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Combination approach could overcome treatment resistance in deadly breast cancer

QIMR Berghofer-led research in collaboration with Australian oncology company, Kazia Therapeutics, has found that combining the drug candidate paxalisib with immunotherapy triggered a molecular epigenetic process that prevented the spread of cancer cells and overcame treatment resistance in preclinical models of triple negative breast cancer.

The research has been published in [*Molecular Cancer Therapeutics*](#), a journal of the American Association for Cancer Research.

The study showed for the first time that inhibiting two key cancer signalling pathways at the same time, the *PI3K* and *mTOR* pathways, disrupted a molecule EZH2 which is known to be critical to the spread of cancer cells.

See video animation [here](#).

The research also found that the combination of paxalisib and immunotherapy in the preclinical models helped make the tumour cells more visible to immune cells, as well as reinvigorating the immune cells.

There is an urgent need to develop new treatments for patients with metastatic breast cancer, which is highly aggressive and difficult to treat. Around half of all triple negative breast cancer patients develop metastatic disease where the cancer spreads to other parts of the body. Standard therapies such as chemotherapy and immunotherapy are only effective for a small number of patients at this advanced stage and, importantly, have not been effective in treating cancer stem cells.

The promising preclinical research findings just published have paved the way for a [clinical trial](#) which is recruiting 24 patients with triple negative or BRCA mutation-associated metastatic breast cancer at three sites in Queensland – the Royal Brisbane & Women's Hospital, Gold Coast University Hospital, and Sunshine Coast University Hospital.

Sponsored by Kazia Therapeutics, the multi-centre, open-label [phase 1b clinical trial](#) is assessing the safety and efficacy of paxalisib given in combination with the standard of care approach of chemo-immunotherapy, or with the targeted PARP inhibitor olaparib.

In a first-of-its kind, QIMR Berghofer researchers are collaborating with the trial investigators to test a new liquid biopsy platform designed to track metastatic cancer cells in the blood of participants and monitor how they are responding to the treatment.

The study will be available at this link <https://aacrjournals.org/mct/article/doi/10.1158/1535-7163.MCT-24-0693> with DOI 10.1158/1535-7163.MCT-24-0693 on publication in *Molecular Cancer Therapeutics*, a journal of the American Association for Cancer Research. An embargoed copy is available on request.

To request an interview with Professor Sudha Rao, please email media@gimrb.edu.au or contact Bridie Barry on 0428 592 194.