

CD19-targeted CAR NK cell therapy achieves promising one-year results in patients with Bcell malignancies

January 18 2024



3D rendering of a B cell. Credit: Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014." WikiJournal of Medicine 1 (2). DOI:10.15347/wjm/2014.010. ISSN 2002-4436. CC BY-SA 4.0

Researchers from The University of Texas MD Anderson Cancer Center have reported promising results in a Phase I/II trial of 37 patients with



relapsed or refractory B-cell malignancies who were treated with cord blood-derived chimeric antigen receptor (CAR) natural killer (NK) cell therapy targeting CD19.

Published in *Nature Medicine*, the findings reveal an overall response (OR) rate of 48.6% at 100 days post treatment, with one-year progression-free survival (PFS) and overall survival (OS) rates of 32% & 68%, respectively. The trial reported an excellent safety profile with no cases of severe cytokine release syndrome (CRS), neurotoxicity, or graft-versus-host disease.

Another key discovery of the trial was the importance of the selection criteria for allogeneic cord blood donors in CAR NK cell manufacturing. Cord blood units that were cryopreserved within 24 hours of collection and those with a low nucleated red blood cell content were associated with markedly better outcomes. CAR NK cells generated from these units resulted in a one-year PFS rate of 69% and an OS rate of 94%, compared to 5% and 48%, respectively, from those units with higher nucleated red blood cell content or longer collection-to-cryopreservation times.

"The responses observed in these patients are very encouraging as we continue to evaluate the long-term efficacy of CAR NK cells in the treatment of these malignancies," said senior author Katy Rezvani, M.D., Ph.D., professor of Stem Cell Transplantation & Cellular Therapy.

"In order to have a successful allogeneic cell therapy, it is also critical that we identify the characteristics of an optimal allogeneic donor for CAR NK manufacturing. We were able to identify two key factors associated with cord blood units most likely to yield a positive clinical response and discerned the biologic mechanisms underlying this phenomenon."



The study also noted encouraging response rates across different types of B-cell malignancies. The OR rate at 30 days post treatment was 100% for patients with low-grade non-Hodgkin lymphoma (NHL), 67% for those with <u>chronic lymphocytic leukemia</u> (CLL) without transformation and 41% in patients with diffuse large B-cell lymphoma (DLBCL).

Researchers also observed durable responses with CAR NK cell treatment. One year after treatment, complete responses were seen in 83% of patients with low grade-NHL, 50% of patients with CLL and 29% of patients with DLBCL. Those with a response at 30 days post treatment were significantly more likely to have PFS at one-year after treatment.

These results build on <u>previous data</u> from this trial, published in the *New England Journal of Medicine*, demonstrating that a single infusion of CAR NK cells achieved remission in 73% of a smaller cohort of patients with B-cell malignancies.

"Our study stresses the importance of identifying donor-specific predictors of response after allogeneic <u>cell therapy</u>, especially since one donor may be used to treat hundreds of patients. CAR NK cells have the potential to be manufactured in advance and stored for off-the-shelf immediate use," Rezvani said. "This could potentially increase patient access to these cell therapies, reduce treatment time and lower cost of therapy."

The selection criteria identified in this study are being applied to select donors for ongoing and future trials at MD Anderson with engineered cord blood NK cells at MD Anderson, extending the platform to target other antigens and malignancies, including solid tumors.

More information: *Nature Medicine* (2024). www.nature.com/articles/s41591-023-02785-8



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

Citation: CD19-targeted CAR NK cell therapy achieves promising one-year results in patients with B-cell malignancies (2024, January 18) retrieved 9 May 2024 from https://medicalxpress.com/news/2024-01-cd19-car-nk-cell-therapy.html

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