blockade. Soluble LAG-3 may be an important biomarker for monitoring the pharmacodynamic activity of FS118 in patients.

Ethics Approval All animal experiments were conducted under a UK Home Office Project Licence and approved by an Animal Welfare and Ethical Review Board (AWERB) in accordance with the UK Animal (Scientific Procedures) Act 1986 and with EU Directive EU 86/609

REFERENCE

1. Kraman M, Faroudi M, Allen N, Kmiecik K, Gliddon D, Seal C, Koers A, Wydro M, Winnewisser J, Young L, Tuna M, Doody J, Morrow M, Brewis N. FS118, a Bispecific Antibody Targeting LAG-3 and PD-L1, Enhances T-Cell Activation Resulting in Potent Antitumor Activity. *Clin Cancer Res* 2020;**26**:3333–3344

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0715

716 CELL-BASED VIROTHERAPY FOR TARGETING CANCERS

[1]Duong Nguyen, [1]Alberto Gomez, [1]Forrest Neuharth, [1]Ashley Alamillo, [2]Thomas Herrmann, [2]Barbara Härtl, [2]Laura Schneider, [1]Ivelina Minev, [1]Boris Minev, [1]Dobrin Draganov*, [1]Antonio Santidrian. *[1]Calidi Biotherapeutics, San Diego, CA, USA; [2]StemVac GmbH, Bernried, Germany*

Background Oncolytic virotherapy has been recognized as a promising new therapy for cancer for decades but only few viruses have been approved worldwide. The therapeutic potential of oncolytic viruses can be severely restricted by innate and adaptive immune barriers making oncolytic virus clinically inefficient. To overcome this obstacle, we utilized adipose-derived stem cells (AD-MSC) loaded with tumor selective CAL1 oncolytic vaccinia virus to generate a new therapeutic agent called SNV1 (SuperNova-1).

Methods CAL1 vaccinia virus was tested for its ability to replicate and selectively kill various human cancer cell lines in vitro and in vivo. Additionally, CAL1 was loaded into adipose-derived mesenchymal stem cells to generate SuperNova1 (SNV1). Both CAL1 and SNV1 were tested for their ability to kill cancer cells in the presence of active complement and neutralizing antibodies in cell culture as well as in mice. Immune cell infiltration of the treated and untreated tumors was analyzed by flow cytometry.

Results CAL1 showed preferential amplification and killed various tested human (PC3, FaDu, MDA-MB-231, RPMI) and mouse cancer cells (CT26, EMT6, TRAMP-C2, RM1). In animals, CAL1 caused tumor regression in PC3 and CT26 mouse models without signs of toxicity. SNV1 significantly enhanced protection of CAL1 virus from clearance by the immune system as compared to naked CAL1 virus, leading to higher therapeutic efficacy in animals. Five days after SNV1 administration, tumor infiltrating lymphocytes (TILs) from both treated and untreated tumors showed increased CD4 and CD8 T-cell infiltrations. Importantly, we documented a 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.

Conclusions CAL1 is potentially used as an oncolytic agent. In addition, SNV1 cell-based platform protects and potentiates oncolytic vaccinia virus by circumventing humoral innate and adaptive immune barriers, resulting in enhanced oncolytic virotherapy. Particularly, SNV1 provided instantly active viral particles for immediate infection and simultaneous release of therapeutic proteins in the injected tumors.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0716

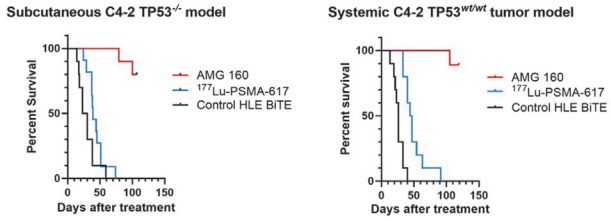
717 AMG 160, A PROSTATE-SPECIFIC MEMBRANE ANTIGEN (PSMA)-TARGETED BITE® IMMUNO-ONCOLOGY THERAPY, IS ACTIVE IN MODELS OF ADVANCED PROSTATE CANCER THAT ARE RESISTANT TO RADIOLIGAND THERAPY

[1]Katharina Lueckerath*, [2]Julie Bailis, [1]Kyle Current, [2]Mark Salvati, [1]Caius Radu, [1]Johannes Czernin. *[1]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [2]Amgen Inc., San Francisco, CA, USA*

Background AMG 160 is an HLE BiTE® (half-life extended bispecific T-cell engager) that binds PSMA on prostate cancer cells and CD3 on T-cells and induces redirected T-cell lysis of PSMA-expressing cells. This mechanism may allow the BiTE molecule to be active in settings where other targeted or immune therapies have failed. Here, we evaluated the activity of AMG 160 in mouse models of advanced prostate cancer that are resistant to ^{177}Lu-PSMA-617, a PSMA-targeted radioligand therapy that has emerged as a promising treatment modality for metastatic castration-resistant prostate cancer (mCRPC).

Methods Two prostate cancer models were tested in 6–8-week-old male NCG mice: one cohort had established subcutaneous C4-2 TP53$^{-/-}$ tumors (C4-2 cells with TP53 knockout), and the other cohort had established systemic C4-2 TP53$^{wt/wt}$tumors that mimic metastatic lesions (intracardiac injection). PSMA levels in both models (~255,000 PSMA/cell) are sufficient for tumor growth inhibition with ^{177}Lu-PSMA-617. Mice were administered a single intravenous (IV) infusion of human T-cells. Three days later, mice were treated with 1 cycle of ^{177}Lu-PSMA-617 (30 MBq, IV), or 3 weekly doses of AMG 160 (1 mg/kg, IV) or of a control HLE BiTE molecule (1 mg/kg, IV; target not expressed on C4-2 cells). Therapeutic efficacy was assessed by tumor burden measurements, time to progression (TTP), and survival.

Results In both prostate cancer models, AMG 160 treatment significantly improved disease control (figure 1). Median TTP was not reached in the AMG 160 group ($p<0.0001$), whereas it was 31d (^{177}Lu-PSMA-617) and 23.5d (control) in the subcutaneous model, and 68d (^{177}Lu-PSMA-617) and 50.5d (control) in the systemic model. Median survival was not reached in the AMG 160 group ($p<0.0001$); it was 39d (^{177}Lu-PSMA-617) and 26.5d (control) in the subcutaneous model, and 77d (^{177}Lu-PSMA-617) and 61d (control) in the systemic model. Following treatment with AMG 160, 2/10 mice with subcutaneous and 7/9 mice with systemic tumors had not progressed at the end of the observation period (>100 days). In contrast, all mice in the ^{177}Lu-PSMA-617 and control groups succumbed to progressive disease.



Abstract 717 Figure 1 AMG 160 treatment extended survival in mouse models of advanced prostate cancer

Conclusions Our study demonstrates potent antitumor activity of AMG 160 monotherapy in models of metastatic CRPC that