Ublituximab + TGR-1202 Demonstrates Activity and Favorable Safety Profile in Relapsed/Refractory B-Cell NHL and High-Risk CLL

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Study Design
Study UTX-TGR-103 (NCT02006485) is an ongoing Phase Ib/II trial evaluating the combination of ublituximab + TGR-1202 in patients with relapsed or refractory NHL. The study is divided into two parts:

- Phase I: 3+3 Dose Escalation evaluating Cycle 1 DLTs (CLL & NHL separately)
- Phase II: Dose Expansion

Ublituximab (TG-1301) is a novel, chimeric monoclonal antibody (mAb) targeting a unique epitope on the CD20 antigen, and glycengineered to enhance affinity for all variants of FyH+ 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 lymphocyte depletion.

TGR-1202

PI3K

- PI3K-δ (S656)
- PI3K-γ (S1047)

Rearrangement

- BCR/ABL
- IGH/CCND1
- MYC

PI3K Generation

- Ublituximab + TGR

Phase II for TGR Dose (QD)

- TGR is a next generation PI3K inhibitor, with a unique structure and activity profile distinct from other PI3K family inhibitors, enabling

- A prolonged half-life that enables once-daily dosing

- A differentiated safety profile from other PI3Kδ inhibitors in development, notably with respect to hepatic toxicity and colitis to date.

Study Objectives

Primary Objectives:

- To assess the Safety and Maximum Tolerated Dose (MTD) of Ublituximab + TGR-1202

Secondary Objectives:

- To assess Efficacy overall response rate, time to response, duration of response, progression free survival increase

Key Eligibility Criteria

- Histologically confirmed B-cell non-Hodgkin’s lymphoma (NHL) at CLL/small lymphocytic lymphoma (SLL) and select other B-cell malignancies

- Relapsed after, or refractory to, at least 1 prior treatment regimen with no limit on prior therapies

- ECOG performance status ≤ 2

- Adequate organ function: Creatinine ≤ 1.5 x upper limit of normal

- Patients with Richter’s Transformation, or refractory to prior PI3Kδ inhibitors or prior BTK inhibitors are eligible

Results

Demographics

Efficacy

- Heavily pre-treated patient population with high-risk features, including ≥50% refractory to last treatment before multiple prior treatments of Rituximab (Rtx) therapy based

- Related AE’s Occurring in ≥ 50% of Patients (n = 55)

- Change from Baseline in Disease Burden

- Patients Treated at the “Higher Doses” of TGR-1202

- Best Percent Change from Baseline in Disease Burden

- Time on Study

- Ublitoximab in combination with TGR-1202 is well tolerated and highly active in a broad population of heavily pretreated and high-risk patients with NHL and CLL

- Grade 3/4 adverse events and discontinuations due to adverse events have been limited (<5%)

- Notably, the activity of the combination has been observed in CLL with high-risk cytogenetics, heavily pretreated indolent NHL, and Germinal Center (GC) diffuse large B-cell lymphoma

- As with single agent TGR-1202, a strong dose-response relationship was observed with the combination

- Safety profile of the combination supports additional multi-drug combination regimens; triple therapy combinations adding novel agents to ublituximab and TGR-1202 are ongoing (including Ibrutinib, ASCO 2015 Abstract #5011 & Lugano (MCL 2015 Abstract #106) with additional triple therapy studies planned

- International Phase III studies for the combination are planned

Conclusions

Time on Study

Patients treated at the “Higher Doses” of TGR-1202

Best Percent Change from Baseline in Disease Burden

- 18 patients have been on study for 6 months

- Ublituximab + TGR-1202 is well tolerated and highly active in a broad population of heavily pretreated and high-risk patients with NHL and CLL.

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- Presented at the 20th Congress of the European Hematology Association (EHA), June 11 – 14, 2015, Vienna, Austria.

- Adverse event profile has been similar to all cohorts to date.

- 3 patients’ (5%) have come off study due to an adverse event, including, (1) Grade 1 pneumonitis, (2) hemorrhage.

- No patients at ≥800 mg micronized TGR-1202 have discontinued due to an AE.

- Neutropenia was managed through dose delays.

- 1 DLT occurred for CLL Cohort 1 (Grade 4 neutropenia in a patient with baseline Gl 3 neutropenia, no other DLT’s were observed permitting continued dose escalation.

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