Long-Term Improvements Observed in Tralokinumab-Treated Patients with Moderate-to-Severe Atopic Dermatitis: an ECZTEND Interim Analysis

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Introduction

- Atopic dermatitis is a chronic inflammatory disease characterized by eczematous skin lesions and multiple symptoms, including pruritus, sleep disturbance, and depression[1–4]
- Tralokinumab is a high-affinity, fully human monoclonal antibody designed to specifically neutralize interleukin-13, a key driver of the underlying inflammation in atopic dermatitis[5–7]
- Phase 3 trials have established the efficacy and safety of tralokinumab for up to 52 weeks in adult patients with moderate-to-severe atopic dermatitis[8,9]
- An ongoing, open-label extension trial, ECZTEND (NCT03587805), is investigating the long-term safety and efficacy of tralokinumab in patients with atopic dermatitis who participated in previous tralokinumab trials

Objective

- To present interim ECZTEND efficacy data collected through April 30, 2020 from a patient cohort receiving tralokinumab for at least 56 weeks

Methods

Patients

- ECZTEND is an ongoing, up to 268-week, open-label, single-arm, multicenter, long-term extension trial in patients with atopic dermatitis who participated in parent tralokinumab trials (ECZTRA 1–8 and TraSki) **(Figure 1)**

Key Inclusion Criteria

- Completed treatment period(s) in a tralokinumab parent trial (ECZTRA 1–8 or TraSki) 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

ECZTEND Trial Design

- Patients received subcutaneous tralokinumab 300 mg every 2 weeks (q2w) plus optional topical corticosteroids (TCS) after a 300 mg or 600 mg loading dose of tralokinumab **(Figure 2)**

ECZTEND Trial Design

- Study primary and secondary endpoints:
  - Number of adverse events from baseline up to Week 268
  - Investigator's Global Assessment (IGA) score of 0/1 from Week 16 to Week 248
  - Eczema Area and Severity Index reduction of at least 75% (EASI-75) a from Week 16 to Week 248

Week 56 interim analysis:

- Included patients from parent trials ECZTRA 1, 2, 3, and 5 enrolled in ECZTEND at least 60 weeks before data cut-off (n=612)
- Efficacy outcomes assessed include:
  - Mean EASI up to Week 56
  - IGA 0/1 response rate at Week 56
  - EASI-50, EASI-75, EASI-90,[a] and EASI <7 response rates at Week 56
  - Mean worst weekly pruritus Numeric Rating Scale (NRS) and eczema-related weekly sleep interference NRS scores up to Week 56

[a]EASI-50, EASI-75, and EASI-90 are calculated based on baseline EASI in parent trial.

Results

Patient Cohorts (Figure 3)

Figure 3. Patient cohorts in ECZTEND interim analysis (April 30, 2020 data cut-off)

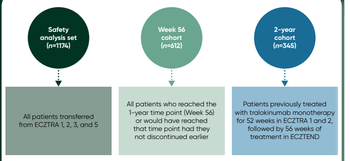
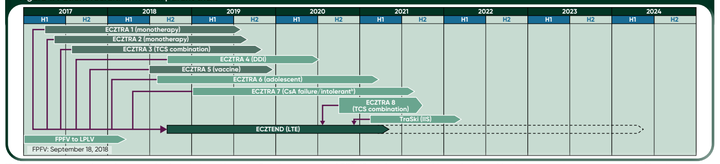


Table 1. Baseline characteristics of all patients from parent trials ECZTRA 1, 2, 3, and 5 enrolled in ECZTEND at data-cut off

Patient demographics	Total (n=1174)
Parent trial, n (%)	
ECZTRA 1 (52-week monotherapy)	450 (38.3)
ECZTRA 2 (52-week monotherapy)	293 (25.0)
ECZTRA 3 (32-week combination therapy)	282 (24.0)
ECZTRA 5 (16-week monotherapy)	149 (12.7)
Median (IQR) age, years	38 (27.0–50.0)
Male, n (%)	675 (57.5)
Region, %	
North America	46.2
Europe	46.5
Japan	7.3
Median (IQR) duration of AD at baseline, years	27 (18.0–40.0)
Median (IQR) BSA at parent trial baseline, %	44.5 (30.0–67.0)
Median (IQR) time from last dose in parent trial, days	36 (15.0–85.0)
Baseline characteristics	**All parent trials** / **ECZTEND**
Median (IQR) EASI score	26.6 (19.7–37.2) / 4.7 (1.8–11.7)
Median (IQR) IGA score	3.0 (3.0–4.0) / 2.0 (1.0–3.0)
Median (IQR) DLQI score	17.0 (11.0–22.0) / 5.0 (2.0–10.0)
Median (IQR) SCORAD	67.4 (59.8–78.0) / 30.2 (18.7–45.0)
Median (IQR) POEM	24.0 (20.0–27.0) / 12.0 (6.0–18.0)

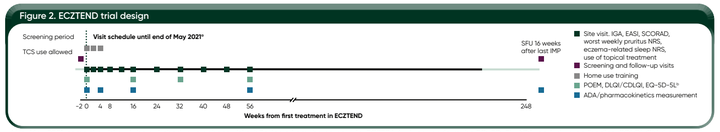
AD, atopic dermatitis; BSA, body surface area; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Invstigator's Global Assessment; IQR, interquartile range; POEM, Patient-Oriented Eczema Measure; SCORAD, SCORing Atopic Dermatitis.

Figure 1. Patient recruitment from parent trials[a]



[a]Previous treatment regimens in parent trials included tralokinumab q2w, q4w, or placebo 6 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; q2w, every 2 weeks; q4w, every 4 weeks; TCS, topical corticosteroids.

Figure 2. ECZTEND trial design



[a]After May 2021, some site visits will be switched to telephone visits; bPatients from the parent trial ECZTRA 6 will not perform the EQ-5D-5L. ADA, anti-drug antibodies; CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EQ-5D-5L, EuroQol 5-Dimension Health Questionnaire 5-Level; IGA, Investigator's Global Assessment; IMP, investigational medicinal product; NRS, Numeric Rating Scale; POEM, Patient-Oriented Eczema Measure; q2w, every 2 weeks; SCORAD, SCOring Atopic Dermatitis; SFU, safety follow-up; TCS, topical corticosteroids.

Baseline Characteristics

- At ECZTEND baseline, patients had mild atopic dermatitis, based on median EASI score, and the median Dermatology Life Quality Index score indicated that atopic dermatitis had a small effect on their quality of life[10,11] **(Table 1)**
- Based on EASI, the overall ECZTEND cohort and Week 56 cohort had similar baseline disease severity

Withdrawal From ECZTEND

- Analysis includes all patients from parent trials ECZTRA 1, 2, 3, and 5 enrolled in ECZTEND at data cut-off (April 30, 2020) **(Table 2)**
- The median (interquartile range) duration from first tralokinumab dose to last visit at data cut-off (follow-up period) was 58.1 (46.4–66.3) weeks

Table 2. Withdrawal from ECZTEND

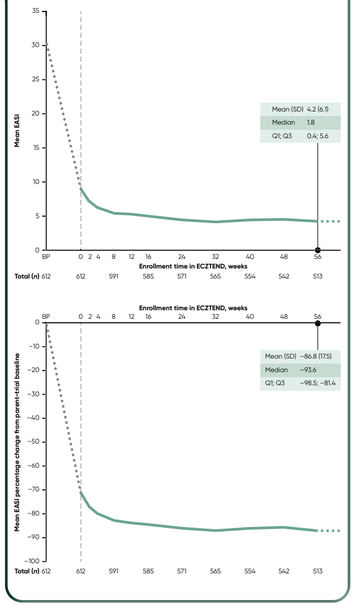
Reason for withdrawal, n (%)[a]	Total (n=1174)
Total patients withdrawing from the study	139 (11.8)
Adverse event	19 (1.6)
Lost to follow-up	29 (2.5)
Withdrawal by patient	16 (1.4)
Lack of efficacy (investigator or patient opinion)	24 (2.0)
Other[b]	51 (4.3)

Analysis includes all patients from parent trials ECZTRA 1, 2, 3, and 5 enrolled in ECZTEND at data cut-off (April 30, 2020).
[a]Data are subject to change as the ongoing ECZTEND study progresses; [b]Withdrawal from ECZTEND due to pregnancy, protocol deviation (concomitant medication/eligibility), physician decision, or administrative reasons (patient moved/relocated/busy/transportation issues/ personal reasons).

Mean EASI up to Week 56 With Tralokinumab

- Mean EASI reduced from a score equivalent to moderate-to-severe atopic dermatitis at parent trial baseline to mild-to-moderate atopic dermatitis at ECZTEND baseline, and was sustained over time in ECZTEND **(Figure 4)**

Figure 4. Mean EASI and percentage change up to Week 56 with tralokinumab (Week 56 cohort[a])

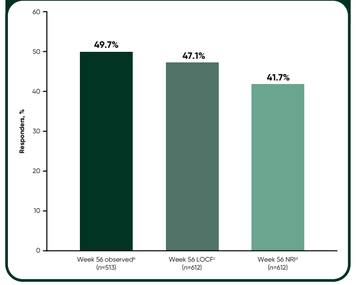


[a]Week 56 cohort included all patients from parent trials ECZTRA 1, 2, 3, and 5 enrolled at least 60 weeks before data cut-off (April 30, 2020). Data were analyzed as observed.
BP, parent trial baseline; EASI, Eczema Area and Severity Index; SD, standard deviation.

IGA 0/1 Response Rate at Week 56 With Tralokinumab

- A high level of IGA 0/1 response rate was sustained with tralokinumab at Week 56 in ECZTEND **(Figure 5)**

Figure 5. IGA 0/1 response rate at Week 56 with tralokinumab (Week 56 cohort[a])



[a]Week 56 cohort included all patients from parent trials ECZTRA 1, 2, 3, and 5 enrolled at least 60 weeks before data cut-off (April 30, 2020); [b]Patients who reached Week 56; [c]Missing data imputed using LOCF; dMissing data imputed as non-response.
IGA, Investigator's Global Assessment; LOCF, last observation carried forward; NRI, non-responder imputation.

Proportion of Patients Achieving EASI-50, EASI-75, and EASI-90 at Week 56 With Tralokinumab

- A high level of EASI-50, EASI-75, and EASI-90 response rates were sustained with tralokinumab at Week 56 in ECZTEND **(Figure 6)**
  - 61% of patients achieved EASI-90 at Week 56
- At Week 56, 79.7% of patients achieved EASI <7, a category corresponding to mild atopic dermatitis

Mean Worst Weekly Pruritus NRS and Eczema-related Weekly Sleep NRS Scores up to Week 56 With Tralokinumab

- Mean worst weekly pruritus NRS and eczema-related weekly sleep NRS scores were sustained over time in ECZTEND with tralokinumab **(Figure 7)**
  - Patients achieved scores equivalent to mild-to-moderate itch and mild sleep interference at Week 56

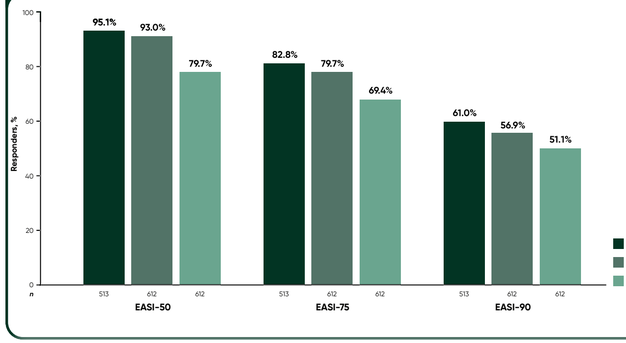
Proportion of Patients Achieving EASI-50, EASI-75, and EASI-90 at Week 56 With Tralokinumab

- Patients treated with tralokinumab for a total of 2 years at ECZTEND data cut-off demonstrated high levels of EASI-50, EASI-75, and EASI-90 response rates, which were consistent with the overall Week 56 cohort **(Figure 8)**

Safety

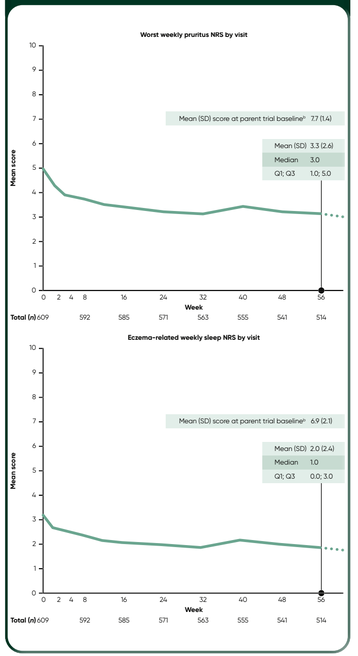
- The overall safety profile of tralokinumab was consistent with parent trials **(Table 3)**

Figure 6. Proportion of patients achieving EASI-50, EASI-75, and EASI-90 at Week 56 with tralokinumab (Week 56 cohort[a])



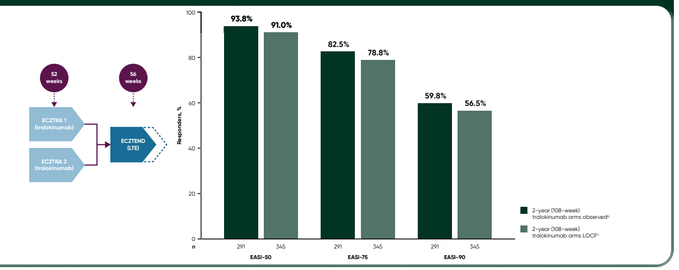
[a]Week 56 cohort included all patients from parent trials ECZTRA 1, 2, 3, and 5 enrolled at least 60 weeks before data cut-off (April 30, 2020); [b]Patients who reached Week 56; [c]Missing data imputed using LOCF; [d]Missing data imputed as non-response. EASI, Eczema Area and Severity Index; LOCF, last observation carried forward; NRI, non-responder imputation.

Figure 7. Mean worst weekly pruritus NRS and eczema-related weekly sleep NRS scores up to Week 56 with tralokinumab (Week 56 cohorta)



[a]Week 56 cohort included all patients from parent trials ECZTRA 1, 2, 3, and 5 enrolled at least 60 weeks before data cut-off (April 30, 2020). Data were analyzed as observed
[b]Parent trial baseline value based on patients from ECZTRA 1, 2, and 3 only.
NRS, Numeric Rating Scale; SD, standard deviation.

Figure 8. Proportion of patients achieving EASI-50, EASI-75, and EASI-90 with tralokinumab at Week 56 (52 weeks in parent study plus 56 weeks in ECZTEND[a])



[a]2-year cohort included all patients who received treatment with tralokinumab for 52 weeks in parent trials ECZTRA 1 and 2, followed by treatment with tralokinumab for 56 weeks in ECZTEND at data cut-off (April 30, 2020); [b]Patients who reached Week 56; [c]Missing data imputed using LOCF. EASI, Eczema Area and Severity Index; LOCF, last observation carried forward; LTE, long-term extension.

Table 3. Overall safety profile of tralokinumab

	AD safety pool (ECZTRA 1, 2, 3, and 5, Phase 2b)[a] Initial treatment period						ECZTEND safety analyses set[b] Trial start to April 30, 2020		
	Tralokinumab q2w 6 TCS (n=1605, PYE=473.19)			Placebo q2w 6 TCS (n=680, PYE=193.1)			Tralokinumab q2w 1 optional TCS (n=1174, PYE=1235.7)		
	n	adj. %	adj. R	n	adj. %	adj. R	n	%	R
All adverse events	1080	65.7	639.5	449	67.2	678.3	844	71.9	237.8
Serious adverse events	37	2.1	7.4	18	2.8	11.9	55	4.7	4.8
Severity									
Mild	881	53.2	429.8	326	49.0	391.0	695	59.2	158.2
Moderate	518	31.5	189.5	258	39.0	254.3	435	37.1	72.1
Severe	77	4.6	20.2	40	6.3	33.0	62	5.3	7.5
Leading to drug withdrawal	38	2.3	9.9	20	2.8	13.3	28	2.4	2.3
Most frequently reported adverse events (>5% of patients)									
Viral upper respiratory tract infection (most commonly reported as common cold)	256	15.7	65.1	78	12.2	53.5	250	21.3	29.3
Atopic dermatitis	272	15.4	68.0	167	26.2	139.7	158	13.5	20.6
Upper respiratory tract infection	92	5.6	20.8	33	4.8	18.5	83	7.1	9.1
Safety areas of interest									
Conjunctivitis, including conjunctivitis, allergic conjunctivitis, bacterial conjunctivitis, viral conjunctivitis, and atopic conjunctivitis	126	7.5	29.0	21	3.2	12.3	65	5.9	6.9

[a]Includes patients from parent trials ECZTRA 1, 2, 3, 5, and Phase 2b; [b]Includes all patients from parent trials ECZTRA 1, 2, 3, and 5 enrolled in ECZTEND at data cut-off (April 30, 2020). %, percentage of patients with ≥1 event; AD, atopic dermatitis; adj. %, adjusted rate calculated using Cochran–Mantel–Haenszel weights; adj. R, adjusted rate calculated using Cochran–Mantel–Haenszel weights; PYE, patient-years of exposure; q2w, every 2 weeks; R, rate (number of adverse events divided by patient-years of exposure multiplied by 100); TCS, topical corticosteroids.

Conclusions

- In this ECZTEND interim analysis of the Week 56 cohort, tralokinumab 300 mg q2w plus optional TCS demonstrated sustained long-term improvements in itch, sleep, and the extent and severity of atopic dermatitis up to Week 56, with maintenance of robust EASI response rates (61% of patients achieved EASI-90 at Week 56)
- Overall, tralokinumab plus optional TCS was well tolerated in patients enrolled in ECZTEND at data cut-off, with a safety profile consistent with the parent trials

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Disclosures

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