Immunotherapy showed promising antileukemia activity in pediatric patients

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Researchers using patients' own immune cells in an immunotherapy approach called "anti-CD19 chimeric antigen receptor (CAR) T-cell therapy," achieved responses in children whose acute lymphocytic leukemia (ALL) had returned after a bone marrow transplant, according to preliminary results presented at the AACR Annual Meeting 2013, held in Washington, D.C., April 6-10.

"Anti-CD19 CAR T-cell therapy using patients' own immune cells is a completely new way of treating childhood cancer," said Daniel W. Lee, M.D., assistant clinical investigator in the Pediatric Oncology Branch of the National Cancer Institute. "It is not chemotherapy; therefore, it has a different side effect profile—we hope better tolerated. In the limited number of post-transplant patients we have treated so far, we're getting acceptable toxicities, and we're not seeing graft-versus-host disease."

More than 95 percent of children initially diagnosed with ALL achieve remission, but a significant number of them relapse, according to Lee. Once they relapse, the prognosis is poor, with ALL accounting for the most deaths from cancer among children.

Other research teams are testing anti-CD19 CAR T-cell therapy in children with ALL that has returned after a bone marrow transplant, according to Lee. However, whether they are using immune cells from the transplant donor, or collecting and preparing the patient's cells, the process is lengthy.

"Often these children with relapsed ALL don't have that kind of time to wait," Lee said. "We wanted something that could be done in a more timely manner. We decided to collect the immune cells, which are called T cells, directly from the patients, even though they'd had bone marrow transplants."

The first three patients in the phase I trial had undergone a previous bone marrow transplant, although the trial is also open to patients who have never had a transplant. One patient had B-cell lymphoma and the other two had ALL.

The researchers collected T cells from the patients and modified them in the laboratory so that they would attach to a protein expressed by the leukemia cells, called CD19, and attack the cancers. The number of modified T cells, now called anti-CD19 CAR T cells, was expanded in the laboratory before they were returned to the patients.

The results so far indicate that this approach is a feasible and active treatment for pediatric patients with ALL, even those who relapse after a bone marrow transplant, according to Lee. One patient had a complete response and a second had a transient complete response, with minimal residual disease remaining. The lone lymphoma patient did not respond.

Cell expansion was robust. "We were able to get very good expansion—on average about 60-fold expansion of these cells during the 11-day culture period," Lee said. "And we were able to insert the receptor, the anti-CD19 CAR, into those T cells with good efficiency."

One patient did not produce a sufficient number of cells, which was likely related to recent intensive chemotherapy and resultant low T-cell count, according to Lee. Despite this, the few cells the patient did receive expanded dramatically and the patient temporarily achieved remission.

Lee and colleagues continue to test this approach in patients whose disease has returned after, or is refractory to, standard treatments whether or not they have had a bone marrow transplant.

"We think that the children who have never had a transplant might experience different toxicities," said Lee. "Our first patient enrolled in this arm of the trial had never achieved disease remission after her initial diagnosis of ALL despite intensive chemotherapy. Strikingly, anti-CD19 CAR T-cell therapy resulted in the complete clearance of any detectable leukemia in this patient, and we were able to send her back to her primary oncologists for a bone marrow transplant."

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