Exploratory endpoints are potential correlations between biomarkers and efficacy. A stratified Cochran Mantel Haenszel method will be used to assess binary endpoints. A Kaplan-Meier method, a stratified log-rank test and a stratified Cox proportional hazards model will be used to assess survival endpoints.Planned enrollment is 406 patients. The study is actively enrolling at 52 Chinese sites.

Results N/A

Conclusions N/A

Acknowledgements N/A

Trial Registration The Clinical trials. gov no NCT04158440

Ethics Approval This study was approved by the Ethics Board of all the involved sites; Approval number of Shanghai Chest Hospital: LS1936

Consent N/A

REFERENCES

1. Forde PM, Chaft JE, Smith KN, *et al*. Neoadjuvant PD-1 blockade in resectable lung cancer *N Engl J Med* 2018;**378**:1976–1986
2. Hellmann MD, Chaft JE, William WN Jr, *et al*. Pathological response after neoadjuvant chemotherapy in resectable non-small-cell lung cancers: proposal for the use of major pathological response as a surrogate endpoint. *Lancet oncol* 2014;**15**:e42–50.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0366

367 A PHASE 1/1B DOSE-ESCALATION STUDY OF INTRAVENOUSLY ADMINISTERED SB 11285 ALONE AND IN COMBINATION WITH ATEZOLIZUMAB IN PATIENTS WITH ADVANCED SOLID TUMORS

[1]Jason Luke*, [2]Filip Janku, [3]Anthony Olszanski, [4]Kevin Leach, [4]Radhakrishnan Iyer, [4]Atif Abbas. *[1]UPMC Hillman Cancer Center, Pittsburgh, PA, USA; [2]MD Anderson Cancer Center, Houston, TX, USA; [3]Fox Chase Cancer Center, Philadelphia, PA, USA; [4]Spring Bank Pharmaceuticals, Hopkinton, MA, USA*

Background Activation of the Stimulator of Interferon Genes (STING) pathway within immune and tumor cells of the tumor microenvironment (TME) results in durable anti-tumor effects via induction of innate and adaptive immunity. SB 11285 is a next-generation immunotherapeutic cyclic dinucleotide that activates the STING pathway leading to stimulation of tumor-resident APCs, NK cells and priming of tumor antigen specific CD8+ T cells. In preclinical studies using multiple tumor-derived cell lines, SB 11285 induced cytokines, such as IFN-α and -β, TNF- α and others consistent with engagement of TBK1 downstream of STING activation. Exposure of SB 11285 directly to tumor also induces cell death by STING-mediated apoptosis. SB 11285 reduced tumor volumes in multiple rodent tumor models when administered intravenously, intraperitoneally or intratumorally, as monotherapy and with amplified effect in combination with CTLA-4 or PD-1 antibodies. The novel properties of SB 11285 facilitate systemic administration which may facilitate trafficking of newly activated CD8+ T cells from the periphery into the TME.

Methods This open-label, multicenter phase 1/1b clinical trial (NCT04096638) will enroll approximately 110 patients in the dose escalation (Part 1) and expansion cohorts (Part 2). Part 1 will includ parallel dose escalations evaluating ascending doses of intravenously administered SB 11285 via 3+3 design with respect to dose-limiting toxicities, maximum tolerated dose, recommended phase 2 dose (RP2D) and the pharmacokinetic/pharmacodynamic profile. Part 2 Expansion Cohorts of the study will explore initial efficacy via overall response rate in pre-specified tumor types (such as Melanoma, Head and Neck Squamous Cell Carcinoma) at the RP2D in combination with atezolizumab. SB 11285 will be administered as monotherapy weekly on Days 1, 8, 15, and 22 of repeated 28-day cycles in escalating doses and in combination with atezolizumab administered Q4W. Biological effects of SB 11285 will be evaluated via changes in immune cell types, serum cytokines, and gene expression patterns indicative of activation of the peripheral and TME immune compartments.

Results 'N/A'

Conclusions 'N/A'

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0367

368 REVEAL: PHASE 1 DOSE-ESCALATION STUDY OF NKTR-262, A NOVEL TLR7/8 AGONIST, PLUS BEMPEGALDESLEUKIN: LOCAL INNATE IMMUNE ACTIVATION AND SYSTEMIC ADAPTIVE IMMUNE EXPANSION FOR TREATING SOLID TUMORS

[1]Adi Diab*, [2]Brendan Curti, [3]Mehmet Bilen, [4]Andrew Brohl, [5]Evidio Domingo-Musibay, [6]Erkut Borazanci, [7]Christie Fanton, [7]Cat Haglund, [7]Mona Vimal, [7]Mann Muhsin, [7]Mario Marcondes, [7]Anh Nguyen, [7]Mary Tagliaferri, [7]Wei Lin, [7]Jonathan Zalevsky, [8]Sandra D'Angelo. *[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Providence Cancer Center and Earle A. Chiles Research Institute, Portland, OR, USA; [3]Winship Cancer Institute of Emory University, Atlanta, GA, USA; [4]H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA; [5]University of Minnesota Medical Center, Minneapolis, MN, USA; [6]HonorHealth Research Institute, Scottsdale, AZ, USA; [7]Nektar Therapeutics, San Francisco, CA, USA; [8]Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, New York, NY, USA*

Background NKTR-262 is a small-molecule agonist of toll-like receptors (TLR) 7/8. Given by intratumoral (IT) injection, NKTR-262 is retained within the tumor microenvironment (TME) and promotes an immunostimulatory milieu and tumor antigen release. Bempegaldesleukin (BEMPEG) is a CD122-preferential IL-2 pathway agonist, which increases proliferation and tumor infiltration of $CD8^+$ T cells and natural killer (NK) cells. Preclinically, NKTR-262 plus BEMPEG combined innate immune signaling and enhanced antigen presentation, with sustained T-cell activation, resulting in tumor growth inhibition of treated and abscopal lesions.

Methods This phase 1 dose-escalation study enrolled patients with relapsed/refractory, advanced/metastatic solid tumors (REVEAL; NCT03435640). Patients received escalating doses of NKTR-262 (0.03 mg to 3.84 mg IT) followed 3 weeks' later by BEMPEG (0.006 mg/kg IV) q3wk utilizing a 3+3 design. The primary endpoint was safety and tolerability, including definition of the recommended phase 2 dose (RP2D). Other endpoints included antitumor activity, pharmacodynamics, and pharmacokinetics.

Results As of June 15, 2020, 36 patients were enrolled. One dose-limiting toxicity, transient transaminase elevation, was observed at the highest NKTR-262 dose (3.84 mg). The most frequent treatment-related adverse events were flu-like symptoms, fatigue, nausea, and pruritus, consistent with the known profile of BEMPEG. Early evidence of clinical activity was observed in patients with metastatic melanoma, with a disease control rate (partial response [PR] + stable disease) of 41.2% (7/17 patients), including two patients with PRs after progression on two prior immunotherapy regimens. Preliminary analyses showed dose-dependent induction of CXCL10 and type 1 interferon genes, consistent with TLR7/8 engagement. $CD11c^+$ target cells were significantly more abundant in baseline melanoma biopsies than other tumor types ($p<0.001$). Induction