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# Oncolytic viruses in brain cancer therapy: advances, challenges, and clinical trial outcomes

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## Abstract

Malignant intracranial tumors are a major cause of morbidity and mortality across age groups. To assess recent progress in glioblastoma (GBM) oncolytic virotherapy, literature was searched in PubMed and Google Scholar using the keywords glioblastoma, oncolytic virus, clinical trials, brain tumor, and oncolytic virotherapy resistance. Relevant studies published through 2024 were reviewed. Brain tumors vary in prevalence, but many have poor prognosis and low survival rates. Among available treatment approaches, oncolytic virotherapy has gained strong attention as a promising cancer therapy. Existing evidence shows that oncolytic viruses (OVs) can produce meaningful anti-tumor effects; however, tumor cells may resist OV activity through several mechanisms. These include alterations in tumor-cell molecular pathways, features of the tumor microenvironment, and physiological barriers within the patient's body. Some OVs have completed in vitro and in vivo studies and are now being evaluated in clinical trials, while others remain in early preclinical development. Clinical success depends on the intrinsic anti-tumor activity of OVs, methods used to enhance them, and their ability to incorporate new genetic and antigenic features. Such modifications may improve immune evasion, tumor targeting, tumor lysis, and anti-tumor immune responses, supporting development of next-generation OVs.

**Keywords:** Brain tumor; clinical trials; glioblastoma; immunogenic cell death; oncolytic virotherapy; oncolytic virus; resistance; tumor microenvironment.

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