Efficacy and Safety of Tralokinumab in Adolescents with Moderate-to-Severe Atopic Dermatitis: Results of the Phase 3 ECZTRA 6 Trial

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Introduction

- Atopic dermatitis (AD) is a chronic, pruritic, inflammatory skin disease that can negatively impact quality of life in adolescents[1]
  - Negative impacts of AD include effects on school performance, social relationships, participation in sports and increased rates of anxiety, depression, and suicidal ideation[2-4]
- Tralokinumab is a fully human, high-affinity, monoclonal antibody that specifically neutralizes interleukin (IL)-13, a key driver of skin barrier dysfunction, inflammation and dysbiosis in AD[5-9]
- In adult phase 3 trials, tralokinumab demonstrated efficacy and safety for treatment of AD[10, 11]

Objective

- To evaluate the efficacy and safety of tralokinumab in adolescents with moderate-to-severe AD in the phase 3 ECZTRA 6 trial (NCT03526861)

Methods

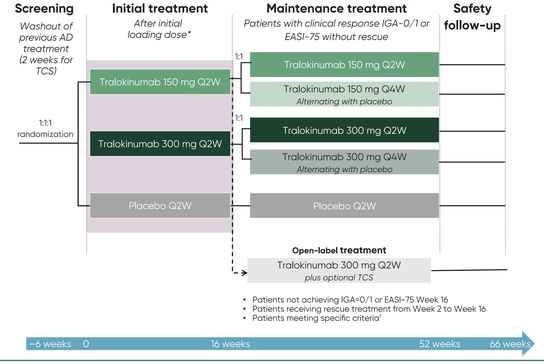
Study design (Figure 1)

- Adolescent patients were randomized 1:1:1 to subcutaneous tralokinumab 150 mg or 300 mg every 2 weeks (Q2W), or placebo for an initial treatment period of 16 weeks
- Primary endpoints were Investigator's Global Assessment (IGA) score 0/1 and ≥75% improvement in Eczema Area and Severity Index (EASI-75) at Week 16
- Patients achieving primary endpoints without rescue treatment were re-randomized to tralokinumab Q2W or every 4 weeks (Q4W), at their same initial dosage for 36 weeks of maintenance treatment as shown in **Figure 1**
- Patients not achieving primary endpoints at Week 16, those receiving rescue treatment from Week 2 to Week 16, and those meeting other specific criteria† were transferred to open-label treatment of tralokinumab 300 mg Q2W plus optional mild-to-moderate strength topical corticosteroids (TCS)

Key inclusion criteria

- Age 12 – 17
- History of AD for ≥1 year
- BSA involvement ≥10% at screening and baseline
- EASI score ≥12 at screening and ≥16 at baseline
- IGA score ≥3 at screening and baseline
- History of TCS and/or topical calcineurin inhibitor treatment failure, or subjects for whom these treatments are medically inadvisable
- Stable dose of emollient ≥2 times daily for ≥14 days before randomization

Figure 1. ECZTRA 6 study design



*loading dose of 600 mg for patients receiving 300 mg Q2W or 300 mg for those receiving 150 mg Q2W
†Patients not achieving EASI-75 over 14 weeks with IGA ≥2 after IGA=0 at Week 16, or with IGA ≥3 after IGA=1 at Week 16, or who had IGA >1 at Week 16; patients who receive rescue treatment after Week 16
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 and endpoints

- EASI-75, IGA 0/1, and secondary endpoint ≥4-point improvement in adolescent pruritus Numerical Rating Scale (NRS) were analyzed using Cochran–Mantel–Haenszel test stratified by geographic region and baseline disease severity
  - Patients receiving rescue therapy between Week 2 and 16 or with missing data at Week 16 were considered non-responders
- Secondary endpoints, change from baseline in SCORing AD (SCORAD) and Children's Dermatology Life Quality Index (CDLQI) were analyzed using a linear mixed model for repeated measurements
  - Data after use of rescue or discontinuation were disregarded
- A closed testing procedure with hierarchical tests, alpha splitting, and alpha recycling were applied for above efficacy endpoints
- The safety population was defined as all randomized patients who received ≥1 injection of study drug

Results

Patient characteristics

- Baseline demographic and clinical characteristics were comparable across treatment groups **(Table 1)**

Table 1. Baseline characteristics

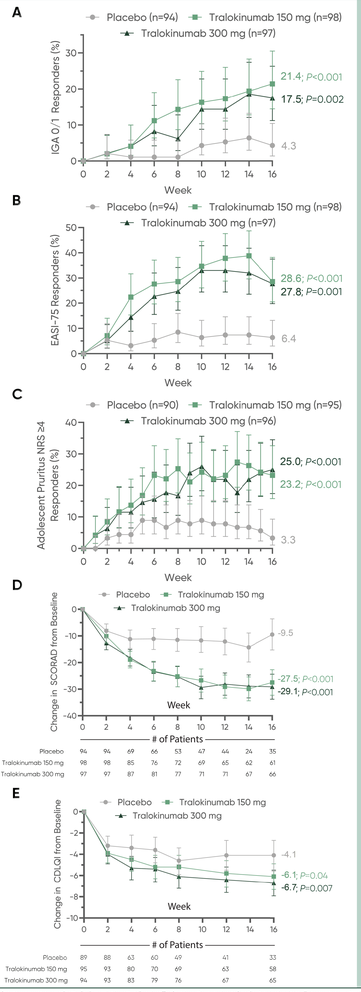
	Placebo (N=94)	Tralokinumab 150 mg Q2W (N=98)	Tralokinumab 300 mg Q2W (N=97)
Mean age, years	14.3	14.8	14.6
Age group, n (%)			
12–14	49 (52.1)	37 (37.8)	45 (46.4)
15–17	45 (47.9)	61 (62.2)	52 (53.6)
Male, n (%)	51 (54.3)	51 (52.0)	47 (48.5)
Race/Ethnicity, n (%)			
White	53 (56.4)	55 (56.1)	56 (57.7)
Black or African American	11 (11.7)	7 (7.1)	14 (14.4)
Asian	23 (24.5)	28 (28.6)	20 (20.6)
Hispanic or Latino	6 (6.4)	10 (10.2)	9 (9.3)
Mean duration of AD, years (SD)	12.7 (3.7)	12.1 (3.7)	12.1 (3.5)
Mean BSA involvement with AD, % (SD)	51.4 (23.9)	52.4 (22.6)	49.6 (23.3)
Severe disease (IGA=4), n (%)	43 (45.7)	44 (44.9)	48 (49.5)
Mean EASI score (SD)	31.2 (14.5)	32.1 (12.9)	31.8 (13.9)
Mean SCORAD score (SD)	67.4 (14.9)	67.7 (14.4)	68.3 (13.7)
Mean CDLQI score (SD)	13.3 (6.0)	12.9 (6.3)	13.4 (7.3)
Mean weekly average worst daily pruritus NRS score (SD)	7.5 (1.7)	7.5 (1.6)	7.8 (1.5)

BSA: Body surface area. AD: Atopic Dermatitis. n: Number of subjects in analysis set. Q2W: Every 2 weeks. IGA: Investigator's Global Assessment. EASI: Eczema Area and Severity Index. SCORAD: Scoring Atopic Dermatitis. CDLQI: Children's Dermatology Life Quality Index. NRS: Numeric rating scale.

Week 16 efficacy analyses

- At Week 16, a significantly greater proportions of patients receiving tralokinumab achieved the primary endpoints of IGA 0/1 and EASI-75 without use of rescue compared to those receiving placebo **(Figures 2A, B)**
- A significantly greater proportions of patients receiving tralokinumab vs placebo achieved ≥4-point improvement in adolescent pruritus NRS at Week 16 without use of rescue **(Figure 2C)**
- Tralokinumab treatment was associated with greater improvement than placebo in SCORAD and CDLQI from baseline to Week 16 **(Figures 2D, E)**

Figure 2. Tralokinumab treatment demonstrated efficacy vs placebo across endpoints at Week 16. A. IGA 0/1 B. EASI-75 C. ≥4-point improvement in adolescent pruritus NRS D. Change in SCORAD E. Change in CDLQI



Error bars show 95% confidence intervals. P-values compare respective tralokinumab dose to placebo. Tables show the number of patients who had a valid measurement value at the specified week.
Q2W: Every 2 weeks. IGA: Investigator's Global Assessment. EASI: Eczema Area and Severity Index. NRS: Numeric rating scale. SCORAD: Scoring Atopic Dermatitis. CDLQI: Children's Dermatology Life Quality Index.

Safety through Week 16

- Through Week 16, percentages of adverse events (AEs), serious AEs, AEs leading to discontinuation, and conjunctivitis events were similar between the tralokinumab (150 mg/300 mg) and placebo treatment groups **(Table 2)**
- The majority of AEs in all treatment groups were mild or moderate in severity and subjects recovered from most of the AEs

Table 2. Summary of AEs from Week 0 to 16

	Placebo (N=94)	Tralokinumab 150 mg Q2W (N=98)	Tralokinumab 300 mg Q2W (N=97)
Patient-Years of Exposure	27.93	29.33	29.48
AEs, n (%)	58 (61.7)	66 (67.3)	63 (64.9)
SAEs, n (%)	5 (5.3)	3 (3.1)	1 (1.0)
AEs leading to discontinuation, n (%)	0	1 (1.0)	0
Severity, n (%)			
Mild	40 (42.6)	48 (49.0)	47 (48.5)
Moderate	31 (33.0)	33 (33.7)	32 (33.0)
Severe	7 (7.4)	5 (5.1)	3 (3.1)
AEs of special interest, n (%)			
Eye disorders	2 (2.1)	4 (4.1)	4 (4.1)
Conjunctivitis	2 (2.1)	4 (4.1)	3 (3.1)
Eczema herpeticum	1 (1.1)	1 (1.0)	0
Skin infections requiring systemic treatment	2 (2.1)	5 (5.1)	2 (2.1)
Injection site reactions	1 (1.1)	9 (9.2)	7 (7.2)

Conclusions

- At Week 16, tralokinumab 150 mg and 300 mg 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 were comparable to those in phase 3 adult tralokinumab trials

References

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Disclosures

Amy Paller has served as an investigator for AbbVie, Anaptysbio, Incyte, Janssen, KrystalBio, LEO Pharma, Regeneron, and UCB, received honorarium for consultancy from AbbVie, Abeona, Almirall, Anaptysbio, Arena, Azitra, BiomX, Boehringer Ingelheim, Castle Biosciences, Catawba, Dermira, Evicure, Forté, Kamari, LEO Pharma, Lilly, LifeMax, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Seanergy, and UCB, and served on a Data Safety Monitory Board for AbbVie, Bausch, Galderma, and Novan. **Andrew Blauvelt** is a scientific adviser and clinical study investigator for AbbVie, Abcentra, Aligos, Almirall, Amgen, Arcutis, Arena, Asian, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly, Evommune, Forte, Galderma, Incyte, Janssen, Landos, LEO Pharma, Novartis, Pfizer, Rapt, Regeneron Pharmaceuticals, Inc., Sanofi Genzyme, Sun Pharma, UCB Pharma. **Weily Soong** has served on the advisory board and received research grants from Abbvie, LEO, Genentech, Inc., Teva, Novartis, and Pfizer; served on the advisory board, received research grants, and was a speaker for Amgen, AstraZeneca, Regeneron, Sanofi, and GlaxoSmithKline; received research grants and was a speaker for Optinose; received research grants from Aimmune, Avillion, Galderma, Gossamer Bio, 3M, and LEO Pharma. **Shinichi Imafuku** is a researcher, consultant, or speaker for Abbvie, Amgen, Celgene, DaiichiSankyo, Eisai, KyowaKirin, Lilly, Taihoyakuhinkogyo, TanabeMitsubishi, Tsumura, Torii, Maruho, Novartis, LEO Pharma and Janssen. **Chih-ho Hong** is a researcher, consultant, and/or advisor for AbbVie, Amgen, Arcutis, Bausch Health, Boehringer Ingelheim, Celgene, Dermavant, Dermira, DS Biopharma, Galderma, GlaxoSmithKline, Incyte, Janssen, LEO Pharma, Lilly, Medimmune, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sun Pharma, and UCB. **Marie L.A. Schuttelaar** has served on advisory boards for Sanofi Genzyme, Pfizer, LEO Pharma, Eli Lilly, Galderma, and Abbvie; as an investigator for AbbVie, Novartis, Regeneron Pharmaceuticals, Inc., Sanofi Genzyme, and Galderma; as a consultant for Regeneron Pharmaceuticals, Inc.; has received research grants from Sanofi Genzyme and Novartis. **Petra Amoudruz, Azra Kurbasic, Lise Soldbro, Katja Lophaven,** and **Shannon Schneider** are employees of LEO Pharma A/S. **Michael Cork** has served as a clinical trial investigator for Astellas, Galapagos, Johnson & Johnson, LEO Pharma, La Roche-Posay, MSD, Novartis, Perrigo, Regeneron, Sanofi Genzyme, and Stiefel; has served as an advisory board member, consultant, and/or invited lecturer for Pfizer Inc., Amgen, Astellas, Bayer, Johnson & Johnson, LEO Pharma, L'Oréal, MSD, Novartis, Regeneron, Sanofi Genzyme, Stiefel, and Unilever; has received honoraria from Astellas, Johnson & Johnson, LEO Pharma, Novartis, Regeneron, Sanofi Genzyme, and Stiefel; and has received research funding from Bayer. **Anthony Bewley** has been a consultant for and received consultancy fees or travel bursaries from AbbVie, Almirall, Eli Lilly, Galderma, Janssen, LEO Pharma, Novartis, Sanofi and UCB Pharma. **Eric Simpson** is a consultant and investigator for Regeneron/Sanofi, Dermira, Menlo Pharmaceuticals, Lilly, Abbvie, Genentech, Medimmune, GSK, LEO Pharma, Celgene, and Pfizer.

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