

Excellent research results for CAR-T Cell therapy against Hodgkin lymphoma

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CAR-T cell therapy, which attacks cancer cells using a person's reprogrammed immune cells, has been used to treat Hodgkin lymphoma with remarkable success for the first time, according to the results of an early phase clinical trial led by researchers at UNC Lineberger Comprehensive Cancer Center and Baylor College of Medicine in Houston.

The clinical trial, whose results are published in the *Journal of Clinical Oncology*, was designed to determine the treatment's safety and efficacy for patients with relapsed Hodgkin lymphoma. Researchers demonstrated that the treatment was safe, but perhaps more importantly, that the treatment was highly active in patients with relapsed/refractory Hodgkin lymphoma. The treatment led to the complete disappearance of tumor in the majority of patients treated at the highest dose level of therapy with almost all patients having clinical benefit after treatment.

"This is particularly exciting because the majority of these patients had lymphomas that had not responded well to other powerful new therapies," said study senior author Barbara Savoldo, MD, Ph.D., professor in the UNC Department of Microbiology and Immunology at the UNC School of Medicine and a UNC Lineberger member.

"Everyone worked tirelessly on the study and I am proud of the collaborative work it fueled between UNC Lineberger and Baylor," Savoldo said.

Chimeric antigen receptor (CAR) T cells are human T cells—a powerful type of immune cell—that have been harvested from a patient and genetically re-engineered to recognize proteins found on the patient's cancer cells. They are reinfused into the patient to circulate in the blood for months as a "living drug" to attack the patient's [cancer cells](#). In some cases, patients are infused with CAR-T cells made from T cells provided by other donors.

CAR-T cell therapies in the past decade have had striking successes in some clinical trials, and so far have been approved by the U.S. Food and Drug Administration for treating two blood cancers, acute lymphoblastic leukemia and diffuse large B-cell lymphoma. These CAR-T cell therapies are designed to target the protein CD19, which is found on malignant cells in these cancers. Inspired by the success of CAR-T cell therapies against these cancers, researchers have been developing the technology for use against cancers that express other cancer-associated proteins.

Savoldo and her colleagues in recent years have been exploring the use of CAR-T cells against Hodgkin lymphoma, a blood cancer that afflicts more than 200,000 people in the United States. While about 85 percent of Hodgkin lymphoma patients are cured or have many cancer-free years following standard chemotherapy and/or radiation regimens, the rest either don't respond to standard therapy or do respond but experience a cancer relapse within a few years. Many of these "refractory/relapsing" patients go through years of further treatments without success, and end up with no good options.

In a pilot study in seven refractory/relapsing Hodgkin lymphoma patients, published in 2017, Savoldo and Baylor colleagues found that a CAR-T cell therapy targeting Hodgkin cell-associated protein CD30 appeared safe but brought about only modest responses.

In the new study, which included 41 patients treated at Baylor and UNC, the researchers used the same anti-CD30 CAR-T cell strategy, but added a preconditioning regimen in which patients' existing lymphocytes—a broad family of white blood cells including T cells—were greatly depleted with chemotherapy drugs prior to the addition of the CAR-T cells.

"Lymphodepletion prior to CAR-T cell infusion seems to produce a more favorable environment for the CAR-T cells to proliferate and attack their cancerous targets," said study co-first author Natalie Grover MD, assistant professor in the UNC Department of Medicine and a UNC Lineberger member.

Carlos Ramos, MD at Baylor College of Medicine is the paper's other co-first author.

Side effects of the lymphodepletion plus CAR-T cell treatment were common and included flu-like symptoms due to an immune chemical storm called cytokine release syndrome, but these events were generally modest. None of the patients experienced the more serious, life-threatening complications, such as brain swelling, that have been seen in CAR-T cell trials against other blood cancers.

Even more promising, the study showed that this anti-CD30 CAR-T cell therapy appeared to be very active even against refractory/relapsing Hodgkin lymphoma.

As the trial progressed, the researchers settled on fludarabine as a key element of the pre-therapy lymphodepletion regimen, since patient outcomes seemed better when it was used. The researchers found that among the 32 patients with active cancer who received fludarabine for lymphodepletion before their CAR-T [cells](#), 19 patients (59 percent) had a complete response.

Of the patients in the study who had a complete response, 61 percent still had no evidence of recurrence a year later. Overall, 94 percent of the treated patients were still alive a year after their treatment.

"This treatment showed remarkable antitumor activity without significant toxicity, and we think it should be considered for patients in earlier stages of refractory/relapsing Hodgkin lymphoma," Savoldo said.

"The activity of this new therapy is quite remarkable and while we need to confirm these findings in a larger study, this treatment potentially offers a new approach for patients who currently have very limited options to treat their [cancer](#)," said Jonathan Serody, MD, the Elizabeth Thomas Professor of Medicine, Microbiology and Immunology at UNC School of Medicine, director of the bone marrow transplant and cellular therapy program at UNC, and a UNC Lineberger member.

"Additionally, unlike other CAR T cell therapies, clinical success was not associated with significant complications from therapy. This means this treatment should be available to patients in a clinic setting and would not require patients to be hospitalized, which is critical in our current environment."

Provided by UNC Lineberger Comprehensive Cancer Center

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