Improvement of the head and neck regions with continuous tralokinumab treatment for up to 4 years in adults with moderate-to-severe atopic dermatitis

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P057

Objectives

- To examine the efficacy of long-term tralokinumab treatment on the head and neck regions through a post hoc analysis of two Phase 3 clinical trials and the on-going ECZTEND open-label trial

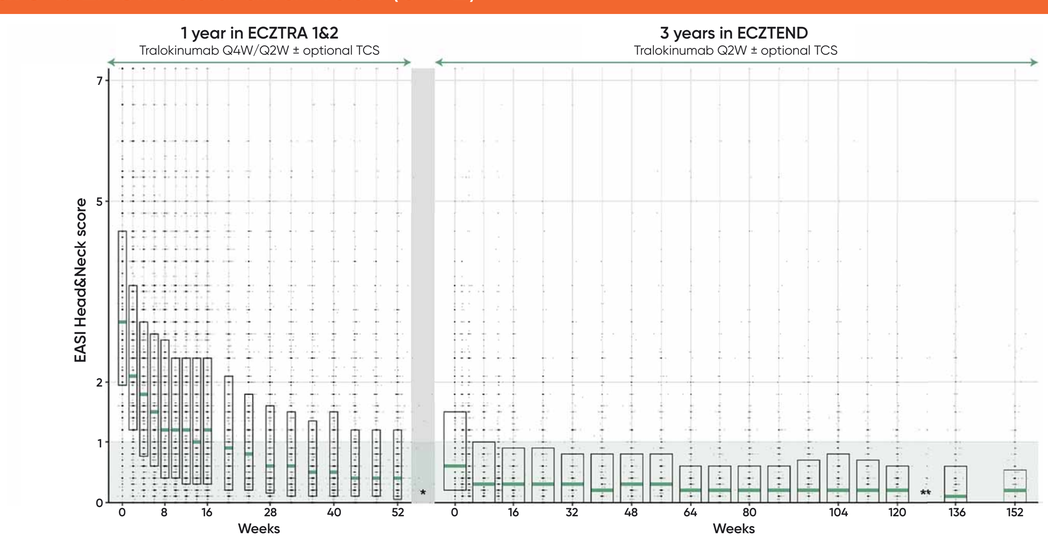
Background

- Atopic dermatitis (AD) is a chronic, inflammatory disease that can affect multiple regions of the body but can be particularly burdensome on exposed areas of skin, such as the head and neck (H&N) regions[1]
- The H&N regions can be difficult to treat, and the use of medium- to high-potency topical corticosteroid (TCS) in this region is not recommended[2]
- Tralokinumab, a high-affinity monoclonal antibody that specifically neutralizes interleukin-13, is approved for the treatment of moderate-to-severe AD in multiple countries[3,4]
- ECZTEND (NCT03587805) is an ongoing open-label, 5-year extension trial investigating the long-term safety and efficacy of tralokinumab plus optional TCS

Results

- In patients treated with tralokinumab for up to a total of 4 years in ECZTRA 1 & 2 and ECZTEND, the median H&N EASI was reduced from 3.0 at parent trial (PT) baseline to 0.2 at Week 152 in ECZTEND. The proportion of patients with H&N EASI≤1 at Week 152 was 87.2% **(Figure 1)**
- In the most severe subgroup, with IGA 4 and high H&N involvement (H&N EASI≥4) at baseline (n=301), the median H&N EASI was reduced from 5.4 at PT baseline to 0.4 at Week 152. The proportion of patients with H&N EASI≤1 at Week 152 was 70.7 **(Figure 2)**
- The median total EASI (0-72) was improved from 28.2 at PT baseline to 1.3 at Week 152. The proportion of patients with EASI≤7 and EASI≤2 at Week 152 were 86.5% and 58.3%, respectively **(Figure 3)**

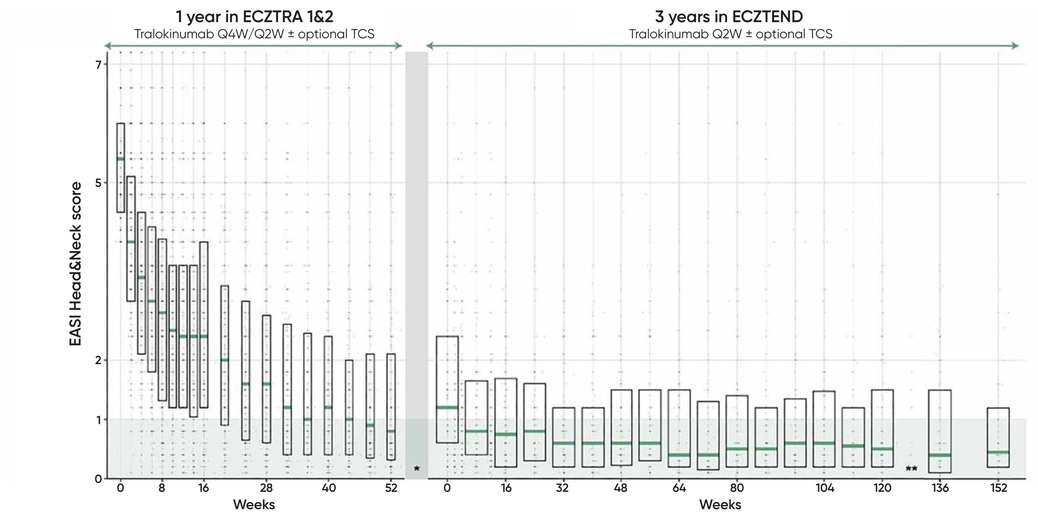
Figure 1. EASI Head and Neck (0-7.2)



Total at risk (N)	1192	1159	1125	930	837	784	523	503	486	467	456	445	426	412	333	267
n	1192	1140	1125	910	815	784	523	503	485	454	416	431	415	408	333	266
EASI H&N = 0 (%)	3.1	11.2	14.6	199	21.6	24.9	20.1	30	34.2	30.6	32.9	37.8	34.2	38.5	45.6	44.4
EASI H&N ≤ 1 (%)	12.2	44.9	48.2	60.1	67.7	71.2	62.3	79.1	81.4	82.2	84.6	85.6	83.6	85	86.8	87.2
Median	3	1.2	1.2	0.6	0.5	0.4	0.6	0.3	0.3	0.3	0.2	0.2	0.2	0.2	0.1	0.2

*Variable time between last treatment in parent trial and fist treatment in ECZTEND. Not all sites participated in ECZTEND and all patients did not consent to continue.
**83 subjects did not re-consent to continue in ECZTEND following a protocol amendment in May 2021 prolonging the trial from up to 3 to up to 5 year and changing the visit frequency from every 8 to every 16 weeks.

Figure 2. EASI Head and Neck (0-7.2) in severe subgroup: IGA 4 and H&N EASI ≥4 at baseline



Total at risk (N)	301	294	282	230	203	186	123	120	119	113	112	109	101	94	78	58
n	301	288	282	221	201	186	123	120	119	110	101	102	98	93	78	58
EASI H&N = 0 (%)	0	3.1	3.5	6.3	8	8.6	4.1	10.8	15.1	9.1	13.9	17.6	9.2	12.9	17.9	17.2
EASI H&N ≤ 1 (%)	0	20.1	23	37.1	48.8	53.8	42.3	60	68.9	66.4	63.4	67.6	69.4	66.7	70.5	70.7
Median	5.4	2.8	2.4	1.6	1.2	0.8	1.2	0.8	0.6	0.6	0.4	0.5	0.6	0.5	0.4	0.4

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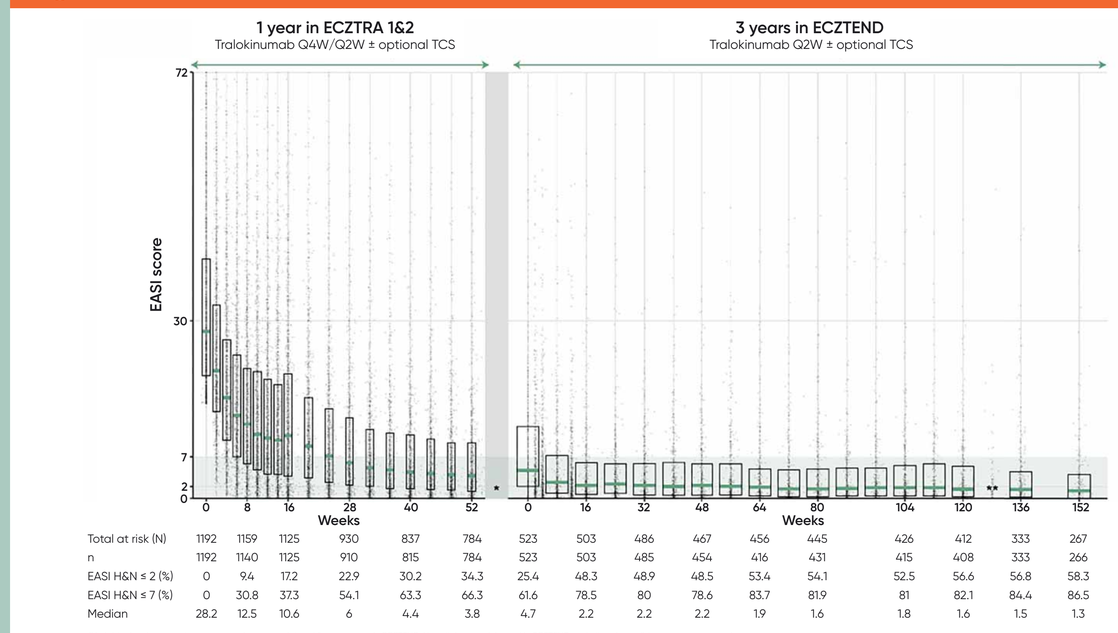
Figure 3. Overall EASI (0-72)



Total at risk (N)	1192	1159	1125	930	837	784	523	503	486	467	456	445	426	412	333	267
n	1192	1140	1125	910	815	784	523	503	485	454	416	431	415	408	333	266
EASI H&N ≤ 2 (%)	0	9.4	17.2	22.9	30.2	34.3	25.4	48.3	48.9	48.5	53.4	54.1	52.5	56.6	56.8	58.3
EASI H&N ≤ 7 (%)	0	30.8	37.3	54.1	63.3	66.3	61.6	78.5	80	78.6	83.7	81.9	81	82.1	84.4	86.5
Median	28.2	12.5	10.6	6	4.4	3.8	4.7	2.2	2.2	2.2	1.9	1.6	1.8	1.6	1.5	1.3

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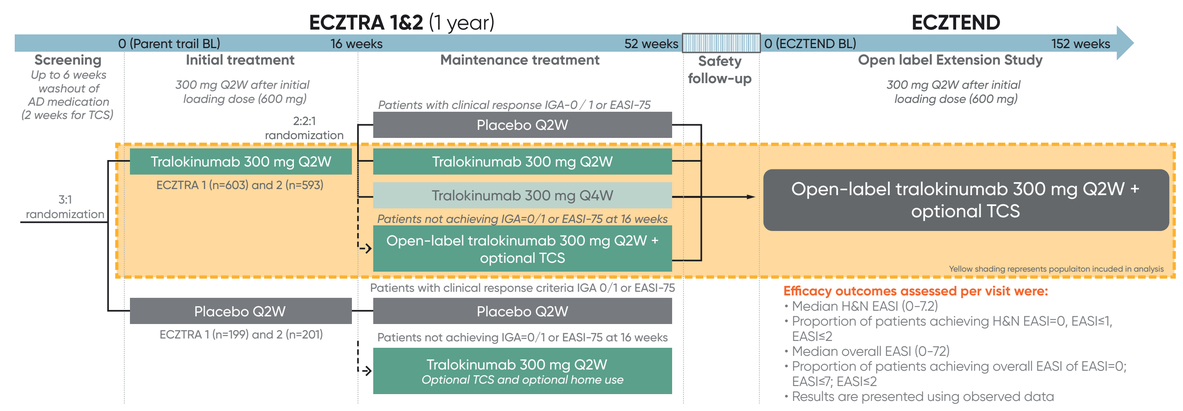
Methods

- Data were obtained from all patients initiated on tralokinumab in ECZTRA 1&2, identically designed phase 3 monotherapy trials conducted in adults with moderate-to-severe AD
- Patients on active treatment were followed for up to 52 weeks in parent trials, and patients that then enrolled in the long-term open-label study ECZTEND were followed up to an additional 152 weeks until the April 30, 2022 data cutoff **(Figure 4)**
- Data from Week 16 responders re-randomized to placebo were not included beyond that timepoint **(Figure 4)**

Analyses

- Overall EASI scores (0-72) were calculated as a composite of the intensity (0–3) and extent of involvement (0–6)
- Head and neck regional scores (H&N EASI; 0-7.2), the intensity of signs (erythema, induration/papulation, excoriation, lichenification) were assessed individually (0-3) and were summated (0–12) and then multiplied by extent of involvement (0–6). Then the % BSA weighting coefficient 0.1 was used
- Results are presented using observed data

Figure 4. Trial Design



Baseline and Disease Characteristics

- Patients generally exhibited substantial disease severity at baseline **(Table 1)**
- 87.8% of patients had H&N involvement at baseline (H&N EASI>1)
- The median treatment duration was 53.1 weeks (IQR 38.4; 199.9) and max 238.5 weeks
- The most common reasons for discontinuation were Lack of efficacy (11.9 %), Other reasons (9.8 %), Adverse events (6.6%), Withdrawal by subject (7.2%), and Lost to follow up (4.2%)

Table 1. Baseline demographics and characteristics

	Initially randomized to tralokinumab Q2W (N=1192)
Mean age, years (SD)	37.9 (14.2)
Male sex, n (%)	708 (59.4)
Mean BSA involvement % (SD)	52.6 (24.8)
Mean duration of AD, years, (SD)	28.1 (15.2)
IGA 4 (severe), n (%)	591 (49.6)
Mean EASI (SD)	32.2 (14.0)
Mean H&N EASI (SD)	3.2 (1.8)

Conclusions

- In this post hoc analysis, tralokinumab provided sustained improvements of head and neck regions in patients with moderate to severe AD for up to 4 years.
- Similarly, sustained improvements were seen in severe patients with substantial head and neck involvement at baseline.
- Improvements in head and neck regions were comparable to overall EASI improvement.

Abbreviations:

AD, atopic dermatitis; **BL**, baseline; **BSA**, body surface area; **EASI**, eczema area and severity index; **H&N**, head and neck; **IGA**, investigator's global assessment; **n**, number of subjects with observed data at the visit analyzed; **N**, Total at risk, or number of subjects with observed data at or later than the visit analyzed; **Q2W**, every 2 weeks; **Q4W**, every 4 weeks; **SD**, standard deviation; **TCS**, topical corticosteroid

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1. Silverberg, J. Ann Allergy Asthma Immunol. 2019;123(2):144–151. **2.** .Sidbury R, Alikhan A, Bercovitch L, et al.J Am Acad Dermatol. 2023;89(1):e1-e20. **3.** Bieber T. Allergy. 2020;75(1):54-62. **4.** Wollenberg A, Blauvelt A, Guttman-Yassky E, et al. Br J Dermatol. 2021;184(3):437-449.

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