Antibody-guided drug works against acute lymphoblastic leukemia

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An antibody packaged with a potent chemotherapy drug to selectively destroy acute lymphoblastic leukemia (ALL) cells eradicated or greatly reduced the disease for 61 percent of 46 patients in a phase II study. It will be presented at the 47th annual meeting of the American Society of Clinical Oncology in Chicago June 3-7.

Patients enrolled in the trial led by investigators at The University of Texas MD Anderson Cancer Center had ALL that resisted other therapies or recurred after treatment.

"A response rate of more than 50 percent in this patient population probably makes inotuzumab ozogamicin the most active single-agent therapy ever for ALL," said Hagop Kantarjian, M.D., professor and chair of MD Anderson's Department of Leukemia and study senior investigator.

ALL is an aggressive form of leukemia in which immature white blood cells, called lymphoblasts, grow rapidly, crowding out normal blood cells.

The drug, also known as CMC-544, links an antibody that targets CD22, a protein found on the surface of more than 90 percent of ALL cells, and the cytotoxic agent calicheamicin. Once the drug connects to CD22, the ALL cell draws it inside and dies.

Response rate for other second options is 20-30 percent

Kantarjian said second-line chemotherapy combinations used for ALL typically have a complete response rate of 20-30 percent. The monoclonal antibody-based drug developed by Pfizer, Inc., also is the first of its type for ALL.

The drug is safe, said Elias Jabbour, M.D., assistant professor in MD Anderson's Department of Leukemia, who will present the study results at ASCO on Monday, June 6. Almost all side-effects were of low grade (1-2) and manageable. Drug-induced fever was the most common side effect, reaching higher grades in nine of 48 patients.

Out of 46 patients evaluable for response, nine had a complete response, 14 had complete response without full recovery of platelets, and 5 had less than 5 percent blasts in their bone marrow without blood count recovery.

Sixteen responders subsequently received a donor blood stem cell transplant, Jabbour noted.

Drug combinations

Combining inotuzumab with other chemotherapy might further improve ALL treatment, Jabbour said. MD Anderson has a phase II clinical trial under way following inotuzumab treatment with another monoclonal antibody drug, rituximab, currently used in some types of non-Hodgkin's lymphoma.

Rituximab targets the CD20 surface protein, which occurs in 50 percent of ALL cells.

In addition to combinations, the authors suggest that a shift from dosing every three weeks to weekly should be explored.

Frontline therapy for ALL is a combination chemotherapy regimen known as HyperCVAD.

The National Cancer Institute estimates that 5,330 people received an ALL diagnosis in 2010 and 1,420 died of the disease.

ALL is the most common type of childhood cancer. Combined chemotherapy regimens have raised long-term survival from 5 percent of pediatric patients in the 1960s to 85 percent today.

Provided by University of Texas M. D. Anderson Cancer Center