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First multicenter trial; CAR T-cell immunotherapy effective for lymphoma

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A late-breaking abstract being presented today during the 58th American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego demonstrates that chimeric antigen receptor (CAR) T-cell therapy is a promising option for treating refractory non-Hodgkin lymphoma and practical to implement in a variety of real-world clinical settings. The study, which involved 22 institutions and tested a product called KTE-C19 (anti-CD19 CAR), is the first multicenter trial of this cellular immunotherapy-based treatment approach for lymphoma.

The study focuses on patients with aggressive non-Hodgkin lymphoma that does not respond to chemotherapy or recurs after autologous stem cell transplant. Such chemorefractory patients have a poor prognosis; median overall survival is just over six months and only about eight percent achieve complete cancer remission with existing therapies. The experimental therapy, KTE-C19, is designed to equip a patient's own immune cells with weapons to find and destroy cancer cells.

"Patients with aggressive non-Hodgkin lymphoma have a major unmet need in terms of available therapies that can induce long-term remission, and there really has been no new treatment for these patients for over 20 years," said lead study author Sattva S. Neelapu, MD, of The University of Texas MD Anderson Cancer Center in Houston. "KTE-C19 could potentially be the solution to that need, and the hope is that this treatment option could be curative for some of these patients."

He said the study, called ZUMA-1, bolsters evidence from previous

trials that reported sustained remission after CAR T-cell therapy with KTE-C19, a treatment in which doctors extract T cells from a patient, genetically engineer the cells with CD19 receptors to seek out cancer cells, expand the population of the engineered cells, and then infuse them back into the patient. In the first phase of ZUMA-1, which was conducted in four institutions, 43 percent of patients have ongoing complete remission at 12 months.

To test the treatment's real-world feasibility, the second phase of ZUMA-1 expanded the study to involve 22 institutions, most of which had no prior experience with CAR T-cell therapy. The new findings report positive results from a pre-specified interim analysis of 51 patients with diffuse large B-cell lymphoma (DLBCL), a common and aggressive form of non-Hodgkin lymphoma. Following KTE-C19 treatment, these patients had an overall response rate of 76 percent (47% complete remission and 29% partial remission) with most responses noted within the first month. As in previous studies, some patients' cancers rebounded after the first few months; by the end of month three, the overall remission rate was 39 percent (33% complete remission and 6% partial remission).

Researchers said the results are encouraging from an efficacy standpoint and also show that CAR T-cell manufacturing, treatment logistics, and the management of adverse events can be successfully implemented across multiple sites. "Efficacy often tends to be lower when you apply a new treatment at multiple centers," said Dr. Neelapu. "It was very gratifying to see that efficacy and side effects are similar to what was observed in previous single-institution studies."

Serious adverse events reported in the total DLBCL cohort of 73 patients that were related to KTE-C19 included neurologic events (25% of patients; typically temporary confusion or disorientation) and grade three or higher cytokine release syndrome, a common, potentially dangerous

reaction to this type of infusion (14% of patients). The most common symptoms of cytokine release syndrome were fever, drop in blood pressure, and shortness of breath, according to Dr. Neelapu. Researchers report one patient died as a result of over-activation of the immune system.

Recent studies of CAR T-cell therapy have improved the ability to manage side effects, researchers said. "We now have guidelines on how to recognize and grade these side effects and how to manage the symptoms, and we were able to implement those across multiple institutions with no prior experience with CAR T-cell therapy," said Dr. Neelapu. "I think it has become much more manageable and safer now."

The team has also separately analyzed results from 20 patients in ZUMA-1's second cohort (abstract #998), which include patients with primary mediastinal B-cell lymphoma or transformed follicular lymphoma, two tumor types that are less common than DLBCL. The overall response rate in this second cohort is 80 percent with a complete remission rate of 55 percent. The researchers will continue to track patient outcomes in these cohorts for 15 years.

More information: Sattva S. Neelapu, MD, The University of Texas MD Anderson Cancer Center, Houston, Texas, will present this study, titled "Kte-C19 (anti-CD19 CAR T Cells) Induces Complete Remissions in Patients with Refractory Diffuse Large B-Cell Lymphoma (DLBCL): Results from the Pivotal Phase 2 Zuma-1," (LBA-6) during the late-breaking abstracts session on Tuesday, December 6 at 7:30 a.m. PST in Hall AB.

Provided by American Society of Hematology