Novel allogeneic CAR T cell therapy shows promising results in patients with metastatic clear cell renal cell carcinoma

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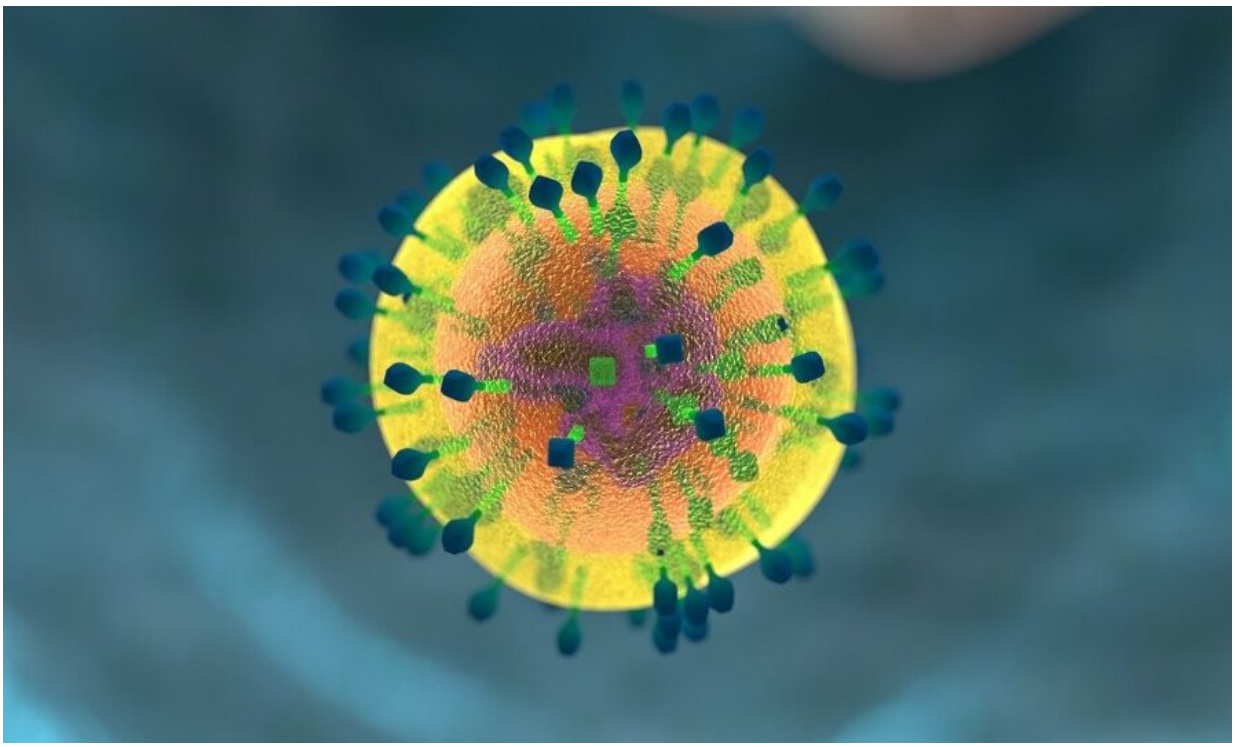

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The CD70-targeting allogeneic chimeric antigen receptor (CAR) T cell therapy, ALLO-316, demonstrated encouraging response rates and disease control rates in patients with metastatic clear cell renal cell

carcinoma (ccRCC), according to results of a Phase I trial led by researchers at The University of Texas MD Anderson Cancer Center and presented today at the American Association for Cancer Research (AACR) Annual Meeting 2023.

The ongoing TRAVERSE trial, led by Samer Srour, M.B.Ch.B., assistant professor of Stem Cell Transplantation & Cellular Therapy, is the first-in-human study evaluating ALLO-316 in patients with metastatic ccRCC who failed both checkpoint and tyrosine kinase inhibitors (TKIs).

In 17 patients, the objective response rate (ORR) was 18% and the disease control rate (DCR) was 82%. For nine patients with confirmed CD70+ disease, the ORR was 33% with a DCR of 100%.

"As we continue to determine the appropriate dose of ALLO-316 for patients, our results demonstrate not only a manageable safety profile but also very encouraging anti-tumor activity," Srour said. "In this trial, we are using an allogeneic 'off-the-shelf' CAR T cell product which offers an additional benefit to our patients because we are able to get this novel treatment to our patients much faster."

ALLO-316 is genetically designed to target CD70, which is expressed in a variety of solid tumor cancers and highly expressed in ccRCC, a subtype of kidney cancer. To reduce the risk of graft-versus-host disease (GVHD), the T cell receptor alpha also was disrupted from ALLO-316 cells. Furthermore, the CD52 gene was knocked out to allow the use of ALLO-647, an anti-CD52 monoclonal antibody that depletes host T cells and improves the persistence of allogeneic CAR T cells.

As of November 2022, 18 patients with metastatic ccRCC were enrolled in this multicenter, single arm clinical trial evaluating the safety and preliminary efficacy of ALLO-316. Seventeen patients received an ALLO-316 infusion. The median age of participants was 63, and 82%

were male. Patients were required to have prior treatment with immune checkpoint inhibitors and TKIs.

Thus far, patients have received ALLO-316 at escalating does of 40—120 X 10^6 CAR T cells. The study allows doses up to 240 million cells. Patients received an ALLO-316 infusion 48 hours after lymphodepletion conditioning with fludarabine/cyclophosphamide, with or without ALLO-647.

Overall, the treatment had a manageable safety profile. Eleven patients (65%) experienced cytokine release syndrome. No cases of GVHD or immune effector cell-associated neurotoxicity syndrome (ICANS) were observed on the study. The maximum tolerated dose has not yet been reached.

"We already know that CAR T cell therapy is effective in patients with hematologic cancers, with several FDA-approved indications. Hence, we are adapting this same strategy for patients with solid tumor cancers," Srour said. "We look forward to our ongoing evaluation of data as we continue to learn about this novel CAR T cell therapy approach in this patient population."

Srour and his colleagues continue to optimize the conditioning and to determine the appropriate dose for the Phase II trial. The trial continues to enroll patients with CD70+ tumors.

More information: Conference: www.aacr.org/meeting/aacr-annual-meeting-2023/

Abstract: www.abstractsonline.com/pp8/#! … 8/presentation/10251

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