

Genetically engineered immunotoxin shows early promise in patients with B-cell malignancies

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Almost all patients with a group of blood cancers called B-cell malignancies have two prominent "fingerprints" on the surface of leukemia and lymphoma cancers, called CD22 and CD19, Vallera explained. To develop the drug, Vallera and colleagues chose two antibody fragments that each selectively bind to CD19 and CD22. They used genetic engineering to attach these two antibodies to a potent toxin, the bacterial diphtheria toxin. When the antibody fragments bind to the two targets on the cancer cell, the entire drug enters the cell, and the toxin kills the cell.

Vallera; Veronika Bachanova, MD, PhD, oncologist and an assistant professor at the University of Minnesota; and colleagues enrolled 25 [patients](#) to the trial. Patients had chemo-refractory pre-B [acute lymphoblastic leukemia](#), [chronic lymphocytic leukemia](#), or non-Hodgkin lymphoma, and had received two to five prior therapies, with eight of them having had previous unsuccessful bone marrow transplantations. All tumors were confirmed to have CD19 and/or CD22 proteins. In this dose-escalation study, all patients received a single cycle of varying doses of the immunotoxin therapy.

Two of the 10 evaluable patients had durable objective responses. One of them had a complete remission after receiving two cycles of treatment. The maximum tolerated dose was not reached but clinical responses occurred between doses 40 to 80 µg/kg administered in four

infusions.

In an interview, Vallera said, "In this phase I trial, we found a safe dose of the [drug](#) that has biological activity. Of the 10 evaluable patients, two of them responded. We are planning a phase II trial with this drug. It will focus on giving more cycles of treatment, which we believe will dramatically enhance the response rates. We were surprised that the drug was effective enough to entirely eliminate the cancer in one of our patients. Further, we expected the patients to make antibodies against the [bacterial toxin](#) and thus reject our drug. Surprisingly, this did not occur in the majority of our patients [70 percent]. We need to study more patients to understand why they did not produce neutralizing antibodies. However, we also have been working to create a less immunogenic form of the toxin for the next-generation drug."

Vallera added, "Another important fact about our drug is that it was home-grown, meaning there was no commercial partner, which is rare. The drug was funded mostly with private donations including individuals that have lost loved ones to cancer."

Provided by American Association for Cancer Research

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