Updated results of the selective Bruton tyrosine kinase (BTK) inhibitor TG-1701, as monotherapy and in combination with ibrutinib and umbralisib (U2) in patients (pts) with B-cell malignancies

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BACKGROUND AND METHODS

- Deep remissions with BTK mono-therapy in CL are rare
- TG-1701 is a covalently bound BTK inhibitor with superior selectivity compared with ibrutinib* (BTK and ILK covalent binding)

The triple combination of TG-1701 with ibrutinib and umbralisib (U2) inhibited tumor growth in BTK- and ILK-resistant xenograft models.

Kinase Selectivity Profiling at 1uM in an in vitro whole kinase screening

Objectives

- Characterize the safety profile of TG-1702.
- Demonstrate the RP2D of TG-1702 as monotherapy and in combination with U2.
- Preliminary antitumor activity, BTK occupancy

Key Eligibility Criteria

- Pts with pathologically confirmed B-cell lymphoma or CLL warranting systemic therapy were included. Previously untreated pts could be enrolled if unsuitable for standard frontline chemoimmunotherapy, in the disease specific cohorts.
- For pts with prior therapy with a BTK inhibitor, any acute or protracted toxicity or condition, consensitum therapy (other than anticoagulation, if allowed), was excluded.

RESULTS

- Ongoing treatments (N(%)): 18 (100). N=18 (100)
- Intra-pd dose escalation N(%) : 2 (10)
- MTD was not reached. Median follow-up: 19 mos

Safety

All Causality AEs (≥15%) TG-1702 Monotherapy

Best % Change in Tumor Burden from Baseline

Efficacy

• CR: 21%
• Median follow up: 15.6 mos

SUMMARY

- TG-1701 exhibits an encouraging safety profile, with clinical and pharmacodynamic activity at all dose levels evaluated that support Q2D dosing.
- The MTD has not been achieved in the monotherapy arm (up to 400 mg QD).
- The combination of TG-1701 with U2 has been well tolerated and dose escalation continues. Combination treatment is associated with encouraging clinical activity, including early complete responses.
- This study (NCT03671590) continues enrollment and future registration trials are being planned.

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