Review Acta Neurol Belg. 2024 Apr 26. doi: 10.1007/s13760-024-02519-8.

Online ahead of print.

CAR T-cell therapy: a potential treatment strategy for pediatric midline gliomas

Anand Kumar Das [#] [1], Mainak Sinha [#] [1], Saraj Kumar Singh [2], Anurag Chaudhary [3], Ashim Kumar Boro [4], Manish Agrawal [3], Sona Bhardwaj [5], Simmi Kishore [6], Katyayani Kumari [7]

Affiliations

PMID: 38669002 DOI: 10.1007/s13760-024-02519-8

Abstract

Pediatric brain tumors are the primary cause of death in children with cancer. Diffuse midline glioma (DMG) and diffuse intrinsic pontine glioma (DIPG) are frequently unresectable due to their difficult access location, and 5-year survival remains less than 20%. Despite significant advances in tumor biology and genetics, treatment options remain limited and ineffective. Immunotherapy using T cells with a chimeric antigen receptor (CAR) that has been genetically engineered is quickly emerging as a new treatment option for these patients. High levels of expression were detected for both disialoganglioside (GD2) and B7-H3 in pediatric DMG/DIPG. Numerous studies have been conducted in recent years employing various generations of GD2-CAR T cells. The two most prevalent adverse effects found with this therapy are cytokine release syndrome, which varies in severity from mild constitutional symptoms to a high-grade disease associated with potentially fatal multi-organ failure, and neurotoxicity, known as CAR T-cell-related encephalopathy syndrome. During the acute phase of anticancer action, peri-tumoral neuro-inflammation might cause deadly hydrocephalus. The initial results of clinical trials show that the outcomes are not highly encouraging as B cell malignancies and myelomas. In vivo research on CAR T-cell therapy for DIPG has yielded encouraging results, but in human trials, the early results have shown potentially fatal side effects and very modest, but fleeting improvements. Solid tumors present a hindrance to CAR T-cell therapy because of the antigenic dilemma and the strong immune-suppressing tumor microenvironment.

Keywords: CAR T therapy; Diffuse midline gliomas; High-grade gliomas (HGG); Immunotherapy; Pediatric brain tumor; Tumor microenvironment (TME).