CD79b is expressed on a majority of B cell-derived malignancies, including nearly all non-Hodgkin lymphomas ( NHL) and chronic lymphocytic leukemia (CLL). Insulin B-cell malignancies remain incurable, as do approximately a third of aggressive NHLs, despite improvements in clinical outcomes of NHL, patients with treatments such as rituximab.

DCDS0780A is a THIOMAB™ antibody drug conjugate (TDC) consisting of the potent anti-mitotic agent, monomethyl auristatin (E), conjugated to a humanized IgG, anti human CD79b monoclonal antibody via a cross-link linker.

The DCDS0780A TDC encompasses THIOMAB™ antibody technology, which allows an essentially homogeneous payload from the conjugation of 2 drugs per antibody engineered cytokines.

OBJECTIVES

To determine the safety, tolerability, pharmacokinetics (PK), maximum tolerated dose (MTD), and dose-limiting toxicities (DLT) of DCDS0780A alone and in combination with rituximab in patients with relapsed/refractory B-NHL.

To determine the recommend Phase II dose (RP2D) and biologic activity of DCDS0780A alone and in combination with rituximab in the same patient population.

METHODS

Patients with histologically confirmed B-cell NHL that had relapsed or failed to respond to at least one prior treatment regimen and for which no suitable curative or higher priority therapy existed were enrolled. Patients received DCDS0780A (0.3–4.8 mg/kg intravenously every 21 days until disease progression or unacceptable toxicity in a standard 3+3 design) DLT were assessed in Cycle 1. Additional patients were enrolled at doses achieving clinically following confirmation of tolerability in order to further evaluate safety and efficacy based on Lugano Classification.

The protocol was approved by Institutional Review Boards prior to patient recruitment and was conducted in accordance with ICH Guidelines, written informed consent was obtained from all patients prior to performing study-related procedures in accordance with federal and institutional policies.

The study was registered on ClinicalTrials.gov (NCT01453087).

RESULTS

Patient characteristics

As of the data cutoff date of 19 Sep, 2017, 60 patients were enrolled (Table 1).

Table 1. Patient Demographics and Baseline Characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DCDS0780A monotherapy</th>
<th>Rituximab + DCDS0780A</th>
<th>Rituximab alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>67 (22–84)</td>
<td>71 (44–82)</td>
<td>71 (40–95)</td>
</tr>
<tr>
<td>Sex: Male/Female</td>
<td>29 (57)</td>
<td>3 (33)</td>
<td>13 (40)</td>
</tr>
<tr>
<td>ECOG performance status</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Type of malignancy</td>
<td>DLBCL</td>
<td>DLBCL</td>
<td>DLBCL</td>
</tr>
<tr>
<td>Prior Rituximab</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Prior rituximab dose</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Prior rituximab duration</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Safety

Adverse event (AE) profile were similar between DCDS0780A monotherapy at 2.4 mg/kg and DCDS0780A + rituximab.

Table 2. AE Profile for DCDS0780A + Rituximab Compared to Rituximab Alone.

<table>
<thead>
<tr>
<th>AE</th>
<th>DCDS0780A + Rituximab (n=25)</th>
<th>Rituximab alone (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 3–4 (n=%)</td>
<td>8 (32)</td>
<td>6 (24)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>7 (28)</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>5 (20)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>3 (12)</td>
<td>0</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>3 (12)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2 (8)</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

Conclusions

The anti-tumor activity of DCDS0780A was encouraging in this Phase I study; patients receiving a dose of ≥ 2.4 mg/kg had 57% overall response rate, including 24% complete response in 43% of DLBCL patients. The overall safety and tolerability profile at that dose was consistent with prior reports of DCDS0780A.

REFERENCES

Cheson et al., J Clin Oncol 2014;32:3059–68.

DISCLOSURES

We thank the patients who participated in the study and their families.

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ASCO 2017 Annual Meeting, December 9-12, Atlanta, GA