Recurrent Glioblastoma Treated with Recombinant Poliovirus.


BACKGROUND: The prognosis of patients with recurrent World Health Organization (WHO) grade IV malignant glioma is dismal, and there is currently no effective therapy. We conducted a dose-finding and toxicity study in this population of patients, evaluating convection-enhanced, intratumoral delivery of the recombinant nonpathogenic polio-rhinovirus chimera (PVSRIPO). PVSRIPO recognizes the poliovirus receptor CD155, which is widely expressed in neoplastic cells of solid tumors and in major components of the tumor microenvironment.

METHODS: We enrolled consecutive adult patients who had recurrent supratentorial WHO grade IV malignant glioma, confirmed on histopathological testing, with measurable disease (contrast-enhancing tumor of ≥1 cm and ≤5.5 cm in the greatest dimension). The study evaluated seven doses, ranging between $10^7$ and $10^{10}$ 50% tissue-culture infectious doses (TCID$_{50}$), first in a dose-escalation phase and then in a dose-expansion phase.

RESULTS: From May 2012 through May 2017, a total of 61 patients were enrolled and received a dose of PVSRIPO. Dose level -1 (5.0×$10^7$ TCID$_{50}$) was identified as the phase 2 dose. One dose-limiting toxic effect was observed; a patient in whom dose level 5 (10$^{10}$ TCID$_{50}$) was administered had a grade 4 intracranial hemorrhage immediately after the catheter was removed. To mitigate locoregional inflammation of the infused tumor with prolonged glucocorticoid use, dose level 5 was deescalated to reach the phase 2 dose. In the dose-expansion phase, 19% of the patients had a PVSRIPO-related adverse event of grade 3 or higher. Overall survival among the patients who received PVSRIPO reached a plateau of 21% (95% confidence interval, 11 to 33) at 24 months that was sustained at 36 months.

CONCLUSIONS: Intratumoral infusion of PVSRIPO in patients with recurrent WHO grade IV malignant glioma confirmed the absence of neurovirulent potential. The survival rate among patients who received PVSRIPO immunotherapy was higher at 24 and 36 months than the rate among historical controls. (Funded by the Brain Tumor Research Charity and others; ClinicalTrials.gov number, NCT01491893.)
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