Effects of Intravenously Administered Recombinant Vesicular Stomatitis Virus (VSV$^{{\Delta M51}}$) on Multifocal and Invasive Gliomas

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Abstract

Background: An ideal virus for the treatment of cancer should have effective delivery into multiple sites within the tumor, evade immune responses, produce rapid viral replication, spread within the tumor, and infect multiple tumors. Vesicular stomatitis virus (VSV) has been shown to be an effective oncolytic virus in a variety of tumor models, and mutations in the matrix (M) protein enhance VSV's effectiveness in animal models.

Methods: We evaluated the susceptibility of 14 glioma cell lines to infection and killing by mutant strain VSV$^{{\Delta M51}}$, which contains a single–amino acid deletion in the M protein. We also examined the activity and safety of this strain against the U87 and U118 experimental models of human malignant glioma in nude mice and analyzed the distribution of the virus in the brains of U87 tumor-bearing mice using fluorescence labeling. Finally, we examined the effect of VSV$^{{\Delta M51}}$ on 15 primary human gliomas cultured from surgical specimens. All statistical tests were two-sided.

Results: All 14 glioma cell lines were susceptible to VSV$^{{\Delta M51}}$ infection and killing. Intratumoral administration of VSV$^{{\Delta M51}}$ produced marked regression of malignant gliomas in nude mice. When administered systemically, live VSV$^{{\Delta M51}}$ virus, as compared with dead virus, statistically significantly prolonged survival of mice with unilateral U87 tumors (median survival: 113 versus 46 days, $P = .0001$) and bilateral U87 tumors (median survival: 73 versus 46 days, $P = .0025$). VSV$^{{\Delta M51}}$ infected multifocal gliomas, invasive glioma cells that migrated beyond the main glioma, and all 15 primary human gliomas. There was no evidence of toxicity.

Conclusions: Systemically delivered VSV$^{{\Delta M51}}$ was an effective and safe oncolytic agent against laboratory models of multifocal and invasive malignant gliomas, the most challenging clinical manifestations of this disease.