What's New and Exciting in the World of RLT



Prof Michael Hofman

Nuclear Medicine Specialist; Director, ProsTIC & Head of PET/CT,
Peter MacCallum Cancer Centre, University of Melbourne

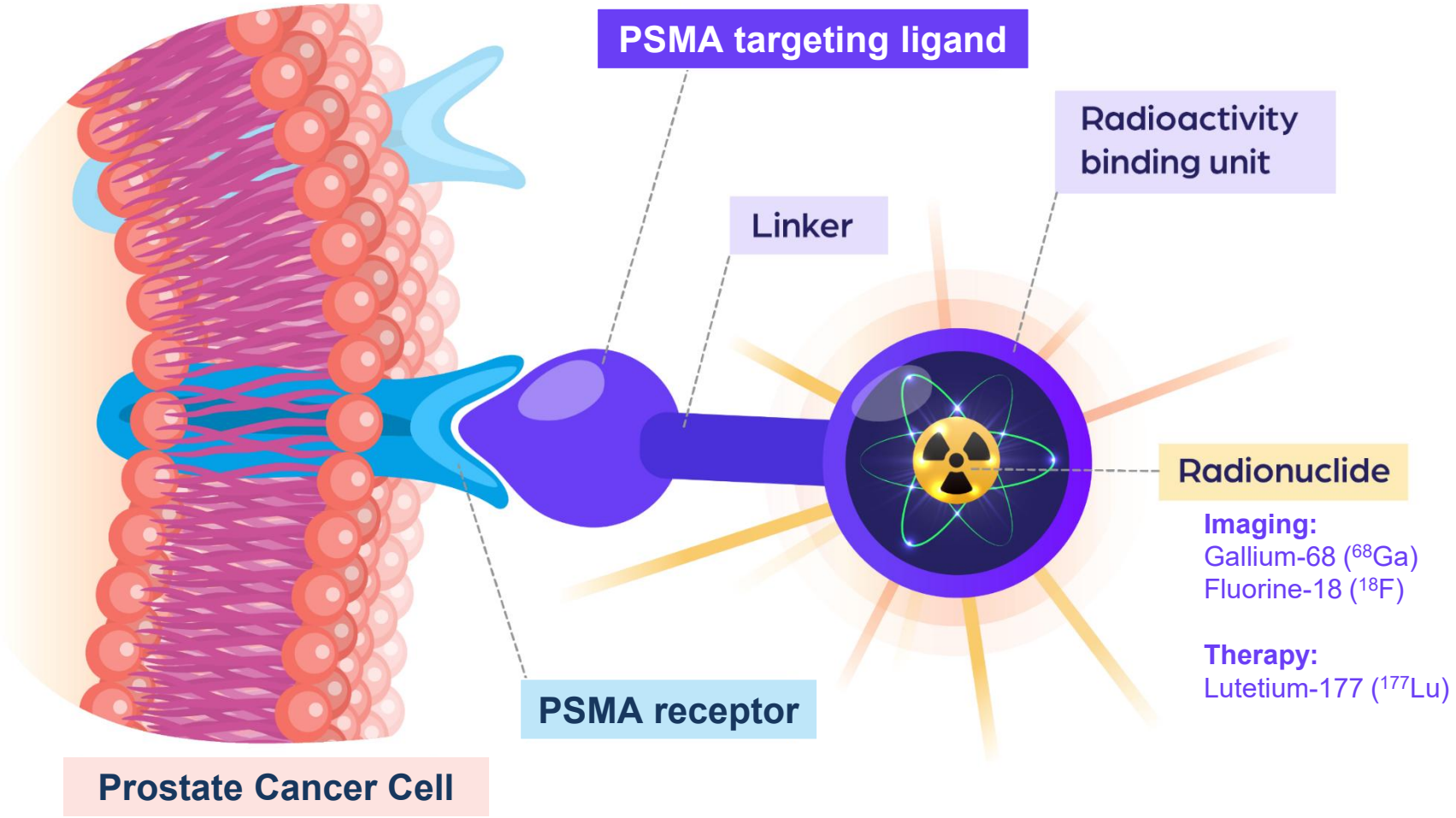
Disclosures

Category	To institution (or unpaid)	Personal
Research support (as principal investigator)	Astra Zeneca, Bayer, GE HealthCare, ITM, Isotopia, Novartis	
Consulting income (advisory board or speaker board)	AdvanCell, ITM	Skops Bio (co-founder), Bicycle, Starget Pharma, Actithera Prior (last 2 years): Astra Zeneca, Johnson & Johnson & MSD
Equity (shares or options)		Skopos Bio, AdvanCell, Starget Pharma, Bicycle
Board	Australasian Association of Nuclear Medicine Specialists (AANMS) (Vice President) (unpaid)	Skopos Bio
Grants (active)	Australian Cancer Research Foundation (ACRF), Prostate Cancer Foundation of Australia, Prostate Cancer Foundation, National Imaging Facility (NIF), NHRMC, Peter MacCallum Foundation	

@DrMHofman

Thera nostics

Therapeutic (beta, alpha, Auger) | **Diagnostic (PET/CT)**

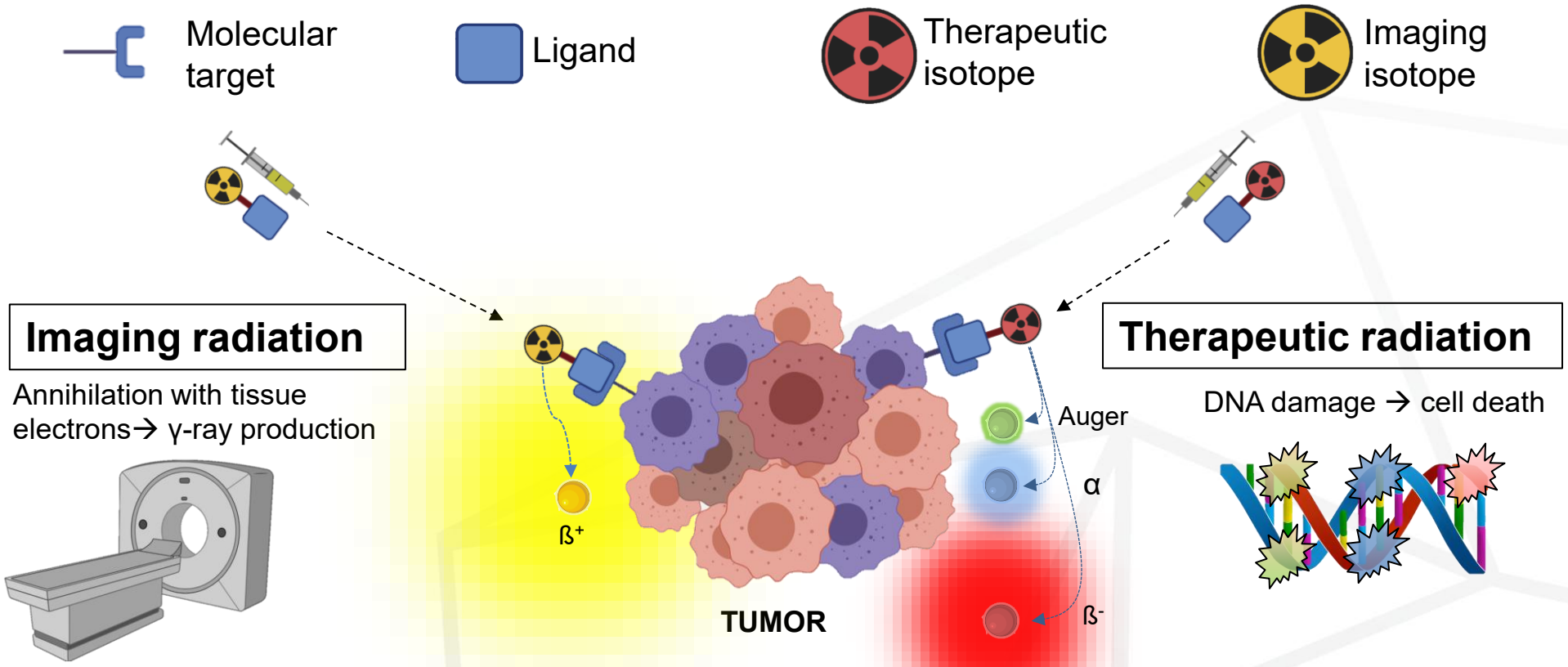


Imaging:
Gallium-68 (^{68}Ga)
Fluorine-18 (^{18}F)

Therapy:
Lutetium-177 (^{177}Lu)

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Victoria Australia

Theranostics: diagnostics & therapy based on the same molecular target



PET Imaging (ß⁺) ► therapeutic radiation (Auger, α or ß⁻)

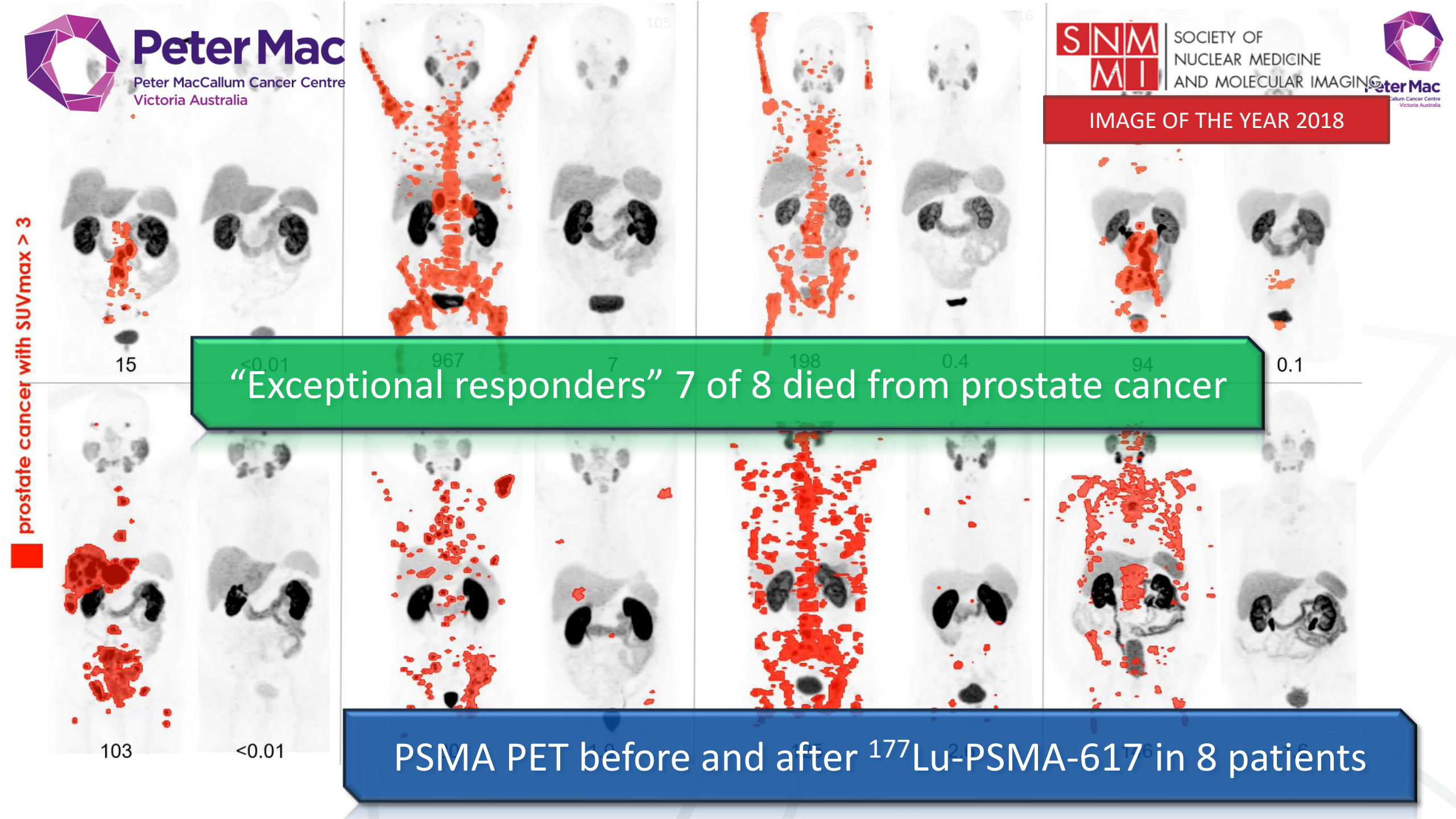
Jewell K et al, Radiology 2024, doi:10.1148/radiol.231703

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SNMMI SOCIETY OF NUCLEAR MEDICINE AND MOLECULAR IMAGING

Peter Mac Callum Cancer Centre Victoria Australia

IMAGE OF THE YEAR 2018



"Exceptional responders" 7 of 8 died from prostate cancer

PSMA PET before and after ^{177}Lu-PSMA-617 in 8 patients

Thirty-Second Annual Prostate Cancer Foundation SCIENTIFIC RETREAT

Landmark Randomised Trials in 2024

phase 3

phase 2

TheraP

pre cabazitaxel



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

Hofman MS et al, Lancet Oncology **2024**
https://doi.org/10.1016/s1470-2045(23)00529-6

VISION

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



post docetaxel

ENZA-P

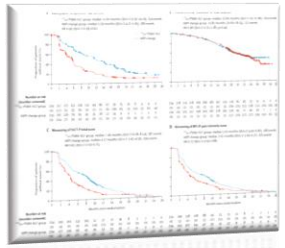
pre docetaxel



Emmett L MS et al, Lancet Oncology **2024**
https://doi.org/10.1016/s1470-2045(23)00529-6

PSMAfore

Morris M et al, Lancet **2024**
https://doi.org/10.1016/s0140-6736(24)01653-2



pre docetaxel

UpFrontPSMA

mHSPC



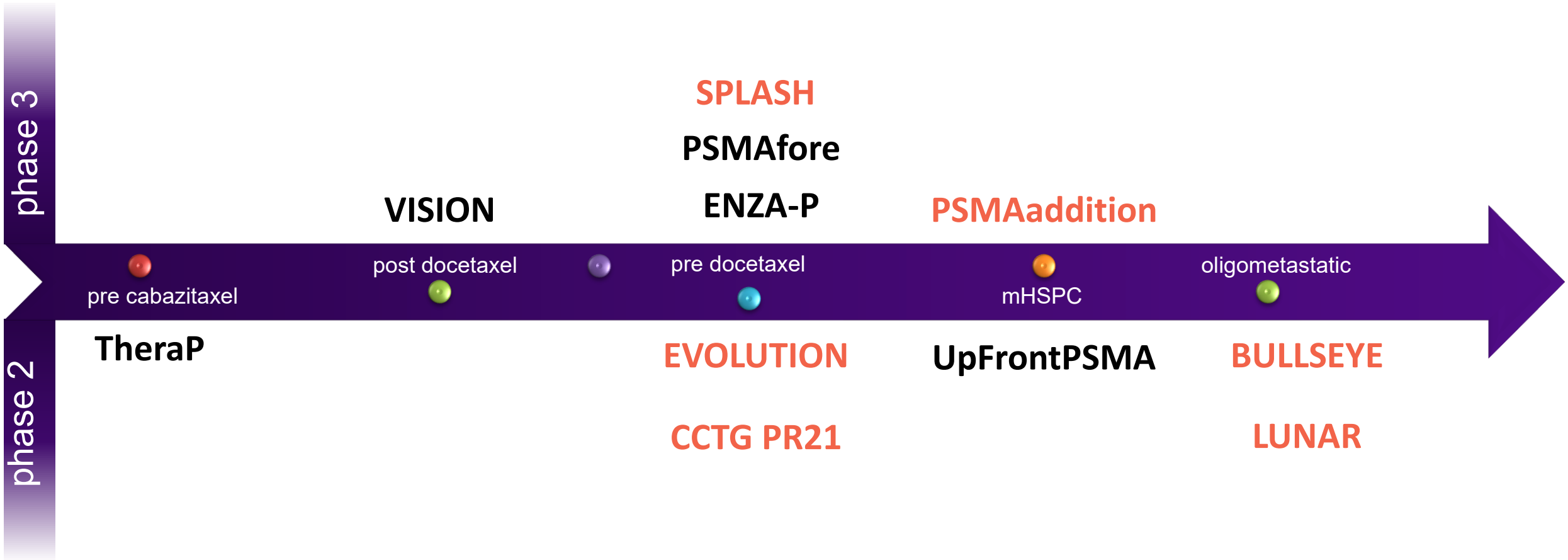
Azad A et al, Lancet Oncology **2024**
https://doi.org/10.1016/s1470-2045(24)00440-6

PROSTATE CANCER FOUNDATION PCF CURING TOGETHER

#PCFRetreat25

Thirty-Second Annual Prostate Cancer Foundation SCIENTIFIC RETREAT

Landmark Randomised Trials in 2025



ProsTIC

Prostate Theranostics Imaging Centre of Excellence

The Next 25 Years
Beginning the End of Cancer

Prostate Cancer Foundation
Curing Together.



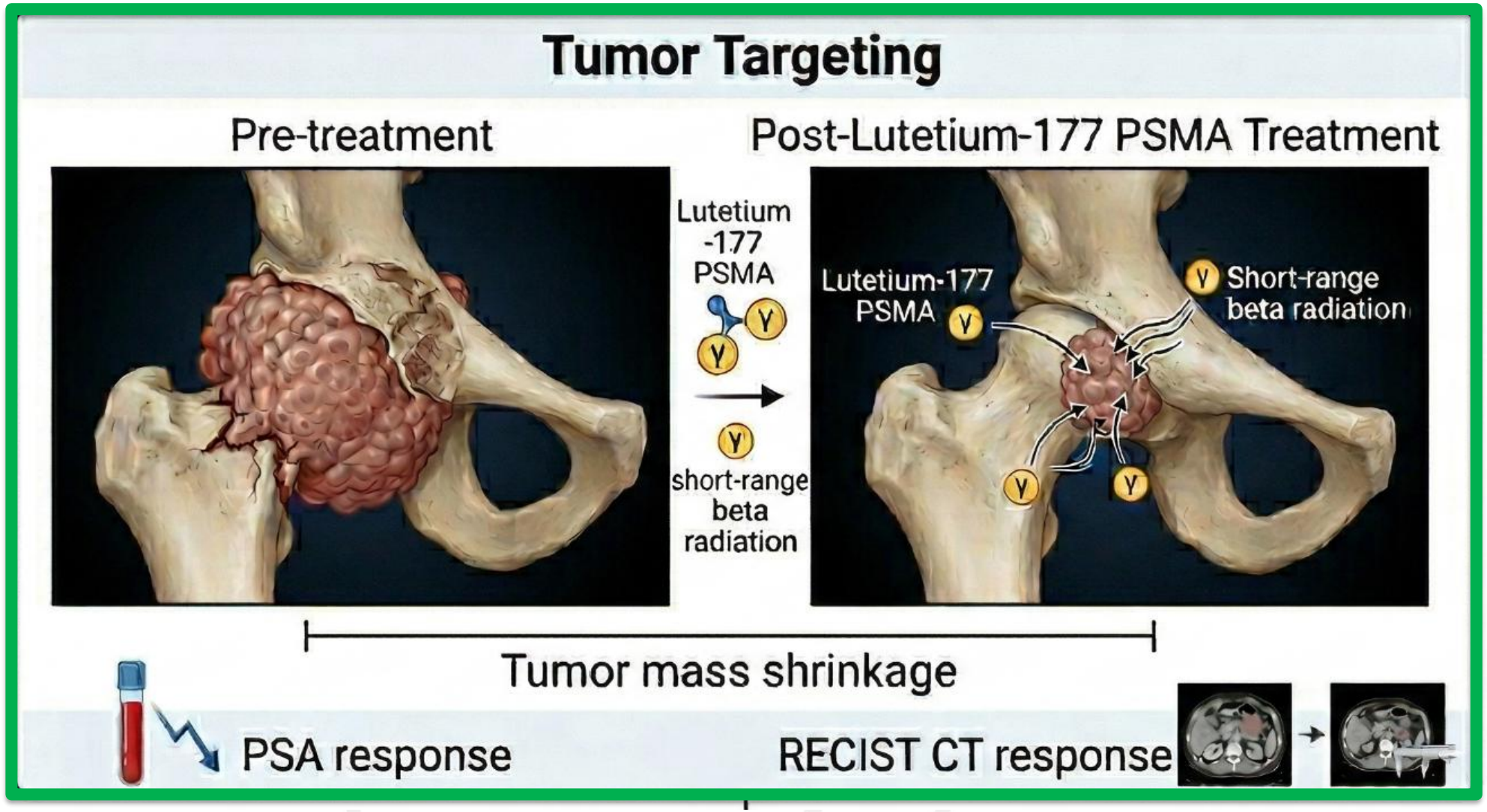
Education & Leadership

Discovery Research

Prostate Theranostics & Imaging Clinical Trials

- **Enable world-class research & innovation; >10 practice-changing clinical trials**
- **Defer ineffective and expensive therapies**
- **https://www.petermac.org/prostic**

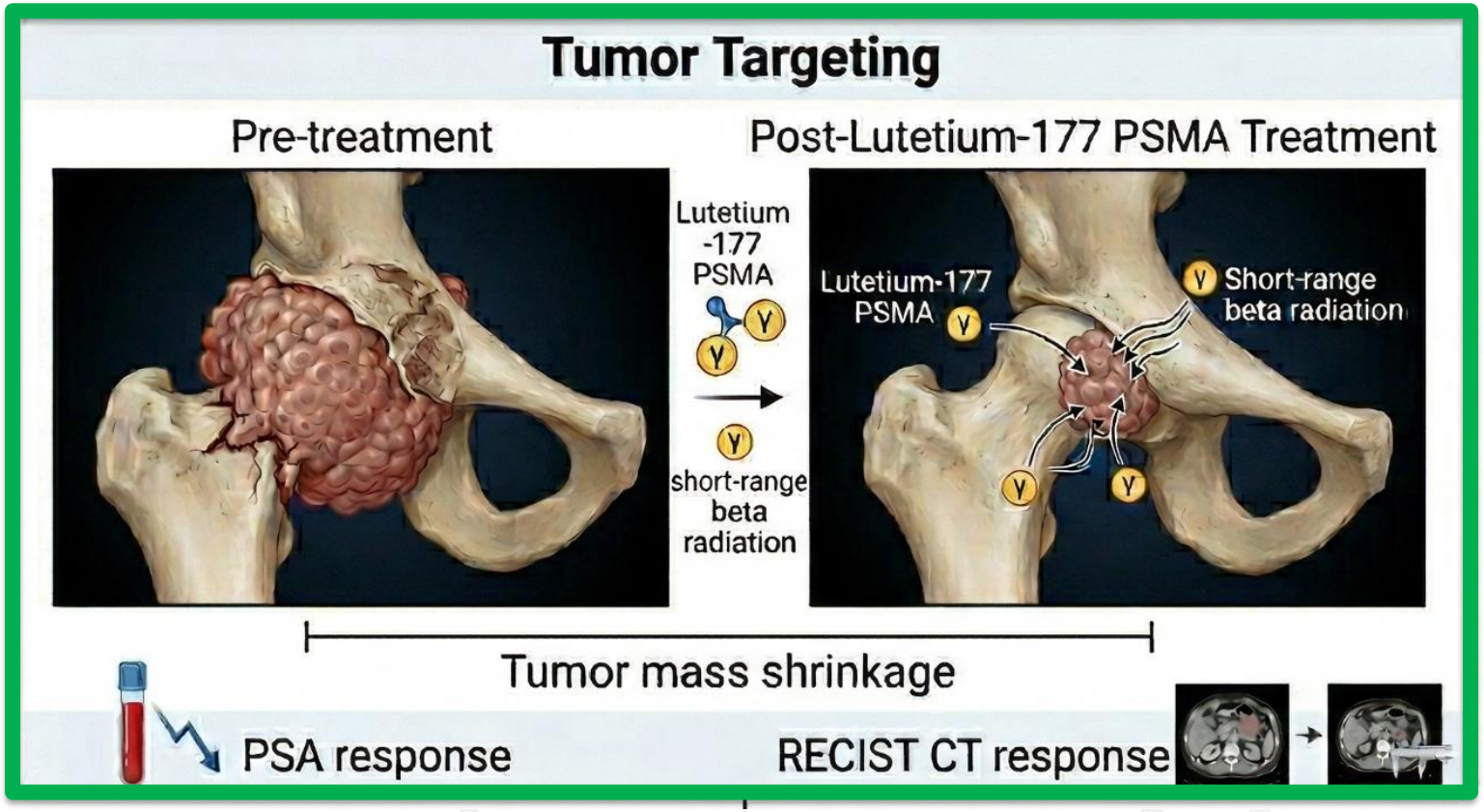
Tumor Targeted ^{177}Lu is Very Effective



Gemini

@DrMHofman

? Less Effective at Stopping New Metastases





✓ ^{177}Lu-PSMA

✓ Taxane Chemo

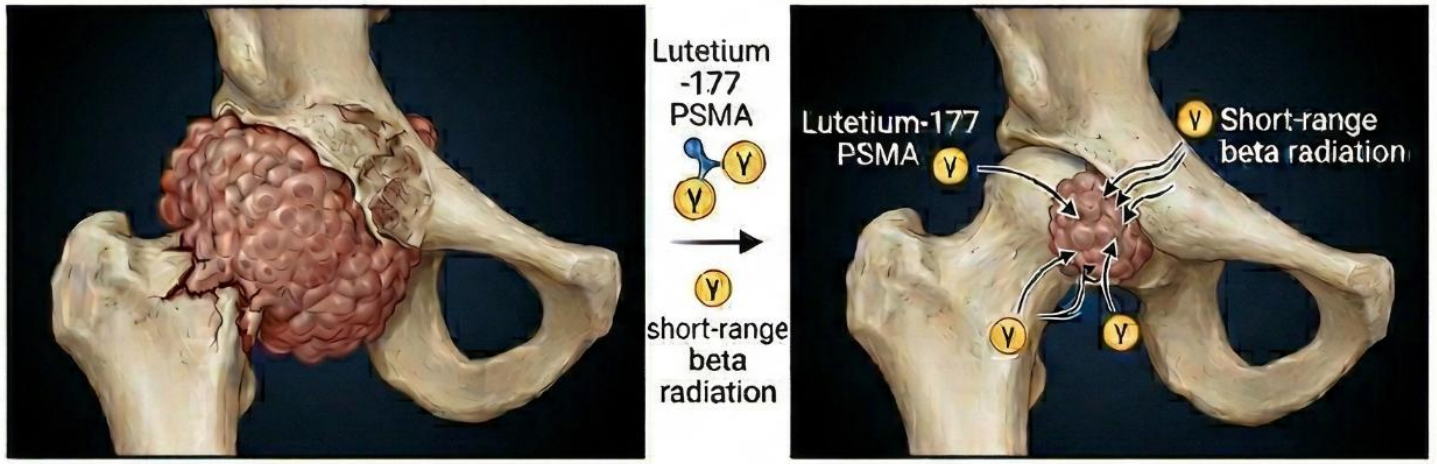
Gemini

@DrMHofman

Tumor Targeting

Pre-treatment

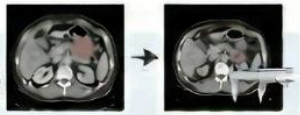
Post-Lutetium-177 PSMA Treatment



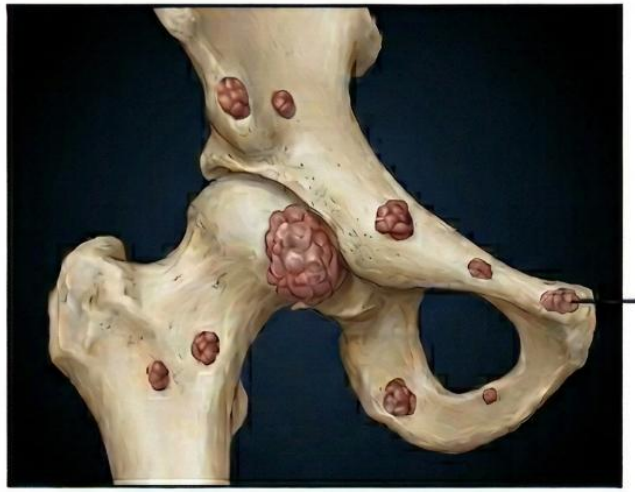
Tumor mass shrinkage

PSA response

RECIST CT response



New Metastasis Formation



Progressing new small tumors



Radiographic PFS



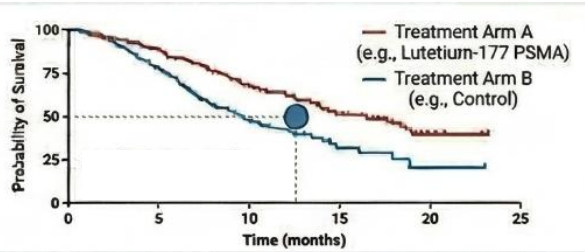
Patient Reported Outcomes (Live Better)





Overall Survival (Live Longer)

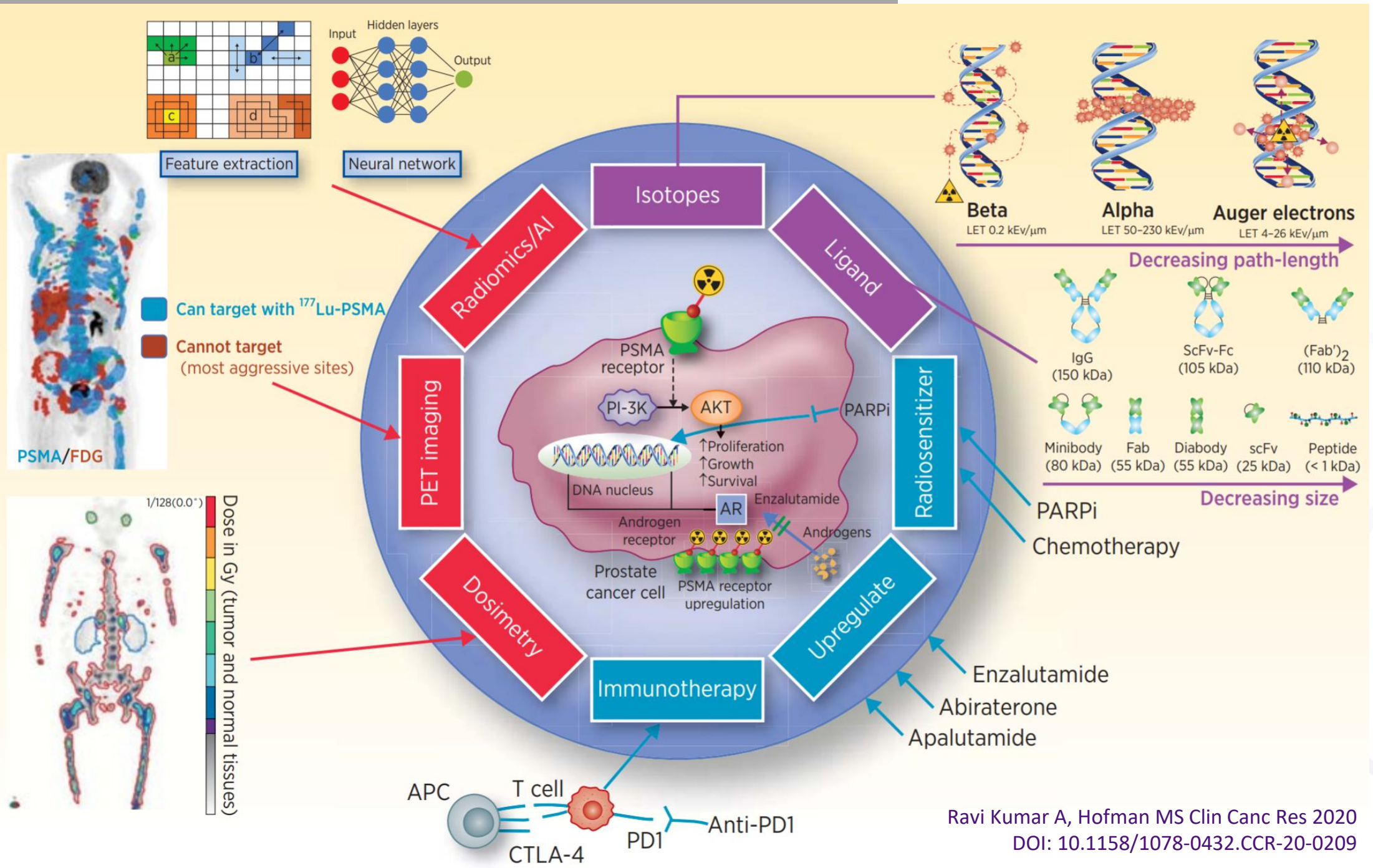




Gemini

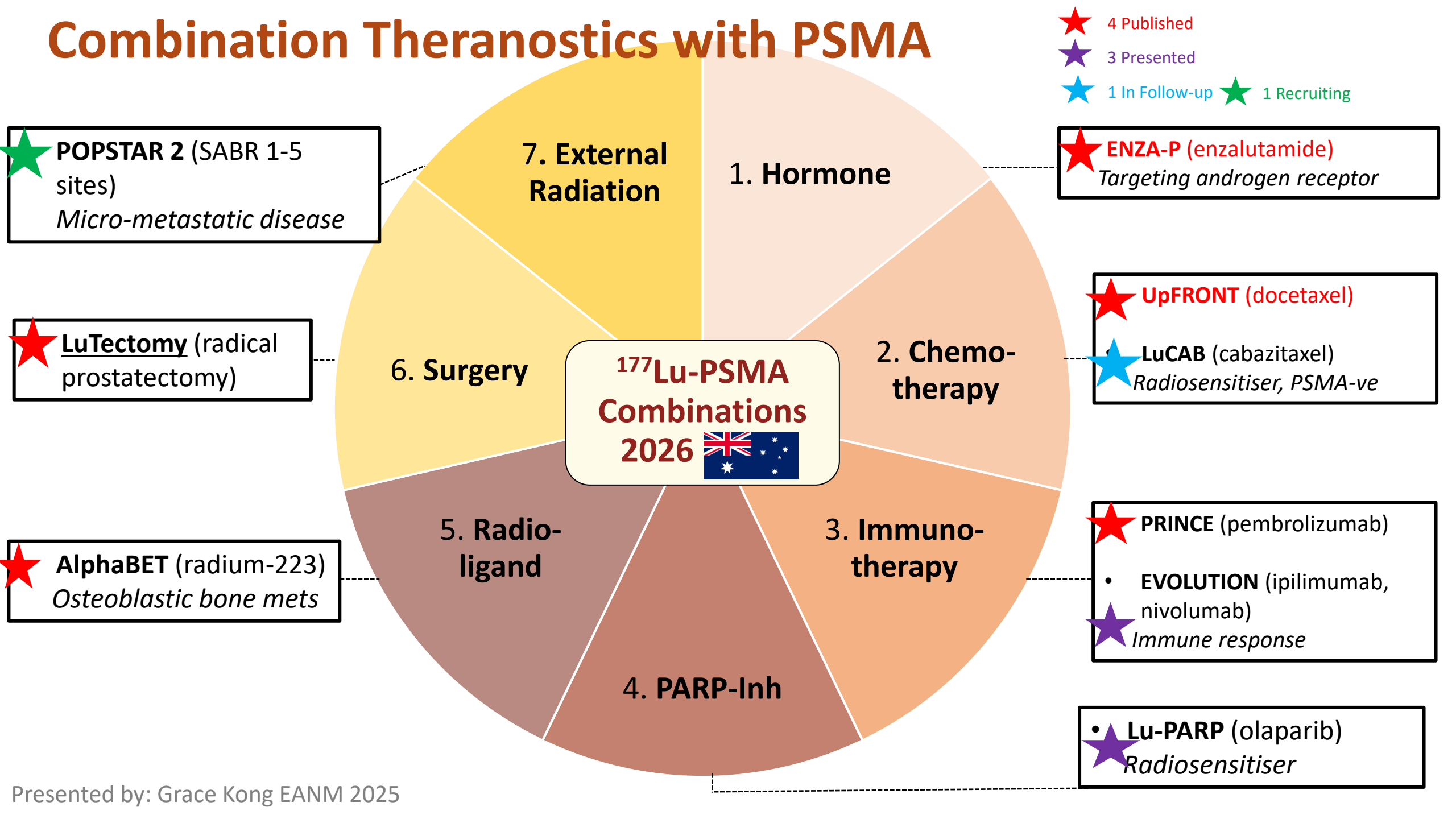
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Advancing PSMA theranostics



Ravi Kumar A, Hofman MS Clin Canc Res 2020
DOI: 10.1158/1078-0432.CCR-20-0209

Combination Theranostics with PSMA



Presented by: Grace Kong EANM 2025

ANZUP 1901

ENZA-P

Randomised Phase II trial

ANZUP Cancer Trials Group Limited

Lutetium-177-PSMA

as a therapeutic target and prognostic indicator

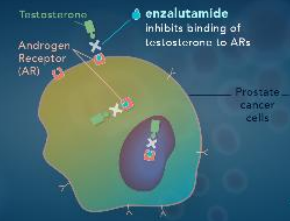
in men with metastatic castration-resistant prostate cancer (mCRPC) treated with

enzalutamide

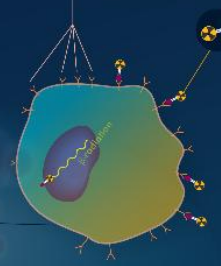
Why this trial?

enzalutamide is a potent **androgen receptor (AR) inhibitor**.

It improves survival in men with metastatic prostate cancer. However, acquired resistance is common.



Prostate specific membrane antigen (PSMA) are expressed abundantly on the surface of prostate cancer cells.



Lu-PSMA-617 is a radiolabelled small molecule that delivers β radiation to cells expressing PSMA.

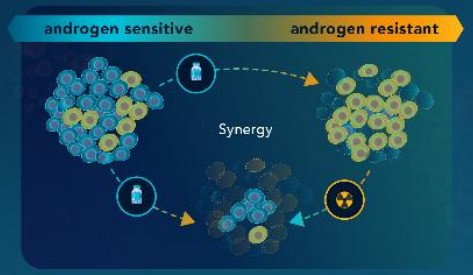
It improves overall survival and is well tolerated in men with CRPC who have progressed despite chemotherapy.

Androgen resistant cells upregulate PSMA expression with androgen blockade, and

reduced PSMA expression following Lu-PSMA-617 may improve sensitivity to AR blockade.

Hypothesis

Simultaneously targeting the PSMA and androgen receptors will lead to an improved treatment response, extending the time men benefit from treatment.



Objectives

1. Determine if the addition of adaptive doses of Lu PSMA to standard enzalutamide effectively addresses treatment resistance.
2. Determine the safety and efficacy of the combined treatments.
3. Develop predictive and prognostic biomarkers to better guide treatment decisions.

Schema

162 participants

Median age: 71

Eligibility

- Confirmed mCRPC with rising PSA and >5ng/mL
- No prior chemotherapy for mCRPC
- Baseline PSMA SUV max ≥ 10 on ^{68}Ga PSMA PET/CT
- ≥ 2 high risk features for early failure on enzalutamide

Randomised 1:1

Enzalutamide 160 mg once daily until disease progression or unacceptable toxicity

Enzalutamide 160 mg once daily + **Lu-PSMA** Adaptive dosing

PSMA / FDG PET	Blood	Tissue biopsy	Baseline
PSMA / PET			Day 15
PSMA / PET	Blood		Day 92
PSMA / FDG PET	Blood	Tissue biopsy	At progression

SPECT scan after each injection

Lu-PSMA 7.5 Gbq

Lu-PSMA 7.5 Gbq

2 to 4 doses dependent on PSMA / PET

Lu-PSMA 7.5 Gbq

Lu-PSMA 7.5 Gbq

Outcomes

Median follow up: **19 months**

1

Progression Free Survival (PFS)

enzalutamide: **7.8 months**

enzalutamide + Lu-PSMA: **13 months**

Radiographic PFS (rPFS)

enzalutamide: **12 months**

enzalutamide + Lu-PSMA: **16 months**

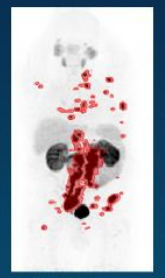
2

PSA Response Rate

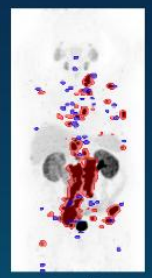
	enzalutamide	enzalutamide + Lu-PSMA
≥ 50% reduction	68%	93%
≥ 90% reduction	37%	78%
Adverse Events	35%	33%

3

Translational research



Baseline



Day 15

Prognostic and predictive biomarkers

Serial quantified molecular imaging with matched timepoint circulating tumor cell and ctDNA analysis will allow comprehensive evaluation of composite biomarkers to develop tools to better guide and personalise treatment decisions.

Sept. 2023 © Louise Emmet
In collaboration of ANZUP, NHMRC Clinical Trials Centre at the University of Sydney

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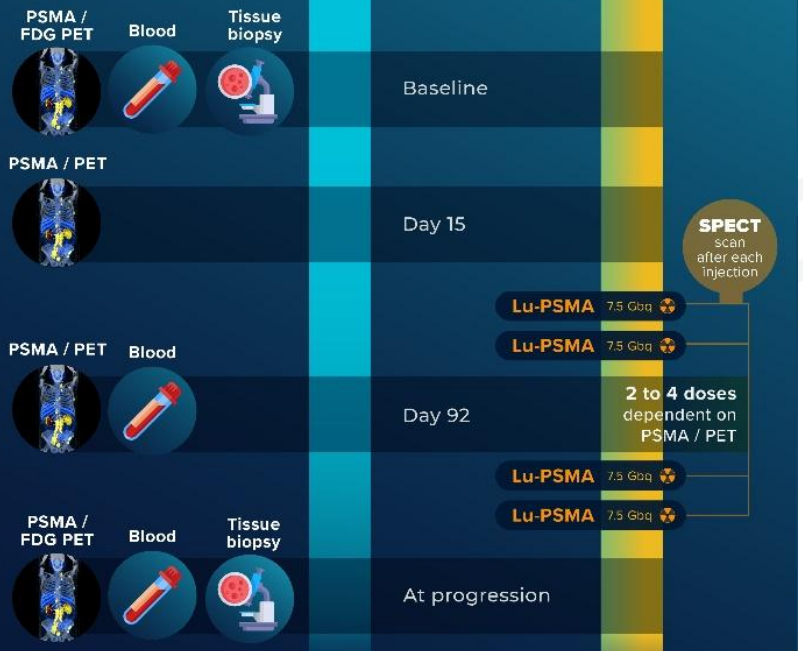
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Randomised 1:1

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Enzalutamide 160 mg once daily + **Lu-PSMA** Adaptive dosing

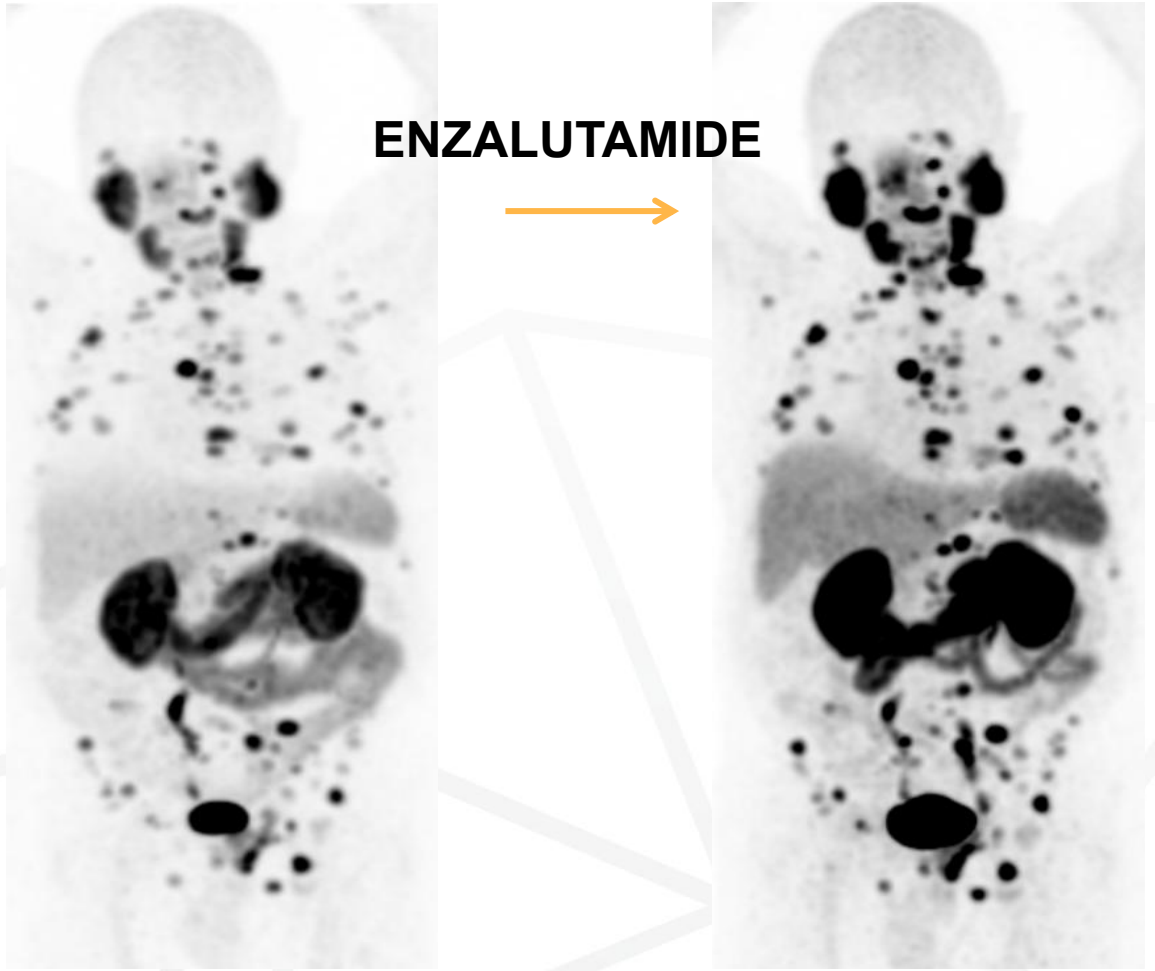


Upregulation of PSMA

PSA 140

ENZALUTAMIDE →

PSA ↓ 98



baseline

D+15

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@drlouiseemmett

Upregulation of PSMA

PSA 140

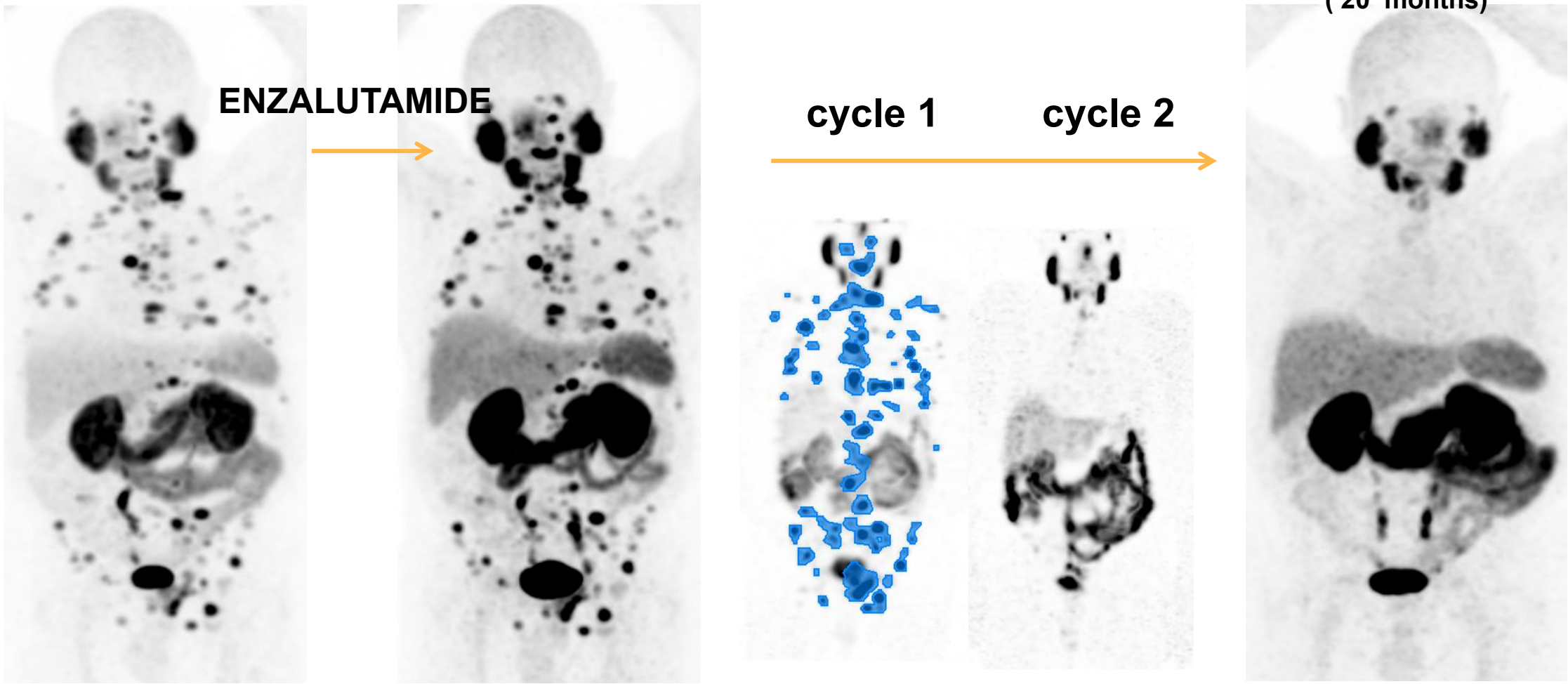
PSA ↓ 98

ENZALUTAMIDE

cycle 1

cycle 2

PSA < 0.02
(20 months)



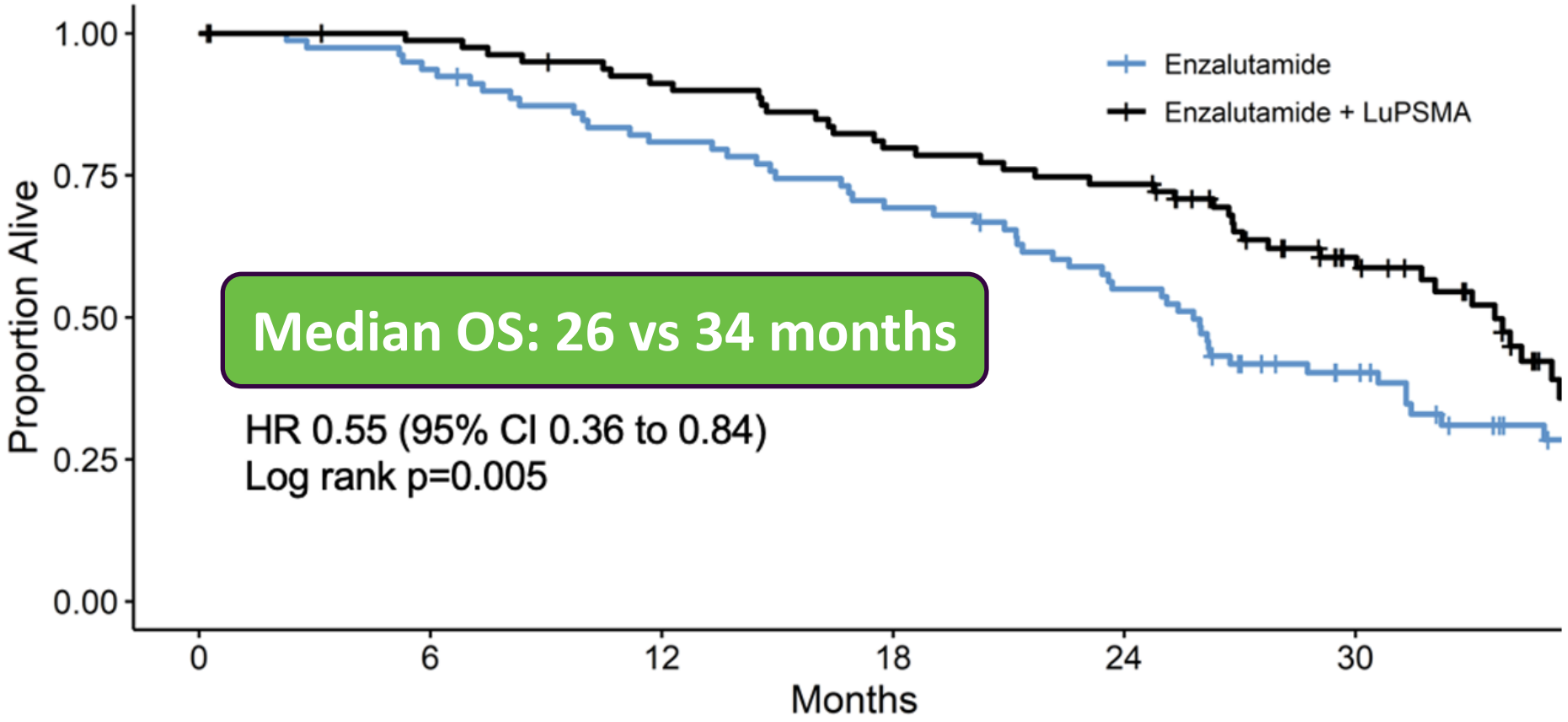
baseline

D+15

D+92

ENZA-P: survival improved with ^{177}Lu-PSMA-617

ASCO Genitourinary Cancers Symposium #GU25

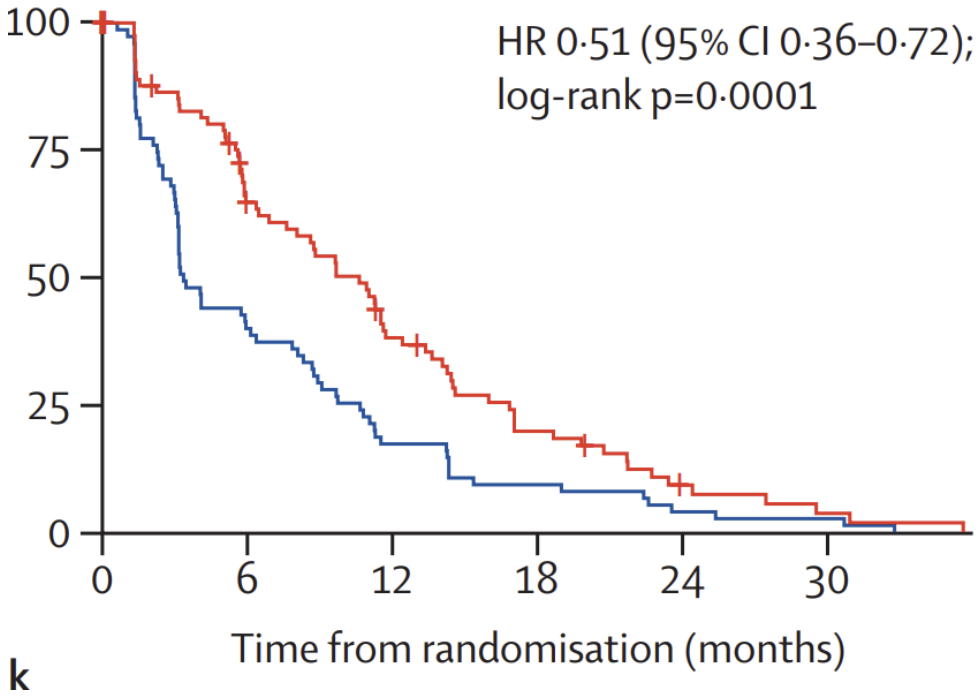


Emmett L, *Lancet Oncology* 2025
doi: 10.1016/ S1470-2045(25)00009-9

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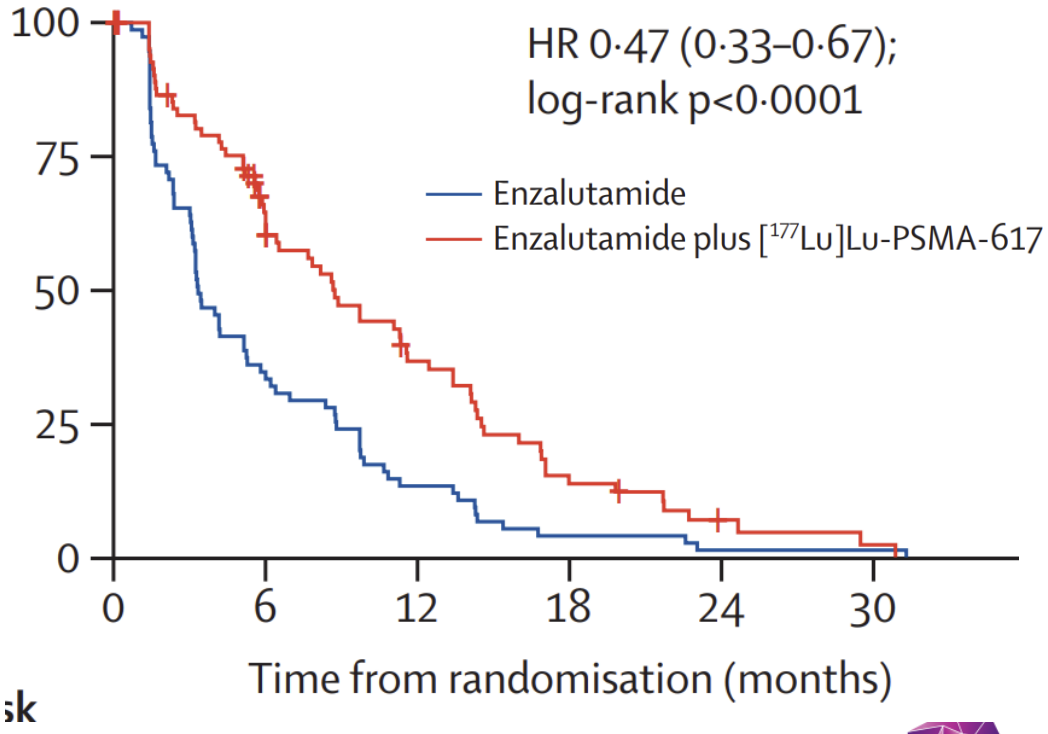
ENZA-P: liver longer with better quality-of-life

Physical Functioning



k

Overall Health Status

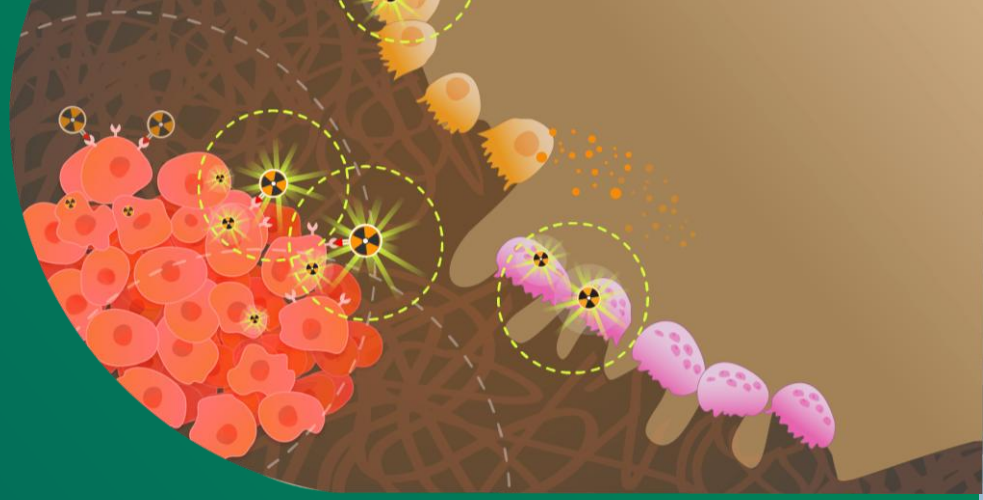


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Emmett L, *Lancet Oncology* **2025**
doi: 10.1016/ S1470-2045(25)00009-9

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Victoria Australia

αLPHA βET



Single-centre, single-arm phase I/II study

Combined Radium-223 (^{223}Ra) and [^{177}Lu]Lu-PSMA-I&T

in patients with metastatic castration-resistant prostate cancer (mCRPC)

Kostos L, …, Hofman MS, Lancet Oncology 2025
https://www.thelancet.com/article/S1470-2045(25)00559-5/

Funding:

PROSTATE CANCER FOUNDATION
PCF
CURING TOGETHER

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ProsTIC
Prostate Theranostics Imaging Centre of Excellence

@DrMHofman
@LouiseKostos

FPN 2386P

αLPHA βET

Single-centre, single-arm phase I/II study

NCT05383079

Co-authors: Louise Kostos, James P Buteau, Jing Xie, Anthony Cardin, Tim Akhurst, Ramin Alipour, Lewis Au, Joanna Chan, Kwang Y Chin, Brittany Emmerson, Luc Furic, Quinn Garcia, Anthony J Hamilton, Mohammad B Haskali, Price A Jackson, Raghava K Kashyap, Grace Kong, Lisa MacFarlane, Prof Declan G Murphy, Prof Belinda S Parker, Aravind S Ravi Kumar, Javad Saghebi, Yang Wang, Ben Tran, Prof Arun A Azad*, Prof Michael S Hofman*

Peter MacCallum Cancer Centre, Melbourne, Australia
University of Melbourne, Melbourne, Australia

*co-senior authors

Published in
THE LANCET Oncology

WHY THIS TRIAL?

^{177}Lu-PSMA and **^{223}Ra** are approved life-prolonging therapies for mCRPC, but resistance and progression, particularly in bones, are common.

^{223}Ra, a bone-seeking **alpha emitter**, has a shorter path length and higher linear energy transfer than **beta emitters** such as **^{177}Lu**, and may be better suited for targeting micrometastatic osseous disease.



TRIAL DESIGN

36 patients

Key eligibility
- Progressive mCRPC after ≥1 ARPI
- ≥2 untreated bone metastases on bone scan
- PSMA-PET positive disease (SUVmax ≥20) with no discordance (FDG-positive with minimal PSMA and bone scan uptake)
- ECOG performance status 0-2

Phase I
3+3 design
9 patients

Up to **6 cycles**

^{177}Lu-PSMA 7.4 GBq every 6 weeks

+ 2 step dose escalation

^{223}Ra 27.5 kBq/kg every 6 weeks → ^{223}Ra 55 kBq/kg every 6 weeks

RP2D: 55 kBq/kg

Phase II
Dose expansion
Recruitment completed: Nov. 2024
27 patients

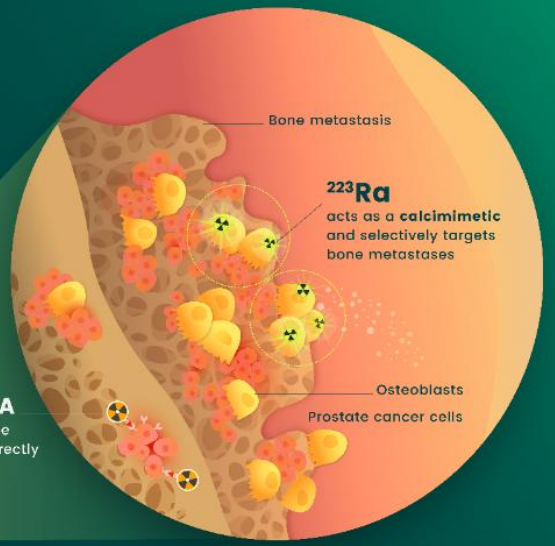
Up to **6 cycles**

^{177}Lu-PSMA 7.4 GBq every 6 weeks + ^{223}Ra 55 kBq/kg every 6 weeks

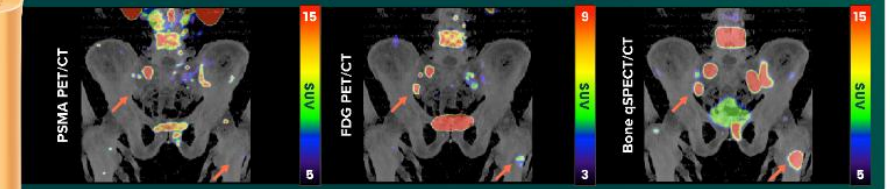
+ Bone protective therapy

The combination of ^{177}Lu-PSMA-I&T and Radium-223 is safe and feasible in patients with mCRPC and bone metastases





Patient with discordant FDG-positive, PSMA-negative osseous metastases that were bone scan-positive, meeting eligibility criteria



RESULTS

Median follow-up: **13.3 months**
Data cut-off: 29th January 2025
5 patients still receiving treatment

53% received **prior docetaxel**

No dose-limiting toxicities

14% experienced **Grade ≥3 treatment-related adverse events**
- Anemia (n=4)
- Neutropenia (n=3)
- Lymphopenia (n=10)
- **No deaths**

PSA50-RR
55%
[95% CI 36 – 72]

PSA90-RR
18%
[95% CI 7 – 35]

Median PSA-PFS
5.3 months
[95% CI 4.0 – 9.0]

Radiographic PFS
10 months
[95% CI 6.7 – 13.5]

Kostos L et al. Front Med (Lausanne) 2022; doi: 10.3389/fmed.2022.1053122

Funding statement: This investigator-initiated trial is funded by a Special Challenge Award from the **Prostate Cancer Foundation (PCF)**, and a **National Health and Medical Research Council (NHMRC)** Investigator Grant. **Bayer** supplied radium-223 and provided funding. The Australian Nuclear Science and Technology Organisation (ANSTO) supplied no carrier added Lu-177.

Disclosure statement from first author: **Louise Kostos** has received honoraria for speaker duties from Bayer, Astrazeneca and Astellas, and from Bayer for participation in an Advisory Board.

Prof Michael Hofman, michael.hofman@petermac.org
Prof Arun Azad, arun.azad@petermac.org

PCF

ProsTIC
Prostate Theranostics Imaging Centre of Excellence

^{177}Lu-PSMA
targets prostate
cancer cells directly

Osteoblasts

Prostate cancer cells

PSA -50%

PSA -90%

Patient with discordant FDG-positive, PSMA-negative osseous metastases that were bone scan-positive, meeting eligibility criteria



rostate Cancer Foundation (PCF), and a **National Health and Medical Research Council (NHMRC)** Investigator Grant.
e and Technology Organisation (ANSTO) supplied no carrier added Lu-177
Bayer, Astrazeneca and Astellas, and from Bayer for participation in an Advisory Board.

Prof Michael Hofman, michael.hofman@petermac.org
Prof Arun Azad, arun.azad@petermac.org

PROSTATE CANCER FOUNDATION
PCF

Outcomes

ALPHABET

FIRST INTERIM ANALYSIS

Median follow-up: 13.3 months

5 patients still receiving treatment

53% received prior docetaxel

No dose-limiting toxicities

14% experienced a Grade ≥ 3 TRAE

- Anaemia (n = 4)
- Neutropaenia (n = 3)
- Lymphopaenia (n = 10)
- No deaths

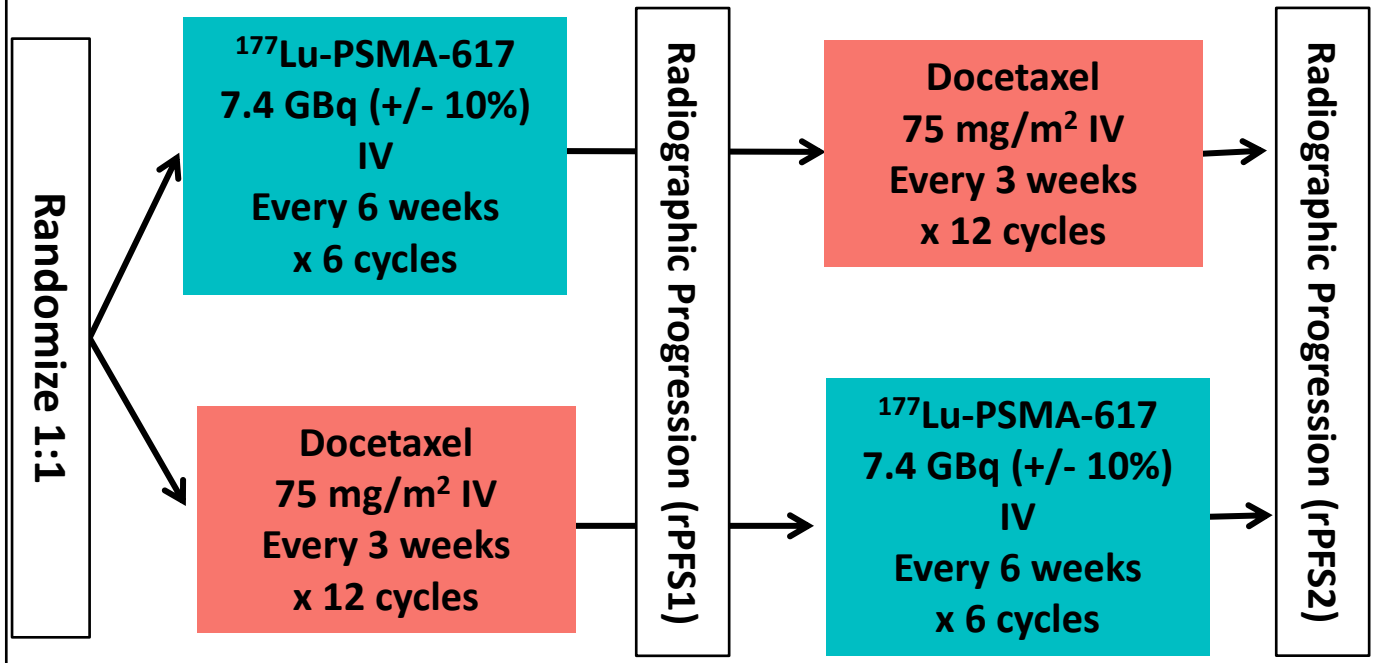
PSA50-RR	**55%** [95%CI 36 - 72]
PSA90-RR	**18%** [95%CI 7 - 35]
PSA-PFS	**5.3 months** **[95% CI 4.0-9.0]**
rPFS	**10.0 months** **[95% CI 6.7-13.5]**
OS	**13.5 months** [95%CI 9.9-NE]

Canadian Cancer Trials Group (CCTG) PR21

Key Eligibility

- Chemotherapy-naïve mCRPC progressing after ARPI
- PSMA PET positive (uptake >liver)
  - Excluded if >50% of extra-osseous lesions or >5 cm soft tissue lesion were PSMA negative
- ANC ≥ 1.5 x 10^9/L
- Platelet count ≥ 100 x 10^9/L
- Hemoglobin ≥ 90 g/L
- CrCl ≥ 30 ml/min
- Bilirubin < 1.5 x ULN
- ALT < 3.5 x ULN (<5 x UN for liver metastases)
- ECOG PS of 0 - 2
- Prior docetaxel for mHSPC permitted if ≥12 months prior

Open label randomized phase II with cross-over



Stratification factors:

- ECOG PS (0-1 vs 2)
- LDH (>ULN, yes vs no)
- Visceral metastases (yes vs no)
- Prior docetaxel for mHSPC (yes vs no)

Primary Objective

- Radiographic Progression Free Survival (rPFS1)

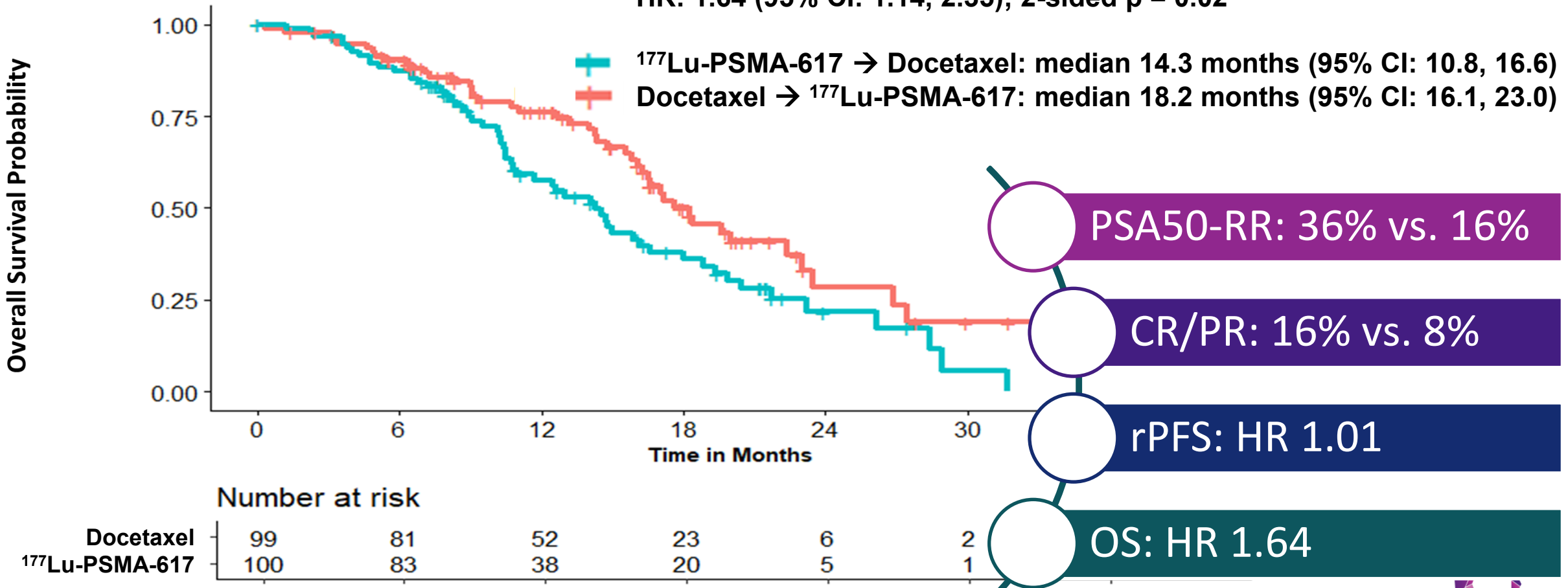
Additional Objectives

- Overall survival
- rPFS2
- PSA decline
- Adverse events
- PRO QoL
- Correlative studies

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

Chi KN et al, ESMO 2025

CCTG PR21: better responses with Lu-PSMA but…



- PSA50-RR: 36% vs. 16%
- CR/PR: 16% vs. 8%
- rPFS: HR 1.01
- OS: HR 1.64

Chi KN et al, ESMO 2025

LUCAB

A Phase I/II investigator-initiated trial

Evaluating [^{177}Lu]Lu-PSMA-617 in combination with cabazitaxel in patients with metastatic castration-resistant prostate cancer (mCRPC)

WHY THIS TRIAL?

[^{177}Lu]Lu-PSMA-617 (^{177}Lu-PSMA) and **cabazitaxel** are both approved, life-prolonging treatments for mCRPC. Despite this, disease progression remains inevitable and many patients are unable to proceed to subsequent lines of treatment.

Concurrent cabazitaxel may improve ^{177}Lu-PSMA efficacy by overcoming heterogeneous PSMA expression and enhancing radiation damage as a radiosensitiser.

TRIAL DESIGN

35 patients treated in total

Key eligibility

- Progressive mCRPC
- PSMA-PET positive disease (SUVmax ≥15) with no discordance on FDG-PET
- Prior exposure to docetaxel and ≥1 androgen receptor pathway inhibitor
- Adequate bone marrow, renal and hepatic function
- ECOG performance status 0-1

Phase I – 3+3 design
Dose escalation

15 patients

Up to **6 cycles**

^{177}Lu-PSMA
7.4 GBq
IV 6 weekly

+

cabazitaxel
Up to 12 doses
IV 3-weekly
Prophylactic G-CSF given after each dose

4 planned dose levels

12.5 mg/m²	(n=3)
15 mg/m²	(n=3)
17.5 mg/m²	(n=3)
20 mg/m²	(n=6)

First dose of cabazitaxel one day after ^{177}Lu-PSMA

No dose-limiting toxicity

Cabazitaxel RP2D: 20mg/m²

Phase II
Dose expansion

Recruitment completed in February 2025

20 patients

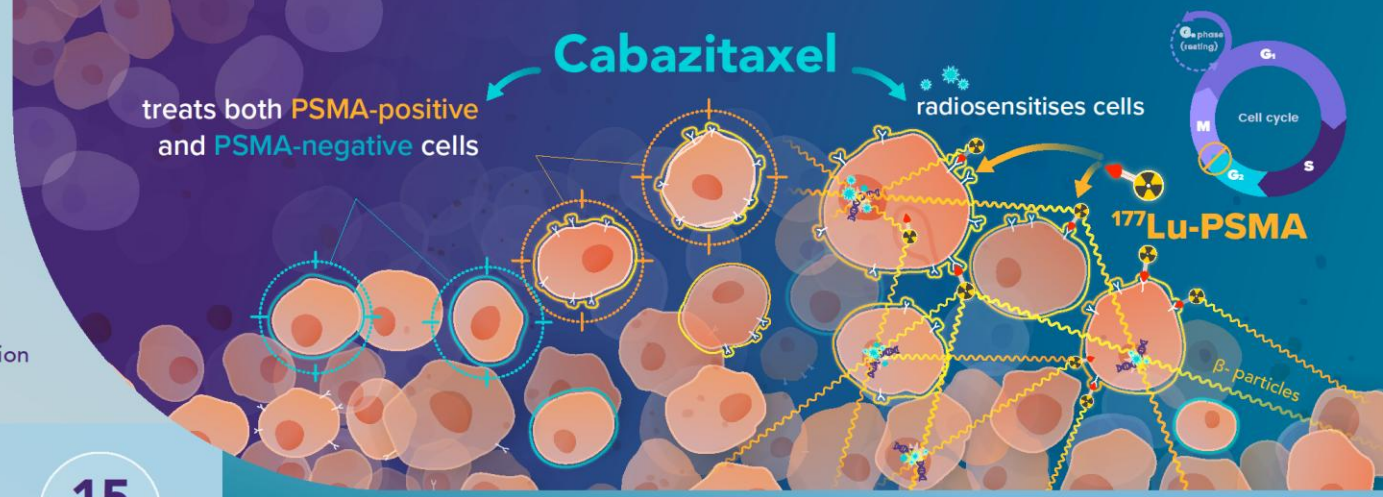
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^{177}Lu-PSMA
7.4 GBq
IV 6 weekly

+

cabazitaxel
IV 3-weekly
Prophylactic G-CSF given after each dose

20 mg/m²



RESULTS

Median follow-up: **20.4 months**
Safety analysis: n=34
Efficacy analysis: n=26 (RP2D cohort)

71% had de novo metastatic disease

29% had M1c disease at baseline

No dose-limiting toxicities

24% experienced **clinically significant Grade ≥3 treatment-related adverse events**

- neutropaenia (n=2)
- anaemia (n=2)
- weight loss (n=1)
- diarrhoea (n=1)
- fatigue (n=1)
- urinary tract infection (n=1)
- **No deaths**

PSA50-RR	**73%** [95% CI 54– 86]
PSA90-RR	**42%** [95% CI 26 – 61]
Median PSA-PFS	**8.5 months** [95% CI 4.8– 12.1]
Radiographic PFS	**10.9 months** [95% CI 10.2 - 13.4]
Overall Survival	**16.5 months** [95% CI 13.4 - 21.8]

The combination of ^{177}Lu-PSMA and cabazitaxel is feasible and safe in heavily pre-treated patients with mCRPC, with encouraging anti-tumour activity.

The findings support further evaluation in a randomised clinical trial.

Accepted in THE LANCET Oncology

We thank the trial participants and their families, trial coordinators, principal investigators and co-investigators at the Peter MacCallum Cancer Centre for making this study possible.

@DrMHofman - @AzadOncology - @LouiseKostos

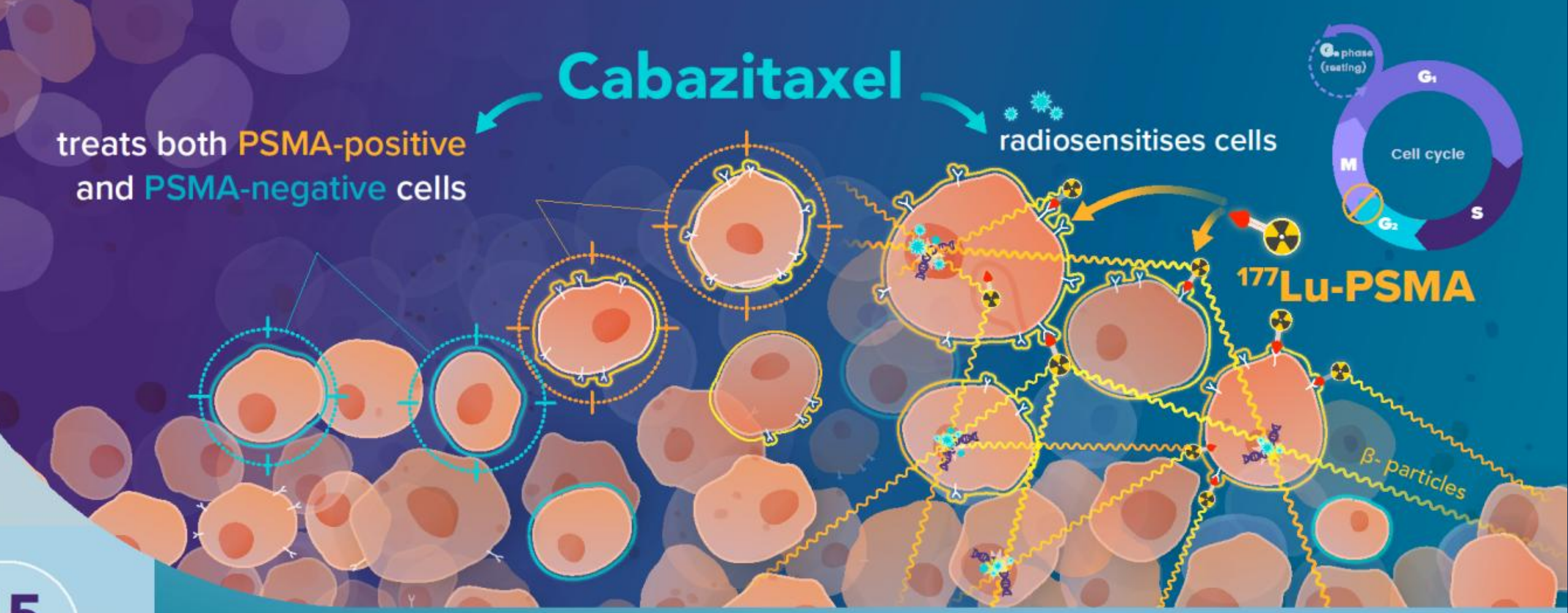
Funding: ProsTIC Prostate Theranostics Imaging Centre of Excellence; PCF Prostate Cancer Foundation

NHMRC Investigator Grants (MSH, AAA)

PCF Young Investigator Award 2026 Louise Kostos

Sponsor: Peter Mac Peter MacCallum Cancer Centre Victoria Australia

PSMA-617 was supplied by Novartis who additionally provided financial support.



5
ients

ose levels
n² (n=3)
(n=3)

RESULTS

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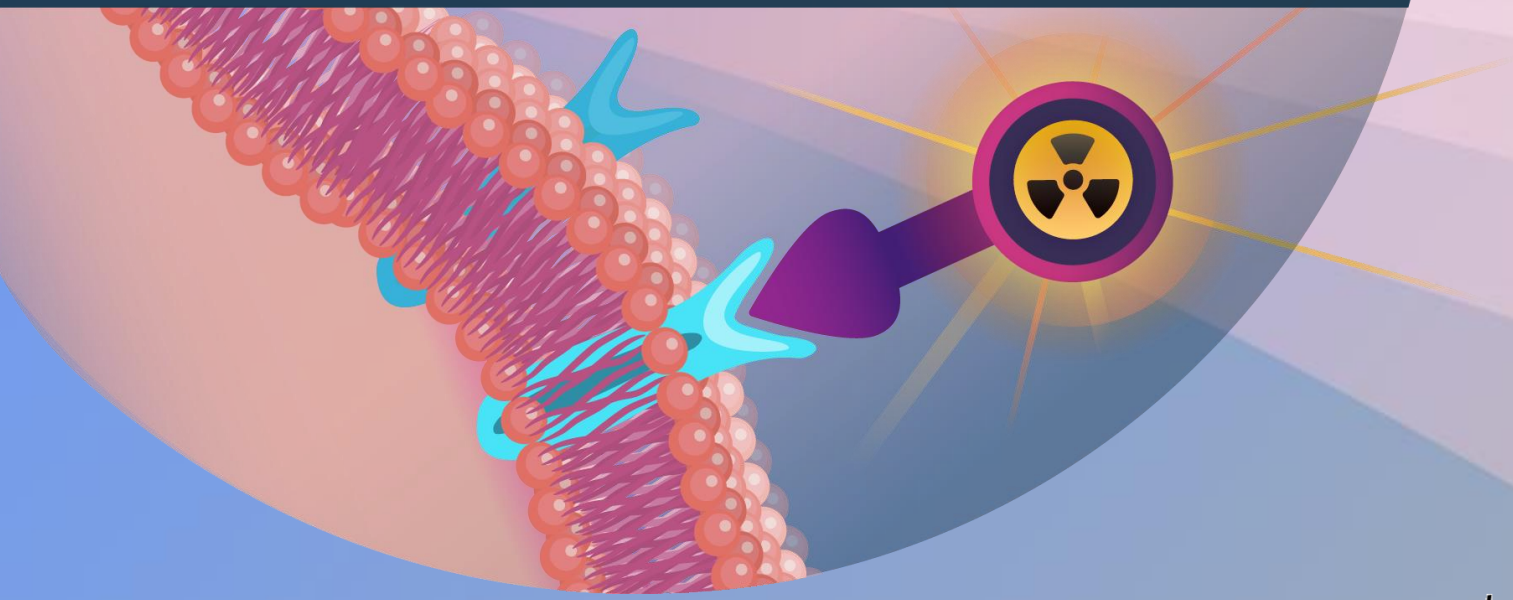
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UpFront PSMA

Phase II study



Sequential [^{177}Lu]Lu-PSMA-617 and docetaxel versus docetaxel in patients with metastatic hormone-sensitive prostate cancer (UpFrontPSMA): a multicentre, open-label, randomised, phase 2 study

Arun A Azad, Mathias Bressel, Hsiang Tan, Mark Voskoboynik, Aneta Suder, Andrew J Weickhardt, Alexander Guminski, Roslyn J Francis, Javad Saghebi, Nattakorn Dhiantravan, Anthony M Joshua, Louise Emmett, Lisa Horvath, Declan G Murphy, Edward Hsiao, Bavanthi Balakrishnar, Peter Lin, Andrew Redfern, William Macdonald, Siobhan Ng, Sze-Ting Lee, David A Pattison, David Nadebaum, Ian D Kirkwood, Michael S Hofman, on behalf of the UpFrontPSMA Study Team*

Sequential ^{177}Lu-PSMA-617 + docetaxel vs docetaxel

in men with newly diagnosed metastatic prostate cancer

A/Prof Arun Azad
& Prof Michael Hofman

Lancet Oncol 2024; published online Sept 15
https://doi.org/10.1016/S1470-2045(24)00440-6

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

ProsTIC
Prostate Theranostics Imaging Centre of Excellence

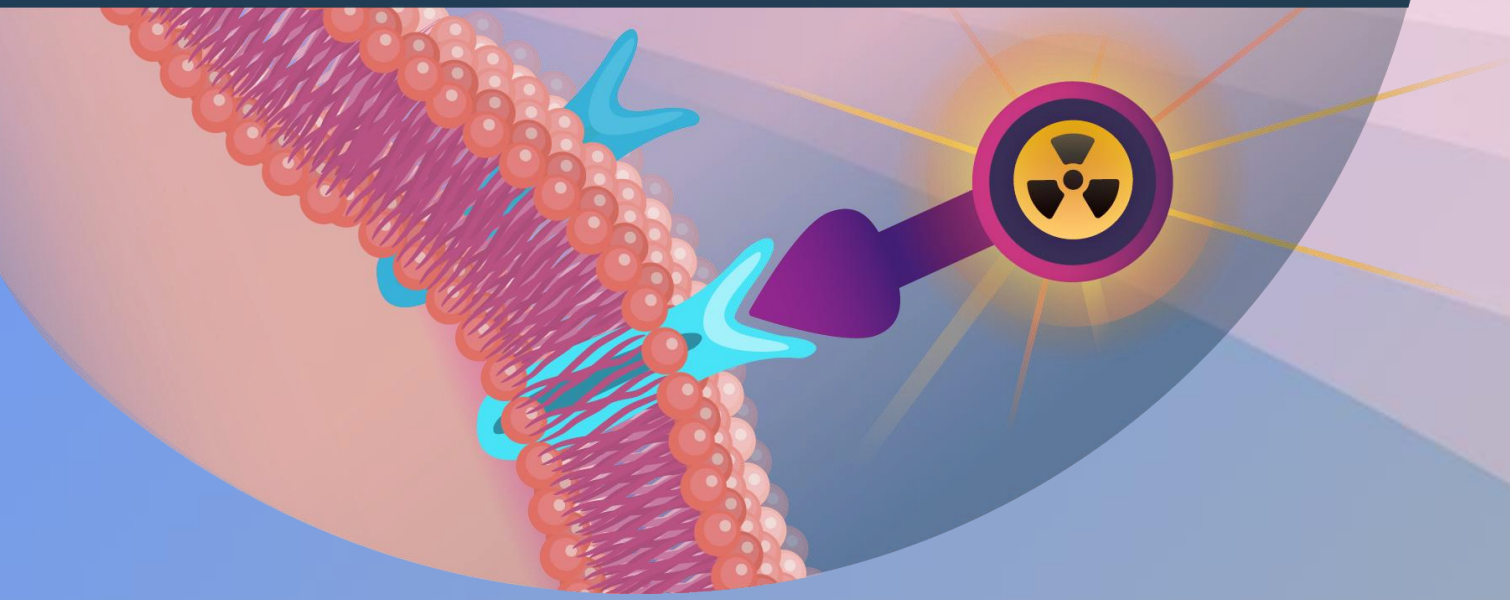
MOVEMBER®
FUNDED PROJECT

CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

clinicaltrials.gov: NCT04343885

UpFront PSMA

Phase II study



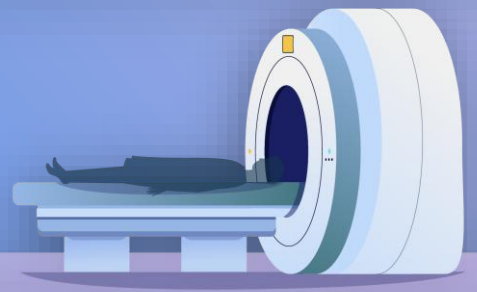
Using PSMA theranostics First-Line rather than Last-Line

UpFrontPSMA

Schema

130 patients
with prostate cancer

- ≤ 12 weeks since diagnosis
- PSA >10 ng/mL at diagnosis
- ≤ 4 weeks on ADT
- metastases on CT and/or bone scan



PET scans x2







Central imaging review

High PSMA tumour uptale + volume disease

Most disease PSMA+

No major discordance

1:1 randomisation

^{177}Lu-PSMA-617 + docetaxel

7.5 GBq
x 2 cycles

75 mg/m^2
x 6 cycles

docetaxel

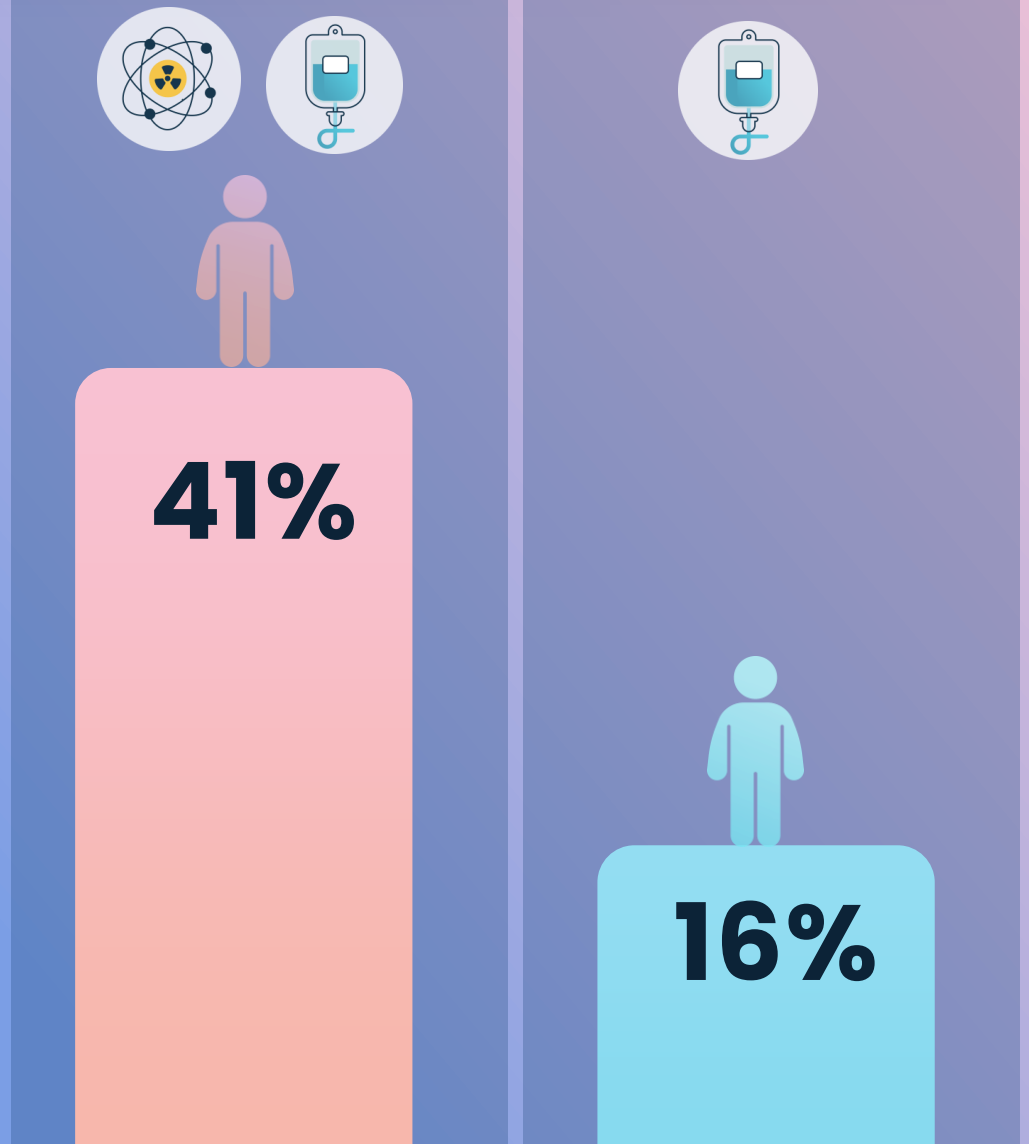
75 mg/m^2
x 6 cycles

UpFrontPSMA

Findings

Undetectable PSA rate a 1 year

(OR 3.9; p=0·002)

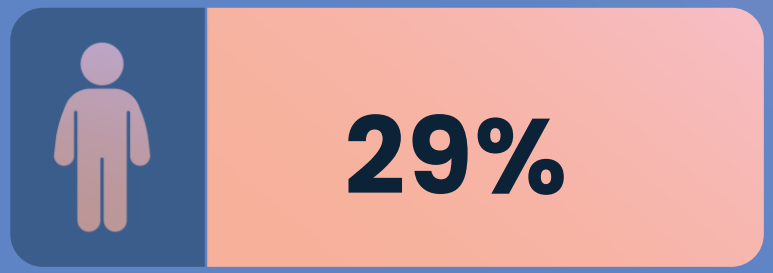


Findings

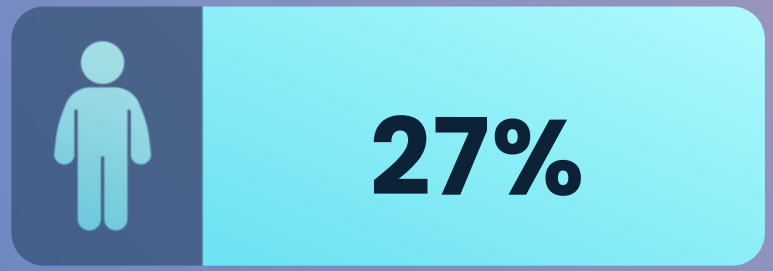
Grade 3 / 4 adverse events

(typically attributable to docetaxel)









Oligometastases & delaying ADT: the final frontier?

LUNAR TRIAL NCT05496959 - STUDY DESIGN

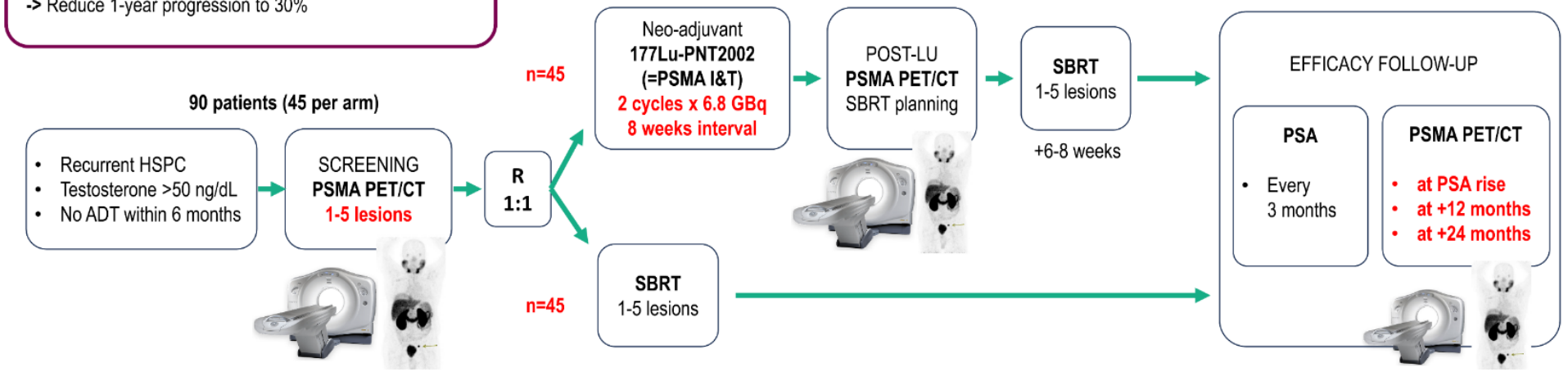
UCLA

Hypothesis:
Adding Lu177-PSMA RLT to SBRT can prolong PFS in patients with oligometastatic recurrent hormone sensitive prostate cancer

Historical data: 1-yr progression rate with SBRT ≈ 50%
Hypothesis 2 cycles of ^{177}Lu-PNT2002 + SBRT:
-> Reduce 1-year progression to 30%

- Single-center randomized, open-label, phase 2 trial
- IIT Supported by POINT biopharma /Lantheus
- PI: Amar U. Kishan (Radiation Oncology), Co-PI: Jeremie Calais (Nuclear Medicine)

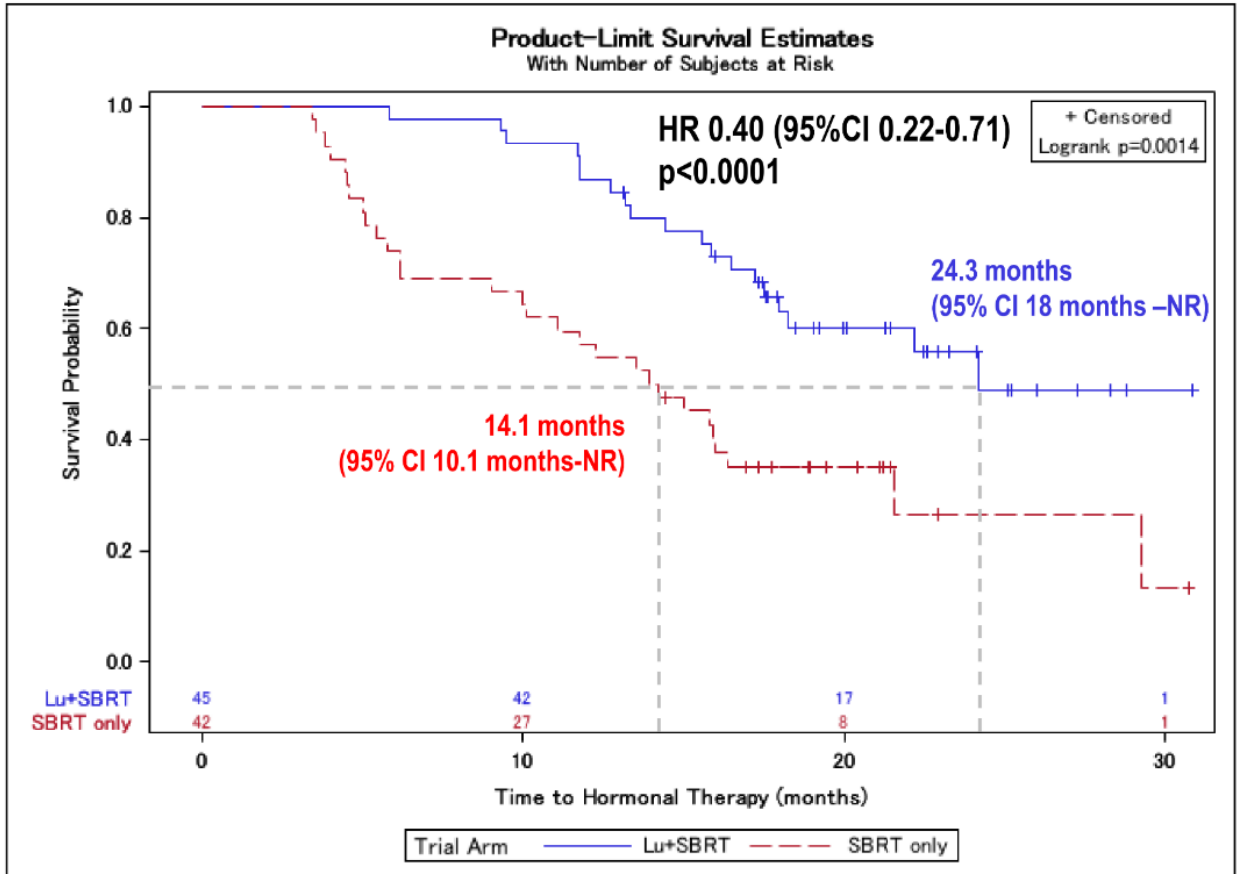
POINT BIOPHARMA LANTHEUS



Ting Martin Ma, …, **Calais J, Kishan AU**, *BJUI* 2023 (protocol)
doi: 10.1111/bju.15988

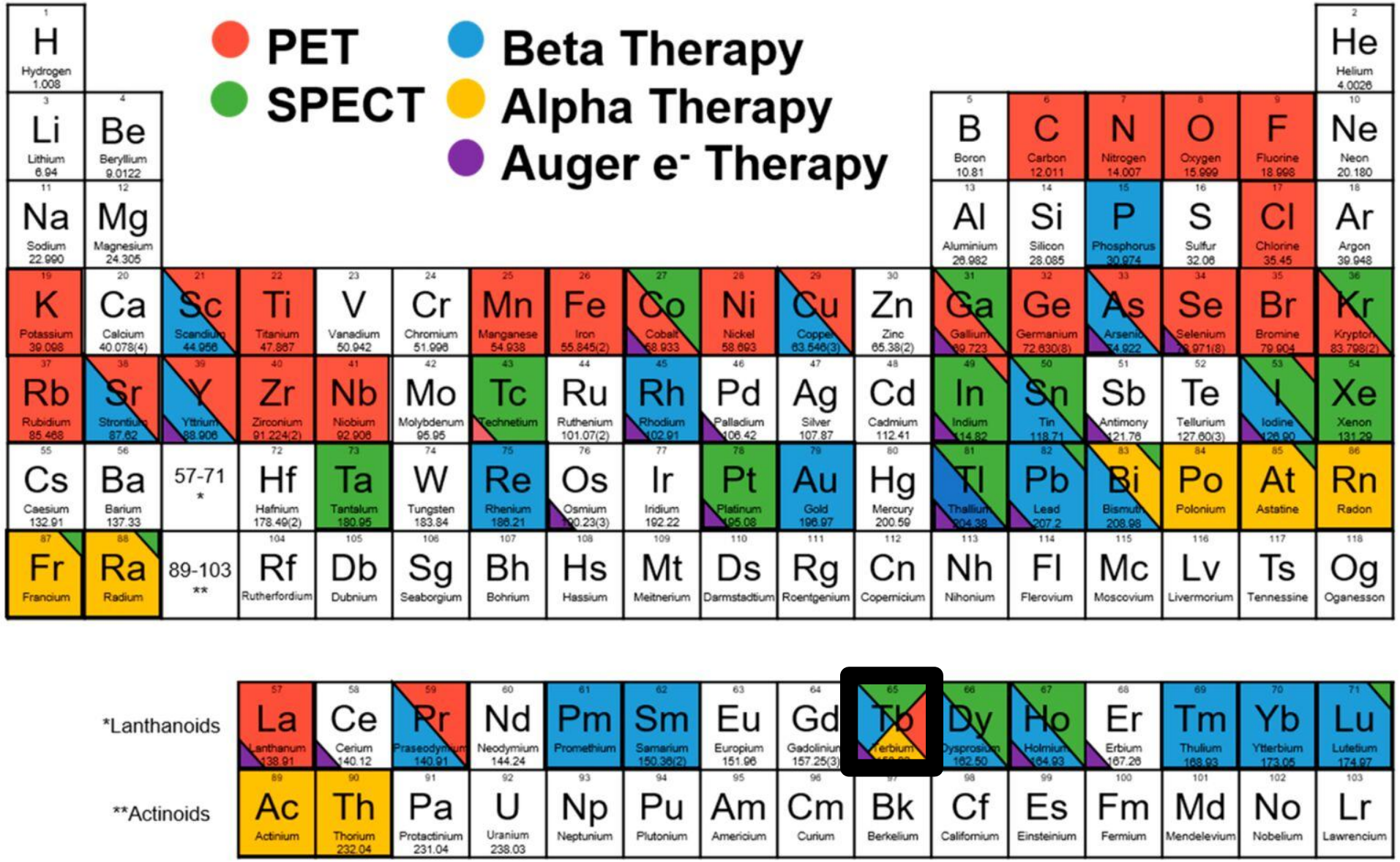
LUNAR: 14.1 months vs. 24.3 month hormone free survival

RESULTS – Salvage Hormonal Therapy HT-free survival



- Criteria for starting **Salvage hormonal therapy** (**HT**)
  - New lesions on PSMA PET/CT (trial-defined progression)
  - PSA >10 ng/mL without identifiable lesions
- **Salvage hormonal therapy** (**HT**) alone
  - SBRT arm: 16 patients (**38%**)
  - 177LuPNT2002+SBRT arm: 9 patients (**20%**)
- **HT** + repeat SBRT to all metastases
  - SBRT arm: 10 patients (24%)
  - 177LuPNT2002+SBRT arm: 10 patients (22%)
- Repeat SBRT only (no HT)
  - SBRT arm: 8 patients (19%)
  - 177LuPNT2002+SBRT arm: 9 patients (20%)

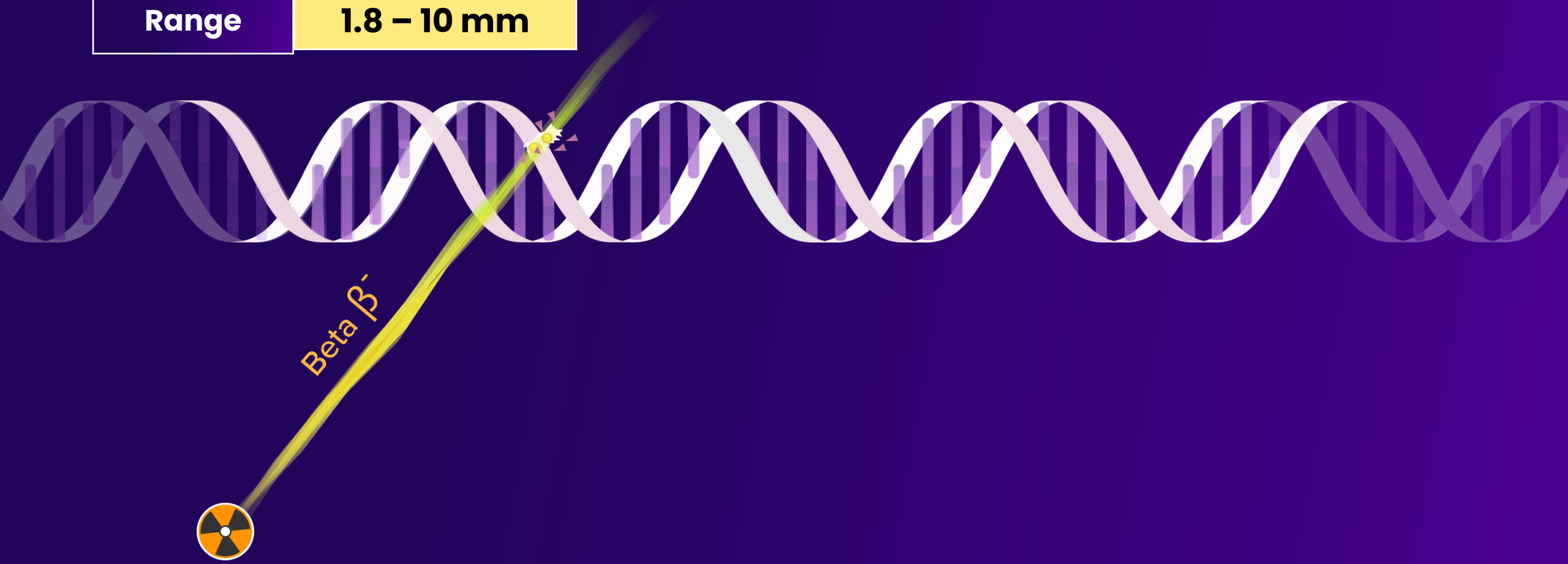
Kishan AU, ASTRO **2025**
Calais J, ESMO **2025**



International Union of Pure and Applied Chemistry 2018

Types of radiation particles

LET	0.2 keV/um
Range	1.8 – 10 mm

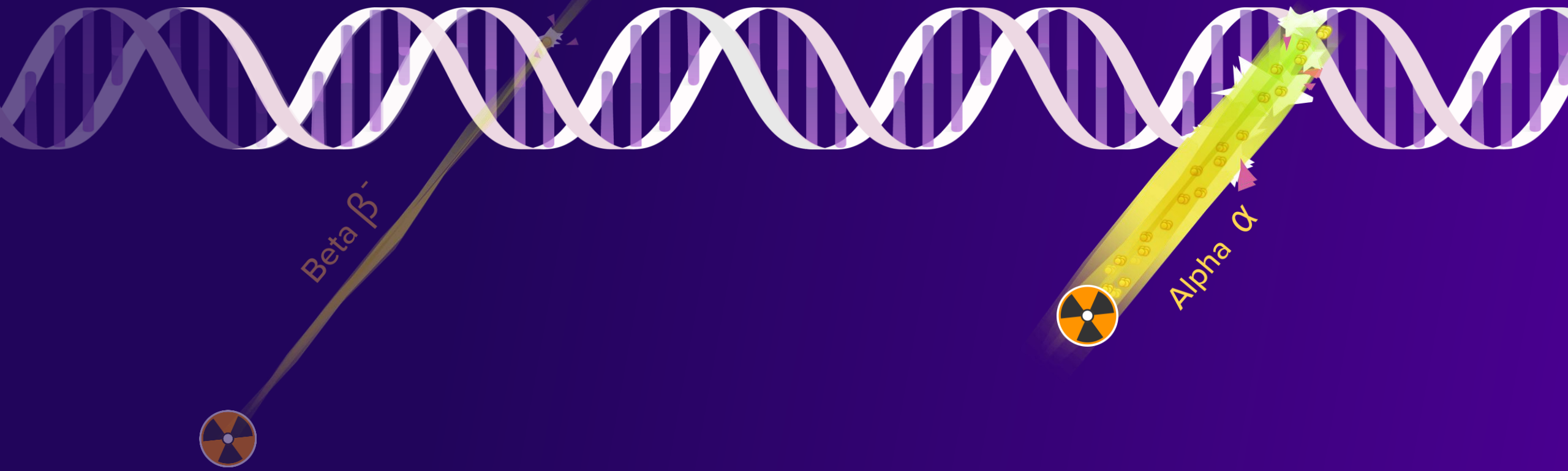


@DrMHofman

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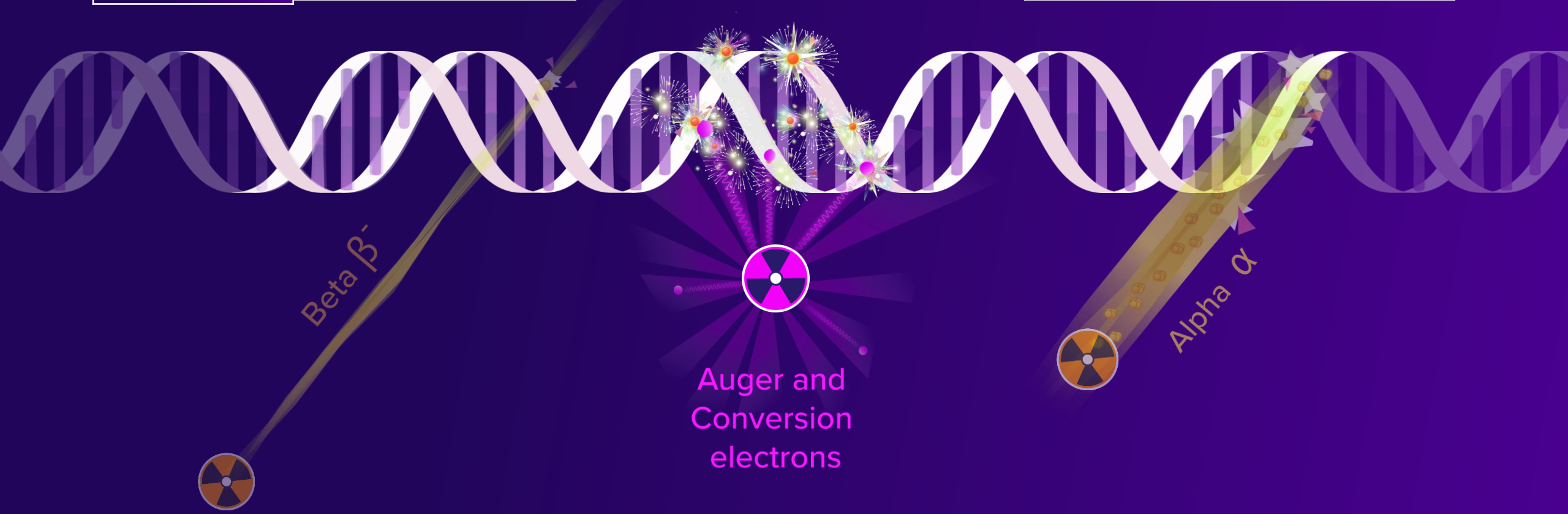
50 – 230 keV/um
40 – 100 nm



@DrMHofman

Types of radiation particles

LET	0.2 keV/um	4 – 26 keV/um	50 – 230 keV/um
Range	1.8 – 10 mm	2 - 500 nm	40 – 100 nm

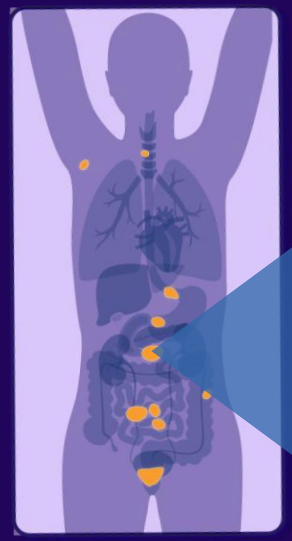


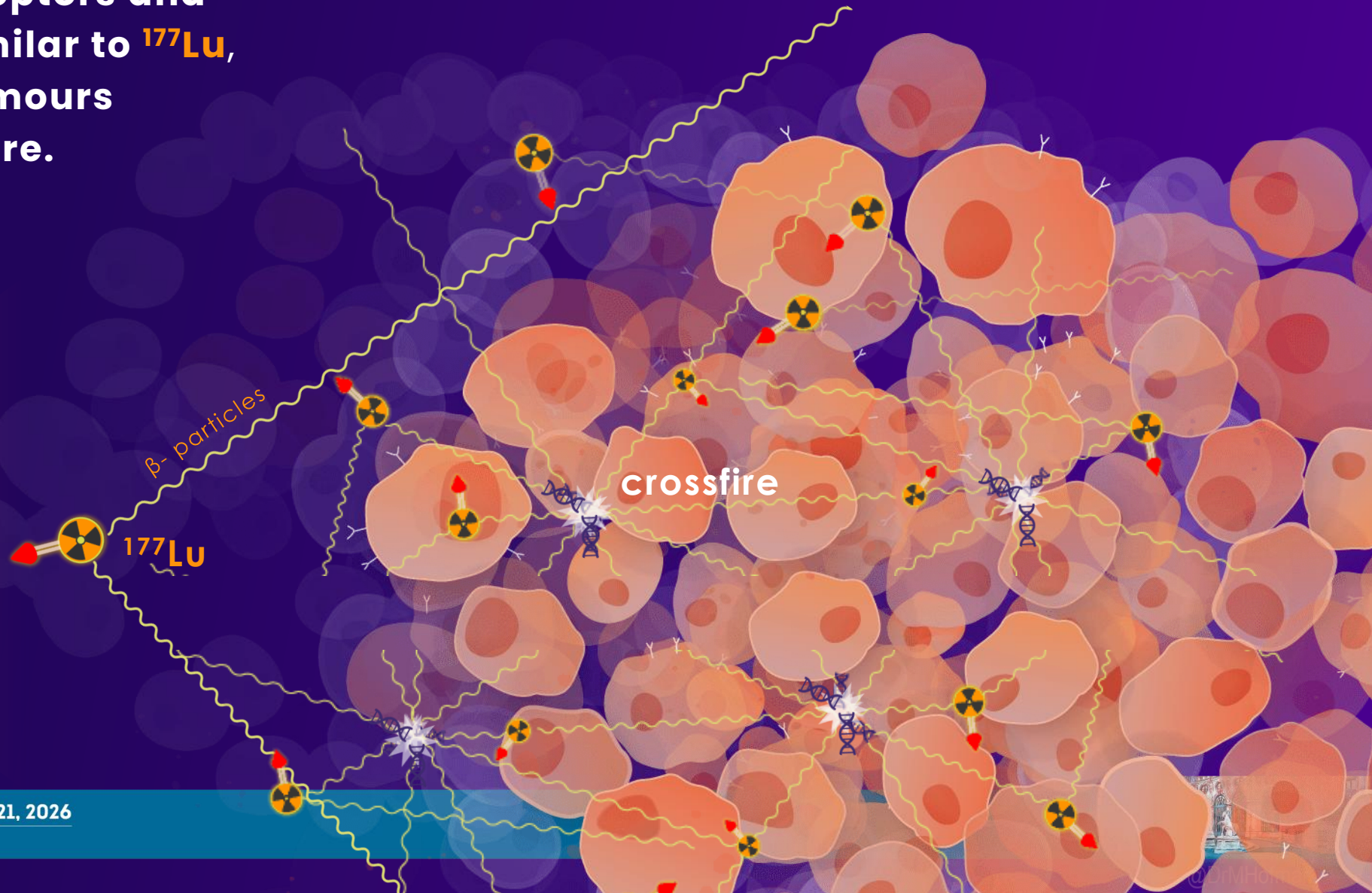


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Terbium-161 (^{161}Tb)

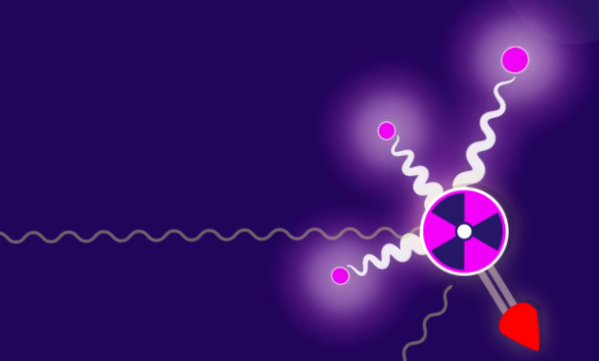
attaches to PSMA receptors and emits β- particles, similar to ^{177}Lu, killing larger sized tumours with abundant crossfire.

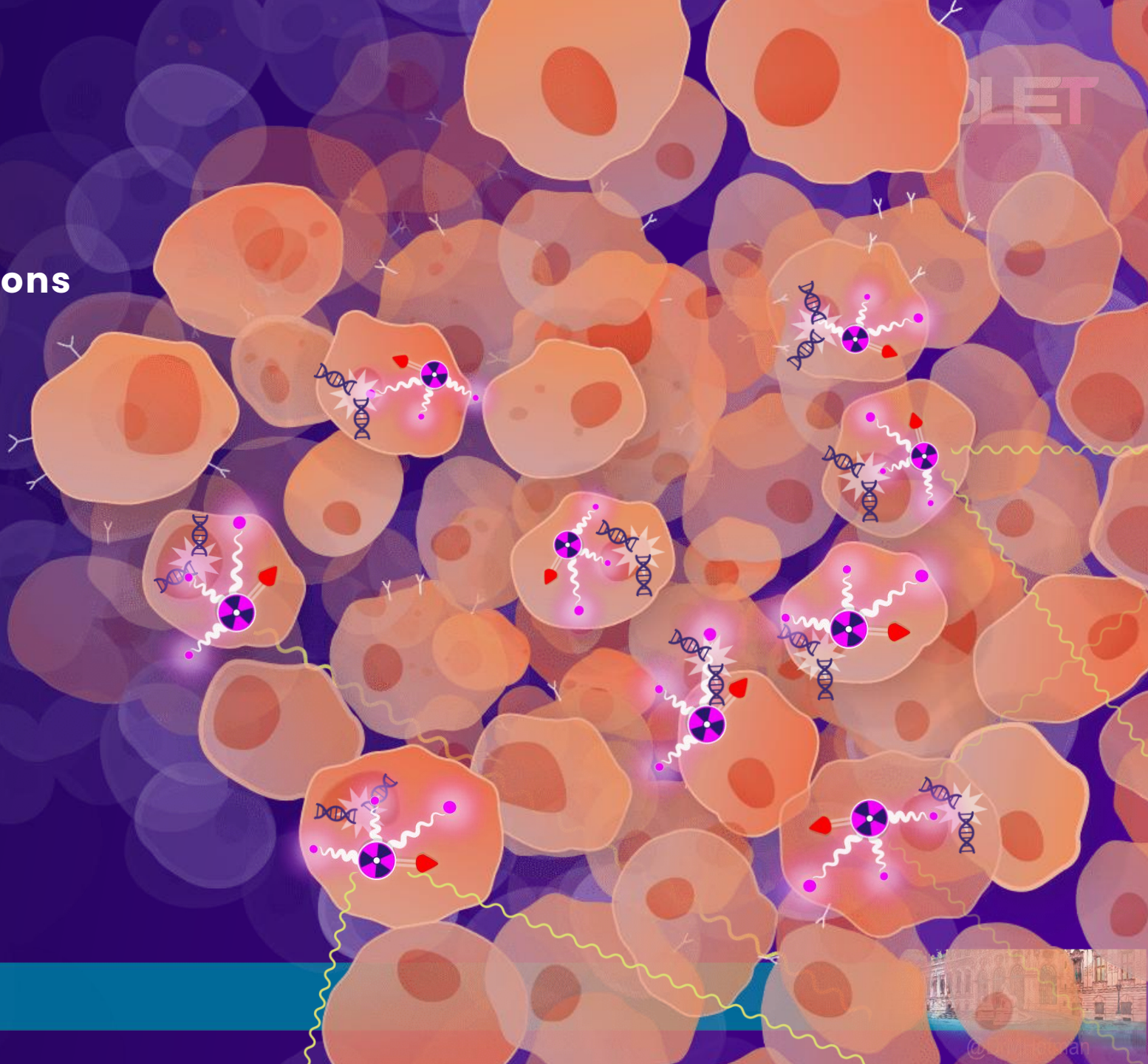




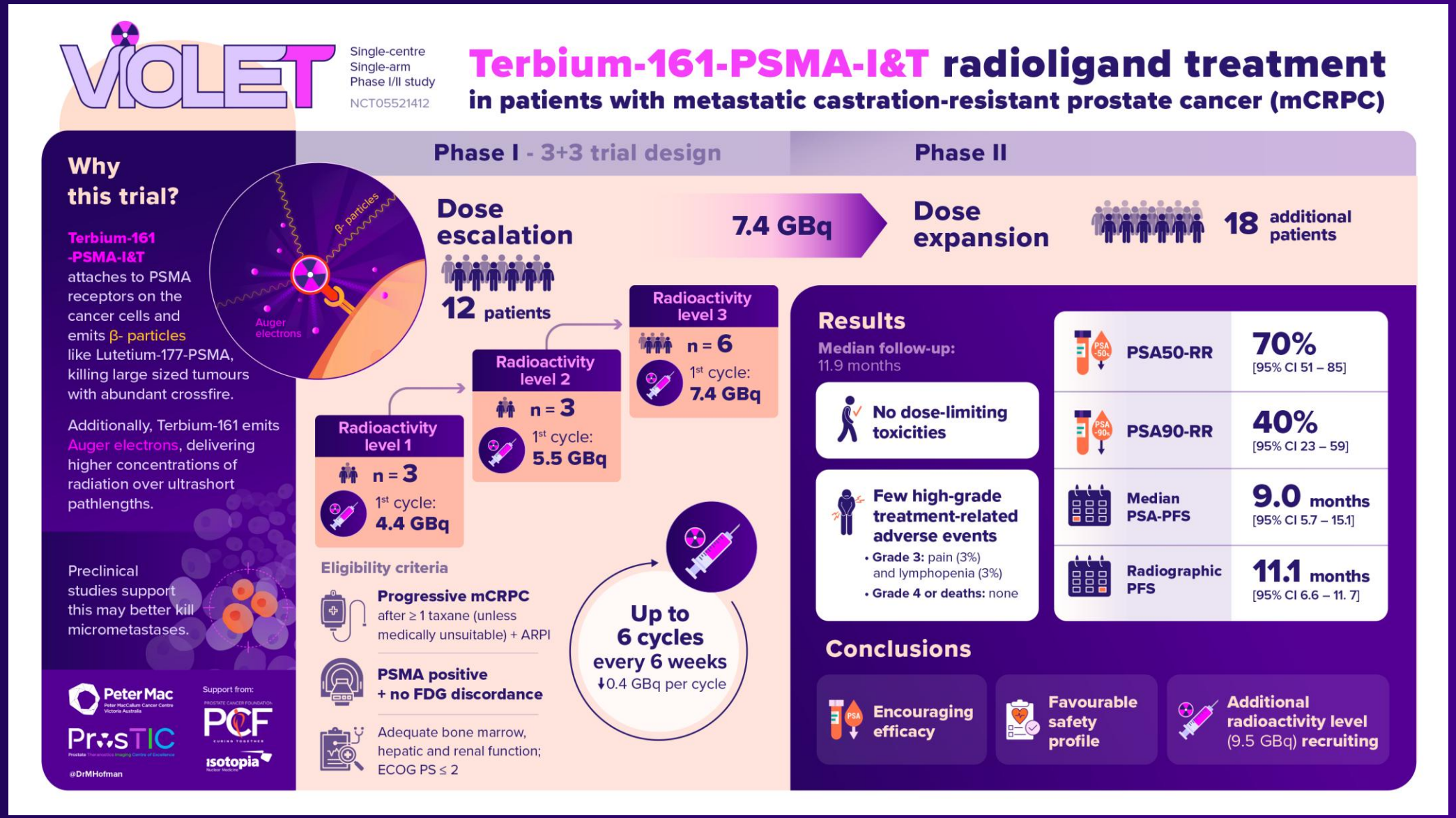
Terbium-161 (^{161}Tb)

also emits additional
Auger and conversion electrons
that delivers higher concentrations of radiation over very short path-lengths, which may kill micrometastases better than ^{177}Lu.





Published VIOLET results (cohort A, n = 30)



Buteau et al. Lancet Oncol 2025; 26: 1009-1017

@DrMHofman

VIOLET cohort A: key results

VIOLET ProsTIC
Prostate Theranostics Imaging Centre of Excellence

Results

Median follow-up:
11.9 months

No dose-limiting toxicities

Few high-grade treatment-related adverse events

- **Grade 3:** pain (3%) and lymphopenia (3%)
- **Grade 4 or deaths:** none

PSA50-RR	**70%** [95% CI 51 – 85]
PSA90-RR	**40%** [95% CI 23 – 59]
Median PSA-PFS	**9.0 months** [95% CI 5.7 – 15.1]
Radiographic PFS	**11.1 months** [95% CI 6.6 – 11. 7]

Conclusions

Encouraging efficacy

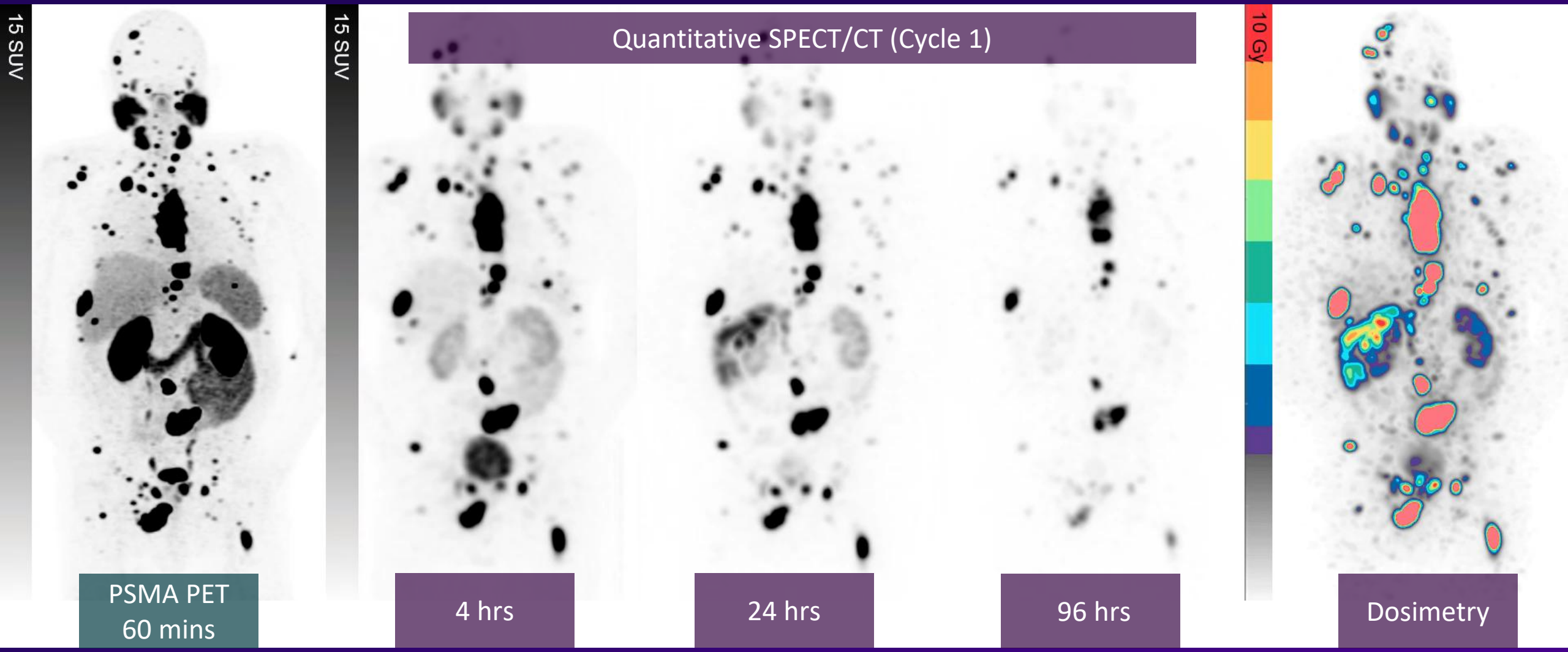
Favourable safety profile

Additional radioactivity level (9.5 GBq) **recruiting**

Buteau et al. Lancet Oncol 2025; 26: 1009-1017

@DrMHofman

Radiation absorbed dose



McIntosh, Jackson et al. EJNMMI Physics (2024) 11:18

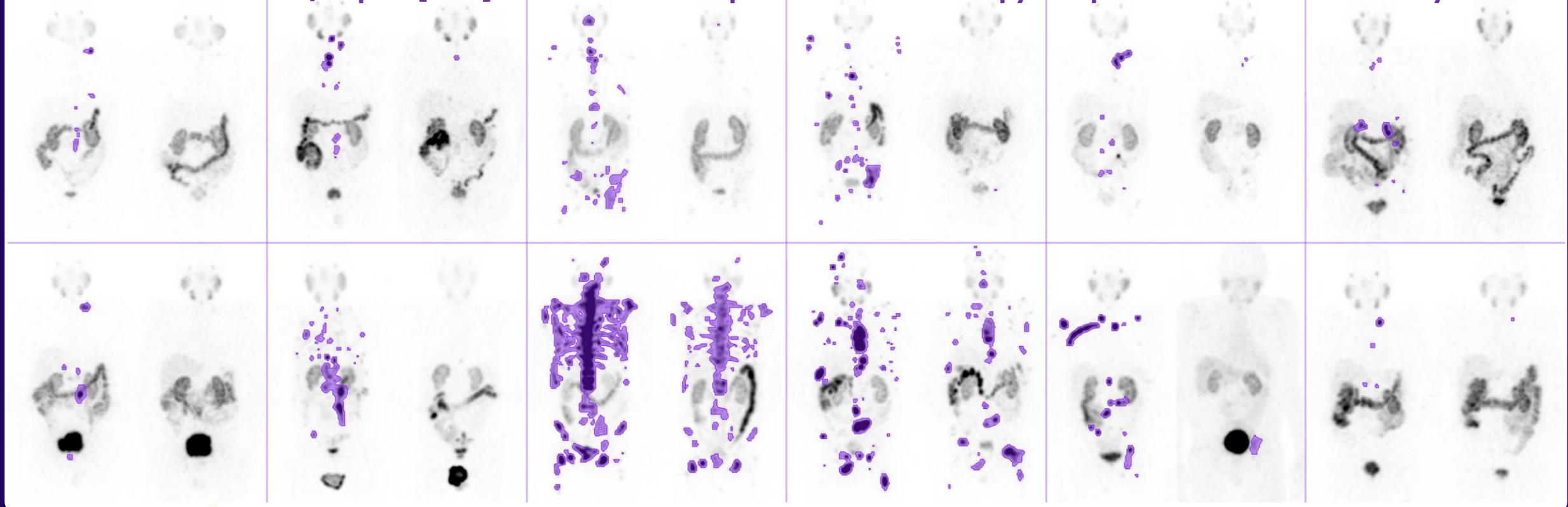
Presentation is property of the author and ASCO. Permission required for reuse; contact permissions@asco.org.

First in-human trial of Terbium-161 PSMA

High rate of deep responses: PSA reduction ≥90% in 40% (12 of 30 pt)

VIOLET
Abstract #251535

Quantitative SPECT/CT post [^{161}Tb]Tb-PSMA-I&T radiopharmaceutical therapy in 12 patients: baseline and last cycle



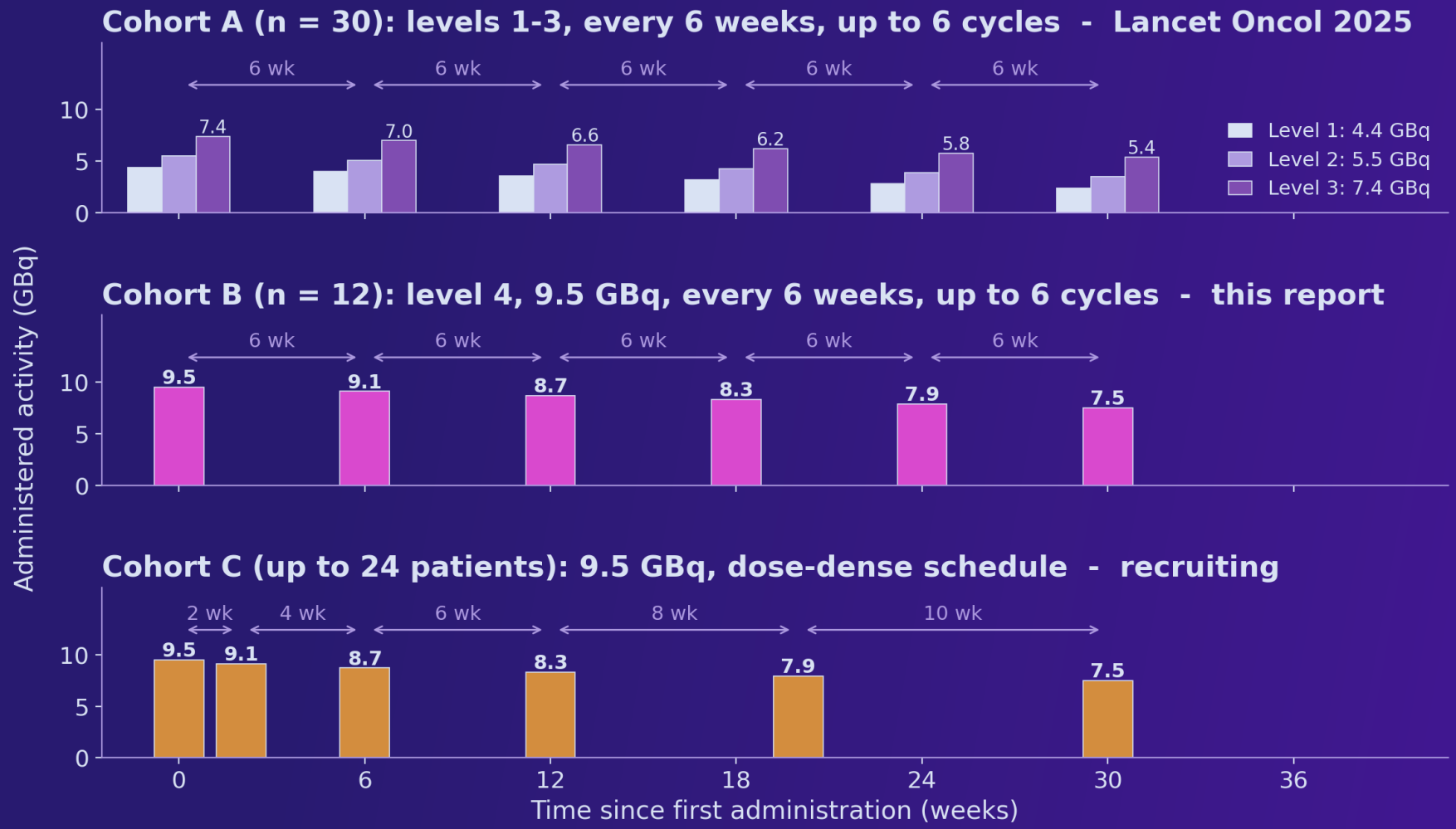


auger & conversion electrons
may better target micrometastases

Encouraging activity

Favorable safety profile at 7.4 GBq

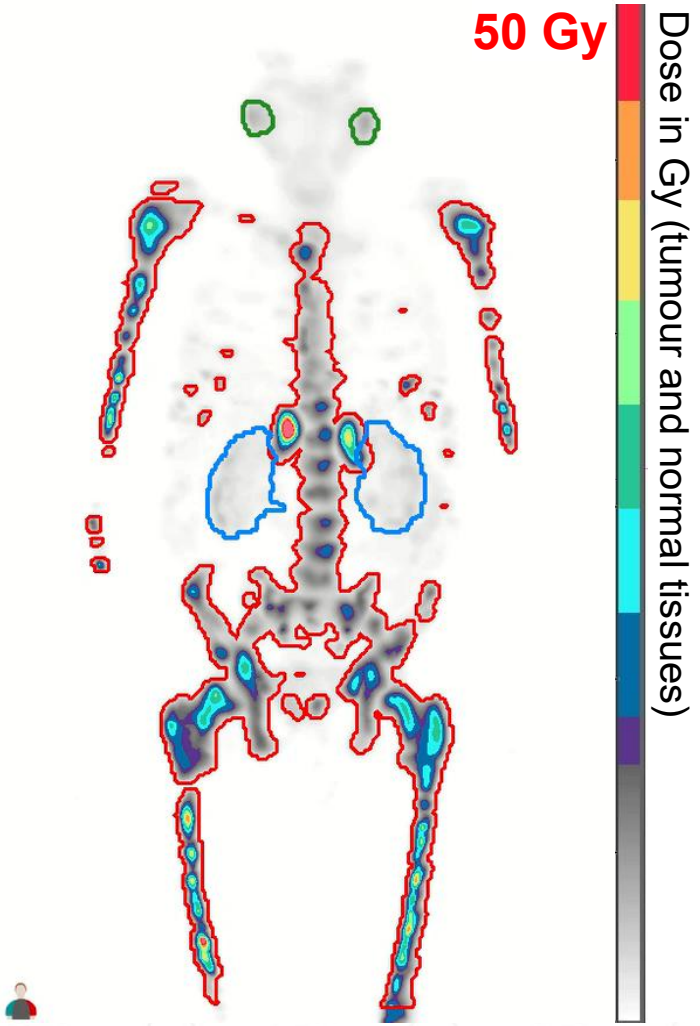
VIOLET: three cohorts



Cohort C: 9.5 GBq at weeks 0, 2, 6, 12, 20 and 30 (shortened intervals between early cycles) - recruiting

@DrMHofman

Not magical:
radiation delivery device



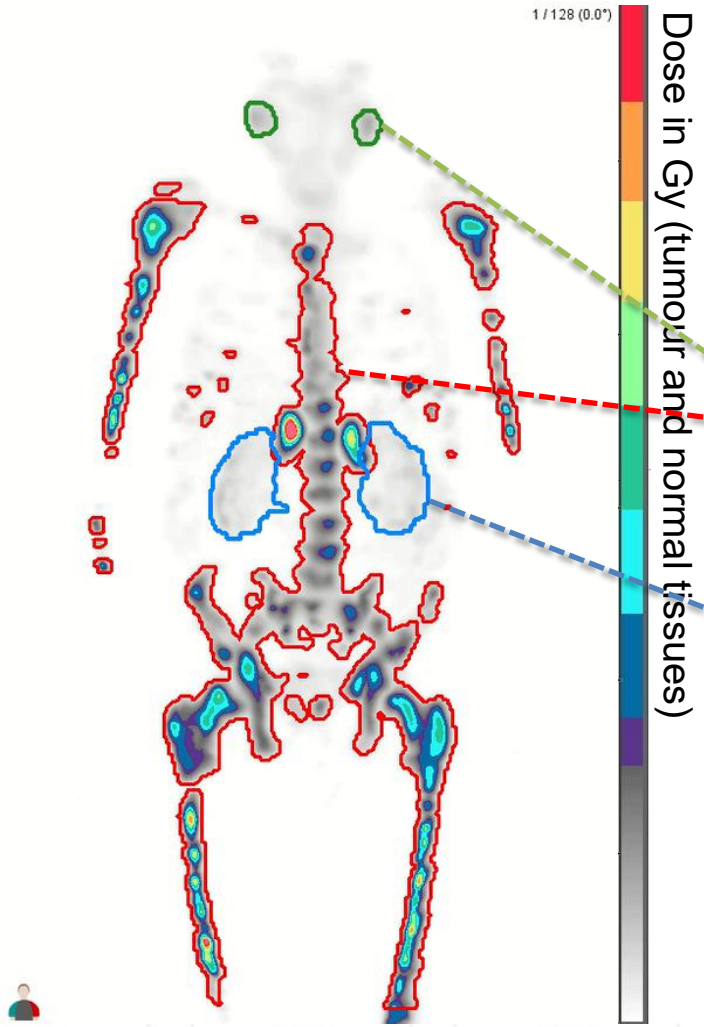
post Lutetium-177 scan

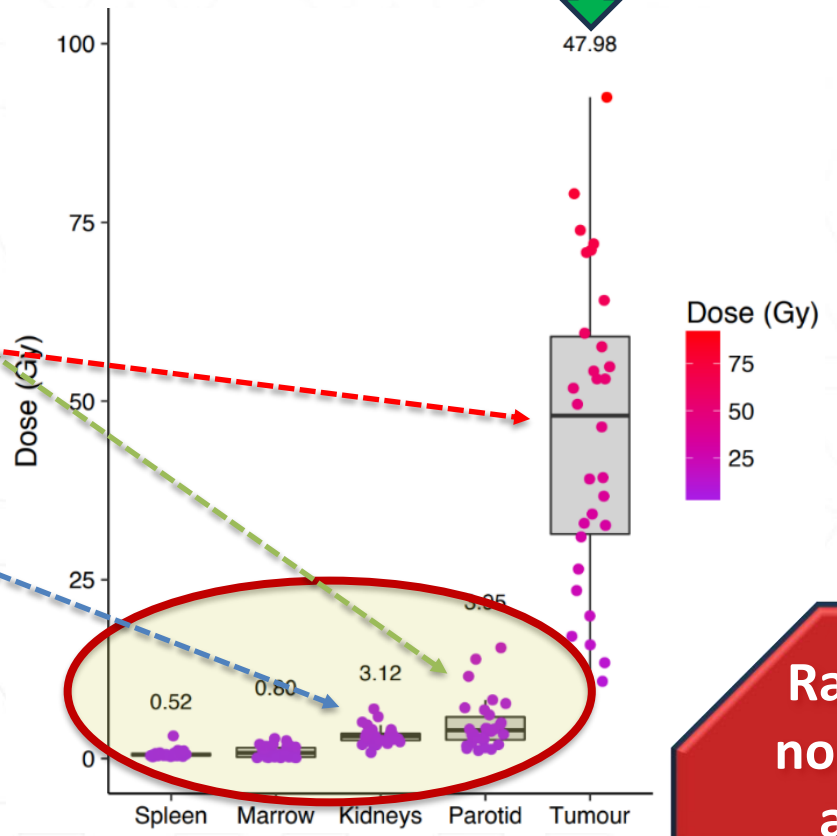
See What You Treat with Theranostics

Violet J et al, JNM 2019 60(4)
doi: 10.2967/jnumed.118.219352

Not magical:
radiation delivery device

Tumour doses:
big variation

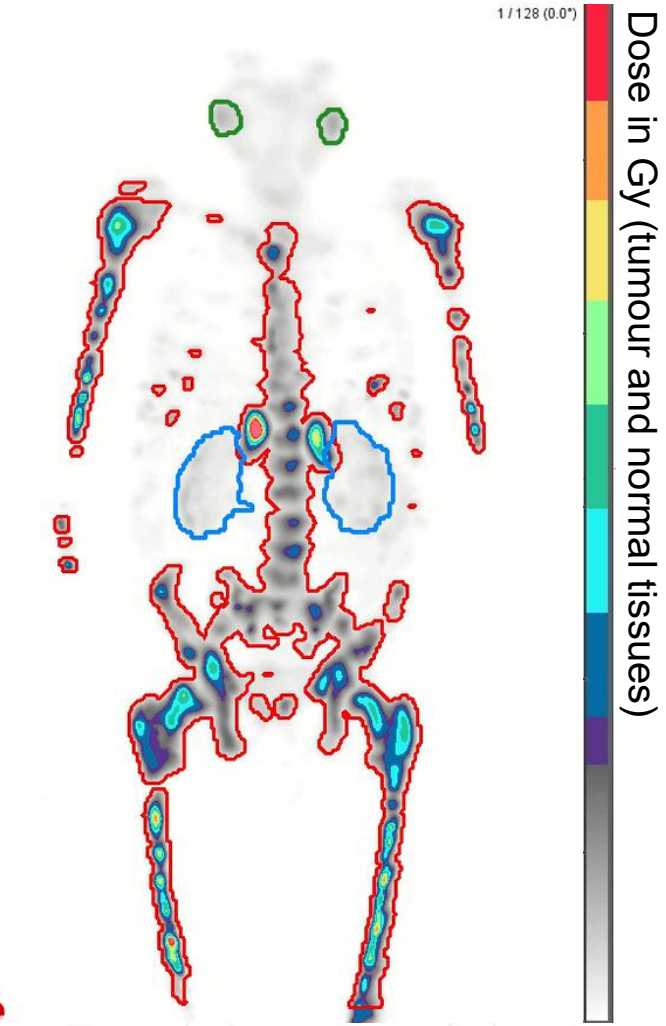




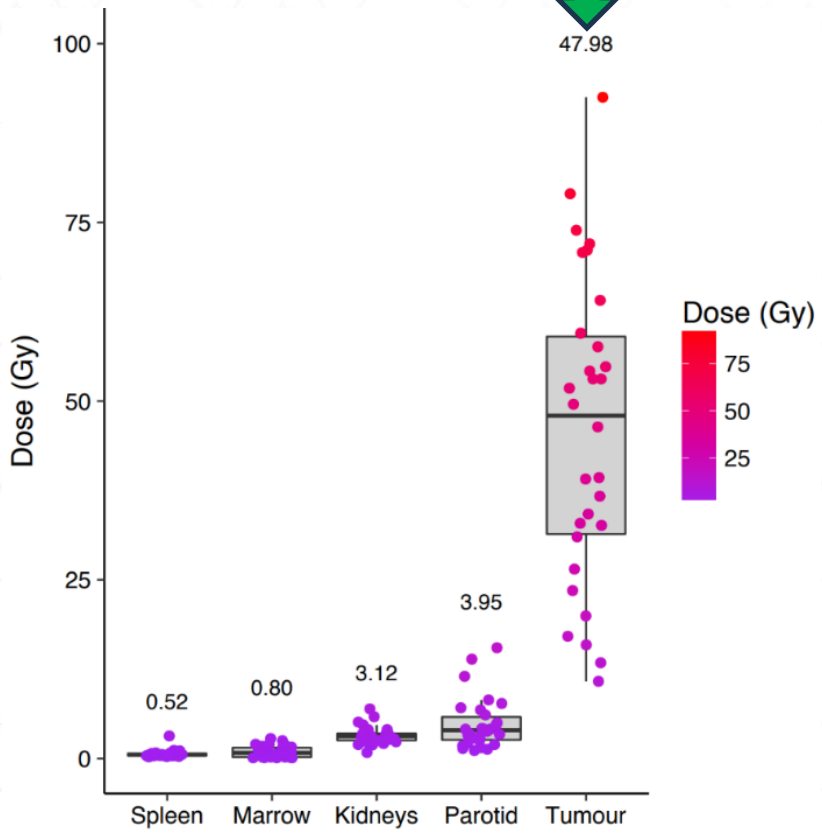
Radiation dose to normal organs low and predicable

Violet J et al, JNM 2019 60(4)
doi: 10.2967/jnumed.118.219352

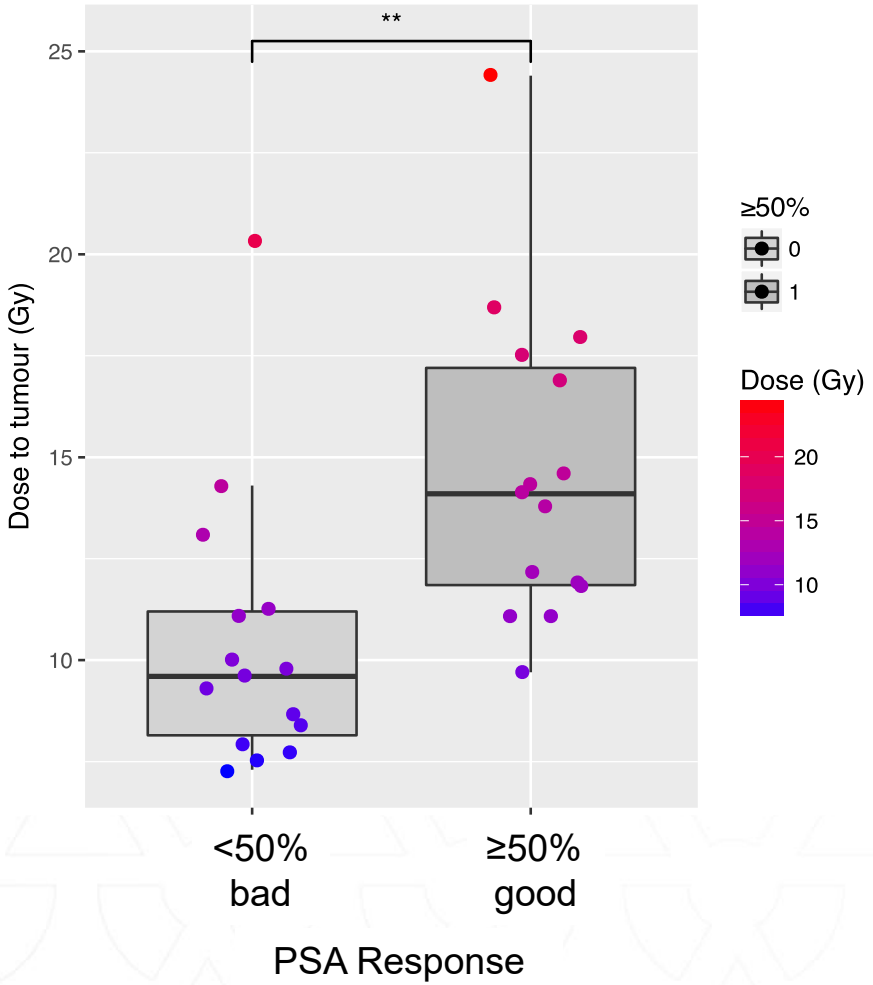
Not magical:
radiation delivery device



Highly variable tumour doses



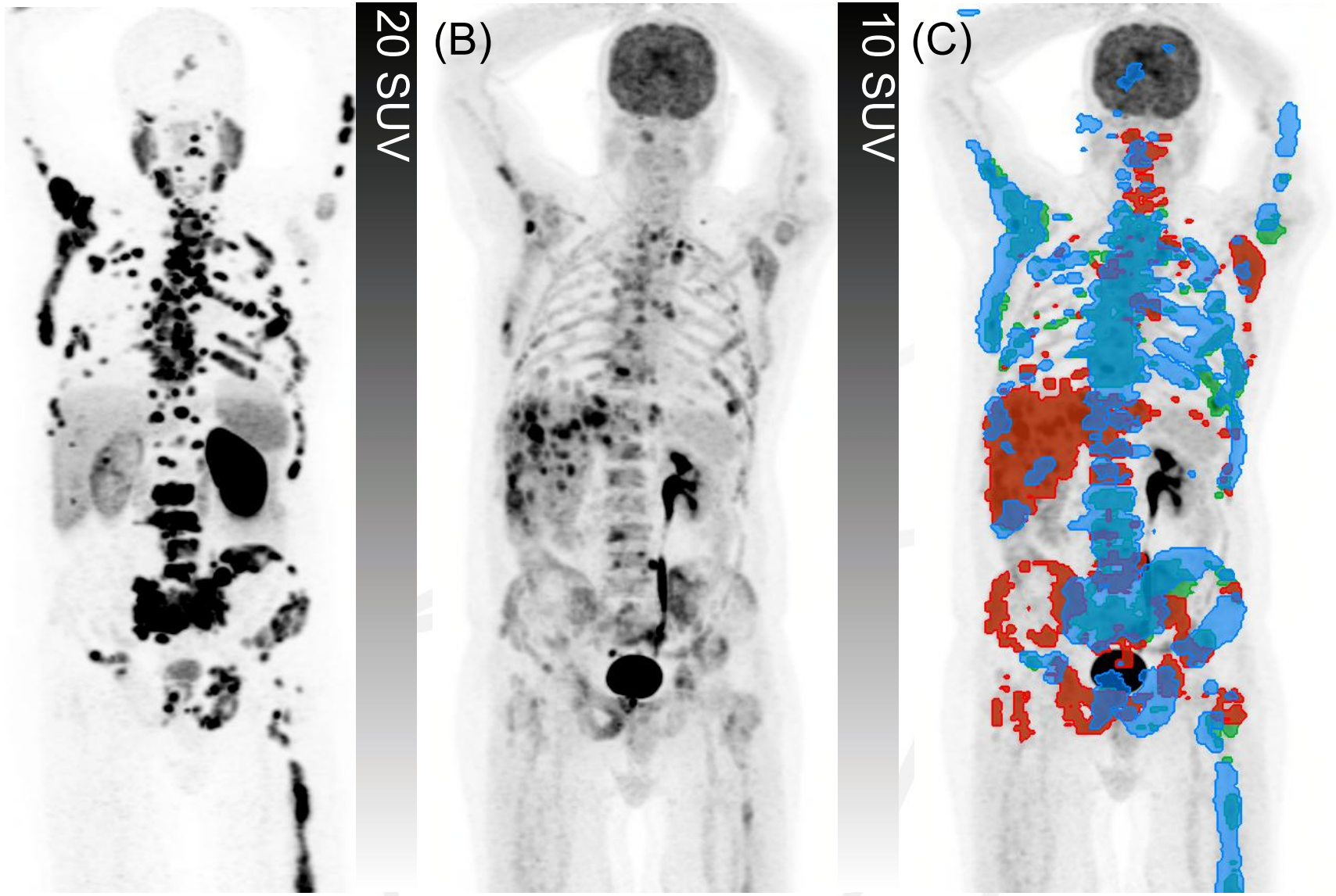
Low dose: response unlikely



Violet J et al, JNM 2019 60(4)
doi: 10.2967/jnumed.118.219352

See What You Treat

PSMA PET | **FDG PET** | **PSMA / FDG**



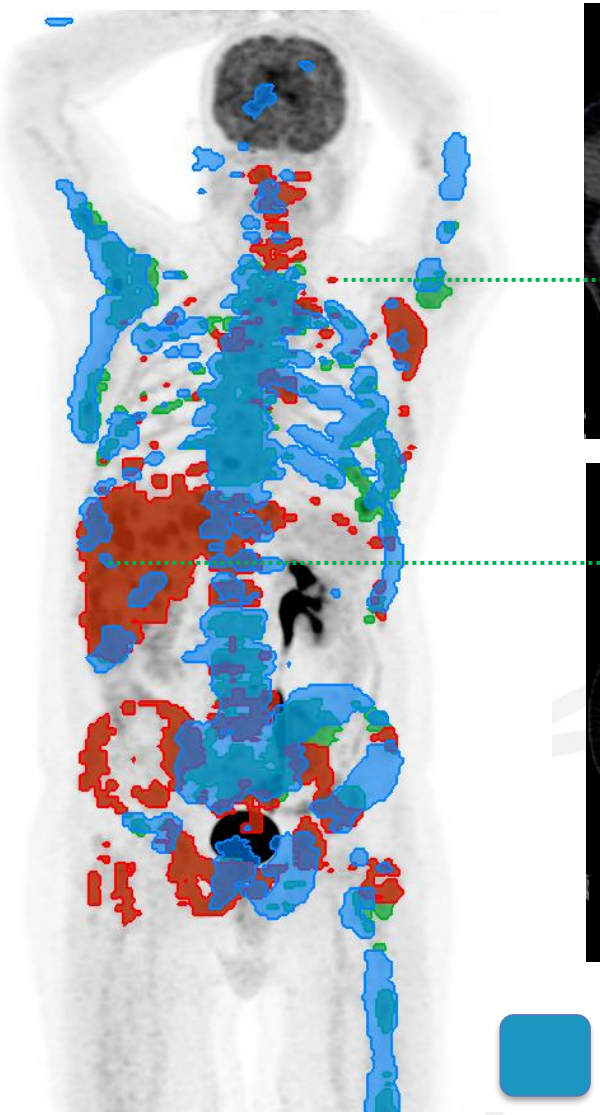
Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

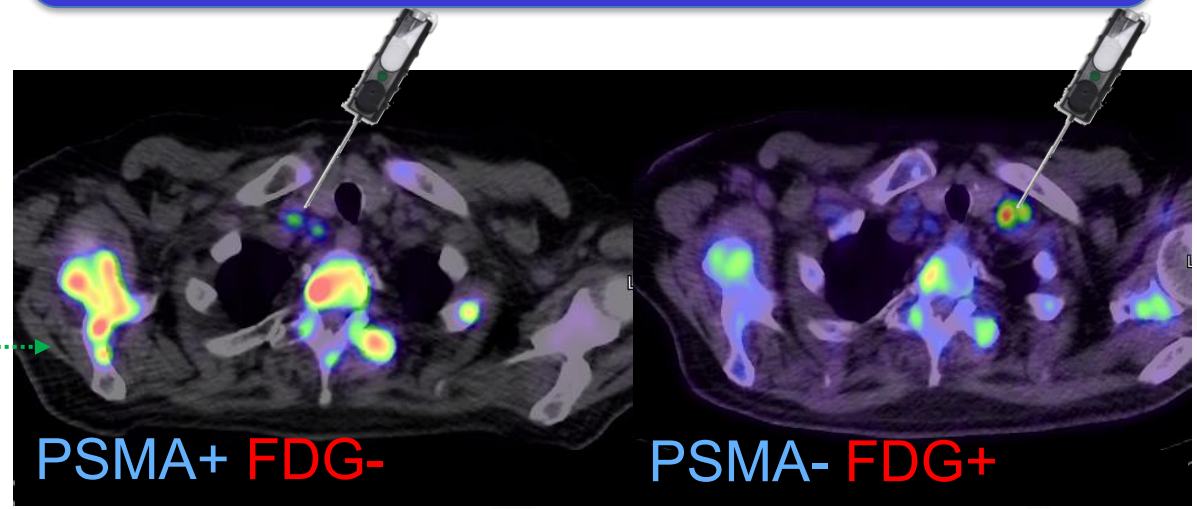
Can target with ^{177}Lu-PSMA

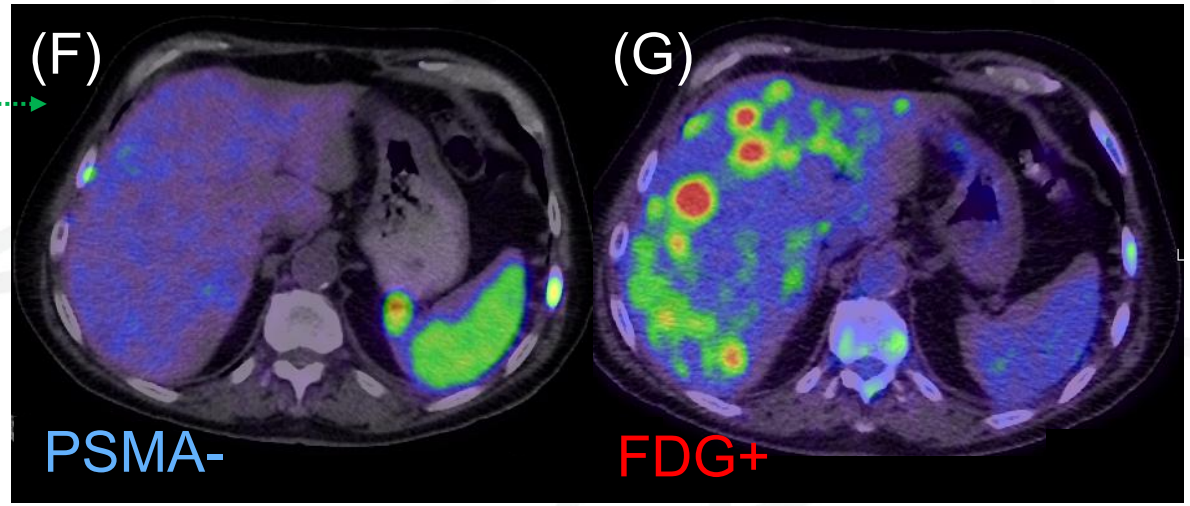
Cannot target (most aggressive sites)

Thang SP et al, *Eur Urology Oncology* 2019

PSMA/FDG enables targeted biopsy, rather than random biopsy

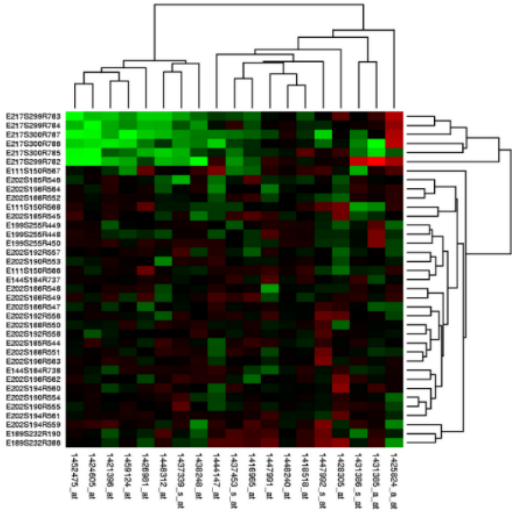






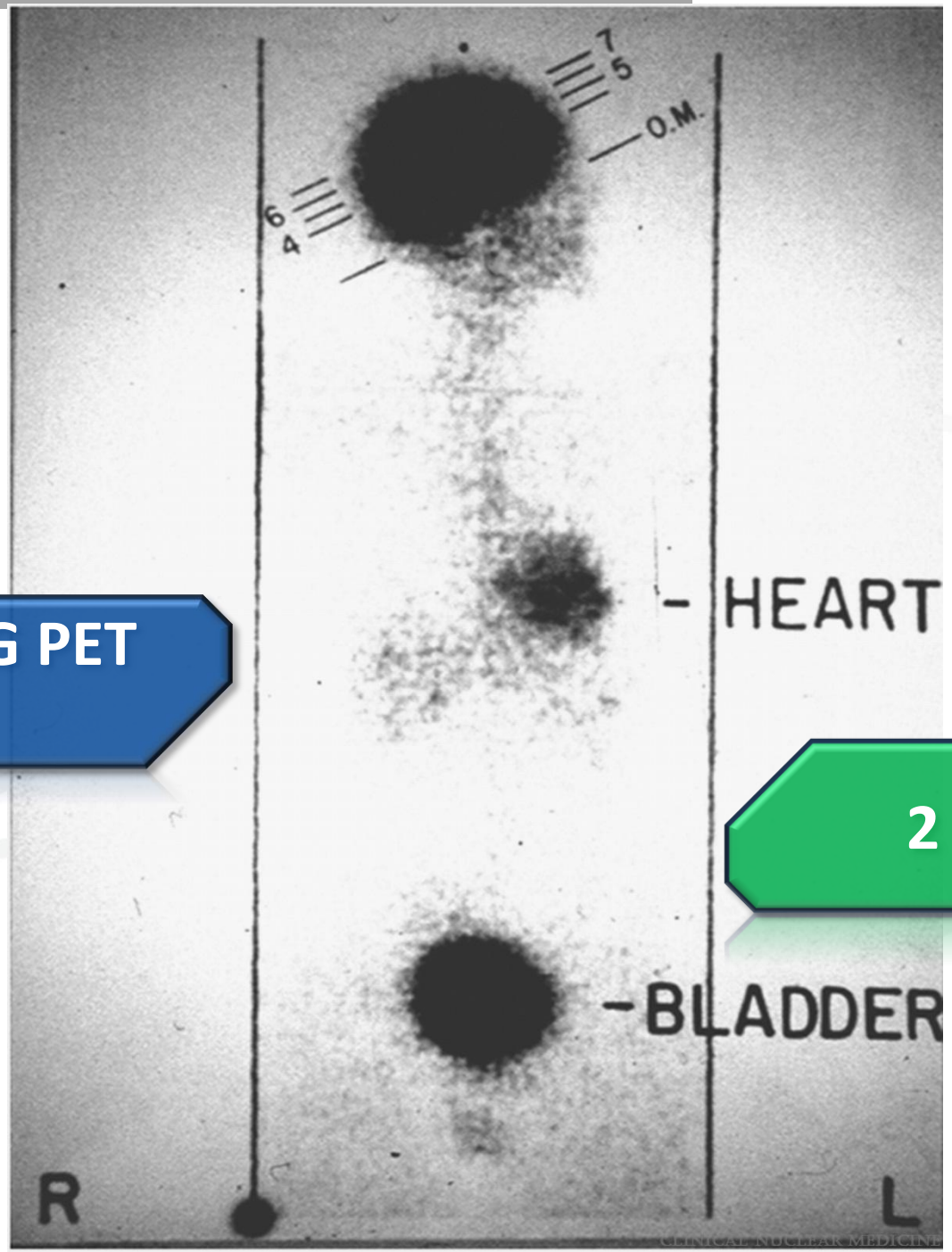
Can target with ^{177}Lu-PSMA

Cannot target





First Whole Body FDG PET
Aug 1976



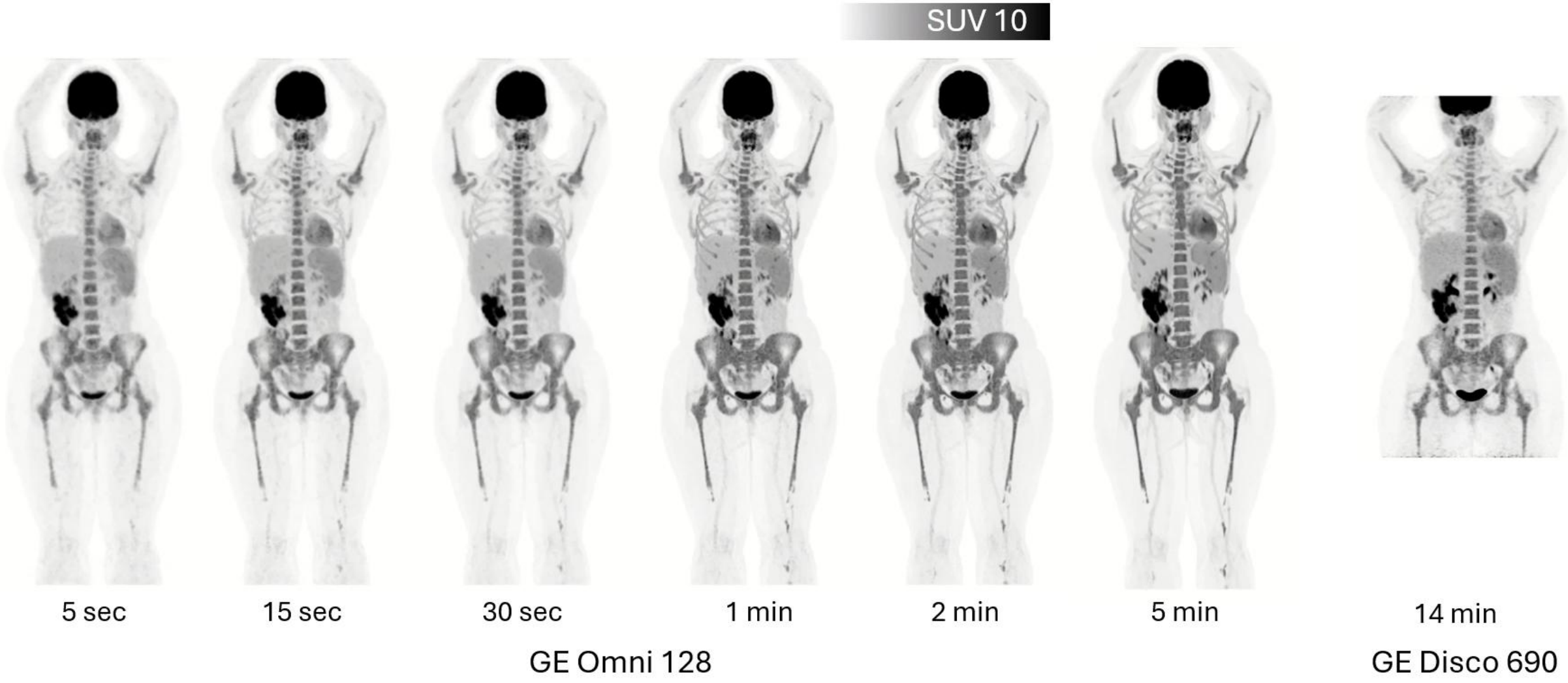
2 hours to scan!

Semin Nucl Med. 2002;32:2–5

FDG PET/CT in 2026



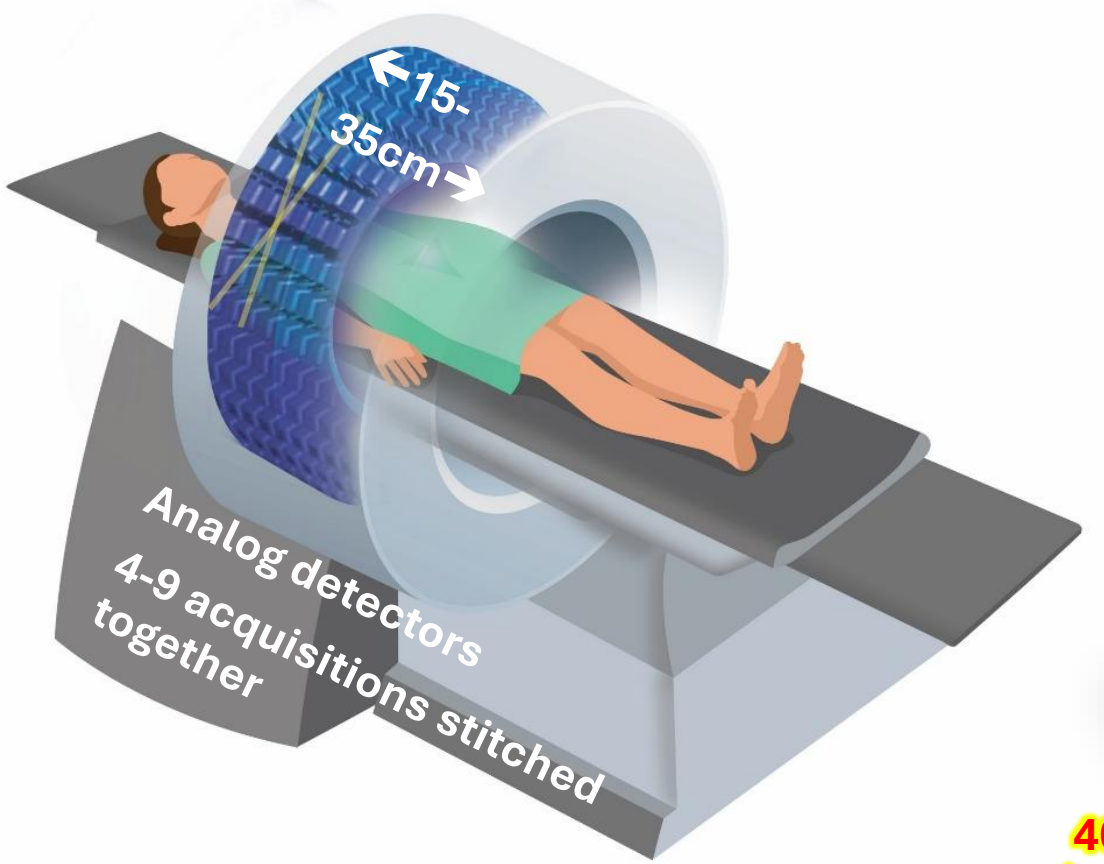
5 second acquisition !!



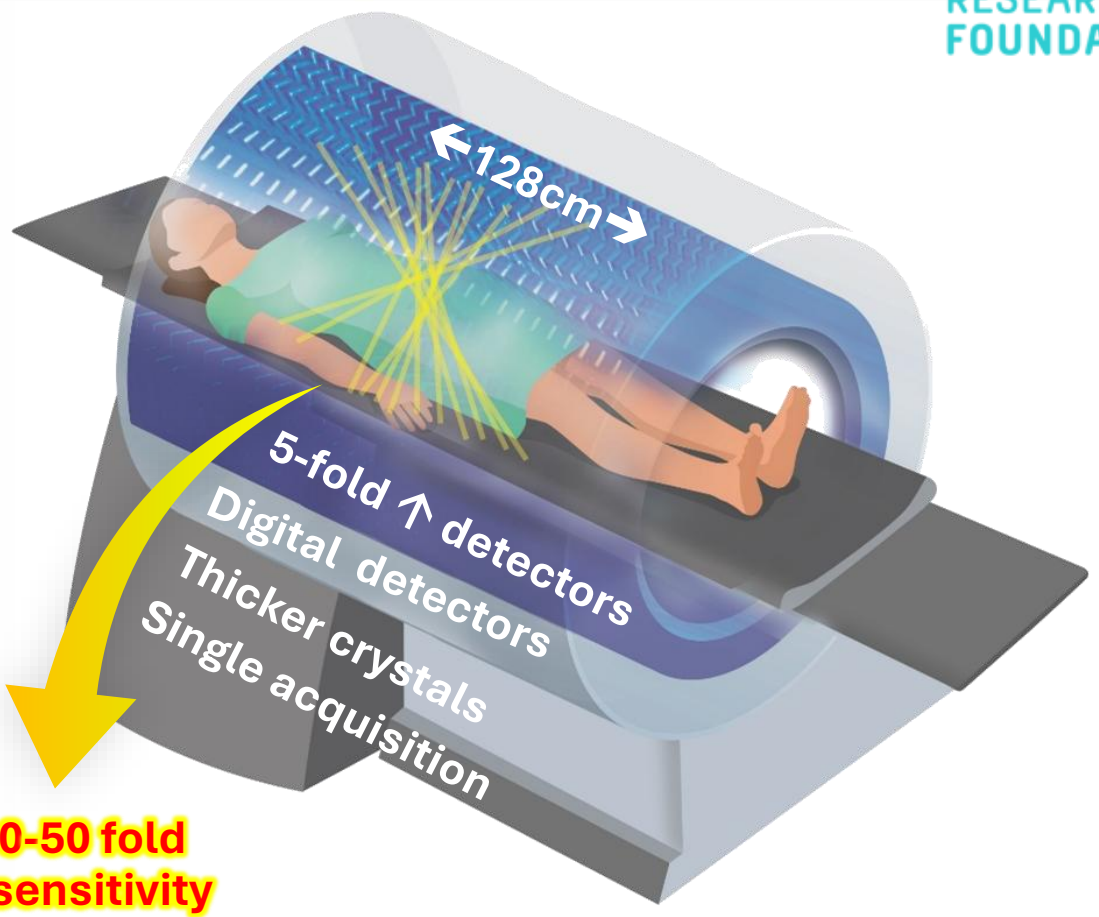
Images from the GE Omni 128cm Large Field of View PET/CT

AUSTRALIAN CANCER RESEARCH FOUNDATION

Conventional PET



Total Body PET



40-50 fold ↑sensitivity

Technical advantages:

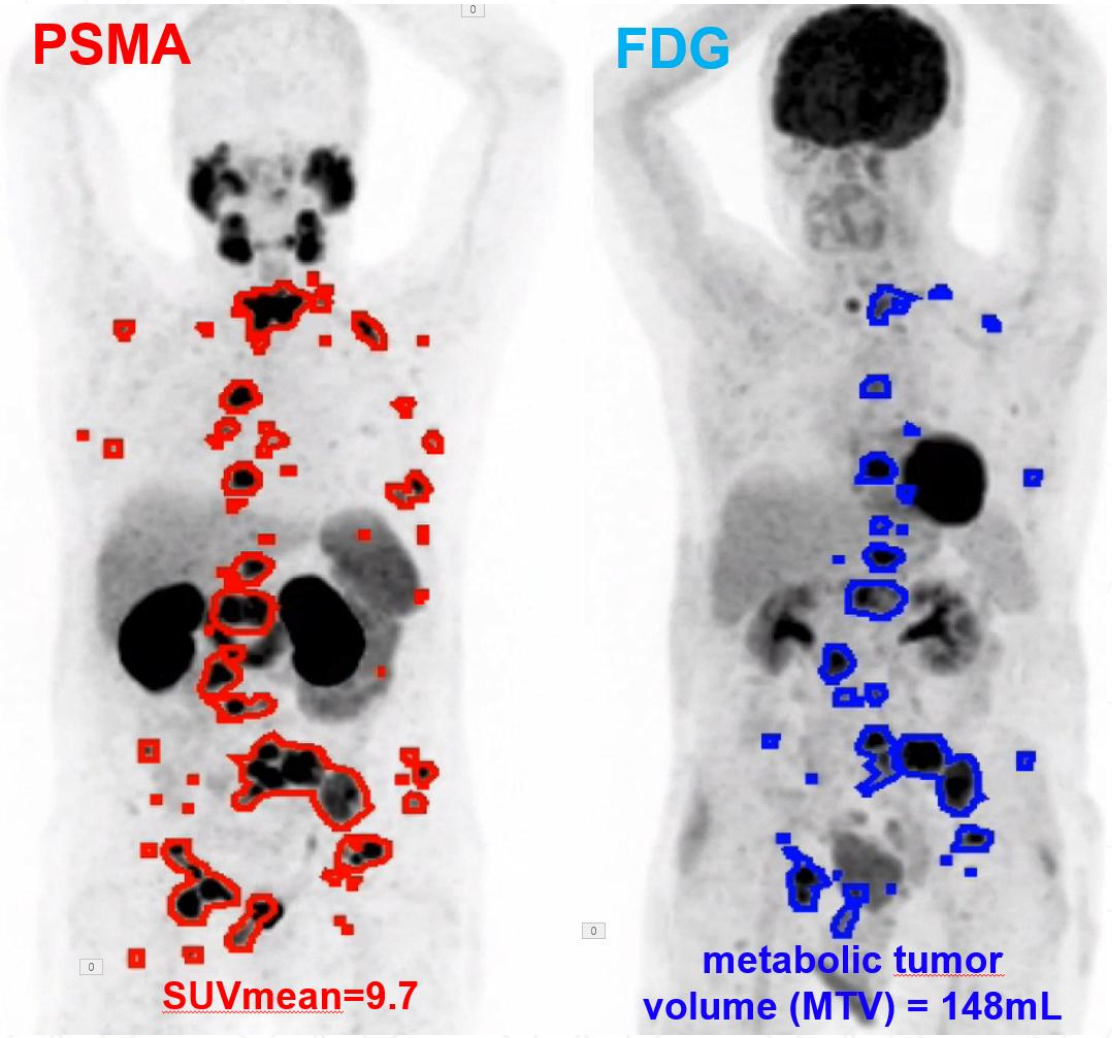
- ^{124}I, ^{68}Ga, ^{89}Zr, ^{64}Cu, ^{11}C — **low count isotopes**
- ↓80% — **faster**
- ↓50+% — **↓ radiation**
- **↑ accuracy**
- **dynamic**

Total Body Pharmacokinetics	Drug development	Cell tracking	ImmunoPET	Paediatric	Multi-tracer



Time-lapse of Peter Mac Total Body PET/CT Installation

Quantitative PET is powerful



Total tumour measures superior to single lesion

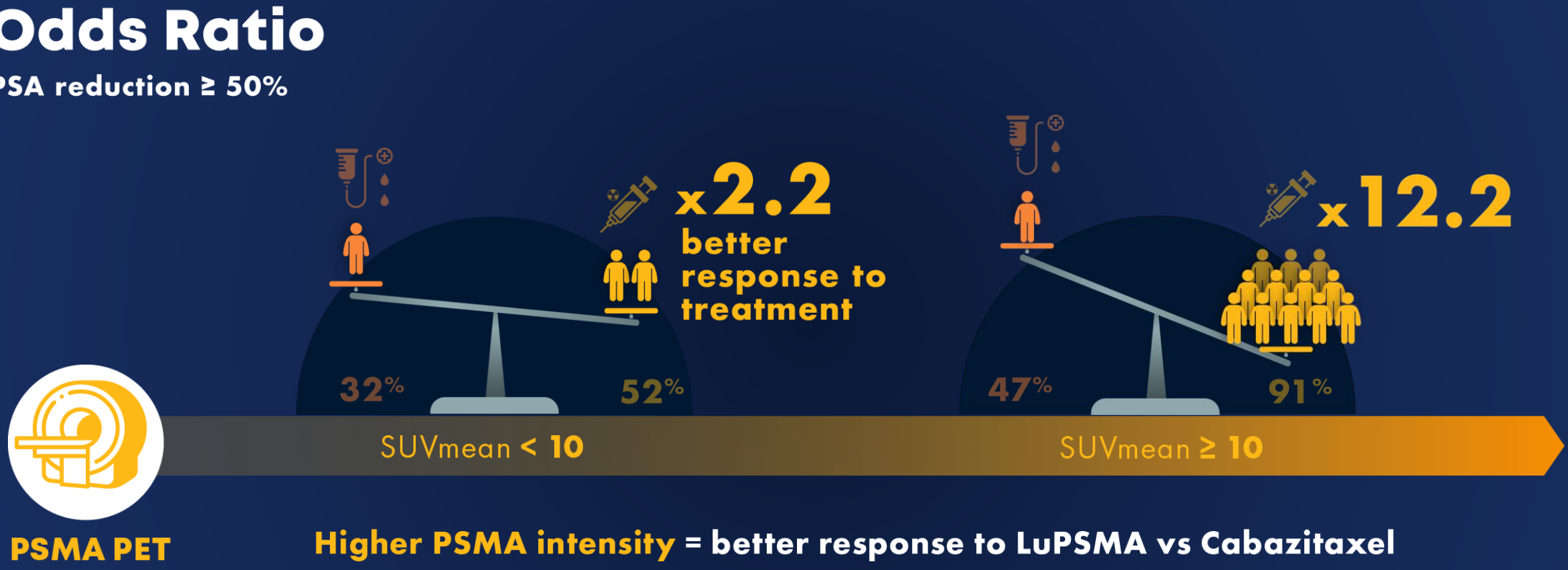
We need automated, reproducible solutions

SUV ≥ 3

SUV > $liver_{mean}$ + 2σ

Buteau J, ..., Hofman MS, **Lancet Oncology** 2022, 23(11)
doi: 10.1016/S1470-2045(22)00605-2

PSMA PET/CT is a predictive biomarker



In TheraP, 91% of pt with SUVmean ≥ 10, had >PSA 50% response

Buteau J, .., Hofman MS, **Lancet Oncology** 2022, 23(11)
doi: 10.1016/S1470-2045(22)00605-2

TheraP ANZUP 1603

Evaluation of PSMA PET as a predictive biomarker FDG PET as a prognostic

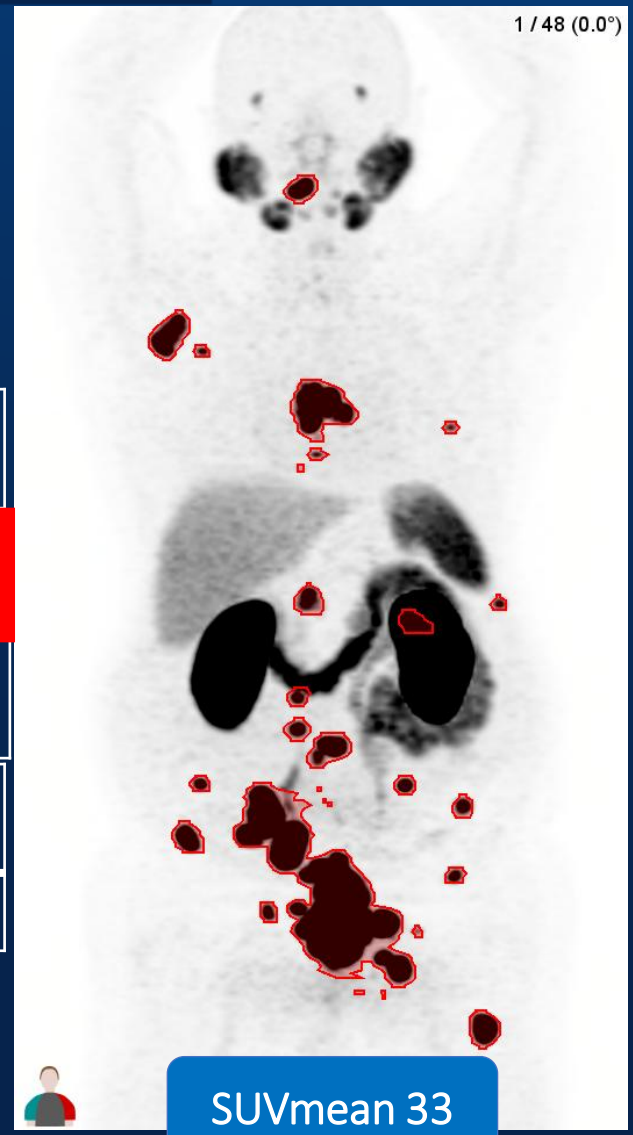
in a randomised phase II trial of CABAZITAXEL versus ^{177}Lu-PSMA-617



SUVmean 4.9

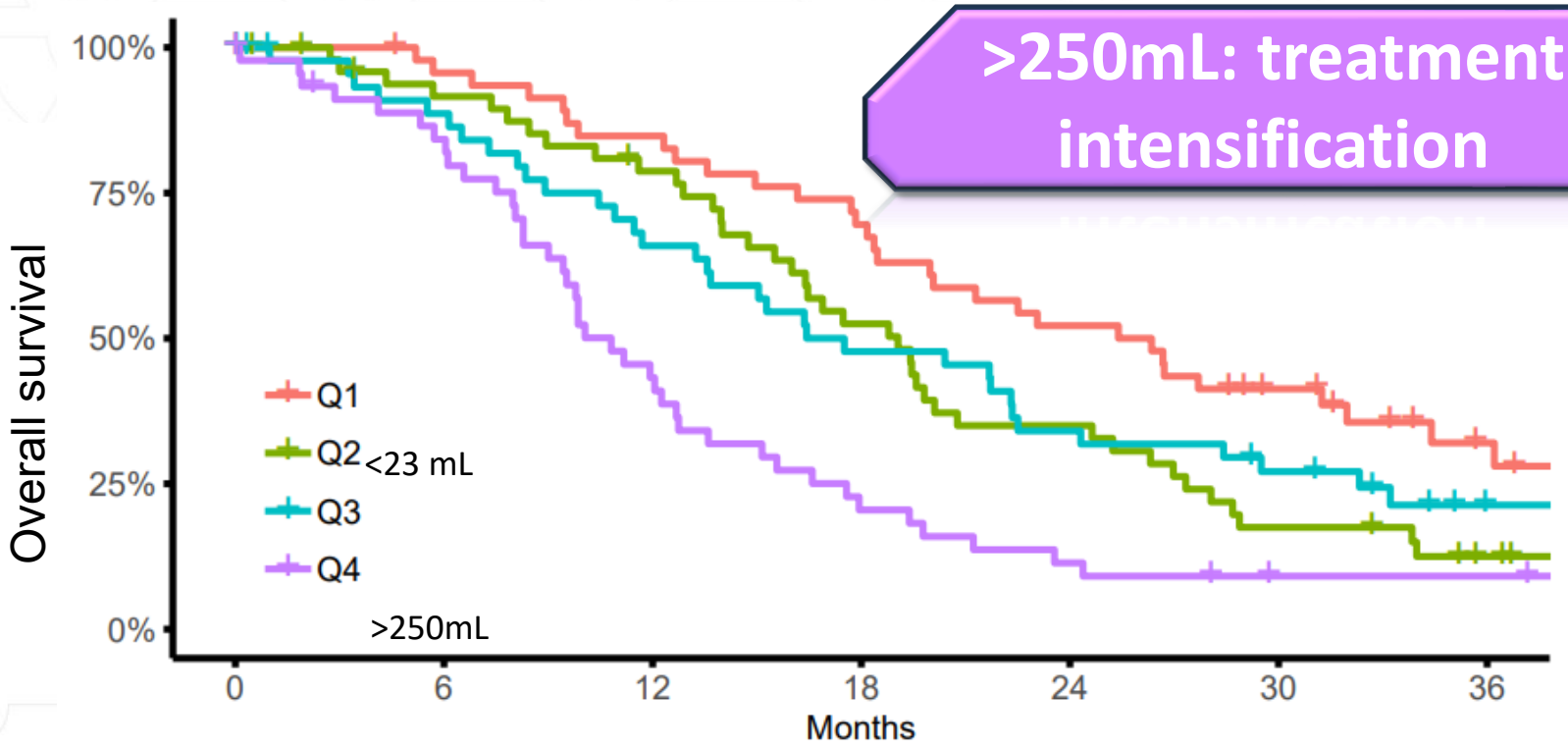
PSMA SUVmean

PSMA SUVmean	Q1 (<6.9)	Q2 (≥6.9 to <8.5)	Q3 (≥8.5 to <10.8)	Q4 (≥10.8)
PSA50-RR (LuPSMA)	6/21 (29%)	18/29 (62%)	17/22 (77%)	24/27 (89%)
PSA50-RR (Cabazitaxel)	12/28 (43%)	3/20 (15%)	11/30 (37%)	11/23 (48%)
OR (95% CI)	0.53 (0.15 -1.74)	9.3 (2.44 – 46.7)	5.9 (1.79 – 22.2)	8.7 (2.25 – 44.4)
p-value	0.3	0.002	0.005	0.003
	?	✓	✓	✓



SUVmean 33

Let's not forget about ^{18}F-FDG



Number at risk (number censored)

Q1	49 (0)	44 (3)	39 (3)	32 (3)	24 (3)	16 (6)	8 (11)
Q2	51 (0)	43 (4)	36 (5)	24 (5)	16 (5)	8 (5)	3 (8)
Q3	50 (0)	39 (6)	29 (6)	21 (6)	15 (6)	11 (7)	4 (12)
Q4	50 (0)	37 (6)	19 (6)	9 (6)	5 (6)	2 (8)	2 (8)

>250mL: treatment intensification

A powerful prognostic biomarker

Superior to conventional biomarkers

ECOG, ALP, haemoglobin, bone metastases, liver metastases

EAU26 | LONDON, GB
13-16 March 2026



PRIMARY 2

NCT 05154162

Multi-centre, randomised, phase III trial

Impact of PSMA PET/CT

in improving diagnosis of prostate cancer

in men with equivocal findings on mpMRI

JP Buteau, D Moon, MT Fahey, MJ Roberts, N Ayati, N Papa, DG Murphy, V Kasivisvanathan, YT Du, AC Hutton, G Jack, SF Lee, ST Lee, S Leslie, SM Levy, C Mitchell, JJ Morigi, A Nguyen, M Patel, DA Pattison, J Yaxley, J Thompson, **MS Hofman***, **L Emmett***
*joint senior authors

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PROSTATE CANCER FOUNDATION
PCF
CURING TOGETHER

ProsTIC
Prostate Theranostics Imaging Centre of Excellence

ANZUP
Cancer Trials Group Limited

Australian Government
National Health and Medical Research Council

©

Trial design

Multicentre, randomised-controlled, investigator-initiated, phase III

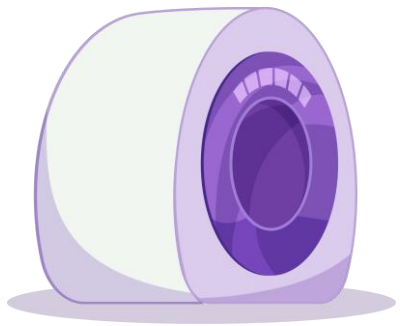
PRIMARY 2

NCT 05154162

primary2.com

660 men

Eligibility criteria:



PSA: **<20 ng/mL**
≤cT2 on DRE
Biopsy naïve

PI-RADS 2
with high clinical risk
(e.g. PSA density >0.1, strong family history)

or

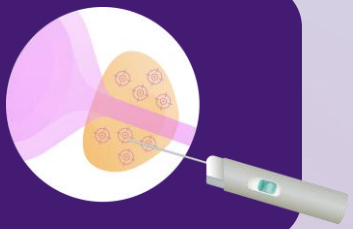
PI-RADS 3

7 Australian hospitals

Randomised 1:1

Control

Standard of Care
Systematic transperineal prostate biopsy



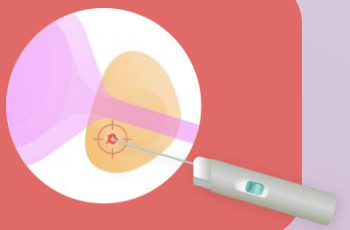
PSMA-PET

[^{68}Ga] Ga-PSMA-11
Pelvic-only



Positive

Targeted biopsy



Negative

No biopsy



Buteau et al. Eur Urol Oncol. 2024; PMID 38061976

European Association of Urology

©

Biopsy avoidance

PRIMARY 2

NCT 05154162

primary2.com



49%

(163/331
[95%CI 44, 55])

p < 0.0001



European Association of Urology

©

Significant prostate cancer

GS 3 + 4 (≥10%) = 7 or higher

PRIMARY 2

NCT 05154162

primary2.com



Difference:

-3·7%

(95% CI -8·9%, 1·5%)

p 0·0093



Control: 51/329 [16%]

PSMA-PET arm: 39/331 [12%]

©


IT'S
JUST
THE
BEGINNING!

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

Peter Mac

Peter MacCallum Cancer Foundation

ProsTIC

Prostate Theranostics Imaging Centre of Excellence

THANKS FOR
YOUR DONATION



DrMHofman

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