Conclusions Alongside our data, we observed multiple effects of IL-7 in these patients, highlighting a complex set of in vivo mechanisms. In the future, knowledge of these effects may help in choosing the best agents to use in combination with IL-7 and/or the best patients to benefit from IL-7 as part of their therapeutic approach.

Trial Registration NCT01881867

Ethics Approval The study was last approved by Fred Hutchinson Cancer Research Center Institutional Review Board, IR file 8037, on January 23, 2020

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0263

Abstract 270 Figure 1

a. Waterfall plot indicating maximum change in baseline tumor measurement following treatment. Crosshatch indicate patients failed therapy and do not have tumor measurements available due to early clinical progression or progression due to new lesions without RECIST measurable changes (N=2). b. Swimmer’s plot of PFS following therapy. Triangles idicated confirmed PR, targets indicate unconfirmed PR and squares indicate SD.

Conclusions Combination therapy with ipilimumab plus nivolumab in thyroid cancer resulted in an ORR of 12% with two partial responses in seventeen treated patients.

Trial Registration NCT02834013

Ethics Approval The study was approved by the NCI Adult Central Institutional Review Board, approval number 02834013.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0270

Abstract 264

Correlation of Virus-Specific CD8+ T Cells to Clinical Response Following Treatment with Pexa-Vec and Cemiplimab in Patients with Advanced Renal Cell Carcinoma

Myles Dillon, Lianjie Li, Jeongsook Bang, Nicholas Gaspar, Jessica Kuhnert, Nathalie Fiaschi, Vladimir Jankovic, Israel Lowy, Gavin Thorton, Glenn Kroog, Kyoung Soo Ha, Raquel Deering, Raquel Deering*, Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; 2Sillajen Inc., Seoul, Korea, Republic of; 3Sillajen Biotherapeutics, San Francisco, CA, USA.

Background To better understand the immune stimulatory mechanisms of Oncolytic virus (OV), we evaluated the circulating OV-specific T cell response in patients during the course of OV therapy. Patients with histologically confirmed advanced clear cell renal cell carcinoma, who were naive or refractory to prior systemic treatment and who had no prior treatment with immune checkpoint inhibitors, were treated with 4 weekly intravenous infusions of Pexa-Vec at 1 × 10^9 plaque forming units starting at Day -7 plus Cemiplimab (350 mg every 3 weeks) from Day 1. Radiographic assessments per RECIST 1.1 were performed centrally every 9 weeks from Day 1. Peripheral blood mononuclear cells (PBMCs) were collected and cryopreserved at baseline and 29 days post initial Pexa-Vec treatment.
Methods
We performed functional IFNg ELISPOT analysis on longitudinal PBMC samples using a custom panel of OV epitopes and culture conditions designed to measure existing OV-specific memory T cell cytolytic activity [1]. PBMC samples were tested for IFNg release following stimulation with OV peptides using two different assay conditions: 1) measurement following direct ex vivo stimulation with OV peptides alone, and 2) measurement following 10 days of T cell expansion in the presence of OV peptides, T cell supportive cytokines (GM-CSF, IL-4, IL-7 and IL-15), and autologous dendritic cells. The number of OV-specific IFNg spots was correlated with the clinical response and tumor regression.

Results
In preliminary analyses, 8 of the 11 (72.7%) patients showed tumor burden reduction, 4 of whom had ≥30% confirmed reduction that qualify as RECIST1.1 PRs (figure 1 and 2). OV-specific IFNg+ T cells were detected in only 3 out of 11 patients in the non-expanded ELISPOT culture conditions (figure 3A), but in 8 out of 11 patients when T cells were first expanded for 10 days in the presence of OV peptides prior to ELISPOT, which trended toward a correlation with the preliminary clinical response assessment (figure 3B). Prolonged stimulation with CMV, EBV and Influenza peptides did not show any correlation (R² = 0.005), suggesting that the treatment and culture expansion influenced relevant OV-specific memory T cell proliferation.

Conclusions
These results suggest that OV-specific T cell responses can be induced by OV therapy. In addition, 10-day expansion of low levels of OV-specific circulating T cells can amplify signals in ELISPOT analysis and might enable systemic tracking of patient responses in blood samples collected at early time points. The observed CD8+ T cell response to oncolytic vaccinia virus in patients supports the rationale for combination treatment with Pexa-Vec and immune checkpoint inhibitors.

Acknowledgements
Sun Young Rha, Yonsei Cancer Center, Severance Hospital, Yonsei University Health System, Seoul, Republic of Korea; Jamie Merchan, University of Miami Health System, Miami, FL, USA; Sung Yong Oh, Dong-A University Hospital, Busan, Republic of Korea; Chan Kim, Cha University Bundang Medical Center, Seongnam, Republic of Korea; Woo Kyun Bae, Chonnam National University Hwasun Hospital, Hwasun, Republic of Korea; Hyun Woo Lee, Ajou University Hospital, Suwon, Republic of Korea.

Trial Registration
NCT03294083

Ethics Approval
The study was approved by University of Miami Institutional Review Board, approval number 20180055.

REFERENCE

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0264