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# Assessing The Combined Efficacy Of AD-RTS-hIL-12 And Veledmix Regimen In Primary And Progressive Glioblastoma Multiforme: A Systematic Review

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Abstract
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## Abstract

**Background**:

Glioblastoma (GBM), classified as a WHO grade IV astrocytoma with IDH wild-type status in 2021, has long posed a clinical challenge. Conventional treatment approaches, including maximal surgical resection, radiation therapy, and chemotherapy, have demonstrated limited efficacy in improving patient outcomes. One significant hurdle lies in the tumor's ability to evade the immune system, necessitating innovative solutions.Thus, gene-based approaches like Ad-RTS-hIL-12 have gained considerable attention. This gene therapy utilizes an adenovirus vector to deliver human interleukin-12 (hIL-12) gene directly into the tumor cells. Interleukin-12 (IL-12), a pivotal cytokine in immune activation, can bolster the local immune response within the tumor microenvironment. The synergy between Ad-RTS-hIL-12 gene therapy and Veledimex represents a promising avenue for enhancing anti-tumor immune responses in the context of GBM management. However, harnessing the potent effects of IL-12 while managing potential side effects remains a critical consideration in its clinical application for GBM treatment. This study aims to uncover the potential impact of this combination therapy in enhancing survival outcomes for Glioblastoma patients.

**Method**:

We conducted a comprehensive systematic search across various electronic databases, such as PubMed, Cochrane, Cochrane Central Register of Controlled Trials (CENTRAL), MIDLINE, and Scopus, to identify relevant studies. This review encompasses both randomized controlled trials and non-randomized controlled trials that investigate the effectiveness of the Ad-RTS-hIL-12 and Veledmix treatment regimen in assessing morbidity and mortality outcomes in patients diagnosed with glioblastoma. This systematic review abides by the PRISMA 2020 guidelines in its applied methodology.

**Results**:

Initially, 151 articles were detected, 27 of which were duplicates, and 122 of which were eliminated according to a preset inclusion criteria. Two articles were selected for this review. In total, 53 patients were involved in two trials. The first trial examined the impact of different doses (10, 20, 30, and 40 mg) of Veledimex (VDX) on overall survival (OS). The results were encouraging for the 20 mg dose, which showed 60%, 26.7%, and 13.3% survival at 12, 18, and 24 months respectively. In contrast, the survival rate for the 10, 30, and 40 mg doses were 0%, 0%, and 30% respectively at 12 months. The second trial focused on the combination of Veledimex (10 and 20 mg) with nivolumab (1 or 3 mg/kg) and their impact on OS. The results showed an OS of 16.9 months for the 10 mg Veledimex with nivolumab and 8.5 months for the 20 mg dose.

**Conclusion**:

The combination of Ad-RTS-hIL-12 and Veledimex (VDX) presents a promising direction for further exploration in the medical treatment of glioblastoma. Our study emphasizes the medical significance of conducting comprehensive dose optimization studies to fully harness the therapeutic potential of Ad-RTS-

hIL-12 and VDX in the context of clinical practice.