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Researchers present advance in re-treatment with CAR T therapy

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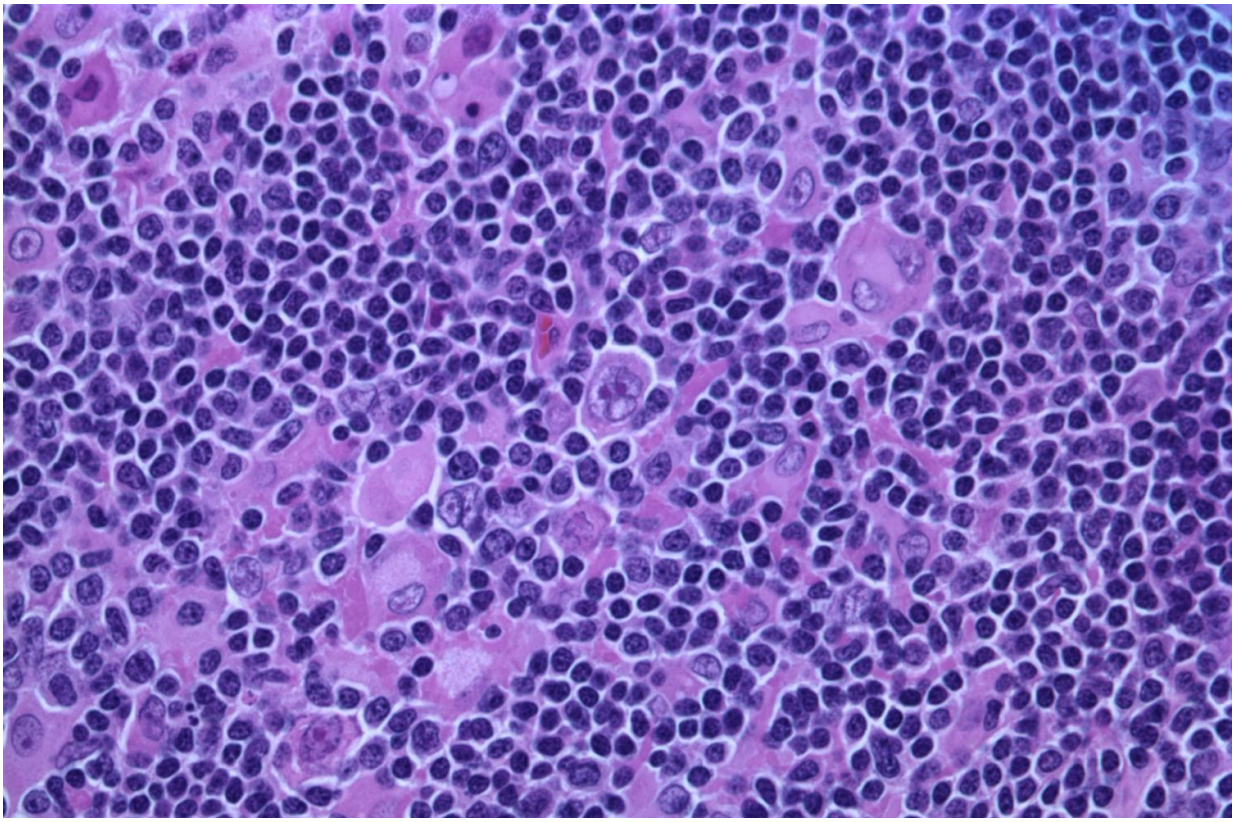

Hodgkin lymphoma, nodular lymphocyte predominant (high-power view) Credit: Gabriel Caponetti, MD./Wikipedia/CC BY-SA 3.0

Researchers from the University of Pennsylvania's Abramson Cancer Center presented preliminary results of an ongoing Phase I clinical trial

demonstrating successful re-treatment with CAR T cell therapy for patients whose cancers relapsed after previous CAR T therapy at the 2022 American Society of Hematology (ASH) Annual Meeting.

CAR T therapies have revolutionized blood cancer treatment over the last decade, providing hope for patients who have run out of conventional treatment options, but patients whose cancers return or stop responding to CAR T therapy have limited options for further treatment.

The first-in-human study (NCT04684563) evaluated a novel fourth-generation CAR T therapy in patients with non-Hodgkin lymphoma (NHL) who had previously received CAR T therapy that failed to stop their cancer. The study is the first clinical trial in the United States with anti-CD19 CAR T cells secreting interleukin 18 (IL 18). The early results show this combination approach is safe and did not result in new or increased side effects compared to other commercially available CAR T therapies.

Senior author and CAR T pioneer Carl June, MD, led the preclinical research that demonstrated IL18 could enhance CAR T activity. "We designed an 'armored' CAR that secretes IL18 and tested it in mice, where we found it to have potent antitumor efficacy in our preclinical studies," said June, who is the Richard W. Vague Professor in Immunotherapy in the department of Pathology and Laboratory Medicine in the Perelman School of Medicine and director of the Center for Cellular Immunotherapies at Penn's Abramson Cancer Center.

Among the first seven patients who received huCART19-IL18—including those who previously did not respond to or relapsed following treatment with commercial CAR T cell therapies—all responded to the therapy (four patients had a complete response and three patients had a partial response). None of the four patients whose cancers completely responded to treatment at month three have seen

their disease return, and all patients are alive at a median follow-up of eight months.

"Patients whose cancers don't respond or become refractory to CAR T therapy tend to have poor outcomes, so we are very motivated to find new options for them," said lead author Jakub Svoboda, MD, an associate professor of Hematology-Oncology at Penn. "Although these are preliminary results, it's encouraging to see how well these patients have done. Our team at Penn is very excited about this ongoing project and these early results continue to motivate us."

The study enrolled patients with CD19+ relapsed/refractory NHL or chronic lymphocytic leukemia (CLL), who had received at least two lines of therapy, including CAR T therapy. The study is continuing to increase the dose of huCART19-IL18 and will enroll patients one at a time until the appropriate dose is determined.

Toxicities related to huCART19-IL18 were temporary and similar to those which have been observed with other CAR T products. Cytokine release syndrome occurred in four patients and neurotoxicity occurred in two patients. No grade four adverse events or study-related deaths have occurred.

Notably, with a three-day manufacturing time, huCART19-IL18 can be ready to administer more quickly than CAR T products with the typical manufacturing time of nine to 14 days, which is especially important for patients with aggressive, fast-growing disease. A previous, preclinical study found the shortened manufacturing time also may enhance the potency of the T cells.

More information: Svoboda will present the abstract in a poster session on Saturday, Dec. 10 from 5:30 to 7:30 p.m. CT in Hall D. Abstract 2016

Provided by Perelman School of Medicine at the University of Pennsylvania