cancer treatment strategy. However, targeting CD47 leads to various hematological toxicities, particularly anemia and thrombocytopenia. Lemzoparlimab (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 lemzoparlimab 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 lemzoparlimab 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). Lemzoparlimab 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 lemzoparlimab 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 Lemzoparlimab 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.

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

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Background HEK-NIZ985 (NIZ985) is a recombinant heterodimer of IL-15/IL-15Rα 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/Ib 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 μg/kg TIW or 2–10 μg/kg QW; CM dosing was 1 μg/kg TIW or 2–4 μg/kg QW. The primary objective was to characterize the safety and tolerability of NIZ985 ± 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 ≥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 μg/kg (bullous pemphigoid, purpura, vasculitis), limiting TIW escalation and initiating QW dose exploration; these were not observed at 1 μg/kg TIW (± spartalizumab) or for QW doses up to 10 μg/kg. CM-TIW dose expansion was therefore at 1 μg/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 ≥1 μg/kg TIW and <10 μg/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

Data are n (%) patients with ≥1 event	SA-TIW (escalation) n=14	SA-QW (escalation) n=13	CM-TIW + CM-QW (escalation) n=20	CM-TIW (expansion) n=36
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.

Conclusions NIZ985 is safe and tolerable at both TIW and QW dosing ± spartalizumab. It displays approximately dose-proportional, time-dependent PK, and a biomarker and lymphocyte response profile consistent with target engagement. Limited antitumor activity was reported during dose escalation; however, preliminary responses in both IO-experienced and IO-naïve patients were seen in combination with spartalizumab that warrant further investigation.

Ethics Approval The study was approved by an independent ethics committee and/or institutional review board at each participating site.

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387 A PHASE II, MULTICENTER STUDY OF THE SAFETY AND EFFICACY OF LAG525 IN COMBINATION WITH SPARTALIZUMAB IN PATIENTS WITH ADVANCED MALIGNANCIES

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Background Expression of LAG-3, an inhibitory immunoreceptor, has been linked to reduced T-cell proliferation and cytokine production. LAG525 is a humanized IgG4 anti-LAG-3 antibody which inhibits LAG-3 binding to MHC class II. Spartalizumab is a humanized IgG4 anti-PD-1 mAb which inhibits PD-1 binding with its ligands PD-L1 and PD-L2. Preclinical data have shown promising antitumor activity when blocking LAG-3 and PD-1.

Methods The Phase II part of the first-in-human study (NCT02460224) explored LAG525 + spartalizumab in patients with advanced/metastatic non-small cell lung cancer (NSCLC), cutaneous and non-cutaneous melanoma, renal cell carcinoma (RCC), mesothelioma, or triple-negative breast cancer (TNBC). The dose/schedule of LAG525 and spartalizumab was 400 mg IV Q3W and 300 mg IV Q3W, respectively. Half of patients with TNBC naïve to anti-PD-1/PD-L1 received LAG525 at 600 mg IV Q4W and spartalizumab at 400 mg IV Q4W. The primary endpoint was overall response rate (ORR) using RECIST v1.1.

Results As of June 1, 2020, 235 patients were enrolled in the Phase II part of the study, including patients with NSCLC (n=42), melanoma (n=42), RCC (n=38), mesothelioma (n=57), or TNBC (n=56). In total, 142 patients were naïve to, and 93 patients were pretreated with, PD-1/PD-L1 inhibitors. Overall, 232 patients (99%) discontinued treatment, 76% due to progressive disease.ORR and disease control rate by indication and prior anti-PD-1/PD-L1 treatment are summarized below (table 1). Best overall response was 3 (1.3%) CR, 23 (9.8%) PR, 84 (35.7%) SD, 95 (40.4%) PD, and 30 (12.8%) unknown. For patients naïve to anti-PD-1/PD-L1, median progression free survival (mPFS) in months (90% CI) was 3.9 (1.7–5.6) for NSCLC, 2.2 (1.6–5.6) for melanoma, 4.4 (2.1–11.1) for RCC, 5.5 (3.5–6.4) for mesothelioma, and 1.9 (1.6–2.6) for TNBC. For patients pretreated with anti-PD-1/PD-L1, mPFS in months (90% CI) was 3.5 (1.9–4.9) for NSCLC, 1.9 (1.8–3.7) for melanoma, 3.0 (1.6–3.9) for RCC, 3.4 (1.8–3.8) for mesothelioma, and 1.7 (1.3–3.4) for TNBC. Adverse events of any grade, regardless of cause, were reported in 233 (99%) patients; the most common (occurring in >20%) were nausea (25%), fatigue (23%), and dyspnea (21%).

Abstract 387 Table 1 Overall response rate (ORR: CR + PR) and disease control rate (DCR: CR + PR + SD) per RECIST v1.1 by indication and prior anti-PD-1/PD-L1 treatment

ORR, % (90% CI)					
Anti-PD-1/PD-L1	NSCLC	Melanoma	RCC	Mesothelioma	TNBC
Naïve	n=20 15% (4.2–34.4)	n=20 15% (4.2–34.4)	n=19 26.3% (11.0–47.6)	n=41 17.1%* (8.3–29.7)	n=42 9.5% (3.3–20.5)
Pretreated	n=22 0% (0.0–12.7)	n=22 9.1%* (1.6–25.9)	n=19 5.3% (0.3–22.6)	n=16 6.3%† (0.3–26.4)	n=14 0% (0.0–19.3)
DCR, % (90% CI)					
Anti-PD-1/PD-L1	NSCLC	Melanoma	RCC	Mesothelioma	TNBC
Naïve	n=20 50% (30.2–69.8)	n=20 45% (25.9–65.3)	n=19 63.2% (41.8–81.2)	n=41 65.9% (51.9–78.0)	n=42 28.6% (17.4–42.1)
Pretreated	n=22 50% (31.1–68.9)	n=22 40.9% (23.3–60.5)	n=19 42.1% (23.0–63.2)	n=16 56.3%† (33.3–77.3)	n=14 21.4% (6.1–46.6)

Conclusions LAG525 + spartalizumab exhibited antitumor activity across different indications, including patients with melanoma, RCC, and mesothelioma who had been pretreated with PD-1/-L1 inhibitors, suggesting that this combination may salvage prior PD-1/-L1 resistance. The combination was well tolerated, and no new safety signals were observed. Biomarker analysis is ongoing.

Trial Registration NCT02460224

Ethics Approval This study was approved by an independent ethics committee or institutional review board at each site.

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