INTRODUCTION

Ublituximab (UXT) 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 FcγRIIa receptors, and thus demonstrates greater ADCC activity than rituximab (RTX) in vitro (Le Gaff-Tavernier, 2011), specifically in low-CD20 tumors (Hoare, 2011). In Non-Hodgkin’s lymphoma in vivo models, ublituximab also displays 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 reported a response rate of 45% (ASH 2011). Herein we report on the Phase I dose escalation of ublituximab in patients with relapsed/refractory B-cell lymphoma.

STUDY DESIGN

Study TG-1101-01 (Clinical Identifier NCT01647971) is a Phase I/II trial currently ongoing with the following endpoints:

- **Primary:** Safety and Maximum Tolerated Dose (MTD)
- **Secondary:** Efficacy as defined by overall response rate (ORR), progression-free survival (PFS), and overall survival (OS).

Phase I Cohort Design: Ublituximab administered weekly x 4 in Cycle 1 (cycle ~ 28 days)

- **Induction:** monthly infusions for patients with SD or better response starting Cycle 3, and infusions every 3 months starting Cycle 6

### Key Inclusion Criteria

- Relapsed or refractory to prior RTX-based regimen (refractory = progressing on or within 6 months of RTX, relapsed > 6 months after RTX)
- B-cell Non-Hodgkin’s Lymphoma with measurable/evaluable disease
- **ECOG ≤ 2, No Hepatitis B/C or HIV**
- Adequate organ / marrow function with baseline ANC > 1,000 cells/µL and platelets ≥ 50,000/µL

### RESULTS

#### Demographics

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Cohort 2</th>
<th>Cohort 3</th>
<th>Cohort 4</th>
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<tbody>
<tr>
<td>450 mg</td>
<td>600 mg</td>
<td>900 mg</td>
<td>1200 mg</td>
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#### Efficacy

- **Cycle 1 Day 1**
  - **Adverse Event**
    - Arthralgia
    - Fatigue
    - Pain
    - Rash
    - Throat irritation
  - **Grade 1**
    - 1
  - **Grade 2**
    - 2
  - **Grade 3**
    - 2
  - **Grade 4**
    - 0

- **Induction**
  - **Adverse Event**
    - Arthralgia
    - Fatigue
    - Pain
    - Rash
    - Throat irritation
  - **Grade 1**
    - 1
  - **Grade 2**
    - 1
  - **Grade 3**
    - 0
  - **Grade 4**
    - 0

#### Safety

All 12 patients received all planned infusions. 4/12 had an infusion interruption. However, all patients finished their dose on the planned day:

- **3 patients** had their dose interrupted in Cycle 1/Day 1 (infusion Related Reaction-IRR)
- **1 patient** had their dose interrupted in Cycle 1/Day 8 (IRR)

### Progression Free Survival Analysis

- **Median:** Not Reached
- **HR:** 0.61
- **95% CI:** (0.49, 0.78)

### CONCLUSION

- Ublituximab has been well tolerated at all dose cohorts with minimal IRIR and limited G 3/4 events reported. Infusion times significantly decreased from the 1st to the 4th infusion.
- A 50% ORR (3 CR’s / 2 PRs) has been achieved with UTX in rituximab refractory patients, and 9/12 patients remain on UTX treatment with median PFS not reached.
- 3/3 MZL patients achieved an objective response (1 CR in RTX refractory, 1 CR & 1 PR in RTX relapsed patients). All MZL patients remain on ublatiximab maintenance treatment now at 5, 7, and 10+ months.
- Cohort expansions identified based on efficacy/safety: 900 and 1200 mg cohorts opened for NHL patients.
- A recent protocol amendment allows for inclusion of CLL patients at 600 mg with future dose escalations planned; enrollment continues in all expansion cohorts.
- Future studies in rituximab refractory/MZL are planned. As ublatiximab has been well tolerated, additional combination studies with novel agents for B-cell lymphoma are in development.