JAMA Neurol. 2026 Jul 13. doi: 10.1001/jamaneurol.2026.2131. Online ahead of print.

Recent Advances and Future Prospects in Gene Delivery Platforms for Glioblastoma: A Review

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PMID: 42440296 DOI: 10.1001/jamaneurol.2026.2131

Abstract

Importance: Glioblastoma (GBM) remains a disease with high mortality despite treatment with maximal safe surgical resection, radiation, and temozolomide. Standard of care for GBM has remained unchanged for decades. Gene therapies using both viral and nonviral platforms have the potential to significantly improve outcomes but have faced challenges related to delivery, intratumoral heterogeneity, and immunologic limitations.

Observations: This review discusses the most recent progress in genetic therapies for gliomas, with a focus on clinical platforms and those nearing clinical translation. Oncolytic and nonlytic replicating viral therapies remain the most clinically advanced, with adeno-associated virus and nonviral systems approaching clinical translation. Treatment efficacy has been variable across trials, platforms, and payloads. Oncolytic herpes simplex virus (G47Δ, teserpaturev) has been conditionally approved for the treatment of gliomas in Japan, while next-generation constructs show a potential association between immunologic activation and survival. Common challenges include the verification and quantification of delivery efficiency, the balance between antivector and antitumor immunity, appropriately designed clinical trials, relevant modeling of vector behavior in the preclinical setting, regulatory clearance, and manufacturing.

Conclusions and relevance: Understanding the potential and limitations of gene therapies for gliomas is vital in navigating the path forward for these promising therapies. The future of these treatments will focus on improved clinical trial design with rapid confirmation and tracking of delivery, biomarker feedback and assay optimization, and combination strategies. A focus on delivery platform development can compress iteration cycles and lead to therapeutic benefit for patients with gliomas and other solid tumors.