Abstract 428: Development of a Novel Chimeric Oncolytic Viral Platform, CF33 and Its Derivatives, for Peritoneal-directed Treatment of Gastric Cancer Peritoneal Carcinomatosis

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Background

- Gastric cancer peritoneal metastasis is fatal without effective therapy.
- Oncolytic viruses (OVs) show promise in the treatment of solid tumors.
- However, need for viral attenuation and high therapeutic dosing have limited their clinical success.
- A novel chimeric OV, CF33 and its derivatives have demonstrated superior anti-tumor activity against a wide-range of solid tumors and is currently under Phase I trials of intratumoral treatment of triple negative breast cancer (CheckVacc, NCT05081492) and intravenous treatment of metastatic solid tumors (VAXINIA, NCT05346484).

Methods

- Chimeric orthopoxvirus CF33, and its derivatives CF33-GFP, CF33-hNIS-antiPDL1
- Virus infection and proliferation assays
- Cytotoxicity assay for in vitro tumor cell killing
- Flow cytometry
- Mouse xenograft model of GCPM using SNU-16-ffluc cells

Results:

- CF33-OVs infects and replicates in a dose dependent manner in both diffuse and intestine subtypes of human GC cell lines without attenuation caused by insertion of human transgenes (**FIG 1**)
- Immunofluorescence imaging showed virus-encoded hNIS and anti-PD-L1 antibody expression in CF33-OV-infected GC cells (**FIG 2**)
- CF33-OVs killed a range of GC cell lines in a dose dependent manner (**FIG 3**)
- Flow cytometry confirmed GC cell surface PD-L1 blockade by virus-encoded anti-PD-L1 (**FIG 4**)
- In the xenograft model (**FIG 5**), CF33-hNIS-antiPDL1 (IP; 3x10^5 pfu x 3 doses) significantly reduced peritoneal tumors (p<0.0001), decreased amount of ascites (62.5% PBS vs. 25% CF33-hNIS-antiPDL1) and prolonged animal survival (p<0.01). At day 91, 6/8 mice were alive in the virus-treated group vs.1/8 in the control group.

FIG 1.

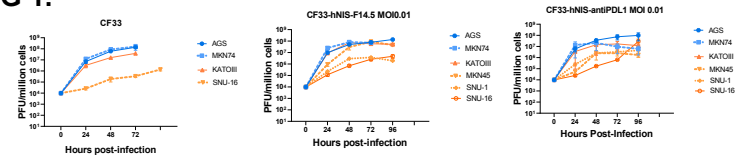


FIG 2.

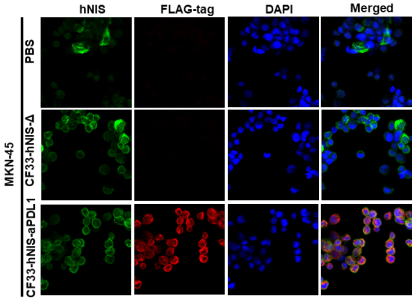


FIG 3.

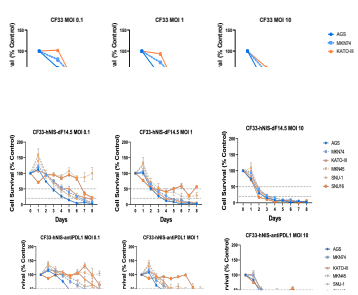


FIG 4.

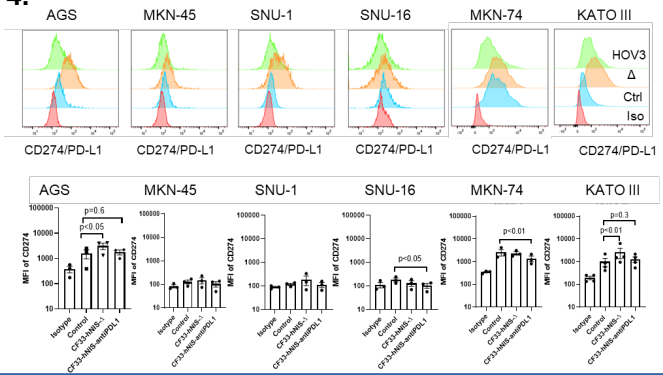
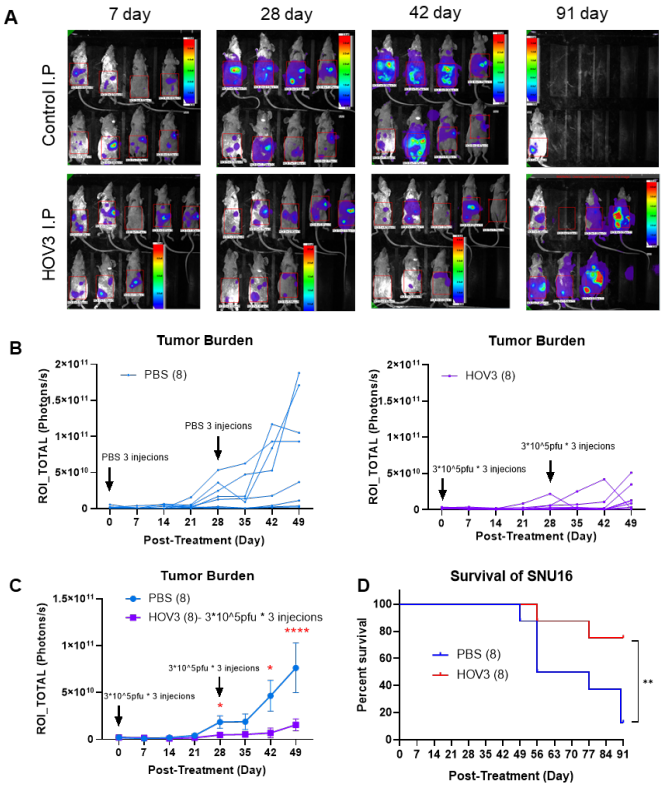


FIG 5.



(**A**) Nude mice were I.P injected with CF33-hNIS-antiPDL1 (HOV3) or PBS 3 times (day 7, day 9, and day 11) at a dose of 3 × 10^5 pfu in 100 µL PBS post tumor inoculation and were treated for the second time on day 35, day 37 and day 39 with the same amount of virus. Graphic representation of luminescence imaging of region of interest (ROI) of intraperitoneal tumor burden were shown. (**B-C**) Tumor burdens are shown as individual (**B**) and analysis (**C**). (**D**) Kaplan-Meier survival analysis of the survival of SNU-16-ffluc peritoneal tumor mice after treatment with CF33-hNIS-antiPDL1 or PBS control. * p<0.05, ** p<0.01, **** p<0.0001

CONCLUSION: CF33-OVs demonstrates robust infection, replication, functional protein delivery and killing of GC in vitro. IP CF33-hNIS-antiPDL1 treatment improves survival of GCPM xenograft mouse models when compared to PBS controls.

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