The impact of tralokinumab on quality of life and school in patients aged 12–17 with atopic dermatitis: results from the phase 3 ECZTRA 6 trial

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Introduction

- Tralokinumab is a fully human monoclonal antibody that binds with high affinity to interleukin-13, a key driver of atopic dermatitis (AD) pathogenesis[1–3]
- AD is a chronic inflammatory skin disease associated with poor quality of life (QoL) and a substantial psychosocial impact in adolescents[4,5]
- AD is associated with poor school behaviours in adolescent patients, including poor task completion, poor connectedness and impulsivity[6]
- The phase 3 ECZTRA 6 trial (NCT03526861) of patients aged 12–17 years with moderate-to-severe AD showed:
  - Tralokinumab monotherapy had superior efficacy to placebo for all primary and key secondary efficacy endpoints, including change in Children's Dermatology Life Quality Index (CDLQI) from baseline to Week 16[7]
- Here we present a detailed analysis of CDLQI results from ECZTRA 6

Objective

- To examine the impact of tralokinumab on AD-related QoL and school in adolescents during Weeks 0–16 of the ECZTRA 6 trial (NCT03526861)

Materials and Methods

Study design

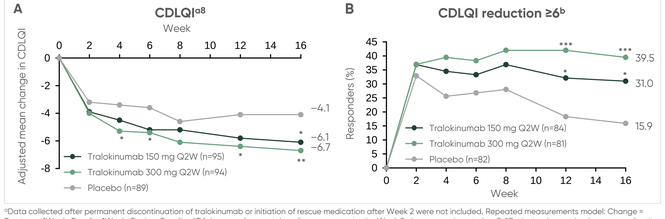
- Adolescents with moderate-to-severe AD (n=289) received tralokinumab 150 mg or 300 mg or placebo every 2 weeks (Q2W) during the initial phase (Weeks 0–16)
- QoL and impact on school was measured using the CDLQI, a 10-item questionnaire assessing patient/caregiver-reported AD impact
  - This analysis presents the results for most of the CDLQI subdomains (excluding 'How Itchy, Sore, Painful' and 'Affected Sleep', which are addressed by other analyses elsewhere)
- Change and proportion of patients with ≥6-point reduction (minimal important difference) from baseline to Week 16 in total CDLQI were evaluated using a linear mixed model for repeated measures and Cochran-Mantel-Haenszel test, respectively
- Individual CDLQI domains were evaluated with the Pearson chi-square test
- Rescue medication [topical calcineurin inhibitor (TCI), TCS, systemic treatment] was used if medically necessary (i.e., to control intolerable AD symptoms)

Results

Change in CDLQI and reduction of CDLQI ≥6: Weeks 0–16

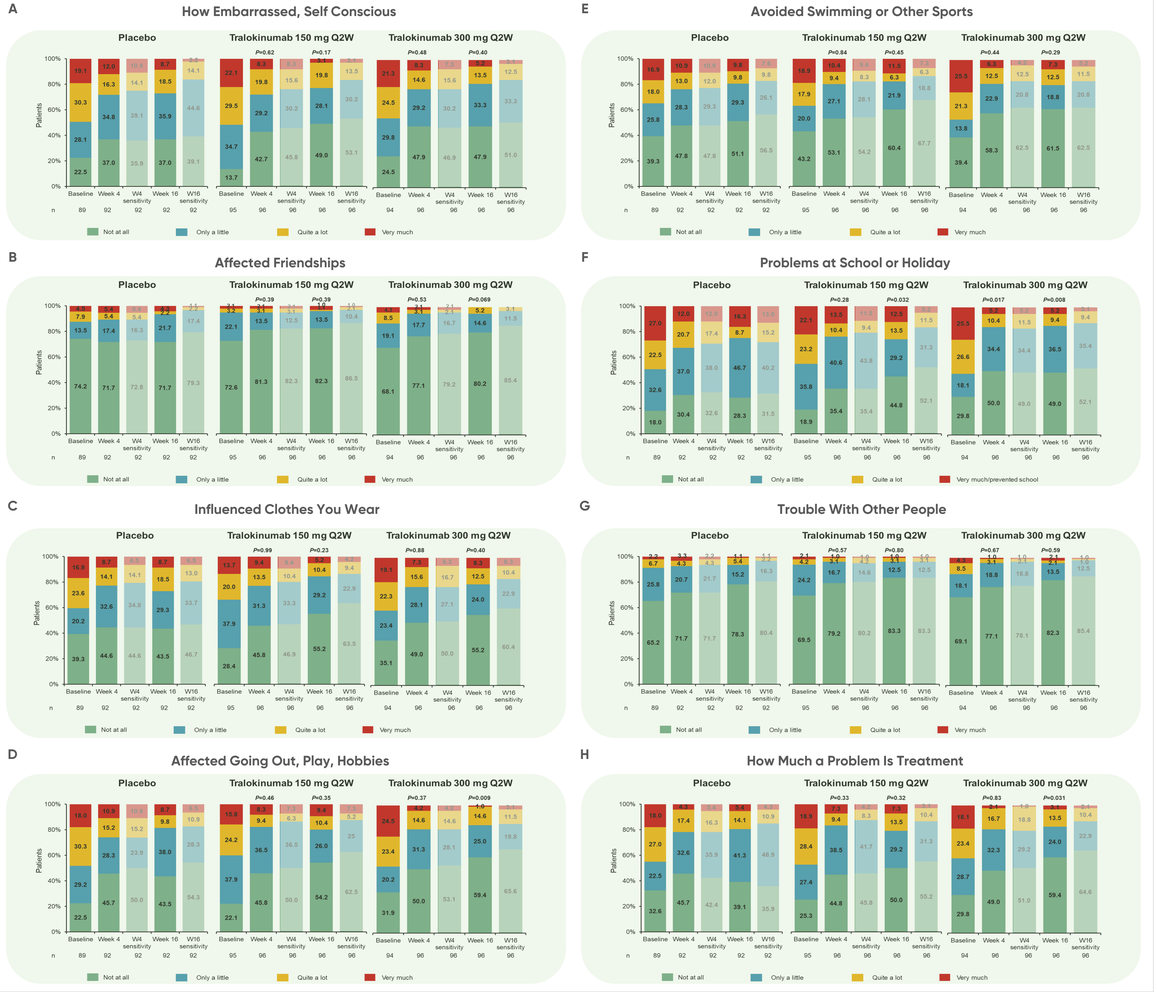
- At Week 16, adjusted mean change from baseline in CDLQI was significantly greater with tralokinumab 150 mg (−6.1) and 300 mg (−6.7) vs placebo (−4.1); difference* −2.0 (p=0.04) and −2.6 (p=0.007) respectively (**Figure 1A**)
- More patients had ≥6-point reduction (minimal important difference in adolescents) with tralokinumab 150 mg (31.0%) and 300 mg (39.5%) vs placebo (15.9%); difference* 14.1% (p=0.029) and 23.9% (p<0.001), respectively (**Figure 1B**)

Figure 1. (A) Adjusted mean change in CDLQI and (B) reduction of CDLQI ≥6 by week



[a]Data collected after permanent discontinuation of tralokinumab or initiation of rescue medication after Week 2 were not included. Repeated measurements model: Change = Treatment*Week+Baseline*Week+Region+Baseline IGA. In case of no post-baseline assessments, the Week 2 change was imputed as 0. [b]Patients who received rescue medication after Week 2 were considered non-responders, as were patients with missing data at Week 16.
*Mantel-Haenszel risk difference compared with placebo, stratified by region and baseline IGA *p<0.05 vs placebo; **p<0.01 vs placebo; ***p<0.001 vs placebo. Patients with at least baseline data available were included in the CDLQI adjusted mean change analysis (A), and patients with CDLQI ≥6 at baseline were included in the CDLQI reduction ≥6 analysis (B).
CDLQI, Children's Dermatology Life Quality Index; IGA, Investigator's Global Assessment; Q2W, every 2 weeks.

Figure 2. Affect of AD on CDLQI domains (Weeks 0–16)



Last observation carried forward (LOCF) was used for patients who used rescue medication or discontinued treatment (observation prior to rescue initiation/treatment discontinuation) or had missing data. Sensitivity analyses used observed data, and LOCF was used for patients missing data. Rescue medication was used by 56.4%, 33.7% and 29.9% in the placebo, tralokinumab 150 mg and 300 mg arms, respectively. Across arms, >70% of patients used topical corticosteroids only.
P values = Pearson chi-square test vs placebo

Affect of AD on CDLQI domains: Weeks 0–16

- At Week 16, AD had 'not at all':
  - affected how embarrassed or self-conscious the patient was over the past 7 days in 49.0/47.9% of tralokinumab (150/300 mg) treated patients vs 37.0% receiving placebo (**Figure 2A**)
  - affected friendships over the past 7 days in 82.3/80.2% of tralokinumab (150/300 mg) treated patients vs 71.7% receiving placebo (**Figure 2B**)
  - influenced clothes you wear over the past 7 days in 55.2/55.2% of tralokinumab (150/300 mg) treated patients vs 43.5% receiving placebo (**Figure 2C**)
  - affected going out, play, or hobbies over the past 7 days in 54.2/59.4% of tralokinumab (150/300 mg) treated patients vs 43.5% receiving placebo (**Figure 2D**)
- At Week 16, 60.4/61.5% of tralokinumab (150/300 mg) treated patients had 'not at all' avoided swimming or other sports due to AD over the past 7 days vs 51.1% receiving placebo (**Figure 2E**)
- At Week 16, AD had 'not at all':
  - affected school/holiday over the past 7 days in 44.8/49.0% of tralokinumab (150/300 mg) treated patients vs 28.3% receiving placebo (**Figure 2F**)
  - impacted trouble with other people over the past 7 days in 83.3/82.3% of tralokinumab (150/300 mg) treated patients vs 78.3% receiving placebo (**Figure 2G**)
- At Week 16, problem with treatment affected patients 'not at all' over the past 7 days in 50.0/59.4% of tralokinumab (150/300 mg) treated patients vs 39.1% receiving placebo (**Figure 2H**)

Conclusions

- Tralokinumab resulted in significantly greater adjusted CDLQI mean change vs placebo, and increased proportions of patients with CDLQI ≥6
- Tralokinumab improved several patient-reported outcomes that encompass psychosocial effects of AD in this vulnerable paediatric age group, as measured by the CDLQI
- Tralokinumab had a substantial benefit on the impact of AD on subdomains in the CDLQI related to school/holiday at Week 16
- There was a trend towards treatment benefit with tralokinumab vs placebo across multiple other psychosocial domains
- The largest improvements in QoL were seen in the tralokinumab 300 mg group

References

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Disclosures

Amy S. 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, Exicure, 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. **Jonathan I. Silverberg** is an investigator for AbbVie, Celgene, Eli Lilly and Company, GSK, Kiniksa, LEO Pharma, Menlo Therapeutics, Realm Therapeutics, Regeneron, Roche, and Sanofi; a consultant for Pfizer Inc., AbbVie, Anacor, AnaptysBio, Arena Pharmaceuticals, Asana Biosciences, Dermira, Dermavant, Eli Lilly and Company, Galderma, GSK, Glenmark, Incyte, Kiniksa, LEO Pharma, MedImmune, Menlo Therapeutics, Novartis, Realm Therapeutics, Regeneron, and Sanofi; a speaker for Regeneron and Sanofi; and is on advisory boards for Pfizer Inc., Dermira, LEO Pharma, and Menlo Therapeutics. **H. 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. **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. **Luis Puig** has received consultancy/speaker's honoraria from and/or participated in clinical trials sponsored by Abbvie, Almirall, Amgen, Baxalta, Biogen, Boehringer Ingelheim, Celgene, Gebro, Janssen, JSC BIOCAD, Leo-Pharma, Lilly, Merck-Serono, MSD, Mylan, Novartis, Pfizer, Regeneron, Roche, Sandoz, Samsung-Bioepis, Sanofi and UCB. **Petra Arlert**, **Azra Kurbasic**, and **Lise Soldbro** are employees of LEO Pharma A/S. **Eric L. 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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