Ublituximab is a novel chimeric mAb targeting a unique epitope (Figure 1) on the CD20 antigen. Ublituximab has been glycoengineered to enhance affinity for all variants of Fcγ receptors, and thus demonstrates greater ADC activity than rituximab (RTX) in vitro (Le Garff-Taverniere, 2011), specifically in low-CD20 tumors (ASH 2011). In non-Hodgkin lymphomas in vivo, Ublituximab also displayed greater antitumor activity than rituximab (ASH 2011). A completed Phase I trial with ublituximab used as a single agent in patients with relapsed/refractory CLL showed manageable toxicity with dose escalation on the Phase I dose-escalation of ublituximab in patients with rituximab (RTX) relapsed/refractory B-cell lymphoma.

**RESULTS**

**Overall Response by Lymphoma Subtype**

<table>
<thead>
<tr>
<th>Lymphoma Subtype</th>
<th>Type</th>
<th>PRs (%)</th>
<th>CRs (%)</th>
<th>SDs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FL</td>
<td>6</td>
<td>2 (17)</td>
<td>2 (17)</td>
<td>4 (33)</td>
</tr>
<tr>
<td>MCL</td>
<td>5</td>
<td>2 -</td>
<td>2 (40)</td>
<td>4 (67)</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>4 (13)</td>
<td>9 (30)</td>
<td>13 (43)</td>
</tr>
</tbody>
</table>

**Efficacy**

- **Best % Change From Baseline in Nodal Size**
- **Median time to CR in ALC 1 Day**

**CONCLUSION**

- Ublituximab is well tolerated even at the highest dose cohort levels tested with no DLT observed. Day 1 IRRs are the most frequent AE (G 1/2 only) and occurred more often in CLL patients. G 3/4 events have been limited. No MTD was reached.
- Infusion times decreased to an average of 90 minutes for the 4th and subsequent infusions.
- Significant single agent activity observed in patients with rituximab relapsed/refractory CLL and indolent NHL patients.
- Rapid and profound circulatory lymphocyte depletion in CLL patients with median time to a peripheral response (>50% reduction) of 1 day.
- Patient responses have been durable (patients in response >1 year on single agent ublituximab) with some having an improvement in response over time with continued ublituximab maintenance.
- Safety profile of ublituximab supports combination therapy with studies of ublituximab in combination with PI3K delta and BTK inhibitors ongoing.
- Phase III studies in B-cell malignancies are currently in development.