Progressive and Sustained Disease Control in Patients with Atopic Dermatitis (AD) Aged 12–17 Years Treated with Tralokinumab 300 mg for 52 Weeks

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Objectives

- To evaluate EASI response and PROs in ECZTRA 6 adolescents treated with tralokinumab 300 mg for the full 52-week treatment period

Results

Tralokinumab 300 mg efficacy at Week 16 (vs placebo) and Week 52

- Cumulative proportions of patients using concomitant TCS (any strength) as rescue therapy during the first 16 weeks were lower with tralokinumab 300 mg (29.9%) versus placebo (56.4%)
- Over 52 weeks, the cumulative proportion of tralokinumab-treated patients using any TCS increased to 47.4%, as TCS were permitted as optional concomitant medication in the open-label arm
- Greater proportions of tralokinumab- vs placebo-treated patients achieved primary endpoints at Week 16 (**Table 1**). Progressive improvement in EASI was seen through Week 52 (**Figure 1**)

Table 1. Tralokinumab 300 mg efficacy at Weeks 16 and 52

	Initial treatment period (Weeks 0–16) at Week 16		Maintenance & open-label period (Weeks 16–52) at Week 52*
Outcome	**Tralokinumab 300 mg Q2W (n=97)**	**Placebo Q2W (n=94)**	**Tralokinumab 300 mg Q4W or Q2W ± optional TCS (n=97)**
IGA 0/1 responders, n/N (%)	20.0/97 (**20.6**)	5.0/94 (**5.3**)	43.5/97 (**44.9**)
Difference vs placebo (95% CI)	**15.5** (6.39–24.55), P=0.008		
EASI-75 responders, n/N (%)	37.3/97 (**38.4**)	22.1/94 (**23.5**)	66.7/97 (**68.8**)
Difference vs placebo (95% CI)	**15.4** (2.57–28.2), P=0.0186		
EASI-90 responders, n/N (%)	23.1/97 (**23.9**)	9.8/94 (**10.4**)	41.5/97 (**42.8**)
Difference vs placebo (95% CI)	**13.6** (2.73–24.5), P=0.0142		
EASI LSM percentage improvement, % (SE)	**59.62** (4.36)	**37.90** (5.16)	**77.95** (2.96)
Difference vs placebo (95% CI)	**21.72** (9.38–34.06), P=0.0006		

*Includes all patients initially randomised to tralokinumab 300 mg Q2W; data for patients withdrawing prior to the maintenance/open-label treatment period are imputed.

Tralokinumab 300 mg disease control at Week 16 (vs placebo) and progressive disease control at Week 52

- Pruritus NRS score was improved for a greater proportion of tralokinumab- vs placebo-treated patients from baseline to Week 16, with further improvement up to Week 52
- Progressive improvements over time were also observed for proportions of patients with reductions of pruritus NRS ≥4, POEM ≥4, and CDLQI ≥6, from baseline (**Table 2**)

Table 2. Tralokinumab 300 mg disease control at Week 16 and progressive disease control at Week 52

	Initial treatment period (Weeks 0–16) at Week 16		Maintenance & open-label period (Weeks 16–52) at Week 52*
Outcome	**Tralokinumab 300 mg Q2W (n=97)**	**Placebo Q2W (n=94)**	**Tralokinumab 300 mg Q4W or Q2W ± optional TCS (n=97)**
Pruritus NRS percentage improvement, mean (SE)	**37.62** (3.32)	**25.80** (3.56)	**46.19** (3.53)
Difference vs placebo (95% CI)	**11.82** (2.28–21.36), P=0.0151		
Pruritus NRS ≥4 from baseline, n/N (%)	35.7/96 (**37.2**)	17.8/92 (**19.3**)	38.7/96 (**40.3**)
Difference vs placebo (95% CI)	**17.88** (4.89–30.87), P=0.0070		
POEM ≥4 from baseline, n/N (%)	71.5/94 (**76.1**)	42.9/87 (**49.3**)	80.9/94 (**86.0**)
Difference vs placebo (95% CI)	**26.39** (12.47–40.31), P=0.0002		
CDLQI ≥6 from baseline, n/N (%)	47.8/94 (**50.8**)	40.4/89 (**45.4**)	52.7/94 (**56.1**)
Difference vs placebo (95% CI)	**4.84** (–9.30, 18.97), P=0.5025		

*Includes all patients initially randomised to tralokinumab 300 mg Q2W; data for patients withdrawing prior to the maintenance/open-label treatment period are imputed.

Safety summary for Weeks 0-16 and Weeks 16-52

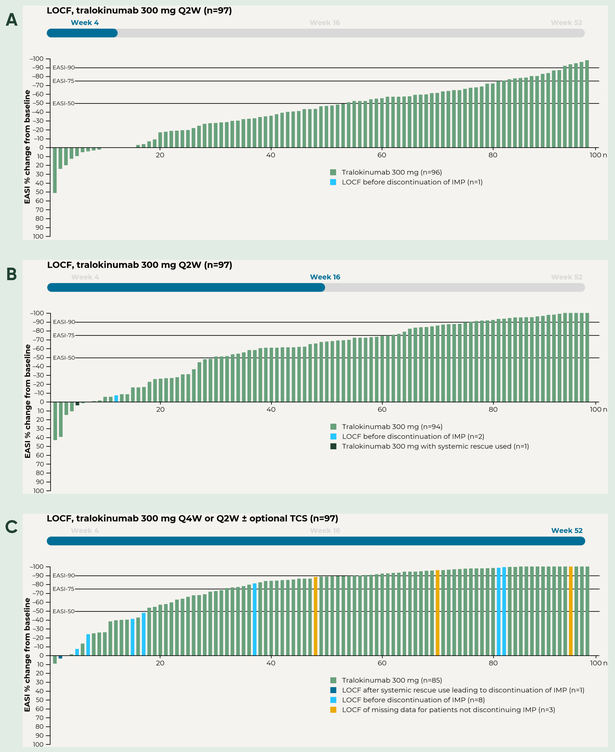
- The safety profile was consistent with prolonged treatment after Week 16; most AEs were mild, with UTRI the most common (**Table 3**)

Table 3. Safety summary for Weeks 0–16 and Weeks 16–52

	Initial treatment period (Weeks 0–16) at Week 16				Maintenance & open-label period (Weeks 16–52) at Week 52*	
	Tralokinumab 300 mg Q2W (n=97; PYE=29.48)		**Placebo Q2W (n=94; PYE=27.93)**		**Tralokinumab 300 mg Q4W or Q2W ± optional TCS (n=94; PYE=63.1)**	
	N (%)	**nE/100 PYE**	**N (%)**	**nE/100 PYE**	**N (%)**	**nE/100 PYE**
Adverse events (AEs)	63 (64.9)	441	58 (61.7)	479.7	61 (64.9)	252.0
Severity						
Mild	47 (48.5)	274.8	40 (42.6)	257.7	44 (46.8)	141.0
Moderate	32 (33.0)	152.6	31 (33.0)	179.0	36 (38.3)	107.8
Severe	3 (3.1)	13.57	7 (7.4)	25.06	2 (2.1)	3.2
Serious AEs	1 (1.0)	3.39	5 (5.3)	17.90	3 (3.2)	4.8
AEs leading to drug withdrawal	0 (0)	–	0 (0)	–	0 (0)	–
Most frequently reported AEs (≥5% of patients)						
Viral URTI†	12 (12.4)	54.27	8 (8.5)	35.80	18 (19.1)	36.4
Dermatitis atopic	7 (7.2)	23.74	12 (12.8)	57.28	7 (7.4)	14.3
URTI	11 (11.3)	37.31	4 (4.3)	17.90	8 (8.5)	17.4
Headache	6 (6.2)	20.35	3 (3.2)	10.74	5 (5.3)	9.5
Asthma	3 (3.1)	10.18	5 (5.3)	21.48	0 (0)	–

*Only patients re-randomised to the maintenance or transferred to the open-label treatment period were included in the analysis set. †Most commonly reported as common cold

Figure 1. Percent change from baseline in EASI through Week 52



*LOCF applied for patients discontinuing IMP (last observation available prior to discontinuing IMP) and for patients with missing data for other reasons at Week 32 (last observation available).

Conclusions

- At Week 16, tralokinumab 300mg Q2W improved EASI and PROs in adolescents with moderate-to-severe AD, with progressive and sustained improvement seen up to Week 52
- Tralokinumab 300 mg Q2W is an efficacious and well-tolerated treatment option for uncontrolled AD in adolescents, with a reassuring long-term safety profile over 52 weeks[1]

Background

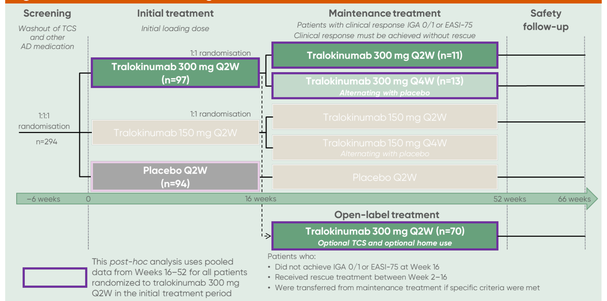
- In the ECZTRA 6 (NCT03526861) phase 3 trial, tralokinumab 300 mg provided progressive and sustained efficacy in adolescent patients with moderate-to-severe AD and was well-tolerated with a reassuring long-term safety profile over 52 weeks[1]

Methods

Study design

- Patients were randomized to tralokinumab 300 mg Q2W (n=97) or placebo (n=94) for 16 weeks (**Figure 2**)
- At Week 16, patients initiated on tralokinumab and achieving primary endpoints (IGA 0/1 and/or EASI-75) without rescue were re-randomized to tralokinumab 300 mg Q2 or Q4W monotherapy for 36 additional weeks; other patients were switched to open-label tralokinumab 300mg Q2W plus optional TCS
- Key inclusion criteria:
  - Age 12 to 17 years
  - History of AD for ≥1 year
  - AD involvement of ≥10% body surface area at screening and baseline
  - History of TCS and/or TCI treatment failure
  - EASI of ≥12 at screening and ≥16 at baseline
  - IGA of ≥3 at screening and at baseline
  - An Adolescent Pruritus NRS average score of ≥4 during the week prior to baseline
- Primary endpoints:
  - IGA 0/1 and/or EASI-75 at Week 16

Figure 2. ECZTRA 6 trial design



*Tralokinumab 300 mg Q2W, with the option of Q4W dosing for patients who achieve clear or almost clear skin after 16 weeks of treatment, is the approved dosing regimen in Europe and Canada.

Statistical methods

- A pre-specified treatment policy approach for the analyses was adopted using observed data, regardless of rescue medication and treatment discontinuation
- Missing data were imputed using multiple imputations; 100 complete datasets were created via imputations
- Treatment differences for the binary endpoints were estimated using the Cochran–Mantel–Haenszel method stratified by region and baseline IGA
- Continuous endpoint data were analyzed using analysis of covariance accounting for the treatment, region, baseline IGA, and baseline outcome value
- Treatment means for the continuous endpoints were estimated using least squares mean
- To combine inference from multiple imputations, the estimated treatment means, treatment differences and standard errors were pooled using Rubin's rule
- *Post hoc* analyses were conducted by pooling Weeks 16–52 data for all patients initially randomised to tralokinumab 300 mg Q2W, regardless of the response achieved at Week 16, the dosing regimen received beyond Week 16, or whether discontinuing treatment before Week 16 (imputed data only)

Abbreviations

AD, atopic dermatitis; AE, adverse event; CDLQI, Children's Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EASI-50/75/90, ≥50/75/90% improvement in EASI; IGA, Investigator's Global Assessment; IMP, investigational medicinal product; LOCF, last observation carried forward; LSM, least squares mean; n, number of patients in the analysis data set; N, number of patients with one or more events; nE, number of events; NRS, numerical rating scale; POEM, Patient-Oriented Eczema Measure; PRO, patient-reported outcome; PYE, patient-years of exposure; Q2, every two weeks; Q4W, every four weeks SE, standard error; TCI, topical calcineurin inhibitors; TCS, topical corticosteroids; URTI, upper respiratory tract infection.

Disclosures

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References

1. Paller AS *et al. JAMA Dermatol.* 2023;159(6):596–605.

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