Tralokinumab Treatment Substantially Improves Patient-Reported Outcomes in Adolescents with Moderate-To-Severe Atopic Dermatitis at 16 Weeks

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Introduction

- Atopic dermatitis (AD) is a chronic inflammatory skin disease that can negatively impact quality of life (QoL) in adolescents through effects on school performance, social relationships, participation in sports, and increased rates of anxiety, depression, and suicidal ideation[1-4]
- Tralokinumab is a fully human, high-affinity, monoclonal antibody that specifically neutralizes interleukin (IL)-13, a key driver of cutaneous barrier dysfunction, inflammation, and dysbiosis in AD[5-9]
- In phase 3 clinical trials, at Week 16, tralokinumab 150 mg and 300 mg every 2 weeks (Q2W) demonstrated significant efficacy vs placebo across primary and secondary endpoints in adolescents with moderate-to-severe AD
- Tralokinumab was well-tolerated; efficacy and safety profiles in adolescents were comparable to those in tralokinumab adult phase 3 trials[10,11]

Objective

- To evaluate the impact of tralokinumab on patient-reported outcomes (PROs) through Week 16 of adolescents in the phase 3 ECZTRA 6 trial (NCT03526861)

Methods

Study Design

- Adolescent patients were randomly assigned 1:1:1 to subcutaneous tralokinumab 150 mg (n=100) or 300 mg (n=101), or placebo (n=100) every 2 weeks (Q2W) for an initial treatment period of 16 weeks. Full analysis set included n=98 patients to tralokinumab 150 mg, n=97 to 300 mg and n=94 to placebo **(Figure 1)**

Patient-reported outcomes (PROs) data collection

Daily via eDiary

- Adolescent worst pruritus Numeric Rating Scale (NRS)
- Eczema-related Sleep Numeric Rating Scale (NRS)

Pruritus NRS: 0 (no itch) – 10 (worst itch)

Sleep NRS: 0 (did not interfere) – 10 (completely interfered)

Scheduled site visits

- Children's Dermatology Life Quality Index (CDLQI)
- Patient-Oriented Eczema Measure (POEM)
- Hospital Anxiety and Depression Scale (HADS)

CDLQI Total: 0 – 30 (↑ score = ↓ QoL)

POEM Total: 0 – 28 (≥8 = moderate eczema; ≥17 = severe eczema)

HADS Total: 0 – 21 (≥8 = anxiety/depression)

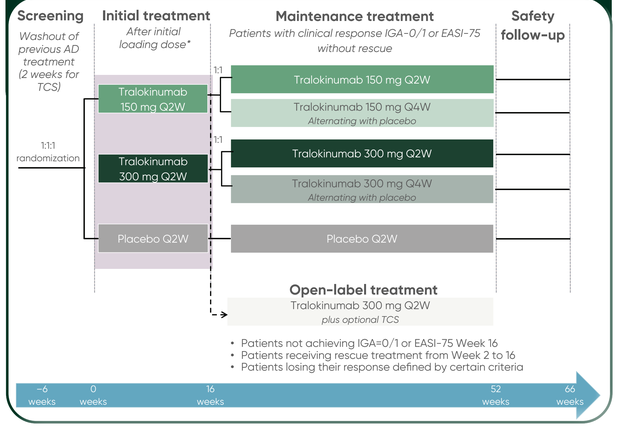
Key inclusion criteria

- Age 12 – 17
- Diagnosis of AD as defined by the Hanifin and Rajka (1980) criteria for AD
- History of AD for ≥1 year
- Body surface area (BSA) involvement ≥10% at screening and baseline
- Eczema Area and Severity Index (EASI) score ≥12 at screening and ≥16 at baseline
- Investigator's Global Assessment (IGA) score ≥3 at screening and baseline
- Adolescent worst pruritus Numeric Rating Scale (NRS) average score ≥4 during the week prior to baseline
- History of topical corticosteroid (TCS) and/or topical calcineurin inhibitor (TCI) treatment failure, or patients for whom these treatments are medically inadvisable
- Stable dose of emollient ≥2 times daily for ≥14 days before randomization

Key exclusion criteria

- Treatment with systemic immunosuppressive/immunomodulating drugs and/or systemic corticosteroid ≤4 weeks before randomization
- TCS, TCI, or topical PDE-4 inhibitor treatment ≤14 days before randomization
- Receipt of any marketed biological therapy or investigational biologic agents, including immunoglobulin, anti-IgE, or dupilumab:
  - Any cell-depleting agents (including but not limited to rituximab) ≤6 months before randomization or other biologics ≤3 months or 5 half-lives before randomization
- Active skin infection ≤1 week before randomization

Figure 1. ECZTRA 6 trial design



*loading dose of 600 mg for patients receiving 300 mg Q2W; 300 mg for those receiving 150 mg Q2W
AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; Q2W, every 2 weeks; Q4W, every 4 weeks; TCS, topical corticosteroids.

Statistical analyses

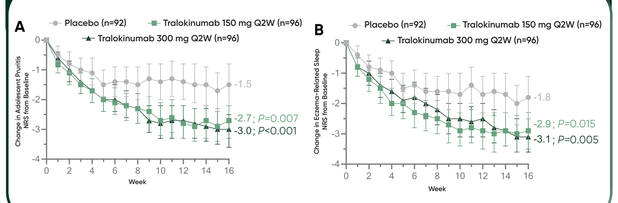
- Change from baseline to Week 16 for adolescent worst pruritus NRS (weekly average), CDLQI, POEM, eczema-related sleep NRS (weekly average), and HADS were analyzed using a linear mixed model for repeated measurements (Change = Treatment * Week + Baseline * Week + Region + Baseline IGA)
  - Data collected after use of rescue (after Week 2) or discontinuation were disregarded from the analysis
- ≥4-point improvement in adolescent worst pruritus NRS (weekly average) and ≥6-point improvement in CDLQI and POEM at Week 16 were analyzed using Cochran-Mantel-Haenszel test stratified by geographic region and baseline IGA
  - Patients receiving rescue therapy after Week 2 or with missing data at Week 16 were considered non-responders

Results

Patient reported itch severity and sleep interference

- Tralokinumab treatment was associated with significantly greater improvement than placebo in adolescent worst pruritus NRS and eczema-related sleep NRS (weekly average) **(Figure 2A, B)**

Figure 2. Tralokinumab treatment vs placebo at Week 16. A. Change in adolescent worst pruritus NRS (weekly average) B. Change in eczema-related sleep NRS (weekly average)

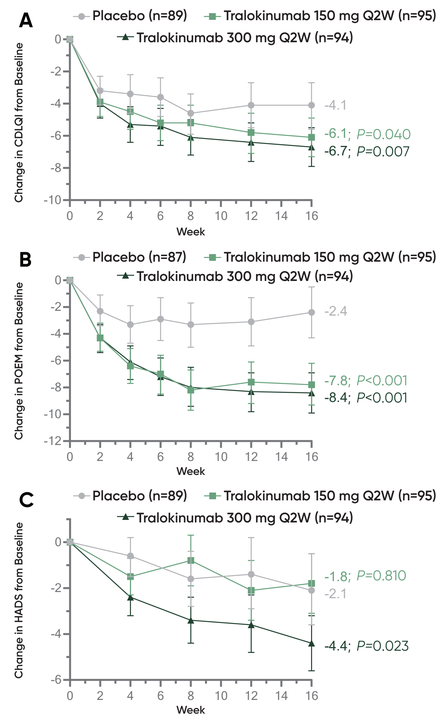


Error bars show 95% confidence intervals. P-values compare respective tralokinumab dose to placebo. n represents number of patients in the full analysis set with a non-missing baseline value.
NRS, Numerical Rating Scale; Q2W, every 2 weeks.

Patient reported QoL, eczema severity, and anxiety/depression

- Tralokinumab treatment was associated with significantly greater improvement than placebo in CDLQI and POEM **(Figure 3A, B)**
- Tralokinumab treatment (300 mg) was associated with significantly greater improvement than placebo in HADS **(Figure 3C)**

Figure 3. Tralokinumab treatment vs placebo at Week 16. A. Change in CDLQI B. Change in POEM C. Change in HADS

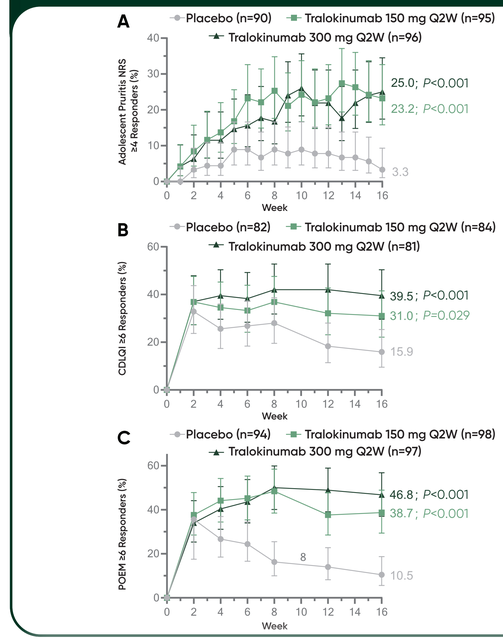


Error bars show 95% confidence intervals. P-values compare respective tralokinumab dose to placebo. n represents number of patients in the full analysis set with a non-missing baseline value.CDLQI, Children's Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale; POEM, Patient-Oriented Eczema Measure; Q2W, every 2 weeks.

Improvement in patient reported itch severity, eczema severity, and QoL

- Significantly greater proportions of patients receiving tralokinumab versus placebo achieved ≥4-point improvement in adolescent worst pruritus NRS (weekly average) **(Figure 4A)**
- Significantly greater proportions of patients receiving tralokinumab vs placebo achieved ≥6-point improvement in CDLQI and POEM **(Figure 4B, C)**

Figure 4. Tralokinumab treatment vs placebo at Week 16. A. Patients with ≥4-point improvement in adolescent worst pruritus NRS from baseline (weekly average) B. Patients with ≥6-point improvement in CDLQI from baseline C. Patients with ≥6-point improvement in POEM from baseline



Error bars show 95% confidence intervals. P-values compare respective tralokinumab dose to placebo. CDLQI, Children's Dermatology Life Quality Index; NRS, Numeric rating scale; POEM, Patient-Oriented Eczema Measure; Q2W, every 2 weeks.

Conclusions

- Tralokinumab significantly improved symptomatic and psychosocial impacts of moderate-to-severe AD in adolescents utilizing clinically relevant PROs at Week 16, including itch, sleep interference, anxiety/depression, and QoL
- The impact of tralokinumab treatment extends beyond improvement in objective signs of AD disease to include patient perceived subjective symptoms which are known to be of major importance for this vulnerable patient group

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