

World-First Clinical Trial of the New Experimental Prostate Cancer Drug c2 at Liverpool Hospital

Flagship Program This Case Study is Attributed to
Targets & Therapeutics (T1/T2)

Translational Pipeline Focus
T1/T2

Type of Cancer(s)
Prostate Cancer

Location(s) Where Research is Based
School of Medicine, Western Sydney University (Trial Sponsor), Ingham Institute for Applied Medical Research (Trial Laboratory), Liverpool Hospital (Trial Site)

Summary

Prostate cancer (CaP) is the most commonly diagnosed cancer in males. Despite intense research no breakthroughs that reduce deaths from CaP have been achieved. Thus, 3,500 Australian men will die of CaP in 2018, an increase of some 400 men compared to 2014 and accounting for 12.7% of all cancer deaths. There remains an urgent need for new therapies for those men where standard therapy has failed.

We have developed a new non-toxic oral medicine called c2 that slows human CaP tumour growth and, in some cases, causes regression following treatment withdrawal in animal models. We have scaled up c2 production and the medicine is being tested in **a world first clinical trial** in men who have failed standard therapy. If successful, this medicine could **revolutionise treatment** in this group of men and **save over 1000 lives per year**.

If the compound can be shown to be safe in humans, it will get significantly closer to being used in hospitals across the world.

The Contribution, Impact or Benefit to Community

Impact on Clinical Oncology. Despite dramatic improvements in the five-year survival for men diagnosed with prostate cancer (CaP), this disease still claims over 3,500 Australian lives each year. For these men, the cancer has progressed to the point where standard therapy has failed and treatment has become palliative. It is clear from recent discoveries, that tumour heterogeneity (not all cancer cells in a tumour are the same) the plasticity of tumour cell metabolism (tumour cells can evolve and develop resistance in response to therapy) and the ability of tumour cells to over-ride the defence mechanisms that would normally clear rogue cells from the body before they can spread, are major challenges that need to be resolved if men with advanced CaP are to be effectively treated. One approach to this problem is to discover new medicines that target previously unrecognised pathways that are important in cancer growth and metastasis. One such oral medicine (c2) is currently in a world-first clinical trial in men with

advanced CaP at Liverpool Hospital. If the safety targets set in this trial are met, the findings will lead to a second larger trial that will seek evidence as to whether the medicine is effective in treating this subgroup of CaP patients.

Impact on Oncology Education. This project is embedded in undergraduate and post-graduate education platforms through Ingham Institute partners, Western Sydney University (WSU) and UNSW Sydney. Dr Adam Cooper and Dr Aflah Rohullah, both enrolled in PhD programs through WSU and supported by partial CONCERT PhD scholarships, are named investigators on the trial protocol. The laboratory component of the trial has provided education opportunities for three medical honours students through UNSW Sydney, six undergraduate science students, one of whom has gained employment in the Liverpool Hospital Cancer Clinical Trials Unit and one current WSU PhD student. The project continues to attract high quality students.

Impact on Oncology Research. In addition to the national and international impacts on clinical oncology described above with respect to therapy, this project identified new research approaches to cancer diagnosis and monitoring within CONCERT. For example, it has led to the ongoing competitive funding applications (eg. APP1161239, currently under review with NHMRC) aimed at:

- 1) developing novel tests to track the effectiveness of c2; and
- 2) to explore novel mechanism(s) of action of the drug.

Discussions are also in progress with Liverpool Hospital staff to develop research projects aimed at exploring the diagnostic imaging possibilities of c2 and associated c2 targets in association with the Academic Units' Program of the local health district.

Impact on Oncology Translation. The c2 clinical trial has had a direct impact on building capacity for the translation of laboratory-based preclinical and clinical research to clinical utility in a hospital environment. The translational impact is evidenced by the demonstration that Liverpool Hospital can offer locally-developed experimental treatment options to patients where standard-of-care therapy has failed. The project has contributed to the case for the recent establishment of an Early Phase Clinical Trials unit embedded within Liverpool hospital. In addition, the trial is also an example of the effectiveness of strategic partnerships between universities (WSU sponsored the trial), research institutes (The Ingham Institute coordinates and carries out the laboratory research components of the trial) and local health districts (The Southwest Sydney LHD is conducting the trial). The importance of these strategic relationships was recently acknowledged with an award from the Western Sydney Leadership Dialogue to each of these partners in recognition of their ability to deliver the c2 trial.

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