Innovando en el abordaje multidisciplinar del cáncer de próstata en Andalucía

Málaga, **27** de **septiembre** de **2023**

Organizado por: En colaboración con:

Sociedad andaluza de oncología médica

SAMN Sociedad Andaluza de Medicina Nuclear

Advanced Accelerator Applications A Novartis Company

17:10h - 17:30h **Evidencia actual acerca del tratamiento del CPRCm; ¿qué nos dicen las guías clínicas? EECC disponibles.**

Dra. Raquel Luque Caro.
Servicio de Oncología Médica.
Hospital Universitario Virgen de las Nieves, Granada

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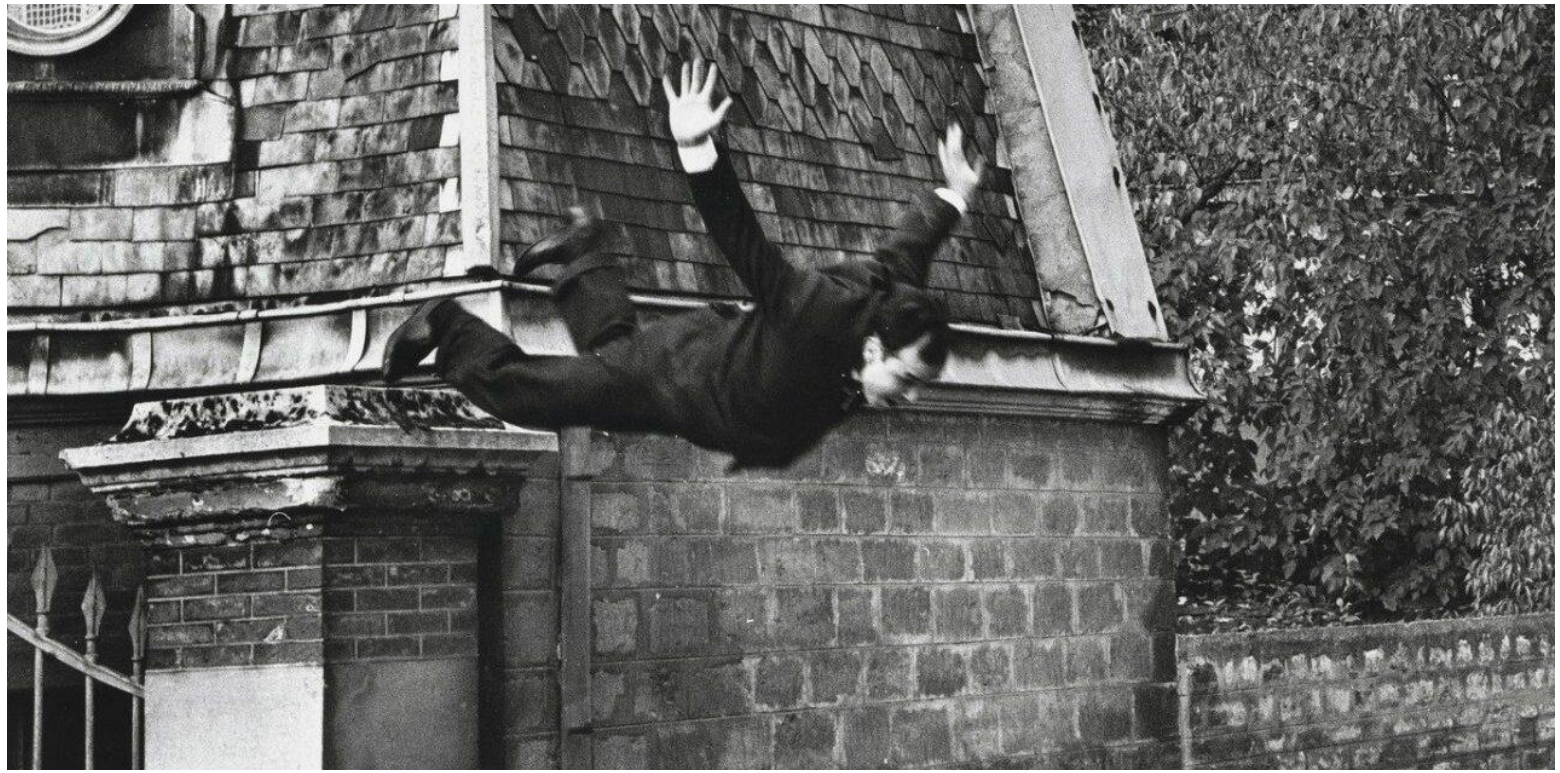

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Radiofármacos

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Estrategia terapéutica CP

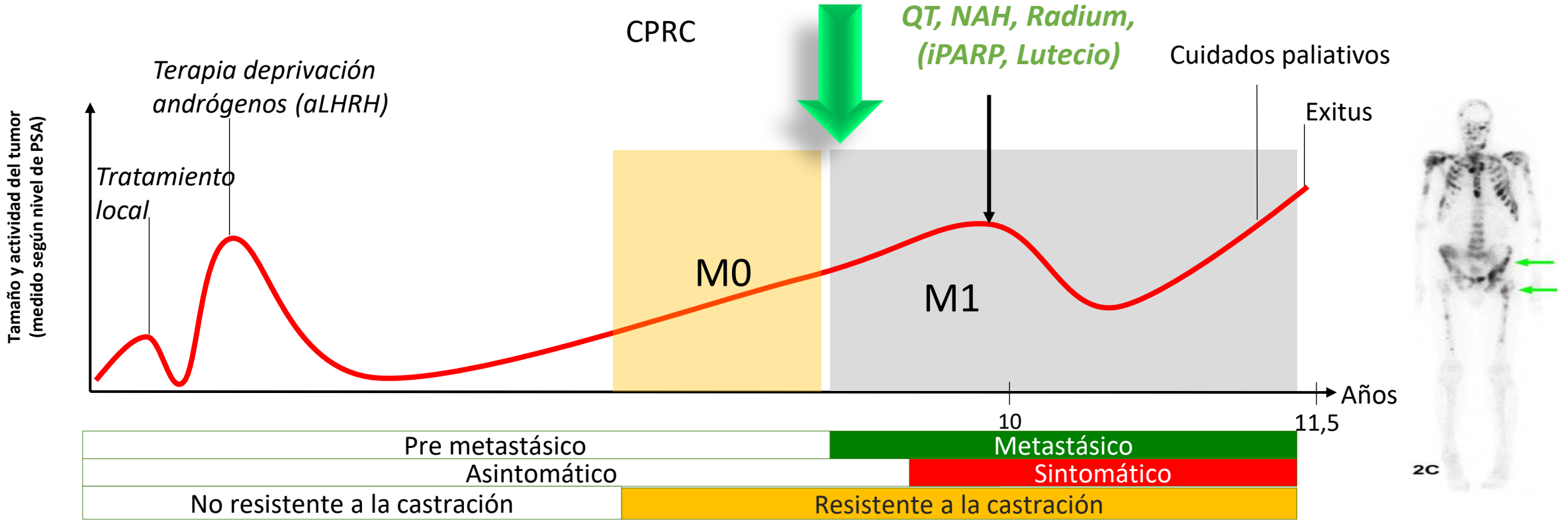
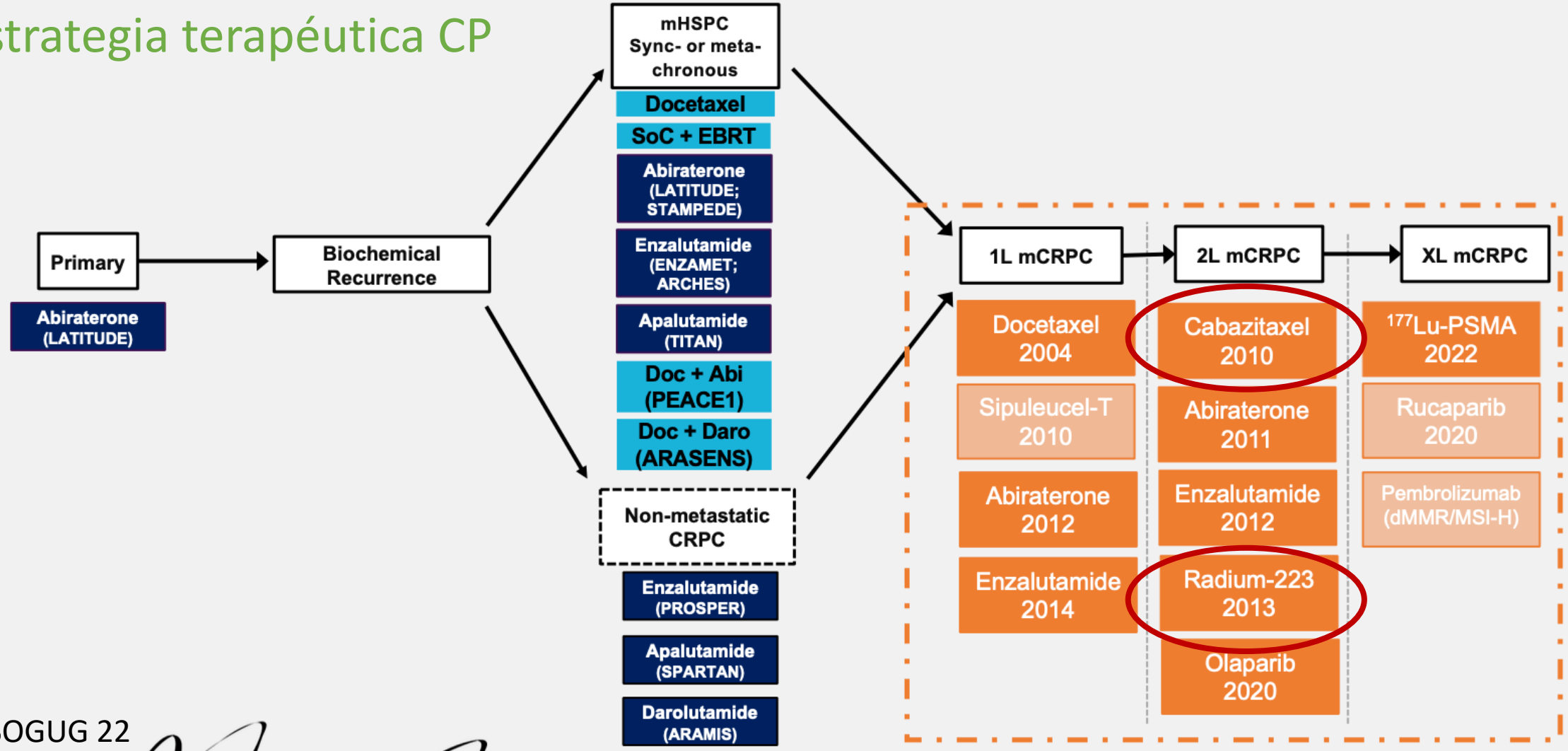


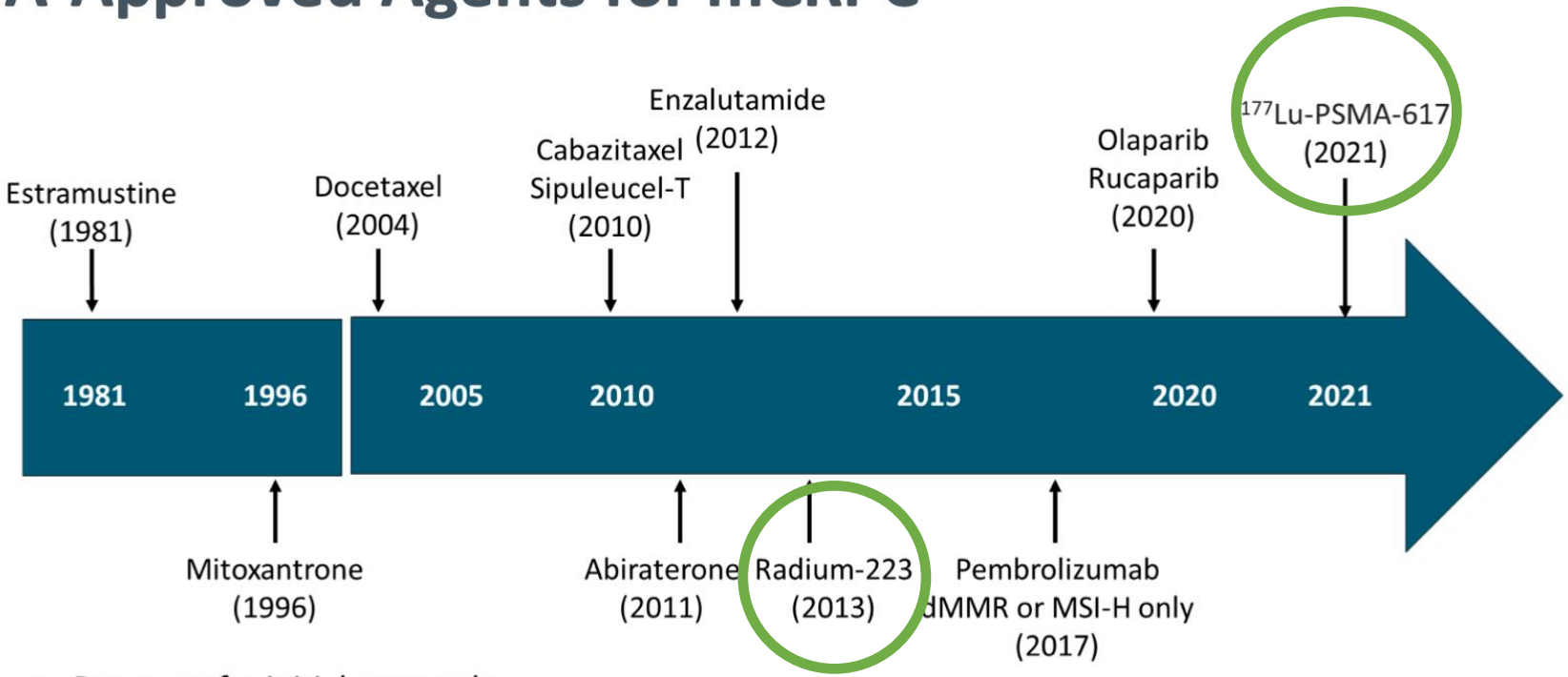
Gráfico adaptado de: 1. Hofland J et al. Cancer Res 2010; 70:1256-1264. 2. Chen Y et al. Lancet Oncol 2009; 10 (10): p981-91 3. Hoimes CJ, Kelly WK. Redefining hormone resiste in prostate cancer. Ther Adv Med Oncol. 2010;2(2):107-123. 4. Scher, H.I. et al. Design and end points of clinical trials for patients with progressive prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Eworking Group. J Clin Oncol. 2008;26(7): 1148-59.

Estrategia terapéutica CP



SOGUG 22

FDA-Approved Agents for mCRPC

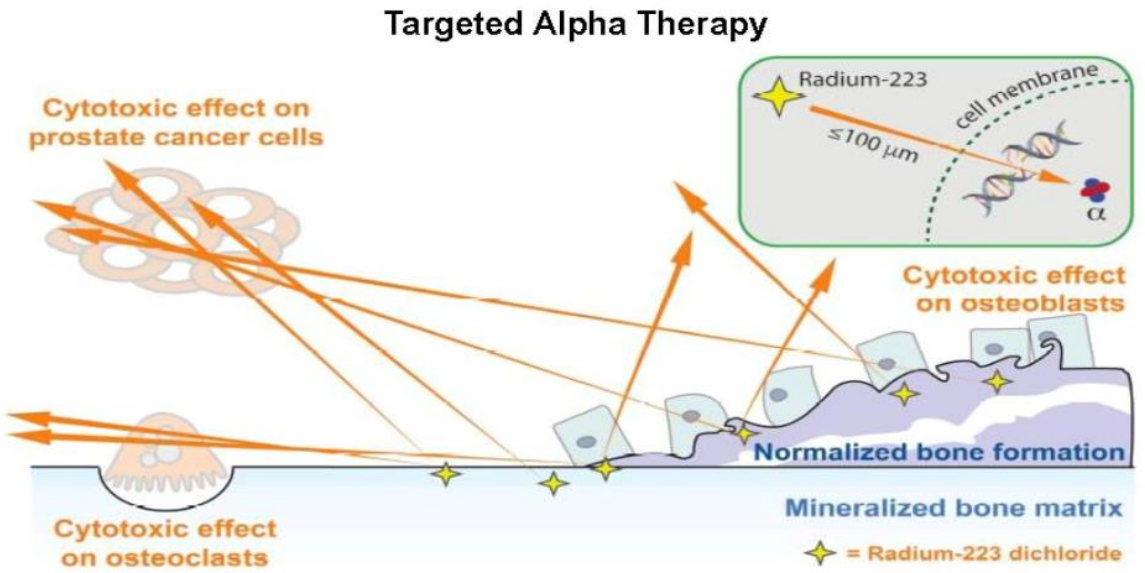


- Dates are for initial approvals

Abiraterone PI. Enzalutamide PI, Docetaxel PI. Cabazitaxel PI. Mitoxantrone PI. Estramustine PI. Sipuleucel-T PI. Pembrolizumab PI. Radium-223 PI. Olaparib PI. Rucaparib PI.


Lutecio
Radium

Radium-223: Mechanism of Action



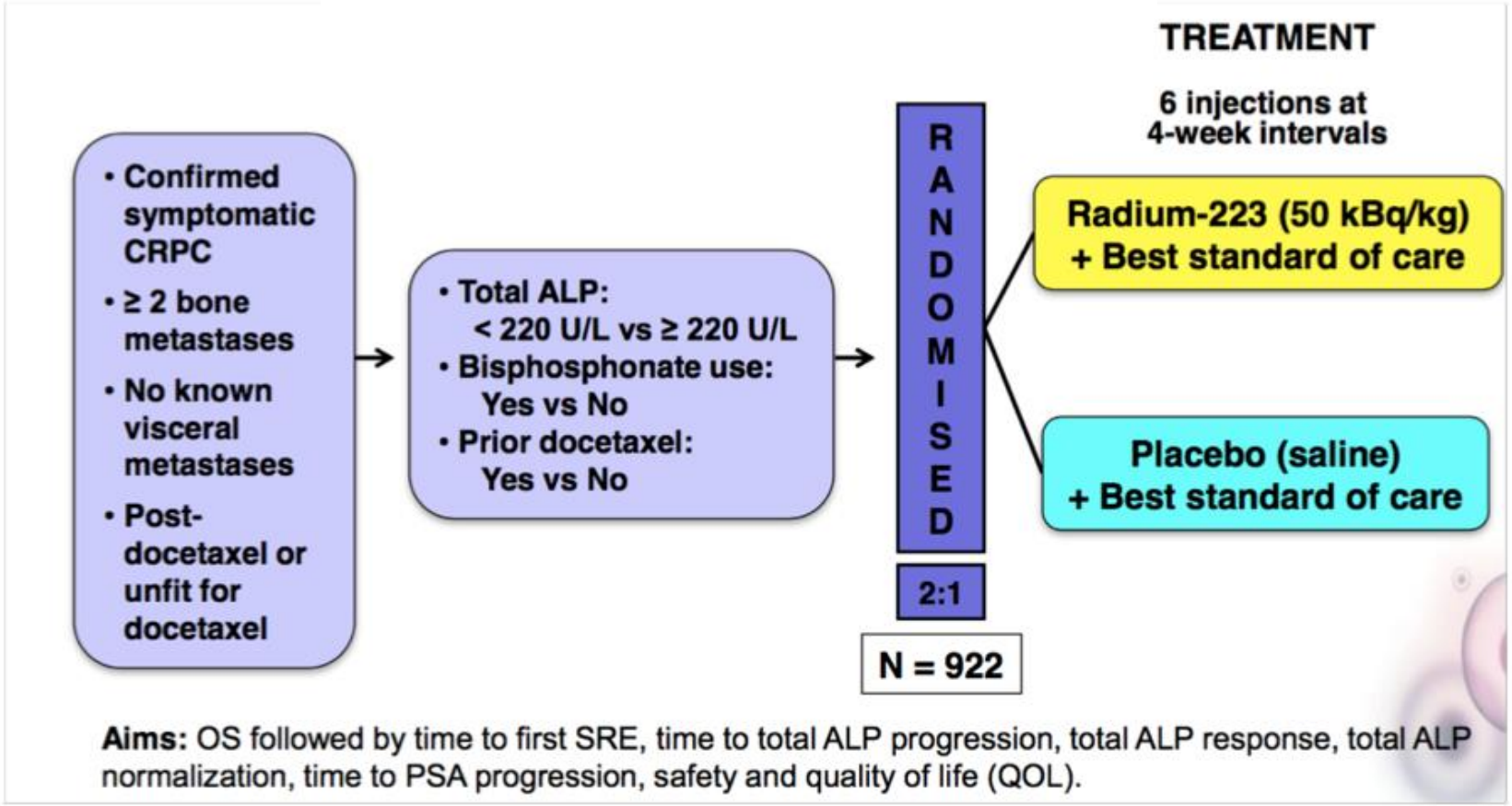
Induces double-stranded DNA breaks in bone metastases, osteoblasts and osteoclasts[1]

Suominen M, et al. Clin Cancer Res. 2017;23:4335–46.

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JULY 18, 2013 VOL. 369 NO. 3

Alpha Emitter Radium-223 and Survival in Metastatic Prostate Cancer

C. Parker, S. Nilsson, D. Heinrich, S.I. Helle, J.M. O'Sullivan, S.D. Fossâ, A. Chodacki, P. Wiechno, J. Logue, M. Seke, A. Widmark, D.C. Johannessen, P. Hoskin, D. Bottomley, N.D. James, A. Solberg, I. Syndikus, J. Kliment, S. Wedel, S. Boehmer, M. Dall'Oglio, L. Franzén, R. Coleman, N.J. Vogelzang, C.G. O'Bryan-Tear, K. Staudacher, J. Garcia-Vargas, M. Shan, Ø.S. Bruland, and O. Sartor, for the ALSYMPCA Investigators*



N Engl J Med 2013;369:213-23.

The NEW ENGLAND JOURNAL of MEDICINE

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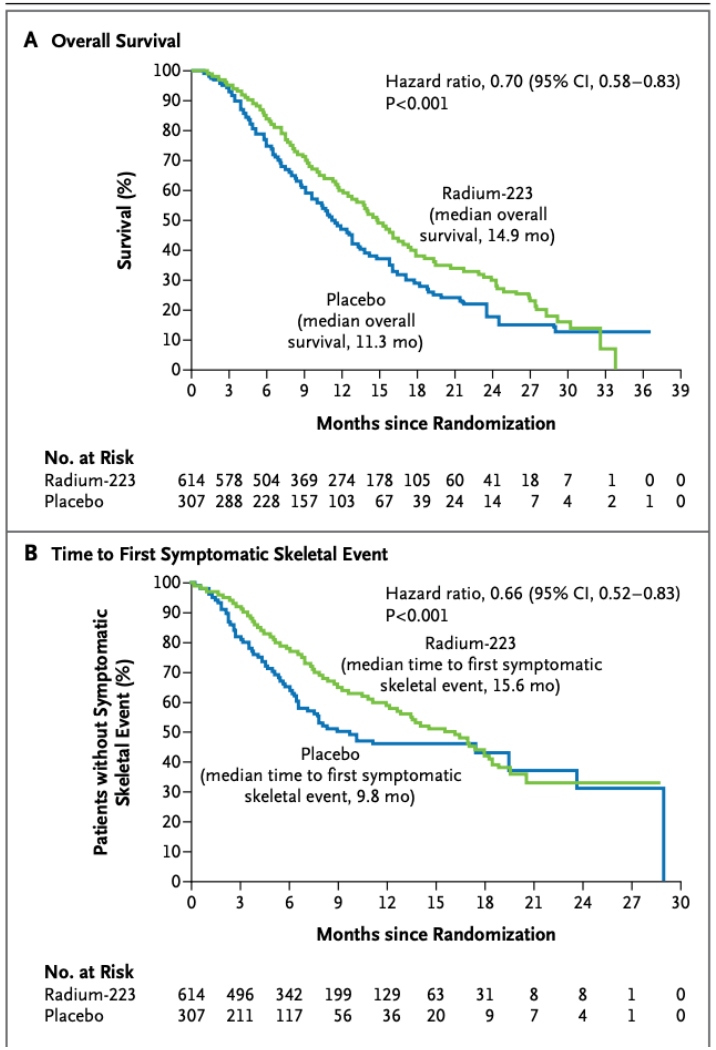

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Table 2. Main Secondary Efficacy End Points in the Intention-to-Treat Population.

End Point	Radium-223 (N=614)	Placebo (N=307)	Hazard Ratio (95% CI)	P Value
Median time to first symptomatic skeletal event — mo	15.6	9.8	0.66 (0.52–0.83)	<0.001
Median time to increase in total alkaline phosphatase level — mo	7.4	3.8	0.17 (0.13–0.22)	<0.001
Median time to increase in PSA level — mo	3.6	3.4	0.64 (0.54–0.77)	<0.001
Patients with ≥30% reduction in total alkaline phosphatase response — no. /total no. (%)	233/497 (47)	7/211 (3)		<0.001
Patients with normalization of total alkaline phosphatase level — no./total no. (%)*	109/321 (34)	2/140 (1)		<0.001

* Only patients who had elevated total alkaline phosphatase levels at baseline are included.

CONCLUSIONS

In this study, which was terminated for efficacy at the prespecified interim analysis, radium-223 improved overall survival. (Funded by Algeta and Bayer HealthCare Pharmaceuticals; ALSYMPCA ClinicalTrials.gov number, NCT00699751.)

N Engl J Med 2013;369:213-23.

- Cómo valoramos el tratamiento
  - FA
  - …PSA
  - ¿dolor?

ERA 223 (NCT02043678)

Study population

- Patients with bone-predominant mCRPC (≥2 bone metastases)
- Asymptomatic or mildly symptomatic
- ECOG PS of 0 or 1
- No prior chemotherapy for CRPC
- No known brain or visceral metastases

Accrual dates 3/2014 – 8/2016

Target accrual N=800

1:1 Randomisation

Abiraterone acetate 1000 mg qd and prednisone/prednisolone 5 mg bid (AAP) + **Radium-223** 55 kBq/kg IV every 4 weeks for 6 cycles

Abiraterone acetate 1000 mg qd and prednisone/prednisolone 5 mg bid (AAP) + **Matching placebo**

Stratification factors

- Geographical region
- Total ALP level at baseline (ALP <90 vs ≥90 U/L)
- Use of bone health agents

Primary endpoint

- SSE-FS

Secondary endpoints

- OS
- rPFS
- Time to chemotherapy
- Time to opiate use for cancer pain
- Safety

Exploratory endpoints

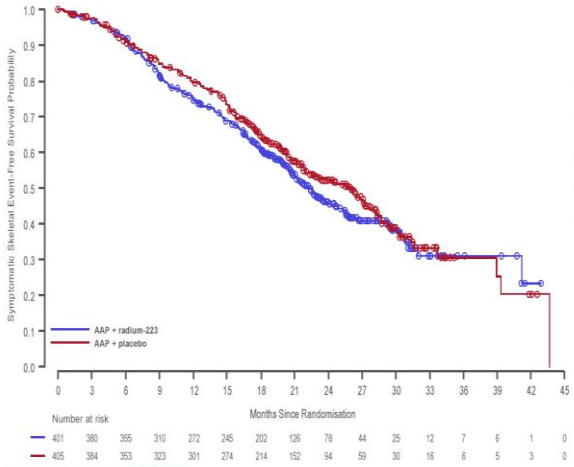
- PSA response
- Time to PSA progression
- ALP response
- Time to ALP progression
- HRQoL

389 events were required to detect a 39% increase in SSE-FS using a test with a 2-sided alpha of 0.05, 90%power and 1:1 randomisation

MUNICH 2018 ESMO congress

Bone health agents (denosumab or bisphosphonates) only permitted in patients receiving them at baseline; initiation during the study prohibited to prevent confounding effects.
ALP, alkaline phosphatase; CRPC, castration-resistant prostate cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; HRQoL, health-related quality of life; IV, intravenous; mCRPC, metastatic castration-resistant prostate cancer; OS, overall survival; PSA, prostate-specific antigen; rPFS, radiological progression-free survival; SSE-FS, symptomatic skeletal event-free survival.

Symptomatic Skeletal Event-Free Survival (ITT)



SSE-FS	AAP + radium-223 N=401	AAP + placebo N=405
Events, n (%)	196 (49)	190 (47)
Median (95% CI), months	22.3 (20.4–24.8)	26.0 (21.8–28.3)
HR (95% CI)	1.122 (0.917–1.374)	
P-value (2-sided)	0.2636	

MUNICH 2018 ESMO congress

AAP, abiraterone acetate and prednisone/prednisolone; ITT, intention-to-treat; SSE-FS, symptomatic skeletal event-free survival.

Most Frequent Treatment-Emergent Adverse Events

TEAEs in ≥15% of patients in either group, n (%)	AAP + radium-223 N=392			AAP + placebo N=394		
	All	Grade 3	Grade 4	All	Grade 3	Grade 4
Back pain	133 (34)	23 (6)	0	121 (31)*	16 (4)	0
Fatigue	89 (23)	4 (1)	0	79 (20)	6 (2)	0
Arthralgia	80 (20)	4 (1)	0	75 (19)	5 (1)	0
Fracture†	103 (26)	35 (9)	1 (0.3)	38 (10)*	12 (3)	0
Hypertension	59 (15)	43 (11)	0	78 (20)	51 (13)	1 (0.3)
ALT increased	69 (18)	29 (7)	5 (1)	59 (15)	28 (7)	0
Constipation	56 (14)	1 (0.3)	0	72 (18)	0	0
Diarrhoea	65 (17)	4 (1)	0	60 (15)	7 (2)	0
Nausea	66 (17)	1 (0.3)	0	59 (15)	1 (0.3)	0
AST increased	61 (16)	18 (5)	1 (0.3)	53 (14)	16 (4)	0
Peripheral oedema	51 (13)	2 (0.5)	0	61 (16)	0	0
Anaemia	57 (15)	24 (6)	0	46 (12)	11 (3)	0

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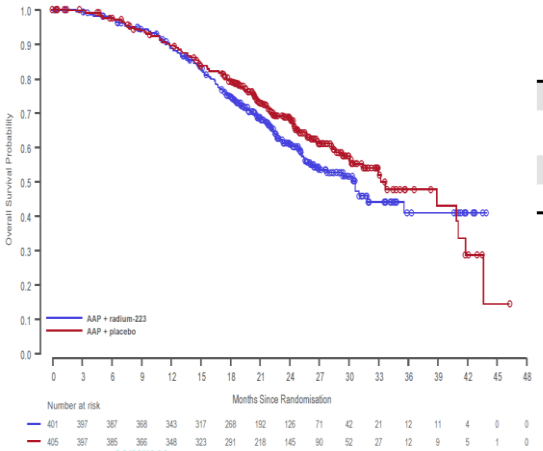
No grade 5 TEAEs reported in ≥10% of patients; *Grade of severity missing for one patient; †Compound term for events of femoral neck, femur, humerus, lumbar vertebral, osteoporotic, pathological, radius, rib, spinal compression, stress, thoracic vertebral, tooth, traumatic and ulna fracture.
AAP, abiraterone acetate and prednisone/prednisolone; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TEAE, treatment-emergent adverse event.

Overall Survival (ITT)



OS	AAP + radium-223 N=401	AAP + placebo N=405
Deaths, n (%)	155 (39)	141 (35)
Median (95% CI), months	30.7 (25.8–NE)	33.3 (30.2–41.1)
HR (95% CI)	1.195 (0.950–1.505)	
P-value (2-sided)	0.1280	

Final OS analysis to be performed after 500 events

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AAP, abiraterone acetate and prednisone/prednisolone; ITT, intention-to-treat; NE, not estimable; OS, overall survival.

Combinación deletérea

EMA restricts use of prostate cancer medicine Xofigo

Medicine to be used only after two previous treatments or when other treatments cannot be taken

On 26 July 2018, the European Medicines Agency concluded its review of the cancer medicine Xofigo (radium-223 dichloride), and recommended restricting its use to patients who have had two previous treatments for metastatic prostate cancer (prostate cancer that has spread to the bone) or who cannot receive other treatments.

Xofigo must also not be used with the medicines Zytiga (abiraterone acetate) and the corticosteroid prednisone or prednisolone. Xofigo should not be used with other systemic cancer therapies, except for treatments to maintain reduced levels of male hormones (hormone therapy). The medicine should also not be used in patients who have no symptoms, in line with the current indication; in addition, the use of Xofigo is not recommended in patients with a low number of bone metastases called osteoblastic bone metastases.

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Junio 2021

EL PAÍS

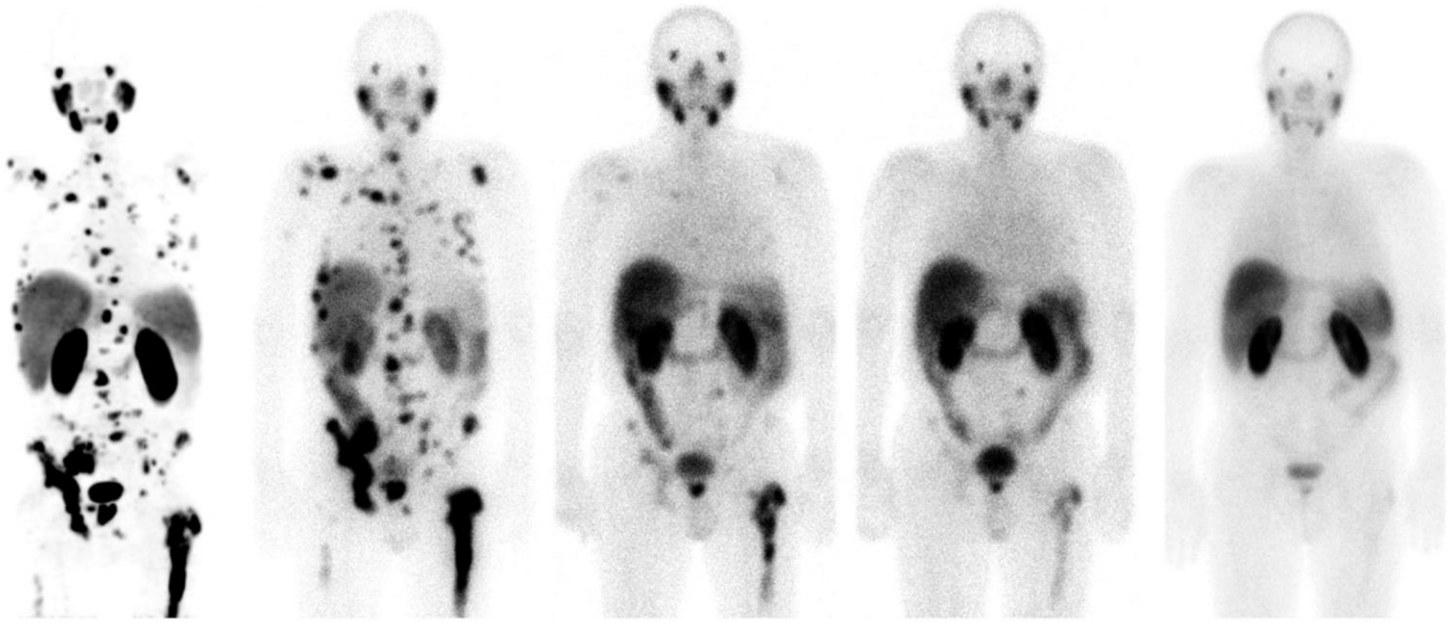
Ciencia / Materia

ASTROFÍSICA · MEDIO AMBIENTE · INVESTIGACIÓN MÉDICA · MATEMÁTICAS · PALEONTOLOGÍA · ÚLTIMAS NOTICIAS

ENFERMEDADES >

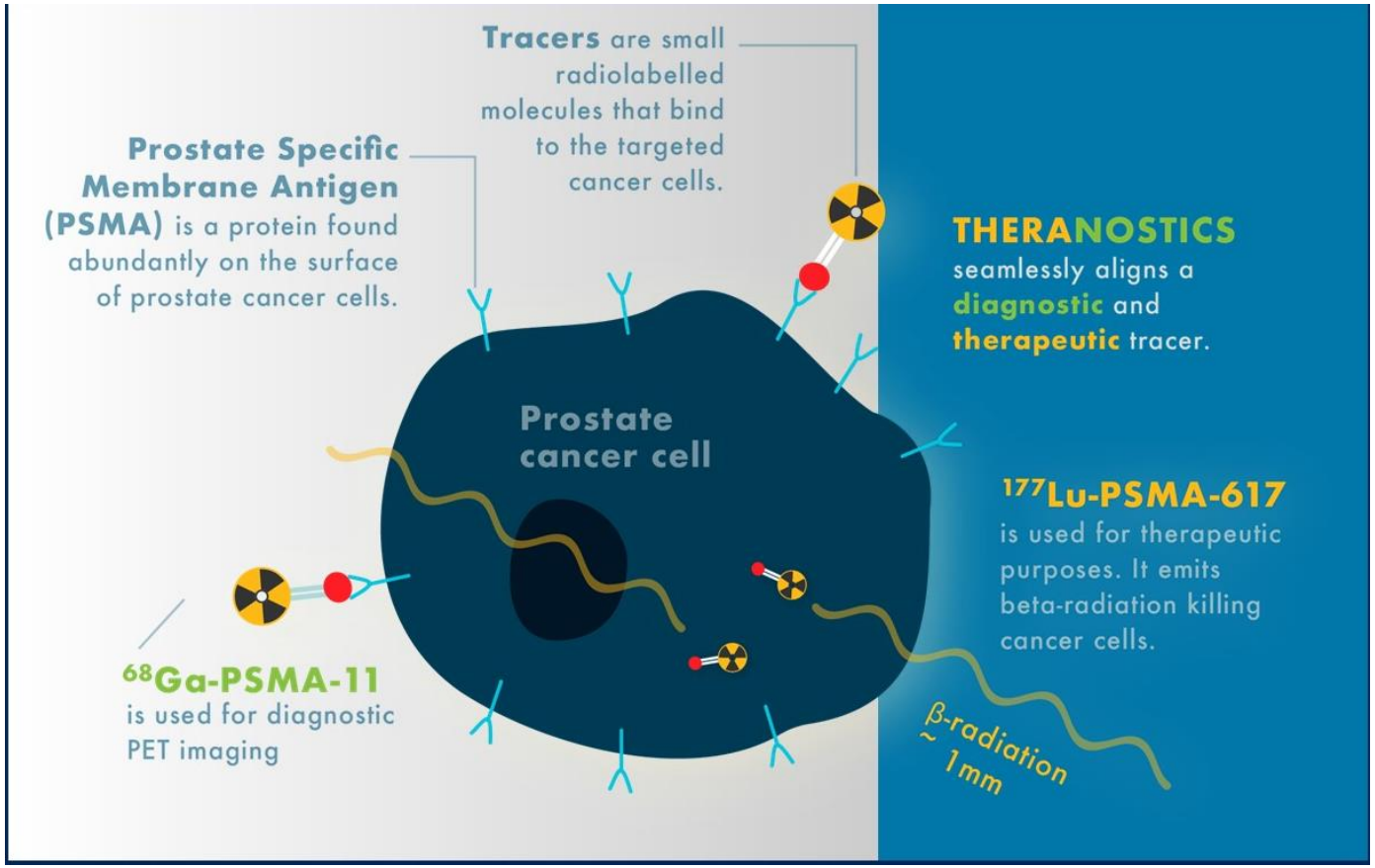
Teragnosis: una nueva esperanza contra el cáncer

La estrategia, que fusiona la terapia y el diagnóstico, logra aumentar un 35% la supervivencia de pacientes con un tumor maligno de próstata terminal

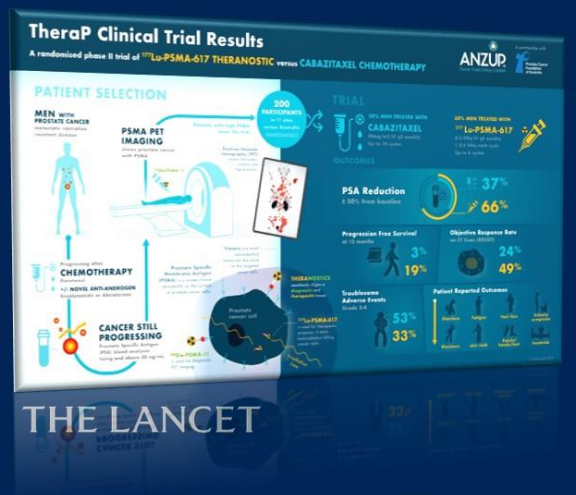


Respuesta a la teragnosis con lutecio-177 en un cáncer de próstata con metástasis, en el Hospital Universitario de Heidelberg (Alemania).

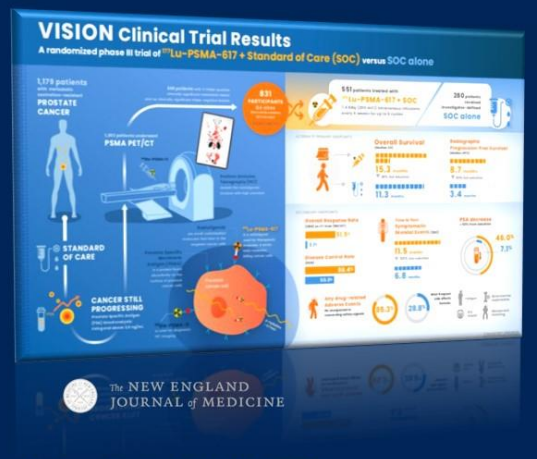
Teragnosis. Lu-PSMA-617



2 RCTs of ^{177}Lu-PSMA-617



Hofman MS et al, The Lancet 2021
https://doi.org/10.1016/S0140-6736(21)00237-3



Sartor O et al, NEJM 2021
nejm.org/doi/full/10.1056/NEJMoa2107322

PRESENTED BY:
Michael Hofman, MBBS @DrMHofman

VISION: an international, prospective, open-label, multicenter, randomized phase 3 study

Eligible patients

- Previous treatment with <u>both:</u>
  - ≥ 1 ARPI
  - 1–2 taxane regimens
- Protocol-permitted SoC planned before randomization
  - Excluding chemotherapy, immunotherapy, radium-223 or other investigational drugs[a]
- ECOG PS 0–2
- Life expectancy > 6 months
- PSMA-positive mCRPC on PET/CT with ^{68}Ga-PSMA-11[b]

2:1

^{177}**Lu-PSMA-617**[c] 7.4 GBq (200 mCi) Q6W up to 6 cycles + Protocol-permitted SoC

Protocol-permitted SoC

Alternate primary endpoints

- rPFS (per PCWG3)
- OS

<u>Randomization stratification</u>

- ECOG PS (0–1 or 2)
- LDH (high or low)
- Liver metastases (yes or no)
- **ARPI in SoC (yes or no)**

[a]Not allowed because of lack of safety data on combining these agents with the investigational drug; [b]At least one PSMA-positive lesion and no PSMA-negative lesions above specific sizes: ≥ 2.5 cm (short axis) in lymph nodes, ≥ 1.0 cm bone metastasis with soft-tissue component, ≥ 1.0 cm solid organ metastasis; [c]Also known as [^{177}Lu]Lu-PSMA-617 and lutetium (^{177}Lu) vipivotide tetraxetan

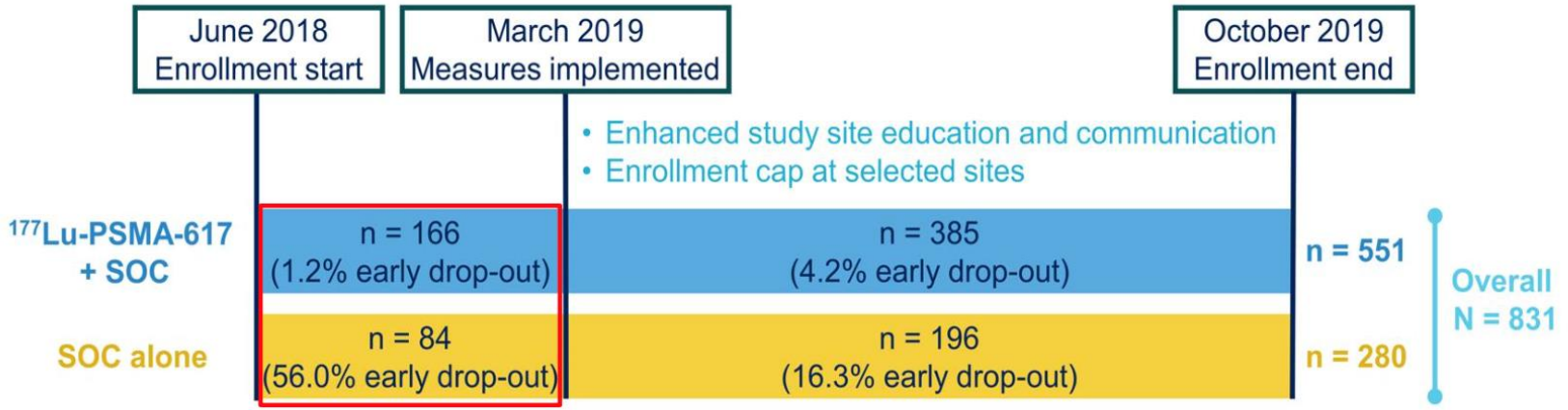
ARPI, androgen receptor pathway inhibitor; CT, computed tomography; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; mCRPC, metastatic castration-resistant prostate cancer; OS, overall survival; PCWG3, Prostate Cancer Clinical Trials Working Group 3; PET, positron emission tomography; PSMA, prostate-specific membrane antigen; Q6W, every 6 weeks; rPFS, radiographic progression-free survival; SoC, standard of care

Sartor O *et al. N Engl J Med* 2021;385:1091–103

Of the 1003 patients who underwent scan- ning, 831 (82.9%) were judged to have met all the trial eligibility criteria,

VISION Phase III trial

High incidence of withdrawal in the control group in the first period



- 2 analysis sets: OS analysis in full randomized population, radiographic PFS in subset after dropout reduction measures implemented

Morris et al. ASCO 2021; LBA4

Prior and concomitant treatments in VISION

- Prior cancer-directed treatments were **well balanced** across treatment arms
- **A majority of patients (65.3%)** in VISION had received only **1 prior taxane regimen**[a]
  - Prior bone health agents in 18.8% of patients, prior ^{223}Ra in 17.4% of patients and prior PARP inhibitors in 5.5% of patients
- **54.8%** of patients received **concomitant ARPIs** as part of SoC (randomization stratification factor)
- **43.9%** of patients received **concomitant bone health agents** as part of SoC

[a]A regimen was defined as the administration of ≥2 cycles of a taxane. Taxane regimen status was unknown in 36/581 patients (6.2%) in the rPFS-FAS and 55/831 patients (6.6%) in the FAS because of no information on number of cycles in case report forms

ARPI, androgen receptor pathway inhibitor; FAS, full analysis set; PARP, poly (ADP-ribose) polymerase; Ra, radium; rPFS, radiographic progression-free survival; SoC, standard of care

Table 1. Characteristics of the Patients at Baseline, According to Analysis Set.*

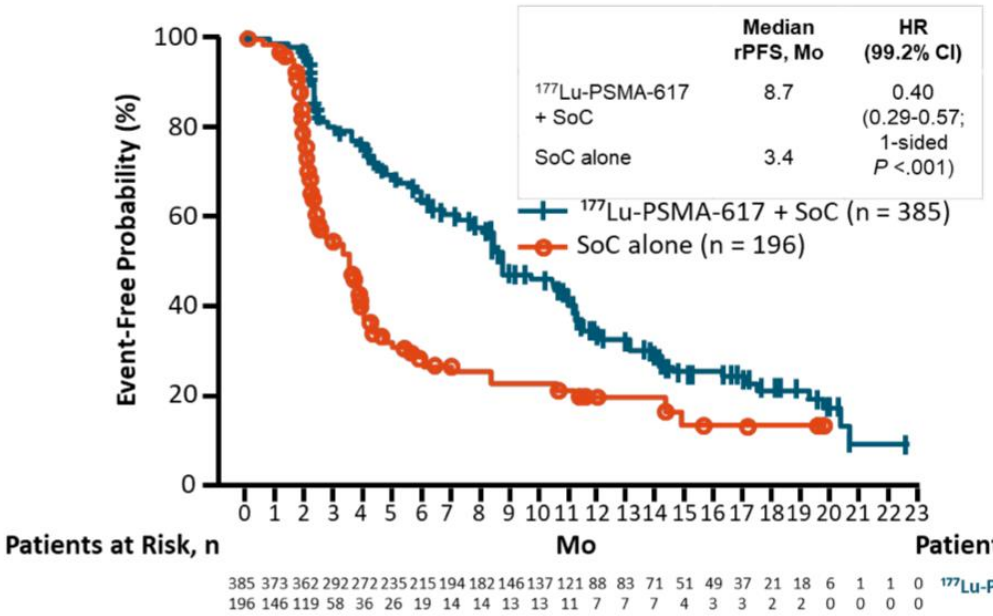
Characteristic	Analysis Set for Imaging-Based Progression-free Survival (N=581)		All Patients Who Underwent Randomization (N=831)	
	^{177}Lu-PSMA-617 plus Standard Care (N=385)	Standard Care Alone (N=196)	^{177}Lu-PSMA-617 plus Standard Care (N=551)	Standard Care Alone (N=280)
Median age (range) — yr	71.0 (52–94)	72.0 (51–89)	70.0 (48–94)	71.5 (40–89)
ECOG performance-status score of 0 or 1 — no. (%)†	352 (91.4)	179 (91.3)	510 (92.6)	258 (92.1)
Site of disease — no. (%)				
Lung	35 (9.1)	20 (10.2)	49 (8.9)	28 (10.0)
Liver	47 (12.2)	26 (13.3)	63 (11.4)	38 (13.6)
Lymph node	193 (50.1)	99 (50.5)	274 (49.7)	141 (50.4)
Bone	351 (91.2)	179 (91.3)	504 (91.5)	256 (91.4)
Median PSA level (range) — ng/ml	93.2 (0–6988)	90.7 (0–6600)	77.5 (0–6988)	74.6 (0–8995)
Median alkaline phosphatase level (range) — IU/liter‡	108.0 (26–2524)	96.0 (34–1355)	105.0 (17–2524)	94.5 (28–1355)
Median LDH (range) — IU/liter‡	230.5 (119–5387)	232.0 (105–2693)	221.0 (88–5387)	224.0 (105–2693)
Median time since diagnosis (range) — yr	7.3 (0.9–28.9)	7.0 (0.7–26.2)	7.4 (0.9–28.9)	7.4 (0.7–26.2)
Gleason score at diagnosis — no. (%)§				
8–10	226 (58.7)	118 (60.2)	324 (58.8)	170 (60.7)
Unknown	28 (7.3)	19 (9.7)	42 (7.6)	24 (8.6)
Previous prostatectomy — no. (%)¶	159 (41.3)	82 (41.8)	240 (43.6)	130 (46.4)
Previous androgen-receptor–pathway inhibitor — no. (%)‖				
One regimen	213 (55.3)	98 (50.0)	298 (54.1)	128 (45.7)
Two regimens	150 (39.0)	86 (43.9)	213 (38.7)	128 (45.7)
More than two regimens	22 (5.7)	12 (6.1)	40 (7.3)	24 (8.6)
Previous taxane therapy — no. (%)**				
One regimen	207 (53.8)	102 (52.0)	325 (59.0)	156 (55.7)
Two regimens	173 (44.9)	92 (46.9)	220 (39.9)	122 (43.6)
Docetaxel	377 (97.9)	191 (97.4)	534 (96.9)	273 (97.5)
Cabazitaxel	161 (41.8)	84 (42.9)	209 (37.9)	107 (38.2)

N Engl J Med 2021;385:1091-103.

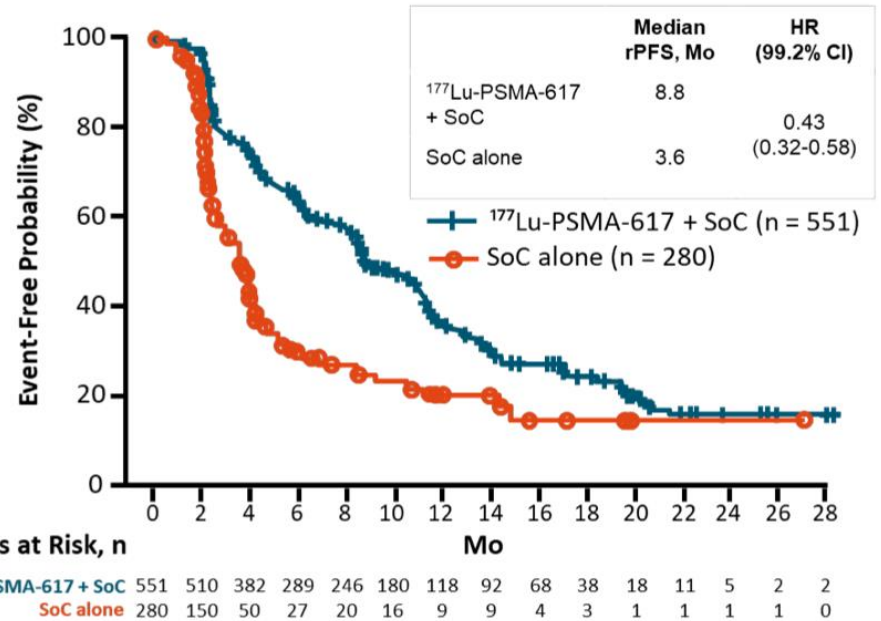
VISION Phase III trial

PFS: Co-Primary Efficacy Outcome

Primary Analysis of rPFS (n = 581)



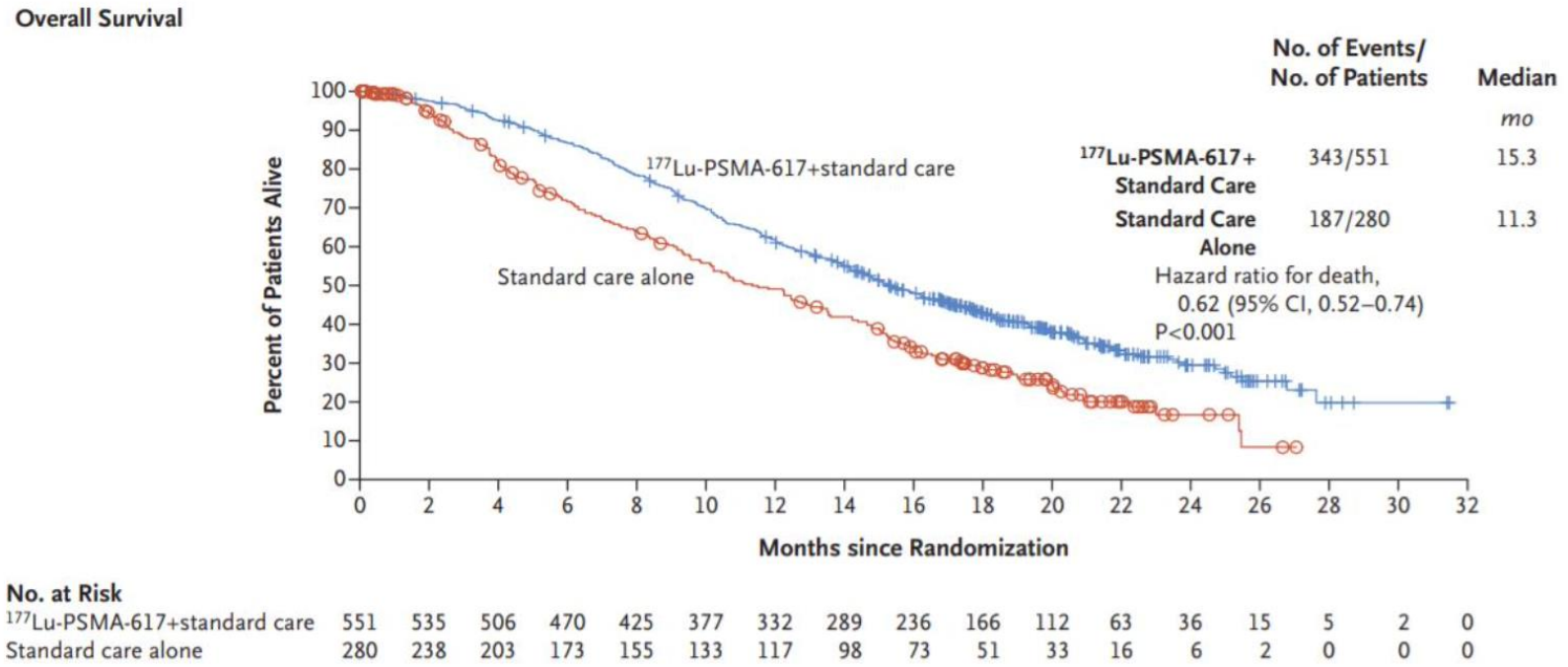
rPFS in OS Analysis Set: All Randomized Patients (N = 831)



Morris. ASCO 2021. Abstr LBA4. Sartor O, et al. NEJM 2021

VISION Phase III trial

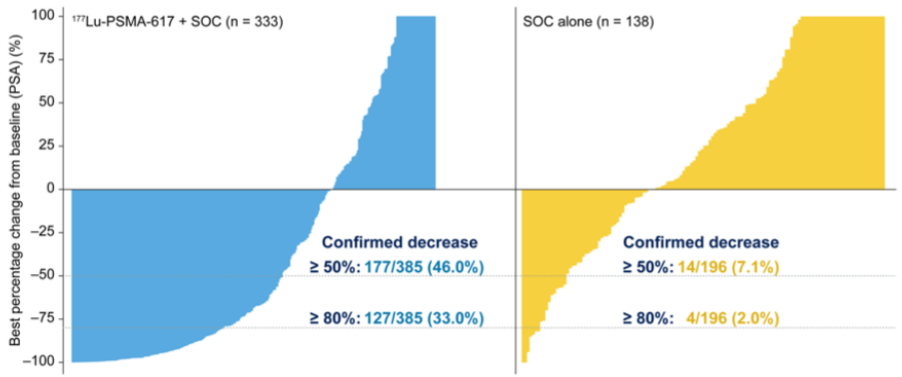
OS: Co-Primary Efficacy Outcome

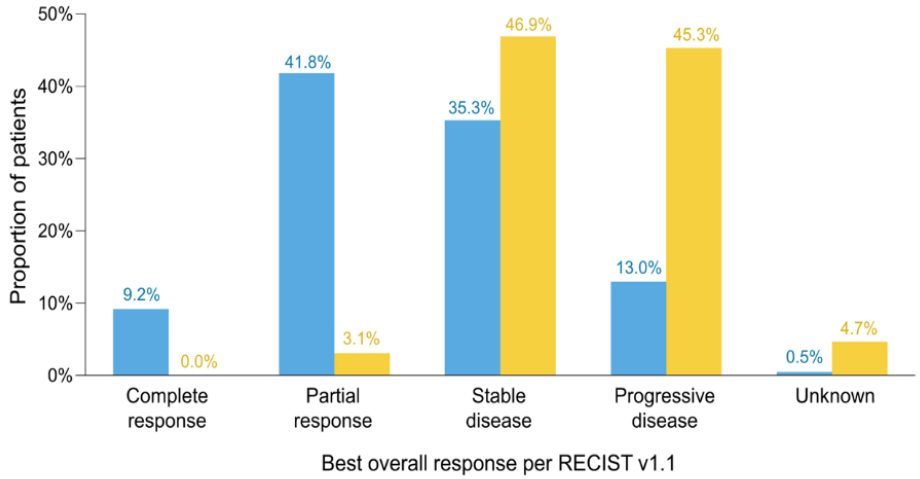


Sartor O, et al. NEJM 2021

Results

- High rate of responses: ***PSA RR50: 46% vs 7,1%, RECIST 29.8% vs 1.7%***





Morris et al. ASCO 2021; LBA4

VISION Phase III trial

Adverse events

- Toxicity profile expected for Beta-emisors

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)
Any TEAE	451 (85.3)	59 (28.8)	150 (28.4)	8 (3.9)
Serious	49 (9.3)	5 (2.4)	43 (8.1)	5 (2.4)
Grade 5	–	–	5 (0.9)	0 (0.0)

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)

Morris et al. ASCO 2021; LBA4

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*

Positivo, con sus peros

CONCLUSIONS

Radioligand th
survival and
vanced PSMA-
Endocyte, a N

mCRPC							
177Lu-PSMA-617 + best standard of care (restricted)	Adult patients with progressive PSMA-positive mCRPC who have been treated with androgen receptor pathway inhibition and taxane-based ChT	VISION[7] Phase III NCT03511664	Best standard of care (restricted) Median OS: 11.3 months	OS gain: 4.0 months	OS: 0.62 (0.52-0.74)	QoL data pending Deteriorated toxicity (based on grade ≥3 AEs): 52.7% versus 38%	4[m] (Form 2a)

N Engl J Med 2021;385:1091-103.

Ann Oncol: 2023: 34

2022 ASCO ANNUAL MEETING

ANZUP Cancer Trials Group Limited

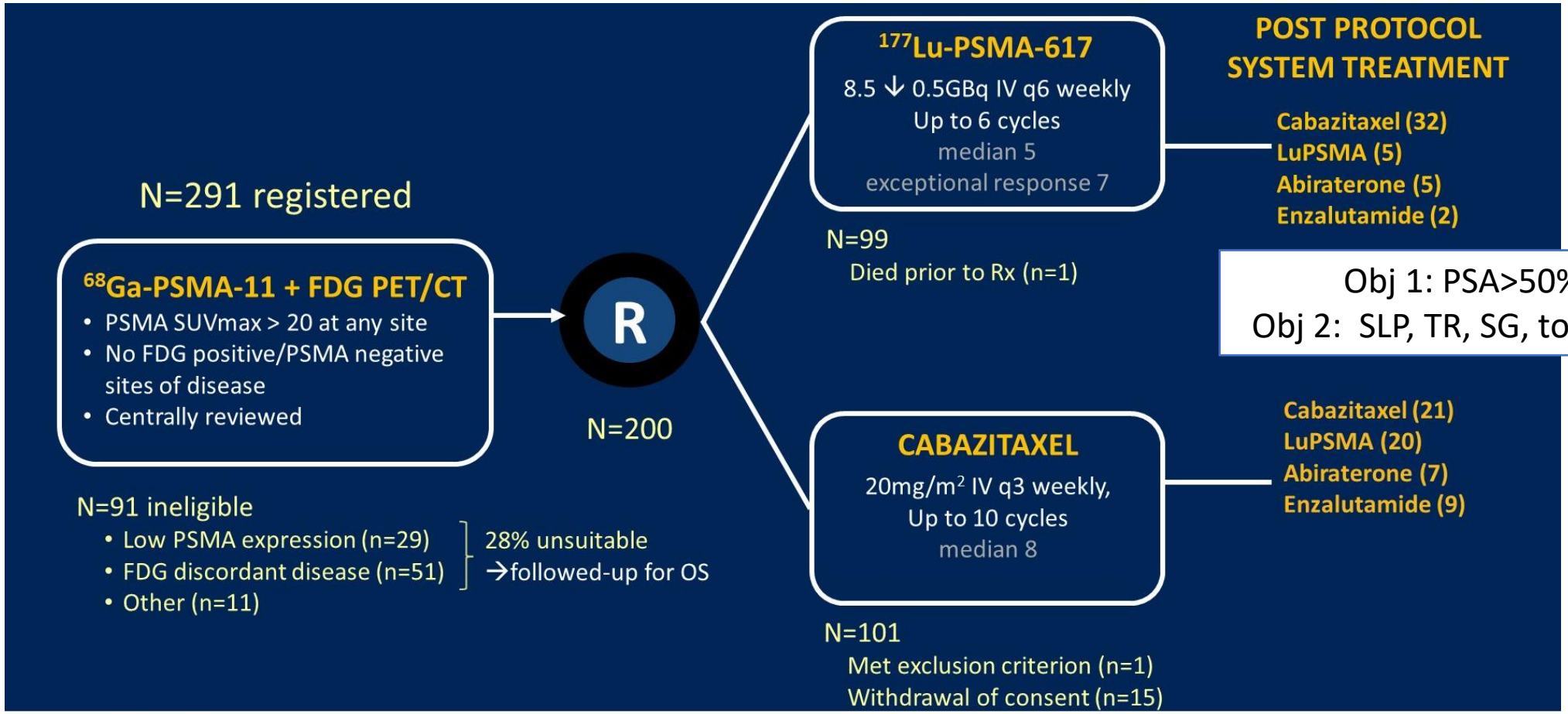
^{177}Lu-PSMA-617 (LuPSMA) versus cabazitaxel in metastatic castration resistant prostate cancer (mCRPC) progressing after docetaxel: overall survival after median follow-up of 3 years

(TheraP ANZUP 1603)

Michael Hofman, Louise Emmett, Shahneen Sandhu, Amir Iravani, Anthony Joshua, Jeffrey Goh, David Pattison, Hsiang Tan, Ian Kirkwood, Siobhan Ng, Roslyn Francis, Craig Gedye, Natalie Rutherford, Andrew Scott, Alison Zhang, Margaret McJannett, Martin Stockler, Scott Williams, Andrew Martin, Ian D. Davis, on behalf of the **TheraP Investigators**

TheraP is a partnership between ANZUP Cancer Trials Group and the Prostate Cancer Foundation of Australia (PCFA) in collaboration with the NHMRC Clinical Trials Centre (CTC) and the Australasian Radiopharmaceutical Trials Network (ARTnet) with support from the Australian Nuclear Science and Technology Organisation (ANSTO) and Endocyte Inc., a Novartis company

Clinicaltrials.gov NCT03392428



Obj 1: PSA>50%
Obj 2: SLP, TR, SG, toxicidad

TheraP: First randomized trial of LuPSMA vs. cabazitaxel[1]

50% MEN TREATED WITH
CABAZITAXEL
20mg/m2 IV q3 weekly
Up to 10 cycles

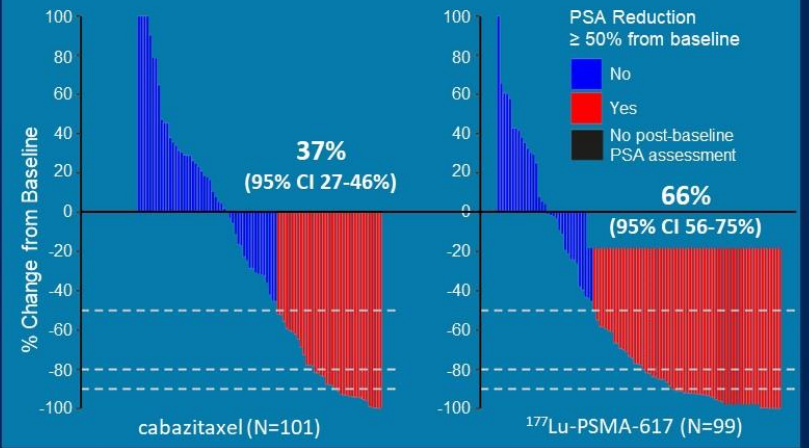
50% MEN TREATED WITH
^{177}Lu-PSMA-617
8.5 GBq IV q6 weekly
↓ 0.5 GBq each cycle
Up to 6 cycles

1º endpoint

PSA Reduction
≥ 50% from baseline

37%
66%

^{177}Lu-PSMA-617: 29% (95% CI 16%-42%; p<0.0001) greater PSA50-RR



2º endpoints

Progression Free Survival
at 12 months

3%
19%

Objective Response Rate
on CT Scan (RECIST)

24%
49%

Troublesome Adverse Events
Grade 3-4

53%
33%

Patient Reported Outcomes

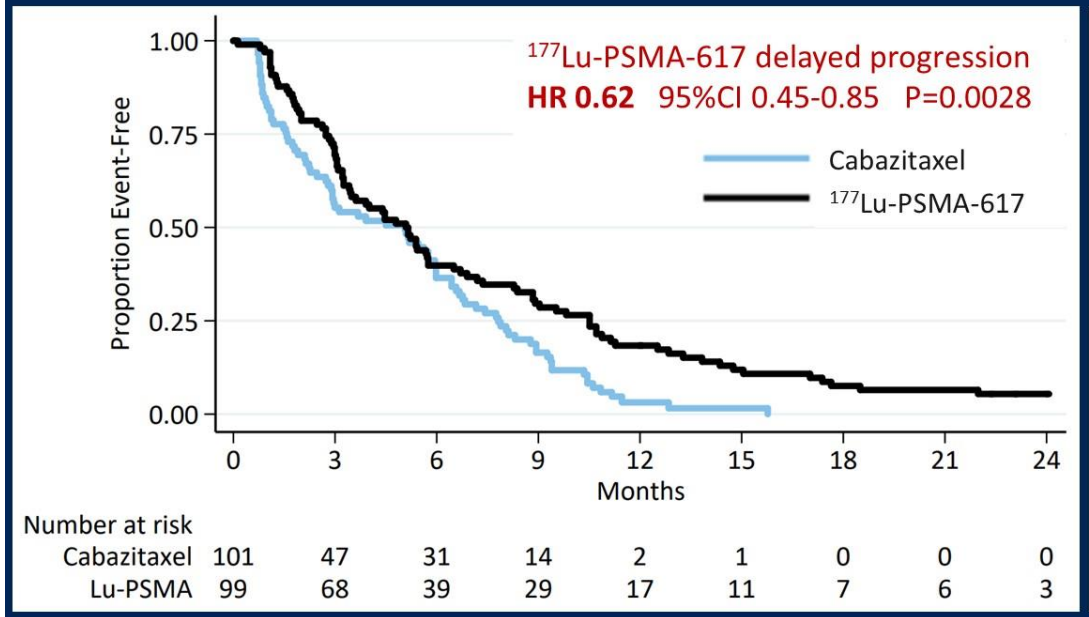
Diarrhea · Fatigue · Hair loss · Urinary symptoms
Dizziness · skin rash · Painful hands/feet · Insomnia

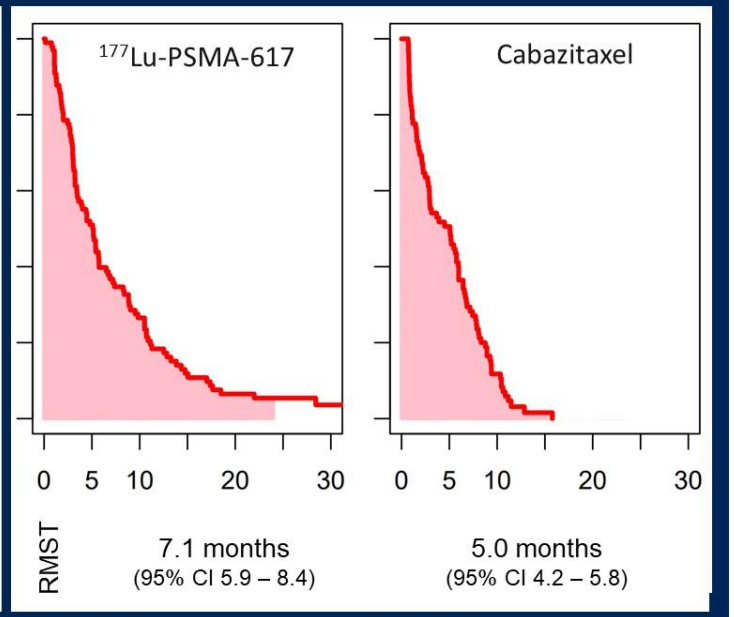
[1] Hofman MS et al, Lancet 2021; 397(10276)

PRESENTED BY: Michael Hofman, MBBS @DrMHofman

Progression Free Survival (PSA and radiographic)

ANZUP Cancer Trials Group Limited





- Treatment effect not constant with respect to time → restricted mean survival time (RMST)
- 177 progression events. Cut-off 31 DEC 2020 for non-OS endpoints.
- Similar HR for rPFS (0.65) and PSA-PFS (0.60), and in per-protocol sensitivity analyses

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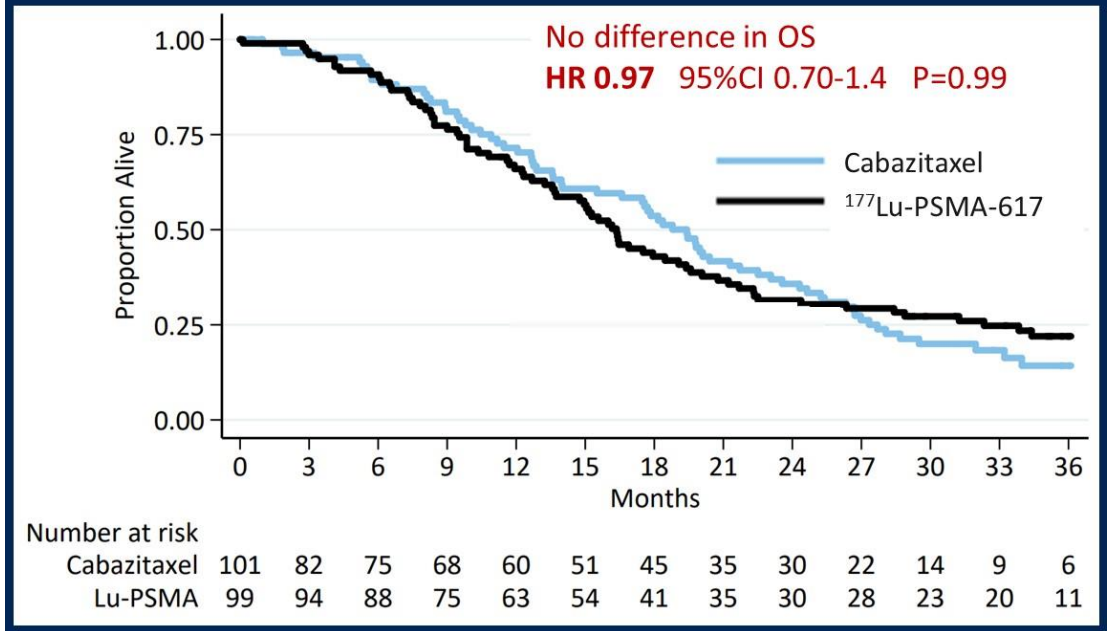
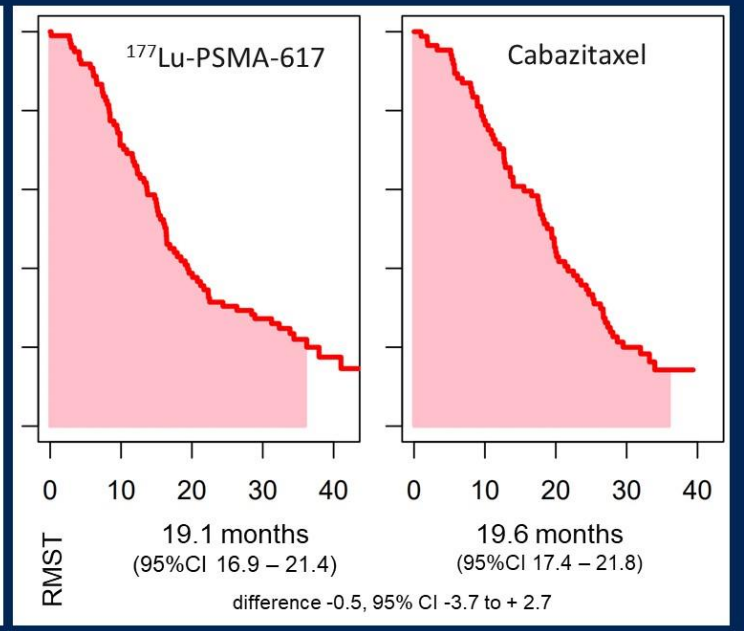
Overall survival (ITT)

ANZUP Cancer Trials Group Limited





- Cut-off 31 DEC 2021 for OS
- At 36 months follow-up, death reported in 147/200; 70/101 assigned cabazitaxel vs. 77/99 assigned LuPSMA
- Per-protocol analysis: no difference in OS
- No additional safety signals with longer follow-up.

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

Interpretation [^{177}Lu]Lu-PSMA-617 compared with cabazitaxel in men with metastatic castration-resistant prostate cancer led to a higher PSA response and fewer grade 3 or 4 adverse events. [^{177}Lu]Lu-PSMA-617 is a new effective class of therapy and a potential alternative to cabazitaxel.

Lancet 2021; 397: 797–804

EMA, Dic 2022

FDA approves Pluvicto for metastatic castration-resistant prostate cancer

Share Tweet Linkedin Email Print

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.

On the same day, the FDA approved Locametz (gallium Ga 68 gozetotide), a radioactive diagnostic agent for positron emission tomography (PET) of PSMA-positive lesions, including selection of patients with metastatic prostate cancer for whom lutetium Lu 177 vipivotide tetraxetan PSMA-directed therapy is indicated. Locametz is the first radioactive diagnostic agent approved for patient selection in the use of a radioligand therapeutic agent.

Pluvicto

Share RSS

lutetium (177Lu) vipivotide tetraxetan

AUTHORISED
This medicine is authorised for use in the European Union.

Table of contents

Overview

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).

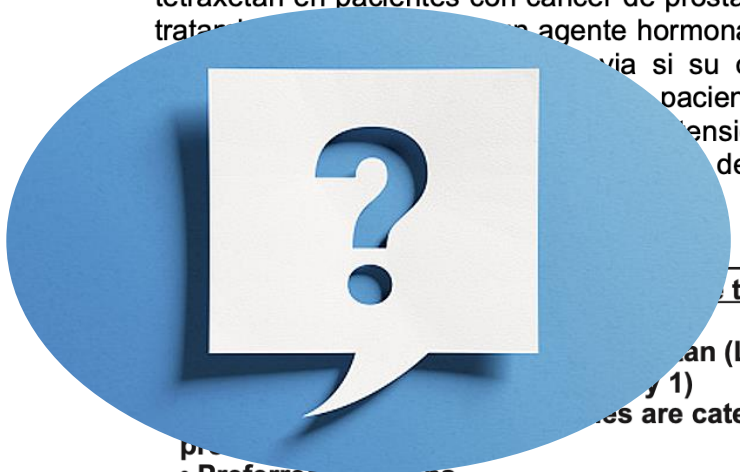
Pluvicto is used together with androgen deprivation therapy (treatment to lower male sex hormones) in adults previously treated with androgen receptor pathway inhibitors (medicines for prostate cancer), and a medicine of the group of cancer medicines known as taxanes. Androgen receptor pathway inhibitors 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 (^{177}Lu) vipivotide tetraxetan.

LUTECIO EN GUIAS

Posicionamiento SEOM

Se propone, por tanto, de acuerdo a la magnitud de beneficio clínico relevante establecido por la Sociedad Europea de Oncología Médica (ESMO MCBS 4), el uso de ^{177}Lutetium vipivotide tetraxetan en pacientes con cáncer de próstata resistente a la castración metastásico bien tras tratar[illegible] agente hormonal y dos líneas de quimioterapia previa, o tras una [illegible]via si su oncólogo considera que no es candidato a una [illegible] pacientes deben presentar enfermedad PSMA positiva [illegible]ensidad de captación (SUVmedia) puede representar [illegible] de pacientes.



NCCN 2023

[illegible] therapy[mmm,ttt]

[illegible]an (Lu-177–PSMA-617) for PSMA-[illegible] 1)

[illegible]es are category 2B if visceral metastases are [illegible]

- **Preferred regimens**
  - **Cabazitaxel**[fff,ooo] **(category 1)**
  - **Docetaxel rechallenge**[fff]
- **Useful in certain circumstances**

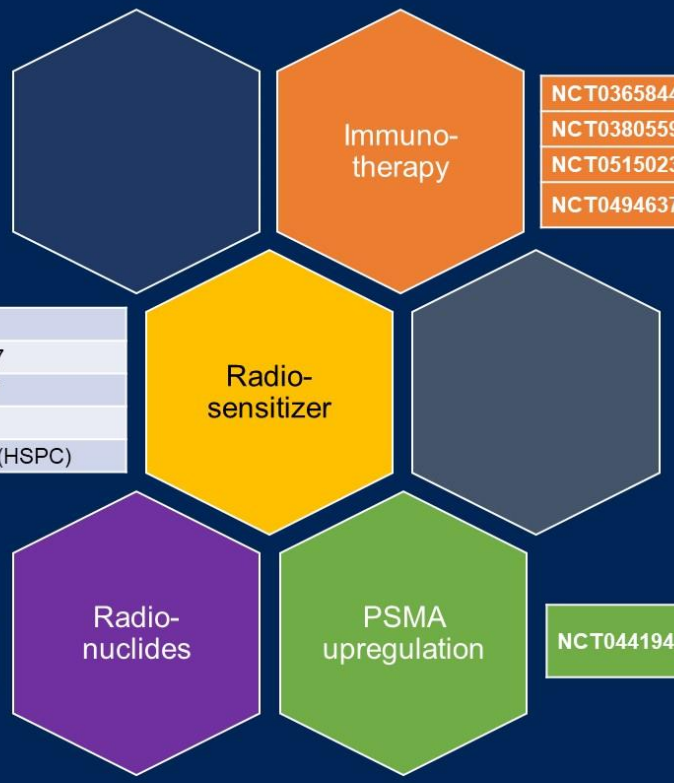
EAU 2023

Novel agents	
Offer poly(ADP-ribose) polymerase (PARP) inhibitors to pre-treated mCRPC patients with relevant DNA repair gene mutations.	Strong
Offer ^{177}Lu-PSMA-617 to pre-treated mCRPC patients with one or more metastatic lesions, highly expressing PSMA (exceeding the uptake in the liver) on the diagnostic radiolabelled PSMA PET/CT scan.	Strong

Metas

- Selección de pacientes
- Combinaciones
- Otros escenarios

Current Lu-PSMA combination trials



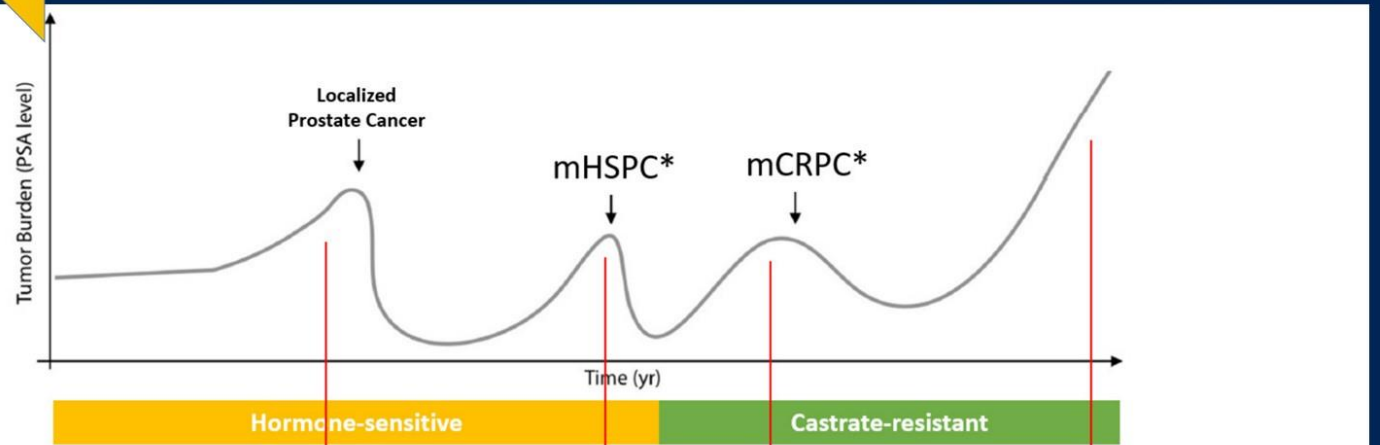
NCT03658447	^{177}LuPSMA-617 + Pembrolizumab
NCT03805594	^{177}LuPSMA-617 + Pembrolizumab
NCT05150236	^{177}Lu-PSMA-617 + Ipilimumab + Nivolumab
NCT04946370	^{225}Ac-J591 + Pembrolizumab + ARPI (eg. enzalutamide)

NCT03874884	Olaparib + ^{177}Lu-PSMA-617
NCT05113537	Abemaciclib + ^{177}Lu-PSMA-617
NCT05340374	Cabazitaxel + ^{177}Lu-PSMA-617
NCT00916123	Docetaxel + ^{177}Lu-J591
NCT04343885	^{177}Lu-PSMA-617 → docetaxel (HSPC)

NCT04886986	^{225}Ac-J591 + ^{177}Lu-PSMA-I&T
AlphaBet	^{233}Ra + ^{177}Lu-PSMA-I&T

NCT04419402	Enzalutamide + ^{177}Lu-PSMA-617

last line to first line



Neoadjuvant therapy for localized disease

1. ^{177}Lu-PSMA-617 (LuTectomy)

First-line therapy for mHSPC

1. ^{177}Lu-PSMA-617 (UpFrontPSMA, PSMAddition)

First-line therapy for mCRPC

1. ^{177}Lu-PSMA-I&T (Bullseye)
2. ^{177}Lu-PSMA-617 + enzalutamide (ENZA-P)

Second-line or later therapy for mCRPC

1. ^{177}Lu-PSMA-617 (LuPSMA,TheraP, VISION)
2. ^{177}Lu-PSMA-617 + olaparib (LuPARP)
3. ^{177}Lu-PSMA-617 + pembrolizumab (PRINCE)
4. ^{177}Lu-PSMA-I&T (SPLASH)
5. ^{225}Ac-PSMA-617 (AcTION)
6. ^{177}Lu-J591 (NCT00538668)
7. ^{225}Ac-J591 (NCT04506567)
8. ^{227}Th-PSMA-TTC (NCT03724747)
9. ^{131}I-MIP-1095 + enzalutamide (ARROW)
10. ^{177}Lu-PSMA-R2 (NCT03490838)

*mHSPC (metastatic hormone-sensitive prostate cancer)
*mCRPC (metastatic castrate-resistant prostate cancer)
*Different colours represent various PSMA-targeted radiopharmaceuticals (^{177}Lu-PSMA-617, ^{177}Lu-PSMA-I&T, ^{177}Lu-J591, ^{225}Ac-J591, ^{227}Th-PSMA-TTC, ^{131}I-MIP-1095, ^{177}Lu-PSMA-R2)

Zhang H et al, *Cancers* 2021

PRESENTED BY: Michael Hofman, MBBS @DrMHofman

Conclusiones

- Ra 223: disponible
  - Mts óseas + dolor
  - Paciente frágil que progresa a NAH
  - Tras NAH y Doc (por ahora)

- Lu-PSMA 617: no disponible…
  - Ga-PSMA-PET positivo
  - tras NAH y Docetaxel y/o cabazitaxel
  - Cuestiones
    - Selección de pacientes
    - Evaluación respuesta
    - nº de ciclos
    - Retratamiento
    - combinaciones

Innovando en el **abordaje multidisciplinar** del **cáncer de próstata** en Andalucía

Málaga, **27** de **septiembre** de **2023**

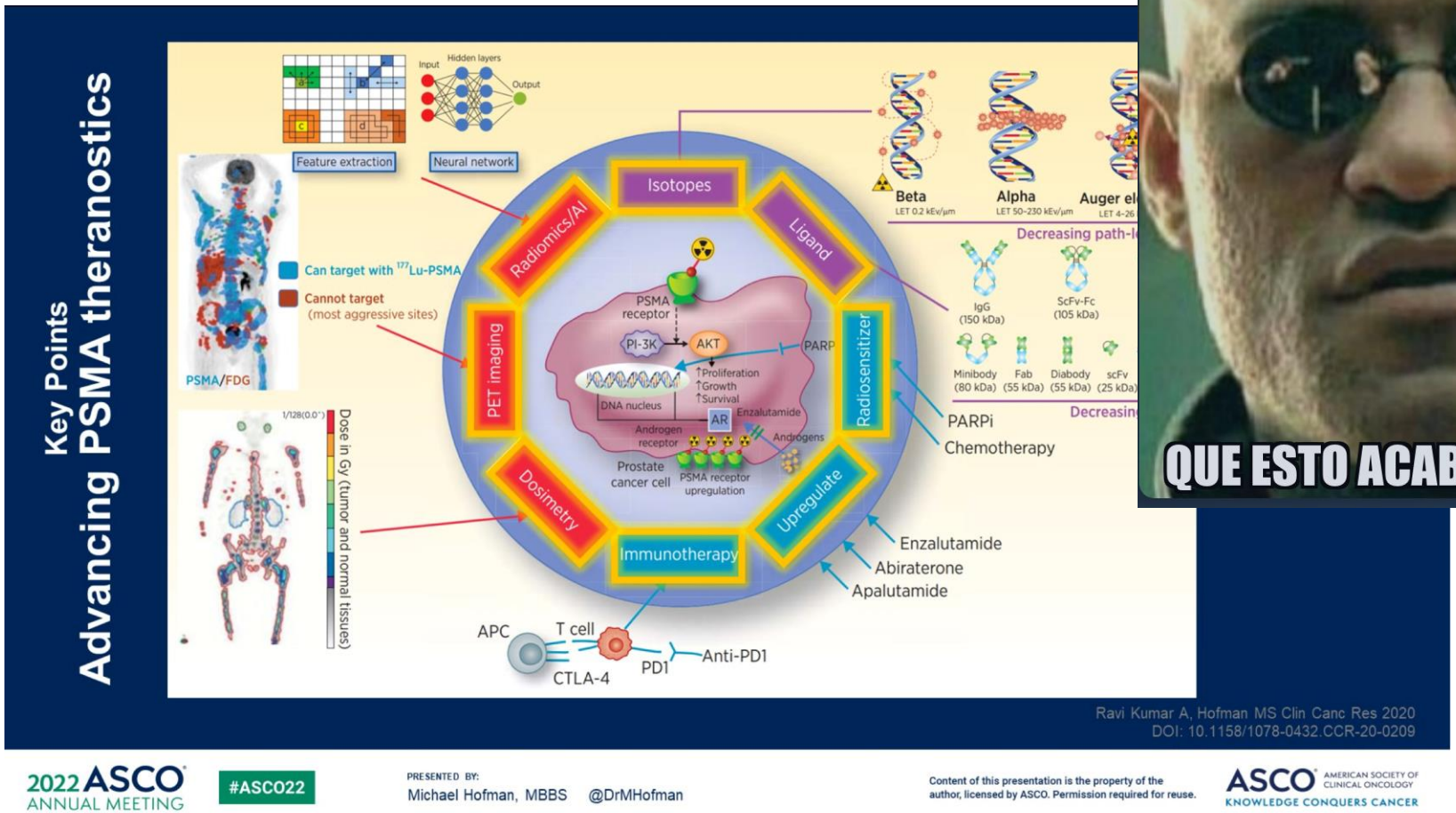
Organizado por:

saom Sociedad andaluza de oncología médica

SAMN Sociedad Andaluza de Medicina Nuclear

En colaboración con:

Advanced Accelerator Applications A Novartis Company



2022 ASCO ANNUAL MEETING #ASCO22

PRESENTED BY: Michael Hofman, MBBS @DrMHofman

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY KNOWLEDGE CONQUERS CANCER

Innovando en el abordaje multidisciplinar del cáncer de próstata en Andalucía

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En colaboración con: Advanced Accelerator Applications, A Novartis Company

17:10h - 17:30h **Evidencia actual acerca del tratamiento del CPRCm; ¿qué nos dicen las guías clínicas? EECC disponibles.**

Dra. Raquel Luque Caro.
Servicio de Oncología Médica.
Hospital Universitario Virgen de las Nieves, Granada

Gracias !!!