

Solid tumors targeted in new CAR T-Cell immunotherapy trial

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Seattle Children's
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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 chimeric antigen receptor (CAR) T-cell immunotherapy trial for children and young adults with relapsed or refractory non-central nervous system EGFR-expressing solid tumors. In the phase 1 trial, [STRIVE-01](#), cancer-fighting CAR T cells will target the EGFR protein expressed in many childhood sarcoma, kidney and neuroblastoma tumors.

Solid tumors, excluding those of the brain, make up about 30 percent of all childhood cancers. Sarcoma, a cancer that develops in the bone and soft tissue; kidney malignancies, including Wilms [tumor](#); and neuroblastoma, a tumor that forms in young nerve [cells](#), are the most common types of non-central nervous system solid tumors diagnosed in children. Even as treatment advances have improved childhood cancer survival rates over the last several decades, these solid tumors remain among the most resistant to standard therapy when the cancer relapses or does not respond to initial treatment.

"Despite employing modern treatments that offer

more intensive therapy or new drug combinations for children with solid tumors, we've been unable to improve outcomes for our highest-risk patient groups," said Dr. Katie Albert, an oncologist at Seattle Children's and lead investigator for the STRIVE-01 trial. "It is those groups that push us to come up with innovative approaches so that we can see all of our patients cured of their cancer."

While CAR T cells engineered to fight cancer have shown promise for curing childhood leukemia in [clinical trials](#) at Seattle Children's, solid tumors pose unique challenges. Solid tumors exist in protective microenvironments that help them evade the immune system, making it more difficult to keep the CAR T cells stimulated.

"In order for this therapy to be effective against solid tumors and induce remission for our patients, we have to find a way to not only get the CAR T cells into the tumor microenvironment, but also ensure they can survive and thrive there," said Albert.

To construct the CAR T cells for STRIVE-01, researchers led by Dr. Mike Jensen at the Ben Towne Center for Childhood Cancer Research at Seattle Children's Research Institute will reprogram a patient's T cells to target the abnormal EGFR protein expressed on the surface of many solid tumor cancer cells. In normal tissues, EGFR is responsible for cell growth and development. When expressed in malignant solid tumors, EGFR has been associated with more aggressive and invasive growth.

By arming the CAR T cells with an antibody known as EGFR806, researchers hope to selectively find and destroy solid tumor cells expressing EGFR with limited toxicity to normal tissues.

As Albert explained, "Normal tissue, including skin, is enriched in EGFR, so it is advantageous to equip the CAR T cells with an antibody that recognizes

EGFR on tumor cells and leaves healthy cells relatively protected."

Anticipating that it will take a multi-faceted approach to overcome solid tumors, STRIVE-01 will include two sequential treatment arms. Children and young adults enrolled in the first arm will receive EGFR806 CAR T cells to first evaluate the toxicity and establish the maximum tolerated dose of the experimental therapy. Once the first arm is complete, the second arm will open. Patients in the second arm will receive CAR T cells reprogrammed to target both EGFR and CD19, a protein expressed on a subset of white blood cells called B lymphocytes.

"By including a CAR T-cell therapy that targets two proteins, we're a step ahead in addressing a known challenge with solid tumors—the cancer-fighting T cells won't hang around long enough to get to the tumor tissues and keep the cancer from coming back," said Albert. "Building on what we've learned in our trials for leukemia, our hope is that the secondary target of CD19 will constantly interact with B lymphocytes in the blood to promote the expansion and persistence of the EGFR-directed CAR T cells."

The study plans to enroll approximately 36 patients across both arms to assess the dosing, safety and tolerability of the CAR T-cell therapies. The results from STRIVE-01 will inform the clinical development of future CAR T-cell trials aimed at finding the most effective targets and therapeutic combinations for pediatric solid tumors.

"We recognize that it will likely require a range of therapeutic strategies to manipulate the immune environment enough to cure patients with hard to treat [solid tumors](#)," said Albert. "I'm excited to have the opportunity to incorporate our most advanced immunotherapy strategies into a solid tumor program that I hope will provide families the most effective and comprehensive CAR T-cell treatment options for their child's cancer."

STRIVE-01 joins a robust pipeline of [T-cell immunotherapy trials](#) underway at Seattle Children's focused on harnessing the immune system to offer better treatment options for children

and young adults with [cancer](#). Seattle Children's is dedicated to improving CAR T-cell immunotherapy for a variety of childhood cancers to the point that it helps patients achieve long-term remission—and ultimately—a cure.

Provided by Seattle Children's Research Institute

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