A cell-based platform to potentiate oncolytic virus: Potential approach for cancer therapies. Presented Thursday, February 6, 2020 ASCO/SITC

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Background:
Oncolytic virotherapy has been pursued by multiple companies and institutions with few candidates reaching the clinic and demonstrating limited efficacy. The therapeutic potential of oncolytic viruses can be severely restricted by innate and adaptive immune barriers. To overcome this obstacle, we load and protect tumor selective CAL1 oncolytic vaccinia virus into adipose-derived stem cells (AD-MSC) to generate a new therapeutic agent called SNV1(SuperNova1).

Methods:
SNV1s were generated by incubating AD-MSC with CAL1 virus. SNV1 was analyzed for its ability to kill cancer cell lines and protect virus in the presence of active neutralizing antibodies and complement. In animals, SNV1 was intratumorally injected in various xenograft and syngeneic models. Viral biodistribution was also evaluated by PCR. Immune infiltration were analyzed using flow cytometry.

Results:
Compared to the naked virus, SNV1 showed improved protection against the humoral barriers and efficient eradication of various human cancer cell lines in vitro. Intratumoral SNV1 treatment showed statistically significant and potentiated tumor growth inhibition compared to control or CAL1 naked virus treatment in all tested models (prostate, breast, melanoma, colon, and prostate cancers). Importantly, local administration of SNV1 induced systemic therapeutic effects. Five days after SNV1 administration, tumor infiltrating lymphocytes (TILs) from both treated and untreated tumors showed increased CD4 and CD8 T-cell populations. As well as decreased frequency of Tregs, and improved effector to Treg ratios, which was associated with inhibition of tumor growth at the treated tumor site and also at distant untreated sites. Ongoing and persistent virus infection could be detected in the treated tumor as late as 15 days after administration.

Conclusions:
This study demonstrates the ability of our cell-based platform to protect and potentiate oncolytic vaccinia virus by circumventing the innate and adaptive immune barriers, resulting in

enhanced oncolytic virotherapy. These findings provide fundamental rationale for the development of cell-based platforms to maximize the therapeutic potential of various oncolytic viruses.