

Nat Med. 2025 Jun 1. doi: 10.1038/s41591-025-03745-0. Online ahead of print.

Intracerebroventricular bivalent CAR T cells targeting EGFR and IL-13R α 2 in recurrent glioblastoma: a phase 1 trial

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PMID: 40451950 DOI: [10.1038/s41591-025-03745-0](https://doi.org/10.1038/s41591-025-03745-0)

Abstract

Glioblastoma (GBM) is the most common primary brain cancer in adults and carries a median overall survival (OS) of 12–15 months. Effective therapy for recurrent GBM (rGBM) following frontline chemoradiation is a major unmet medical need. Here we report the dose escalation and exploration phases of a phase 1 trial investigating intracerebroventricular delivery of bivalent chimeric antigen receptor (CAR) T cells targeting epidermal growth factor receptor (EGFR) epitope 806 and interleukin-13 receptor alpha 2 (IL-13R α 2), or CART-EGFR-IL13R α 2 cells, in patients with EGFR-amplified rGBM. Primary endpoints included dose-limiting toxicity, determination of the maximum tolerated dose and recommended dose for expansion, and occurrence of adverse events. Secondary endpoints included objective radiographic response, duration of response, progression-free survival and OS. A total of 18 patients received CART-EGFR-IL13R α 2 cells. The maximum tolerated dose was determined to be 2.5×10^7 cells. Of the 18 patients, 10 (56%) experienced grade 3 neurotoxicity; none had grade 4–5 neurotoxicity. Of 13 patients, 8 (62%) with measurable disease at the time of CAR T cell infusion experienced tumor regression, with one confirmed partial response by Modified Response Assessment in Neuro-Oncology criteria (objective radiographic response, 8%; 90% confidence interval, 0–32%) and one patient with ongoing durable stable disease lasting over 16 months. Median progression-free survival was 1.9 months (90% confidence interval, 1.1–3.4 months), and median OS was not yet reached at the time of data cut-off (median follow-up time, 8.1 months). These findings indicate that intracerebroventricular delivery of bivalent CART-EGFR-IL13R α 2 is feasible and appears safe. CART-EGFR-IL13R α 2 cells are bioactive and exhibit a signal of antitumor effect in rGBM. ClinicalTrials.gov registration: [NCT05168423](https://clinicaltrials.gov/ct2/show/study/NCT05168423).

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