Combination of Ublituximab, TGR-1202, and Bendamustine Demonstrates Significant Benefits in Patients with Advanced DLBCL and Follicular Lymphoma

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Background

- Ublituximab (TG-1110, UTX) is a novel, chimeric monoclonal antibody targeting a unique epitope combining the CD20 antigen, and glyceroenriched to enhance affinity for all variants of FcγRIIIa receptors, thereby demonstrating greater antibody-dependent cellular cytotoxicity (ADCC) activity than rituximab and ofatumumab.
- Ublituximab is currently in Phase 3 development in combination with ibritumomab or TGR-1202 for patients with chronic lymphocytic leukemia (CLL), and in Phase 2b studies for patients with Diffuse Large B-Cell Lymphoma (DLBCL).

TGR-1202

- TGR-1202 (TGR) is a next generation PI3K inhibitor, with a unique structural similarity profile distinct from other PI3K inhibitors in development, including:
  - High selectivity to the 6 isoform of PI3K
  - A prolonged half-life that enables once-daily dosing
  - A differentiated safety profile from other PI3K inhibitors in development, notably with respect to hepatic toxicity and colitis observed to date

Study Design

Study UTX-TGR-1202 (NCT02004485) is a Ph1b/2 trial evaluating the combination of ublituximab + TGR-1202 in patients with relapsed or refractory NHL and CLL. Following safety evaluation of the UTX + TGR, a triple cohort was opened evaluating the combination of UTX + TGR + bendamustine restricted to enrollment for DLBCL and Follicular Lymphoma patients:

Dose Escalation Schema:

<table>
<thead>
<tr>
<th>Ublituximab Dose</th>
<th>TGR-1202 Dose</th>
<th>Bendamustine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 mg</td>
<td>1202 mg</td>
<td>1 g/m²</td>
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</table>

Treatment Schedule: Efficacy is assessed at Week 8 and every 12 weeks thereafter. After Month 12, all patients remain on TGR-1202 single agent.

Results

Demographics

- Evaluable for Safety (n) = 34
- Evaluable for Efficacy (n) = 15
- Median Age, years (range) = 68 (31 – 81)
- Male/Female = 11/8

Histology

- DLBCL 11
- FL 8
- Others 5

ECOG, 0/1/2 = 3/15/1

Prior Therapy Regimens, median = 2 (1 – 6)

Patients with ≥ 3 Prior Therapies, n (%) = (37%)

Refractory to Prior Therapy, n (%) = (47%)

Refractory to Previous Regimen, n (%) = (58%)

Analysis

- All CAE Patients Occurring in ≥ 5% of Patients (n = 35)
- Adverse Event
  - N (%) = 1
  - Diarrhea 7 (37%) 1 (5%)
  - Decreased appetite 6 (32%) 1 (5%)
  - Nausea 6 (32%) 1 (5%)
  - Anemia 4 (21%) 2 (11%)
  - Neutropenia 4 (21%) 4 (22%)
  - Vitamin D decreased 4 (21%) 1 (5%)
  - Arthralgia 3 (16%) -
  - Asthenia 3 (16%) -
  - Dyspnea 3 (16%) 1 (5%)
  - Hypogammaglobulinemia 3 (16%) -
  - Infusion related reaction 3 (16%) -
  - Rash 3 (16%) 1 (5%)
  - Thrombocytopenia 3 (16%) -
  - Upper respiratory infection 2 (11%) -
  - Diarrhea 2 (11%) -

- Mean time on study 6 cycles
- No patient has discontinued due to a treatment-related AE
- Growth factor support was restricted during Cycle 1 for DLT evaluation purposes
- No Grade 3/4 transaminase elevations have been reported
- 1 transient event of Grade 3 diarrhea (duration of 1 day) was reported
- No events of pneumonia or pneumonitis have been reported to date

Efficacy

- Best Percent Change from Baseline in Disease Burden

- Type
  - PD
  - CR
  - PR
  - ORR
  - SD
  - PG

- Histology
  - DLBCL
  - FL

- Ref

- Prior Therapies
  - Combination of Ublituximab, TGR-1202, and Bendamustine
  - 1

- Best CR

- Combination of Ublituximab, TGR-1202, and Bendamustine is well tolerated and highly active in patients with advanced indolent and aggressive NHL, with an encouraging CR rate observed (40%)

- The non-chemotherapy doublet of ublituximab + TGR-1202 is a safe and efficacious backbone regimen on which to build novel multi-drug combinations with several triple therapy combination ongoing (including withibrutinib, pemolizumab, and bendamustine).

- The ublituximab + TGR-1202 doublet regimen is in registration directed UNITY-CLL Phase 3 study and UNITY-DLCL Study, with additional registration studies planned in the UNITY program

- The activity demonstrated with the triple combination of ublituximab + TGR-1202 + bendamustine is intended to be explored further in registration directed studies

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