Tralokinumab improves signs and symptoms of moderate-to-severe atopic dermatitis in patients aged 12 years and older with and without atopic comorbidities

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Background

- Atopic dermatitis (AD) is an inflammatory skin disease associated with atopic comorbidities, including asthma, food allergy, hay fever, and allergic conjunctivitis[1,2]
- The presence of comorbidities can impact treatment selection in patients with AD[2]
- Tralokinumab, a high-affinity monoclonal antibody that specifically targets IL-13, is approved for the treatment of moderate-to-severe AD in multiple countries[3,4]
- This post-hoc analysis presents data from the adult ECZTRA 1, 2 , and 3, and the adolescent ECZTRA 6, trials

Objectives

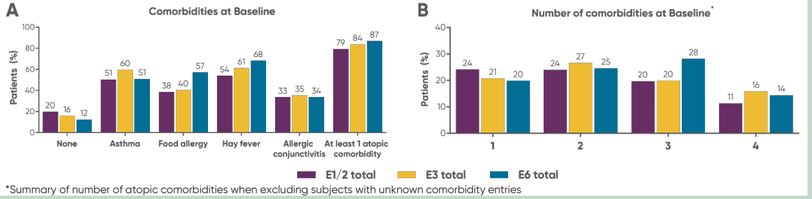
- To assess the impact of atopic comorbidities on the efficacy and safety of tralokinumab vs. placebo for moderate-to-severe AD in patients age ≥12 years in the ECZTRA 1, 2, 3, and 6 phase 3 clinical trials

Results

Baseline atopic comorbidities by trial (pooled placebo and tralokinumab)

- Proportions of patients in all parent trials reporting history of atopic comorbidities were largely similar, although more adolescent patients reported food allergy (**Figure 1A**)
- Patients in all trials largely had between 1 and 3 comorbidities at baseline and were overall similar, except patients in ECZTRA 6 reported a higher proportion of 3 comorbidities (**Figure 1B**)

Figure 1. Baseline comorbidities by trial

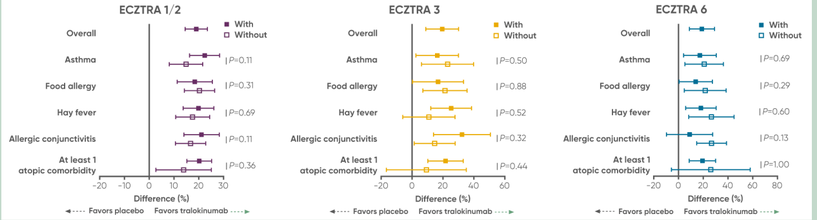


*Summary of number of atopic comorbidities when excluding subjects with unknown comorbidity entries

Efficacy analyses at Week 16 – defined by baseline atopic comorbidities

- In all subgroups at Week 16, higher proportions of patients receiving tralokinumab vs. placebo achieved EASI-75 (**Figure 2**) and IGA 0/1 (**Figure 3**) regardless of type or presence of atopic comorbidity

Figure 2. Analyses of EASI-75 at Week 16*

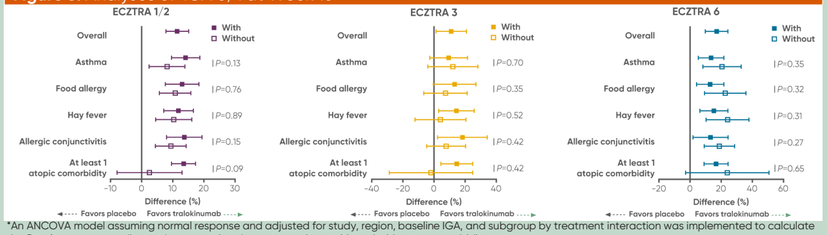


*An ANCOVA model assuming normal response and adjusted for study, region, baseline IGA, and subgroup by treatment interaction was implemented to calculate the *P*-values corresponding to the comparison between patients with and without a comorbidity.

Conclusions

- 16 weeks of tralokinumab treatment improved AD signs and symptoms in adult and adolescent patients with and without atopic comorbidities, regardless of type or number of atopic comorbidities (**Figure 4**)
- In the full population of the adult trials, response rates improved beyond Week 16 up through Week 52 for ECZTRA 1 and 2, and Week 32 for ECZTRA 3[4,5]
- The safety profile of tralokinumab was consistent between patients with and without atopic comorbidities

Figure 3. Analyses of IGA 0/1 at Week 16*



*An ANCOVA model assuming normal response and adjusted for study, region, baseline IGA, and subgroup by treatment interaction was implemented to calculate the *P*-values corresponding to the comparison between patients with and without a comorbidity.

Safety at Week 16

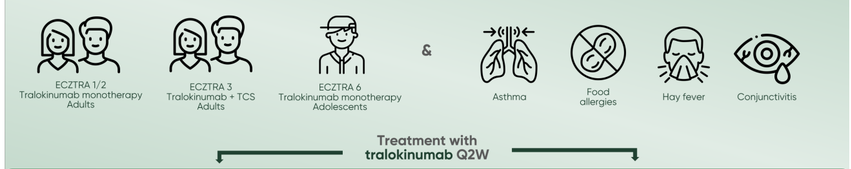
- In the overall population, safety across subgroups was consistent with the safety profile of tralokinumab observed in adults and adolescents (**Table 1**)
- The proportion of patients with asthma AEs was higher in patients with at least 1 atopic comorbidity vs. none, and lower in the tralokinumab group than the placebo group for both adults (E1/2/3 pooled) and adolescents (E6) among patients with at least 1 atopic comorbidity (**Table 1**)

Table 1. Safety at Week 16

	At least 1 atopic comorbidity				No atopic comorbidities			
	ECZTRA 1/2/3 (N=1550)		ECZTRA 6 (N=251)		ECZTRA 1/2/3 (N=368)		ECZTRA 6 (N=36)	
	Tralo (N=1137)	Placebo (N=413)	Tralo (N=167)	Placebo (N=84)	Tralo (N=273)	Placebo (N=95)	Tralo (N=26)	Placebo (N=10)
All AEs, n (%)	830 (73.0)	310 (75.1)	115 (68.9)	54 (64.3)	162 (59.3)	53 (55.8)	13 (50.0)	4 (40.0)
Serious AEs, n (%)	29 (2.6)	16 (3.9)	4 (2.4)	5 (6.0)	5 (1.8)	1 (1.1)	0 (0.0)	0 (0.0)
Severity, n (%)								
Mild	690 (60.7)	228 (55.2)	85 (50.9)	38 (45.2)	128 (46.9)	42 (44.2)	9 (34.6)	2 (20.0)
Moderate	406 (35.7)	193 (46.7)	61 (36.5)	29 (34.5)	68 (24.9)	18 (18.9)	4 (15.4)	2 (20.0)
Severe	65 (5.7)	35 (8.5)	7 (4.2)	7 (8.3)	6 (2.2)	4 (4.2)	1 (3.8)	0 (0.0)
AEs leading to discontinuation of study drug, n (%)	31 (2.7)	9 (2.2)	1 (0.6)	0 (0.0)	4 (1.5)	3 (3.2)	0 (0.0)	0 (0.0)
Most frequently reported AEs, n (%)*								
Dermatitis atopic	210 (18.5)	137 (33.2)	17 (10.2)	10 (11.9)	50 (18.3)	15 (15.8)	3 (11.5)	2 (20.0)
Viral upper respiratory tract infection	203 (17.9)	65 (15.7)	29 (17.4)	8 (9.5)	30 (11.0)	6 (6.3)	2 (7.7)	0 (0.0)
Upper respiratory tract infection	78 (6.9)	23 (5.6)	16 (9.6)	3 (3.6)	9 (3.3)	2 (2.1)	3 (11.5)	1 (10.0)
Conjunctivitis	79 (6.9)	11 (2.7)	2 (1.2)	0 (0.0)	10 (3.7)	0 (0.0)	0 (0.0)	0 (0.0)
AEs of special interest, n (%)								
Conjunctivitis	109 (9.6)	18 (4.4)	6 (3.6)	2 (2.4)	15 (5.5)	1 (1.1)	0 (0.0)	0 (0.0)
Keratoconjunctivitis	4 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Keratitis	4 (0.4)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.8)	0 (0.0)
Eczema herpeticum	5 (0.4)	6 (1.5)	1 (0.6)	1 (1.2)	1 (0.4)	2 (2.1)	0 (0.0)	0 (0.0)
Skin infections requiring systemic treatment	32 (2.8)	32 (7.7)	7 (4.2)	2 (2.4)	6 (2.2)	1 (1.1)	0 (0.0)	0 (0.0)
Malignancies diagnosed after randomization	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Asthma, n (%)**	22 (1.9)	11 (2.7)	3 (1.8)	5 (6.0)	1 (0.4)	0 (0.0)	0 (0.0)	0 (0.0)

*Most frequent preferred terms: Reported if more than 5% of subjects in the total arm of one the study pools experience the event; **Preferred terms Asthma and Asthmatic crisis

Figure 4. Summary of ECZTRA 1/2, 3, and 6 *post-hoc* analyses



Treatment with tralokinumab for 16 weeks was safe and efficacious regardless of type or number of comorbidities at baseline

Abbreviations

AD, atopic dermatitis; AE, adverse event; CDLQI, children's DLQI; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EASI-75, at least 75% improvement in Eczema Area and Severity Index; FDA, Food and Drug Administration; IGA 0/1, achievement of clear (0) or almost clear (1) in Investigator's Global Assessment; IL, interleukin; NRS, numerical rating scale; Q2W, every two weeks; SCORAD, SCORing atopic dermatitis; SD, standard deviation; TCS, topical corticosteroids; Tralo, tralokinumab; USPI, United States Prescribing Information.

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Baseline Demographics and Clinical Characteristics

- Baseline demographics and clinical characteristics were similar between the trials/subgroups, although E3 had a higher percentage of white patients in the tralokinumab group, and mean age was lower in E6
- Clinical characteristics were largely similar between trials and treatment groups for patients with at least 1 atopic comorbidity and no atopic comorbidities, although the no atopic comorbidities subgroup trended toward more moderate disease (**Table 2**)

Table 2. Baseline Demographics and Clinical Characteristics

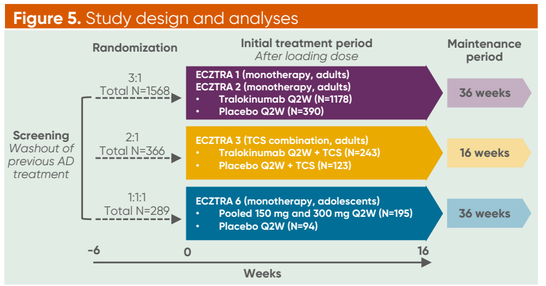
	At least 1 atopic comorbidity						No atopic comorbidities					
	ECZTRA 1/2 N=1568		ECZTRA 3 N=366		ECZTRA 6* N=289		ECZTRA 1/2 N=1568		ECZTRA 3 N=366		ECZTRA 6* N=289	
	Tralo N=929	Placebo N=315	Tralo N=207	Placebo N=99	Tralo N=167	Placebo N=84	Tralo N=237	Placebo N=73	Tralo N=35	Placebo N=23	Tralo N=26	Placebo N=10
Age												
Mean (SD)	37.4 (13.9)	37.2 (14.3)	39.1 (15.1)	37.0 (14.9)	14.7 (1.7)	14.3 (1.7)	39.8 (15.4)	36.8 (17.0)	38.4 (12.0)	39.8 (14.9)	15.1 (1.8)	14.8 (1.1)
Sex												
Male, n (%)	554 (59.6)	182 (57.8)	103 (49.8)	68 (68.7)	82 (49.1)	48 (57.1)	135 (57.0)	46 (63.0)	16 (45.7)	14 (60.9)	14 (53.8)	3 (30.0)
Female, n (%)	375 (40.4)	133 (42.2)	104 (50.2)	31 (31.3)	85 (50.9)	36 (42.9)	102 (43.0)	27 (37.0)	19 (54.3)	9 (39.1)	12 (46.2)	7 (70.0)
Race												
White, n (%)	638 (68.7)	219 (69.5)	161 (77.8)	64 (64.6)	95 (56.9)	47 (56.0)	147 (62.0)	40 (54.8)	32 (91.4)	16 (69.6)	15 (57.7)	6 (60.0)
Black, n (%)	50 (5.4)	18 (5.7)	21 (10.1)	10 (10.1)	18 (10.8)	9 (10.7)	22 (9.3)	8 (11.0)	1 (2.9)	2 (8.7)	3 (11.5)	2 (20.0)
Asian, n (%)	207 (22.3)	67 (21.3)	15 (7.2)	20 (20.2)	41 (24.6)	21 (25.0)	64 (27.0)	24 (32.9)	2 (5.7)	4 (17.4)	6 (23.1)	2 (20.0)
IGA												
Moderate Disease, n (%)	436 (46.9)	144 (45.7)	101 (48.8)	50 (50.5)	90 (53.9)	44 (52.4)	146 (61.6)	43 (58.9)	26 (74.3)	13 (56.5)	11 (42.3)	7 (70.0)
Severe Disease, n (%)	493 (53.1)	171 (54.3)	106 (51.2)	49 (49.5)	77 (46.1)	40 (47.6)	91 (38.4)	30 (41.1)	9 (25.7)	10 (43.5)	15 (57.7)	3 (30.0)
EASI, n	929	315	207	99	167	84	237	73	35	23	26	10
Mean (SD)	33.3 (14.3)	33.5 (13.8)	29.2 (11.9)	30.7 (12.9)	32.0 (13.7)	31.9 (15.0)	28.6 (12.3)	31.1 (14.1)	28.1 (12.9)	29.8 (13.4)	31.6 (12.1)	25.0 (7.0)
SCORAD, n	929	315	207	99	167	84	237	73	35	23	26	10
Mean (SD)	70.8 (13.2)	71.4 (12.4)	67.2 (13.4)	68.5 (13.3)	67.9 (14.2)	68.4 (15.1)	67.8 (13.0)	70.1 (13.0)	67.7 (13.4)	70.7 (13.5)	68.7 (13.4)	58.5 (9.7)
DLQI, n**	917	312	205	98	162	79	235	72	35	23	25	10
Mean (SD)	17.6 (6.9)	17.6 (6.9)	17.9 (6.9)	17.3 (7.0)	13.0 (6.7)	13.8 (6.0)	16.1 (7.6)	17.5 (7.4)	18.1 (7.1)	17.7 (8.0)	14.8 (7.5)	9.7 (5.5)
Worst Daily Pruritus NRS (weekly average), n	922	313	207	99	164	83	235	72	34	23	26	9
Mean (SD)	7.8 (1.4)	7.9 (1.3)	7.8 (1.4)	8.0 (1.5)	7.7 (1.6)	7.6 (1.6)	7.7 (1.5)	7.6 (1.5)	7.7 (1.8)	7.8 (1.3)	7.8 (1.5)	6.8 (1.7)

*Includes pooled 150 mg and 300 mg doses; **CDLQI was assessed in ECZTRA 6

Methods

- The ECZTRA 1 and 2 (NCT03131648 and NCT03160885), ECZTRA 3 (NCT03363854), and ECZTRA 6 (NCT03526861) phase 3 trials are described elsewhere[4–6] (**Figure 5**)
- Data from the initial 16-week treatment period of ECZTRA 1 and 2 (pooled), ECZTRA 3, and ECZTRA 6 (pooled 150 mg and 300 mg tralokinumab) were analyzed and used as per FDA label and USPI
- The proportion of patients achieving EASI-75 and IGA 0/1 at Week 16 according to patient-reported current or past atopic comorbidity are presented as observed regardless of rescue medication use; missing data were imputed as non-responders

Figure 5. Study design and analyses



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Disclosures

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