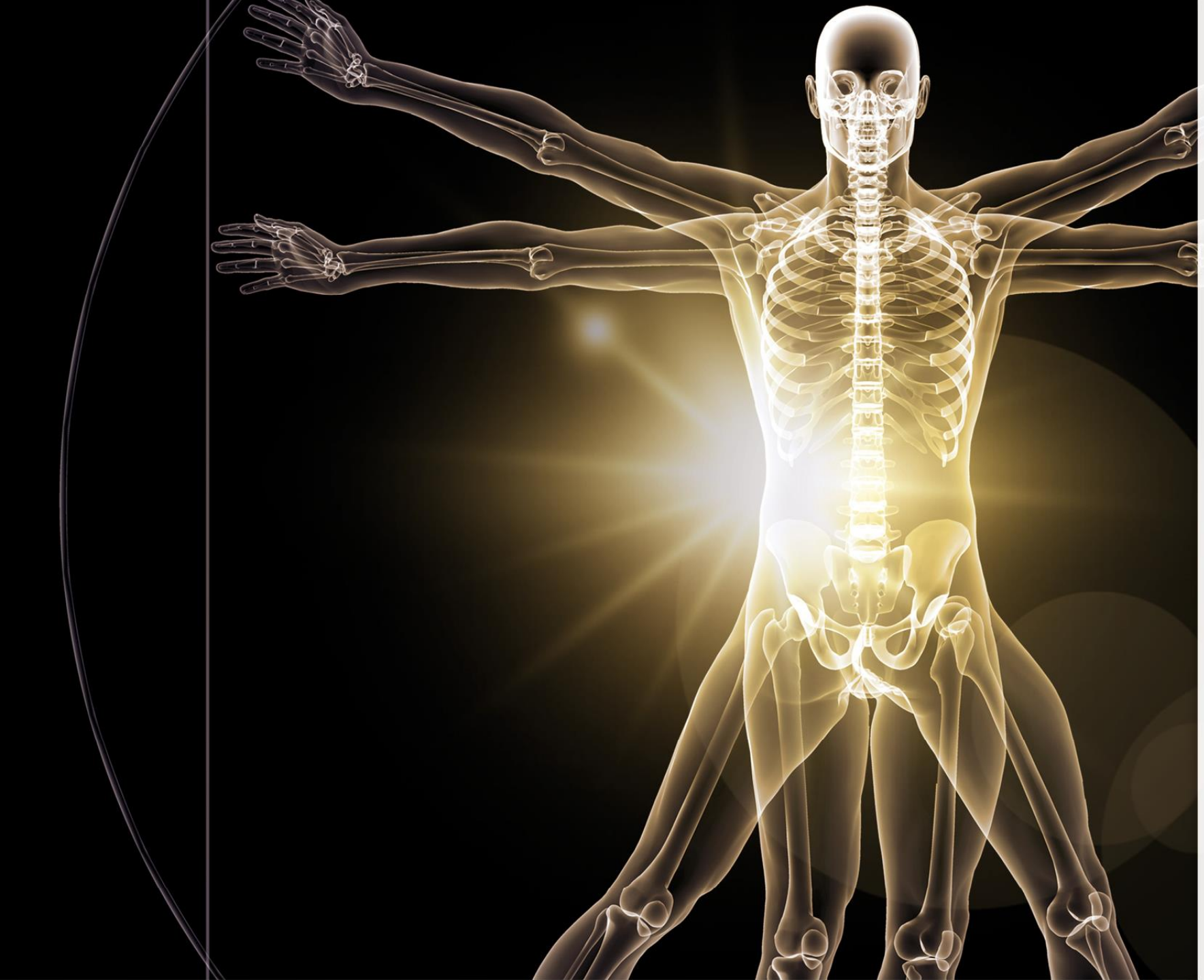


IS3R 2023

Berlin/Germany

August 24–26, 2023

Molecular Imaging and Theranostics – Where are we heading?

Ken Herrmann

DISCLOSURES (ACCORDING TO EANM)

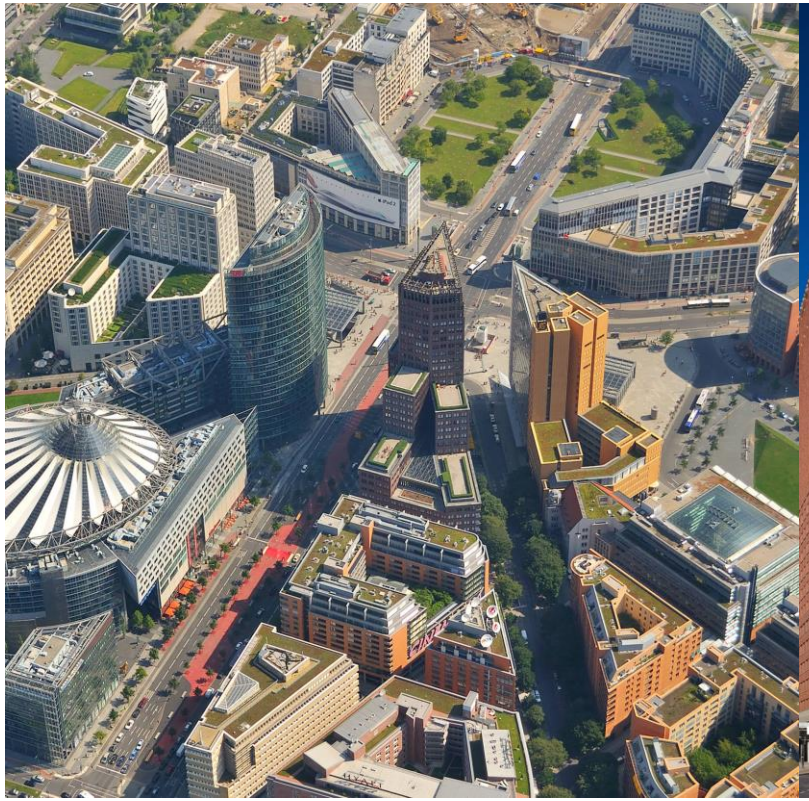
1) I or one of my co-authors hold a position as an employee, consultant, assessor or advisor for a pharmaceutical, device or biotechnology company. **Consultant/Advisor of Bayer, IPSEN, Sofie Biosciences, Aktis Oncology, MPM Capital, Bain Capital, SIRTEX, Curium, ABX, BTG/BSC, Adacap/Novartis, Endocyte, Janssen, Amgen, Telix, Fusion, Theragnostics, GE and Siemens.**

2) I or one of my co-authors receive support from or hold stocks or shares (greater than 5% equity) in a pharmaceutical, device or biotechnology company. **None.**

3) I or one of my co-authors hold property rights/patents for (radio)pharmaceuticals, medical devices or medical consulting firms. **None.**

4) I or one of my co-authors have written articles for (radio)pharmaceutical, medical device, biotechnology or consulting companies during the last 5 years. **None.**

Potsdamer Platz (1989 / 2023)



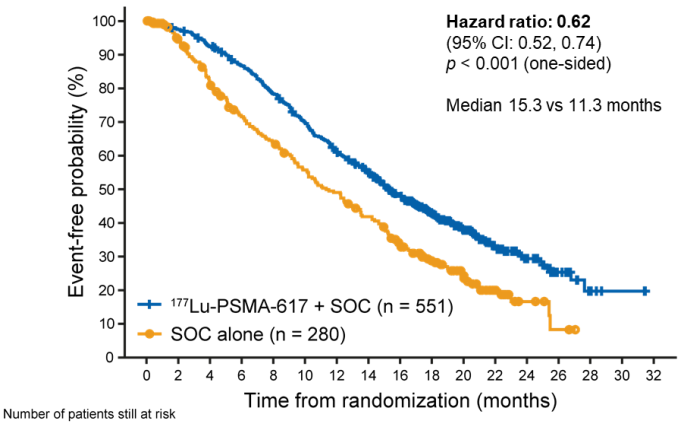
https://www.mauer-fotos.de/fotos/f-023601/

https://www.h-hotels.com/de/berlin/sehenswuerdigkeiten/potsdamer-platz

PATIENT BENEFIT

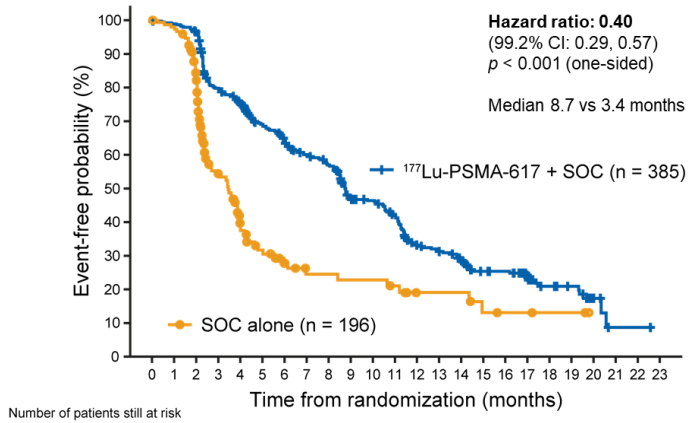
^{177}Lu-PSMA-617 prolonged overall survival

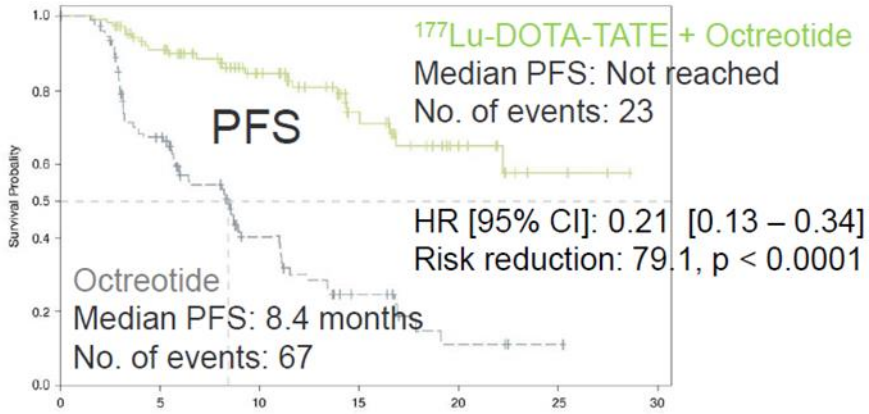
All randomized patients (N = 831)



^{177}Lu-PSMA-617 improved rPFS

rPFS analysis set (n = 581)

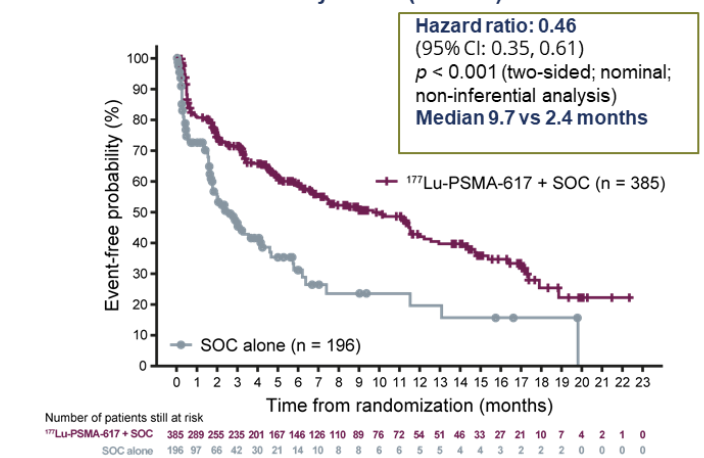




Ad hoc analyses

FACT-P total score
Time to worsening favoured the ^{177}Lu-PSMA-617 arm

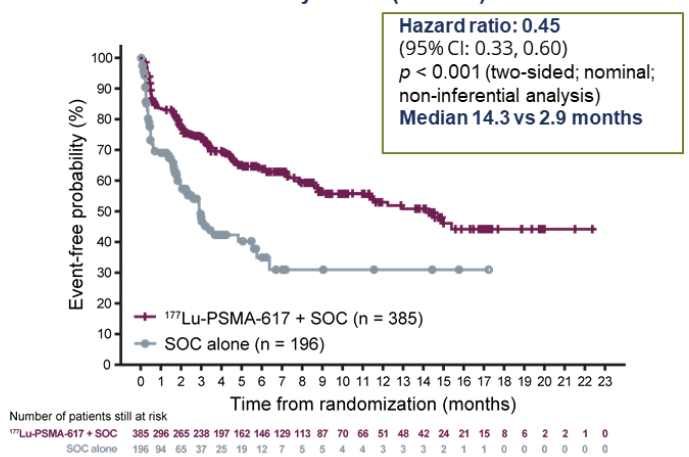
rPFS analysis set (n = 581)



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

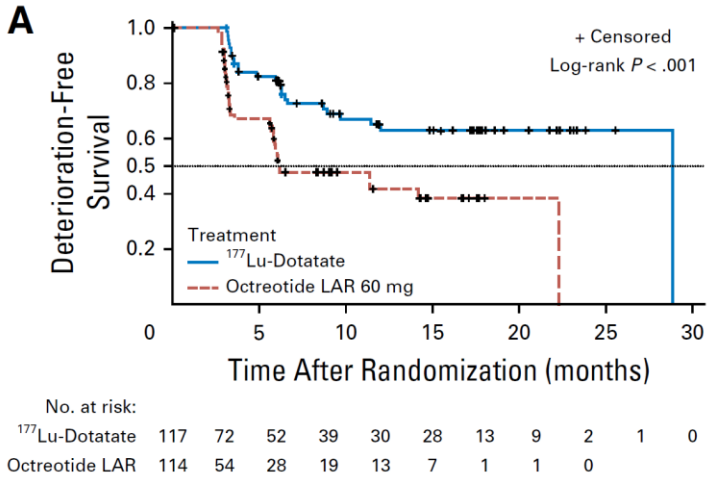
BPI-SF pain intensity
Time to worsening favoured the ^{177}Lu-PSMA-617 arm

rPFS analysis set (n = 581)



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

A



Strosberg et al. , NEJM 2017; Strosberg et al., J Clin Oncol 2018; Sartor et al., NEJM 2021; Fizazi et al., Lancet Oncol in press

Market Predictions

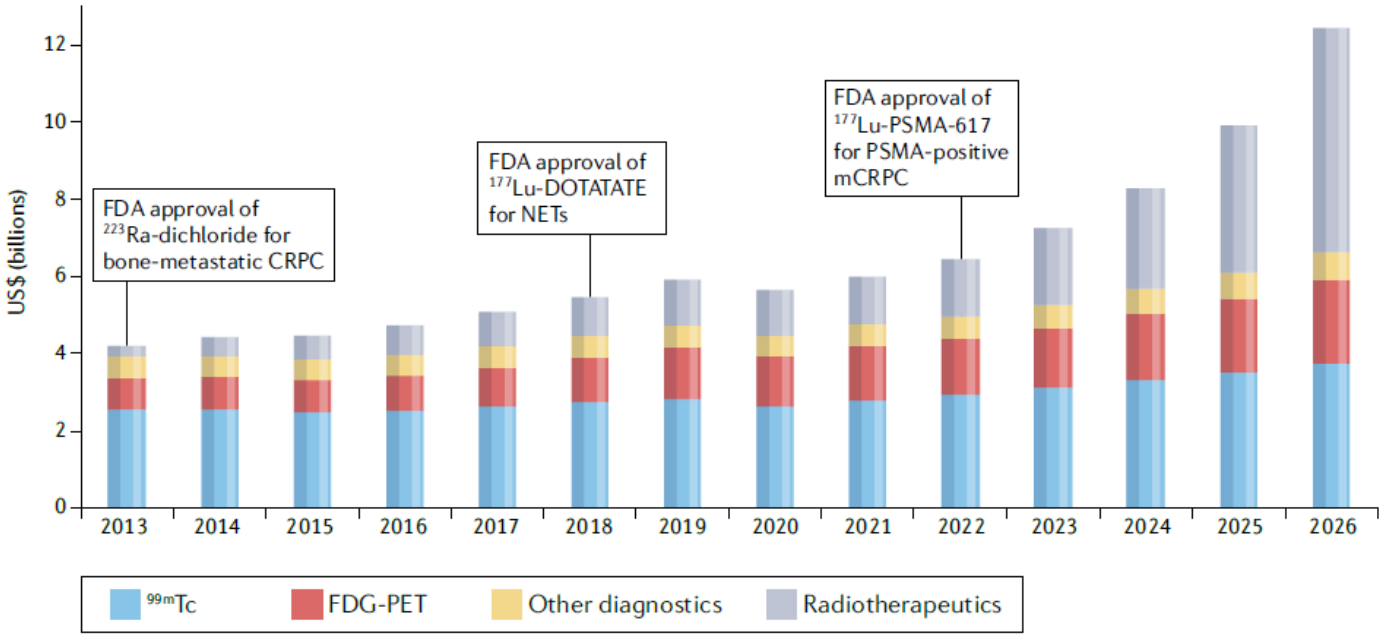


Fig. 3 | **The predicted global nuclear medicine market 2013–2026.** This projected market growth likely reflects the availability of a greater number of agents, implementation at an increasing number of centres and projected increases in the numbers of patients with cancer globally. ©MEDraysintell Nuclear Medicine Report & Directory, Edition 2021. CRPC, castration-resistant prostate cancer; mCRPC, metastatic CRPC; NET, neuroendocrine tumour; PSMA, prostate-specific membrane antigen.

Three fold increase in revenues 2013 to 2026 (50% 2013 to 2022) with an estimated 12 bn USD in 2026

Main driver: radiotherapeutics (10 fold increase!)

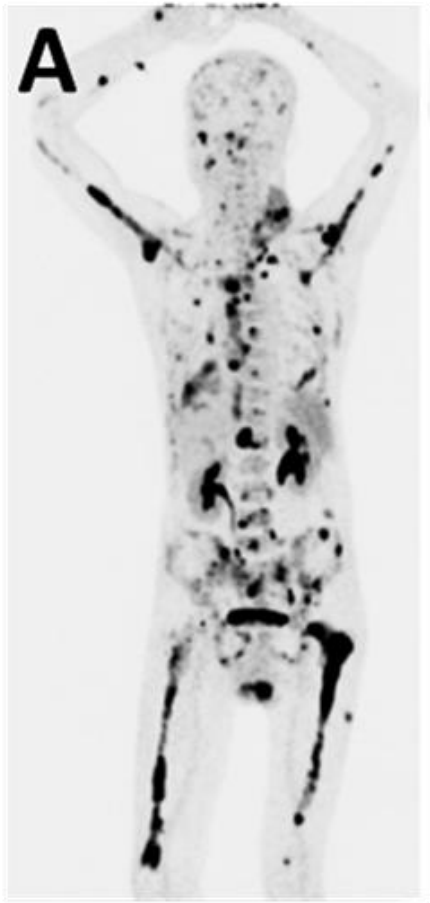
New developments:

- New targets
- New radionuclides
- New indications of approved concepts
- New administration pathways
- Combination treatment
- New Dos(ing) concepts

Bodei, Herrmann, …. and Lewis, Nat Rev Clin Oncol 2022

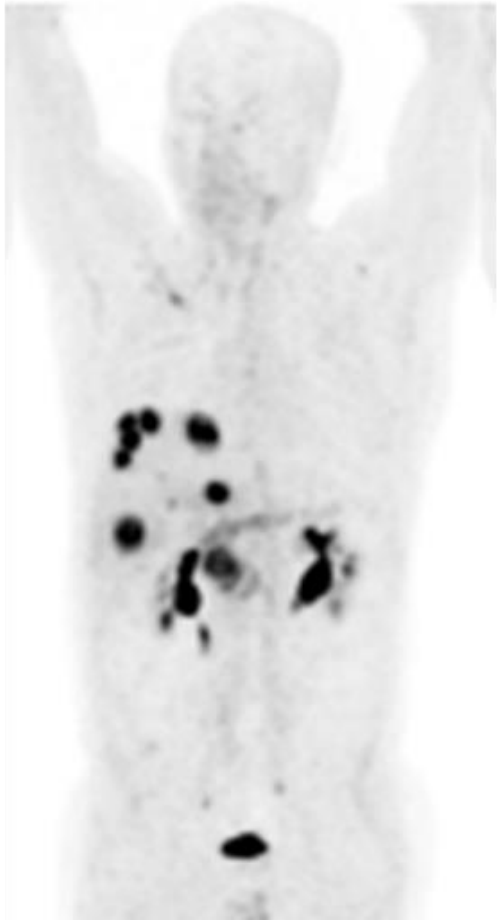
New Targets

^{68}Ga-Pentixafor



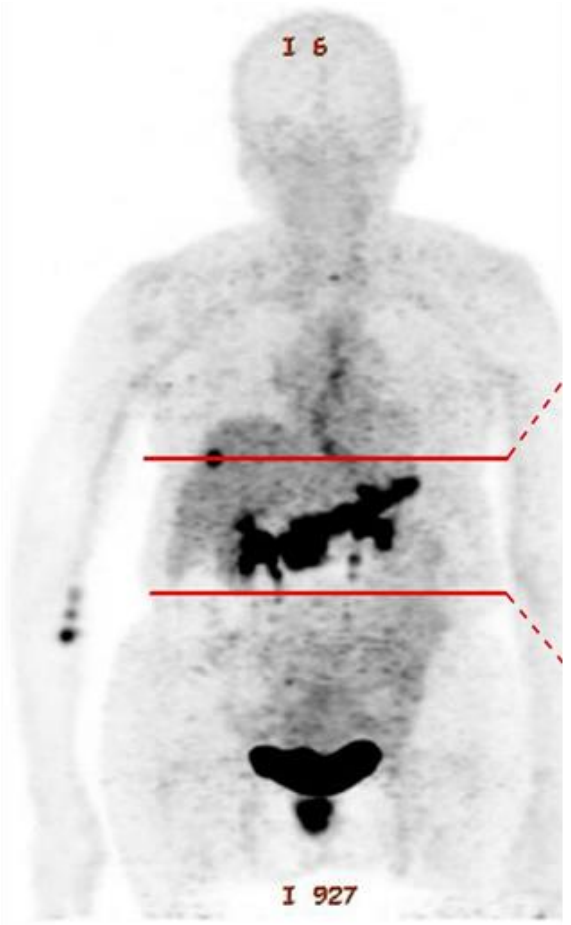
CXCR4

^{68}Ga-FAPI



FAP

^{68}Ga-NeoB



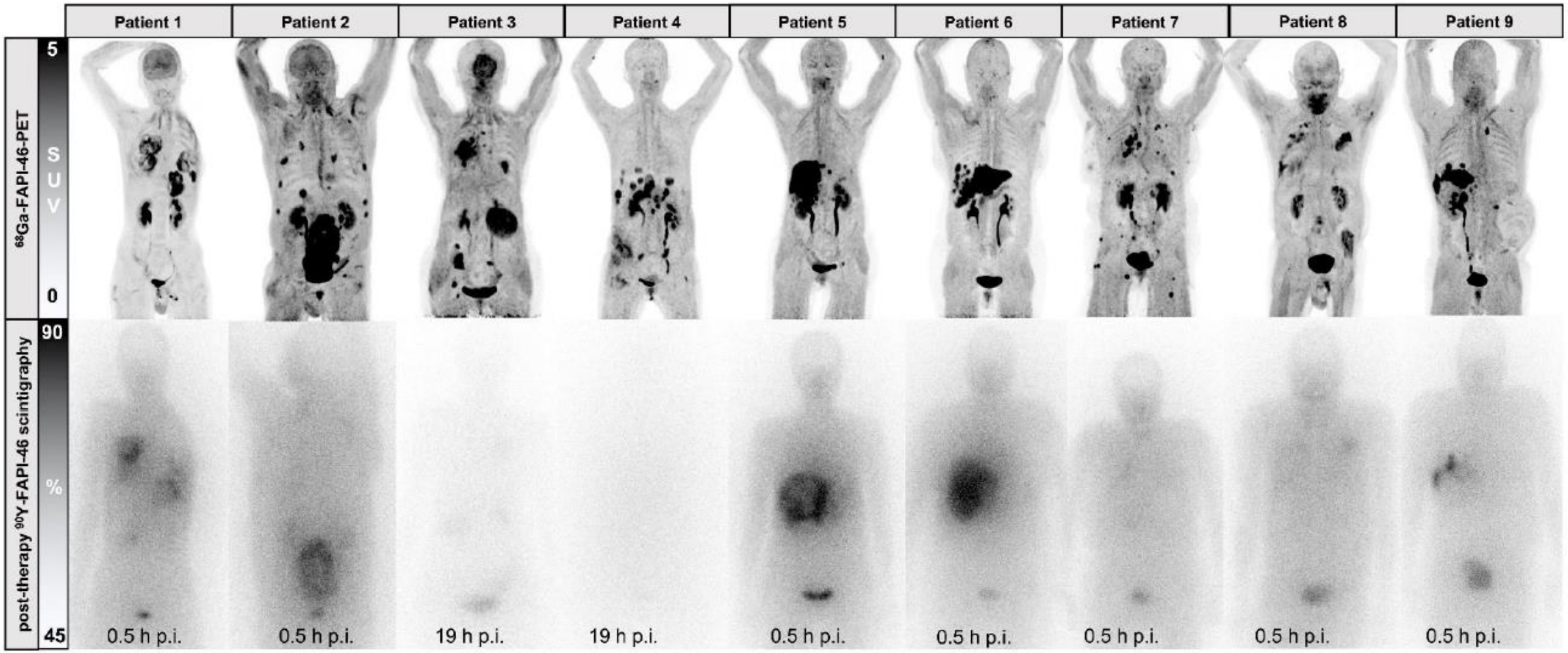
GRP

^{89}Zr-Girentuximab

CAIX

NEW TARGETS

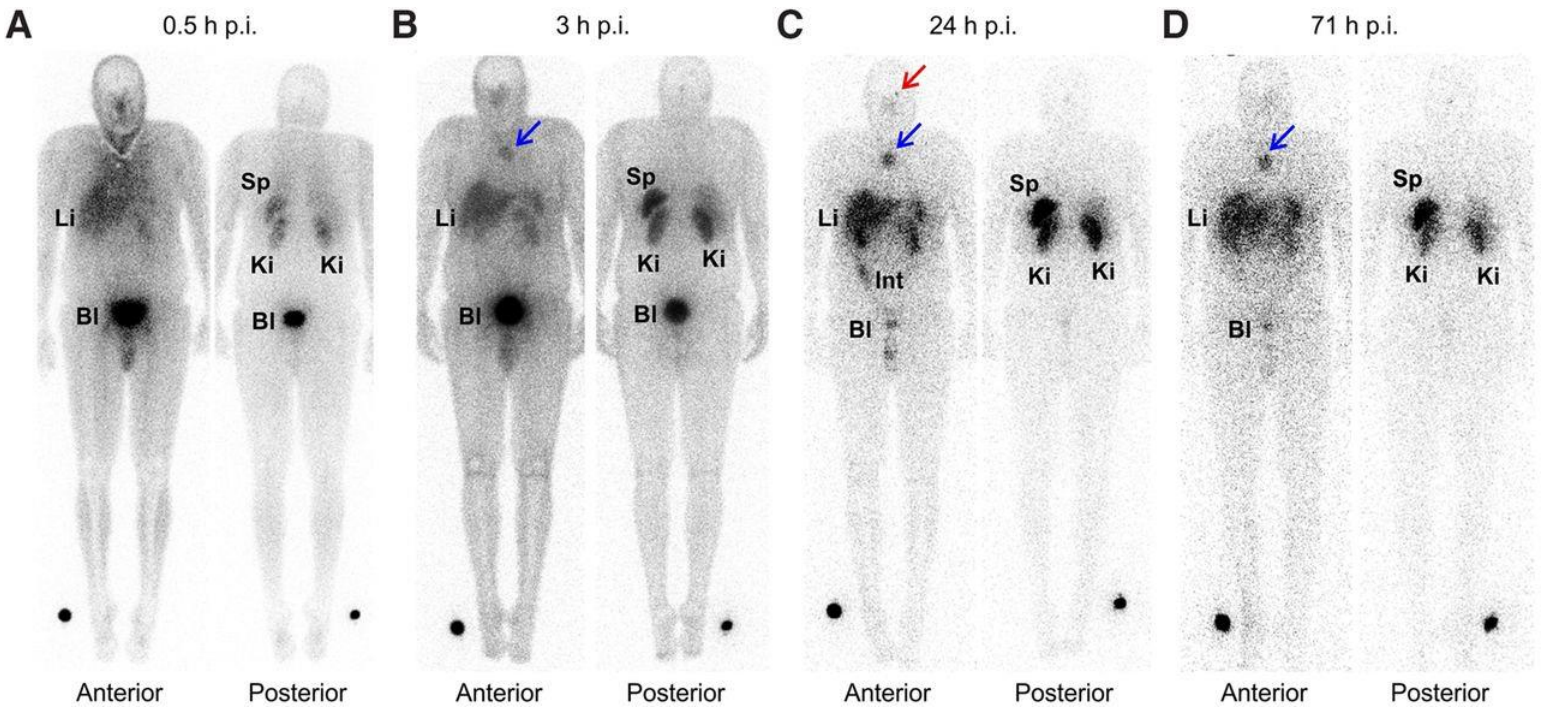
Figure 1: Pre-therapeutic ^{68}Ga-FAPI-46 PET images and post-treatment ^{90}Y-FAPI-46 bremsstrahlung scintigraphies after first cycle of ^{90}Y-FAPI-46 radioligand therapy



Ferdinandus et al., J Nucl Med 2022

New Radionuclides

New Radionuclides such as ^{212}Pb, ^{161}Tb, ^{67}Cu, ^{211}At etc.



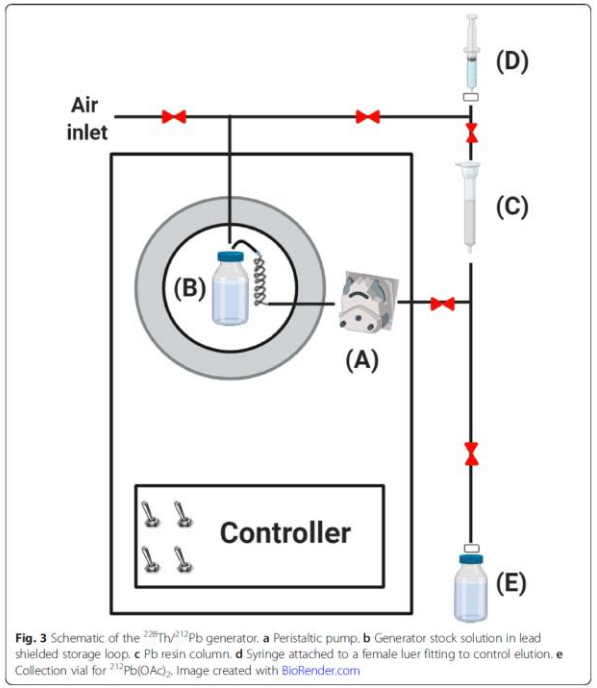
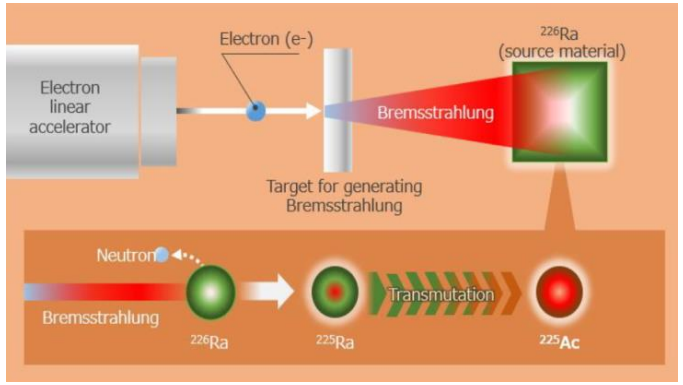


Fig. 3 Schematic of the $^{228}Th/^{212}Pb$ generator. **a** Peristaltic pump. **b** Generator stock solution in lead shielded storage loop. **c** Pb resin column. **d** Syringe attached to a female luer fitting to control elution. **e** Collection vial for $^{212}Pb(OAc)_2$. Image created with BioRender.com

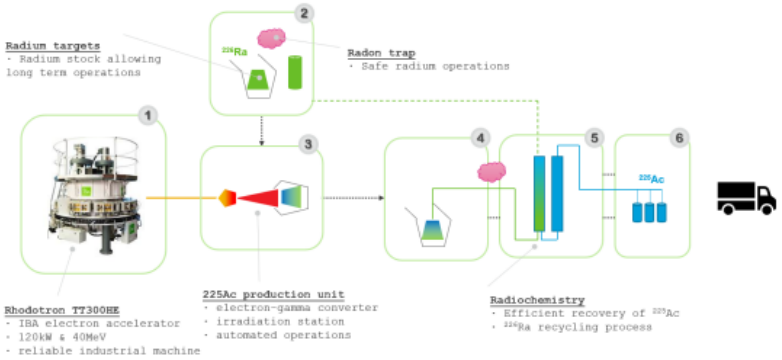
Baum et al., J Nucl Med 2021;
McNeil et al., EJNMMI Radiopharmacy and Chemistry 2021; https://advancell.com.au/technology

New (Production Pathways of) Radionuclides

Linear Accelerator Pathway



Rhodotron Pathway



Technologies Under Development and Operating Sites for ^{225}Ac Production, Including Estimated Present and 2032 Capacities

Technology	Source	Yearly production capacity (GBq/y/site) 2023	2032	Total (GBq/y) in 2032	Comment
A: [(^{233}U→) ^{229}Th→^{225}Ac] (generator)	ORNL, United States	26	26	Up to 3,000 [80]	Highest quality of *nca* ^{225}Ac; may enter price competitivity
	IPPE, Russia	37 (est.)	150 (est. 2025) to 300 (est. 2030)		
	JRC-ITU, Germany	11	11		
	TRIUMF, Canada	0.4	0.4		
	TerraPower, United States	>10	≤2,700		
	Pantera, Belgium	0	>70		TerraPower source
B: [^{232}Th(p,x)^{225}Ac+^{227}Ac] (high-energy accelerator)	BNL/ORNL LANL; Tri-Lab, United States	16.7	Potential, >3,700	>9,000 [>240]	Contaminated with ^{227}Ac (0.2% EOB - ~1.5% at calibration); not suitable for large scale routine use
	CNL/TRIUMF, Canada; BWXT/ITM, United States/Germany	>1	Idem >3,700		
	INR, Russia		≤1,000		
	SpectronRx, United States	>1	>200		
	Others: Arronax, France; IsoDar, Japan; CIAE, China	First GBq in 2024	Potential, >200 each		
C: [+ … +^{225}Ra→^{225}Ac] (as side product)	~10% of above; CNL/TRIUMF, Canada	0.3	>370 (theory)	>370 [>10]	High level of waste - expensive
D: [^{226}Ra(p,2n)^{225}Ac] (cyclotron)		First GBq		>4,500 [>120]	Additional sites under evaluation in other countries (Asia)
	SpectronRx, United States	2023	>500		
	Ionetix, United States	2023	1,900		
	Eckert&Ziegler, Germany	2024	550		
	Alfarim, Netherlands	2025	450–850		
	N-MediPhysics, Japan	>2023	>500		
	KIRAMS, South Korea	>2025	>500		
D: [^{226}Ra(d,3n)^{225}Ac] (linear accelerator)	Nusano, United States		≤160,000		Under evaluation
E: [^{226}Ra(γ,n)^{225}Ra→^{225}Ac] (photoconverter)	NorthStar, United States	2023	3,700–15,000	>37,000 [>1,000]	Rhodotron: *nca* ^{225}Ac
	Pantera, Belgium	2027	3,700–5,000		
	TerraPower, United States	2029	3,700–5,000		
	Niowave, United States	2023	≤18,000		Linac: *nca* ^{225}Ac
	Hitachi, Japan	>2024	>3,700		
F: [^{226}Ra(n,2n)^{225}Ra→^{225}Ac] (n from d on beryllium target)	Nusano, United States		≤44,000		Under evaluation

Journal of Nuclear Medicine, published on August 17, 2023 as doi:10.2967/jnumed.123.265907

EDITORIAL

Is Actinium Really Happening?

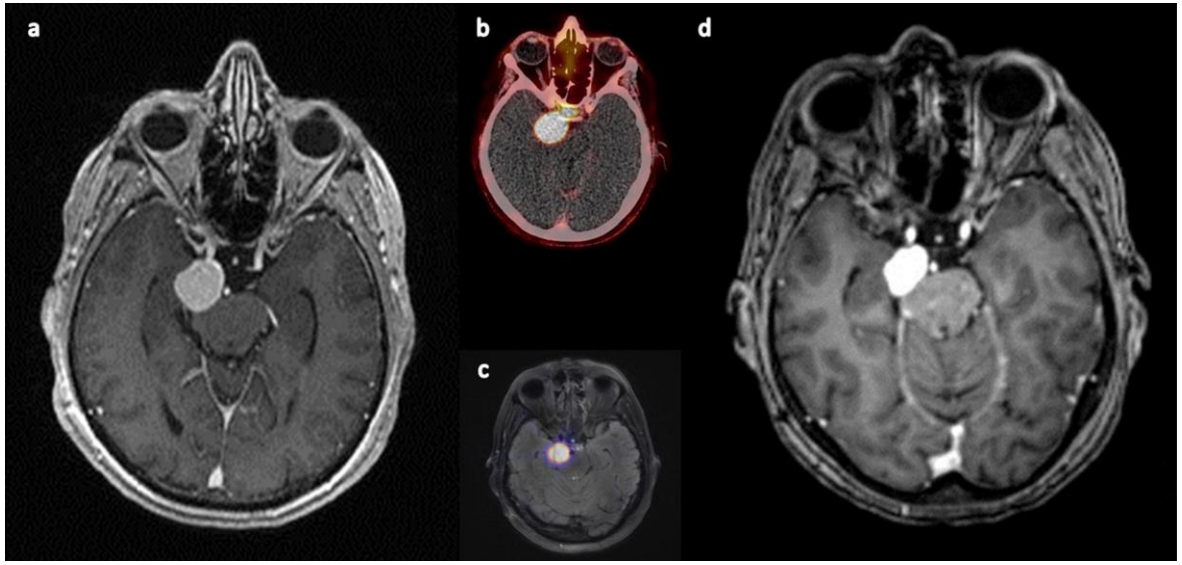
Richard Zimmermann

Chrysalium Consulting, Lalaye, France; MEDraysintell, Louvain-la-Neuve, Belgium; and Oncidium Foundation, Mont-Saint-Guibert, Belgium

https://www.iba-radiopharmasolutions.com/sites/default/files/2022-11/PANTERA-Set-up%20of%20a%20commercial%20225Ac%20production%20facility_Poster_TRP_2022.pdf
https://www.world-nuclear-news.org/Articles/New-isotope-initiatives-address-supply-challenges

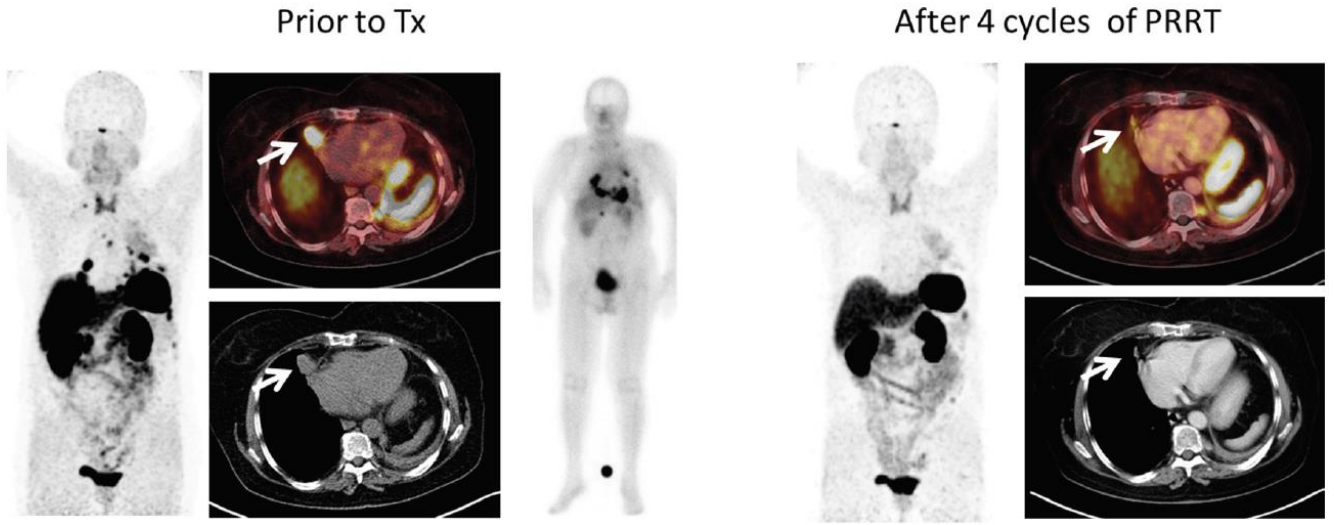
EXPLORING PRRT BEYOND NETS

MENIGNIOMA



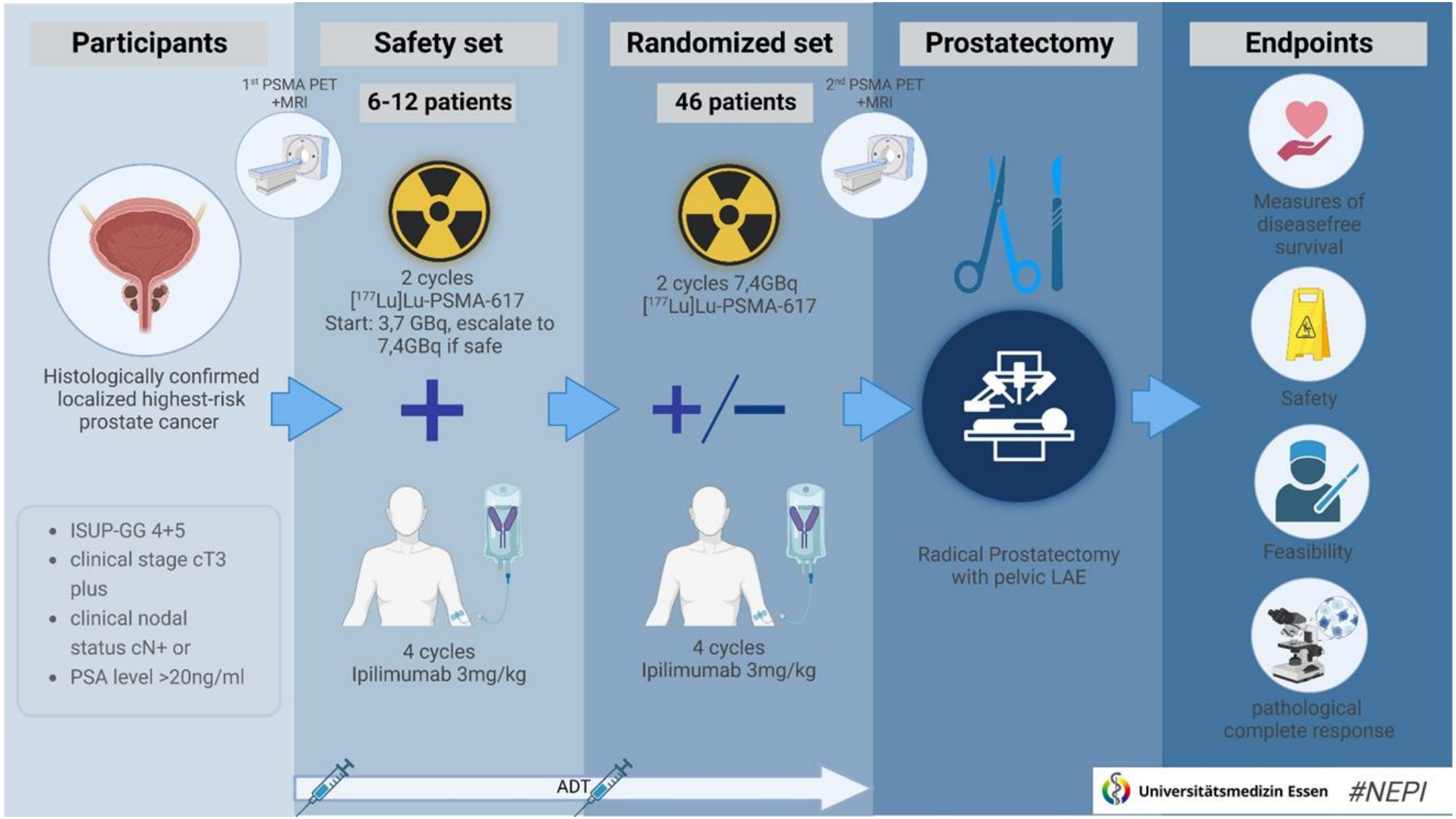
Hartrampf et al.
Clinical and Translational Radiation Oncology 2020; DOI: 10.1016/j.ctro.2020.03.002

SCLC

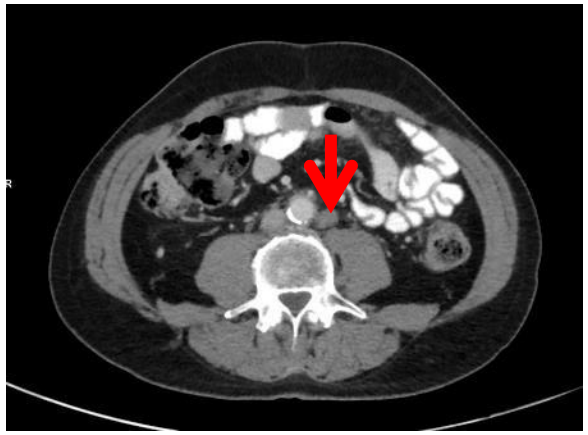


Lapa et al.
Oncotarget 2016
DOI: 10.18632/oncotarget.7706

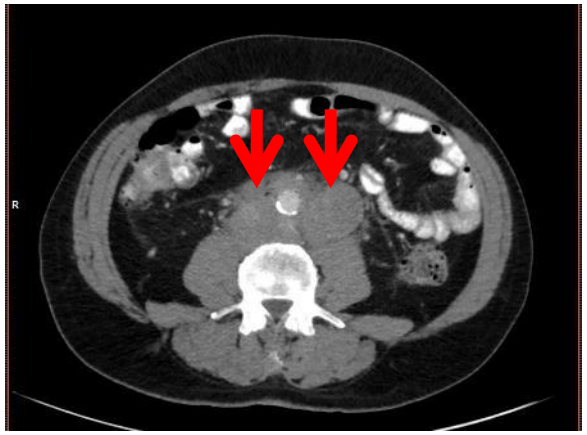
New Administration Pathways



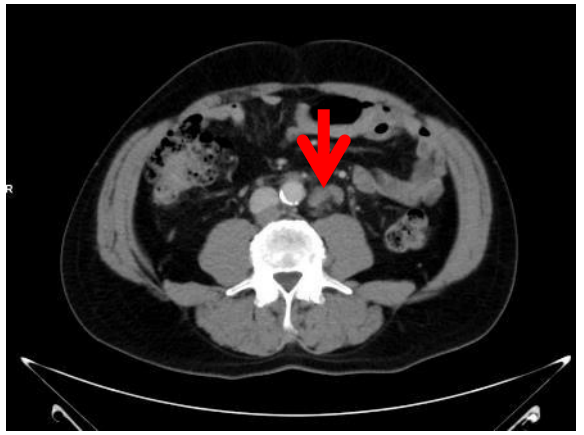
Combination Treatment



anti-PD1

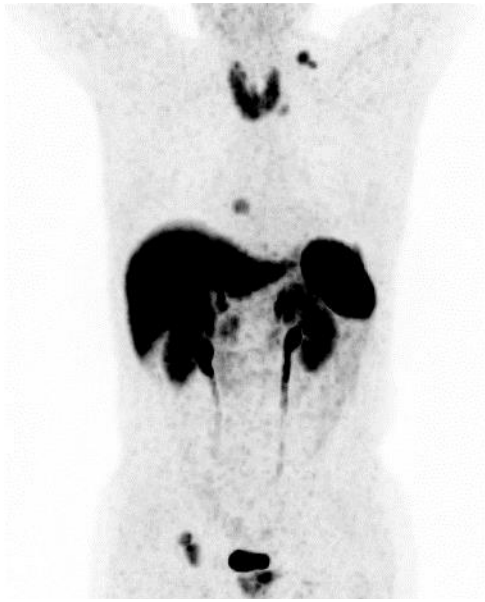


PRRT
+
anti-PD1



Metastatic Merkel Cell Carcinoma
Progressive Disease Status Post
2x Radiotherapy
5x ImmunoTx

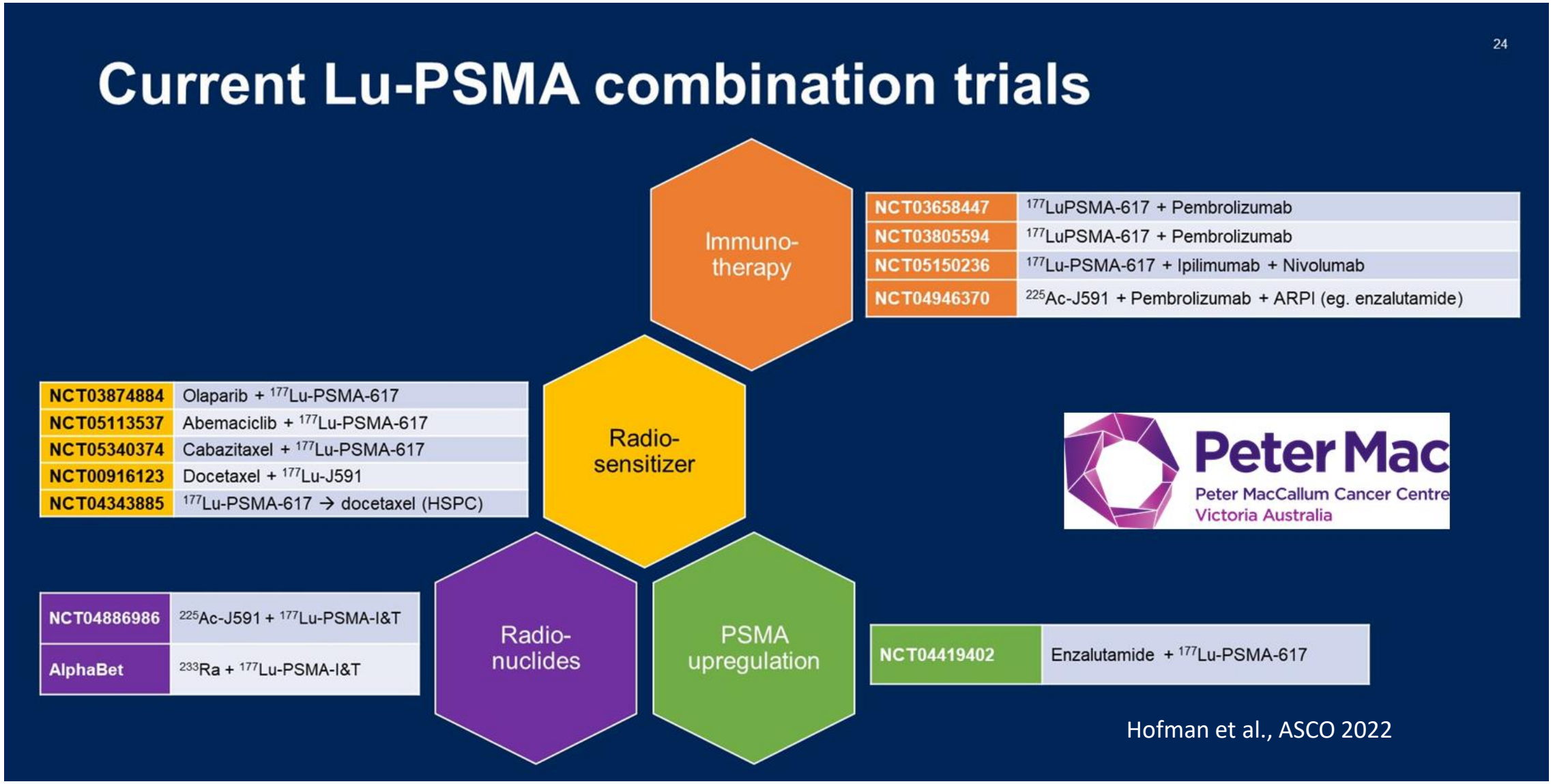
Baseline DOTATOC PET



Follow-up DOTATOC PET

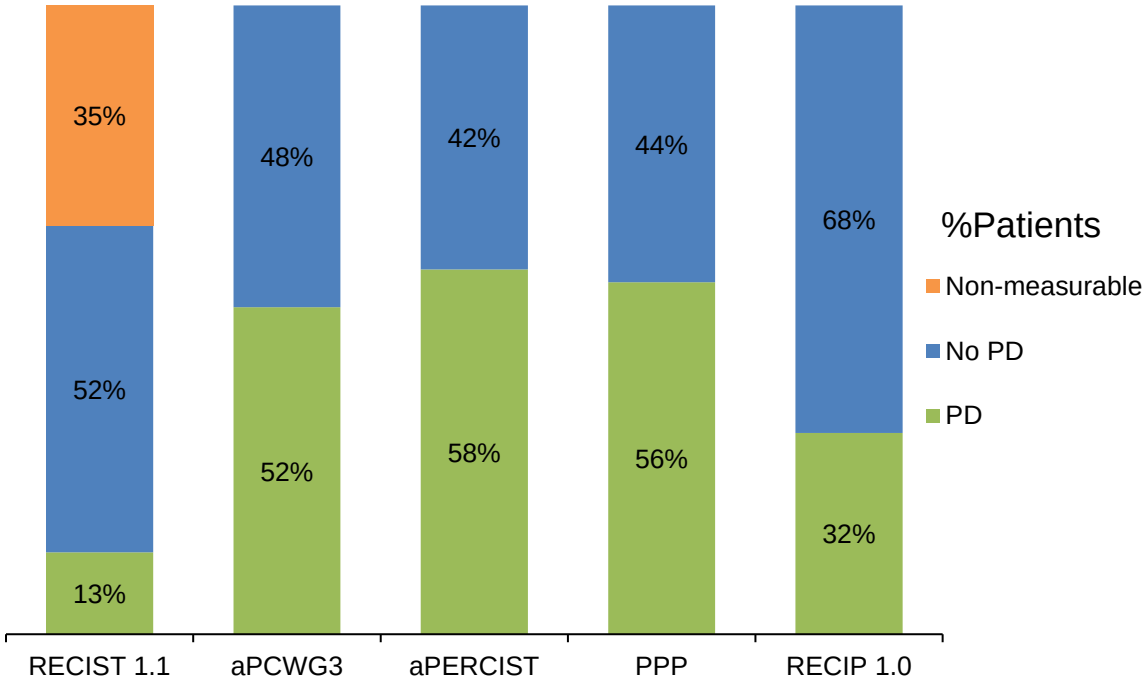
Ferdinandus et al.
J Nucl Med. 2021
doi: 10.2967/jnumed.121.262344.

COMBINATION TREATMENT

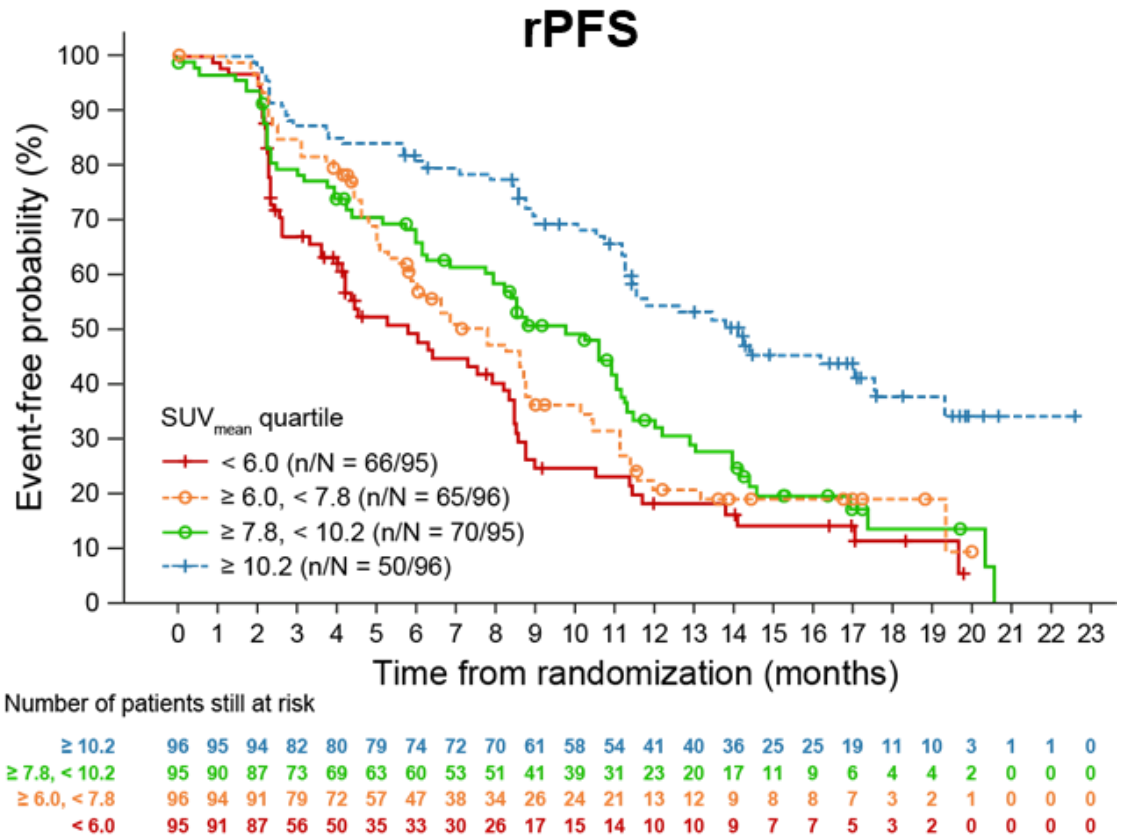


Establishing (PSMA) PET for Patient Selection and Response Monitoring

Interpretation of response among criteria for response evaluation at 12 weeks after ^{177}Lu-PSMA radioligand therapy[1]



PSMA PET SUV_{mean} at baseline as a predictor of response to ^{177}Lu-PSMA-617 radioligand therapy[2]



aPERCIST, adapted Positron Emission Tomography Response Criteria in Solid Tumors; aPCWG3, adapted Prostate Cancer Working Group Criteria; PD, progressive disease; PET, positron emission tomography; PPP, PSMA PET progression; PSMA, prostate-specific membrane antigen; RECIP, Response Evaluation Criteria In PSMA-Imaging; RECIST, Response Evaluation Criteria in Solid Tumors; rPFS, radiographic progression-free survival; SUV, standardized uptake value.

1. Gafita A, et al. Eur J Nucl Med Mol Imaging 2022;doi:10.1007/s00259-022-05882-x; 2. Kuo P, et al. J Clin Oncol 2022;40(no. 16_suppl):5002.

Major Challenges for Scale Up

Last Mile Challenge

1. Lack of Professionals
2. Patient Referral
3. Economics

European Journal of Nuclear Medicine and Molecular Imaging
https://doi.org/10.1007/s00259-022-05785-x

GUIDELINES

Check for updates

Joint EANM, SNMMI and IAEA enabling guide: how to set up a theranostics centre

Ken Herrmann[1,2] · Luca Giovanella[3] · Andrea Santos[4] · Jonathan Gear[5] · Pinar Ozgen Kiratli[6] · Jens Kurth[7] · Ana M. Denis-Bacelar[8] · Roland Hustinx[9,10] · Marianne Patt[11] · Richard L. Wahl[12] · Diana Paez[13] · Francesco Giammarile[13] · Hossein Jadvar[14] · Neeta Pandit-Taskar[15] · Munir Ghesani[16] · Jolanta Kunikowska[17]

Received: 15 March 2022 / Accepted: 25 March 2022

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Joint EANM, SNMMI and IAEA Enabling Guide: How to Set Up a Theranostics Centre

Ken Herrmann[1], Luca Giovanella[2], Andrea Santos[3], Jonathan Gear[4], Pinar Ozgen Kiratli[5], Jens Kurth[6], Ana M Denis-Bacelar[7], Roland Hustinx[8], Marianne Patt[9], Richard L. Wahl[10], Diana Paez[11], Francesco Giammarile[11], Hossein Jadvar[12], Neeta Pandit-Taskar[13], Munir Ghesani[14] and Jolanta Kunikowska[15]

SUMMARY

- Radiotheranostics is a success story
- New targets, radionuclides and combination approaches driving next wave
- Challenge Last Mile
- Fast Track Pathways needed, Leveraging Companion Imaging

https://phillbarron.wordpress.com/2012/04/04/once-in-a-lifetime/

Theranostics: Field of Growth

Thank you very much for your attention!

Twitter: #ProfKHerrmann

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Klinik für Nuklearmedizin