JOHNS HOPKINS MEDICINE | JOHNS HOPKINS ALL CHILDREN'S HOSPITAL

Three Nonprofit Organizations Step Up to Fund Unique, Pediatric Cancer Clinical Trial

Posted on Feb 27, 2023

Jonathan Metts, M.D.
By Randolph Fillmore

In an effort to make an advanced cancer treatment available to pediatric patients with certain cancers, researchers at Johns Hopkins All Children's Hospital and colleagues have developed a clinical trial protocol to study the safety and feasibility of a treatment that expands and enhances a patient's own immune cells to fight cancer. The treatment, known as "adoptive cell therapy," has been approved and has been successful in treating adult patients with certain cancers, but has never been studied as treatment exclusively for pediatric cancer patients.

Jonathan Metts, M.D.

The Phase 1 clinical study, titled "Tumor Infiltrating Lymphocytes in Pediatric Malignant Solid Tumors: A Prospective Biobanking Study and Phase I Clinical Trial," is slated to begin later this year pending U.S. Food and Drug Administration (FDA) approval. The study will seek to enroll pediatric cancer patients with malignant, high-risk, non-cranial solid tumors.

Three nonprofit charities — each of which have missions to develop treatments for pediatric cancer patients — have provided funding.

Cannonball Kids' cancer Foundation, a nonprofit dedicated to finding cures for all childhood cancers by funding critical research, has awarded Metts and his colleagues $200,000 to conduct the clinical trial. In a letter in response to the researcher's application for competitive funding, the Cannonball Kids cancer Foundation said that the Foundation's Scientific Advisory Board "favorably scored and highly ranked" the grant application. The Foundation's executive director also extended best wishes for success and added their "admiration for your vision and dedication to finding a cure for pediatric cancers."

Swim Across America, a charity that funds cancer research, clinical trials and patient programs by hosting charity swims, provided pre-clinical funding, which laid the groundwork for the research. The Benjamin Gilkey Fund that funds investigative physician researchers within the Johns Hopkins All Children's Cancer & Blood Disorders Institute in St. Petersburg, Florida, is providing the bulk of funds, covering the areas not funded by the other organizations.

According to Jonathan Metts, M.D., an assistant professor of oncology in the Johns Hopkins University School of Medicine Department of Oncology, a physician in the Johns Hopkins All Children's Cancer & Blood Disorders Institute and the principal investigator for the upcoming clinical trial, the study may provide hope for pediatric cancer patients and their families.

"High-risk pediatric patients with non-cranial malignant solid tumors comprise about 30-40% of pediatric cancers," explains Metts. "Despite chemotherapy, surgery and radiation, if these patients relapse, they often have no good treatment options."

For Metts, the goal of the proposed clinical trial is personal.

"Finding new therapeutic strategies is a top priority," he says. "My inspiration, and my goal, is to try to find innovative, curative therapies that have fewer long-term side effects."

TIL — A "Personalized" Cancer Therapy

Tumor Infiltrating Lymphocyte Therapy is a "personalized" type of cancer therapy that involves infusion of immune cells called tumor-infiltrating lymphocytes (TILs) from patients with certain cancers. In the laboratory, these cells are "enhanced" and "expanded," in a sense "revved up." The patient's own immune cells are then "enlisted" into the fight against cancer when they are infused back into their donors.

While TILs have been successful in shrinking tumors and providing cancer remission in adults with certain cancers, the procedure has not been studied as a treatment exclusively for pediatric cancer patients. However, establishing TIL therapy as being safe and feasible for treating high-risk pediatric cancer patients could open new doors to needed, advanced treatments.

Here, safety means having no resulting toxicities from TIL therapy while feasibility means that at least 50% of the tumor samples can satisfactorily produce the massive number of revved up cells that are to be infused back into the patients.

Metts explains some of the challenges.

"These cancers in pediatric patients are rare, so it is difficult to find enough patients to enroll," Metts says. "These patients are also often small and, relative to the patient's overall size, their tumors are small and require careful surgery to remove tumor tissue samples."

Metts also says the TIL therapy procedure requires a massive number of T cells that have been "revved up" with cytokines in the lab. Thousands of cells would be insufficient. The actual number required? A billion (yes, that's billion, with a "B").

The researchers have established in the preclinical phase of research that 78% of these tumors are able to produce viable TIL cultures and presented their findings at the Society for Immunotherapy of Cancer Annual Meeting in 2021.

Complicated Steps to “Rev Up” Immune Cells

Metts explains that there are three phases to the TIL therapy procedure. The first phase is surgically obtaining a sample of the tumor. The sample is then sent to the laboratory. At the lab, the cells undergo an expansion manufacturing process, which produces a massive expansion of the T cells (specialized immune cells). These “revved-up” cells will be infused back into the patient. The next phase uses chemotherapy to deplete the immune system of immune cells. This step “makes room for” the eventual reinfusion of the expanded cells.

The third phase is the post-TIL observation period during which there is an infusion of Interleukin-2, a type of white blood cell signaling molecule in the immune system. This step aims at boosting the effectiveness of the TIL therapy procedure.

The Team Approach

The Johns Hopkins All Children’s Pediatric Biorepository, which assists researchers and doctors worldwide in processing, cryopreserving and storing blood, tissue and other specimens for archival and hypothesis-driven research, will play a key role in conducting the study.

According to Metts, the biorepository will have the important task of receiving the tumor samples and making sure they reach the laboratories of the Cell Therapy Facility at Moffitt Cancer Center and Research Institute in Tampa in the best possible condition for growing, multiplying, and manufacturing the right cell products for the eventual reinfusion into study patients.

As in previous studies, Metts will also be working John Mullinax, M.D., a surgical oncologist and associate member in Moffitt’s Sarcoma Program and members of his lab.

During the study, Metts will also work closely with Ajay Gupta, M.D., an assistant professor of oncology in the Department of Pediatric Oncology at the Roswell Park Oishei Children’s Cancer and Blood Disorders Program at the Roswell Park Comprehensive Cancer Center where some of the patients on the study will be treated.

Getting Underway Soon

The launch date of the trial is now in the hands of the U.S. Food and Drug Administration (FDA), Metts says. The FDA is requiring that the researchers, in “trial runs,” twice demonstrate their ability to generate the correct amount and best quality of cells for infusion. So far, the researchers have satisfied the FDA once and a review of another batch of cells is underway.

“We anticipate that the first patient will receive TIL therapy in about nine to 12 months,” Metts says.

The researchers are already designing a phase 2 clinical trial that will look at the TIL therapy efficacy with a larger number of pediatric patients once safety and feasibility are demonstrated in the phase 1 trial.