ABSTRACT

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Oncolytic DNX-2401 Virus for Pediatric Diffuse Intrinsic Pontine Glioma.

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Comment in
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BACKGROUND: Pediatric patients with diffuse intrinsic pontine glioma (DIPG) have a poor prognosis, with a median survival of less than 1 year. Oncolytic viral therapy has been evaluated in patients with pediatric gliomas elsewhere in the brain, but data regarding oncolytic viral therapy in patients with DIPG are lacking.

METHODS: We conducted a single-center, dose-escalation study of DNX-2401, an oncolytic adenovirus that selectively replicates in tumor cells, in patients with newly diagnosed DIPG. The patients received a single virus infusion through a catheter placed in the cerebellar peduncle, followed by radiotherapy. The primary objective was to assess the safety and adverse-event profile of DNX-2401. The secondary objectives were to evaluate the effect of DNX-2401 on overall survival and quality of life, to determine the percentage of patients

who have an objective response, and to collect tumor-biopsy and peripheral-blood samples for correlative studies of the molecular features of DIPG and antitumor immune responses.

RESULTS: A total of 12 patients, 3 to 18 years of age, with newly diagnosed DIPG received 1×1010 (the first 4 patients) or 5×1010 (the subsequent 8 patients) viral particles of DNX-2401, and 11 received subsequent radiotherapy. Adverse events among the patients included headache, nausea, vomiting, and fatigue. Hemiparesis and tetraparesis developed in 1 patient each. Over a median follow-up of 17.8 months (range, 5.9 to 33.5), a reduction in tumor size, as assessed on magnetic resonance imaging, was reported in 9 patients, a partial response in 3 patients, and stable disease in 8 patients. The median survival was 17.8 months. Two patients were alive at the time of preparation of the current report, 1 of whom was free of tumor progression at 38 months. Examination of a tumor sample obtained during autopsy from 1 patient and peripheral-blood studies revealed alteration of the tumor microenvironment and T-cell repertoire.

CONCLUSIONS: Intratumoral infusion of oncolytic virus DNX-2401 followed by radiotherapy in pediatric patients with DIPG resulted in changes in T-cell activity and a reduction in or stabilization of tumor size in some patients but was associated with adverse events. (Funded by the European Research Council under the European Union's Horizon 2020 Research and Innovation Program and others; EudraCT number, 2016-001577-33; ClinicalTrials.gov number, NCT03178032.).

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