Abstract 786 Figure 4 Lack of host IFN-g and IL-17 eliminates aPD-L2 efficacy In the image.

Abstract 786 Figure 5 PD-L1 KO aged mice challenged with PD-L1 KO B16 In the image.

Abstract 786 Figure 6 Immune cell immune checkpoint expression In the image.

Conclusions Treatment differences in aged versus young could depend on immune checkpoint or TCSC differences, which could be related to CD8+ T-cell infiltration, including TCSC. aPD-1 efficacy in aged PD-L1KO mice challenged with PD-L1KO B16 suggests that aPD-1 efficacy is through PD-L2 block in aged. PD-L2 expression differences and anatomical compartment differences in tumor microenvironment may also contribute to treatment efficacy differences. We are now identifying mechanisms for increased PD-L2 and other mechanisms for aPD-L2 efficacy in aged, and testing TCSC effects. Our work can improve cancer immunotherapy in aged hosts and provides insights in treatment failures, including in young hosts.

Acknowledgements South Texas MSTP training grant (NIH T32GM113896), TLITR002647, Graduate Research in Immunology Program training grant (NIH T32 AI138944), R01 CA231325, Samuel Waxman Cancer Research Foundation Grant

Ethics Approval The study was approved by UTHSA IACUC, approval number 20180021.

REFERENCES


http://dx.doi.org/10.1136/jitc-2020-SITC2020.0786

Clinical trials completed

787 ABSTRACT WITHDRAWN

788 PEMBROLIZUMAB FOR PATIENTS WITH LEPTOMENINGEAL METASTASIS FROM SOLID TUMORS: EFFICACY, SAFETY AND CEREBROSPINAL FLUID BIOMARKERS

1 Jarushka Naidoo*, 2 Karisa Schreck, 2 Wei Fu, 2 Chen Hu, 2 Roisin Connolly, 2 Cesar Santa-Maria, 2 Evan Lipson, 2 Matthias Holdhoff, 2 Patrick Forde, 2 Joanne Riemer, 2 Amanda Barnes, 2 Nafi Aygun, 2 Lawrence Kleinberg, 2 Krishn Redmond, 2 Christopher Douville, 2 Chetan Bettegowda, 2 Arun Venkatesan, 2 Stuart Grossman, 2 Julie Brahmer, 1 Johns Hopkins Sidney Kimmel Cancer Center, Baltimore, MD, USA; 2 SKCC at Johns Hopkins University, Baltimore, MD, USA

Background Immune checkpoint inhibitors (ICI) have anti-cancer activity in selected patients with central nervous system (CNS) metastases. However, the benefit of ICIs in patients with leptomeningeal metastases (LMM) is unknown. We hypothesized that pembrolizumab would lead to CNS responses in patient with LMM from solid tumors, and that genomic and immunologic features of the cerebrospinal fluid (CSF) may identify biomarkers of LMM response.

Methods We undertook a single-center investigator-initiated phase 2 trial of pembrolizumab in patients with LMM from solid tumors. Eligible patients had radiologic (>3mm on MRI) or cytologic (+CSF cells) LMM and ECOG PS 0-1. Pembrolizumab was administered IV at 200mg q3W until disease progression or unacceptable toxicity. The primary endpoint was CNS response (complete response=CR, partial response=PR or stable disease=SD) after 4 cycles, defined radiologically/cytologically. Radiologic response was assessed by RECIST v1.1 and irRC. Secondary endpoints were CNS-progression-free survival (PFS), overall survival (OS) and safety. Baseline and serial CSF samples were assessed by tumor-derived DNA aneuploidy assay (t-DNA), 16-color flow cytometry and multiplex cytokine analysis.

Results Thirteen of a planned 18 patients were treated between 04/2017-12/2019. The study closed early due to poor accrual. Median age was 57 years (range 22-79); 54% were female. The majority of patients had tumors not traditionally responsive to ICI (62%; hormone-receptor+ breast carcinoma=39%; high-grade glioma=23%), while 38% had ICI-responsive tumors (NSCLC=23%, head&neck carcinoma=8%, cutaneous squamous carcinoma=8%). CNS response was observed in 38% of patients (95% CI 13.9-68.4%). Two patients achieved durable CRs (cutaneous
squamous carcinoma=1, OS 3+yrs; MET-exon14+ NSCLC=1, OS 9 mos.), 1 PR (7.7%, OS 6 mos), and 2 SDs (15.4%) in the CNS. Median CNS-PFS and OS were 2.9 mos (95% CI: 1.3-NR) and 4.9 mos (95% CI: 3.7-NR), respectively. There were no unacceptable safety signals. Sensitivity for LMM detection by t-DNA was 84.6% (95% CI: 54.6-98.1%), and 46.2% (95%CI: 19.2-74.9%) by cytopathology. Pre and on-therapy CSF cytokine analysis showed complete responders clustered together, while progressors clustered differently.

Conclusions Patients with LMM from solid tumors have a dismal prognosis and limited treatment options. In this phase 2 trial, we identified an impressive 38% CNS response rate for pembrolizumab in patients with LMM, deep and durable responses in selected patients with ICI-responsive tumors, and that pembrolizumab was well-tolerated. CSF t-DNA may be more sensitive for detection of LMM than cytopathology, and immunologic subsets of ICI-response based on cytokine profiles warrant further study. These data support investigation of pembrolizumab in larger populations with LMM.

Trial Registration NCT03091478
Ethics Approval The study was approved by John’s Hopkins University’s Institutional Ethics Board, approval number J1655
Consent All participants provided informed consent as per the study protocol

---

**789** INTRATUMORAL PLASMID IL-12 EXPANDS CD8+ T CELLS AND INDUCES A CLINICALLY VALIDATED CXCR3 SIGNATURE IN TRIPLE-NEGATIVE BREAST CANCER

Erika Crosby*, Hiroshi Nagata, Melinda Telli, Chaitanya Acharya, Irene Wapnit, Kaitlin Zablotsky, Erica Browning, Reneta Hermiz, Lauren Svenson, Donna Bannavong, Kellei Malloy, David Cantor, Christopher Twitty, Tatsuya Osada, Herbert Lyerly, Duke University, Durham, NC, USA; Stanford University, Stanford, CA, USA; OncoSec Medical Inc., San Diego, CA, USA

Background Triple-negative breast cancer (TNBC) is an aggressive disease with limited therapeutic options. Immune checkpoint inhibitors (ICI) have entered the therapeutic landscape in TNBC, but only a minority of patients benefit. Interleukin-12 (IL-12) is a pro-inflammatory cytokine involved in the generation of an inflammatory tumor microenvironment and is critical in eliciting a productive anti-tumor immune response. It has been investigated as an anti-cancer therapeutic using various delivery routes, but intratumoral injection of plasmid IL-12 (tavokinogene telseplasmid; tavo) followed by electroporation is a gene therapy approach with minimal systemic immune-related toxicity.

Methods Intratumoral injection of tavo was tested in several preclinical models of TNBC and single cell RNA sequencing (scRNAseq) was used to evaluate changes in the tumor microenvironment following treatment. These findings were then applied to the analysis of patient samples from a single arm, prospective clinical trial of tavo monotherapy (OMS-I140; NCT02531425).

Results A comprehensive analysis of cellular networks using ligand-receptor interactions identified CXCR3 (expressed by APCs) to be positively correlated with CXCL9/10/11 secreted by CD8 T cells. Further investigation of tavo treated murine tumors resulted in a 50-gene CXCR3 gene expression signature that is associated with a decrease in granulocytes, enhanced antigen presentation, increased T cell infiltration, and induction of PD-1/PD-L1. A deeper look at paired TCR alpha and beta chains on tumor infiltrating T cells (TILs) demonstrated a dramatic shift in TIL clonality and frequency following tavo treatment. There was a significant increase in not only the number of expanded (>10) clones, but also a robust activation signature that was absent in control tumors. Treatment of mice with tavo prior to anti-PD1 therapy led to complete tumor regression and long-term survival in a significant proportion of mice, while none of the mice treated with anti-PD1 alone exhibited this therapeutic efficacy. As a proof of concept, we utilized nanostring data from OMS-I140 to show a significant enhancement in this signature in patients who demonstrated a greater than 2-fold increase in CD8 TILs by IHC post-treatment. Further, we show a single patient who had previously been non-responsive to ICI that went on to receive anti-PD1 as their immediate next treatment after participating in OMS-I140, and demonstrated a significant clinical response.

Conclusions Together these data identify a clinically relevant CXCR3-associated gene signature that represents both a potential biomarker for response to ICIs and a potentially targetable pathway for therapeutic intervention in TNBC.

---

**790** A PHASE II STUDY (TACTI-002) OF EFTILAGIMOD ALPHA (A SOLUBLE LAG-3 PROTEIN) WITH PEMBROLIZUMAB IN PD-L1 UNSELECTED PATIENTS WITH METASTATIC NON-SMALL CELL LUNG(NSCLC) OR HEAD AND NECK CARCINOMA(HNSCC)

Matthew Krebs*, Mariganta Majen, Enriqueta Felip, Martin Forster, Bernard Doder, Tim Clay, Erric Carcereny, Julio Peguero, Leora Horn, Pawan Bajaj, Patricia Rosburgh, Chrysselle Brignone, Christian Mueller, Frederic Triebel, The Christie NHS Foundation Trust, Manchester, Manchester, UK; Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; Vall d’ Hebron Institute of Oncology, Barcelona, Spain; University College London Hospitals NHS, London, UK; Fundacion Jimenez Diaz, Madrid, Spain; St John of God Subiaco Hospital, Perth, Australia; Institut Catalá d’Oncologia Badalona, Badalona, Spain; Oncology Consultants P.A., Houston, Texas, USA; Vanderbilt University Medical Center (VU, Nashville, TN, USA); Tramsan Oncology, Queensland Australia; Beatson West of Scotland Cancer Center, Glasgow, UK; Immutep S.A.S, Paris, France; Immutep, Berlin, Germany

Background Eftilagimod alpha (efi) is a soluble LAG-3 protein that binds to a subset of MHC class II molecules to mediate antigen presenting cell (APC) and CD8 T-cell activation. The stimulation of the dendritic cell network and subsequent T cell recruitment may lead to stronger anti-tumor responses in combination with pembrolizumab than observed with pembrolizumab alone. We report results from stage 1 of all parts of the study (NCT03625323).