

383

FIRST-IN-MAN CLINICAL TRIAL OF INTRATUMORAL INJECTION OF CLOSTRIDIUM NOVI-NT SPORES IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH TREATMENT-REFRACTORY ADVANCED SOLID TUMORS

¹Filip Janku*, ²Siqing Fu, ²Ravi Murthy, ²Daniel Karp, ²David Hong, ²Apostolia Tsimberidou, ²Maura Gillison, ²Abha Adat, ²Anjali Raina, ²Greg Call, ³Brent Kreider, ³David Tung, ³Mary Varterasian, ⁴Khashayarsha Khazaie. ¹The University of Texas MD Anderson Cancer Center, Houston, TX, USA; ²MD Anderson Cancer Center, Houston, TX, USA; ³BioMed Valley Discoveries Inc., Kansas City, MO, USA; ⁴Mayo Clinic, Rochester, MN, USA

Background Intratumorally injected Clostridium novyi-NT (non-toxic), an attenuated strain of *C. novyi* that lacks production of the lethal alpha toxin, replicates within hypoxic tumor regions and elicits tumor-confined cell lysis. Early clinical and translational data suggest that intratumoral injection of *C. novyi*-NT is feasible, demonstrates early signals of anti-tumor activity and induction of the host immune response, which supports additional studies in combination with immune checkpoint inhibitors.

Methods This first-in-human study (NCT03435952) enrolls patients with injectable, treatment-refractory solid tumors to receive a single intratumoral injection of *C. novyi*-NT across 4 dose cohorts (3 × 10⁴ to 100 × 10⁴ spores, 3+3 dose-escalation design) in combination with intravenous pembrolizumab 200 mg every 3 weeks for up to 24 months to determine dose-limiting toxicities (DLTs), and the maximum tolerated dose (MTD).

Results As of August 24, 2020, 9 patients (breast cancer, n=2; colorectal cancer, n=1; fibrous histiocytoma, n=1; anal cancer, n=1; chondrosarcoma, n=1; appendiceal cancer, n=1; tongue squamous cell cancer, n=1; nasopharyngeal cancer, n=1) were treated. There were no DLTs to date. Signs and symptoms of *C. novyi*-NT germination (infection) including fever, injection site pain, erythema, swelling, tenderness, and in some cases, ulceration, spontaneous drainage, tissue sloughing, bleeding, and malodor were observed in 5 patients. Partial responses were noted in 2 of 9 patients (tongue squamous cell cancer, nasopharyngeal cancer).

Conclusions Single intratumoral injection of *C. novyi*-NT in combination with pembrolizumab has been demonstrating manageable toxicity profile and encouraging signals of anti-cancer activity. The enrolment continues.

Trial Registration NCT03435952

Ethics Approval The study was approved by MD Anderson IRB

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0383>

384

A PHASE 1 STUDY TO EVALUATE THE SAFETY, PK, AND ANTITUMOR ACTIVITY OF AK117, AN ANTI-CD47 MONOCLONAL ANTIBODY, IN SUBJECTS WITH RELAPSED/REFRACTORY ADVANCED OR METASTATIC SOLID TUMORS OR LYMPHOMAS

¹Amy Prawira*, ²Jermaine Coward, ³Anna Mislav, ⁴Adnan Nagrial, ⁵Hui Gan, ⁶Xiaoping Jin, ⁶Baiyong Li, ⁶Zhongmin Maxwell Wang, ⁶Kon Yew Kwek, ⁶Dennis Xia, ⁶Yu Xia. ¹St Vincent's Hospital, Sydney, Australia; ²Icon Cancer Centre, Brisbane, Australia; ³Adelaide Cancer Centre, Kurrallta Park, Australia; ⁴Blacktown Hospital, Blacktown, Australia; ⁵Austin Health, Melbourne, Victoria, Australia; ⁶Akeso Biopharma Inc, Zhongshan city, China

Background AK117 is a novel humanized IgG4 monoclonal antibody (mAb) targeting CD47, a macrophage immune checkpoint and 'don't eat me' signal that allows tumor cells to

evade immune destruction by phagocytic cells. Most human cancers express CD47 to varying degrees, making CD47 a universal target. The efficacy of anti-CD47 therapy has been studied, as monotherapy and in combination with other anti-neoplastic agents, in various malignancies, including acute myeloid leukemia, diffuse large B-cell lymphoma, multiple myeloma, colorectal cancer, hepatocellular carcinoma and breast cancer. Anemia is common with anti-CD47 therapy because CD47 is ubiquitously expressed on senescent red blood cells (RBCs). However, in comparison to other anti-CD7 mAbs, AK117 exhibits significantly weaker binding to human RBCs than tumor cells. In both in vitro and in vivo nonclinical studies, AK117 demonstrated robust anti-tumor activity without causing significant agglutination of human RBCs in vitro or anemia in monkeys.

Methods This is a first-in-human, Phase 1, multicenter, open label, single arm, dose escalation and dose expansion study of AK117 administered intravenously to adult subjects with relapsed/refractory advanced or metastatic solid tumors or lymphomas. The primary objective is to assess the safety and tolerability of AK117 monotherapy; and determine the maximum tolerated dose (MTD). Antitumor activity, PK, pharmacodynamic profile and immunogenicity of AK117 will be studied as secondary objectives. The dose escalation parts of the study uses a 3+3+3 design to determine the Recommended Phase 2 Dose (RP2D) dose between 0.3 mg/kg to 45 mg/kg QW. Dose escalation is performed exclusively in solid tumors; and any dose escalation cohort not exceeding the MTD may be expanded up to a maximum of approximately 18 subjects, with a minimum of 6 subjects with lymphomas, to provide additional clinical data to inform the optimal dose level and treatment schedule for tumor type-specific dose expansion and subsequent clinical studies. In the dose expansion phase, AK117 will be studied in cohorts of 30 subjects each with selected solid tumors and selected lymphomas. Subjects with active or prior autoimmune disease that may relapse, history of hemolytic anemia of any cause within 3 months of first dose, hemophagocytic lymphohistiocytosis, defects in RBC production; or defects in hemoglobin production or metabolism will not be eligible for this study.

Results N/A

Conclusions N/A

Trial Registration NCT04349969

Ethics Approval The study was approved by Bellberry Human Research Ethics Committee (Application No. 2020-02-016).

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0384>

385

A FIRST-IN-HUMAN STUDY OF LEMZOPARLIMAB, A DIFFERENTIATED ANTI-CD47 ANTIBODY, IN SUBJECTS WITH RELAPSED/REFRACTORY MALIGNANCY: INITIAL MONOTHERAPY RESULTS

¹Jordan Berlin*, ²Wael Harb, ³Alex Adjei, ⁴Yan Xing, ⁵Paul Swiecicki, ³Mahesh Seetharam, ⁶Lakshminarayanan Nandagopal, ⁷Ajay Gopal, ⁸Cong Xu, ⁸Cong Xu, ⁸Yuan Meng, ⁸Linda Lee, ⁸Yonggang Zhao, ⁸Zhengyi Wang, ⁸Joan Huaqiong Shen. ¹Vanderbilt University, Nashville, TN, USA; ²Horizon Oncology, Lafayette, IN, USA; ³Mayo Clinic, Rochester, MN, USA; ⁴City of Hope, Duarte, CA, USA; ⁵University of Michigan, Ann Arbor, MI, USA; ⁶University of Alabama, Birmingham, AL, USA; ⁷University of Washington, Seattle, WA, USA; ⁸I-Mab Biopharma, Gaithersburg, MD, USA

Background CD47 blockade using SIRPα-Fc or anti-CD47 antibodies results in inhibition of the 'do not eat' signal and activation of phagocytosis and has emerged as a promising

cancer treatment strategy. However, targeting CD47 leads to various hematological toxicities, particularly anemia and thrombocytopenia. Lenzoparlimab (also known as TJ011133 or TJC4) is a fully human, anti-CD47 IgG4 antibody that is endowed with a red blood cell (RBC) sparing property and unique binding epitope, potentially differentiating itself from other CD47 axis targeting therapies.

Methods This phase 1 study (NCT03934814) is comprised of 2 parts. Part 1 consists of lempzarlimab monotherapy dose escalation and 2 separate dose escalations of combination therapy with pembrolizumab or rituximab. The study is a standard 3+3 design. Part 2 is a dose expansion study. During monotherapy dose escalation, patients with relapsed/refractory solid tumors were administered an intravenous weekly dose (1 to 30 mg/kg) of lempzarlimab to determine tolerability, safety, pharmacokinetics (PK), pharmacodynamics (PD) and anti-tumor activity based on Response Evaluation Criteria in Solid Tumors (RECIST v1.1) and iRECIST. Preliminary data from fully enrolled monotherapy cohorts in Part 1 are reported as of 17 July 2020.

Results Twenty patients with relapsed/refractory solid tumors were enrolled to monotherapy dose escalation cohorts (1, 3, 10, 20 and 30 mg/kg). Lenzoparlimab toxicity was manageable up to 30 mg/kg without a dose-limiting toxicity (DLT) observed. The most common treatment-related adverse events (TRAEs) were anemia (30.0%, n=6), fatigue (25.0%, n=5), infusion-related reactions (20.0%, n=4), and diarrhea (15.0%, n=3). All TRAEs were Grade 1 or 2. A transient, non-dose-dependent average reduction of 1.5 mg/dL (range: 0.4–2.6 mg/dL) in hemoglobin during the first cycle was observed across all cohorts consistent with the results of pre-clinical good laboratory practice toxicity studies. Laboratory or clinical evidence of hemolysis was not observed in any cohort. Preliminary results indicate the PK of lempzarlimab appears to be linear at mid- to high dose levels following a single dose. CD47 receptor occupancy shows complete saturation on peripheral T cells at peak concentrations of 20 mg/kg and above.

Conclusions Lenzoparlimab appears safe up to 30 mg/kg with favorable PK and PD characteristics in patients with relapsed/refractory solid tumors to date. No TRAEs greater than Grade 2 have been observed. Results will be updated at presentation including available tumor response data.

Trial Registration NCT03934814

Ethics Approval The study was approved by IRB, approval number 20190733.

<http://dx.doi.org/10.1136/jitc-2020-SITC2020.0385>

386

PHASE I/IB FIRST-IN-HUMAN STUDY OF HEK-NIZ985, A RECOMBINANT IL-15/IL-15R α HETERODIMER, ALONE AND IN COMBINATION WITH SPARTALIZUMAB, IN ADULTS WITH ADVANCED AND METASTATIC SOLID TUMORS

¹Rom Leidner, ²Andrea Wang-Gillam, ³Sumati Gupta, ⁴Robert Wesolowski, ⁵Douglas McNeel, ⁶Kevin Conlon, ⁷Nehal Parikh, ⁷Jessica O’Keeffe, ⁸Niladri Roy Chowdhury, ⁷Xiaoli Wang, ⁷Ryan Sullivan, ⁹John Thompson. ¹Providence EACRI, Portland, OR, USA; ²Washington University School of Medicine, St. Louis, MO, USA; ³University of Utah, Salt Lake City, UT, USA; ⁴The Ohio State University, Columbus, OH, USA; ⁵University of Wisconsin Clinical Science Center, Madison, WI, USA; ⁶National Cancer Institute, Bethesda, MD, USA; ⁷Novartis Institutes for BioMedical Research, inc. (NIBR), Cambridge, MA, USA; ⁸Novartis Pharmaceuticals, East Hannover, NJ, USA; ⁹University of Washington Seattle Cancer Care, Seattle, WA, USA

Background HEK-NIZ985 (NIZ985) is a recombinant heterodimer of IL-15/IL-15R α that expands effector lymphocytes and antitumor activity in animal models and a human clinical trial. We report interim data from the first-in-human study of NIZ985.

Methods CNIZ985X2102J is an open-label Phase I/II dose-escalation/expansion trial evaluating the safety of subcutaneous NIZ985 three-times-weekly (TIW; 2-weeks-on/2-weeks-off) or once-weekly (QW; 3-weeks-on/1-week-off) as a single agent (SA) or in combination (CM) dosing with 400 mg of the PD-1 inhibitor spartalizumab every 4 weeks, in adults with metastatic/unresectable solid tumors. SA dosing was 0.25–4 μ g/kg TIW or 2–10 μ g/kg QW; CM dosing was 1 μ g/kg TIW or 2–4 μ g/kg QW. The primary objective was to characterize the safety and tolerability of NIZ985 \pm spartalizumab. Data are presented for dose escalation, and CM-TIW expansion.

Results Overall, 83 patients entered dose escalation (n=47) or CM-TIW expansion (n=36), of whom 63.8% (30/47) and 69.4% (25/36), respectively, had received \geq 3 prior lines of antineoplastic treatment. At data cut-off (March 2, 2020), 91.6% (76/83) had discontinued study treatment. Adverse events (AEs) are summarized below (table 1). There were no dose-limiting toxicities during the first 28-day cycle in any cohort. Systemic skin AEs (Cycle 2) occurred in three SA-TIW patients receiving 2 or 4 μ g/kg (bullous pemphigoid, purpura, vasculitis), limiting TIW escalation and initiating QW dose exploration; these were not observed at 1 μ g/kg TIW (\pm spartalizumab) or for QW doses up to 10 μ g/kg. CM-TIW dose expansion was therefore at 1 μ g/kg; the recommended QW expansion dose is currently undetermined. For SA NIZ985, best overall response (RECIST 1.1) was stable disease (SD; 8/27 patients [29.6%]). Objective responses for NIZ985 plus spartalizumab (3/56 partial response [PR; 5.3%], 15/56 SD [26.8%]) occurred in both immuno-oncology treatment (IO)-naïve and IO-experienced patients, including 5/8 IO-experienced melanomas (cutaneous: 3 SD, 1 PR; uveal: 1 SD). Systemic NIZ985 exposure was approximately dose-proportional after first dose for \geq 1 μ g/kg TIW and <10 μ g/kg QW, with time-dependent clearance without accumulation. Proliferation of peripheral CD8+ and NK lymphocytes, and increased inflammatory cytokines, were observed for both dosing schedules.

Abstract 386 Table 1 Adverse event summary

	SA-TIW (escalation) n=14	SA-QW (escalation) n=13	CM-TIW + CM-QW (escalation) n=20	CM-TIW (expansion) n=36
<i>Data are n (%) patients with \geq1 event</i>				
Any AE	14 (100)	13 (100)	20 (100)	35 (97.2)
Grade 3–4 AEs	6 (42.9)	10 (76.9)	12 (60.0)	16 (44.4)
Treatment-related	6 (42.9)	2 (15.4)	5 (25.0)	4 (11.1)
SAEs	5 (35.7)	7 (53.8)	10 (50.0)	14 (38.9)
Treatment-related	3 (21.4)	1 (7.7)	1 (5.0)	1 (2.8)
Discontinuations for AEs	3 (21.4)	1 (7.7)	1 (5.0)	0
Common AEs (all-cause >20% in all patients)				
Injection site reaction	14 (100)	10 (76.9)	20 (100)	34 (94.4)
Fatigue	9 (64.3)	8 (61.5)	14 (70.0)	15 (41.7)
Chills	10 (71.4)	3 (23.1)	8 (40.0)	7 (19.4)
Nausea	5 (35.7)	7 (53.8)	13 (65.0)	10 (27.8)
Decreased appetite	4 (28.6)	9 (69.2)	10 (50.0)	9 (25.0)
Diarrhea	3 (21.4)	2 (15.4)	11 (55.0)	5 (13.9)
Pyrexia	7 (50.0)	3 (23.1)	8 (40.0)	7 (19.4)
Arthralgia	5 (35.7)	3 (23.1)	8 (40.0)	4 (11.1)
Vomiting	3 (21.4)	3 (23.1)	8 (40.0)	12 (33.3)
Abdominal pain	1 (7.1)	6 (46.2)	9 (45.0)	9 (25.0)
Dizziness	1 (7.1)	4 (30.8)	7 (35.0)	9 (25.0)
Influenza-like illness	1 (7.1)	3 (23.1)	4 (20.0)	13 (36.1)
Myalgia	3 (21.4)	2 (15.4)	6 (30.0)	8 (22.2)

AE, adverse event; CM, combination treatment (NIZ985 + spartalizumab); QW, once weekly; SA, NIZ985 single agent; SAE, serious AE; TIW, three times weekly.