**BACKGROUND**

Ublituximab (TG-1101) is a novel, chimeric monoclonal antibody (mAb) targeting a unique epitope on the CD20 antigen. Ublituximab has been glycengineered to enhance affinity for all variants of FcγRIIIa receptors and therefore displays greater antibody-dependent cytotoxicity (ADCC), activity in rituximab- and ofatumumab-pretreated patients, particularly against tumor cells that express low CD20 levels. A recent protocol amendment allows for inclusion of CLL Cohort expansions identified based on efficacy/safety: ECOG ≤ 150. A 50% ORR (3 CR's / 2 PR's) has been achieved with UTX in CLL patients. Tolerability varies, the protocol was amended during Cohort 2 to allow a revised dose escalation. Phase I/II studies are currently ongoing with ublituximab in patients with rituximab relapsed and refractory B-cell lymphoma. TG-1101-310 is a study of single agent ublituximab in three patient populations; while TG-1101-315 is a study of ublituximab administered in combination with lenalidomide, an immunomodulating agent that has demonstrated activity in lymphomas and has been shown to enhance the ADCC activity of anti-CD20 antibodies. Herein we report on the Phase I dose-escalation portion of both these ongoing studies.

**STUDY DESIGN**

Study TG-1101-3101 (Clinical Identifier NCT01647997) is a Phase I/II that currently enrolling with the following endpoints:
- Primary: Safety and Maximum Tolerated Dose (MTD)
- Secondary: Efficacy in defined by overall response rate (ORR, PR + CR) + Pharmacokinetic (PK) and PFS

Phase I Cohort Design: 3 + 3 dose-escalation design of 4 cohorts

**RESULTS**

**DEMOGRAPHICS**

### TG-1101-102: Ublituximab + Lenalidomide in Rituximab Relapsed and Refractory Patients

**Key Inclusion Criteria**
- Relapsed or refractory to rituximab and/or CHOP
- Measurable disease
- serum LDH within 1.5 times upper limit of normal
- Adequate organ function

**RESULTS**

Among the 12 patients treated in the dose-escalation phase I component of this study, no DLTs have been observed, and thus no MTD has been achieved. All adverse events (CTCAE v.4.0) are summarized as follows:

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pruritus</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dysphonia</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Key Inclusion Criteria**
- Relapsed or refractory to rituximab and/or CHOP
- Measurable or evaluable disease
- CD19+ B-NHL

**Safety**

Infections and infusion-related reactions were the most frequent adverse events observed in this study. The incidence of infections was 90% (9/10 patients), with 2 cases of grade 3 infection and 1 case of grade 4 infection. Infusion-related reactions were observed in 90% of patients (9/10), with 2 cases of grade 3 reaction and 1 case of grade 4 reaction. No deaths were reported during the study. Therefore, the MTD of Ublituximab in combination with Lenalidomide was not reached.

**Dosing Schedule**

Ublituximab is administered on Days 1, 8, and 15 of Cycles 1 and 2 (Cycle = 28 days) during the induction period, followed by maintenance infusions for patients achieving stable disease or better on Day 1 of Cycles 3, 6, and every 3 months thereafter.

**CONCLUSIONS**

- Ublituximab in combination with lenalidomide was well tolerated in patients with relapsed or refractory B-cell lymphoma.
- Further studies in rituximab-relapsed/refractory patients are warranted.
- Pharmacokinetic data will be provided to support further development of this combination.

**Abstract**

**Presentation**

Presented at the 18th Congress of the European Hematology Association (EHA) June 13 – 16, 2013, Stockholm, Sweden