Clinical Activity and Safety of TGR-1202, a Novel Once-Daily PI3Kδ Inhibitor, in Patients with CLL and B-Cell Lymphoma

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Study Design

- **Key Eligibility Criteria**
  - Histologically confirmed B-cell non-Hodgkin lymphoma (NHL), CLL, Hodgkin’s lymphoma (HL), and select other B-cell disorders
  - Relapsed, or refractory to, at least 1 prior treatment regimen with no limit on prior therapies
  - ECOG performance status ≤ 2
  - Adequate organ system function: ANC ≥ 7500/µL, platelets ≥ 100 K/µL
  - Patients with prior therapy with an antibody that specifically targets PI3K and/or mTOR are excluded in dose-escalation cohorts only

- **Study Objectives**
  - Primary: To determine the Safety, Pharmacokinetics (PK), and Maximum Tolerated Dose (MTD) of TGR-1202
  - Secondary: To determine the Pharmacodynamics of TGR-1202 and assess Efficacy (overall response rate and duration of response)

- **Background**
  - TGR-1202 is a next generation PI3Kδ inhibitor with a unique structure and activity profile distinct from other PI3Kδ inhibitors in development including:
    - A prolonged half-life and accumulation 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

- **Adverse Events in TGR-1202 Treated Patients**
  - All Events in >10% of Patients (N=81)

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- **Results**

- **Demographics**
  - Median Age, years (range): 65 (22–85)
  - Male/Female: 53/28

- **Histology**
  - 21 CLL
  - 6 MCL
  - 22 FL
  - 5 MZL
  - 14 DLBCL
  - 2 WM
  - 1 HL
  - 1 T-Cell

- **Median ECOG**
  - 1
  - Prior Therapies, median (range): 3 (1–14)
  - Patients with ≥3 Prior Therapies (%): 46 (57%)

- **Patients Refractory to Prior Therapy (%)**: 40 (49%)

- **Patients treated with >2 prior regimens (100% of those with ≥3 prior regimens were included): 6 were Too Early To Evaluate, 2 Non-Compliant (both ≥1800 mg), 3 removed per investigator discretion, and 1 failed inclusion/exclusion (Baseline Marker’s Transformation)

- **Characteristics by Cohort**
  - Cohort 1: 50 mg
  - Cohort 2: 100 mg
  - Cohort 3: 150 mg
  - Cohort 4: 200 mg
  - Cohort 5: 300 mg
  - Cohort 6: 400 mg
  - Expansion Cohort 7: 400 mg
  - Expansion Cohort 8: 800 mg
  - Expansion Cohort 9: 1200 mg
  - Expansion Cohort 10: 1200 mg
  - Expansion Cohort 11: 2000 mg
  - Expansion Cohort 12: 2400 mg

- **Conclusions**

- **TGR-1202 is a once-daily PI3Kδ inhibitor with single agent activity observed in patients with a variety of relapsed/refractory hematologic malignancies**

- **Long term safety has been well characterized with many patients on daily TGR-1202 for over 12 cycles, upwards of 34+ cycles (2.5+ years)**

- **To date, no events of colitis have been observed**

- **No long term trends in toxicity have been observed**

- **Adverse event profile to date appears differentiated from other PI3Kδ inhibitors, especially with respect to hepatoxicity and colitis**

- **Marked single-agent activity has been observed at doses ≥ 800 mg of initial formulation or any dose of micronized formulation, in patients with**

  - **Relapsed refractory CLL, with a 94% nodal response rate and an ORR of 50% based on iwCLL (Hallek 2008) criteria; and**

  - **Relapsed refractory FL, including a preliminary ORR of 38% with median tumor reductions of ~48%, and many patients on study pending further efficacy assessments**

- **Safety and efficacy profile supports combination therapy with other novel targeted agents (including ibrutinib, ASH Abstract #1538)**

- **TGR-1202 is now in Phase 3 for patients with CLL (UNITY-CLL Study)**

- **Presented at the 57th American Society of Hematology (ASH) Annual Meeting and Exhibition, December 5 – 8, 2015, Orlando, FL**