



Team Progress Updates

SU2C-Lustgarten Foundation Pancreatic Cancer Dream Team: "Transforming Pancreatic Cancer to Treatable Disease"



Pancreatic ductal adenocarcinoma (PDA) is resistant to most forms of therapy and is one of the deadliest types of cancer. Studies in mice and humans have shown that the environment surrounding a PDA tumor, called the microenvironment, has unique characteristics that are thought to limit the efficacy of treatment.

The Dream Team uses a "convergence" approach, in which leading individuals in different scientific fields work together toward understanding and treating PDA.

The Dream Team has been conducting numerous clinical trials using combinations of drugs and is gaining insight as to which molecules can be measured as indicators, or biomarkers, of tumor microenvironment reprogramming. The team's trials are focusing on new ways to reverse immune suppression in the tumor, either in combination with a vaccine that activates anticancer immune cells called T cells, or in combination with chemotherapy. These trials will also contribute to the establishment of a national PDA biobank for identification of immune biomarkers.

The team has reported the following progress:

December 2017

- The Team has treated 93 patients with metastatic pancreatic adenocarcinoma with cancer vaccines, with and without an antibody that targets a protein called PD-1. The Team is now analyzing the data so that they can make conclusions about this study.
- Promising results were seen by the Team in their Phase I study of an inhibitor against a protein called CXCR4. Because of this, a Phase II trial is being considered where this inhibitor may be combined with immunotherapy.

June 2017

- Clinical trial with an antibody against a new target, CD47 is actively enrolling patients with about 90% enrollment completed.
- Enrollment of clinical trial with the chemokine inhibitor is approaching 70%.
- The Team established a centralized program to effectively analyze samples from various trials to understand how drugs work and how to select patients to receive the maximal benefits from various treatments.

December 2016





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- Three clinical trials of combination therapy are continuing to accrue with the focus on novel immune suppressive pathways within the tumor and stroma.
 - The first study testing a vaccine approach with checkpoint blockade therapy is 100% enrolled.
 - The second study combines chemotherapy with a "BTK" inhibitor (ibrutinib) and is continuing enrollment at two sites.
 - The third study is testing an antibody combined with chemotherapy has completed 40% enrollment and will open a third site.
- Two additional clinical trials, each testing tumor-targeted agents are actively enrolling patients.
- The Team is analyzing the first set of patient samples (from 24 subjects) using a multiplex immunohistochemistry biomarker assay, which was developed by this Team.

June 2016

- All five clinical trials are open and actively enrolling patients.
- The preclinical mouse studies are active and producing data that suggests rational drug combination strategies combining immune checkpoint inhibition with the current drugs that are being tested by this Team.

December 2015

- The Team's five clinical trials, testing one or more agents that have been shown in laboratory studies to alter a novel immune suppressive pathway in PDA, are all open and enrolling patients.
- One of the studies has banked enough patient samples to begin biomarker identification work.
- Laboratory studies are being conducted alongside the clinical trials to establish novel combination treatment approaches and to develop biomarkers that will drive the next generation of clinical trials.
- The Team's central data repository, LabKey, used for storing clinical, correlative, and laboratory data and protocols is being enhanced and refined.

June 2015

During the 7-12 month reporting period, the Stand Up To Cancer-Lustgarten Pancreatic Cancer Convergence Dream Team has made progress on all of their specific aims.

- Five pancreatic cancer clinical trials have been designed
 - Two clinical trials are actively enrolling patients;
 - One is completing the optimization of the drug dosing phase;
 - Two have IRB approval;
- Secured additional funding to perform an enhanced analysis called RNA-Seq on tumor biopsies from one of the clinical trials before and after patients receives treatment.



Team Progress Updates

- Assays to measure biomarkers, and tools to analyze the results, were developed.
- Mouse studies to determine which drug combinations should be tried in humans are currently being conducted.
- A database to capture the clinical and preclinical data is under development.

December 2014

- Five pancreatic cancer clinical trials have been designed
 - One clinical trial has begun enrolling patients,
 - One is IRB approved,
 - Three are rapidly moving toward regulatory approval.
- Biomarker assays have been established, and a set of standard operating procedures for the procurement, processing, and analysis of biosamples across all trials, were established.
- Standard operating procedures for mouse studies have been set up.
- The computational biology working group, which will help catalog all the data generated by the Dream Team, is being formed.