

Dual-Target CAR T-Cell Therapy Slows Growth of Aggressive Brain Cancer

Penn Medicine researchers have demonstrated encouraging tumor reductions rarely seen in recurrent glioblastoma following Phase I clinical trials.

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A dual-target [CAR T-cell therapy](#) approach shows promise for slowing tumor growth in a notoriously aggressive and fast-growing brain cancer. Tumors became smaller after the experimental CAR T-cell therapy in nearly two-thirds of patients. While survival data is still accumulating, several patients lived 12 months or longer after receiving the investigational therapy, which is notable given the typical survival for this patient population is less than a year.

The findings were presented [June 1] at the [2025 American Society of Clinical Oncology \(ASCO\) Annual Meeting \(Abstract 102\)](#) and simultaneously published in [Nature Medicine](#) by researchers from Penn's [Abramson Cancer Center](#) (ACC) and [Perelman School of Medicine](#).

The results build on the [hopeful momentum of an early report](#) from the same phase I clinical trial [published last year](#), alongside similar findings from other researchers across the United States.

[Glioblastoma \(GBM\)](#) is the most common—and deadly—brain cancer in adults, with average life expectancies of 12-18 months after diagnosis, despite decades of focused research efforts. Even after aggressive treatment, the cancer grows back, or recurs, in nearly all patients. The median survival rate for recurrent GBM typically ranges from six to ten months.

“Seeing recurrent GBM tumors shrink like this is extraordinary because the immunotherapy drugs that we’ve tried in the past have been unable to do that,” says principal investigator [Stephen Bagley](#), an assistant professor of hematology-oncology and neurosurgery. “Before the trial, many of these patients had tumors that were growing rapidly, and the treatment changed the trajectory of their disease, which is very meaningful to patients with GBM.”

Penn-developed dual-target CAR T therapy

CAR T-cell therapy is a form of personalized immunotherapy that uses a patient’s own immune cells to treat their cancer. While widely successful in blood cancers, CAR T-cell therapy has yet to make significant inroads against solid tumor cancers, like brain cancer.

The Penn-developed CAR-T product used in this study is unique in that it targets not one, but two proteins commonly found in brain tumors—epidermal growth factor receptor (EGFR) and interleukin-13 receptor alpha 2 (IL13R α 2)—and is administered through an injection into the cerebrospinal fluid. The dual-target CAR was created in the laboratory of [Donald M. O'Rourke](#), the John Templeton, Jr., MD Professor in Neurosurgery and director of the Glioblastoma Translational Center of Excellence in the Abramson Cancer Center at Penn Medicine, who was scientific advisor to the trial.

Temporary decrease in tumor size in most patients

The study enrolled 18 patients with recurrent GBM who underwent surgery to remove as much of the tumor as possible, followed by infusion of the dual-target CAR T-cell therapy directly into the cerebrospinal fluid. The tumors became smaller after CAR T-cell therapy in eight of the 13 patients (62 %) who still had at least 1cm of tumor remaining after surgery. While the tumors grew back after one to three months in most patients, there were encouraging signals:

- Two patients (11%) remain alive with stable disease that has continued beyond six months.
- Of the seven patients with at least 12 months' follow-up time, three (43%) were still alive after a year.
- This includes one individual whose cancer has remained stable, with no tumor growth for more than 16 months, despite advanced disease spread and rapid growth at the time of enrollment.

The researchers also found signs that the therapy remains in the immune system after the infusion to prevent tumor growth over time. In one patient who underwent surgery again due to tumor regrowth after the CAR T-cell therapy, the researchers detected positive effects of the treatment in the removed tissue. These effects included infiltration of T cells throughout the tumor and clearance of the tumor by immune cells called macrophages. The researchers were able to see similar signals of the therapy stimulating the immune system through spinal fluid samples from the other patients, including one patient whose spinal fluid still had detectable CAR T-cells one year after receiving the treatment.

"These results reaffirm that we're onto something with our dual target therapy, and that we have a good template that we can begin refining for even better outcomes," O'Rourke says. "Periods of stability, when tumors shrink or don't grow, vastly improve the quality of a patient's life. Our goal is to refine the treatment so that more patients experience longer-lasting results."

In the final cohort of this study, the team plans to give patients more than one dose of the CAR T-cell therapy, to see if repeat dosing extends the time before the tumors grow back.

With safety established, next clinical trials to open soon

Ten of 18 patients (56%) experienced grade 3 neurotoxicity, with no new or unexpected side effects reported, beyond the known side effects of other FDA-approved CAR T-cell therapies. The neurotoxicity was managed successfully, and the therapy was determined to be safe and feasible.

Based on these results, the researchers determined the maximum tolerated dose level to carry forward in upcoming clinical trials, the first of which will be for patients with newly diagnosed GBM. ([See study information and enrollment contacts at clinicaltrials.gov.](#))

“By the time GBM recurs, it has become even more challenging to treat, and the patient has already been through a lot,” Bagley says. “We’re hopeful that by moving quickly to test this CAR T-cell therapy in the newly diagnosed setting, the cancer will be more vulnerable to therapy and more patients will see a benefit.”

This study was funded by Kite, a Gilead Company, the Abramson Cancer Center Glioblastoma Translational Center of Excellence, the Templeton Family Initiative in Neuro-Oncology, and the Maria and Gabriele Troiano Brain Cancer Immunotherapy Fund.

Information for patients interested in joining a clinical trial: visit Penn Medicine’s [Abramson Cancer Center Clinical Trial Information Service](#) online or call 1-855-216-0098 to speak to a clinical trial navigator.

Editor’s note: O’Rourke is an inventor on multiple patents related to CAR T-cell therapy in solid tumors that have been licensed by the University of Pennsylvania and has received royalties from these license agreements. O’Rourke is a paid consultant for Kite Pharma. Penn has received and may receive in the future, sponsored research funding and certain intellectual property license-related payments from Kite Pharma.

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