MADRID 2017 ESMO congress

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

Lutetium-177 PSMA (LuPSMA) Theranostic Phase II trial: Efficacy, safety and QoL in patients with castrate-resistant prostate cancer treated with LuPSMA

M. S. Hofman, S. Sandhu, P. Eu, P. Jackson, T. Akhurst, A. Iravani, G. Kong, A. Ravi Kumar, S. Williams, S. Thang, D. Murphy, M. Scalzo, R.J. Hicks, J. Violet

Peter MacCallum Cancer Centre, Melbourne, Australia

Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, Australia

✉ Associate Professor Michael Hofman, MBBS, FRACP, FAANMS
michael.hofman@petermac.org

esmo.org

Prostate 785O

DISCLOSURE AND ACKNOWLEDGEMENTS

- Authors declare no conflicts of interest
- Lutetium-177 (no carrier added) supplied by Australian Nuclear Science & Technology Organisation (ANSTO, Australia)
- PSMA617 supplied by Advanced Biochemical Compounds (ABX, Germany)
- ANSTO and ABX provided no input into trial design, execution or analysis
- Supported by a Clinical Fellowship Award (MH) from the Peter MacCallum Foundation

Australian Government | ansto Nuclear-based science benefiting all Australians

ABX advanced biochemical compounds

Prostate specific membrane antigen (PSMA)

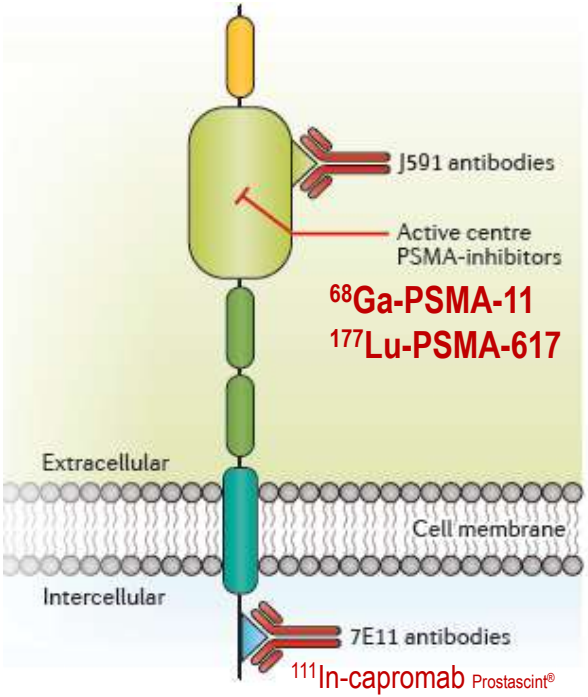
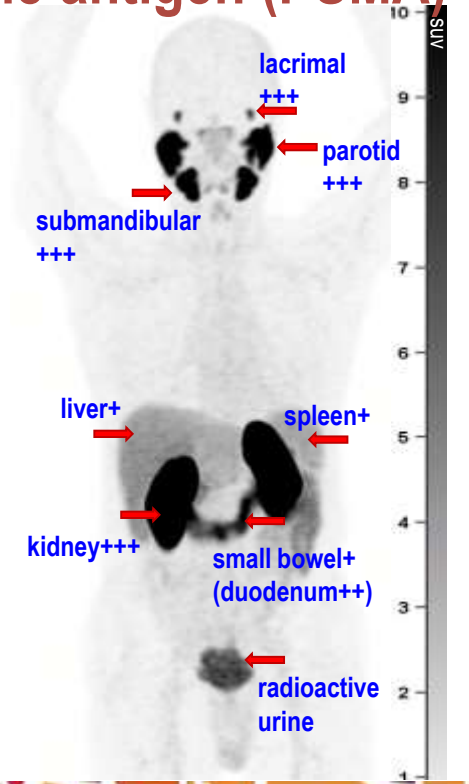


Image from Maurer T et al. Nat Rev Urol. 2016 Apr;13(4):226-35



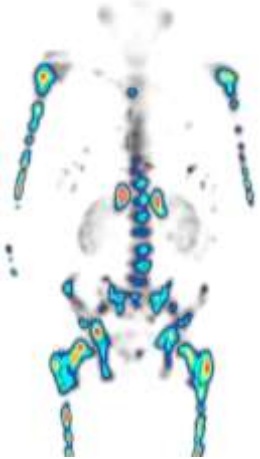
- Type II transmembrane glycoprotein (FOLH1)
- Highly over-expressed in prostate cancer
- ↑↑ castrate-resistant metastatic disease

PSMA PET
normal biodistribution

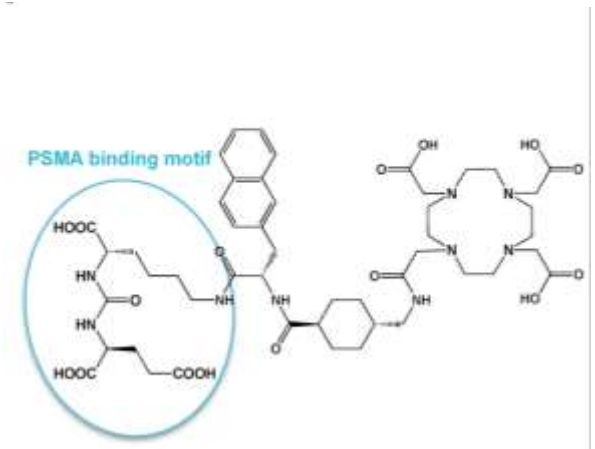
THERANOSTICS

TARGETED THERAPEUTIC + DIAGNOSTIC COMPANION

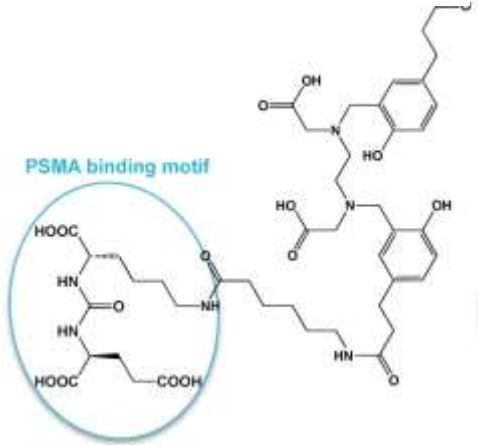
^{177}Lu-PSMA-617

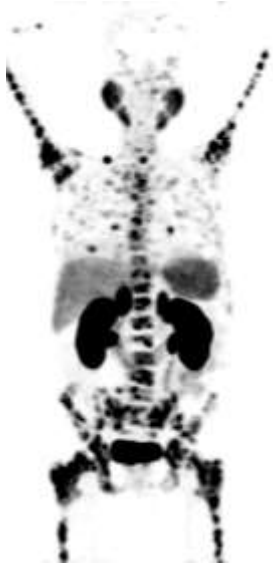


Post-therapy
SPECT/CT



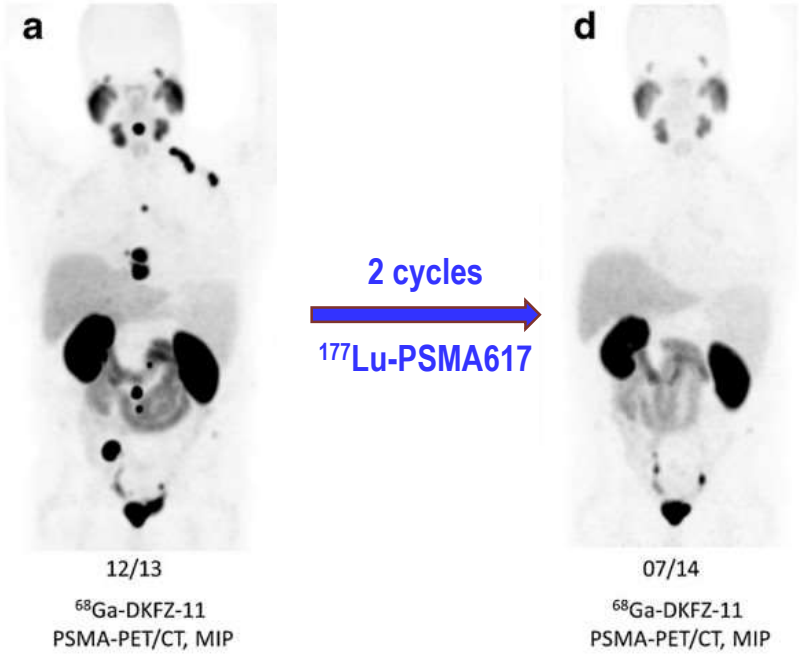
^{68}Ga-PSMA-11 PET/CT





Pre-therapy
PET/CT

First report of ^{177}Lu-PSMA617



Cratochwil et al, *Eur J Nucl Med Mol Imaging* 2015. DOI 10.1007/s00259-014-2978-1

STUDY SYNOPSIS

Hypothesis

- ^{177}Lu-PSMA will result in the effective delivery of therapeutic beta-irradiation to sites of malignancy with an acceptable safety profile.
- Observe clinically significant benefit

Design

- 30 patient prospective, open label, single arm non-randomised pilot study

Intervention

- Up to four cycles of ^{177}Lu-PSMA
  4 – 8 GBq ± 10% adjusted according to tumor burden, renal function and body weight

ANZCTR Australian New Zealand Clinical Trials Registry, ACTRN12615000912583

ENDPOINTS

Primary

- Toxicity (CTCAE 4)
- Activity
  - PSA response (PCWG2)
  - Quality of life (EORTC QLQ-C30, BPI-SF)
  - Imaging response (RECIST, bone scan, PSMA/FDG PET)

Secondary

- Dosimetry to tumors and normal tissue
- Progression free and overall survival

Study data collected using REDCap hosted at the University of Melbourne. Statistical analysis: R-Statistics with ggplot2

PATIENT ELIGIBILITY

Inclusion

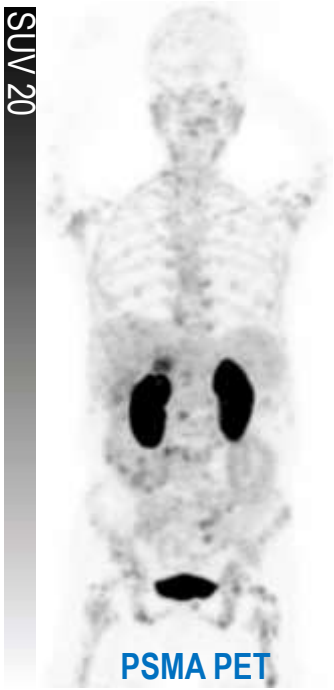
- Castration-resistant
- Documented progression after (unless contraindicated or patient refused)
  - Docetaxel
  - Enzalutamide or abiraterone
- ECOG ≤ 2
- High uptake on PSMA PET

Exclusion

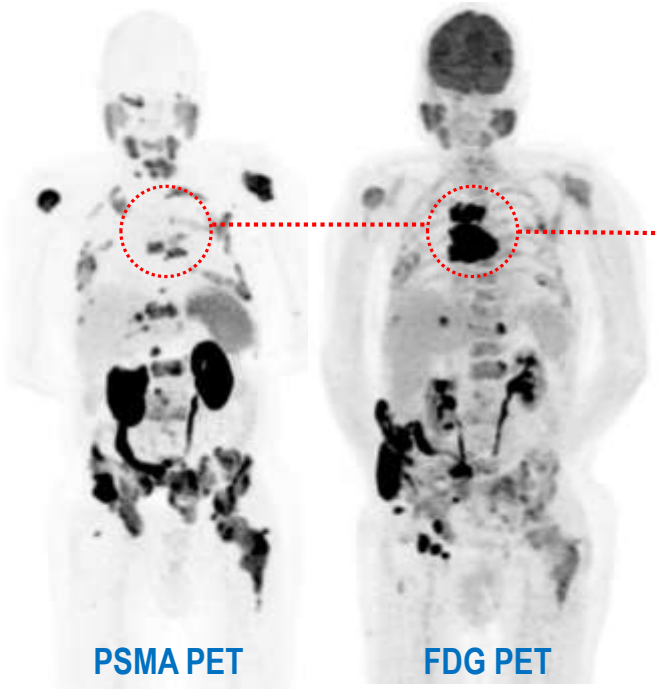
- GFR < 40 ml/min
- Platelet < 75,000
- Neutrophil < 1.5
- Hb < 9.0
- Albumin < 25
- FDG PET/CT demonstrating discordant disease

SCREENING FAILURE

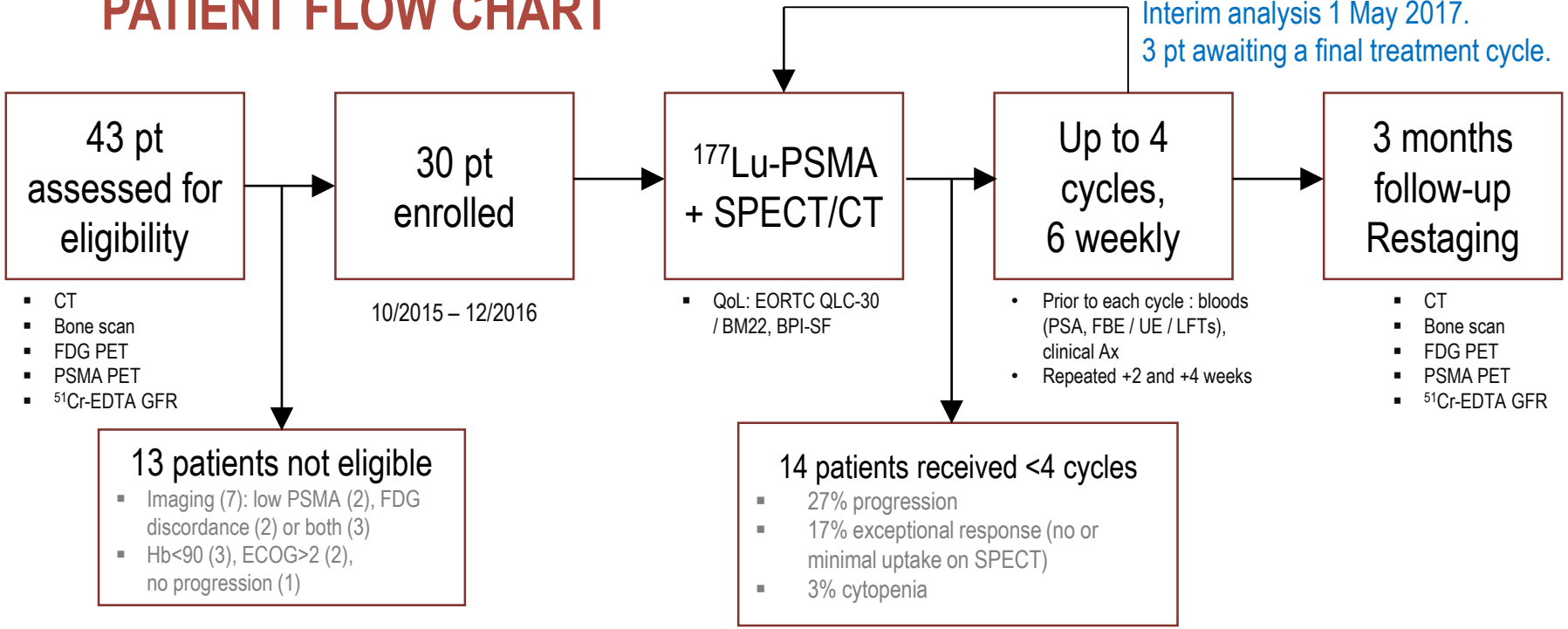
1. LOW PSMA EXPRESSION



2. DISCORDANT FDG+ PSMA-



PATIENT FLOW CHART

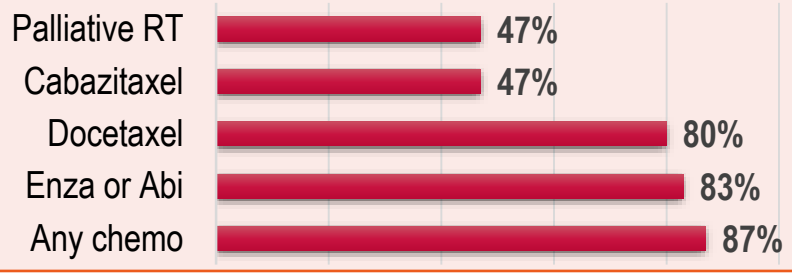


Lu-177 PSMA617 administrated via slow intravenous infusion. Oral hydration encouraged. No pre-medication. Day admission.

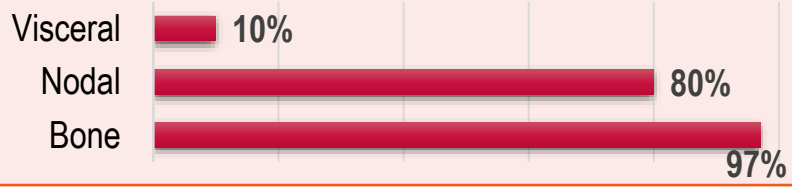
PATIENT CHARACTERISTICS

Characteristic	Mean	SD (Range)		
Age	**70.1**	7.3 (50 – 86)		
Years since diagnosis	**9**	(2 – 17)		
PSA (ng/ml)	**552.6**	929 (13 – 4022)		
PSA doubling time (mnths)	**3.6**	8.0 (0.5 – 42.1)		
ALP	**160.4**	123.5 (52 –542)		
Haemoglobin	**117**	15.5 (92 –161)		
ECOG	**0: 37%**	**1: 47%**	**2: 17%**	
Prior chemo regimens	**0: 13%**	**1: 40%**	**≥2: 47%**	

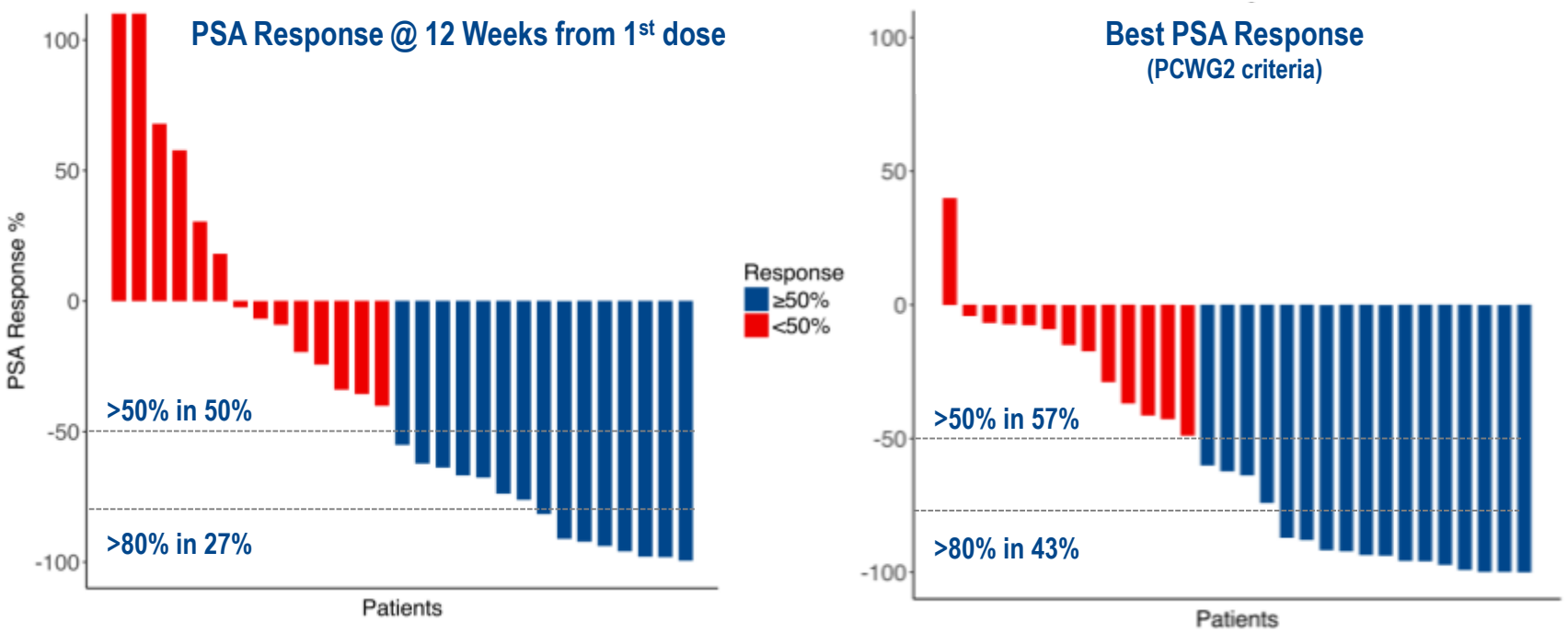
Prior treatments



Sites of disease on PSMA PET/CT



1º ENDPOINT: PSA RESPONSE



TOXICITY

Non haematological attributable to LuPSMA:

Toxicity	G1/2 (%)	G3/4 (%)
Dry mouth	63	0
Nausea*	50	0
Vomiting*	20	0
Fatigue	17	3
Dry eyes	7	0
Bone pain	7	3
Anorexia	7	0
Infusion related reactions	0	0
Renal toxicity	0	0

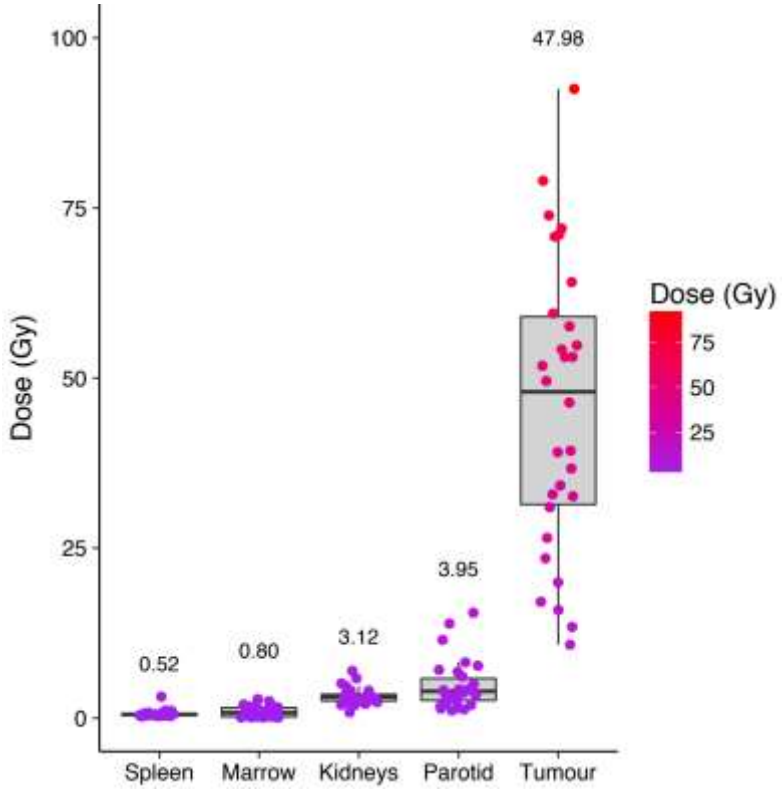
Haematoxicity:

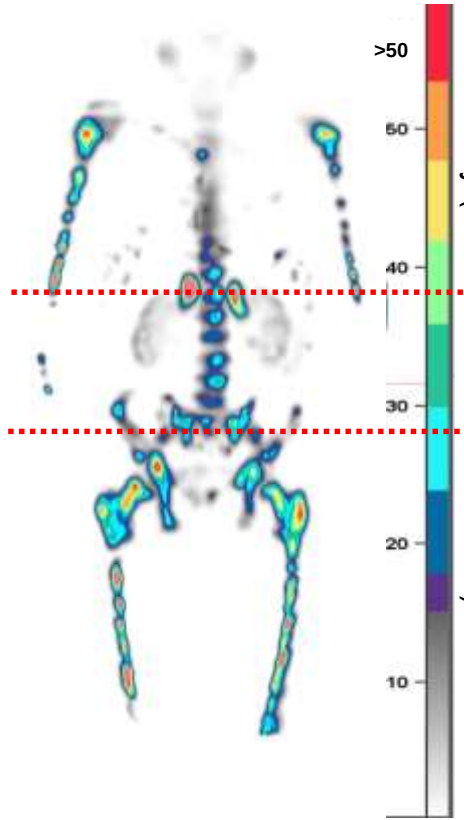
Toxicity	G1/2 (%) (baseline)	G1/2 (%) (any cause)	G3/4 (%) (any cause)	G3/4 (%) (LuPSMA)
Haemoglobin	80	73	23	7
Neutrophils**	0	40	10	7
Platelets	17	43	27	13

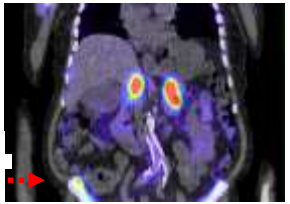
* transient and self-limiting within first 24 hours
** no episodes of febrile neutropenia

CTCAE version 4: adverse events that occurred within 12 weeks after last injection of LuPSMA, or more than 12 weeks if determined to be related to LuPSMA

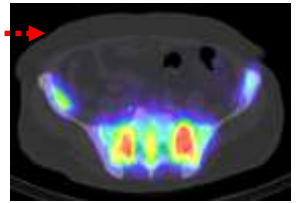
Dosimetry from 1st cycle







Adrenal mets: 68 Gy



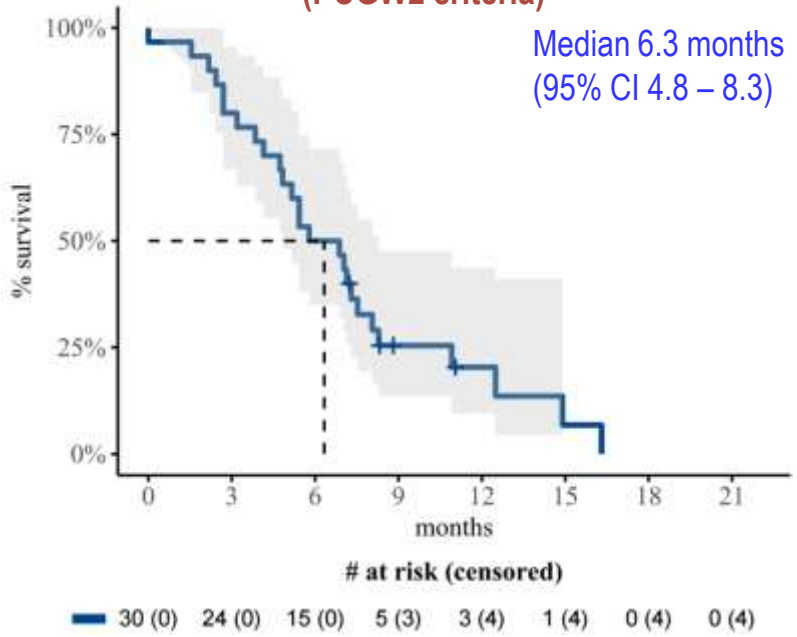
Bone mets: 33 Gy

Parotid: 4 Gy
Kidney: 3 Gy

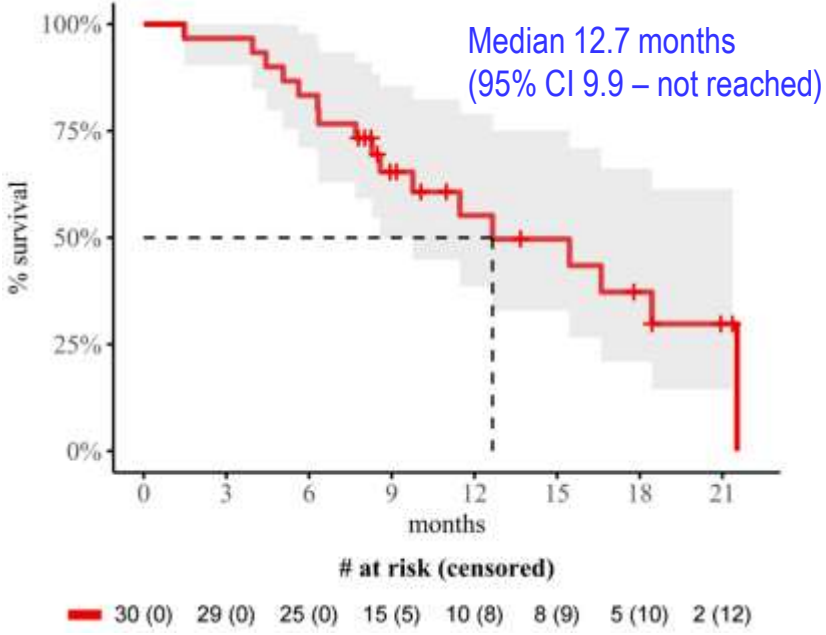
Voxel-based Monte-Carlo dosimetry from 4, 24 & 96hr qSPECT/CT (8GBq ^{177}Lu-PSMA617)

PSA PROGRESSION FREE SURVIVAL

(PCGW2 criteria)

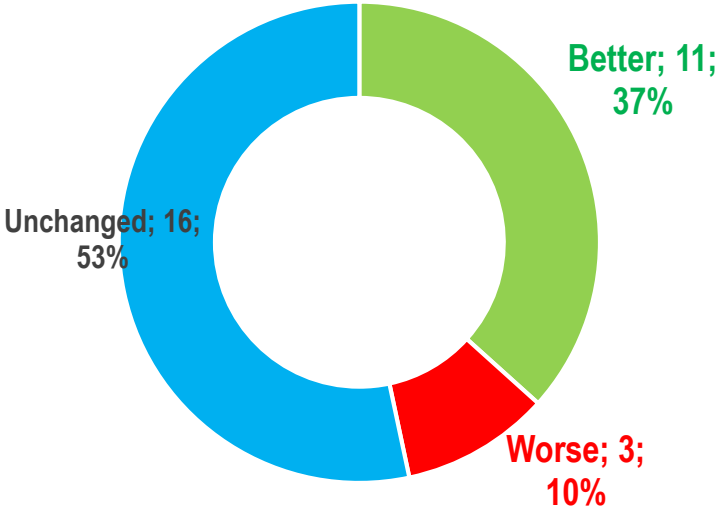


OVERALL SURVIVAL

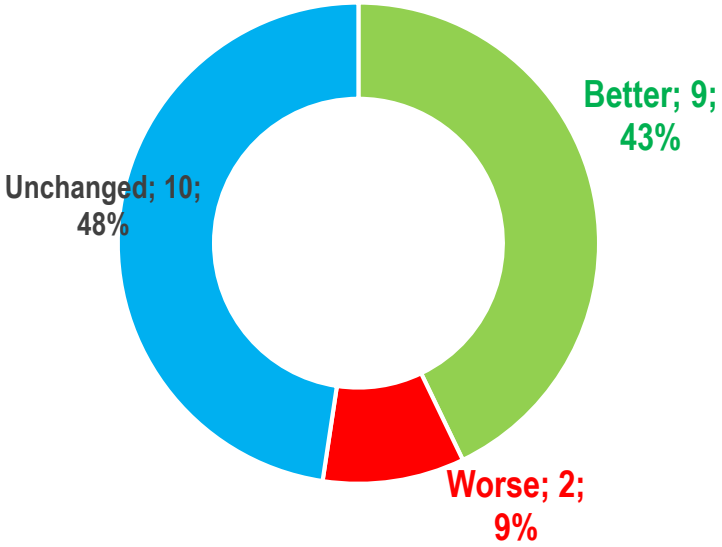


Kaplan-Meier Plot with 95% confidence interval

QUALITY OF LIFE BASELINE → 2ND CYCLE



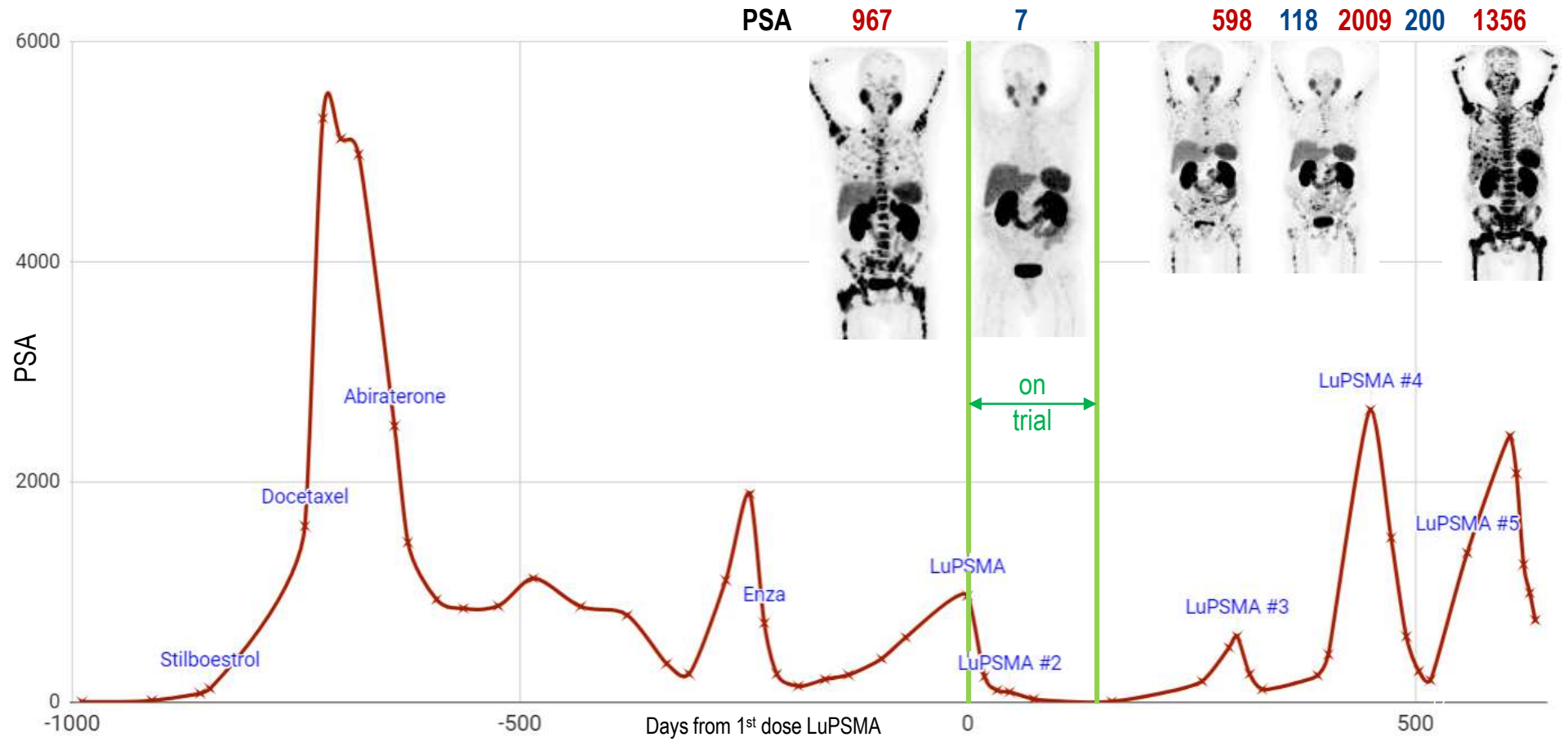
EORTC Global Health Score
n=30



BPI Mean Severity Score
n=21 with pain

EORTC QLQ-C30 / BPI-SF better: +10 points | worse: -10 points or not completed owing to progression/death

Follow-Up Case: Intermittent Further Rx



STRENGTHS

- Important need
- First prospective data of LuPSMA
- Theranostics: see what you treat
- Encouraging activity: PSA>50% in 57%
- Highly targeted: limited toxicity

LIMITATIONS

- Single-centre study
  >10 years experience in ^{177}Lu therapy (DOTATATE in NET)
  radiopharmacy expertise
- Longer follow-up to identify any delayed toxicities
- No comparator arm: limits interpretation of PFS / OS and toxicity data

CONCLUSIONS

In men with mCRPC who have progressed after standard therapies with PSMA-avid disease, LuPSMA has high response rates, limited toxicity with improvements in pain and well-being.

Warrants further evaluation:

- "TheraP Trial": 200 pt multi-centre phase II RCT vs cabazitaxel (ANZUP / PCFA / ABX / ANSTO)
- LuPSMA + anti-PD1 Ab pilot study (Victorian Cancer Agency)
- LuPSMA + PARPi phase I study (PCF Challenge Award)

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✉ **michael.hofman@petermac.org**