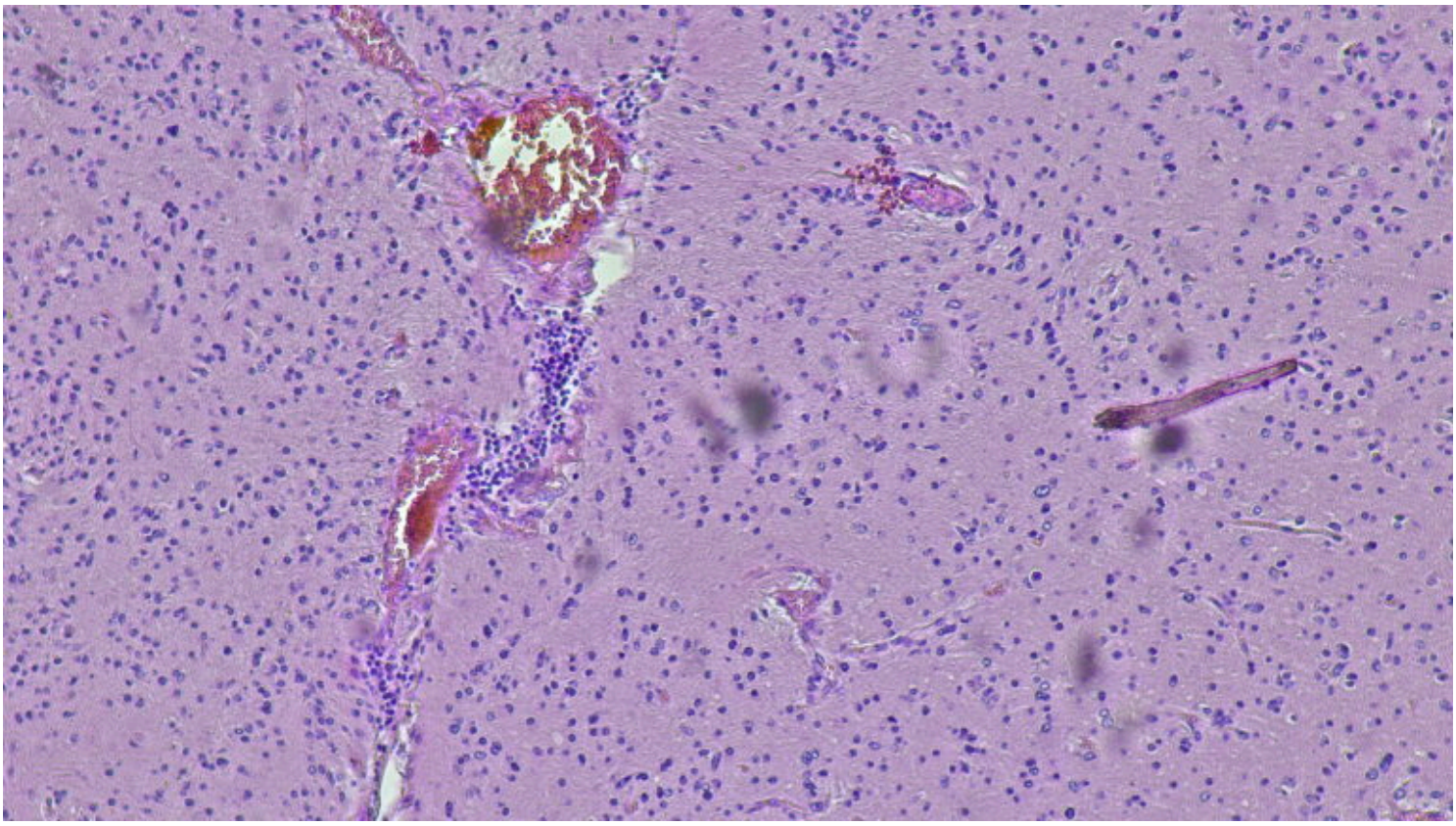
STAT PLUS
BIOTECH

Defying death two years after brain cancer diagnosis: studies build hope in CAR-T

Most patients in two small glioblastoma trials responded to treatment for months, and some much longer



Glioblastoma multiforme, a type of brain cancer. Adobe

By Angus Chen June 2, 2025

Cancer Reporter

CHICAGO — New data on two studies are bolstering hopes that CAR-T therapy, which uses engineered immune T cells to fight cancer, may be able to overcome one of the most

difficult to treat cancers of the brain, glioblastoma.

The data are very early, involving only a handful of patients, and typical indicators of efficacy in clinical trials like overall survival are not yet available. It will take longer follow up and more patients in larger trials to truly determine efficacy, experts said. Still, experts added, the fact that many of them are responding to treatment and — in a couple cases — experiencing long lasting remission is remarkable.

“As time goes on, we see these patients alive, and they come back to clinic. We’re filled with complete bewilderment at how well some patients are doing on the study. I think we’re continuing to try to understand why that is,” said Bryan Choi, a neurosurgeon and cancer researcher from Mass General Hospital who presented one of the studies here at the American Society of Clinical Oncology. “It’s true that patients have had different levels of response, but this disease hasn’t had an answer.”

The other study is from a group at the University of Pennsylvania. The presentations are updates from earlier results that the groups published separately in the New England Journal of Medicine and Nature Medicine last year. In those studies, researchers saw rapid shrinkage of tumors and the first signs CAR-T therapies were active in a few patients. Now, the new data include several more patients and are providing clues into how researchers might improve the therapy.

“Both of the studies are exciting to me,” said Graeme Woodworth, a neurosurgeon and cancer researcher at the University of Maryland who didn’t work on either study. “They show signs that the treatments are active in the patients.”

In glioblastoma, 95% of patients die within five years of their diagnosis. Patients who have experienced a recurrence, like those in these trials, typically die within six to eight months. In Choi’s study, which had a total of 10 patients including three from an earlier safety arm, seven continue surviving longer than eight months, and three have passed away. Seven of these 10 patients also received multiple infusions of CAR-T cells.

The Penn study, also presented at ASCO and published in Nature Medicine on Sunday, had 18 patients. Thirteen of these had a measurable tumor when they received the cell therapy, and eight of those experienced tumor regression, including one patient whose tumor shrank by more than 50%. All patients on the Penn trial except one have seen their

disease return, and the median progression free survival was 1.9 months. Kite Pharma sponsored the Penn study.

Notably, one patient from each trial now remains alive and has been without evidence of disease progression for roughly two years since treatment. In a separate trial from City of Hope, which wasn't presented at the meeting, one glioblastoma patient remains alive almost five years after CAR-T cell therapy treatment. That's raising the hope that this technology might one day be able to offer cures for glioblastoma patients, something that has been practically unheard of in the history of the disease.

"If it's five years out and the tumor doesn't come back, then he's cured because these tumors don't stay around for that long. It's shown us that given the right patient, and the right immune milieu, this can really work," said Stephen Bagley, a cancer researcher at the U. Penn and lead author on the Nature paper. "We're shrinking tumors. We're seeing in this one patient, it can get rid of it long term. But the vast majority of folks still relapse. The holy grail is why."

One possibility is that the body's natural immune system is developing a response to the CAR-T cell therapy, destroying the therapy before it has much of a chance to take effect. The MGH scientists saw that after infusion of the CAR-T cells, which go directly into the patients' cerebrospinal fluid, the patients' immune systems would create antibodies against the therapy.

"That is unfortunate and may be a limitation of this technology," said Behnam Badie, a cancer researcher at City of Hope who also studies CAR-T in glioblastoma but didn't work on these two trials. Finding ways to make sure that these cells can persist in the central nervous system may be very important to making them work for more patients long term, Badie said.

In one attempt to do that, the MGH researchers began giving chemotherapy to the patients before infusing the CAR-T cells, hoping to knock down the immune system and give the cells more of a chance to take hold. The data showed some early signs that could be helping, as each time the scientists infused CAR-T cells, the cells lasted longer if chemotherapy was given first. The team also plans to use rituximab, a therapy which

targets antibody-producing B cells, to further help the cells from being rejected by the body.

The one patient who's still alive in that trial nearly two years out notably didn't have an antibody response to his CAR-T cells.

In the Penn trial, the one patient still alive nearly two years after treatment had a tumor along the leptomeninges, the outer membrane of the brain and spinal cord. That area is more exposed to the cerebrospinal fluid, where the CAR-T cells are infused for the therapy, which may have made it more possible for the engineered cells to attack the tumor, Penn's Bagley hypothesized.

The therapies may still need future iterations before it's ready to seek approval for glioblastoma though, other experts said. "We need more time to investigate and understand how this works and how to improve efficacy," said City of Hope's Badie, though he added that commercial investment into the field would make a big difference. "These are really expensive trials."

Still, the data are promising enough that groups are looking to continue expanding the work. Mass General's researchers have begun spinning out a new company to further develop the therapy. "It's in stealth right now," said Marcela Maus, a CAR-T scientist at Mass General who also led the work.

Hopefully, she said, that investment will help build the technology so that soon, there might be more patients experiencing lasting remission from a cancer that has long been considered incurable. "We have a lot of hope this can change the trajectory of the disease," she said. "It's definitely ready for clinical development."