**INTRODUCTION AND METHODS**

Ublituximab (T25, TG-1101) is a novel chimeric monoclonal antibody (mAb) that targets a unique epitope on the CD20 antigen. It is also glycoengineered to enhance affinity for all variants of FcγRIIa receptors, thereby demonstrating greater antibody-dependent cell-mediated cytolysis (ADCC) activity than maximals and off-targets.

In an earlier study, ubliltuximab demonstrated 100 times greater natural killer (NK) cell-mediated ADCC than rituximab in patient-derived GLL cells for Geoff Toftevoll et al., 2012).

**Binding Epitopes of Anti-CD20 Antibodies**

**METHOD & STUDY DESIGN**

To date, over 1000 patients with various B cell malignancies have been treated with ubliltuximab and two multicenter Phase III trials are complete or in progress (GENUINE and UNITI, respectively). Completed oncology studies have demonstrated robust efficacy with excellent safety and tolerability. In addition to the oncology studies, two Phase III trials in MS are ongoing.

The objective for the ubliltuximab-RMS Phase 2 program is to determine whether the enhanced ADCC potency of ubliltuximab can translate into additional clinical benefits for MS patients, in terms of slower disease progression and faster infusions than current anti-CD20 infused therapies.

**RESULTS**

**Methods & Study Design**

Ublituximab (UTX; TG-1101) is a novel chimeric mAb that targets a unique epitope on the CD20 antigen. It is also glycoengineered to enhance affinity for all variants of FcγRIIa receptors, thereby demonstrating greater ADCC activity than maximals and off-targets.

No T1 Gd-enhancing lesions detected in any subjects at Week 24 or 48 (100% reduction; p=0.003). Subjects saw 10.6% reduction in total T2 lesion volume from baseline to Week 48 (p=0.002).

Annualized Relapse Rate (ARR) of 0.07 was observed at Week 48, with 93% of subjects being relapse free. 74% of subjects fulfilled the criteria for NEDA.

**Safety & Tolerability**

Ublituximab was well tolerated and no drug-related discontinuations occurred. The most common Adverse Events (AEs) were Infusion Related Reactions (IRR), all Grade 1 or 2. IRRs were most frequent with the first infusion (Day 1) and infused in 100% of total infusions. Most frequently reported AEs were Infusion Related Reaction (48%), Rash (22%), Pain (8%), Headache (8%), Infusion Related Reaction (48%), Rash (22%), Pain (8%), Headache (8%).

**DISCUSSION**

The objective for the ubliltuximab-RMS Phase 2 program is to determine whether the enhanced ADCC potency of ubliltuximab can translate into additional clinical benefits for MS patients, in terms of slower disease progression and faster infusions than current anti-CD20 infused therapies.

**SUMMARY**

Ublituximab was well tolerated and no drug-related discontinuations occurred. The most common Adverse Events (AEs) were Infusion Related Reactions (IRR), all Grade 1 or 2. IRRs were most frequent with the first infusion (Day 1) and infused in 100% of total infusions. Most frequently reported AEs were Infusion Related Reaction (48%), Rash (22%), Pain (8%), Headache (8%).

**REFERENCES**

1. Central Texas Neurology Consultants, The Ohio State University, Microbial Infection and Immunity, Akamai Neurology Center, Assistive Speech & Motor Center, TG Therapeutics, Inc.
2. Tavernier et al, 2011
3. **NEDA is defined as subjects without relapses, MRI activities (no T1 Gd-enhancing lesions and 26% had ≥4 T1 Gd lesions)**

**CONCLUSIONS**

Ublituximab was well tolerated and no drug-related discontinuations occurred. The most common Adverse Events (AEs) were Infusion Related Reactions (IRR), all Grade 1 or 2. IRRs were most frequent with the first infusion (Day 1) and infused in 100% of total infusions. Most frequently reported AEs were Infusion Related Reaction, Rash, Pain, Headache, Infusion Related Reaction.

A rapid infusion time, as low as one hour, 450mg was well tolerated, produced high levels of B cell depletion and is now being studied in the Phase 3 clinical trials in MS.

**PRESENTATION**

Final Results of a Placebo Controlled, Phase 2 Multicenter Study of Ublituximab (UTX), a Novel Glycoengineered Anti-CD20 Monoclonal Antibody (mAb), in Patients with Relapsing Forms of Multiple Sclerosis (RMS)