

PSMA and FDG-PET as predictive and prognostic biomarkers in patients given [¹⁷⁷Lu]Lu-PSMA-617 versus cabazitaxel for metastatic castration-resistant prostate cancer (TheraP ANZUP 1603): a biomarker analysis from a randomised, open-label, phase 2 trial

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for the TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group

TOP Trials Session 1: Best International Trials

Sunday, October 16, 2022

EANM'22 Annual Congress



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@DrMHofman

#TheraP

EANM Disclosure of Interest Statement

1. I hold a position as an employee, consultant, assessor or advisor for a pharmaceutical, device or biotechnology company.

No

2. I receive support from a pharmaceutical, device or biotechnology company.

No

3. I hold property rights/patents for (radio)pharmaceuticals, medical devices or medical consulting firms.

No

4. I have written articles for (radio)pharmaceutical, medical device, biotechnology or consulting companies during the last 5 years.

No

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Co-authors (unrelated to this work)

MSH reports grants from Novartis, ANSTO, Bayer, Isotopia; and consulting fees for lectures or advisory boards from Astellas, AstraZeneca, Janssen, Merck Sharp and Dohme (MSD), Mundipharma, and Point Biopharma.

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All other authors declare no competing interests.

PSMA and FDG-PET as predictive and prognostic biomarkers in patients given [^{177}Lu]Lu-PSMA-617 versus cabazitaxel for metastatic castration-resistant prostate cancer (TheraP): a biomarker analysis from a randomised, open-label, phase 2 trial



*James P Buteau, Andrew J Martin, Louise Emmett, Amir Iravani, Shahneen Sandhu, Anthony M Joshua, Roslyn J Francis, Alison Y Zhang, Andrew M Scott, Sze-Ting Lee, Arun A Azad, Margaret M McJannett, Martin R Stockler, Scott G Williams, Ian D Davis, Michael S Hofman, for the TheraP Trial Investigators and the Australian and New Zealand Urogenital and Prostate Cancer Trials Group**

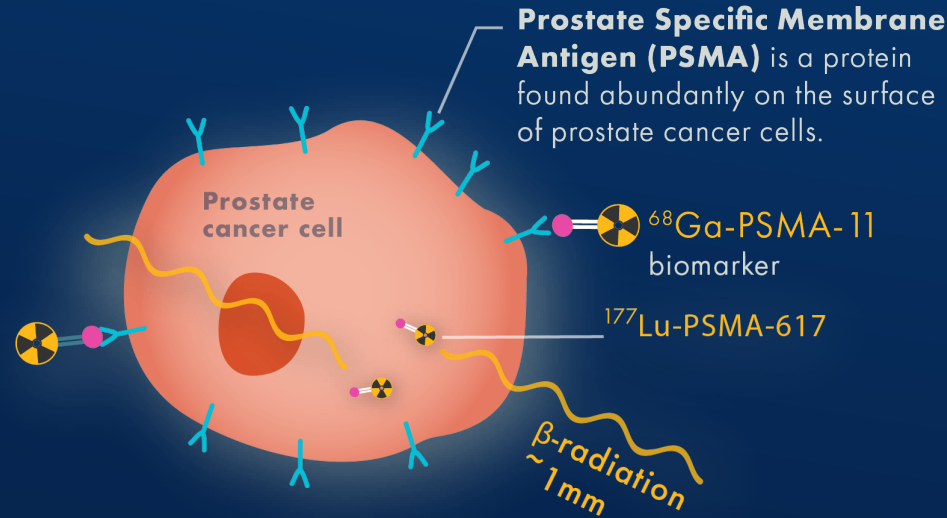
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PSMA PET as a predictive FDG PET as a prognostic biomarker

in a randomised phase II trial of **CABAZITAXEL** versus **¹⁷⁷Lu-PSMA-617**



TheraP: first randomized trial comparing LuPSMA vs. cabazitaxel¹

- 1° endpoint: PSA-50RR 66% vs. 37% (29% difference [95%CI 16-42]; p < 0.001)
- 2° endpoint: Lu-PSMA delayed progression HR 0.63 (95%CI 0.46-0.86 P=0.0028)

¹ Hofman MS Lancet 2021; 397: 797-804

PSMA PET as a predictive FDG PET as a prognostic biomarker

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Patient selection



PSMA PET

to measure intensity
of PSMA uptake
(SUVmean)



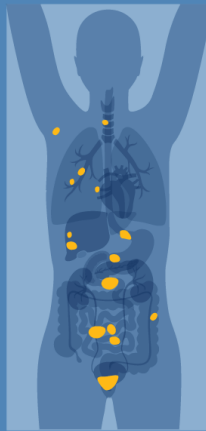
FDG PET

to measure
Metabolic Tumor
Volume (MTV)

SUVmax ≥ 20 on ⁶⁸Ga-PSMA at
a site of disease

No sites of disease
FDG positive/PSMA negative

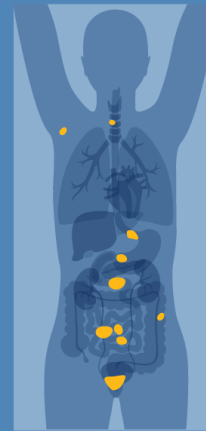
PSMA
positive



FDG
negative



PSMA
positive



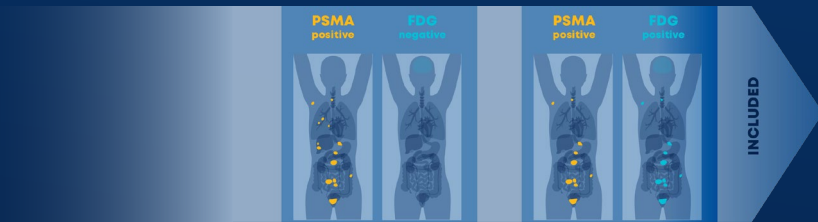
FDG
positive



INCLUDED

PSMA PET as a predictive FDG PET as a prognostic biomarker

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200

PATIENTS

across Australia
RANDOMISED

Hypotheses

- ↑PSMA intensity: ↑response to LuPSMA vs. Cabazitaxel
- ↑FDG volume: ↓response to either



50% patients treated with
CABAZITAXEL

20mg/m² IV q3 weekly
Up to 10 cycles



50% patients treated with
¹⁷⁷Lu-PSMA-617

8.5 GBq IV q6 weekly
0.5 GBq each cycle
Up to 6 cycles

Responses defined according to PSA50-RR (1° endpoint), and PSA-PFS and rPFS (2° endpoints)

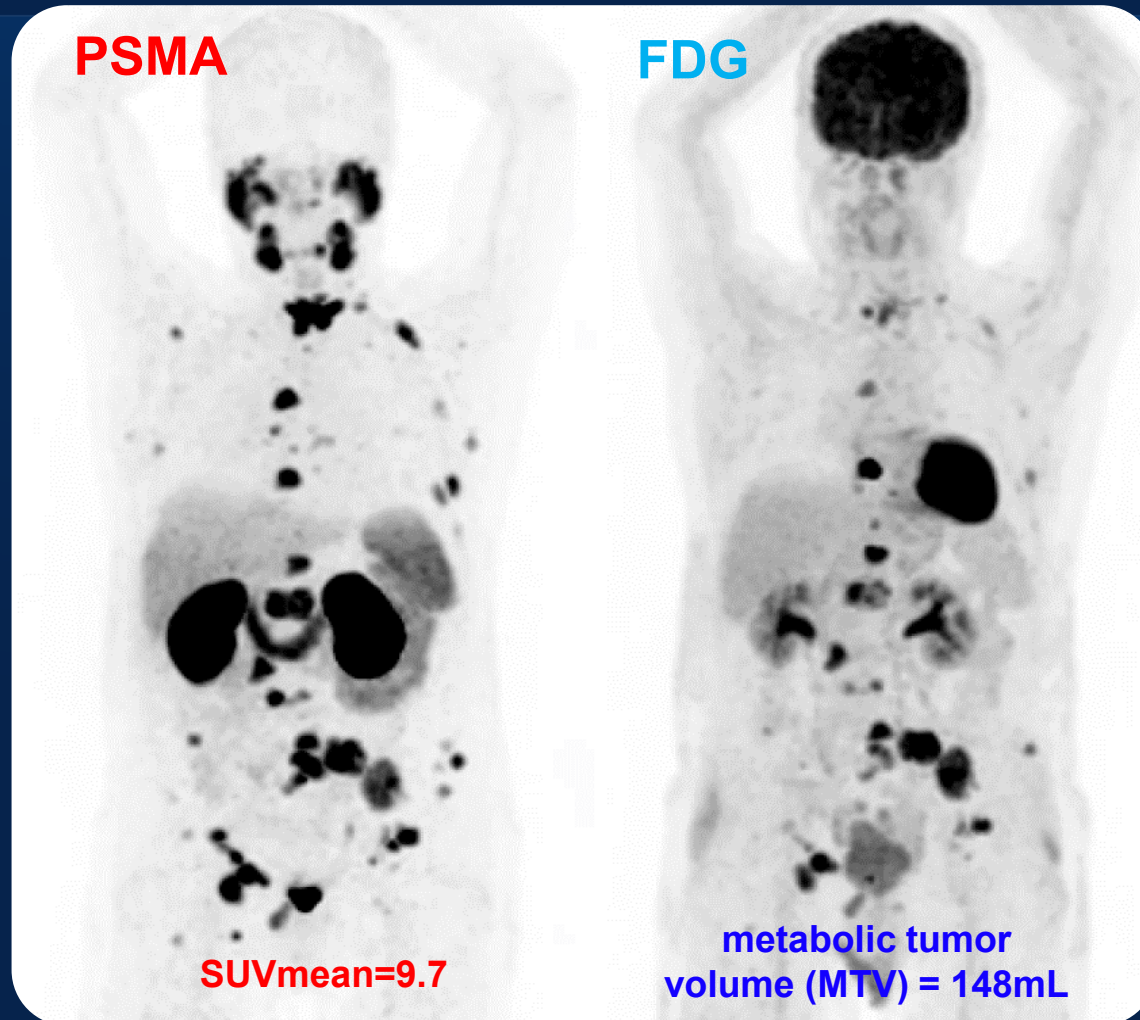
Binary and PFS endpoints were analysed using logistic and Cox regression, respectively.

Data cut-off as per Lancet 2021¹

¹ Hofman MS Lancet 2021; 397: 797-804

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SUV ≥ 3



SUV > liver_{mean} + 2 SD

PET scan quantification

- Centrally collected with WIDEN²
- Prospectively contoured with MIM Software
- Pre-defined cut-off points for contouring³

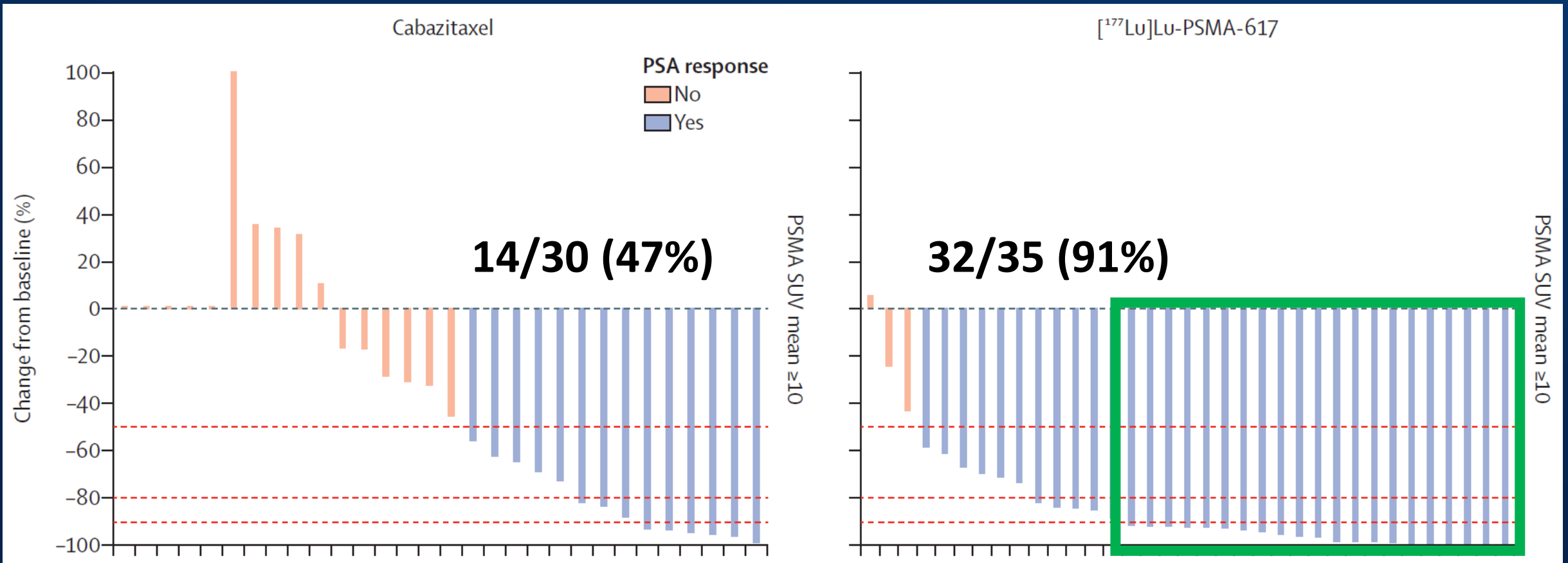
Baseline characteristics

	Cabazitaxel (n = 101)	Lu-PSMA (n = 99)
PSMA SUVmean ≥ 10	30/101 (30%)	35/99 (35%)
FDG volume ≥ 200 mL	30/101 (30%)	30/99 (30%)

² Chauvie S Clin Trials 2014; 11: 355-361

³ Ferdinandus J Eur J Nucl Med Mol Imaging 2020;47:2322-2327

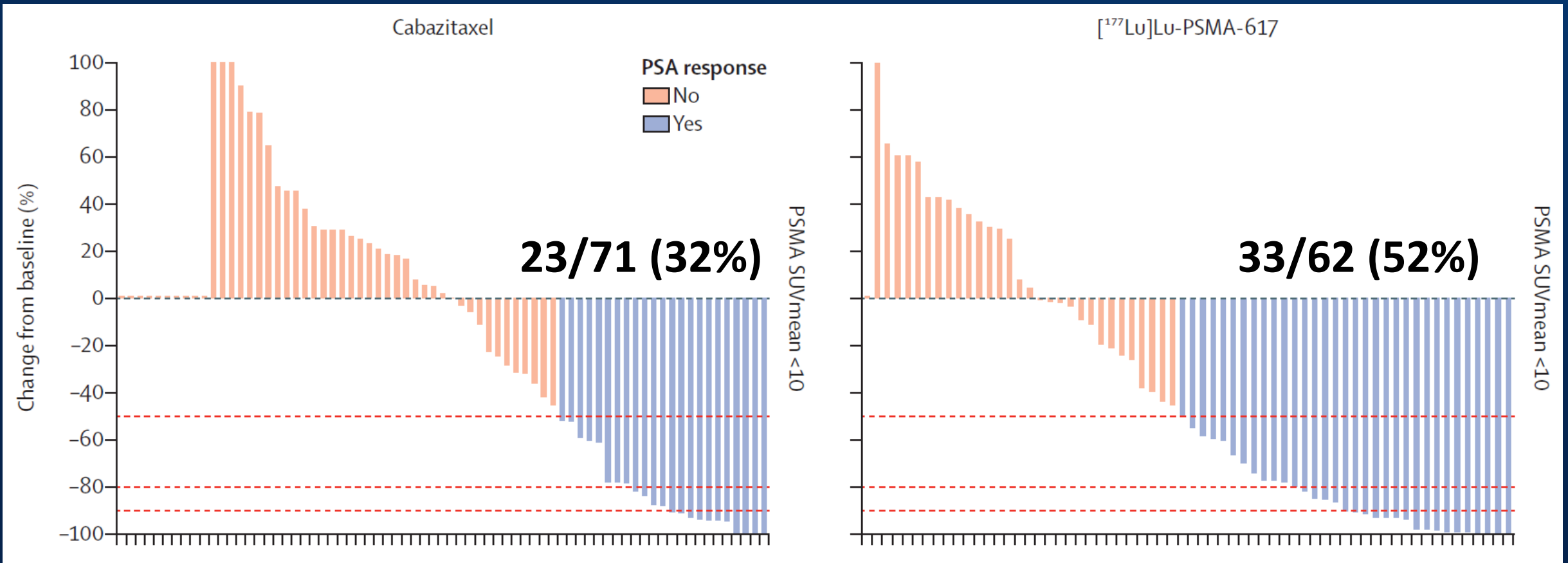
PSMA intensity: predictive biomarker (PSA50-RR)



PSMA PET as a predictive FDG PET as a prognostic biomarker

in a randomised phase II trial of **CABAZITAXEL** versus **¹⁷⁷Lu-PSMA-617**

PSMA intensity: predictive biomarker (PSA50-RR)



PSMA PET as a predictive FDG PET as a prognostic biomarker

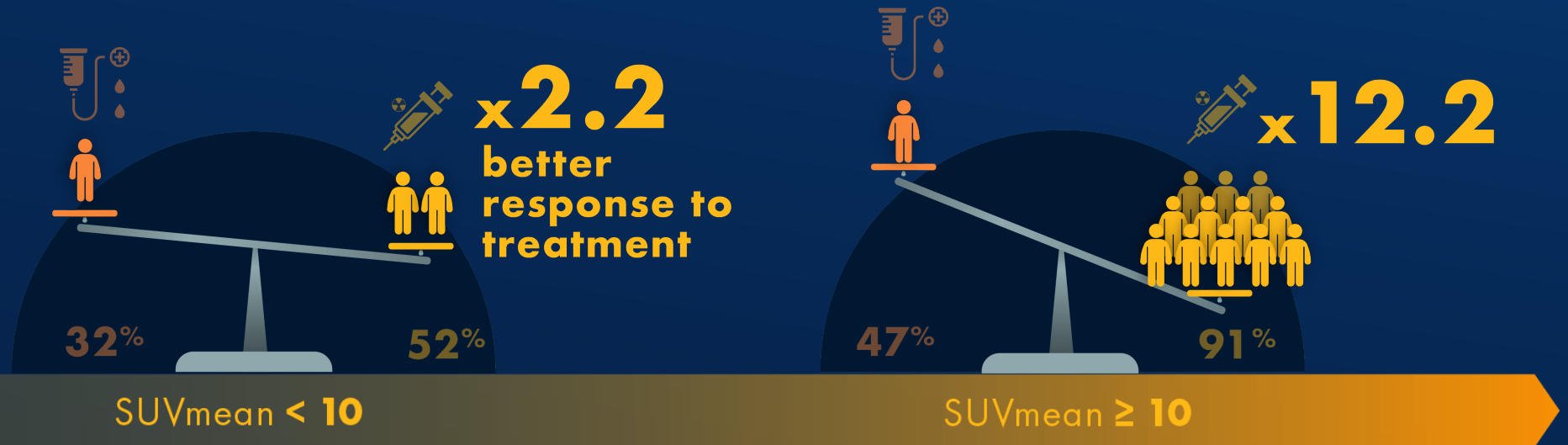
in a randomised phase II trial of **CABAZITAXEL** versus **¹⁷⁷Lu-PSMA-617**

Odds Ratio

PSA reduction $\geq 50\%$



PSMA PET



Higher PSMA intensity = better response to LuPSMA vs Cabazitaxel

$p=0.031$; $p_{\text{adj}} = 0.039$

PSMA PET as a predictive biomarker

FDG PET as a prognostic biomarker

in a randomised phase II trial of **CABAZITAXEL** versus **¹⁷⁷Lu-PSMA-617**



PSMA SUVmean

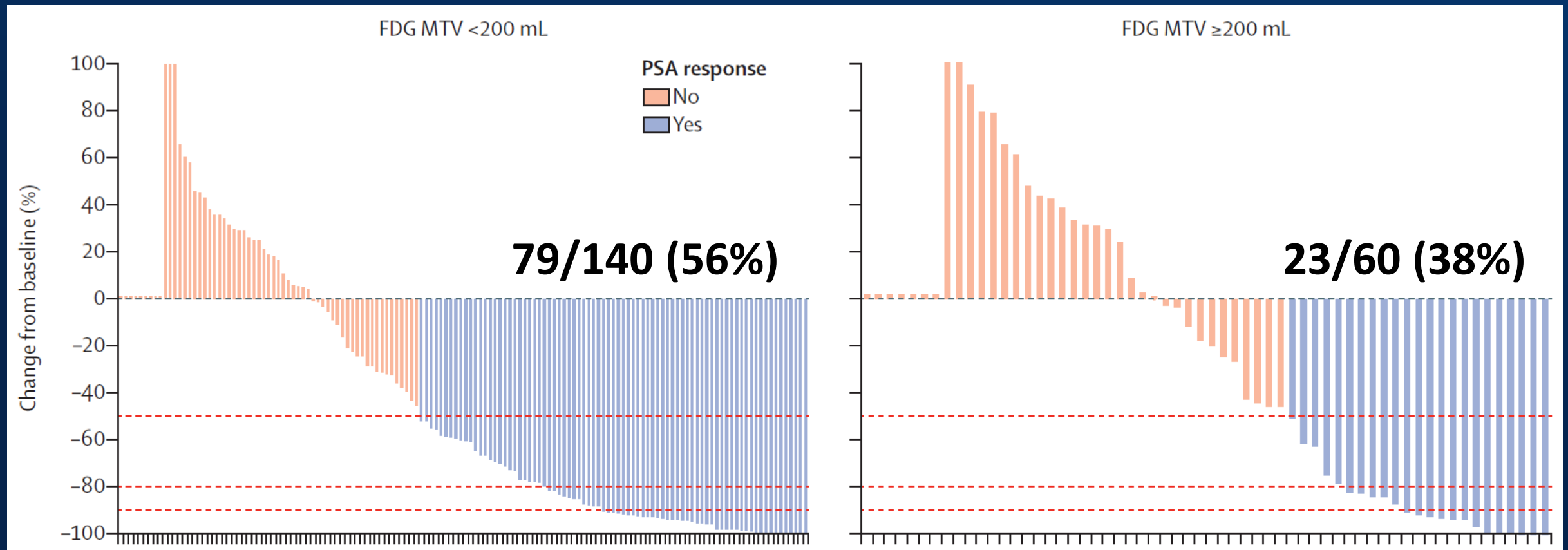
PSMA SUVmean	Q1 (<6.9)	Q2 (≥6.9 to <8.5)	Q3 (≥8.5 to <10.8)	Q4 (≥10.8)
PSA50-RR (LuPSMA)	6/21 (29%)	18/29 (62%)	17/22 (77%)	24/27 (89%)
PSA50-RR (Cabazitaxel)	12/28 (43%)	3/20 (15%)	11/30 (37%)	11/23 (48%)
OR (95% CI)	0.53 (0.15 - 1.74)	9.3 (2.44 - 46.7)	5.9 (1.79 - 22.2)	8.7 (2.25 - 44.4)
p-value	0.3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



SUVmean 4.9

SUVmean 33

FDG volume: prognostic biomarker (PSA50-RR)

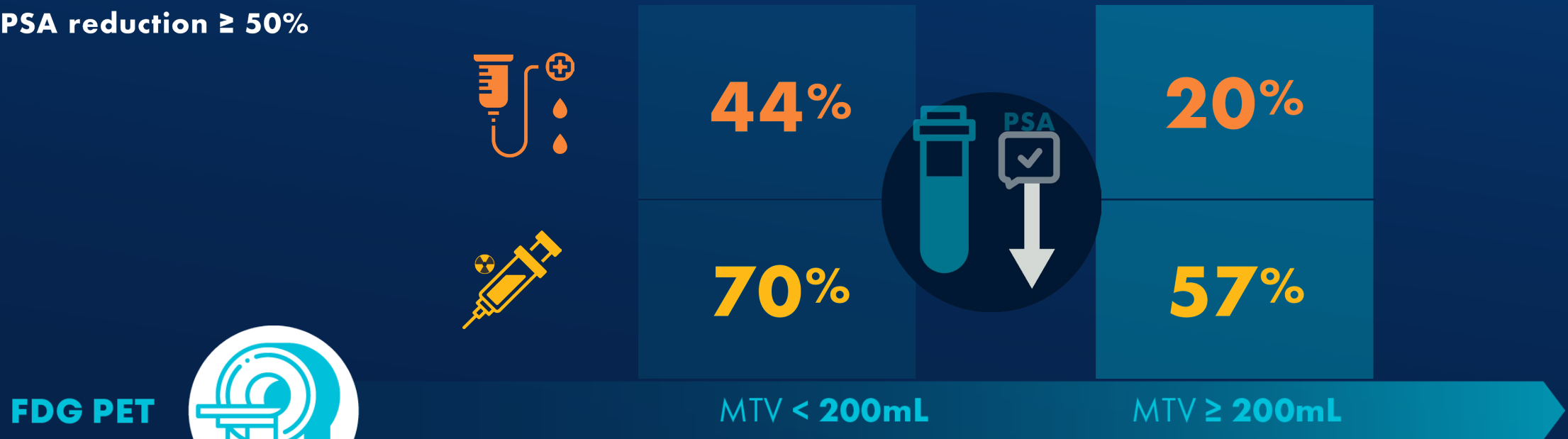


PSMA PET as a predictive FDG PET as a prognostic biomarker

in a randomised phase II trial of **CABAZITAXEL** versus **¹⁷⁷Lu-PSMA-617**

Response Rate

PSA reduction $\geq 50\%$

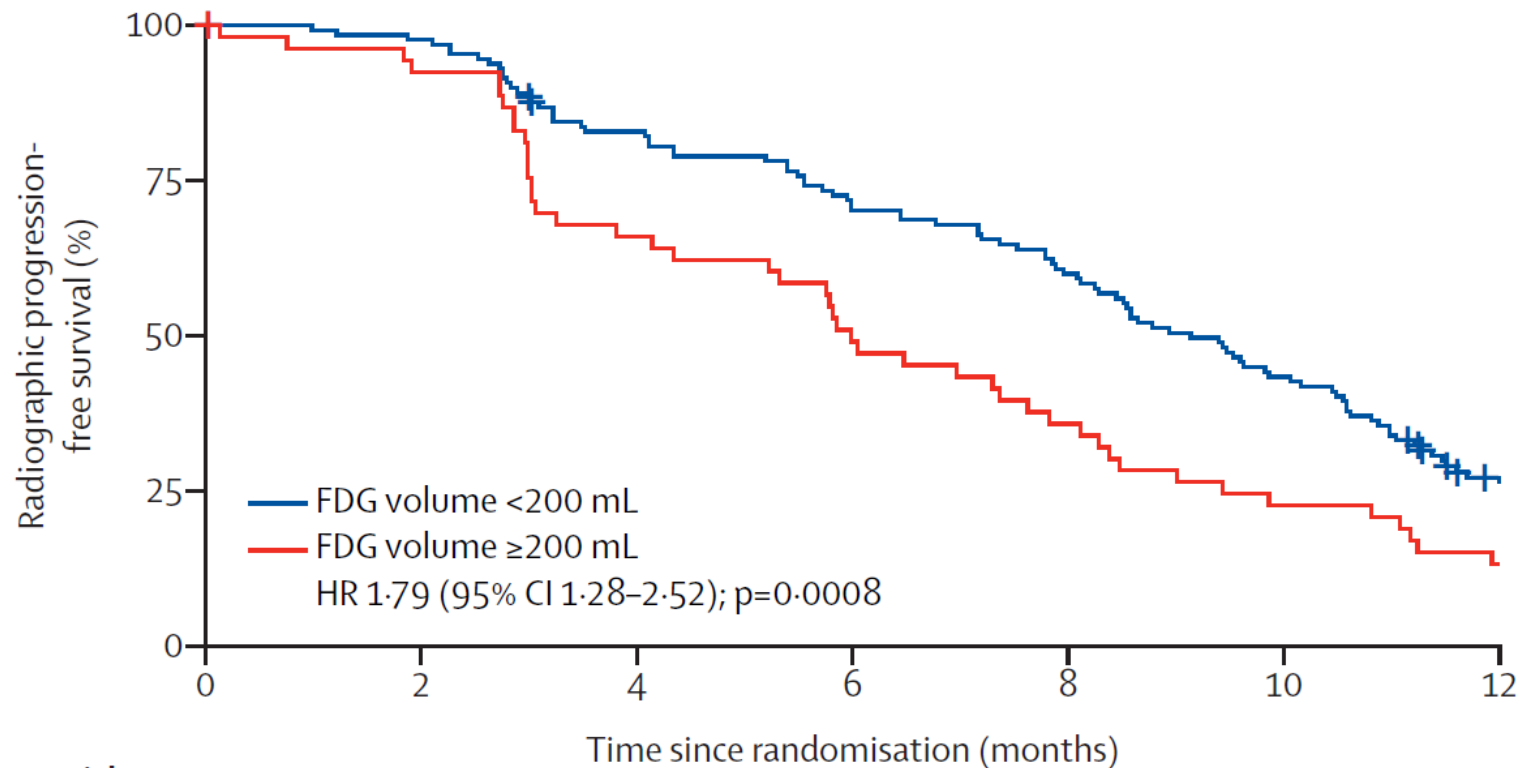


Higher FDG volume = worse response to either LuPSMA or Cabazitaxel
Odds ratio 0.44; $p=0.014$, $p_{adj}=0.35$

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

in a randomised phase II trial of **CABAZITAXEL** versus **¹⁷⁷Lu-PSMA-617**

FDG volume: prognostic biomarker (rPFS)



	Time since randomisation (months)						
	Number at risk (number censored)						
FDG volume < 200 mL	140 (0)	126 (11)	105 (13)	89 (13)	76 (13)	55 (13)	28 (13)
FDG volume ≥200 mL	60 (0)	49 (7)	35 (7)	26 (7)	19 (7)	12 (7)	7 (7)

PSMA PET as a predictive FDG PET as a prognostic biomarker

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Strengths

Prospective,
randomized, multi-
center

PSMA + FDG

Pre-specified
predictive and
prognostic biomarkers

Weaknesses

Manual contouring:
labor intensive

No information in
patients with lower
PSMA expression
(>liver, SUVmax<20)

No OS (analysis
planned)

Clinical Implications

High PSMA uptake
Prioritize LuPSMA

High FDG volume
Research for treatment
intensification

Quantitative PET
parameters valuable

Conclusion

In patients with mCRPC,

High PSMA expression (SUVmean \geq 10) was *predictive* of a higher likelihood of favorable response to LuPSMA than cabazitaxel

A high volume of disease on FDG PET (MTV $>$ 200mL) was associated with worse *prognosis* regardless of randomly assigned treatment

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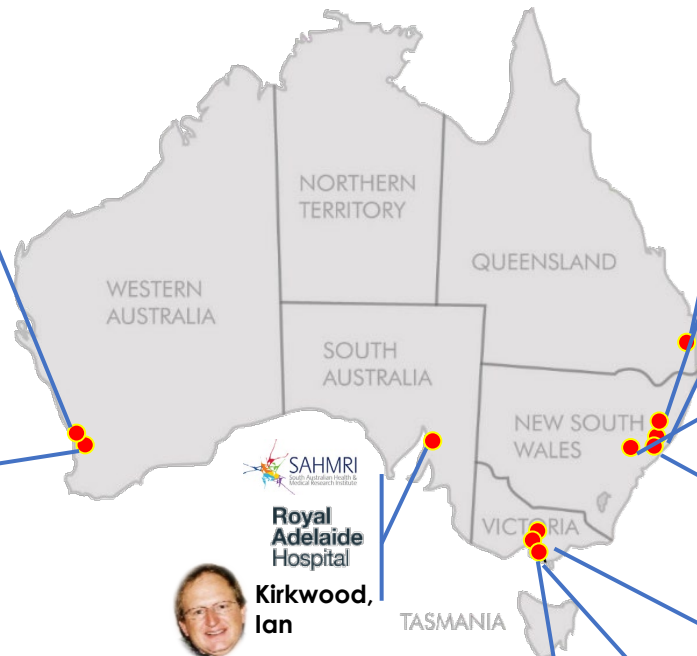
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All slides can be downloaded at:
www.anzup.org.au/therap

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- Nuclear medicine technologists
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- Australasian Radiopharmaceutical Trials Network (ARTnet)



TheraP ANZUP 1603

Evaluation of

PSMA PET as a predictive **FDG PET as a prognostic** **biomarker**

in a randomised phase II trial of **CABAZITAXEL** versus **¹⁷⁷Lu-PSMA-617**



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[Clinicaltrials.gov NCT03392428](https://clinicaltrials.gov/NCT03392428)