Rapid and sustained improvements in itch and sleep with tralokinumab treatment in patients with moderate-to-severe Atopic Dermatitis, a post hoc analysis of pooled data from ECZTRA 1 and 2

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Introduction

- Atopic dermatitis (AD) is a chronic skin disease associated with significant itch and sleep disturbances that profoundly affect 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
- In two pivotal phase 3 trials (ECZTRA 1, NCT03131648; ECZTRA 2, NCT03160885) in adults with moderate-to-severe AD, tralokinumab monotherapy demonstrated superiority compared to placebo for each primary and secondary endpoint at Week 16 and was well tolerated up to 52 weeks of treatment[1]

Objective

To evaluate the timing and effect of tralokinumab on itch and sleep in adult patients with moderate-to-severe AD pooled from two identical Phase 3 trials.

Methods

Trial design

- ECZTRA 1 and 2 were two identically designed, multinational, double-blind, randomized, placebo-controlled, 52-week trials (**Figure 1**)
- Patients were randomized 3:1 to subcutaneous 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

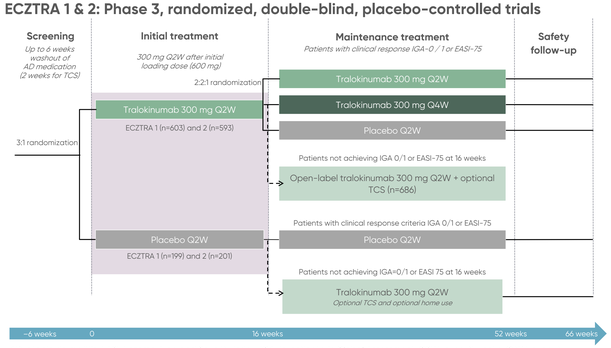
Key eligibility criteria

- ≥18 years of age
- Confirmed diagnosis of atopic dermatitis for ≥1 year
- EASI score ≥12 at screening and ≥16 at baseline
- IGA score ≥3
- AD involvement of ≥10% body surface area
- Worst daily pruritus numeric rating scale (NRS) average score ≥4 during week prior to baseline
- Candidates for systemic therapy due to a recent (within 1 year) history of inadequate response or intolerance to topical treatment

Outcomes

- EASI and IGA were assessed at baseline and at scheduled biweekly visits throughout the trials
- 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 (11-point scale with 0 indicating that it "did not interfere" and 10 indicating that it "completely interfered")

Figure 1. ECZTRA 1 and 2 trial design.



AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; Q2W, every 2 weeks; Q4W, every 4 weeks; TCS, topical corticosteroid. Wollenberg A et al. *Br J Dermatol* 2020.

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 6) in post-hoc analyses using a mixed model for repeated measures with fixed effects of planned treatment, region, baseline IGA, trial and interactions between treatment and visit and baseline value and visit. Data collected after permanent discontinuation or initiation of rescue medication (including TCS) were set to missing
  - Difference in worst daily pruritus and eczema-related sleep interference response rates (NRS ≥2 and NRS≥4) were assessed using the single worst daily measures (Baseline to Day 12) in post-hoc analyses 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
  - *p* values are nominal without multiplicity adjustment

Results

Patients, demographics, and clinical characteristics

- 802 and 794 patients were randomized in ECZTRA 1 and 2, respectively (tralokinumab, n=1196; placebo, n=400)
- Baseline demographics and clinical characteristics were well balanced between treatment groups (**Table 1**)

Table 1. Baseline demographics and clinical characteristics.

	All randomized (N=1596)	Tralokinumab Q2W (n=1196)	Placebo (n=400)
Mean age in years (SD)	37.8 (14.4)	37.9 (14.2)	37.2 (14.8)
Male, n (%)	947 (59.3)	710 (59.4)	237 (59.3)
Region, n (%)			
North America	559 (35.0)	419 (35.0)	140 (35.0)
Europe	711 (44.5)	533 (44.6)	178 (44.5)
Australia	121 (7.6)	90 (7.5)	31 (7.8)
Asia	205 (12.8)	154 (12.9)	51 (12.8)
Mean affected BSA, %	52.9 (24.9), *n=1595*	52.7 (24.8)	53.6 (25.3), *n=399*
Mean disease duration, years (SD)	28.2 (15.2), *n=1594*	28.1 (15.2), *n=1195*	28.5 (14.9), *n=399*
Severe Disease (IGA 4), n (%)	794 (49.7)	591 (49.4)	203 (50.8)
Mean EASI (SD)	32.3 (14.0), *n=1590*	32.2 (14.0), *n=1192*	32.7 (13.9), *n=398*
Mean total SCORAD (SD)	70.4 (13.0), *n=1590*	70.2 (13.2), *n=1192*	71.1 (12.4), *n=398*
Mean DLQI (SD)	17.3 (7.1), *n=1572*	17.2 (7.1), *n=1178*	17.5 (7.0), *n=394*
Mean weekly average worst daily pruritus NRS (SD)	7.8 (1.4), *n=1577*	7.8 (1.4), *n=1182*	7.8 (1.4), *n=395*
Mean weekly average eczema related sleep NRS (SD)	7.0 (2.0), *n=1577*	7.0 (2.0), *n=1182*	7.0 (2.0), *n=395*

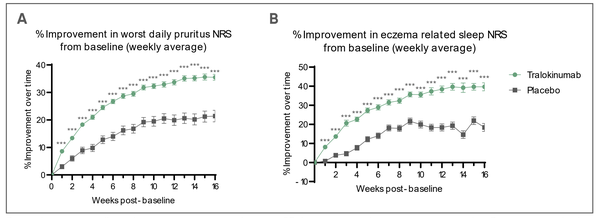
IGA 0/1 and EASI-75 at Week 16

- Significantly more patients achieved the primary endpoints of IGA 0/1 (tralokinumab 19.0%, placebo 9.0%; $p<0.001$) and a 75% reduction in Eczema Area and Severity Index (EASI-75; tralokinumab 29.0%, placebo 12.1%; $p<0.001$) at Week 16 with tralokinumab versus placebo†

Effect on itch and sleep over 16 weeks

- At Week 16, tralokinumab had a greater adjusted mean percentage improvement from baseline in weekly average of worst daily pruritus NRS (tralokinumab 35.5%, placebo 21.4%; $p<0.001$) and eczema-related sleep interference (tralokinumab 39.7%, placebo 18.4%; $p<0.001$) compared to placebo (**Figure 2**)

Figure 2. Percent improvement from baseline in weekly average over 16 weeks in: **A.** worst daily pruritus NRS **B.** eczema related sleep NRS

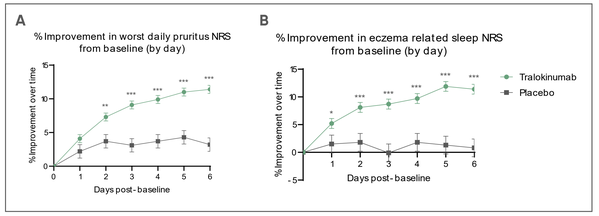


Data shown are adjusted mean percentage change ±SE from repeated measurements model. Data collected after permanent discontinuation or initiation of rescue medication (including TCS) were set to missing. *$p<0.05$; **$p<0.01$; ***$p<0.001$.

Timing of the effect on itch and sleep

- A greater improvement from baseline was seen in worst daily pruritus NRS from Day 2 ($p=0.001$), and in eczema-related sleep interference from Day 1 ($p<0.05$) with tralokinumab compared to placebo (**Figure 3**)

Figure 3. Percent improvement from baseline by day in: **A.** worst daily pruritus NRS **B.** eczema related sleep NRS



Data shown are adjusted mean percentage change ±SE from repeated measurements model. Data collected after permanent discontinuation or initiation of rescue medication (including TCS) were set to missing. *$p<0.05$; **$p<0.01$; ***$p<0.001$.

- Relative to the placebo group, a significantly greater proportion of patients in the tralokinumab group achieved ≥2 or ≥4 point improvement after:†
  - 3 days for **worst daily pruritus NRS ≥2** (at Day 3, tralokinumab: 29.7%, placebo: 20.0%; difference [95% CI]: 11.9 % [7.4%, 16.4%]; $p<0.001$)
  - 4 days for **worst daily pruritus NRS ≥4** (at Day 4, tralokinumab: 10.1%, placebo: 7.5%; difference: 3.7 % [1.5%, 6.0%]; $p=0.008$)
  - 2 days for **eczema related sleep NRS ≥2** (Day 2, tralokinumab: 29.7%, placebo: 24.0%; difference: 6.2 % [1.3%, 11.2%]; $p=0.018$)
  - 3 days for **eczema related sleep NRS ≥4** (at Day 3, tralokinumab: 11.0%, placebo: 8.2%; difference: 4.3 % [1.8%, 6.8%]; $p=0.005$)

†Missing data or data after collected after rescue medication (including TCS) were imputed as non-response.

Conclusions

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

References

1. Wollenberg A et al. *Br J Dermatol.* 2020 Sep 30. doi: 10.1111/bjd.19574. Online ahead of print.

Disclosures

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