AT THE FOREFRONT OF KIDS' MEDICINE®
UChicago Medicine
Comer Children's

Update for the Greenfield Family from Ami Desai, MD
December 2023

Phase I Clinical Trial of SBRT Plus Immunotherapy in Children with Neuroblastoma

As outlined in the proposal for your gift, Dr. Desai has worked diligently on convening the team of experts and support staff at Comer Children's Hospital, the University of Chicago Medicine, and beyond, to solidify the crucial partnerships necessary to conduct this unique clinical trial. The team includes physician scientists from radiation oncology, pharmacy, and oncology and other medicine-focused laboratories conducting the correlative biology studies that will play a pivotal role in the study.

At the time of our last update, we were awaiting final approval of the clinical trial full protocol by the pharmaceutical company. Although the concept was approved, the pharmaceutical company subsequently put investigator initiated research proposals on hold during the acquisition of their company. We reconnected with the new company once research activities resumed, and we are excited to announce that they have approved our investigator-initiated study and will provide an anti-GD2 antibody (dinutuximab-beta) that has been tested in Europe but not previously used in North America for this study. We are currently undergoing regulatory approvals and contracting associated with the study. The issues with our industry partner were unanticipated; however, it was critical to have continued conversations and solidify their partnership. With this partnership, we are able to incorporate dinutuximab-beta with a unique administration schedule that may decrease toxicity for our patients and allow them to receive part of their therapy in the outpatient setting.

Your gift has enabled Dr. Desai to align these internal and external partners, and we continue to be exceedingly grateful for your support while Dr. Desai navigates final approvals and anticipates enrolling patients in this important trial.

Related Research in Neuroblastoma for the SBRT Trial

In addition to the work described above on the clinical trial, Dr. Desai has several other important research projects that are creating the ideal environment to conduct the new study.

Recently published papers (enclosed):

- High-risk neuroblastoma patients with end-induction residual disease commonly receive post-induction ("bridge") therapy in an effort to increase survival by improving response prior to autologous stem cell transplant (ASCT). This project, developed at the University of Chicago with Dr. Desai as the first author, looked at outcomes of patients with less than a complete response to induction therapy and investigated the efficacy of this approach through a multicenter, retrospective study. One of the main findings was that patients with end-Induction metastatic stable disease benefited from bridge therapy prior to moving on to ASCT. This paper was published and highlighted in Cancer in 2022 with an accompanying editorial as well as media attention. This trial outlined in the proposal is relevant for patients with refractory neuroblastoma.

- Immunotherapy with dinutuximab (an anti-GD2 antibody, similar to the the intended antibody for the SBRT trial) was found to improve outcomes for high-risk neuroblastoma patients enrolled on the randomized portion of a Children's Oncology Group study (Yu, et al. NEJM 2010). After randomization ended, patients were non-randomly assigned to immunotherapy to refine event-free and overall survival estimates and obtain additional toxicity and correlative biology data in a larger group of patients. This analysis confirmed the survival and toxicity outcomes published in the original paper. In addition, among patients with available correlative biology data, dinutuximab level and FCGR3A genotype were associated with higher event-free survival. Dr. Desai served as the first author of this paper which was published in the Journal of Clinical Oncology in 2022.

- Racial/ethnic disparities in neuroblastoma were reported by our group greater than a decade ago (Henderson, et al. Journal of Clinical Oncology, 2009). Dr. Desai and colleagues at the University of Chicago conducted a project to determine if these disparities persisted in the current era (2010-2019) using the INRG data commons. They found that Black patients continued to have a higher proportion of disease compared to with White patients. Among patients with high-risk disease, Hispanic patients had worse overall survival compared to White patients. Black and Hispanic patients assigned to receive post-Consolidation dinutuximab (anti-GD2 antibody) on clinical trials had worse overall survival compared to White patients. These findings were recently published in European Journal of Cancer: Paediatric Oncology in 2023.

- Dr. Desai served as the Study Chair for the Children's Oncology Group Study ANBL19P1, a pilot study to assess the feasibility of administering chemoimmunotherapy in post-Consolidation, which is the last phase of frontline therapy for high-risk neuroblastoma. The study was recently closed in June 2023 and Dr. Desai is working on the final analysis of this trial with the study team.

Updates on Research Related to the Correlative Biology Studies for the SBRT Trial:

- Embedded Microbiome Study (Dr. Desai in collaboration with the University of Chicago Ducchosois Family Institute led by Dr. Eric Pamer): First batch of samples were analyzed from patients with newly diagnosed neuroblastoma and patients with relapsed or refractory disease to describe the landscape of the microbiome in patients with neuroblastoma. Preliminary results (unpublished) demonstrate that the gut microbiome differs among healthy controls and patients with neuroblastoma. In high-risk patients, the dysbiosis and decreased microbial diversity detected during Consolidation therapy with ASCT persists during post-Consolidation therapy. To note, there is data from work in adult cancers that the microbiome may impact response to therapy (immunotherapy, chemotherapy) and radiation.

- Liquid biopsy/cell free DNA-5hmc profiles (Dr. Mark Applebaum and Dr. Sue Cohn): This work is correlated with response to therapy for neuroblastoma. The team has secured three grants for this work, including one from the National Institutes of Health.

- Immunophenotyping (Dr. James Labelle): This lab is working towards describing the immune cell profiles in patients with neuroblastoma during immunotherapy with anti-GD2 antibody. Dr.

LaBelle's preliminary work has been completed in neuroblastoma and will be analyzed in the SBRT trial as well.

Thank you

Thank you for your support of Dr. Desai in her work towards better outcomes for neuroblastoma patients. Your gift drives vital collaboration and research, altering the future of cancer treatment for this disease and beyond.

We are inspired by your commitment and generosity, and we are excited for the progress that we will make together.