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Seattle Children's opens CD22 CAR T-cell immunotherapy trial for children and young adults

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After seeing promising results in phase 1 of the Pediatric Leukemia Adoptive Therapy (PLAT-02) trial with 93 percent of patients with relapsed or refractory acute lymphoblastic leukemia (ALL) achieving complete initial remission, researchers at Seattle Children's are continuing their quest to improve the experimental therapy and reduce the rate of relapse, which is about 50 percent. Researchers have now opened a phase 1 clinical trial, PLAT-04, for children and young adults with relapsed or refractory CD22-positive ALL. They will examine the safety and feasibility of administering cancer-fighting chimeric antigen receptor (CAR) T cells that have been reprogrammed to target the CD22 protein expressed by some leukemia cells.

"We're at a pivotal point where we're building upon what we've learned in the PLAT-02 trial and opening new trials, like PLAT-04, with the goal of improving this therapy to the point that it becomes a long-term cure for all of our leukemia patients," said Dr. Corinne Summers, an oncologist at Seattle Children's and the lead investigator of the PLAT-04 trial.

Summers and the research team, led by Dr. Mike Jensen at the Ben Towne Center for Childhood Cancer Research at Seattle Children's Research Institute, are opening PLAT-04 after discovering that of the patients who relapsed in the PLAT-02 trial, approximately 40 percent of them relapsed with a leukemia that evolved to circumvent the CAR T

cells that were reprogrammed to detect and destroy cancer.

In PLAT-02, the CAR T cells are reprogrammed to recognize and target the CD19 protein that is expressed by most precursor B acute lymphoblastic leukemia cells. However, in some patients, the leukemia recurred without the CD19 target and expressed a protein that the CAR T cells were unable to recognize—CD22. With the PLAT-04 trial, researchers will now be able to reprogram CAR T cells to detect and destroy leukemia cells that express the CD22 protein. Researchers hope to enroll more than 30 patients in the trial over the next two to three years.

"Leukemia cells evolve in order to find ways to survive," said Summers. "For the patients who relapse with CD22-positive leukemia, we are very pleased to now be able to offer a treatment option that will hopefully lead them to finally achieving long-term remission."

The PLAT-04 trial follows the PLAT-03 trial that Seattle Children's opened in May. PLAT-03 institutes another strategy aimed at increasing long-term remission—introducing T-cell "boosters" intended to improve the persistence of CAR T cells. Researchers are also working to develop a trial where they will reprogram CAR T cells to identify the CD19 and CD22 proteins simultaneously, enabling them to target the cancer cells from more than one angle with the initial round of T-cell immunotherapy.

"We believe T-cell immunotherapy has tremendous potential," said Summers. "This is why we're diligently working to employ several strategies that we hope will lead us to reaching our ultimate goal of developing the best therapy possible—a therapy that can be given to patients as a first line of defense, greatly reducing the side effects of cancer treatment and leading to a cure."

Provided by Seattle Children's Research Institute