Two-Year Maintenance of Response with Tralokinumab in Moderate-to-Severe Atopic Dermatitis: Interim Analysis of the ECZTEND Open-Label Extension Trial

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Introduction

- Atopic dermatitis is associated with intense itch, sleep disturbance, and impaired quality of life[1–4]
- Tralokinumab is a high-affinity, fully human, monoclonal antibody designed to specifically neutralize interleukin-13, a key driver of underlying inflammation in atopic dermatitis[5–7]
- Phase 3 trials established tralokinumab efficacy and safety for up to 52 weeks in adult patients with moderate-to-severe atopic dermatitis[8,9]
- ECZTEND (a 5-year, open-label extension trial [NCT03587805]) is ongoing and evaluates long-term safety and efficacy of tralokinumab in patients who participated in previous tralokinumab trials

Objective

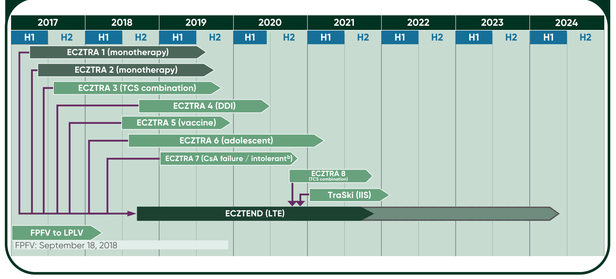
- To investigate 2-year efficacy and safety of continued tralokinumab treatment and the ability to regain treatment response after pausing and reinitiating tralokinumab

Materials and Methods

Parent trials

- This analysis included patients who received tralokinumab for the full 52 weeks in the parent trials ECZTRA 1 and 2, and had been enrolled ≥60 weeks in ECZTEND as of April 30, 2020 **(Figure 1)**

Figure 1. Parent trials within ECZTEND[a]

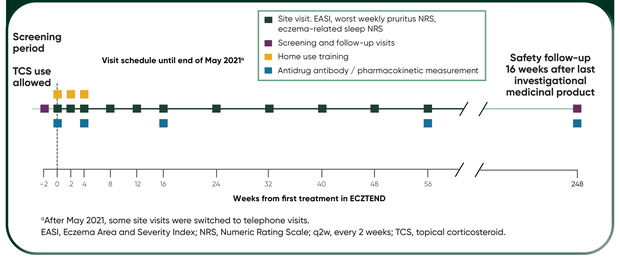


[a]Previous treatment regimens in parent trials included tralokinumab q2w, q4w, or placebo + / - TCS.
[b]Study in patients with atopic dermatitis who are not adequately controlled with or have contraindications to oral CsA.
CsA, cyclosporine; DDI, drug–drug interaction; FPFV, first patient first visit; IIS, investigator-initiated study; LPLV, last patient last visit; LTE, long-term extension; q4w, every 4 weeks; TCS, topical corticosteroid.

Study design

- The ECZTEND study design is shown in **Figure 2.** In ECZTEND, patients receive subcutaneous tralokinumab 300 mg every 2 weeks plus optional topical corticosteroids
- Patients were analyzed in 3 cohorts, defined by the interval between last parent trial dose and first ECZTEND dose: ≤5 weeks, 6–15 weeks, and >15 weeks
- Long-term control at 56 weeks in ECZTEND was assessed as percentage improvement from parent trial baseline in Eczema Area and Severity Index (EASI) and achievement of ≥50, 75, and 90% improvement in EASI (EASI-50, -75, -90)
- Worst weekly pruritus Numeric Rating Scale (NRS) and weekly eczema-related sleep interference NRS were assessed

Figure 2. Study design



[a]After May 2021, some site visits were switched to telephone visits.
EASI, Eczema Area and Severity Index; NRS, Numeric Rating Scale; q2w, every 2 weeks; TCS, topical corticosteroid.

Key inclusion criteria

- Completed treatment period(s) in a tralokinumab parent trial without any safety concerns
- Complied with the clinical trial protocol in the parent trial
- Able and willing to self-administer tralokinumab, or have it administered by a caregiver, at home after the initial 3 injection visits at trial site
- Applied a stable dose of emollient (minimum twice daily) for at least 14 days before baseline

Endpoints and analyses

Interim analysis:

- Included patients who received tralokinumab for the full 52 weeks in parent trials ECZTRA 1 and 2 and had been enrolled in ECZTEND ≥60 weeks prior to April 30, 2020
- Patients were analysed in 3 cohorts defined by the interval between the last parent trial dose and the first ECZTEND dose:
  - ≤5 weeks (continuous treatment); 6–15 weeks (interrupted treatment); >15 weeks (washout)

Endpoints:

- Efficacy outcomes assessed were:
  - Percentage improvement from parent trial baseline in EASI at Week 56
  - EASI-50, EASI-75, and EASI-90 response rates at Week 56
  - Worst weekly pruritus NRS and eczema-related weekly sleep NRS up to Week 56
- EASI-50, EASI-75, and EASI-90 are calculated based on baseline EASI in parent trial

Results

Baseline characteristics

- Baseline characteristics of enrolled patients are shown in **Table 1.** Overall, median age was 42 years, 59% of patients were male, and median duration of atopic dermatitis was 30 years
- Median time between last tralokinumab dose in the parent trial and first dose in ECZTEND was 63 days

Table 1. Baseline characteristics

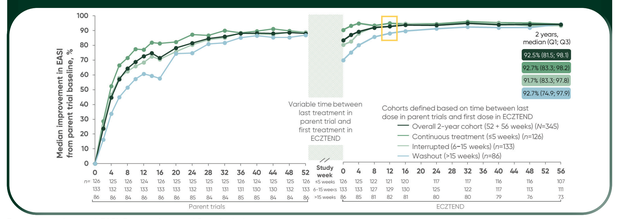
	Continuous treatment (n=126)	Interrupted treatment (n=133)	Washout (n=86)	Total (n=345)
Patient demographics				
Median (IQR) age, years	42.5 (31.0–52.0)	42.0 (29.0–53.0)	40.5 (29.0–51.0)	42.0 (30.0–52.0)
Male, n (%)	75 (59.5)	72 (54.1)	56 (65.1)	203 (58.8)
Median (IQR) atopic dermatitis duration at baseline, years	32.0 (19.0–44.0)	30.0 (21.0–43.0)	26.0 (18.0–40.0)	30.0 (19.0–43.0)
Median (IQR) BSA at parent trial baseline	43.5 (29.0–67.0)	51.0 (33.0–73.0)	35.5 (23.0–50.0)	44.0 (29.0–67.0)
ECZTEND baseline characteristics				
Median (IQR) EASI	2.8 (1.2–6.3)	5.8 (2.8–13.1)	7.6 (4.0–17.2)	4.7 (2.2–12.3)
Median (IQR) IGA score	2.0 (1.0–2.0)	2.0 (2.0–3.0)	3.0 (2.0–3.0)	2.0 (1.0–3.0)
Median (IQR) worst pruritus score	4.0 (2.0–6.0)	6.0 (4.0–8.0)	6.0 (4.0–8.0)	5.0 (3.0–8.0)
Median (IQR) sleep interference score	2.0 (0.0–4.0)	3.0 (1.0–6.0)	3.5 (2.0–7.0)	3.0 (1.0–5.0)
Median (IQR) time from exposure in parent trial, days	14.0 (14.0–26.0)	70.0 (58.0–86.0)	122.0 (112.0–130.0)	63.0 (21.0–105.0)

BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; IQR, interquartile range.

EASI with tralokinumab

- Median EASI with tralokinumab in parent trials and ECZTEND is shown in **Figure 3.** At Week 52 of the parent trials, median (IQR) EASI improvement from baseline was 99.0% (78.4–96.1)
- At ECZTEND baseline, median EASI improvement from parent trial baseline was 88.9% (80.5–95.3) for participants with continuous tralokinumab; 78.8% (55.9–91.6) for interrupted tralokinumab; 68.6% (37.1–82.6) for participants with tralokinumab washout
- At Week 56 in ECZTEND, i.e. after 2 years of tralokinumab treatment, median EASI improvement from parent trial baseline was 92.7% (83.3–98.2) for participants with continuous tralokinumab; 91.7% (83.3–97.8) for interrupted tralokinumab; 92.7% (74.9–97.9) for participants with tralokinumab washout
- Median EASI improvement equivalent to parent trial levels was maintained for participants with continuous tralokinumab, was regained by Week 8 for the interrupted cohort, and Week 16 for the washout cohort

Figure 3. Median EASI with tralokinumab in parent trials and ECZTEND over 2 years of tralokinumab treatment

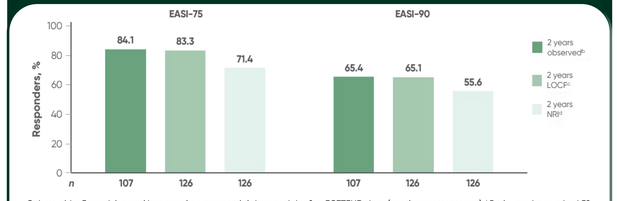


Data are as observed. EASI, Eczema Area and Severity Index.

Patients in ECZTEND achieving EASI-75 and EASI-90

- High levels of EASI-75 and EASI-90 response rates were sustained in the continuous treatment cohort at 2 years of tralokinumab therapy in ECZTEND **(Figure 4)**
  - 65% of patients achieved EASI-90 at 2 years of tralokinumab treatment

Figure 4. Proportion of patients in ECZTEND achieving EASI-75 and EASI-90 at 2 years of tralokinumab treatment (continuous treatment cohort[a])

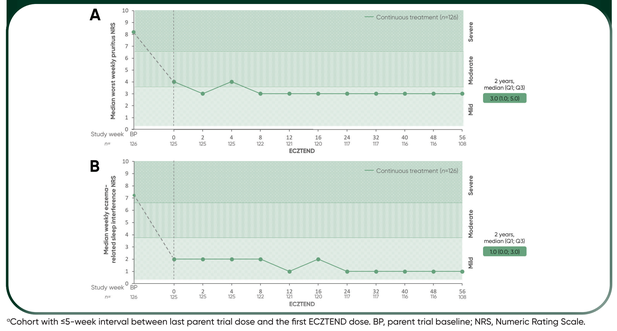


[a]Cohort with ≤5-week interval between last parent trial dose and the first ECZTEND dose (continuous treatment). [b]Patients who reached 52 weeks in parent trial and 56 weeks in ECZTEND. [c]Missing data imputed using LOCF. [d]Missing data imputed as non-response. Selection of the efficacy analysis set is conducted at Week 0 of ECZTEND, ie, 100% of subjects are present at Week 0 in the efficacy analysis set. Thus, subjects who terminated the study or had missing observations at Week 56 in ECZTEND and formed part of the efficacy analysis set will have LOCF or non-responder imputations for EASI-75/EASI-90. EASI, Eczema Area and Severity Index; LOCF, last observation carried forward; NRI, non-responder imputation.

Median worst weekly pruritus and eczema-related sleep

- At Week 56, median worst weekly pruritus NRS was 3 (mild) in all cohorts and median weekly eczema-related sleep interference NRS was similar across cohorts **(Figure 5)**

Figure 5. A. Median worst weekly pruritus and B. Eczema-related sleep NRS in parent trials and ECZTEND over 2 years of tralokinumab treatment (continuous treatment cohort[a])



[a]Cohort with ≤5-week interval between last parent trial dose and the first ECZTEND dose. BP, parent trial baseline; NRS, Numeric Rating Scale.

Tralokinumab safety profile

- The adverse event profile was consistent with the ECZTEND overall safety population, as of 30 April 2020 (n=1174) **(Table 2)**

Table 2. Overall safety profile of tralokinumab

	Patients from ECZTRA 1 and 2 enrolled in ECZTEND ≥60 weeks prior to data cut-off (April 30, 2020) – safety analysis set		ECZTEND Safety analysis set[a] Trial start to April 30, 2020	
	Tralokinumab, overall 2-year cohort (n=345, PYE=420.8)		Tralokinumab q2w + optional TCS (n=1174, PYE=1235.7)	
	n (%)	R	n (%)	R
All adverse events	280 (81.2)	246.0	844 (71.9)	237.8
Serious adverse events	17 (4.9)	4.0	55 (4.7)	4.8
Severity				
Mild	223 (64.6)	158.0	695 (59.2)	158.2
Moderate	152 (44.1)	78.4	435 (37.1)	72.1
Severe	24 (7.0)	9.5	62 (5.3)	7.5
AEs leading to withdrawal from trial **Most frequently reported adverse events (≥5% of patients)[b]**	7 (2.0)	1.7	19 (1.6)	1.5
Viral upper respiratory tract infection (most commonly reported as common cold)	95 (27.5)	32.3	250 (21.3)	29.3
Atopic dermatitis	50 (14.5)	16.6	158 (13.5)	20.6
Upper respiratory tract infection	34 (9.9)	11.6	83 (7.1)	9.1
Conjunctivitis	17 (4.9)	5.5	45 (3.8)	4.5
Headache	17 (4.9)	5.7	49(4.2)	5.7

[a]Includes all patients from parent trials ECZTRA 1, 2, 3, and 5 enrolled in ECZTEND at data cut-off (April 30, 2020). [b]According to MedDRA preferred term. %, percentage of patients with ≥1 event; PYE, patient-years of exposure; q2w, every 2 weeks; R, rate (number of adverse events divided by patient years of exposure multiplied by 100); MedDRA, Medical Dictionary for Regulatory Activities; TCS, topical corticosteroid

Conclusions

- Continued tralokinumab treatment (≤5 weeks from last dose in parent trial to first in ECZTEND) was associated with consistent long-term control for signs and symptoms from parent trial through ECZTEND
- Median EASI improvements among patients with a >5-week interruption between doses returned to parent trial levels by week 12
- Over 2 years, tralokinumab provided long-term control of the extent and severity of atopic dermatitis, as well as improved itch and reduced sleep interference responses in patients treated with tralokinumab

References

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Disclosures

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