3 years of tralokinumab treatment provides long-term disease control as demonstrated by clinically meaningful outcomes in moderate-to-severe atopic dermatitis

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Introduction

- Atopic dermatitis (AD) is a chronic skin disease which may impact patients throughout their lifespan, requiring efficacious long-term treatment options with a favorable safety profile[1]
- The European guidelines (EuroGuiDerm) define disease control or remission as satisfactory reduction of the signs and symptoms of AD whilst being on a safe long-term anti-inflammatory treatment[2]
  - An international consensus previously defined a set of core decision points for systemic therapies at 6 months, including EASI ≤ 7, itch NRS ≤ 4 and DLQI ≤ 5 representing mild/no disease[3]
- Tralokinumab, a specific, high-affinity interleukin-13 inhibitor, is approved in Europe, Canada, and the United States for the treatment of adults with moderate-to-severe AD
- ECZTEND (NCT03587805) is an ongoing open-label extension trial assessing the safety and efficacy of tralokinumab over 5 years after the completion of parent trials (PT)
  - A recently presented interim safety analysis of adult patients with up to 42 months of exposure confirmed the safety profile of tralokinumab[4]

Objective

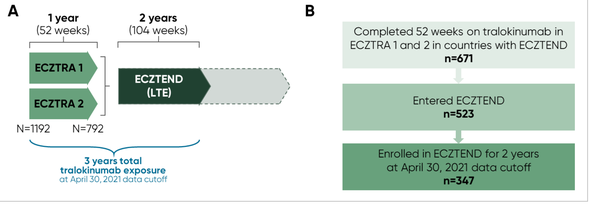
To evaluate the efficacy and safety of 3 years of tralokinumab treatment, using clinically relevant outcomes indicating disease control, for adults with moderate-to-severe AD

Materials and Methods

Patients and treatment

- In ECZTEND, patients who completed PT of tralokinumab received open-label tralokinumab 300 mg every two weeks (Q2W, home use) plus optional topical corticosteroids (TCS, US class ≥4 or Europe class ≤3) or topical calcineurin inhibitor (TCI), with visits every 8 weeks
  - For key inclusion and exclusion criteria, please see Blauvelt et al[5]
  - Multiple tralokinumab PT of varying duration will contribute to the ECZTEND population (ECZTRA 1-8 and the investigator-initiated study TraSki, conducted in 11 countries)
  - While ECZTRA 3-5 and 7 were completed at data cutoff (April 30, 2021), participants in these trials did not receive 52 weeks of tralokinumab and therefore were not included in the 3-year efficacy analysis set
- This *post hoc* analysis assessed tralokinumab efficacy in a homogenous group of participants with the longest tralokinumab treatment duration at data cutoff (April 30, 2021)
  - Data are presented from eligible adult patients with moderate-to-severe AD who completed 3 years of tralokinumab treatment irrespective of response in the PT ECZTRA 1 and 2 (1 year in PT, 2 years in ECZTEND; **Figure 1**; N=347 of 1442 total enrolled in ECZTEND at data cutoff)

Figure 1. Schematic of (A) ECZTEND interim analysis of patients previously treated with tralokinumab monotherapy for 52 weeks in ECZTRA 1 and 2, followed by 104 weeks of treatment in ECZTEND and (B) patient disposition at parent trial completion, ECZTEND baseline, and at April 30, 2021 data cutoff



Analyses

- Efficacy outcomes assessed were:
  - Proportion of patients with 3 years total tralokinumab treatment achieving EASI-75/90, IGA 0/1, and EASI ≤ 7
  - Percentage of patients achieving mild or no disease, defined as EASI ≤ 7, itch NRS ≤ 4, or DLQI ≤ 5, after 3 years of tralokinumab treatment
  - Proportion of time with mild/no disease during 3 years total tralokinumab treatment
- For EASI-75/90 and IGA 0/1 response rates, as observed data are presented, and intermittent missing data are presented using last observation carried forward (LOCF). Modified non-responder imputation (mNRI) sets discontinuation from ECZTEND due to adverse event(s) or lack of efficacy as non-response and uses LOCF for other missing data

Results

Baseline demographics and characteristics

- This *post hoc* analysis included 347 patients from the PTs ECZTRA 1 and 2 who had entered ECZTEND and consistently received tralokinumab for a total of 3 years at data cutoff, April 30, 2021 (**Fig. 1B, Table 1**)
- Amongst patients who completed 3 years of tralokinumab treatment (N=347), median EASI improved from 26.7 (IQR 19.7; 38.4) at PT baseline to 3.0 (IQR 1.0; 6.7) after one year of PT

Table 1. Baseline demographic and disease characteristics of patients with 3 years total tralokinumab treatment (ECZTEND interim efficacy analysis set)

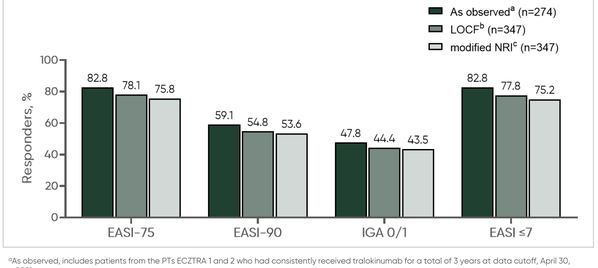
	ECZTEND interim efficacy analysis set n=347	
Age Median years (IQR)	42.0 (30.0; 53.0)	
Sex n (%) Male Female	205 (59.1) 142 (40.9)	
Race n (%)[a] White Black Asian	259 (74.6) 20 (5.8) 56 (16.1)	
Parent trial n (%) ECZTRA 1 ECZTRA 2	224 (64.6) 123 (35.4)	
Age at onset of AD Median years (IQR)	3.0 (1.0; 15.0)	
Duration of AD Median years (IQR)	29.0 (19.0; 43.0)	
	Parent Trial Baseline	**ECZTEND Baseline**
IGA severity n (%) Clear/minimal (score=0/1) Mild (score=2) Moderate (score=3) Severe (score=4)	– – 172 (49.6) 175 (50.4)	98 (28.2) 123 (35.4) 106 (30.5) 20 (5.8)
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), *n*	17.0 (11.0; 23.0), *n*=343	5.0 (2.0; 10.0), *n*=332
Worst weekly pruritus NRS[a] Median (IQR), n	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.

Sustained improvement in lesion extent and severity with continued tralokinumab

- Amongst patients who completed 3 years of tralokinumab treatment at data cutoff,
  - EASI-75 and EASI-90 were achieved in 76% (263/347) and 54% (186/347) of patients by mNRI, respectively (**Figure 2**)
  - IGA 0/1 was achieved in 44% (151/347) by mNRI (**Figure 2**)
  - EASI ≤7 was achieved by 75% (261/347) by mNRI (**Figure 2**)

Figure 2. Proportion of patients with 3 years total tralokinumab treatment achieving EASI-75, EASI-90, IGA 0/1, and EASI ≤7

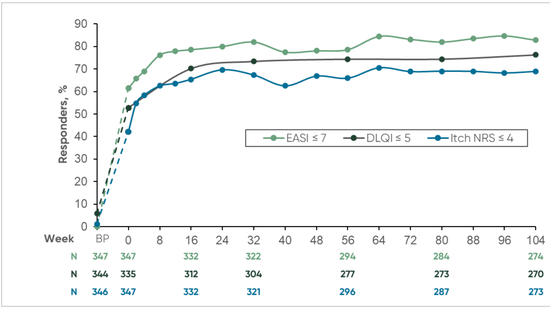


[a]As observed, includes patients from the PTs ECZTRA 1 and 2 who had consistently received tralokinumab for a total of 3 years at data cutoff, April 30, 2021.
[b]Intermittent missing data imputed using LOCF.
[c]Discontinuation from ECZTEND due to adverse event(s) or lack of efficacy set as non-response, other missing imputed with LOCF.

Maintained improvements in clinically relevant outcomes at 3 years of tralokinumab treatment

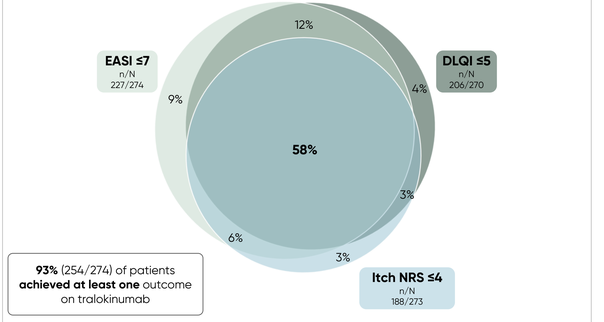
- Patients were controlled (mild/no disease) for the majority of the 3 years of tralokinumab treatment (**Figure 3**)
- At 3 years of tralokinumab treatment, 93% (254/274, as observed) of patients achieved at least one outcome (**Figure 4**)
- Median duration of response during PT and ECZTEND up to week 104, as observed:
  - >80% of visits with EASI ≤ 7 response [84.7 (Q1,Q3; 55.8, 93.8)%]
  - >80% of visits with DLQI ≤ 5 [84.1 (43.1, 96.9)%]
  - >70% of visits with Itch NRS ≤ 4 [73.8 (31.7, 91.3)%]
- Using mNRI, 84% of patients achieved at least one clinically meaningful improvement, and 51% achieved clinically meaningful improvements of all three measures

Figure 3. Percent response from parent trial baseline in disease severity, itch, and life quality over 3 years



In ECZTEND, worst itch NRS was assessed based on recall of the previous week before the visit

Figure 4. Percentage of patients achieving mild or no disease by at least one outcome after 3 years of tralokinumab treatment



Data as observed. Denominator is the smallest number of patients with DLQI, EASI, and itch NRS measurements(s) in category, except for individuals with no response where largest number is used. No response includes non-evaluable patients, e.g., for category DLQI≤5 + EASI≤7 where DLQI is not measured for one or more patient(s).

No new safety signals with continued tralokinumab treatment

- The safety profile was consistent with the PTs[6] and the overall ECZTEND population (n=1442),[4] with no new safety signals arising with continued tralokinumab (**Table 2**)

Table 2. Summary of adverse events (AEs) in patients with 3 years total tralokinumab treatment

	AEs in ECZTEND ECZTEND interim efficacy analysis set[a] Tralokinumab Q2W + optional TCS (n=347; PYE=707.7)				AEs up to Week 16 in parent trials initial tralokinumab treatment[b] Tralokinumab Q2W ± TCS (n=1605; PYE=473.2)			Placebo Q2W ± TCS (n=680; PYE=193.1)		
	n (%)	Rate[c] [(nP/PYE)*100]	E	Rate[d] [(nE/PYE)*100]	*n* (adj. %)[d]	E	Adj. Rate[d,e] [(nE/PYE)*100]	*n* (adj. %)[d]	E	Adj. Rate[d,e] [(nE/PYE)*100]
All AEs	295 (85.0)	144.2	1422	200.9	1080 (65.7)	3148	639.5	449 (67.2)	1276	678.3
AEs related to study drug[f]	102 (29.4)	18.3	251	35.5	463 (28.0)	1025	207.6	176 (26.8)	365	195.6
Severity										
Mild	247 (71.2)	80.5	917	129.6	881 (53.2)	2127	429.8	326 (49.0)	738	391.0
Moderate	180 (51.9)	40.6	450	63.6	518 (31.5)	917	189.5	258 (39.0)	478	254.3
Severe	31 (8.9)	4.6	55	7.8	77 (4.6)	104	20.2	40 (6.3)	60	33.0
Serious AEs	31 (8.9)	4.6	34	4.8	37 (2.1)	38	7.4	18 (2.8)	22	11.9
Leading to withdrawal from trial	9 (2.6)	1.3	9	1.3	34 (2.0)	42	8.6	12 (1.8)	15	8.0

[a]Includes 347 patients from the PTs ECZTRA 1 and 2 who had consistently received tralokinumab for a total of 3 years at data cutoff, April 30, 2021.
[b]Includes patients from a pooled safety analysis set from parent trials ECZTRA 1, 2, 3, 5, and Phase 2b, previously presented at RAD Virtual 2020[1]; AEs related to study drug and AEs leading to withdrawal during initial treatment sourced from data on file; TCS rules varied across parent trials with mandatory TCS in ECZTRA 3, and TCS use not part of treatment regimen in ECZTRA 1, ECZTRA 2, and ECZTRA 5.
[c]Rate calculated by number of patients divided by PYE until first event, multiplied by 100.
[d]Rate calculated by number of events divided by PYE, multiplied by 100.
[e]For PTs, Cochran-Mantel-Haenszel weights were applied to calculate adjusted AE incidences and rates to account for different randomization ratios across PTs.[7]
[f]AEs related to study drug comprise AEs considered possibly or probably related by the investigator and AEs with missing causality.

Limitations

- The analysis presented here represents a subgroup of patients who were eligible, chose to enter from two of the PTs and were treated for two years in ECZTEND by the time of data cutoff, and as such, the data may not be generalizable to the full tralokinumab population (see **Figure 1B**). Analyses on the full two-year cohort were previously presented[4])

Conclusions

- Clinically meaningful improvements were observed in AD signs and symptoms in patients with moderate-to-severe AD treated with tralokinumab for 3 years
- Nine out of ten patients achieved at least one of the clinically relevant outcomes of EASI ≤ 7, itch NRS ≤ 4, or DLQI ≤ 5, representing mild/no AD; approximately 60% achieved clinically meaningful outcomes by all three measures
- The response rates were maintained over time with patients having EASI ≤ 7 for more than 80% of visits during the 3 years of treatment
- These data, in combination with the favorable safety profile, suggest tralokinumab as an efficacious and well-tolerated treatment option for long-term disease control in patients with moderate-to-severe AD

Abbreviations

%, percentage of patients with ≥1 event; adj., adjusted (for PTs, Cochran-Mantel-Haenszel weights were applied to calculate adjusted AE incidences and rates to account for different randomization ratios across PTs)[7]; AE, adverse event; AD, atopic dermatitis; BP, parent trial baseline; DLQI, dermatology life quality index; E, number of adverse events; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; IQR, interquartile range; Itch NRS, peak worst weekly itch NRS; LOCF, last observation carried forward; mNRI, modified non-responder imputation; n, number of patients achieving the indicated metric, or with ≥1 event; nE, number of events; nP, number of patients; N, number of patients with recorded observation; NRS, numerical rating scale; PYE, patient-years of exposure; PT, parent trial; Q2W, every 2 weeks; SCORAD, scoring atopic dermatitis; SD, standard deviation; TCI, or topical calcineurin inhibitor; TCS, topical corticosteroids.

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Disclosures

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