# Tralokinumab provides progressive improvements beyond week 16 in patients with atopic dermatitis who have an initial partial response

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## Introduction

- Atopic dermatitis (AD) is a chronic type 2 inflammatory skin disease characterised by excessive skin dryness, inflamed skin and intense itch[1-3]
- Tralokinumab is a fully human immunoglobulin G4 monoclonal antibody that specifically binds to the interleukin 13 (IL-13) cytokine with high affinity, preventing interaction with the IL-13 receptor and subsequent downstream IL-13 signalling, thus inhibiting its pro-inflammatory activity[4-8]
- An Investigator's Global Assessment (IGA) score of 0/1 (IGA-0/1) [clear/almost clear skin] and 75% improvement in Eczema Area and Severity Index (EASI) [EASI-75] are standard regulatory outcome measures for AD trials
  - IGA-0/1 and EASI-75 are stringent endpoints; hence, achievement of mild disease severity (IGA-2) and a 50% improvement in EASI (EASI-50) may be considered clinically relevant improvements in AD
- In the pivotal Phase 3 trials ECZTRA 1 and ECZTRA 2, tralokinumab monotherapy provided significant and early improvements in AD severity and symptoms in adults with moderate-to-severe AD[9]
  - In both trials, significantly more patients receiving tralokinumab monotherapy achieved the primary endpoints of IGA-0/1 and EASI-75 compared with placebo
  - Patients who did not achieve IGA-0/1 or EASI-75 during the 16-week initial treatment period were transferred to open-label tralokinumab plus optional topical corticosteroids (TCS) as needed for a further 36 weeks

## Objective

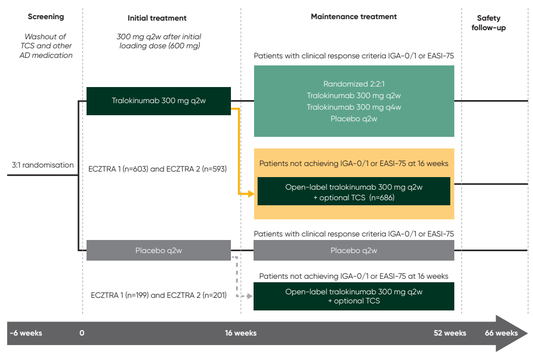
- The objective of this post hoc analysis was to assess clinical responses during open-label treatment in tralokinumab-treated patients who did not achieve IGA-0/1 or EASI-75 at week 16

## Methods

### Study design and patients

- ECZTRA 1 (NCT03131648) and ECZTRA 2 (NCT03160885) were identically designed, multinational, double-blind, randomized, placebo-controlled, 52-week trials of tralokinumab monotherapy in patients with moderate-to-severe AD
- Eligible patients were ≥18 years of age, with a confirmed diagnosis of AD for >1 year, EASI score ≥16, IGA score ≥3, and pruritus Numeric Rating Scale ≥4, and were candidates for systemic therapy due to a recent (within 1 year) history of inadequate response or intolerance to topical treatment
- Patients were stratified by region and baseline disease severity (IGA-3 [moderate AD] or IGA-4 [severe AD]) and were randomized 3:1 to receive either subcutaneous tralokinumab 300 mg or placebo every 2 weeks (q2w) for an initial treatment period of 16 weeks **(Figure 1)**

**Figure 1. ECZTRA 1 and ECZTRA 2 trial designs**




This *post hoc* analysis focused on pooled data of patients from ECZTRA 1 and ECZTRA 2 who were initially treated with tralokinumab and transferred to open-label treatment at week 16.

- At week 16, responders (IGA-0/1 and/or EASI-75) were re-randomized 2:2:1 to maintenance treatment with tralokinumab 300 mg q2w or every 4 weeks (q4w), or placebo
- Patients who did not achieve IGA-0/1 and/or EASI-75 at week 16 were transferred to open-label treatment with tralokinumab 300 mg q2w, with optional use of TCS up to week 52

### *Post hoc* analysis

- This analysis pooled data from ECZTRA 1 and ECZTRA 2 on IGA-0/1 and EASI-75 responses in patients who initially received tralokinumab and were transferred to open-label tralokinumab plus optional TCS at week 16

### Statistical analysis

- The primary analysis approach assessed treatment effect, irrespective of TCS use. Patients with missing data were imputed as non-responders
- An alternative analysis was also performed in which patients who used anti-inflammatory treatments (including TCS) were considered non-responders and patients with missing data were imputed as non-responders

## Results

### Patient demographics at baseline

- In total, 686 patients combined in ECZTRA 1 and ECZTRA 2 who were initially treated with tralokinumab transferred to open-label treatment **(Table 1)**

**Table 1. Demographics of patients transferred to open-label treatment with tralokinumab at week 16**

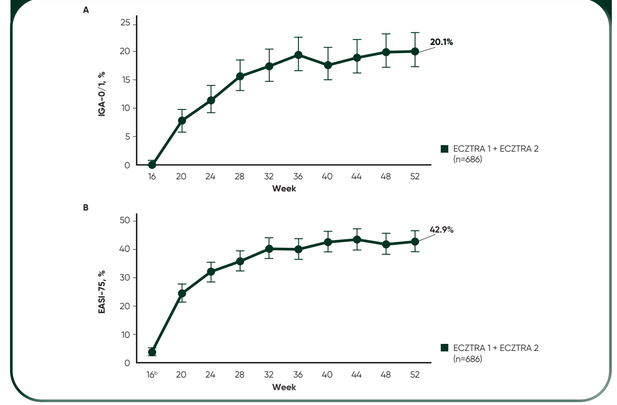
| | ECZTRA 1 + ECZTRA 2 |
|---|---|
| | Patients initially treated with tralokinumab q2w (n=686) |
| Age, years (SD) | 379 (14.2) |
| Male, n (%) | 438 (63.8) |
| Race, n (%) | |
| White | 472 (68.8) |
| Black or African American | 30 (4.4) |
| Asian | 161 (23.5) |
| American Indian or Alaska Native | 3 (0.4) |
| Native Hawaiian or other Pacific Islander | 1 (0.1) |
| Other | 18 (2.6) |
| Missing | 1 (0.1) |
| Region, n (%) | |
| North America | 207 (30.2) |
| Europe | 337 (49.1) |
| Australia | 57 (8.3) |
| Asia | 85 (12.4) |

In ECZTRA 1, patients were enrolled from Europe (Germany, France and Spain), North America (USA) and Asia (Japan). In ECZTRA 2, patients were enrolled from Europe (UK, Italy, Denmark, Poland and Russia), North America (USA and Canada), Asia (Korea) and Australia. SD, standard deviation.

### Pooled analysis

- Overall, 686/1196 (57.4%) tralokinumab-treated patients (360 and 326 from ECZTRA 1 and ECZTRA 2, respectively) were transferred to open-label treatment at week 16
- IGA-0/1 at week 52 was achieved by 138/686 (20.1%; 95% confidence interval [CI] 17.3, 23.3) patients receiving open-label tralokinumab plus optional TCS
- EASI-75 at week 52 was achieved by 296/686 (42.9%; 95% CI 39.2, 46.6) patients receiving open-label tralokinumab plus optional TCS
- More than half of the responder proportions at week 52 were achieved within 8 weeks of starting open-label treatment **(Figure 2)**
  - 11.4% (95% CI 9.2, 14) and 31.9% (95% CI 28.5, 35.5) achieved IGA-0/1 and EASI-75, respectively, by week 24

**Figure 2. Proportion of patients achieving (A) IGA-0/1 and (B) EASI-75 at week 52 in the open-label phase[a]**

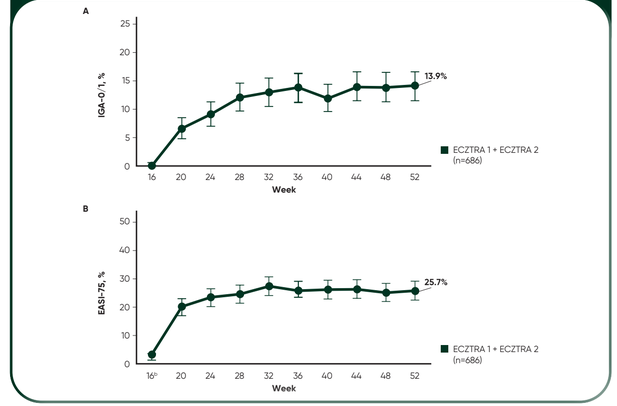



[a]Data were pooled from ECZTRA 1 and ECZTRA 2 and included all patients transferred to the open-label phase, irrespective of anti-inflammatory treatment (including TCS use). Missing data were imputed as non-response. All patients were initially randomized to tralokinumab up to week 16; [b]25 patients (3.64%) were incorrectly transferred to open-label treatment despite achieving EASI-75 at week 16.

### Alternative analysis

- In an alternative analysis to assess if the increased response over time was due to the addition of optional TCS or to extended tralokinumab treatment alone, 338/686 (49.3%) patients who used anti-inflammatory treatment, mainly TCS, were considered non-responders
  - IGA-0/1 was achieved by 95/686 (13.9%; 95% CI 11.5, 16.6) and EASI-75 was achieved by 176/686 (25.7%; 95% CI 22.5, 29.1) patients at week 52 with tralokinumab without optional TCS **(Figure 3)**

**Figure 3. Proportion of patients achieving (A) IGA-0/1 and (B) EASI-75 at week 52 in the open-label phase without use of anti-inflammatory treatment[a]**

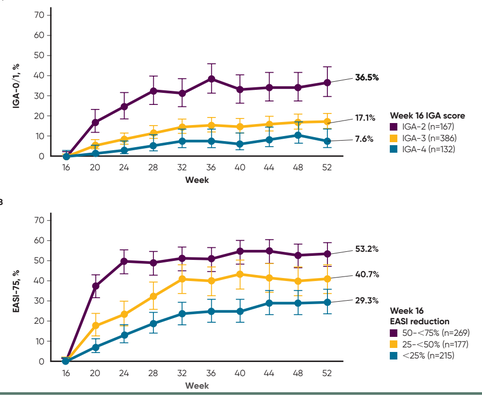



[a]Patients who received anti-inflammatory treatment were considered non-responders. Missing data were imputed as non-response. All patients were initially randomized to tralokinumab up to week 16; [b]15 patients (2.19%) were incorrectly transfered to open-label treatment despite achieving EASI-75 at week 16 without receiving anti-inflammatory treatment.

### Response by AD disease activity at week 16

- In an analysis by AD disease activity at week 16 in all patients initially treated with tralokinumab and transferred to the open-label phase, irrespective of TCS use, 36.5% (95% CI 29.6, 44.4) of patients who had IGA-2 at week 16 achieved IGA-0/1 at week 52, whereas 17.1% (95% CI 13.7, 21.2) and 7.6% (95% CI 4.2, 13.4) of patients with IGA-3 and IGA-4 at week 16 achieved IGA-0/1 at week 52, respectively **(Figure 4)**
- 53.2% (95% CI 47.2, 59.0) of patients who had EASI-50 to EASI-74 at week 16 achieved EASI-75 at week 52, whereas 40.7% (95% CI 33.7, 48.0) and 29.3% (95% CI 23.6, 35.7) of patients with a reduction in EASI score of 25–<50% and <25% at week 16 achieved EASI-75 at week 52, respectively

**Figure 4. Proportion of patients achieving (A) IGA-0/1 and (B) EASI-75 based on level of disease activity at week 16[a]**




[a]Data were pooled from ECZTRA 1 and ECZTRA 2 and included all patients transferred to the open-label phase, irrespective of anti-inflammatory treatment (including TCS use). Missing data were imputed as non-response. All patients were initially randomized to tralokinumab up to week 16.

## Conclusions

- This post hoc analysis indicates that some tralokinumab-treated patients who did not achieve the primary endpoints (IGA-0/1 or EASI-75) at week 16 progressively improved with continued tralokinumab treatment beyond week 16
- More than half of the responder proportions at week 52 were achieved within 8 weeks of starting open-label treatment
- Patients achieving an initial clinically relevant response with tralokinumab monotherapy at week 16 (EASI-50 or IGA-2) progressively improved with continued tralokinumab plus optional TCS treatment to achieve EASI-75 or IGA-0/1 over time
  - Of the week-16 EASI-50 or IGA-2 responders, 53.2% achieved EASI-75 and 36.5% achieved IGA-0/1 at week 52
  - The progressive clinical response with continued treatment beyond week 16 was mainly driven by continued tralokinumab treatment and not by the addition of optional TCS
- These data suggest that a substantial proportion of patients not achieving EASI-75 or IGA-0/1 at week 16 may improve with continued tralokinumab therapy beyond week 16

**References**

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**Disclosures**

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