**Efficacy and safety of tralokinumab plus topical corticosteroids in patients with severe atopic dermatitis and prior history of dupilumab treatment: a post hoc subgroup analysis from ECZTRA 7 trial**

**Introduction**

- **AD** is a chronic inflammatory disease, characterized by eczematous skin lesions and multiple symptoms, including pruritus, sleep disturbance, and depression.
- Tralokinumab is a high-affinity, fully human, monoclonal antibody designed to specifically neutralize interleukin-13, a key driver of the underlying inflammation in AD.

- The Phase 3 ECZTRA 7 trial (NCT03761537) met its primary endpoint of EASI-75 at Week 16, confirming tralokinumab plus topical corticosteroids (TCS) is superior to placebo plus TCS in treating severe atopic dermatitis (AD) in patients not adequately controlled by, or with contraindications to, or cyclosporine A.

- Patients not adequately controlled with currently available treatment options may require additional therapeutic options.

- There can be inadequate disease control with currently available treatment options and with additional treatments.

**Objective**

To describe the efficacy and safety of tralokinumab in a subgroup of ECZTRA 7 patients with severe AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IGA, Investigator’s Global Assessment; Q2W, every 2 weeks; TCS, topical corticosteroids.

**Methods**

- **ECZTRA 7** was a randomized, double-blinded, multicenter, placebo-controlled Phase 3 trial (Figure 1).
- **Inclusion criteria** for ECZTRA 7:
  - Adult patients with AD for ≥6 weeks who did not respond adequately to previous systemic treatments.
  - Disease activity at study entry (EASI score ≥10% body surface area).
  - Women of childbearing potential agreed to use an effective method of contraception.
  - No prior systemic or biological therapy within the last 6 months.

- **Exclusion criteria** for ECZTRA 7:
  - Prior history of tumor necrosis factor-α inhibitors.
  - Use of systemic glucocorticoids within the last 12 months.
  - Worsening of AD within the last 2 weeks.

**Table 1. Baseline demographics and clinical characteristics for randomized subjects in ECZTRA 7**

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (n=263)</th>
<th>AD duration, years</th>
<th>Age, years</th>
<th>Disease area (%)</th>
<th>Worsening of disease within the last 2 weeks</th>
<th>Itch NRS≥4*</th>
<th>IGA 0/1</th>
<th>Tralokinumab + TCS</th>
<th>Placebo + TCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tralokinumab-Naive</td>
<td></td>
<td>263</td>
<td>26.3 (25.0, 34.0)</td>
<td>51.5 (43.0, 57.0)</td>
<td>7.0 (4.0, 10.0)</td>
<td>5.0 (4.0, 6.0)</td>
<td>0.0 (0.0, 0.0)</td>
<td>3.0 (2.0, 4.0)</td>
<td></td>
</tr>
<tr>
<td>Tralokinumab-Experienced</td>
<td></td>
<td>137</td>
<td>33.0 (25.0, 45.0)</td>
<td>55.0 (45.0, 65.0)</td>
<td>16.0 (10.0, 26.0)</td>
<td>11.0 (10.0, 16.0)</td>
<td>1.0 (0.0, 2.0)</td>
<td>2.0 (1.0, 3.0)</td>
<td></td>
</tr>
</tbody>
</table>

**Results**

- **Patient characteristics**
  - Tralokinumab-Naive (n=140) and dupilumab-naïve (n=23) cohorts had comparable baseline characteristics, except that median (interquartile range, IQR) age was 51.5 (43.0, 57.0) years for dupilumab-experienced patients and 33.0 (25.0, 45.0) years for dupilumab-naïve patients (Table 1).
  - Median (IQR) EASI and percentage of patients with an IGA of 0 were 35.3 (24.2, 39.6) and 57% among dupilumab-experienced patients and 28.7 (22.4, 39.5) and 67% among dupilumab-naïve patients, respectively.

- **Among dupilumab-experienced patients, baseline characteristics and clinical stability were comparable to the tralokinumab + TCS vs. placebo + TCS as needed (n=140) group (Table 1)**
  - 50% of patients in each of these two groups discontinued dupilumab due to either lack of efficacy or safety concerns.

- **Efficacy and safety of tralokinumab plus topical corticosteroids in patients with severe atopic dermatitis and prior history of dupilumab treatment**
  - Tralokinumab + TCS as needed were consistent with the pooled analysis of tralokinumab in moderate-to-severe AD.

- **Safety**
  - No serious adverse events occurred in either treatment group.
  - From a safety perspective, there were two patients who had previously discontinued dupilumab due to conjunctivitis, adverse events of conjunctivitis were not reported for either patient during 26 weeks of dupilumab + TCS treatment.

**Conclusions**

This post hoc subgroup analysis indicates that dupilumab-experienced patients can benefit from tralokinumab + TCS as needed.

- **Overall**, four percent of adverse events in dupilumab-experienced patients treated with tralokinumab + TCS as needed were consistent with the pooled analysis of tralokinumab in moderate-to-severe AD.

- **Due to the small sample size, further data involving more patients are needed to confirm these findings.**

**References**

5. Bieber T. Allergy. 2020;75:54–62;

**Disclosures**

- The authors have no conflicts of interest.

- This study was funded by Sanofi-Genzyme, Regeneron, LEO Pharma, AbbVie, Novartis and Galderma, and is involved in performing clinical trials with Sanofi-Genzyme, Regeneron, LEO Pharma, AbbVie, Novartis and Galderma.

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**Table 2. Binary efficacy endpoints in dupilumab-experienced subjects**

<table>
<thead>
<tr>
<th>Visit</th>
<th>Endpoint</th>
<th>Tralokinumab + TCS</th>
<th>Placebo + TCS</th>
<th>Difference (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 16</td>
<td>IGA 0/1</td>
<td>6 /6 (100.0%)</td>
<td>4 /6 (66.7%)</td>
<td>2.0 (0.0, 4.0)</td>
</tr>
<tr>
<td></td>
<td>itch NRS≤4*</td>
<td>3 /6 (50.0%)</td>
<td>3 /6 (50.0%)</td>
<td>0.0 (-1.0, 1.0)</td>
</tr>
<tr>
<td>Week 26</td>
<td>IGA 0/1</td>
<td>6 /6 (100.0%)</td>
<td>5 /6 (83.3%)</td>
<td>1.7 (0.0, 3.4)</td>
</tr>
<tr>
<td></td>
<td>itch NRS≤4*</td>
<td>3 /6 (50.0%)</td>
<td>3 /6 (50.0%)</td>
<td>0.0 (-1.0, 1.0)</td>
</tr>
</tbody>
</table>

*Any adverse event: an event that, if serious, resulted in death, was life-threatening, required hospitalization, resulted in persistent or significant disability/incapacity, or was a congenital anomaly/birth defect.*

†Any serious adverse event: an event that resulted in death, was life-threatening, required hospitalization, resulted in persistent or significant disability/incapacity, or was a congenital anomaly/birth defect.