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 lezmoparlimab 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 lezmoparlimab 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 lezmoparlimab appears to be linear 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 1 were 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.

Abstract

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 CNI985X2102J 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 underdetermined. 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)-naive 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

<table>
<thead>
<tr>
<th>Event Category</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common AEs</td>
<td>4 (37)</td>
<td>2 (19)</td>
<td>2 (19)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Skin AEs</td>
<td>21 (190)</td>
<td>12 (110)</td>
<td>4 (37)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vascular AEs</td>
<td>6 (54)</td>
<td>3 (27)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

AE, adverse event; CM, combination treatment (NIZ985 ± spartalizumab); QW, once weekly; SA, NIZ985 single agent; SIIE, single agent IO expansion; SD, stable disease; TIW, three-times-weekly; WO, weeks-off.
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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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

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 PD-1/-L1 with PD-1/PD-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.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0387