Atopic dermatitis (AD) is a chronic skin disease associated with significant itch and sleep disturbances that profoundly affects patients’ daily lives. Tralokinumab is a fully human, high-affinity, monoclonal antibody that specifically neutralizes the interleukin-13 cytokine, a key driver of AD signs and symptoms.

Rescue treatment could be used at the discretion of the investigator to control intolerable symptoms.

Prior to randomization, AD treatments were washed out: 4 weeks for systemic therapy in adults with moderate-to-severe AD, tralokinumab monotherapy demonstrated superiority compared to placebo in a proof-of-concept, randomised, controlled trial at Week 16 and was well tolerated up to 52 weeks of treatment.

### Methods

#### Trial design

- **ECZTRA 1** and **2** were two identically designed, multinational, double-blind, randomized, placebo-controlled, 52-week trials.
- **Patients** were randomized to stratified subgroups of tralokinumab 300 mg or placebo every 2 weeks for an initial 16 weeks.
- Prior to randomization, AD treatments were washed out: 4 weeks for systemic treatments and 2 weeks for TCS and other topical treatments.
- Rescue treatment could be used at the discretion of the investigator to control intolerable symptoms.

#### Key eligibility criteria

- **38 years of age**
- **Confirmed diagnosis of atopic dermatitis for ≥1 year**
- **ASI score ≥2 at screening and week 0**
- **ASI score ≥2 at screening and week 0**
- **AD involvement of ≥10% body surface area**

#### Outcomes

- **ASI and IGA** were assessed at baseline and at scheduled biweekly visits throughout the trial.
- **itch and sleep interference** were recorded daily by patients using:
  - Numeric Rating Scale (NRS) for worst daily pruritus (11-point scale with 0 being ‘no itch’ and 10 being ‘worst itch imaginable’)
  - NRS for eczema-related sleep interference

#### Analyses

- **This post hoc analysis was conducted of pooled data from ECZTRA 1 and ECZTRA 2 trials through Week 16**.
- **Statistical analyses followed pre-specifications**:
  - Difference in IGA 0/1 and EASI-75 response rates were assessed at Week 16 in a pre-specified pooled analysis of the primary endpoints using the Cochran-Mantel-Haenszel stratified by region, baseline Investigator’s Global Assessment (IGA) and trial. Missing data or data after rescue medication (including TCS) were imputed as non-response.
  - Change from baseline in worst daily pruritus, eczema-related sleep interference were assessed both as weekly averages of worst daily measures (Baseline to Week 16) as well as the single worst daily measures (Baseline to Day 0) and in post-hoc analyses using a mixed model for repeated measures with effects of planned treatment, region, baseline IGA, trial and interactions between treatment and visit and baseline value and visit. Data collected after optional discontinuation or initiation of rescue medication (including TCS) were set to missing.
  - **Conclusion**
  - At Week 16, tralokinumab had a greater adjusted mean percentage improvement from baseline in worst daily pruritus NR S (Tralokinumab 35.5%, placebo 21.4%, p<0.001) and eczema-related sleep interference (_tralokinumab 30.7%, placebo 18.4%, p<0.001_)
  - **Effect on itch and sleep over 16 weeks**
  - **Week 16, tralokinumab** had a greater adjusted mean percentage improvement from baseline in worst daily pruritus NR S: (Tralokinumab 35.5%, placebo 21.4%, p<0.001) and eczema-related sleep interference (tralokinumab 30.7%, placebo 18.4%, p<0.001) compared to placebo.

#### Results

- **Patients, demographics, and clinical characteristics**
  - **1204 patients** were randomized in ECZTRA 1 and 2, respectively (tralokinumab: n=1196, placebo: n=402).
  - **Baseline demographics and clinical characteristics** were well balanced between treatment groups (Table 1).

#### Conclusions

- **Tralokinumab monotherapy showed reduced and sustained improvements from baseline in itch and sleep relative to placebo, starting from Day 2 after the first dose.**

Data shown are adjusted mean percentage change (Δ% from baseline) measured over all weeks of treatment. Data collected after rescue medication (including TCS) were imputed as non-response.

- **Relative to the placebo group, a significantly greater proportion of patients in the tralokinumab group achieved ≥20% and ≥40% improvement after 16 weeks**:
  - **3 days for worst daily pruritus NR S (22.3%, p<0.01; 29.7%, p<0.001)**
  - **3 days for worst daily NR S (24.4%, p<0.001; 29.7%, p<0.001)**
  - **2 days for eczema-related sleep NR S (22.8%, p<0.01; 20.2%, ns)**

*Placebo data: data collected after rescue medication including TCS were imputed as non-response.

*Data: data collected after rescue medication including TCS were imputed as non-response.

- **Overall, improvements from baseline in worst daily pruritus NR S were observed in the ECZTRA 1 and 2 trials as early as Week 2.**

- **Patient safety**: No new, unexpected or unexpected severe adverse events (SADs) were identified in tralokinumab or placebo groups. The most frequently reported AEs were similar to the placebo group and were generally mild to moderate in severity. The most frequent SADs were infusion reactions, infections, and pyrexia. The incidence of skin disorders was low and similar in the tralokinumab and placebo groups. There was no evidence of immunogenicity for tralokinumab.

### References


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