CAML

Centro Académico de Medicina de Lisboa

Welcome

PRISMAP Public Event
"Challenges in nuclear medicine"

28 November 2023
Lisbon School of Medicine, Aula Magna
Santa Maria Hospital Building

This public event will be organised at the Lisbon School of Medicine, in person only.

In the first session Portuguese and Spanish researchers will present their recent findings and invite to discuss challenges in nuclear medicine.

In the second session PRISMAP news, results from the project and its user projects and needs of the User Forum will be in the focus.

More information and registration (in-person only):
www.prismap.eu/news/events-feed/challenges-in-nuclear-medicine/

Morning session "Challenges in nuclear medicine" Chairs: António Paulo, Luís Costa		
9.00	Welcome	Luís Costa (Hospital de Santa Maria; Faculdade de Medicina de Lisboa, Instituto de Medicina Molecular)
9.15	New approaches in cancer treatment: facts and expectations with medical radionuclides	Luis Costa
9.45	Delivering on the promise of theranostics - a pillar of progress in IPO Porto	Gonçalo Ferreira (IPO Porto)
10.10	Short break	
10:25	ICNAS: 15 years of acceleration	Francisco Alves (ICNAS—Institute for Nuclear Sciences Applied to Health, University of Coimbra)
11.00	Phase 1 clinical trials with medical radionuclides	Bernard Doger (START Madrid- Jimenez Diaz Foundation University Hospital)
11:30	Round table discussion	Chairs: António Paulo, Luís Costa
12.30	Group photo	All
12.45	Lunch break	

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Afternoon session "Recent findings of PRISMAP and its user projects" Chair: Charlotte Duchemin		
14.00	PRISMAP – a short introduction	Thierry Stora (CERN)
14.15	Dedicated phantom measurements to develop and validate quantitative Ac-225-(micro)SPECT imaging	Michel Koole (KULeuven)
14.45	Development of a single-domain antibody for nuclear imaging and therapy of mesothelin expressing tumours	Alexis Broisat (INSERM)
15.15	Optimized cyclotron production of astatine: activity balance of At-211, At-210 and Po-210 after extraction chromatography.	Matthijs Sevenois (VUB)
15.45	Short break	
16.15	Optimization of the radiotheragnostic concept: Investigations of the next generation radionuclides	Cristina Müller (PSI)
16.45	User forum: Needs and active involvement	Thomas Elias Cocolios (KULeuven), Kristoff Muylle (VUB)
17.15	Conclusions	Charlotte Duchemin (CERN)
17.30 - End of the meeting		

New approaches in cancer treatment: facts and expectations with medical radionuclides

Luís Costa, MD, PhD

PRISMAP Public Event
"Challenges in nuclear medicine"

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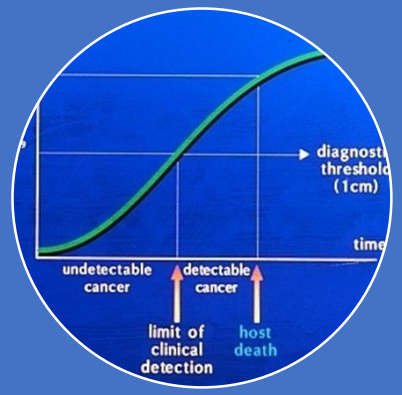
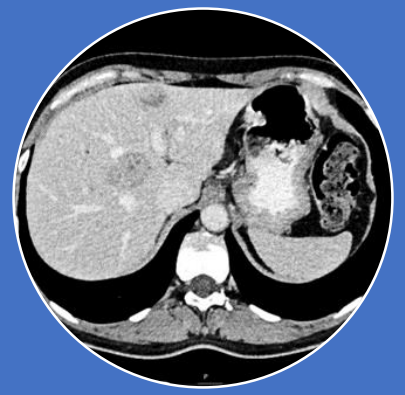
The chance to beat cancer: Major obstacles

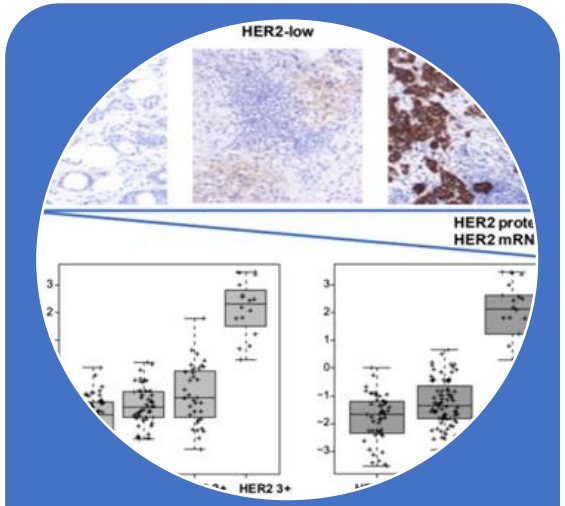


Time



Volume

(Tumor Burden)



Biology

Host (patient individuality)

Natural History of Cancer

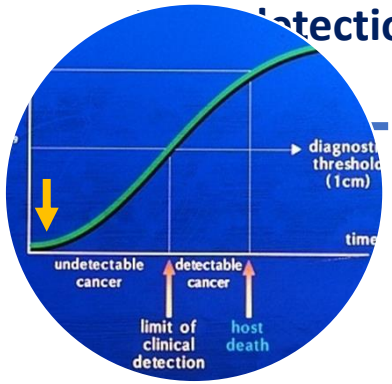
Before cancer | Premalignant lesions | Early stage | Advanced stage

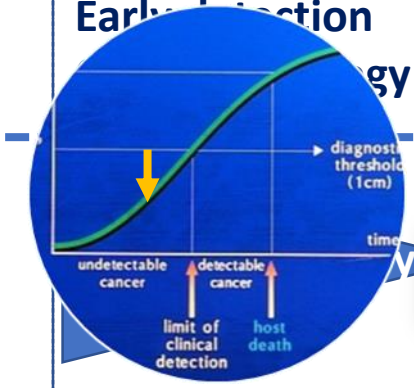
Prevention / Chemoprevention

Carcinogens

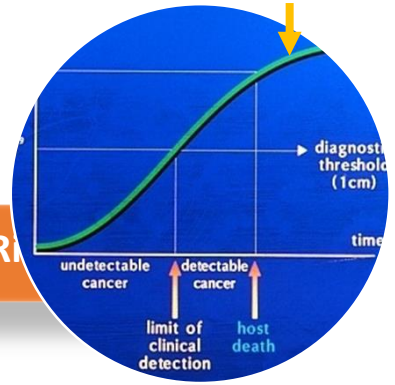
Risk factors
Lifestyle

Genetic susceptibility





Palliative:
Increase survival
Symptom control
Curative (?) (a few)



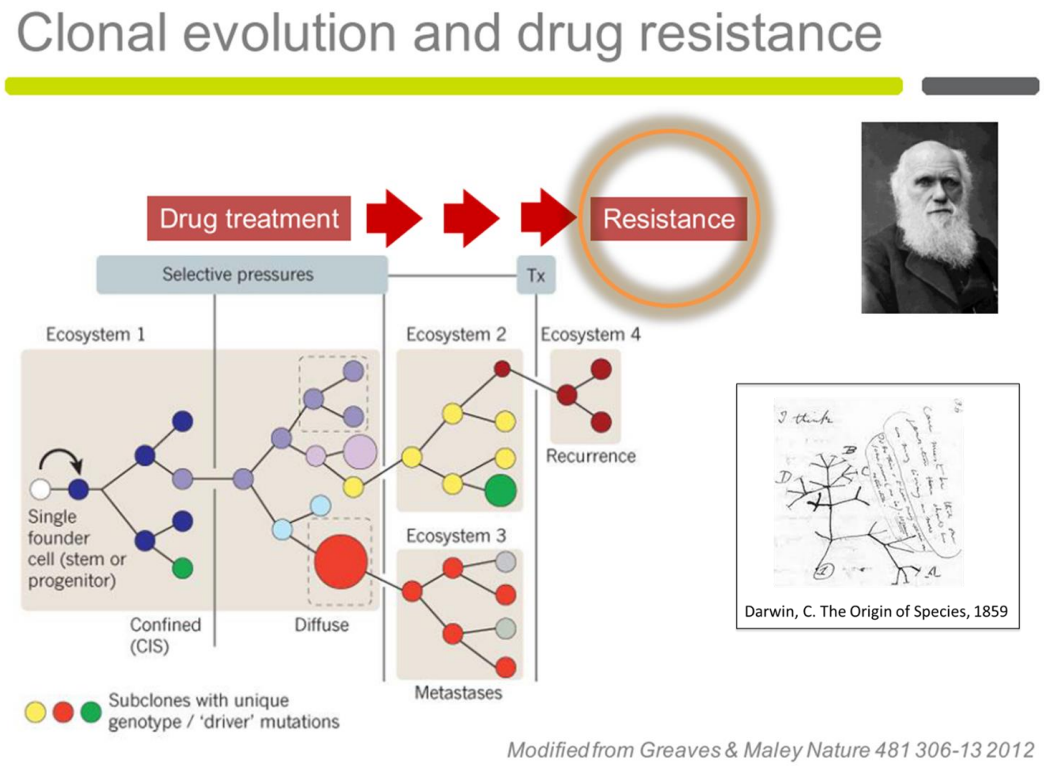
Pace of publications in cancer: 1973-October 2023

Cancer Biology: 397,036 results
Cancer Therapy: 937,651 results
Cancer Diagnosis: 1,896,700 results

Role of surgery in prevention

Metastatic *de novo*

Volume (burden)



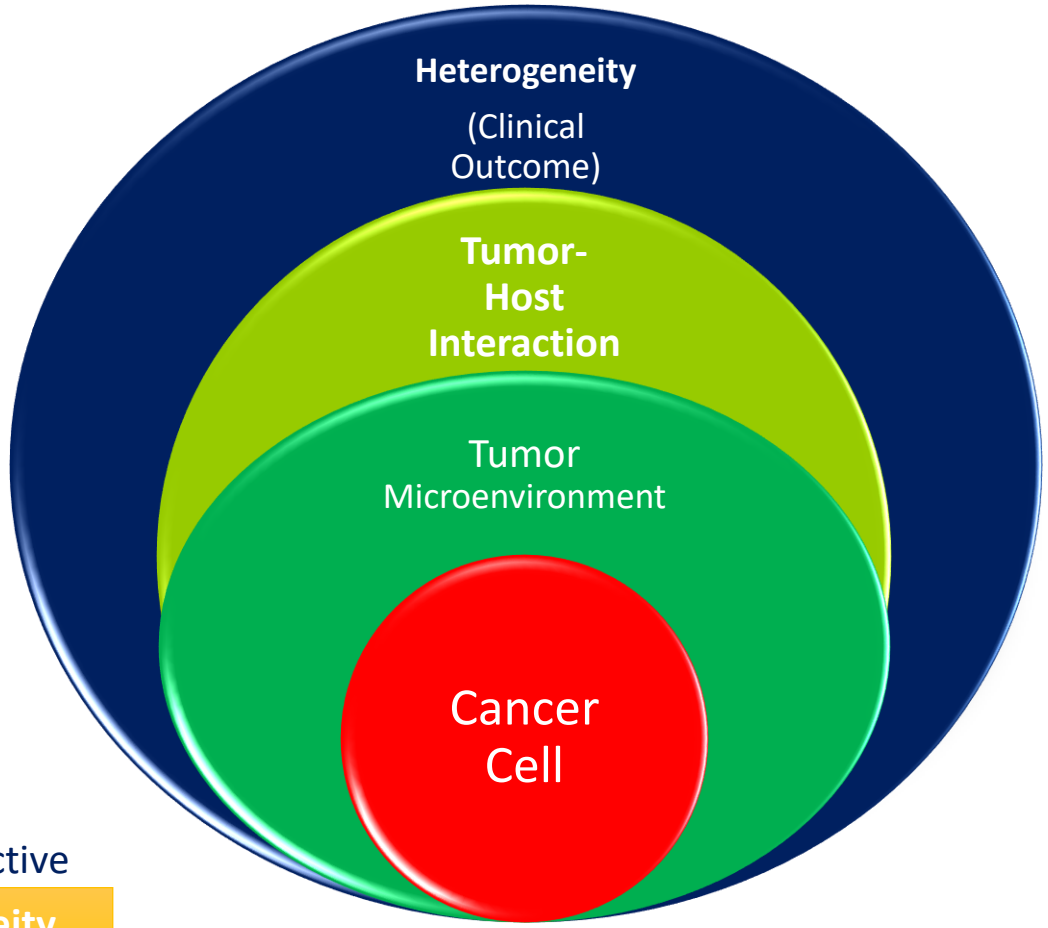
Overcoming resistance in advanced cancer:

Primary goal of pharmaceutical industry research for the past 15 years

Early diagnosis
Earlier treatment

Successful cure

Cancer Biology:
Questions with major clinical relevance



Cancer Biology Perspective

Intratumor Heterogeneity

Intertumoral Heterogeneity

Cancer Treatment Options

Surgery	**Removal of all visible tumor**
Radiotherapy	**Kill tumor cells; Locoregional therapy**

Chemotherapy	**Kill cells in division; systemic therapy**
Antibody-Drug Conjugates (ADCs)	**Target specific cancer cells and release a toxic drug into the cancer cell**
Endocrine therapy	**Inhibits the use of hormones as growth factors. Induces apoptosis; systemic therapy**
Targeted therapy	**Inhibition of specific sites (signal transduction pathway) required for cell survival; systemic therapy**
Immunotherapy	**Activates T-Cell response against tumor cell; systemic therapy**

Medical Radionuclides in Oncology

Radiopharmaceutical therapy (RPT) in cancer

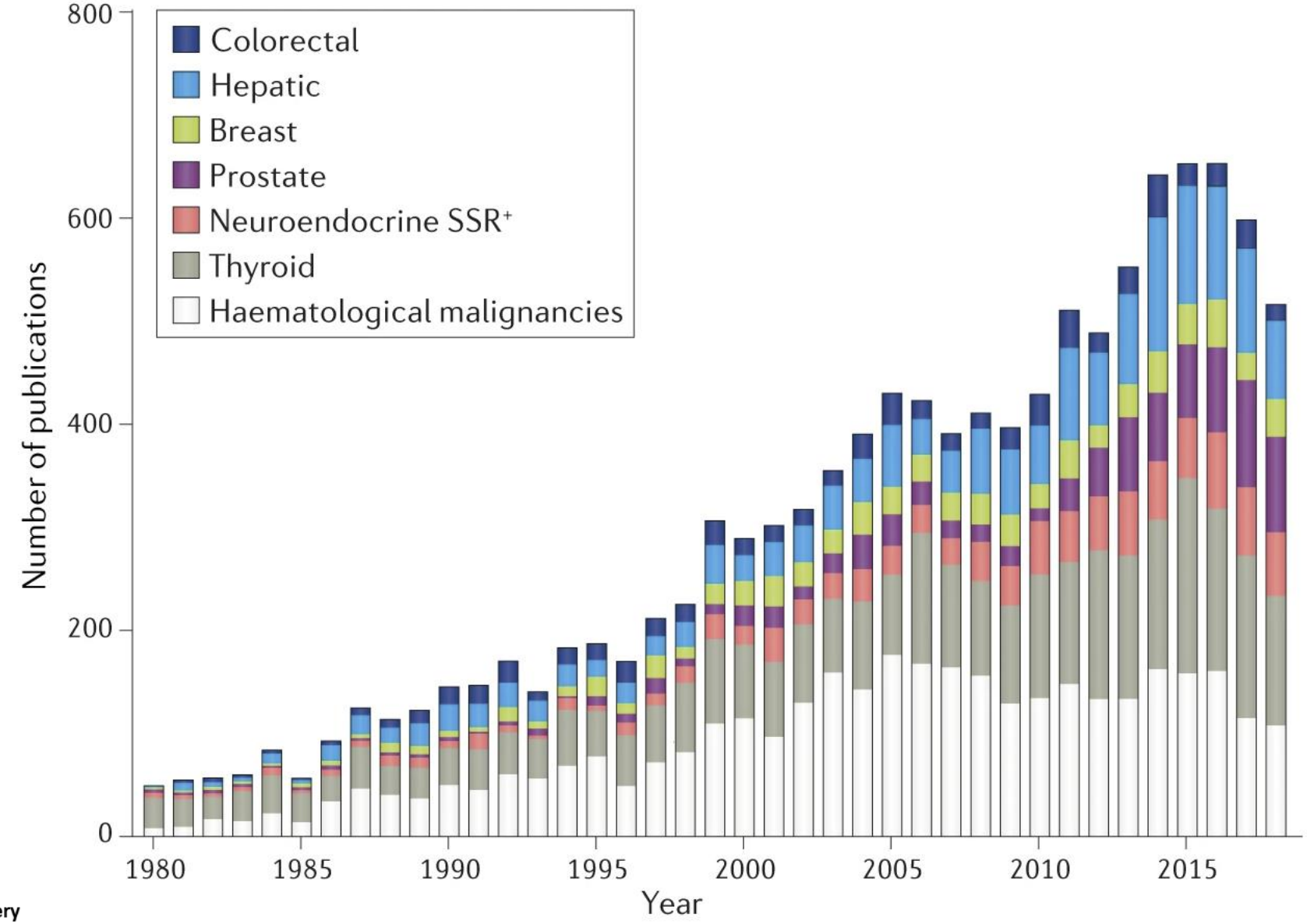
Delivery of radioactive atoms to tumour- associated targets.
Systemic Therapy

"In almost all cases, the radionuclides may be visualized by nuclear medicine imaging techniques to assess targeting of the agent, which provides a substantial advantage over existing therapeutic approaches and enables a precision medicine approach to RPT delivery."

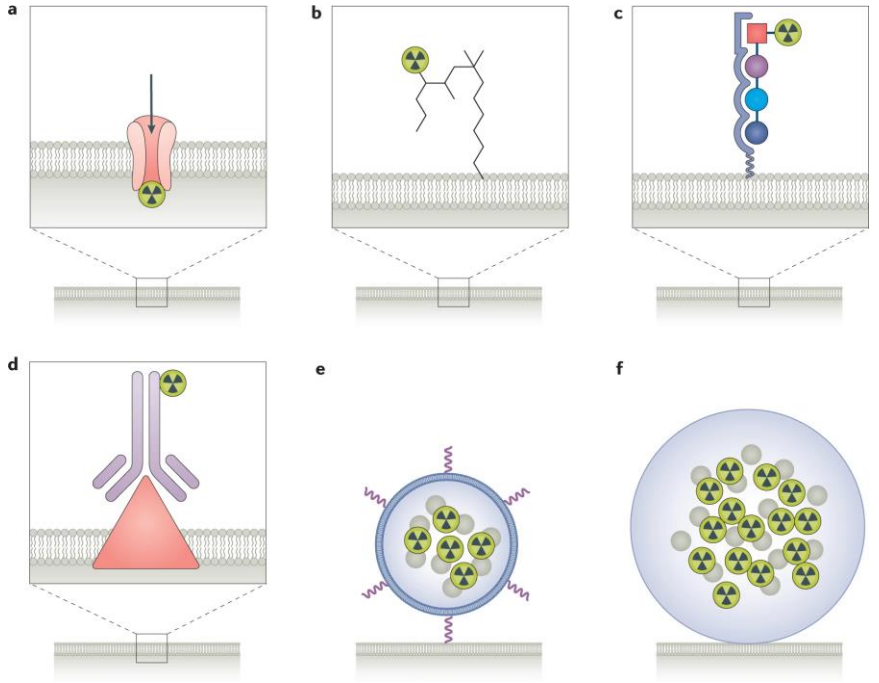
Dosimetry

"The biological effects of radionuclide therapy are mediated by a well- defined physical quantity, the absorbed dose.
In chemotherapy, targeted biologic therapy and immunotherapy, there is no dosimetry analogue.

Nature Reviews | Drug Discovery- September 2020



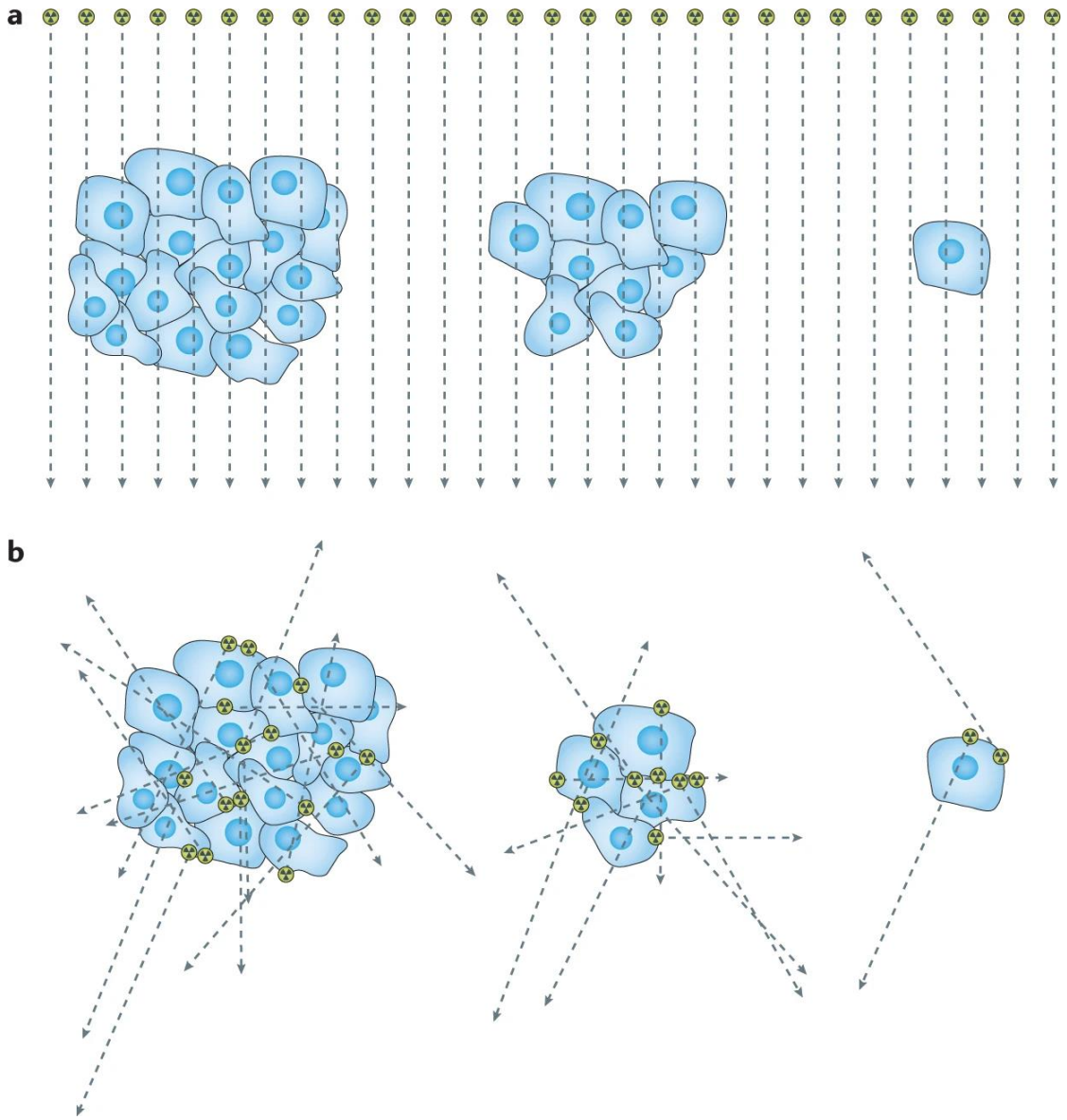
Nature Reviews | Drug Discovery
September 2020



- The various radiopharmaceutical therapy (RPT) constructs that have been used to deliver radiation are illustrated: radioactive element (part a); small molecule (part b); peptide (part c); antibody (part d); nanoconstruct (part e); microsphere (part f).

Nature Reviews | Drug Discovery
September 2020

Radiolabelled antibodies must overcome a number of barriers before they can effectively irradiate solid tumour targets. They must extravasate and diffuse across an interstitial fluid space that is characterized by pressure gradients opposing macromolecular transport



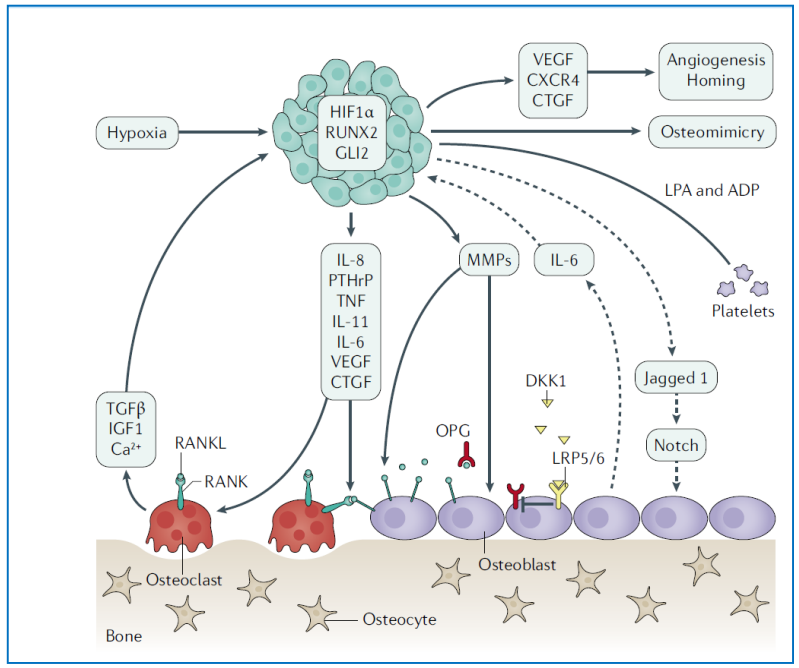
Nature Reviews | Drug Discovery
September 2020

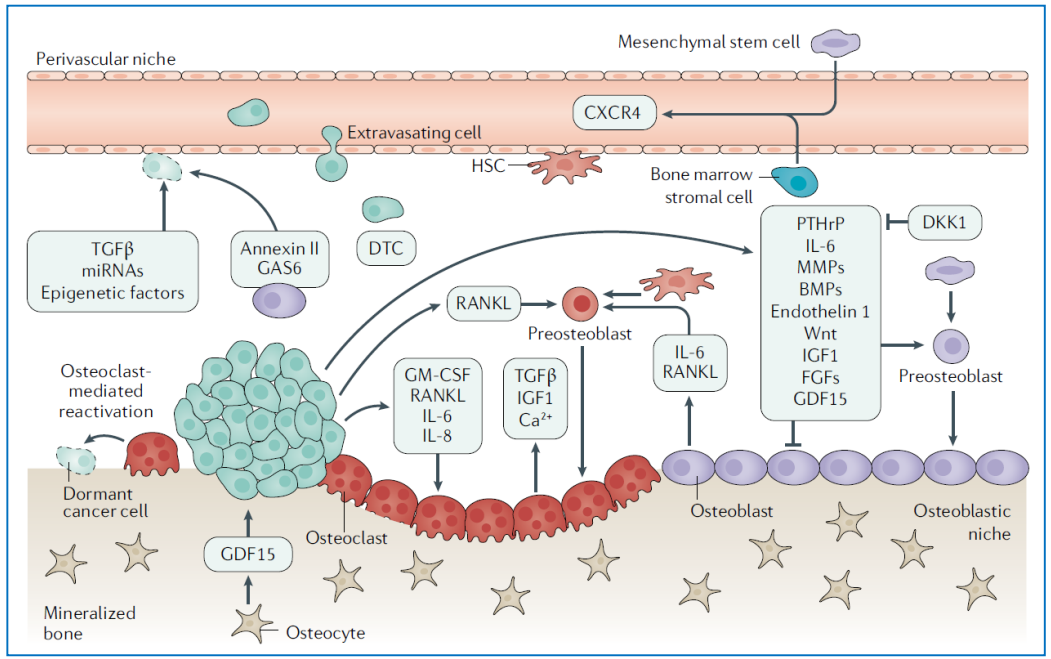
PRIMER

Check for updates

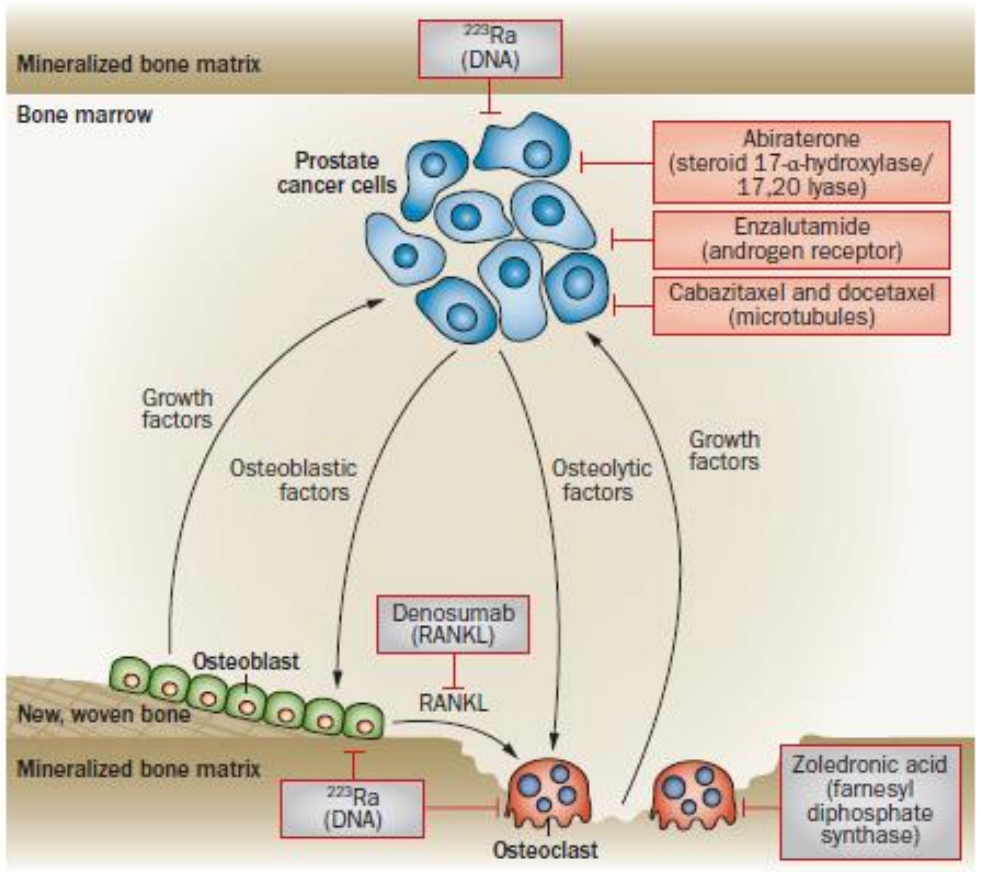
Bone metastases

Robert E. Coleman[1] ✉, Peter I. Croucher[2,3], Anwar R. Padhani[4], Philippe Clézardin[1,5], Edward Chow[6], Marie Fallon[7], Theresa Guise[8], Simone Colangeli[9], Rodolfo Capanna[9] and Luis Costa[10]





Osteoblastic bone metastases



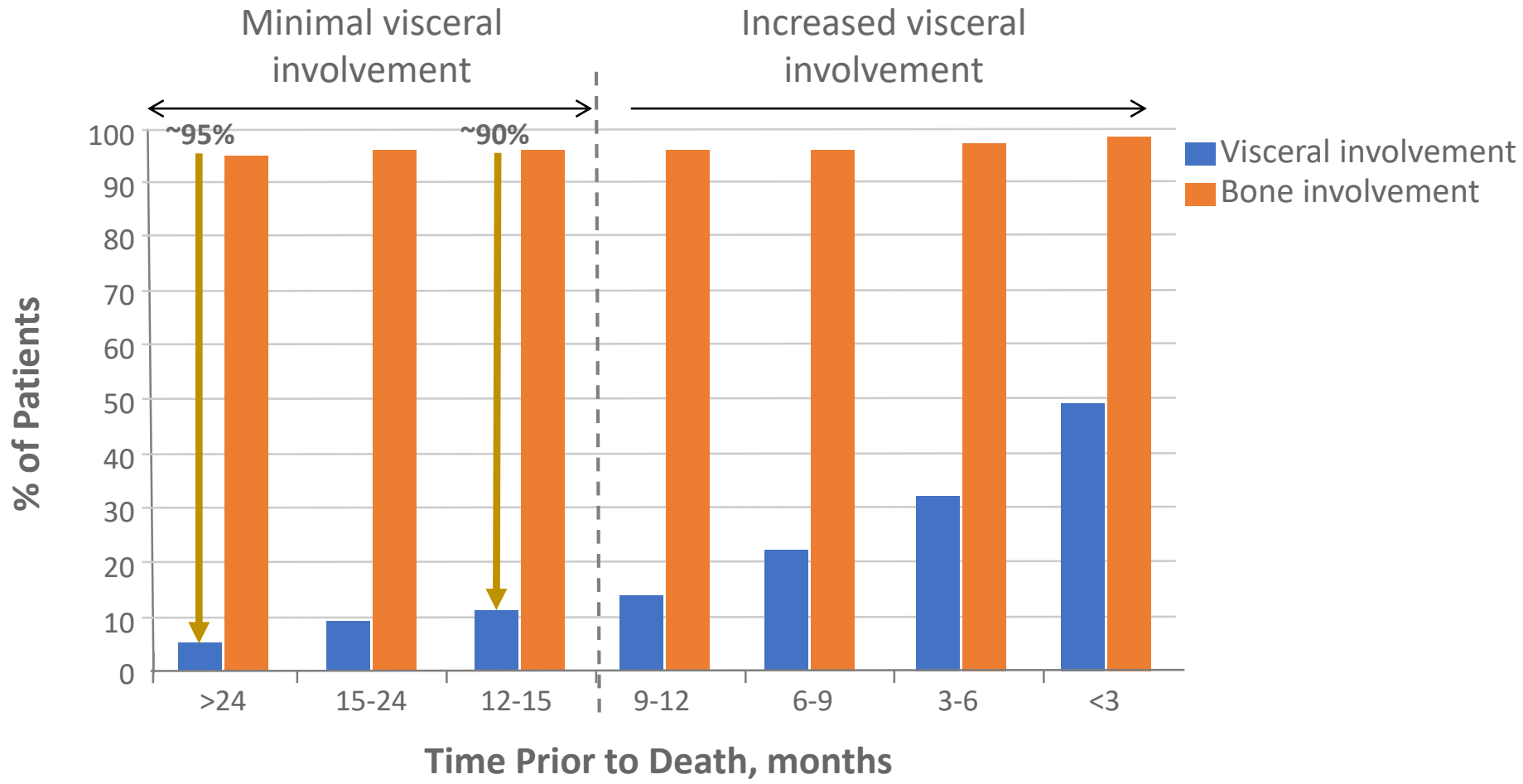
Radium-223 is a bone targeted therapy: targets cancers cells and the microenvironment.

Targeting bone metastases in prostate cancer: improving clinical outcome.

Jean-Jacques Body, Sandra Casimiro and Luís Costa

NATURE REVIEWS | UROLOGY

Most Patients With mCRPC Develop Visceral Metastases in the Final Stages of the Disease



Reference: Pezaro CJ et al. *Eur Urol*. 2014;65:270-273.

Impact of Extraskeletal Metastases on Skeletal-Related Events in Metastatic Castration-Resistant Prostate Cancer with Bone Metastases

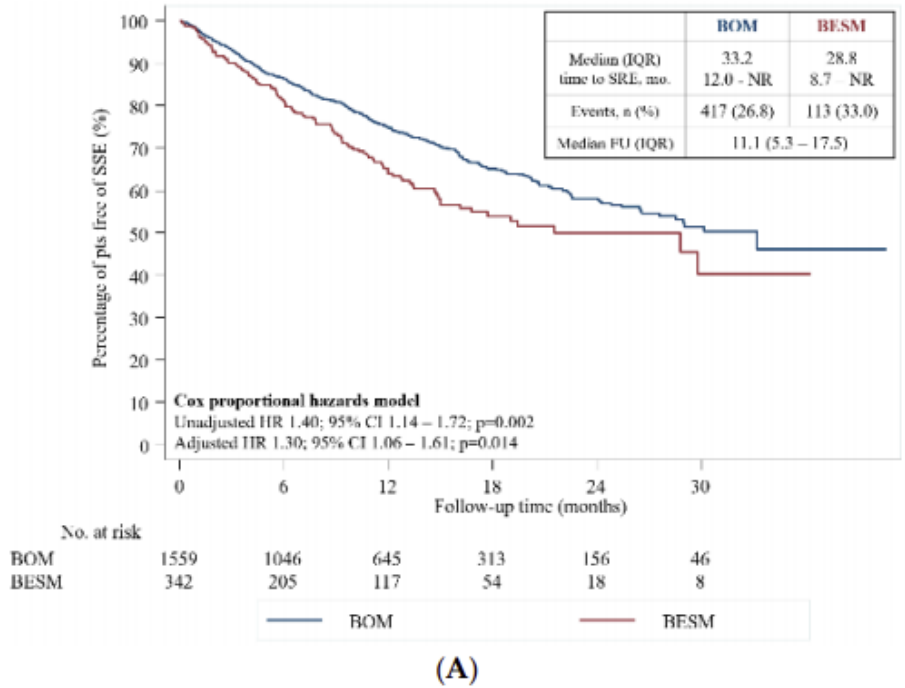
cancers

MDPI

Article

Impact of Extraskeletal Metastases on Skeletal-Related Events in Metastatic Castration-Resistant Prostate Cancer with Bone Metastases

Soraia Lobo-Martins [1,2,†], Arlindo R. Ferreira [2,3,†], André Mansinho [1,2], Sandra Casimiro [2], Kim Leitzel [4], Suhail Ali [4], Allan Lipton [4] and Luís Costa [1,2,*]



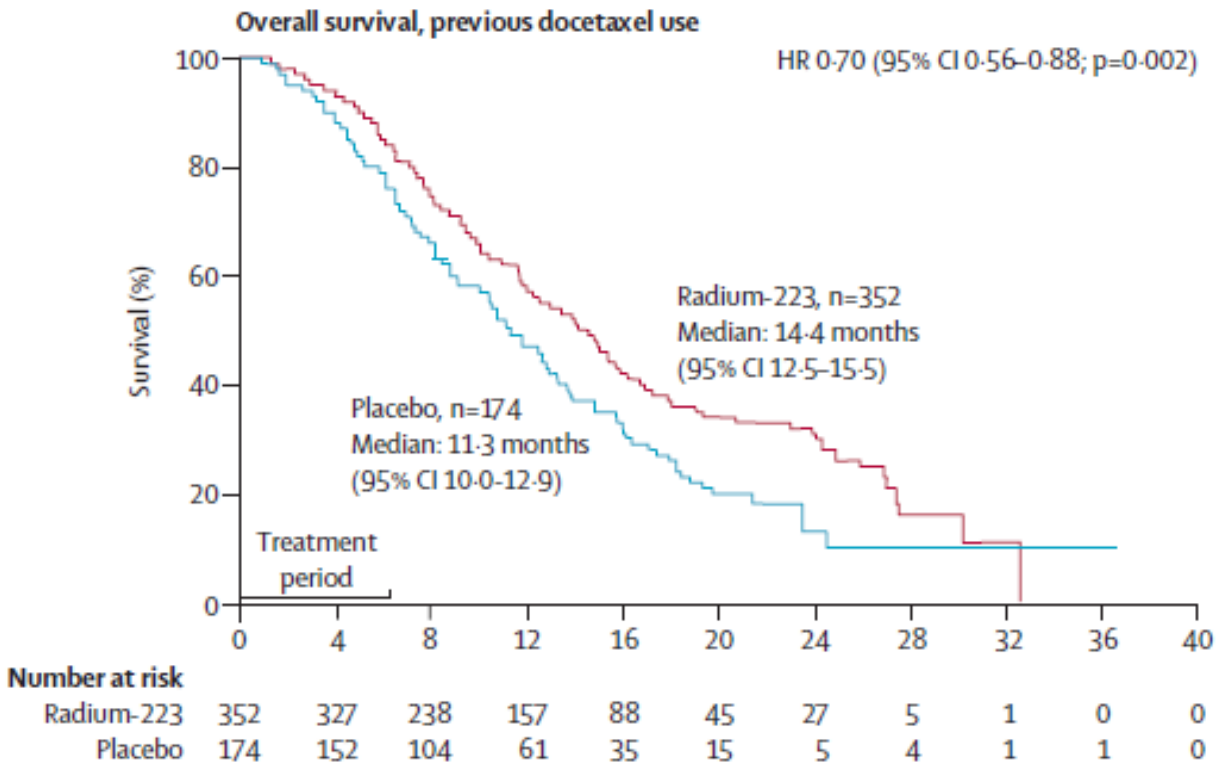
(A)

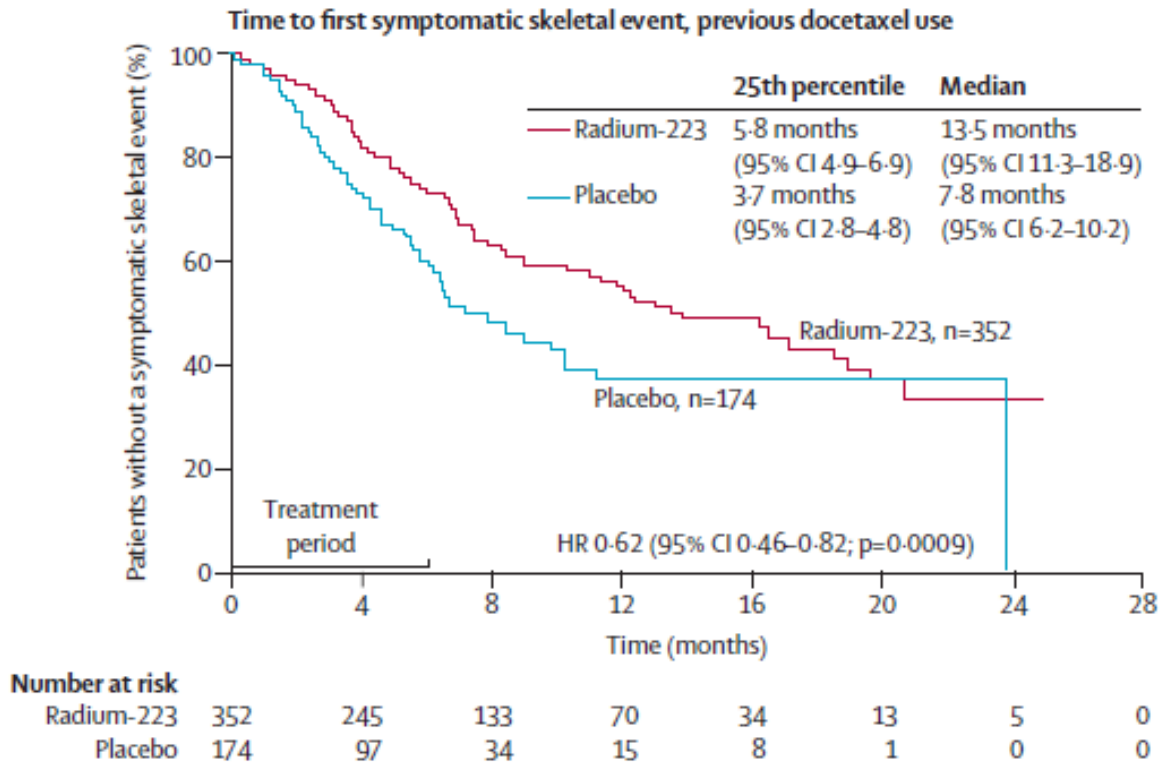
Figure 3. *Cont.*

BOM, bone metastases only. BESM, bone metastases and extraskeletal metastases

RADIUM-223

ALSYMPCA TRIAL





Hoskin P, *et al*. The Lancet Oncology. 2014;15(12):1397-406

Radium-223

Real-world data: HSM Cohort 2017-2022

Treatment	n=70
Previous ChT	62 (89%)
223Ra 6cy	40 (57%)
223Ra <6cy	27 (36%): Hematological toxicity, 8 (11%) Visceral progression, 7 (10%) Death, 6 (9%) Other clinical causes, 6 (9%)

Outcomes	n=70
Overall survival, median	17 months
High tumor burden (>20 met)	12 months
Low tumor burden (<6 met)	25 months

Pena H, *et al.* Eur J Nucl Med Mol Imaging. 2022;49(Suppl 1):S1-S751.

Radium-223

Real-world data: HSM Cohort 2017-2022

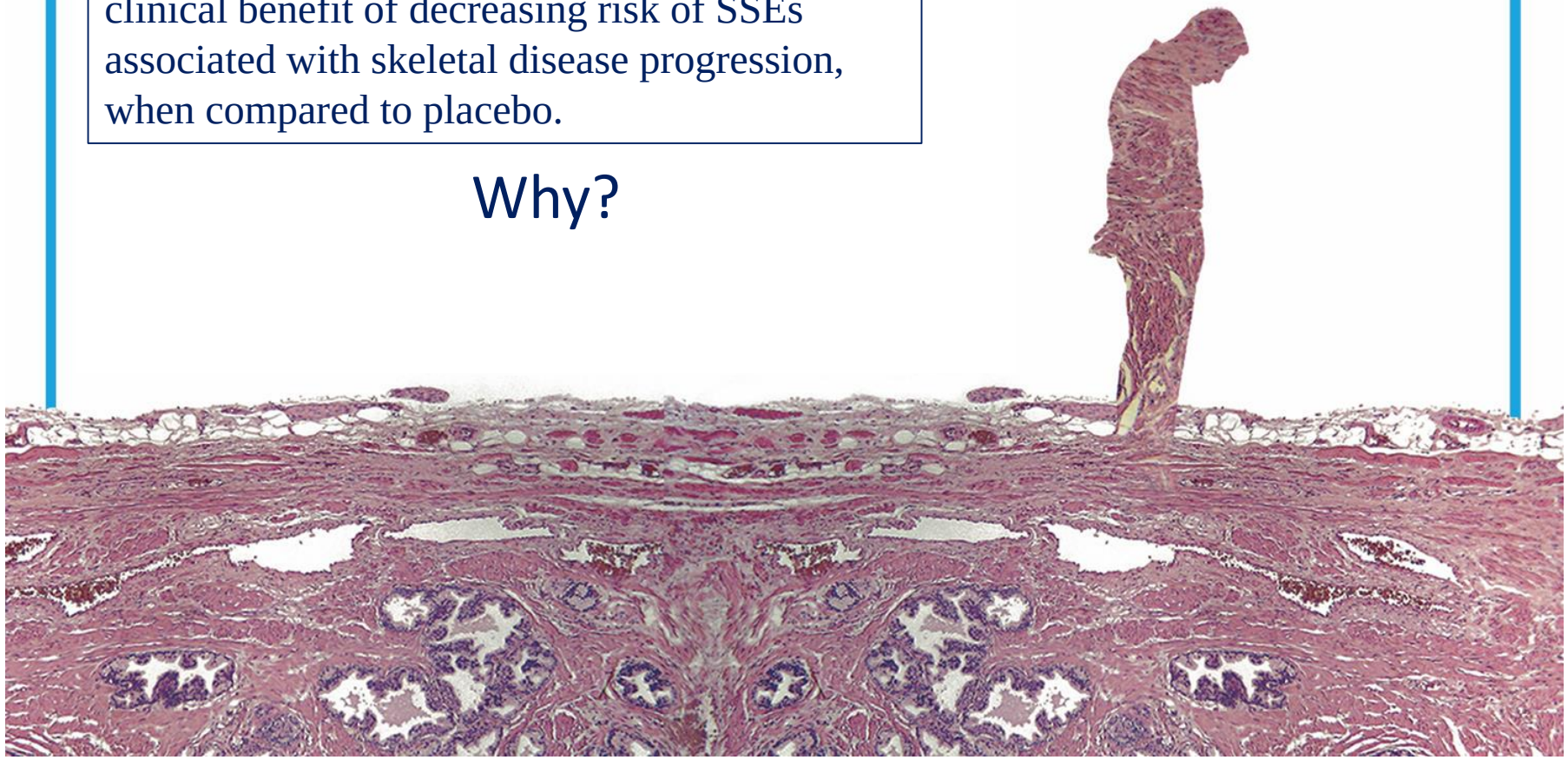
Outcomes	n=70
ALP, mean increase	41%
LDH, mean increase	2%
tPSA, mean increase	397%
tPSA increase, n	67 (96%)
tPSA decrease (>30%), n	2 (3%)

Safety	n=70
Hematological toxicity, mean decrease	
hemoglobin	13%
neutrophils	24%
platelets	22%
G3 anemia	3 (4%)
G3 neutropenia	1 (1%)
G3 thrombocytopenia	5 (7%)
SRE	0 (0%)

Pena H, *et al.* Eur J Nucl Med Mol Imaging. 2022;49(Suppl 1):S1-S751.

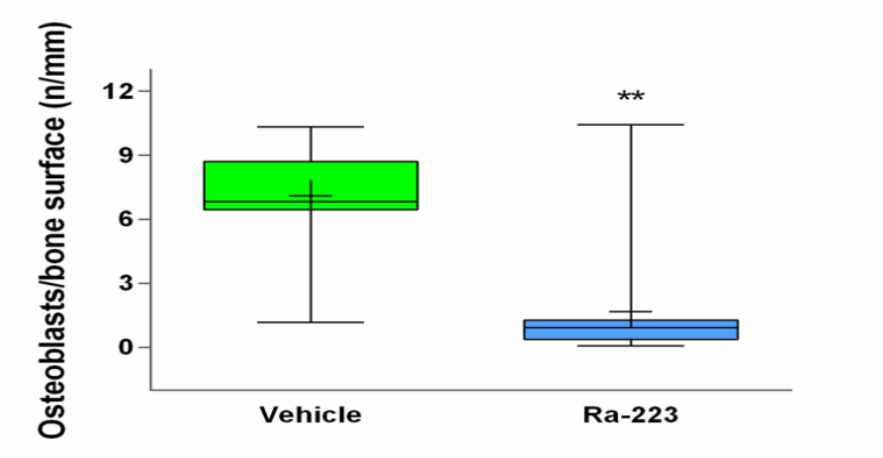
Radium-223 prolongs survival with the added clinical benefit of decreasing risk of SSEs associated with skeletal disease progression, when compared to placebo.

Why?

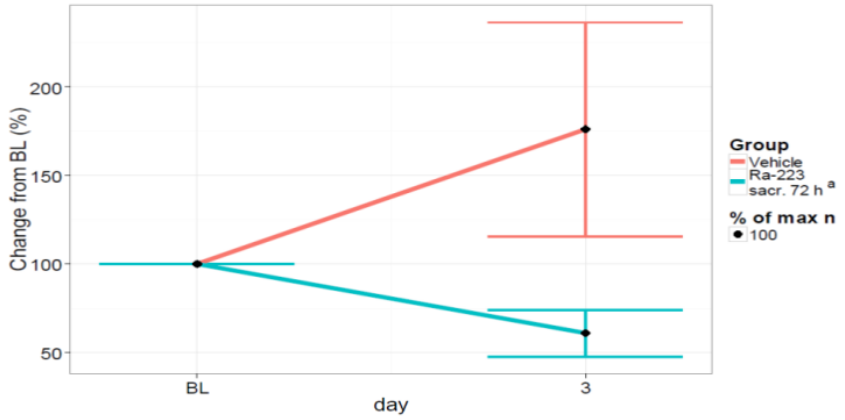


MoA in LuCaP-58 osteoblastic prostate PDX
- Autoradiography upon a single dose of Ra-223 -

Number of osteoblasts



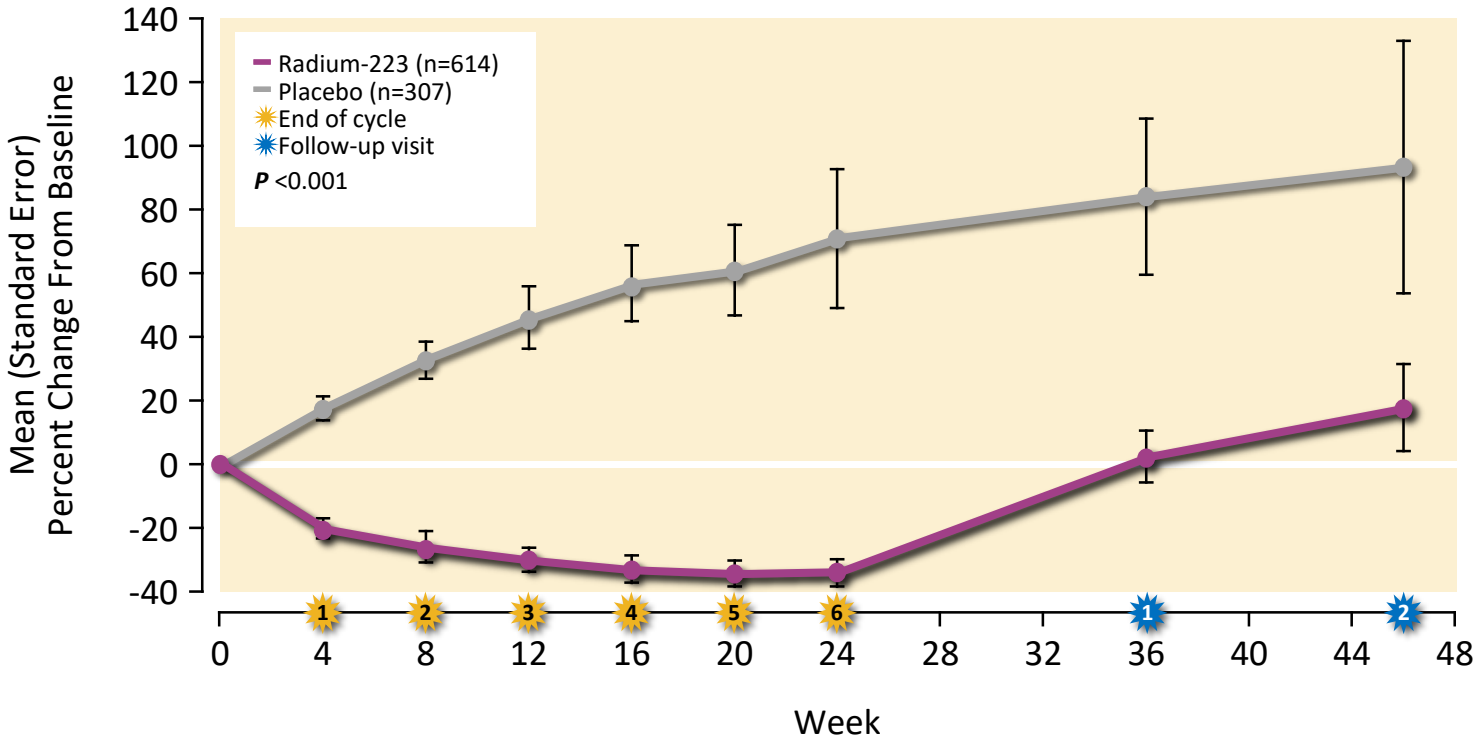
Serum-PSA



- Reduction of osteoblast number (72 h post dosing)
- Decline of serum PSA levels upon Ra-223 treatment (significant difference 72 h post dosing)

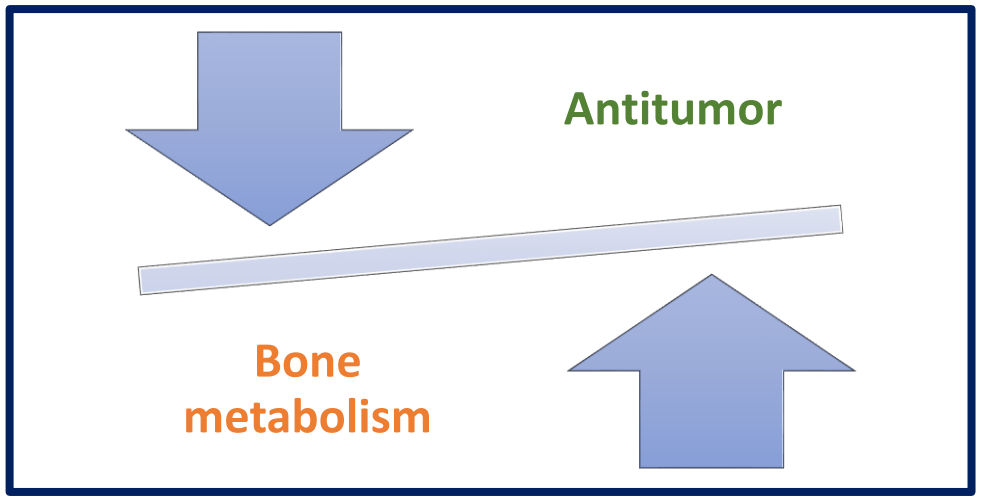
Suominen et al, EORTC-NCI-AACR 2014 poster
ECTS-IBMS 2015 poster 139, oral poster CABS OP4.3

ALSYMPCA: ALP dynamics



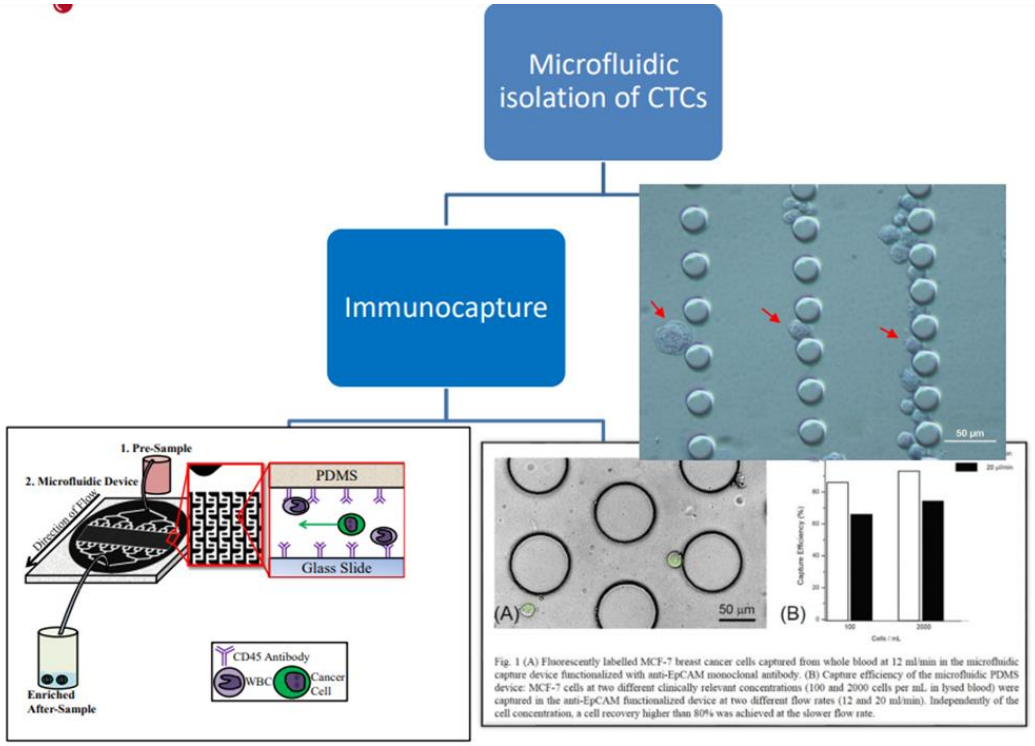
Radium-223	614	582	561	517	465	413	353		336		252
Placebo	307	286	260	231	193	159	130		136		100

Sartor O, et al. *J Clin Oncol.* 31, 2013 (suppl; abstr 5080). Annals of Oncol (28): 1090-1097, 2017.



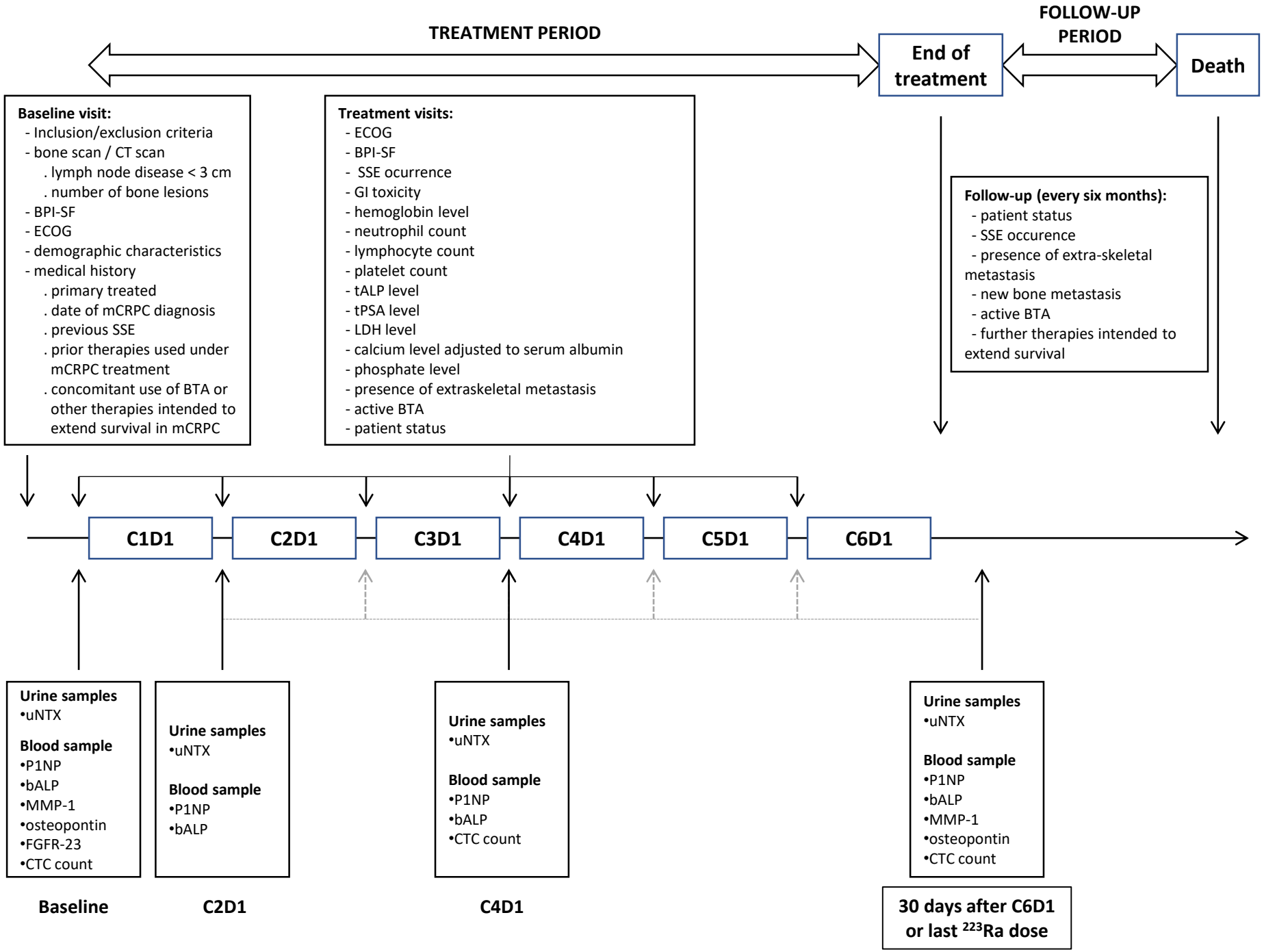
RAMBO-223

RAdium-223 Dichloride Effect in the **M**etabolism of **BO**ne Turnover Markers



In collaboration with INL (Lorena Dieguez)

- **Currently in practice:** tPSA, LDH, ALP
- **Possible future use:**
  - BALP
  - uNTX
  - P1NP
  - FGF23
  - MMP1
  - Osteopontin


TREATMENT PERIOD
FOLLOW-UP PERIOD
End of treatment
Death
Baseline visit:
- Inclusion/exclusion criteria
- bone scan / CT scan
. lymph node disease < 3 cm
. number of bone lesions
- BPI-SF
- ECOG
- demographic characteristics
- medical history
. primary treated
. date of mCRPC diagnosis
. previous SSE
. prior therapies used under mCRPC treatment
. concomitant use of BTA or other therapies intended to extend survival in mCRPC
Treatment visits:
- ECOG
- BPI-SF
- SSE ocurrence
- GI toxicity
- hemoglobin level
- neutrophil count
- lymphocyte count
- platelet count
- tALP level
- tPSA level
- LDH level
- calcium level adjusted to serum albumin
- phosphate level
- presence of extraskeletal metastasis
- active BTA
- patient status
Follow-up (every six months):
- patient status
- SSE occurence
- presence of extra-skeletal metastasis
- new bone metastasis
- active BTA
- further therapies intended to extend survival
C1D1
C2D1
C3D1
C4D1
C5D1
C6D1
Urine samples
•uNTX
Blood sample
•P1NP
•bALP
•MMP-1
•osteopontin
•FGFR-23
•CTC count
Urine samples
•uNTX
Blood sample
•P1NP
•bALP
Urine samples
•uNTX
Blood sample
•P1NP
•bALP
•CTC count
Urine samples
•uNTX
Blood sample
•P1NP
•bALP
•MMP-1
•osteopontin
•CTC count
Baseline
C2D1
C4D1
30 days after C6D1 or last 223Ra dose

Radiopharmaceuticals for prostate cancer bone metastases

JAMA Oncology | Original Investigation

Overall Survival in Men With Bone Metastases From Castration-Resistant Prostate Cancer Treated With Bone-Targeting Radioisotopes

A Meta-analysis of Individual Patient Data From Randomized Clinical Trials

Safae Terrisse, MD; Eleni Karamouza, MSc; Chris C. Parker, MD; A. Oliver Sartor, MD; Nicholas D. James, MD; Sarah Pirrie, MSc; Laurence Collette, PhD; Bertrand F. Tombal, MD; Jad Chahoud, MD; Sigbjørn Smeland, MD; Bjørn Erikstein, MD, PhD; Jean-Pierre Pignon, MD, PhD; Karim Fizazi, MD, PhD; Gwénaël Le Teuff, PhD; for the MORPHEP Collaborative Group

Terrisse S, et al. JAMA Oncology. 2020; 6(2):206-216

Radiopharmaceuticals for prostate cancer bone metastases

Figure 1. Overall Survival and Subgroup Analysis of Trials Comparing Patients Receiving Radioisotopes (RIs) With Patients Receiving No RIs by Type of Radiation

A Overall survival analysis

Source	No. of Deaths/No. Entered: RI	No RI	O-E	Variance	HR (95% CI)	P Value
α-Emitting RIs						
Nilsson et al,[28] 2007	23/33	27/31	-6.6	11.9	0.57 (0.33-1.01)	
ALSYMPCA[15]	333/614	195/307	-37.6	110.0	0.71 (0.59-0.86)	
Subtotal	356/647	222/338	-44.2	121.9	FE: 0.70 (0.58-0.83) RE: 0.70 (0.58-0.83)	.47[a] 0[b]
β-Emitting RIs						
Oosterhof et al,[27] 2003	97/101	97/102	13.7	47.0	1.34 (1.01-1.78)	
Tu et al,[25] 2001	14/36	27/36	-10.4	9.8	0.34 (0.18-0.65)	
Smeland et al,[26] 2003	30/30	34/34	0	15.5	1.00 (0.61-1.64)	
TRAPEZE[29]	308/378	310/379	-12.3	153.1	0.92 (0.79-1.08)	
Subtotal	449/545	468/551	-9.0	225.3	FE: 0.96 (0.84-1.10) RE: 0.88 (0.60-1.29)	.001[a] 0.11[b]
Total	805/1192	690/889	-53.2	347.2	0.86 (0.77-0.95)	

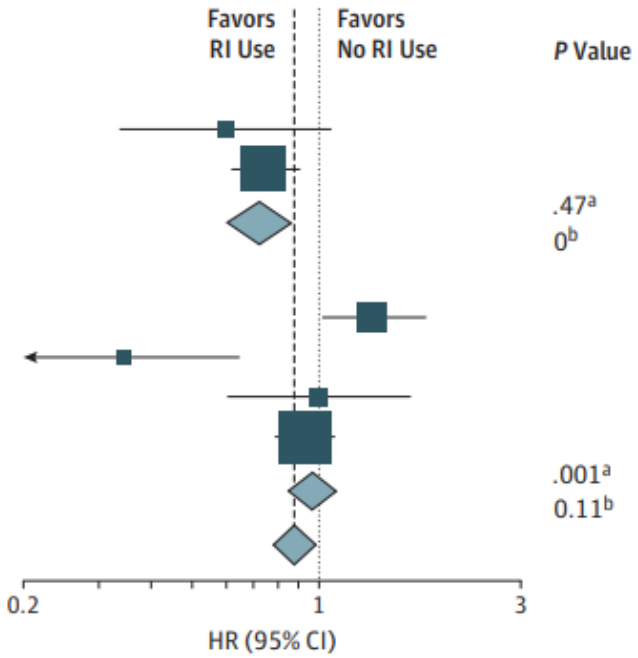
Test for heterogeneity: $\chi^2_5 = 24.46$; $P < .001$; $I^2 = 80\%$

Test for interaction: $\chi^2_1 = 8.24$; $P = .004$

Residual heterogeneity: $\chi^2_4 = 16.22$; $P = .003$

RE model: HR, 0.80; 95% CI, 0.61-1.06; $P = .12$; $\tau^2 = 0.08$

RE effect: $P = .004$



Ra223

Sr89

Terrisse S, et al. JAMA Oncology. 2020; 6(2):206-216

Radium-223

Table 1. Selected Ongoing Clinical Trials of Ra-223 in mCRPC

Trial Acronym	Regimen	Patient Population	Phase	NCT Identifier	Estimated Primary Completion Date
TRANCE	Ra-223 + dexamethasone	First-line therapy for mCRPC	IV	NCT03432949	December 2022
COMRADE	Ra-223 + olaparib	mCRPC with bone metastases	II	NCT03317392	November 2023
PEACE III	Ra-223 + enzalutamide vs enzalutamide monotherapy	Asymptomatic or mildly symptomatic mCRPC	III	NCT02194842	March 2024
–	Ra-223 + nivolumab	Bone-only mCRPC	I/II	NCT04109729	April 2024
–	Ra-223 vs NAH	Bone-dominant mCRPC progressing on/after one line of NAH	IV	NCT04597125	May 2025
DORA	Ra-223 + docetaxel vs docetaxel monotherapy	Progressing mCRPC and more than two bone lesions	III	NCT03574571	February 2026
ALPHABET	Ra-223 + LuPSMA	Progressing mCRPC and more than two bone lesions	I/II	NCT05383079	December 2026

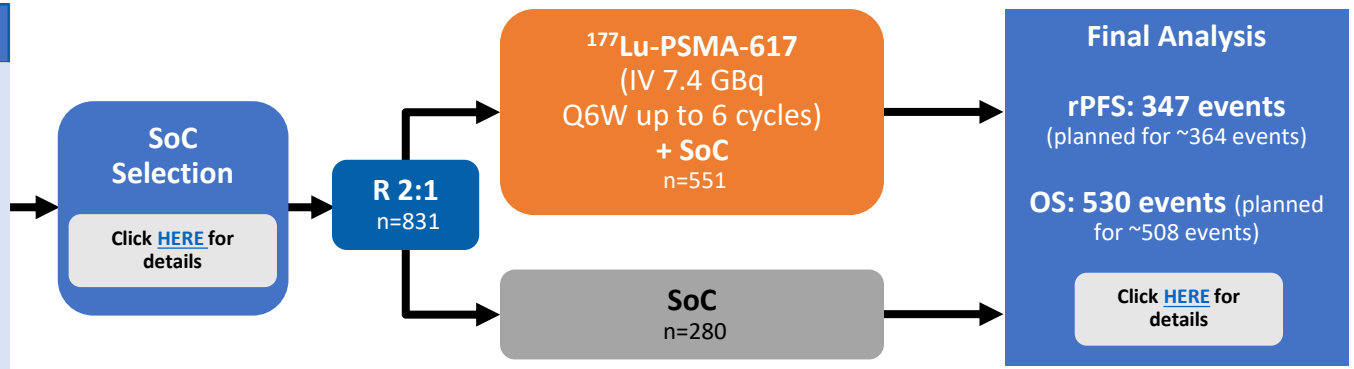
Sartor O and Maughan BL. ASCO Post. 2023.

VISION Trial Design

An international, multicenter, randomized, open-label Phase 3 trial[1–3]

Population

- Progressive[a] mCRPC
- PSMA-positive with ^{68}Ga-PSMA-11 PET/CT scan (per pre-defined criteria[b])
- Previous taxane (≤2 regimens) therapy and previous ARPI (≥1 regimen)
- ECOG PS 0–2
- Life expectancy >6 months



Treated until radiographic progression, unacceptable toxicity, lack of clinical benefit, or requirement for a prohibited treatment

Alternate Primary Endpoints

- rPFS (per PCWG3)
- OS

Key Secondary Endpoints (with α control)

- RECIST v1.1 response: ORR and DCR
- Time to first SSE

Stratification Factors

- Serum LDH (≤ 260 IU/L vs >260 IU/L)
- Presence of liver metastases (yes vs no)
- ECOG PS (0–1 vs 2)
- Inclusion of ARPI in SoC (yes vs no) at time of randomization

Additional Secondary Endpoints

- Safety and tolerability
- HRQoL: EQ-5D-5L, FACT-P and BPI-SF
- Health economics
- Composite PFS (radiological, clinical or PSA progression)
- Biochemical response: PSA, ALP and LDH levels

.

[a] Rising PSA according to PCWG3 criteria (2 rising values above a baseline at a minimum of 1-week intervals) and PSA ≥2.0 ng/mL. [b] PSMA-positive disease sites were defined as ≥1 PSMA-positive lesions anywhere in the body, with PSMA PET imaging ligand uptake ≥ liver. No size criteria were applied on PSMA-positive lesions.

ADT, androgen deprivation therapy; AE, adverse event; ALP, alkaline phosphatase; ARPI, androgen receptor pathway inhibitor; SoC, standard of care; BPI-SF, Brief Pain Inventory–Short Form; CT, computed tomography; DCR, disease control rate; ECOG PS, Eastern Cooperative Oncology Group performance status; EQ-5D-5L; European Quality of Life Five Dimension Five Level Scale; FACT-P, Functional Assessment of Cancer Therapy–Prostate; ^{68}Ga, gallium-68; GBq, gigabecquerel; HRQoL, health-related quality of life; IV, intravenous; ^{177}Lu, lutetium-177; LDH, lactate dehydrogenase; mCRPC, metastatic castrate-resistant prostate cancer; ORR, overall response rate; OS, overall survival; PET, positron emission tomography; PCWG3, Prostate Cancer Working Group 3; PFS, progression-free survival; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; Q6W, every 6 weeks; R, randomized; RECIST, Response Evaluation Criteria in Solid Tumors; rPFS, radiographic progression-free survival; SSE; symptomatic skeletal event.

1. Endocyte. Protocol no. PSMA-617-01, v4.0; 2. ClinicalTrials.gov. NCT03511664. https://clinicaltrials.gov/ct2/show/NCT03511664 (accessed April 2021); 3. . Morris M, et al. Oral presentation at the 2021 ASCO Annual Meeting; June 6, 2021; Abstract LBA4. 4. Sartor O, et al. N Engl J Med. 2021 Jun 23. doi: 10.1056/NEJMoa2107322. Online ahead of print.

LUTETIUM-177 PSMA-617

MECHANISM OF ACTION: β- and γ-emitting PSMA-617 targeting radioisotope

VISION TRIAL:

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

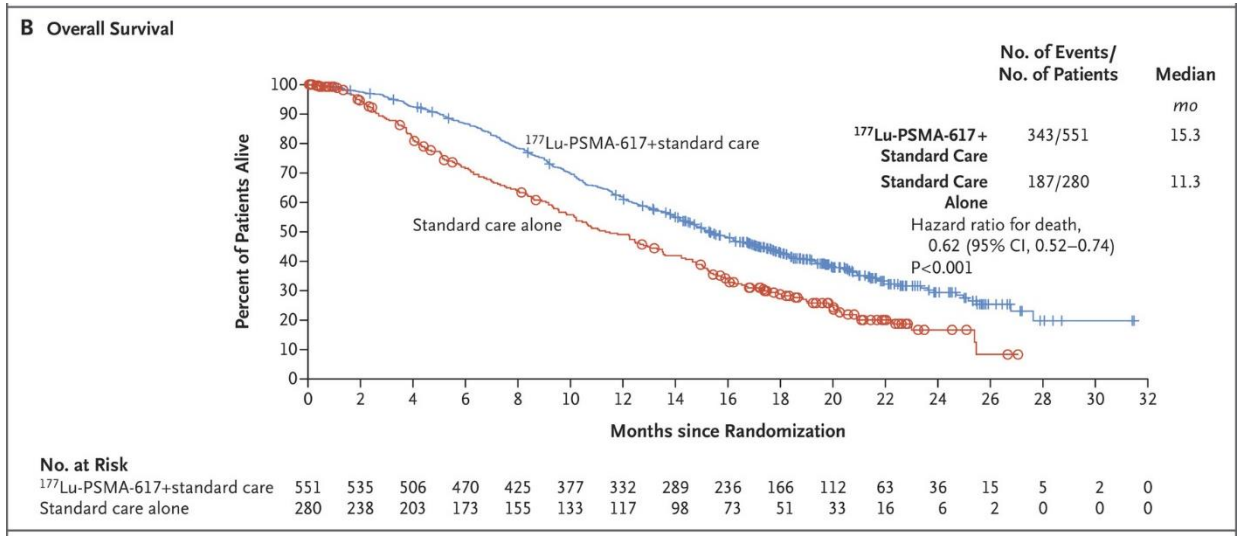
Characteristic	Analysis Set for Imaging-Based Progression-free Survival (N=581)		All Patients Who Underwent Randomization (N=831)	
	^{177}Lu-PSMA-617 plus Standard Care (N=385)	Standard Care Alone (N=196)	^{177}Lu-PSMA-617 plus Standard Care (N=551)	Standard Care Alone (N=280)
Median age (range) — yr	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)

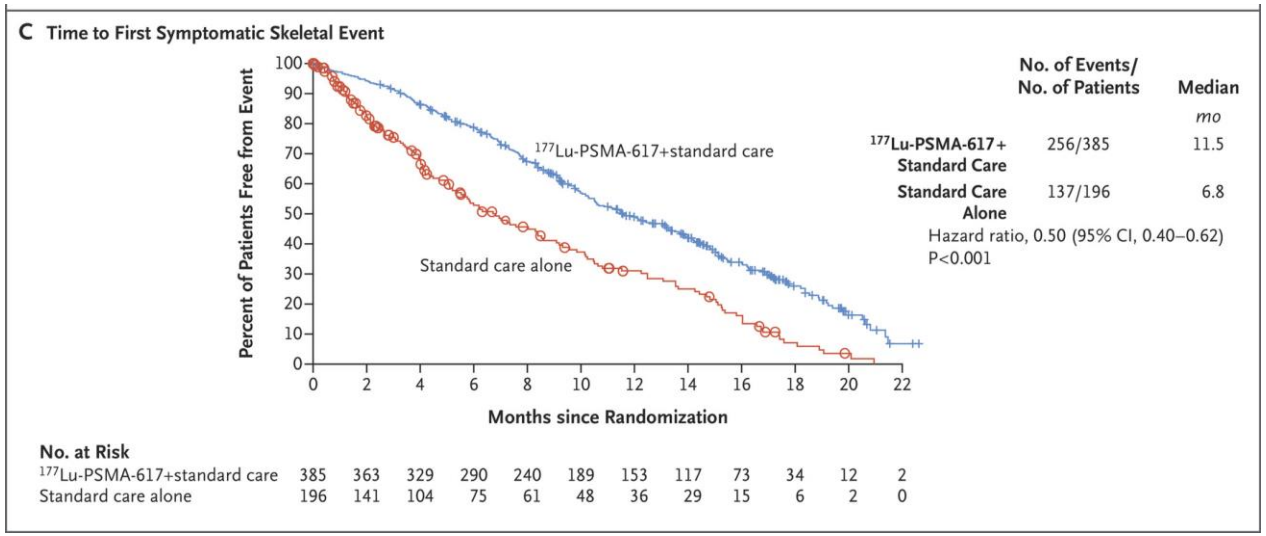
Gonzalez BD, *et al.* ASCO-GU. 2022.

LUTETIUM-177 PSMA-617

MECHANISM OF ACTION: β- and γ-emitting PSMA-617 targeting radioisotope

VISION TRIAL:





Gonzalez BD, *et al.* ASCO-GU. 2022.

LUTETIUM-177 PSMA-617

MECHANISM OF ACTION: β- and γ-emitting PSMA-617 targeting radioisotope

Meeting Abstract | 2022 ASCO Genitourinary Cancers Symposium

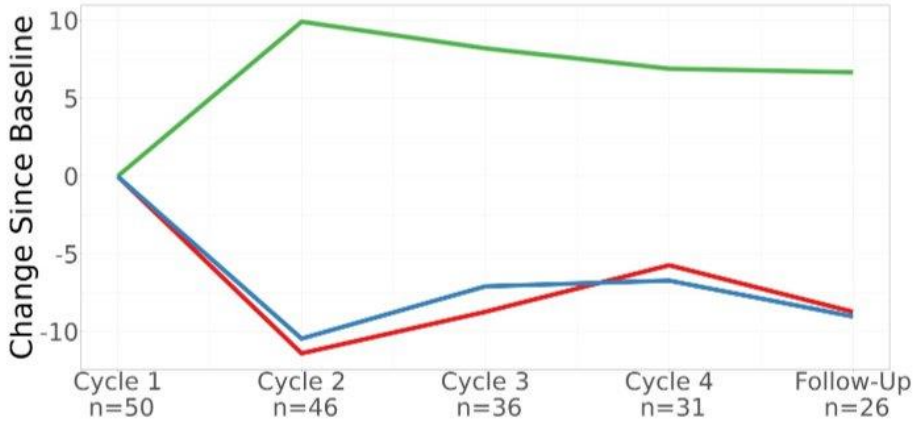
PROSTATE CANCER - ADVANCED

Improvements in symptoms related to bone metastasis in recipients of Lutetium-177 PSMA-617 for prostate cancer.

Brian D. Gonzalez, Naomi C. Brownstein, Wenyi Fan, Adam P. Dicker, Laura B. Oswald, Haryana M. Dhillon, ...

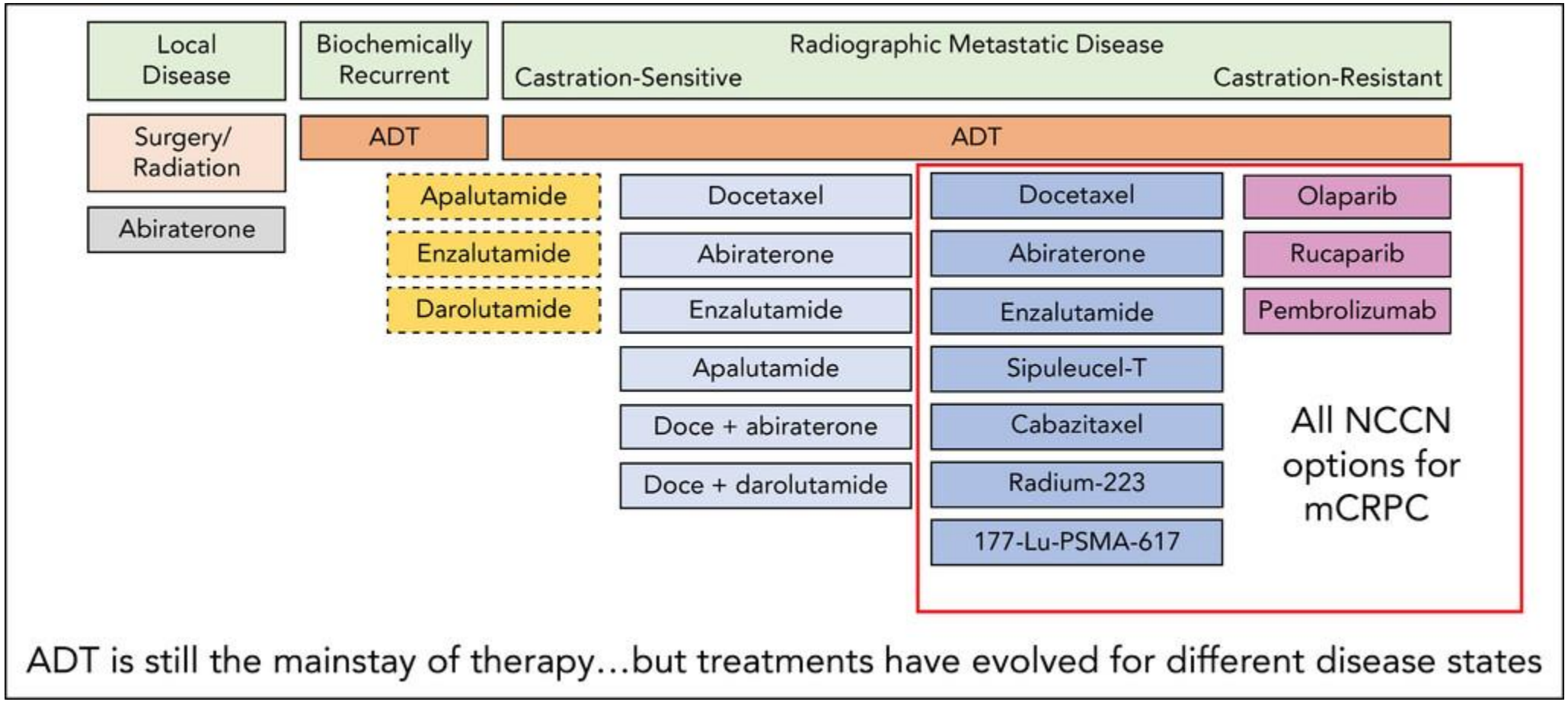
Average scores for BM-related outcomes improved over time:

- Increased functional ability despite BM-related pain ($p<.01$)
- Decreased severity of BM-related pain ($p=.01$)
- Decreased consistency, intermittency, and difficulty alleviating BM-related pain ($p=.01$)



Gonzalez BD, *et al.* ASCO-GU. 2022.

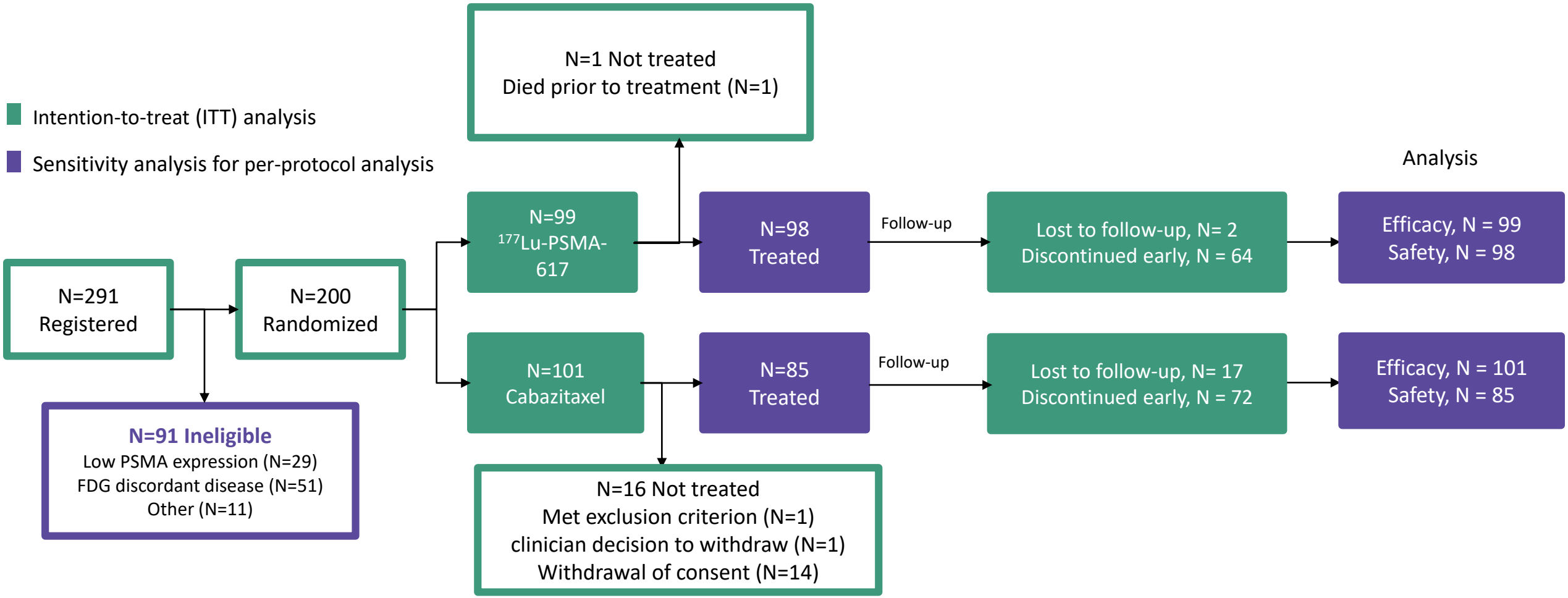
RADIOPHARMACEUTICALS FOR METASTATIC PROSTATE CANCER



Ajmera A, *et al.* Journal of the National Comprehensive Cancer Network 2023;21(5.5)

TheraP investigator-initiated trial

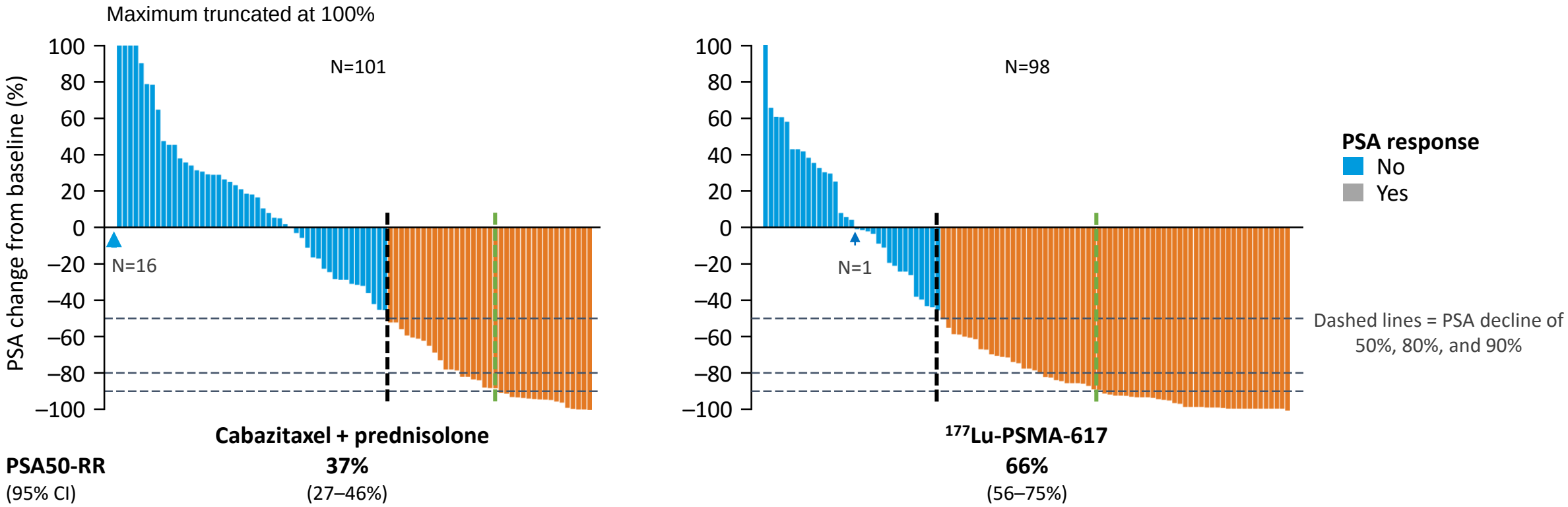
177Lu-PSMA-617 versus cabazitaxel in metastatic castration-resistant prostate cancer: a randomized, open-label, phase 2 trial



FDG, fluorodeoxyglucose; IIT, investigator-initiated trial; ITT, Intention-to-treat; Lu, lutetium; PSMA, prostate-specific membrane antigen.

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

Primary endpoint: PSA50 response rate*



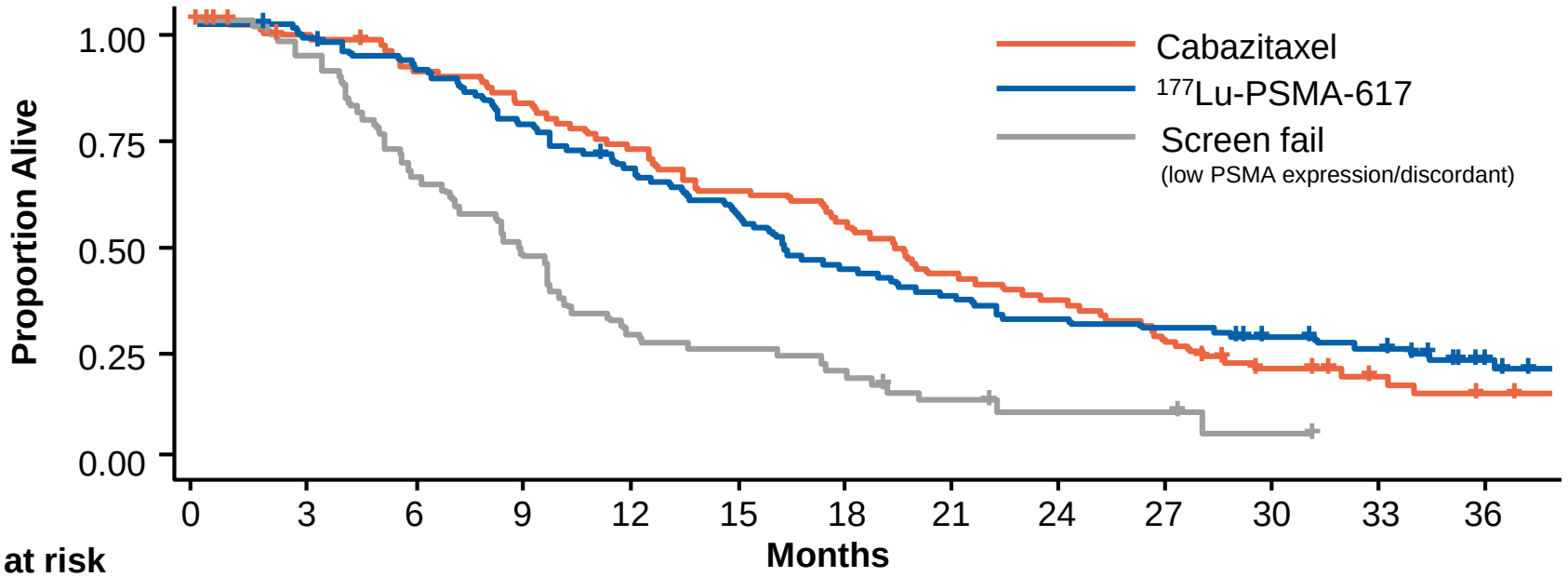
Patients treated with ^{177}Lu-PSMA-617 had 29% greater PSA response rate (95% CI: 16%–42%; p <0.0001) compared with cabazitaxel. For sensitivity analysis per-protocol, the difference was 23% (95% CI: 9%–37%; p = 0.0016)

*PSA reduction of ≥50% from baseline. Each bar represents an individual, with the vertical grey dashed line corresponding to 90% of patients.

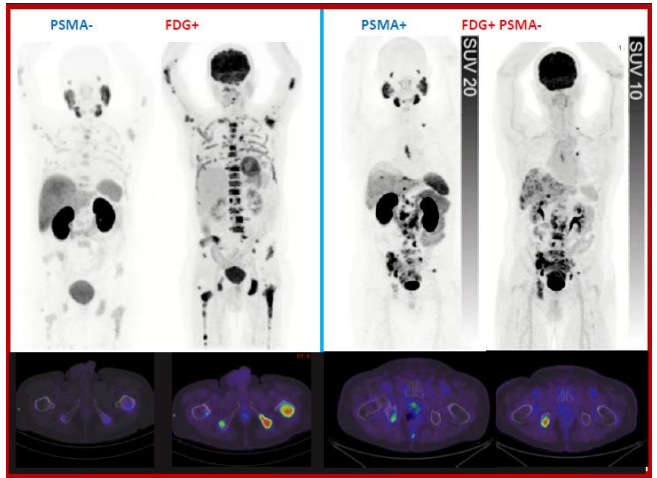
CI, confidence interval; IIT, investigator-initiated trial; Lu, lutetium; PSA, prostate-specific antigen; PSA50-RR, prostate-specific antigen ≥50 response rate; PSMA, prostate-specific membrane antigen. Figures were reproduced with the consent of the author.

1. Hofman MS, et al. Oral presentation at the 2021 Virtual ASCO-GU cancers symposium; Feb 11, 2021; Abstract 6. 2. Hofman M, et al. *The Lancet.* 2021; in press. https://doi.org/10.1016/S0140-6736(21)00237-3

Secondary endpoint: OS



Number at risk													
Cabazitaxel	101	82	75	68	60	51	45	35	30	22	14	9	6
^{177}Lu-PSMA-617	99	94	88	75	63	54	41	35	30	28	23	20	11
Screen fail*	61	56	39	30	17	15	12	7	4	4	1	0	0



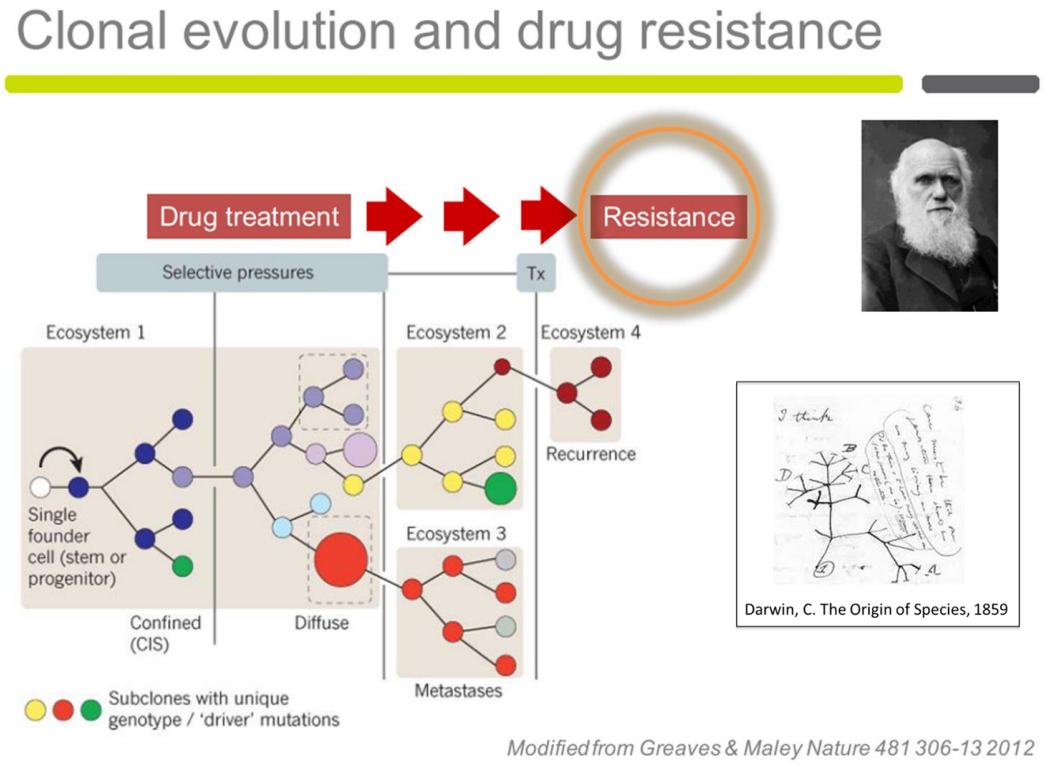
Compared with randomized treatment arms, OS was notably worse for screen fail* patients

* Of n=80 patients who were excluded before randomization due to low PSMA expression or discordant disease, n=61 consented to follow up and were included in this analysis. Next line of treatment for screen fail group: cabazitaxel n=29 (48%); enzalutamide n=4 (7%); ^{177}Lu-PSMA-617 n=3 (5%); carboplatin n=3 (5%); other n=3 (5%); mitoxantrone n=1 (2%)

CI, confidence interval; FDG, fluorodeoxyglucose; Lu, lutetium; OS, overall survival; PSMA, prostate-specific membrane antigen. Figures were reproduced with the consent of the author.

Hofman MS, et al. *J Clin Oncol*. 2022;40(suppl.16):Abstract 5000.

Volume (burden)



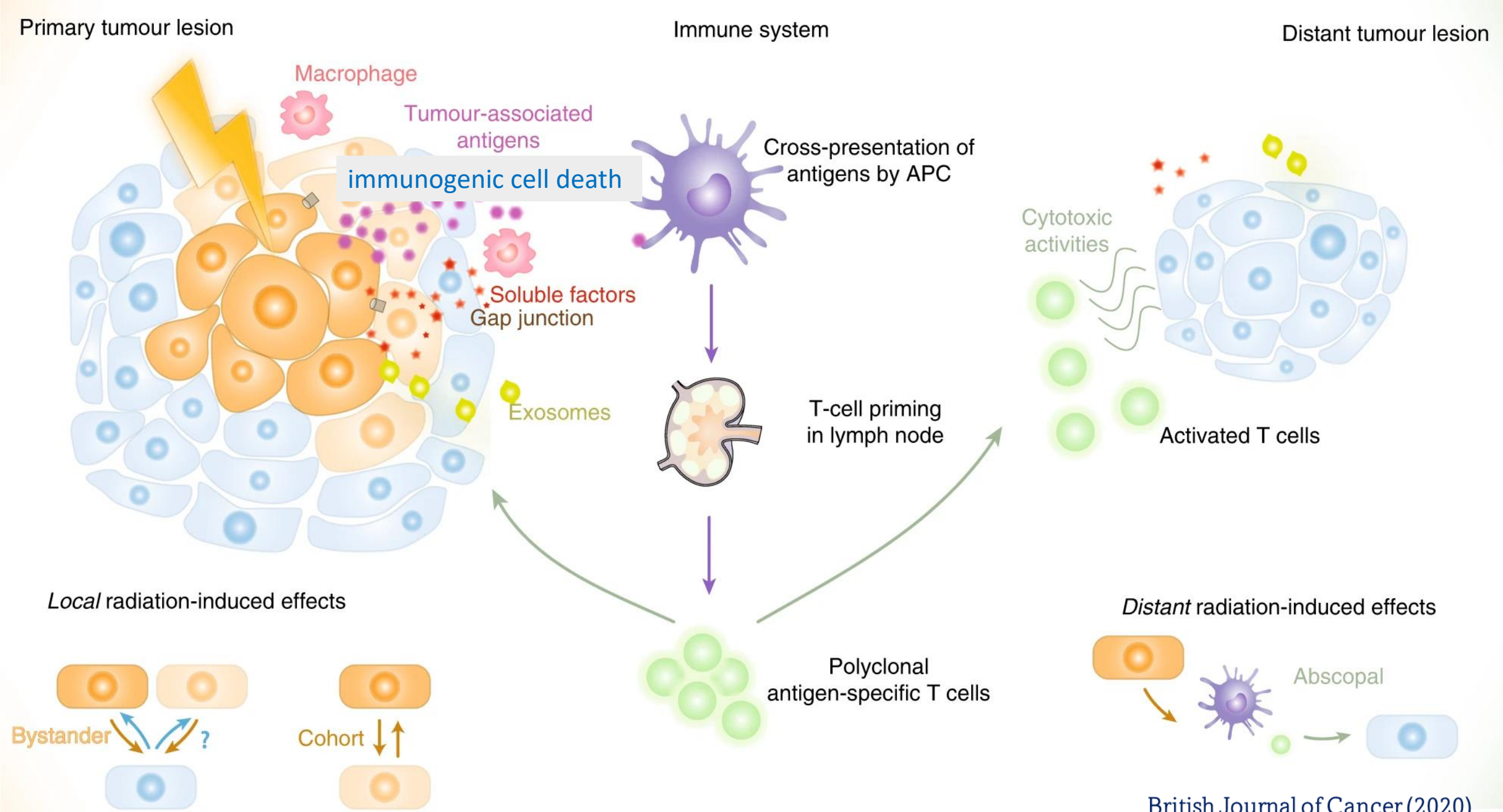
Immunotherapy (host-dependent)

Identification of sub-clones Through Molecular Imaging / Liquid Biopsy

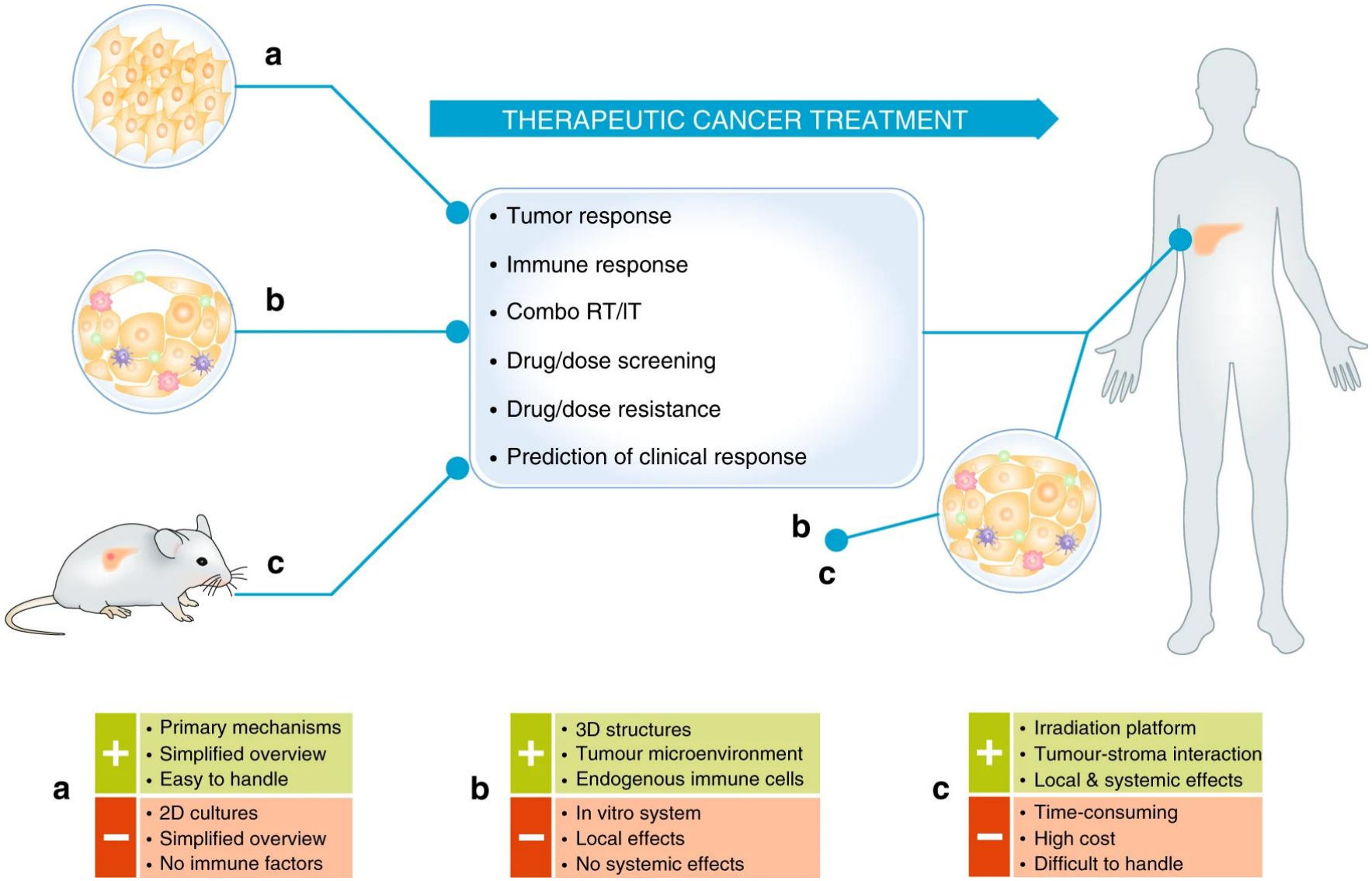
Selected RPT agents that are on the market

RPT agent	Company	Indication	Properties
Radium-223 chloride[a]	Bayer	Bone metastasis	Calcium analogue
^{90}Y-loaded glass microspheres	BTG	Hepatic malignancies	Radioembolization of liver microvasculature
^{90}Y-loaded resin microspheres	CDH Genetech/ Sirtex	Hepatic malignancies	Radioembolization of liver microvasculature
^{131}I radioiodine	Jubilant Draximage/ Malklincrodt	Thyroid cancer	Active uptake through Na–I symporter and storage in follicular cells
^{153}[Sm]lexidronam	Lantheus	Cancer bone pain	Binding to hydroxyapatite matrix
^{177}Lu-labelled DOTATATE	Novartis/AAA	Neuroendocrine tumours	SSR-mediated binding
[^{131}I]mIBG	Progenics	Adrenergic receptor^{+} tumours	Active uptake mechanism via the adrenaline transporter and storage in presynaptic neurosecretory granules
^{177}Lu-labelled PSMA-617	Novartis/ Endocyte	Prostate cancer, tumour neovasculature	PSMA-mediated binding

Adapted from Nature Reviews September 2020



British Journal of Cancer (2020)

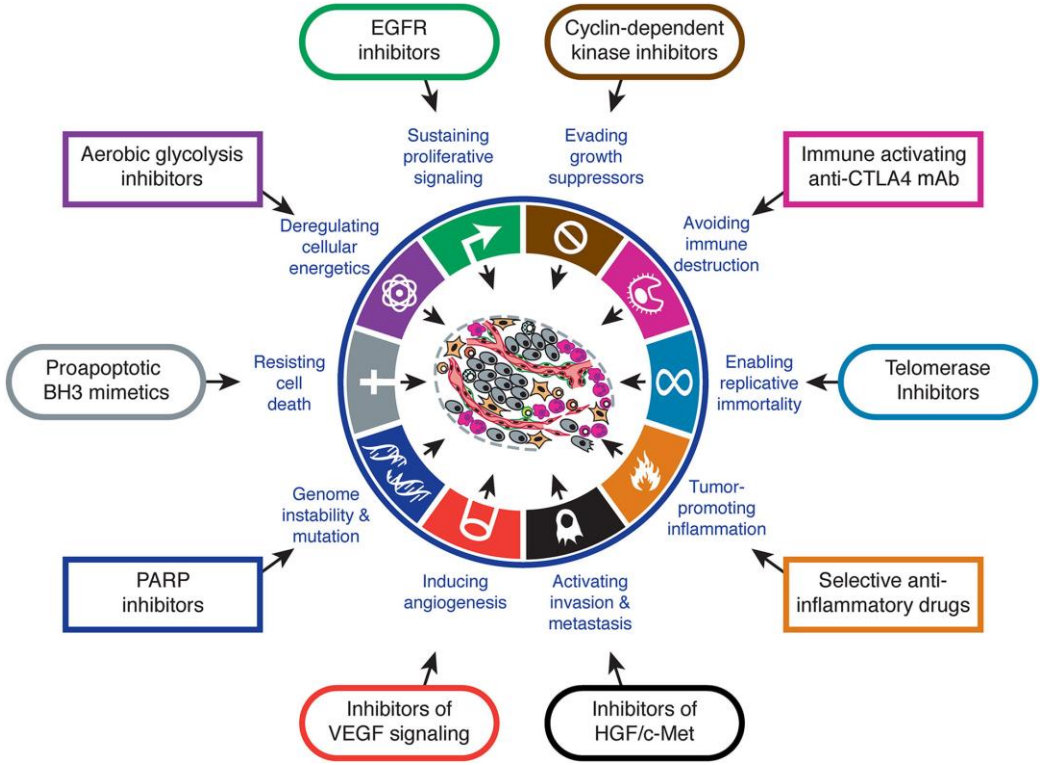


a Co-cultures, b mouse or patient-derived tumour organoids and c genetically engineered mouse models or patient-derived tumour xenografts

British Journal of Cancer (2020)

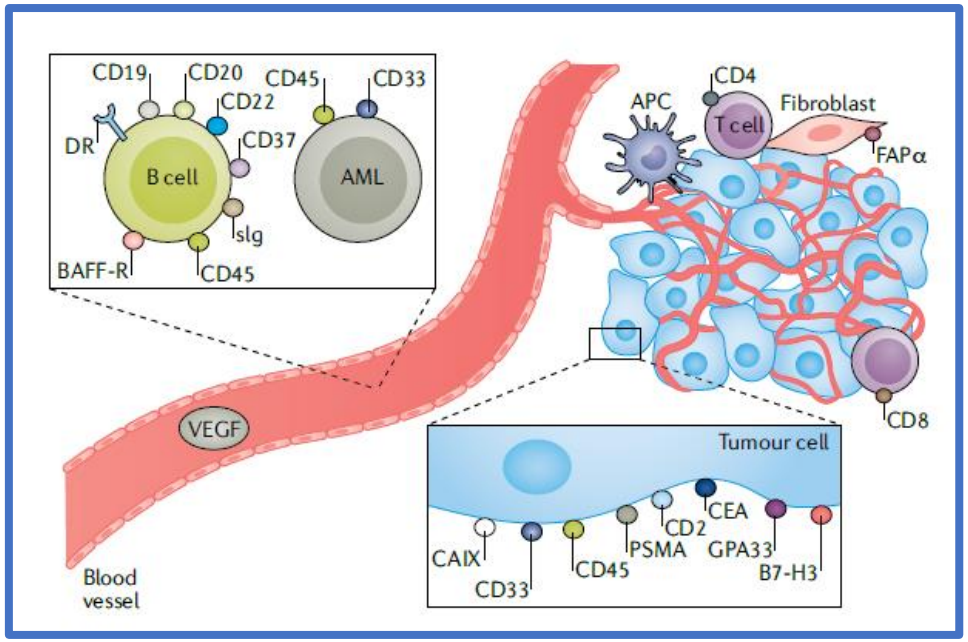
Radiopharmaceutical therapy (RPT) in cancer

Cancer Cell / Tumor Microenvironment



Douglas Hanahan, et al. The Hallmarks of Cancer

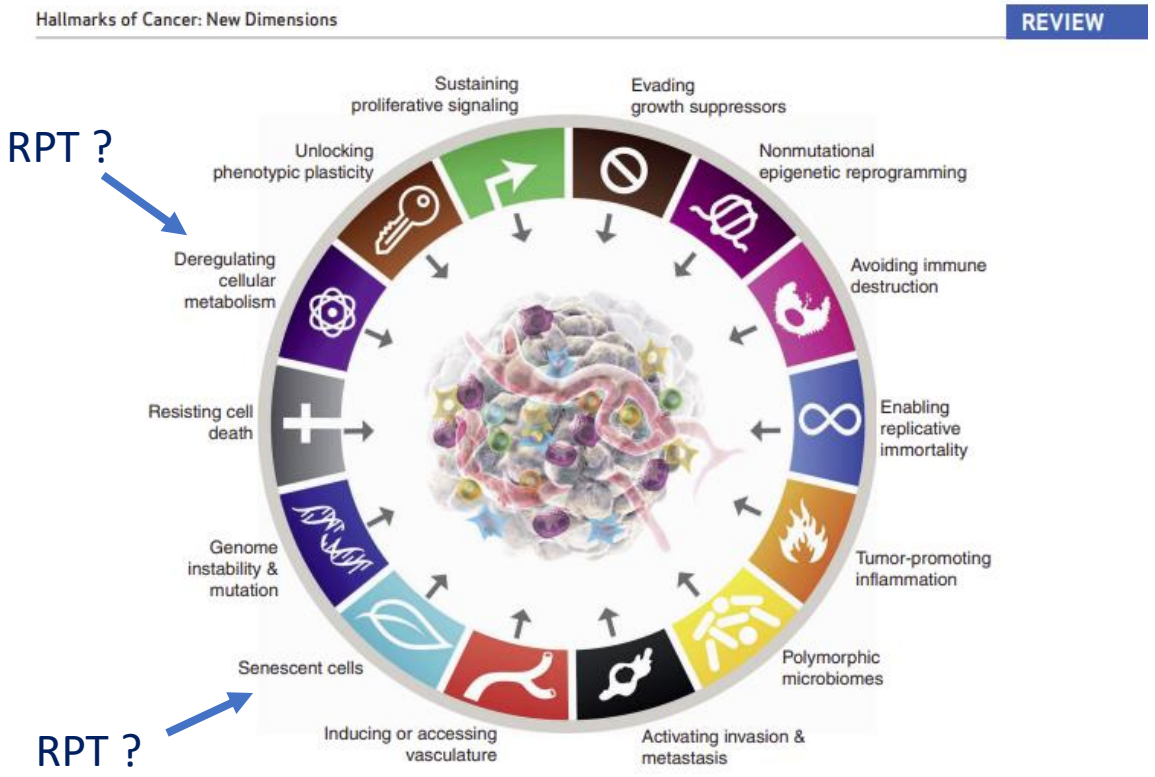
Nature Reviews | Drug Discovery
September 2020



Radiopharmaceutical therapy (RPT) in cancer

Selecting Patients through Molecular Imaging

Hallmarks of Cancer: New Dimensions



Douglas Hanahan. JANUARY 2022 CANCER DISCOVERY

New approaches in cancer treatment: facts and expectations with medical radionuclides

Luís Costa, MD, PhD

Thank you for your attention

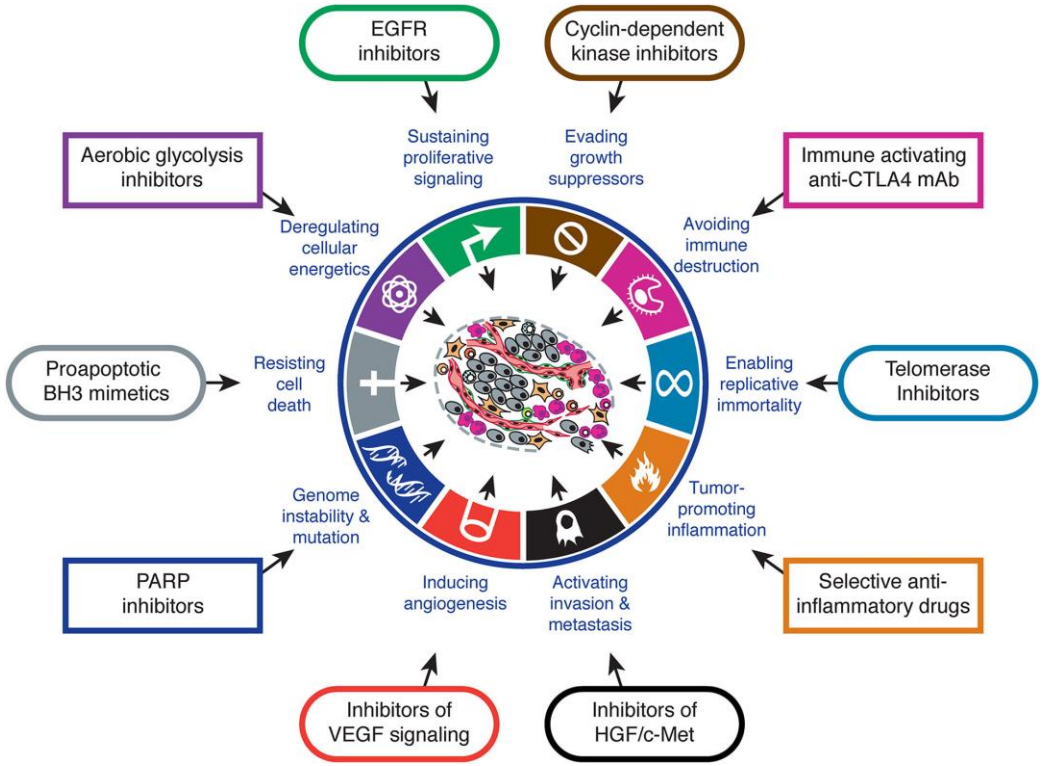
PRISMAP Public Event
"Challenges in nuclear medicine"

28 November 2023
Lisbon School of Medicine, Aula Magna
Santa Maria Hospital Building

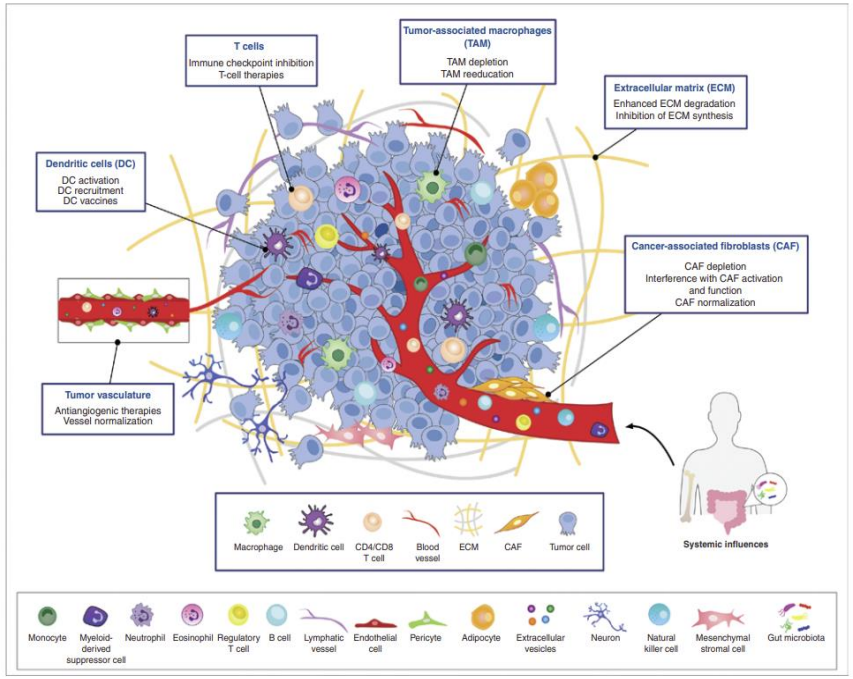
CAML
Centro Académico de Medicina de Lisboa

Radiopharmaceutical therapy (RPT) in cancer

Cancer Cell / Tumor Microenvironment



Douglas Hanahan, et al. The Hallmarks of Cancer



CANCER DISCOVERY 10TH ANNIVERSARY ISSUE April 2021

Radiopharmaceutical therapy (RPT) in cancer

Selecting Patients through Molecular Imaging