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Recombinant polio-rhinovirus immunotherapy for recurrent paediatric high-grade glioma: a phase 1b trial

Eric M Thompson [1], Daniel Landi [2], Michael C Brown [1], Henry S Friedman [1], Roger McLendon [3], James E Herndon 2nd [4], Evan Buckley [5], Dani P Bolognesi [6], Eric Lipp [7], Kristin Schroeder [8], Oren J Becher [9], Allan H Friedman [1], Zachary McKay [10], Ashley Walter [7], Stevie Threatt [7], Denise Jaggers [7], Annick Desjardins [1], Matthias Gromeier [1], Darell D Bigner [1], David M Ashley [11]

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Abstract

Background: Outcomes of recurrent paediatric high-grade glioma are poor, with a median overall survival of less than 6 months. Viral immunotherapy, such as the polio-rhinovirus chimera lerapolturev, is a novel approach for treatment of recurrent paediatric high-grade glioma and has shown promise in adults with recurrent glioblastoma. The poliovirus receptor CD155 is ubiquitously expressed in malignant paediatric brain tumours and is a treatment target in paediatric high-grade glioma. We aimed to assess the safety of lerapolturev when administered as a single dose intracerebrally by convection enhanced delivery in children and young people with recurrent WHO grade 3 or grade 4 glioma, and to assess overall survival in these patients.

Methods: This phase 1b trial was done at the Duke University Medical Center (Durham, NC, USA). Patients aged 4-21 years with recurrent high-grade malignant glioma (anaplastic astrocytoma, glioblastoma, anaplastic oligoastrocytoma, anaplastic oligodendroglioma, or anaplastic pleomorphic xanthoastrocytoma) or anaplastic ependymoma, atypical teratoid rhabdoid tumour, or medulloblastoma with infusible disease were eligible for this study. A catheter was tunnelled beneath the scalp for a distance of at least 5 cm to aid in prevention of infection. The next day, lerapolturev at a dose of 5×10^7 median tissue culture infectious dose in 3 mL infusate loaded in a syringe was administered via a pump at a rate of 0·5 mL per h as a one-time dose. The infusion time was approximately 6·5 h to compensate for volume of the tubing. The primary endpoint was the proportion of patients with unacceptable toxic effects during the 14-day period after lerapolturev treatment. The study is registered with ClinicalTrials.gov, NCT03043391.

Findings: Between Dec 5, 2017, and May 12, 2021, 12 patients (11 unique patients) were enrolled in the trial. Eight patients were treated with lerapolturev. The median patient age was 16·5 years (IQR 11·0-18·0), five (63%) of eight patients were male and three (38%) were female, and six (75%) of eight patients were White and two (25%) were Black or African American. The median number of previous chemotherapeutic regimens was 3·50 (IQR 1·25-5·00). Six of eight patients had 26 treatment-related adverse events attributable to lerapolturev. There were no irreversible (ie, persisted longer than 2 weeks) treatment-related grade 4 adverse events or deaths. Treatment-related grade 3 adverse events included headaches in two patients and seizure in one patient. Four patients received low-dose

bevacizumab on-study for treatment-related peritumoural inflammation or oedema, diagnosed by both clinical symptoms plus fluid-attenuated inversion recovery MRI. The median overall survival was 4·1 months (95% CI 1·2-10·1). One patient remains alive after 22 months.

Interpretation: Convection enhanced delivery of lerapolturev is safe enough in the treatment of recurrent paediatric high-grade glioma to proceed to the next phase of trial.

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