**INTRODUCTION & PURPOSE**

Ublituximab (UTX, TG-1101) is a novel chimeric monoclonal antibody (mAb) that targets a unique epitope on CD20. Ublituximab is glycoengineered to enhance affinity for all activating FcγRIIIa receptors, thereby demonstrating greater antibody-dependent cellular cytotoxicity (ADCC) activity than rituximab, ofatumumab or obinutuzumab.

In vitro studies, ublituximab demonstrated 100 times greater natural killer (NK) cell-mediated ADCC than rituximab in patient donor chronic lymphocytic leukemia (CLL) cells (Ja-Guirr-Taverin et al, 2011).

To date, over 1500 patients with various B cell mediated diseases have been treated with ublituximab, with completed relapsing multiple sclerosis (RMS) and oncology studies demonstrating robust activity, with favorable safety tolerability. In addition, two Phase III trials in RMS are fully enrolled, the UBLATEX I & II trials.

**METHODS PHASE 2 & OLE**

TG1101-1MS201 (NCT01758171) was a 52 week randomized, placebo controlled, multicenter Phase 2 study to test the safety and efficacy of ublituximab at a range of infusion times, with a goal of rapid infusions.

To qualify for the study, subjects needed to have a diagnosis of relapsing MS, by 2010 McDonald Criteria, and either one confirmed MS relapse in the past year, 2 relapses in the past two years, or at least one active Gd-enhancing T1 lesion at the screening MRI.

To qualify for the OLE, subjects must have completed three infusions of ublituximab, have completed the scheduled assessments up to the Week 48 visit of TG-1101-1MS201, and be in good health with stable disease.

**RESULTS**

**OLE SAFETY UPDATE**

All AEs Deemed at Least Possibly Related to UTX

<table>
<thead>
<tr>
<th>Phase (N=48)</th>
<th>OLE (N=45)</th>
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</thead>
<tbody>
<tr>
<td>Regrettable</td>
<td>Related to UTX</td>
</tr>
<tr>
<td>Patients with an AE</td>
<td>48 (100%)</td>
</tr>
<tr>
<td>Patients with a Grade 3/4 AE</td>
<td>8 (17%)</td>
</tr>
<tr>
<td>AEs leading to withdrawal</td>
<td>1 (2%)</td>
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</tbody>
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1. Excludes infusion related reactions (IRRs)

**OLE STUDY DESIGN**

- All subjects enrolled on the OLE, regardless of their cohort assignment in the Phase 2, will receive 450mg of ublituximab administered in a one hour infusion every 24 weeks with the first infusion given within 60 days of completing the Phase 2.
- Each infusion visit is accompanied by routine physical exam, routine blood chemistry, and an assessment of adverse events to evaluate long-term safety and tolerability.
- EDSS assessments are conducted every 48 weeks to assess long-term disability outcomes.

**PATIENT DEMOGRAPHICS & DISPOSITION**

**OBJECTIVES**

- The objective for the ublituximab RMS Phase 2 study (TG-1101-1MS201) was to determine whether the enhanced ADCC potency of ublituximab translates into additional clinical benefits for MS patients, in the form of lower doses and faster infusion times than current anti-CD20 infused therapies.
- The objective for the Open Label Extension (OLE) of the Phase 2 study is to evaluate the long-term safety and tolerability and long-term disability outcomes of ublituximab treatment in subjects continuing treatment after completion of TG-1101-1MS201 Phase 2 trial.

**CONCLUSIONS**

- Ublituximab continues to be well tolerated, with a median duration of follow-up of 124.7 weeks.
- No drug related discontinuations occurred during the Phase 2 or on the OLE.

**INFUSION RELATED REACTIONS (IRRs)**

All patients on the OLE received 450mg administered in a one hour infusion, with 100% of patients receiving at least one infusion, and 96% of patients receiving 2 or more infusions.

86% were infrequent during the OLE, occurring in 5 patients (11%), all Grade 1 or 2, with no patient experiencing an RR for the first time on the OLE.

During the Phase 2, IRRs were most frequent on Day 1, with 33% of patients experiencing an RR on Day 1 when given 150mg of UTX over 4 hours (the Phase 3 Day 1 dose).

**FINAL PHASE 2 WEEK 48 EFFICACY RECAP**

- No T1 Gd lesions were detected in any subjects at Week 24 or at Week 48 (100% reduction; p<0.003).
- Ublituximab (UTX) was well tolerated with a median duration of follow-up of 124.7 weeks.
- No drug related discontinuations occurred during the Phase 2 or on the OLE.

**Adverse Event (AE) Summary**

- All AEs considered at least possibly related to UTX.
- 86% of subjects experienced ≥1 relapse in the year prior to screening.
- Mean number of relapses = 1.45.
- Median number of relapses = 2.
- OLE: 45 subjects entered the OLE.
- Mean Age: 41 years
- 64% Female

**Phase 2**

- 86% of subjects experienced ≥1 relapse in the year prior to screening.
- Mean number of relapses = 1.45.
- Median number of relapses = 2.

**OLE**

- 45 subjects entered the OLE.
- Mean Age: 41 years
- 64% Female

**All patients on the OLE received 450mg administered in a one hour infusion, with 100% of patients receiving at least one infusion, and 96% of patients receiving 2 or more infusions.**

**IRRs were infrequent during the OLE, occurring in only 5 patients (11%), all Grade 1 or 2, with no patient experiencing an RR for the first time on the OLE.**

**During the Phase 2, IRRs were most frequent on Day 1, with 33% of patients experiencing an RR on Day 1 when given 150mg of UTX over 4 hours (the Phase 3 Day 1 dose).**

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