Efficacy and safety of tralokinumab plus topical corticosteroids in patients with severe atopic dermatitis and prior history of dupilumab treatment: a post hoc subgroup analysis from ECZTRA 7 trial

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Introduction

- AD is a chronic inflammatory disease,[1] characterized by eczematous skin lesions and multiple symptoms, including pruritus, sleep disturbance, and depression[2–4]
- Tralokinumab is a high-affinity, fully human, monoclonal antibody designed to specifically neutralize interleukin-13, a key driver of the underlying inflammation in AD[5–7]
- The Phase 3 ECZTRA 7 trial (NCT03761537) met its primary endpoint of EASI-75 at Week 16, confirming tralokinumab plus topical corticosteroids (TCS) is superior to placebo plus TCS in treating severe atopic dermatitis (AD) in patients not adequately controlled by, or with contraindications to, oral cyclosporine A
- There can be inadequate disease control with currently available treatment options and many patients with severe AD continue to experience high disease burden

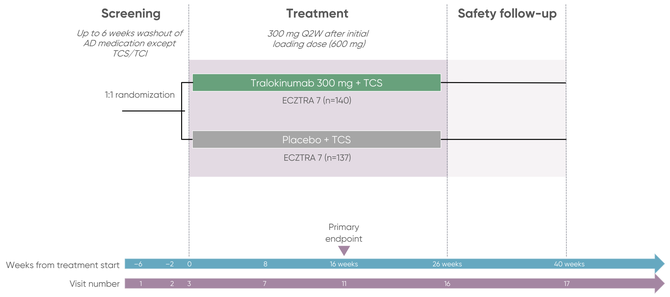
Objective

To describe the efficacy and safety of tralokinumab in a subgroup of ECZTRA 7 patients with prior history of dupilumab treatment

Methods

- ECZTRA 7 was a randomized, double-blinded, multicenter, placebo-controlled Phase 3 trial (**Figure 1**)
- Key inclusion criteria for ECZTRA 7:
  - Adult patients with AD for ≥1 year with inadequate response to topical or documented systemic medication in the past year
  - Disease not adequately controlled with, or patients with contraindications to, use of oral cyclosporine A
  - AD involvement of ≥10% body surface area
  - EASI ≥20 and IGA ≥3 at screening and at baseline
  - Worst daily pruritus numeric rating scale (NRS) average score of ≥4 during the week prior to baseline

Figure 1. ECZTRA 7 trial design.



AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; Q2W, every 2 weeks; TCS, topical corticosteroid.

- Eligible patients were randomized 1:1 to subcutaneous tralokinumab 300 mg every 2 weeks with TCS as needed or placebo with TCS as needed for a treatment period of 26 weeks, following a 600 mg loading dose on Day 0
- For this analysis, prior history of dupilumab treatment was confirmed and further details were collected via queries before trial unblinding
- Dupilumab-experienced patients are defined as those with a confirmed history of dupilumab use prior to the trial
- Cochran-Mantel-Haenszel with treatment as only strata was used for analysis

Results

Patient characteristics

- Dupilumab-experienced (n=14) and dupilumab-naïve (n=263) cohorts had comparable baseline characteristics, except that median (interquartile range, IQR) age was 51.5 (43.0, 57.0) years for dupilumab-experienced patients and 33.0 (25.0, 45.0) years for dupilumab-naïve patients (**Table 1**)
- Median (IQR) EASI and percentage of patients with an IGA of 4 were 35.5 (24.8, 39.6) and 57.1% among dupilumab-experienced patients and 28.7 (22.4, 39.5) and 49.0% among dupilumab-naïve patients, respectively
- Among dupilumab-experienced patients, baseline and clinical characteristics were similar between the tralokinumab + TCS as needed (n=6) and placebo + TCS as needed (n=8) groups (**Table 1**)
  - 50% of patients in each of these two groups discontinued dupilumab due to either lack of efficacy or safety concerns

Table 1. Baseline demographics and clinical characteristics for randomized subjects in **ECZTRA 7**.

	Dupilumab-Naive			Dupilumab-Experienced								
	All (N=263)			All (N=14)			Tralokinumab + TCS (n=6)			Placebo + TCS (n=8)		
Variable	n	Median	IQR	n	Median	IQR	n	Median	IQR	n	Median	IQR
AD duration, years	262	26.0	18.0, 34.0	14	34.0	15.0, 44.0	6	17	15.0, 43.0	8	34.0	21.0, 47.5
Age, years	263	33.0	25.0, 45.0	14	51.5	43.0, 57.0	6	50.0	43.0, 56.0	8	51.5	42.0, 62.5
BSA (%)	263	52.0	35.0, 70.0	14	56.5	34.0, 70.0	6	58.5	50.0, 72.0	8	54.5	33.5, 65.0
DLQI	257	16.0	11.0, 21.0	14	15.0	8.0, 18.0	6	11.0	7.0, 16.0	8	16.5	10.5, 21.5
EASI	261	28.7	22.4, 39.5	14	35.5	24.8, 39.6	6	37.3	29.0, 39.6	8	32.3	23.5, 38.9
SCORAD	261	68.9	61.5, 78.9	14	73.6	61.2, 77.0	6	72.6	58.0, 73.8	8	76.7	64.7, 82.2
Worst daily pruritus NRS (weekly average)	259	7.4	6.6, 8.3	14	6.7	5.4, 8.0	6	5.9	5.3, 7.6	8	7.4	6.2, 8.9
IGA 4, n (%)	263	129 (49.0)		14	8 (57.1)		6	5 (83.3)		8	3 (37.5)	

Tralokinumab response in dupilumab-experienced patients

- Among dupilumab-experienced patients at Week 16, 100% (n/N, 6/6) of patients receiving tralokinumab + TCS achieved EASI-75 without the use of rescue therapy, compared to 50% (4/8) of those receiving placebo + TCS (difference [95% CI]: 50.0 [15.4, 84.6]; **Table 2**)
- Numerically higher proportions of dupilumab-experienced patients receiving tralokinumab + TCS achieved IGA 0/1 (4/6, 66.7%; placebo + TCS: 3/8, 37.5%; difference: 29.2 [-21.3, 79.6]) and improvement in worst daily pruritus NRS (weekly average) ≥4 points (3/6, 50%; placebo + TCS: 3/8, 37.5%; difference: 12.5 [-39.7, 64.7]) at Week 16
- Similarly, at Week 26, numerically higher proportions of dupilumab-experienced patients receiving tralokinumab + TCS achieved EASI-75 (6/6, 100%; placebo + TCS: 3/8, 37.5%; difference: 62.5 [29.0, 96.0]), IGA 0/1 (4/6, 66.7%; placebo + TCS: 2/8, 25%; difference: 41.7 [-6.5, 89.9]), and improvement in worst daily pruritus NRS (weekly average) ≥4 points (3/6, 50%; placebo + TCS: 3/8, 37.5%; difference: 12.5 [-39.7, 64.7]), compared to placebo + TCS

Safety

- Through the 26 weeks, 66.7% (4/6) of dupilumab-experienced patients receiving tralokinumab + TCS reported any adverse event, compared to 87.5% (7/8) of those receiving placebo + TCS (**Table 3**)
- One placebo patient reported 2 events of conjunctivitis, 1 mild and 1 of moderate severity; 1 tralokinumab patient reported 1 mild event of conjunctivitis

Table 2. Binary efficacy endpoints in dupilumab-experienced subjects.

Visit	Endpoint	Tralokinumab + TCS (n=6)	Placebo + TCS (n=8)	Difference (95% CI)†
Week 16	EASI75	6 /6 (100.0%)	4 /8 (50.0%)	50.0 (15.4,84.6)
	IGA 0/1	4 /6 (66.7%)	3 /8 (37.5%)	29.2 (-21.3,79.6)
	Itch NRS≥4*	3 /6 (50.0%)	3 /8 (37.5%)	12.5 (-39.7,64.7)
Week 26	EASI75	6 /6 (100.0%)	3 /8 (37.5%)	62.5 (29.0,96.0)
	IGA 0/1	4 /6 (66.7%)	2 /8 (25.0%)	41.7 (-6.5,89.9)
	Itch NRS≥4*	3 /6 (50.0%)	3 /8 (37.5%)	12.5 (-39.7,64.7)

†Estimated treatment difference and 95% CI from Mantel-Haenszel analysis with treatment as only strata
*Improvement in worst daily pruritus NRS (weekly average) ≥4 points from baseline

- No serious adverse events occurred in either treatment group
- From a safety perspective, there were 2 patients who had previously discontinued dupilumab due to conjunctivitis; adverse events of conjunctivitis were not reported for either patient during 26 weeks of tralokinumab + TCS treatment

Table 3. Adverse events in dupilumab-experienced subjects through 26 weeks

	Tralokinumab + TCS (n=6)	Placebo + TCS (n=8)
Any adverse event	4 /6 (66.7%)	7 /8 (87.5%)
Any serious adverse event	0 /6 (0.0%)	0 /8 (0.0%)
Conjunctivitis*	1 /6 (16.7%)	1/8 (12.5%)

*Search was done for adverse event of special interest: conjunctivitis

Conclusions

This post hoc subgroup analysis indicates that dupilumab-experienced patients can benefit from tralokinumab + TCS as needed.

- Overall frequencies of adverse events in dupilumab-experienced patients treated with tralokinumab + TCS as needed were consistent with the pooled analysis of tralokinumab Phase 2 and 3 trials[8]
- Due to the small sample size, further data involving more patients are needed to confirm these findings

References

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