



Team Progress Updates

SU2C Canada–Canadian Cancer Society Breast Cancer Dream Team: “Translational Development of Novel Drugs Targeting Tumor Vulnerabilities”

Breast cancer remains the second-leading cause of cancer death in women in Canada and the United States. For triple-negative breast cancer and other aggressive forms of the disease, treatment options have been limited. The Dream Team seeks to expand the range of options by accelerating the development of three new drugs.

The first drug, called CFI-400945, inhibits an enzyme that drives division and proliferation of cancer cells. The second, CFI-402257, inhibits a molecule that also seems to drive the cancer process. The third, CX5461, works by binding to the replicating DNA and stopping the cell's copying machinery in its tracks.

The team is also using state-of-the-art approaches to help determine how the three drugs can be used most effectively against breast cancer. All three are in early-stage clinical trials to pave the way to larger trials. This team was originally launched as the SU2C Canada -Canadian Breast Cancer Foundation Breast Cancer Dream Team.

To date the team has:

January 2019

- As planned, trials of three agents are underway and are enrolling patients:
 - The Phase I trial of CFI-400945 in patients with advanced solid tumors have completed the dose escalation phase,
 - With CX-5461, the team is in the dose escalation phase,
 - The Phase I trial of CFI-402257 monotherapy continues in dose escalation with no evidence of toxicity, and,
 - A phase Ib/II trial of CFI-402257 in combination with paclitaxel has been initiated.

June 2018

- The team is finishing up phase I clinical trials for three compounds to treat breast cancer.
- Two of the compounds show no dose-limiting toxicity and clinical responses. These two compounds are being prepared for phase 2 clinical trials.
- Preclinical studies have identified potential biomarkers for predictive use in the compounds.



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- The team continues to develop and analyze data generated from drug testing in patient-donated breast tumors. These data have been integrated into a computational platform to facilitate data analysis, incorporating genetic characterization of the tumors with an aim to discover new biomarkers and predict why some tumors respond to therapy while others do not.
- The team continues to study the impact of the tumor microenvironment on drug response variability.

December 2017

- Continued clinical trial of drug CX5461.
- Launched clinical trials of drugs CFI-402257 and CFI-400945.
- Completed genomic characterization of patient-donated tumor models, permitting the team to test its predictions of drug response.

June 2017

- Obtained preliminary results of clinical trials, allowing the usage of higher doses of the drug than initially anticipated without unexpected toxicity ("side effects").

December 2016

- Launched clinical trial of drug CX5461 – developed by team leaders and the first agent of its kind to be tested as a treatment for breast cancer.
- Obtained encouraging observations on the use of new drugs on patient-derived tumors being grown in animal models.
- Applied new technologies to predict which changes in a tumor cell will kill the cell, or render it more less likely to be killed by drugs being investigated.

June 2016

- Three agents were tested using a panel of more than 50 breast cancer cell lines, helping the team determine which tumour cell features ("biomarkers") can predict a response to a given drug.
- Prepared clinical trials of new drug agents.