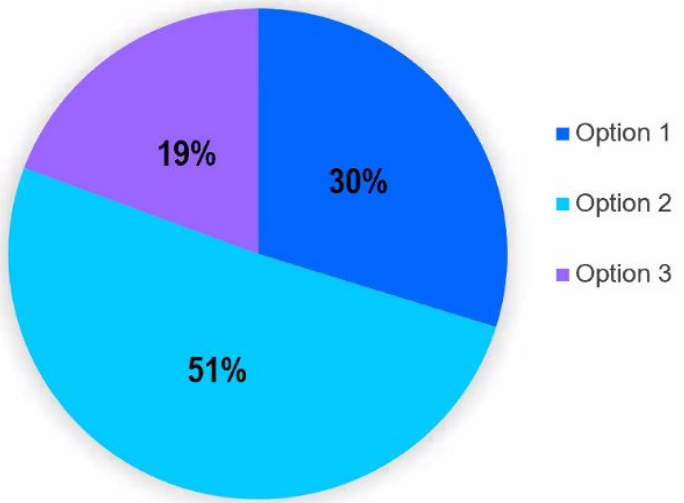
Patient selection

Is it safe to recommend treatment with Lutetium-PSMA in a patient with mCRPC with and impaired renal function (e.g. GFR 30- 49 ml/min)?

1. Yes
2. Yes, but reduced dose of Lutetium-PSMA
3. No



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Gracias.

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