Novel NK cell therapy shows strong response in lymphoma patients

University of Texas M. D. Anderson Cancer Center Apr 4 2025

A novel cell therapy approach using cord blood-derived natural killer (NK) cells pre-complexed with AFM13, or acimtamig, a CD30/CD16A bispecific antibody, was safe and generated strong response rates for patients with refractory CD30-positive lymphomas, according to a new study from The University of Texas MD Anderson Cancer Center.

Results from the Phase I trial, published today in *Nature Medicine,* demonstrated an overall response rate of 92.9% and a complete response of 66.7% in 42 heavily pretreated patients. These findings suggest this unique cell therapy approach has promise for specific patients with lymphoma, but it may be adapted for more cancer types in the future.

> *We observed rapid and strong responses to this novel approach of treating patients with AFM13-NK, and we continue to evaluate the efficacy of this therapy for these hard-to-treat malignancies. These data lend to this approach being considered as a possible curative treatment for some patients and a bridge to a stem cell transplant for others."*
>
> *Yago Nieto, M.D., Ph.D., principal investigator, professor of Stem Cell Transplantation & Cellular Therapy*

The trial's novel approach uses Affimed's AFM13 bispecific antibody, which is designed to bind to CD16A on NK cells and CD30 on lymphoma cells. Therefore, pre-complexed AFM13-NK cells are more readily able to find and eliminate CD30-positive lymphoma cells. The NK cells first are activated with cytokines, expanded in the presence of artificial antigen-presenting cells and complexed with AFM13 before being infused into a patient.

The technique was first developed in the laboratory of collaborating author Katy Rezvani, M.D., Ph.D., Sally Cooper Murray Endowed Chair in Cancer Research, professor of Stem Cell Transplantation & Cellular Therapy, and vice president

and head of MD Anderson's Institute for Cell Therapy Discovery & Innovation. Through the institute, Rezvani and her team continue to develop and advance impactful cell therapies for a variety of conditions.

This trial enrolled 37 adult patients with CD30-positive Hodgkin lymphoma and five with T-cell lymphoma. Patients were heavily pretreated and were refractory to brentuximab vedotin and anti-PD1 immune checkpoint inhibitors. The median age for trial participants was 43 years. Patients had received a median of seven prior lines of therapy.

Trial participants were treated with two to four cycles of chemotherapy followed by AFM13-NK cell infusion at three dose levels and three weekly infusions. At day 28 of each cycle, each patient's response to treatment was evaluated, with a follow-up assessment every three months thereafter.

The overall response rate (ORR) and complete response (CR) in study patients was 92.9% and 66.7%, respectively. Among patients with Hodgkin lymphoma, the ORR and CR were 97.3% and 73%, respectively. At a median follow-up of 20 months, the two-year event-free survival (EFS) and overall survival (OS) rates for all participants were 26.2% and 76.2%, respectively, which is encouraging given the heavily pretreated and refractory nature of the patients' tumors.

The median EFS was 8.8 months, and median OS had not yet been reached at data cut-off – a signal of positive results. Eleven patients remained in complete response for at least 14 months, and some remained in complete response up to 40 months post-therapy. Five patients maintained their complete remission without any additional therapy, and six went on to receive a stem cell transplant.

The AFM13-NK cell treatment was well tolerated, with no identified cases of cytokine release syndrome, immune cell associated neurotoxicity syndrome or graft-versus-host disease. There was one case of Grade 2 infusion-related reaction.

Cord blood units for each cycle, used for the NK cells, were selected from the MD Anderson Cancer Center Cord Blood Bank and chosen based on the criteria previously identified for optimal cord blood units. Donor NK cells peaked in patients' blood one day post-infusion and persisted up to three weeks and

trafficked to tumor sites.

"Our trial showed the favorable safety profile and encouraging activity of AFM13-NK cells in patients with heavily pretreated refractory CD30-positive Hodgkin lymphoma," said Nieto. "This approach, involving cytokine-induced memory cord blood-derived NK cells precomplexed with AFM13 not only holds promise for the treatment of Hodgkin lymphoma but also supports future research into the clinical applications of NK cells with bispecific engagers."

The trial was supported by Affimed. Additional study support was provided by MD Anderson and the National Institutes of Health (P30CA016672). Nieto received financial support from Affimed to conduct this trial.

Source:

University of Texas M. D. Anderson Cancer Center

Journal reference:

Nieto, Y., *et al*. (2025). Allogeneic NK cells with a bispecific innate cell engager in refractory relapsed lymphoma: a phase 1 trial. *Nature Medicine*. doi.org/10.1038/s41591-025-03640-8.