Ublituximab (TG-1101), a Novel Glycoengineered Anti-CD20 Monoclonal Antibody, in Combination with Ibrutinib Is Highly Active in Patients with Relapsed and/or Refractory Mantle Cell Lymphoma: Results of a Phase II Trial

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Background

Ublituximab is a novel, chimeric monoclonal antibody (mAb) targeting a unique epitope on the CD20 antigen, and is glycoengineered to enhance affinity for all variants of FcRyIIa receptors, thereby demonstrating greater antibody-dependent cellular cytotoxicity (ADCC) than rituximab and ofatumumab, particularly against tumor cells that express low CD20 levels.

Results

Study Design

- **Ublituximab IV**: 900 mg on Days 1, 8, and 15 in Cycle 1 followed by Day 1 of Cycles 2 – 6.
- **Ibrutinib**: 560 mg on Day 1 and continued daily through Cycle 6.

A safety run-in (Part 1) of the study was designed to enroll 6 patients. If no unacceptable safety concerns were observed, enrollment opened to the expansion phase (Part 2). Efficacy was assessed at 3 and 6 months.

Study Endpoints

- **Primary endpoints**: Safety and ORR
- **Secondary**: Time to Response and CR rate

Key Eligibility Criteria

- Patients with previously treated MCL with measurable disease requiring treatment according to standard criteria for MCL (Cheson et al., 2007)
- No limit on prior type or # of therapies or regimens
- ECOG ≤ 2 with adequate organ / marrow function with baseline
- ANC ≥ 1,000/µL and platelets ≥ 50k/µL for Part 1; and
- ANC ≥ 750/µL and platelets ≥ 30k/µL for Part 2
- Prior treatment with a BTK inhibitor and/or a PI3K inhibitor was permitted
- 21 day washout from prior therapy; Prior allogeneic SCT was excluded

Phase 3 GENUINE Study in High-Risk CLL

- **A Phase 3 Study of Ibrutinib vs. Ublituximab + Ibrutinib**
  - **Design, Endpoints, and Statistics** agreed to via Special Protocol Assessment (SPA)
  - Enrolling 330 patients with High-Risk CLL (IPI > 2, high grade, and/or p53 mutation)
  - Study Chair: Jeff Sharram, MD
  - Clinical trials.gov #: NCT02301156

CONCLUSIONS

- Data from this Phase 2 study suggests ublituximab, a glycoengineered anti-CD20 mAb, in combination with ibrutinib is a well-tolerated and highly active regimen for patients with relapsed or refractory MCL
- An 87% ORR with a 33% CR rate in patients with advanced MCL compares favorably to historical single agent ibrutinib (66% ORR and 17% CR rate; ibrutinib prescribing information, 2015)
- Increased depth of response as measured by greater CR rate compared to historical ibrutinib single agent data suggests the potential for better long-term outcomes
- Enhanced ORR and depth of response is consistent with results seen for the combination in rel/ref CLL with a 95% ORR (25% achieved CR and/or MRD negativity) in high-risk CLL (ICML 2015)
- A randomized Phase 3 trial with ibrutinib +/- ublituximab (GENUINE) is currently ongoing in high-risk CLL pts and future studies using this combination in MCL are being evaluated