Abstracts

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

C Daniel De Magalhaes Filho*, Chung-Wei Lee, Nikolai Suslov, Jerry Fong, Miguel Garcia-Guzman, Rakuten Medical, San Diego, CA, USA

Background RM-1929 is an antibody-dye conjugate comprised of cetuximab covalently linked to the photoactivatable 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/II 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±2.8 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 Institution Ethics Boards and IRB: UCSF Institutional Review Board (#17-21904), Thomas Jefferson University, IRB (#16C.328), University of Oklahoma Health Sciences Center Institutional Review Board (#S723), 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 (CHIRI) Institutional Review Board (CHIRI) (# IRB00009715).

Consent N/A

623 IMMUNO-STATS: LEVERAGING PROTEIN ENGINEERING TO EXPAND T Target RESPONSE TO TREAT CANCER PATIENTS IN VIVO

1Stad Zeigler, 2Andrew Woodham, 1Mengyan Li, 2Elia Zeyang, 2Stephen Kefifrah, 4Mohammad Rashidian, 1Kaitlyn O’Connor, 2Rodolfo Chaparro, 4Ronald Seidel, 2Maia Meyninger, 2Ross Cheholo, 2Jason Dealing, 1Phaneendra Duddempudi, 1Alex Celikgil, 2Scott Garforth, 2Alan Packard, 2Harris Goldstein, 2Hidde Plugheg, 2Steven Almo*, 1Albert Einstein College of Medicine, Bronx, NY, USA; 2Massachusetts Institute of Technology, Cambridge, MA, USA; 3Dana Farber Cancer Institute, Boston, MA, USA; 4Cue Biopharma, Cambridge, MA, USA

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 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.