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FINAL REPORT

Project / Program Title		Role of Lutetium-177 Radiolabeled Small Molecule Targeting Prostate Specific Membrane Antigen (PSMA) as an Early Treatment Option in Prostate Cancer
Name		Dr Nattakorn Dhiantravan
Award Received		2020 Arnott Research Entry Scholarship in Cancer Research
Report Date		10/03/2021
Funding Period	Start Date:	03/02/2020
	Finish Date:	06/02/2023

PROJECT SUMMARY

My project focuses on a novel radiopharmaceutical called Lutetium-177 radiolabeled small molecule targeting prostate specific membrane antigen (177Lu-PSMA) and its clinical role as an early treatment option for men with prostate cancer. The research component involves two clinical trials, a multi-centre large scale clinical trial and a local clinical trial. Both trials have commenced and actively recruiting. My project also focuses on utility of molecular imaging biomarkers in prostate cancer, through application of artificial intelligence.

PROJECT AIMS / OBJECTIVES

My project has two distinct but interconnect components, clinical component and development molecular imaging biomarkers component.

The clinical component aims to explore clinical activity and efficacious of 177Lu-PSMA as an early treatment option for men with high volume metastatic hormone naïve prostate cancer and for men with high risk localised prostate cancer.

This aim is being achieved through two separate clinical trials, which are actively recruiting. The first clinical trial is a randomised phase 2 study of sequential 177Lu-PSMA and Docetaxel versus Docetaxel in metastatic hormone-naïve prostate cancer. For this trial, we plan to recruit 140 patients across 12 participating study centres. The hypothesis is 177Lu-PSMA with docetaxel achieves a higher undetectable PSA rate at 12 months compared to docetaxel in patients with metastatic hormone-naïve prostate cancer. We have recruited 41 patients to date. We anticipate recruitment completion by early 2022. The molecular imaging data from this trial should be available for analysis upon completion of enrolment.

The second clinical trial is a phase I/II study of dosimetry, safety and potential benefit of 177Lu-PSMA prior to radical prostatectomy in men with high risk localised prostate cancer. For this trial, we plan to recruit 20 patients across 2 participating study sites. The hypothesis is neo-adjuvant 177Lu-PSMA is safe and can delivery clinically relevant radiation to prostate cancer prior to radical prostatectomy. We have recruited 7 patients to date and anticipate

recruitment completion by the end of 2021. Dosimetry data and early safety data should be

available for analysis upon completion of trial treatment of the last patient.

The development of molecular imaging biomarker component aims to establish novel predictive and prognostic imaging biomarkers in prostate cancer through integration of artificial intelligence data processing with radiomics features. The hypothesis is imaging quantitative features outperform visual assessment as prognostic biomarkers of overall outcome and as predictive biomarkers of treatment response to 177Lu-PSMA or Cabazitaxel.

For this study, we will analyse imaging data from TheraP trial, a randomised phase 2 clinical of 177Lu-PSMA versus Cabazitaxel in men with progressive metastatic castration resistant prostate cancer. TheraP trial, with result recently published in the Lancet in February 2021, has a large dataset of molecular imaging PSMA PET/CT and FDG PET/CT of up to 240 patients. To date, we have developed a visual assessment scoring system, designed to offer simplified quantification of the disease heterogeneity captured on PSMA PET/CT and FDG PET/CT. The system is ready for testing using the TheraP imaging data set. Additionally, we have developed methodology for artificial intelligence assisted imaging segmentation and radiomics features extraction.

I have successfully completed by 1-year confirmation hearing for this PhD project in February 2021.

SIGNIFICANCE AND OUTCOMES

Through a collaborative team effort through the past 12 months, we have published two clinical trial protocols.

• Clinical Trial Protocol for LuTectomy: A Single-arm Study of the Dosimetry, Safety, and Potential Benefit of 177Lu-PSMA-617 Prior to Prostatectomy. Eur Urol Focus. 2020 Nov 7:S24 05-4569(20)30284-4

• UpFrontPSMA: A Randomised Phase 2 Study of Sequential 177Lu-PSMA-617 and Docetaxel versus Docetaxel in Metastatic Hormone-Naïve Prostate Cancer. BJU Int. 2021 Mar 7. doi: 10 .1111/bju.15384

We have submitted two posters to ASCO GU 2021, for UpFrontPSMA Trial Protocol and LuTectomy Trial protocol.

We have also published an editorial piece.

• Actinium-225 Prostate-specific Membrane Antigen Theranostics: Will α Beat β? Eur Urol. 2021 Jan 9:S0302-2838(20)30959-3.

Under supervision, I have also started and now co-chair a weekly Prostate Radionuclide Therapy Multidisciplinary Meeting.

ACKNOWLEDGEMENTS

I am tremendously grateful of the generosity received from the RACP Foundation. In both published clinical trial protocols (mentioned above), it has been acknowledged that Dr. Nattakorn Dhiantravan is a recipient of the RACP Arnott Research Entry Scholarship in Cancer Research.

Clinical Trial Protocol for LuTectomy: A Single-arm Study of the Dosimetry, Safety, and Potential Benefit of 177Lu-PSMA-617 Prior to Prostatectomy. Eur Urol Focus. 2020 Nov 7:S24 05-4569(20)30284-4

UpFrontPSMA: A Randomised Phase 2 Study of Sequential 177Lu-PSMA-617 and Docetaxel versus Docetaxel