**BACKGROUND**

- Lymphotoxin-α (LTα; also known as TNFSF1) is a member of the tumour necrosis factor (TNF) superfamily. LTα forms a homotrimer that binds to the TNF receptor 1 (TNFR1) and 2 (TNFR2) with high affinity. LTα also forms a heterotrimer with LTβ (or TNFSF3) and this heterotrimer binds to LTβRII. LTα is expressed as both soluble and membrane isoforms of lymphotoxin-alpha being investigated as a targeted therapy for RA.

- Pateclizumab (PTZ) is a novel, humanized IgG1 antibody against soluble and membrane isoforms of lymphotoxin-alpha being investigated as a targeted therapy for RA.

**METHODS**

Study Design, Patient Eligibility, and Assessments

- The safety and efficacy of PTZ was evaluated and compared with adalimumab (ADA), an anti-TNF biology drug, in a randomized, double-blind, placebo-controlled Phase 2 study.

**RESULTS**

Patient Disposition

- 214 patients were enrolled. Baseline demographics and disease characteristics were balanced across groups (Table 1).

Table 1. Patient Characteristic.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pateclizumab (n=85)</th>
<th>Adalimumab (n=85)</th>
<th>Placebo (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>51 (10)</td>
<td>54 (11)</td>
<td>51 (13)</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>51%</td>
<td>52%</td>
<td>44%</td>
</tr>
<tr>
<td>Race (white)</td>
<td>63%</td>
<td>63%</td>
<td>66%</td>
</tr>
<tr>
<td>Region (US and ES)</td>
<td>98%</td>
<td>98%</td>
<td>100%</td>
</tr>
<tr>
<td>Duration of RA (yr), mean (SD)</td>
<td>10.7 (8.5)</td>
<td>10.4 (8.8)</td>
<td>13.1 (9.1)</td>
</tr>
<tr>
<td>DAS28 (ESR), mean (SD)</td>
<td>5.9 (1.2)</td>
<td>5.9 (1.2)</td>
<td>6.3 (1.9)</td>
</tr>
<tr>
<td>Prednisone use (%)</td>
<td>9%</td>
<td>10%</td>
<td>13%</td>
</tr>
<tr>
<td>Deaths</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Safety

- No dose-limiting toxicities, deaths, or pregnancies were reported on study.

- No safety signals were associated with PTZ. Total adverse events (AEs), serious adverse events (SAEs) and infectious AEs in the PTZ cohort were less than placebo. Infections were the most common AE, occurring with comparable frequency across arms.

- There were no SAEs in the PTZ-treated cohort. Of the 6 total SAEs, 2 (both in ADA group) were judged by the investigator to be related to study drug: 1 patient had pulmonary tuberculosis and the other had lymphopenia.

Pharmacokinetics and Immunogenicity

- Pateclizumab displayed linear PK with an apparent half-life ~12 days, typical for an IgG antibody.

- Treatment emergent anti-therapeutic antibodies were uncommon in PTZ-treated patients (4 positive/66 total exposures) and were not associated with changes in pharmacokinetics, efficacy, or safety.

**CONCLUSIONS**

- PTZ had no treatment effect on DAS28-ESR (primary endpoint) and modest clinical activity (ACR20 responses, secondary endpoint) compared to placebo but was inferior to ADA on DAS28-ESR response and in all ACR20/50/70 responses after 10 weeks of treatment.

- CXCL13 levels decreased rapidly and significantly in patients treated with PTZ, demonstrating evidence of on target pharmacology (p<0.01 vs. placebo, Day 85, Figure 1).

- ADA treatment also decreased CXCL13 levels significantly (p<0.01 vs. placebo).

**ACKNOWLEDGMENTS**

- We thank the patients and families who participated in the study.

- Genentech provided support for this poster.

**REFERENCES**