

Review [Curr Treat Options Oncol.](#) 2024 Jun 19. doi: 10.1007/s11864-024-01211-6.

Online ahead of print.

An Update on the Clinical Status, Challenges, and Future Directions of Oncolytic Virotherapy for Malignant Gliomas

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PMID: 38896326 DOI: [10.1007/s11864-024-01211-6](https://doi.org/10.1007/s11864-024-01211-6)

Abstract

Malignant gliomas are common central nervous system tumors that pose a significant clinical challenge due to the lack of effective treatments. Glioblastoma (GBM), a grade 4 malignant glioma, is the most prevalent primary malignant brain tumor and is associated with poor prognosis. Current clinical trials are exploring various strategies to combat GBM, with oncolytic viruses (OVs) appearing particularly promising. In addition to ongoing and recently completed clinical trials, one OV (Tesperaturev, Delytact®) received provisional approval for GBM treatment in Japan. OVs are designed to selectively target and eliminate cancer cells while promoting changes in the tumor microenvironment that can trigger and support long-lasting anti-tumor immunity. OVs offer the potential to remodel the tumor microenvironment and reverse systemic immune exhaustion. Additionally, an increasing number of OVs are armed with immunomodulatory payloads or combined with immunotherapy approaches in an effort to promote anti-tumor responses in a tumor-targeted manner. Recently completed oncolytic virotherapy trials can guide the way for future treatment individualization through patient preselection, enhancing the likelihood of achieving the highest possible clinical success. These trials also offer valuable insight into the numerous challenges inherent in malignant glioma treatment, some of which OVs can help overcome.

Keywords: Glioblastoma; Immunotherapy; Immunovirotherapy; Malignant glioma; Oncolytic virotherapy; Oncolytic virus.

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