MedicalXpress

Patient's immune status associated with outcome following third-generation CAR T-cell therapy

September 6 2017

Treatment with third-generation CAR T–cell therapy led to a complete response in six of 15 patients with a CD19-positive B-cell malignancy and overall survival was associated with the patient's immune status, according to data from a phase I/IIa clinical trial presented at the Third CRI-CIMT-EATI-AACR International Cancer Immunotherapy Conference: Translating Science into Survival, held Sept. 6–9.

"CD19-specific CAR T–cell therapy has yielded remarkable response rates for patients who have B-cell acute lymphoblastic leukemia," said Tanja Lövgren, PhD, a researcher in the Department of Immunology, Genetics and Pathology at Uppsala University in Sweden. "However, many patients relapse. In addition, response rates are more variable for patients who have other CD19-positive B-cell malignancies and many patients experience serious adverse events.

"We set out to investigate the safety and effectiveness of a third-generation CD19-specific CAR T–cell therapy and to identify potential biomarkers of treatment outcome," said Lövgren. "We found that the treatment was generally safe and effective, and that an immunostimulatory environment was associated with improved overall survival while immunosuppressive cells and factors were associated with treatment failure and decreased overall survival."

Although further studies are needed to confirm these data, they suggest

that it is probably best to combine CAR T–cell therapy with a therapy reducing immunosuppressive cells and/or factors in most cases, according to Lövgren.

Lövgren and colleagues enrolled 15 patients who had relapsed or refractory CD19-positive B-cell malignancy in the clinical trial. Eleven had a CD19-positive B-cell lymphoma and four had a CD19-positive B-cell leukemia. Tumor responses were followed by bone marrow/blood analysis and/or radiology depending on the type of malignancy. Blood samples were collected before infusion of the CD19-specific CAR T cells and at multiple times after infusion.

Six patients, four with lymphoma and two with leukemia, had an initial complete response. The median duration of the complete responses was five months. Although the four lymphoma patients relapsed, they responded well to subsequent conventional therapy.

Four patients had serious adverse events; three had cytokine-release syndrome and two had central nervous system–related toxicity. All serious adverse events resolved spontaneously or with appropriate treatment.

Analysis of patient blood samples showed that high levels of immunosuppressive immune cells called monocytic myeloid-derived suppressive cells prior to treatment was associated with decreased overall survival and increased levels of these cells after treatment preceded treatment failure. In addition, high plasma levels of immunosuppressive factors such as PD-L1 and PD-L2 after treatment were associated with decreased overall survival.

High plasma levels of biomarkers of an immunostimulatory environment, including IL-12, DC-LAMP, TRAIL, and FasL before administering CAR T–cell therapy was associated with increased overall

survival.

"We are hoping to follow up this study with another clinical trial that will combine CAR T–cell therapy with chemotherapy known to decrease the number of monocytic myeloid-derived suppressive cells," said Lövgren. "We are also looking to further optimize the CAR T–cell therapy."

According to Lövgren, the main limitations of the study are that it was a small study with only 15 patients; that the patients had several different types of B-cell malignancy; and that some patients may have been too sick to respond to any treatment.

Provided by American Association for Cancer Research