Efficacy and safety of tralokinumab plus concomitant topical corticosteroids in adult patients with moderate-to-severe atopic dermatitis: results from the 32-week, Phase 3 ECZTRA 3 trial

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Introduction

Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterized by exacerbations and remissions. The disease affects >20% of the world's population and is associated with a significant burden of quality of life, work productivity, and healthcare costs.

Randomization and washout of TCS and other AD medication

300 mg q2w after initial loading dose (600 mg) was supplied proactively from randomization to the end of treatment. Concomitant TCS use during ECZTRA 3 was associated with improved efficacy and safety with tralokinumab plus TCS compared with placebo plus TCS. All participants were treated with a concomitant topical glucocorticoid plus TCS were either in or on residence, with only a minority discontinuing treatment.

Methods

Participants

Eligible patients were ≥18 years of age with a confirmed diagnosis of AD for ≥1 year and with an Investigator Global Evaluation of AD (Eye, Scalp, and Extremities) score >4, and an Eczema Area and Severity Index (EASI) score of ≥10. Patients were randomized 1:1 to receive either tralokinumab q2w plus TCS (n=253) or placebo q2w plus TCS (n=127) over the initial 16-week treatment period. Non-responders received tralokinumab q2w plus TCS for an additional 16 weeks. Placebo responders continued with placebo and alfinitumab, while non-responders received tralokinumab q2w plus TCS for an additional 16 weeks.

Study design

The objective of the ECZTRA 3 trial (NCT03363854) was to evaluate the efficacy and safety of tralokinumab plus concomitant topical corticosteroids in adult patients with moderate-to-severe atopic dermatitis. Additional eligibility requirements

Primary endpoints

- Efficacy endpoints: Eczema Area and Severity Index (EASI) -75
- Safety endpoints: Adverse events

Secondary endpoints

- Tralokinumab plus TCS significantly improved outcomes for all key secondary endpoints

Concomitant TCS use during ECZTRA 3

Concomitant TCS use during ECZTRA 3 was associated with improved efficacy and safety with tralokinumab plus TCS compared with placebo plus TCS.

Safety

- All primary and secondary endpoints at week 16 demonstrated superior clinically meaningful improvements in both efficacy and safety with tralokinumab plus TCS compared with placebo plus TCS.
- Approximately 90% of patients treated with tralokinumab q2w plus TCS who responded at week 16 maintained their response at week 32 with tralokinumab q2w plus TCS.
- Less frequent (q4w) dosing of tralokinumab could be explored.
- Continuation treatment with tralokinumab q2w plus TCS improved the initial response in many patients beyond 16 weeks.
- The overall frequency of adverse events was comparable across treatment groups and did not increase with prolonged treatment.

Statistical analyses

- Primary and secondary endpoints were analyzed in the intent-to-treat population at week 16. All statistical comparisons were performed using the t tests for continuous variables and the chi-square test for categorical variables.

Table 1. Patient demographics and disease characteristics at baseline

<table>
<thead>
<tr>
<th></th>
<th>Tralokinumab q2w plus TCS Mean ± SD</th>
<th>Placebo q2w plus TCS Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>EASI</td>
<td>26.8 ± 16.9</td>
<td>31.2 ± 16.2</td>
</tr>
<tr>
<td>SCORAD</td>
<td>33.6 ± 23.3</td>
<td>38.8 ± 23.6</td>
</tr>
<tr>
<td>DLQI</td>
<td>23.7 ± 9.0</td>
<td>28.5 ± 9.3</td>
</tr>
<tr>
<td>Pruritus</td>
<td>6.6 ± 3.7</td>
<td>7.5 ± 4.0</td>
</tr>
<tr>
<td>Risk of eczema flares</td>
<td>2.1 ± 1.1</td>
<td>2.3 ± 1.2</td>
</tr>
</tbody>
</table>

Table 2. Summary of adverse events in the initial 16-week treatment period

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Tralokinumab q2w plus TCS</th>
<th>Placebo q2w plus TCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
<td>16/253 (6.3%)</td>
<td>9/127 (7.1%)</td>
</tr>
<tr>
<td>Serious infections</td>
<td>3/253 (1.2%)</td>
<td>1/127 (0.8%)</td>
</tr>
<tr>
<td>Discontinuations due to adverse events</td>
<td>15/253 (6.0%)</td>
<td>11/127 (8.6%)</td>
</tr>
</tbody>
</table>

Conclusions

- All primary and secondary endpoints at week 16 demonstrated superior clinically meaningful improvements in both efficacy and safety with tralokinumab plus TCS compared with placebo plus TCS.
- Approximately 90% of patients treated with tralokinumab q2w plus TCS who responded at week 16 maintained their response at week 32 with tralokinumab q2w plus TCS.
- Less frequent (q4w) dosing of tralokinumab could be explored in some patients.
- Less TCS was used by tralokinumab-treated patients compared with those who received placebo through the initial 16-week treatment period.
- Continued treatment with tralokinumab q2w plus TCS improved the initial response in many patients beyond 16 weeks.
- The overall frequency of adverse events was comparable across treatment groups and did not increase with prolonged treatment.

References