A Pioneering CAR-T trial for CNS tumors at Children's Hospital of Seattle

Bella Smith

Abstract

The Seattle Children's Hospital launched a pioneering clinical trial of chimeric antigen receptors (CAR) T-cell immunotherapy for relapsed or refractory HER2-positive CNS tumors in children and young adults. Among them, CAR-T cells will be delivered directly to the brain. In a Phase 1 trial of BrainChild-01, depending on the location of the tumor, CAR-T cells will be catheterized into the cavity or CNS ventricular system where the tumor has been removed.

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CNS tumors found in the brain and spine are the most common forms of childhood cancer and are the leading cause of cancer deaths in children under the age of 19. In the United States, more than 4,000 children are diagnosed with brain tumors each year. Although approximately 70% of newly diagnosed children with CNS tumors survive after receiving standard treatment, the disease is often fatal in approximately 30% of relapsed children.

Dr. Nick Vitanza, a neurosurgeon at Seattle Children’s Hospital and chief researcher of the BrainChild-01 trial, said: “Although the survival rate has improved, many of the children we care about have relapsed without life-saving treatment options. We must find one. This approach gives them a life after they have relapsed, and at the same time can ultimately provide initial treatment with fewer long-term side effects.”

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

Compared with hematological tumors, the goals of solid tumor therapy are very challenging because they express multiple proteins and are difficult to reach. They look for markers that are present in many types of tumors but not in healthy brain tissue. At the time, we were pleased to discover that HER2 may be a common clue to help us target several brain tumors we treat in children."

Vitanza and a team led by Dr. Mike Jensen of the Ben Towne Children's Cancer Research Center at the Seattle Children's Institute plan to recruit at least 18 patients during the trial. After the researchers confirmed HER2 expression, the patients were divided into two groups according to their location. After reprogramming the patient's T cells, those children in the first group will be intubating their T cells into the tumor resection cavity. The second group of children will inject their T cells into their CNS ventricular system via a catheter.

By injecting CAR T cells directly into the brain rather than into the bloodstream, the researchers believe that this delivery will be more effective because T cells do not need to penetrate the blood-brain barrier (which tends to prevent drugs from reaching the brain to reach the necessary concentration). Researchers also hope that patients may have fewer side effects, such as neurotoxicity and cytokine release syndrome, because reprogrammed T cells do not circulate extensively in the blood. This clinical trial will examine the safety and feasibility of this method.

Patients will receive one dose of CAR-T cell infusion per week, and in this study, they may need to receive up to six doses of treatment. Based on the patient's response to the experimental treatment and tolerance, they can choose to continue to receive more doses.

BrainChild-01 is Seattle's next step for children seeking to use the immune system to bring better treatment and treatment to children around the world. With clinical trials of T-cell immunotherapy open to children and young adults, Seattle Children's Hospital will work to improve this treatment for childhood cancer to help patients achieve their ultimate goal of long-term remission. Considering the goal of long-term treatment of CNS tumors, Vitanza said: "BrainChild-01 may be just the beginning. With the emergence of a large number of tumor types and more aggressive tumors, this study may also be directed to different or multiple proteins. "

Vitanza said: "Our final research goal is to find a safe and effective treatment and use it as a platform to combine multiple targets to treat the most aggressive cancers because there are a lot of clinical ones. Children with invasive or recurrent brain tumors are not treated effectively and I was therefore inspired to get into the path of neuronal tumors. With CAR T technology, we decided to develop a treatment that allows these children to have treatment options for the future to help them live a longer, more fulfilling life."

Author Bio

As a global company, Creative Biolabs has more than 200 talented and well-trained scientists located in different continents working closely with partners from the entire world to develop and produce medicines of tomorrow. Specifically, we are the established leading expert in TCR T cell nd CAR T&NK cell immune therapy development, as we offer the one-stop custom services that cover the entire new drug development pipeline. Additionally, we also offer an exclusive line of ready-to-use TCR technology K cell construction products, such as virus packaging, purification, expansion and titer determination kits. Furthermore, we have built up a unique unparalleled CAR construction and production platform for all four CAR generations.