3. Zammarchi, F., *et al*., A CD25-targeted pyrrolobenzodiazepine dimer-based antibody-drug conjugate shows potent anti-tumor activity in pre-clinical models of solid tumors either alone or in combination with a PD-1 inhibitor. *Journal for ImmunoTherapy of Cancer* 2018. 6(Supplement 1).
4. Zammarchi, F., *et al*., A CD25-targeted antibody-drug conjugate depletes regulatory T cells and eliminates established syngeneic tumors via antitumor immunity. *Journal for ImmunoTherapy of Cancer* 2020. In press.

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622 PD-L1 IS A POTENTIAL PREDICTIVE BIOMARKER FOR RESPONSE TO RM-1929 TREATMENT IN RECURRENT HEAD AND NECK SQUAMOUS CELL CARCINOMA PATIENTS

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Background RM-1929 is an antibody-dye conjugate comprised of cetuximab covalently linked to the photoactivable dye, IRDye® 700DX (IR700). After systemic infusion of RM-1929, illumination of the tumor with 690 nm non-thermal red light activates the drug and results in targeted and rapid tumor necrosis. Previous preclinical data have shown that RM-1929 treatment triggers immunogenic cell death and activates the innate and adaptive immune response. A retrospective analysis of PD-L1 expression from the phase I/IIa clinical trial in patients with recurrent head and neck squamous cell carcinoma (rHNSCC) (NCT02422979) was conducted. The analysis explored correlations of PD-L1 expression, including combined proportion score (CPS) and tumor proportion score (TPS), with clinical outcomes such as response rate and overall survival.

Methods PD-L1 expression prior to RM-1929 treatment was assessed by immunohistochemistry in 18 out of 30 patients enrolled in Part II of the trial, based on sample availability. PD-L1 expression was evaluated using TPS and CPS. Responders were defined as patients that achieved complete response or partial response, and non-responders had either stable disease or progressive disease. Overall survival (OS) was analyzed using the Kaplan-Meier method.

Results Responders (n=10) had a TPS of 4.3±2.4 (mean ±SEM), which was substantially lower than in non-responders (n=8) with a TPS of 39.4±11.8. Similarly, CPS was lower in responders (8.6±3.6) compared to non-responders (50.0 ±13.5). The best target response rate for all patients included in this analysis was 56%. Patients with CPS=40 had a response rate of 76.9% (n=13) compared to 0% in patients with CPS>40 (n=5). This suggests that a CPS cut-off of =40 led to enrichment of the best target response rate. The median OS of patients with CPS=40 (13.0±0.8 months) was also higher than in patients with CPS>40 (3.1±0.8 months) and in all patients (12.0±2.9 months).

Conclusions These results suggest that rHNSCC patients with lower PD-L1 expression levels may be more responsive to RM-1929 treatment and CPS/TPS could potentially be predictive biomarkers in identifying patients with a higher probability of benefiting from this treatment. Given the limited number of patients in this analysis, additional clinical trials will be needed to validate PD-L1 expression as an effective predictive biomarker for RM-1929 treatment.

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Trial Registration NCT02422979

Ethics Approval The trial was approved by the following Instution Ethics Boards and IRB# as listed: UCSF Institutional Review Board (#17-21904), Thomas Jefferson University, IRB (#16C.328), University of Oklahoma Health Sciences Center Institutional Review Board (#5723), University of Texas MD Anderson Cancer Center - Institutional Review Board (#IRB 2 IRB00002203), Quorum Review IRB (#30458/1), Rush University Medical Center Institutional Review Board (#15030601-IRB01), and Catholic Health Initiatives Institute for Research and Innovation (CIRI) Institutional Review Board (CHIRB) (# IRB00009715).

Consent N/A

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623 IMMUNO-STATS: LEVERAGING PROTEIN ENGINEERING TO EXPAND AND TRACK ANTIGEN-SPECIFIC T CELLS IN VIVO

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Background Immunotherapies are highly promising and effective strategies for the treatment of cancer; however, continuing challenges persist, including 1) untargeted global immune modulation, resulting in serious side effects; 2) lack of therapeutics capable of in vivo expansion of tumor-specific T cells; 3) inability to visualize in vivo tumor-specific T cell responses; and 4) lack of flexible platforms to rapidly and efficiently explore new therapeutic strategies and immune-escape mechanisms. To address these challenges, we developed a novel class of precision biologics to treat cancer, autoimmune diseases and infectious diseases. We describe a modular platform constructed around an Fc-based covalent pMHC dimer, referred to as synTac (artificial synapse for T cell activation; also termed Immuno-STATs for Selective Targeting and Alteration of T cells), which selectively delivers different cargoes, including costimulatory, coinhibitory or cytokine signals and other modalities to primary T cells of defined specificity. The inherent modularity supports broad applications. Changing the encoded peptide enables targeting of different T cell specificities to address different diseases, while altering the cargo allows for evaluation of different co-modulatory mechanisms or the delivery of mechanistically informative probes.

Methods Sortase A-mediated enzymatic coupling supported site-specific and stoichiometric installation of positron emission tomography (PET)-active radiolabels on synTacs to visualize the in vivo localization of antigen-specific T cells. The NSG humanized mouse model allowed for the evaluation of synTacs/Immuno-STATs to drive the in vivo antigen-specific expansion of human CD8 T cells.