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CHAPTER FIVE - Oncolytic viruses as treatment for adult and pediatric high-grade gliomas: On the way to clinical success

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Abstract

High-grade gliomas (HGGs) are the most common and aggressive primary brain tumors in both adult and pediatric populations. Despite the multimodal treatment modality currently available for HGG, the prognosis is dismal, with a low overall survival rate at two years after diagnosis. In the last decade, oncolytic virotherapy has emerged as a promising and feasible therapeutic tool in management of these tumors due to its oncolytic and immunostimulatory properties. Various oncolytic viruses, such as herpes simplex virus, adenovirus, poliovirus, reovirus, parvovirus and others, have been evaluated in the early stages of the clinical setting with regard to improving the outcome of patients with HGG. In this review, we summarize completed and ongoing clinical trials of oncolytic virotherapy for adult and pediatric malignant gliomas in terms of safety and efficacy, followed by a brief discussion about the current status and future directions of this therapy in the brain tumor field.

Section snippets

High-grade gliomas

Diffuse gliomas are the most common primary central nervous system (CNS) tumors in both adult and pediatric populations, with average annual age-adjusted incidence rates of 8.72 and 0.47 per 100,000, respectively (Ostrom et al., 2022). According to the 2021 World Health Organization classification, diffuse gliomas are divided into low-grade (LGGs) and high-grade (HGGs) gliomas, the latter of which include adult glioblastoma (GB) and pediatric diffuse midline glioma, H3 K27-altered (DMG), among…

Oncolytic viruses

Oncolytic viruses have gained considerable interest as immune therapeutic agents due to their dual therapeutic effect against tumors: they are capable of selectively infecting, replicating in, and killing tumor cells while healthy cells remain intact (Jafari et al., 2022), triggering antitumor immune responses (Bartlett et al., 2013, Guo et al., 2019). Oncolytic cell death causes tumor cells to release tumor-associated antigens, damage-associated molecular patterns (DAMPs, such as calreticulin, …

Herpes simplex virus type-1(HSV-1)

Herpes simplex virus type-1 (HSV-1) is an enveloped, double-stranded DNA virus with a large genome (152 kb) belonging to the *Herpesviridae* family. Since the approval of T-VEC, six oncolytic HSV-1 strains have been engineered and examined in clinical trials for treatment of adult GB: G207, G47Δ, HSV1716, rQNestin34.5v.2, M032 and C134 (Kaufman et al., 2015). G207 is a genetically modified HSV-1 that contains deletions in two loci of the $\gamma_1 34.5$ neurovirulence gene, as well as a disruption of the …

Pediatric high-grade glioma clinical trials

The first completed clinical trial of oncolytic virotherapy for pediatric brain tumors was a phase 1 trial using HSV-1 G207 alone or in combination with a single radiation dose in children with recurrent or progressive supratentorial HGG (NCT02457845). A total of twelve patients with an age range of 7–18 years old were infused with a dose of 1×10^7 or 1×10^8 PFU of G207 through intratumoral catheters alone or with 5 Gy of radiation; there were no complications, demonstrating the procedure's…

Discussion and future perspectives

Implementation of oncolytic virotherapy in cancer has revolutionized the therapeutic landscape of high-grade brain tumors in the last decade. Overall, the results of the clinical trials described in this review largely confirm the safety profile of different oncolytic viruses in adult and pediatric patients with HGG, without serious viral therapy-related adverse events. Such is the confidence in this approach that a new G47Δ-based drug called Teserpaturev has been authorized for treating…

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