Long-term safety and efficacy of tralokinumab in adults and adolescents with moderate-to-severe atopic dermatitis treated for up to 6 years

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Objectives

- To assess the safety and efficacy of long-term treatment with tralokinumab in the final results of the 5-year extension study ECZTEND

Results

Safety

- Patients were exposed to tralokinumab for up to 1 year in the parent trials and up to 5 years in ECZTEND (**Table 1**)
- The overall long-term safety profile of tralokinumab in ECZTEND was similar to the safety profile observed in the initial placebo-controlled treatment period of the parent trials (**Tables 2 and 3**)
  - AEs and SAEs were reported at lower rates in ECZTEND
  - The majority of AEs were mild-to-moderate

Table 1. Exposure time to tralokinumab

	ECZTEND N=1672; PYE=4466.2	Parent trial + ECZTEND N=1664; PYE=5487.6
PYE		
Mean (SD)	2.7 (1.3)	3.3 (1.4)
Median (min;max)	2.6 (0.00;5.14)	3.3 (0.00;6.14)
Exposure time, n (%)		
≥16 weeks	1592 (95.2)	1647 (99.0)
≥52 weeks (1 year)	1422 (85.0)	1551 (93.2)
≥104 weeks (2 years)	1184 (70.8)	1331 (80.0)
≥156 weeks (3 years)	701 (41.9)	978 (58.8)
≥208 weeks (4 years)	321 (19.2)	571 (34.3)
≥256 weeks (~5 years)	61 (3.6)	239 (14.4)
≥304 weeks (~6 years)	-	46 (2.8)

n, number of patients with recorded observation.

Table 2. Summary of AEs in treatment period

	ECZTEND (up to Week 268) Tralokinumab N=1672; PYE=4466.2			Placebo-controlled parent trials (up to Week 16)[a] Tralokinumab N=1939; PYE=587.2			Placebo N=913; PYE=271.3		
	E	n (%)	IR	E	n (adj %)	Adj IR	E	n (adj %)	Adj IR
Overall summary of treatment-emergent AEs									
All AEs	8119	1421 (85.0)	114.33	3894	1325 (67.5)	424.8	1746	616 (68.1)	475.3
SAEs	189	151 (9.0)	3.54	44	43 (2.0)	6.7	36	29 (3.3)	11.1
AEs leading to permanent discontinuation of study drug	79	76 (4.5)	1.71	51	42 (2.0)	6.8	24	18 (2.0)	7.0
Outcome									
Fatal	1[b]	1 (0.1)	0.02	1[c]	1 (0.1)	0.3	0	0 (0.0)	-
Treatment-emergent AEs (≥5% in ECZTEND) by PT									
Dermatitis atopic	632	357 (21.4)	9.28	394	299 (13.5)	50.9	292	194 (23.0)	99.5
Nasopharyngitis	599	372 (22.2)	10.09	378	313 (15.9)	58.6	141	114 (12.6)	46.5
Coronavirus infection[d]	322	299 (17.9)	7.22	0	0 (0)	-	0	0 (0)	-
Upper respiratory tract infection	233	147 (8.8)	3.57	134	122 (6.2)	21.3	46	42 (4.6)	16.3
Headache	143	114 (6.8)	2.66	128	95 (5.1)	17.7	52	40 (4.4)	15.0
Conjunctivitis	131	103 (6.2)	2.41	115	100 (4.9)	16.9	15	14 (1.6)	5.4

[a]Study size-adjusted % and IR; [b]A patient in their 50's was treated with study drug for 1 year in the parent trial and 3.5 years (1271 days) in ECZTEND and had previously received cyclosporine and azathioprine. The patient was diagnosed with COVID-19 infection and subsequently hospitalized for 31 days in the ICU for respiratory distress and extensive pneumopathy, during which the patient was diagnosed with cutaneous T-cell lymphoma (CTCL) and re-hospitalized 25 days later with febrile dyspnea, worsening of interstitial lung disease, and major biological inflammatory syndrome with hypereosinophilia. The patient died 5 days later due to multiple organ failure and refractory hypoxemia, later classified as worsening of an interstitial lung disease related to CTCL and possible sequelae of COVID-19; [c]The details of the reported death in the initial period of the of the vaccine study (ECZTRA 5) have been previously published[1]; [d]The difference between ECZTEND and the parent trials for coronavirus infection was consistent with the timing of trials relative to the COVID-19 pandemic.

Conclusions

- Long-term use of tralokinumab, up to 1 year in parent trials plus up to 5 years in ECZTEND, was well-tolerated with no new safety signals identified in patients aged 12 and up with moderate-to-severe AD
- Tralokinumab treatment demonstrated robust long-term efficacy with sustained improvements in AD signs, symptoms, and quality of life

- In ECZTEND most AESI eye disorder events (97%) were mild to moderate and only 7 (0.5%) patients discontinued treatment due to AESI eye disorders (**Table 3**)

Table 3. Summary of AESIs in treatment period

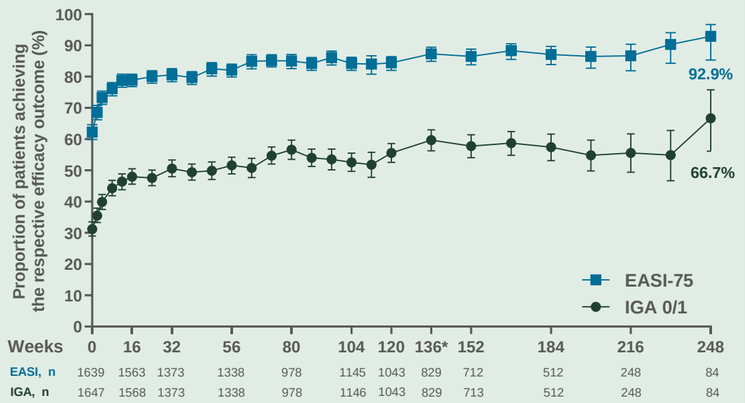
	ECZTEND (up to Week 268) Tralokinumab N=1672; PYE=4466.2			Placebo-controlled parent trials (up to Week 16)[a] Tralokinumab N=1939; PYE=587.2			Placebo N=913; PYE=271.3		
	E	n (%)	IR	E	n (adj%)	Adj IR	E	n (adj %)	Adj IR
Eye disorders[b]	260	189 (11.3)	4.59	184	158 (8.0)	27.8	35	30 (3.4)	11.4
Skin infections requiring systemic treatment	82	61 (3.6)	1.39	55	48 (2.3)	7.7	54	45 (5.1)	18.1
Eczema herpeticum[c]	30	23 (1.4)	0.52	9	9 (0.5)	1.6	12	12 (1.4)	4.8
Malignancy diagnosed after treatment assignment[d]	17	17 (1.0)	0.38	1	1 (<0.1)	0.1	1	1 (0.1)	0.4

[a]Study size-adjusted % and IR; [b]Eye disorders category includes several PTs, such as conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, keratitis, keratitis viral, ulcerative keratitis, and atopic keratoconjunctivitis; [c]Eczema herpeticum category includes PTs such as eczema herpeticum and kaposi's varicelliform eruption; [d]Malignancies diagnosed after dosing (excluding basal cell carcinoma, localized squamous cell carcinoma of the skin, and carcinoma in situ of the cervix).

Efficacy

- Long-term treatment with tralokinumab demonstrated sustained efficacy, with EASI-75 and IGA 0/1 observed in 92.9% and 66.7% of patients at Week 248, respectively (**Fig. 1**)
- Itch, sleep, and life quality improvements were sustained at levels equivalent to no-to-mild disease (**See online supplement, available via QR code**)

Figure 1. Proportion of patients achieving IGA 0/1 and EASI-75 as observed over 248 weeks of treatment in ECZTEND



Error bars represent 95% CI; *Study duration varied based on patients' consent to the amendment to prolong the study from 3 to 5 years and the country of enrollment (**see online supplement, available via QR-code**).

Abbreviations: AD, atopic dermatitis; AE, adverse event; AESI, AE of special interest; CI, confidence interval; COVID-19, coronavirus disease 2019; CTCL, cutaneous T-cell lymphoma; DLQI, dermatology life quality index; E, number of AEs; EASI, Eczema Area and Severity Index; EASI-75, 75% improvement in EASI; IGA, Investigator's Global Assessment; IR, Incidence rate (n/100PYE), for IR calculations, patient exposure was censored at the time of first event; n, number of patients with ≥1 event (unless otherwise specified); N, number of patients in indicated treatment set; PT, preferred term; PYE, patient years of exposure; Q2W, every 2 weeks; SAE, serious AE; SCORAD, SCORing AD; SD, standard deviation; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid.

References: **1.** Merola J, Bagel J, Almgren P, et al. *JAAD.* 2021;85(1):71-78. **2.** Simpson E, Blauvelt A, Silverberg J, et al. *AJCD.* 2024;25(1):139-148. **3.** Reich K. et al. *SKIN.* 2024;8(2):s375. **4.** Blauvelt A. et al. *JAAD.* 2022;87(4):815-824.

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Background

- Tralokinumab, a monoclonal antibody that specifically neutralizes IL-13, is indicated for the treatment of moderate-to-severe AD in patients aged ≥12 years[2]
- ECZTEND (NCT03587805) is a long-term open-label extension study evaluating the long-term safety and efficacy of tralokinumab for up to 5 years in adults and adolescents with moderate-to-severe AD
- Interim analyses have previously demonstrated the benefit-risk profile of tralokinumab in patients followed up to 3.5 years in ECZTEND[3,4]

Methods

Patients and treatment

- Patients who completed one of multiple tralokinumab parent trials at participating sites were eligible to enroll in ECZTEND, regardless of previous treatment or response in parent trials (**See online supplement, available via QR code**)
- Patients enrolled in ECZTEND received open-label tralokinumab 300 mg Q2W (home use) provided at site visits every 8-16 weeks and were allowed to use mild-to-moderate potency TCS or TCI at the investigators' discretion

Analyses

- AEs were coded over the course of the trial according to the Medical Dictionary for Regulatory Activities (MedDRA©) system
- Due to the absence of a comparator arm in ECZTEND, data from the initial 16-week treatment period of 7 placebo-controlled parent trials (NCT03131648, NCT03160885, NCT03363854, NCT03562377, NCT03526861, NCT03761537, NCT04587453) are provided as a basis for comparison[3]
- Exposure adjusted IRs were calculated as the number of patients reporting an event per PYE
  - PYE was defined as the time until the first event or exposure end, whichever came first, and incidence was defined as the first event
- Efficacy results are presented using observed data

Baseline Demographics and Clinical Characteristics

- Baseline demographics and clinical characteristics for the final ECZTEND results were similar to previous analyses[3,4] (**Table 4**)

Table 4. Baseline demographics and clinical characteristics

	ECZTEND total population N=1672; PYE=4466.2	
Demographics		
Age, median years (min ; max)	36.0 (13.0 ; 87.0)	
Age group, years, n (%)		
12-17	103 (6.2)	
≥18	1569 (93.8)	
Female, n (%)	709 (42.4)	
Race, n (%)		
White	1194 (71.4)	
Asian	312 (18.7)	
Black	120 (7.2)	
Age at onset of AD, median years (min ; max)	3.0 (0.0 ; 84.0)	
Clinical characteristics		
	Parent trial baseline N=1664	**ECZTEND baseline N=1672**
IGA score, n (%)		
0/1 – clear/almost clear	-	525 (31.4)
2 – mild	-	608 (36.4)
3 – moderate	890 (53.5)	443 (26.5)
4 – severe	774 (46.5)	96 (5.7)
EASI, median (Q1 ; Q3)	27.0 (20.6 ; 37.9)	4.6 (1.6 ; 11.7)
SCORAD, median (Q1 ; Q3)	*n = 1664* 67.7 (59.8 ; 78.0)	*n = 1670* 29.4 (18.0 ; 43.8)
DLQI, median (Q1 ; Q3)	*n = 1488* 16.0 (11.0 ; 21.0)	*n = 1504* 5.0 (2.0 ; 9.0)

n, number of patients with recorded observation; Q1, 1st quartile (25th percentile); Q3, 3rd quartile (75th percentile).

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