The B lymphocyte-derived malignancies represent a diverse group of diseases, including non-Hodgkin’s lymphoma (NHL) and chronic lymphocytic leukemia (CLL). Compared to chemotherapy alone, XmAb13676 is being studied in two separate NHL safety populations: BRUK17001 and BRUK17002. Considered a humanized antibody that binds to CD20, expressing target cells and to CD3, to recruit and activate T cells, XmAb13676 is being studied in two groups of patients with relapsed or refractory B-cell malignancies, both NHL and CLL.

### Methods

#### Study Design:
- **Objective:** Phase 1, dose-escalation and expansion study to assess the safety and tolerability of XmAb13676 monotherapy

- **Study Population:**
  - Part A: weekly dosing to establish a "dosing window" initially selected as 80 µg/kg and subsequently reduced to 45 µg/kg in the NHL group
  - Part B: escalating 3-dose cohorts with an initial "peak" dose of 80 µg/kg
  - Cycle 1 Day 1 followed by higher step-up doses to determine MTD/DRD

- **Key Inclusion criteria:
  - Adult (age ≥ 18 years)
  - Diagnosis of either B-cell NHL or CLL
  - ECOG performance status of 0-2

- **Key Exclusion criteria:
  - Refusal or is not a candidate for hematopoietic stem cell transplantation

### Results

#### Patient disposition, treatment exposure, baseline characteristics, and prior treatments

- As of 8 November 2019, 53 patients (45 NHL and 8 CLL GLL) were treated with XmAb13676 monotherapy and are included in the safety analysis (ECOG performance status 0-2)

- Patients with diffuse large B-cell lymphoma (DLBCL) receiving highest doses of 80-170 µg/kg are included in analyses to define clinical activity (Table 2).

#### Safety

- **Most events were mild or moderate in severity (Table 3).**
- **Nervous system disorders occurred in 26 (49.1%) patients (data not shown).**
  - The most common nervous system events were dizziness (17%), headache (17%), paresthesia (9.4%), and lethargy (5.7%).
  - One (2.2%) patient experienced overt short-term encephalopathy (Grade 2) during a cytokine release syndrome (CRS) event that resolved concomitantly with discontinuation of the CRS.
  - One (2.2%) patient lost consciousness (Grade 1) during a bowel movement (likely vasovagal).

- **Cytokine Release Syndrome (CRS):**
  - **At least 1 CRS event occurred in 28 (52.8%) patients (Table 4).
  - Of these 28 CRS events, 25 (89%) were Grade 1 or 2 in severity (data not shown).
  - Of the 25 patients who experienced CRS, 23 patients had prior treatment exposure to ECOG Cooperative Eastern Group (ECOG) performance status 0-2.**

- **Relapsed/progression after last systemic therapy:**
  - Yes: 14 (77.8)
  - No: 3 (16.7)

#### Table 2: Baseline characteristics and Prior treatments

<table>
<thead>
<tr>
<th>Event, n(%)</th>
<th>NHL</th>
<th>CLL</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRS, n (%)</td>
<td>25 (89)</td>
<td>22 (88)</td>
<td>47 (89)</td>
</tr>
<tr>
<td>Responsive Hct</td>
<td>14 (77.8)</td>
<td>16 (60)</td>
<td>30 (57)</td>
</tr>
<tr>
<td>Non-responsive Hct</td>
<td>5 (27.8)</td>
<td>5 (17.2)</td>
<td>10 (19)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (11.1)</td>
<td>1 (4)</td>
<td>3 (5.7)</td>
</tr>
</tbody>
</table>

#### Table 3: Summary of TEAEs

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#### Table 4: Best ORR with DLBCL Patients

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</table>

#### Clinical Activity

- **Clinical Activity:**
  - The data cut-off date for the analyses to define clinical activity was 8 November 2019 and includes patients who achieved a high dose with XmAb13676 was 80 µg/kg and above (Table 4).

- **Time on treatment and treatment exposure in DLBCL safety population:**
  - Two patients had dose reductions due to toxicity, one dose reduction for fatigue and one dose reduction for neutropenia.

#### References


#### Conclusions

- In the ongoing dose-escalation phase 1 study in B-cell malignancies, the CD20xCD3 bispecific antibody XmAb13676 was generally well tolerated.
- CRS, an AE associated with this class of agents, was observed in 52.8% of patients.
- Other events that may be consistent with symptoms of CRS were observed in an additional 22.6% of patients.
- Most CRS events occurred with the first dose of XmAb13676 and were Grade 1 and 2 by the Lee criteria.
- There were no Grade 3 or 4 CRS events once treatment was initiated.
- XmAb13676 demonstrated clinical activity in DLBCL at doses of 80 µg/kg and higher (top dose tested 170 µg/kg in a dose-dependent manner).
- In DLBCL, the objective response rate was 71% (38.9%), and the complete response rate was 5/18 (27.8%).
- Additional responses have been observed in Waldenström macroglobulinemia and Richter transformation of CLL, both CRS and both at 20 µg/kg, with one CRS event and one step-up to 170 µg/kg, also a CR (1/5 at 80 µg/kg).
- PK was dose proportional (data not shown). Doxorubicin and schedule optimization are ongoing.

Acknowledgments