Continuous tralokinumab treatment over 4 years in adults with moderate-to-severe atopic dermatitis provides long-term disease control

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Results

- After 4 years of total tralokinumab treatment (1 year in parent trial and 3 years in ECZTEND):
  - Median improvement in EASI from PT baseline was 94.7% (**Figure 1A**)
  - IGA 0/1 [% (n/N)] was observed in 52.6% (92/175), EASI-75 in 84.5% (147/174), EASI-90 in 64.4% (112/174), EASI ≤7 (mild disease) in 84.5% (147/174), and EASI ≤2 in 55.2% (96/174) of patients (**Figure 1B**)
  - EASI-75 {% (n/N) [95% CI]} was achieved in 84.5% (147/174) [78.4, 89.1] of patients as observed, and in 73.4% (254.8/347) [68.6, 78.3] using mNRI. EASI-90 {% (n/N) [95% CI]} was achieved in 64.4% (112/174) [57.0, 71.1] of patients as observed, and in 53.4% (185.2/347) [47.8, 59.0] using mNRI (**Figure 1C**)
- After 3 years of tralokinumab treatment in ECZTEND, worst weekly pruritus NRS ≤4 (no to mild itch) and DLQI ≤5 (no to small effect of AD on quality of life) were observed in 68.0% (119/175) and 79.0% (128/162) of patients, respectively (**Figure 1D**)
- The findings were consistent with the known safety profile of tralokinumab, with no new safety signals detected (**Table 1**)

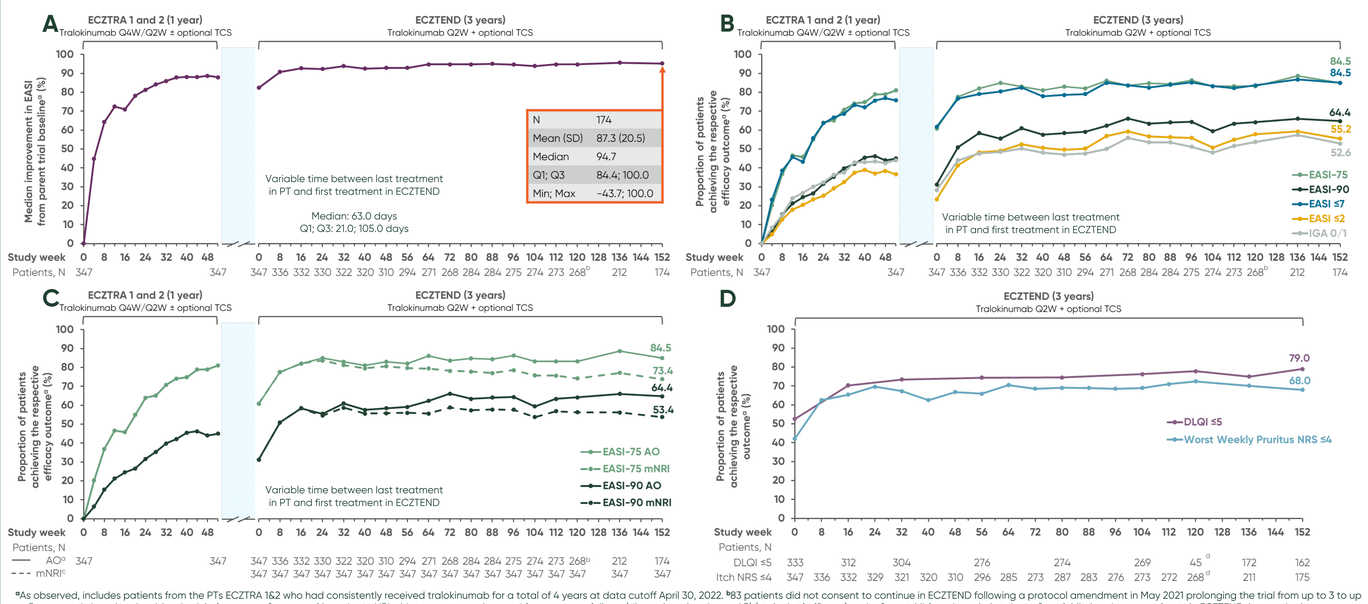
Objectives

- To assess the efficacy of long-term tralokinumab treatment by conducting a *post hoc* interim subgroup analysis restricted to the largest, most homogenous patient population, with the longest treatment duration.

Background

- AD is a chronic skin disease that may impact patients throughout their lifespan, requiring efficacious long-term treatment options with a favorable safety profile[1]
- Tralokinumab, a monoclonal antibody that specifically neutralizes interleukin-13, is approved for the treatment of moderate-to-severe AD in multiple countries
- Phase 3 clinical trials of up to 52-week duration showed that tralokinumab was effective and well tolerated as monotherapy and in combination with topical therapy[2,3]
- ECZTEND (NCT03587805) is an ongoing open-label, 5-year extension trial investigating the long-term safety and efficacy of tralokinumab plus optional TCS

Figure 1. Efficacy over 4 years of tralokinumab treatment. **(A)** Median improvement in EASI relative to PT baseline. **(B)** Proportion of patients achieving the respective efficacy endpoint. **(C)** Sensitivity analyses for EASI-75/90. **(D)** Proportion of patients achieving Itch NRS ≤4 and DLQI ≤5 over 3 years of tralokinumab treatment in ECZTEND.



[a]As observed, includes patients from the PTs ECZTRA 1&2 who had consistently received tralokinumab for a total of 4 years at data cutoff April 30, 2022. [b]83 patients did not consent to continue in ECZTEND following a protocol amendment in May 2021 prolonging the trial from up to 3 to up to 5 years and changing the visit schedule from every 8 to every 16 weeks. [c]mNRI with non-response imputed for treatment failures (discontinuation due to AE(s) or lack of efficacy) and a 2-step MI for other missing data. Step 1: Missing data up to 1 year in ECZTEND imputed using a standard regression-based MI method; Step 2: Missing data post 1 year imputed by carrying forward the within-subject AUC of days in-response. [d]83 patients did not consent to continue in ECZTEND following a protocol amendment in May 2021 prolonging the trial from up to 3 to up to 5 years, and the low N for DLQI ≤5 is related to a change in the visit schedule from every 8 to every 16 weeks.

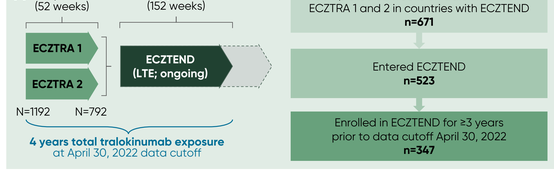
Methods

- This *post hoc* analysis included 347 patients who were continuously treated with tralokinumab ± optional TCS for 52 weeks in the PT, ECZTRA 1 or ECZTRA 2, and for up to 152 weeks in ECZTEND as of the April 30, 2022 data cutoff (**Figure 2**)
- The median treatment duration from first dose to discontinuation was 155.6 weeks (IQR 132.1; 174.4)
  - The most common reasons for discontinuation were lack of efficacy (7.5%), other reasons (6.1%), adverse events (5.8%), and withdrawal by patient (5.8%)

Analyses

- Efficacy outcomes included % improvement from PT baseline in EASI and proportions of patients achieving: IGA 0/1, EASI-75/90 relative to PT baseline, EASI ≤7/≤2, worst weekly pruritus (itch) NRS ≤4, and DLQI ≤5
- Results are presented using observed data
- A summary of the number (%) of AEs, severe AEs, SAEs, withdrawals from the trial due to AEs, and the rate of AEs, are presented

Figure 2. ECZTEND (**A**) study design and (**B**) patient disposition.



Baseline demographics and characteristics

- 347 adults with a mean age (SD) of 42.2 (14.5) years and a mean EASI (SD) of 30.8 (13.7) at PT baseline were included (**Table 2**)

Table 2. Baseline demographics and characteristics.

	ECZTEND interim efficacy analysis set (n=347)	
Age (ECZTEND baseline) Median years (IQR)	42.0 (30.0; 53.0)	
Sex % (n)		
Male	59.1 (205)	
Female	40.9 (142)	
Race % (n)[a]		
White	74.6 (259)	
Black	5.8 (20)	
Asian	16.1 (56)	
Age at onset of AD Median years (IQR)	3.0 (1.0; 15.0)	
Duration of AD (ECZTEND baseline) Median years (IQR)	29.0 (19.0; 43.0)	
	Parent Trial Baseline	**ECZTEND Baseline**
IGA severity % (n)		
Clear/minimal (score=0/1)	-	28.2 (98)
Mild (score=2)	-	35.4 (123)
Moderate (score=3)	49.6 (172)	30.5 (106)
Severe (score=4)	50.4 (175)	5.8 (20)
EASI Median (IQR)	26.7 (19.7; 38.4)	4.7 (2.2; 12.4)
SCORAD Median (IQR)	68.1 (60.8; 78.1)	32.8 (20.6; 46.9)
DLQI Median (IQR)	17.0 (11.0; 23.0), *n*=344	5.0 (2.0; 10.0), *n*=333
Worst weekly pruritus NRS[a] Median (IQR)	7.9 (6.9; 8.9), *n*=346	5.0 (3.0; 8.0), *n*=347

[a]In PTs, worst pruritus NRS was assessed daily; in ECZTEND, worst pruritus NRS was assessed based on recall of the previous week before the visit.

Table 1. Summary of AEs.

	AEs in ECZTEND[a]		AEs in ECZTRA 1&2 Initial 16-week treatment period[b]				AEs in ECZTRA 1&2 OL treatment arm Week 16–52[c]	
	Tralokinumab Q2W + optional TCS (n=347; PYE=913.5)		Tralokinumab Q2W (n=1194; PYE=354.5)		Placebo Q2W (n=396; PYE=114.5)		Tralokinumab Q2W + optional TCS (n=1121; PYE=664.9)	
	% (n)	Rate (nE/100 PYE)	adj. % (n)	Rate (nE/100 PYE)	adj. % (n)	Rate (nE/100 PYE)	adj. % (n)	Rate (nE/100 PYE)
All AEs	88.2 (306)	189.1	69.0 (824)	699.4	71.5 (283)	785.3	72.6 (814)	431.6
Severity								
Mild	75.8 (263)	120.6	56.4 (673)	466.6	51.5 (204)	436.8	60.0 (673)	286.8
Moderate	56.5 (196)	61.4	34.3 (409)	206.8	46.0 (182)	305.7	38.1 (427)	133.5
Severe	10.4 (36)	7.0	5.4 (65)	26.0	8.1 (32)	42.8	4.2 (47)	11.3
Serious AEs	10.7 (37)	4.6	2.8 (33)	9.6	3.3 (13)	14.9	3.8 (43)	7.4
Leading to withdrawal from trial	5.8 (20)	2.3	2.4 (29)	9.6	2.8 (11)	14.0	2.5 (28)	5.0

[a]Includes 347 patients from the PTs ECZTRA 1&2 who had consistently received tralokinumab for up to 4 years at data cutoff April 30, 2022. [b]Includes patients from a pooled safety analysis set from PTs ECZTRA 1&2 placebo controlled initial 16-week treatment period. [c]Includes patients from a pooled safety analysis set from PTs ECZTRA 1&2 open-label 36-week continuation treatment with tralokinumab + optional TCS.

Conclusions

- Continuous use of tralokinumab ± optional TCS for up to 4 years provided long-term disease control in adult patients with moderate-to-severe AD
- These data, in combination with the favorable safety profile, suggest tralokinumab as an efficacious and well-tolerated long-term treatment option for moderate-to-severe AD

Abbreviations

%, percentage of patients; AD, atopic dermatitis; adj., adjusted; AE, adverse event; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EASI-75/90, at least 75/90% improvement in EASI relative to PT baseline; IGA, Investigator's Global Assessment; IQR, interquartile range; LOCF, last observation carried forward; LTE, long-term extension; Max, maximum; Min, minimum; mNRI, modified NRI with discontinuations due to adverse event(s) or lack of efficacy set as non-response, other missing data imputed with LOCF; n, number of patients achieving the indicated metric; nE, number of events; NRS, numeric rating scale; OL, open-label; PT, parent trial; PRO, patient-reported outcome; PYE, patient-years of exposure; Q, quartile; Q2W/Q4W, every 2/4 weeks; SAE, serious AE; SCORAD, SCORing Atopic Dermatitis; SD, standard deviation; TCS, topical corticosteroids.

References

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