COMPARISON OF TWO OHSV VECTORS FOR THE TREATMENT OF Glioblastoma

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 rQNestin34.5v1 replicated more effectively and generally induced greater viral mediated cytotoxicity. In syngeneic mice, rQNestin34.5v1 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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591

ENHANCING THE THERAPEUTIC POTENTIAL OF ONCOlytic ADENOVIRUSES WITH VSEns™ TECHNOLOGY

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. 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. To overcome these limitations, we developed a novel proprietary