**BACKGROUND**

Ublituximab (TG-1001, previously LUBR020) is a novel, chronic monoclonal antibody (mAb) targeting a unique epitope on the CD20 antigen. Ublituximab has been designed to enhance affinity to all variants of FcγR receptors and therefore demonstrates greater antibody-dependent cellular cytotoxicity (ADCC) activity than rituximab and ofatumumab, particularly against tumor cells that express low levels of CD20. A two-part, first-in-human study was conducted, evaluating ublituximab monotherapy in patients with relapsed and refractory Chronic lymphocytic leukemia (CLL). In the dose-escalation Part 1 of this study, a weekly 4 dose regimen was found to be safe, rapid, and sustained blood lymphocyte depletion in patients with advanced stage IGL (SGI 2010, #3447). The second part of the study (Phase II) was designed to evaluate a fixed, weekly 3 dose regimen for safety, pharmacokinetics (PK) and efficacy of ublituximab in the same population herein. We report the final results of the Phase II study.

**UBLITUXIMAB**

Ublituximab, a next generation anti-CD20 antibody currently in clinical development, is characterized by a specific glycopattern containing a high percentage of non-fucosylated antibody molecules at the Fc region. This specific pattern of glycosylation increases the affinity of antibodies for human FcγRIIIA (CD16a), resulting in an increased antibody dependent cell-mediated cytotoxicity (ADCC) by human FcγRIIIA-expressing effector cells.

**RESULTS**

**Safety**

- All patients except one received all 8 planned infusions without any dose reduction. Patients D1-D6 was withdrawn from the study after the second ublituximab infusion due to a concomitant secondary AEs. A total number of 57 drug-related AEs were included resulting 23 grade 3-4 AEs.
- No drug-related mortality was recorded, and there were no deaths on study.

**Pharmacokinetics**

Main PK findings are summarized as follows: mean Css, AUC0-24h and terminal half-life increased and mean clearance decreased from the first to the 8th infusion of ublituximab.

**METHODS**

**Study Regimen**

Ublituximab was administered once weekly for 8 weeks with an initial 150 mg loading infusion in the first week, followed by 7 weekly doses at 450 mg (total 3100 mg) ublituximab. Response assessment was conducted at Week 16, with a confirmatory assessment conducted at Week 24 for responders.

**Pharmacokinetic Evaluation**

PA was expanded on blood samples collected over the 12 month study period, with PK profiles after the 1st infusion. PK results were compared to the results of a 1st infusion in a first-in-human study performed at 3 different sites in the USA and France.

**CONCLUSION**

- Ublituximab induced a durable 45% ORR in patients with advanced CLL at a relatively low dose regimen
- Ublituximab showed a manageable and consistent anti-CD20 directed therapy, allowing for development of combination therapies
- Future development strategies in CLL and other low-CD20 expressing tumors, in addition to rituximab-refractory/refractory patient is warranted and underway.