Introduction

Ultra-tribulin (UTX; TG1101) is a novel (human) monoclonal antibody that targets CD20 antigen. It also glucosylates to enhance affinity for all classes of FcγRIIIa receptors, thereby demonstrating greater antibody-dependent cellular cytotoxicity (ADCC) activity than rituximab, ofatumumab, or obinutuzumab. In vitro studies, ultra-tribulin demonstrated 100% greater affinity for the human FcγRIIIa receptor than rituximab or obinutuzumab variants in patientderived CD20+ Jurkat (DeWitt et al. 2012). 

Objective

The objective for the ultra-tribulin RMS Phase 2 study (TG1101-RM01) was to determine whether the added Ancillary panel of adverse events translates into additional nadir benefits for RMS patients, in the form of fewer, slower flare reactions than current anti-CD20 infused therapies.

Methods & Study Design

Phases 1 and 2: All patients on the OLE received 450mg administered in a one hour infusion, with 100% of patients receiving at least one infusion.

Phase 2:

1. Subjects and Placebo

<table>
<thead>
<tr>
<th></th>
<th>cohort</th>
<th>Gender (%)</th>
<th>Placebo</th>
<th>UTX</th>
<th>Placebo</th>
<th>UTX</th>
<th>Placebo</th>
<th>UTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>15.4</td>
<td>80</td>
<td>46</td>
<td>7.1</td>
<td>1101</td>
<td>80</td>
<td>150</td>
<td>9.6</td>
</tr>
</tbody>
</table>

Disease Duration

EDSS assessments are conducted every 48 weeks to assess longterm disability outcomes of ublituximab treatment in subjects continuing treatment after completion of TG332-201 and be in good health with stable disease.

OLI Safety Update

Adverse Event (AE) Summary 1

All AEs At Least Possibly Related to UTX

Phase 2:

80% of subjects experienced 21 relapses in the year prior to screening

Mean number of relapses = 1.45

Median number of relapses = 2

OLE:

45 subjects entered the OLE

Mean Age: 41 years

64% Female

Results

INFECTION

1. All patients on the OLE received 450mg administered in a one hour infusion, with 100% of patients receiving at least one infusion, and 96% of patients receiving 2 or more infusions.

2. No drug-related discontinuations occurred during the Phase 2 or on the OLE.

Infusion Related Reactions

All patients on the OLE received 450mg administered in a one hour infusion, with 100% of patients receiving at least one infusion, and 96% of patients receiving 2 or more infusions.

- No infusion related reactions

- No subjects discontinued due to an AE related to ublituximab on the Phase 2 or during the OLE.

Conclusions

Ulbituximab is considered to be well tolerated, with a median duration of follow-up of 124.7 weeks.

All AEs deemed at least possibly related to UTX were infrequent during the OLE with all doses of 450mg administered in a one hour infusion (Phase 3 dose).

Infusion Related Reactions (IRRs) were rare during the OLE, occurring in only 5 patients (11%), all Grade 1 or 2. No subjects discontinued due to an AE related to ublituximab on the Phase 2 or during the OLE.

At the conclusion of the Phase 2 an ARR of 0.07 was observed at Week 48, with 93% of subjects being relapse free and 74% of subjects fulfilling the criteria for NEDA. Additionally, no T1 Gd enhancing lesions were detected in any subjects at Week 24 or 48 (100% reduction; p=0.003).

Phase 2 efficacy data and long term safety data support the full enrolled Phase 3 ULTIMATE trials evaluating a one hour infusion of 450mg of ublituximab in patients with Relapsing Forms of Multiple Sclerosis (RMS).