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TITLE: A Phase 2 Trial of Combined Lutetium-PSMA Theranostics and Docetaxel in Newly Diagnosed Metastatic Hormone-Naïve Prostate Cancer

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CONTRACTING ORGANIZATION: University of Melbourne, Parkville, Australia

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14. ABSTRACT

This research will conduct a randomised phase II multi-centre trial of ¹⁷⁷Lu-PSMA + ADT followed by standard-of-care docetaxel in comparison to standard-of-care alone (ADT + docetaxel) will be conducted. We postulate that the addition of up-front treatment with ¹⁷⁷Lu-PSMA will more effectively eradicate disease resulting in a higher proportion of patients with undetectable PSA at 12 months. This is an open label, randomised, and stratified, 2-Arm, multi-centre, phase 2 clinical trial recruiting 140 patients at 11 Australian centres. Patients with *de novo* high-volume metastatic hormone-naïve prostate cancer will be randomised to the experimental Arm (¹⁷⁷Lu-PSMA followed by docetaxel) or standard-of-care Arm (docetaxel alone) in a 1:1 ratio. The **primary objective** is to compare the undetectable prostate specific antigen (PSA) rate at 12 months after commencement of protocol therapy in male patients with newly-diagnosed high-volume metastatic hormone-naïve prostate cancer (mHNPC) treated with sequential ¹⁷⁷Lu-PSMA and docetaxel versus those treated with docetaxel alone.

Progress: Target recruitment for the Peter MacCallum Site as part of this DoD Prostate Cancer Impact Award is 100%. Total recruitment across all sites >75%. This is an active RCT.

15. SUBJECT TERMS

Lutetium-177, PSMA, Prostate Cancer, docetaxel chemotherapy, hormone therapy, mHNPC, PSMA PET

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1. INTRODUCTION:

In our research, we will conduct a randomised study comparing the addition of up-front ¹⁷⁷Lu-PSMA to the existing standard-of-care of Androgen Deprivation Therapy (ADT) + Docetaxel in 140 men with high-volume metastatic hormone-naive prostate cancer (mHNPC). Patients will be recruited from 12 Australian sites experienced in theranostics. The primary endpoints will be achievement of PSA ≤ 0.2ng/mL at 12 months and safety. We anticipate the results we derive will provide evidence of the safety, feasibility and activity of ¹⁷⁷Lu-PSMA in high-volume mHNPC. We anticipate our results will provide a compelling rationale for developing later-phase studies that could transform clinical practice in prostate cancer.

2. KEYWORDS:

Lutetium-177, PSMA, Prostate Cancer, docetaxel chemotherapy, hormone therapy, mHNPC, PSMA PET

3. ACCOMPLISHMENTS:

We registered 36 patients at the Peter MacCallum Cancer Centre, and randomized 31 (Arm A = 14/Arm B = 17), meeting the statement of work for this grant.

In 2022 Clinical trial activity increased significantly as COVID-19 restrictions easing Australia-wide from late 2021. This grant specifically supports UpFrontPSMA patients recruited to Peter MacCallum Cancer Centre.

As per the 2nd annual report the COVID-19 global pandemic is still a disruptive influence in the local landscape. While site activation has caught up patient recruitment is still affected. As government and institutional regulatory advice updates, so too does the activity of the study.

Due to the effect of COVID 19 an overall no cost extension was granted by study co-funders PCRA Movember/Medical Research Future Fund (formerly Cancer Australia). The extension is until June 30 2022. Currently 11 sites are active, with 1 site still in negotiation. Recruitment is ongoing to reach target of 140 patients, we anticipate this is completed in Q4 2022. The screen fail rate has been higher than expected at 29%. Peter MacCallum Cancer Centre is currently the highest recruiter.

Major Task 1: Study start-up phase (Months 1-3)

Milestones achieved

Please note all of Major Tasks in this section were completed in year 1.

Major Task 2: Patient accrual & treatment (Months 9-27)

Subtask 1: Commence and undertake Study

- Screen, recruit, randomise, deliver therapy as per randomised-arm and follow-up patients as per protocol. Complete study case report forms. Monitor for serious adverse events.

Milestones Achieved

Study begins: 1st participant consented, screened and enrolled	First patient consented on 20 April 2020 and enrolled during COVID-19 pandemic. Reported in Year 1
Monitor study quarterly, specifically patient recruitment quarterly, percentage of case report forms completed and review of serious adverse events by the data safety monitoring committee.	Ongoing. Study is regularly monitored with fortnightly meetings held between PIs and the study management team. DSMB meeting held in August 2022 as per protocol with no study concerns raised.
Complete patient recruitment	Patient recruitment for the DoD-funded patients at the Peter MacCallum Cancer Centre has been successfully completed. The broader study continues. At 15 August 2022, 148 patients are registered to study and 106 patients have been randomized. 53 in each arm. Screen fail rate is 29%, significantly higher than expected and will be explored further. Expected date for complete recruitment Q4 2022. This target will continue to be monitored and adjusted accordingly dependent on COVID-19 status in Australia, and communication with sites. Healthcare Workforce shortages have created significant disturbances across Australia as the most recent Influenza and COVID waves

	impacted over the 2022 Winter. This has contributed significantly to recruitment.
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Major Task 3: Data Analysis (Months 33-36)

Sub Task 1: Report findings of study

- Perform statistical analysis to determine primary objectives (refer to objectives on p1).
- Perform statistical analysis to determine secondary objectives (refer to objectives on p1).
- Disseminate study findings through presentations at international scientific meetings and scientific journals.

Milestones Achieved

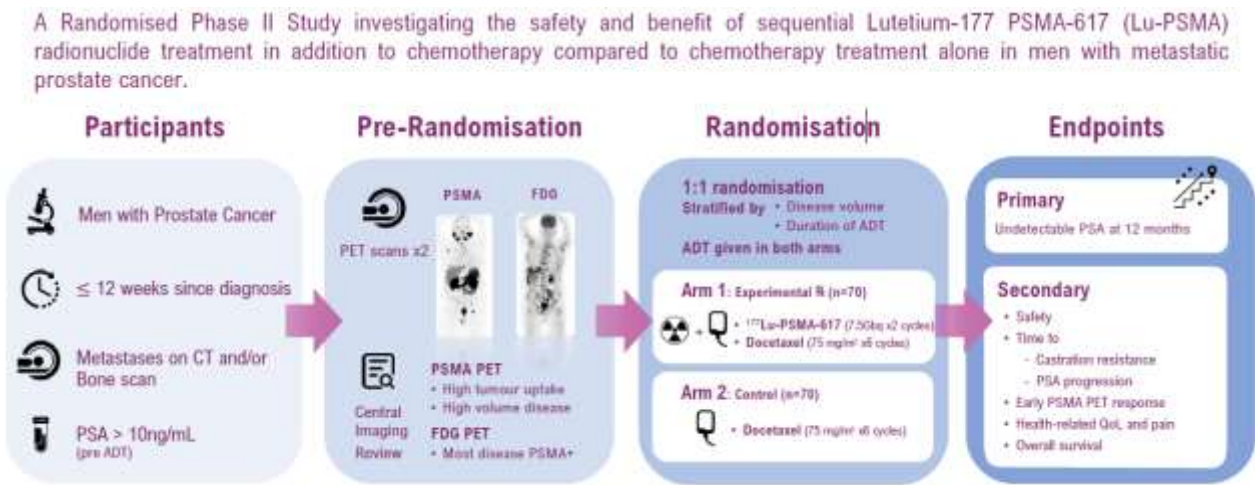
This milestone is yet to be reached.

The Research team are yet to begin analysis on UpFrontPSMA samples as trial accrual is ongoing (patient #107 to be randomized). We have collected correlative samples from all patients on trial as specified in the protocol. Analysis will begin in 2023 when recruitment is complete.

All findings will be reported back to U.S. Army Medical Research and Development Command.

What was accomplished under these goals?

Methodology (as presented in year 1 & 2 Reports):



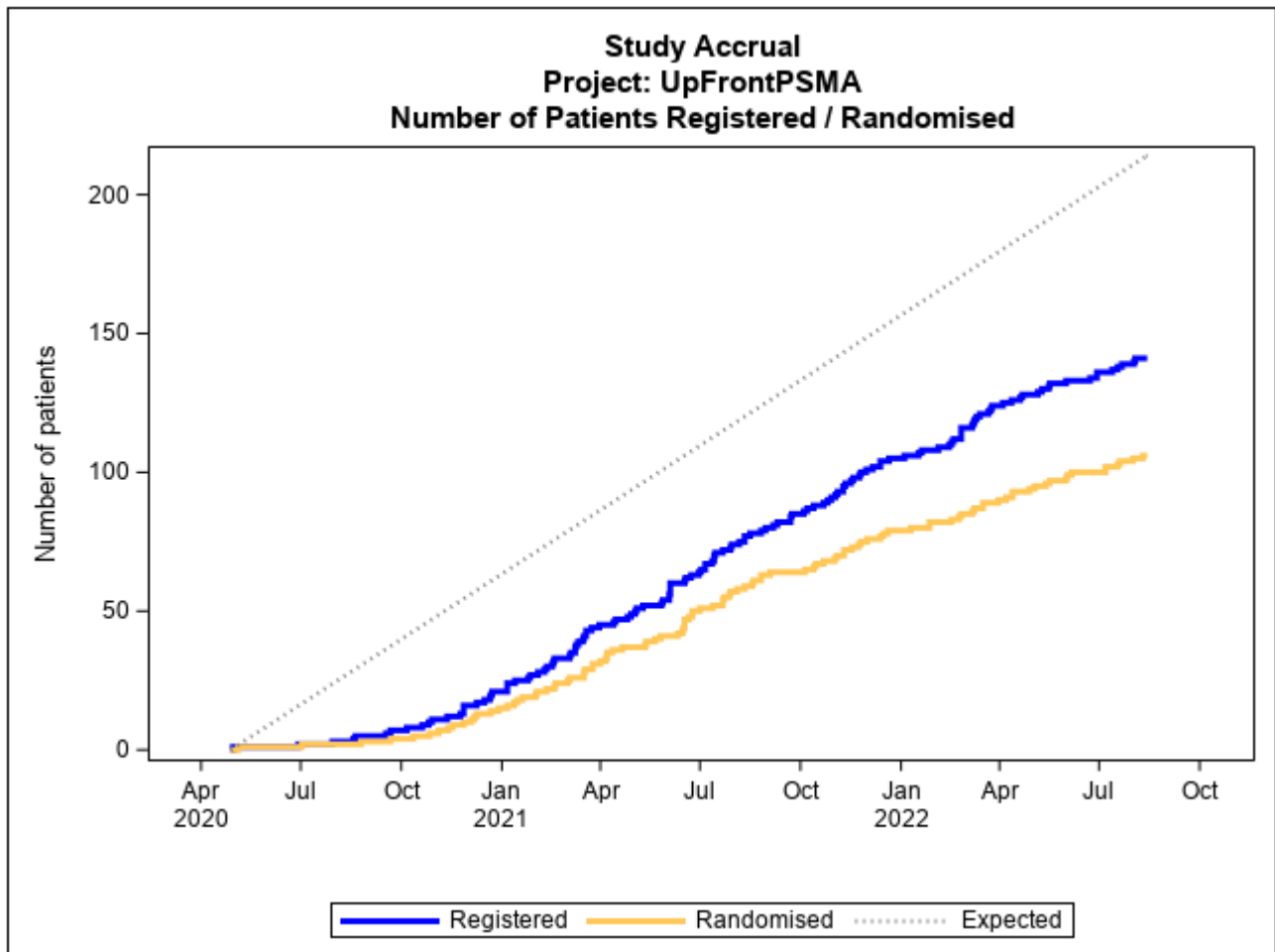
In spite of a challenging external and internal environment brought on by the COVID 19 pandemic – year 3 activity for the study is successful. 11 sites are now actively participating in recruitment and screening of patients. Our third annual grant information event was held on 28 January 2022 (via zoom). All DoD

co-investigators were present. This is an important communication tool for disseminating information, and was well attended by study co-investigators and researchers.

At the start of 2022 COVID restrictions eased nationally and borders opened to national and international travelers. Recruitment of patients to the study received a significant boost as more sites opened throughout 2021/2022. The study is 75% recruited. Deadlines however are still impacted. Recruitment will unlikely be complete until well into the second half of 2022.

2021/2022 12 month highlights are:

- Activation of 11 study sites.
- Randomisation of 106/140 Men to #UpFrontPSMA
- Trial Management Committee meeting held April 2022 with no concerns raised
- DSMB meeting held August 2022 with no concerns raised
- 6 issues of Study newsletter produced and circulated to stakeholders
- 3rd grant education session held for all CIs in January 2022
- Ongoing effective and supportive relationships with entire study team BaCT, ANZUP, ARTnet, PMCC OCR, Study sites and Investigators, Movember, USDoD, ANSTO, Endocyte/AAA/Novartis, University of Melbourne.
- DoD quarterly reporting milestones met



What opportunities for training and professional development has the project provided?

In 2022, two new PhD candidates were added to the PSMA Theranostics program at Peter Mac. Medical Oncologist Dr Louise Kostos & Nuclear Medicine Research Fellow Dr James Buteau.

Dr James Buteau

Title: Breaking Barriers in Prostate Cancer: Novel Clinical Uses of Imaging with PSMA PET/CT and Therapy.

Supervisors: Prof Michael Hofman & A/Prof Arun Azad

Dr Louise Kostos:

Title: Optimising the efficacy of radionuclide therapy in advanced prostate cancer

Supervisors: A/Prof Arun Azad, Prof Michael Hofman, Dr Luc Furic

Preceptorship 2022: The inaugural Prostate Cancer Theranostics and Imaging Centre of Excellence (ProSTIC) Preceptorship “How we do PSMA” was held as a hybrid meeting from 1-2 April 2022. While not funded directly by the DoD, this event is a direct result of the high volume PSMA research being conducted at PMCC that UpFrontPSMA is spearheading.

This premier PSMA Theranostics education event attracted 413 registrations from 38 Countries. Specialised multidisciplinary presentations, including 2 MDT sessions, were delivered by 34 national and international guest presenters. A highlight was hosting Prof Tom Hope (UCSF) and Dr Andrei Gafita (UCLA) in person. The 2 day event was live streamed to over 240 online delegates who amassed a total 67,738 minutes viewing time.

The Preceptorship partnered with the Prostate Cancer Foundation of Australia to deliver a comprehensive 2 hour consumer session that included 6 multidisciplinary presentations. The Preceptorship content has been packaged as an online education resource <https://procticpreceptorship2022.org/>.

How were the results disseminated to communities of interest?

The UpFrontPSMA alliance has adapted and adopted all online meeting and webinar activities. In 2021/2022 there has been continued online engagement. While not all reported presentations below specifically relate to the study, they encompass the ongoing research in PSMA Theranostics currently. UpFront SMA, as one of the world's pioneering studies in the early use of Lu-PSMA Theranostics, has been referred to as the next generation research paradigm. The multidisciplinary team consistently reference all the PSMA clinical and preclinical research being conducted.

The active participation in webinars and podcasts has had a dramatic effect on our international outreach capability, which is significant. The PMCC team engages the world's foremost Theranostics thought leaders on a regular basis.

- **Invited Lectures International**

1. Hofman MS, TheraP 3 year follow-up, Best of ASCO Malaysia, July 24-25, 2022. [Online].
2. Moon D, NGI in prostate cancer diagnostics: what should be the PRIMARY tool?, Singapore Urological Association UroFair 2022, July 14-16, 2022.
3. Hofman MS, Advancing Cancer Care with Nuclear Medicine: PET/CT and Theranostics, National Undergraduate Oncology Conference, Jun 25, 2022. [Online].
4. Hofman MS, ARTnet PSMA Study Updates; Patient Selection and Imaging Biomarkers for PSMA Theranostics; Single-centre experience of treating men with metastatic castration-resistant prostate cancer with Lutetium-177 PSMA-I&T using TheraP-like treatment algorithm, ANZSNM Annual Scientific Meeting, May 13-15, 2022. Australia.
5. Hofman MS, The Future of Theranostics: From Seeing to Quantifying What You Treat. ANZSNM Annual Scientific Meeting, MIM Software User Meeting, May 14th, 2022. Australia.
6. Medhurst, L, Prostate cancer theranostics: nursing implications, ASM USANZ, 25 June 2022.
7. Hofman MS, Advances in Dosimetry in Theranostics, Advanced Prostate Cancer Consensus Conference (APCCC), Apr 27, 2022. Switzerland.
8. Hofman MS, When low volume on conventional imaging goes into high volume on next generation imaging in mHSPC- How Frequent Is This Situation?, Advanced Prostate Cancer Consensus Conference (APCCC), Apr 27, 2022. Switzerland.
9. Risbridger G, Prostate Cancer Research Program, Biggest Ever Blokes' Lunch, Mar 4, 2022. Australia.
10. Hofman MS, When do I use PSMA PET/CT in staging and biochemical recurrence: urologists perspective; Will PSMA PET/CT replace mpMRI for diagnosis of prostate cancer?; PSMA PET/CT "live" cases: pearls and pitfalls; Guiding current practice with best available evidence: TheraP and VISION; How I Select Patients; Aussie leading the way with Investigator Initiated Trials: emerging combinations in mCRPC "Novel Radionuclide Treatment Combinations"; Next generation research - How I do it; Nuclear medicine technologist: administration and post therapy imaging; Nurse specialist: fully integrated; Medical Physicist "Dosimetry in Lu-PSMA Therapy: Practical and Technical Considerations"; Medical oncologist: bringing it all together; Radiopharmacy: how the kitchen operates - a unique medicinal environment; How I sequence LuPSMA in the landscape of increasing options for mCRPC?; Prognostic and predictive imaging biomarkers: PSMA and FDG

- PET/CT; Other biomarkers in prostate cancer: CTCs, ctDNA and beyond, Peter MacCallum Cancer Centre ProstIC Preceptorship, Apr 1-2, 2022. [Hybrid].
11. Hofman MS, Predictors and Real-World Utilization of Prostate-Specific Radioligand Therapy: PSMA and Beyond, Educational session chaired by Hofman MS with speakers including Calais J (UCLA), Schuster D (Emory, Penn). Resistance Mechanisms and Combinatorial Approaches to Enhance PSMA-Based Radioligand Responses presented by Hofman MS.
 12. Hofman MS, ProPSMA Trial, Celebrating International Clinical Trials Day: MISCH Hub and University of Melbourne, Methods and Implementation Support for Clinical and Health research Hub (MISCH), May 20, 2022.
 13. Hofman MS, Future Perspectives on PC Management: Radio-Ligand-Treatment, Radboudumc 3rd Nijmegen Prostate Cancer Prospects, Mar 22-23, 2022 [hybrid].
 14. Ravi Kumar A, VISION update, BNMS Spring Meeting Glasgow UK, May 15-18, 2022.
 15. Buteau JP. The Future of Theranostics: From Seeing to Quantifying What You Treat. ANZSNM Annual Meeting, MIM Software User Meeting, Brisbane, May 14th, 2022.
 16. Hofman MS, Molecular Imaging for Personalised medicine: PET/CT to select for and guide radioligand therapies, ESMO Targeted Anticancer Therapies, Mar 7-8, 2022 [Online].
 17. Ravi Kumar A, LuPSMA in prostate cancer – options, indications and responses, 26th annual meeting of SNM India Southern Chapter, Feb 6, 2022. [Online].
 18. Risbridger G, Women in Urology (Invited speaker and panelist), Australasian Prostate Cancer Conference, Dec 2-3, 2021.
 19. Hofman MS, Role of PSMA and FDG PET/CT in selecting patients for Lutetium 177 PSMA theranostics, 11th Shanghai Genitourinary Oncology International Symposium & 2021 Annual Meeting of China Anti-Cancer Association-Genitourinary Cancer Committee, Dec 10-11, 2021.
 20. Hofman MS, Utilizing Diagnostics to Inform Patient Stratification and Selection in Clinical Trials, Targeted Radiopharmaceuticals Summit, Dec 7-9, 2021.
 21. Debate: Third-line treatment of mCRPC- The Case for Lu-PSMA, Belgian Association of Urology 2021 (BAU2021), Dec 3-4, 2021
 22. Metastatic castration-resistant prostate cancer: Standard of care in 2021, ESMO Virtual Advanced Course on Clinical questions in prostate cancer, December 8-11, 2021.
 23. State of the art management of MO Castrate-Resistant Prostate Cancer (CRPC), ESMO Virtual Advanced Course on Clinical questions in prostate cancer, December 8-11, 2021.
 24. Hofman MS, Breaking ground in diagnostics: how PSMA can be optimised for imaging techniques in prostate cancer, PROSPECT21 national meeting, Nov 27, 2021 [Virtual Live]. Sponsored by Astellas
 25. Hofman MS, Strengthening the pipeline for clinical research: PSMA Therapy, Australian Clinical Trials Alliance (ACTA) Annual Scientific Meeting, 12 Nov 2021 [Online]. Included panel discussion with Allyson Essex (Assistant Secretary, Department of Health), Dan Grant, Jason Kovacic, Lillian Leigh, John Simes, Peter Meikle, Tony Keech, Anna Lene Seidler.
 26. Overview of advances in systemic therapy in prostate cancer, Brisbane Cancer Conference, November 25-16, 2021.
 27. Hofman MS, PSMA Therapy, The Canadian Association of Nuclear Medicine (CANM) Annual Scientific Meeting 2021, Nov 2021 [Online]. With live Q&A. <https://youtu.be/6yEKnTcOHQg>
 28. Hofman MS, LuPSMA: The Newest Treatment Class for Advanced Prostate Cancer, 28th Annual Prostate Cancer Foundation (PCF) Scientific Retreat, Oct 28-29, 2021. Inc. Session Chair and Moderate for Q&A Session [Virtual]. <https://youtu.be/DI4XZOaL7iM>

29. Hofman MS, Tech23 Impact Circles: Next Generation Cancer Treatments, 1 Oct 2021 [Online]. <https://www.youtube.com/watch?v=rjSEAUV-uSY>
30. Buteau J, All Things PSMA: Revolutionizing Primary Staging to Advanced Metastatic Prostate Cancer. Annual Medical Imaging Scientific Day, Sherbrooke (Canada), October 27, 2021.
31. The influence of next generation imaging (NGI) on future management paradigms in prostate cancer. ACEXclusive 2 Asia Pacific Prostate Cancer Conference, October 12-17, 2021.
32. Hofman MS, Do we need the second PET (FDG) for patient selection? (including SUV for selection of PSMA therapy), Advanced Prostate Cancer Centre Consensus Conference (APCCC), 9 Oct ,2021. <https://youtu.be/iU3EyoXd2Po>
33. ¹⁷⁷Lu-PSMA Lutetium Therapy: Guide for Nurses, Advanced Prostate Cancer Centre Consensus Conference (APCCC), 9 Oct ,2021.
34. Hofman MS, PSMA PET/CT Imaging in Prostate Cancer, British PET/CT Imaging Course, October 8, 2021. [Online]
35. Medhurst L, Theranostics: Nursing Implications, Prostate Cancer Foundation of Australia, education day, October 2021.
36. Paradigm Change in Non-Metastatic Castrate Resistant Prostate Cancer Treatment Landscape: The Window of Opportunity. 32nd Annual Scientific Congress of the Malaysian Oncological Society (ASCOMOS), October 29-31, 2021.
37. Hofman MS, MDT Masterclass: Prostate (advanced), ANZUP ASM 2021, October 17-18, 2021. Panel with Lisa Horvarth, Colin Tang, Melissa Caruso and Anis Hamid.
38. Medhurst L, Establishing a prospective registry for Lutetium-177 PSMA and a developing role for an advanced practice nurse within the nuclear medicine team, ANZUP ASM 2021, October 17-18, 2021.
39. PSMA Theranostics in Prostate Cancer, RANZCR NZ ASM New Zealand, Aug 6-8, 2021. [Online].

Awards and Honors

1. James Buteau, **2022 1st Place Winner Therapy Center of Excellence Young Investigator Award at Society of Nuclear Medicine and Molecular Imaging 2022 meeting** (Vancouver) for paper "Time-savings analysis of total tumor burden quantification on ⁶⁸Ga-PSMA-11 PET/CT with deep learning auto-segmentation of organs for automatic physiological uptake removal in men with metastatic castration-resistant prostate cancer (mCRPC), Oncology: Clinical Therapy & Diagnosis"
2. M Hotta, SNMMI 2022 Best Poster Award at **Society of Nuclear Medicine and Molecular Imaging 2022 meeting** (Vancouver) for paper "PSMA PET tumor-to-Salivary Glands ratio (PSG score) to predict response to Lu-177 PSMA radioligand therapy: an international multicenter retrospective study" (Hofman MS co-author)
3. Laura Evangelisa, **2022 European Urology Oncology #SoMe award** (most influential article according to PlumX Metrics), for paper "[⁶⁸Ga]Ga-PSMA Versus [¹⁸F]PSMA Positron Emission Tomography/Computed Tomography in the Staging of Primary and Recurrent Prostate Cancer. A Systematic Review of the Literature" (Hofman MS co-author)
4. Kostos L, **2022 Vincent Fairfax Family Foundation Research Entry Scholarship**, for PhD titled "Optimising Efficacy of Radionuclide Therapy in Advanced Prostate Cancer"
5. Dr Jeremy Ong, **2021 Radiological Society of North America (RSNA) Cum Laude Award for Education Exhibit** titled "Tumour Heterogeneity" (Hofman MS co-author)

6. Prof Michael Hofman, **2021 European Urology Best Scientific Paper** for the PRIMARY trial, co-author and Peter Mac PI
awarded to first author Prof. Louise Emmett
7. Dr Wolfgang Fendler, 2021 EAU Prostate Cancer Research Award, for paper “Prostate-Specific Membrane Antigen Ligand Positron-Emission Tomography in Men with Nonmetastatic Castration-Resistant Prostate Cancer” (Hofman MS co-author)
8. Prof Michael Hofman, **2021 Society of Nuclear Medicine and Molecular Imaging (SNMMI) International Best Abstract Award for Australia**, ¹⁷⁷Lu-PSMA-617 Versus Cabazitaxel in Metastatic Castration-Resistant Prostate Cancer: A Randomised, Open-Label, Phase 2 Trial (TheraP)
9. Prof Michael Hofman, **2021 Invited Delegate, Saul Hertz and the Medical uses of Radio-iodine: A National Historic Landmark**, Dedicated at Massachusetts General Hospital, Boston, on Oct. 8, 2021 <https://youtu.be/hY51SWncNto>
<https://www.acs.org/content/acs/en/education/whatischemistry/landmarks/medical-uses-of-radioiodine.html>
10. Prof Michael Hofman on behalf of the ProPSMA Team, **2021 Australian Clinical Trial Alliance (ACTA) Trial of the Year Winner**,
<https://www.petermac.org/news/peter-mac-wins-clinical-trial-year>

What do you plan to do during the next reporting period to accomplish the goals?

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Based on the plan for Milestones as submitted in the Project Grant application, year 3/4 activities for UpFrontPSMA are centered on completing patient recruitment and monitoring of study activities. We anticipate beginning Major task 3: Data Analysis by Q1. 2023, and reporting study findings.

4. IMPACT:

In the USA March 23, 2022, the FDA approved Pluvicto (¹⁷⁷Lu-PSMA617) for the treatment of patients with (PSMA) - positive (mCRPC) who have been treated with androgen receptor (AR) pathway inhibition and taxane-based chemotherapy. FDA Also approved Locametz (⁶⁸Ga gozetotide), a radioactive diagnostic agent for positron emission tomography (PET) of PSMA-positive lesions. Locametz is the first radioactive diagnostic agent approved for patient selection in the use of a radioligand therapeutic agent. UpFrontPSMA represents the first trial using these new FDA-approved agents in the hormone-sensitive setting. Accordingly, we results are eagerly awaited by the global prostate cancer community.

What was the impact on other disciplines?

PSMA PET/CT and radioligand therapy is having a great impact on the broader management with prostate cancer. This was highlight at the recent Advanced Prostate Cancer Consensus Conference (APCCC) held in Lugano, Switzerland 2022. PI Hofman and PI Murphy both featured in the panel of experts. Both are also participating in a Lancet Commission on Prostate Cancer, with results expected to be published in 2023.

The impact of PSMA radioligand therapy is also being noted by other cancer specialties. There are more than 20 start-up companies globally focusing efforts of identifying effective theranostics in other tumour type.

What was the impact on technology transfer?

Nothing to report

What was the impact on society beyond science and technology?

Nothing to report

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to report

Actual or anticipated problems or delays and actions or plans to resolve them

COVID-19 Pandemic

As previously reported the global COVID-19 pandemic continues to affect patient recruitment and the ability for our study to meet initial timelines. A 12 month no cost extension has been granted to the wider PCRA program to assist with fulfilling requirements.

Changes that had a significant impact on expenditures

Budget expenditure has been met

*Salaries as per budget

*Material and supplies in line with increased patient recruitment in year 3. Research progress spend will be realized with expenditure in 2023

*Foreign Travel and Publication costs lagged due to COVID 19 travel restrictions and delays in patient recruitment

An application to adjust the budget to include the purchase of an HPLC machine was approved in year 2. The equipment (QC item). For noting: the HPLC-scanner is a flexible controlling unit designed for the remote detection of a wide range of radioisotopes with TLC and HPLC for highest level control of our radiopharmaceutical production of LuPSMA617 – the therapy being used in our trial.

The extra volume of production our trial is creating, along with the strict QC parameters identified this need. Permission was granted as budget expenditure adjustments were possible, and the purchase did not change the overall grant funding allocation.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use or care of vertebrate animals

Nothing to report

Significant changes in use of biohazards and/or select agents

Nothing to report

6. PRODUCTS:

Nothing to report

Books or other non-periodical, one-time publications.

Nothing to report

Other publications, conference papers and presentations.

Publication & Citation		
Publication	Journal Impact Factor	No. of Citation
Ong S, Pascoe C, Kelly BD, Ballok Z, Webb D, Bolton D, Murphy D, Sengupta S, Bowden P, Lawrentschuk N. PSMA PET-CT Imaging Predicts Treatment Progression in Men with Biochemically Recurrent Prostate Cancer-A Prospective Study of Men with 3 Year Follow Up. Cancers (Basel). 2022 May 31;14(11):2717. doi: 10.3390/cancers14112717.	6.1	0
Gaudreault M, Chang D, Hardcastle N, Jackson P, Kron T, Hanna GG, Hofman MS, Siva S. Utility of Biology-Guided Radiotherapy to De Novo Metastases Diagnosed During Staging of High-Risk Biopsy-Proven Prostate Cancer. Front Oncol. 2022 Apr 12;12:854589.	6.2	0
Gaudreault M, Chang D, Hardcastle N, Jackson P, Kron T, Hofman MS, Siva S. Feasibility of biology-guided radiotherapy using PSMA-PET to boost to dominant intraprostatic tumour. Clin Transl Radiat Oncol. 2022 May 17;35:84-89. doi: 10.1016/j.ctro.2022.05.005.	4.5	0
Gafita A, Marcus C, Kostos L, Schuster DM, Calais J, Hofman MS. Predictors and Real-World Use of Prostate-Specific Radioligand Therapy: PSMA and Beyond. Am Soc Clin Oncol Educ Book. 2022 Apr;42:1-17. doi: 10.1200/EDBK_350946.	1	0
Pathmanandavel S, Crumbaker M, Yam AO, Nguyen A, Rofe C, Hovey E, Gedye C, Kwan EM, Hauser C, Azad AA, Eu P, Martin AJ, Joshua AM, Emmett L. ¹⁷⁷Lu-PSMA-617 and Idronoxil in Men with End-Stage Metastatic Castration-Resistant Prostate Cancer (LuPIN): Patient Outcomes and Predictors of Treatment Response in a Phase I/II Trial. J Nucl Med. 2022 Apr;63(4):560-566. doi: 10.2967/jnumed.121.262552.	6.5	1
Ptasznik G, Papa N, Kelly BD, Thompson J, Stricker P, Roberts MJ, Hofman MS, Buteau J, Murphy DG, Emmett L, Moon D. High prostate-specific membrane antigen (PSMA) positron emission tomography (PET) maximum standardized uptake value in men with PI-RADS score 4 or 5 confers a high probability of significant prostate cancer. BJU Int. 2022 Apr 1. doi: 10.1111/bju.15736	5.9	0

Emmett LM, Papa N, Buteau J, Ho B, Liu V, Roberts M, Thompson J, Moon D, Sheehan-Dare G, Alghazo O, Agrawal S, Murphy DG, Stricker P, Hope TA, Hofman M. The PRIMARY Score: Using intra-prostatic PSMA PET/CT patterns to optimise prostate cancer diagnosis. J Nucl Med. 2022 Mar 17;jnumed.121.263448. doi: 10.2967/jnumed.121.263448.	6.5	1
Jackson P, Hofman M, McIntosh L, Buteau JP, Ravi Kumar A. Radiation Dosimetry in 177Lu-PSMA-617 Therapy. Semin Nucl Med. 2022 Mar;52(2):243-254. doi: 10.1053/j.semnuclmed.2021.11.003.	4.4	4
Emmett L, Buteau J, Papa N, Moon D, Thompson J, Roberts MJ, Rasiah K, Pattison DA, Yaxley J, Thomas P, Hutton AC, Agrawal S, Amin A, Blazeovski A, Chalasani V, Ho B, Nguyen A, Liu V, Lee J, Sheehan-Dare G, Kooner R, Coughlin G, Chan L, Cusick T, Namdarian B, Kapoor J, Alghazo O, Woo HH, Lawrentschuk N, Murphy D, Hofman MS, Stricker P. The Additive Diagnostic Value of Prostate- specific Membrane Antigen Positron Emission Tomography Computed Tomography to Multiparametric Magnetic Resonance Imaging Triage in the Diagnosis of Prostate Cancer (PRIMARY): A Prospective Multicentre Study. Eur Urol. 2021 Aug 28:S0302-2838(21)01946- <i>Awarded EAU Scientific Manuscript of the Year 2021</i>	20.1	42
Medhurst E, Alipour R, Akhurst T, Azad AA, Buteau J, Cardin A, Dhiantravan N, Jackson P, Kong G, Murphy DG, Ong JSL, Kashyap R, Kostos L, Kumar AR, Saghebi J, Sandhu S, Spain L, Tran B, Haskali MB, Scalzo M, Hofman MS. Single-centre experience of treating men with metastatic castration-resistant prostate cancer with Lutetium-177 PSMA-I&T using TheraP-like treatment algorithm. Internal Medicine Journal. 2022	8.9	0
Kostos L, Murphy DG, Azad AA. Double or Triple Trouble in Metastatic Hormone-sensitive Prostate Cancer? European Urology Oncology, 2022. In Press.	7.5	0
Williams I, McVie A, O'Brien J, Perera S, Kostos L, Chen, Kasivisvanathan V, Siva S, Azad AA, Lawrentschuk N, Murphy DG, Frydenberg M. More Good, Less Harm: Modern Paradigms for Prostate Cancer Detection and Management. Medical Journal of Australia. 2022. Accepted for publication.	7.7	0
Chen K, Kostos L, Azad AA. Future directions in systemic treatment of metastatic hormone-sensitive prostate cancer. World Journal of Urology. 2022. Accepted for publication.	4.2	0
Mak B, Lin H-M, Kwan EM, Fettke H, Tran B, Davis ID, et al. Combined impact of lipidomic and genetic aberrations on clinical outcomes in metastatic castration-resistant prostate cancer. BMC Med. 2022;20(1):112.	8.7	1
Kwan EM, Spain L, Anton A, Gan CL, Garrett L, Chang D... Fettke H, et al. Avelumab Combined with Stereotactic Ablative Body Radiotherapy in Metastatic Castration-resistant Prostate Cancer: The Phase 2 ICE-PAC Clinical Trial. Eur Urol. 2022;81(3):253-62	20.1	6
Kwan EM*, Dai C*, Fettke H*, Hauser C, Docanto MM, Bukczynska P, et al. Plasma Cell-Free DNA Profiling of PTEN-PI3K-AKT Pathway Aberrations in Metastatic Castration-Resistant Prostate Cancer. JCO Precision Oncology. 2021(5):622-37.	5.4	10

Fettke H, Kwan EM, Bukczynska P, Steen JA, Docanto M, Ng N, et al. Independent prognostic impact of plasma NCOA2 alterations in metastatic castration-resistant prostate cancer. The Prostate. 2021;81(13):992-1001.	4.1	1
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*these manuscripts do not all directly relate to UpFrontPSMA. The findings, however, have contributed indirectly to this research and DoD is consistently acknowledged as funders of future research activity like UpFrontPSMA

Website(s) or other Internet site(s)

Webinars and Podcasts

Hosted **2 new ProSTIC-PCF Global Knowledge Exchange Webinars** (>950 registrants from 62 countries). <https://www.youtube.com/ProSTICTV>

- Jul 2022: "New Era of Lutetium-PSMA Post Approval: Perspectives, Challenges & Future" Featuring Ken Herrmann, Silke Gillesen, Louise Kostos;
- Jul 2021: phase 3 VISION trial. >750 registrants from 62 countries. Featuring Michael Morris, Oliver Sartor, Alicia Morgans, Sze Ting Lee and James Buteau;

GU Cast sessions focussing on PSMA with 8 new (Jul 21-22). <https://www.gucast.org/>
Includes:

- Post-ASCO Vision deep dive with Dr Michael Morris,
- GU Case PROSPECT Summer Series,
- FDA approves PSMA PET/CT! We chat with UCSF team.
- Going Nuclear | GU Oncology highlights from #EANM20,
- #ESMO20 highlights with Ben Tran and Ciara Conduit, (6) PSMA PET/CT prior to biopsy? PRIMARY trial in Eur Urol;
- VISION - "a dilapidated, delinquent, unethical control arm",
- PRIMARY 2 opens - another fantastic randomised trial of PSMA PET/CT, (9) Late night PSMA chat at the ProSTIC Preceptorship,
- Translational scientists working on PSMA theranostics update - A/Prof Arun Azad, Dr Louise Kostos, Dr Luc Furic, Dr Heidi Fettke;
- GU Cast APCCC Highlights Part 2;
- PSMA Highlights at ASCO 22

- **Technologies or techniques**

Nothing to report

- **Inventions, patent applications, and/or licenses**

Nothing to report

- **Other Products**

Nothing to report

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

In 2021/2022 there were no changes to staffing

Name:	Professor Michael Hofman
Project Role:	PI
Research Identifier:	ORCID 0000-0001-8622-159X
Nearest Person Month Worked:	7
Contribution to Project	PI Study design Writing Protocols Submitting Ethics documents
Funding Support	n/a

Name:	Associate Professor Arun Azad
Project Role:	Co-PI
Research Identifier:	ORCID 0000-0002-0579-4052
Nearest Person Month Worked:	6
Contribution to Project	Co PI Study design Writing Protocols Submitting Ethics documents
Funding Support	n/a

Name:	Professor Declan Murphy
Project Role:	Co-PI
Research Identifier:	ORCID 0000-0002-7500-5899
Nearest Person Month Worked:	2
Contribution to Project	Co PI Protocol Review
Funding Support	n/a

Name:	Professor Scott Williams
Project Role:	Co-PI
Research Identifier:	ORCID 0000-0002-1357-0884
Nearest Person Month Worked:	2
Contribution to Project	Co PI Study design Writing Protocols
Funding Support	n/a

Name:	Dr Javad Saghebi
Project Role:	Central Review Consultant
Research Identifier:	N/A
Nearest Person Month Worked:	2
Contribution to Project	Consultant seeing trial patients Central Review team member
Funding Support	DoD 20%

Name:	Mr Gaurav Sharma
Project Role:	Project Officer/Research Coordinator
Research Identifier:	N/A
Nearest Person Month Worked:	4
Contribution to Project	Administration support
Funding Support	DoD (50%)

Other Collaborating Organisations

- Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP): Review of protocol, clinical expertise network, information sharing and project promotion, co-badging partner.
- Centre for Biostatistics and Clinical Trials (BaCT): Will provide biostatistics support for the study
- Australasian Radiopharmaceutical Trials network (ARTnet): Review of protocol and providing Nuclear Medicine expertise.
- Australian Nuclear Science and Technology Organisation (ANSTO): Supplier of subsidised Lutetium-177
- Endocyte/Advanced Accelerator Applications (AAA), the radioligand business of Novartis, manufacturer of PSMA-617: supplying FOC PSMA-11 & PSMA-617 to patients on experimental arm of study and financial support.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report

What other organizations were involved as partners?

Nothing to report

7. SPECIAL REPORTING REQUIREMENTS

- **Equipment purchased with Award funds**

HPLC-Scan. A flexible controlling unit designed for the remote detection of a wide range of radioisotopes with TLC and HPLC for highest level control of our radiopharmaceutical production of LuPSMA617.

8. APPENDICES

Revised approved budget attached RR_Budget_1_4-V1.4_W81XWH1910651.pdf (includes purchase of HPLC-Scan).