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Tumor-targeted interferon-α gene therapy for glioblastoma: a phase 1 trial

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Abstract

Glioblastoma (GBM) is an immunologically cold brain tumor with poor outcome, characterized by a myeloid-driven immunosuppressive microenvironment. Here we report an interim analysis of a first-in-human phase 1/2a dose-escalation study evaluating Temferon-a genetically engineered autologous stem cell transplant designed to deliver interferon-α2 by means of myeloid progeny recruited to the GBM TME and locally activate antitumor immunity. Twenty-four newly diagnosed patients with GBM and unmethylated MGMT promoter were treated across eight cohorts following surgical resection and radiotherapy, testing Temferon doses ranging from 0.5×10^6 to 4.0×10^6 $CD34^+$ cells kg^{-1} and different conditioning regimens (BCNU or busulfan, with or without thiotepa). The primary endpoint was safety and tolerability within 90 days after infusion. Secondary endpoints included long-term safety, dose and conditioning regimen selection, Temferon engraftment, clinical response, quality of life and survival. No dose-limiting toxicities were observed up to the highest dose level of temferon tested. Busulfan conditioning was selected for further development. Adverse events included laboratory abnormalities, cytopenias and infections consistent with autologous stem cell transplant. Median overall survival and progression-free survival were 16.7 months and 8.1 months from diagnosis, respectively, with most patients maintaining good performance status and quality of life. Genetically engineered cells were detected long term in the bone marrow and the blood, where minimal amounts of interferon-α were measured. Temferon is a safe and tolerable immunotherapeutic strategy in patients with newly diagnosed GBM. ClinicalTrials.gov: NCT03866109 .