New immunotherapy trial for children with central nervous system tumors opens

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Seattle Children's mission is to provide hope, care and cures to help every child live the healthiest and most fulfilling life possible. Credit: Seattle Children's

Seattle Children's has opened a pioneering chimeric antigen receptor (CAR) T-cell immunotherapy trial for children and young adults with relapsed or refractory HER2-positive central nervous system (CNS) tumors where CAR T cells will be delivered directly into the brain. In

the phase I trial, BrainChild-01, cancer-fighting CAR T cells will be infused through a catheter, either into the cavity where the tumor has been removed or the CNS ventricular system, depending on the location of the tumor.

CNS tumors, which are found in the brain and spine, are the most common form of childhood cancer and are the leading cause of cancer-related death in children under the age of 19. More than 4,000 children in the U.S. are diagnosed with brain tumors each year. While approximately 70% of children with newly diagnosed CNS tumors survive with standard therapy, the disease is often fatal for the approximately 30% of children who relapse.

"While survival rates have improved, many of the children we care for have no life-saving therapy options if their disease recurs," said Dr. Nick Vitanza, a neuro-oncologist at Seattle Children's and lead investigator for the BrainChild-01 trial. "We have to find a way to give them a life after they recur—and ultimately—be able to offer initial treatments with fewer long-term side effects."

In the BrainChild-01 trial, T cells will be reprogrammed to target the protein HER2, which is widely known for its presence in breast cancer, but also expressed by many common brain tumors in children, including medulloblastoma, ependymoma, and glioma. In targeting this protein, the CAR T cells will be able to find and destroy the cancerous tumor cells while preserving healthy brain tissue, which does not express HER2.

"Solid tumors are challenging to target compared to blood cancers because they express a diverse array of proteins and are harder to reach," said Vitanza. "In looking for a common denominator that is present on many types of tumors, but not present in healthy brain tissue, we were pleased to find that HER2 could be a common thread that helps us target several of the brain tumors we treat in children and young adults."

Vitanza and the research team, led by Dr. Mike Jensen at the Ben Towne Center for Childhood Cancer Research at Seattle Children's Research Institute, plan to enroll a minimum of 18 patients over the course of the trial. Patients will be enrolled in one of two arms based on the location of their tumor after researchers confirm it expresses HER2. Once the patient's CAR T cells have been reprogrammed, those children in the first arm will have their T cells infused through a catheter into the tumor resection cavity. Children in the second arm will have their T cells infused through a catheter into their CNS ventricular system.

By infusing the CAR T cells directly into the brain instead of into the blood intravenously, researchers believe the delivery will be more effective since the T cells will not need to penetrate the blood-brain barrier, which often prevents drugs from getting into the brain at the necessary concentrations. Researchers also hope patients may have fewer side effects, like neurotoxicity and cytokine release syndrome, since the reprogrammed T cells will not circulate widely through the blood. This clinical trial will examine the safety and feasibility of this approach.

Patients will receive one dose of CAR T cells weekly, up to six doses on the study. Depending on the patient's response and tolerability to the experimental therapy, they will have the option to continue receiving doses.

BrainChild-01 is the next step in Seattle Children's quest to harness the immune system and bring better therapies and cures to children worldwide. With one of the most robust pipelines of open T-cell immunotherapy clinical trials for children and young adults, Seattle Children's is dedicated to working to improve this therapy for a variety of childhood cancers to the point that it helps patients achieve long-term remission—and ultimately—a cure.

With this long-term goal in mind for treating CNS tumors, Vitanza said

BrainChild-01 will likely only be the beginning. With the vast array of tumor types and more aggressive tumors, this research may also open new doors to treatment strategies that involve targeting different or multiple proteins simultaneously.

"Our eventual goal with this research is to find a therapy that is safe, curative and serves as a platform to combine multiple targets in order to treat the most aggressive cancers," said Vitanza. "I was inspired to go into neuro-oncology after experiencing too often how little can be done for most kids with aggressive or recurrent brain tumors. Using CAR T cells, we are determined to develop a therapy that will give these kids an option that they desperately need—that will help them be able to live a longer and fuller life."

The T-cell immunotherapy trials at Seattle Children's are funded in part by Strong Against Cancer, a national philanthropic initiative with worldwide implications for potentially curing childhood cancers. If you are interested in supporting the advancement of immunotherapy and cancer research, please visit Strong Against Cancer's donation page.

Provided by Seattle Children's Research Institute