Neuro Oncol. 2025 Mar 12:noaf064. doi: 10.1093/neuonc/noaf064. Online ahead of print.

Locoregional Infusion of EGFR806-CAR T Cells for Recurrent or Refractory Pediatric CNS Tumors: Results of the Completed BrainChild02 Phase 1 Clinical Trial

Juliane Gust [1 2 3], Bonnie L Cole [4], Rebecca Ronsley [3 5 6], Ashley L Wilson [7], Kristy Seidel [7], Jason Wendler [7], Sowmya Pattabhi [7], Christopher Brown [7 8], Stephanie D Rawlings-Rhea [7], Nadezhda Shtanukhina [7], Samuel R Browd [9], Jason S Hauptman [1 9], Amy Lee [9], Jeffrey G Ojemann [1 9], Erin E Crotty [3 5 6], Sarah E S Leary [3 5 6], Francisco A Perez [10], Jason N Wright [10], Catherine M Albert [3 5 6], Navin Pinto [3 5 6], Rebecca A Gardner [3 5 6], Nicholas A Vitanza [3 5 6], Michael C Jensen [3 5 6], Julie R Park [3 5 6]

Affiliations
PMID: 40070357 DOI: 10.1093/neuonc/noaf064

Abstract

Background: Relapsed/refractory pediatric CNS tumors have a poor prognosis. EGFR is commonly overexpressed, but EGFRvIII mutations are uncommon. To target these tumors, we used chimeric antigen receptor (CAR) T cells with a binder based on mAb806 which recognizes ectopically expressed wild-type EGFR and EGFRvIII.

Methods: In this open-label phase 1 clinical trial, patients age 1-26 years with EGFR+ CNS tumors received weekly infusions of 1-2.5 x 107 CAR T cells into the tumor resection bed or the lateral ventricle via an implanted catheter. No lymphodepletion was used.

Results: Eleven patients were enrolled. Four (3 with high-grade glioma, 1 with atypical teratoid-rhabdoid tumor) were treated and received 5-10 CAR T cell infusions without dose-limiting toxicities. The trial closed prior to reaching planned dose regimens. All treatment-related adverse events were no higher than CTCAE grade 2. The most common were headache and nausea. One patient had a grade 1 seizure, and three had new sensory changes, weakness and/or urinary changes (grade 1-2) that were possibly related to CAR T cell infusion. Three of the four treated patients had progressive disease. One patient with spinal cord diffuse midline glioma had progressive peritumoral edema that could not be conclusively attributed to either progression or pseudoprogression and was therefore defined as stable disease, followed by a complete response to subsequent chemotherapy.

Conclusions: Intracranially infused EGFR806-CAR T cells were tolerable at tested doses, with a best response of stable disease. EGFR is a potentially useful target for cellular therapy against pediatric brain tumors, particularly high-grade gliomas.

Keywords: CAR T cell; CNS tumor; EGFR; locoregional; pediatric.