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ORIGINAL RESEARCH

Clinical Laboratory Parameters in Adolescents with Moderate-to-Severe Atopic Dermatitis Treated with Tralokinumab Up to Week 52 in the Phase 3 ECZTRA 6 Trial

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ABSTRACT

Introduction: Tralokinumab is approved for the treatment of moderate-to-severe atopic dermatitis (AD) in patients aged ≥ 12 years. Here, we examined clinical laboratory parameters in adolescents with moderate-to-severe AD who were treated with tralokinumab for up to 1 year.

Methods: This analysis assessed data from adolescents in the ECZTRA 6 (NCT03526861) phase 3 trial initiated on tralokinumab (150 mg or 300 mg) or placebo for 16 weeks. Additionally, pooled data from tralokinumab-treated patients who continued treatment beyond Week 16 were analyzed regardless of Week 16 response or tralokinumab dosing regimen (i.e., blinded 150 mg or 300 mg every 2 or 4 weeks or open-label tralokinumab 300 mg plus optional topical corticosteroids or calcineurin inhibitors).

Results: Median levels of most laboratory parameters were within respective reference ranges at baseline, Week 16, and Week 52, with comparable values across treatment groups at baseline and Week 16. Baseline levels for

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eosinophils and immunoglobulin E (IgE) were elevated across treatment groups. Few patients shifted from normal baseline eosinophil levels to moderate eosinophilia by Week 16 (150 mg, 3.4%; 300 mg, 2.0%; placebo, 0.0%). In tralokinumab-treated patients who continued treatment beyond Week 16, median eosinophil levels at Week 52 (0.48×10^9/L) were similar to baseline levels ($P = 0.70$). No adverse events of "eosinophilia" or "eosinophil count increased" were reported. IgE levels decreased from baseline to Week 16 in the tralokinumab groups but increased in the placebo group (median change: 150 mg, −186 IU/mL; 300 mg, −105 IU/mL; placebo: +41 IU/mL). Among tralokinumab-treated patients, median IgE was significantly lower at Week 52 (1183 IU/mL) versus baseline ($P < 0.01$).
Conclusion: Similar to previous findings in adults, tralokinumab treatment for up to 1 year did not have any clinically relevant impact on laboratory parameters in adolescents with moderate-to-severe AD, supporting its use without required laboratory monitoring.
Trial Registration: ClinicalTrials.gov identifier, NCT03526861 (ECZTRA 6); study start date: June 19, 2018; primary completion date: April 15, 2020; study completion date: March 16, 2021.

Keywords: Adolescent; Tralokinumab; Clinical laboratory parameters; Atopic dermatitis; ECZTRA 6; Phase 3

Key Summary Points

Why carry out this study?
In the ECZTRA 6 tralokinumab monotherapy phase 3 trial, adolescents treated with tralokinumab (150 or 300 mg) exhibited improvements in atopic dermatitis (AD) signs and symptoms compared with those in the placebo group
Previous work has shown no clinically significant changes in laboratory parameters in adults with moderate-to-severe AD from the tralokinumab clinical trials
Here, we examined clinical laboratory parameters in adolescents with moderate-to-severe AD who were treated with tralokinumab for up to 1 year in the ECZTRA 6 trial
What was learned from the study?
Nearly all hematology and biochemistry clinical laboratory parameters, except for eosinophils and immunoglobulin E (IgE), were within respective reference ranges at baseline, Week 16, and Week 52, with comparable values across tralokinumab and placebo groups at baseline and Week 16
Tralokinumab-treated patients showed a transient elevation in median eosinophil levels from baseline to Week 16, whereas median IgE levels decreased from baseline to Week 16 in the tralokinumab groups but increased in the placebo group
Tralokinumab treatment (150 or 300 mg) for up to 1 year does not have any clinically relevant impact on laboratory parameters in adolescents with moderate-to-severe AD, supporting the use of tralokinumab without routine laboratory monitoring

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease with an estimated 1-year prevalence of 14.8% in adolescents aged 12–17 years old [1]. Although AD can persist into adulthood [2] and often requires patients to undergo long-term treatment, many treatment options are not recommended for long-term use. Established systemic immunosuppressants (e.g., azathioprine, mycophenolate, cyclosporine, systemic corticosteroids) are limited by safety concerns

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and/or lack of evidence for long-term efficacy [3]. Newer treatments, such as systemic Janus kinase inhibitors (e.g., abrocitinib, upadacitinib, baricitinib), require screening and ongoing laboratory monitoring for potential adverse effects [4], which can potentially increase disease burden and negatively impact treatment adherence. Current AD biologics are strongly recommended by professional dermatology and allergy/immunology guidelines as systemic treatments for patients with moderate-to-severe AD [4–7] and do not have laboratory monitoring requirements [8–11].

Tralokinumab, a fully human immunoglobulin G4 (IgG4) high-affinity monoclonal antibody that specifically binds to and neutralizes interleukin (IL)-13 [12, 13], is currently approved in multiple countries for the treatment of moderate-to-severe AD in both adults and adolescents [8, 14–17]. In the ECZTRA 6 tralokinumab monotherapy phase 3 trial, significantly more adolescents with moderate-to-severe AD in the tralokinumab groups (150 or 300 mg) exhibited improvements in AD signs and symptoms compared with those in the placebo group [18]. Additionally, tralokinumab demonstrated a safety profile in adolescents that was consistent with previous observations in adults [18]. Previous analyses of tralokinumab phase 2 and 3 clinical trials in adults with moderate-to-severe AD revealed no clinically significant changes in clinical laboratory parameters [19, 20].

Clinical laboratory parameters in tralokinumab-treated adolescents have not yet been comprehensively reported. Here, we examined clinical laboratory parameters in adolescents with moderate-to-severe AD who were treated with tralokinumab for up to 1 year in the ECZTRA 6 phase 3 trial.

METHODS

Study Design and Patient Population

This analysis examined clinical laboratory parameters from adolescents in the ECZTRA 6 (NCT03526861) phase 3 trial who were initiated on tralokinumab (150 mg or 300 mg) or placebo. Additionally, pooled data from tralokinumab-treated patients who continued treatment beyond Week 16 were analyzed regardless of Week 16 response or tralokinumab dosing regimen [i.e., blinded 150 mg or 300 mg every 2 (Q2W) or 4 weeks (Q4W) or open-label tralokinumab 300 mg plus optional topical corticosteroids (TCS) or calcineurin inhibitors (TCI)].

The trial design and eligibility criteria have been previously described [18]. Briefly, ECZTRA 6 was a multinational, double-blinded, randomized, placebo-controlled, 52-week phase 3 trial of tralokinumab monotherapy in adolescents (aged 12–17 years old) with moderate-to-severe AD. In the initial treatment period, patients were randomized 1:1:1 to receive either subcutaneous tralokinumab, 150 or 300 mg (after an initial loading dose on Day 0, which was twice the dosage of their respective tralokinumab group) or placebo every other week (Q2W) for 16 weeks. Tralokinumab-treated patients who achieved the pre-specified primary endpoints, an Investigator's Global Assessment (IGA) score of clear (0) or almost clear (1) skin or ≥ 75% improvement from baseline in the Eczema Area and Severity Index (EASI-75) at Week 16 without any rescue use (including TCS, TCI, or systemic AD treatment), were re-randomized 1:1 to blinded maintenance treatment of either tralokinumab Q2W or every 4 weeks (Q4W) at their initially assigned dosage (150 or 300 mg) until Week 52. Patients initially assigned to the placebo group who achieved the primary endpoints continued to receive placebo Q2W until Week 52 to maintain blinding of the study. Patients who did not achieve IGA 0/1 or EASI-75 at Week 16 were transferred to open-label treatment (tralokinumab 300 mg Q2W plus optional weak to moderate potency TCS or TCI) after Week 16. During the 36-week maintenance treatment period, patients were transferred to open-label treatment if they exhibited a decline in response defined by pre-defined transfer criteria (Figure S1) [18].

The trial protocol was approved by all relevant ethics committees and institutional review boards [18]. The trial was conducted according to the principles of the Declaration of Helsinki and the International Council on Harmonization Guidelines for Good Clinical Practice and

conformed with all relevant country-specific laws and regulations. All patients, or their legal representatives, provided written informed consent.

Clinical Laboratory Measurements and Statistical Analyses

Blood samples for hematology and serum biochemistry laboratory testing were collected at Weeks 0, 8, 16, 28, and 52 and analyzed by a central laboratory utilizing validated assays. Categories of clinical laboratory parameters reported here include red blood cells, platelets, white blood cells, electrolytes, total immunoglobulin E (IgE), lipids, and liver and renal function (Table S1). All laboratory results outside the reference range were evaluated by the investigator and determined to be either "clinically significant" or "not clinically significant," with "clinically significant" abnormal tests repeated for confirmation. Any laboratory abnormality considered clinically significant by the investigator was reported as an adverse event (AE).

Clinical laboratory parameters were descriptively summarized at baseline, Week 16, and Week 52. Additionally, for eosinophils and IgE, comparisons between the tralokinumab and placebo groups were analyzed using the non-parametric Dwass-Steel-Critchlow-Fligner method, which accounts for multiplicity. Within-group comparisons across time points were analyzed using non-parametric pairwise Wilcoxon tests for difference in location, without adjustment for multiplicity.

For eosinophils, the proportions of patients with grades 1, 2, or 3 levels (worst observation used per patient) were reported. Grades were defined per the Nordic MPN Study group recommendation, in which grade 1 is mild (≥ 0.5 to $\leq 1.5 \times 10^9$/L), grade 2 is moderate (>1.5 to $\leq 5.0 \times 10^9$/L), and grade 3 is severe ($>5.0 \times 10^9$/L) [21]. For neutrophils and platelets, the proportions of patients with grades 1, 2, 3, or 4 levels (worst observation used per patient) were reported. Grades were defined per Common Terminology Criteria for Adverse Events (CTCAE) version 5.0, in which grade 1 is mild, grade 2 is moderate, grade 3 is severe or medically significant but not immediately life-threatening, and grade 4 is potentially life-threatening [22].

RESULTS

Patient Disposition and Baseline Characteristics

Overall, 289 patients were included in the analysis. Baseline demographics and clinical characteristics were comparable between the tralokinumab (150 and 300 mg) and placebo groups (Table 1). The percentages of patients who had moderate (IGA 3) or severe disease (IGA 4) at baseline were 53.3% (154/289) and 46.7% (135/289), respectively. Likewise, the mean EASI (tralokinumab 150 mg, 32.1 [SD, 12.9]; tralokinumab 300 mg, 31.8 [13.9]; placebo, 31.2 [14.5]) and mean SCORAD (tralokinumab 150 mg, 67.7 [14.4]; tralokinumab 300 mg, 68.3 [13.7]; placebo, 67.4 [14.9]) were indicative of severe AD (EASI, 21–50; SCORAD, >50). Mean Adolescent Worst Pruritus Numeric Rating Scale (NRS) was 7.5 (SD, 1.6), 7.8 (1.5), and 7.5 (1.7), respectively, and at least half of patients reported a current or history of asthma, food allergy, or hay fever. More than 80% of patients had elevated IgE levels (≥158.0 IU/mL) at baseline (150 mg, 87.0%; 300 mg, 87.0%; placebo, 88.2%; Table 1).

Clinical Laboratory Parameters

Median levels of most hematologic and biochemical clinical laboratory parameters were within respective reference ranges at baseline (Table S2), Week 16 (Table S3), and Week 52 (Table S3), with comparable values across the tralokinumab and placebo groups at baseline (Table S2) and Week 16 (Table S3).

Eosinophils

Median levels of eosinophils across tralokinumab and placebo groups were greater than the upper limit (M, 0.30×10^9/L; F, 0.20×10^9/L) of the reference range (Table S1) at both baseline

Table 1 Baseline demographics and clinical characteristics for adolescents with moderate-to-severe AD in the ECZTRA 6 trial

	Placebo (*N* = 94)	**Tralokinumab 150 mg (*N* = 98)**	**Tralokinumab 300 mg (*N* = 97)**
Age (years), mean (SD)	14.3 (1.6)	14.8 (1.7)	14.6 (1.7)
Age group, *n* (%)			
12–14	49 (52.1)	37 (37.8)	45 (46.4)
15–17	45 (47.9)	61 (62.2)	52 (53.6)
Sex, *n* (%)			
Female	43 (45.7)	47 (48.0)	50 (51.5)
Male	51 (54.3)	51 (52.0)	47 (48.5)
Race, *n* (%)			
White	53 (56.4)	55 (56.1)	56 (57.7)
Black or African American	11 (11.7)	7 (7.1)	14 (14.4)
Asian	23 (24.5)	28 (28.6)	20 (20.6)
American Indian or Alaska Native	1 (1.1)	2 (2.0)	0 (0)
Native Hawaiian or Other Pacific Islander	2 (2.1)	0 (0)	2 (2.1)
Other	4 (4.3)	6 (6.1)	5 (5.2)
Body mass index (kg/m^2), mean (SD)	23.3 (6.1)	22.3 (4.7)	23.0 (4.9)
Duration of AD (years), mean (SD)	12.1 (3.5)	12.7 (3.7)	12.1 (3.7)
BSA involvement with AD (%), mean (SD)	51.4 (23.9)	52.4 (22.6)	49.6 (23.3)
IGA, *n* (%)			
IGA 3 (moderate)	51 (54.3)	54 (55.1)	49 (50.5)
IGA 4 (severe)	43 (45.7)	44 (44.9)	48 (49.5)
EASI, mean (SD)	31.2 (14.5)	32.1 (12.9)	31.8 (13.9)
SCORAD, mean (SD)	67.4 (14.9)	67.7 (14.4)	68.3 (13.7)
CDLQI, mean (SD)	13.3 (6.0), *N* = 89	12.9 (6.3), *N* = 95	13.4 (7.3), *N* = 94
Adolescent worst pruritus NRS[a], mean (SD)	7.5 (1.7), *N* = 92	7.5 (1.6), *N* = 96	7.8 (1.5), *N* = 96
Current/past atopic comorbidities, *n* (%)			
Asthma	49 (52.1)	49 (50.0)	49 (50.5)
Food allergy	52 (56.5), *N* = 92	64 (67.4), *N* = 95	49 (51.6), *N* = 95

Table 1 continued

	Placebo ($N=94$)	Tralokinumab 150 mg ($N=98$)	Tralokinumab 300 mg ($N=97$)
Hay fever	69 (73.4)	71 (73.2), $N=97$	57 (59.4), $N=96$
IgE, *n* (%)			
≥ 158.0 IU/mL	82 (88.2), $N=93$	80 (87.0), $N=92$	80 (87.0), $N=92$

[a]Patients assessed their worst itch over the past 24 h each day using an 11-point NRS ("0", no itch; "10", worst itch possible), and the weekly average was calculated. Individual row *N* values are shown when different from the respective total number of patients in the group

AD atopic dermatitis, *BSA* body surface area, *CDLQI* Children's Dermatology Life Quality Index, *EASI* Eczema Area and Severity Index, *IGA* Investigator's Global Assessment, *IgE* immunoglobulin E, *IU/mL* international units per milliliter, *NRS* numeric rating scale, *N* total number of patients per group, *n* number of patients meeting indicated metric, *SCORAD* SCORing Atopic Dermatitis, *SD* standard deviation

(150 mg, 0.40×10^9/L; 300 mg, 0.48×10^9/L; placebo, 0.44×10^9/L; Table S2) and Week 16 (150 mg, 0.51×10^9/L; 300 mg, 0.62×10^9/L; placebo, 0.43×10^9/L; Table S3). No significant differences were observed between tralokinumab and placebo groups at either baseline (150 mg or 300 mg vs. placebo, $Ps=0.75$) or Week 16 (150 mg vs. placebo, $P=0.38$; 300 mg vs. placebo, $P=0.09$). Similarly, there were no significant differences between tralokinumab doses at either timepoint (baseline: 150 mg vs. 300 mg, $P=0.33$; Week 16: 150 mg vs. 300 mg, $P=0.77$). Median eosinophil levels numerically increased from baseline to Week 16 across tralokinumab treatment groups (median change: 150 mg, $+0.10\times10^9$/L; 300 mg, $+0.05\times10^9$/L) but not in the placebo group (-0.01×10^9/L). No significant differences between baseline and Week 16 were observed for either the tralokinumab (150 mg, $P=0.09$; 300 mg, $P=0.21$) or placebo group ($P=0.79$). Few patients shifted from normal baseline eosinophil levels ($\leq0.5\times10^9$/L) to moderately elevated levels (i.e., eosinophilia) by Week 16 (150 mg, 3.4%; 300 mg, 2.0%; placebo, 0.0%). In tralokinumab-treated patients who continued treatment beyond Week 16, median eosinophil levels at Week 52 (0.48×10^9/L) were not significantly different from baseline ($P=0.70$; Table S3), though they remained above the upper limit of the reference range. The percentages of tralokinumab-treated patients who exhibited mild (42.2%), moderate (14.6%), or severe (1.1%) eosinophilia were similar in the post-Week 16 period to the percentages observed during the initial treatment period (Table 2). No AEs of "eosinophilia" or "eosinophil count increased" were reported during the trial.

IgE

Median levels of total IgE across tralokinumab and placebo groups were markedly greater than the upper limit (≤ 158.0 IU/mL) of the reference range at baseline (150 mg, 2467 IU/mL; 300 mg, 1768 IU/mL; placebo, 1846 IU/mL; Table S2) and Week 16 (150 mg, 1550 IU/mL; 300 mg, 1472 IU/mL; placebo, 2121 IU/mL; Table S3). No significant differences were observed between tralokinumab and placebo groups at either baseline (150 mg vs. placebo, $P=0.82$; 300 mg vs. placebo, $P=0.90$) or Week 16 (150 mg vs. placebo, $P=0.63$; 300 mg vs. placebo, $P=0.45$). Similarly, there were no significant differences between tralokinumab doses at either timepoint (baseline: 150 mg vs. 300 mg, $P=0.44$; Week 16: 150 mg vs. 300 mg, $P=0.97$). IgE levels numerically decreased from baseline to Week 16 in both tralokinumab groups (median change: 150 mg, –186 IU/mL; 300 mg, –105 IU/mL) but increased in the placebo group (median change: + 41 IU/mL). No significant differences between baseline and Week 16 median IgE levels

Table 2 Percentages of adolescents with moderate-to-severe AD with CTCAE grades 1–4 for neutropenia or thrombocytopenia and Nordic MPN Study Group grades 1–3 for eosinophilia

	Initial treatment period (Weeks 0–16)			Maintenance and open-label treatment period (Weeks 16–52)
	Placebo Q2W ($N=94$)	Tralokinumab 150 mg Q2W ($N=98$)	Tralokinumab 300 mg Q2W ($N=97$)	Pooled tralokinumab-treated ($N=185$)[a]
Platelets (10^9/L), *n*/*N*2 (%)				
Grade 1 (mild): < LLN to 75×10^9/L	1/91 (1.1)	2/91 (2.2)	0/95 (0.0)	3/185 (1.6)
Grade 2 (moderate): < 75 to 50×10^9/L	0/91 (0.0)	0/91 (0.0)	0/95 (0.0)	0/185 (0.0)
Grade 3 (severe): < 50 to 25×10^9/L	0/91 (0.0)	0/91 (0.0)	0/95 (0.0)	0/185 (0.0)
Grade 4 (potentially life-threatening): < 25×10^9/L	0/91 (0.0)	0/91 (0.0)	0/95 (0.0)	0/185 (0.0)
Neutrophils, segmented (10^9/L), *n*/*N*2 (%)				
Grade 1 (mild): < LLN to 1.5×10^9/L	1/91 (1.1)	0/93 (0.0)	1/95 (1.1)	3/185 (1.6)
Grade 2 (moderate): < 1.5 to 1.0×10^9/L	1/91 (1.1)	1/93 (1.1)	2/95 (2.1)	5/185 (2.7)
Grade 3 (severe): < 1.0 to 0.5×10^9/L	0/91 (0.0)	0/93 (0.0)	0/95 (0.0)	0/185 (0.0)
Grade 4 (potentially life-threatening): < 0.5×10^9/L	0/91 (0.0)	0/93 (0.0)	1/95 (1.1)	0/185 (0.0)
Eosinophils (10^9/L), *n*/*N*2 (%)				
Grade 1 (mild): 0.5 to 1.5×10^9/L	40/91 (44.0)	42/93 (45.2)	50/95 (52.6)	78/185 (42.2)
Grade 2 (moderate): > 1.5 to 5.0×10^9/L	4/91 (4.4)	12/93 (12.9)	11/95 (11.6)	27/185 (14.6)
Grade 3 (severe): > 5.0×10^9/L	0/91 (0.0)	2/93 (2.2)	1/95 (1.1)	2/185 (1.1)

[a]Patients initially treated with tralokinumab (150 mg or 300 mg) who continued treatment beyond Week 16 regardless of Week 16 response or tralokinumab dosing regimen (i.e., blinded 150 mg or 300 mg Q2W or Q4W or open-label tralokinumab 300 mg plus optional TCS or TCI). Worst observation per patient in count and percent

LLN lower limit of normal, *N* total number of patients per group, *n/N2* number of patients with grade/number of patients with available data, *Q2W* every 2 weeks, *Q4W* every 4 weeks, *TCI* topical calcineurin inhibitors, *TCS* topical corticosteroids

were observed for either tralokinumab (150 mg, $P=0.28$; 300 mg, $P=0.65$) or placebo groups ($P=0.83$). In tralokinumab-treated patients who continued treatment beyond Week 16, median IgE levels at Week 52 (1183 IU/mL) were significantly lower than at baseline ($P<0.01$; Table S3), though they remained above the upper limit of the reference range.

Other

The percentages of patients who exhibited lowered neutrophil levels (i.e., neutropenia) were similar across treatment groups during the initial treatment period, as one to two patients in each treatment group showed grade 1 or 2 neutropenia (Table 2). Grade 4 neutropenia was observed and reported as an AE for a single patient (tralokinumab 300 mg) (Table 2). The AE was moderate in severity, resolved without changes to the treatment regimen, and assessed as not related to tralokinumab. Among patients initiated on tralokinumab who continued treatment beyond Week 16, three patients (1.6%) showed grade 1 neutropenia, and five (2.7%) exhibited grade 2 neutropenia (Table 2). The percentages of patients who exhibited elevated levels of neutrophils (i.e., neutrophilia) were similar across treatment groups during the initial treatment period (150 mg, 3.2%; 300 mg, 5.3%; placebo, 5.5%), with no notable increases in events among patients initiated on tralokinumab who continued treatment beyond Week 16. No AEs for "neutrophilia" were reported during the trial.

The percentages of patients who exhibited lowered platelet levels (i.e., thrombocytopenia) were similar across treatment groups during the initial treatment period, as one to two patients in the tralokinumab (150 mg only) and placebo groups showed grades 1 or 2 thrombocytopenia (Table 2). No patients in the tralokinumab or placebo groups exhibited grade 2, 3, or 4 thrombocytopenia in the initial treatment period (Table 2). Of the tralokinumab-treated patients who continued treatment beyond Week 16, three (1.6%) exhibited grade 1 thrombocytopenia, and no patients exhibited grades 2, 3, or 4 thrombocytopenia (Table 2). Greater percentages of patients exhibited thrombocytosis during the initial treatment period in the placebo group (16.5%) than in the tralokinumab groups (150 mg, 5.5%; 300 mg, 5.3%), with no notable increases in events among patients initiated on tralokinumab who continued treatment beyond Week 16. No AEs for "thrombocytopenia" or "thrombocytosis" were reported during the trial.

DISCUSSION

Data from this analysis of adolescents with moderate-to-severe AD in the ECZTRA 6 clinical trial revealed no clinically relevant changes in the hematologic and biochemical clinical laboratory parameters through Week 52 of tralokinumab treatment. Tralokinumab monotherapy has been shown to be efficacious in adolescents with moderate-to-severe AD [18], and these data expand tralokinumab's previously reported favorable safety and tolerability profile [18]. Additionally, these data corroborate previous clinical laboratory parameters from the adult tralokinumab clinical trials [19, 20], which supported the use of tralokinumab without routine laboratory monitoring.

Elevated levels for eosinophils and/or IgE have commonly been observed in both adults and adolescents with moderate-to-severe AD [19, 23–25], and previous work has revealed a significant association between higher levels of eosinophils and/or IgE and AD disease severity [26]. In this study, tralokinumab-treated patients showed mild increases in median eosinophil levels by Week 16, which returned to near baseline values by Week 52. This transient increase in eosinophil levels has been observed in adults in the tralokinumab clinical trials [19] and in adults and adolescents in the dupilumab clinical trials [25, 27, 28]. A potential explanation is that inhibition of the IL-13 pathway reduces eotaxin expression in the skin, resulting in the temporary accumulation of eosinophils in the peripheral blood before proinflammatory signals in the bone marrow subside.

Reductions in IgE levels from baseline to Week 16 have been observed in adults treated with tralokinumab [29] and in adult and pediatric populations treated with dupilumab

[24, 30, 31]. In this study, median IgE levels decreased from baseline to Week 16 in the tralokinumab groups, but not in the placebo group, and median IgE levels in tralokinumab-treated patients at Week 52 were lower those observed at baseline. Importantly, no clinical consequences appeared to be directly related to the elevated eosinophil or IgE levels observed throughout the trial.

Eosinophils and/or IgE elevations are especially common in patients with moderate-to-severe AD who have a current or past history of asthma and/or hay fever [32]. Likewise, in our patient population, we observed elevated median eosinophil and IgE levels across treatment groups and noted that more than half of patients reported a current or past history of asthma, food allergy, or hay fever at baseline. As IgE plays a central role in allergen-induced inflammatory processes, tralokinumab-mediated reduction of IgE may improve both AD and allergy-related signs and symptoms in patients with AD and atopic comorbidities. Previous work has shown that tralokinumab treatment improved AD severity at Week 16 in adults and adolescents regardless of the presence or number of self-reported (current or past) atopy history at baseline [33].

Potential limitations of this analysis include the pooling of patients after re-randomization to distinct dosing regimens at Week 16, the use of segmented neutrophil count rather than absolute neutrophil count for CTCAE severity grading, and that specific IgE was not analyzed. A strength of the current article was the long-term (up to Week 52) data collection as most previous laboratory data analyses for AD biologics in pediatric populations have only examined up to Week 16 [25, 34].

CONCLUSIONS

Tralokinumab treatment for up to 1 year does not have any clinically relevant impact on laboratory parameters in adolescents with moderate-to-severe AD, supporting its use without required laboratory monitoring. Importantly, the transient increase in eosinophil levels from baseline to Week 16 across tralokinumab treatment groups, which showed no clinical consequences, returned to baseline levels by Week 52.

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Data Availability. The data supporting the findings of this publication are available to qualified external researchers on reasonable request to LEO Pharma. These requests are reviewed on a case-by-case basis based on scientific merit.

Declarations

Conflict of interest. Amy S. Paller has served as an investigator for AbbVie, Biomendics, Dermavant, Eli Lilly, Incyte, Johnson & Johnson Innovative Medicine, Regeneron, and UCB; serves as a consultant for Abeona, Arcutis, BioCryst, Boehringer-Ingelheim, Castle Creek, Chiesi, Dermavant, Johnson & Johnson Innovative Medicine, Krystal, LEO Pharma, Lilly, L'Oreal, MoonLake Immunotherapeutics, Peltheos, Quoin, Regeneron, and Sanofi; and on the data safety monitoring board for for AbbVie, Abeona, Biocryst, Daiichi Sankyo, and Galderma. Michael J. Cork has served as a clinical trial investigator for Astellas, Galapagos, Johnson & Johnson, LEO Pharma, La Roche-Posay, MSD, Novartis, Perrigo, Regeneron, Sanofi Genzyme, and Stiefel; has served as an advisory board member, consultant, and/or invited lecturer for Pfizer Inc., Amgen, Astellas, Bayer, Johnson & Johnson, LEO Pharma, L'Oréal, MSD, Novartis, Regeneron, Sanofi Genzyme, Stiefel, and Unilever; has received honoraria from Astellas, Johnson & Johnson, LEO Pharma, Novartis, Regeneron, Sanofi Genzyme, and Stiefel; and has received research funding from Bayer. Norito Katoh has received honoraria as a speaker/consultant for Sanofi, Maruho, Abbvie, Ely-Lilly Japan, Taiho Pharmaceutical, Torii Pharmaceutical, and LEO Pharma, and has received grants as an investigator from Maruho, Ely-Lilly Japan, Sun Pharma, Taiho Pharmaceutical, Torii Pharmaceutical, Boehringer Ingelheim Japan, Kyowa Kirin, Jansen Pharma, Boehringer Ingelheim Japan, Abbvie, and LEO Pharma. H. Chih-ho Hong is a researcher, consultant, and/or advisor for AbbVie, Amgen, Arcutis, Aslan, Bausch Health, Boehringer Ingelheim, Bristol Meyers Squibb, Celgene, Dermavant, Dermira, DS Biopharma, Eli Lilly, Evelo, Galderma, GlaxoSmithKline, Incyte, JAMP Pharma, Janssen, LEO Pharma, MedImmune, Novartis, Organon, Oruka, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sun Pharma, Takeda, and UCB. Weily Soong reports grants from LEO Pharma during the conduct of the study; personal fees from LEO Pharma, Regeneron, Sanofi, Genentech, Lilly, AbbVie, Pfizer, Amgen, and AstraZeneca; grants from Regeneron, Genentech, Lilly, Glenmark, Allakos, AbbVie, Pfizer, Incyte, Aslan, and Amgen; serving on the advisory boards of and receiving research grants from Incyte, Lilly, Genentech, Novartis, and UCB; serving on the advisory boards, receiving research grants, and serving as a speaker for AbbVie, LEO Pharma, Amgen, AstraZeneca, Pfizer, Regeneron, and Sanofi; and receiving research grants from Allakos, Dermavant, and Galderma. Shannon K. R. Schneider and Hannah Lo are employees of LEO Pharma Inc. Frank Vinther is an employee of LEO Pharma A/S. Patrick Thøgersen was an employee of LEO Pharma A/S. Andreas Wollenberg has received grants, personal fees, or nonfinancial support from AbbVie, Almirall, AMGEN, Beiersdorf, Bioderma, BMS, Chugai, Galapagos, Galderma, GSK, Hans Karrer, Janssen, LEO Pharma, Lilly, L'Oreal, Maruho, MedImmune, Merck, MSD, Novartis, Pfizer, Pierre Fabre, Regeneron, Sandoz, Santen, Sanofi-Aventis, and UCB.

Ethical Approval. The trial protocol was approved by all relevant ethics committees and institutional review boards [18]. The trial was conducted according to the principles of the Declaration of Helsinki and the International Council on Harmonization Guidelines for Good Clinical Practice and conformed with all relevant country-specific laws and regulations. All patients, or their legal representatives, provided written informed consent.

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