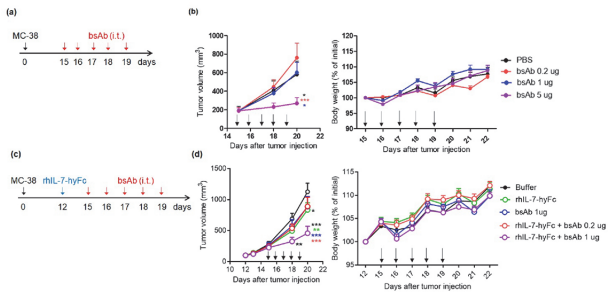

Abstract 450 Figure 4 (a-b) Mice bearing MC-38 tumors were treated i.t. with bsAb as indicated in (a) (n = 6–7 per group). (b) Shown are mean tumor growth curves (left) and body-weight changes (right). (c-d) Mice bearing MC-38 tumors were treated either 1.25 mg/kg of rhIL-7-hyFc (s.c.), indicated doses of BsAb (i.t.), or combination of each therapy as indicated in (c). (n = 9–10 per group). (d) Shown are mean tumor growth curves (left) and body-weight changes (right). Arrows indicate the dosing of bsAb. Data are represented as mean ± SEM. Statistical significance was analyzed by two-way ANOVA with bonferroni's multiple comparisons for tumor growth graphs. *P<0.05; **P<0.01;***P<0.001

Conclusions The combination treatment of anti-PD-L1xCD3ϵ bsAb with rhIL-7-hyFc enhances antitumor efficacy.Both systemic and intratumoral administration of bsAb with rhIL-7-hyFc augments antitumor effects, and intratumoral administration induced less weight loss than systemic administration.The activation of PD-1$^-$ bystander CD8$^+$ T cells in tumors by the combination of bsAb and rhIL-7-hyFc suggests that antitumor response may be partially mediated by the targeted activation of bystander CD8$^+$ T cells. Our results serve as a proof-of-concept that the combination of rhIL-7-hyFc, a strong T cell amplifier, with bsAb, a tumor-targeted T-cell stimulator, would be a promising strategy for cancer immunotherapy.

Acknowledgements This research was supported by the Bio & Medical Technology Development Program of the National Research Foundation (NRF) funded by the Korean government (MSIT)(NRF-2020M3H1A1075314) and the grants from Research Institute of NeoImmuneTech, Inc.

Ethics Approval This study was approved by POSTECH institutional animal care and use committee; approval number POSTECH-2020-0057.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0450

451 COMBINING BEMPEGALDESLEUKIN (CD122-PREFERENTIAL IL-2 PATHWAY AGONIST) AND NKTR-262 (TLR7/8 AGONIST) PAIRS LOCAL INNATE ACTIVATION WITH SYSTEMIC CD8+ T CELL EXPANSION TO ENHANCE ANTI-TUMOR IMMUNITY

[1]Annah Rolig*, [1]Daniel Rose, [2]Saul Kivimae, [2]Werner Rubas, [1]William Redmond. *[1]Earle A. Chiles Research Institute, Portland, OR, USA; [2]Nektar Therapeutcs, San Francisco, CA, USA*

Background Previously, we demonstrated that radiation therapy (RT) combined with Bempegaldesleukin (BEMPEG;NKTR-214), a first-in-class CD122-preferential IL-2 pathway agonist, led to enhanced anti-tumor efficacy through a T cell-dependent mechanism. However, we observed only modest systemic responses to BEMPEG/RT across several murine tumor models. Therefore, we explored alternative approaches to improve systemic tumor-specific immunity. We evaluated whether intratumoral NKTR-262, a polymer-modified toll-like receptor (TLR) 7/8 agonist, combined with systemic BEMPEG treatment resulted in improved tumor-specific immunity and survival compared to BEMPEG combined with RT. We hypothesized that BEMPEG/NKTR-262 immunotherapy would promote synergistic activation of local immunostimulatory innate immune responses followed by systemic adaptive immunity to significantly improve tumor regression and overall survival.

Methods Tumor-bearing mice (CT26; EMT6) received BEMPEG (0.8 mg/kg; iv), RT (12 Gy x 1), and/or intratumoral NKTR-262 (0.5 mg/kg). Flow cytometry was used to evaluate CD4+ and CD8+ T cell activation status in the blood and/or tumor (7 days post-treatment) and NK cell activity in the tumor (1, 3 days post-treatment). The contribution of specific immune subsets was determined by depletion of CD4+, CD8+, or NK cells. CD8+ T cell activity was determined in vitro by tracking apoptosis in an Incucyte assay. Data are representative of 1–2 independent experiments (n=5–14/group) and statistical significance was determined by 1-way ANOVA (p-value cut-off of 0.05).

Results BEMPEG/NKTR-262 resulted in significantly improved survival compared to BEMPEG/RT. BEMPEG/NKTR-262 efficacy was NK and CD8+ T cell-dependent, while BEMPEG/RT primarily relied on CD8+ T cells. Response to BEMPEG/NKTR-262 was characterized by a significant expansion of activated CD8+ T cells (GzmA+; Ki-67+; ICOS+; PD-1+) in the blood, which correlated with reduced tumor size (p<0.05). In the tumor, NKTR-262/BEMPEG induced higher frequencies of GzmA+ CD8+ T cells exhibiting reduced expression of suppressive molecules (PD-1+, TIM-3+), compared to BEMPEG/RT. Indeed, CD8+ T cells isolated from BEMPEG/NKTR-262-treated tumors had greater cytolytic capacity than those from BEMPEG/RT-treated mice. CD8+ T cell expansion (blood) and activity (tumor) depended upon the initial NK response, as neither occurred in the absence of NK cells. BEMPEG/NKTR-262 uniquely induced the expansion of early and high effector NK cells.

Conclusions Combining BEMPEG with NKTR-262 lead to an early and robust NK cell expansion not observed in the BEMPEG/RT combination. The improved tumor regression and survival was dependent on the NKTR-262 driven expansion of NK cells. A clinical trial of BEMPEG/NKTR-262 for patients with metastatic solid tumors is in progress (NCT03435640).

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0451

452 COMBINATION TREATMENT USING KISIMA^{TM} PROTEIN-BASED CANCER VACCINE AND SYSTEMIC STING AGONIST RESULTS IN PROFOUND MODULATION OF TUMOR MICROENVIRONMENT AND IMPROVED TUMOR CONTROL

Matteo Rossi *, Elodie Belnoue, Susanna Carboni, Wilma Besson-Di Berardino, Erika Riva, Marie-Laure Santiago-Raber, Madiha Derouazi. *AMAL Therapeutics, Geneva, Switzerland*

Background KISIMA^{TM} platform allows the development of protein-based cancer vaccines able to induce a potent, tumor-specific CD8 and CD4 T cells response. While the cell penetrating peptide and the Anaxa portions confer, respectively, the cell delivery and self-adjuvanticity properties, the multiantigenic domain allows the targeting of different cancer antigens, resulting in anti-tumoral efficacy in different murine models.[1] The first clinical candidate developed from KISIMA^{TM} is currently tested, together with anti-PD-1 blockade, in a phase I study in metastatic colorectal cancer patients. Stimulator of