Outcomes of patients with relapsed or refractory (R/R) B-cell acute lymphoblastic leukemia (B-ALL) remain dismal, with 5-year survival rates <20%,1 2 CD19, which is normally expressed during B-cell development, is universally present in B-cell malignancies.3–5 ADCT-402 (loncastuximab tesirine [Lonca-T]) is an antibody drug conjugate composed of a human CD19-targeting monoclonal antibody conjugated to tesirine, a pyrrolobenzodiazepine (PBD) dimer cytotoxin (Figure 1).

**RESULTS**

**Patient characteristics**

- As of October 30, 2017, 29 patients (18 male, 11 female) with B-ALL have been treated with Lonca-T (Table 2).
- Patients had a median (min, max) of 2 (1, 12) years from first treatment to enrollment.
- Eleven (37.9%) patients had priorreceive concomitant chemotherapy.
- No dose-limiting toxicities (DLTs) have been observed up to the highest evaluated dose of 150 µg/kg once every 3 weeks (q3w).
- The most recently treated cohort received Lonca-T at a dose of 50 µg/kg once weekly.

**TABLE 2. Patient baseline characteristics (analysis safety set)**

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Total (N=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%)</td>
<td>Females (11/27)</td>
</tr>
<tr>
<td>Age, years</td>
<td>Median (min, max) = 18 (0–12)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>Black or African American (5/20)</td>
</tr>
<tr>
<td>Number of previous chemotherapies</td>
<td>Median (min, max) = 2 (0–6)</td>
</tr>
<tr>
<td>Number of previous chemotherapies</td>
<td>Median (min, max) = 2 (0–6)</td>
</tr>
</tbody>
</table>

**Lonca-T TK data**

PK data show PBD-conjugated antibody and total antibody concentrations below quantifiable levels of 5.0 and 20 ng/mL, respectively, well before end of the 21-day treatment cycle (Figure 5). PK data were largely below measurable levels throughout the course time, justifying a change to weekly dosing.

**Lonca-T safety**

Treatment-emergent adverse events (TEAEs) were reported by 28/39 (72.3%) patients with 265 TEAEs reported in total. Twelve (41.4%) patients reported adverse events deemed to be possibly or probably related to Lonca-T. The most common TEAEs were:
- Nausea (n=9)
- Fatigue (n=7)
- Febrile neutropenia (n=7)
- Headache (n=7)

Grade 3/4 TEAEs were reported in 24/29 (82.8%) patients, of which febrile neutropenia (n=7) and neutrophil count decrease (n=7) were the most common (Table 3).

Two patients experienced TEAEs with fatal outcomes (lung infection and sepsis), both from the 120 µg/kg q3w dosing group.

Four patients experienced TEAEs leading to a dose delay or reduction, but no TEAEs led to treatment withdrawal.

- Liver toxicity events were reported in 7 patients, leading to dose delay in 1 patient (owing to hepatic steatosis).

- Four patients experienced Grade 3 liver toxicity events, including during Cycle 1, all were reversible (median [range] duration) 11.5 [6–36] days) and not related to veno-occlusive disease.

- There were 3 infection-related reactions, including 1 case each of Grade 2 infusion-related reaction and cytokine release syndrome, and 1 case of Grade 1 tachycardia.

- The MTD has not yet been reached.

**CONCLUSIONS**

- In this Phase 1 study in patients with R/R B-ALL, single-agent Lonca-T was well tolerated with no DLTs and showed 2 MRD-negative complete remissions in a heavily pretreated population.

- Dose escalation will continue to find the MTD for a weekly regimen.

- A dose-expansion phase in part 2 of the study is planned to further evaluate the tolerability, safety, PK, and activity of Lonca-T.

**Acknowledgments**

The authors would like to thank and acknowledge the participating patients and their families, and all study personnel involved in the Lonca-T clinical development program. Loncastuximab tesirine is given intravenously on Day 1 of each 21-day cycle. Lonca-T has excellent stability in preclinical in vivo models.8 Lonca-T is given intravenously on Day 1 of each 21-day cycle for patients treated every 3 weeks, and on Days 1, 8, and 15 for patients assigned to a weekly dosing regimen (Figure 4). Part 2 will further evaluate the safety, tolerability, PK, and clinical activity of Lonca-T the dose recommended from part 1.

**Completes response is defined as achieving each of the following:**

- Bone marrow differential showing ≤5% blast cells
- Absolute neutrophil count ≥1.5 × 10⁹/L and platelet count ≥100 × 10⁹/L
- Absence of extramedullary disease
- Patient is independent of red blood cell transfusions.

**REFERENCES**

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