CAR T cell therapy effective as first-line treatment for high-risk large B-cell lymphoma

December 7 2020

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A study led by researchers at The University of Texas MD Anderson Cancer Center found that axi-cel, an autologous anti-CD19 chimeric antigen receptor (CAR) T cell therapy, is a safe and effective first-line therapy for patients with high-risk large B-cell lymphoma (LBCL), a group with an urgent need for new and effective treatments.

These results were presented at the virtual 2020 Annual Meeting of the American Society of Hematology.

Historically, around half of patients with high-risk LBCL, a subgroup of the disease in which patients have double- or triple-hit lymphoma or additional clinical risk factors identified by the International Prognostic Index (IPI), do not reach long-term disease remission with typical treatment approaches like chemoimmunotherapy.

"This trial is a step toward moving CAR T cell therapy to first-line therapy for patients with aggressive B-cell lymphoma," said principal investigator Sattva S. Neelapu, M.D., professor of Lymphoma and Myeloma. "Currently, patients with newly diagnosed aggressive B-cell lymphoma receive approximately six months of chemotherapy. If successful, CAR T cell therapy could change it to a one-time infusion with therapy completed within one month."

Axi-cel is currently approved for treatment of adults with relapsed or refractory LBCL who already have received two or more lines of systemic therapies, based on the pivotal study, ZUMA 1. The Phase 2, open-label, single-arm, multicenter ZUMA-12 trial expands on the

ZUMA-1 findings to evaluate the use of axi-cel as first-line therapy for patients with high-risk LBCL.

The interim analysis of ZUMA-12 shows that 85% of patients treated with axi-cel experienced overall response, and 74% experienced complete response. Seventy percent of the patients enrolled had an ongoing response at the data cutoff, after median follow-up of 9.3 months.The most common adverse events associated with axi-cel treatment included white blood cell count decrease, encephalopathy, anemia and cytokine release syndrome. All adverse events were resolved by the time of data analysis.

Additionally, the peak level of CAR T cells present within the blood, as well as the median CAR T cell expansion, was increased in this trial of first-line CAR T cell therapy, compared to when the immunotherapy products were generated from patients who have already received several lines of chemotherapy.

"This T cell fitness could be associated with improved effectiveness of treatment, leading to better outcomes for patients," Neelapu said.

Following the promising interim results of ZUMA-12, the investigators plan to conduct continued follow-up to confirm durability of the patients' responses to the treatment.

"If the responses are durable after longer follow-up, a randomized clinical trial would be needed to definitively demonstrate that CAR T cell therapy is superior to existing standard of care with chemoimmunotherapy in these high-risk patients," Neelapu said. "Furthermore, it raises the question of whether CAR T cell therapy also should be evaluated in intermediate-risk patients with large B-cell lymphoma."

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