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Oncolytic virotherapy for the treatment of pediatric brainstem gliomas

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Abstract

Diffuse intrinsic pontine glioma (DIPG) is the most frequent brainstem glioma and the most lethal brain tumor in childhood. Despite transient benefit with radiotherapy, the prognosis of children with this disease remains dismal with severe neurological morbidity and median survival less than 12months. Oncolytic immunovirotherapy is emerging as a potential therapeutic approach in neuro-oncology. The oncolytic adenovirus Delta-24-RGD has shown efficacy in adult patients with recurrent GBM. Our group has demonstrated that Delta-24-RGD has oncolytic activity and triggers immune response in preclinical models of DIPG, and has a synergistic effect with radiotherapy in animal models of this disease. In this scenario, we conducted a first-in-human phase 1 clinical trial to evaluate the safety and efficacy of intratumoral injection of Delta-24-RGD in pediatric patients with newly diagnosed DIPG prior to standard radiotherapy. The study confirmed the feasibility of this treatment with an acceptable safety profile and encouraging efficacy results. Correlative analyses showed a biological activity from Delta-24-RGD in DIPG. Further advanced trials are needed to validate these results. Meanwhile, plenty of opportunities to increase the potential contribution of oncolytic viruses in the management of devastating tumors with no current effective treatment such as DIPG need to be explored and exploited.

Keywords: Brainstem glioma; DIPG; Delta-24-RGD; Oncolytic virus; Virotherapy.