A Phase I Trial Of Ublituximab, A Novel Glycoengineered Anti-CD20 mAb, In Combination With TGR-1202, A Next Generation PI3Kδ Inhibitor, In Patients With Chronic Lymphocytic Leukemia And Non-Hodgkin’s Lymphoma

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Background

- Ublituximab (TG-1101) is a novel, chimeric monoclonal antibody (mAb) targeting a unique epitope on the CD20 antigen, and glycoengineered to enhance affinity for all variants of FcγRIIIa receptors, thereby demonstrating greater antibody-dependent cellular cytotoxicity (ADCC) activity than rituximab and ofatumumab.
- Two Phase I trials of single agent ublituximab in patients with relapsed/refractory CLL reported response rates of 67% (ASCO 2014) and 45% (EHA 2013), with rapid and sustained lymphocytosis.

Study Design

- Study UTX-TGR-103 (NCT02004485) is an ongoing Phase I/II trial evaluating the combination of ublituximab + TGR-1202 in patients with relapsed or refractory NHL and CLL.
- The study is divided into two parts:
  - Phase I: 3+3 Dose Escalation evaluating Cycle 1 DLTs for CLL & NHL separately
  - Phase II: Dose confirmation

Key Eligibility Criteria

- Combined CD20-negative, non-Hodgkin lymphoma (NHL) or CLL/small lymphocytic lymphoma (SLL), and select other B-cell lymphoproliferative disorders
- Relapsed after, or refractory to, at least 1 prior treatment regimen with no limit on prior therapies
- ECOG performance status ≤ 2
- Adequate organ system function: ANC ≥ 750/μL; platelets ≥ 100,000
- Patients with Richter’s Transformation, or refractory to prior PI3Kδ inhibitors or prior BTK inhibitors are eligible

Study Objectives

- To assess safety, and Maximum Tolerated Dose (MTD) of UTX + TGR
- To assess efficacy (overall response rate, time to response, duration of response, progression free survival)

Objectives for Primary Efficacy

- Primary Efficacy
  - Hematologic and surrogate responses
  - Safety
- Secondary Efficacy
  - Hematologic and surrogate responses
  - Safety

Efficacy

- Related AE’s occurring in ≥ 2 Patients (n = 21)
- Adverse Event
  - Total AEs
  - UTX-related AEs
  - UTX-related AEs ≥ Grade 3/5

Safety

- Patients were hematoxynally, and included high risk subgroups:
  - ≥3 prior treatments including ≥2 lines of BTK (≥2 TG-1202 doses)
  - ≤5 doses of DLI with patients who have relapsed TGR-1202

Conclusions

- Preliminary data suggests ublituximab in combination with TGR-1202 is well tolerated and highly active in a heavily pre-treated population of patients with relapsed or refractory NHL and CLL.
- No drug related increases in ALT/AST observed to date.
- Notta and Neopterin were monitored through dose levels
- Neopterin related dose related met for a DLT in a CLL patient at UTX-600 mg (TGR-800 mg), neutrophilia enrollment of additional patients into this cohort
- No patients had their UTX or TGR dose reduced
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