Tralokinumab Versus Dupilumab for the Treatment of Moderate-to-Severe Atopic Dermatitis With Hand Involvement: a Matching-Adjusted Indirect Comparison

April Armstrong,[1] Leon Kircik,[2] Andrei Metelitsa,[3] Richard B Warren,[4] Adrian Rodriguez,[5] Sebastian Volc,[6] Naiem Issa,[7] Raj Chovatiya,[8] Rie von Eyben,[9] Teodora Festini,[9] Pierre Johansen,[9] Benjamin Ehst[10]

[1]Department of Dermatology, University of California Los Angeles, Los Angeles, CA, USA; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; Indiana University School of Medicine, Indianapolis, IN, USA; [3]Division of Dermatology, University of Calgary, Calgary, AB, Canada; Beacon Dermatology, Calgary, AB, Canada; [4]Dermatology Centre, Northern Care Alliance NHS Foundation Trust & Division of Musculoskeletal and Dermatological Sciences, Manchester NIHR Biomedical Research Centre, Manchester Academic Health Science Centre, University of Manchester, UK; [5]Nashville Skin Comprehensive Dermatology Center, Nashville, TN, USA; [6]Department of Dermatology, Eberhard Karls University Tuebingen, Germany; [7]Forefront Dermatology, Vienna, VA, USA; University of Miami School of Medicine, FL, USA; George Washington University School of Medicine and Health Sciences, Washington, DC, USA; [8]Rosalind Franklin University of Medicine and Science Chicago Medical School, Chicago, IL, USA; Center for Medical Dermatology + Immunology Research, North Chicago, IL, USA; [9]LEO Pharma A/S, Ballerup, Denmark; [10]Oregon Medical Research Center, Portland, OR, USA

Conclusions

- Treatment with tralokinumab resulted in significantly more patients achieving HECSI-90 versus dupilumab at 16 weeks, indicating a deeper response.
- Patients treated with tralokinumab also had a significantly greater improvement in the ability to perform regular daily activities (not including work) compared with dupilumab.
- Other endpoints (HECSI-75, HECSI percent reduction, reduction in itch, ≥4-point improvement in itch, and reduction in pain) were numerically in favor of tralokinumab.

Objective

- To compare the efficacy of tralokinumab and dupilumab in patients with moderate-to-severe atopic dermatitis (AD) with hand involvement in an anchored matching-adjusted indirect comparison (MAIC).

Background

- Tralokinumab is a high-affinity interleukin (IL)-13 inhibitor while dupilumab targets the IL-4/IL-13 pathway via inhibition of the IL-4 receptor α.[1] Both are approved for the treatment of moderate-to-severe AD, including on the hands where AD often presents an additional burden and treatment challenges.[2]
- As no head-to-head studies have been conducted, the 16-week efficacy of tralokinumab and dupilumab were compared in patients with AD with hand involvement in an anchored MAIC based on two phase 3 trials, ADHAND[3] and LIBERTY-AD-HAFT.[4]

Methods

- ADHAND (NCT05958407) was a phase 3 trial in which adults with moderate-to-severe AD with hand involvement were randomized 2:1 to double-blind treatment with tralokinumab 300 mg or placebo every 2 weeks for 16 weeks (Figure 1A).
- LIBERTY-AD-HAFT (NCT04417894) was a phase 3 trial in which adults and adolescents (aged ≥12 to <17 years) with moderate-to-severe AD with hand and/or foot involvement were randomized to 300 mg (200 mg in adolescents with body weight <60 kg) or placebo every 2 weeks for 16 weeks (Figure 1B).
- An anchored MAIC was conducted using individual patient data from the ADHAND trial and aggregate published data from the LIBERTY-AD-HAFT trial with placebo as the common anchor. Individual patient data from ADHAND were weighted to match age, sex, race, and baseline Hand Eczema Severity Index (HECSI) score in LIBERTY-AD-HAFT.
- Endpoints compared at Week 16 were the proportions of patients with Investigator's Global Assessment (IGA) scores of 0/1 (IGA-Atopic Hand Eczema [AHE] in ADHAND and Hand and Foot [HF]-IGA in LIBERTY-AD-HAFT), HECSI-75 and HECSI-90, percentage reduction in HECSI, and ability to perform regular daily activities other than work using the Percent Routine Activity Impairment domain of the Work Productivity and Activity Index. Reductions in itch and pain (assessed with 11-point numerical rating scales) were also compared, as were the proportions of patients with ≥4-point improvement in itch.
- For binary endpoints, missing data due to use of rescue medication, treatment discontinuation, and other reasons were assessed using non-responder imputation. For continuous endpoints, missing data due to rescue medication or treatment discontinuation because of adverse events or lack of efficacy were imputed by worst observation carried forward and data missing for other reasons were imputed using Markov chain Monte Carlo estimation.

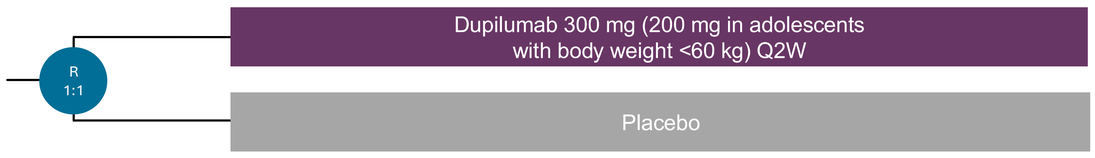
Figure 1 Trial designs

A. ADHAND: Adults with moderate-to-severe AD with hand involvement



Primary endpoint: IGA-AHE score 0/1 at Week 16	
Score 0:	No signs of erythema, scaling, hyperkeratosis/lichenification, vesiculation, edema or fissures
Score 1:	Barely perceptible erythema, rare scaling, and/or minimal lichenification. No signs of hyperkeratosis, vesiculation, edema or fissures

B. LIBERTY-AD-HAFT: Adults and adolescents with moderate-to-severe AD with hand and/or foot involvement



Primary endpoint: HF-IGA score 0/1 at Week 16	
Score 0:	No signs of erythema, scaling, hyperkeratosis/lichenification, vesiculation, edema or fissures
Score 1:	Barely perceptible erythema, scaling, lichenification and/or edema. No signs of vesiculation/erosions or fissures
Severity can be stepped down if the extent of the lesions is limited; i.e. a patient could score a 2 based on the signs present but if extent is limited then this could be stepped down to a 1	

Results

Patient characteristics

- LIBERTY-AD-HAFT included 133 patients (dupilumab, n=67, placebo, n=66) while ADHAND included 235 patients (tralokinumab, n=156; placebo, n=79). The effective sample size after matching was 99 (tralokinumab, n=76, placebo, n=23).
- In the matched active treatment arms, over two-thirds of patients were female (67.2%) and most were White (79.1%) with mean age of 36 years and mean HECSI score of 46 at baseline.

Table 1 Baseline characteristics

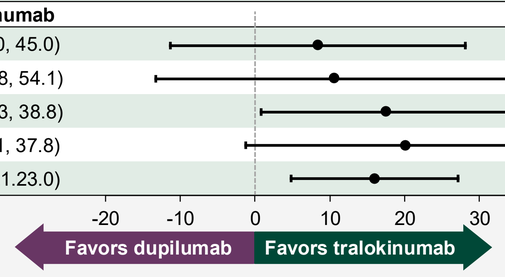
	ADHAND All patients (N=235)		ADHAND Matched (N=99)		LIBERTY-AD-HAFT (N=133)	
	Tralokinumab (N=156)	Placebo (N=79)	Tralokinumab (N=76)	Placebo (N=23)	Dupilumab (N=67)	Placebo (N=66)
Age, years, mean (SD)	39.1 (14.9)	41.5 (13.7)	35.8 (15.6)	33.4 (11.1)	35.8 (17.1)	33.4 (14.7)
Sex, female, n (%)	94 (60.3)	55 (69.6)	51 (67.2)	13 (57.6)	45 (67.2)	38 (57.6)
Race, White, n (%)	104 (66.7)	54 (68.4)	60 (79.1)	18 (80.3)	53 (79.1)	53 (80.3)
HECSI score, mean (SD)	83.9 (51.8)	77.7 (41.4)	46.2 (26.5)	47.4 (19.7)	46.2 (14.4)	47.4 (18.5)

Matching-adjusted indirect comparison

- Anchor-adjusted relative treatment differences significantly favored tralokinumab over dupilumab for the proportions of patients achieving HECSI-90 (*P*=0.040) and decrease in Percent Routine Activity Impairment (*P*=0.005).
- Relative differences for other endpoints favored tralokinumab over dupilumab but were not significantly different between treatments.

Figure 2 Relative treatment differences at 16 weeks in IGA, HECSI and activity impairment for tralokinumab versus dupilumab

Patients (%) at Week 16	Risk difference vs placebo		Tralokinumab vs dupilumab risk difference (95% CI)	*P* value
	Dupilumab	Tralokinumab		
IGA score 0/1	23.6 (8.8, 38.4)	32.0 (19.0, 45.0)	8.4 (-11.3, 28.1)	0.403
HECSI-75	25.3 (9.6, 41.1)	36.0 (17.8, 54.1)	10.7 (-13.3, 34.7)	0.383
HECSI-90	9.5 (-2.4, 21.4)	27.0 (15.3, 38.8)	17.5 (0.8, 34.2)	0.040
HECSI reduction (%)	34.9 (47.5, 22.3)	55.0 (72.1, 37.8)	20.1 (-1.2, 41.3)	0.064
Routine Activity Impairment reduction (%)	15.1 (22.8, 7.5)	31.1 (39.1.23.0)	16.0 (4.8, 27.1)	0.005

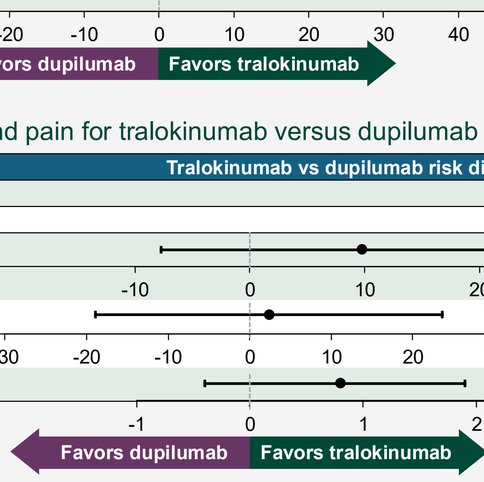


Strengths and limitations

- Both trial designs were similar with populations matched on age, sex, race, and baseline HECSI. Comparing relative treatment effects in the two studies (i.e., active treatment versus placebo) indirectly adjusted for prognostic factors that were not directly matched.
- Differences in trial populations included that, unlike ADHAND, LIBERTY-AD-HAFT included patients with foot involvement only (n=4, 3%) and adolescents (aged ≥12 to <17 years) (n=27, 20%); however, populations were matched for age in the MAIC.
- There were minor differences between trials in the scales used to assess IGA and the numeric rating scales used to assess itch and pain.

Figure 3 Relative treatment differences at 16 weeks in itch and pain for tralokinumab versus dupilumab

Patients (%) at Week 16	Risk difference vs placebo		Tralokinumab vs dupilumab risk difference (95% CI)	*P* value
	Dupilumab	Tralokinumab		
Itch percentage change	-36.7 (-48.8, -24.6)	-46.5 (-59.2, -33.8)	-9.8 (-27.4, 7.7)	0.273
Itch ≥4-point improvement	38.6 (24.1, 53.2)	41.0 (25.5, 56.4)	2.4 (-18.9, 23.6)	0.827
Pain change	-2.7 (-3.6, -1.8)	-3.5 (-4.2.-2.7)	-0.8 (-1.9, 0.4)	0.213



Itch and pain were assessed by 11-point numeric rating scales in both ADHAND and LIBERTY-AD-HAFT; In ADHAND, patients used the Hand Eczema Symptom Diary, in which 10 = severe symptoms, while in LIBERTY-AD-HAFT, patients used the Hand and Foot Peak pruritus and pain scales, in which 10 = 'worst scratching/itching or pain possible'. Risk differences are based on percentage change from baseline in weekly average of daily score for itch and absolute change from baseline in weekly average of daily score for pain, as reported for LIBERTY-AD-HAFT.[4]

Abbreviations AD, atopic dermatitis; CI, confidence interval; HECSI, Hand Eczema Severity Index; HF-IGA, Hand and Foot-Investigator's Global Assessment; IGA-AHE, Investigator's Global Assessment-Atopic Hand Eczema; IL, interleukin; N, number of patients in the analysis set; n, number of patients with observation; Q2W, every 2 weeks; SD, standard deviation.

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References **1.** Davis DMR, et al. *J Am Acad Dermatol*. 2024;90:e43-e56; **2.** Silverberg JI, et al. *J Am Acad Dermatol*. 2023;89:519-528; **3.** Ehst B, et al. Presented at the Georg RAJKA International Symposium on Atopic Dermatitis (ISAD), Melbourne, Australia, 24-26 October 2025; **4.** Simpson EL, et al. *J Am Acad Dermatol*. 2024;90:1190-1199.

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