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Repeated peripheral infusions of anti-EGFRvIII CAR T cells in combination with pembrolizumab show no efficacy in glioblastoma: a phase 1 trial

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Abstract

We previously showed that chimeric antigen receptor (CAR) T-cell therapy targeting epidermal growth factor receptor variant III (EGFRvIII) produces upregulation of programmed death-ligand 1 (PD-L1) in the tumor microenvironment (TME). Here we conducted a phase 1 trial (NCT03726515) of CAR T-EGFRvIII cells administered concomitantly with the anti-PD1 (aPD1) monoclonal antibody pembrolizumab in patients with newly diagnosed, EGFRvIII^{+} glioblastoma (GBM) (n = 7). The primary outcome was safety, and no dose-limiting toxicity was observed. Secondary outcomes included median progression-free survival (5.2 months; 90% confidence interval (CI), 2.9-6.0 months) and median overall survival (11.8 months; 90% CI, 9.2-14.2 months). In exploratory analyses, comparison of the TME in tumors harvested before versus after CAR + aPD1 administration demonstrated substantial evolution of the infiltrating myeloid and T cells, with more exhausted, regulatory, and interferon (IFN)-stimulated T cells at relapse. Our study suggests that the combination of CAR T cells and PD-1 inhibition in GBM is safe and biologically active but, given the lack of efficacy, also indicates a need to consider alternative strategies.