

CD19 CAR NK-cell therapy achieves 73% response rate in patients with leukemia and lymphoma

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Katy Rezvani, M.D., Ph.D. Credit: MD Anderson Cancer Center

According to results from a Phase I/IIa trial at The University of Texas MD Anderson Cancer Center, treatment with cord blood-derived chimeric antigen receptor (CAR) natural killer (NK)-cell therapy

targeting CD19 resulted in clinical responses in a majority of patients with relapsed or refractory non-Hodgkin's lymphoma (NHL) and chronic lymphocytic leukemia (CLL), with no major toxicities observed.

The trial results were published today in the *New England Journal of Medicine*. Of the 11 patients participating in the study, eight (73%) responded to therapy and seven of those achieved a complete response, meaning they no longer showed evidence of disease at a median follow-up of 13.8 months. Post-remission therapy was administered to five of the responding patients. No patients experienced cytokine release syndrome or neurotoxicity.

Responses to the CD19 CAR NK cell therapy were evident within one month following infusion, and persistence of these [cells](#) was confirmed out to one year post-infusion.

"We are encouraged by the results of the clinical trial, which will launch further clinical studies to investigate allogeneic cord blood-derived CAR NK cells as a potential treatment option for patients in need," said corresponding author Katy Rezvani, M.D., Ph.D., professor of Stem Cell Transplantation & Cellular Therapy.

Rezvani led the development of MD Anderson's CAR NK platform with the support of the adoptive cell therapy (ACT) platform, Chronic Lymphocytic Leukemia Moon Shot and B-Cell Lymphoma Moon Shot, all part of the institution's Moon Shots Program, a collaborative effort to rapidly develop scientific discoveries into meaningful clinical advances that save patients' lives.

CAR NK cells are allogeneic, meaning the cells are taken from a non-related healthy donor rather than the patient themselves. Thus, CAR NK cells have the potential to be manufactured in advance and stored for off-the-shelf immediate use. In contrast, currently commercially available

CAR T cells require the use of a patient's own genetically modified T cells, created through a multi-week manufacturing process.

At MD Anderson, NK cells are isolated from donated umbilical cord blood and genetically engineered to express the desired CAR, which recognizes cancer-specific targets. The CAR NK cells also are 'armored' with IL-15, an immune signaling molecule that is designed to enhance proliferation and survival of the cells. The CD19 CAR NK cells used in this study were designed to target B-cell malignancies.

On the clinical trial, 11 patients received a single dose of cord blood-derived CD19 CAR NK cells, administered at one of three dose levels. Five patients had CLL and six had NHL. All patients were treated with a minimum of three and maximum of 11 lines of prior therapy. The first nine patients treated received CD19 CAR NK cells that were partially matched according to the individual's [human leukocyte antigen](#) (HLA) type, but the protocol allowed the final two patients to be treated with no HLA matching.

Side effects experienced by participants were primarily related to the conditioning chemotherapy given before cell infusion and were resolved within one to two weeks, said Rezvani. No patient required admission to an intensive care unit for management of treatment side effects.

"Due to the nature of the therapy, we've actually been able to administer it in an outpatient setting," said Rezvani. "We look forward to building upon these results in larger multi-center trials as we work with Takeda to make this therapy available more broadly."

MD Anderson's CAR NK cell therapy platform was licensed to Takeda Pharmaceutical Company Limited in 2019. As part of the license agreement and research agreement, Takeda has exclusive rights to develop and commercialize up to four CAR NK programs, including the

CD19 CAR NK cell [therapy](#) (TAK-007) and B-cell maturation antigen (BCMA)-targeted CAR NK cells.

With continued support from the ACT platform, the Department of Lymphoma and Myeloma, and MD Anderson's Therapeutics Discovery division, Takeda and MD Anderson are collaborating to initiate a pivotal clinical trial for the CD19 CAR NK-[cell therapy](#) TAK-007 in 2021. MD Anderson will implement an Institutional Conflict of Interest Management and Monitoring Plan for this research.

More information: Enli Liu et al, Use of CAR-Transduced Natural Killer Cells in CD19-Positive Lymphoid Tumors, *New England Journal of Medicine* (2020). DOI: 10.1056/NEJMoa1910607 , www.nejm.org/doi/full/10.1056/NEJMoa1910607

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

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