

CD19-targeting CAR T-cell immunotherapy yields high responses in treatment-resistant CLL

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In a small, early phase trial, a high percentage of patients who had exhausted most traditional treatments for chronic lymphocytic leukemia saw their tumors shrink or even disappear after an infusion of a highly targeted, experimental CAR T-cell immunotherapy developed at Seattle's Fred Hutchinson Cancer Research Center.

Fred Hutch researchers will present their findings in an oral presentation on Dec. 3 at the American Society of Hematology Annual Meeting and Exposition in San Diego.

Almost all of the 24 patients in the study had cancer that had advanced despite treatment with a newly approved drug called ibrutinib - an ominous indicator for patient survival. Most patients also had chromosomal markers in their leukemia cells that put them at high risk - "predictors of a bad response to most standard therapies," said Dr. Cameron Turtle, a hematologist/oncologist in the Clinical Research Division at Fred Hutch who co-leads the trial with colleagues Drs. David Maloney and Stanley Riddell.

Turtle's presentation will focus on the results in a subgroup of patients who received the CAR T-cell infusion using preferred chemotherapy and CAR T-cell doses that evolved from recent trial data. Fourteen of the 19 restaged patients experienced a partial or complete regression of the disease in their lymph nodes. Of the 17 who had leukemia in their marrow when they enrolled in the trial, 15 saw the marrow become cancer-free after receiving CAR T-cells.

"These are all heavily pretreated patients who've gone through many previous therapies," Turtle said. "It's very pleasing to see patients with refractory disease respond like this."

Participants with the highest number of CAR T-cells in their blood after infusion were the most likely to have their disease disappear from bone marrow after CAR T-cell infusion. Side effects included high fevers, due to activation of CAR T-cells, and neurologic symptoms. Although one patient died from severe toxicity, the side effects experienced by other patients in the study were temporary.

In a separate poster presentation from 5:30 to 7:30 p.m. on Dec. 3, the researchers will share their findings in a detailed characterization of the side effects of CD19 CAR T-cells. The poster session presentation is embargoed until 9 a.m. Dec. 3 - just over an hour after the embargo lifts for the CLL study results. Turtle and his colleagues identified certain biomarkers in [patients'](#) blood the day after infusion that were associated with the later development of the most severe toxicities. The researchers hope these biomarkers could eventually lead to tests to predict and mitigate the most serious side effects.

CAR T-cell therapy is accomplished by engineering T cells extracted from each patient's blood. A modified virus delivers genetic instructions into the cells for making a CAR, or chimeric antigen receptor, a synthetic molecule that allows T cells to recognize and kill cells bearing a particular target. In this case, the target is CD19, a molecule found on the surface of certain blood cells, including CLL cells, and the T cells are carefully selected, one-to-one combination of two functionally different subsets of T cells. After the CAR T-cells are grown in the lab and the patient has received chemotherapy, the new CAR T-cells are infused back into the patient.

CD19 CAR T-cell studies at Fred Hutch are unique because the researchers engineer specific subsets

of cells from the patient and formulate the cell product to be uniform. By creating CAR T-cells with a defined composition of T cell subsets, the researchers can improve the link between the dose of [cells](#) a patient receives and what they experience afterward - not just benefits, but also potential [side effects](#).

Patients in the trial are seen at Seattle Cancer Care Alliance, Fred Hutch's clinical care partner.

Provided by Fred Hutchinson Cancer Research Center

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