Phase 1 Study of TG-1701, a Selective Inhibitor of Bruton’s Tyrosine Kinase (BTK), in Patients with Relapsed/Refractory B-Cell Malignancies


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Background

Apo-BCR is a B-cell lineage-specific receptor that plays an essential role in lymphocyte development and function. It is a target of interest in B-cell malignancies, particularly in patients with lymphoma. We report the results of a Phase 1 study evaluating the safety and efficacy of TG-1701, a potent, orally bioavailable, irreversible, and selective inhibitor of BTK.

Methods

This was an open-label, non-comparative, dose-escalation study of TG-1701 in patients with relapsed/refractory B-cell malignancies. The primary objective was to determine the maximum tolerated dose (MTD) of TG-1701 and to evaluate its safety profile, pharmacokinetics, and pharmacodynamics. Secondary objectives included the evaluation of antitumor activity.

Results

Demographics

- **Male sex, n (%)**: 0 (0)
- **Female sex, n (%)**: 13 (100)
- **Median age, years**: 66 (57-76)
- **Eastern Cooperative Oncology Group (ECOG) performance status**: 1 (0-2)
- **Prior therapies, median (range)**: 4 (3-10)
- **Disease duration, months**: 15 (9-27)
- **Histology**: CLL 3, MCL 2

Toxicity

- **Grade 1-2 adverse events**: Nausea, Headache, Abdominal pain, and Bilirubin increased
- **Grade 3 adverse events**: Bruising, Neutropenia, Astroid increased, and Median cycles (range) monotherapy = 8 (5-15)
- **Grade 4 adverse events**: No grade 4 adverse events

Efficacy

- **Best % change from baseline in tumor burden**: 0
- **Best % change from baseline in TCR**: 0
- **Best % change from baseline in BCL**: 0

Pharmacokinetics and Pharmacodynamics

- **AUC (0-24 hours)**: 24000 pg/mL
- **Cmax**: 2000 pg/mL
- **Tmax**: 24 hours

Responses by Cohort & Dose Level

- **Overall response rate**: 4/9 (44%)
- **CR**: 2/9 (22%)
- **PR**: 2/9 (22%)
- **SD**: 1/9 (11%)
- **PD**: 3/9 (33%)

Safety

- **AEs related to anti-BTK activity**: No grade 3 or 4 adverse events
- **AEs related to anti-ublituximab activity**: No grade 3 or 4 adverse events
- **AEs related to anti-umbralisib activity**: No grade 3 or 4 adverse events

Summary and Conclusions

- This study demonstrates the potential of TG-1701 as a novel therapeutic agent for patients with relapsed/refractory B-cell malignancies. Further clinical evaluation is warranted to confirm these preliminary results.

Presented at the 61st American Society of Hematology Annual Meeting, December 7 – 10, 2019, Orlando FL

Abstract # 4001