2022 ASCO® ANNUAL MEETING

ANZUP® Cancer Trials Group Limited

^{177}Lu-PSMA-617 (LuPSMA) versus cabazitaxel in metastatic castration resistant prostate cancer (mCRPC) progressing after docetaxel: overall survival after median follow-up of 3 years

(TheraP ANZUP 1603)

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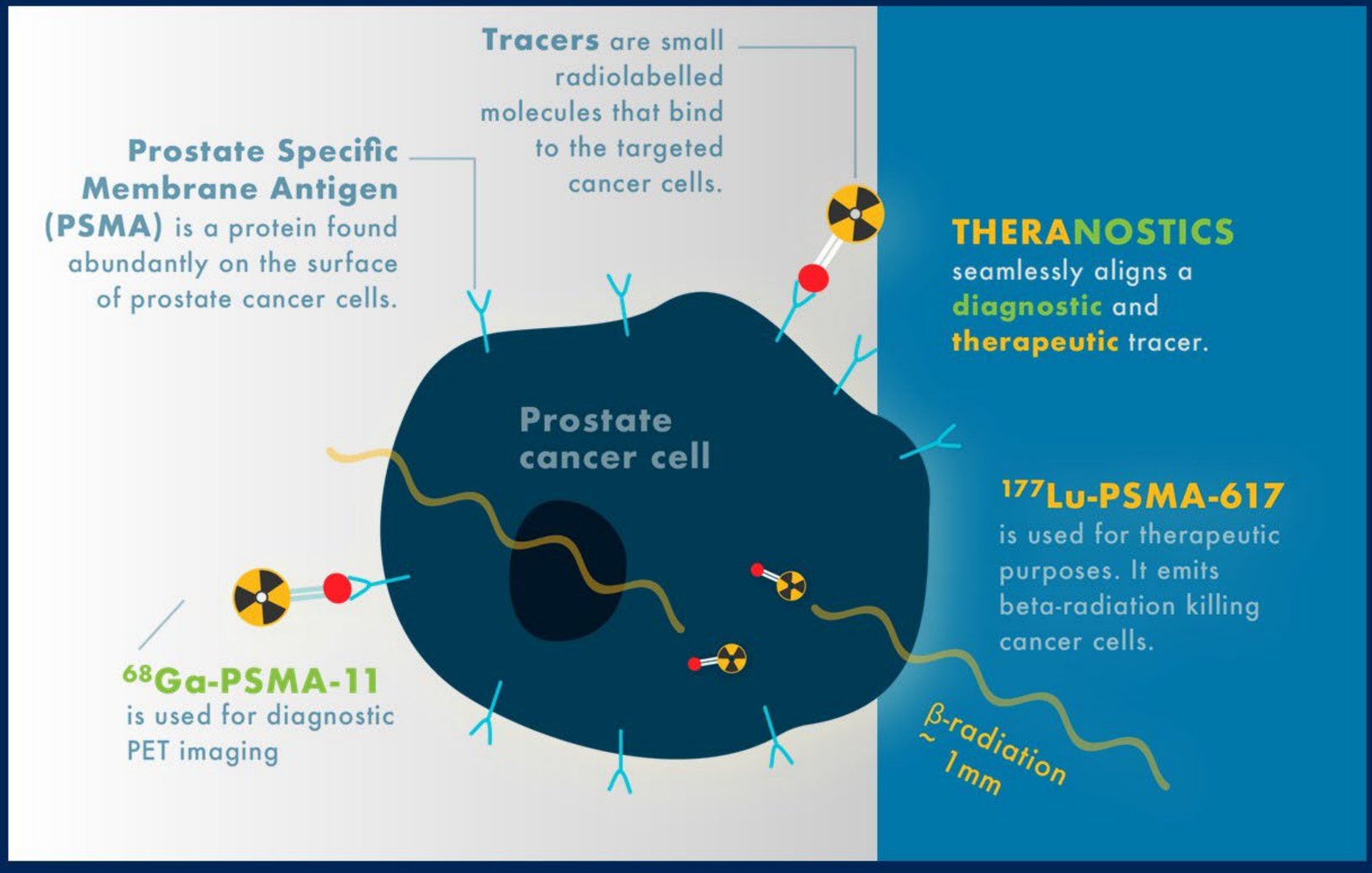
TheraP is a partnership between ANZUP Cancer Trials Group and the Prostate Cancer Foundation of Australia (PCFA) in collaboration with the NHMRC Clinical Trials Centre (CTC) and the Australasian Radiopharmaceutical Trials Network (ARTnet) with support from the Australian Nuclear Science and Technology Organisation (ANSTO) and Endocyte Inc., a Novartis company

Clinicaltrials.gov NCT03392428

^{177}Lu-PSMA-617: ↑OS and QoL in mCRPC[1]



[1] Sartor O et al, NEJM 2021; 385

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TheraP: First randomized trial of LuPSMA vs. cabazitaxel[1]

50% MEN TREATED WITH
CABAZITAXEL
20mg/m2 IV q3 weekly
Up to 10 cycles

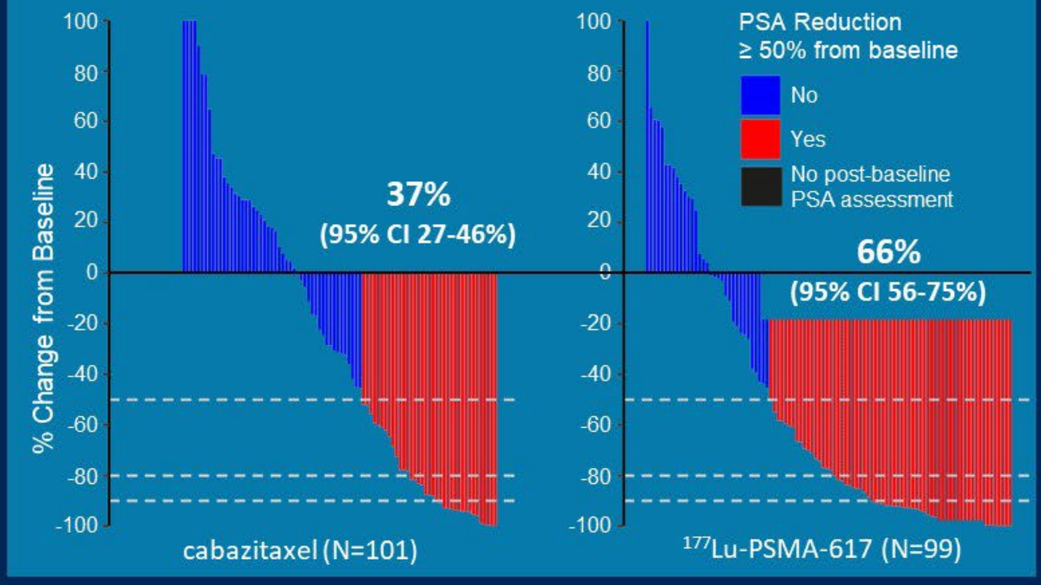
50% MEN TREATED WITH
^{177}Lu-PSMA-617
8.5 GBq IV q6 weekly
↓ 0.5 GBq each cycle
Up to 6 cycles

1º endpoint

PSA Reduction
≥ 50% from baseline

37%
66%

^{177}Lu-PSMA-617: 29% (95% CI 16%-42%; p<0.0001) greater PSA50-RR



2º endpoints

Progression Free Survival
at 12 months

3%
19%

Objective Response Rate
on CT Scan (RECIST)

24%
49%

Troublesome Adverse Events
Grade 3-4

53%
33%

Patient Reported Outcomes

- Diarrhea
- Fatigue
- Hair loss
- Urinary symptoms
- Dizziness
- skin rash
- Painful hands/feet
- Insomnia

[1] Hofman MS et al, Lancet 2021; 397(10276)

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Michael Hofman, MBBS @DrMHofman

TheraP Trial Schema

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KEY ELIGIBILITY
- mCRPC post docetaxel
- Rising PSA and PSA ≥ 20 ng/mL
- ECOG 0-2

^{68}Ga-PSMA-11 + FDG PET/CT
- PSMA SUVmax > 20 at any site
- No FDG positive/PSMA negative sites of disease
- Centrally reviewed

R

^{177}Lu-PSMA-617
8.5 GBq IV q6 weekly
↓ 0.5GBq each cycle
Up to 6 cycles

SPECT/CT @ 24 hours
suspend Rx if no or minimal uptake (centrally reviewed)

200 men 1:1 randomisation
11 sites in Australia
Stratified by:
- Disease burden (>20 sites vs ≤ 20 sites)
- Prior enzalutamide or abiraterone
- Study site

CABAZITAXEL
20mg/m^2 IV q3 weekly,
Up to 10 cycles

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Aim: report secondary endpoint of OS

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N=291 registered

^{68}Ga-PSMA-11 + FDG PET/CT
- PSMA SUVmax > 20 at any site
- No FDG positive/PSMA negative sites of disease
- Centrally reviewed

N=200

R

N=91 ineligible
- Low PSMA expression (n=29)
- FDG discordant disease (n=51)
- Other (n=11)

28% unsuitable
→followed-up for OS

^{177}Lu-PSMA-617
8.5 ↓ 0.5GBq IV q6 weekly
Up to 6 cycles
median 5
exceptional response 7

N=99
Died prior to Rx (n=1)

POST PROTOCOL SYSTEM TREATMENT
- Cabazitaxel (32)
- LuPSMA (5)
- Abiraterone (5)
- Enzalutamide (2)

CABAZITAXEL
20mg/m^2 IV q3 weekly,
Up to 10 cycles
median 8

N=101
Met exclusion criterion (n=1)
Withdrawal of consent (n=15)

- Cabazitaxel (21)
- LuPSMA (20)
- Abiraterone (7)
- Enzalutamide (9)

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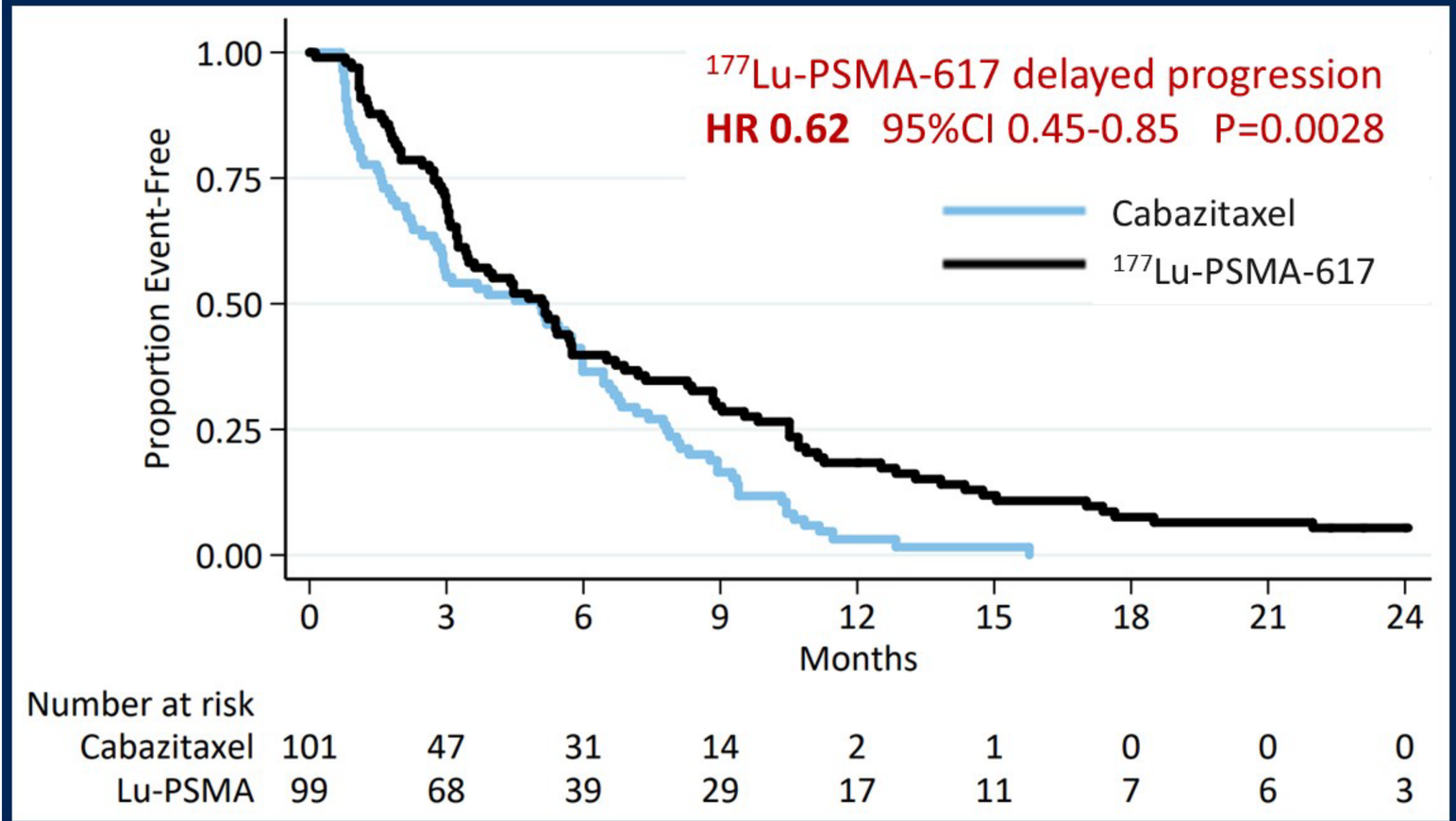
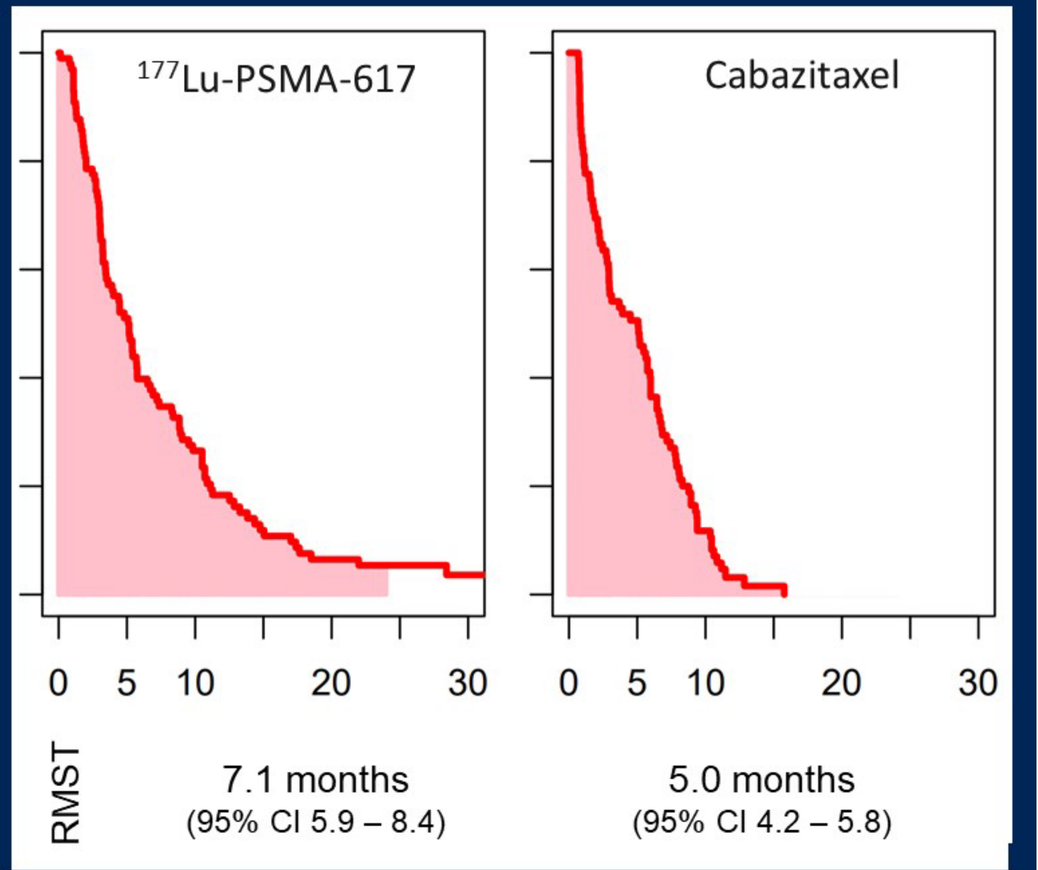
Progression Free Survival (PSA and radiographic)





- Treatment effect not constant with respect to time → restricted mean survival time (RMST)
- 177 progression events. Cut-off 31 DEC 2020 for non-OS endpoints.
- Similar HR for rPFS (0.65) and PSA-PFS (0.60), and in per-protocol sensitivity analyses

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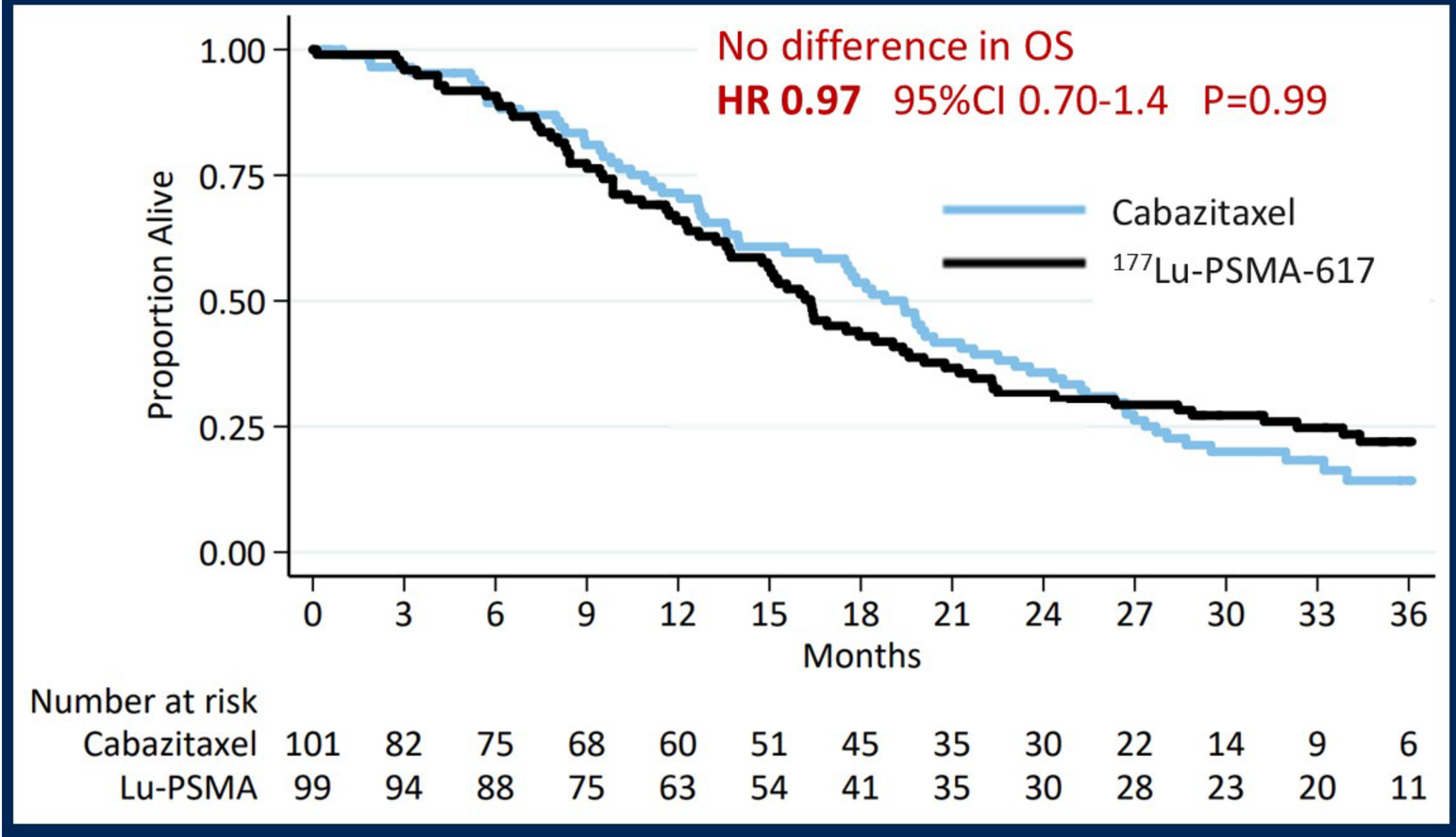
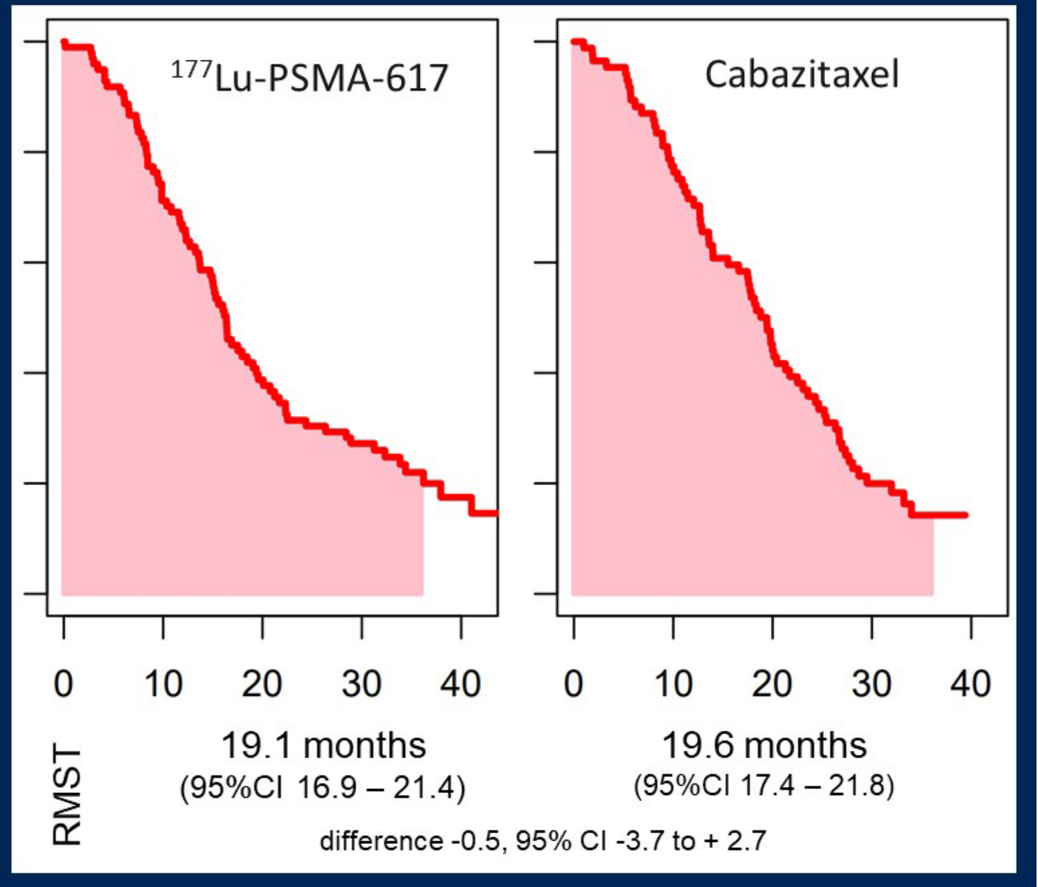
Overall survival (ITT)





- Cut-off 31 DEC 2021 for OS
- At 36 months follow-up, death reported in 147/200; 70/101 assigned cabazitaxel vs. 77/99 assigned LuPSMA
- Per-protocol analysis: no difference in OS
- No additional safety signals with longer follow-up.

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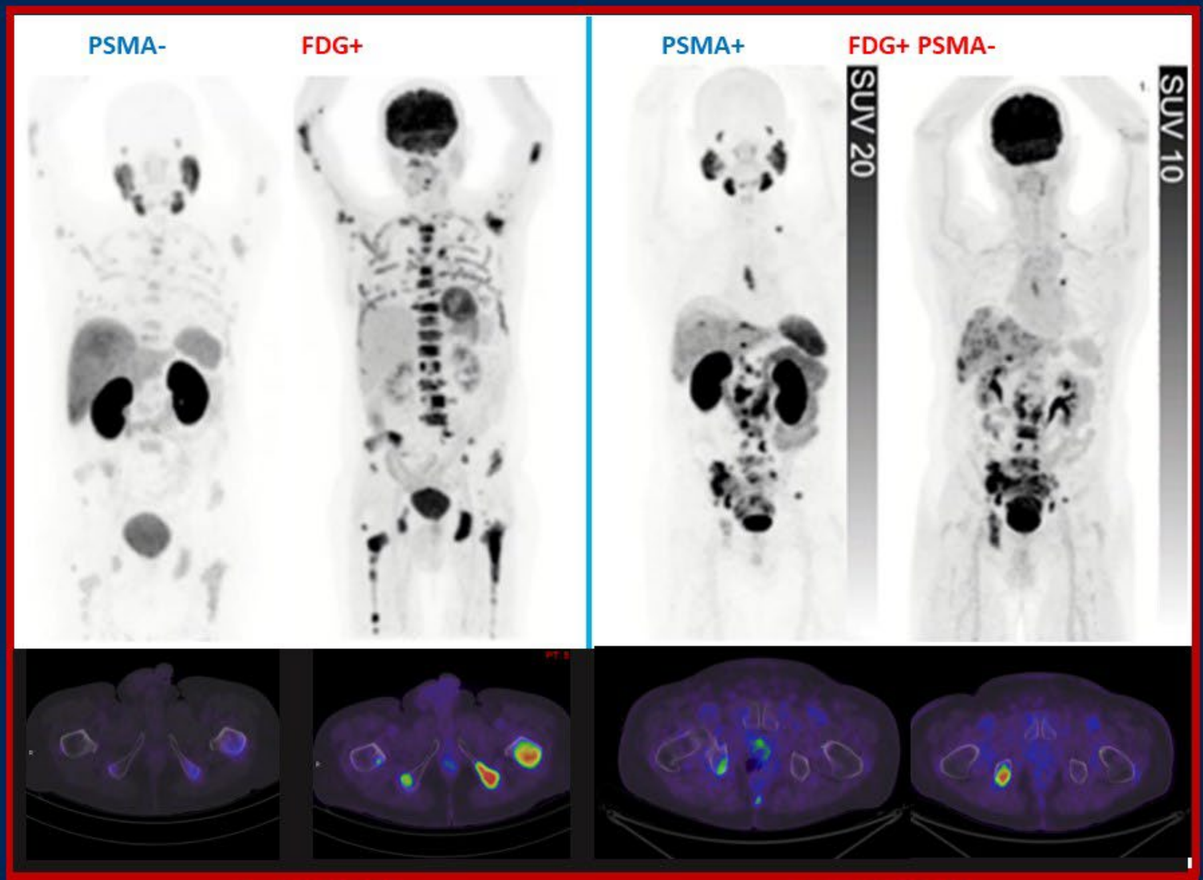
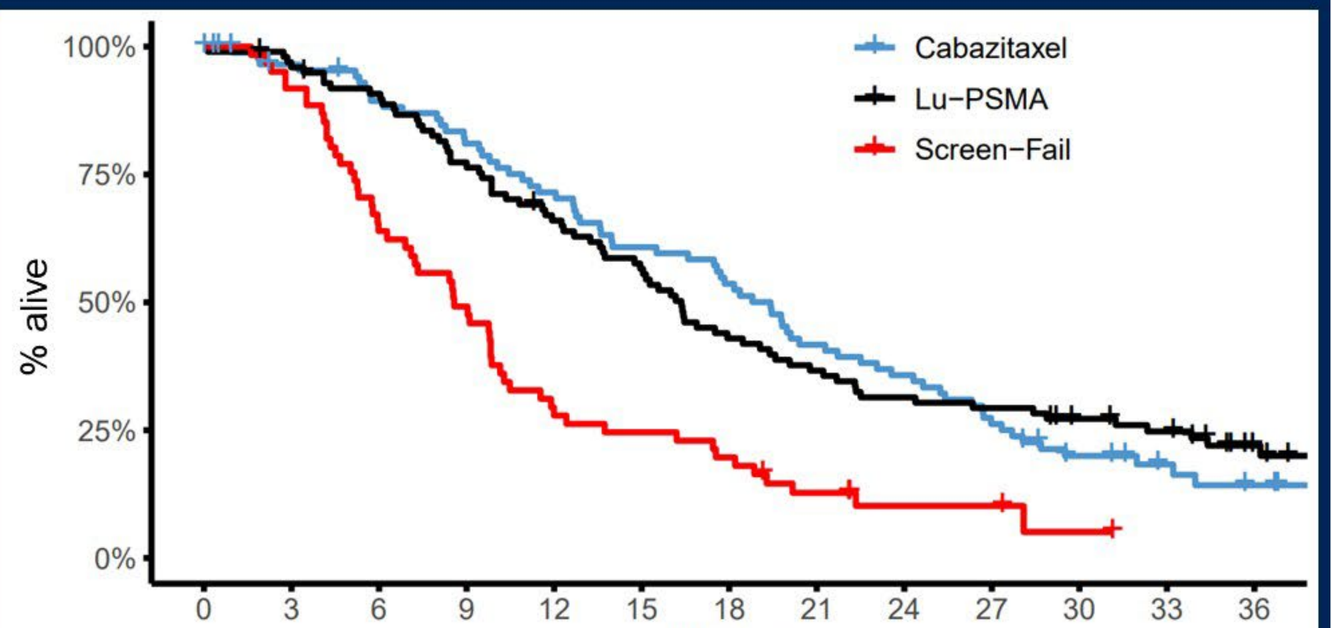
OS of PSMA/FDG PET Screen Failures



n=51(18%) n=29 (10%)

Ineligible (n=80, 28%)

Patients met other TheraP trial eligibility criteria.
61 of 80 consented for follow-up



Number at risk

Cabazitaxel	101	82	75	68	60	51	45	35	30	22	14	9	6
Lu−PSMA	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

Next line of treatment: cabazitaxel 29 (48%), enzalutamide 4 (7%), LuPSMA 3 (5%), carboplatin 3 (5%), other 3 (5%), mitoxantrone 1 (2%)

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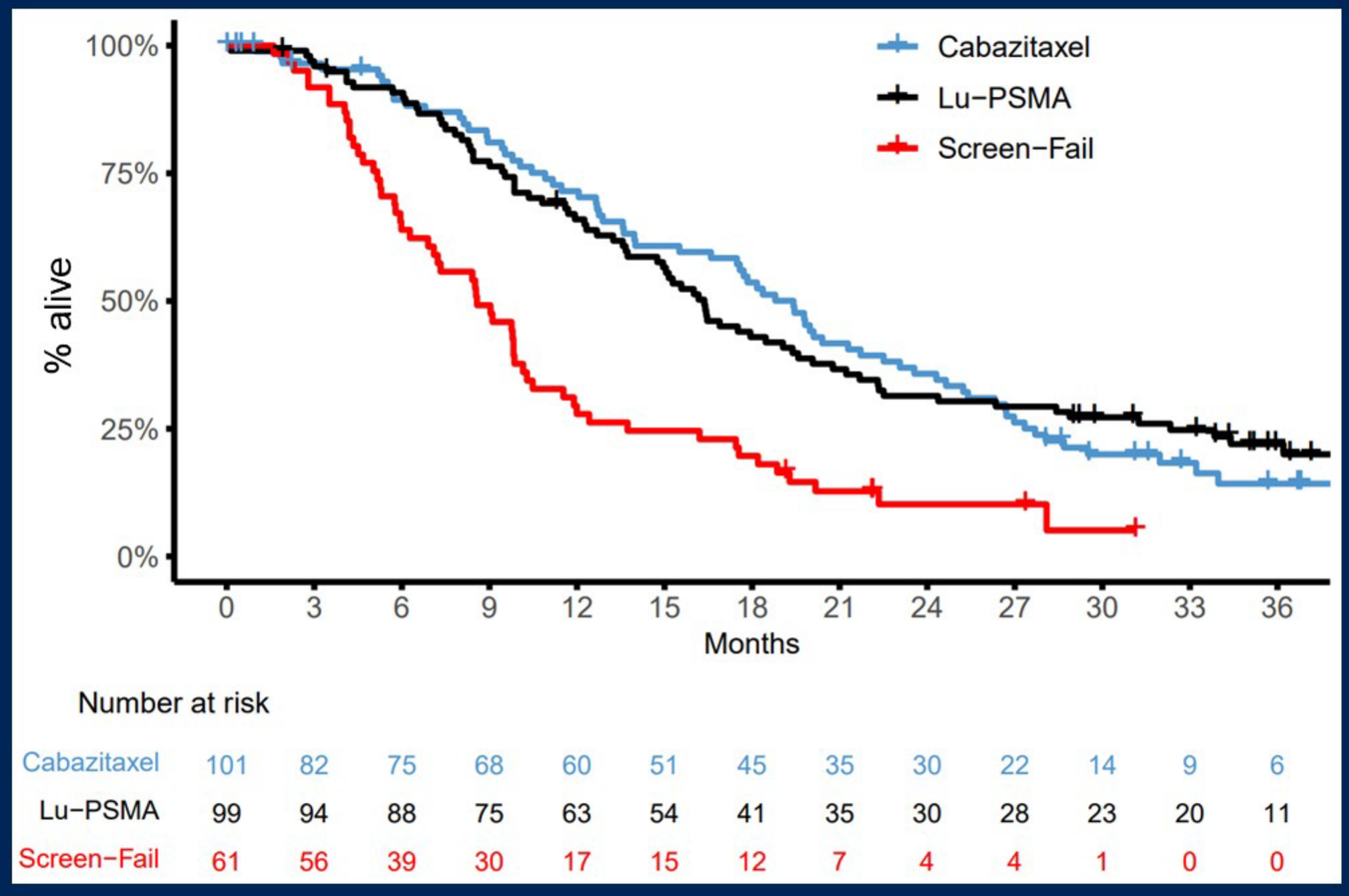
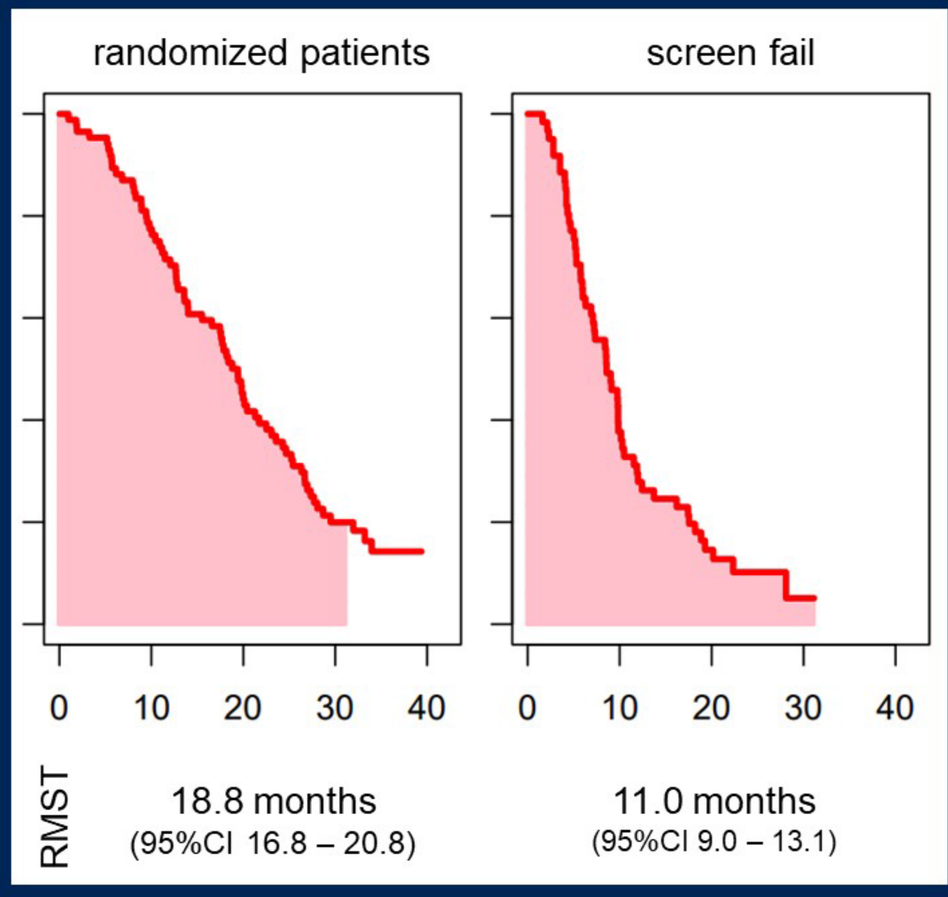
OS of PSMA/FDG PET Screen Failure





Next line of treatment: cabazitaxel 29 (48%), enzalutamide 4 (7%), LuPSMA 3 (5%), carboplatin 3 (5%), other 3 (5%), mitoxantrone 1 (2%)

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Discussion

Strengths

- Prospective, randomized, multi-center
- 3 years follow-up
- Active control arm[1] (vs. VISION)

Limitations

- Post protocol cross-over confounds OS
- Withdrawal post randomization in cabazitaxel arm
- OS a 2º endpoint (underpowered)

Clinical Implications

- LuPSMA: >greater activity
  PSA50-RR, RECIST, rPFS, PSA-PFS
- Similar OS to cabazitaxel, a life prolonging treatment[1]
- Fewer AEs, better patient reported outcomes

[1] de Wit R et al, NEJM 2019; 381

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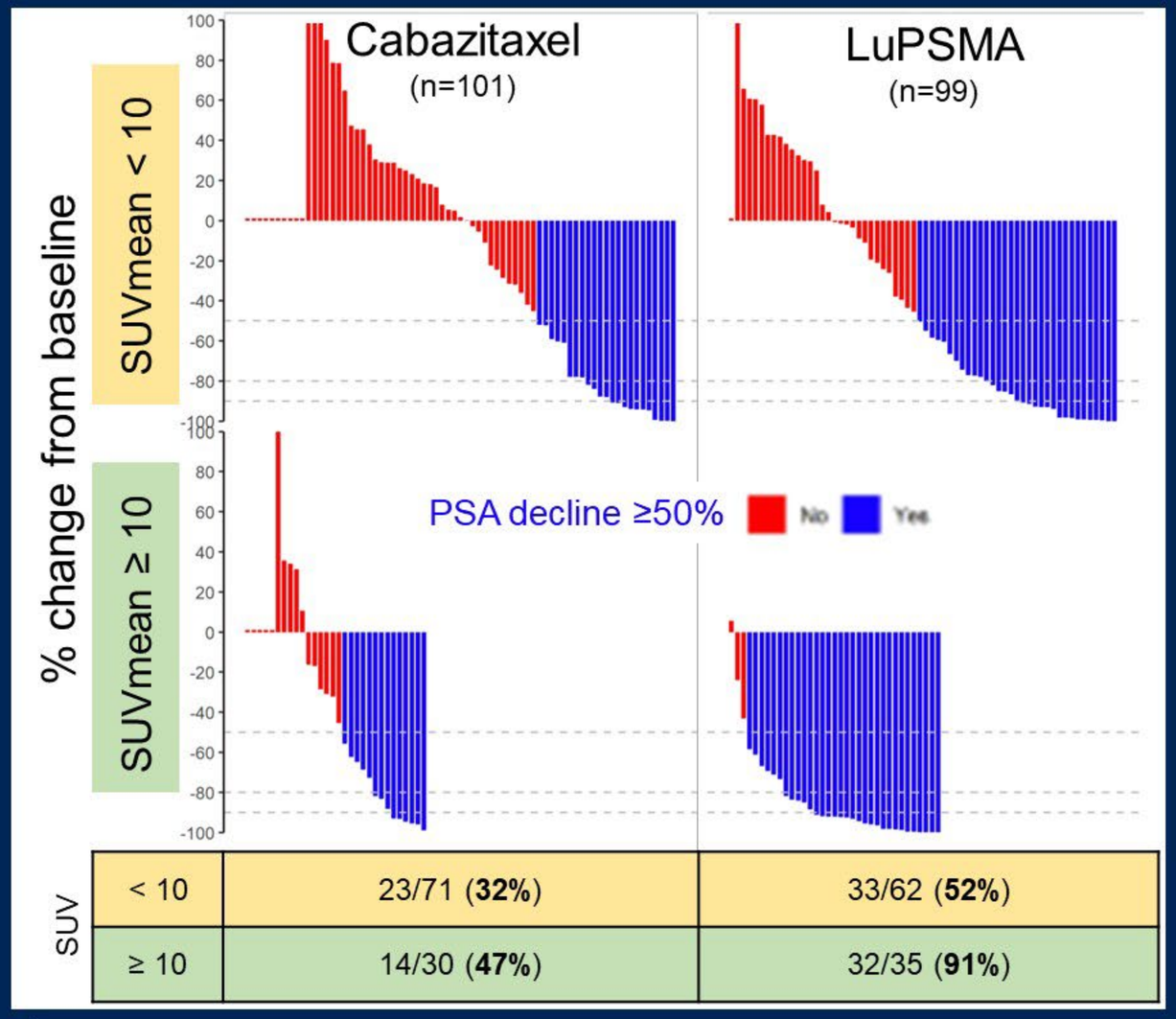
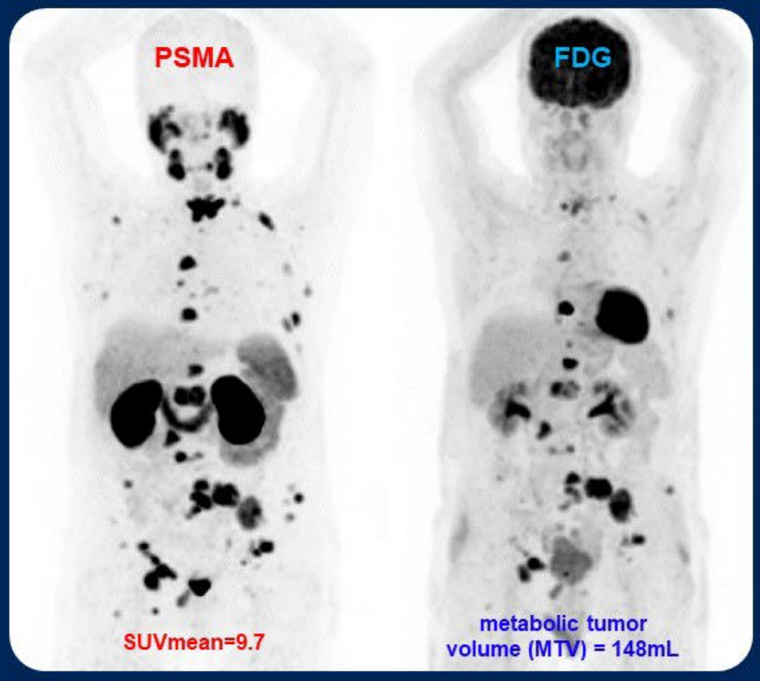
Discussion: PSMA as predictive biomarker[1] (PSA50-RR)



SUV		Cabazitaxel (n=101)	LuPSMA (n=99)
SUV	< 10	23/71 (**32%**)	33/62 (**52%**)
SUV	≥ 10	14/30 (**47%**)	32/35 (**91%**)



Odds of PSA50-RR to LuPSMA *vs* cabazitaxel

	OR (95% CI)
PSMA SUVmean < 10	2.2 (1.1 – 4.5)
PSMA SUVmean ≥ 10	12.2 (3.4 - 59)

P=0.03

Further analysis to be performed including OS

[1]Buteau J et al, ASCO GU 2022. doi:10.1200/JCO.2022.40.6_suppl.010

Conclusion

The TheraP data support the choice of ^{177}Lu-PSMA-617 over cabazitaxel for patients with PSMA-positive, progressive mCRPC after docetaxel and androgen-receptor pathway inhibitor, on the basis of its higher PSA response rate, greater PFS benefit, QoL benefits, favorable safety profile and dosing schedule, and similar survival outcomes.

Survival was considerably shorter for patients excluded on PSMA/FDG-PET with either low PSMA-expression, or discordant disease.

Acknowledgements

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

We thank:

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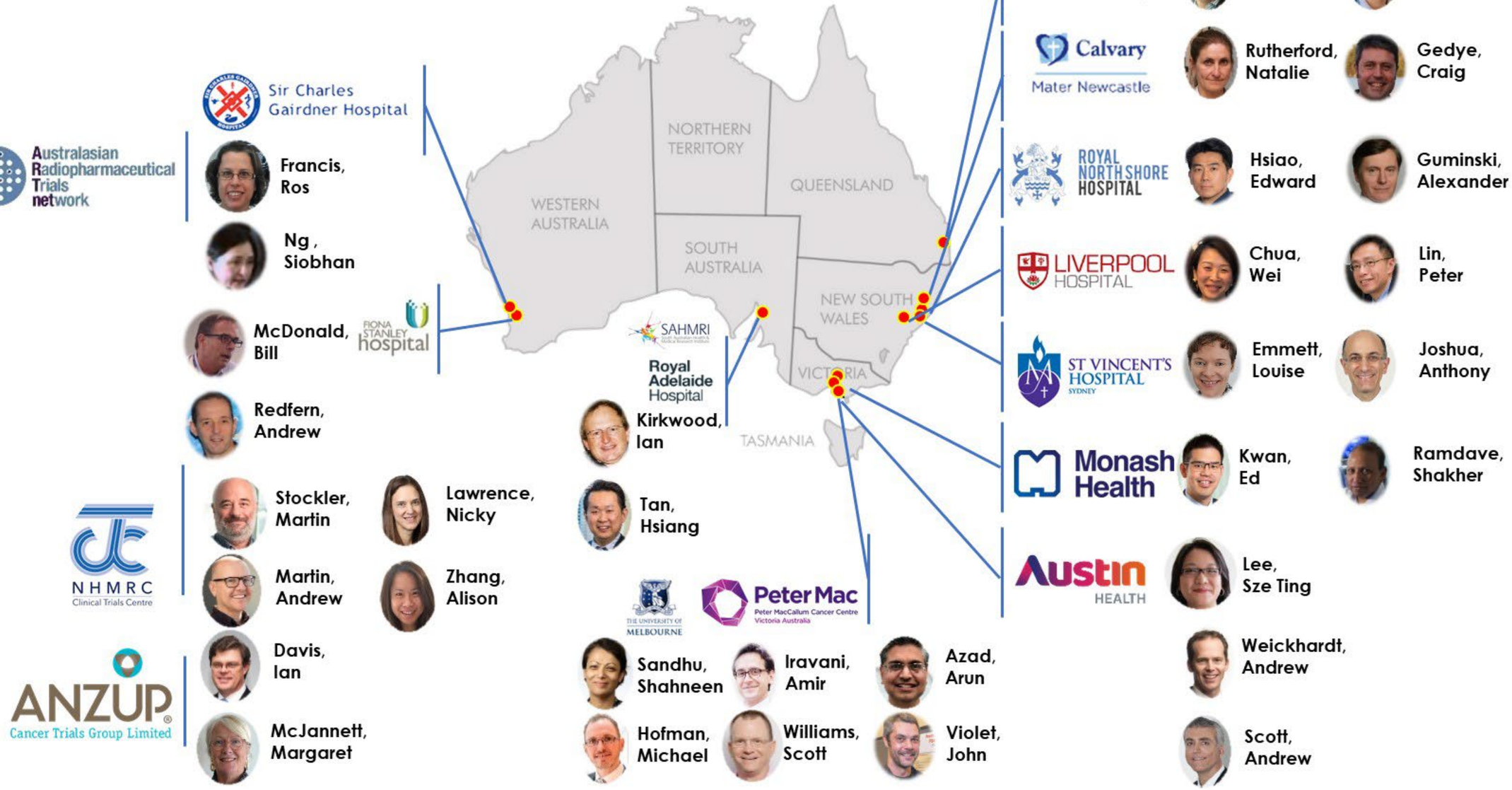
- Australasian Radiopharmaceutical Trials Network (ARTnet)

#TheraP Study Team



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