Combination of TGR-1202, Ublituximab, is Safe and Highly Active in Patients with Advanced DLBCL and Follicular Lymphoma

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Background

Study Rationale

Ublituximab (UBX-1201, UTX) is a novel, chimeric monoclonal antibody targeting a unique epitope on the CD20 antigen, and glycoengineered to enhance affinity for all variants of the FRα receptor, thereby demonstrating a novel ratio-dependent antibody-dependent cellular toxicity (ADCC) activity as compared to rituximab and ofatumumab.

Ublituximab is currently in Phase 3 development in combination with durvalumab for patients with chronic lymphocytic leukemia (CLL), and in Phase 2b study for patients with Non-Hodgkin’s Lymphoma (NHL).

Study Design

Study Schema

Study UTX-TGR-103 (NCT02005489) is a Phase Ib/II trial evaluating the combination of ublitzumab + umbralab (TGR-1202) in patients with relapsed or refractory NHL, and CLL. Following safe evaluation of the UTX + TGR1 doublet, a triplet cohort was opened evaluating the combination of UTX + TGR1 + bendamustine restricted to enrollment for DLBCL and Follicular lymphoma, which included patients with measurable disease to any prior prior, and those not able to tolerate aggressive chemotherapy, stem-cell transplant, or CAR T-cells directed therapy.

Toxicity Dose Escalation

Treatment Schema

Criteria: Effective at Week 8 and every 12 weeks thereafter. After Month 12, all patients remain on TGR-1202 single agent.

UBILTUXIMAB INFUSIONS

Cycle 2 Cycle 3 Cycle 4 Cycle 5 Cycle 6 Cycle 7 Cycle 8 Cycle 9 Cycle 10 Cycle 11 Cycle 12

Results

Efficacy

Best Overall Response Rate at Month 3

<table>
<thead>
<tr>
<th>Type</th>
<th>CR</th>
<th>PR</th>
<th>ORR</th>
<th>SD</th>
<th>PD</th>
<th>DCR</th>
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</thead>
<tbody>
<tr>
<td>UTX</td>
<td>2 (50%)</td>
<td>5 (20%)</td>
<td>6 (100%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>TGR</td>
<td>1 (50%)</td>
<td>6 (30%)</td>
<td>7 (40%)</td>
<td>-</td>
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Safety

Overall Response Rate at Month 3

<table>
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<tr>
<th>Type</th>
<th>CR</th>
<th>PR</th>
<th>ORR</th>
<th>SD</th>
<th>PD</th>
<th>DCR</th>
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<tbody>
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<td>7 (60%)</td>
<td>10 (30%)</td>
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<td>TGR</td>
<td>3 (33%)</td>
<td>5 (30%)</td>
<td>8 (20%)</td>
<td>-</td>
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</tbody>
</table>

Combined | 4 (34%) | 6 (40%) | 15 (10%) | - | - | - |

Key Eligibility Criteria

- Confirmed diagnosis of Diffuse Large B-Cell (DLBCL) or Follicular Lymphoma (FL)
- Relapsed after or refractory to at least 1 prior treatment regimen with no prior on triple therapies
- ECOC performance status ≤ 2
- Prior rituximab or BTK inhibitors are eligible. Relapse from prior activity will stem-cell transplant after 50 days are eligible

Time on Study (Days)

- >= 30 days
- >= 90 days
- >= 180 days

Conclusions

- The non-comparative doublet of ublitzumab + TGR-1202 is a safe and efficacious backbone regimen on which to build upon for novel multi-drug combinations.
- The combination of ublitzumab + TGR-1202 + bendamustine is well tolerated and highly active in patients with advanced indolent and aggressive NHL, including those not eligible for HDT/ASCT or CD38 CAR T-cell therapy.
- A 100% ORR with 50% CR rate in relapsed DLBCL; 40% ORR with 24% CR rate in refractory DLBCL with durable CR and PR responses observed; and 82% ORR with 50% CR rate in relapsed or indolent indolent NHL.
- The activity demonstrated with the triple combination of ublitzumab + TGR-1202 + bendamustine is further explored in the ongoing registration directed studies (UNITY-NHL).