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THE HEART OF MEDICAL EDUCATION

NURSING SUPPORT FOR METASTATIC CASTRATE RESISTANT PROSTATE CANCER (mCRPC) PATIENTS DURING RADIOPHARMACEUTICAL TREATMENTS

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CLINICAL TAKEAWAYS

- Radiopharmaceuticals such as radium-223 and ^{177}Lu-PSMA-617 offer a survival benefit to mCRPC patients as well as managing bone pain and QoL
- They are able to deliver targeted radiation to prostate cancer cells thereby minimising toxicity to normal healthy tissue
- Real-world data support using ^{177}Lu-PSMA-617 in patients who previously received Ra-223
- Nurses and patients should be aware of post-treatment precautions, but radiopharmaceuticals are an effective and manageable treatment option for mCRPC patients

mCRPC, metastatic castrate-resistant prostate cancer; PSMA, prostate-specific membrane antigen; QoL, quality of life

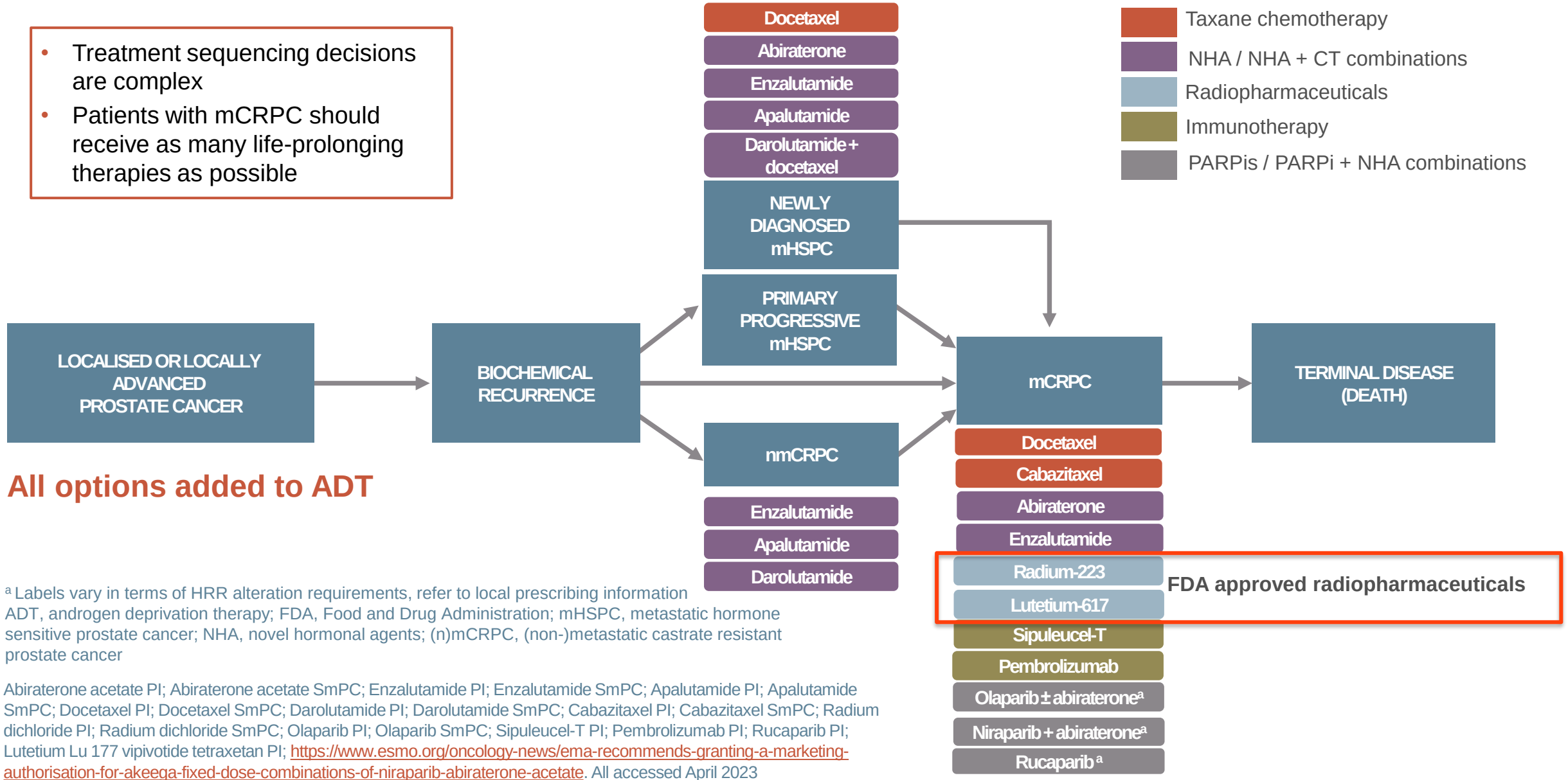
EDUCATIONAL OBJECTIVES

- Recognise the considerations for **treatment selection** for mCRPC in clinical practice, minimising the impact of treatment on patient lives
- Understand the clinical application of recent data to treatment sequencing in **bone dominant mCRPC**
- Be able to **educate and support patients** during treatment to ensure patients understand what to expect

mCRPC, metastatic castrate-resistant prostate cancer

THE PROSTATE CANCER LANDSCAPE IS COMPLICATED!

- Treatment sequencing decisions are complex
- Patients with mCRPC should receive as many life-prolonging therapies as possible



All options added to ADT

[a] Labels vary in terms of HRR alteration requirements, refer to local prescribing information
ADT, androgen deprivation therapy; FDA, Food and Drug Administration; mHSPC, metastatic hormone sensitive prostate cancer; NHA, novel hormonal agents; (n)mCRPC, (non-)metastatic castrate resistant prostate cancer

Abiraterone acetate PI; Abiraterone acetate SmPC; Enzalutamide PI; Enzalutamide SmPC; Apalutamide PI; Apalutamide SmPC; Docetaxel PI; Docetaxel SmPC; Darolutamide PI; Darolutamide SmPC; Cabazitaxel PI; Cabazitaxel SmPC; Radium dichloride PI; Radium dichloride SmPC; Olaparib PI; Olaparib SmPC; Sipuleucel-T PI; Pembrolizumab PI; Rucaparib PI; Lutetium Lu 177 vipivotide tetraxetan PI; https://www.esmo.org/oncology-news/ema-recommends-granting-a-marketing-authorisation-for-akeega-fixed-dose-combinations-of-niraparib-abiraterone-acetate. All accessed April 2023

FDA-APPROVED THERAPEUTIC RADIOPHARMACEUTICALS FOR mCRPC PATIENTS

Radiopharmaceuticals	Radioactive particles	Description	Survival Benefit
Strontium-89	β-emitter	Palliative agent for chemotherapy-refractory mCRPC patients with bone metastasis	No survival benefit
Samarium-153	β-emitter	Provides significant pain relief to patients with bone metastasis	No survival benefit
Radium-223	α-emitter	Improves overall survival in symptomatic bone-predominant mCRPC without visceral metastasis	2.8-month improvement in OS compared to placebo (HR 0.70, 95% CI: 0.58-0.83, p<0.001)
^{177}Lu-PSMA-617	β-emitter	Improves overall survival in PSMA-positive mCRPC patients previously treated with ARPI and taxane-based chemotherapy	4-month improvement in OS compared to SoC (HR 0.62, 95% CI: 0.52-0.74, p<0.001)

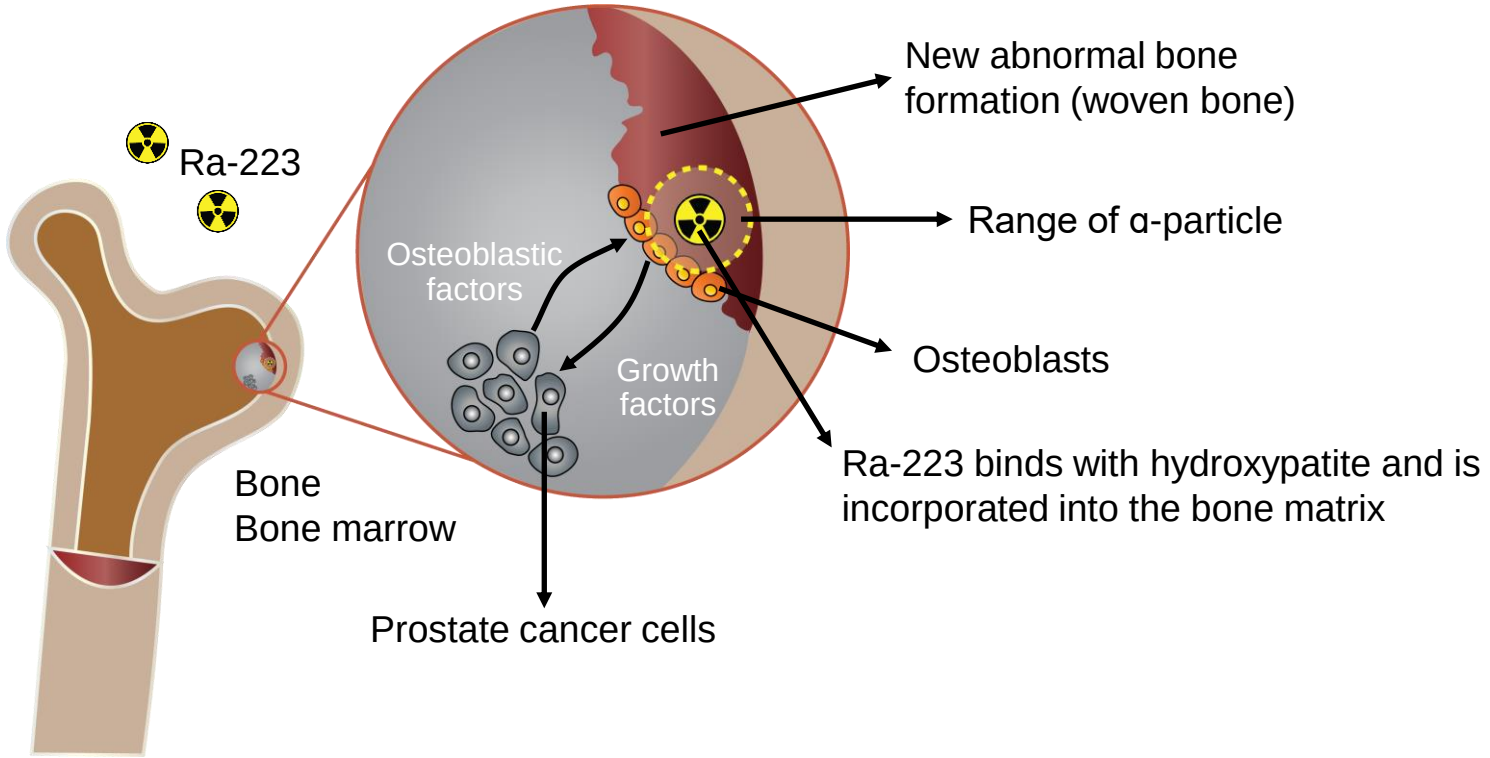
^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; ARPI, androgen receptor pathway inhibitor; CI, confidence interval; FDA, Food and Drug Administration; HR, hazard ratio; mCRPC, metastatic castrate-resistant prostate cancer; OS, overall survival; SoC, standard of care

Ramnaraign B, et al. Oncologist. 2023;28:392-401; Parker C, et al. N Engl J Med 2013; 369: 213-223; Sartor O, et al. N Eng J Med. 2021;385:1091-103

RADIUM-223

RADIUM-223: MECHANISM OF ACTION

- Radiopharmaceutical targets bone metastasis
- Radium-223 mimics calcium
- Taken up by the bone mets, emit alpha radiation causing double stranded DNA breaks



mets, metastases

Radium-223 Prescribing Information Dec 2019

Figure adapted from: Faria T, et al. Br J Cancer Res 2018; 1(2): 156-161

RADIUM-223 ADMINISTRATION AND DOSE

- Ra-223 should be administered only by persons authorised to handle radiopharmaceuticals in designated clinical settings and after evaluation of the patient by a qualified physician

- The dose is 55 kBq (1.49 microcurie) per kg body weight

The volume to be administered to a given patient is calculated as follows:

$$\text{Volume to be administered (mL)} = \frac{\text{Body weight in kg} \times 55\ \text{kBq/kg body weight}}{\text{Decay factor} \times 1100\ \text{kBq/mL}} \quad \textbf{OR} \quad \frac{\text{Body weight in kg} \times 1.49\ \text{mCi/kg body weight}}{\text{Decay factor} \times 30\ \text{mCi/mL}}$$

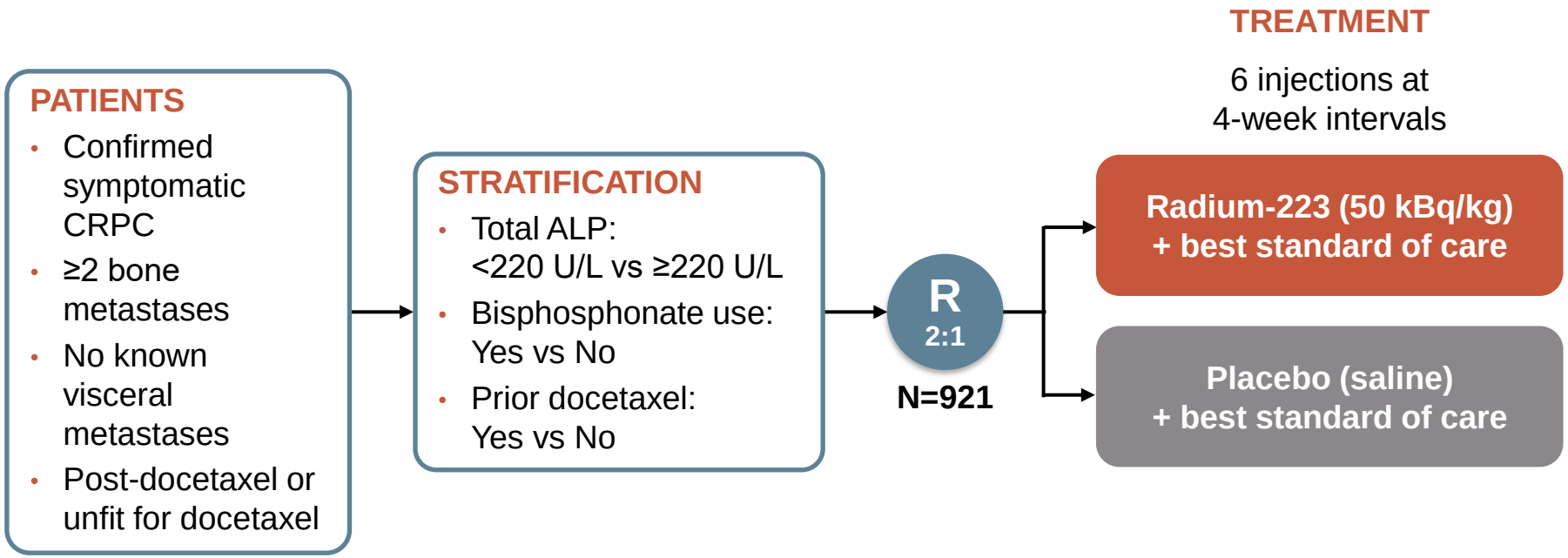
- Patient treated as an outpatient

kBq, kilobecquerel; mCi, microcurie; Ra-233, radium-233

Radium-223 US Prescribing Information (Dec 2019); Radium-223 SmPC

ALSYMPCA STUDY

- Phase 3 study in mCRPC patients with symptomatic bone metastases and no known visceral mets

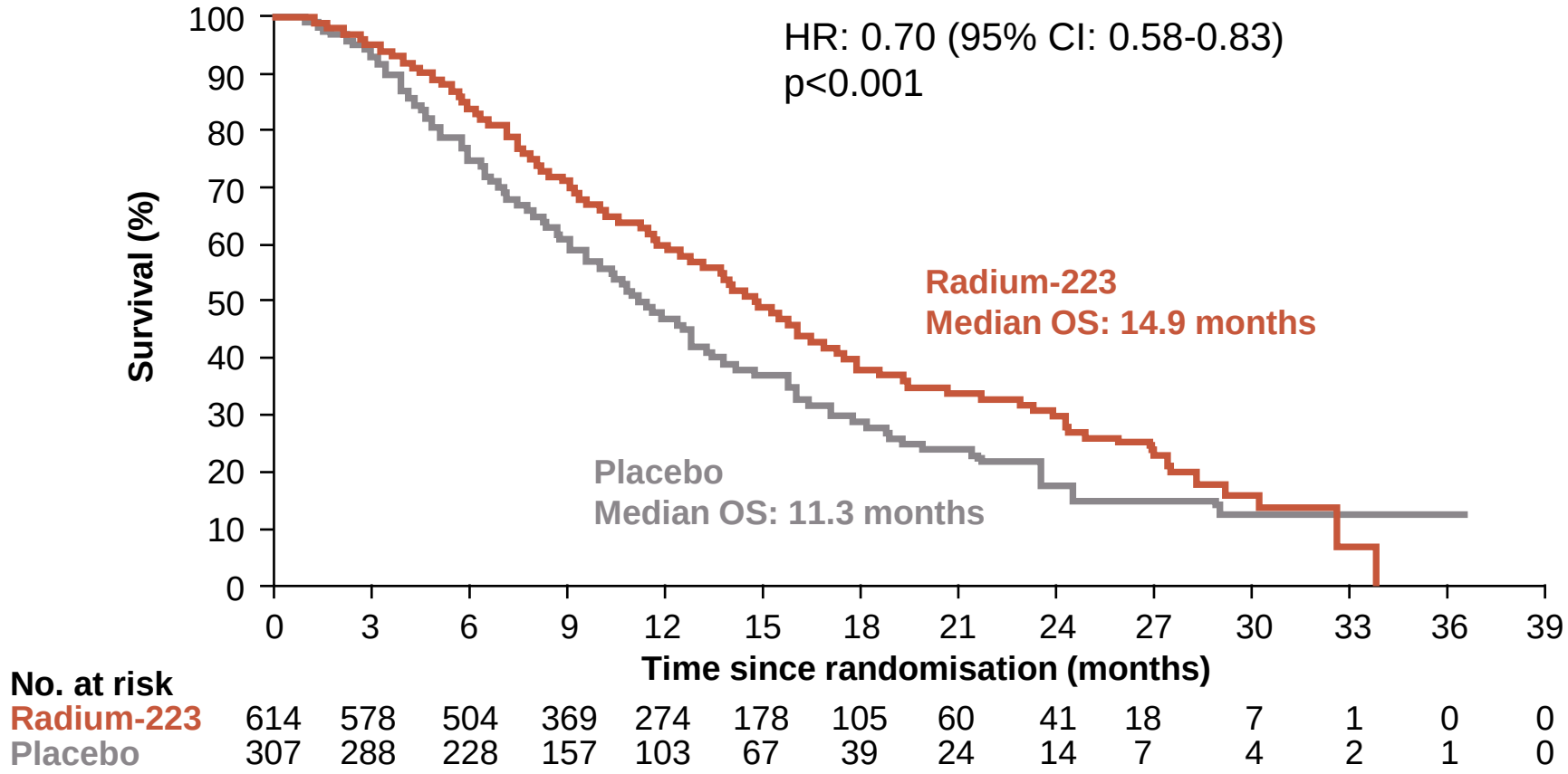


ALP, alkaline phosphatase; kBq, kilobecquerel; (m)CRPC, (metastatic) castrate resistant prostate cancer; mets, metastases; R, randomisation

Parker C, et al. N Engl J Med. 2013;369:213-23 (inc. protocol)

ALSYMPCA: Ra-223 PROLONGS OVERALL SURVIVAL

- Radium-223 significantly improved overall survival compared to placebo in mCRPC patients with symptomatic bone metastases

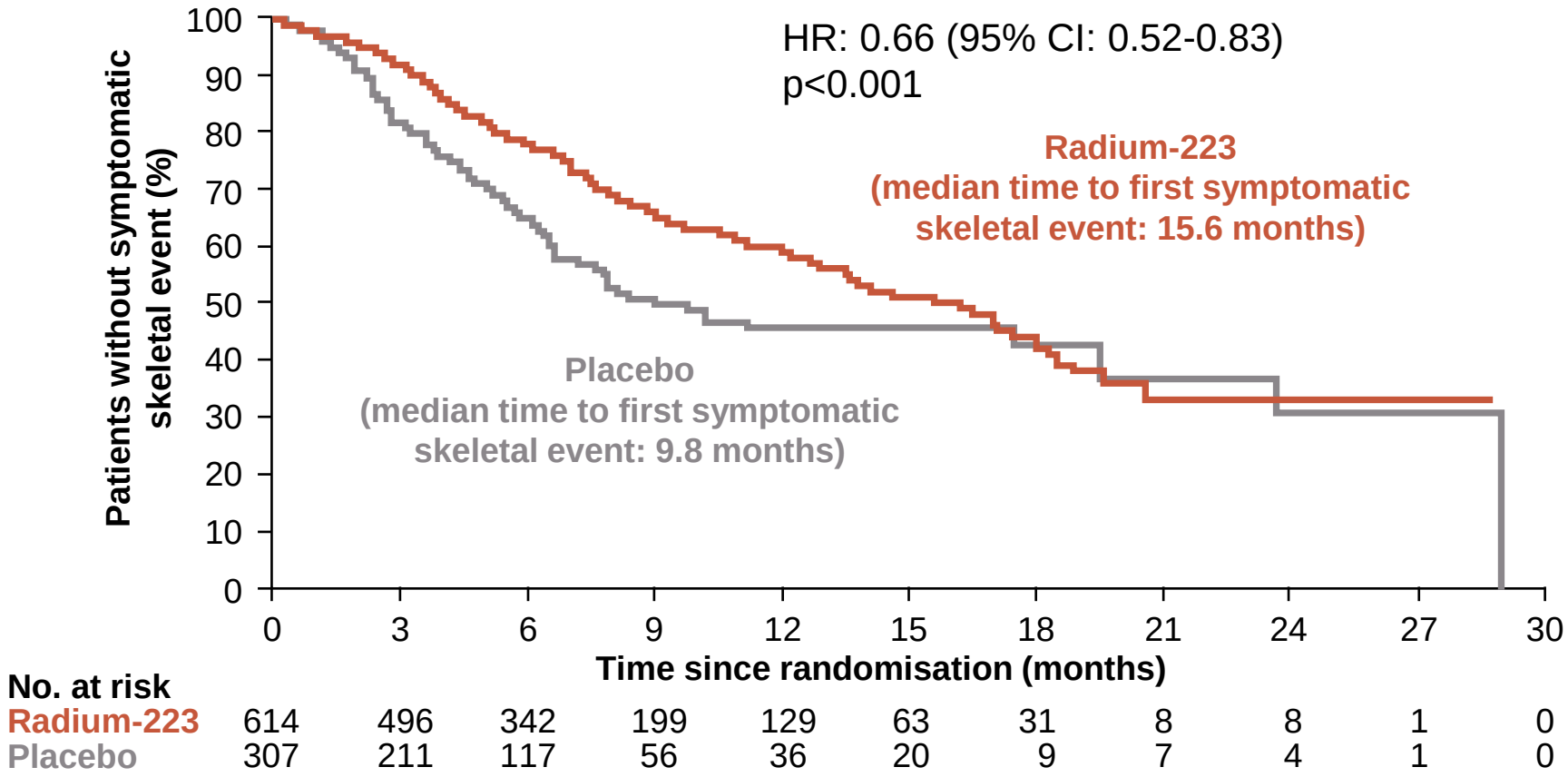


CI, confidence interval; HR, hazard ratio; mCRPC, metastatic castrate resistant prostate cancer; OS, overall survival; Ra-223, radium-223

Parker C, et al. N Engl J Med. 2013;369:213-23

ALSYMPCA: Ra-223 DELAYS TIME TO FIRST SSE

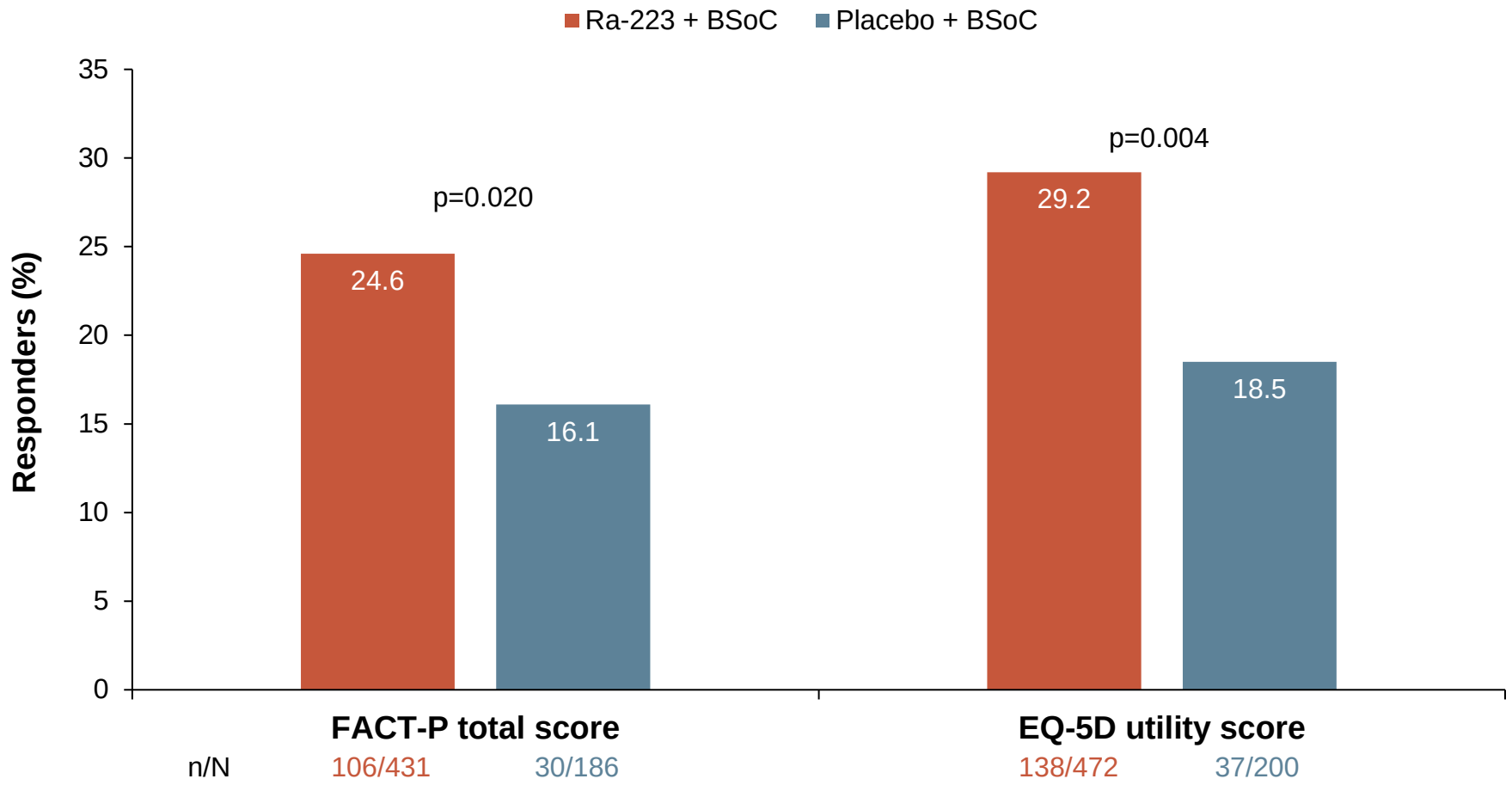
TIME TO FIRST SYMPTOMATIC SKELETAL EVENT



CI, confidence interval; HR, hazard ratio; Ra-223, radium-223; SSE, symptomatic skeletal event

Parker C, et al. N Engl J Med. 2013;369:213-23

ALSYMPCA: Ra-223 RESULTS IN A MEANINGFUL IMPROVEMENT IN QoL



BSoC, best standard of care; EQ-5D, EuroQoL 5D; FACT-P, Functional Assessment of Cancer Therapy Prostate; QoL, quality of life; Ra-223, radium-223

Adapted from Nilsson S, et al. Ann Oncol. 2016;27:868-74

ALSYMPCA: SAFETY DATA

Event, n (%)[1]	Radium-223 dichloride (n=600)				Placebo (n=301)			
	All grades	Grade 3	Grade 4	Grade 5[a]	All grades	Grade 3	Grade 4	Grade 5[a]
Haematological AEs								
Anaemia	187 (31)	65 (11)	11 (2)	0	92 (31)	37 (12)	2 (1)	1 (<1)
Thrombocytopenia	69 (12)	20 (3)	18 (3)	1 (<1)	17 (6)	5 (2)	1 (<1)	0
Neutropenia	30 (5)	9 (2)	4 (1)	0	3 (1)	2 (1)	0	0
Non-haematological AEs								
Constipation	108 (18)	6 (1)	0	0	64 (21)	4 (1)	0	0
Diarrhoea	151 (25)	9 (2)	0	0	45 (15)	5 (2)	0	0
Nausea	213 (36)	10 (2)	0	0	104 (35)	5 (2)	0	0
Vomiting	111 (18)	10 (2)	0	0	41 (14)	7 (2)	0	0
Asthenia	35 (6)	5 (1)	0	0	18 (6)	4 (1)	0	0
Fatigue	154 (26)	21 (4)	3 (1)	0	77 (26)	16 (5)	2 (1)	0
General physical health deterioration	27 (4)	9 (2)	2 (<1)	5 (1)	21 (7)	8 (3)	2 (1)	2 (1)
Peripheral oedema	76 (13)	10 (2)	0	0	30 (10)	3 (1)	1 (<1)	0
Pyrexia	38 (6)	3 (1)	0	0	19 (6)	3 (1)	0	0
Pneumonia	18 (3)	9 (2)	0	4 (1)	16 (5)	5 (2)	2 (1)	0

[a] Only one grade 5 haematological AE was considered possibly related to study drug: thrombocytopenia in one patient in the radium-223 group

- Final 3-year safety analysis of ALSYMPCA showed that radium-223 remained well tolerated, with low myelosuppression incidence and no new safety concern[2]

AE, adverse event

1. Parker C, et al. N Engl J Med. 2013;369:213-23; 2. Parker C, et al. Eur Urol. 2018;73:427-35

RADIUM-223: SIDE EFFECT MANAGEMENT

- **Diarrhoea and sickness**
  - Monitor oral intake and fluid status to prevent dehydration
- **Low blood cell count** – risk of infection/anaemia/bruising
  - Haematological evaluation at baseline and prior to every dose of radium-223
- **Increased bone pain in the area of bone disease** for a few days after treatment
  - Increase pain medication during this period
  - Levels of pain decrease with progressive cycles of radium-223
- **Peripheral oedema**
  - Gentle exercise, raise swollen areas on chair
  - Treat with diuretics if required

Radium-223 SmPC and US Prescribing Information; Local guidelines University College London Hospital, Janet Forgenie personal communication

WHEN TO USE Ra-223

Radium-223 FDA-approved indication[1]

Indicated for the treatment of patients with castrate-resistant prostate cancer, **symptomatic bone metastases** and **no known visceral metastatic disease**

Radium-223 EMA-approved indication[2]

Indicated as monotherapy or in combination with an LHRH analogue for the treatment of adult patients with mCRPC, **symptomatic bone metastases** and **no known visceral metastases**, who are in **progression after at least two prior lines of systemic therapy** for mCRPC (other than LHRH analogues), or ineligible for any available systemic mCRPC treatment

FDA, Food and Drug Administration; LHRH, luteinising hormone-releasing hormone; mCRPC, metastatic castrate-resistant prostate cancer; Ra-223, radium-223

1. Radium-223 US prescribing information (Dec 2019); 2. Radium-223 SmPC (Jun 2018)

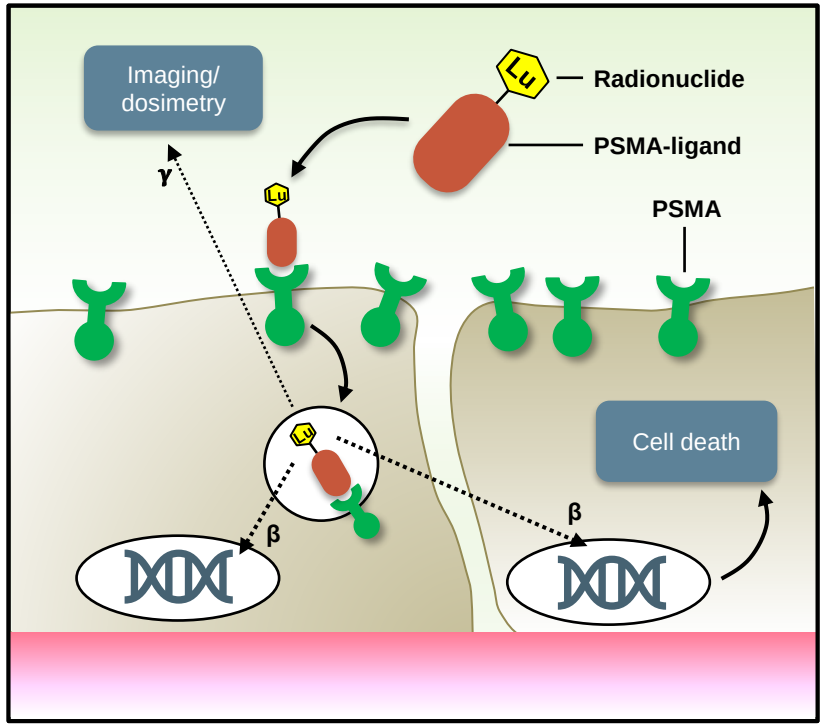
^{177}LU-PSMA-617

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617

^{177}LU-PSMA-617: MECHANISM OF ACTION

MECHANISM OF ACTION

- ^{177}Lu-PSMA is a radionuclide therapy that is directed to PSMA expressing prostate cancer
- ^{177}Lu-PSMA-617 pairs PSMA targeting ligand (PSMA-617) to radioactive atom (^{177}lutetium)
- “Ligand” is a small molecule designed to bind to PSMA, a protein highly expressed on the cell surface of most prostate cancer cells
- Once bound, the ^{177}lutetium atom releases an energetic beta particle that kills cancer cell



ADMINISTRATION

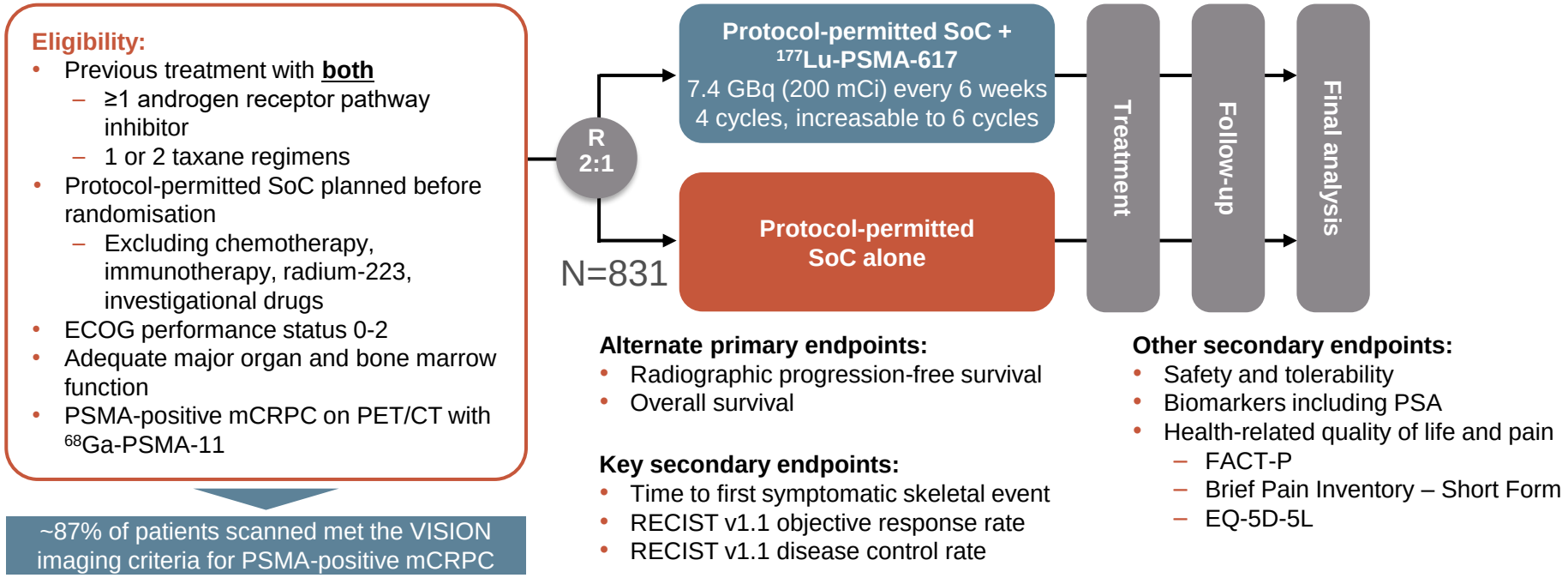
- Administered as 6 fractions of treatment (once every 6 weeks ± 1 week)
  - 7.4 GBq (± 10%) of ^{177}Lu-PSMA-617 will be administered
  - Treatment will be administered on an outpatient basis in the Department of Nuclear Medicine

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; β, β particle; GBq, gigabecquerel; PSMA, prostate specific membrane antigen; RLT, radioligand therapy

Ferdinandusa J, et al. Curr Opin Urol. 2018;28:197-204; Lutetium Lu 177 vipivotide tetraxetan US Prescribing Information (Oct 2022)

VISION STUDY: BACKGROUND AND DESIGN

- Prostate-specific membrane antigen (PSMA) is highly expressed on the surface of prostate cancer cells, including metastatic lesions, and is only expressed on a few normal tissues such as the salivary and lacrimal glands
- Studies have confirmed that PSMA-bound imaging is highly specific for PET-based imaging of prostate cancer
- The VISION trial randomised patients with mCRPC who had ≥1 PSMA-PET positive metastatic lesion and no PSMA-negative metastatic lesions to receive either ^{177}Lu-PSMA-617 plus ongoing standard of care or standard of care



Alternate primary endpoints:
- Radiographic progression-free survival
- Overall survival

Key secondary endpoints:
- Time to first symptomatic skeletal event
- RECIST v1.1 objective response rate
- RECIST v1.1 disease control rate

Other secondary endpoints:
- Safety and tolerability
- Biomarkers including PSA
- Health-related quality of life and pain
  - FACT-P
  - Brief Pain Inventory – Short Form
  - EQ-5D-5L

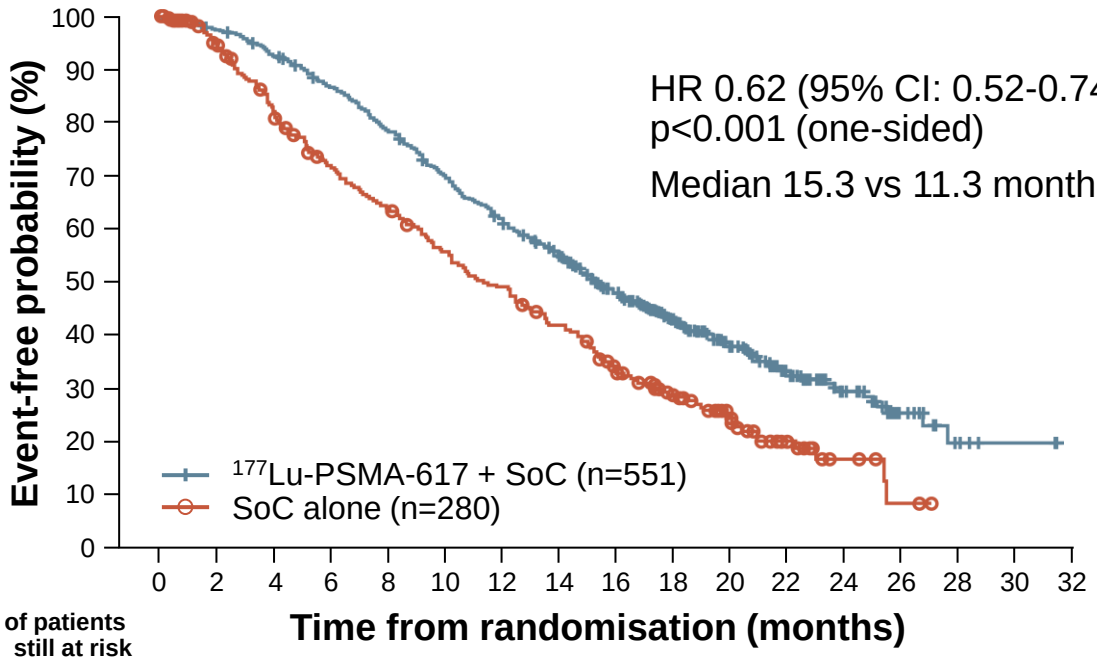
^{68}Ga-PSMA-11; gallium-68-prostate-specific membrane antigen-11; ^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; EQ-5D-5L, European Quality of Life (EuroQol)–5 domain 5 level scale; FACT-P, Functional Assessment of Cancer Therapy–Prostate; mCi, microcurie; mCRPC, metastatic castrate-resistant prostate cancer; PET, positron-emission tomography; PSA, prostate-specific antigen; PSMA prostate-specific membrane antigen; R, randomisation; RECIST, Response Evaluation Criteria in Solid Tumours; SoC, standard of care

Morris MJ, et al. J Clin Oncol. 2021;39 suppl 15:LBA4 (ASCO 2021 oral presentation); Ferdinandusa J, et al. Curr Opin Urol. 2018;28:197-204 ; Sartor O, et al. N Eng J Med. 2021;385:1091-103 (Supplementary Appendix)

VISION STUDY: ^{177}LU-PSMA-617 PROLONGS OS IN PTS WHO HAVE RECEIVED ≥1 ARI, AND 1 OR 2 PRIOR TAXANE-BASED CT REGIMENS

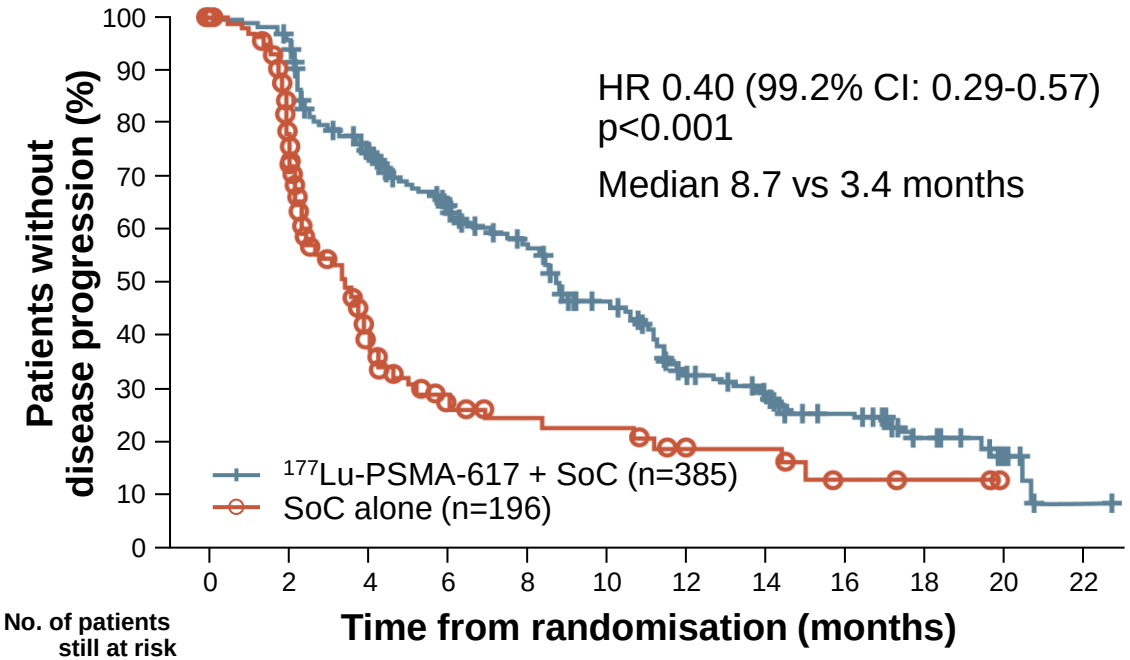
ALTERNATE PRIMARY ENDPOINTS

OS all randomised patients (N=831)



No. of patients still at risk																	
^{177}Lu-PSMA-617 + SoC	551	535	506	470	425	377	332	289	236	166	112	63	36	15	5	2	0
SoC alone	280	238	203	173	155	133	117	98	73	51	33	16	6	2	0	0	0

Imaging-based progression-free survival (n=581)



No. of patients still at risk												
^{177}Lu-PSMA-617 + SoC	385	362	272	215	182	137	88	71	49	21	6	1
SoC alone	196	119	36	19	14	13	7	7	3	2	0	0

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; ARI, androgen receptor inhibitor; CI, confidence interval; CT, chemotherapy; ^{177}Lu-PSMA-617, lutetium-177-prostate specific membrane antigen-617; HR, hazard ratio; OS, overall survival; pt, patient; SoC, standard of care

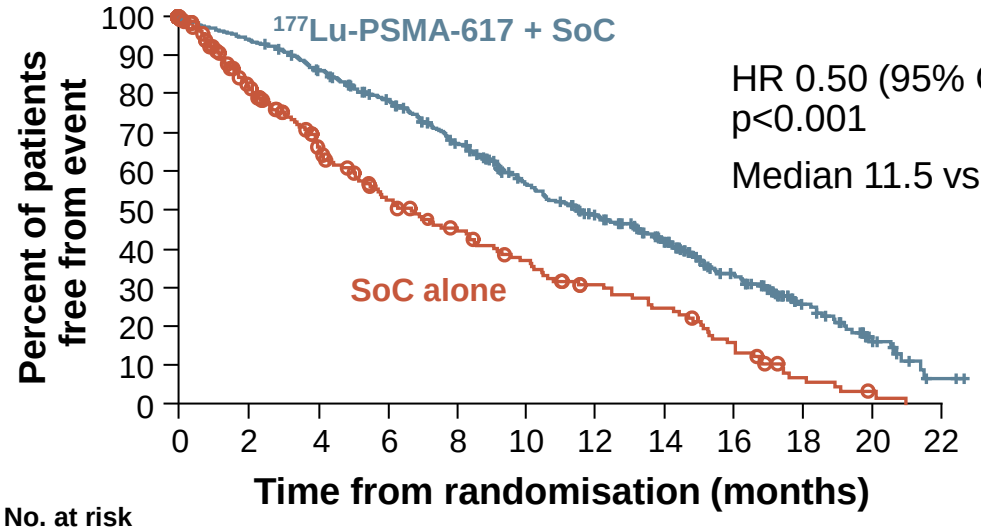
Sartor O, et al. N Eng J Med. 2021;385:1091-103

VISION STUDY: ^{177}LU-PSMA-617 SIGNIFICANTLY IMPROVES ALL SECONDARY ENDPOINTS

INCLUDING TIME TO FIRST SYMPTOMATIC SKELETAL EVENT, ORR AND DCR

Patients with evaluable disease at baseline	^{177}Lu-PSMA-617 + SoC (N=319)	SoC (N=120)
ORR, n (%)	95 (29.8)	2 (1.7)
	OR 24.99 (95% CI: 6.05-103.24) p<0.001	
DCR, n (%)	284 (89.0)	80 (66.7)
	OR 5.79 (95% CI: 3.18-10.55) p<0.001	

Time to first symptomatic skeletal event



HR 0.50 (95% CI: 0.40-0.62)
p<0.001

Median 11.5 vs 6.8 months

No. at risk

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

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; CI, confidence interval; DCR, disease control rate; HR, hazard ratio; mo, months; OR, odds ratio; ORR, overall response rate; SoC, standard of care

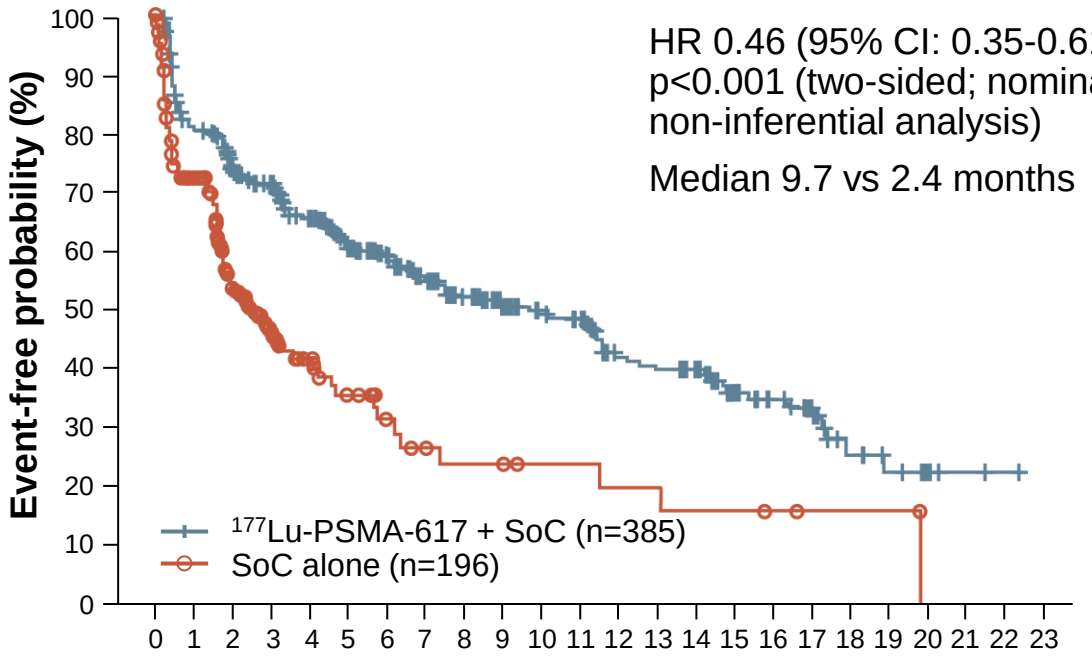
Sartor O, et al. N Engl J Med. 2021;385:1091-103 (Supplementary Appendix)

VISION STUDY: ^{177}LU-PSMA-617 BENEFICIAL EFFECT ON PAIN AND QoL

FACT-P TOTAL SCORE

Time to worsening favoured the ^{177}Lu-PSMA-617 arm

rPFS analysis set (N=581)



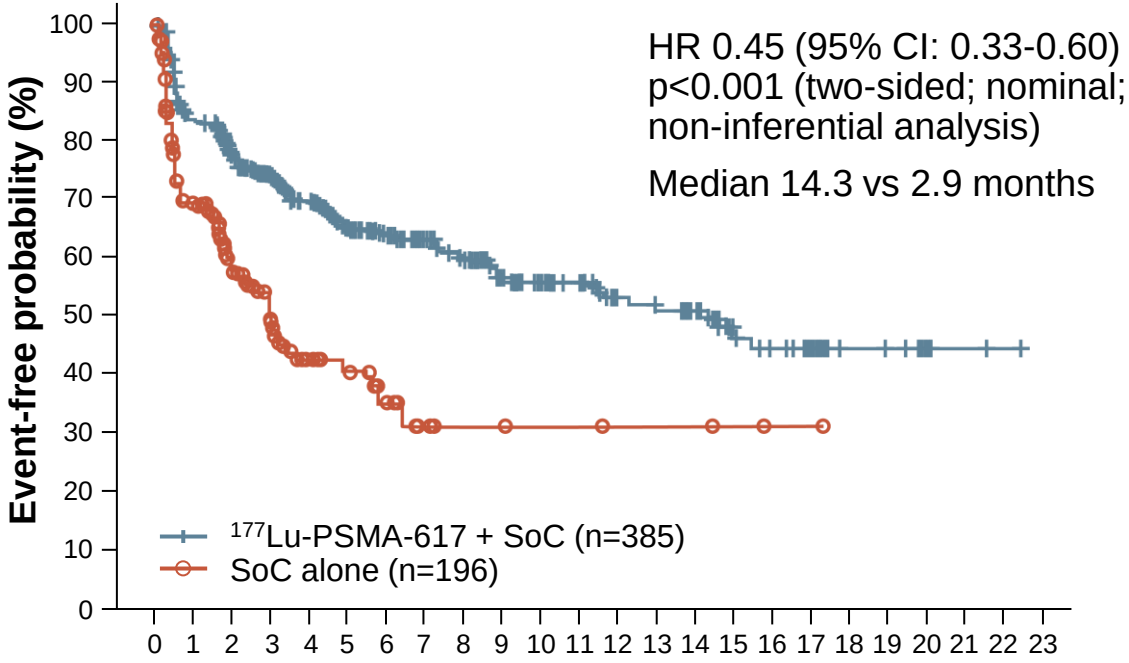
No. of patients still at risk																								
^{177}Lu-PSMA-617 + SoC	385	289	255	235	201	167	146	126	110	89	76	72	54	51	46	33	27	21	10	7	4	2	1	0
SoC alone	196	97	66	42	30	21	14	10	8	8	6	6	5	5	4	4	3	2	2	2	0	0	0	0

Time to the first occurrence of ≥10-point decrease in FACT-P total from baseline

BPI-SF PAIN INTENSITY

Time to worsening favoured the ^{177}Lu-PSMA-617 arm

rPFS analysis set (N=581)



No. of patients still at risk																								
^{177}Lu-PSMA-617 + SoC	385	296	265	238	197	162	146	129	113	87	70	66	51	48	42	24	21	15	8	6	2	2	1	0
SoC alone	196	94	65	37	25	19	12	7	5	5	4	4	3	3	3	2	1	1	0	0	0	0	0	0

Time to the first occurrence of ≥30-point or ≥2-point increase in BPI-SF pain intensity from baseline

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; BPI-SF, Brief Pain Inventory–Short Form; CI, confidence interval; FACT-P, Functional Assessment of Cancer Therapy– Prostate; HR, hazard ratio; QoL, quality of life; rPFS, radiographic progression-free survival; SoC, standard of care

Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S627-8 (ESMO 2021 oral presentation)

VISION STUDY: SIDE EFFECTS

TREATMENT-EMERGENT ADVERSE EVENTS

Patients, n (%)	^{177}Lu-PSMA-617 + SoC (N=529)		SoC alone (N=205)	
	All grades	Grade 3 to 5	All grades	Grade 3 to 5
Any drug-related TEAE	451 (85.3)	150 (28.4)	59 (28.8)	8 (3.9)
Serious	49 (9.3)	43 (8.1)	5 (2.4)	5 (2.4)
Grade 5[a]	5 (0.9)	5 (0.9)	0 (0.0)	0 (0.0)
TEAEs grouped by topics of interest				
Fatigue	260 (49.1)	37 (7.0)	60 (29.3)	5 (2.4)
Bone marrow suppression	251 (47.4)	124 (23.4)	36 (17.6)	14 (6.8)
Leukopenia	66 (12.5)	13 (2.5)	4 (2.0)	1 (0.5)
Lymphopenia	75 (14.2)	41 (7.8)	8 (3.9)	1 (0.5)
Anaemia	168 (31.8)	68 (12.9)	27 (13.2)	10 (4.9)
Thrombocytopenia	91 (17.2)	42 (7.9)	9 (4.4)	2 (1.0)
Dry mouth	208 (39.3)	0 (0.0)	2 (1.0)	0 (0.0)
Nausea and vomiting	208 (39.3)	8 (1.5)	35 (17.1)	1 (0.5)
Renal effects	46 (8.7)	18 (3.4)	12 (5.9)	6 (2.9)
Second primary malignancies	11 (2.1)	4 (0.8)	2 (1.0)	1 (0.5)
Intracranial haemorrhage	7 (1.3)	5 (0.9)	3 (1.5)	2 (1.0)

[a] There were five drug-related treatment-emergent adverse events leading to death in the ^{177}Lu-PSMA-617 arm: pancytopenia, n=2; bone-marrow failure, n=1; subdural haematoma, n=1; intracranial haemorrhage, n=1

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; SoC, standard of care; TEAE, treatment-emergent adverse event

Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S627-8 (ESMO 2021 oral presentation)

WHEN TO USE ^{177}LU-PSMA-617


^{177}Lu-PSMA-617 FDA and EMA approved indications[1,2]

^{177}Lu-PSMA-617 is approved by the FDA and EMA for the treatment of adult patients with progressive PSMA-positive mCRPC who have been previously treated with ARPI and taxane-based chemotherapy [1,2]

- The pivotal VISION trial supports the use of ^{177}Lu-PSMA-617 in patients previously treated with an ARPI and docetaxel in a setting currently occupied with cabazitaxel[3]
- The phase 2, TheraP trial performed a direct comparison between ^{177}Lu-PSMA-617 and cabazitaxel[4]:
  - ^{177}Lu-PSMA-617 led to a higher PSA response (66 vs 37%, p<0.0001) and fewer grade 3 to 4 AEs (33 vs 53%)
  - Based on these results, cabazitaxel - ^{177}Lu-PSMA-617 sequence could be reversed
- However, the 3-year follow up of the TheraP study showed no difference in OS between the treatments (19.1 vs 19.6 months, difference -0.5, 95% CI -3.7 to + 2.7)[5]

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; ADT, androgen deprivation therapy; AE, adverse event; ARPI, androgen receptor pathway inhibitor; CI, confidence interval; EMA, European Medicines Agency; FDA, Food and Drug Administration; mCRPC, metastatic castrate-resistant prostate cancer; OS overall survival; PSA, prostate-specific antigen; PSMA, prostate specific membrane antigen

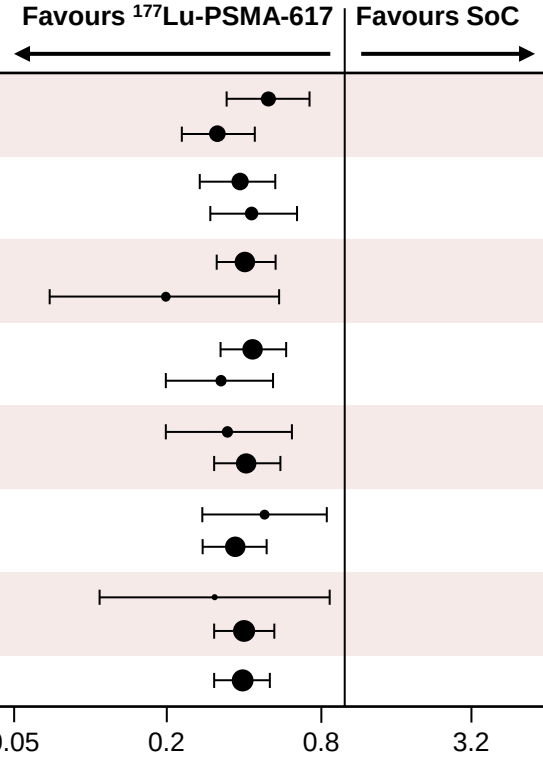
1. Lu-PSMA US Prescribing Information; 2. Lu-PSMA SmPC; 3. Sartor O, et al. N Engl J Med. 2021;385:1091-103; 4. Hofman M, et al. Lancet. 2021;397:797-804; 5. Hofman M, et al. J Clin Oncol. 2022;40, no. 16_suppl:5000-5000

SEQUENCING RADIOPHARMACEUTICALS

VISION STUDY: rPFS BY PRIOR TREATMENTS (BICR)

- ~78% of patients had received ≥3 lines of prior therapy in the VISION trial

n/N (%)		^{177}Lu-PSMA-617 + SoC (n=385)	SoC alone (n=196)	HR (95% CI)
ARPIs	1	138/209 (66.0)	42/97 (43.3)	0.51 (0.35, 0.73)
	≥2	116/176 (65.9)	51/99 (51.5)	0.32 (0.23, 0.45)
Taxane regimens	1	142/224 (63.4)	49/110 (44.5)	0.39 (0.27, 0.54)
	≥2	94/134 (70.1)	40/77 (51.9)	0.44 (0.30, 0.66)
Non-taxane regimens	0	230/347 (66.3)	88/183 (48.1)	0.41 (0.32, 0.54)
	≥1	24/38 (63.2)	5/13 (38.5)	0.20 (0.07, 0.56)
Immunotherapies	0	199/306 (65.0)	65/146 (44.5)	0.44 (0.33, 0.59)
	≥1	55/79 (69.6)	28/50 (56.0)	0.33 (0.20, 0.53)
Bone health agents	Yes	45/66 (68.2)	21/35 (60.0)	0.35 (0.20, 0.62)
	No	209/319 (65.5)	72/161 (44.7)	0.42 (0.31, 0.56)
^{223}Ra	Yes	43/63 (68.3)	19/36 (52.8)	0.49 (0.28, 0.87)
	No	211/322 (65.5)	74/160 (46.3)	0.38 (0.28, 0.50)
PARP inhibitors	Yes	18/24 (75.0)	5/11 (45.5)	0.31 (0.11, 0.89)
	No	236/361 (65.4)	88/185 (47.6)	0.41 (0.31, 0.53)
All patients		**254/385 (66.0)**	**93/196 (47.4)**	**0.40 (0.31, 0.52)**



- rPFS benefits with ^{177}Lu-PSMA-617 were consistent across all prior treatment groups, including prior treatment with the radiopharmaceutical Ra-223

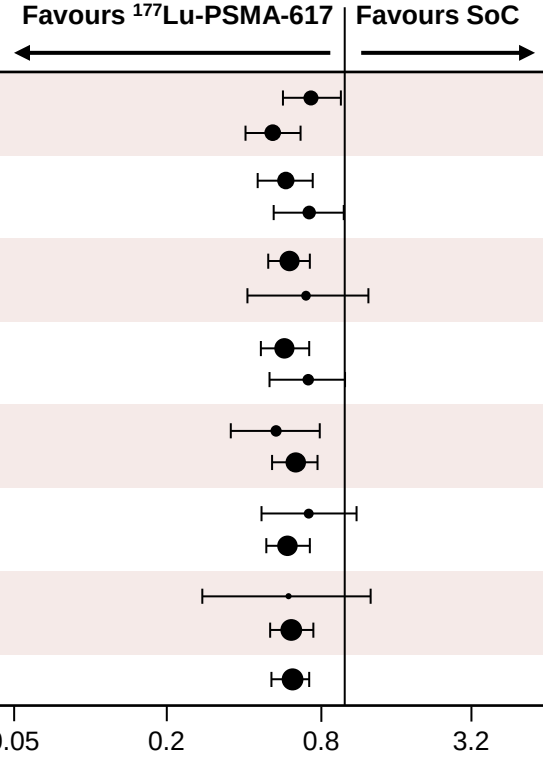
ARPI, androgen receptor pathway inhibitor; CI, confidence interval; HR, hazard ratio; PARP, poly (ADP-ribose) polymerase; PSMA, prostate-specific membrane antigen; Ra, radium; rPFS, radiographic progression-free survival; SoC, standard of care

Sartor O, et al. N Eng J Med. 2021;385:1091-103 (supplementary data appendix); Vaishampayan N, et al. ASCO 2022; abstract #5001 (oral presentation)

VISION STUDY: OS BY PRIOR TREATMENTS (BICR)

- OS benefits with ^{177}Lu-PSMA-617 were consistent across all prior treatment groups

n/N (%)		^{177}Lu-PSMA-617 + SoC (n=551)	SoC alone (n=280)	HR (95% CI)
ARPIs	1	182/296 (61.5)	83/130 (63.8)	0.74 (0.57, 0.97)
	≥2	161/255 (63.1)	104/150 (69.3)	0.52 (0.41, 0.67)
Taxane regimens	1	206/342 (60.2)	108/165 (65.5)	0.59 (0.46, 0.75)
	≥2	113/170 (66.5)	70/99 (70.7)	0.73 (0.53, 0.99)
Non-taxane regimens	0	299/485 (61.6)	167/252 (66.3)	0.61 (0.50, 0.74)
	≥1	44/66 (66.7)	20/28 (71.4)	0.71 (0.42, 1.23)
Immunotherapies	0	255/414 (61.6)	134/200 (67.0)	0.58 (0.47, 0.73)
	≥1	88/137 (64.2)	53/80 (66.3)	0.72 (0.51, 1.01)
Bone health agents	Yes	66/99 (66.7)	43/57 (75.4)	0.54 (0.36, 0.80)
	No	277/452 (61.3)	144/223 (64.6)	0.64 (0.52, 0.79)
^{223}Ra	Yes	59/97 (60.8)	31/48 (64.6)	0.73 (0.47, 1.13)
	No	284/454 (62.6)	156/232 (67.2)	0.60 (0.49, 0.73)
PARP inhibitors	Yes	22/30 (73.3)	11/16 (68.8)	0.60 (0.28, 1.28)
	No	321/521 (61.6)	176/264 (66.7)	0.62 (0.51, 0.75)
All patients		**343/551 (62.3)**	**187/280 (66.8)**	**0.62 (0.52, 0.74)**

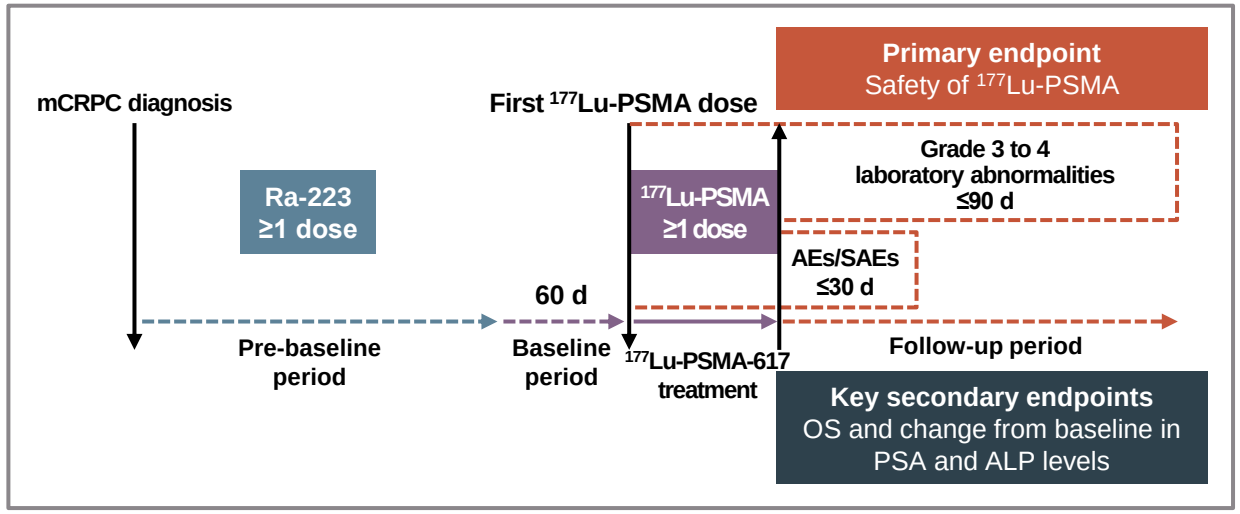


ARPI, androgen receptor pathway inhibitor; CI, confidence interval; HR, hazard ratio; OS, overall survival; PARP, poly (ADP-ribose) polymerase; PSMA, prostate-specific membrane antigen; Ra, radium; SoC, standard of care

Sartor O, et al. N Eng J Med. 2021;385:1091-103 (supplementary data appendix); Vaishampayan N, et al. ASCO 2022; abstract #5001 (oral presentation)

RALU STUDY: ^{177}LU-PSMA-617 IN PATIENTS PREVIOUSLY TREATED WITH RA-223

- **The RALU study was a retrospective, multicentre medical chart review evaluating the safety and clinical outcomes of sequential radium-223/^{177}Lu-PSMA therapy in mCRPC patients**



RESULTS

- Low rates of overall and hematologic AEs indicated an acceptable safety profile when using ^{177}Lu-PSMA-617 after Ra-223
- Median OS was 12.6 and 31.4 mo from the first dose of ^{177}Lu-PSMA-617 and Ra-223, respectively, and 39% of patients had at least a 30% decline in PSA

- The use of novel mechanisms of action with life-prolonging benefits, such as Ra-223 and ^{177}Lu-PSMA-617, can be achieved in heavily pretreated mCRPC patients
- The data support using ^{177}Lu-PSMA-617 in patients who previously received Ra-223

^{177}Lu-PSMA, lutetium-177-prostate-specific membrane antigen; AE, adverse event; ALP, alkaline phosphatase; d, days; mCRPC, metastatic castrate resistant prostate cancer; mo, months; OS, overall survival; PSA, prostate specific antigen; Ra-223, radium-223; SAE, serious adverse event

Rahbar K, et al. J Nucl Med. 2023; 64:574-8

NURSE MANAGEMENT OF PATIENTS

RISK ASSESSMENT: DETERMINE PATIENTS MEDICAL & PERSONAL CIRCUMSTANCES

- Do they have any urinary or faecal incontinence?
- Do they have a urinary catheter/urostomy or stoma bag?
- Does the patient have a separate toilet at home they can use for one week post treatment?
- Does the patient need any personal care?
- Does the patient care for anyone?
- Is the patient sexually active (should not father a child for 6 months post-treatment and use of a condom recommended)?
- Does the patient share their accommodation with any pregnant/breastfeeding women or children
- Is the patient solely or chiefly responsible for care of any children
  - They need to avoid prolonged close contact e.g. sitting on the sofa watching television, contact with babies and small children under 16 for the first 3 days
  - No isolation from family or friends is required
- Consider patient's occupation/activities/family commitments and social life
  - Does the patient work, or do they carry out any tasks outside of the house?
  - Any important upcoming family/social events (e.g. wedding)?

Local Questionnaire and guidelines University College London Hospital, Janet Forgenie personal communication

BEST PRACTICE: MANAGING BODILY FLUIDS DURING TREATMENT

- Bodily fluids are slightly radioactive for the first 7 days therefore precautions are required
  - Sit to void & double flush with the lid down after each use
  - Does the patient have a separate toilet at home they can use for one week post treatment?
  - If a shared toilet, wipe the toilet seat after use
  - Wipe carefully after bowel movement/some patients use gloves
  - When handling bodily fluids, simply wearing gloves and hand washing will protect caregivers
  - Soiled clothing should be washed promptly and separately from other clothing

Local Guidelines University College London Hospital, Janet Forgenie personal communication

RADIUM-223: SAFETY/RADIATION CONSIDERATIONS

- **Patients should stay well hydrated**, and their oral intake, fluid status, and urine output should be monitored while on treatment
  - Patients should promptly report signs of dehydration, hypovolemia, urinary retention, or renal failure / insufficiency
- There are **no restrictions regarding personal contact** (visual or physical proximity) with other people after receiving Ra-223
- **Male patients should use condoms and their female partners of reproductive potential should use effective contraception** during and for 6 months following completion of treatment
- **Perform complete blood counts prior to treatment initiation and before every dose of Ra-223**:
  - Discontinue treatment if haematologic values do not recover within 6 to 8 weeks after treatment. Monitor patients with compromised bone marrow reserve closely. Discontinue treatment in patients who experience life-threatening complications despite supportive care measures

ANC, absolute neutrophil counts; Ra-223, radium-223

Radium-223 SmPC and US Prescribing Information

^{177}LUTETIUM-PSMA-617: SAFETY/RADIATION CONSIDERATIONS

- **Ensure patients increase oral fluid intake** and advise patients to void as often as possible to reduce bladder radiation
- Advise patients to **limit close contact (less than 3 feet) with household contacts** for 2 days or with children and pregnant women for 7 days
- Following administration of ^{177}Lutetium-PSMA-617:
  - advise patients to **refrain from sexual activity for 7 days**
  - advise patients to **sleep in a separate bedroom from household contacts for 3 days**, from children for 7 days, or from pregnant women for 15 days
  - Advise male patients with female partners of reproductive potential to **use effective contraception during treatment and for 14 weeks after the last dose**
- **Perform complete blood counts before and during treatment with ^{177}Lutetium-PSMA-617**
  - withhold, reduce dose, or permanently discontinue treatment and clinically treat patients based on the severity of myelosuppression
- **Perform kidney function laboratory tests**
  - withhold, reduce dose, or permanently discontinue treatment based on severity

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617

^{177}Lu-PSMA-617 SmPC and US Prescribing Information

MANAGING BONE HEALTH

MUSCULOSKELETAL EVENTS

- Bone is the most common site of prostate cancer metastases and is associated with significant morbidity[1]
- Bone decay with ADT is associated with an increase in fracture risk[2]
- When treated with ADT, over 58% of men with risk factors for skeletal complications develop at least one fracture within 12 years[3]
  - Men who sustained a fracture within 48 months experienced an almost 40% higher risk of mortality than those who did not

ADT, androgen-deprivation therapy

1. Coleman RE. Clin Cancer Res. 2006;12:6243-9s; 2. Cheung AS, et al. Endocr Relat Cancer. 2014;21:R371-94; 3. Shao YH, et al. BJU Int. 2013;111:745-52

THE EFFECTS OF PROSTATE CANCER TREATMENT ON BONE

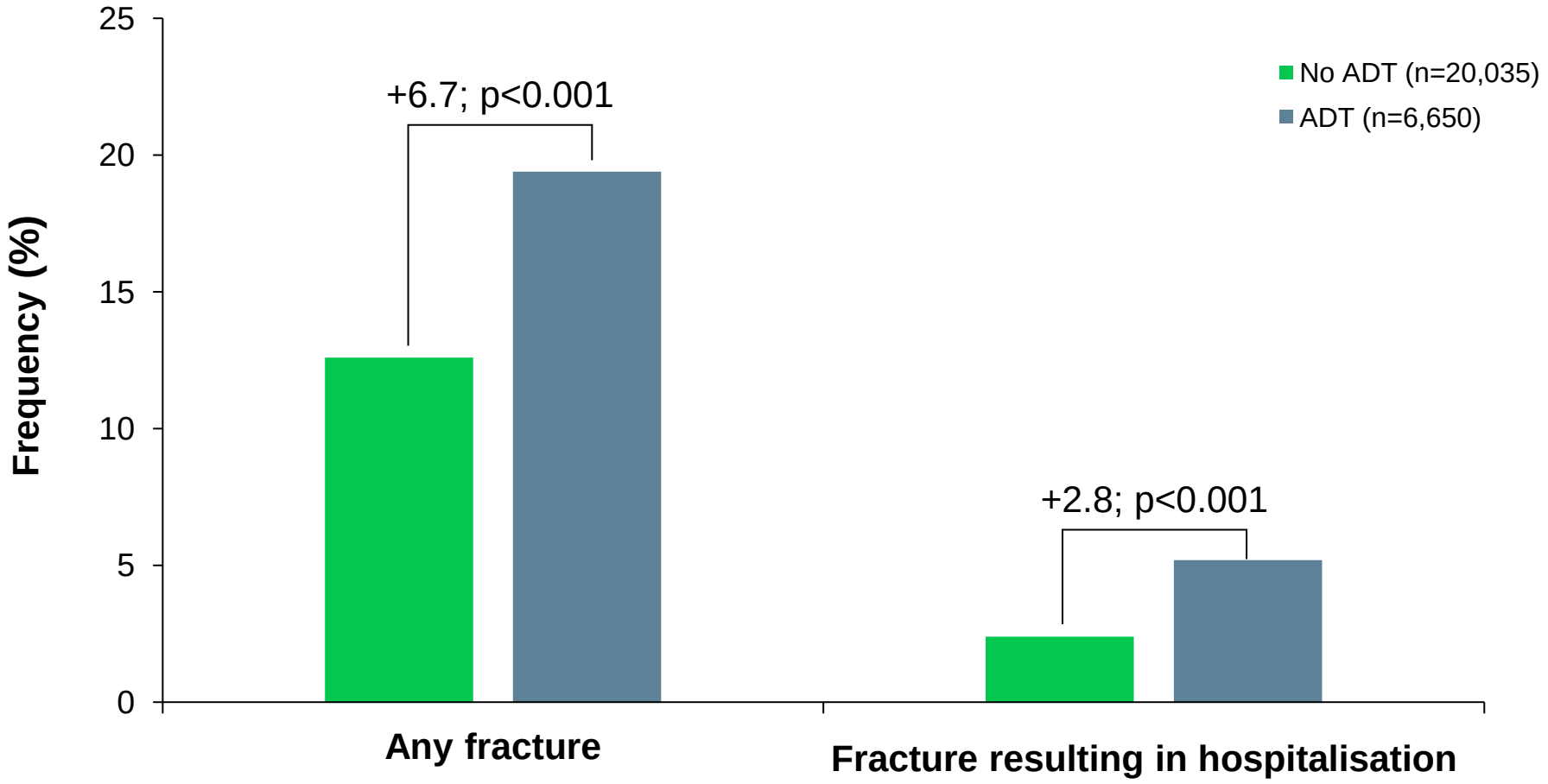
- Bone mass loss is associated with ADT
- We see skeletal related events in patient with bone mets
- Pathological fractures resulting in pain/risk of MSCC and reduce QoL
- Giving active therapy to treat bone mets can prolong survival
- Bone loss is most pronounced during initial ADT exposure but persists throughout treatment, increasing the longer patients are exposed
- Ultimately prevention is better than cure – hormone therapy is associated with a 34% increase in fracture risk among men with non-metastatic PC and a 51% increase in fracture risk among men with metastatic PC
- Concomitant use of bone health agent is recommended to minimise fracture risk

ADT, androgen deprivation therapy; mets, metastases; MSCC, metastatic spinal cord compression; PC, prostate cancer; QoL, quality of life

1. Suzman D, et al. Cancer Metastasis Rev. 2014;33:619-28; 2. El Badri S, et al. Curr Osteoporos Rep. 2019;17:527-37;
3. Hussain A, et al. Crit Rev Oncol Hematol 2019; 139: 108-16; 4. Beebe-Dimmer JL, et al. Pharmacoepidemiol Drug Saf. 2012;21(1):70-8.

PROPORTION EXPERIENCING FRACTURES 1-5 YEARS AFTER PROSTATE CANCER DIAGNOSIS

ADT RESULTED IN 21% - 54% INCREASE IN RELATIVE RISK OF FRACTURE



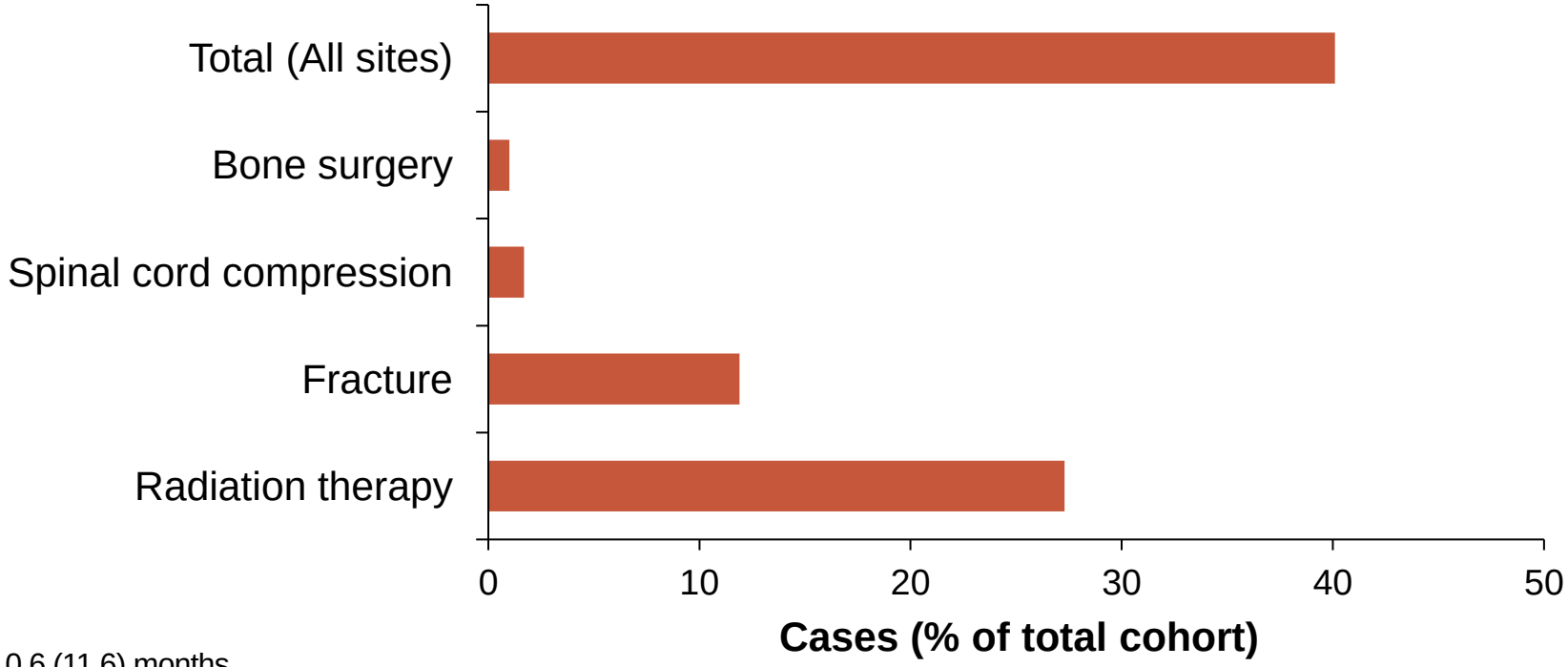
ADT, androgen deprivation therapy

Shahinian VB, et al. N Engl J Med. 2005;352:154-64

BONE METASTASES AND SREs

- Approx. 90% of patients with mCRPC develop bone metastases[1,2]
- Approx. 50% of PC patients with bone metastases will have SREs[3]

NUMBER OF FIRST CASES OF SRE[4]



Mean (SD) follow-up was 10.6 (11.6) months

mCRPC, metastatic castrate resistant prostate cancer; PC, prostate cancer; SREs, skeletal related events

1. Bubendorf L, et al. Hum Pathol. 2000;31:578-83; 2. Tannock IF, et al. N Engl J Med. 2004;352:1502-12; 3. Yong C, et al. Curr Opin Oncol. 2014;26:274-83; 4. Kawai A, et al. Prostate Cancer. 2019;2019:5971615

THINKING AHEAD

- DEXA studies show that **bone mineral density falls by 2% to 6% per year at the lumbar spine** and by **2% to 4% at the total hip during the first 1-2 years of ADT**[1-4]
  - This is a significantly faster rate of bone loss than in healthy controls or prostate cancer patients who are not receiving ADT[1-4]
- **Bone loss is most pronounced during initial ADT exposure**, it persists throughout treatment. In one study of 390 men receiving long-term ADT for prostate cancer, the prevalence of osteoporosis was 35% at baseline, 43% after 2 years, 49% after 4 years, 66% after 8 years, and 81% after 10 or more years of ADT[5]
- Studies also have estimated the extent to which ADT increases fracture risk. In an analysis of SEER-Medicare linked records from more than 80,000 prostate cancer patients, **gonadotropin-releasing hormone (GnRH) agonist therapy was associated with a 34% increase in risk of fracture among** men with non-metastatic prostate cancer, and a 51% increase in risk of fracture among men with metastatic prostate cancer[6]

ADT, androgen deprivation therapy; DEXA, dual-energy X-ray absorptiometry; SEER, Surveillance, Epidemiology, and End Results

1. Choo et al. International Journal of Radiation Oncology. 2013; 85(5):1239-4; 2. Alibhai SM, et al. Osteoporos Int. 2013;24(10):2571-2579.; 3. Brown SA, et al. Crit Rev Eukaryot Gene Expr. 2009;19:47–60; 4. Greenspan SL, et al. J Clin Endocrinol Metab. 2005;90:6410–6417; 5. Morote J, et al. Urology. 2007;69(3):500-504; 6. Beebe-Dimmer JL, et al. Pharmacoepidemiol Drug Saf. 2012;21(1):70-8.

SUMMARY

- The **landscape for mCRPC patients has evolved rapidly** over the past few years providing clinicians with a greater choice of treatments, including radiopharmaceuticals
  - Radiopharmaceuticals such as **Ra-223 and 177Lu-PSMA-617 offer a survival benefit to mCRPC patients** as well as managing bone pain and QOL[1-4]
- **~90% of men with advanced PC will develop bone metastasis** which often lead to skeletal-related events[5-7]
  - Bone health agents are therefore recommended for patients with advanced prostate cancer
- **Combining bisphosphonates or denosumab with newer therapies may improve outcomes**. *Post hoc* data suggest that additive effects for such combinations are possible but further evaluation required[8]
- Real-world data supports using ^{177}Lu-PSMA in patients who previously received Ra-223[9]
- Nurses and patients should be aware of post-treatment precautions, but **radiopharmaceuticals are an effective and manageable treatment option for mCRPC patients**

^{177}Lu-PSMA-617, lutetium-177-prostate-specific membrane antigen-617; mCRPC, metastatic castrate-resistant prostate cancer; mets, metastases; (m)PC, (metastatic) prostate cancer; QoL, quality of life

1. Parker C, et al. N Engl J Med. 2013;369:213-23; 2. Nilsson S, et al. Ann Oncol. 2016;27:868-74; 3. Sartor O, et al. N Engl J Med. 2021;385:1091-103; 4. Fizazi K, et al. Ann Oncol. 2021;32 suppl 5:S627-8; 5. Bubendorf L, et al. Hum Pathol. 2000;31:578-83; 6. Tannock IF, et al. N Engl J Med. 2004;352:1502-12; 7. Suzman D, et al. Cancer Metastasis Rev. 2014;33:619-283. 8. Saad F, et al. Cancer Treat Rev 2018; 68:25-37; 9. Rahbar K, et al. J Nucl Med 2023; 64:574–578

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