

Tralokinumab Treatment In Patients With Atopic Dermatitis and Moderate-to-Severe Hand Involvement: Results From the 32-week Phase 3b ADHAND Trial

Benjamin Ehst,¹ Richard B Warren,² H. Chih-ho Hong,³ Dong Hun Lee,⁴ Andrei Metelitsa,⁵ Sebastian Volc,⁶ Marie Tauber,⁷ Farzaneh Safavimanesh,⁸ Ann-Marie Tindberg,⁸ Linda Stein Gold⁹

¹Oregon Medical Research Center, Portland, OR, USA; ²Dermatology 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; ³Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada; ⁴Department of Dermatology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Republic of Korea; ⁵Division of Dermatology, Department of Medicine, University of Calgary, Calgary, Alberta, Canada; ⁶Department of Dermatology, University Hospital Tübingen, University of Tübingen, Tübingen, Germany; ⁷Department of Allergology and Immunology, Centre Hospitalier Lyon Sud, Pierre-Bénite, France; ⁸LEO Pharma A/S, Ballerup, Denmark; ⁹Henry Ford Health System, Detroit, MI, USA

Key Takeaways

- Tralokinumab monotherapy rapidly and significantly improved signs, symptoms and quality of life in patients with atopic dermatitis (AD) and moderate-to-severe hand involvement
- Response rates continued to improve through Week 32
- Tralokinumab was well tolerated with a favorable safety profile consistent with previous clinical trials
- These results support tralokinumab as a treatment option for this high-burden, difficult-to-treat population of patients with AD

Objective

To evaluate the 32-week efficacy and safety of tralokinumab compared with placebo in patients with AD and moderate-to-severe hand involvement, who were candidates for systemic therapy

Background

- AD with hand involvement imposes a significant burden on individuals, affecting quality of life, emotional well-being, and ability to work¹⁻³
- Hand involvement occurs in up to 56% of patients with AD, and reported by 58% of patients to be the most bothersome lesion location^{1,2}
- Hand involvement in AD is often difficult to treat³⁻⁴
- There is a clear, unmet need for long-term treatments with a favorable benefit-risk profile for patients with AD and hand involvement

Methods

ADHAND (NCT05958407)⁵ was a phase 3b, interventional, international, multicenter, randomized, 32-week, double-blind, placebo-controlled, parallel-group, adaptive clinical trial with a 16-week, open-label treatment period of tralokinumab monotherapy in adults with AD and moderate-to-severe hand involvement, who were candidates for systemic therapy

Study eligibility and key endpoints

Inclusion criteria^a

- Adult patients with moderate-to-severe AHE (IGA-AHE 3 or 4)
- HESD itch score (weekly average) score of ≥ 4 at baseline
- Recent (within 1 year) inadequate response to topical prescription medications
- AD involvement of ≥ 1 body location other than hands/wrists

Primary endpoint

- IGA-AHE 0 or 1 at Week 16

Key secondary endpoints

- HECSI-50/-75/-90 at Week 16
- ≥ 4 -point reductions in HESD itch and pain scores from baseline to Week 16
- Percentage changes in HECSI, HEIS, DLQI scores from baseline to Week 16

Exclusion criteria included: Active subtypes of hand eczema other than atopic hand eczema (AHE) considered to be the predominant cause of the current hand eczema, prior failure on tralokinumab (lack of efficacy or safety concern) or dupilumab (lack of efficacy), use of systemic medication within the prior 4 weeks or topical medication within the prior 1 week of trial start. ^aParticipants in the tralokinumab group received a loading dose of 600 mg on Day 1.

Results

Patients

- See the [online supplement](#) via the QR code for details of patient disposition, baseline demographics and disease characteristics and the use of rescue medication

Clinician-reported outcomes

Investigator Global Assessment – Atopic Hand Eczema (IGA-AHE)

- The **primary endpoint** was met at Week 16, with 40.0% of patients who received tralokinumab achieving IGA-AHE 0/1 compared with 10.6% of patients who received placebo (treatment difference [95% CI]: 29.7% [19.0, 40.4], $P < 0.001$; **Figure 1**; **Table 1**)
 - Response rates continued to improve through Week 32, with 57.9% (77/133) of patients continuing tralokinumab achieving IGA-AHE 0/1 (as observed)

Hand Eczema Severity Index (HECSI)

- The number of patients achieving **HECSI-50**, **HECSI-75** or **HECSI-90** was significantly greater for tralokinumab compared with placebo at Week 16 (**Table 1**)
 - 41.7% of patients who received tralokinumab achieved **HECSI-90** compared with 10.9% of patients who received placebo (treatment difference [95% CI]: 30.8% [20.0, 41.5], $P < 0.001$); **Figure 2**; **Table 1**)
- Further improvements were observed through Week 32 on all HECSI outcomes

Results (cont.)

Figure 1 Proportion of responders with IGA-AHE 0/1 (clear/almost clear skin) up to Week 32

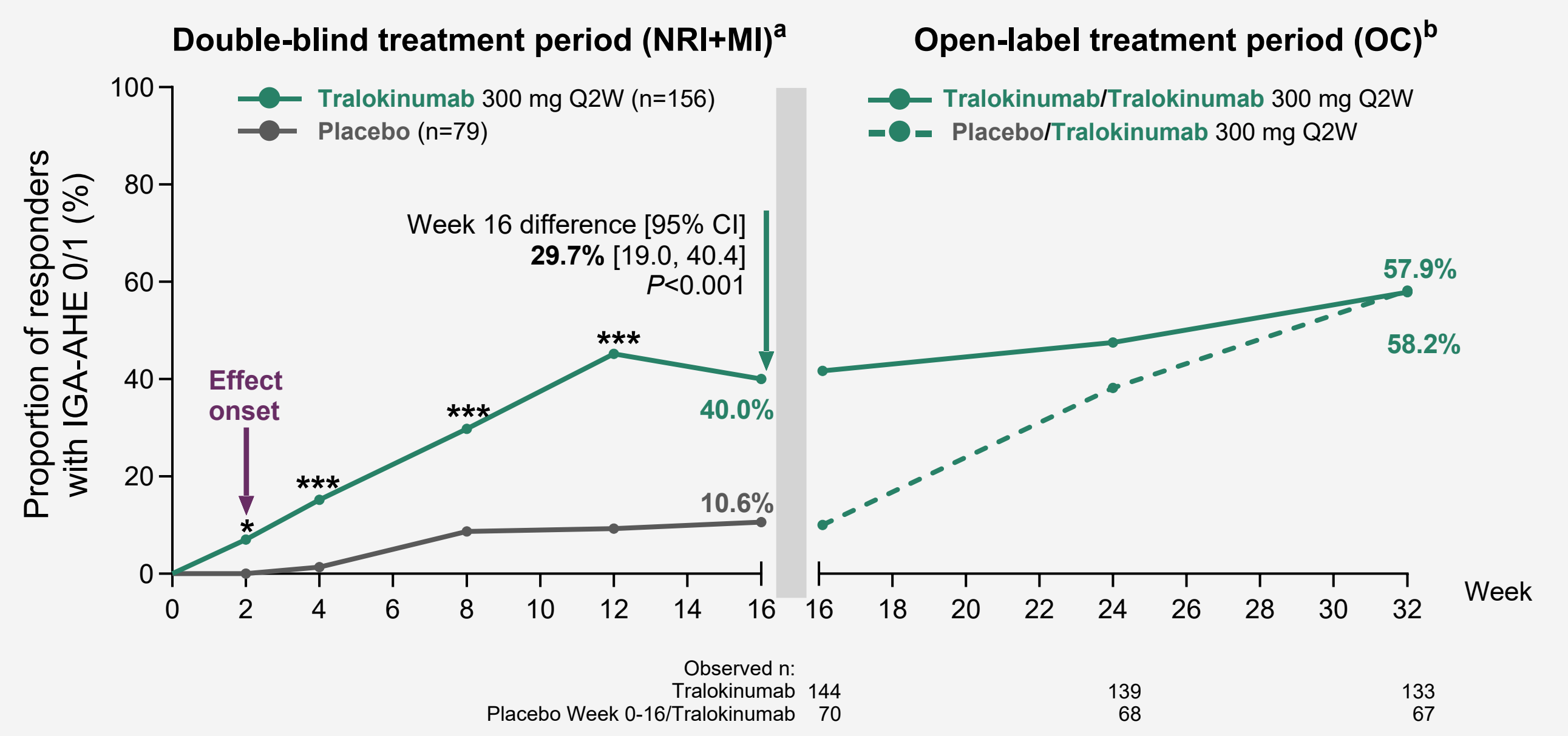
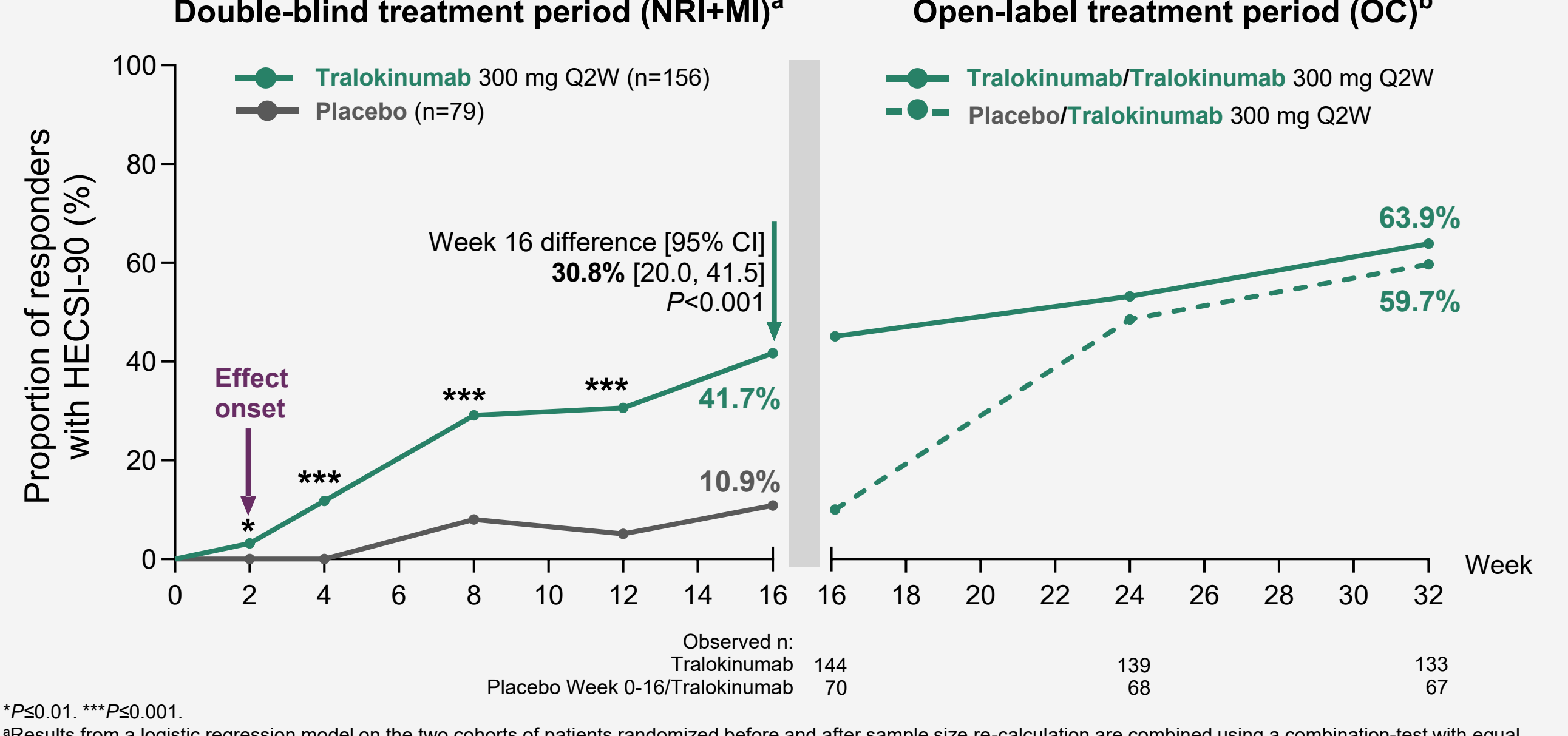


Figure 2 Proportion of responders with HECSI-90 up to Week 32



Patient-reported outcomes

Hand Eczema Symptom Diary (HESD) itch and pain

- At Week 16, significantly more patients achieved a ≥ 4 -point reduction in HESD itch and HESD pain with tralokinumab compared with placebo (**HESD itch** treatment difference: 26.6% [95% CI: 14.6, 38.7]; $P < 0.001$; **HESD pain** treatment difference: 32.0% [95% CI: 20.8, 43.1] $P < 0.001$; **Table 1**)
 - Further improvements in **HESD itch** and **pain** were observed through Week 32 (**Table 1**)
- The mean **percentage change from baseline** in HESD itch and HESD pain was greater for tralokinumab compared with placebo from Week 1 and onwards (See [online supplement](#) via the QR code)

Safety

- The proportion of patients experiencing at least one adverse event (AE) was comparable between tralokinumab (60.3%) and placebo (60.8%) (**Table 2**)
- Safety data for patients who switched from placebo to tralokinumab are available in the [online supplement](#)

Table 1 Primary and key secondary endpoints

	Double-blind period at Week 16 ^a		P value	Open-label period at Week 32 (OC) ^c	
	Tralokinumab (N=156)	Placebo (N=79)		Tralokinumab to Tralokinumab, % (N=133)	Placebo to Tralokinumab, % (N=67)
Proportion of patients, % (95% CI)					
IGA-AHE 0/1	40.0 (31.3, 49.4)	10.6 (5.0, 20.9)	<0.001	57.9	58.2
HECSI-50	79.7 (71.9, 85.8)	50.7 (38.7, 62.7)	<0.001	94.0	92.5
HECSI-75	64.1 (55.3, 72.0)	33.8 (23.4, 46.0)	<0.001	77.4	76.1
HECSI-90	41.7 (33.0, 50.9)	10.9 (5.2, 21.4)	<0.001	63.9	59.7
HESD itch ≥ 4 , [n] ^b	47.3 (38.4, 56.4) [153]	20.7 (12.6, 31.9) [78]	<0.001	59.7 [124]	66.1 [56]
HESD pain ≥ 4 , [n] ^b	45.3 (36.0, 55.0) [138]	13.3 (7.1, 23.4) [73]	<0.001	74.3 [113]	64.7 [51]
Mean change from baseline, % (95% CI)					
HECSI	-69.9 (-77.5, -62.3)	-31.4 (-42.2, -20.6)	<0.001	-86.3	-83.6
HEIS [n]	-64.9 (-71.1, -58.7) [154]	-28.5 (-37.4, -19.7) [77]	<0.001	-75.7 [130]	-76.2 [62]
DLQI [n]	-60.9 (-68.8, -53.0) [154]	-21.0 (-32.1, -9.9) [77]	<0.001	-72.9 [129]	-73.0 [62]

^aBinary endpoints were analyzed using NRI for data following discontinuation due to an AE or lack of efficacy. Data following all other reasons for discontinuation was set to missing and, together with any other missing data, was imputed from a linear model using MI. Continuous endpoints were analyzed using last observation carried forward (LOCF) for data following discontinuation due to an AE or lack of efficacy and data after receipt of rescue medication. Data following all other reasons for discontinuation was set to missing and, together with any other missing data, was imputed from a linear model using MI. ^bOnly patients with a baseline value ≥ 4 were included in the analysis. ^cData analyzed as OC.

Table 2 Safety summary

Category, n (%)	Double-blind period		Open-label period
	Tralokinumab (N=156)	Placebo (N=79)	Tralokinumab to Tralokinumab (N=144)
All AEs	94 (60.3)	48 (60.8)	63 (43.8)
Mild	72 (46.2)	28 (35.4)	42 (29.2)
Moderate	48 (30.8)	25 (31.6)	31 (21.5)
Severe	2 (1.3)	3 (3.8)	2 (1.4)
Serious AEs	3 (1.9)	1 (1.3)	2 (1.4)
AE leading to withdrawal	3 (1.9)	2 (2.5)	1 (0.7)
Most frequent AEs ($\geq 3\%$ in any group)			
Nasopharyngitis	26 (16.7)	6 (7.6)	12 (8.3)
COVID-19	8 (5.1)	0	0
Upper respiratory tract infection	6 (3.8)	4 (5.1)	4 (2.8)
Conjunctivitis	5 (3.2)	2 (2.5)	2 (1.4)
Injection site reaction	10 (6.4)	1 (1.3)	8 (5.6)
Fatigue	5 (3.2)	3 (3.8)	0
Dermatitis atopic	9 (5.8)	4 (5.1)	4 (2.8)
Hand dermatitis	2 (1.3)	7 (8.9)	4 (2.8)

Clinical images of tralokinumab-treated patients

- Clinical images showing improvement of AD in tralokinumab-treated patients are shown in **Figures 3** and **4**

Figure 3 Male patient treated with tralokinumab

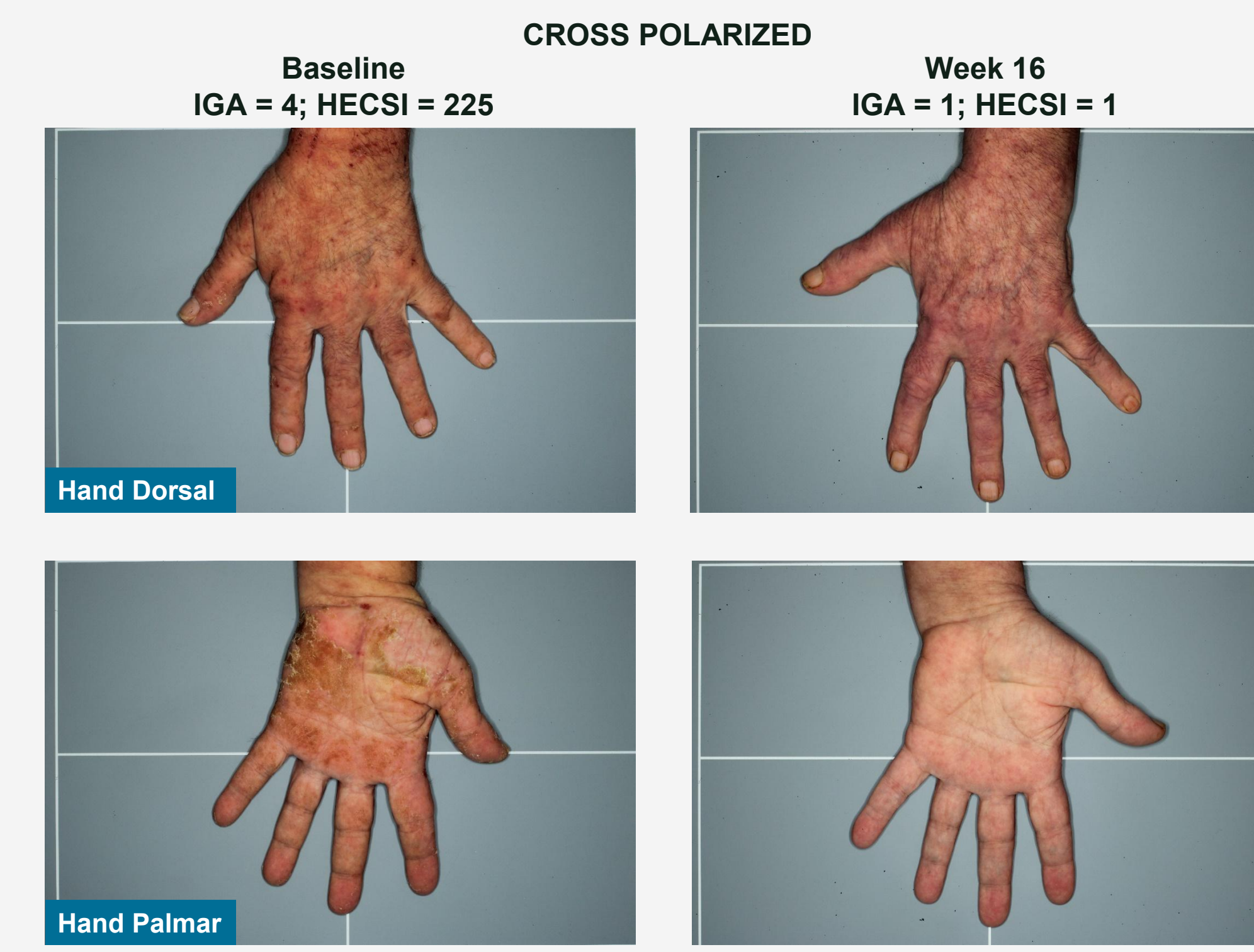


Figure 4 Female patient treated with tralokinumab

