Phase 2 Multicenter Study Results of Ublituximab, a Novel Glycoengineered AntiCD20 Monoclonal Antibody (mAb), in Patients with Relapsing Multiple Sclerosis (RMS)

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Ublituximab (TG-1101)

- Novel Glycoengineered Anti-CD20 mAb
- Unique protein sequence
- Type 1 Chimeric IgG1 mAb
- Potential advantages over current standard of care:
  - Glycoengineered for significantly enhanced ADCC
  - Activity in “low” CD20 expressing cell lines, a characteristic of rituximab resistance
  - Binds to a novel epitope on CD20

Source: Adapted from Ruuls et al 2008
Ublituximab Phase II: Design

**Study Week**

Drug Administration: Dose and Infusion Time Varies by Cohort

**Screen**

**EDSS Assessments**

**B-Cell Measures and Safety Labs**

**MRI Analyses**

**Clinic Assessment**

**B cell & Labs**

**MRI**

**Infusion**

**Placebo Phase**

Week 48 Final Study Visit
### Ublituximab Phase II: Design

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Randomization</th>
<th>Treatment</th>
<th>Day 1/ Infusion Time</th>
<th>Day 15/ Infusion Time</th>
<th>Week 24/ Infusion Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Placebo (n=2)</td>
<td>Placebo</td>
<td>4h</td>
<td>Placebo / 3h</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>150 mg</td>
<td>4h</td>
<td>450 mg / 3h</td>
<td>450 mg / 1.5h</td>
</tr>
<tr>
<td>2</td>
<td>Placebo (n=2)</td>
<td>Placebo</td>
<td>4h</td>
<td>Placebo / 1.5h</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>150 mg</td>
<td>4h</td>
<td>450 mg / 1.5h</td>
<td>450 mg / 1h</td>
</tr>
<tr>
<td>3</td>
<td>Placebo (n=2)</td>
<td>Placebo</td>
<td>4h</td>
<td>Placebo / 1h</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>150 mg</td>
<td>4h</td>
<td>450 mg / 1h</td>
<td>600 mg / 1h</td>
</tr>
<tr>
<td>4</td>
<td>Placebo (n=2)</td>
<td>Placebo</td>
<td>3h</td>
<td>Placebo / 1h</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>150 mg</td>
<td>3h</td>
<td>600 mg / 1h</td>
<td>600 mg / 1h</td>
</tr>
<tr>
<td>5</td>
<td>Placebo (n=2)</td>
<td>Placebo</td>
<td>2h</td>
<td>Placebo / 1h</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>150 mg</td>
<td>2h</td>
<td>600 mg / 1h</td>
<td>600 mg / 1h</td>
</tr>
<tr>
<td>6</td>
<td>Placebo (n=2)</td>
<td>Placebo</td>
<td>1h</td>
<td>Placebo / 1h</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>150 mg</td>
<td>1h</td>
<td>600 mg / 1h</td>
<td>600 mg / 1h</td>
</tr>
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</table>
TG1101-RMS201
PHASE II PRELIMINARY RESULTS:

• 24 Week Data, All Cohorts
• 48 Week Data, Cohorts 1 and 2
## Ublituximab Phase II Results: Baseline Characteristics

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Subjects and treatment</th>
<th>Age (Years)(^1)</th>
<th>Gender (% Female)</th>
<th>Disease Duration (Years)(^{1,2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Placebo (n=2)</td>
<td>39±14</td>
<td>50%</td>
<td>15.5±20.4</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>43±12</td>
<td>67%</td>
<td>7.1±7.3</td>
</tr>
<tr>
<td>2</td>
<td>Placebo (n=2)</td>
<td>44±1</td>
<td>0%</td>
<td>0.9±1.2</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>33±10</td>
<td>100%</td>
<td>5.3±6.4</td>
</tr>
<tr>
<td>3</td>
<td>Placebo (n=2)</td>
<td>38±7</td>
<td>50%</td>
<td>11.5±7.5</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>40±11</td>
<td>67%</td>
<td>13.4±10.0</td>
</tr>
<tr>
<td>4</td>
<td>Placebo (n=2)</td>
<td>31±1</td>
<td>67%</td>
<td>6.8±7.7</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>39±12</td>
<td>50%</td>
<td>0.20±0.10</td>
</tr>
<tr>
<td>5</td>
<td>Placebo (n=2)</td>
<td>36±12</td>
<td>100%</td>
<td>15.4±9.6</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>46±1</td>
<td>100%</td>
<td>6.3±5.6</td>
</tr>
<tr>
<td>6</td>
<td>Placebo (n=2)</td>
<td>28±1</td>
<td>50%</td>
<td>5.7±2.5</td>
</tr>
<tr>
<td></td>
<td>UTX (n=6)</td>
<td>40±8</td>
<td>33%</td>
<td>8.5±8.4</td>
</tr>
</tbody>
</table>

**Total**

| N=48 | 40±10 | 65% | 8.0±8.1 |

\(^1\) Mean ± Standard Deviation

\(^2\) Distribution of time from diagnosis: 22 subjects (46%) were less than 5 years, 10 (21%) were 5-10 years, and 16 (33%) were greater than 10 years
Ublituximab Phase II Results: Patient Disposition

- 48 subjects were randomized to treatment in Cohort 1 through Cohort 6

- 46/48 subjects completed 6 months of ublituximab treatment; 12 subjects (2 per cohort) received placebo infusions, before crossing over to the ublituximab arm
  - One subject in Cohort 2 withdrew from the study due to pregnancy, after having received 2 ublituximab infusions, but continued to be followed with safety lab monitoring and immunological analyses
  - One subject in Cohort 6 missed the week 24 infusion
Ublituximab Phase II Results: Safety & Tolerability

All AEs >10% Regardless of Causality

<table>
<thead>
<tr>
<th>Event, n (%)</th>
<th>(N=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse event¹</td>
<td>41 (85%)</td>
</tr>
<tr>
<td>Most frequently reported adverse events²</td>
<td>All Grades</td>
</tr>
<tr>
<td>Infusion-related reaction</td>
<td>20 (42%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>12 (25%)</td>
</tr>
<tr>
<td>Headache</td>
<td>11 (23%)</td>
</tr>
<tr>
<td>Numbness</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>Common Cold</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>7 (15%)</td>
</tr>
<tr>
<td>Upper Respiratory Infection</td>
<td>7 (15%)</td>
</tr>
</tbody>
</table>

1 Reflects total number of patients that experienced one or more adverse event.
2 These events were reported by at least 10% of patients and are listed by decreasing incidence.

- Median duration of follow up ~11 months
- Ublituximab was well tolerated and no drug related discontinuations from study have occurred to date.
- No Grade 3/4 Adverse Events (AEs) were deemed possibly related to ublituximab.
- A total of 41 infusion related reactions (IRRs) were reported in 20 subjects. All were Grade 1 or Grade 2.
- No events of death reported on study.
- The Data Safety Monitoring Board (DSMB) has reviewed safety labs & adverse events for all subjects, and has not found any lab abnormalities or safety signals that would warrant a change in protocol.
At week 4, median 99% B cell depletion was observed and maintained at Week 24 (n=44)
Ublituximab Phase II 24 Week Results: MRI-Gd Enhancing Lesions

- No T1 Gd-enhancing lesions detected in any subjects at Week 24 (n=44; p=0.003)
- Mean number of T1 Gd lesions at baseline was 3.80

Subject T1 Gd MRI at Baseline and Week 24
No T1 Gd-enhancing lesions detected in any subjects in Cohorts 1-2 at Week 48 (n=14)

Mean number of T1 Gd lesions at baseline for Cohorts 1-2 was 3.64 (n=14)
There was a decrease of 7.67% (p=0.004) in T2 lesion volume at Week 24 compared to baseline.

The mean number of New/Enlarging T2 lesions from baseline to Week 24 was 0.2 ± 0.45.
There was a decrease of 10.5% in T2 lesion volume at Week 48 compared to baseline for Cohorts 1-2 (n=14)
83% of subjects showed improved or stable EDSS

Mean EDSS at baseline was 2.41 ±1.41; Median=2.5

At Week 24, the mean EDSS was 2.12. The mean change from baseline was an improvement of 0.29 ±0.93 points.

* 2 of the total 48 patients did not complete the week 24 EDSS evaluation
Ublituximab Phase 2 RMS Update: NEDA at Week 24

- At Week 24, 43* of 48 subjects had received all assessments to be evaluated for NEDA:
  - 98% of subjects were relapse free
  - 93% of subjects did not experience 24 week confirmed disability progression
  - 100% of subjects did not have any Gd-enhancing lesions
  - 84% of subjects did not have any new/enlarging T2 lesions
  - 76% of subjects achieved clinical and MRI outcomes consistent with NEDA

<table>
<thead>
<tr>
<th>NEDA 77%</th>
<th>No 24 Wk CDP 93%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No T1 Gd+Lesions 100%</td>
<td>No Evidence of MRI Disease 84%</td>
</tr>
<tr>
<td>No Relapses 98%</td>
<td>No Evidence of Clinical Disease 91%</td>
</tr>
</tbody>
</table>

* 3 of the total 48 patients did not have week 24 MRI, 1 patient did not have week 24 MRI or week 24 EDSS evaluation and 1 additional patient did not have a week 24 EDSS evaluation therefore only 43 patients had received all assessments to be evaluated for NEDA.

CDP is defined as an increase of ≥ 1.0 point from the baseline EDSS score that is not attributable to another etiology (e.g. fever, concurrent illness, or concomitant medication) when the baseline score is 5.5 or less, and ≥ 0.5 when the baseline score is above 5.5.
Ublituximab Phase II Results: Cumulative ARR

- Annualized Relapse Rate of 0.07
  - ARR calculated cumulatively, based on 48 subjects with a mean of approximately 11 months of follow-up
Conclusions

- B-cells are efficiently depleted in most patients within 24 hours of receiving the first dose of ublituximab, with >99% depletion in all patients by Week 4, and significant reductions from baseline maintained at Week 24

- Ublituximab was well tolerated and the most frequent AEs were infusion related reactions (IRRs); all Grade 1 or 2

- A rapid infusion time, as low as one hour, of 450mg was well tolerated, produced high levels of B cell depletion and is now being studied in the Phase 3 ULTIMATE trials
Conclusions

- **Cumulative Annualized Relapse Rate (ARR) of 0.07**

- No T1 Gd-enhancing lesions were detected in any subjects at Week 24 (n=44) or at Week 48 (n=14)

- 7.67% Reduction in T2 lesion volume at Week 24 from baseline, suggestive of a decrease in burden of disease (n=44)
  - 10.5% reduction in T2 lesion volume at Week 48 from baseline (n=14)

- Final Week 48 results from this Phase 2 are expected to be presented at an upcoming major medical meeting and support the currently ongoing ULTIMATE Phase 3 trials in relapsing forms of Multiple Sclerosis (RMS)
Thank You to Our Study Sites

- Hope Neurology, Knoxville, TN: Sibyl Wray, MD
  - Coordinator: Brenda Whitehead, CCRP
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  - Coordinator: Lillie Denny
- Phoenix Neurological Associates: Barry Hendin, MD
  - Coordinator: Lynn Flynn