reovirus as a pre-conditioning regimen performed significantly better than the simultaneous or preceding administration of bsAbs. This combination treatment also induced regressions of non-injected distant lesions, suggesting that this therapy might be effective for metastatic disease.

Conclusions Oncolytic reovirus administration represents an effective strategy to induce a local IFN response and strong T cell influx, thereby sensitizing the tumor microenvironment for subsequent CD3-bsAb therapy (figure 1). Our data advocate for the inclusion of oncolytic viruses as a pre-conditioning strategy in T cell engaging antibody trials for solid tumors. Since both CD3-bispecific antibodies and oncolytic viruses are in advanced clinical development as monotherapies, efficient translation of this combination seems feasible.

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Ethics Approval All mouse studies were approved by the institutional Animal Welfare Body of Leiden University Medical Center and carried out under project licenses AVD1160020187004 or AVD116002015271, issued by the competent authority on animal experiments in the Netherland (named CCID).

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COMPARISON OF TWO OHSV VECTORS FOR THE TREATMENT OF Glioblastoma

Background Glioblastoma multiforme (GBM) is the most common human brain cancer. Despite a well-established standard of care, the 5-year mortality rate of GBM patients is 95%, highlighting the need for innovative therapeutic approaches. A variety of oncolytic viruses, including those derived from herpes simplex virus (oHSV), have been designed for GBM therapy, but early-phase clinical trials have reported few complete responses and no evidence of durable anti-tumor immunity. Potential reasons for the lack of efficacy are limited vector potency (i.e., virulence) and the presence of a highly immunosuppressive tumor microenvironment (TME) comprised of few adaptive immune cell types within the TME was not observed at 2 days post oHSV treatment.

Conclusions oHSV impacted survival outcomes in the more permissive CT2A model. Analysis, of either the GL261N4 or CT2A TME two days post virus administration revealed that both viruses had reduced microglia cell frequency, induced the influx of tumor associated macrophages and polymorphonuclear cells, but did not alter the frequency of mononuclear MDSCs, natural killer cells, CD8+ or CD4+ T-cells.

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