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 CCD).

REFERENCES

1. Benonisson H, Altıntaş I, Sluijter M, Verploegen S, Labrijn AF, Schuurhuis DH, Houtkamp MA, Verbeek JS, Schuurman J and van Hall T. CD3-Bispecific antibody therapy turns solid tumors into inflammatory sites but does not install protective memory. *Mol Cancer Ther* 2019; **18**(2):312–322.
2. Groeneveldt, C, van Hall, T, van der Burg, SH, ten Dijke, P and van Montfoort, N. Immunotherapeutic potential of TGF-β inhibition and oncolytic viruses. *Trends Immunol* 2020; **41**(5):406–420.

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591 COMPARISON OF TWO OHSV VECTORS FOR THE TREATMENT OF GLIOBLASTOMA

[1]Joseph Jackson*, [1]Bonnie Hall, [1]Lisa Bailey, [2]E Chiocca, [1]Justus Cohen. *[1]The University of Pittsburgh, Pittsburgh, USA; [2]Harvard Medical School and Brigham and W, Boston, MA, USA*

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 interventions. 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 activated lymphocytes, large numbers of immunosuppressive myeloid cells (macrophages, myeloid derived suppressor cells [MDSCs], microglia), and an agglomerate of immunosuppressive cytokines (IL-10, VEGF, MIF, etc.).[1] Herein we explore these obstacles by comparing the anti-tumor activity two different oHSV designs, an HSV-1 KOS strain derivative designated KG4:T124, and an F strain derivative designated rQNestin34.5v.1 (a similar oHSV, rQNestin34.5v.2, is currently in a phase I clinical trial for GBM).[2]

Methods Using the murine syngeneic GBM models, GL261N4 and CT2A, we compared the anti-tumor activity of KG4:T124 and rQNestin34.5v1. In vitro, we evaluated the viral entry, replication capacity, and cytotoxicity of both oHSVs. In vivo, we measured the impact of both vectors on tumor progression, TME immune cell composition, and animal survival.

Results Virus entry into cancer cells of KG4:T124 or rQNestin34.5v1 was relatively similar, but rQNestin34.5v.1 replicated more effectively and generally induced greater viral mediated cytotoxicity. In syngeneic mice, rQNestin34.5v.1 reduced orthotopic GL261N4 tumor burden and enhanced animal survival compared to KG4:T124. However, preliminary data indicate that multiple injections of KG4:T124 but not rQNestin34.5 enhance GL261N4 survival outcome. Neither oHSV impacted survival outcomes in the more pernicious 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 monocytic MDSCs, natural killer cells, CD8+ or CD4+ T-cells.

Conclusions rQNestin34.5 had greater oncolytic activity In vivo and in vitro, but did not benefit from multiple oHSV injections. Both viruses induced similar changes in the TME immune cell composition. However, the presence of vital adaptive immune cell types within the TME was not observed at 2 days post oHSV treatment.

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REFERENCES

1. Muller S, Kohanbash G, Liu SJ, Alvarado B, Carrera D, Bhaduri A, Watchmaker PB, Yagnik G, Di Lullo E, Malatesta M, Amankulor NM, Kriegstein AR, Lim DA, Aghi M, Okada H, Diaz A. Single-cell profiling of human gliomas reveals macrophage ontogeny as a basis for regional differences in macrophage activation in the tumor microenvironment. *Genome Biol*. 2017;**18**(1):234. Epub 2017/12/22. doi: 10.1186/s13059-017-1362-4. PubMed PMID: 29262845; PMCID: PMC5738907.
2. Chiocca EA, Nakashima H, Kasai K, Fernandez SA, Oglesbee M. Preclinical Toxicology of rQNestin34.5v.2: An Oncolytic Herpes Virus with Transcriptional Regulation of the ICP34.5 Neurovirulence Gene. *Mol Ther Methods Clin Dev* 2020;17:871–93. Epub 2020/05/07. doi: 10.1016/j.omtm.2020.03.028. PubMed PMID: 32373649; PMCID: PMC7195500.

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592 ENHANCING THE THERAPEUTIC POTENTIAL OF ONCOLYTIC ADENOVIRUSES WITH VSENS™ TECHNOLOGY

Goo-Young Kim*, Ji Yeon Son, So Jin Lee, Sang Woo Jo, Changhoon In, Sang Hoon Kim, Joon Young Park, So-Young Kim, Gyu-Young Moon, Ji-Hye Choi, Suk-Hwan Kim, Minhyuk Yun, Hye Yeong Nam, Helen Cho. *Samyang Biopharmaceuticals Corporation, Gyeonggi-do, Korea, Republic of*

Background Oncolytic viro-therapeutics is a promising treatment for cancer. Among the different strains of oncolytic viruses currently being developed, potent cytolytic activity, manageable safety profiles, large genomic capacity for addition of transgenes and available advanced manufacture processes make adenovirus (Ad) a great choice.[1] However, the delivery of Ad for clinical application is limited due to 1) neutralization by pre-existing neutralizing antibodies (nAb) in bloodstream and 2) receptor restricted tumor-cellular entry.[2] To overcome these limitations, we developed a novel proprietary