Conduct Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

REFERENCE


http://dx.doi.org/10.1136/jitc-2020-SITC2020.0801

802 | RAMUCIRUMAB PLUS ATEZOLIZUMAB IN PATIENTS WITH STAGE IV NON- small CELL LUNG CANCER PREVIOUSLY TREATED WITH IMMUNE CHECKPOINT BLOCKADE

Brett Herzog*, Saimaa Waqar, Siddhartha Devarakonda, Jeffrey Ward, Ramaswamy Govindan, Daniel Morgensztern. Washington University in St. Louis, Saint Louis, MO, USA

Background T-cell trafficking to the tumor is inhibited via vascular endothelial growth factor (VEGF)-mediated downregulation of important adhesion molecules on tumor-associated blood vessels and progression of disease on immune checkpoint blockers (ICBs) has been associated with decreased tumor-infiltrating immune cells. 1, 2 We hypothesized that inhibiting VEGF signaling through its receptor, VEGFR2, would increase intratumoral T cells. Therefore we sought to evaluate the combination of ramucirumab, an anti-VEGF receptor 2 monoclonal antibody, and atezolizumab in patients with advanced-stage, non-small cell lung cancer (NSCLC) patients who have previously progressed on at least one line of ICB. Here, we report on the first twelve patients enrolled on trial.

Methods Advanced stage NSCLC patients with an ECOG performance status of ≤1 who had previously been treated with ICBs were eligible with no limitation on prior lines of ICB therapy. Patients with untreated brain metastasis, recent hemoptysis, gastrointestinal bleeding or perforation or fistula were excluded. The study was conducted with a two-stage MiniMax design. Peripheral blood and repeated biopsies, when feasible, were collected for correlative analysis.

Results Twelve patients were enrolled in the first stage of the trial. The median age was 68 (range 47-78), 10 of the patients are female, and 10 had non-squamous histology. Patients had an average of 3.5 prior lines of therapy and 1.6 lines of prior immunotherapy. Overall, treatment was well-tolerated with no grade 3 or 4 adverse events. The most common adverse events were grade 1 or 2 hypertension (35%), nausea (25%) and vomiting (25%). There were no objective responses and 11 patients (91%) achieved stable disease. The median progression-free survival is 3 months with 3 patients (25%) on trial for more than 12 months. The median overall survival (OS) at the time of the latest data cutoff on 9/15/20 is 11.5 months.

Conclusions The preliminary data from our study showed that combination of ramucirumab and atezolizumab is well-tolerated and associated with prolonged overall survival in a subset of heavily pretreated patients who progressed on prior ICB. The trial is still accruing patients and exploratory analyses are planned.

Ethics Approval The study was approved by the Washington University Institutional Review Board.

REFERENCES


http://dx.doi.org/10.1136/jitc-2020-SITC2020.0802

803 | PHASE 1/2 STUDY USING ENB-003, A FIRST-IN-CLASS SELECTIVE ETBRI, IN COMBINATION WITH PEMBROLIZUMAB IN SUBJECTS WITH ADVANCED REFRAC TORY SOLID TUMORS

1Sumayah Jamal*, 2Adnan Nagrial, 3Anthony Joshua, 4Richard Eiek, 5Sumayah Jamal. 1ENB Therapeutics Inc, New York, NY, USA; 2Blacktown Cancer and Haematology, Blacktown, Australia; 3Kinghorn Cancer Centre, Darlinghurst, Australia; 4Border Medical Oncology Research Unit, Albury, Australia

Background The endothelin B receptor (ETBR) is upregulated in many types of cancer and is associated with poor overall survival and a paucity of TILs (tumor infiltrating lymphocytes). 1 The ETBR prevents T-cell extravasation and tumor infiltration by a mechanism involving adhesion molecule downregulation in the tumor vasculature. Thus ETBR expression may mediate resistance to immunomodulatory therapy. ENB-003 is a small molecule ETBRI (ETBR inhibitor) which overcomes resistance to anti-PD1 across multiple cancer types in preclinical studies. Part 1 of this study seeks to evaluate the safety and tolerability of ENB-003 in combination with pembrolizumab in refractory advanced ETBR+ solid tumors. Part 2 of the study is an expansion cohort basket trial assessing the efficacy of ENB-003 in combination with pembrolizumab in anti-PD1 refractory melanoma, platinum resistant ovarian cancer and refractory pancreatic cancer.

Methods Study ENB-003-101 (MK-3475-951) is a multicenter, Phase 1/2, open-label study of ENB-003 in combination with pembrolizumab in adult subjects with advanced solid tumors. The part 1 dose escalation is enrolling subjects with ETBR+ tumors and includes 5 doses of ENB-003 in combination with a fixed dose of pembrolizumab. The primary objective of part 1 is to assess safety and tolerability, the secondary objective is to evaluate anti-tumor effect (RECISt 1.1 and iRECIST). Exploratory objectives are to examine biomarkers/pharmacodynamics.

Results ENB-003, as a single agent and in combination with anti-PD1, was investigated in a variety of syngeneic preclinical models. ENB-003 enhanced the anti-tumor activity of anti-PD1 in anti-PD1 resistant models of melanoma, ovarian cancer, pancreatic cancer, bladder cancer and SCC. For example, the combination of ENB-003 plus anti-PD1 in an anti-PD1-resistant melanoma model resulted in complete tumor eradication in 21 days as well as the formation of TLOs (tertiary lymphoid organs). The combination of ENB-003 plus pembrolizumab was well tolerated in the first 2 cohorts of the ongoing Phase 1 trial in patients with advanced refractory solid tumors that are ETBR+. Best overall responses from the first 2 cohorts (n=6) demonstrates disease stabilization (SD) in 2 patients as well as a partial response (PR) in an ovarian cancer patient with ~60% reduction in target lesions.

Conclusions ETBRI is a novel approach to overcoming immunotherapy resistance. The combination of ENB-003 and pembrolizumab is well tolerated thus far and is demonstrating promising early signals of anti-tumor efficacy. Trial updates will be reported.