Efficacy and safety of up to two years of tralokinumab treatment in adults of different racial subgroups with 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]
- Although AD is highly prevalent in patients with skin of color, data on the efficacy of AD therapies in these patients is limited since most clinical trials enroll predominately White patients[2]
  - Several standard measures, including EASI, can underestimate AD severity in dark skin[2]
- 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)

Objective

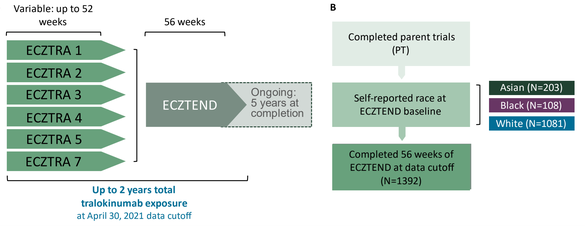
To evaluate the efficacy and safety of up to 2 years of tralokinumab treatment by self-identified racial subgroup (Asian, Black, White) in adults with moderate-to-severe AD

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) after a 600 mg loading dose plus optional topical corticosteroids (US class ≥4 or Europe class ≤3) or topical calcineurin inhibitor, with visits every 8 weeks
  - All patients who completed PT at sites with ECZTEND were eligible to enroll in ECZTEND, regardless of prior treatment or response
  - For key inclusion and exclusion criteria, please see Blauvelt et al[3]
- Adult patients included in this post hoc analysis completed 56 weeks of open-label tralokinumab treatment in ECZTEND by the data cutoff (April 30, 2021) (**Figure 1A**)
- Patients self-reported race at baseline of ECZTEND (**Figure 1B**)

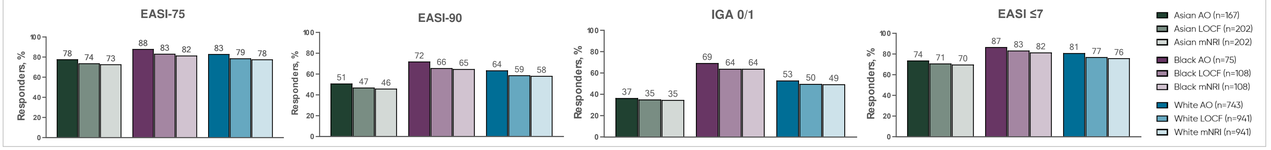
Figure 1. Schematic of (A) ECZTEND interim analysis of adult patients and (B) patient disposition at parent trial completion, ECZTEND baseline, and at April 30, 2021 data cutoff



Analyses

- Proportion of patients achieving EASI-75/90, IGA 0/1, EASI≤7, Worst Weekly Pruritus NRS≤ 3, and DLQI ≤ 5 were assessed. EASI-75/90 determined relative to PT baseline
- Data are presented as observed. 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
- To account for potential baseline confounders with racial subgroup, logistic regression analysis adjusting for country, weight, EASI, ethnicity and age (all at ECZTEND baseline) in addition to racial subgroup were conducted. Estimated proportions from these analyses were expressed relative to US non-Hispanic patients
- Data were used as per Food and Drug Administration (FDA) label and United States Prescribing Information (USPI)

Figure 2. Proportion of patients by racial subgroup achieving EASI-75, EASI-90, IGA 0/1, and EASI≤7 at Week 56 of ECZTEND



Results

Patients, Demographics, and Clinical Characteristics

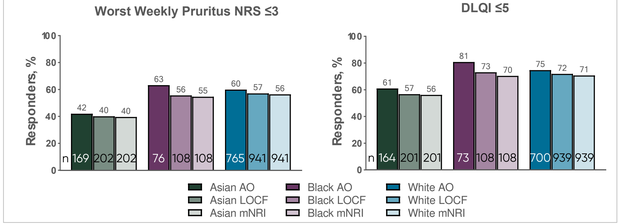
- This post hoc analysis included 1392 adult patients who had completed 56 weeks of tralokinumab in ECZTEND (up to 2 years total) at data cutoff, April 30, 2021 and self-reported their race as Asian, Black, or White (**Figure 1B, Table 1**)
  - Among patients who had completed 56 weeks of tralokinumab in ECZTEND at data cutoff, 24% had skin of color (self-reported race as Asian, Black, or Other)
  - Very few patients self-reported their race as other than Asian, Black, or White (N=38 patients total) and therefore were not included in this analysis
- Baseline demographic and disease characteristics were largely balanced across subgroups (**Table 1**), although regional differences were present

Table 1. Baseline demographic and disease characteristics of patients by racial subgroup

	Asian N=203		Black N=108		White N=1081	
Mean age, y (SD)	37.9 (13.9)		39.6 (13.4)		39.4 (14.1)	
Male, n (%)	125 (61.6)		45 (41.7)		637 (58.9)	
Ethnicity, n (%) Hispanic or Latino Not Hispanic or Latino	2 (1.0) 201 (99.0)		5 (4.6) 103 (95.4)		79 (7.3) 1002 (92.7)	
Country, n (%)	United States, 49 (24.1) Canada, 55 (27.1) Germany, 2 (1.0) Great Britain, 9 (4.4) Spain, 1 (0.5) France, 1 (0.5) Japan, 86 (42.4)		United States, 94 (87.0) Canada, 7 (6.5) Germany, 3 (2.8) Great Britain, 3 (2.8) France, 1 (0.9)		United States, 187 (17.3) Canada, 137 (12.7) Poland, 178 (16.5) Germany, 246 (22.8) Great Britain, 52 (4.8) Spain, 123 (11.4) Belgium, 62 (5.7) France, 61 (5.6) Italy, 15 (1.4) Czech Republic, 20 (1.9)	
Baseline scores	**Parent trial**	**ECZTEND**	**Parent trial**	**ECZTEND**	**Parent trial**	**ECZTEND**
IGA, n (%) 3 4	89 (43.8) 114 (56.2)	51 (25.1) 14 (6.9)	73 (67.6) 35 (32.4)	22 (20.4) 7 (6.5)	575 (53.2) 506 (46.8)	308 (28.5) 63 (5.8)
Mean EASI (SD)	32.5 (14.5)	9.2 (11.7)	27.9 (12.0)	6.9 (11.0)	30.7 (12.7)	8.6 (10.0)
Mean SCORAD score (SD)	70.0 (13.5)	33.5 (18.5)	65.3 (12.4)	27.6 (18.6)	69.2 (12.7)	33.5 (19.1)
Mean POEM (SD), n	22.6 (4.7), 199	13.2 (6.8), 197	20.4 (6.2), 99	10.6 (7.2), 106	22.3 (5.1), 1037	12.4 (7.4), 1048
Mean DLQI (SD), n	16.4 (6.9), 200	6.9 (5.8), 197	16.0 (7.7), 100	6.9 (6.4), 106	16.6 (6.9), 1041	6.7 (6.0), 1048
Mean Worst Pruritus NRS (SD), n	7.9 (1.3), 180	5.3 (2.5), 202	8.0 (1.8), 63	4.6 (2.9)	7.6 (1.5), 971	4.9 (2.7), 1080
Mean Sleep Interference NRS (SD), n	7.2 (1.9), 180	3.6 (2.8), 202	7.4 (2.2), 63	3.0 (3.1)	6.8 (2.0), 971	3.1 (2.8), 1080

[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.

Figure 3. Percentage of patients achieving Worst Weekly Pruritus NRS ≤3 and DLQI ≤5 by racial subgroup at Week 56 of ECZTEND



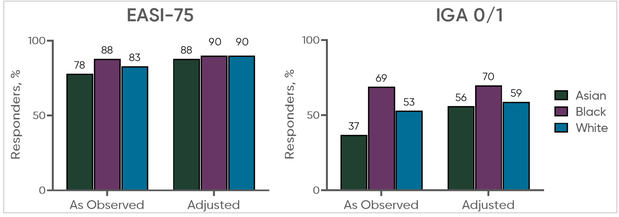
Comparable efficacy across racial subgroups with up to two years of tralokinumab treatment

- At Week 56 in ECZTEND
  - EASI-75 was achieved in 78% (130/167) of Asian patients, 88% (66/75) of Black patients and 83% (186/347) of White patients, as observed (**Figure 2**)
  - Worst weekly pruritus NRS ≤3 was achieved in 42% (71/169) of Asian patients, 63% (48/76) of Black patients, and 60% (458/765) of White patients, as observed (**Figure 3**)
  - Similar patterns of response were observed for EASI-90, EASI ≤7, IGA 0/1, and DLQI ≤5, and when using LOCF or mNRI to account for missing data (**Figures 2 and 3**)

Adjusting for differences in baseline characteristics and country between subgroups impacts estimated responder proportions

- Adjusted for race and country as main effects, EASI-75 was achieved in 88% of Asian patients, 90% of Black patients, and 90% of White patients (**Figure 4**)
- Similar patterns of estimated response were observed for IGA 0/1 (**Figure 4**) and when adjusting for region as main effect or the interaction between region and race

Figure 4. Percentage of patients achieving EASI-75 and IGA 0/1 by racial subgroup before and after adjusting for baseline differences



The safety profile of up to 2 years of tralokinumab treatment was consistent across racial subgroups

- Through Week 56 in ECZTEND, rates of adverse events (AEs), serious AEs, and AEs leading to drug withdrawal were comparably low across racial subgroups (**Table 2**)
- The majority of AEs in all subgroups were mild or moderate in severity and subjects recovered from most of the AEs

Table 2. Summary of AEs in ECZTEND by racial subgroup

	Asian (*n*=203; PYE=386.2)		Black (n=108; PYE=169.7)		White (n=1081; PYE=1808.0)	
	n **(%)**	**Rate (nE/100 PYE)**	***n*** **(%)**	**Rate (nE/100 PYE)**	***n*** **(%)**	**Rate (nE/100 PYE)**
All AEs	162 (79.8)	167.8	71 (65.7)	142.6	850 (78.6)	208.2
Severity						
Mild	143 (70.4)	130.2	57 (52.8)	101.9	717 (66.3)	134.1
Moderate	67 (33.0)	34.7	35 (32.4)	35.3	503 (46.5)	66.8
Severe	10 (4.9)	2.8	7 (6.5)	5.3	80 (7.4)	7.4
Serious AEs	12 (5.9)	3.4	7 (6.5)	4.7	81 (7.5)	5.4
Leading to withdrawal from trial	2 (1.0)	0.5	2 (1.9)	1.2	30 (2.8)	1.7
Outcome						
Not recovered/ not resolved	68 (33.5)	28.0	23 (21.3)	24.2	269 (24.9)	23.7
Recovering/resolving	18 (8.9)	5.4	12 (11.1)	10.0	153 (14.2)	12.2
Recovered/resolved	151 (74.4)	133.1	65 (57.4)	106.0	799 (73.9)	169.2
Recovered/resolved with sequelae	1 (0.5)	0.3	3 (2.8)	1.8	16 (1.5)	1.0
Unknown	3 (1.5)	1.0	1 (1.0)	0.6	28 (2.6)	1.9

Conclusions

- Improvements in disease severity, itch, and quality of life were comparable across different racial subgroups following up to two years of tralokinumab treatment in adults with moderate-to-severe AD
- Limitations of this analysis include the lack of a placebo arm in ECZTEND, disparate sample sizes across racial subgroups, and possible confounders not considered
- The lower response rates observed for the Asian subgroup relative to other racial subgroups could be partially explained by adjusting for country

Abbreviations

adj., adjusted; AE, adverse event; AD, atopic dermatitis; DLQI, dermatology life quality index; E, number of adverse events; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; LOCF, last observation carried forward; mNRI, modified non-responder imputation; n, number of patients achieving the indicated metric, or with ±1 event; *n*E, number of events; N, number of patients with recorded observation; NRS, numerical rating scale; PYE, patient-years of exposure; PT, parent trial; Q2W, every 2 weeks; SD, standard deviation

References

1. Weidinger S, Novak N. *Lancet*. 2016;387(10023):1109-1122. **2.** Kaufman B, et al. *Exp Dermatol* 2018; 27: 340-357. **3.** Blauvelt A, *et al. J Am Acad Dermatol.* 2022;S0190-9622(22)02345-3.

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