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Published 07/12/2024

Efficacy Of Adenovirus-mediated Delivery Of Herpes Simplex Virus Thymidine Kinase (ADV-TK) Gene Therapy Combined With Antiviral Agents In Giloblastoma Treatment : A Systematic Review And Meta-analysis

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Categories: Neurology, Neurosurgery, Oncology
Keywords: ganciclovir, thymidine kinase, adenovirus, antiviral agents, genetic therapy, brain neoplasms, glioblastoma

How to cite this abstract
Arafeh Y, El-Samahy M, Eid S, et al. (July 12, 2024) Efficacy Of Adenovirus-mediated Delivery Of Herpes Simplex Virus Thymidine Kinase (ADV-TK) Gene Therapy Combined With Antiviral Agents In Giloblastoma Treatment : A Systematic Review And Meta-analysis . Cureus 16(7): a1277

Abstract

Background:

Glioblastoma (GBM), the most common malignant primary brain tumour in adults, is associated with a grim prognosis. Despite the aggressive conventional treatments employed such as adjuvant postoperative radiation therapy and chemotherapy, its median overall survival remains poor, with 10-12 months duration. This unfavourable prognosis can be attributed to GBM's highly infiltrative growth patterns, intricate involvement of critical brain structures, genetic heterogeneity, micro-environmental factors, immune evasion mechanisms, and sub-optimal drug delivery across the Blood-Brain Barrier. In the era of precision medicine, viral vectors, particularly adenovirus, have shown promise in improving outcomes, with notable enhancements in overall Progression-Free Survival (PFS) and overall survival (OS) within adenovirus-thymidine kinase (ADV-TK) treated patients. Adenovirus-tk is a gene-mediated cytotoxic immunotherapy. It functions by converting ganciclovir into GCV triphosphate, its active form. This study aims to assess the effectiveness of Adenovirus-mediated herpes simplex virus thymidine kinase (Adv-tk) gene therapy in conjunction with antiviral therapy for the treatment of GBM patients.

Materials and Methods:

This systematic review was conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guideline. A computerised literature search was conducted on several databases spanning from 1946 to April 2023. We included randomised controlled trials and non-randomized controlled trials that examine the efficacy of the AdV-tk and antiviral therapy regimen on morbidity and mortality in patients with Glioblastoma. We evaluated overall survival and progression-free survival differences between the "Control" and "Experimental" groups through a comprehensive approach. Initially, Kaplan-Meier analysis was employed to provide survival estimates for both groups, followed by the application of the log-rank test to assess differences in survival estimates. Subsequently, a Cox Proportional Hazards Regression model was utilised to estimate the hazard ratio of the "Experimental" group relative to the "Control" group.

Results:

The "Experimental" group demonstrated significantly improved overall survival (median 15.9 months, 95% CI: [11.3-23.4]) compared to the "Control" group (median 12.1 months, 95% CI: [10.6-14.9]), supported by a significant log-rank test ($p = 0.005$) and a hazard ratio of 0.64 in favour of the "Experimental" group. Additionally, in terms of progression-free survival, the "Experimental" group also exhibited enhanced outcomes (median 7.9 months, 95% CI: [6.75-10.35]) compared to the "Control" group (median 6.94 months, 95% CI: [5.57-7.68]), with a significant log-rank test ($p = 0.008$) and a hazard ratio of 0.65 indicating favorable survival outcomes for the "Experimental" group.

Conclusion:

Our study demonstrates that Adenovirus-mediated herpes simplex virus thymidine kinase (Adv-tk) gene therapy with antiviral treatment significantly enhances overall and progression-free survival in GBM patients. These findings offer valuable insights for patients, clinicians, and researchers seeking innovative approaches to improve Glioblastoma outcomes.