Efficacy and Safety of Apremilast for the Treatment of Japanese Patients With Palmoplantar Pustulosis: 52-Week Results From a Phase 3, Randomized, Placebo-Controlled Study

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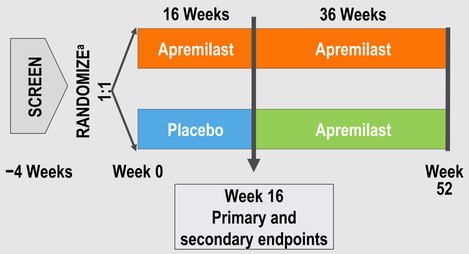
Background

- Palmoplantar pustulosis (PPP) is a difficult to treat condition in patients with chronic dermatitis with limited treatment options[1]
- Apremilast is an oral phosphodiesterase 4 inhibitor internationally approved for use in plaque psoriasis, psoriatic arthritis, and oral ulcers associated with Behçet's disease
- Apremilast has previously demonstrated significant efficacy in Japanese patients with moderate to severe PPP in a phase 2 trial[2]
- A phase 3 trial was conducted to confirm the results of the phase 2 trial
  - In this phase 3 trial, apremilast 30 mg twice daily showed superior efficacy with statistically significant differences for primary and secondary endpoints compared with placebo at Week 16[3]

Objective: Report apremilast efficacy and safety in patients with moderate to severe PPP over 52 weeks

Study Design

- Phase 3, multicenter, randomized, placebo-controlled, double-blind trial conducted in Japan (NCT05174065)
- Patients with moderate to severe PPP were treated with apremilast 30 mg twice daily or placebo for 16 weeks followed by a 36-week apremilast extension phase



[a]Randomization was stratified by rounded PPPASI total score (≤20/21–30/≥31) at baseline and baseline focal infection status (yes/no).

Key Inclusion Criteria

- ✓Adults with a PPP diagnosis with or without pustular arthro-osteitis (PAO) for no less than 24 weeks before screening
- ✓PPP Area and Severity Index (PPPASI) total score ≥12 at baseline
- ✓PPPASI pustules/vesicles severity score ≥2
- ✓Inadequate response to topicals before or at screening

Excluded treatments

- xTopical or systemic therapies that could affect PPP or the efficacy evaluation
- xSystemic therapy for PAO

For key exclusion criteria, scan the QR code

Assessment through week 52 for primary, secondary, exploratory, and safety endpoints

Efficacy

- ≥50%, 75%, or 90% reduction in PPPASI total score (**PPPASI-50, -75, or -90**), change from baseline in **PPPASI total score**, change from baseline in Palmoplantar Pustulosis Severity Index (**PPSI**) **total score**, change from baseline in patient's visual analog scale (**VAS**) assessment for PPP symptoms (**pruritus**), change from baseline in patient's **VAS** assessment for PPP symptoms (**pain/discomfort**), change from baseline in Dermatology Life Quality Index (**DLQI**)

Safety

- Treatment-emergent adverse events (TEAEs)

Baseline demographics and clinical characteristics were balanced across groups

- Of 176 patients randomized (apremilast: 88, placebo: 88), 164 (93.2%) completed Week 52 (apremilast/apremilast: 84 [95.5%], placebo/apremilast: 80 [90.9%])

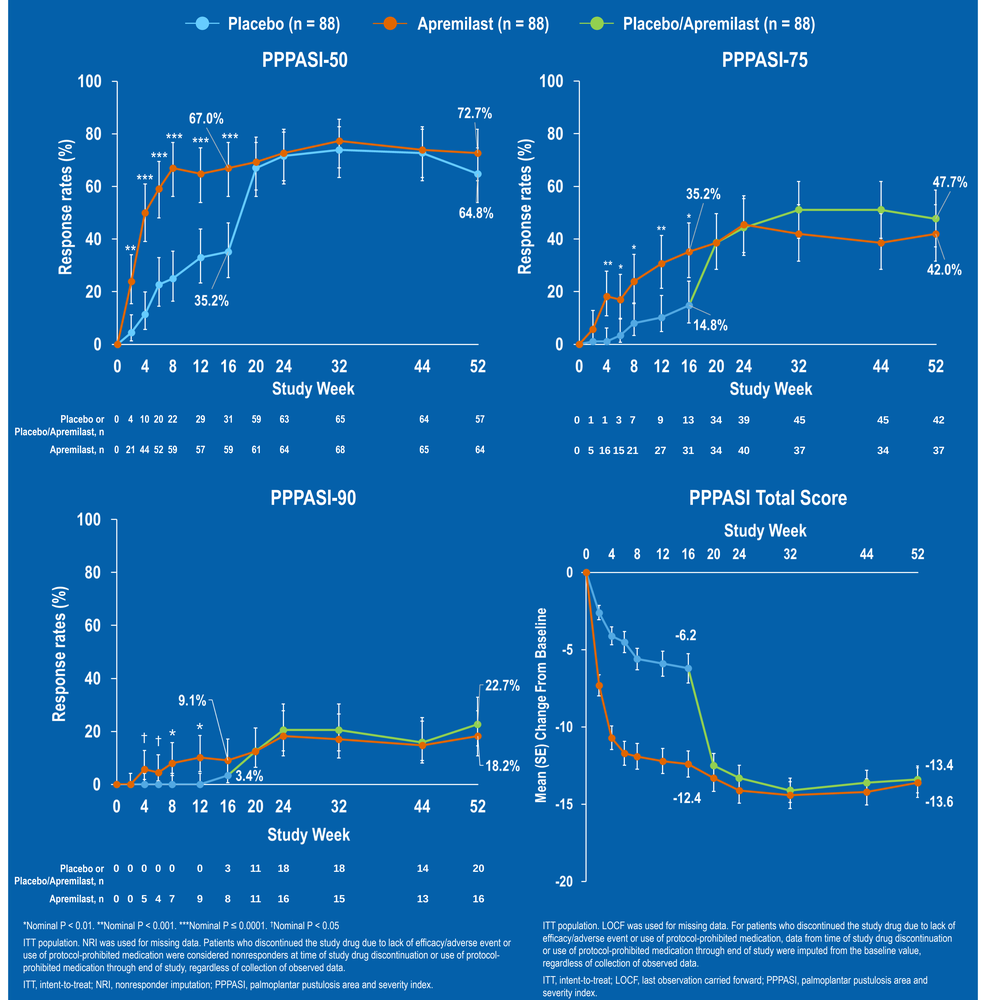
	Placebo (n = 88)	Apremilast (n = 88)	Total (N = 176)
Age, mean (SD), years	56.0 (11.4)	57.0 (11.3)	56.5 (11.3)
Female, n (%)	72 (81.8)	69 (78.4)	141 (80.1)
Duration of PPP, mean (SD), years	6.0 (7.5)	6.7 (7.6)	6.4 (7.5)
PPPASI total score (0–72), mean (SD)	22.0 (8.4)	22.1 (8.1)	22.1 (8.2)
PPSI total score (0–12), mean (SD)	8.0 (1.7)	8.1 (1.6)	8.1 (1.6)
Pruritus VAS (0–100 mm), mean (SD)	51.2 (29.6)	48.7 (29.1)	50.0 (29.3)
Pain/discomfort VAS (0–100 mm), mean (SD)	45.8 (29.9)	43.3 (29.6)	44.5 (29.7)
DLQI (0–30), mean (SD)	6.7 (4.9)	5.7 (4.6)	6.2 (4.8)
Tobacco use, n (%)			
Current	42 (47.7)	42 (47.7)	84 (47.7)
Former	24 (27.3)	28 (31.8)	52 (29.5)
Never	22 (25.0)	18 (20.5)	40 (22.7)
Presence of PAO	16 (18.2)	13 (14.8)	29 (16.5)
Presence of focal infection	57 (64.8)	59 (67.0)	116 (65.9)

ITT population.
DLQI, Dermatology Life Quality Index; ITT, intent-to-treat; PAO, pustular arthro-osteitis; PPPASI, palmoplantar pustulosis area and severity index; PPSI, palmoplantar pustulosis severity index; SD, standard deviation; VAS, visual analog scale.

Key Takeaways

- **Improvements in PPP seen with apremilast at Week 16 were maintained or further improved through Week 52 in patients continuing apremilast, including improvements in PPP severity, symptoms (pruritus and pain/discomfort), and patient-reported quality of life**
- **Improvements were also observed when patients transitioned from placebo to apremilast at Week 16 through Week 52**
- **No new safety signals were observed**

Improvements by PPPASI achieved at week 16 were maintained or further improved through week 52



*Nominal P < 0.01. **Nominal P < 0.001. ***Nominal P ≤ 0.0001. †Nominal P < 0.05

ITT population. NRI was used for missing data. Patients who discontinued the study drug due to lack of efficacy/adverse event or use of protocol-prohibited medication were considered nonresponders at time of study drug discontinuation or use of protocol-prohibited medication through end of study, regardless of collection of observed data.

ITT, intent-to-treat; NRI, nonresponder imputation; PPPASI, palmoplantar pustulosis area and severity index.

ITT population. LOCF was used for missing data. For patients who discontinued the study drug due to lack of efficacy/adverse event or use of protocol-prohibited medication, data from time of study drug discontinuation or use of protocol-prohibited medication through end of study were imputed from the baseline value, regardless of collection of observed data.

ITT, intent-to-treat; LOCF, last observation carried forward; PPPASI, palmoplantar pustulosis area and severity index.

References: **1.** Obeid G et al. *Cochrane Database Syst Rev*. 2020;20(1):CD011628. **2.** Terui T et al. *Am J Clin Dermatol*. 2023;24(5):837-847. **3.** Terui T et al. Oral presentation at the Annual Meeting of the American Academy of Dermatology; March 8-12, 2024; San Diego, CA. **4.** Mease PJ, et al. *Am J Clin Dermatol*. 2023;24:809-20.

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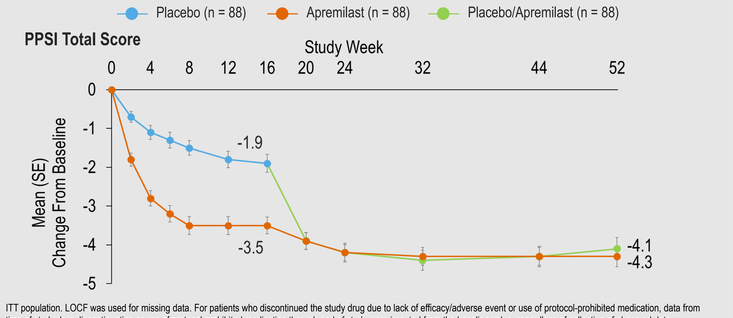
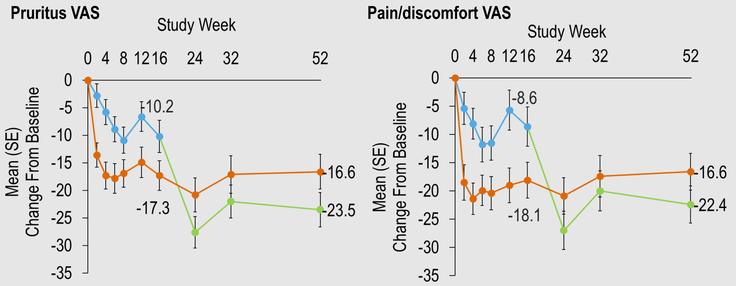
For additional eligibility criteria and author disclosures, scan the QR code

Decreases in PPSI total score were maintained from Week 16 to Week 52



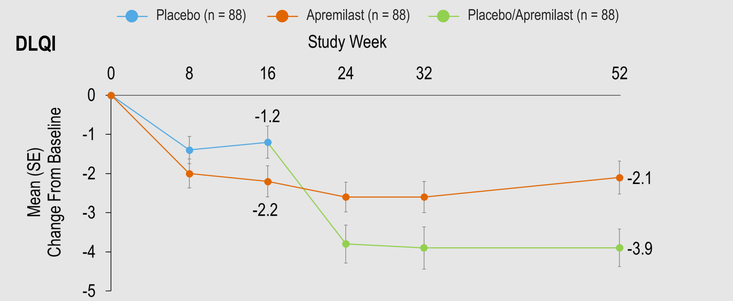
ITT population. LOCF was used for missing data. For patients who discontinued the study drug due to lack of efficacy/adverse event or use of protocol-prohibited medication, data from time of study drug discontinuation or use of protocol-prohibited medication through end of study were imputed from the baseline value, regardless of collection of observed data.
ITT, intent-to-treat; LOCF, last observation carried forward; PPPASI, palmoplantar pustulosis area and severity index.

Improvements in pruritus and pain/discomfort were observed as early as 2 weeks after initiating apremilast and maintained to week 52



ITT population. LOCF was used for missing data. For patients who discontinued the study drug due to lack of efficacy/adverse event or use of protocol-prohibited medication, data from time of study drug discontinuation or use of protocol-prohibited medication through end of study were imputed from the baseline value, regardless of collection of observed data.
ITT, intent-to-treat; LOCF, last observation carried forward; VAS, visual analog scale.

Improvements in DLQI were maintained from week 16 to week 52



ITT population. LOCF was used for missing data. For patients who discontinued the study drug due to lack of efficacy/adverse event or use of protocol-prohibited medication, data from time of study drug discontinuation or use of protocol-prohibited medication through end of study were imputed from the baseline value, regardless of collection of observed data.
DLQI, Dermatology Life Quality Index; ITT, intent-to-treat; LOCF, last observation carried forward.

Safety outcomes over 52 weeks were consistent with other apremilast clinical studies[4]

	Apremilast patients as treated N = 174, PY = 143.0	
	n (%)	EAIR/100 PY
Any TEAE	148 (85.1)	347.9
Any severe TEAE	6 (3.4)	4.3
Any serious TEAE	9 (5.2)	6.4
Any serious treatment-related TEAE	0 (0.0)	0.0
Any TEAE leading to treatment withdrawal	5 (2.9)	3.5
Any fatal TEAE	0 (0.0)	0.0
TEAEs occurring in ≥10% of patients		
Diarrhea	31 (17.8)	26.1
Nasopharyngitis	28 (16.1)	21.1
Nausea	23 (13.2)	18.3
Faeces soft	22 (12.6)	17.6
Headache	19 (10.9)	14.8
COVID-19	18 (10.3)	13.4

Includes patients who were treated with apremilast 30 mg BID from randomization and patients who were treated with placebo at randomization and switched to apremilast 30 mg BID at Week 16.
COVID, coronavirus disease; EAIR, exposure adjusted incidence rate; PY, patient-years; TEAE, treatment-emergent adverse event.

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Efficacy and Safety of Apremilast in Pediatric Patients With Moderate-to-Severe Plaque Psoriasis: 52-Week Results From the SPROUT Randomized Controlled Trial

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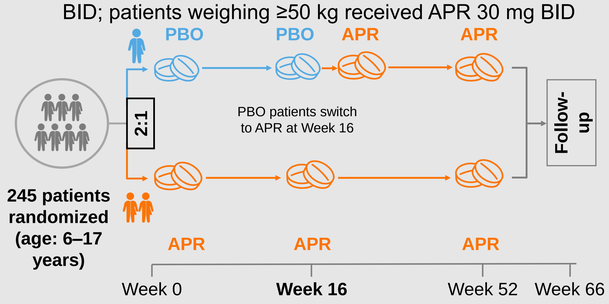
Background & Objective

- Treatment options for pediatric patients with moderate to severe plaque psoriasis are limited, with apremilast the only approved oral systemic treatment
- SPROUT evaluated the efficacy and safety of apremilast (APR) compared with placebo (PBO) in pediatric patients

Study Design & Patient Population

- **Design:** Phase 3, multicenter, randomized, double-blind, PBO-controlled, parallel-group study (NCT03701763)
  - Randomization (2:1) was stratified by age group
  - Patients weighing ≥20 to <50 kg received APR 20 mg BID; patients weighing ≥50 kg received APR 30 mg BID



- **Main Inclusion Criteria:** Age 6-17 years, with moderate to severe psoriasis (Psoriasis Area and Severity Index [PASI] ≥12, affected body surface area [BSA] ≥10%, static Physician Global Assessment [sPGA] ≥3) inadequately controlled by or intolerant to topical therapy
- **Primary Endpoint:** sPGA response (score 0 [clear] or 1 [almost clear] with a ≥2-point reduction from baseline) at Week 16
- **Major Secondary Endpoint:** ≥75% reduction from baseline in PASI score (PASI-75)
- **Exploratory Endpoint:** APR pharmacokinetics
- *Scan the QR code for patient disposition*

Baseline Characteristics

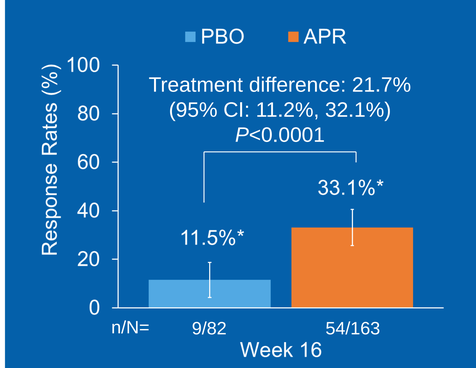
	PBO (n=82)	APR (n=163)	Total (N=245)
Age, mean (SD), y	12.2 (3.25)	12.3 (3.32)	12.2 (3.29)
6–11, n (%)	34 (41.5)	67 (41.1)	101 (41.2)
12–17, n (%)	48 (58.5)	96 (58.9)	144 (58.8)
Male, n (%)	43 (52.4)	74 (45.4)	117 (47.8)
Duration of plaque psoriasis, mean (SD), y	4.0 (3.39)	4.3 (3.35)	4.2 (3.36)
sPGA score, n (%)			
3 (Moderate)	63 (76.8)	122 (74.8)	185 (75.5)
4 (Severe)	19 (23.2)	41 (25.2)	60 (24.5)
PASI score, mean (SD)	19.5 (7.94)	20.0 (8.16)	19.8 (8.07)
Affected BSA, mean (SD), %	30.8 (19.04)	31.9 (18.45)	31.5 (18.62)

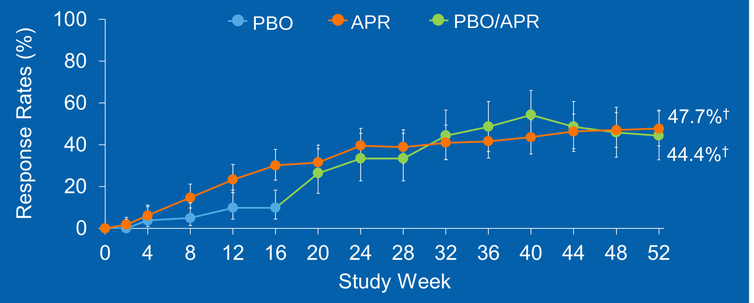
- A total of 221 patients (PBO: 72 [87.8%]; APR: 149 [91.4%]) completed the PBO-controlled phase and 186 (PBO/APR: 61 [74.4%]; APR: 125 [76.7%]) completed 52 weeks (*scan the QR code for baseline information*)

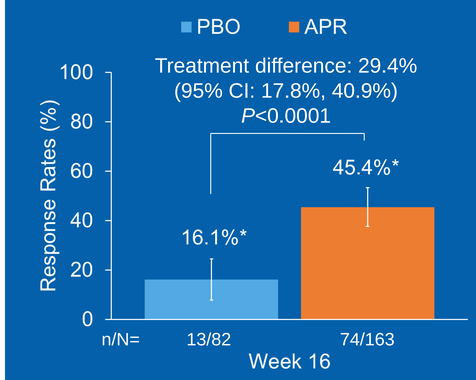
Key Takeaways

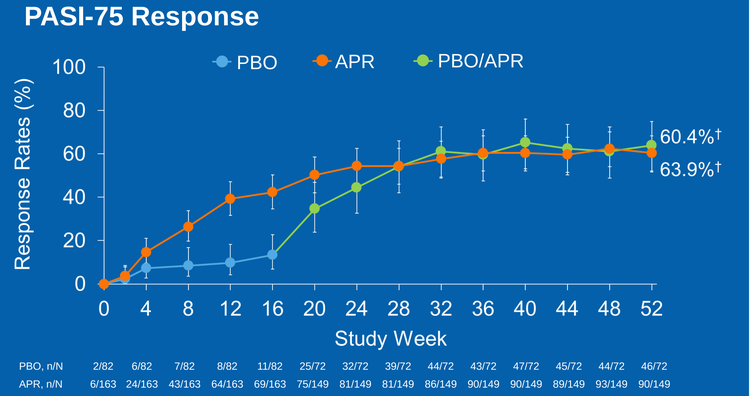
- **Improvements in psoriasis severity and skin involvement in pediatric patients treated with apremilast were maintained from 16 to 52 weeks**
- **Adverse events were consistent with the known safety profile of apremilast in adults**
- **Apremilast plasma exposures were similar between the two body weight categories (20 to <50 kg and ≥50 kg) and dose groups (20 mg BID and 30 mg BID)**

Sustained improvements in sPGA and PASI responses were observed from Week 16 to Week 52 with APR treatment









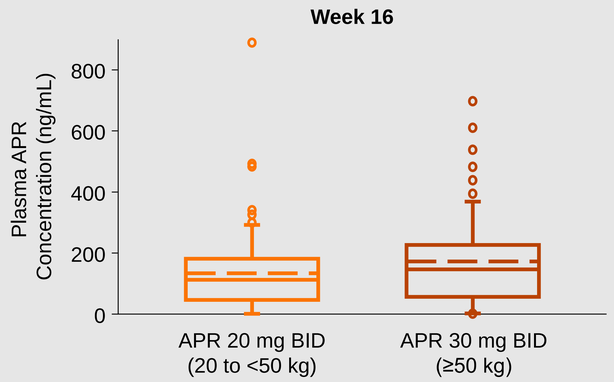
Intent-to-treat population. Error bars represent 95% CI. *Multiple imputations. †Nonresponder imputation. Two-sided *P* value is based on the Cochran-Mantel-Haenszel test adjusting for the stratification factors.
PBO/APR=patients who switched from PBO to APR at Week 16.

Safety and Tolerability

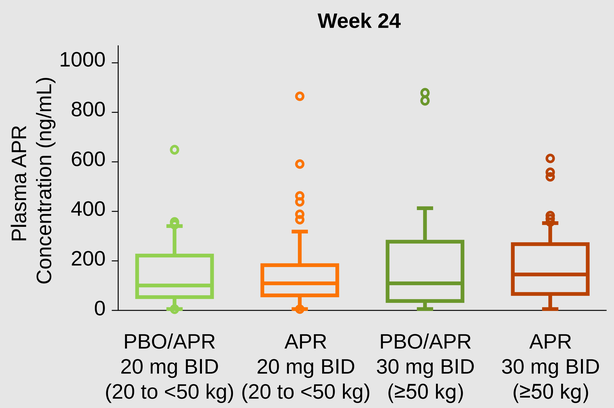
- During both the PBO-controlled and extension phases, adverse events (AEs) and tolerability were consistent with the known safety profile of APR in adults; no new safety signals were observed[1,2]
- The most common AEs (>10%) throughout the study were nausea, diarrhea, abdominal pain, vomiting, and headache
- *Scan the QR code for an overview of treatment-emergent AEs*

Pharmacokinetics

- APR plasma concentrations at Week 16 were similar between patients weighing ≥20 to <50 kg and those weighing ≥50 kg



- APR plasma concentrations at Week 24 were similar between dose groups, and between patients who switched from PBO to APR and those who were initially randomized to APR



Boxes show median (solid horizontal lines), mean (dashed horizontal lines), 25th percentiles (bottom of boxes), and 75th percentiles (top of boxes); whiskers above and below the boxplot represents the 90th and the 10th percentiles, respectively, and circles outside the whiskers represent outliers.
PBO/APR=patients who switched from PBO to APR at Week 16.

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References: 1. Papp K, et al. *J Am Adad Dermatol*. 2015;73:37-49. **2.** Paul C, et al. *Br J Dermatol*. 2015;173:1387-1399.

For patient disposition, baseline characteristics of those who completed 52 weeks, and additional safety information, scan the QR code

Patient-Reported Outcomes With Roflumilast Foam 0.3% in Patients With Scalp and Body Psoriasis in the Phase 3 ARRECTOR trial

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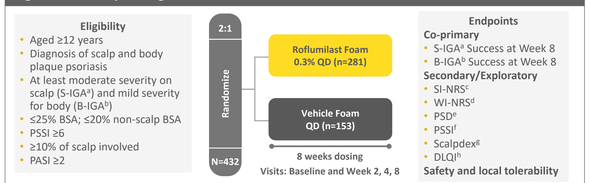
INTRODUCTION

- Plaque psoriasis is a chronic inflammatory skin condition that negatively impacts quality of life, including in patients in which the disease is not extensive[1]
  - Up to 80% of patients with psoriasis experience scalp psoriasis[2-4]
  - Disease severity scores may underestimate the impact of disease on overall quality of life[1]
- Roflumilast is a potent phosphodiesterase 4 (PDE4) inhibitor formulated as a water-based cream and foam
  - Roflumilast potency is ~25- to >300-fold higher than apremilast and crisaborole, with roflumilast more closely mimicking cyclic adenosine monophosphate (cAMP) binding to PDE4[5,6]
  - Formulations do not contain ethanol, propylene glycol, or fragrances that can irritate skin

METHODS

- ARRECTOR was a Phase 3, parallel-group, double-blind, vehicle-controlled trial (NCT05028582) enrolling patients ≥12 years of age with diagnosis of scalp and body psoriasis of at least moderate severity on the Scalp-Investigator Global Assessment (S-IGA) and mild severity on the Body-Investigator Global Assessment (B-IGA; **Figure 1**)
  - The co-primary efficacy endpoints were S-IGA Success and B-IGA Success at Week 8, which were defined as achievement of Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline
  - Patient-reported outcomes included Worst Itch Numeric Rating Scale (WI-NRS) and Scalp Itch Numeric Rating Scale (SI-NRS), Psoriasis Symptom Diary (PSD), Psoriasis Scalp Severity Index (PSSI), Scalpdex, and Dermatology Life Quality Index (DLQI)
- Safety and local tolerability were also assessed

Figure 1. Study Design



S-IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline
B-IGA Success = Clear or Almost Clear IGA status plus ≥2-grade improvement from baseline

[a]A 5-point scale (ranging from 0 [Clear] to 4 [Severe]) assessing severity of psoriasis on the scalp. [b]A 5-point scale (ranging from 0 [Clear] to 4 [Severe]) assessing severity of psoriasis on the body. [c]An 11-point scale assessing scalp itch, ranging from 0 (no itch) to 10 (worst itch imaginable). [d]An 11-point scale assessing itch of non-scalp body regions, ranging from 0 (no itch) to 10 (worst itch imaginable). [e]A 161-point scale assessing various psoriasis symptoms, including itch, pain, and scaling. [f]A 72-point scale based on psoriasis disease intensity and total affected body area. [g]A 23-item survey assessing quality of life in patients with scalp psoriasis. [h]A 30-point scale assessing patients' quality of life.
B-IGA: Body-Investigator Global Assessment; BSA: body surface area; DLQI: Dermatology Life Quality Index; PASI: Psoriasis Area and Severity Index; PSD: Psoriasis Symptom Diary; PSSI: Psoriasis Scalp Severity Index; QD: once daily; S-IGA: Scalp-Investigator Global Assessment; SI-NRS: Scalp Itch Numeric Rating Scale; WI-NRS: Worst Itch Numeric Rating Scale.

RESULTS

- Baseline disease characteristics were consistent between groups (**Table 1**)

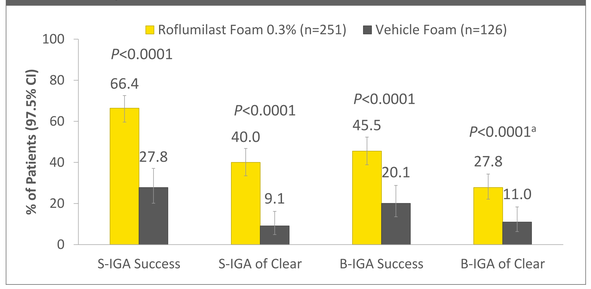
Table 1. Baseline Disease Characteristics

	Roflumilast Foam 0.3% (n=281)	Vehicle Foam (n=151)
Baseline S-IGA, mean (SD)	3.1 (0.4)	3.1 (0.3)
3 (Moderate), n (%)	239 (85.1)	131 (86.8)
4 (Severe), n (%)	42 (14.9)	20 (13.2)
Baseline B-IGA, mean (SD)	2.8 (0.5)	2.8 (0.5)
2 (Mild), n (%)	76 (27.0)	43 (28.5)
3 (Moderate), n (%)	191 (68.0)	99 (65.6)
4 (Severe), n (%)	14 (5.0)	9 (6.0)
SI-NRS, mean (SD)	5.8 (2.6)	6.1 (2.3)
WI-NRS, mean (SD)	5.7 (2.6)	5.5 (2.6)
PSD total score, mean (SD)	73.4 (40.2)	75.2 (36.9)
PSD aggregate score (itch/pain/scaling), mean (SD)	15.7 (7.3)	16.2 (6.7)
PSSI, mean (SD)	21.4 (11.1)	22.2 (11.0)
Scalpdex, mean (SD)	47.2 (22.9)	50.5 (20.4)
DLQI, mean (SD)	7.1 (5.3)	7.3 (4.8)
BSA (%), mean (SD)	6.1 (4.3)	6.0 (4.3)
Extent of scalp involvement (%), mean (SD)	34.4 (25.0)	36.0 (25.8)

SD: standard deviation.

- Roflumilast provided significant improvement in scalp and body psoriasis, as indicated by improvements in S-IGA and B-IGA (**Figure 2**)

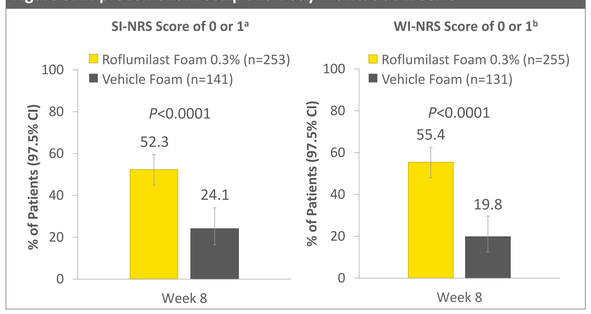
Figure 2. Proportion of Patients Achieving S-IGA Success, S-IGA of Clear, B-IGA Success, and B-IGA of Clear at Week 8



Multiple imputation of missing data.
[a]Nominal *P* value.
CI: confidence interval.

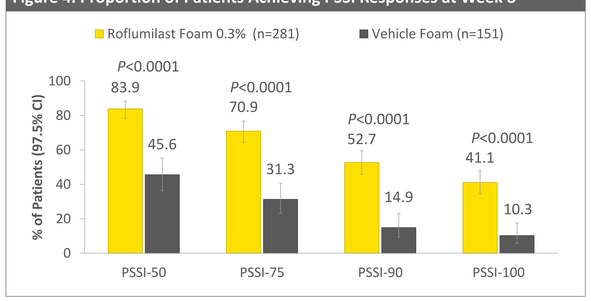
- Once-daily treatment with roflumilast foam 0.3% also resulted in significant improvement in patient-reported outcomes
- In patients with SI-NRS and WI-NRS ≥2 at baseline, more roflumilast-treated than vehicle-treated patients achieved a score of 0 or 1 at Week 8 (**Figure 3**)
- At Week 8, significantly more roflumilast-treated than vehicle-treated patients achieved a PSD total score of 0 (19.6% vs 7.1%; *P*=0.0002)
  - Least squares (LS) mean change from baseline (CfB) in PSD items related to itching/pain/scaling was significantly greater with roflumilast than with vehicle at Week 8 (LS mean CfB: −10.87 vs −5.75; *P*<0.0001)
- Significantly more roflumilast-treated than vehicle-treated patients achieved ≥50%, ≥75%, ≥90%, and 100% reductions in PSSI scores (**Figure 4**)
- At Week 8, LS mean CfB in Scalpdex total score was also significantly greater with roflumilast than with vehicle (**Figure 5**)
- Roflumilast treatment also resulted in a significantly greater LS mean CfB in DLQI score at Week 8 (roflumilast: −4.37, n=276; vehicle: −2.44, n=149; *P*<0.0001)

Figure 3. Improvement in Scalp and Body Pruritus at Week 8



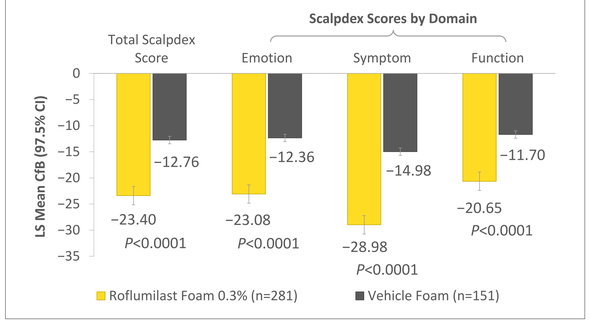
[a]SI-NRS score of 0 or 1 evaluated in patients with baseline SI-NRS ≥2.
[b]WI-NRS score of 0 or 1 evaluated in patients with baseline WI-NRS ≥2.
CI: confidence interval.

Figure 4. Proportion of Patients Achieving PSSI Responses at Week 8



Multiple imputation of missing data. PSSI-50/75/90/100: ≥50%/≥75%/≥90%/100% reduction in PSSI from baseline.
CI: confidence interval.

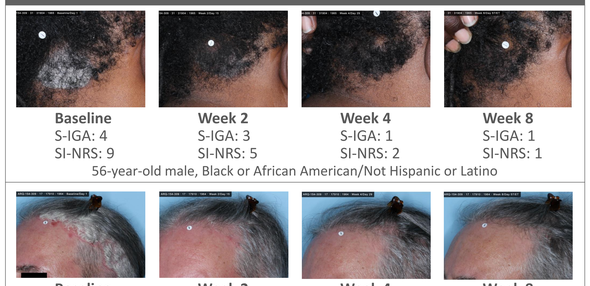
Figure 5. Improvement in Scalpdex Score at Week 8



Missing data were not imputed.
CfB: change from baseline; CI: confidence interval; LS: least squares.

- Two series of photographs of patients with improvement in psoriasis following roflumilast treatment is shown in **Figure 6**

Figure 6. Improvement in Patients With Psoriasis Treated With Roflumilast Foam 0.3%



S-IGA and SI-NRS are global assessments.

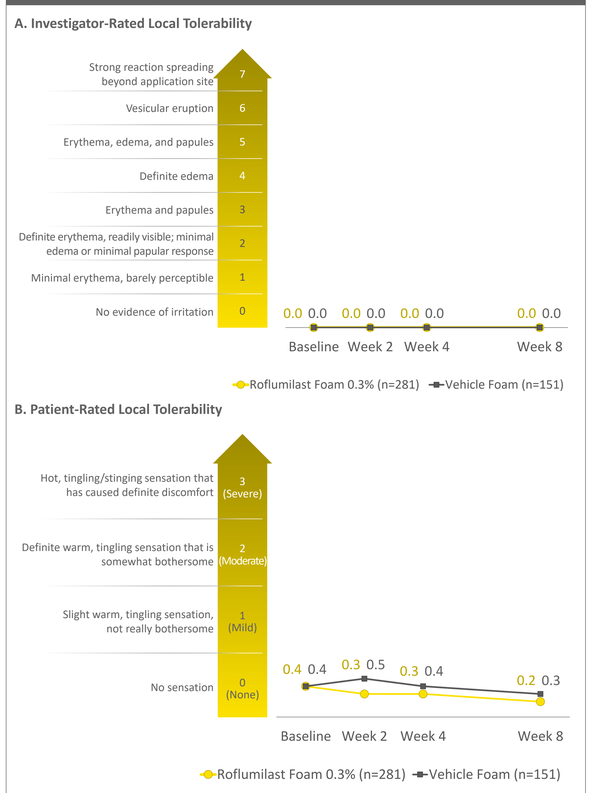
- Incidence of treatment-emergent adverse events was low in both treatment groups (**Table 2**)
- Investigator- and patient-rated local tolerability was similar to that observed with vehicle (**Figure 7**)

Table 2. Safety

Patients, n (%)	Roflumilast Foam 0.3% (n=281)	Vehicle Foam (n=151)
Any TEAE	75 (26.7)	25 (16.6)
Any treatment-related TEAE	16 (5.7)	3 (2.0)
Any treatment-emergent SAE[a]	2 (0.7)	1 (0.7)
Any treatment-related SAE	1 (0.4)	0
Discontinued trial drug due to an AE	7 (2.5)	2 (1.3)
Discontinued trial due to AE	5 (1.8)	2 (1.3)
Most common TEAEs by Preferred Term, ≥1% in any group		
Headache	13 (4.6)	3 (2.0)
Diarrhea	9 (3.2)	4 (2.6)
COVID-19	8 (2.8)	4 (2.6)
Nasopharyngitis	4 (1.4)	2 (1.3)
Nausea	6 (2.1)	0
Hypertension	3 (1.1)	2 (1.3)
Urinary tract infection	2 (0.7)	2 (1.3)
Upper respiratory tract infection	3 (1.1)	0

[a]SAEs include bipolar disorder (roflumilast; unrelated); gastritis (roflumilast; possibly related); joint dislocation, peripheral artery occlusion, and radius fracture (vehicle; all unrelated).
AE: adverse event; COVID-19: coronavirus disease 2019; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Figure 7. (A) Investigator- and (B) Patient-Rated Local Tolerability



CONCLUSION

- In patients with scalp and body psoriasis, treatment with once-daily roflumilast foam 0.3% demonstrated greater improvement compared with vehicle across multiple patient-reported efficacy endpoints
  - Significant improvement in both scalp and body psoriasis occurred as early as 2 weeks after treatment initiation, the first time point measured
  - Significant improvement in patient-reported outcomes occurred, indicating relief from itching, pain, and scaling that was associated with improved quality of life
- Treatment with roflumilast foam 0.3% was associated with low rates of adverse events, few discontinuations because of adverse events, and local tolerability that was similar to vehicle

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DISCLOSURES

MJG, JB, SBF, LHK, MW, BL, and JS are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; DK, SK, DRB, and DHC are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.

PRESENTED AT ELEVATE DERM-WEST CONGRESS; NOVEMBER 7–10, 2024; SCOTTSDALE, AZ, USA

Once-Daily Roflumilast Cream 0.15% for the Treatment of Atopic Dermatitis in Patients With Diverse Skin Types: Pooled Subgroup Analysis From the Phase 3 INTEGUMENT-1 and -2 Trials

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INTRODUCTION

- The epidemiology and clinical presentation of atopic dermatitis (AD) may differ based on race, ethnicity, and Fitzpatrick skin type[1-3]
- In the INTEGUMENT-1 (NCT04773587) and INTEGUMENT-2 (NCT04773600) Phase 3 trials, roflumilast cream 0.15% was well tolerated and demonstrated efficacy in patients aged ≥6 years with mild-to-moderate AD[4,5]

METHODS

- INTEGUMENT-1 and INTEGUMENT-2 were identically designed, randomized, parallel-group, double-blind, vehicle-controlled, multicenter trials enrolling patients aged ≥6 years with mild-to-moderate AD
- The primary endpoint was Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) Success (0 [clear] or 1 [almost clear] plus ≥2-grade improvement) at Week 4
  - vIGA-AD: 5-point scale ranging from clear (0) to severe (4) that assesses inflammatory signs of AD
- Secondary endpoints included vIGA-AD Success at Weeks 1 and 2; vIGA-AD 0/1 at Weeks 1, 2, and 4; Worst Itch-Numeric Rating Scale (WI-NRS) Success (≥4-point improvement in patients aged ≥12 years with baseline score ≥4) at Weeks 1, 2, and 4; and ≥75% reduction from baseline in Eczema Area and Severity Index (EASI-75) at Week 4
  - WI-NRS: 11-point scale ranging from 0 (no itch) to 10 (worst itch imaginable)
- Safety and tolerability were also assessed

Study Design

Eligibility
- Diagnosis of mild or moderate AD (vIGA-AD = 2 or 3)
- Aged ≥6 years
- BSA ≥3%
- EASI ≥5

Randomize 2:1 → Roflumilast Cream 0.15% QD; Vehicle Cream QD

4 weeks[a]

[a]Nonmedicated emollients or moisturizers could be applied QD, but only to untreated areas of the patient's skin.
BSA: body surface area; EASI: Eczema Area and Severity Index; QD: once daily.

OBJECTIVE

- Assess the efficacy of roflumilast cream 0.15% in patients with AD based on race (White, Black or African American, Asian, or other race), ethnicity (Hispanic or Latino, or Not Hispanic or Latino), and Fitzpatrick skin type (I–III or IV–VI) using pooled data from Phase 3 randomized controlled trials

RESULTS

- Baseline weekly average WI-NRS and EASI did not differ by race
- Roflumilast cream 0.15% provided consistent and meaningful improvements in signs and symptoms of AD in patients across race, ethnicity, and Fitzpatrick skin types

Patient Demographics

		Roflumilast Cream 0.15% (n=884)	Vehicle Cream (n=453)
Age, years, mean (SD) [range]		27.9 (19.4) [6–91]	27.3 (19.0) [6–84]
Female at birth, n (%)		489 (55.3)	272 (60.0)
Ethnicity, n (%)	Hispanic or Latino	150 (17.0)	72 (15.9)
	Not Hispanic or Latino	730 (82.6)	377 (83.2)
	Not reported[a]	4 (0.5)	4 (0.9)
Race, n (%)	White	529 (59.8)	267 (58.9)
	Black or African American	176 (19.9)	96 (21.2)
	Asian	114 (12.9)	62 (13.7)
	Other race[b]	65 (7.4)	28 (6.2)
Fitzpatrick skin type, n (%)	I–III	481 (54.4)	238 (52.5)
	IV–VI	403 (45.6)	215 (47.5)

[a]Patients not reporting ethnicity were not included in subgroup analyses based on ethnicity; [b]Other race category includes patients reporting races as American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, multiple races, and those patients who chose to describe their race rather than select 1 of the provided options, as well as patients who did not report their race.

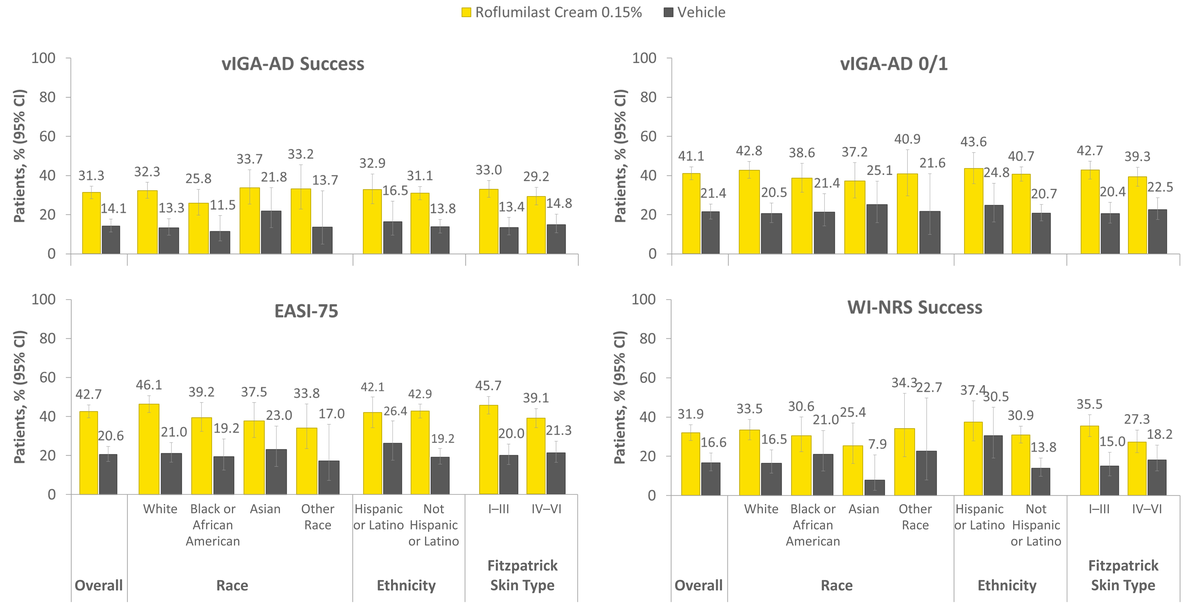
Baseline Disease Characteristics

		Roflumilast Cream 0.15% (n=884)	Vehicle Cream (n=453)
Overall	vIGA-AD 2 (Mild), n (%)	211 (23.9)	112 (24.7)
	vIGA-AD 3 (Moderate), n (%)	673 (76.1)	341 (75.3)
	EASI, mean (SD)	10.1 (5.7)	10.0 (5.2)
	Weekly WI-NRS, mean (SD)	6.1 (2.2)	5.9 (2.2)
White	vIGA-AD 2 (Mild), n (%)	134 (25.3)	70 (26.2)
	vIGA-AD 3 (Moderate), n (%)	395 (74.7)	197 (73.8)
	EASI, mean (SD)	9.7 (5.1)	10.0 (5.1)
	Weekly WI-NRS, mean (SD)	6.0 (2.1)	5.8 (2.2)
Black or African American	vIGA-AD 2 (Mild), n (%)	45 (25.6)	28 (29.2)
	vIGA-AD 3 (Moderate), n (%)	131 (74.4)	68 (70.8)
	EASI, mean (SD)	9.5 (4.6)	9.4 (5.3)
	Weekly WI-NRS, mean (SD)	6.0 (2.3)	6.0 (2.4)
Asian	vIGA-AD 2 (Mild), n (%)	18 (15.8)	8 (12.9)
	vIGA-AD 3 (Moderate), n (%)	96 (84.2)	54 (87.1)
	EASI, mean (SD)	11.6 (7.7)	10.6 (5.5)
	Weekly WI-NRS, mean (SD)	6.1 (2.1)	5.8 (2.3)
Other race	vIGA-AD 2 (Mild), n (%)	14 (21.5)	6 (21.4)
	vIGA-AD 3 (Moderate), n (%)	51 (78.5)	22 (78.6)
	EASI, mean (SD)	12.4 (8.3)	10.6 (5.0)
	Weekly WI-NRS, mean (SD)	6.1 (2.3)	6.0 (2.4)

Safety

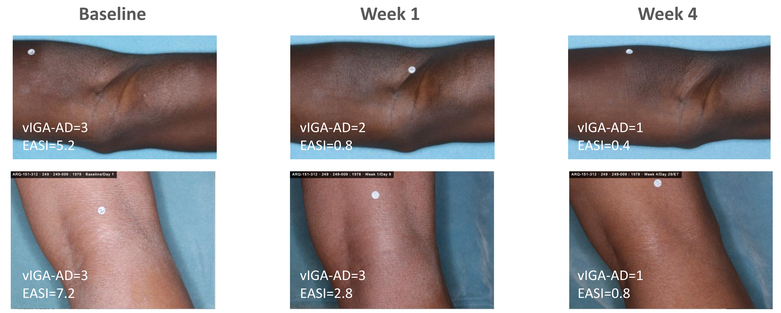
- Safety findings were generally consistent across subgroups
- Overall, the most frequently reported (≤2.9%) treatment-emergent adverse events across subgroups included headache, nausea, application site pain, diarrhea, and vomiting
- Investigator-rated and patient-reported tolerability by race were consistent with the overall population

Proportion of Patients Achieving vIGA-AD Success, vIGA-AD 0/1, EASI-75, and WI-NRS Success at Week 4



CI: confidence interval.

Improvement in Patients With AD Treated With Roflumilast Cream 0.15%



vIGA-AD and EASI are global measures.

CONCLUSIONS

- Once-daily nonsteroidal roflumilast cream 0.15% provided meaningful improvements in signs and symptoms of AD
  - Improvements in outcomes were generally consistent across race, ethnicity, and Fitzpatrick skin type subgroups of patients and with the overall trial results
- Safety and local tolerability were generally consistent across race, ethnicity, and Fitzpatrick skin type subgroups and similar between both roflumilast and vehicle treatment groups

ABBREVIATIONS

AD: atopic dermatitis; BSA: body surface area; CI: confidence interval; EASI: Eczema Area and Severity Index; QD: once daily; vIGA-AD: Validated Investigator Global Assessment for Atopic Dermatitis; WI-NRS: Worst Itch-Numeric Rating Scale.

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DISCLOSURES

VHP, JCB, MG, HCH, and ELS are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; MSS, DK, PB, DRB, RCH, and DHC are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.

PRESENTED AT ELEVATE DERM-WEST CONGRESS; NOVEMBER 7–10, 2024; SCOTTSDALE, AZ, USA

Deucravacitinib in plaque psoriasis: laboratory parameters through 4 years of treatment in the phase 3 POETYK PSO-1, PSO-2, and LTE trials

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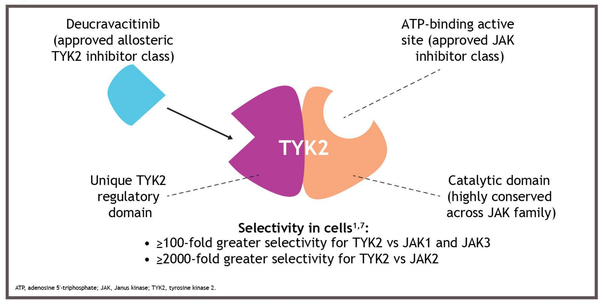
Introduction

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of select inflammatory cytokines (eg, interleukin [IL]-23, IL-12, Type I interferons [IFNs])[1]
  - IL-23 and Type I IFNs are involved in psoriasis pathogenesis[1]
- Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, is approved in the US, EU, and other countries for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy[2-6]
- Deucravacitinib uniquely binds to the TYK2 regulatory domain rather than to the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind[1,7] (**Figure 1**), driving its selectivity for TYK2 and representing the first in a new class of oral drugs

Figure 1. Mechanism of action of deucravacitinib



- Two global, 52-week, phase 3 trials, POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751), demonstrated that deucravacitinib was significantly more efficacious than placebo and apremilast at Week 16 and was well tolerated in patients with moderate to severe plaque psoriasis[8,9]
- Patients who completed the POETYK PSO-1 and PSO-2 parent trials could enroll in the ongoing POETYK long-term extension (LTE) (NCT04036435) trial and receive open-label deucravacitinib
  - Clinical efficacy was maintained through 1 year in the parent trials and 2 additional years in the POETYK LTE trial (total, 3 years), with no new safety signals observed compared with the first year[10,11]
  - No clinically meaningful changes from baseline or trends were observed in laboratory parameters through 3 years[10,11]

Objectives

- To determine whether there were clinically relevant changes in blood laboratory parameters through 4 years (Week 208; data cutoff, November 1, 2023) in deucravacitinib-treated patients with moderate to severe plaque psoriasis in the POETYK PSO-1, PSO-2, and LTE trials
- To evaluate whether deucravacitinib treatment elicits changes in laboratory parameters known to occur with JAK1,2,3 inhibitors

Methods

Study designs

- POETYK PSO-1 and PSO-2 were 52-week, multinational, phase 3, double-blind trials that randomized adults with moderate to severe plaque psoriasis 1:2:1 to oral placebo, deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily
  - Placebo patients crossed over to deucravacitinib at Week 16
  - In POETYK PSO-2, deucravacitinib-treated patients who achieved ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) at Week 24 were rerandomized 1:1 to continue deucravacitinib treatment or switch to placebo through Week 52
- At Week 52, eligible patients were allowed to enroll in the POETYK LTE trial and receive open-label deucravacitinib 6 mg once daily

Laboratory assessments

- Adverse events (AEs) and treatment discontinuations due to laboratory abnormalities (Common Terminology Criteria for Adverse Events [CTCAE] version 5.0) were evaluated through 4 years (Week 208)
  - Safety data were reported as exposure-adjusted incidence rate (EAIR) per 100 person-years (PY) and calculated as 100 * (number of patients with an AE) / (total exposure time for all patients at risk [time to initial AE occurrence for patients with AE + total exposure time for patients without AE])
- Select laboratory parameters of note in the blood that are known to be associated with JAK1,2,3 inhibitors were assessed periodically through 4 years
  - Changes in laboratory parameters assessed included:
    - Hematology: hemoglobin, neutrophils, lymphocytes, platelets
    - Chemistry: alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, creatine phosphokinase (CPK), total bilirubin
    - Lipids: total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides

Results

Patients

- A total of 1519 patients received ≥1 dose of deucravacitinib across the parent trials (POETYK PSO-1 and PSO-2) and the POETYK LTE trial
  - Total deucravacitinib exposure through 4 years was 4392.8 PY
  - Median duration of exposure was 185 weeks
    - ≥52 weeks, n = 1203 (79.2%) patients
    - ≥208 weeks, n = 542 (35.7%) patients
- Baseline patient demographics and disease characteristics are presented in **Table 1**

Table 1. Baseline patient demographics and disease characteristics

Parameter	POETYK PSO-1 + PSO-2 + LTE Deucravacitinib (n = 1519)
Age, mean (SD), y	46.6 (13.4)
Weight, mean (SD), kg	90.6 (21.6)
Body mass index, mean (SD), kg/m²	30.5 (6.8)
Female, n (%)	493 (32.5)
Race, n (%)	
White	1325 (87.2)
Asian	153 (10.1)
Black or African American	23 (1.5)
Other	18 (1.2)
Age at disease onset, mean (SD), y	28.8 (14.9)
Disease duration, mean (SD), y	18.7 (12.7)
PASI score, mean (SD)	21.1 (8.1)
sPGA score, n (%)	
3 (moderate)	1211 (79.7)
4 (severe)	308 (20.3)
BSA involvement, mean (SD), %	26.2 (15.8)

BSA, body surface area; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; SD, standard deviation; sPGA, static Physician Global Assessment.

Laboratory assessments

- The most common laboratory abnormality AEs (EAIR ≥1/100 PY) were blood CPK increased (n = 93/1519; EAIR, 2.20) and ALT increased (n = 47/1519; EAIR, 1.08), which all resolved spontaneously on continuing treatment with deucravacitinib
- Discontinuations due to laboratory abnormality AEs were low and balanced across treatment groups over the first 52 weeks in the parent trials and continued to be low through 4 years (**Table 2**)
  - No patients discontinued deucravacitinib treatment due to the minimal triglyceride elevations noted below

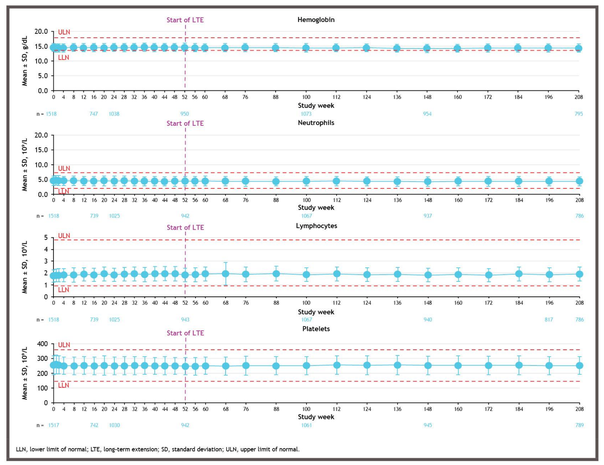
Table 2. Laboratory abnormality AEs leading to treatment discontinuation through 1 year and 4 years

	At 1 year (POETYK PSO-1 + PSO-2, Weeks 0-52)						At 4 years (POETYK PSO-1 + PSO-2 + LTE, Weeks 0-208)	
	Placebo (n = 666) Total exposure = 240.9 PY		Deucravacitinib (n = 1364) Total exposure = 969.0 PY		Apremilast (n = 422) Total exposure = 221.1 PY		Deucravacitinib (n = 1519) Total exposure = 4392.8 PY	
	n (%)	EAIR/ 100 PY	n (%)	EAIR/ 100 PY[a]	n (%)	EAIR/ 100 PY	n (%)	EAIR/ 100 PY[a]
Lymphopenia	0	0	1 (0.1)[b]	0.1	0	0	1 (0.1)[b]	0.02
Blood CPK increased	0	0	2 (0.1)[c]	0.2	1 (0.2)	0.4	3 (0.2)[c]	0.1
Hepatic function abnormal	1 (0.2)	0.4	1 (0.1)[b]	0.1	0	0	1 (0.1)[b]	0
ALT increased	0	0	0	0	0	0	1 (0.1)[d]	0
AST increased	0	0	0	0	1 (0.2)	0.4	1 (0.1)[d]	0

[a]Incidences are expressed as EAIRs/100 PY to account for variable exposure due to treatment switches at Weeks 16 and 24. [b]This AE was considered treatment-related. [c]Two CPK events were considered treatment-related and 1 CPK event was considered not related. [d]This AE was considered not related to treatment.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; EAIR, exposure-adjusted incidence rate; LTE, long-term extension; PY, person-years.

- No clinically meaningful mean changes were observed through 4 years (Weeks 0-208) in any of the evaluated hematology (**Figure 2**), chemistry (**Figure 3**), or lipid (**Figure 4**) laboratory parameters
  - Laboratory parameters remained within normal ranges for the vast majority of patients throughout this period
  - As expected, due to comorbidities known to be present in this population, such as obesity and metabolic syndrome,[12] baseline levels of cholesterol and triglycerides were elevated
    - A minimal increase (<10 mg/dL) in the mean change from baseline (150 mg/dL) in serum triglycerides was observed with deucravacitinib during the first year of treatment and was:
      - Not considered clinically relevant
      - Not associated with increases in LDL levels (<3 mg/dL)
      - Stable over time
  - Signature changes in mean laboratory parameters seen with 1 or more JAK1,2,3 inhibitors, such as lymphopenia, anemia, thrombocytopenia, liver enzyme elevations, creatinine increases, and cholesterol increases,[13] were not observed with deucravacitinib treatment

Figure 2. Changes in hematology parameters over 4 years in patients treated with deucravacitinib in POETYK PSO-1 + PSO-2 + LTE



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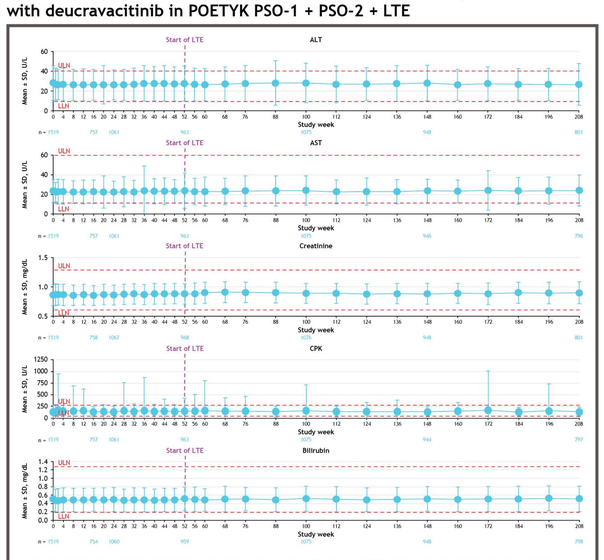

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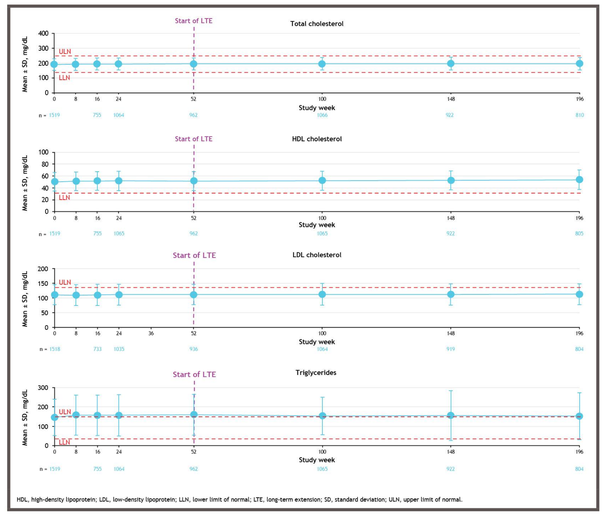

Conclusions

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  - Signature changes in mean values of laboratory analytes observed with JAK1,2,3 inhibitors (eg, increased cholesterol, creatinine, serum transaminases, CPK levels, cytopenias)[13] were not observed over 4 years of deucravacitinib treatment
- Discontinuations due to laboratory abnormalities were rare (7 events) through 4 years of deucravacitinib treatment
- This laboratory parameter profile further supports the selectivity of deucravacitinib for TYK2 and highlights that the JAK1,2,3 pathways are not impacted by selective, allosteric TYK2 inhibition

References

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NJK: Advisory board and consulting fees: AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Janssen, Leo Pharma, Lilly, Novartis, Principia, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB; Grant support/principal investigator: AbbVie, Amgen, Argenx, Bristol Myers Squibb, Celgene, Chemocentryx, Galderma, Kyowa Kirin, Leo Pharma, Lilly, Menlo Therapeutics, Principia, Prothena, Rhizen, Syntimmune, Trevi, and XBiotech; Speaker: AbbVie, Janssen, Lilly, Novartis, Regeneron, and Sanofi Genzyme. **TP:** Advisory board and consulting fees: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Galderma, Incyte, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Sanofi Genzyme, Sun Pharma, and UCB. **YO:** Research grants: AbbVie, Eisai, Maruho, Shiseido, Sun Pharma, and Torii; Honoraria: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eisai, Janssen Pharma, Jimro, Kyowa Kirin, Leo Pharma, Lilly, Maruho, Novartis, Pfizer, Sanofi, Sun Pharma, Taiho, Tanabe-Mitsubishi, Torii, and UCB; Clinical trials: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Janssen, Leo Pharma, Lilly, Maruho, Pfizer, Sun Pharma, and UCB. **JB:** Research funds payable to the Psoriasis Treatment Center of New Jersey: AbbVie, Amgen, Arcutis, Boehringer Ingelheim, Bristol Myers Squibb, CorEvitas Psoriasis Registry, Dermavant, Dermira/UCB, Glenmark, Janssen Biotech, Kadmon, Leo Pharma, Lilly, Lycera, Menlo Therapeutics, Novartis, Pfizer, Regeneron, Sun Pharma, Taro, and Valeant; Consultant: AbbVie, Amgen, Janssen Biotech, Lilly, Novartis, Sun Pharma, and Valeant; Speaker: AbbVie, Celgene, Janssen Biotech, Lilly, and Novartis. **RBW:** Research grants: AbbVie, Almirall, Amgen, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, and UCB; Consulting fees: AbbVie, Almirall, Amgen, Astellas, Boehringer Ingelheim, Dice Therapeutics, GSK, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Sanofi, UCB, and Union Therapeutics. **LS:** Consultant, paid investigator, advisory board and/or speaker: AbbVie, Amgen, Anacor, Ascend, Astellas, AstraZeneca, Blaze Bioscience, Boehringer Ingelheim, Botanix, Bristol Myers Squibb, Celgene, Connect Biopharma, Dermira, Enkang, Equillium Inc, Evelo Biosciences, Genesis Care, Galderma, Genentech, GSK, Hexima, Incyte, Inflarx GmbH, Invion, Janssen, Kiniksa, Koblo Labs, LG Chem, Lilly, Lipidio Pharma, Leo Pharma, Mayne, Medimmune, Merck, Merck-Serono, Novartis, Nektar Therapeutics, Olix, Otsuka, Pfizer, Phosphagenics, Photon MD, Principia, Regeneron, Ribon, Samumed, Sanofi Genzyme, SHR Pharmacy, Sun Pharma, Takeda, UCB, and Zai Lab. **KW:** Consulting: AbbVie, AstraZeneca, Bristol Myers Squibb, Galapagos, Gilead, GSK, Lilly, Novartis, Pfizer, Regeneron, Roche, Sanofi, and UCB; Research support: Bristol Myers Squibb and Pfizer. **KH:** Consultant: Bristol Myers Squibb via Syneos Health. **TS and SB:** Employees at the time of study conduct and shareholders: Bristol Myers Squibb. **DT:** Research support and principal investigator (clinical trial funds to institution): AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Galderma, Janssen-Cilag, Leo Pharma, Lilly, Novartis, Pfizer, Regeneron, Sanofi, and UCB; Consultant: AbbVie, Almirall, Boehringer Ingelheim, Bristol Myers Squibb, Leo Pharma, Novartis, Pfizer, and UCB; Lecturer: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Roche-Posay, Sanofi, Target RWE, and UCB; Scientific advisory board: AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Janssen-Cilag, Leo Pharma, Lilly, Novartis, Pfizer, Sanofi, and UCB. **MS:** Consultant (honoraria): AbbVie, Amgen, Arcutis, Bristol Myers Squibb, Dermavant, Galderma, Janssen, Leo Pharma, Lilly USA, Novartis, Ortho Dermatologics, Sanofi-Genzyme, Regeneron, UCB; Speaker: AbbVie, Arcutis, Bristol Myers Squibb, Lilly USA, Janssen, Dermavant, Leo Pharma, Pfizer, and UCB; Investigator: AbbVie, Cara Therapeutics, CorEvitas Psoriasis and Atopic Dermatitis Registry, Dermira, Dermavant, Mindera Health, Novartis, and Union Therapeutics. **LSG:** Consultant, advisory board member, and/or speaker: AbbVie, Amgen, Arcutis, Aslan, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Galderma, Incyte, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB.

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Deucravacitinib in plaque psoriasis: laboratory parameters through 4 years of treatment in the phase 3 POETYK PSO-1, PSO-2, and LTE trials

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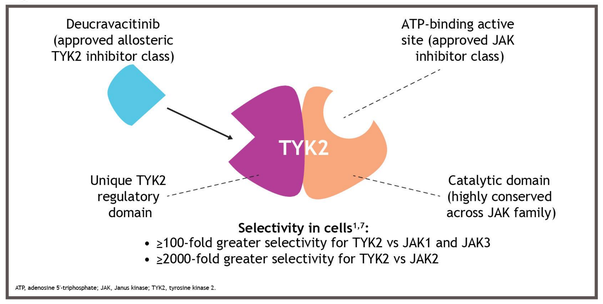
Introduction

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of select inflammatory cytokines (eg, interleukin [IL]-23, IL-12, Type I interferons [IFNs])[1]
  - IL-23 and Type I IFNs are involved in psoriasis pathogenesis[1]
- Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, is approved in the US, EU, and other countries for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy[2-6]
- Deucravacitinib uniquely binds to the TYK2 regulatory domain rather than to the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind[1,7] (**Figure 1**), driving its selectivity for TYK2 and representing the first in a new class of oral drugs

Figure 1. Mechanism of action of deucravacitinib



- Two global, 52-week, phase 3 trials, POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751), demonstrated that deucravacitinib was significantly more efficacious than placebo and apremilast at Week 16 and was well tolerated in patients with moderate to severe plaque psoriasis[8,9]
- Patients who completed the POETYK PSO-1 and PSO-2 parent trials could enroll in the ongoing POETYK long-term extension (LTE) (NCT04036435) trial and receive open-label deucravacitinib
  - Clinical efficacy was maintained through 1 year in the parent trials and 2 additional years in the POETYK LTE trial (total, 3 years), with no new safety signals observed compared with the first year[10,11]
  - No clinically meaningful changes from baseline or trends were observed in laboratory parameters through 3 years[10,11]

Objectives

- To determine whether there were clinically relevant changes in blood laboratory parameters through 4 years (Week 208; data cutoff, November 1, 2023) in deucravacitinib-treated patients with moderate to severe plaque psoriasis in the POETYK PSO-1, PSO-2, and LTE trials
- To evaluate whether deucravacitinib treatment elicits changes in laboratory parameters known to occur with JAK1,2,3 inhibitors

Methods

Study designs

- POETYK PSO-1 and PSO-2 were 52-week, multinational, phase 3, double-blind trials that randomized adults with moderate to severe plaque psoriasis 1:2:1 to oral placebo, deucravacitinib 6 mg once daily, or apremilast 30 mg twice daily
  - Placebo patients crossed over to deucravacitinib at Week 16
  - In POETYK PSO-2, deucravacitinib-treated patients who achieved ≥75% reduction from baseline in Psoriasis Area and Severity Index (PASI 75) at Week 24 were rerandomized 1:1 to continue deucravacitinib treatment or switch to placebo through Week 52
- At Week 52, eligible patients were allowed to enroll in the POETYK LTE trial and receive open-label deucravacitinib 6 mg once daily

Laboratory assessments

- Adverse events (AEs) and treatment discontinuations due to laboratory abnormalities (Common Terminology Criteria for Adverse Events [CTCAE] version 5.0) were evaluated through 4 years (Week 208)
  - Safety data were reported as exposure-adjusted incidence rate (EAIR) per 100 person-years (PY) and calculated as 100 * (number of patients with an AE) / (total exposure time for all patients at risk [time to initial AE occurrence for patients with AE + total exposure time for patients without AE])
- Select laboratory parameters of note in the blood that are known to be associated with JAK1,2,3 inhibitors were assessed periodically through 4 years
  - Changes in laboratory parameters assessed included:
    - Hematology: hemoglobin, neutrophils, lymphocytes, platelets
    - Chemistry: alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, creatine phosphokinase (CPK), total bilirubin
    - Lipids: total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides

Results

Patients

- A total of 1519 patients received ≥1 dose of deucravacitinib across the parent trials (POETYK PSO-1 and PSO-2) and the POETYK LTE trial
  - Total deucravacitinib exposure through 4 years was 4392.8 PY
  - Median duration of exposure was 185 weeks
    - ≥52 weeks, n = 1203 (79.2%) patients
    - ≥208 weeks, n = 542 (35.7%) patients
- Baseline patient demographics and disease characteristics are presented in **Table 1**

Table 1. Baseline patient demographics and disease characteristics

Parameter	POETYK PSO-1 + PSO-2 + LTE Deucravacitinib (n = 1519)
Age, mean (SD), y	46.6 (13.4)
Weight, mean (SD), kg	90.6 (21.6)
Body mass index, mean (SD), kg/m²	30.5 (6.8)
Female, n (%)	493 (32.5)
Race, n (%)	
White	1325 (87.2)
Asian	153 (10.1)
Black or African American	23 (1.5)
Other	18 (1.2)
Age at disease onset, mean (SD), y	28.8 (14.9)
Disease duration, mean (SD), y	18.7 (12.7)
PASI score, mean (SD)	21.1 (8.1)
sPGA score, n (%)	
3 (moderate)	1211 (79.7)
4 (severe)	308 (20.3)
BSA involvement, mean (SD), %	26.2 (15.8)

BSA, body surface area; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; SD, standard deviation; sPGA, static Physician Global Assessment.

Laboratory assessments

- The most common laboratory abnormality AEs (EAIR ≥1/100 PY) were blood CPK increased (n = 93/1519; EAIR, 2.20) and ALT increased (n = 47/1519; EAIR, 1.08), which all resolved spontaneously on continuing treatment with deucravacitinib
- Discontinuations due to laboratory abnormality AEs were low and balanced across treatment groups over the first 52 weeks in the parent trials and continued to be low through 4 years (**Table 2**)
  - No patients discontinued deucravacitinib treatment due to the minimal triglyceride elevations noted below

Table 2. Laboratory abnormality AEs leading to treatment discontinuation through 1 year and 4 years

	At 1 year (POETYK PSO-1 + PSO-2, Weeks 0-52)						At 4 years (POETYK PSO-1 + PSO-2 + LTE, Weeks 0-208)	
	Placebo (n = 666) Total exposure = 240.9 PY		Deucravacitinib (n = 1364) Total exposure = 969.0 PY		Apremilast (n = 422) Total exposure = 221.1 PY		Deucravacitinib (n = 1519) Total exposure = 4392.8 PY	
	n (%)	EAIR/ 100 PY	n (%)	EAIR/ 100 PY[a]	n (%)	EAIR/ 100 PY	n (%)	EAIR/ 100 PY[a]
Lymphopenia	0	0	1 (0.1)[b]	0.1	0	0	1 (0.1)[b]	0.02
Blood CPK increased	0	0	2 (0.1)[c]	0.2	1 (0.2)	0.4	3 (0.2)[c]	0.1
Hepatic function abnormal	1 (0.2)	0.4	1 (0.1)[b]	0.1	0	0	1 (0.1)[b]	0
ALT increased	0	0	0	0	0	0	1 (0.1)[d]	0
AST increased	0	0	0	0	1 (0.2)	0.4	1 (0.1)[d]	0

[a]Incidences are expressed as EAIRs/100 PY to account for variable exposure due to treatment switches at Weeks 16 and 24. [b]This AE was considered treatment-related. [c]Two CPK events were considered treatment-related and 1 CPK event was considered not related. [d]This AE was considered not related to treatment.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; EAIR, exposure-adjusted incidence rate; LTE, long-term extension; PY, person-years.

- No clinically meaningful mean changes were observed through 4 years (Weeks 0-208) in any of the evaluated hematology (**Figure 2**), chemistry (**Figure 3**), or lipid (**Figure 4**) laboratory parameters
  - Laboratory parameters remained within normal ranges for the vast majority of patients throughout this period
  - As expected, due to comorbidities known to be present in this population, such as obesity and metabolic syndrome,[12] baseline levels of cholesterol and triglycerides were elevated
    - A minimal increase (<10 mg/dL) in the mean change from baseline (150 mg/dL) in serum triglycerides was observed with deucravacitinib during the first year of treatment and was:
      - Not considered clinically relevant
      - Not associated with increases in LDL levels (<3 mg/dL)
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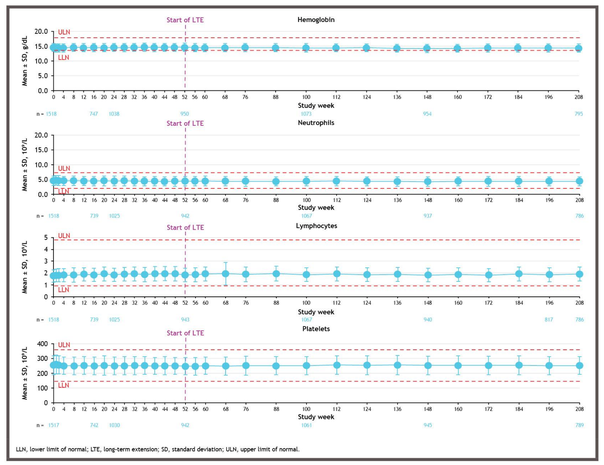

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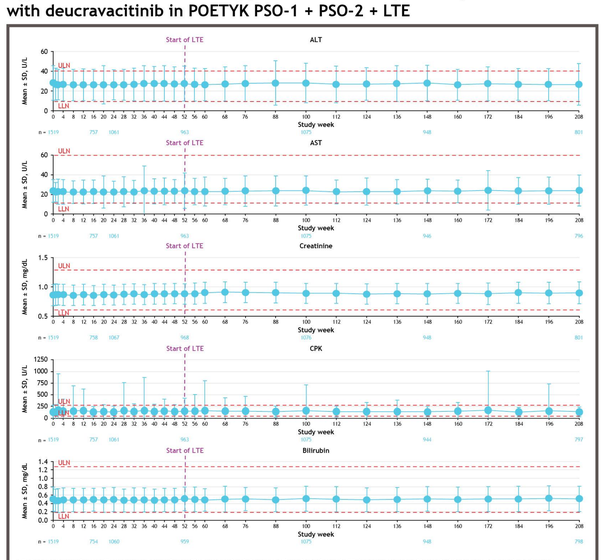

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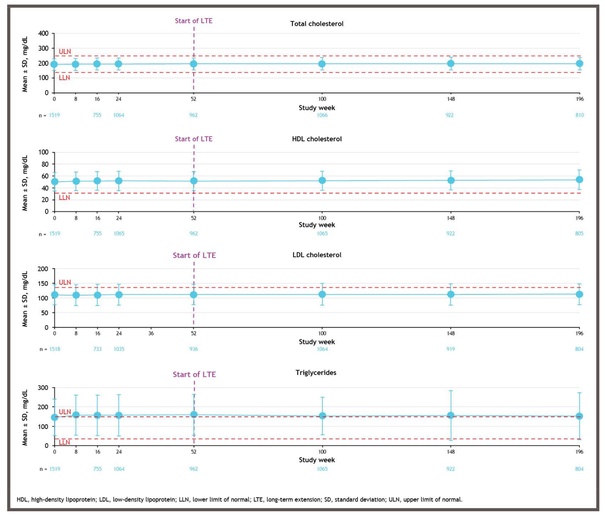

Conclusions

- In the global, phase 3 POETYK PSO-1, PSO-2, and LTE trials in patients with plaque psoriasis, no trends or clinically meaningful mean changes from baseline in hematology, chemistry, or lipid (including triglycerides) laboratory parameters were observed in 1519 patients with 4392.8 PY of deucravacitinib exposure
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Disclosures

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Expected spesolimab plasma exposure following intravenous and subcutaneous dosing in patients with generalized pustular psoriasis

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Aim: To simulate the PK of IV vs SC doses of spesolimab to compare drug exposure profiles and support dosing recommendations in patients with GPP

Background

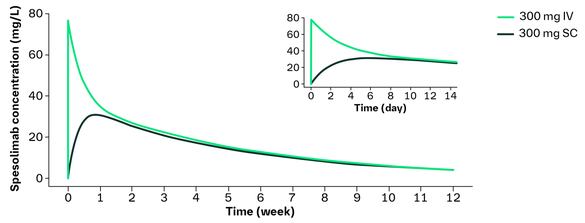
- GPP is a rare, chronic, and potentially life-threatening inflammatory skin disease characterized by episodic flares of widespread pustular eruptions and erythema
- Spesolimab is a first-in-class anti-interleukin-36 receptor monoclonal antibody approved in 48 countries as an IV dosage in adults to treat GPP flares, and in the US and China in both adults and pediatric patients aged 12 years or older and weighing at least 40 kg, as an IV dosage to treat GPP flares and as a SC dosage to treat GPP when not experiencing a flare[1]
- A population PK model was developed using clinical PK data collected in patients treated with spesolimab to simulate the plasma drug exposure levels over time in patients following administration of IV spesolimab vs SC spesolimab

Methods

- A population PK model was developed using individual-level PK, ADA, and covariate data from 18 studies in which patients were treated with IV or SC spesolimab[2]
- The mathematical model quantified the PK of spesolimab following IV and SC administration, including the effect of patient-specific factors on PK (e.g. body weight, disease state, ADA titer)
- The resulting population PK model was used to simulate concentration–time profiles over 12 weeks (84 days) of various IV and SC doses:
  - IV spesolimab 300 mg and 900 mg administered over 90 minutes, as 1 dose or 900 mg as 2 doses (1 week apart), and
  - SC spesolimab 300 mg, 600 mg, 900 mg, and 2250 mg injections, as 1 dose or as 2 doses (1 week apart)
- For each dose, C_{max}, T_{max}, and AUC over 14 and 84 days were summarized

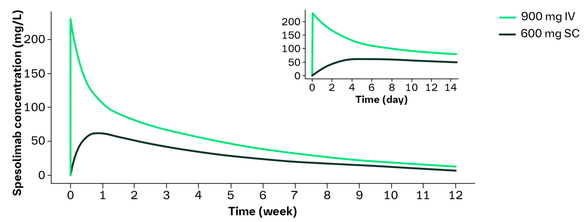
Results

Figure 1. Model-predicted concentration–time profiles of 300 mg IV vs 300 mg SC spesolimab



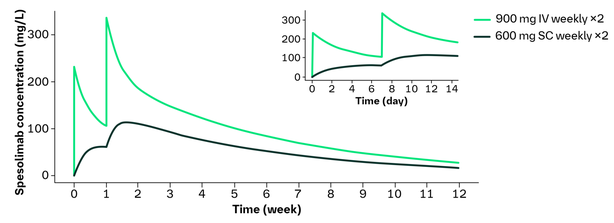
The simulated C_{max} was approximately 2.5-fold greater with 300 mg IV vs 300 mg SC spesolimab. The T_{max} was at the end of the 90-minute infusion for IV spesolimab vs approximately 1 week after dosing for SC spesolimab

Figure 2. Model-predicted concentration–time profiles of 900 mg IV vs 600 mg SC spesolimab



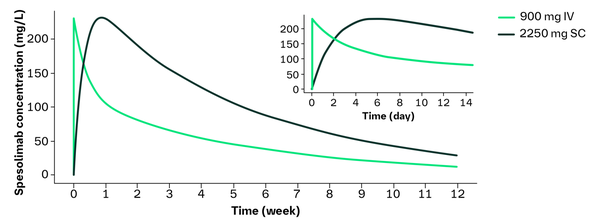
The simulated C_{max} was approximately 3.7-fold greater with 900 mg IV vs 600 mg SC spesolimab. The T_{max} was at the end of the 90-minute infusion for IV spesolimab vs approximately 1 week after dosing for SC spesolimab

Figure 3. Model-predicted concentration–time profiles of 900 mg IV ×2 vs 600 mg SC ×2 spesolimab



When administered as a 2-dose regimen, exposure increased due to accumulation. However, the C_{max} was still approximately 3-fold greater with IV vs SC dosing after the second dose. Similarly, the T_{max} occurred approximately 1 week after each dose of SC compared with immediately after the end of each 90-minute IV infusion

Figure 4. Model-predicted concentration–time profiles of 900 mg IV vs 2250 mg SC spesolimab



A SC dose of 2250 mg was required to attain a target C_{max} equivalent to that of 900 mg IV spesolimab. With the SC dose, T_{max} was delayed 1 week and AUC was almost twice as large; most importantly, a SC injection of this size is not clinically feasible (equivalent to 15 injections of the 150 mg SC pre-filled syringe)

Summary exposure metrics after single IV or SC dose in patients with GPP

Dose (mg)	C_{max} (mg/L)	T_{max} (day)	AUC (mg/L*day) 14-day	AUC (mg/L*day) 84-day
IV				
300	77.1	0.07	557	1400
900	231	0.07	1670	4230
IV weekly ×2				
900	337	7.07	2710	8370
SC				
2250	232	6.09	2750	8710
300	30.9	6.08	367	1150
600	61.8	6.09	734	2310
900	92.8	6.09	1100	3470
SC weekly ×2				
600	115	11.9	1070	4580

Simulated spesolimab exposures demonstrated that the C_{max} and AUC of the single-dose 900 mg IV route of administration consistently exceeded that of all feasible single doses of SC spesolimab. A similar trend was observed for the IV and SC 2-dose regimens. Slow absorption is expected with the SC formulation, with T_{max} attained immediately following 90-minute infusion for single IV doses vs approximately 1 week after SC injection

Conclusions

- PK data from this simulation suggest that treatment with IV and SC spesolimab can result in differences in drug exposure in clinical practice
- Significantly higher C_{max} and more rapid T_{max} was observed for the IV vs SC doses of spesolimab
- To match the C_{max} of the 900 mg IV dose, a SC dose 2.5× greater (2250 mg, equivalent to 15 injections of the 150 mg SC pre-filled syringe) would be required
- The immediate and high bioavailability of IV spesolimab compared with SC spesolimab are supportive of the use of IV spesolimab in acute GPP flare treatment and SC spesolimab in treating GPP when not experiencing a flare

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Abbreviations

ADA, anti-drug antibody; AUC, area under the curve; C_{max}, peak plasma concentration; GPP, generalized pustular psoriasis; IV, intravenous; PK, pharmacokinetics; SC, subcutaneous; T_{max}, time to peak plasma concentration

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Four-weekly dosing intervals with subcutaneous spesolimab appear to be required for optimal prevention of generalized pustular psoriasis flares: Data from the Effisayil® 2 and Effisayil® ON trials

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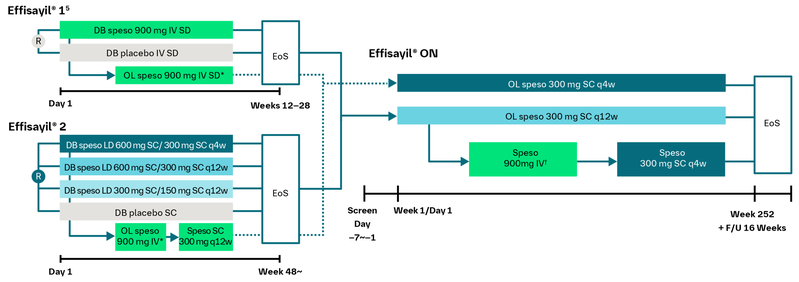
Aim: To present data from the Effisayil® 2 and Effisayil® ON OLE trials, comparing the relative efficacy of a q4w vs q12w dosing schedule of spesolimab SC for preventing GPP flares

Background

- GPP is a chronic, heterogeneous, unpredictable, and potentially life-threatening neutrophilic inflammatory skin disease that exerts a considerable burden on patients and healthcare systems[1]
- Spesolimab is a first-in-class anti-interleukin-36 receptor monoclonal antibody approved in 48 countries as an IV dosage in adults to treat GPP flares, and in the US and China in adults and pediatric patients aged 12 years or older and weighing at least 40 kg, as an IV dosage to treat GPP flares and as a SC dosage to treat GPP when not experiencing a flare[2]
- Effisayil® 2, a randomized, placebo-controlled, Phase IIb trial (NCT04399837),[3] provided dose-ranging data for three SC dose regimens, and evaluated the efficacy, safety, and tolerability of spesolimab for the prevention of GPP flares compared with placebo
- Effisayil® ON (NCT03886246)[4] is a non-randomized, long-term extension study to assess the efficacy and safety of spesolimab in preventing reoccurrence of flares

Methods

Figure 1. Study designs



*900 mg IV dose given for GPP flare during DB treatment period. †900 mg IV dose given for GPP flare during treatment period.

Effisayil® 2

- Participants:
  - History of GPP and GPPGA score of 0 or 1* at screening/randomization
  - ≥2 past GPP flares with fresh pustulation†
- Spesolimab dosing regimens were LD 300 mg SC/ 150 mg SC q12w, LD 600 mg SC/300 mg SC q12w, or LD 600 mg SC/300 mg SC q4w
- Primary endpoint was time to GPP flare‡ and key secondary endpoint was the occurrence of at least one GPP flare, both up to Week 48

Effisayil® ON

- Participants completed the treatment period in prior spesolimab trials, including Effisayil® 2, without premature discontinuation
- Dose selection based on treatment response in previous trials:
  - Patients who did not require OL spesolimab 900 mg IV in previous trial, or patients who received placebo, received OL spesolimab 300 mg SC q12w
  - Patients who required OL spesolimab 900 mg IV during the previous trial received an intensified treatment regimen with OL spesolimab 300 mg SC q4w
  - Dose regimen could be escalated or de-escalated based on specific criteria related to changes in GPPGA total score and pustulation subscore, and history of flares in previous trial
- Primary endpoint was TEAEs up to Week 252; secondary endpoints were reoccurrence of a GPP flare§ and time to achievement of a GPPGA score of 0 or 1¶

*GPPGA score of 0 or 1 is clear or almost clear skin. †Participants not on concurrent GPP treatment at randomization must have had ≥2 flares in the previous year; those on concurrent GPP treatment within 12 weeks prior to randomization must have a history of flaring during, or after dose reduction, or discontinuation of, concurrent treatment. ‡GPP flare defined as an increase in GPPGA total score of ≥2 and pustulation subscore of ≥2. §GPP flare defined as a ≥2-point increase in GPPGA total score with pustulation subscore of ≥2 (GPPGA score 0 or 1 at screening), or ≥1-point increase in GPPGA score and presence of fresh pustulation (GPPGA score 2 at screening); further reoccurrence of GPP flare was defined based on the participant's GPPGA score improvement after each rescue treatment. ¶Secondary endpoint was in participants who received 900 mg IV spesolimab for flare treatment.

Results

Effisayil® 2

- Spesolimab 300 mg SC q4w* versus 300 mg SC q12w* data indicate the need for q4w dosing
- Spesolimab 300 mg SC q4w* led to nearly two-thirds fewer participants experiencing GPP flares (10.0% [3/30] of participants [12.7% when exposure adjusted] in the q4w arm vs 29.0% [9/31] in the q12w arm)
- Effisayil® 2 demonstrated an 84% reduction in GPP flares for participants in the q4w arm compared with placebo

Table 1. Time to the GPP flare, up to Week 48

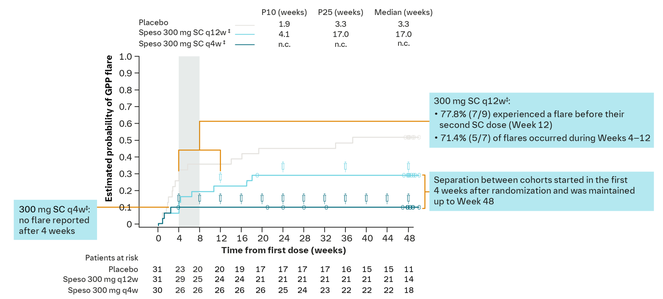
	Placebo	Spesolimab 300 mg SC q12w*	Spesolimab 300 mg SC q4w*
Participants, N (%)	31 (100.0)	31 (100.0)	30 (100.0)
Participants with GPP flares, n (%)	16 (51.6)	9 (29.0)	3 (12.7¶)
Probability of GPP flare at Week 48, Kaplan–Meier estimate (95% CI)		0.290 (0.163, 0.484)	0.100 (0.33, 0.279)
HR for time to GPP flare vs placebo (98% CI)†		0.468 (0.206, 1.064)	0.157 (0.046, 0.541)
P-value‡		0.0269	0.0005
Risk difference for GPP flare occurrence vs placebo (95% CI)§		−0.225 (−0.462, 0.013)	−0.390 (−0.621, −0.159)
P-value			0.0013

*Following a 600 mg SC loading dose. †Cox regression model stratified by the use of systemic GPP medications at randomization. ‡Log-rank test stratified by the use of systemic GPP medications at randomization. §Cochran–Mantel–Haenszel test after multiple imputations, stratified by the use of systemic GPP medications at randomization. ¶Exposure adjusted.

Effisayil® ON

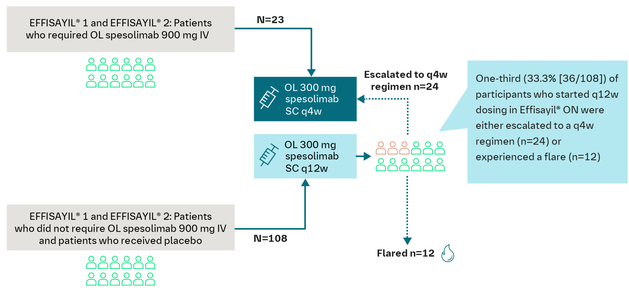
- OL spesolimab SC dosing (300 mg q12w) data from Effisayil® ON further support the need for q4w dosing when initiating treatment for prevention of GPP flares

Figure 2. Time to GPP flare, up to Week 48 (EM, PM) in Effisayil® 2*†



*EM, primary estimand for randomized treatment period, where any use of rescue medication with spesolimab IV or investigator-prescribed standard of care is considered as GPP flare; PM, primary method for censoring, which is made at the earliest date of end of study – Day 351 if no intercurrent event. †Probability of event is estimated by the Kaplan–Meier approach. ‡Following a 600 mg SC loading dose.

Figure 3. Effisayil® ON



Conclusions

- **Effisayil® 2 and Effisayil® ON results suggest that spesolimab 300 mg SC q4w* is the optimal dosing regimen for prevention of GPP flares**
- **Further research is needed to understand the mechanisms underlying superior flare prevention with q4w dosing**

*Following a 600 mg SC loading dose.

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Abbreviations

DB, double-blind; EM, Primary estimand for the randomized maintenance treatment period in Effisayil® 2 with use of investigator prescribed standard of care for GPP or use of OL spesolimab IV for GPP flare treatment regarded as event or treatment failure; EoS, end of study; F/U, follow-up; GPP, generalized pustular psoriasis; GPPGA, Generalized Pustular Psoriasis Physician Global Assessment; HR, hazard ratio; IV, intravenous; LD, loading dose; n.c., not calculable; OL, open-label; OLE, open-label extension; PM, Primary method for handling missing data for time-to-event endpoints; q4w, every 4 weeks; q12w, every 12 weeks; R, randomization; SC, subcutaneous; SD, single dose; Speso, spesolimab; TEAE, treatment-emergent adverse event.

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Boehringer Ingelheim

Enabling access to prognostic gene expression profile (GEP) testing for invasive melanoma by

Background

- Melanoma diagnoses can be challenging to achieve definitively.[1-3]
- Ancillary testing, typically utilized by the pathologist, can disambiguate problematic lesions and help provide a definitive diagnosis.[4]
- The 23-GEP provides test results of suggestive of benign lesion, suggestive of malignant lesion, or intermediate (cannot exclude malignancy) and is recommended by guideline organizations including the National Comprehensive Cancer Network, American Society of Dermatopathology: Appropriate Use Criteria for Ancillary Diagnostic Testing, the American Academy of Dermatology Guidelines of Care for the Management of Primary Cutaneous Melanoma, and the Skin Cancer Prevention Working group.[4-7]
- The **diagnostic 23-GEP** test has demonstrated accuracy metrics of 90.4 – 94.9% sensitivity and 92.5 – 96.2% specificity including 3 studies with known outcomes.[8-12]
- The **prognostic 31-GEP** test stratifies, independent of clinicopathologic factors, patients with cutaneous melanoma into groups at low, intermediate, or high risk of recurrence, metastasis, or death based on the patient's molecular risk.[13-17]
- Clinicians use the 31-GEP results to make risk-aligned decisions about sentinel lymph node biopsy, surveillance imaging, adjuvant therapy, and follow-up schedule decisions.[18-20]
- Both diagnostic ancillary tests and prognostic tests require tissue to perform, which is a limited resource. Some ancillary testing can take weeks to months to provide results leading to a definite diagnosis.
- The 23-GEP ancillary diagnostic test utilizes the **same base material, RNA**, as the 31-GEP test and is performed in the same laboratory.[21,22]
- **Here, we describe clinical trends that help achieve a definitive diagnosis and provide access to vital prognostic testing utilizing the same tissue.**

Methods

- The study includes clinical cases submitted to Castle Biosciences for 23- and/or 31-GEP testing with results reported between March 1 and July 31, 2023.

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Diagnostic 23-GEP clinical orders

Table 1. Patient Characteristics

	Gender (%)	Age (median, (range))
Female (%)	57.4%	49 (4 – 90+)
Male (%)	42.6%	49 (5 – 90+)

Table 2. Biopsy Type

Biopsy Description*	
Shave	88.4%
Punch	7.3%
Excisional	3.6%
Re-excision, WLE	0.1%

*Biopsy percentage was calculated from orders where biopsy type was provided. Biopsy type was provided for 68.1% of orders.

Table 3. 23-GEP Turnaround Time

Turnaround Time*	
Median	4 days

*Turnaround time was calculated as the number of business days (Monday – Friday) from the date the tissue was received until the report date.

- 23-GEP results are returned quickly (43% provided in 3 days or less), avoiding delayed diagnoses for difficult lesions.

Table 4. Clinical result stratification

23-GEP Test Result	Orders (%)
Benign	60.1%
Malignant	19.9%
Intermediate	13.4%
MGF/Fail	6.7%

Table 5. Lesions with resolved ambiguity

Actionable Test Result*	
Resolved ambiguity	79.9%

*23-GEP results of either benign or malignant are considered actionable.

Prognostic 31-GEP Eligibility

- Clinicians can order 23-GEP and 31-GEP on the sam tumor tissue specimen for most samples that receiv a 23-GEP malignant result.

Table 6. Biopsies eligible for 31-GEP

31-GEP Eligible*	
≥ 40% tumor content	81.5%

*Of patients with 23-GEP malignant results, percentage with ≥ 40% tumor volume (minimum tumor content required for 31-GEP).

Conclusions

- ~80% of cases tested with 23-GEP receive an actionable result in a median of 4 business days.
- ~60% of ambiguous lesions received a benign 23-GEP test result, reducing overdiagnosis and overtreatment for diagnostically challenging lesions.
- ~80% of clinically tested lesions with 23-GEP malignant results have sufficient biopsy tumor content for 31-GEP testing without requesting additional tissue.

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Skin Clearance, Treatment Response Off-therapy, and Safety of Tapinarof Cream 1% Once Daily: Results from ADORING 3, a 48-week Phase 3 Trial in Adults and Children Down to 2 Years of Age with Atopic Dermatitis

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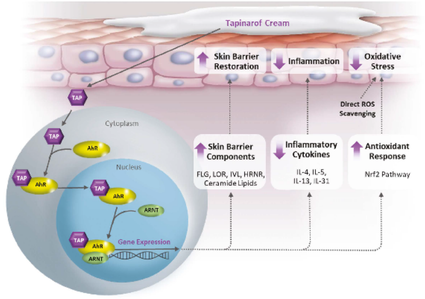
INTRODUCTION

- Topical therapies remain the cornerstone of atopic dermatitis (AD) treatment, regardless of disease severity or age[1,2]
  - However, there can be a significant treatment burden due to requirements for frequent application (e.g., twice daily) or preventative long-term treatment (e.g., twice weekly) due to rapid loss of response after stopping therapy[1–3]
  - Continuous, long-term therapy may also increase the risk of adverse events[1,2]
- There is a need for well-tolerated, efficacious, non-steroidal topicals suitable for all patients, with less frequent application, both for acute and long-term treatment, including as maintenance and with treatment-free intervals with a sustained response
- Tapinarof (VTAMA®, Dermavant Sciences, Inc.) is a non-steroidal, topical aryl hydrocarbon receptor (AhR) agonist, approved by the FDA for the treatment of plaque psoriasis in adults,[4] with no restrictions on duration, location, or extent of use
- Tapinarof binds to and activates AhR to restore the skin barrier through upregulation of skin barrier components, to downregulate pro-inflammatory cytokines, and to reduce oxidative stress (**Figure 1**)[2]
- In two phase 3 AD trials, ADORING 1 and 2, tapinarof cream 1% once daily (QD) demonstrated superior efficacy versus vehicle and was well tolerated in adults and children down to 2 years of age[5]
  - The primary efficacy endpoint of Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD™) score of 0 or 1 and ≥2-grade improvement from baseline was highly statistically significant with tapinarof versus vehicle in both trials: 45.4% vs 13.9% and 46.4% vs 18.0% (both $P<0.0001$)
- In a 4-week maximal usage pharmacokinetics (MUPK) trial, tapinarof cream 1% QD was well tolerated with no-to-minimal systemic exposure in children aged 2–17 years, even with extensive AD (up to 90% body surface area [BSA]; mean 42.8%)[6]
- The ADORING phase 3 program in patients down to 2 years of age with AD evaluated the same dose and frequency as the adult psoriasis trials

Figure 1. Proposed Mechanism of Action of Tapinarof[2]



AhR, aryl hydrocarbon receptor; ARNT, aryl hydrocarbon receptor nuclear translocator; FLG, filaggrin; HRNR, hornerin; IL, interleukin; IVL, involucrin; LOR, loricrin; Nrf2, nuclear factor erythroid 2-related factor 2; ROS, reactive oxygen species; TAP, tapinarof.

OBJECTIVE

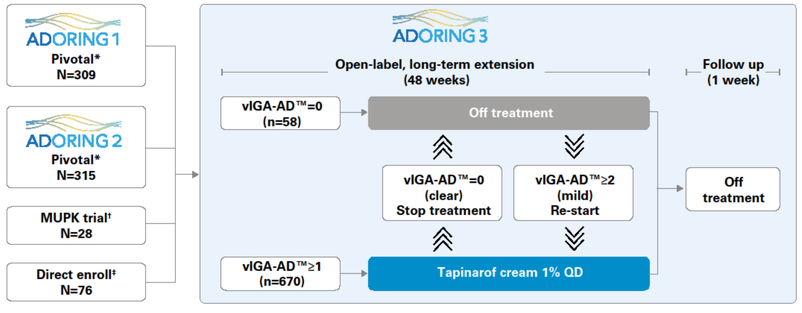
- To present skin clearance rates, treatment response off therapy, safety, and tolerability outcomes from ADORING 3, a 48-week, open-label, long-term extension trial

METHODS

Trial Design

- In the long-term extension trial, ADORING 3, eligible patients from ADORING 1 and 2, from a 4-week maximal usage pharmacokinetics trial, and tapinarof-naive patients with mild AD, or moderate or severe AD, that did not meet inclusion criteria for ADORING 1 or 2, received up to 48 weeks of open-label tapinarof cream 1% QD, followed by a 1-week follow-up period off-treatment (**Figure 2**)
- Patients were treated with tapinarof based on their vIGA-AD™ score:
  - **Complete disease clearance**: Patients entering ADORING 3 with any disease activity (vIGA-AD™≥1) were treated with tapinarof until complete disease clearance (vIGA-AD™=0 [clear])
  - **Treatment-free interval**: After achieving complete disease clearance, patients discontinued therapy and were monitored to determine the duration of the treatment-free interval (maintenance of clear or almost clear skin off treatment)
  - **Recapture of response and absence of tachyphylaxis**: Patients whose AD returned to mild (vIGA-AD™≥2) were re-treated until complete clearance was achieved again

Figure 2. ADORING 3 Trial Design



The vIGA-AD™ scale is copyright ©2017 Eli Lilly and Company – Used with the permission under a Creative Commons Attribution-NoDerivatives 4.0 International License. Patients could use moisturizers but only on non-lesional skin. *Patients were adults and children down to 2 years of age with a clinical diagnosis of AD by Hanifin and Rajka criteria,[7] a vIGA-AD™ score of ≥3 (moderate or severe), an EASI score of ≥6, and BSA involvement of 5–35% at screening and baseline. †Patients were adolescents and children aged 2–17 years with a clinical diagnosis of AD by Hanifin and Rajka criteria,[7] a vIGA-AD™ score of ≥3 (moderate or severe) and BSA involvement of ≥35% for children aged 2–11 years or ≥25% for adolescents aged 12–17 years. ‡Pediatric patients aged 2–17 years with mild AD (vIGA-AD™=2), or moderate or severe AD, that did not meet inclusion criteria for ADORING 1 and 2.
AD, atopic dermatitis; BSA, body surface area; EASI, Eczema Area and Severity Index; MUPK, maximal usage pharmacokinetics; QD, once daily; vIGA-AD™, Validated Investigator Global Assessment for Atopic Dermatitis™.

Outcome Measures

Efficacy

- **Complete disease clearance**: The proportion of patients entering with or achieving complete disease clearance (vIGA-AD™=0)
- **Clear or almost clear skin**: The proportion of patients entering with or achieving a vIGA-AD™ score of 0 (clear) or 1 (almost clear)
- **Treatment-free interval**: Mean duration of the treatment-free interval, defined as maintenance of clear or almost clear skin (vIGA-AD™=0 or 1) off treatment, after first achieving complete disease clearance (vIGA-AD™=0) and discontinuing treatment
- **Maintenance of response**: Maintenance of clear or almost clear skin (vIGA-AD™=0 or 1) on either continuous or intermittent treatment (absence of tachyphylaxis) over 48 weeks

Safety and Tolerability

- Safety assessments included the incidence and frequency of treatment-emergent adverse events (TEAEs)
- Adverse events of special interest (AESI)
- Investigator- and patient- or parent/caregiver-assessed Local Tolerability Scale (LTS) scores

Statistical Analyses

- Efficacy endpoints were summarized descriptively using observed cases in the intention-to-treat population
- Safety assessments were summarized descriptively for the intention-to-treat population

RESULTS

ADORING 3 Baseline Patient Demographics and Disease Characteristics

- 728 patients enrolled in ADORING 3; this included 76 children who enrolled directly (**Table 1**)
  - Pediatric patients (aged 2–17 years) comprised 83.0% of the trial population
  - ~47% patients were non-white (White, 52.6%; Black or African American, 30.1%; Asian, 11.1%; other race categories, 4.4%)
- Patients had a wide spectrum of AD at baseline, from clear (vIGA-AD™=0) to severe (vIGA-AD™=4), depending on their route into ADORING 3 (**Table 1**)
- Tapinarof-treated patients from ADORING 1 and 2 had less severe disease at ADORING 3 baseline than vehicle-treated patients or patients from the other arms

Table 1. ADORING 3 Baseline Patient Demographics and Disease Characteristics

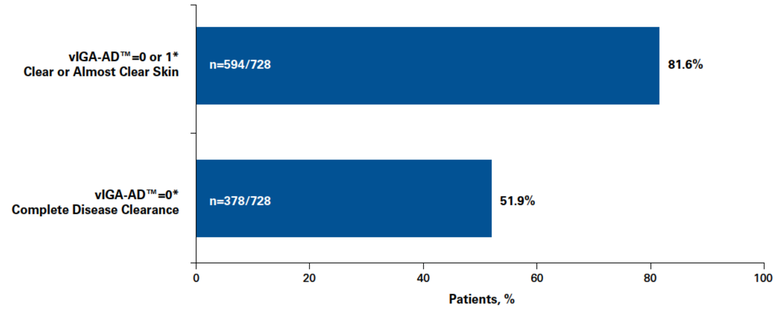
	ADORING 3				
	ADORING 1 and 2 (pivotal trials)		MUPK trial	Direct enroll	Overall
	Tapinarof cream 1% QD (n=431)	Vehicle QD (n=193)	Tapinarof cream 1% QD (n=28)	Tapinarof naïve (n=76)	Total (N=728)
Age, years, mean (SD)	16.1 (16.3)	16.4 (15.8)	8.8 (4.9)	7.9 (4.8)	15.0 (15.3)
Male, n (%)	201 (46.6)	85 (44.0)	19 (67.9)	34 (44.7)	339 (46.6)
vIGA-AD™, n (%)					
0 – Clear	51 (11.8)	6 (3.1)	1 (3.6)	0 (0.0)	58 (8.0)
1 – Almost clear	157 (36.4)	26 (13.5)	6 (21.4)	0 (0.0)	189 (26.0)
2 – Mild	153 (35.5)	63 (32.6)	12 (42.9)	40 (52.6)	268 (36.8)
3 – Moderate	69 (16.0)	88 (45.6)	9 (32.1)	16 (21.1)	182 (25.0)
4 – Severe	1 (0.2)	10 (5.2)	0 (0.0)	20 (26.3)	31 (4.3)
EASI, mean (SD)	3.3 (3.5)	8.2 (6.7)	9.2 (5.6)	17.6 (16.3)	6.3 (8.2)
BSA, %, mean (SD)	5.7 (6.5)	12.4 (10.7)	18.0 (11.7)	31.6 (27.8)	10.6 (14.3)

BSA, body surface area; EASI, Eczema Area and Severity Index; MUPK, maximal usage pharmacokinetics; QD, once daily; SD, standard deviation; vIGA-AD™, Validated Investigator Global Assessment for Atopic Dermatitis™.

Patients Achieving Complete Disease Clearance (vIGA-AD™=0) and Clear or Almost Clear Skin (vIGA-AD™=0 or 1)

- Overall, 51.9% (n=378/728) of patients achieved complete disease clearance (vIGA-AD™=0 [clear]) at least once during the trial (**Figure 3**)
- In addition, 81.6% (n=594/728) achieved a vIGA-AD™ score of 0 (clear) or 1 (almost clear) at least once during the trial (**Figure 3**)

Figure 3. Proportion of Patients who Achieved Clear or Almost Clear Skin (vIGA-AD™=0 or 1) and Complete Disease Clearance (vIGA-AD™=0)



*Patients entering with or achieving the outcome at any time at least once during ADORING 3.
Intention-to-treat; observed cases.
QD, once daily; vIGA-AD™, Validated Investigator Global Assessment for Atopic Dermatitis™.

Treatment-free Interval After Complete Disease Clearance

- After first achieving complete clearance and discontinuing treatment (n=378), the mean duration of the first treatment-free interval was 79.8 consecutive days off therapy (standard deviation [SD], 81.4 days)
- Recapture of response was demonstrated
  - After achieving vIGA-AD™=0 and discontinuing tapinarof, patients whose vIGA-AD™ score returned to ≥2 (mild) off treatment could regain vIGA-AD™=0 when re-treated
  - The overall mean duration of treatment-free intervals across the trial was 74.7 consecutive days (SD, 76.0 days), demonstrating the ability for a patient to achieve complete disease clearance repeatedly and experience almost 3 months off therapy

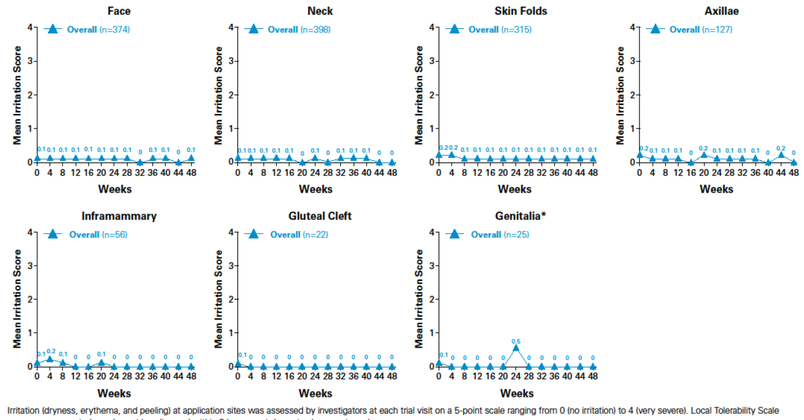
Maintenance of Response (No Tachyphylaxis)

- Tapinarof demonstrated maintenance of clear or almost clear skin (vIGA-AD™=0 or 1) on either continuous or intermittent therapy, with no tachyphylaxis, for up to 48 weeks

Tolerability

- Tapinarof cream was well tolerated, with mean patient or parent/caregiver evaluations indicating no or minimal burning/stinging and itching with long-term treatment for 48 weeks, even with intermittent treatment
- Mean investigator evaluations indicated that patients had no or minimal irritation (LTS=0) at all visits over the 48-week trial, with improvements in tolerability scores compared with ADORING 3 pre-treatment baseline
- Tapinarof was well tolerated locally, even when applied on sensitive skin across all evaluations for 48 weeks (**Figure 4**)
  - At baseline in ADORING 3, 72.5% of patients had AD affecting the head and neck region

Figure 4. Excellent Tolerability Across Sensitive Skin Areas in ADORING 3



Irritation (dryness, erythema, and peeling) at application sites was assessed by investigators at each trial visit on a 5-point scale ranging from 0 (no irritation) to 4 (very severe). Local Tolerability Scale scores were reported pre-dose at baseline and within 2 hours post dose at subsequent weeks.
*A mean irritation score of 0.5 was observed at Week 24 (mean of scores for all affected patients); this was due to one patient who had molluscum contagiosum affecting the genitalia, which the investigator determined was unrelated to treatment. QD, once daily.

Safety

- The most frequent TEAEs included folliculitis (12.1%), nasopharyngitis (6.9%), and upper respiratory tract infection (6.9%); trial discontinuations due to TEAEs were low (2.6%)
- AESI of follicular events, contact dermatitis, and headache were mostly mild or moderate and associated with low discontinuation rates (1.0%, 0.4%, and 0%, respectively)

CONCLUSIONS

- Tapinarof cream 1% QD monotherapy demonstrated a high rate of complete disease clearance (51.9%) in a diverse population of adults and children down to 2 years of age with AD
- After discontinuing tapinarof, patients maintained clear or almost clear skin for almost 3 consecutive months (~80 days)
- Clinical response did not decline over time with continuous or intermittent use of tapinarof monotherapy
- There were no new safety signals and low rates of trial discontinuations due to TEAEs
- Long-term application of tapinarof cream demonstrated favorable local tolerability, even on sensitive skin areas including the face and neck and on either continuous or intermittent therapy
- Tapinarof is a once-daily non-steroidal cream that is efficacious and well tolerated with long-term use in AD, and has the potential to be used without restrictions on duration of use, extent of BSA treated, or sites of application

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Ltd., Eli Lilly, EOS, Exeltis, Ferndale Laboratories, Inc., Ferrer, Foamix Pharmaceuticals, Galderma, Genentech, Inc., GlaxoSmithKline, Glenmark Pharmaceuticals, Healthpoint, Ltd, Idera Pharmaceuticals, Incyte, Intendis, Innocutis, Innovail, ISDIN, Johnson & Johnson, Kyowa Kirin, Laboratory Skin Care Inc., LEO Pharma, L'Oréal, 3M, Maruho Co., Ltd., Medical International Technologies, Merck, Medicis Pharmaceutical Corp., Merz Pharma, NanoBio, Novartis AG, Noven Pharmaceuticals, Nucryst Pharmaceuticals Corp., Obagi, Onset Dermatologics, Ortho Neutrogena, Pediapharma, Pfizer, Promius Pharma, PuraCap, Pharmaderm, QLT, Inc., Quinnova Pharmaceuticals, Quatrix, Regeneron, Sanofi, Serono (Merck Serono International SA), SkinMedica, Inc., Stiefel Laboratories, Inc., Sun Pharma, Taro Pharmaceutical Industries, Toler Rx, Triax Pharmaceuticals, UCB Pharma, Valeant Pharmaceuticals Intl., Warner Chilcott, XenoPort, and ZAGE. 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Real-world effectiveness of tralokinumab in adults with atopic dermatitis: Interim data on improvements in patients with head and neck atopic dermatitis after up to 9 months of treatment in the TRACE study

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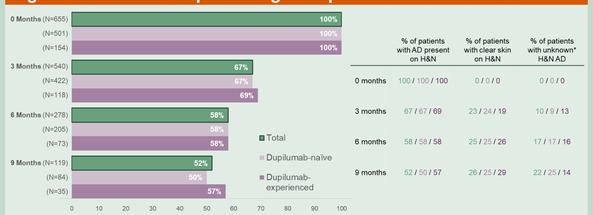
Objectives

- To evaluate the effectiveness of tralokinumab treatment on AD signs and symptoms in patients with head and neck (H&N) AD in an interim analysis of the noninterventional TRACE study

Results

- In patients with baseline H&N AD, the percentages who still reported H&N AD decreased through 9 months of tralokinumab (**Fig. 1**)

Figure 1. Decrease in percentages of patients with H&N AD.

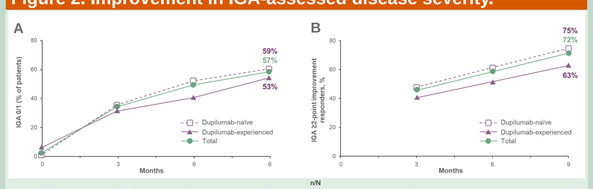


	% of patients with AD present on H&N	% of patients with clear skin on H&N	% of patients with unknown* H&N AD
0 months	100 / 100 / 100	0 / 0 / 0	0 / 0 / 0
3 months	67 / 67 / 69	23 / 24 / 19	10 / 9 / 13
6 months	58 / 58 / 58	25 / 25 / 26	17 / 17 / 16
9 months	52 / 50 / 57	26 / 25 / 29	22 / 25 / 14

*Information on AD localization not available. Percentages are rounded to the nearest whole number.

- Percentages of patients with IGA 0/1 increased from 1% at baseline to 34% at 3 months and 57.4% at 9 months of tralokinumab (**Fig. 2A**)
- In patients with baseline IGA ≥2, the percentages achieving ≥2 improvement in IGA increased from 46% at 3 months to 72% at 9 months of tralokinumab (**Fig. 2B**)

Figure 2. Improvement in IGA-assessed disease severity.

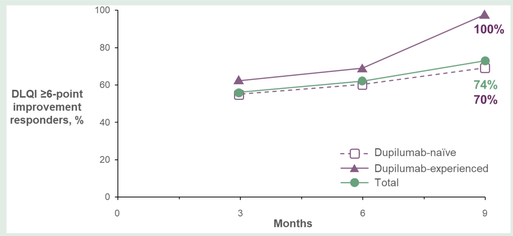


n/N			
Dupilumab-naïve	1/497	138/401	96/187	42/71
Dupilumab-experienced	8/153	34/111	25/63	16/30
Total	9/650	172/512	121/250	58/101
Dupilumab-naïve	181/378	110/179	51/68
Dupilumab-experienced	39/96	30/58	17/27
Total	220/474	140/237	68/95

Percentages are rounded to the nearest whole number.

- In patients with baseline DLQI ≥6, the majority (57.9%) achieved ≥6 improvement in DLQI by 3 months of tralokinumab (**Fig. 3**)
- Percentages of patients with RECAP<6 increased from baseline to 9 months of tralokinumab treatment (**Fig. 4**)
- Mean PP-NRS and Sleep NRS improved from baseline to 9 months of tralokinumab treatment (**Fig. 5**)

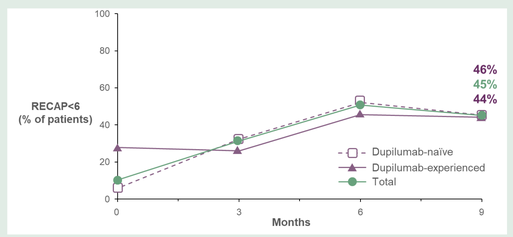
Figure 3. Clinically meaningful improvement in DLQI.



n/N			
Dupilumab-naïve	71/125	39/63	26/37
Dupilumab-experienced	13/20	10/14	6/6
Total	84/145	49/77	32/43

Percentages are rounded to the nearest whole number.

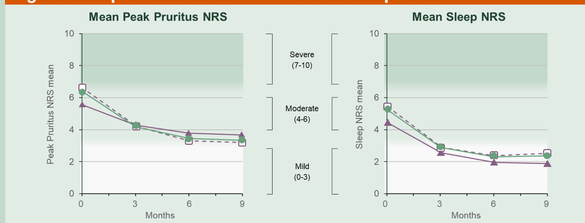
Figure 4. Improvement in patient-reported eczema control.



n/N				
Dupilumab-naïve	10/162	31/95	21/40	10/22
Dupilumab-experienced	11/39	5/19	6/13	4/9
Total	21/201	36/114	27/53	14/31

RECAP<6 identifies patients whose AD is considered completely controlled (RECAP score: 0-1) or mostly controlled (RECAP score: 2-5). Percentages are rounded to the nearest whole number.

Figure 5. Improvements in PP-NRS and Sleep NRS.



N				
Dupilumab-naïve	293	164	78	43
Dupilumab-experienced	94	49	33	16
Total	387	213	111	59
Dupilumab-naïve	242	140	67	40
Dupilumab-experienced	63	30	17	13
Total	305	170	84	53

- Similar improvements were observed across endpoints in both dupilumab-naive and dupilumab-experienced patients

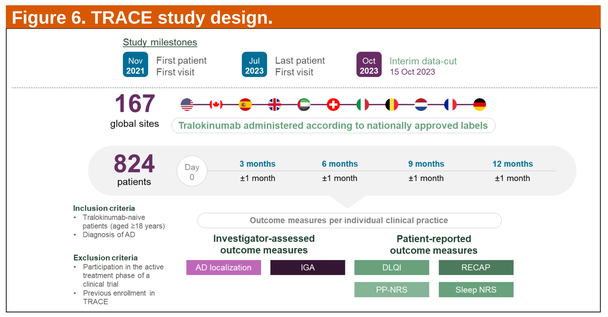
Background

- AD is an inflammatory skin disease that can affect multiple body areas[1]
- H&N region involvement is reported in 72% of patients with moderate-to-severe AD[1]
- AD with involvement of H&N, more than other body regions, is associated with social embarrassment, stigmatization, and negative impact on patients' quality of life and mental health[2]
- Tralokinumab is a high-affinity monoclonal antibody that specifically targets IL-13 and is indicated for treatment of moderate-to-severe AD[3,4]

Methods

- TRACE is a prospective, noninterventional, international, single-cohort study of adult patients with AD who were prescribed tralokinumab according to national approved labels (**Fig. 6**)
- Patients from 167 sites from 11 countries across Europe, North America, and the Middle East, were enrolled in TRACE between November 2021 and July 2023
- At data cutoff for this interim analysis (15 October 2023), not all patients had completed all visits
- This subanalysis included patients with AD involvement on the face, scalp, and/or neck at baseline
- Outcome measures collected included IGA, DLQI, RECAP, PP-NRS, and Sleep NRS, as per individual clinical practice
- Data presented as observed for baseline, 3-, 6-, and 9-month visits

Figure 6. TRACE study design.



Baseline and Disease Characteristics

- At baseline, 655 of 824 (80%) patients reported H&N AD (**Table 1**)
- Baseline demographics were similar, but dupilumab-naïve patients had higher baseline disease severity and greater impact on QoL vs dupilumab-experienced patients (**Table 1**)

Table 1. Baseline demographics and clinical characteristics.

	Dupilumab-naïve (N = 501)	Dupilumab-experienced (N = 154)	Total (N = 655)
Age (years), mean (SD)	41.1 (17.3)	45.2 (17.9)	42.1 (17.5)
Gender, n (%)			
Female	228 (45.5%)	80 (51.9%)	308 (47.0%)
Male	273 (54.5%)	74 (48.1%)	347 (53.0%)
Race, n (%)			
American Indian or Alaska Native	1 (0.2%)	1 (0.6%)	2 (0.3%)
Asian	29 (5.8%)	10 (6.5%)	39 (6.0%)
Black or African American	14 (2.8%)	7 (4.5%)	21 (3.2%)
Native Hawaiian or Pacific Islander	1 (0.2%)	1 (0.6%)	2 (0.3%)
White	387 (77.2%)	115 (74.7%)	502 (76.6%)
Multiple	2 (0.4%)	1 (0.6%)	3 (0.5%)
BMI (kg/m^2), mean (SD)	26.5 (5.7)	27.2 (5.5)	26.7 (5.7)
Disease duration (years), mean (SD)	19.3 (17.0) *N = 489*	24.8 (19.9) *N = 153*	20.6 (17.8) *N = 642*
IGA 4 (severe disease), n (%)	193 (38.8%)	52 (34.0%)	245 (37.7%)
DLQI, mean (SD)	13.8 (7.7) *N = 287*	10.8 (7.2) *N = 78*	13.2 (7.7) *N = 365*
RECAP<6, n (%)	10 (6.2%) *N = 162*	11 (28.2%) *N = 39*	21 (10.4%) *N = 201*
Peak Pruritus NRS, mean (SD)	6.7 (2.4) *N = 293*	5.6 (2.9) *N = 94*	6.4 (2.6) *N = 387*
Sleep NRS, mean (SD)	5.4 (3.1) *N = 242*	4.4 (3.0) *N = 63*	5.2 (3.1) *N = 305*

Abbreviations

AD, atopic dermatitis; BMI, body mass index; DLQI, Dermatology Life Quality Index; H&N, head and neck; IGA, Investigator's Global Assessment; IL, interleukin; n, number of patients with the indicated metric; N, number of patients with available data; NRS, numeric rating scale; PP-NRS, Peak Pruritus NRS; PRO, patient-reported outcome; QoL, quality of life; RECAP, Recap for atopic eczema; SD, standard deviation; TRACE, Tralokinumab Real World Clinical Use.

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Disclosures

AA has served as a research investigator and/or scientific advisor to AbbVie, Almirall, Arcutis Biotherapeutics, ASLAN, Beiersdorf, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Dermira, EPI, Incyte Corporation, Janssen, LEO Pharma A/S, Lilly, Modmed, Nimbus, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, Sun Pharma, and UCB. **AA** has been a speaker, advisor, and/or investigator for AbbVie, Bayer, Boehringer Ingelheim, Ego Pharmaceuticals, Galderma, Jamjoom Pharma, Janssen, LEO Pharma A/S, Lilly, Novartis, Organon, Pfizer, Sanofi, and Viatris. **JB** has worked in clinical trials for tralokinumab, dupilumab, and upadacitinib. **TF**, **UI**, and **IV** are employees of LEO Pharma A/S. **AEP** has acted as advisor, speaker, investigator, received educational support from or received research funding from LEO Pharma A/S, Novartis, UCB, AbbVie, Almirall, Amgen, BMS, Boehringer Ingelheim, Janssen, La Roche-Posay, Lilly, Pfizer, Celgene, and Sanofi.

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Conclusions

- H&N involvement was common in patients with AD in previous reports,[1] and present at baseline in 80% of patients in the real-world TRACE study
- Among patients with baseline H&N AD, tralokinumab treatment reduced the proportion with H&N involvement to 67% at 3 months and 52% at 9 months
- Tralokinumab improved AD severity and QoL at 3 months (IGA 0/1: 34%; DLQI ≥6 improvement: 58%), with further improvement up to 9 months (IGA 0/1: 57%; DLQI ≥6 improvement: 74%)

Anchored matching-adjusted indirect comparison of the long-term maintenance of efficacy of tralokinumab and lebrikizumab in treating moderate-to-severe atopic dermatitis

Matthias Augustin[1], April Armstrong[2], Naiem Issa[3-5], Anne Sohrt Petersen[6], Rie von Eyben[6], Teodora Festini[6], Tiago Torres[7,8]

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Objectives

- To conduct an anchored matching-adjusted indirect comparison (MAIC) of the efficacy of tralokinumab and lebrikizumab at Week 52 in Week 16 responders

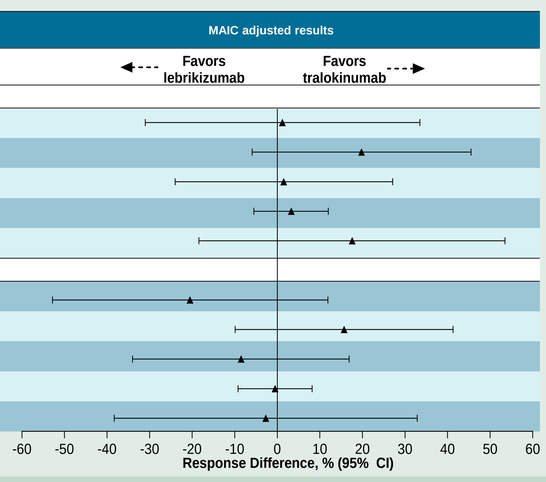
Results

Tralokinumab and lebrikizumab had comparable maintenance of efficacy across endpoints at Week 52

- The MAIC comparison at Week 52 was numerically in favor of tralokinumab for all endpoints with Q2W dosing (**Figure 1**)
  - There were no statistically significant differences between tralokinumab and lebrikizumab for the MAIC comparison for all endpoints
- The MAIC comparison between tralokinumab and lebrikizumab at Week 52 with Q4W dosing showed no significant differences in maintenance of efficacy with:
  - IGA 0/1 and EASI-90 numerically in favor of lebrikizumab (**Figure 1**)
  - EASI-75 numerically in favor of tralokinumab (**Figure 1**)
  - EASI % change from baseline and worst pruritus NRS ≥4-point improvement comparable between lebrikizumab and tralokinumab (**Figure 1**)
- The sensitivity analysis confirmed that there were no significant differences between tralokinumab and lebrikizumab

Figure 1. Response difference for achieving efficacy endpoints for tralokinumab vs lebrikizumab at Week 52

	Lebrikizumab vs. Placebo		Tralokinumab vs. Placebo		Tralokinumab vs. Lebrikizumab		MAIC adjusted results
	Response Difference, %	SE	Response Difference, %	SE	Response Difference, % (95% CI)	*P*-value*	
Q2W							
IGA 0/1 and ≥ 2-pt improvement	18.9	9.7	20.1	13.3	1.2 (-31.0, 33.5)	0.94	
EASI-75	10.0	8.0	29.8	10.4	19.8 (-5.9, 45.5)	0.13	
EASI-90	18.6	7.9	20.1	10.4	1.5 (-24.0, 27.1)	0.91	
EASI % change from baseline	8.1	3.2	11.4	3.1	3.3 (-5.5, 12.0)	0.46	
Pruritus NRS ≥ 4-pt improvement	5.4	11.3	23.0	14.4	17.6 (-18.4, 53.5)	0.34	
Q4W							
IGA 0/1 and ≥ 2-pt improvement	26.7	9.6	6.2	13.4	-20.5 (-52.8, 11.9)	0.22	
EASI-75	13.5	7.8	29.2	10.5	15.7 (-9.9, 41.3)	0.23	
EASI-90	21.5	7.9	13.0	10.4	-8.5 (-34.0, 16.9)	0.51	
EASI % change from baseline	11.3	3.2	10.8	3.1	-0.5 (-9.2, 8.2)	0.91	
Pruritus NRS ≥ 4-pt improvement	12.6	11.1	9.9	14.4	-2.7 (-38.3, 32.9)	0.88	



*A *P*-value of ≤0.05 was considered statistically significant.

Study Limitations

- As with all indirect comparisons, bias due to observed and unobserved differences across the trials cannot be ruled out

Conclusion

- The maintenance of efficacy after 52 weeks was comparable between tralokinumab and lebrikizumab in Week 16 responders
- The differences were not statistically significant for any outcomes
- All Q2W endpoints were numerically in favor of tralokinumab

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Abbreviations

AD, atopic dermatitis; BMI, body mass index; CI, confidence interval; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; IL, interleukin; IPD, individual patient data; LOCF, last observation carried forward; MAIC, Matching-Adjusted Indirect Comparison; N, sample size; N_{eff}, effective sample size after adjusted matching; NRS, numerical rating scale; PDE, phosphodiesterase; Q2W, every 2 weeks; Q4W, every 4 weeks; SD, standard deviation; SE, standard error; TCI, topical calcineurin inhibitors; TCS, topical corticosteroids.

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Background

- Atopic Dermatitis (AD) is a chronic, relapsing, inflammatory skin condition, associated with a high disease burden that impacts patients' lives[1,2]
- Patients with moderate-to-severe AD often require long-term treatment, and biologics are currently recommended as first-line systemic treatment to prevent flares and maintain disease control[3,4]
- Tralokinumab (fully human) and lebrikizumab (humanized) are monoclonal antibodies specifically targeting IL-13 that have demonstrated efficacy in patients with moderate-to-severe AD up to 52 weeks of treatment[5,6]
  - There are no direct head-to-head comparisons of tralokinumab and lebrikizumab
  - Without head-to-head data, indirect comparison methods that adjust for cross-trial differences can be used to compare therapies[7]

Table 1. Key Study Characteristics

	ECZTRA 1 & 2[5,10] Tralokinumab 300 mg	ADvocate 1 & 2[6,11] Lebrikizumab 250 mg
Design	Randomized, double-blind, multicenter, placebo-controlled phase 3	Randomized, double-blind, multicenter, placebo-controlled phase 3
Loading Dose	600 mg on day 0	500 mg at day 0 **and week 2**
Inclusion Criteria	• Age ≥ 18 years with moderate-to-severe AD • History of AD ≥ 1 year • Inadequate response to topical therapy or topicals not advised • EASI ≥ 12 at screening and ≥ 16 at baseline • IGA ≥ 3 • AD involvement of ≥ 10% of the body • Worst daily pruritus NRS ≥ 4 average	• Adults (≥ 18 years) and **adolescents (12-18 years, ≥ 40 kg)** with moderate-to-severe AD • History of AD ≥ 1 year • Inadequate response to topical therapy or topicals not advised • EASI ≥ 16 • IGA ≥ 3 • AD involvement of ≥ 10% of the body
Exclusion Criteria	• Previous enrollment in a tralokinumab trial • Active conditions that may confound AD diagnosis • Treatment within the previous 4 weeks of a systemic immunosuppressant/ immunomodulator, systemic corticosteroid, or 3+ bleach baths in any week • Treatment with TCS, TCI, or topical PDE-4 inhibitor for **2 weeks** prior to randomization	• Previous treatment with lebrikizumab, dupilumab, or tralokinumab • Treatment within the previous 4 weeks of an immunosuppressant/ immunomodulator or photochemotherapy • Use of an investigational drug within 5 half-lives of baseline • Uncontrolled chronic disease that may require oral corticosteroids • Treatment with TCS, TCI, or topical PDE-4 inhibitor for **1 week** prior to baseline visit
TCS during maintenance period	Used at the discretion of the investigator for intolerable symptoms	Intermittent use of **TCS permitted**
Transfer to escape arm	≥2 point increase in IGA and/or lack of EASI-75 response for 4 weeks[a]	**Lack of EASI-50 response**

[a]Specifically, patients with IGA 0 at Week 16 who have IGA ≥ 2 and do not achieve EASI-75 over at least a 4-week period (i.e. over 3 consecutive visits), patients with IGA 1 at Week 16 who have IGA ≥ 3 and do not achieve EASI-75 over at least a 4-week period, or patients with IGA > 1 at Week 16 not achieving EASI-75 over at least a 4-week period were transferred to open-label treatment (tralokinumab 300 mg Q2W with optional use of TCS) and continued their scheduled visit sequence. Transfer to open-label could occur no earlier than Week 22.

Methods

Matching-adjusted indirect comparison

- An anchored MAIC analysis[8,9] was conducted using individual patient data (IPD) from patients in the ECZTRA 1 & 2 tralokinumab trials[5,10], and aggregate data from patients in the ADvocate 1 & 2 lebrikizumab trials[6,11] (**Table 1**)
  - Placebo-adjusted values were utilized for IPD from ECZTRA 1 & 2 patients
- Tralokinumab IPD were weighted to match the baseline and Week 16 characteristics of the lebrikizumab patients
  - Baseline characteristics matched: age, sex, race, BMI, mean AD duration, proportion of IGA 3, mean EASI, and mean worst daily pruritus NRS
  - Week 16 characteristics matched: mean EASI, proportion of IGA 0/1, and mean pruritus NRS

Patient cohort

- Only patients who received active treatment and achieved response at Week 16 were included in the analyses, where response was defined as EASI-75 or IGA 0/1 with ≥ 2-point improvement without use of topical or systemic rescue medication[11]

Outcomes

- Maintenance of efficacy at Week 52: EASI-75 and IGA 0/1 & ≥ 2-point improvement
  - EASI-75 response was assessed in the subset of patients with EASI-75 response at Week 16
  - IGA 0/1 response was assessed in the subset of patients with IGA 0/1 response at Week 16
- Efficacy at Week 52: EASI-90, EASI percent change from baseline, and pruritus NRS ≥ 4-point improvement
  - EASI-90 and EASI percent change from baseline were assessed in the subset of patients with EASI-75 response at Week 16
  - Pruritus NRS ≥ 4-point improvement was assessed in the subset of patients with pruritus ≥ 4-point response at Week 16
- Patients who received rescue medication such as TCS or TCI, discontinued treatment, or transferred to the escape arm were imputed as non-response for binary endpoints and imputed as last observation carried forward (LOCF) for continuous endpoints

Sensitivity analysis

- A sensitivity analysis was made by comparing the analyses generated by using the two estimands reported in the ADvocate 1 & 2 trials
- For the 36-week maintenance period:
  - Patients who received systemic rescue medication, discontinued treatment due to lack of efficacy, or transferred to the escape arm were imputed as non-response
  - Patients who received topical rescue medication or discontinued treatment for any other reasons had values set to missing after this time through to Week 52, and Monte Carlo Markov Chain Multiple imputation was used to impute the missing data

Baseline and Disease Characteristics

- Though baseline characteristics were overall similar between trials (**Table 2**), the following differences were noted:
  - For the treatment groups with dosing schedule Q2W and Q4W as well as the placebo groups, the baseline disease duration was longer in the tralokinumab trials
  - For the treatment groups with dosing schedule Q2W, the proportions of patients with baseline IGA 3 (moderate disease) and Week 16 IGA 0/1 (clear/almost clear disease) response were higher in the tralokinumab trials
  - For the treatment groups with dosing schedule Q4W, the proportions of patients with baseline IGA 3 (moderate disease) and Week 16 IGA 0/1 (clear/almost clear disease) response were higher in the lebrikizumab trials
  - For the placebo groups, the proportions of patients with baseline IGA 3 (moderate disease) and Week 16 IGA 0/1 (clear/almost clear disease) response were similar between the trials

Table 2. Baseline and Week 16 characteristics

		ADvocate 1 & 2[11]	ECZTRA 1 & 2		ADvocate 1 & 2[11]	ECZTRA 1 & 2		ADvocate 1 & 2[11]	ECZTRA 1 & 2	
		Placebo	Placebo		Lebrikizumab Q2W	Tralokinumab Q2W		Lebrikizumab Q4W	Tralokinumab Q4W	
		Baseline characteristics	Baseline characteristics	Weighted summary	Baseline characteristics	Baseline characteristics	Weighted summary	Baseline characteristics	Baseline characteristics	Weighted summary
		N = 60	N = 71	N_{eff} = 28	N = 113	N = 127	N_{eff} = 71	N = 118	N = 130	N_{eff} = 68
Baseline	Age, years (SD)	34 (17)	38 (13)	34 (12)	36 (17)	37 (13)	36 (13)	36 (17)	39 (16)	36 (15)
	Sex, % male	40	56	40	53	57	53	42	51	42
	Mean BMI, kg/m^2 (SD)	25 (5)	26 (6)	25 (6)	26 (7)	26 (5)	26 (6)	26 (6)	26 (6)	26 (6)
	Disease duration, years (SD)	20 (15)	30 (16)	20 (13)	22 (14)	27 (16)	22 (14)	23 (15)	27 (16)	23 (15)
	Race, % white	55	62	55	71	68	71	73	70	73
	IGA 3, %	62	62	62	62	72	62	66	56	66
	Mean DLQI (SD)	15 (8)	17 (6)	15 (6)	15 (7)	16 (8)	15 (7)	15 (8)	15 (7)	15 (7)
	Mean Pruritus NRS (SD)	8 (2)	8 (1)	8 (1)	7 (2)	8 (2)	7 (1)	7 (2)	8 (1)	7 (2)
Week 16	Mean EASI (SD)	2 (2)	3 (3)	2 (2)	3 (3)	3 (3)	3 (3)	2 (3)	3 (3)	2 (2)
	IGA 0/1, %	67	65	67	68	72	68	67	62	67
	Mean Pruritus NRS (SD)	3 (2)	4 (3)	3 (2)	3 (2)	3 (2)	3 (2)	3 (2)	4 (3)	3 (2)

Delgocitinib cream reduces itch and pain in adults with moderate to severe Chronic Hand Eczema: pooled analyses of the Phase 3 DELTA 1 and 2 trials

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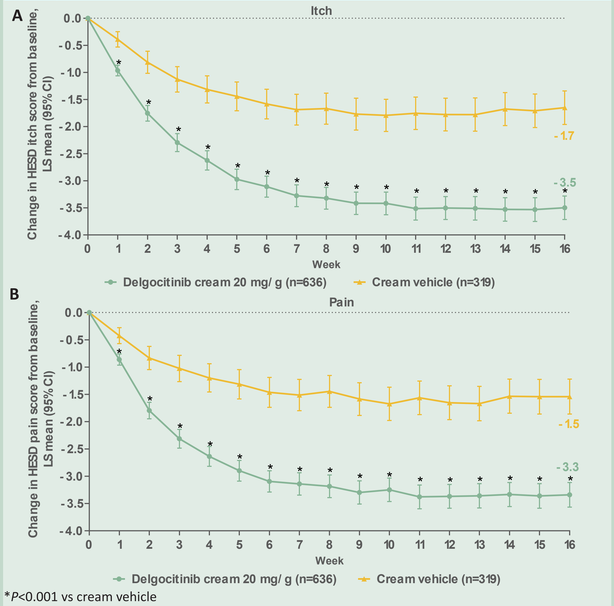
Objectives

- To assess the effect and speed of onset following twice-daily applications of delgocitinib cream 20 mg/g on itch and pain, versus cream vehicle, in adults with moderate to severe Chronic Hand Eczema (CHE)

Results

- For itch, a significant mean reduction from baseline was detected 1 day after the first application of delgocitinib cream (0.75 vs 0.32 cream vehicle; *P*<0.001; **Figure 1A**)
- For pain, a significant mean reduction was detected 3 days after the first application of delgocitinib cream (0.98 vs 0.58 cream vehicle; *P*=0.001; **Figure 1B**)
- Delgocitinib cream 20 mg/g treatment reduced mean itch and pain through to Week 16 versus cream vehicle (**Figure 2**)

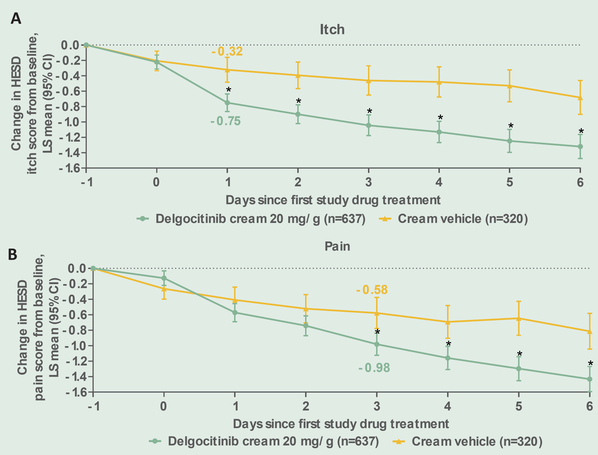
Figure 2. Change in HESD score for itch and pain from baseline to Week 16 (FAS, WOCF)



*P<0.001 vs cream vehicle

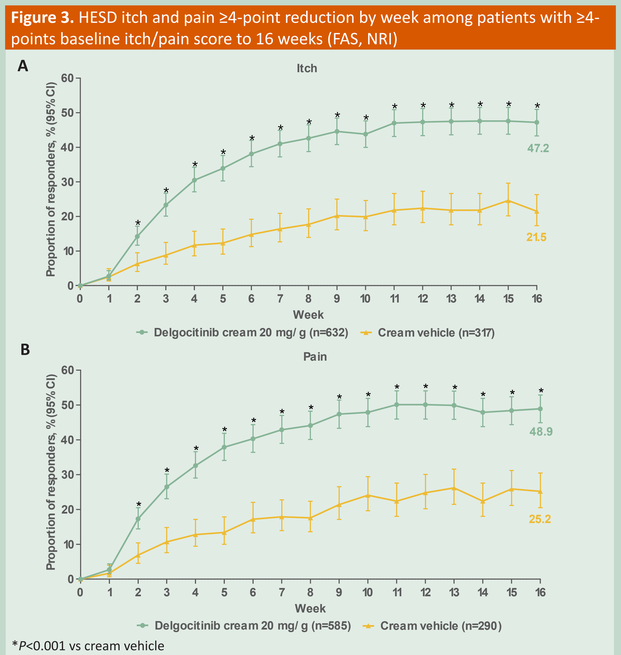
- A clinically meaningful ≥4-point reduction in itch and pain was observed from Week 2 in the delgocitinib group versus the cream vehicle group among patients with ≥4-points baseline itch/pain score (**Figure 3**)
  - A ≥4-point reduction in itch was achieved by significantly more patients applying delgocitinib cream from Week 2 (14.2%) versus cream vehicle (6.3%, *P*<0.001) and maintained through to Week 16 (47.2% vs 21.5%, respectively; *P*<0.001)
  - Similarly, a ≥4-point reduction in pain was achieved by significantly more patients applying delgocitinib cream from Week 2 (17.3% vs 6.9% cream vehicle; *P*<0.001) and maintained through to Week 16 (48.9% vs 25.2%, respectively; *P*<0.001)

Figure 1. Change in **daily** HESD score for itch and pain from baseline to Day 6 (FAS, WOCF)



*P≤0.001 vs cream vehicle

Figure 3. HESD itch and pain ≥4-point reduction by week among patients with ≥4-points baseline itch/pain score to 16 weeks (FAS, NRI)



*P<0.001 vs cream vehicle

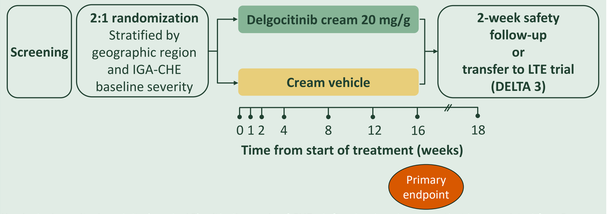
Background

- CHE is the most frequent chronic inflammatory disease affecting hands, with itch and pain being two of the most common and burdensome symptoms[1-7]
  - There are no topical treatments specifically developed and approved for CHE[5,6], and patients with CHE are seeking alternative treatment options that do not involve TCS[7]
- Delgocitinib is a topical pan-JAK inhibitor impacting JAK enzymatic activity and targeting key mediators of CHE[8]
  - Sustained itch and pain reductions have been reported in a Phase 2b trial[9]
  - The current pooled analysis of the DELTA 1 and 2 trials was designed to assess early changes in itch and pain following the application of delgocitinib cream 20 mg/g

Methods

- Data were pooled from Phase 3 DELTA 1 (NCT04871711) and DELTA 2 (NCT04872101) (**Figure 4**)
- HESD is a validated 6-item PRO instrument designed to assess severity of CHE signs and symptoms (itch, pain, cracking, redness, dryness, and flaking)
  - HESD captured patient-reported worst severity of itch and pain over the past 24 hours on an 11-point numeric rating scale (0=no itch/pain to 10=severe itch/pain)
- Daily scores were recorded using an eDiary

Figure 4. DELTA 1 and 2 trial design



Key inclusion criteria: adults (aged ≥18) with diagnosis of CHE, defined as hand eczema that has persisted for >3 months or returned ≥2 times within past 12 months; IGA-CHE score of 3 (moderate) or 4 (severe); HESD itch score (weekly average) of ≥4 points; medical history of inadequate response to TCS (within past 12 months) or TCS medically inadvisable.
Results presented are from the main analysis of primary estimand (composite strategy) where patients who discontinue study treatment (any reason) or initiate rescue treatment are considered non-responders with missing values being considered non-response. Changes in itch and pain from baseline were assessed daily during Week 1 and weekly from Week 1 to Week 16. Analyses were pre-specified in the SAP for the clinical summary of efficacy before unblinding of the DELTA 1 and DELTA 2 trials.
DELTA 3: ClinicalTrials.gov ID NCT04949841.

Conclusions

- The reductions in itch and pain were significantly (*P*≤0.001) greater in the delgocitinib 20 mg/g group than the cream vehicle group at Day 1 (itch) and Day 3 (pain), and were maintained through to Week 16
- In patients with HESD itch and pain scores ≥4 points at baseline, a greater proportion of patients in the delgocitinib cream 20 mg/g group achieved ≥4-point reduction from Week 2 (itch: 14.2%; pain: 17.3%) versus the cream vehicle group (itch: 6.3%; pain: 6.9%)

Baseline Demographics and Characteristics

- This DELTA 1 and 2 pooled analysis included 960 patients (delgocitinib cream 20 mg/g [N=639]; cream vehicle [N=321])
  - Overall, baseline demographics and patient characteristics were similar between delgocitinib cream 20 mg/g and cream vehicle groups (**Table 1**)

Table 1. Baseline demographics and characteristics

	Total (N=960)	Delgocitinib cream 20 mg/g (N=639)	Cream vehicle (N=321)
Age, median years, (min–max)	44.0 (18–87)	45.0 (18–87)	42.0 (18–86)
Sex, n (%)			
Male	342 (35.6)	233 (36.5)	109 (34.0)
Female	618 (64.4)	406 (63.5)	212 (66.0)
Age at onset of CHE, median, years (min–max)	33.0 (0–87)	34.0 (0–87)	32.0 (0–77)
Duration of CHE, median, years (min–max)	5.0 (0–61)	5.0 (0–61)	5.0 (0–53)
IGA-CHE, n (%)			
Moderate	687 (71.6)	457 (71.5)	230 (71.7)
Severe	273 (28.4)	182 (28.5)	91 (28.3)
HESD itch (weekly average)			
N	955	636	319
Median (min-max)	7.2 (1.9–10.0)	7.1 (1.9–10.0)	7.2 (2.6–10.0)
≥4, n (%)	949 (99.4)	632 (99.4)	317 (99.4)
HESD pain (weekly average)			
N	955	636	319
Median (min-max)	6.9 (0–10.0)	6.9 (0–10.0)	6.9 (0.9–10.0)
≥4, n (%)	875 (91.6)	585 (92.0)	290 (90.9)

Note: Discrepancies in patient numbers for some assessments is due to some patients missing assessments at baseline.

Abbreviations

CHE, Chronic Hand Eczema; CI, confidence interval; FAS, full analysis set; HESD, Hand Eczema Symptoms Diary; HRQoL, health-related quality of life; IGA-CHE, Investigator's Global Assessment for CHE; JAK, Janus kinase; LS, least squares; LTE, long-term extension; N, number of patients in analysis set; n, number of patients with data available at baseline; NRI, non-responder imputation; WOCF, worst observation carried forward.

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Disclosures

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Efficacy and safety of delgocitinib cream in adults with moderate to severe Chronic Hand Eczema: pooled results of the Phase 3 DELTA 1 and 2 trials

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Objectives

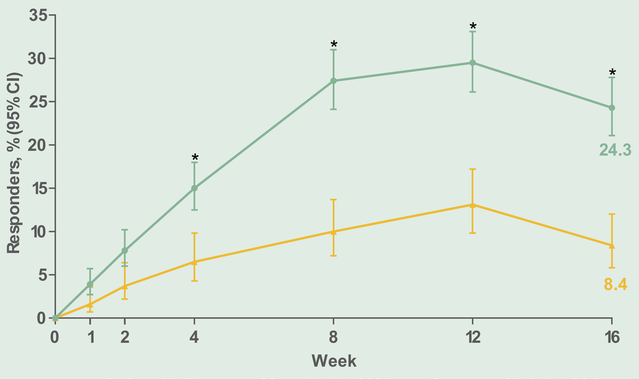
- To study the efficacy and safety of twice-daily delgocitinib cream 20 mg/g compared with cream vehicle in adults with moderate to severe Chronic Hand Eczema (CHE) up to Week 16 in a pooled analysis of the DELTA 1 and 2 trials

Results

Efficacy Results

- At Week 16, a greater proportion of delgocitinib-treated patients achieved IGA-CHE treatment success versus cream vehicle (24.3% vs 8.4%; P<0.001; **Figure 1**)

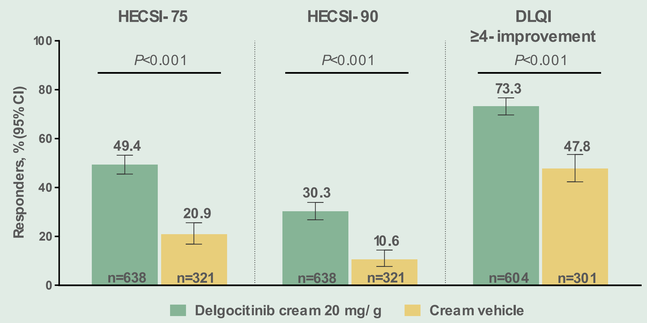
Figure 1. Proportion of patients achieving IGA-CHE treatment success[a] from baseline to Week 16



[a]IGA-CHE treatment success by visit was defined as IGA-CHE score of 0/1 (clear/almost clear, i.e., no/barely perceptible erythema and no other signs) with at least a two-step improvement from baseline. *Nominal *P*<0.001 versus cream vehicle.

- Higher proportions of patients treated with delgocitinib cream 20 mg/g achieved HECSI-75, HECSI-90, and a ≥4-point DLQI improvement from baseline at Week 16 versus cream vehicle (**Figure 2**)

Figure 2. Proportion of patients achieving HECSI-75, HECSI-90 and a ≥4-point DLQI improvement from baseline at Week 16 (key secondary endpoints)



[a]Among patients with baseline ≥4 points DLQI score. Nominal *P*-values compare delgocitinib cream 20 mg/g versus cream vehicle. The number of patients are represented within each respective bar.

Safety Results

- Treatment with delgocitinib cream for 16 weeks was well tolerated (**Table 1**)
  - Delgocitinib cream had a similar safety profile as cream vehicle over 16 weeks
  - Overall, 0.5% of delgocitinib-treated patients reported AEs leading to treatment discontinuation vs 3.4% of those in the cream vehicle group

Table 1. Summary of AEs

	Delgocitinib cream 20 mg/g (N=638; PYO=196.7)			Cream vehicle (N=321; PYO=93.9)		
	n (%)	E	R	n (%)	E	R
All events	291 (45.6)	579	294.3	153 (47.7)	307	326.9
Serious AEs	11 (1.7)	12	6.1	6 (1.9)	8	8.5
Severity of AEs						
Mild	223 (35.0)	391	198.8	120 (37.4)	199	211.9
Moderate	118 (18.5)	167	84.9	60 (18.7)	92	98.0
Severe	15 (2.4)	21	10.7	9 (2.8)	16	17.0
AEs probably or possibly related to study drug	34 (5.3)	47	23.9	24 (7.5)	32	34.1
AEs leading to discontinuation of study drug	3 (0.5)	3	1.5	11 (3.4)	12	12.8
Frequent AEs (≥2% in any treatment group)						
COVID-19	71 (11.1)	71	36.1	34 (10.6)	34	36.2
Nasopharyngitis	44 (6.9)	49	24.9	24 (7.5)	26	27.7

- No specific treatment-emergent safety concerns were identified with delgocitinib cream 20 mg/g treatment
  - Few SAEs were reported, with all being assessed as not related to study drug; no SAE led to any safety concerns
  - No AEs of special interest were reported for eczema herpeticum, deep vein thrombosis, or pulmonary embolism
  - No changes or differences between treatment groups in haematology, biochemistry, vital signs, physical examination, or electrocardiogram were assessed to be of clinical relevance

Conclusions

- In this pooled analysis, delgocitinib cream 20 mg/g was shown to be:
  - clinically effective in clinician-reported outcomes (IGA-CHE treatment success and HECSI) and patient-reported outcomes (DLQI) measured
  - well-tolerated over 16 weeks with no identified safety concerns
- These data suggest delgocitinib cream is efficacious and well-tolerated in patients with Chronic Hand Eczema where there are no topical treatments specifically developed and approved for this disease

Background

- Delgocitinib is a first-in-class, topical, pan-JAK inhibitor[1]
  - In two phase 3 trials (DELTA 1 and 2), twice-daily delgocitinib cream 20 mg/g up to 16 weeks demonstrated significantly greater efficacy, versus cream vehicle, and was well-tolerated in adults with moderate to severe CHE[2,3]

Methods

- In Phase 3 DELTA 1 (NCT04871711) and DELTA 2 (NCT04872101), patients were randomized 2:1 to twice-daily delgocitinib cream 20 mg/g or cream vehicle for 16 weeks
  - The primary endpoint was IGA-CHE treatment success at Week 16, defined as an IGA-CHE score of 0/1 (clear/almost clear, i.e., no/barely perceptible erythema and no other signs), with a ≥2-step improvement from baseline
  - Key safety evaluations included treatment-emergent AEs, SAEs, and rates of AEs related/leading to discontinuation of study drug
  - Results presented are from the main analysis of primary estimand (composite strategy) where patients who discontinue study treatment (any reason) or initiate rescue treatment are considered non-responders with missing values being considered non-response

Baseline Demographics and Characteristics

- In this DELTA 1 and 2 pooled analysis (delgocitinib cream: n=639; cream vehicle: n=321), baseline demographics and patient characteristics were similar between the two groups (**Tables 2 and 3**)

Table 2. Previous CHE treatments

	Total (N=960)	Delgocitinib cream 20 mg/g (N=639)	Cream vehicle (N=321)
TCS			
Inadequate response in last 12 months, n (%)	950 (99.0)	634 (99.2)	316 (98.4)
Medically inadvisable, n (%)	195 (20.3)	127 (19.9)	68 (21.2)
TCI, n (%)	349 (36.4)	234 (36.6)	115 (35.8)
Phototherapy and other procedures, n (%)	191 (19.9)	125 (19.6)	66 (20.6)
Oral retinoids, n (%)	143 (14.9)	97 (15.2)	46 (14.3)
Oral corticosteroids, n (%)	137 (14.3)	96 (15.0)	41 (12.8)
Oral methotrexate, n (%)	50 (5.2)	35 (5.5)	15 (4.7)
Oral cyclosporine, n (%)	31 (3.2)	20 (3.1)	11 (3.4)
Other previous CHE treatments*, n (%)	212 (22.1)	144 (22.5)	68 (21.2)

*The most frequently reported (>2% of patients) included antihistamines, select emollients and protectives, and antibiotics.

Table 3. Baseline demographics and characteristics

	Total (N=960)	Delgocitinib cream 20 mg/g (N=639)	Cream vehicle (N=321)
Age, median years (min-max)	44.0 (18-87)	45.0 (18-87)	42.0 (18-86)
Sex, n (%)			
Male	342 (35.6)	233 (36.5)	109 (34.0)
Female	618 (64.4)	406 (63.5)	212 (66.0)
Race, n (%)			
White	868 (90.4)	578 (90.5)	290 (90.3)
Black or African American	7 (0.7)	5 (0.8)	2 (0.6)
Asian	34 (3.5)	22 (3.4)	12 (3.7)
Other/Not reported	51 (5.3)	34 (5.3)	17 (5.3)
Age at onset of CHE, median years (min-max)	33.0 (0-87)	34.0 (0-87)	32.0 (0-77)
Duration of CHE, median years (min-max)	5.0 (0-61)	5.0 (0-61)	5.0 (0-53)
IGA-CHE, n (%)			
Moderate	687 (71.6)	457 (71.5)	230 (71.7)
Severe	273 (28.4)	182 (28.5)	91 (28.3)
HECSI, median (min-max)	62.0 (7-280)	63.0 (7-275)	60.0 (8-280)
DLQI			
Median (min-max)	11.0 (0-30)	11.0 (0-30)	11.0 (2-30)
≥4, n (%)	905 (95.5)	604 (95.7)	301 (95.0)

Abbreviations

AE, adverse event; CHE, Chronic Hand Eczema; CI, confidence interval; DLQI, Dermatology Life Quality Index; E, number of events; HECSI, Hand Eczema Severity Index; HECSI-75/90, ≥75%/≥90% improvement in Hand Eczema Severity Index; IGA-CHE, Investigator's Global Assessment for CHE; JAK, Janus kinase; LTE, long-term extension; N, number of patients in analysis set; n, number of patients with data available at baseline; PYO, patient-years of observation; R, rate calculated as (E/PYO)*100; SAE, serious adverse event; TCI, topical calcineurin inhibitors; TCS, topical corticosteroids.

References

1. Tanimoto A, *et al. Inflamm Res.* 2015;64(1):41-51. **2.** Bissonnette R, *et al.* Late Breaker presentation on 18th March 2023 at the 81st Annual Meeting of the American Academy of Dermatology (AAD) in New Orleans, LA, USA. **3.** Schliemann S, *et al.* Poster presentation at 32nd Annual Congress of the EADV, 11-14 October 2023 in Berlin, Germany.

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Long-term safety and efficacy of tralokinumab in adults and adolescents with moderate-to-severe atopic dermatitis treated for up to 6 years

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Objectives

- To assess the safety and efficacy of long-term treatment with tralokinumab in the final results of the 5-year extension study ECZTEND

Results

Safety

- Patients were exposed to tralokinumab for up to 1 year in the parent trials and up to 5 years in ECZTEND (**Table 1**)
- The overall long-term safety profile of tralokinumab in ECZTEND was similar to the safety profile observed in the initial placebo-controlled treatment period of the parent trials (**Tables 2 and 3**)
  - AEs and SAEs were reported at lower rates in ECZTEND
  - The majority of AEs were mild-to-moderate

Table 1. Exposure time to tralokinumab

	ECZTEND N=1672; PYE=4466.2	Parent trial + ECZTEND N=1664; PYE=5487.6
PYE		
Mean (SD)	2.7 (1.3)	3.3 (1.4)
Median (min;max)	2.6 (0.00;5.14)	3.3 (0.00;6.14)
Exposure time, n (%)		
≥16 weeks	1592 (95.2)	1647 (99.0)
≥52 weeks (1 year)	1422 (85.0)	1551 (93.2)
≥104 weeks (2 years)	1184 (70.8)	1331 (80.0)
≥156 weeks (3 years)	701 (41.9)	978 (58.8)
≥208 weeks (4 years)	321 (19.2)	571 (34.3)
≥256 weeks (~5 years)	61 (3.6)	239 (14.4)
≥304 weeks (~6 years)	-	46 (2.8)

n, number of patients with recorded observation.

Table 2. Summary of AEs in treatment period

	ECZTEND (up to Week 268) Tralokinumab N=1672; PYE=4466.2			Placebo-controlled parent trials (up to Week 16)[a] Tralokinumab N=1939; PYE=587.2			Placebo N=913; PYE=271.3		
	E	n (%)	IR	E	n (adj %)	Adj IR	E	n (adj %)	Adj IR
Overall summary of treatment-emergent AEs									
All AEs	8119	1421 (85.0)	114.33	3894	1325 (67.5)	424.8	1746	616 (68.1)	475.3
SAEs	189	151 (9.0)	3.54	44	43 (2.0)	6.7	36	29 (3.3)	11.1
AEs leading to permanent discontinuation of study drug	79	76 (4.5)	1.71	51	42 (2.0)	6.8	24	18 (2.0)	7.0
Outcome									
Fatal	1[b]	1 (0.1)	0.02	1[c]	1 (0.1)	0.3	0	0 (0.0)	-
Treatment-emergent AEs (≥5% in ECZTEND) by PT									
Dermatitis atopic	632	357 (21.4)	9.28	394	299 (13.5)	50.9	292	194 (23.0)	99.5
Nasopharyngitis	599	372 (22.2)	10.09	378	313 (15.9)	58.6	141	114 (12.6)	46.5
Coronavirus infection[d]	322	299 (17.9)	7.22	0	0 (0)	-	0	0 (0)	-
Upper respiratory tract infection	233	147 (8.8)	3.57	134	122 (6.2)	21.3	46	42 (4.6)	16.3
Headache	143	114 (6.8)	2.66	128	95 (5.1)	17.7	52	40 (4.4)	15.0
Conjunctivitis	131	103 (6.2)	2.41	115	100 (4.9)	16.9	15	14 (1.6)	5.4

[a]Study size-adjusted % and IR; [b]A patient in their 50's was treated with study drug for 1 year in the parent trial and 3.5 years (1271 days) in ECZTEND and had previously received cyclosporine and azathioprine. The patient was diagnosed with COVID-19 infection and subsequently hospitalized for 31 days in the ICU for respiratory distress and extensive pneumopathy, during which the patient was diagnosed with cutaneous T-cell lymphoma (CTCL) and re-hospitalized 25 days later with febrile dyspnea, worsening of interstitial lung disease, and major biological inflammatory syndrome with hypereosinophilia. The patient died 5 days later due to multiple organ failure and refractory hypoxemia, later classified as worsening of an interstitial lung disease related to CTCL and possible sequelae of COVID-19; [c]The details of the reported death in the initial period of the of the vaccine study (ECZTRA 5) have been previously published[1]; [d]The difference between ECZTEND and the parent trials for coronavirus infection was consistent with the timing of trials relative to the COVID-19 pandemic.

Conclusions

- Long-term use of tralokinumab, up to 1 year in parent trials plus up to 5 years in ECZTEND, was well-tolerated with no new safety signals identified in patients aged 12 and up with moderate-to-severe AD
- Tralokinumab treatment demonstrated robust long-term efficacy with sustained improvements in AD signs, symptoms, and quality of life

- In ECZTEND most AESI eye disorder events (97%) were mild to moderate and only 7 (0.5%) patients discontinued treatment due to AESI eye disorders (**Table 3**)

Table 3. Summary of AESIs in treatment period

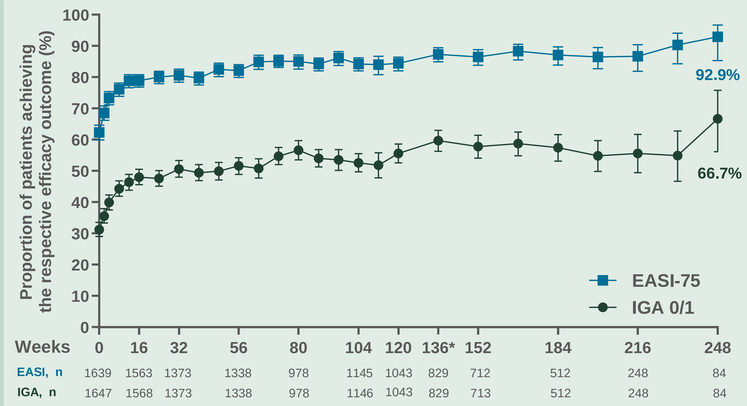
	ECZTEND (up to Week 268) Tralokinumab N=1672; PYE=4466.2			Placebo-controlled parent trials (up to Week 16)[a] Tralokinumab N=1939; PYE=587.2			Placebo N=913; PYE=271.3		
	E	n (%)	IR	E	n (adj%)	Adj IR	E	n (adj %)	Adj IR
Eye disorders[b]	260	189 (11.3)	4.59	184	158 (8.0)	27.8	35	30 (3.4)	11.4
Skin infections requiring systemic treatment	82	61 (3.6)	1.39	55	48 (2.3)	7.7	54	45 (5.1)	18.1
Eczema herpeticum[c]	30	23 (1.4)	0.52	9	9 (0.5)	1.6	12	12 (1.4)	4.8
Malignancy diagnosed after treatment assignment[d]	17	17 (1.0)	0.38	1	1 (<0.1)	0.1	1	1 (0.1)	0.4

[a]Study size-adjusted % and IR; [b]Eye disorders category includes several PTs, such as conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, keratitis, keratitis viral, ulcerative keratitis, and atopic keratoconjunctivitis; [c]Eczema herpeticum category includes PTs such as eczema herpeticum and kaposi's varicelliform eruption; [d]Malignancies diagnosed after dosing (excluding basal cell carcinoma, localized squamous cell carcinoma of the skin, and carcinoma in situ of the cervix).

Efficacy

- Long-term treatment with tralokinumab demonstrated sustained efficacy, with EASI-75 and IGA 0/1 observed in 92.9% and 66.7% of patients at Week 248, respectively (**Fig. 1**)
- Itch, sleep, and life quality improvements were sustained at levels equivalent to no-to-mild disease (**See online supplement, available via QR code**)

Figure 1. Proportion of patients achieving IGA 0/1 and EASI-75 as observed over 248 weeks of treatment in ECZTEND



Error bars represent 95% CI; *Study duration varied based on patients' consent to the amendment to prolong the study from 3 to 5 years and the country of enrollment (**see online supplement, available via QR-code**).

Abbreviations: AD, atopic dermatitis; AE, adverse event; AESI, AE of special interest; CI, confidence interval; COVID-19, coronavirus disease 2019; CTCL, cutaneous T-cell lymphoma; DLQI, dermatology life quality index; E, number of AEs; EASI, Eczema Area and Severity Index; EASI-75, 75% improvement in EASI; IGA, Investigator's Global Assessment; IR, Incidence rate (n/100PYE), for IR calculations, patient exposure was censored at the time of first event; n, number of patients with ≥1 event (unless otherwise specified); N, number of patients in indicated treatment set; PT, preferred term; PYE, patient years of exposure; Q2W, every 2 weeks; SAE, serious AE; SCORAD, SCORing AD; SD, standard deviation; TCI, topical calcineurin inhibitor; TCS, topical corticosteroid.

References: **1.** Merola J, Bagel J, Almgren P, et al. *JAAD*. 2021;85(1):71-78. **2.** Simpson E, Blauvelt A, Silverberg J, et al. *AJCD*. 2024;25(1):139-148. **3.** Reich K. et al. *SKIN*. 2024;8(2):s375. **4.** Blauvelt A. et al. *JAAD*. 2022;87(4):815-824.

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Background

- Tralokinumab, a monoclonal antibody that specifically neutralizes IL-13, is indicated for the treatment of moderate-to-severe AD in patients aged ≥12 years[2]
- ECZTEND (NCT03587805) is a long-term open-label extension study evaluating the long-term safety and efficacy of tralokinumab for up to 5 years in adults and adolescents with moderate-to-severe AD
- Interim analyses have previously demonstrated the benefit-risk profile of tralokinumab in patients followed up to 3.5 years in ECZTEND[3,4]

Methods

Patients and treatment

- Patients who completed one of multiple tralokinumab parent trials at participating sites were eligible to enroll in ECZTEND, regardless of previous treatment or response in parent trials (**See online supplement, available via QR code**)
- Patients enrolled in ECZTEND received open-label tralokinumab 300 mg Q2W (home use) provided at site visits every 8-16 weeks and were allowed to use mild-to-moderate potency TCS or TCI at the investigators' discretion

Analyses

- AEs were coded over the course of the trial according to the Medical Dictionary for Regulatory Activities (MedDRA©) system
- Due to the absence of a comparator arm in ECZTEND, data from the initial 16-week treatment period of 7 placebo-controlled parent trials (NCT03131648, NCT03160885, NCT03363854, NCT03562377, NCT03526861, NCT03761537, NCT04587453) are provided as a basis for comparison[3]
- Exposure adjusted IRs were calculated as the number of patients reporting an event per PYE
  - PYE was defined as the time until the first event or exposure end, whichever came first, and incidence was defined as the first event
- Efficacy results are presented using observed data

Baseline Demographics and Clinical Characteristics

- Baseline demographics and clinical characteristics for the final ECZTEND results were similar to previous analyses[3,4] (**Table 4**)

Table 4. Baseline demographics and clinical characteristics

	ECZTEND total population N=1672; PYE=4466.2	
Demographics		
Age, median years (min ; max)	36.0 (13.0 ; 87.0)	
Age group, years, n (%)		
12-17	103 (6.2)	
≥18	1569 (93.8)	
Female, n (%)	709 (42.4)	
Race, n (%)		
White	1194 (71.4)	
Asian	312 (18.7)	
Black	120 (7.2)	
Age at onset of AD, median years (min ; max)	3.0 (0.0 ; 84.0)	
Clinical characteristics		
	Parent trial baseline N=1664	ECZTEND baseline N=1672
IGA score, n (%)		
0/1 – clear/almost clear	-	525 (31.4)
2 – mild	-	608 (36.4)
3 – moderate	890 (53.5)	443 (26.5)
4 – severe	774 (46.5)	96 (5.7)
EASI, median (Q1 ; Q3)	27.0 (20.6 ; 37.9)	4.6 (1.6 ; 11.7)
SCORAD, median (Q1 ; Q3)	*n = 1664* 67.7 (59.8 ; 78.0)	*n = 1670* 29.4 (18.0 ; 43.8)
DLQI, median (Q1 ; Q3)	*n = 1488* 16.0 (11.0 ; 21.0)	*n = 1504* 5.0 (2.0 ; 9.0)

n, number of patients with recorded observation; Q1, 1st quartile (25th percentile); Q3, 3rd quartile (75th percentile).

Scan to download a copy of this poster and an online data supplement

DELTA FORCE trial: 24-week Phase 3 trial comparing the efficacy and safety of topical delgocitinib cream with oral alitretinoin capsules in adults with severe Chronic Hand Eczema

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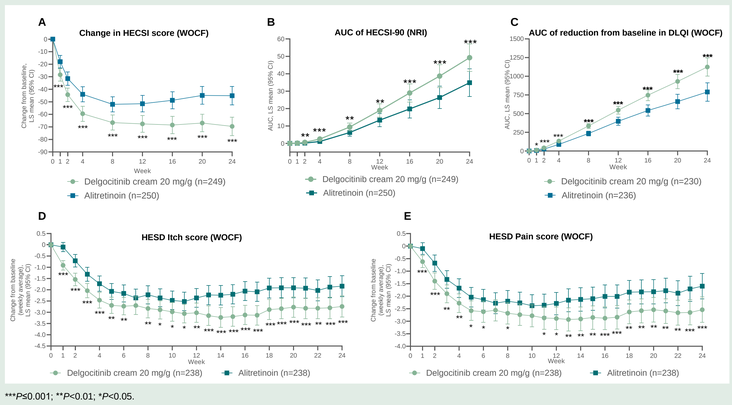
Objective

- This head-to-head, phase 3 DELTA FORCE trial (NCT05259722) evaluated the efficacy, effect on HRQoL, and safety of twice-daily topical delgocitinib cream 20 mg/g compared with once-daily oral alitretinoin capsules in adult patients with severe CHE

Results

- Superiority of delgocitinib cream was shown for the primary endpoint and all secondary efficacy endpoints (**Table 1**)
  - Consistently higher efficacy rates in the delgocitinib cream group were observed throughout the treatment period, with differences between treatment groups observed from Week 1 (**Figure 1**)
- Delgocitinib cream was well-tolerated and showed a favourable safety profile versus alitretinoin (**Table 2**)
  - Fewer patients in the delgocitinib cream group than in the alitretinoin group reported AEs, serious AEs, and AEs leading to trial drug discontinuation (**Table 2**)
- Permanent discontinuations of trial drug were more frequent in the alitretinoin group (35.9%) than in the delgocitinib cream 20 mg/g group (13.4%; **Figure 2**)

Figure 1. Consistently higher efficacy rates in the delgocitinib cream group throughout the treatment period (full analysis set)



***P≤0.001; **P<0.01; *P<0.05.

Figure 2. Time to permanent discontinuation of trial drug (full analysis set)

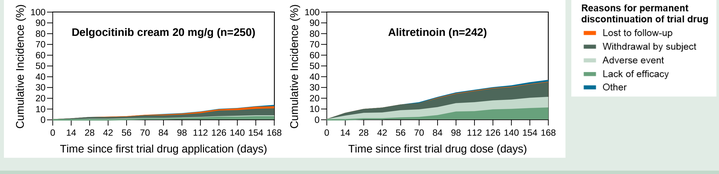


Table 1. Summary of efficacy results in the DELTA FORCE trial (full analysis set)

	Delgocitinib 20 mg/g (N=250)	Alitretinoin (N=253)	Difference (95% CI)	*P*-value
Primary endpoint				
Change in HECSI score (WOCF), Week 12 LS mean	n=249 -67.6	n=250 -51.5	-16.1 (-23.3 to -8.9)	<0.001
Key secondary endpoints				
HECSI-90 (NRI), Week 12 n (%)	n=249 96 (38.6)	n=250 65 (26.0)	12.6 (4.3 to 20.8)	0.003
IGA-CHE TS (NRI), Week 12 n (%)	n=250 68 (27.2)	n=253 42 (16.6)	10.6 (3.3 to 17.9)	0.004
Change in HESD itch (WOCF), Week 12 LS mean	n=238 -3.0	n=238 -2.4	-0.7 (-1.1 to -0.2)	0.005
Change in HESD pain (WOCF), Week 12 LS mean	n=238 -2.9	n=238 -2.3	-0.6 (-1.1 to -0.1)	0.018
AUC of HECSI-90 (NRI), Week 24 LS mean	n=249 49.2	n=250 34.9	14.3 (5.8 to 22.9)	<0.001
AUC of reduction in DLQI score (WOCF), Week 24 LS mean	n=230 1124.7	n=236 790.7	334.0 (195.7 to 472.3)	<0.001
Change in HECSI score (WOCF), Week 24 LS mean	n=249 -69.6	n=250 -45.1	-24.5 (-32.6 to -16.4)	<0.001

Missing data were imputed with WOCF (continuous endpoints) or non-response (binary endpoints). Data after initiation of rescue treatments or permanent discontinuation of trial drug were treated as missing. Two-sided *P*-values are reported. The order of endpoints in this table reflects the order of the testing hierarchy. IGA-CHE TS was defined as achieving an IGA-CHE score of 0 (clear) or 1 (almost clear i.e., barely perceptible erythema only). The AUC of HECSI-90 from baseline up to Week 24 represents the number of days with 90% reduction in HECSI score until Week 24. The AUC of reduction from baseline in DLQI score up to Week 24 represents the cumulative improvement in DLQI score until Week 24.

Table 2. Summary of adverse events in the DELTA FORCE trial (safety analysis set)

	Delgocitinib 20 mg/g (N=253, PYO=120.9)			Alitretinoin (N=247, PYO=104.0)		
	n (%)	**E**	**R**	**n (%)**	**E**	**R**
All AEs	125 (49.4)	280	231.5	188 (76.1)	620	596.1
Serious AEs	5 (2.0)	5	4.1	12 (4.9)	12	11.5
Severity						
Mild	92 (36.4)	168	138.9	151 (61.1)	397	381.7
Moderate	68 (26.9)	108	89.3	104 (42.1)	198	190.4
Severe	4 (1.6)	4	3.3	14 (5.7)	25	24.0
AEs probably or possibly related to trial drug	24 (9.5)	30	24.8	134 (54.3)	311	299.0
AEs leading to permanent discontinuation of trial drug	3 (1.2)	4	3.3	25 (10.1)	44	42.3
AEs of special interest						
Eczema Herpeticum	0	0	0	0	0	0
Deep Vein Thrombosis	0	0	0	1 (0.4)	1	1.0
Pulmonary Embolism	0	0	0	0	0	0
Frequent AEs (≥5% in any treatment group)						
Headache	10 (4.0)	19	15.7	80 (32.4)	114	109.6
Nasopharyngitis	30 (11.9)	38	31.4	34 (13.8)	46	44.2
Nausea	1 (0.4)	1	0.8	14 (5.7)	15	14.4

AEs starting or worsening in severity after first trial drug dose and reported on or before Week 26 were reported. Relation to trial drug was based on investigator's assessment. AEs were coded using MedDRA Version 24.0 dictionary.

Conclusions

- Topical delgocitinib cream 20 mg/g demonstrated superior clinical treatment effects and HRQoL improvements, and a more favourable safety profile compared with oral alitretinoin over 24 weeks across the primary and all secondary endpoints in patients with severe `CHE
- Delgocitinib cream 20 mg/g was well-tolerated over 24 weeks, with no treatment-emergent safety concerns identified
- These data support the benefits of delgocitinib cream 20 mg/g as an efficacious and well tolerated topical treatment in this patient population which faces a high disease burden and has unmet treatment needs

Background

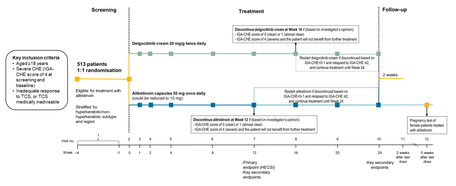
- Chronic Hand Eczema (CHE) is one of the most common chronic inflammatory disorders affecting the hands and wrists that can negatively impact patient HRQoL and occupational capabilities[1-4]
- Alitretinoin, an oral systemic retinoid, is currently the only drug specifically approved in a few countries worldwide for the treatment of severe CHE[2,5,6]
- Delgocitinib cream is a topical pan-JAK inhibitor impacting the activation of multiple JAK-STAT pathways involved in skin barrier dysfunction and the inflammation associated with CHE pathogenesis[7,8]
  - In phase 3 trials in patients with moderate to severe CHE,[9,10] delgocitinib cream demonstrated significant improvement in all primary and secondary efficacy endpoints versus cream vehicle and was well tolerated when used long-term as needed

Methods

- DELTA FORCE was a phase 3, randomised, assessor-blinded, active-controlled, parallel-group, multi-site trial
- Adults (aged ≥18 years) with severe CHE (defined as Investigator's Global Assessment for CHE [IGA-CHE] score of 4) were randomised 1:1 to twice-daily topical delgocitinib cream 20 mg/g (n=254) or once-daily oral alitretinoin 30 mg* (n=259) for up to 24 weeks (**Figure 3**)
- The primary endpoint was change in Hand Eczema Severity Index (HECSI) score from baseline to Week 12
- Safety endpoints included numbers of adverse events (AEs), AEs leading to trial drug discontinuation, and serious AEs
- Data presented are from the composite estimand, where data collected after initiation of rescue treatment or after permanent discontinuation of the trial drug, as well as any other missing data, were imputed with worst observation carried forward (WOCF; including baseline value, for continuous endpoints) or non-response (for binary endpoints)

*The alitretinoin dose could be reduced to 10 mg in the event of unacceptable adverse reactions (as according to the product label). If the alitretinoin dose was decreased to 10 mg due to safety issues, it was not permitted to increase the dose at a later point during the trial; local safety requirements for alitretinoin use was followed.

Figure 3. DELTA FORCE trial design



For patients treated with medications requiring a 28-day washout period prior to baseline, the duration of the screening period was extended up to 31 days to ensure appropriate washout. For women of childbearing potential, the duration of the screening period was extended up to 42 days to ensure compliance with contraceptive and pregnancy prevention program requirements.

Efficacy endpoints were assessed based on the full analysis set (n=503), which comprised all eligible randomised patients. Safety endpoints were assessed in the safety analysis set (n=500), which comprised all patients who were exposed to the trial drugs.

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Abbreviations: AE, adverse event; AUC, area under the curve; CHE, Chronic Hand Eczema; CI, confidence interval; DLQI, dermatological life quality index; E, number of events; FAS, full analysis set; HECSI, hand eczema severity index; HECSI-90, at least 90% improvement in HECSI score from baseline; HESD, hand eczema symptom diary; HRQoL, health-related quality of life; IGA-CHE, Investigator's Global Assessment for CHE; IGA-CHE TS, IGA-CHE treatment success, i.e. an IGA-CHE score of 0 (clear) or 1 (almost clear); JAK, Janus kinase; LS mean, Least Squares mean; max, maximum; MedDRA, Medical Dictionary for Regulatory Activities; min, minimum; n, number of patients with observation; N, total number of patients; NRI, non-response imputation; %, percentage of patients with observation; PYO, patient years of observation; Q1, first quartile; Q3, third quartile; R, rates (E/PYO)×100; SD, standard deviation; STAT, signal transducer and activator of transcription; TCS, topical corticosteroids; WOCF, worst observation carried forward.

Baseline demographics and characteristics

- Baseline demographics and disease characteristics were comparable in the two treatment groups (**Table 3**)

Table 3. Patient demographics and baseline characteristics in the DELTA FORCE trial (randomised population)

	Delgocitinib 20 mg/g (n=254)	Alitretinoin (n=259)	Overall (N=513)
Age (years) Median (min;max)	46.0 (18;77)	44.0 (18;75)	45.0 (18;77)
Female sex, n (%)	167 (65.7)	167 (64.5)	334 (65.1)
Race, n (%)			
White	237 (93.3)	240 (92.7)	477 (93.0)
Asian	9 (3.5)	5 (1.9)	14 (2.7)
Black or African American	1 (0.4)	3 (1.2)	4 (0.8)
Multiple	2 (0.8)	0	2 (0.4)
Other/Not reported	5 (2.0)	11 (4.2)	16 (3.1)
Region, n (%)			
Europe	229 (90.2)	230 (88.8)	459 (89.5)
North America	25 (9.8)	29 (11.2)	54 (10.5)
Age at onset of CHE, Median years (min;max)	37.5 (0;72)	36.0 (0;72)	37.0 (0;72)
Duration of CHE, Median years (min;max)	4.0 (0;50)	4.0 (0;48)	4.0 (0;50)
IGA-CHE, n (%)			
Severe	254 (100.0)	258 (99.6)	512 (99.8)
Mild	0	1 (0.4)[a]	1 (0.2)[a]
HECSI Median (Q1;Q3)	n=252 79.5 (52.5; 114.5)	n=256 80.0 (52.0; 119.0)	n=508 80.0 (52.0; 117.0)
DLQI Median (Q1;Q3)	n=233 12.0 (8.0; 17.0)	n=242 12.0 (8.0; 17.0)	n=475 12.0 (8.0; 17.0)
HESD itch (weekly average)[b] Median (Q1;Q3) ≥4, n (%)	n=240 6.1 (3.8; 8.0) 177 (69.7)	n=244 6.4 (4.1; 8.0) 185 (71.4)	n=484 6.2 (3.9; 8.0) 362 (70.6)
HESD pain (weekly average)[b] Median (Q1;Q3) ≥4, n (%)	n=240 5.6 (3.1; 7.6) 163 (64.2)	n=244 6.1 (3.6; 8.0) 176 (68.0)	n=484 6.0 (3.3; 7.9) 339 (66.1)

[a]Patient with baseline IGA-CHE = mild was excluded from the full analysis set due to inclusion criteria not being met. [b]Baseline weekly average was defined as the average of the daily observations during the 7 days preceding the randomization date. IGA-CHE scores: 0-clear, 1-almost clear, 2-mild, 3-moderate, and 4-severe. HECSI ranges from 0–360. DLQI scores range from 0–30. HESD itch and HESD pain scores range from 0–10.

Disclosures: **AMGA** is or recently was a speaker and/or advisor for and/or has received research funding from Almirall, Amgen, AstraZeneca, Avene, Blueprint, Celldex, Escient Pharmaceuticals, Genentech, GSK, Harmonic Bio, Instituto Carlos III- FEDER, Jaspers, LEO Pharma A/S, Menarini, Mitsubishi Tanabe Pharma, Noucor, Novartis, Sanofi–Regeneron, Septerna, Servier, Thermo Fisher Scientific, Uriach Pharma. **AP** has served as an investigator and/or speaker and/or advisor for AbbVie, Almirall-Hermal, Amgen, Biogen Idec, Biontec, Boehringer-Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, GSK, Eli-Lilly, Galderma, Hexal, Janssen, LEO Pharma A/S, MC2, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pascoe, Pfizer, Tigercat Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi-Genzyme, Schering-Plough, UCB Pharma, and Zuellig Pharma. **WS** received travel support for participation in congresses and / or (speaker) honoraria and / or research grants from AbbVie, Almirall, Amgen, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, GSK, Janssen, LEO Pharma A/S, Lilly, medi GmbH Bayreuth, MSD, Novartis, Pfizer, Roche, Sanofi Genzyme, and UCB. **ZR** has received consulting fees and honoraria from: AbbVie, Almirall, Amgen, Avene, Bristol Myers Squibb, Celgene, Cerave, GSK, Janssen-Cilag, La Roche Posay, LEO Pharma A/S, Lilly, Medac, MSD, Novartis, Pierre Fabre Dermatologie, Pfizer, UCB, and Sanofi. Investigator for: AbbVie, Actelion, Almirall, Amgen, Bayer, Boehringer-Ingelheim, Bristol Myers Squibb, Forward Pharma, GSK, Galderma, Genentec, Incyte, Janssen Cilag, LEO Pharma A/S, Novartis, Pfizer, Roche, Regeneron, UCB, and Sanofi. **RW** has received travel support for participation in congresses and / or (speaker) honoraria and / or research grants from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eli Lilly, Galderma, Janssen-Cilag, LEO Pharma A/S, Novartis, Pfizer, Sanofi, and UCB. **CL** has been a speaker and/or consultant to: AbbVie, Amgen, Aralez, Arcutis, Bausch Health, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cipher, Dermavant, Devonian, Eli Lilly, Fresnius Kabi, Galderma, GSK, InCyte, Innovaderm, Intega Skin, Janssen, Kyowa Kirin, La Roche Posay, LEO Pharma A/S, L'Oreal, Medexus, MedX, Merck, Novartis, P&G, Pediapharm, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sandoz, Sentrex, SunPharma, TEVA, Tribute, UCB, Valeant, Viatris, and Volo Health; and has been a principal investigator for: AbbVie, Acelyrin, Akros, Altius, Amgen, Aralez, Arcutis, Avillion, Bausch Health, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Cipher, Concert, Dermavant, Devonian, Eli Lilly, Evelo, Galderma, GSK, Incyte, Innovaderm, Intega Skin, Janssen, Kyowa Kirin, La Roche Posay, LEO Pharma A/S, L'Oreal, Medexus, MedX, Merck, MoonLake, Novartis, P&G, Pediapharm, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sandoz, Sentrex, SunPharma, TEVA, Tribute, UCB, Valeant, Viatris, and Volo Health. **FJL** has received consulting fees and/or honoraria for lectures, presentations, speaker's bureaus, manuscript writing or education events; participated on advisory boards; and/or served as an investigator for: AbbVie, Almirall, Amgen, Celgene, DS Biopharma, Eli Lilly and Company, Galderma, Incyte, Janssen Cilag, Kiniksa Pharmaceuticals, LEO Pharma A/S, Menlo Therapeutics, Novartis, Pelpharma, Pfizer, Regeneron, Sanofi, Trevi Therapeutics and Vitor Pharma. **AC** has served as advisory board member and consultant and has received fees and speakers honoraria or has participated in clinical trials for AbbVie, Almirall, Amgen LEO Pharma A/S, Lilly, Galderma, Incyte, Janssen, Novartis, Sanofi Genzyme, Boehringer-Ingelheim, and UCB. **JFS** has been an investigator, speaker, and/or advisor for AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, Lilly, Galderma, Incyte, LEO Pharma A/S, Novartis, Pfizer, Regeneron, and Sanofi Genzyme. **BFH** is a former employee of LEO Pharma A/S. **NM**, **UP**, and **LR** are employees of LEO Pharma A/S. **AB** has been a speaker/advisor/investigator and/or received research funding from AbbVie, Almirall, Amgen, AstraZeneca, Biofrontera, Blueberry Therapeutics, Bristol Myers Squibb, Celldex, Centogene, Escient, Galderma, Genentech, Gilead, Jasper, Incyte, LEO Pharma A/S, Lilly, L'Oréal, Novartis, Sanofi, Regeneron, and Takeda.

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Systemic exposure and safety profile of delgocitinib cream in adults with moderate to severe Chronic Hand Eczema in the Phase 3 DELTA 2 trial

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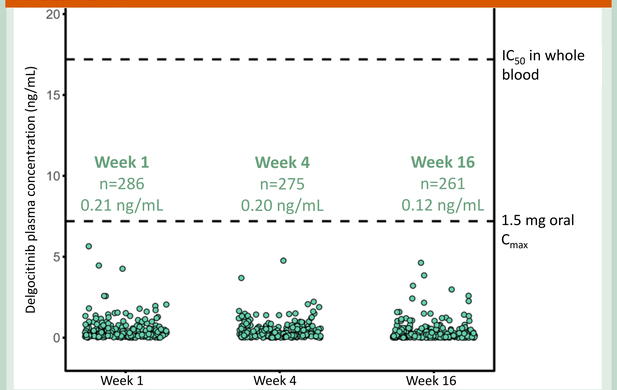
Objectives

- To examine systemic exposure of delgocitinib cream 20 mg/g in adults with moderate to severe Chronic Hand Eczema (CHE) in the randomized, double-blind, vehicle-controlled DELTA 2 trial
- To compare DELTA 2 systemic exposure with corresponding data following oral administration of delgocitinib in a Phase 1 trial
- To present a summary of delgocitinib cream safety from the randomized, double-blind, vehicle-controlled DELTA 2 trial

Results

- In DELTA 2, the geometric mean plasma concentration of delgocitinib was 0.21, 0.20 and 0.12 ng/mL at Weeks 1, 4 and 16, respectively (**Figure 1**)
- The geometric mean IC_{50} of delgocitinib in an IL-4 release assay (*in vitro* spiking of whole blood from healthy adults) was 17.2 ng/mL
- In the Phase 1 trial, the lowest oral delgocitinib dose tested (1.5 mg; n=8) showed a peak systemic exposure (geometric mean C_{max}) of 7.2 ng/mL (**Table 1**)

Figure 1. Box plot of delgocitinib concentration by visit at Weeks 1, 4, and 16 in the DELTA 2 trial[a]



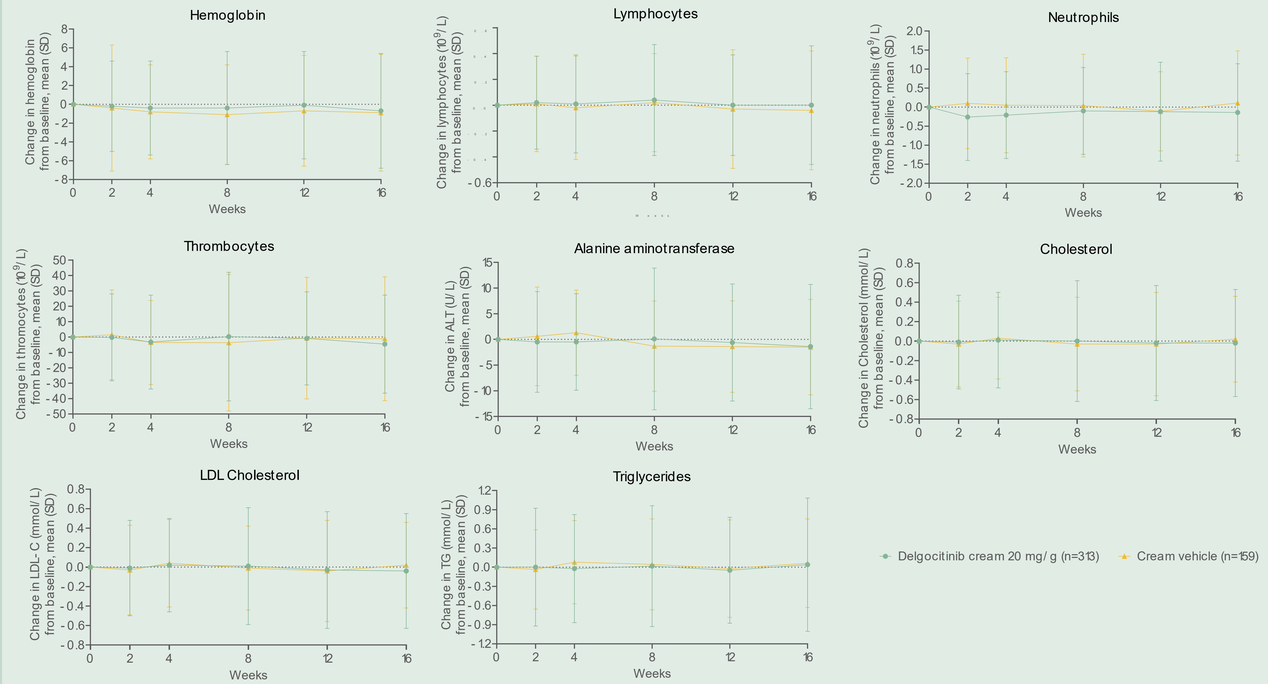
Horizontal dashed lines represent geometric mean values.
[a]One patient was excluded from this analysis due to an outlier value at Week 4.

Table 1. Systemic exposure in the oral Phase 1 trial

Dose (mg)	n	$AUC_{0-\infty}$ (h*ng/mL)	C_{max} (ng/mL)	t_{max} (h) median	$t_{1/2}$ (h)
1.5	8	39.6	7.2	1.0	2.0
3	8	66.6	18.4	0.84	2.3
6	8	211.0	51.0	0.83	2.9
12	8	408.0	99.3	1.0	2.8

- In DELTA 2, delgocitinib cream treatment was well tolerated, with AEs being reported by 45.7% (n=143/313) of patients in the delgocitinib cream group and 44.7% (n=71/159) of those in the cream vehicle group, and COVID-19 being most common (11.5% vs 12.6%, respectively)
  - The proportion of subjects with possibly or probably related AEs was low and similar between delgocitinib cream (7.0% [n=22/313]) and cream vehicle (6.9% [n=11/159])
  - Few serious AEs were reported (delgocitinib cream: 1.6% [n=5/313]; cream vehicle: 1.9% [n=3/159]) with none assessed as related to the study drug; no deaths were reported
  - No AEs of special interest were reported (eczema herpeticum, deep vein thrombosis, or pulmonary embolism)
  - No malignancies, major adverse cardiovascular events or venous thromboembolisms were reported in patients treated with delgocitinib cream
  - No changes or differences between the delgocitinib cream 20 mg/g and cream vehicle in laboratory parameters were assessed to be of clinical relevance (**Figure 2**)

Figure 2. Mean (SD) change in laboratory parameters from baseline by study visit in DELTA 2



Conclusions

- In the DELTA 2 trial, twice-daily application of delgocitinib cream 20 mg/g demonstrated:
  - minimal systemic exposure in association with a favorable safety profile in patients with moderate to severe CHE treated for 16 weeks
  - no safety findings to support any causal relationship with systemic adverse events, with no AEs of special interest being reported
  - no clinically meaningful changes in laboratory parameters versus cream vehicle
- No systemic pharmacological effects are expected from twice-daily applications of delgocitinib cream 20 mg/g in patients with moderate to severe CHE

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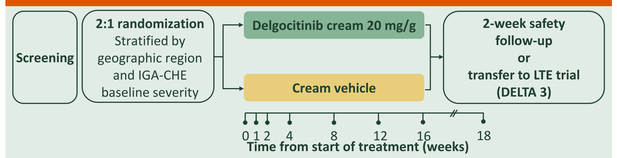
Background

- The pathogenesis of CHE involves JAK-STAT signaling pathways[1,2]
- The cream formulation of delgocitinib, a pan-JAK inhibitor, has been developed for topical use
  - Delgocitinib cream was well tolerated and demonstrated significant improvement in all efficacy endpoints in the identical DELTA 1 (NCT04871711) and DELTA 2 (NCT04872101) pivotal phase 3 trials for treatment of moderate to severe CHE[3,4]

Methods

- The DELTA 2 pivotal Phase 3 clinical trial was randomized, double-blind and vehicle-controlled (**Figure 3**)
  - Adults (aged ≥18 years) with moderate to severe CHE were randomized 2:1 to twice-daily delgocitinib cream 20 mg/g (n=314) or cream vehicle (n=159) for 16 weeks followed by either 2-weeks safety follow up or transfer to a 36-week extension trial
  - Pharmacokinetic blood sampling was performed 2-6 hours after delgocitinib cream application at Weeks 1, 4, and 16 using an LC/MS-based method with a lower limit of quantitation of 5 pg/mL
- In the Phase 1 trial (NCT05050279), single oral doses of delgocitinib 1.5, 3, 6, and 12 mg) were tested in healthy volunteers (n=40) with sampling performed 30 minutes prior to administration and at 13 timepoints for up to 24-hours post-administration
- IC_{50} of delgocitinib was assessed using an *in vitro* IL-4 release assay based on whole blood of healthy adults (n=4)

Figure 3. DELTA 2 trial design[a]



[a]Systemic exposure samples collected at Weeks 1, 4, and 16 (2-6 hours after delgocitinib cream application).
Key inclusion criteria: adults (aged ≥18) with diagnosis of CHE, defined as hand eczema that has persisted for >3 months or returned ≥2 times within past 12 months; IGA-CHE score of 3 (moderate) or 4 (severe); HESD itch score (weekly average) of ≥4 points; medical history of inadequate response to TCS (within past 12 months) or TCS medically inadvisable.
Results presented are from the main analysis of the primary estimand (composite strategy) where patients who discontinue study treatment (any reason) or initiate rescue treatment are considered non-responders with missing values being considered non-response.
DELTA 3: ClinicalTrials.gov ID NCT04949841.

Abbreviations

AE, adverse event; ALT, alanine aminotransferase; $AUC_{0-\infty}$, extrapolated area under the plasma concentration-time curve; CHE, Chronic Hand Eczema; C_{max}, peak drug plasma concentration; CV, coefficient of variation (calculated based on log-normal distribution assumption); HESD, hand eczema symptom diary; HRQoL, health-related quality of life; IC_{50}, concentration of drug required for 50% inhibition; IGA-CHE, Investigator's Global Assessment for CHE; JAK, Janus kinase; LC, liquid chromatography; LDL-C, low-density lipoprotein cholesterol; LTE, long-term extension; min, minimum; max, maximum; MS, mass spectrometry; N, number of patients in analysis set; n, number of patients with data available at baseline; Q1, first quartile; Q3, third quartile; TCS, topical corticosteroids; TG, triglycerides; t1/2, time required for drug plasma concentration to decrease by 50%; t_{max}, time to peak drug plasma concentration.

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3. Bissonnette R, *et al.* Late Breaker presentation on 18th March 2023 at the 81st Annual Meeting of the American Academy of Dermatology (AAD) in New Orleans, LA, USA. **4.** Schliemann S, *et al.* Poster presentation at 32nd Annual Congress of the EADV, 11-14 October 2023 in Berlin, Germany.

Disclosures

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Long-term safety and efficacy of delgocitinib cream for up to 36 weeks in adults with Chronic Hand Eczema: results of the Phase 3 open-label extension DELTA 3 trial

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Objectives

- To evaluate the long-term safety and efficacy of as-needed treatment with twice-daily applications of delgocitinib cream 20 mg/g in adults with CHE in the DELTA 3 trial

Results

Across DELTA 1, 2, and 3, no safety concerns were identified

- No increase in AE rates was seen in DELTA 3 long term as-needed treatment vs DELTA 1 and 2 (**Table 1**)
- Few SAEs were observed, with all being evaluated as non-related to study drug
- Delgocitinib cream 20 mg/g was generally well tolerated across all three trials
  - In DELTA 3, most patients reported no or mild tolerability issues[a] from Week 1 (83.9%), with tolerability improving up to Week 36 (90.2%)

Table 1. DELTA 1, 2, and 3 safety

	DELTA 1 delgocitinib cream 20 mg/g (N=325, PYO=100.85)			DELTA 2 delgocitinib cream 20 mg/g (N=313, PYO=95.87)			DELTA 3 (N=801, PYO=535.65)		
	n (%)	E	R	n (%)	E	R	n (%)	E	R
All events	147 (45.2)	308	305.41	143 (45.7)	269	280.60	495 (61.8)	1238	231.12
Serious events	6 (1.8)	7	6.94	5 (1.6)	5	5.22	27 (3.4)	36	6.72
Severity									
Mild	106 (32.6)	193	191.38	116 (37.1)	196	204.45	390 (48.7)	771	143.94
Moderate	68 (20.9)	99	98.17	50 (16.0)	68	70.93	242 (30.2)	429	80.09
Severe	12 (3.7)	16	15.87	3 (1.0)	5	5.22	28 (3.5)	38	7.09
Probably or possibly related to IMP	12 (3.7)	17	16.86	22 (7.0)	30	31.29	27 (3.4)	31	5.79
AEs leading to permanent discontinuation of study drug	2 (0.6)	2	1.98	1 (0.3)	1	1.04	7 (0.9)	8	1.49

[a]Defined as 'Worst stinging/burning' reported as 'none' or 'mild'.

DELTA 3 - Most frequent AEs were similar based on previous treatment

- No difference in proportion of patients who experienced the frequent AEs (≥2% of total subjects) was identified (**Table 2**)
- No clinically relevant changes were identified for vital signs, investigator-assessed ECGs and laboratory parameters

Table 2. Most frequently reported AEs

	Previous delgocitinib cream 20 mg/g (N=560, PYO=378.03)			Previous cream vehicle (N=241, PYO=157.62)			Total (N=801, PYO=535.65)		
System organ class/Preferred term[a]	n (%)	E	R	n (%)	E	R	n (%)	E	R
Infections and infestations									
COVID-19	95 (17.0)	99	26.19	39 (16.2)	39	24.74	134 (16.7)	138	25.76
Nasopharyngitis	91 (16.3)	117	30.95	37 (15.4)	44	27.91	128 (16.0)	161	30.06
Upper respiratory tract infection	24 (4.3)	28	7.41	8 (3.3)	8	5.08	32 (4.0)	36	6.72
Influenza	20 (3.6)	20	5.29	8 (3.3)	8	5.08	28 (3.5)	28	5.23
Skin and subcutaneous tissue disorders									
Hand dermatitis[b]	20 (3.6)	24	6.35	11 (4.6)	12	7.61	31 (3.9)	36	6.72
Eczema[c]	7 (1.3)	7	1.85	10 (4.1)	14	8.88	17 (2.1)	21	3.92
Musculoskeletal and connective tissue disorder									
Back pain	12 (2.1)	13	3.44	8 (3.3)	8	5.08	20 (2.5)	21	3.92
Nervous system disorder									
Headache	15 (2.7)	18	4.76	7 (2.9)	9	5.71	22 (2.7)	27	5.04

[a]Any clinically significant aggravation/exacerbation/worsening of any medical condition comparted to screening had to be reported; [b]Reporting exacerbation or worsening of CHE, which exceeded normal fluctuation or appeared in areas not normally affected by CHE; [c]Preferred term designated for non-specific eczemas on areas other than hands and wrists.

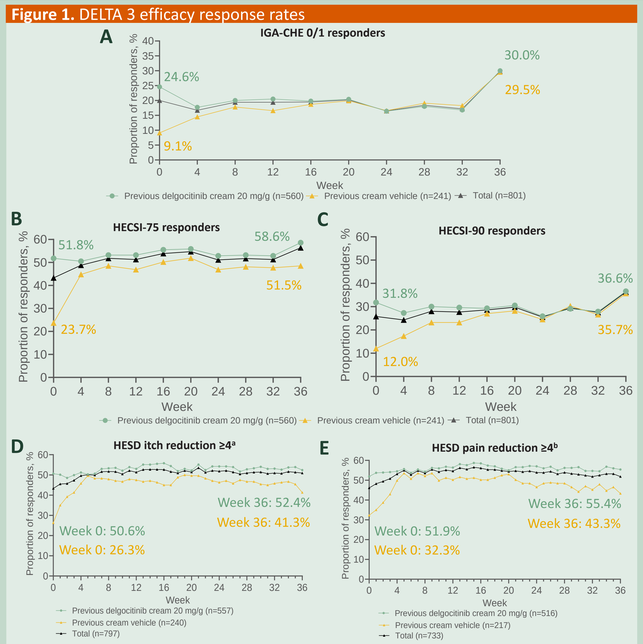
DELTA 3 efficacy response rates were maintained over time

- In DELTA 3, IGA-CHE 0/1 was maintained among subjects previously treated with delgocitinib cream 20 mg/g (**Fig. 1A**)
  - In DELTA 3, the IGA-CHE 0/1 response rate improved among subjects previously treated with cream vehicle
- Among subjects previously treated with delgocitinib cream 20 mg/g, HECSI-75/90 scores were maintained in DELTA 3 (**Fig. 1B and C**)
  - Among subjects previously treated with cream vehicle, the HECSI-75/90 score response rates improved in DELTA 3
- In DELTA 3, ≥4-point HESD itch/pain reductions were maintained among subjects previously treated with delgocitinib cream 20 mg/g (**Fig. 1D and E**)
  - In DELTA 3, ≥4-point HESD itch/pain reductions were improved among subjects previously treated with cream vehicle

Conclusions

- Overall, with delgocitinib cream 20 mg/g treatment no safety concerns were identified
  - Consistent with DELTA 1 and 2, delgocitinib cream 20 mg/g remained well tolerated in DELTA 3
- Efficacy rates were maintained among subjects treated with delgocitinib cream 20 mg/g in the parent trials (DELTA 1 and DELTA 2)
  - Efficacy further improved among subjects previously treated with cream vehicle
- These DELTA 3 data support the benefit of long-term as-needed use of delgocitinib cream 20 mg/g in patients with moderate to severe CHE

Figure 1. DELTA 3 efficacy response rates

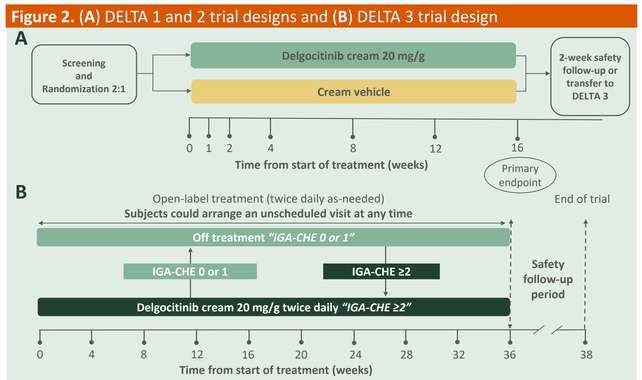


Missing data and data after initiation of rescue medication imputed as non-response. [a]Only includes subjects with parent trial baseline itch score ≥4; [b]Only includes subjects with parent trial baseline pain score ≥4.

Methods

- DELTA 3 (NCT04949841) was a Phase 3, 36-week, open-label, multi-site, extension trial in adults with CHE who completed DELTA 1 or DELTA 2 (**Fig. 2**)
  - DELTA 1 and 2 studied the effect of twice-daily applications of delgocitinib cream 20 mg/g versus cream vehicle in adults with moderate to severe CHE
  - In DELTA 3, patients with IGA-CHE 0 or 1 were not assigned to treatment while patients with IGA-CHE ≥2 were assigned to delgocitinib cream 20 mg/g treatment

Figure 2. (**A**) DELTA 1 and 2 trial designs and (**B**) DELTA 3 trial design



During DELTA 3, patients stopped treatment when IGA-CHE 0 or 1 was achieved and re-initiated treatment when they experienced IGA-CHE ≥2. Subjects experiencing discontinuation of study drug, initiation of rescue treatment, or withdrawal from trial, were imputed as non-responders. Otherwise, missing values were not imputed.

Background

- CHE is one of the most frequent chronic inflammatory diseases affecting hands and wrists, and is associated with pain, itch, as well as significant functional, social, and psychological burden[1-4]
  - There are no topical treatments specifically developed and approved for CHE[5,6]
  - There is a preference from patients for novel steroid-free topical alternatives for CHE treatment[7]
- Delgocitinib is a first-in-class topical pan-JAK inhibitor that targets the key mediators of CHE pathogenesis[8]
  - In the pivotal Phase 3 DELTA 1 (NCT04871711) and DELTA 2 (NCT04872101) trials, delgocitinib cream 20 mg/g demonstrated greater improvements in both patient- and clinician-reported efficacy outcomes versus cream vehicle and was well tolerated over 16 weeks[9,10]

Baseline Demographics and Characteristics

	Previous delgocitinib cream 20 mg/g (N=560)	Previous cream vehicle (N=241)	Total (N=801)
Age, median years (min-max)	46.0 (18-83)	44.0 (18-86)	45.0 (18-86)
Sex, female, n (%)	355 (63.4)	157 (65.1)	512 (63.9)
Race, n (%)			
White	513 (91.6)	219 (90.9)	732 (91.4)
Asian	15 (2.7)	9 (3.7)	24 (3.0)
Black or African American	3 (0.5)	1 (0.4)	4 (0.5)
Other/Not reported	29 (5.2)	12 (5.0)	41 (5.1)
Region, n (%)			
Europe	447 (79.8)	192 (79.7)	639 (79.8)
North America	113 (20.2)	49 (20.3)	162 (20.2)
IGA-CHE, n (%)			
Clear or almost clear	138 (24.6)	22 (9.1)	160 (20.0)
Mild	256 (45.7)	89 (36.9)	345 (43.1)
Moderate	145 (25.9)	98 (40.7)	243 (30.3)
Severe	21 (3.8)	32 (13.3)	53 (6.6)
HECSI, median	13.0	36.0	20.0
HESD itch (weekly average), median	2.7	4.9	3.4
HESD pain (weekly average), median	2.1	4.4	3.0
Age at onset of CHE, median years (min-max)	35.0 (0-83)	33.0 (0-72)	34.0 (0-83)
Duration of CHE, median years (min-max)	5.0 (0-61)	5.0 (0-53)	5.0 (0-61)
CHE subtype, main diagnosis, n (%)			
Atopic hand eczema	192 (34.3)	89 (36.9)	281 (35.1)
Hyperkeratotic eczema	120 (21.4)	48 (19.9)	168 (21.0)
Irritant contact dermatitis	111 (19.8)	45 (18.7)	156 (19.5)
Allergic contact dermatitis	74 (13.2)	45 (18.7)	119 (14.9)
Vesicular hand eczema (pompholyx)	63 (11.3)	14 (5.8)	77 (9.6)
Contact urticaria/protein contact dermatitis	0	0	0

HECSI ranges from 0-360.

Abbreviations

AE, adverse event; CHE, Chronic Hand Eczema; E, number of events; HECSI, Hand Eczema Severity; HECSI-75/90, ≥75%/90% improvement in HECSI score from baseline; HESD, Hand Eczema Symptom Diary (HESD itch score and HESD pain score ranges from 0-10); IGA-CHE, Investigator's Global Assessment for Chronic Hand Eczema (IGA-CHE scores: 0-clear, 1-almost clear, 2-mild, 3-moderate and 4-severe); IMP, investigational medicinal product; JAK, Janus kinase; min, minimum; max, maximum; PYO, patient years of observation; R, event rate calculated as (E/PYO)*100.

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1. Capucci S, *et al.* Dermatitis. 2020;31(3):178-184; **2.** Thyssen JP, *et al.* Contact Dermatitis. 2022;86(5):357-378; **3.** Politiek K, *et al.* Contact Dermatitis. 2016;75(2):67-76; **4.** Kouris A, *et al.* Contact Dermatitis. 2015;72(6):367-70; **5.** Dubin C, *et al.* Ther Clin Risk Manag. 2020;16:1319-1332; **6.** Lee HG, *et al.* Dermatol Ther. 2019;32(3):e12840; **7.** Egeberg A, *et al.* JAAD Int. 2024;14:77-83; **8.** Tanimoto A, *et al.* Inflamm Res. 2015;64(1):41-51; **9.** Bissonnette R, *et al.* Late Breaker presentation on 18th March 2023 at the 81st Annual Meeting of the American Academy of Dermatology (AAD) in New Orleans, LA, USA; **10.** Schliemann S, *et al.* Poster presentation at 32nd Annual Congress of the EADV, 11-14 October 2023 in Berlin, Germany.

Disclosures

MG has been an investigator, speaker and/or advisor for: AbbVie, Acelyrin, Amgen, Akros, AnaptysBio, Arcutis Biotherapeutics, Aristea Therapeutics, ASLAN Pharmaceuticals, Apogee, Bausch Health, BMS, Boehringer Ingelheim, Cara Therapeutics, Celgene, Dermira, Dermavant, Eli Lilly, Galderma, Inmagene Biopharmaceuticals, Incyte, Inmagene Biopharmaceuticals, Janssen, LEO Pharma A/S, Medimmune, Meiji Seika Pharma, Moonlake, Nimbus, Novartis, Pfizer, Regeneron, Reistone Biopharma, Roche, Sanofi Genzyme, Sun Pharma, Tarsus, Takeda Pharmaceuticals, UCB, and Ventyx. **SM** has received honoraria as consultant/advisor or speaker and/ or grants from Abbvie, Almirall, Aralez, Arcutis, Basilea, Bausch and Lomb, Bristol Myer Squibb, Boehringer-Ingelheim, Evidera, Galderma, GSK, Incyte, LEO Pharma A/S, Lilly, Novartis, Pfizer, Sanofi, Sun Pharma and UCB. She is currently investigator for Novartis and LEO Pharma A/S. **RB** is an Advisory Board Member, Consultant, Speaker and/or Investigator for and receives honoraria and/or grant from AbbVie, Amgen, Apogee, Arcutis, Asana BioSciences, Bellus Health, BioMimetix, Bluefin Biomedicine, Boehringer-Ingelheim, Boston, CARA Therapeutic, Clexio, Dermavant, Eli Lilly, Escient, Evidera, Fresh Tracks (Brickell), Galderma, GlaxoSmithKline, Incyte, Inmagene Bio, Janssen, LEO Pharma A/S, Merck, Novartis, Opsidio, Pfizer, RAPT Therapeutic, Regeneron, Sanofi, Target RWE, Vyne Therapeutics and Zencor. **NW** reports grants and personal fees from from AbbVie Deutschland, Allergopharma, Aimmune, ALK-Abello, Almirall S. A., Amgen GmbH, Biotest, Bristol-Myers Squibb GmbH & Co., DBV Technologies, KGaA, Mylan Germany, LEO Pharma A/S, Lilly Deutschland, Regeneron Pharmaceuticals, Sanofi Aventis, Novartis, and Pfizer Deutschland GmbH, outside the submitted work and is past WAO co-chair of the anaphylaxis committee. **MNC** is a consultant, advisory board member, investigator, and/or speaker for AbbVie, Eli Lilly, LEO Pharma A/S, Novartis, Pfizer, and Sanofi-Genzyme. **LS** has been principal investigator in clinical trials sponsored by and/or and has received personal fees for participation in advisory board from Abbvie, Amgen, LEO Pharma A/S, Eli Lilly, Novartis, and Sanofi, outside the submitted work. **RW** has received research grants or consulting fees from AbbVie, Almirall, Amgen, Arena, Astellas, Avillion, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, DICE, GSK, Janssen, Lilly, LEO Pharma A/S, Novartis, Pfizer, Sanofi, Sun Pharma, UCB and UNION. **SS** is a consultant, advisory board member, investigator, and/or speaker for LEO Pharma A/S and Sanofi-Aventis. **CLBC** and **MLO** are employees of LEO Pharma A/S. **TA** has been a speaker/consultant/advisor for AbbVie, Almirall, Eli Lilly, LEO Pharma A/S, Pfizer, and Sanofi-Genzyme.

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Real-world effectiveness of tralokinumab in adults with atopic dermatitis: Interim data on improvements in physician-assessed disease severity after up to 9 months of follow-up in the TRACE study

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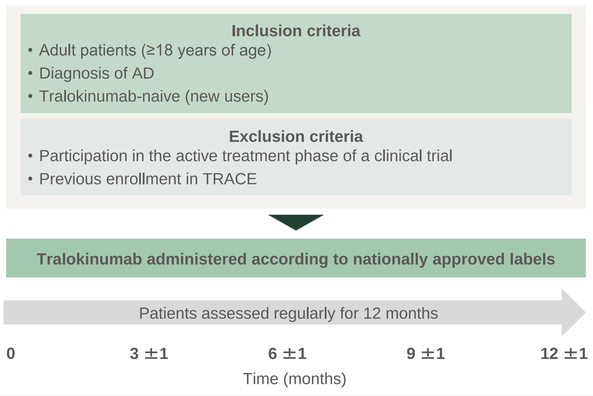
Background

- AD is a chronic inflammatory skin disease that is associated with substantial disease burden, often requiring long-term treatment[1]
- Tralokinumab, a high-affinity monoclonal antibody that specifically targets IL-13, is indicated for the treatment of moderate-to-severe AD[2,3]
- Phase 3 clinical trials have shown that tralokinumab is effective and well tolerated
- TRACE is a global, real-world, up to 12-month study of adult patients with AD that aims to better understand the use of tralokinumab in clinical practice[4]

Methods

- TRACE is a prospective, noninterventional, multicenter study of adult patients with AD who were prescribed tralokinumab according to national approved labels (**Fig. 1**)
- Patients from 167 sites from 11 countries across Europe, North America, and the Middle East, were enrolled in TRACE between November 2021 and July 2023
- This interim analysis, with data cutoff of October 15th, 2023, assessed patients at baseline, 3-, 6- and 9-month visits
- This analysis included 824 patients who received ≥1 dose of tralokinumab
- Physician-assessed outcome measures included: EASI and/or IGA, according to individual clinical practice
- All data presented are as observed

Figure 1. TRACE study design



Baseline and Disease Characteristics

- Overall, baseline demographics were similar between dupilumab-naive (N=627) and dupilumab-experienced (N=197) patients; however, dupilumab-naive patients exhibited higher baseline disease severity (**Table 1**)

Table 1. Baseline demographics and disease characteristics

	Dupilumab-naive (N=627)	Dupilumab-experienced (N=197)	Total (N=824)
Mean age, years (SD)	43.2 (17.9)	46.7 (17.6)	44.1 (17.9)
Gender, n (%)			
Male	338 (53.9)	92 (46.7)	430 (52.2)
Race, n (%)			
Asian	33 (5.3)	11 (5.6)	44 (5.3)
Black or African American	24 (3.8)	13 (6.6)	37 (4.5)
White	480 (76.6)	144 (73.1)	624 (75.7)
Multiple/Unknown/Other	90 (14.3)	29 (14.7)	119 (14.4)
BMI (kg/m^2), mean (SD)	*n=539,* 26.6 (5.7)	*n=176,* 27.7 (6.0)	*n=715,* 26.9 (5.8)
EASI	*n=499*	*n=132*	*n=631*
mean (SD)	20.9 (10.9)	16.9 (10.8)	20.1 (11.0)
≤7, %	11.0	26.0	14.0
IGA	*n=616*	*n=192*	*n=808*
3 (moderate disease), n (%)	321 (52.1)	80 (41.7)	401 (49.6)
4 (severe disease), n (%)	214 (34.7)	61 (31.8)	275 (34.0)
PP-NRS	*n=364*	*n=120*	*n=484*
Mean (SD)	6.6 (2.4)	5.5 (2.8)	6.3 (2.6)
DLQI	*n=351*	*n=95*	*n=446*
Mean (SD)	13.4 (7.5)	10.7 (7.3)	12.8 (7.5)
Sleep NRS	*n=298*	*n=74*	*n=372*
Mean (SD)	5.2 (3.2)	4.4 (2.9)	5 (3.2)

Objective

- To evaluate changes in physician-assessed disease severity of AD in an interim analysis of the global noninterventional TRACE study

Results

- Mean EASI improved from 20.1 at baseline to 6.4 at 3 months, 5.4 at 6 months, and 3.6 at 9 months of tralokinumab treatment (**Fig. 2**)
- The proportion of patients with EASI ≤7 (no or mild disease) increased from 14% at baseline to 72% at 3 months, 77% at 6 months, and 80% at 9 months (**Fig. 3**)
- Among the patients with baseline IGA ≥2 (mild to severe disease), the proportion with at least a 2-point improvement in IGA increased from 46% at 3 months to 58% at 6 months, and 70% at 9 months of treatment (**Fig. 4**)
- Dupilumab-naive and dupilumab-experienced patients showed similar improvement across all efficacy endpoints, despite higher baseline disease severity in dupilumab-naive patients

Figure 3. Percentage of patients with EASI ≤7 with tralokinumab

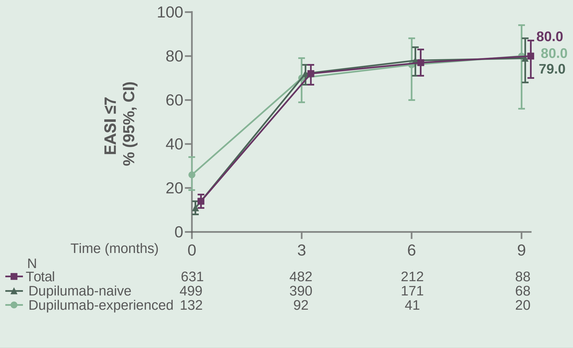
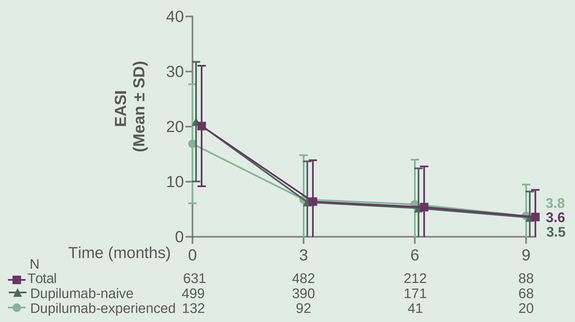
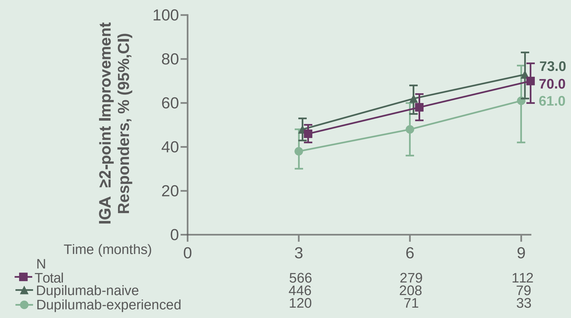


Figure 2. Mean EASI with tralokinumab



Some error bars are clipped at the axis.

Figure 4. Percentage of patients with IGA ≥2-point improvement with tralokinumab (among patients with baseline IGA ≥2)



Conclusions

- Results from the interim analysis (up to 9 months) of the global non-interventional TRACE study show effectiveness of tralokinumab treatment in adult patients with AD in a real-world setting
- Improvements were similar regardless of prior dupilumab use, and consistent with progressive improvements with tralokinumab in phase 3 clinical trials

Disclosures: **EP** has been consultant, clinical trial investigator and speaker for LEO Pharma A/S, Abbvie, Pfizer, Novartis, Sanofi Genzyme, Galderma, Boehringer Ingelheim, and Janssen. **MC** has served as a clinical trial investigator for Astellas, Galapagos, Johnson & Johnson, LEO Pharma A/S, 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 A/S, L'Oréal, MSD, Novartis, Regeneron, Sanofi Genzyme, Stiefel, and Unilever; has received honoraria from Astellas, Johnson & Johnson, LEO Pharma A/S, Novartis, Regeneron, Sanofi Genzyme, and Stiefel; and has received research funding from Bayer. **JB** has served as an investigator, speaker, advisor/consultant for and/or received grants/honoraria from AbbVie, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Concert, Galderma, Eli Lilly, Incyte, Janssen, Johnson and Johnson, LEO Pharma A/S, L'Oréal Group, Novartis, Pfizer, Reistone, Sanofi Genzyme, and UCB. **AR** is an investigator and consultant/advisor or speaker for: Abbvie, Arcutis, Bristol Myers Squibb, Eli Lilly, Incyte, Janssen, LEO Pharma A/S, Novartis, Sun, and UCB. **IV, TF, and UI** are employees of LEO Pharma A/S. **DT** has served as an investigator and/or consultant/adviser for AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celltrion, Eli Lilly, Galderma, Janssen-Cilag, LEO Pharma, L'Oreal, Meiji, NewBridge, Novartis, Regeneron, Sanofi, Pfizer, Target-RWE, UCB, and Vichy. He has received grants from AbbVie, LEO Pharma, and Novartis.

Abbreviations: AD, atopic dermatitis; BMI, body mass index; CI, confidence interval; DLQI, dermatology life quality index; EASI, eczema area and severity index; IGA, investigator's global assessment; IL, interleukin; n, patients in the analysis set; NRS, numerical rating scale; PP-NRS, peak pruritus numeric rating scale; PRO, patient-reported outcome; SD, standard deviation; TRACE, tralokinumab real world clinical use.

References: **1.** Weidinger S, Novak N. *Lancet.* 2016;387(10023):1109-1122. **2.** Bieber T. *Allergy.* 2020;75(1):54-62. **3.** Wollenberg A, Blauvelt A, Guttman-Yassky E, et al. *Br J Dermatol.* 2021;184(3):437-449. **4.** Thaçi D, et al. Presented at Revolutionizing Atopic Dermatitis (RAD) Conference 2023 (Abstract #418).

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Real-world effectiveness of tralokinumab in adults with atopic dermatitis on the genitals: Interim data on improvements in physician-assessed disease severity and patient-reported outcomes in up to 3 months of treatment in the TRACE study

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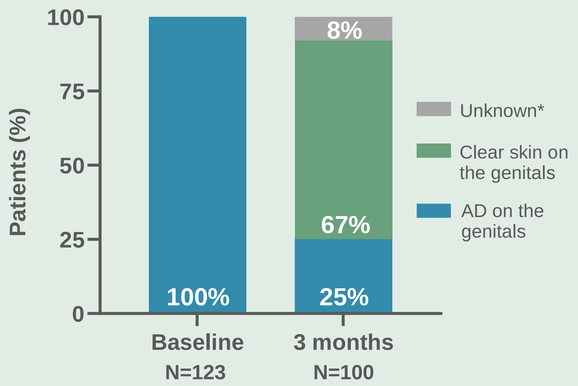
Objectives

- To evaluate changes in investigator-assessed disease severity and patient-reported outcomes in patients with AD on the genitals in an interim analysis of the noninterventional TRACE study

Results

- Among the patients who had AD on the genitals at baseline, the majority (67%) reported clear skin on the genitals by 3 months of tralokinumab treatment (**Fig. 1**)

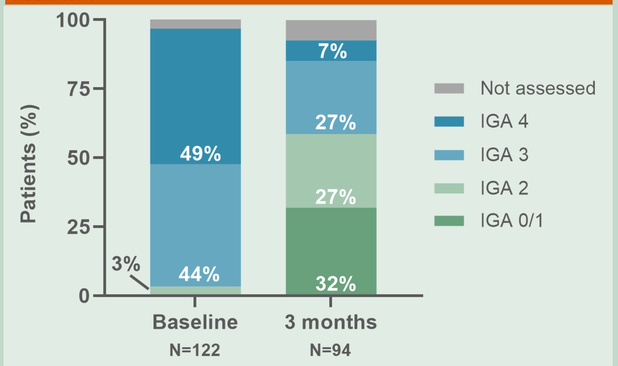
Figure 1. Proportion of patients with AD on the genitals at baseline and after 3 months of tralokinumab treatment



*Information on AD localization not available.

- The proportion of patients with IGA 0/1 (clear or almost clear disease) increased from 0% at baseline to 32% by 3 months of treatment, and the proportion of patients with IGA 4 (severe disease) decreased from 49% at baseline to 7% at 3 months (**Fig. 2**)
- Among patients with IGA ≥2 at baseline, approximately half of patients achieved an IGA reduction of ≥2 at 3 months (**Table 1**)

Figure 2. Improvement in IGA after 3 months of tralokinumab treatment



Percentages are rounded to the nearest whole number.

- Among patients with DLQI ≥6 at baseline, the majority achieved a DLQI reduction of ≥6 at 3 months (**Table 1**)
- Mean sleep NRS improved by approximately half from baseline to 3 months (**Table 1**)

Table 1. Improvement in additional endpoints from baseline to 3 months of tralokinumab treatment

Endpoint	Baseline	3 months
IGA reduction ≥2 n/N (%)	-	44/90 (48.9)
DLQI reduction of ≥6 n/N (%)	-	14/22 (63.6)
Sleep NRS Mean (lower error ; upper error)	N=50 6.16 (5.72 ; 6.60)	N=26 3.54 (2.90 ; 4.17)

Conclusions

- An increased awareness of involvement of AD on the genitals and treatment options for this neglected area is essential
- Among adult patients with AD on the genitals at baseline, two-thirds reported clear skin on the genitals, with only 25% still reporting AD on the genitals, at 3 months of tralokinumab treatment in TRACE
- Patients with AD on the highly impactful genital region showed substantial improvements in AD severity and PROs with tralokinumab treatment in a real-world setting, including the proportion of patients with IGA ≤2 (clear-to-mild) increasing from 3% at baseline to 59% at 3 months

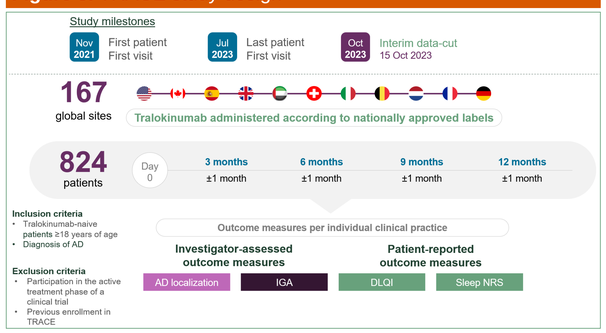
Background

- AD is an inflammatory skin disease that can involve any part of the body, including the genital region[1,2]
- The presentation of AD on the genitals is often overlooked and underreported due to patients' reluctance to discuss this sensitive area with the clinician and the lack of routine examination of this region[1-3]
- Presence of AD in the genital area can have a significant negative impact on quality of life, including pain, sleep, mood, sexual function, and personal relationships[4,5]
- Tralokinumab, a high-affinity monoclonal antibody that specifically targets IL-13, is indicated for the treatment of moderate-to-severe AD[6,7]
- Recent case series have demonstrated successful use of tralokinumab in the treatment of AD on the genitals[1,2]

Methods

- TRACE is a prospective, non-interventional, international, single-cohort study of adult patients with AD who were prescribed tralokinumab according to national approved labels (**Fig. 3**)
- Patients from 167 sites from 11 countries across Europe, North America, and the Middle East, were enrolled in TRACE between November 2021 and July 2023
- This subanalysis included patients with AD on the genitals at baseline with a data cutoff of October 15, 2023
- Outcome measures collected included: IGA, DLQI, and sleep NRS, as per individual clinical practice

Figure 3. TRACE study design



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Baseline demographics

- Of the 824 patients in the total population, 14.9% had AD on the genitals at baseline (**Table 2**)
- Baseline demographics were similar between the total population and patients with AD on the genitals, though patients with AD on the genitals tended to have higher baseline disease severity, and a greater proportion were male, White, and in Europe

Table 2. Baseline characteristics

	Patients with genital AD (N=123)	Total population (N=824)
Mean age, years (SD)	42.2 (17.1)	44.1 (17.9)
Gender, male, n (%)	78 (63.4)	430 (52.2)
Race, n (%)		
White	100 (81.3)	624 (75.7)
Asian	5 (4.1)	44 (5.3)
Black or African American	3 (2.4)	37 (4.5)
Unknown	5 (4.1)	45 (5.5)
BMI (kg/m^2)	*N=115*	*N=715*
Mean (SD)	27.1 (6.0)	26.9 (5.8)
Country, n (%)		
Germany	57 (46.3)	226 (27.4)
Italy	20 (16.3)	149 (18.1)
United States	15 (12.2)	137 (16.6)
Canada	8 (6.5)	93 (11.3)
France	5 (4.1)	58 (7.0)
Switzerland	5 (4.1)	12 (1.5)
Belgium	4 (3.3)	24 (2.9)
Netherlands	4 (3.3)	18 (2.2)
Spain	3 (2.4)	40 (4.9)
Great Britain	1 (0.8)	29 (3.5)
United Arab Emirates	1 (0.8)	38 (4.6)
AD disease duration (years)	*N=120*	*N=807*
Mean (SD)	19.2 (16.6)	18.9 (17.8)
IGA, n (%)		
0 (Clear disease)	0 (0.0)	3 (0.4)
1 (Almost clear disease)	0 (0.0)	13 (1.6)
2 (Mild disease)	4 (3.3)	67 (8.3)
3 (Moderate disease)	54 (44.3)	401 (49.6)
4 (Severe disease)	60 (49.2)	275 (34.0)
DLQI	*N=61*	*N=446*
Mean (SD)	15.8 (7.6)	12.8 (7.5)
Sleep NRS	*N=50*	*N=372*
Mean (SD)	6.2 (3.1)	5.0 (3.2)

Abbreviations: AD, atopic dermatitis; BMI, body mass index; DLQI, Dermatology Life Quality Index; IGA, Investigator's Global Assessment; IL, interleukin; n, number of patients who achieved the indicated metric; N, number of patients with available data; NRS, numeric rating scale; PRO, patient-reported outcome; SD, standard deviation; TRACE, Tralokinumab Real World Clinical Use.

References: **1.** Paolino G, Narcisi A, Carugno A, et al. *J Dermatolog Treat*. 2024;35(1):2351489. **2.** Paolino G, Sernicola A, Di Nicola M, et al. *Clin Exp Dermatol*. 2022;47(1):176-178. **3.** Napolitano M, Fabbrocini G, Martora F, et al. *Dermatol Ther.* 2022; 35(12):e15901. **4.** Rodríguez-Pozo JA, Montero-Vílchez T, Díaz Calvillo P, et al. *Acta Derm Venereol.* 2024;104:adv35107. **5.** Yang E and Murase J. *Int J Womens Dermatol.* 2018;4(4):223-226. **6.** Bieber T. *Allergy*. 2020;75(1):54-62. **7.** Wollenberg A, Blauvelt A, Guttman-Yassky E, et al. *Br J Dermatol.* 2021;184(3):437-449.

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Real-world effectiveness of tralokinumab in adults with atopic dermatitis: Interim data on improvements in patients with atopic dermatitis with hands and feet involvement after up to 9 months of treatment in the TRACE study

Diamant Thaçi,[1] Pierre André Becherel,[2] Adrian Rodriguez,[3] Teodora Festini,[4] Ulla Ivens,[4] Ida Vittrup,[4] Mahreen Ameen[5]

[1]University of Luebeck, Germany, [2]Antony Hospital, France, [3]Nashville Skin, USA, [4]LEO Pharma A/S, DK, [5]Royal Free London National Health Services Foundation Trust, UK

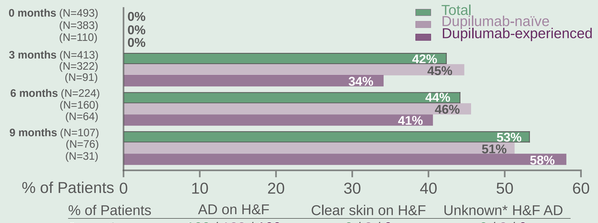
Objectives

- To evaluate the effectiveness of tralokinumab treatment on AD signs and symptoms in patients with hands and/or feet (H&F) AD in an interim analysis of the noninterventional TRACE study

Results

- Among patients who had H&F AD at baseline, 42.4% had clear skin on the H&F area at 3 months, which increased to 53.3% at 9 months of tralokinumab **(Fig. 1)**

Figure 1. Percentages of patients with clear skin on the H&F area

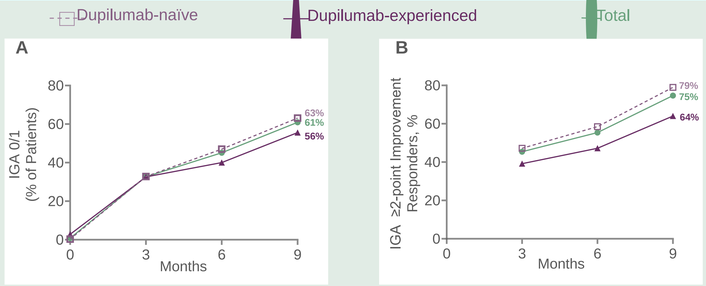


% of Patients	AD on H&F	Clear skin on H&F	Unknown* H&F AD
0 months	100 / 100 / 100	0 / 0 / 0	0 / 0 / 0
3 months	47 / 44 / 57	42 / 45 / 34	10 / 11 / 9
6 months	39 / 38 / 42	44 / 46 / 41	17 / 16 / 17
9 months	25 / 25 / 26	53 / 51 / 58	22 / 24 / 16

Percentages are rounded to the nearest whole number. *Information on AD localization not available.

- Percentages of patients with IGA 0/1 increased from 0.8% at baseline to 32.7% at 3 months, and further increased to 60.9% at 9 months of tralokinumab **(Fig. 2A)**
- Among patients with baseline IGA ≥2, percentages achieving ≥2-point improvement in IGA increased from 45.4% at 3 months to 74.7% at 9 months **(Fig. 2B)**

Figure 2. Improvement in IGA-assessed disease severity

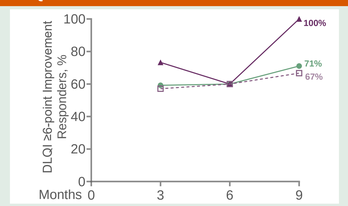


n/N				
Dupilumab-naïve	1/379	99/302	70/149	41/65
Dupilumab-experienced	3/109	28/86	22/55	15/27
Total	4/488	127/388	92/204	56/92

n/N				
Dupilumab-naïve	133/282	83/142	49/62	
Dupilumab-experienced	31/79	25/53	16/25	
Total	164/361	108/195	65/87	

- Among patients with baseline DLQI ≥6, percentages achieving ≥6-point reduction in DLQI increased from 59.2% at 3 months to 71.1% at 9 months of tralokinumab **(Fig. 3)**

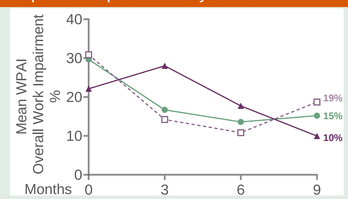
Figure 3. Improvement in QoL



n/N			
Dupilumab-naïve	60/105	33/55	22/33
Dupilumab-experienced	11/15	6/10	5/5
Total	71/120	39/65	27/38

- WPAI (percent overall work impairment) due to AD decreased from 29.7% at baseline to 16.7% at 3 months, and 15.2% at 9 months of tralokinumab **(Fig. 4)**

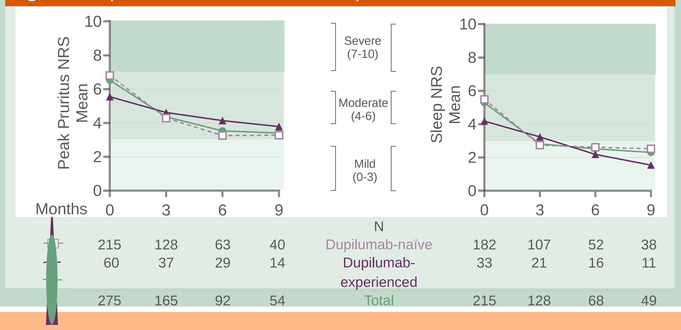
Figure 4. Improvement in patient-reported ability to work



N				
Dupilumab-naïve	75	41	12	9
Dupilumab-experienced	12	9	8	6
Total	87	50	20	15

- Mean peak pruritus and Sleep NRS scores improved by 3 months, with further improvement by 9 months of tralokinumab **(Fig. 5)**

Figure 5. Improvement in Pruritus and Sleep NRS



N				
Dupilumab-naïve	215	128	63	40
Dupilumab-experienced	60	37	29	14
Total	275	165	92	54

N				
Dupilumab-naïve	182	107	52	38
Dupilumab-experienced	33	21	16	11
Total	215	128	68	49

Conclusions

- 42% of patients with baseline H&F AD reported clear skin on the H&F area after 3 months of tralokinumab, which increased to 53% at 9 months
  - Among dupilumab-experienced patients with baseline H&F involvement, 58% showed clear skin on the H&F area at 9 months of tralokinumab
- In this TRACE interim analysis, tralokinumab improved signs, symptoms, QoL, and work productivity in patients with H&F AD in a real-world setting

Background

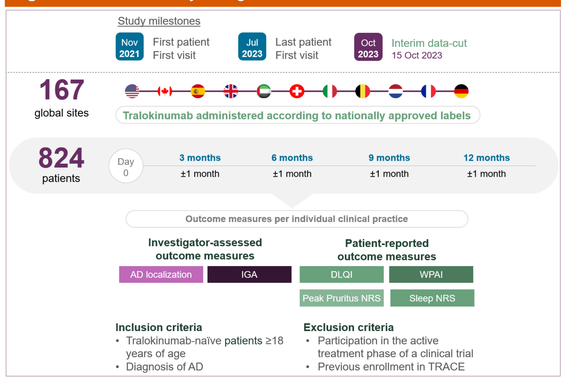
- AD is a chronic inflammatory skin disease that is associated with substantial disease burden[1]
- AD often affects the H&F, which are considered high-impact areas, due to significant negative impact on patients' quality of life and ability to work[2,3]
- Tralokinumab, a high-affinity monoclonal antibody that specifically targets IL-13, is indicated for the treatment of moderate-to-severe AD[4,5]

Methods

- TRACE is a prospective, noninterventional, single-cohort study of adult patients with AD who were prescribed tralokinumab according to national approved labels (**Fig. 6**)
- Patients from 167 sites from 11 countries across Europe, North America, and the Middle East, were enrolled in TRACE between November 2021 and July 2023
- This interim analysis, with a data cutoff of October 15, 2023, assessed patients with AD involvement on hands and/or feet at baseline
- Outcomes collected included AD localization, and overall AD measures; IGA, DLQI, WPAI, Peak Pruritus NRS, and/or Sleep NRS according to individual clinical practice
- Data presented as observed from baseline, 3-, 6-, and 9-month visits*

*Not all patients included in the analysis had completed all visits at the time of interim analysis data cutoff

Figure 6. TRACE study design



Baseline and Disease Characteristics

- In patients with baseline H&F AD (59.8% of full analysis set), dupilumab-naïve patients reported slightly higher baseline disease severity and impact on QoL than dupilumab-experienced patients (**Table 1**)

Table 1. Baseline characteristics

	Dupilumab-naïve (N=383)	Dupilumab-experienced (N=110)	Total (N=493)
Mean age, years (SD)	41.6 (17.1)	48.1 (17.5)	43.0 (17.4)
Gender, n (%)			
Male	206 (53.8%)	51 (46.4%)	257 (52.1%)
Race, n (%)			
Asian	23 (6.0%)	7 (6.4%)	30 (6.1%)
Black/African American	7 (1.8%)	8 (7.3%)	15 (3.0%)
White	301 (78.6%)	79 (71.8%)	380 (77.1%)
Multiple	1 (0.3%)	1 (0.9%)	2 (0.4%)
Mean disease duration, years (SD)	19.7 (16.9) *n=375*	23.1 (20.9) *n=110*	20.5 (17.9) *n=485*
BMI (kg/m^2), mean (SD)	26.7 (5.4)	28.1 (6.2)	27.1 (5.6)
IGA 4 (severe), n (%)	144 (38.0%)	41 (37.6%)	185 (37.9%)
DLQI, Mean (SD)	14.3 (7.5) *n=217*	12.1 (7.8) *n=49*	13.9 (7.5) *n=266*
WPAI, Mean	30.9 *n=75*	22.1 *n=12*	29.7 *n=87*
Peak Pruritus NRS, Mean (SD)	6.8 (2.4) *n=215*	5.6 (2.6) *n=60*	6.5 (2.5) *n=275*
Sleep NRS, Mean (SD)	5.5 (3.1) *n=182*	4.2 (2.7) *n=33*	5.3 (3.0) *n=215*

Abbreviations

AD, atopic dermatitis; BMI, body mass index; DLQI, dermatology life quality index; H&F, hands and feet; IGA, investigator's global assessment; IL, interleukin; n, number of patients with the indicated metric; N, number of patients with available data; NRS, numeric rating scale; QoL, quality of life; RECAP, recap for atopic eczema; SD, standard deviation; WPAI, work productivity and activity impairment; TRACE, tralokinumab real world clinical use.

References

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3. Lee HJ, Ha SJ, Ahn WK, et al. *Pediatr Dermatol*, 2001;18(2):102-106.; 19(10):943-948. **4.** Bieber T. *Allergy*. 2020;75(1):54-62. **5.** Wollenberg A, Blauvelt A, Guttman-Yassky E, et al. *Br J Dermatol*. 2021;184(3):437-449.

Disclosures

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Lebrikizumab Improves Atopic Dermatitis in Adult and Adolescent Patients With Skin of Color: 16-Week Results From the ADmirable Study

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[1]Weill Cornell Medicine, New York, USA, [2]Comprehensive Dermatology Center, Detroit, USA, [3]Miami Dermatology and Laser Institute, Miami, USA, [4]Wallace Skin Research Center, Los Angeles, USA, [5]Skin Care Physicians of Georgia, Macon, USA, [6]First OC Dermatology Research, Fountain Valley, USA, [7]Solutions Through Advanced Research, Jacksonville, USA, [8]Eli Lilly and Company, Indianapolis, USA, [9]Baylor University Medical Center, Dallas, Arlington Research Center, Arlington, and Arlington Center for Dermatology, Arlington, USA

OBJECTIVES

- Results on efficacy and safety outcomes from ADmirable (NCT05372419), the first Phase 3, open-label, 24-week trial of lebrikizumab in adult and adolescent patients with moderate-to-severe AD and skin of color, a historically under-represented patient population, were first reported at AAD 2024[1]
- This analysis reports the 16-week efficacy and safety outcomes, including innovative measures of post-inflammatory hyperpigmentation and hypopigmentation

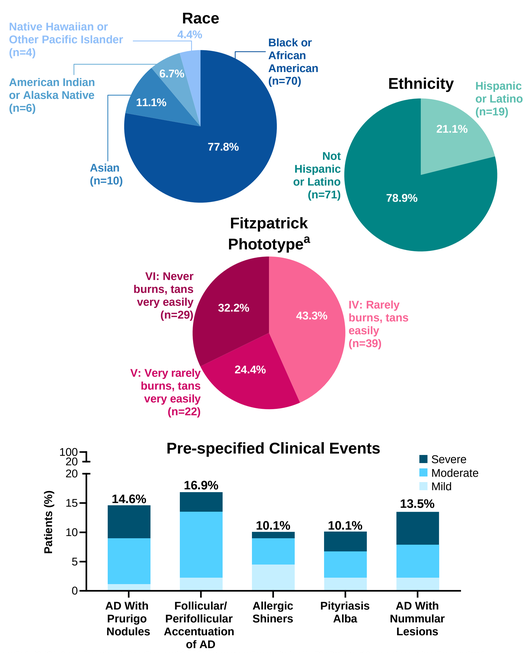
CONCLUSIONS

- ADmirable is the first clinical trial to report data from patients with moderate-to-severe AD and skin of color (78% Black or African American patients) using novel tools and scales to evaluate signs and symptoms that matter to patients
- Lebrikizumab improved AD signs and symptoms after 16 weeks of treatment
  - The majority of patients achieved 75% or greater improvement in skin clearance and showed improved symptoms of itch and quality of life
- Based on the novel PDCA-Derm™ scale, lebrikizumab improved hypopigmented and hyperpigmented lesions
- Lebrikizumab's safety profile was consistent with that reported in Phase 3 trials[3-6]
  - No SAEs were reported

Elevate-Derm West Conference; Scottsdale, AZ, USA; November 7-10, 2024

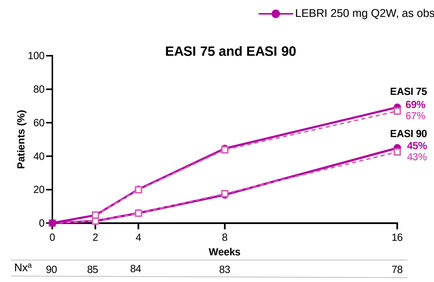
Baseline Demographics and Disease Characteristics

	LEBRI 250 mg Q2W (N=90)
Age, years	40.7 (19.6)
Adult (≥18 years), n (%)	76 (84.4)
Adolescent (≥12 to <18 years), n (%)	14 (15.6)
Female, n (%)	39 (43.3)
BMI, kg/m^2	30.1 (7.7)
BMI category, n (%)	
Underweight (<18.5 kg/m^2)	3 (3.3)
Normal (≥18.5 and <25 kg/m^2)	19 (21.1)
Overweight (≥25 and <30 kg/m^2)	30 (33.3)
Obese (≥30 and <40 kg/m^2)	26 (28.9)
Extreme obese (≥40 kg/m^2)	12 (13.3)
Duration since AD onset, years	19.7 (16.1)
IGA[b]	
3 (Moderate), n (%)	62 (68.9)
4 (Severe), n (%)	27 (30.0)
EASI	26.4 (12.2)
BSA % affected	37.8 (20.5)
POEM	17.3 (6.5)
Pruritus NRS[c]	7.0 (2.2)
≥3, n (%)	73 (93.6)
≥4, n (%)	70 (89.7)
Sleep-Loss scale[c]	2.0 (1.1)
DLQI[d]	13.2 (7.4)
cDLQI[d]	12.2 (8.2)
PO-SCORAD[e]	57.1 (17.8)
PDCA-Derm™[f]	
Hypopigmented lesion(s), n (%)	16 (17.8)
Hyperpigmented lesion(s), n (%)	52 (57.8)



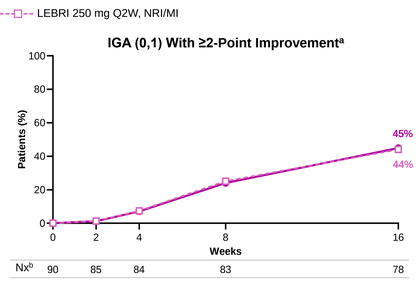
[a]Based on the patient's reported cutaneous reaction to sun exposure; [b]1 patient inadvertently enrolled with IGA=2 and discontinued when discovered they did not meet enrollment criteria; [c]Nx=78; [d]Patients <16 years of age at baseline completed cDLQI [Nx=10]; others completed DLQI [Nx=77]. [e]Nx=87; [f]A scale used to compare post-inflammatory lesions to unaffected, adjacent normal skin.
Notes: Data in table are mean (SD) unless stated otherwise. Percent values for pre-specified clinical events were calculated using 86 as the denominator.

69% of Patients Achieved EASI 75 (Primary Endpoint), and 45% of Patients Achieved EASI 90 at Week 16



[a]As observed:
Notes: NRI/MI analyses are based on all N=90 patients at each timepoint. Patients who discontinued treatment due to lack of efficacy were imputed as non-responders; all other missing data were imputed using MI.

45% of Patients Achieved IGA (0,1) With ≥2-Point Improvement From Baseline at Week 16



[a]ITT population with baseline IGA ≥2; [b]As observed.
Notes: NRI/MI analyses are based on all N=90 patients at each timepoint. Patients who discontinued treatment due to lack of efficacy were imputed as non-responders; all other missing data were imputed using MI.

33% of Patients Showed Improved Hypopigmentation and 63% Showed Improved Hyperpigmentation at Week 16, as measured by PDCA-Derm™

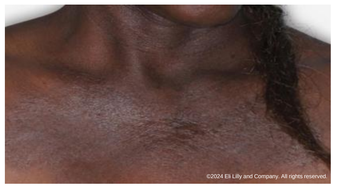
At Week 16:

[a]The analysis was performed on patients with a hypopigmentation lesion at baseline and non-missing data at Week 16 (N=12); [b]The analysis was performed on patients with a hyperpigmentation lesion at baseline and non-missing data at Week 16 (N=46).
Notes: For patients with multiple hypopigmented or hyperpigmented lesions at baseline, only the lesion with the most severe score was included in the analysis for each lesion type. In the event of a tie, the lesion reflecting a smaller improvement or worsening in condition from baseline to Week 16 was included.

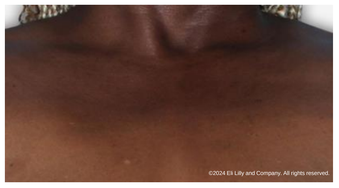
Results

Photographs Showing Improvement in AD With Lebrikizumab in a Patient With Skin of Color

50-year-old Black/African American, non-Hispanic female



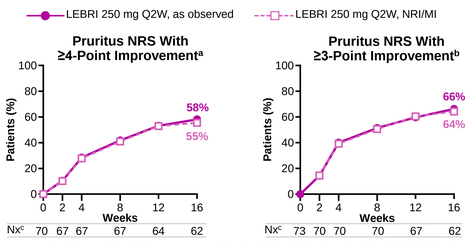
Baseline	
IGA	EASI
3	19.35



Week 16		
IGA	EASI	EASI % CFB
1	2.4	88%

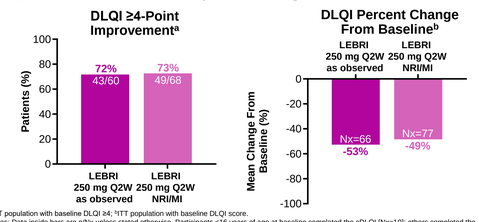
- Information on the ADmirable Study Design, Key Eligibility Criteria, Methods, and Use of Concomitant Topical and Systemic Therapy are described in **Supplemental Materials**

58% of Patients Achieved ≥4-Point Improvement, and 66% Achieved ≥3-Point Improvement in Pruritus NRS at Week 16



[a]ITT population with baseline Pruritus NRS ≥4; [b]ITT population with baseline Pruritus NRS ≥3; [c]As observed. Notes: NRI/MI analyses are based on all N=70 (Pruritus NRS with ≥4-point improvement) or N=73 (Pruritus NRS with ≥3-point improvement) patients at each timepoint. Patients who discontinued treatment due to lack of efficacy were imputed as non-responders; all other missing data were imputed using MI.

72% of Patients Achieved ≥4-Point Improvement in DLQI, and DLQI Scores Decreased by an Average of 53% at Week 16



[a]ITT population with baseline DLQI ≥4; [b]ITT population with baseline DLQI score.
Notes: Data inside bars are n/Nx unless stated otherwise. Participants <16 years of age at baseline completed the cDLQI [Nx=10]; others completed the DLQI [Nx=77]. Patients who discontinued treatment due to lack of efficacy were imputed as non-responders; all other missing data were imputed using MI.

Adverse Events

	LEBRI 250 mg Q2W (N=90)
TEAE[a]	21 (23.3)
Mild	11 (12.2)
Moderate	9 (10.0)
Severe	1 (1.1)
SAE	0
Death	0
TEAE related to study treatment[b]	4 (4.4)
AE leading to treatment discontinuation[b]	0
TEAE within special safety topics	
Infections[c]	6 (6.7)
Skin infections	2 (2.2)
Potential hypersensitivity[d]	1 (1.1)
Injection site reactions	0
Keratitis cluster	0
Conjunctivitis cluster[e]	0
Malignancies[f]	0
AD exacerbation	1 (1.1)
Hepatic events	0

[a]Patients with multiple events with different severity are counted under the highest severity; [b]As assessed by investigator; [c]No cases of herpes infection or helminthic infection were reported; [d]Events that occurred on the day of drug administration and captured using the Hypersensitivity, Angioedema, and Anaphylaxis Standardized MedDRA Queries. The Preferred Term for the potential hypersensitivity event was dermatitis atopic; [e]Defined using the following MedDRA Preferred Terms: conjunctivitis, conjunctivitis allergic, and conjunctivitis bacterial; [f]Includes cases with and without NMSC.
Notes: Data are n (%). Severe TEAE includes back pain.

Abbreviations: *AAD=American Academy of Dermatology; AD=atopic dermatitis; AE=adverse event; BMI=body mass index; BSA=body surface area; cDLQI=Children's DLQI; CFB=change from baseline; DLQI=Dermatology Life Quality Index; EASI=Eczema Area and Severity Index; EASI 75/90=≥75/90% improvement from baseline in EASI; IGA=Investigator's Global Assessment; IGA (0,1)=IGA response of clear or almost clear; ITT=intent-to-treat; IP=investigational product; JAK=Janus kinase; LD=loading dose; LEBRI=lebrikizumab; MedDRA=Medical Dictionary for Regulatory Activities; MI=multiple imputation; NMSC=non-melanoma skin cancer; NRI=non-responder imputation; NRS=Numeric Rating Scale; Nx=number of patients with non-missing values; PDE-4=phosphodiesterase 4; POEM=Patient-Oriented Eczema Measure; PO-SCORAD=Patient-Oriented SCORing of Atopic Dermatitis; Q2W=every 2 weeks; Q4W=every 4 weeks; QoL=quality of life; SAE=severe adverse event; SD=standard deviation; TCI=topical calcineurin inhibitor; TCS=topical corticosteroids; TEAE=treatment-emergent adverse event*

References:

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Medical writing assistance was provided by Heidi Tran, PhD, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company

Previously presented at Fall Clinical 2024; Las Vegas, USA; 24-27 October 2024

Supplemental Materials

Scan the QR code for additional Methods and Results

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Effectiveness of Biologics in Clinical Practice: Interim Month 24 Results From the International Observational Psoriasis Study of Health Outcomes (PSoHO)

April W. Armstrong,[1] Julia-Tatjana Maul,[2,3] Antonio Costanzo,[4] Saxon D. Smith,[5] Bruce Konicek,[6] Meghan Feely McDonald,[6,7] Natalie Haustrup,[6] Anastasia Lampropoulou,[6] Alan Brnabic,[6] Andreas Pinter[8]

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OBJECTIVE

- To evaluate PASI 100 response rates at Week 12 and Months 6, 12, 18, and 24 for patients with moderate-to-severe PsO treated with biologics in a real-world setting

CONCLUSION

- Building on previous Week 12, Month 6, and Month 12 PSoHO data,[2-4] this interim analysis demonstrates the continued high-level effectiveness of anti–IL-17A biologics through Month 24 and the varying effectiveness of individual biologics, including ixekizumab, in a real-world setting

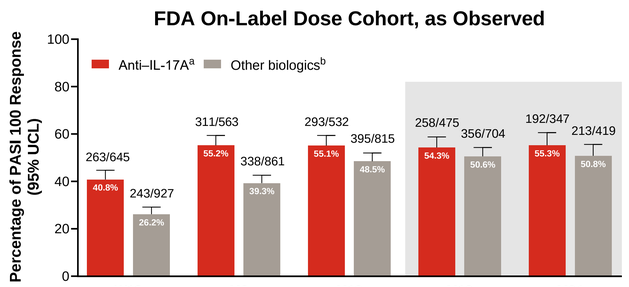
Elevate-Derm West Conference; Scottsdale, AZ, USA; November 7-10, 2024

BACKGROUND

- PsO severely impacts the health and quality of life of patients, and disease management is an ongoing challenge[1]
- PSoHO is an ongoing international, prospective, observational study comparing the effectiveness of anti–IL-17A biologics to other approved biologics for the treatment of PsO[2,3]
  - Preliminary Month 12 data reported higher PASI 100 response rates for patients treated with anti–IL-17A biologics compared with other biologics and durability of treatment effectiveness[4]

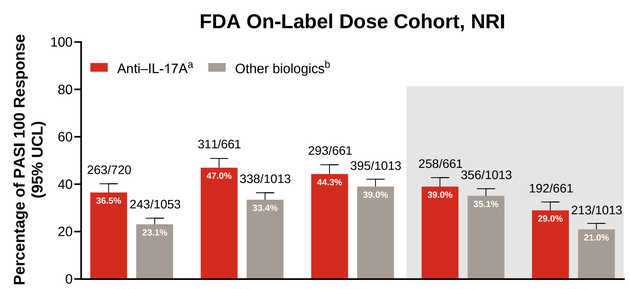
KEY RESULTS

The Anti–IL-17A Cohort Had Numerically Higher PASI 100 Response Rates Than the Other Biologics Cohort Through to Month 24



[a] Ixekizumab and secukinumab; [b] Adalimumab, brodalumab, certolizumab, etanercept, guselkumab, infliximab, risankizumab, tildrakizumab, and ustekinumab
Note: Grey shading indicates interim data

NRI Data Showed a Consistent, but Lower, Trend of PASI 100 Response Rates Compared With Observed Data Through to Month 24



[a] Ixekizumab and secukinumab; [b] Adalimumab, brodalumab, certolizumab, etanercept, guselkumab, infliximab, risankizumab, tildrakizumab, and ustekinumab
Note: Grey shading indicates interim data

METHODS

Analysis Population

- This 4th interim analysis includes 2 cohorts of PSoHO patients:
  - FDA On-Label Dose Cohort: Patients who received FDA-approved on-label dosing
  - EMA On-Label Dose Cohort: Patients who received EMA-approved on-label dosing
- Week 12 data correspond to patients who received FDA/EMA-approved on-label dosing up to Week 12
- Months 6 and 12 data correspond to patients who received FDA/EMA-approved on-label dosing up to Month 12
- Months 18 and 24 interim data are preliminary, not inclusive of the FDA/EMA adjudication populations

FDA- and EMA-Approved On-Label Dosing

Treatment	FDA-Approved On-Label Dosing for PsO	EMA-Approved On-Label Dosing for PsO
Ixekizumab	160 mg at W0, then 80 mg Q2W until W12, then Q4W thereafter	As per FDA
Secukinumab	300 mg weekly at W0-4, then 300 mg Q4W. For some patients, a dose of 150 mg may be acceptable	300 mg weekly at W0-4, then monthly dosing. 300 mg Q2W maintenance dose may provide additional benefit for patients with a body weight of ≥90 kg
Guselkumab	100 mg at W0 and W4, then Q8W thereafter	As per FDA
Risankizumab	150 mg at W0 and W4, then Q12W thereafter	As per FDA

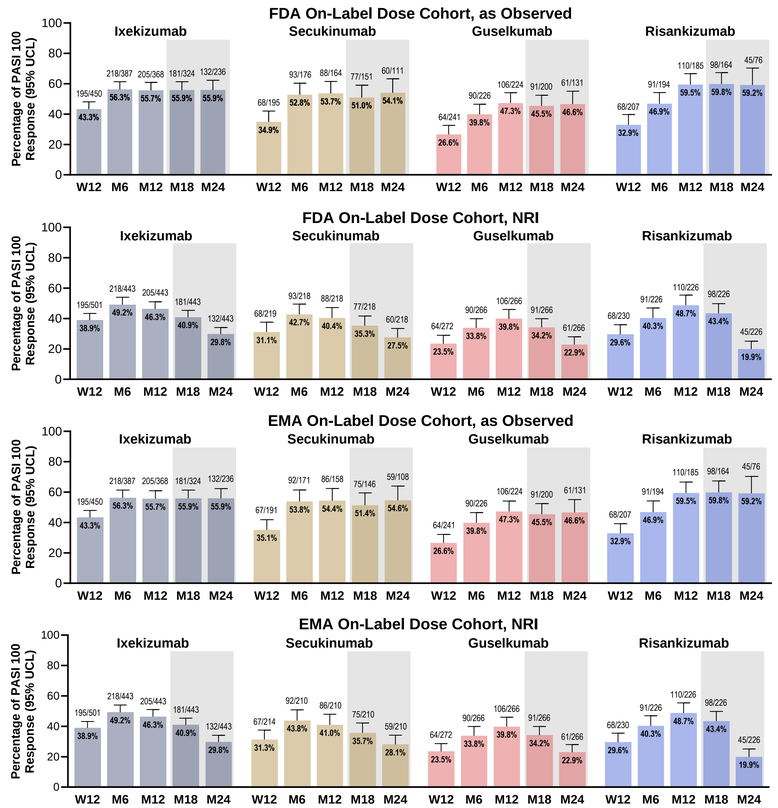
Note: See Supplementary Data for FDA- and EMA-approved on-label dosing for adalimumab, brodalumab, certolizumab, etanercept, infliximab, tildrakizumab, and ustekinumab

Supplemental Materials

Scan or click the QR code to access:

- Eligibility Criteria
- Statistical Analyses
- FDA and EMA On-Label Dosing for Other Biologics
- EMA On-Label Dose Cohort Percentage of PASI 100 Response for Anti–IL-17A vs. Other Biologics

Individual Biologics Showed Varying Effectiveness (PASI 100) Over Time



Note: Grey shading indicates interim data

Limitations

- As an observational study, PSoHO is subject to various forms of bias, including selection or participation bias, or measurement error
- Grouping of non-anti–IL-17A biologics into a single category may not reflect variabilities within the class, particularly as some individual drugs were used by only small numbers of patients
- Months 18 and 24 interim data are preliminary, not inclusive of the FDA/EMA adjudication populations
- No comparative analysis was conducted and no adjustments were made for measured confounders

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1. Feldman S, et al. *Am Health Drug Benefits*. 2016;9:504-513.
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Abbreviations: *CI=confidence interval; EMA=European Medicines Agency; FDA=US Food and Drug Administration; IL=interleukin; M=Month; NRI=non-responder imputation; PASI=Psoriasis Area and Severity Index; PASI 100=100% improvement in PASI from baseline (total clearance); PsO=psoriasis; PSoHO=Psoriasis Study of Health Outcomes; QW=every week; Q2W=every 2 weeks; Q4W=every 4 weeks; Q8W=every 8 weeks; Q12W=every 12 weeks; UCL=upper confidence limit; W=Week*

Disclosures: A. W. Armstrong has served as a consultant, speaker, and/or investigator for: AbbVie, Almirall, Arcutis, ASLAN Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, EPI Health, Incyte Corporation, Janssen, LEO Pharma, Modernizing Medicine, Nimbus Therapeutics, Novartis, Ortho Dermatologics, PAREXEL, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma; **J-T. Maul** has served as an advisor and/or received speaking fees and/or participated in clinical trials sponsored by: AbbVie, Almirall, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly and Company, Incyte Corporation, LEO Pharma, Janssen Cilag, Merck Sharp & Dohme, Novartis, Pfizer, Pierre Fabre, Roche, Sanofi, and UCB Pharma; **A. Costanzo** has served as an advisory board member or consultant and/or has received speaker's honoraria or has participated in clinical trials for: AbbVie, Almirall, Biogen, Eli Lilly and Company, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi Genzyme, and UCB Pharma; **S. D. Smith** has been an advisor for and/or received speaking fees and/or served as an investigator in clinical trials for: AbbVie, Amgen, Biogen, Bristol Myers Squibb, Eli Lilly and Company, Janssen Cilag, LEO Pharma, Novartis, Pfizer, Sanofi Genzyme, and UCB Pharma; **B. Konicek**, **N. Haustrup**, **A. Lampropoulou**, and **A. Brnabic** are employees and shareholders of: Eli Lilly and Company; **M. Feely McDonald** is associate staff at: Mount Sinai Hospital, Mount Sinai West, and Mount Sinai Morningside; is an employee and shareholder of: Eli Lilly and Company; and has received consulting, travel, or speaker fees from: Aerolase, American Academy of Dermatology, Castle Biosciences, CeraVe-L'Oréal, DREAM USA, Galderma Aesthetics, Glow Recipe, La Roche-Posay-L'Oréal, Revian, Sonoma Pharmaceuticals, Sun Pharma, and Suneva Medical; **A. Pinter** has served as an investigator and/or speaker and/or advisor for: AbbVie, Almirall Hermal, Amgen, Biogen, BioNTech, Boehringer Ingelheim, Celgene, Eli Lilly and Company, Galderma, GlaxoSmithKline, Hexal, Janssen, LEO Pharma, MC2 Therapeutics, Medac, Merck Serono, Merck Sharp & Dohme, Mitsubishi Tanabe Pharma, Novartis, Pascoe Natural Healthcare, Pfizer, Regeneron, Roche, Sandoz, Sanofi Genzyme, Schering-Plough, Tigercat Pharma, and UCB Pharma

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Previously presented at American Academy of Dermatology San Diego, USA; 8-12 March 2024

Systemic Therapy Improves Patient-Reported Treatment Satisfaction, Adherence, and Reduces Therapy Burden in Patients with Atopic Dermatitis: Advanced Practice Provider and Patient Perspectives

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Sponsored by Eli Lilly and Company

OBJECTIVE

- This study evaluates APPs' perceptions of patients' treatment challenges and patients' perceptions of treatment adherence and satisfaction in patients with a history of moderate-to-severe AD.

CONCLUSIONS

- The addition of systemic therapy to topical treatment resulted in a higher proportion of patients being "extremely or very satisfied" with their therapy.
- The primary reason for patients' dissatisfaction in both treatment groups was that their AD was not improving as expected.
- Additionally, systemics±topicals therapy resulted in low rates of issues related to the mode of administration and therapy inconvenience.
- Systemics±topicals therapy may increase compliance/adherence compared to topical-only treatment, but overall compliance could be improved.
- It is crucial for APPs to set appropriate therapy expectations initially and continually reassess them, ensuring alignment with patient understanding and treatment progress for optimal care outcomes.
- Considering the potential benefits of adding systemic therapy to the topical treatment, newer advanced systemics with strong efficacy and flexible dosing may further help to improve compliance/adherence and reduce treatment challenges.

LIMITATIONS

- The APPs captured patient information retrospectively within the patient record forms, which may have introduced recall bias – a common limitation of survey data.
- The study sample included consecutive patients who consulted the APPs. Therefore, the sample may not truly represent the overall AD population, as patients who consulted frequently were more likely to be included in the sample.

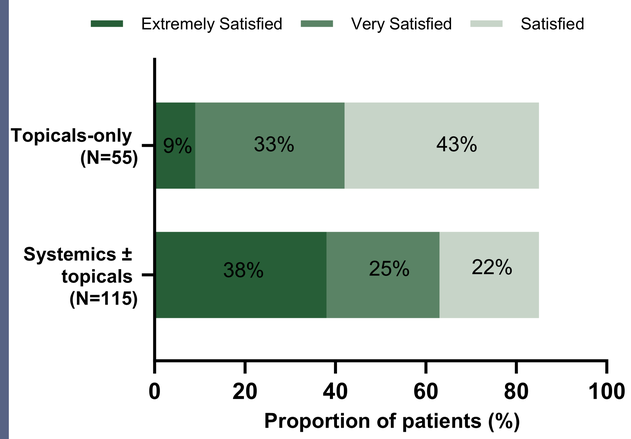
Elevate-Derm West; Scottsdale, AZ; 7-10, November 2024

BACKGROUND

- Atopic dermatitis (AD) is a chronic heterogeneous skin condition associated with a profound symptom burden affecting patients' quality of life.[1]
- Despite therapeutic advances, patients with AD often face challenges with treatment adherence and satisfaction.[2,3]
- Dermatology advanced practice providers (APPs) are often involved in patient care.[4] However, their perceptions of patients' treatment challenges have not been explored.

KEY RESULTS

Patient-reported satisfaction with the current treatments



Footnote: Neither satisfied nor dissatisfied: 7% (n=8) in systemics±topicals group and 11% (n=6) in the topicals-only group; Patients dissatisfied: 8% (n=9) in systemics±topicals group and 4% (n=2) in the topicals-only group.

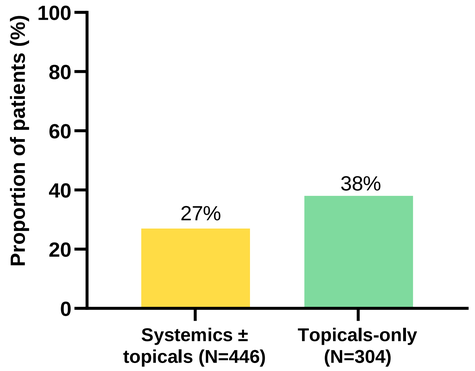
- The proportion of patients extremely or very satisfied with the current prescribed treatment was numerically higher in the systemics±topicals group than in the topicals-only group.

Reasons for patients' dissatisfaction with current treatments

Reason for patients' dissatisfaction	Systemics ± topicals (N=17)	Topicals-only (N=08)
AD not improving as expected, (n)	11	3
Side effects with medication, (n)	3	1
Inconvenience with the mode of administration, (n)	2	2
Medication is expensive, (n)	1	1

- The primary reason for patients' dissatisfaction in both treatment groups was that their AD was not improving as expected.

APP-reported proportion of patients experiencing issues with their current treatments

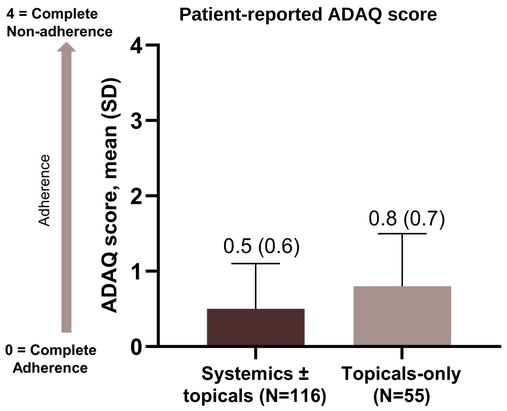


APP-reported issues experienced by patients with current treatments

APP-reported issues experienced by patients with current treatments	Systemics ± topicals (N=122)	Topicals-only (N=116)
Loss of response over time (%)	28	25
Failure to resolve all symptoms (%)	25	25
Lack of compliance (%)	16	23
AD worsened (%)	16	21
Inconvenient/burdensome therapy (%)	5	16
Struggles with mode of administration (%)	5	14

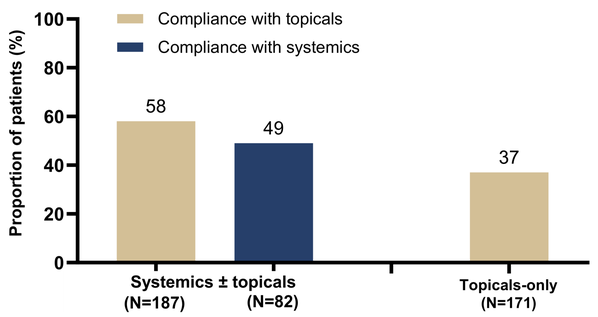
- Loss of response over time and failure to resolve all symptoms were most frequently reported issues in both treatment groups.
- APPs reported that patients receiving topicals-only had experienced more inconvenience with therapy, struggled with mode of administration, and lack of compliance than patients receiving systemics±topicals.

Patient-reported ADAQ score



- Patients receiving topicals-only were slightly less adherent than those receiving systemics±topicals.

APP-reported patient's compliance with current treatments



- APPs reported that full compliance with topical and systemic treatments was numerically higher among patients receiving systemics±topicals.

METHODS

STUDY DESIGN

- A cross-sectional, real-world survey including retrospective data collection from APP-reported medical records and patient surveys

DATA SOURCE AND SURVEY DURATION

- Adelphi AD Disease Specific Programme™ conducted in the United States between February 2021 and February 2022

TREATMENT GROUPS

- Patients with AD were grouped into two categories based on their current treatment:

Systemics± topicals	Systemic treatment* with or without topical treatment.
Topicals-only	This group included only topical treatments** (no systemic treatment)

*Systemic treatments included injectable biologics, oral and injected corticosteroids, and conventional immunosuppressants.
**Topical treatments included corticosteroids, calcineurin inhibitors, and crisaborole.

KEY INCLUSION CRITERIA

APPs

- Nurse practitioners and physician assistants
- Affiliated with a dermatologist or allergist
- Actively managing/co-managing AD patients
- Treating ≥10 patients with moderate-to-severe AD in a month

Patients

- Adult patients (≥18 years) with a history of moderate-to-severe AD
- Currently not enrolled in any AD clinical trial

DATA COLLECTION AND ANALYSIS

- APPs (nurse practitioners [n=34] and physician assistants [n=53]) completed 914 patient record forms to provide retrospective patient data for demographics, disease characteristics (AD severity, body surface area involvement, subjective flare status), issues, and compliance with current treatments.
- Of these,171 patients reported their current treatment satisfaction and completed the Adelphi Adherence Questionnaire (ADAQ; 11-item, 0=complete adherence, 4=complete non-adherence).[5]
- Descriptive statistics were reported with means, standard deviations, and percentages.

Patient Demographics and Clinical Characteristics*

	Systemics±topicals (N=446)	Topicals-only (N=304)
Age		
Mean (SD), years	41.5 (17.6)	40.9 (18.3)
Sex, n (%)		
Female	234 (53)	168 (55)
Race, n (%)		
White/Caucasian	296 (66)	188 (62)
African American	78 (17)	65 (22)
Asian[$]	25 (6)	19 (6)
Other^	18 (4)	10 (3)
Ethnicity, n (%)		
Hispanic/Latino	29 (7)	22 (7)
AD Severity, n (%)		
Mild	232 (52)	133 (44)
Moderate	166 (37)	150 (49)
Severe	48 (11)	21 (7)
BSA Involvement, (%)	**N=406**	**N=256**
Mean (SD)	13.9 (17)	12.3 (13.6)
Flare Status, n (%)	**N=316**	**N=217**
Currently flaring	106 (34)	99 (46)

*APPs (34 NPs, 53 PAs) provided data for a total of 914 patients. Here, we present data for patients receiving systemics±topicals or topicals-only
[$]Indian/Southeast Asian/Other Asian subcontinent
^Other include Native Americans, Middle Eastern, Mixed race, or APP-reported other race.
The overall assessment of the current severity of AD was based on the NP/PA's personal definitions of the terms mild, moderate, and severe AD. Flare was not defined in the study protocol and was left to the interpretation of the APPs.

Disclosures:

▪**EC**: Consultant and/or speaker for: Bristol Myers Swibb, Dermavant, Lilly, AbbVie, Arcutis, Sanofi Genzyme/Regeneron, Beiersdorf, Johnson & Johnson, LEO. **LP**: Consultant and/or speaker for Abbvie, Arcutis, Biersdorf Inc., Boehringer Ingelheim International, Bristol Meyers Squibb Company, Dermavant Sciences Inc., Galderma, Johnson & Johnson, Leo Pharma, Eli Lilly and Company, Novartis, Pfizer Inc., Sanofi S.A., Regeneron Pharmaceuticals, UCB. **DD**: Consultant and/or speaker for: Dermavant, Lilly, AbbVie, Arcutis, Amgen, Sanofi Genzyme/Regeneron, Beiersdorf, Johnson & Johnson, LEO, UCB. **ZD** and **EP**: Employment and stockholder, Lilly. **PA, JP, and SM**: Full-time employees of Adelphi Real World. **KG**: Consultant/Speaker for Leo, AbbVie,OrthoDerm, ArCutis, Lilly. **JS**: speaker for Lilly, Abbvie. **SJ**: Speaker and advisor for Abbvie, Amgen, Leo, Lilly Johnson and Johnson, UCB, BMS, Regeneron, Sanofi, Incyte, Dermavant, Arcutis, Galderma.

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Abbreviations: AD, Atopic dermatitis; ADAQ, Adelphi Adherence Questionnaire; APP, Advanced practice providers; BSA, Body surface area; N, Total population; NPs, Nurse practitioners; PAs, Physician assistants; SD, Standard deviation; US, United States

Acknowledgments: Sankara Narayana Doddam, an employee of Eli Lilly Services India Pvt. Ltd., provided medical writing support.

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Effectiveness of Ixekizumab on Skin, Itch and Quality of Life Through 24 Weeks From the Second Interim Analysis of a US Observational Psoriasis Study

David Fivenson[1], Brandon Kirsch[2], Bartley Joseph Gill[3], William Malatestinic[4], Mwangi Murage[4], Ali Sheikhi Mehrabadi[4], Edward Herman[5]

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Sponsored by Eli Lilly and Company

OBJECTIVE

- To evaluate the effectiveness of ixekizumab treatment on skin, itch, and quality of life of patients with PsO in the prospective PsO in Special Areas (PSoSA) study

CONCLUSION

- Patients initiating ixekizumab in a real-world setting demonstrated improvements in PASI, Itch, and DLQI scores starting as early as Week 4 and continuing through Week 24
- Patients reached PASI 100, Itch NRS (0), and DLQI (0,1) as early as Week 4, with the percentages of patients achieving these scores increasing over 24 weeks
- This second interim analysis of the PSoSA study further confirms the effectiveness of ixekizumab in real-world settings

Limitations

- As an interim analysis, the results should be interpreted with caution, because the number of patients completing later timepoints was small

Elevate-Derm West Conference; Scottsdale, AZ, USA; November 7-10, 2024

BACKGROUND

- Ixekizumab, a highly selective interleukin-17A monoclonal antibody, has demonstrated effectiveness in treating moderate-to-severe plaque PsO, including in challenging body areas such as nails and scalp[1-3]
- However, real-world data relating to its effects on these areas are limited

KEY RESULTS

Effectiveness Continued to Increase From 4 Weeks to 24 Weeks of Treatment With Ixekizumab

	Week 4	Week 12	Week 24
Mean PASI percent CFB	-52.6 (-59.9 to -45.3) [n=138]	-74.7 (-81.7 to -67.7) [n=113]	-82.3 (-91.6 to -73.0) [n=69]
PASI 90	18.8 (13-26) [n=138]	54.0 (44-63) [n=113]	69.6 (57-80) [n=69]
PASI 100	10.9 (6-17) [n=138]	27.4 (19-37) [n=113]	43.5 (32-56) [n=69]
Itch NRS (0)	17.8 (12-25) [n=135]	29.7 (21-39) [n=111]	41.8 (30-54) [n=67]
Itch NRS ≥4-Point Improvement	41.9 (33-51) [n=124]	45.0 (35-55) [n=100]	57.6 (44-70) [n=59]
DLQI (0, 1)	22.2 (16-30) [n=135]	42.9 (34-53) [n=112]	61.2 (49-73) [n=67]

Note: Data are % (95% CI) of patients achieving the endpoints.

RESULTS

Baseline Demographics and Disease Characteristics

Characteristic	Patients in Second Interim Analysis of PSoSA (N=187)
Age, years	50.4 (15.3)
Male, n (%)	106 (56.7)
BMI, kg/m²	30.1 (7.2)
Time since PsO diagnosis, years	12.6 (13.6)
BSA % involvement	18.4 (19.1)
PASI	10.4 (11.7)
Itch NRS	4.3 (3.1)
Previous biologic therapy, n (%)	55 (29.4)
Concomitant PsO therapy,[a] n (%)	36 (19.3)

[a]Included 1 patient receiving apremilast, 1 patient receiving intralesional triamcinolone intradermal injection, 1 patient receiving phototherapy, and 35 patients receiving topical therapy (8 calcineurin inhibitors, 31 corticosteroids, 5 vitamin D3 analogues, 1 salicylic acid, 1 coal tar, 2 roflumilast, and 5 other) (patients can contribute to >1 category).
Note: Data are mean (SD) unless stated otherwise.

METHODS

PSoSA Patient Population

- PSoSA is a US-based, single-arm, prospective, multicenter, observational, real-world study

Inclusion Criteria

- Adult patients (age ≥18 years) who present within the usual course of care
- Eligible for ixekizumab treatment in accordance with FDA labeling with a diagnosis of moderate-to-severe plaque PsO, as determined by the investigator
- Nail involvement (mNAPSI >0)
- First-time treatment with ixekizumab

Exclusion Criteria

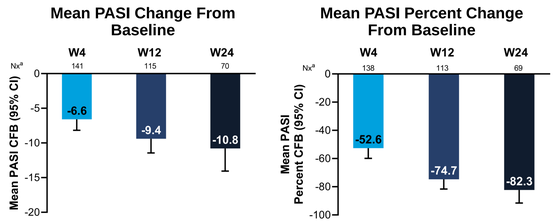
- Overt onychomycosis or any significant disease in the fingernails other than PsO, as determined by the investigator
- Treatment initiation contraindicated due to US-approved indication
- Current participation in another PsO or PsA study that includes treatment with ixekizumab or an investigational product and/or intervention

Statistical Analyses and Assessments

- A descriptive analysis of the second interim data from the PSoSA study
- The following outcomes were assessed at Weeks 4, 12, and 24:
  - Mean change and percent change from baseline in:
    - PASI, a measure of PsO, with higher scores (range, 0-72) indicating greater severity
  - Response rates for:
    - PASI 90: ≥90% improvement from baseline in PASI
    - PASI 100: 100% improvement from baseline in PASI
    - Itch NRS 0: Indicating no itch
    - Itch NRS ≥4-point improvement from baseline: Clinically meaningful improvement in itch, measured in patients with Itch NRS ≥4 at baseline
    - DLQI (0,1): Indicating no or minimal impact of disease on quality of life

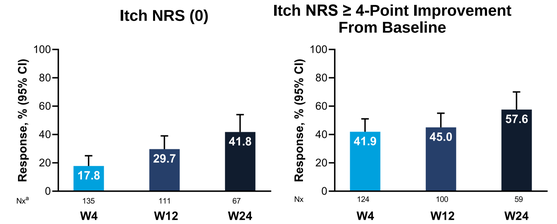
RESULTS

PASI Change and Percent Change From Baseline Was Observed as Early as Week 4 and Improved Up to Week 24



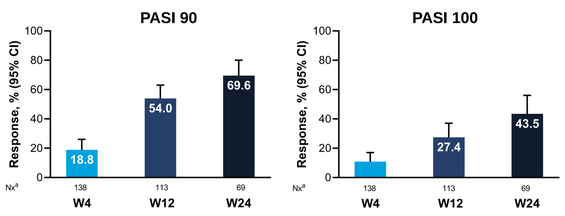
[a]This interim analysis included patients who had completed W4, or W12, or W24, respectively; Nx excluded patients with a baseline score of 0.

Improvement in Itch Was Observed as Early as Week 4 and Continued Up to Week 24



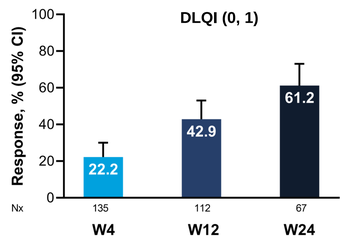
[a]This interim analysis included patients who had completed W4, or W12, or W24, respectively; Nx excluded patients with a baseline score of 0.

PASI 90/100 Responses Were Observed as Early as Week 4 and Continued to Increase Up to Week 24



[a] This interim analysis included patients who had completed W4, or W12, or W24, respectively.

Percentage of Patients Achieving DLQI (0,1) Scores Increased Through Week 24



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Abbreviations: *BMI=body mass index; BSA=body surface area; CFB=change from baseline; CI=confidence interval; DLQI=Dermatology Life Quality Index; DLQI (0,1)=DLQI response of clear or almost clear; FDA=US Food and Drug Administration; mNAPSI=modified Nail Psoriasis Severity Index; NRS=Numeric Rating Scale; Nx=number of patients with non-missing values; PASI=Psoriasis Area and Severity Index; PASI 90/100=≥90/100% improvement from baseline in PASI; PsA=psoriatic arthritis; PsO=psoriasis; PSoSA=PSOriasis in Special Areas; SD=standard deviation; W=Week*

Disclosures: D. Fivenson has been principal investigator and has received speaker's honoraria for: Eli Lilly and Company; **B. Kirsch** has no conflict of interests to declare; **B. J. Gill** has served as a contracted speaker and/or received speaker fees for and has been a principal investigator for: Eli Lilly and Company; **W. Malatestinic**, **M. Murage**, and **A. S. Mehrabadi** are current employees and shareholders of: Eli Lilly and Company; **E. Herman** has received consulting fees from: AbbVie, Bristol Myers Squibb, LEO Pharma, and Sanofi/Regeneron

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Lebrikizumab Improves Atopic Dermatitis and Quality of Life in Patients With Moderate-to-Severe Atopic Dermatitis Previously Treated With Dupilumab: Results From the ADapt Trial

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OBJECTIVES

- In real-world settings, approximately 18-20% of patients with moderate-to-severe AD discontinue dupilumab within 3-4 years of treatment, and the primary reasons are loss of efficacy (26-40%), AEs (20%), and cost issues and insurance coverage (18%)[1,2]
- The open-label, Phase 3b, 24-week ADapt trial (NCT05369403) aims to assess the efficacy and safety of lebrikizumab in patients previously exposed to dupilumab
  - Other clinical questions include:
    - How are patients with inadequate response to dupilumab likely to respond to lebrikizumab?
    - Are patients who stopped dupilumab because of an AE likely to experience the same AE with lebrikizumab?
- This analysis reports the efficacy and safety of lebrikizumab following 24 weeks of treatment in patients with moderate-to-severe AD previously treated with dupilumab in the ADapt trial

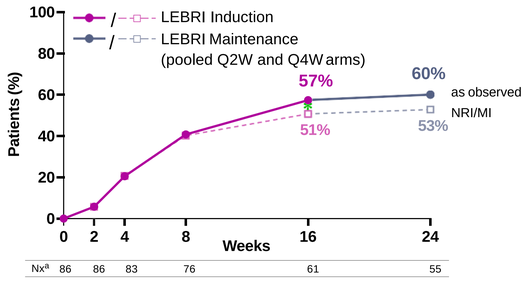
CONCLUSIONS

- Lebrikizumab provides meaningful improvements in skin (including face and hand) clearance, itch, and QoL in patients with moderate-to-severe AD who were previously treated with dupilumab
- The ADapt safety profile is consistent with other lebrikizumab phase 3 trials[3-6]

Elevate-Derm West Conference; Scottsdale, AZ, USA; November 7-10, 2024

How Efficacious Is Lebrikizumab in Patients Previously Exposed to Dupilumab?

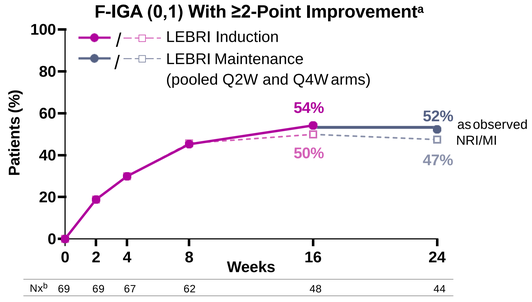
EASI 75



These results are similar to Phase 3 monotherapy trials of lebrikizumab in patients with moderate-to-severe AD **without** prior dupilumab exposure:

* The EASI 75 response rate at Week 16 using pooled ADvocate 1 & 2 data was 55.4%[4,b]

F-IGA (0,1) With ≥2-Point Improvement[a]

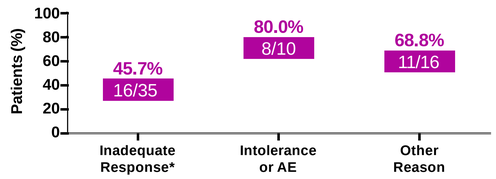


[a]As observed; [b]In ADvocate 1 and ADvocate2, patients who discontinued treatment due to loss of efficacy or initiated protocol-defined rescue therapy were imputed as non-responders in the NRI/MI analysis.
Notes: NRI/MI analyses are based on all N=86 patients at each timepoint and were performed for Week 0 to Week 24 after pooling together the LEBRI 250 mg Q2W and Q4W arms. Patients who discontinued treatment due to lack of efficacy were imputed as non-responders; all other missing data were imputed using MI.

[a]ITT population with baseline F-IGA ≥2; [b]As observed.
Notes: NRI/MI analyses are based on all N=69 patients at each timepoint and were performed for Week 0 to Week 24 after pooling together the LEBRI 250 mg Q2W and Q4W arms. Patients who discontinued treatment due to lack of efficacy were imputed as non-responders; all other missing data were imputed using MI.

How Are Patients With Inadequate Response to Dupilumab Likely to Respond to Lebrikizumab?

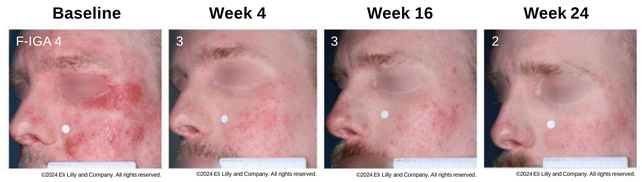
Achievement of EASI 75 at Week 16 by Reason for Prior Dupilumab Discontinuation



*Dupilumab inadequate response subgroup (n/Nx): 2/3 had no response to dupilumab; 7/21 had partial response to dupilumab; and 7/11 lost response to dupilumab

Notes: 61 patients had observed data at Week 0 and Week 16 and were included in this subgroup analysis. Data inside the bars are n/Nx. Reasons for dupilumab discontinuation were patient-reported. The inadequate response group consists of patients who discontinued dupilumab due to no response to treatment, defined as having a peak response for skin and itch that did not improve at all and/or improved less than 25%; partial response to treatment, defined as having a peak response for skin and itch that only improved partially and/or improved between 25% and 50%; or lost response to treatment, defined as "initially responded but lost response to dupilumab" with respect to skin and/or itch. Other reasons included being unable to afford treatment, health insurance changes, and previous open-label clinical trial participation that completed with no discontinuation for AEs. Due to the small sample size of all subgroups, no conclusions can be drawn from these analyses.

In a Patient Who Discontinued Dupilumab Due to Loss of Response, Lebrikizumab Shows Improvement in Facial Atopic Dermatitis



Lebrikizumab Improved Hand Dermatitis Through Week 24

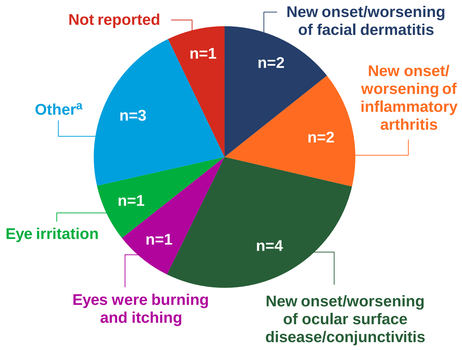
- In dupilumab-experienced patients with moderate-to-severe hand dermatitis at baseline (N=41), defined by mTLSS ≥12, mTLSS decreased by an average of 69% (as observed; NRI/MI, 64%) at Week 16 and by 75% (as observed; NRI/MI, 68%) at Week 24

Notes: NRI/MI analyses are based on all N=41 patients at each timepoint and were performed for Week 0 to Week 24 after pooling together the LEBRI 250 mg Q2W and Q4W arms. Patients who discontinued treatment due to lack of efficacy were imputed as non-responders; all other missing data were imputed using MI.

Are Patients Who Stopped Dupilumab Because of an AE Likely to Experience the Same AE With Lebrikizumab?

Primary Intolerance or AE Leading to Prior Dupilumab Discontinuation

N=14



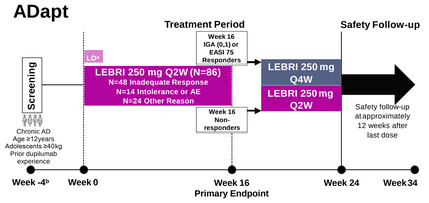
[a]Other includes increased itching; weight gain and worsening of itch; hives, rash, pruritus, and swelling (n=1 each).

In the ADapt Trial

- Of the 10 patients who reported eye-related events, facial dermatitis, or inflammatory arthritis as the reason for prior dupilumab discontinuation, none reported similar events with lebrikizumab
- Of the 14 patients with prior dupilumab discontinuation due to AEs
  - 2 discontinued treatment with lebrikizumab due to anAE:
    - Dermatitis atopic, n=1
    - Immune-mediated rash, n=1

Study Design

ADapt



[a]Patients received LD of 500 mg given SC at Week 0 and Week 2; [b]Screening window was up to 30 days.
Notes: The use of low- and/or mid-potency TCS, TCIs, topical PDE-4 inhibitors, or high-potency TCS up to 10 days was permitted. Patients requiring rescue therapy (high-potency TCS >10 days, topical JAK inhibitors, phototherapy, systemic medication) were discontinued from the study.

Results

Lebrikizumab Improved QoL and Symptoms of Itch Through Week 24

- Of dupilumab-experienced patients with baseline DLQI ≥4 (N=77), 83% (as observed) achieved ≥4-point improvement in DLQI from baseline at Weeks 16 and 24 (NRI/MI, 81% and 80%, respectively)
- Of dupilumab-experienced patients with baseline Pruritus NRS ≥4 (N=62), 53% and 62% (as observed) achieved ≥4-point improvement in Pruritus NRS from baseline at Week 16 and 24 (NRI/MI, 49% and 48%), respectively

Notes: NRI/MI analyses are based on all N=77 or N=62 patients at each timepoint and were performed for Week 0 to Week 24 after pooling together the LEBRI 250 mg Q2W and Q4W arms. Patients who discontinued treatment due to lack of efficacy were imputed as non-responders; all other missing data were imputed using MI.

Baseline Demographics and Disease Characteristics

Characteristic	All LEBRI (N=86)	Reason for Dupilumab Discontinuation[a] Inadequate Response (N=48)	Intolerance or AE (N=14)	Other Reason (N=24)
Age, years	46.4 (20.0)	43.0 (20.8)	53.1 (15.8)	49.1 (20.0)
Adult (≥18 years), n (%)	77 (89.5)	40 (83.3)	14 (100.0)	23 (95.8)
Adolescent (≥12 to <18 years), n (%)	9 (10.5)	8 (16.7)	0	1 (4.2)
Female, n (%)	41 (47.7)	21 (43.8)	7 (50.0)	13 (54.2)
BMI, kg/m²	27.9 (6.0)	27.2 (5.5)	29.3 (6.7)	28.7 (6.7)
Age at AD onset, years	26.6 (25.9)	22.3 (25.2)	27.4 (25.4)	34.7 (26.6)
Duration since AD onset, years	20.2 (19.9)	21.1 (20.8)	26.2 (21.6)	14.8 (16.2)
IGA, n (%)				
3 (Moderate)	65 (75.6)	33 (68.8)	13 (92.9)	19 (79.2)
4 (Severe)	21 (24.4)	15 (31.3)	1 (7.1)	5 (20.8)
F-IGA, n (%)				
2 (Mild)	21 (24.4)	15 (31.3)	2 (14.3)	4 (16.7)
3 (Moderate)	40 (46.5)	25 (52.1)	6 (42.9)	9 (37.5)
4 (Severe)	8 (9.3)	3 (6.3)	3 (21.4)	2 (8.3)
Pruritus NRS	6.6 (2.4)	6.5 (2.5)	7.0 (2.4)	6.6 (2.2)
≥4, n (%)	62 (87.3)	32 (84.2)	11 (91.7)	19 (90.5)
EASI	24.1 (10.7)	25.8 (12.2)	20.2 (4.3)	22.8 (9.6)
BSA % affected	32.2 (18.5)	35.3 (19.9)	24.8 (11.5)	30.3 (17.7)
DLQI[b]	14.4 (7.0)	15.1 (6.9)	15.4 (7.2)	12.7 (6.8)
mTLSS[c]	10.0 (5.0)	10.4 (5.0)	9.0 (4.4)	9.8 (5.3)
Number of prior systemic treatments,[d] n (%)				
1	50 (58.1)	27 (56.2)	6 (42.9)	17 (70.8)
2	22 (25.6)	13 (27.1)	4 (28.6)	5 (10.8)
≥3	14 (16.3)	8 (16.7)	4 (28.6)	2 (8.3)

[a]Reasons for dupilumab discontinuation were patient-reported. The dupilumab inadequate response subgroup consists of patients who discontinued dupilumab due to no response to treatment, defined as having a peak response for skin and itch that did not improve at all and/or improved less than 25%; partial response to treatment, defined as having a peak response for skin and itch that only improved partially and/or improved between 25% and 50%; or lost response to treatment, defined as "initially responded but lost response to dupilumab" with respect to skin and/or itch. Other reasons included being unable to afford treatment, health insurance changes, previous open-label clinical trial participation that completed with no discontinuation for adverse events; [b]Patients <16 years of age at baseline completed the cDLQI and continued to complete the cDLQI for the duration of the study; [c]41 patients in the all lebrikizumab cohort had mTLSS ≥12, and the mean (SD) score among these patients was 14.0 (2.0); [d]1=dupilumab only, 2=dupilumab and 1 other prior systemic treatment, 3=dupilumab and ≥2 other prior systemic treatments.
Notes: Data are mean (SD) unless stated otherwise. Number of patients with non-missing data was used as the denominator.

AEs[a] Through Week 24

	Pooled LEBRI 250 mg Q2W and Q4W (N=86)
TEAE[b]	46 (53.5)
Mild	26 (30.2)
Moderate	17 (19.8)
Severe	3 (3.5)
SAE	2 (2.3)
Death	0
AE leading to treatment discontinuation[c]	5 (5.8)
TEAE within special safety topics	
Infections	19 (22.1)
Skin infections	1 (1.2)
Potential hypersensitivity[d]	5 (5.8)
Dermatitis atopic	4 (4.7)
Urticaria	1 (1.2)
Injection site reactions[e]	4 (4.7)
Conjunctivitis cluster[f]	3 (3.5)
Malignancies	1 (1.2)
NMSC	1 (1.2)
Malignancies excluding NMSC	0
AD exacerbation	7 (8.1)
Hepatic events	1 (1.2)
Alanine aminotransferase increased	1 (1.2)
Aspartate aminotransferase increased	1 (1.2)

- 3 participants reported TEAEs of conjunctivitis, which were mild or moderate and did not lead to discontinuation

[a]Assessed in patients who received ≥1 dose of LEBRI; [b]Patients with multiple events with different severity were counted under the highest severity; [c]Determined to be due to dermatitis atopic, drug eruption, immune-mediated dermatitis, rash morbilliform, and headache (n=1 each); [d]Events that occurred on the day of drug administration identified using a narrow algorithm search; [e]Injection site reactions are defined using MedDRA high-level term of injection site reactions excluding joint-related Preferred Terms; [f]Defined using the following MedDRA Preferred Terms: conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, and giant papillary conjunctivitis.
Note: Data are n (%).

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Abbreviations: *AD=atopic dermatitis; AE=adverse event; BMI=body mass index; BSA=body surface area; cDLQI=Children's DLQI; DLQI=Dermatology Life Quality Index; EASI=Eczema Area and Severity Index; EASI 75=75% improvement from baseline in EASI; F-IGA=Face-IGA; IGA=Investigator's Global Assessment; IGA (0,1)=IGA response of clear or almost clear; ITT=intent-to-treat; JAK=Janus kinase; LD=loading dose; LEBRI=lebrikizumab; mTLSS=modified Total Lesion Symptom Score; MI=multiple imputation; NMSC=non-melanoma skin cancer; NRI=non-responder imputation; NRS=Numeric Rating Scale; N=number of patients with non-missing values; PDE-4=phosphodiesterase-4; Q2W=every 2 weeks; Q4W=every 4 weeks; QoL=quality of life; SAE=serious adverse event; SC=subcutaneous; SD=standard deviation; TCI=topical calcineurin inhibitor; TCS=topical corticosteroids; TEAE=treatment-emergent adverse event; W=Week*

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Supplemental Materials
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Impact of Age on Efficacy and Safety of Fixed-Dose Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel in Participants with Moderate-to-Severe Acne

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SYNOPSIS

- Acne affects patients of all ages, but there are age-related differences in clinical presentation and efficacy and safety of acne treatments[1]
- Topical clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% (CAB) gel is the only fixed-dose, triple-combination formulation approved for the treatment of acne, and is indicated for use in patients aged ≥12 years[2]
- In three clinical studies of participants with moderate-to-severe acne, once-daily CAB gel demonstrated superior efficacy to vehicle and component dyads, with good safety and tolerability[3,4]

OBJECTIVE

- This post hoc analysis was performed to evaluate the efficacy and safety of CAB in pediatric, adolescent, and adult participants

METHODS

- In a phase 2 (NCT03170388) and two phase 3 (NCT04214652, NCT04214639) studies, participants aged ≥9 years with moderate-to-severe acne were randomized to once-daily CAB or vehicle gel; data for participants randomized to the component dyad gels (phase 2 study) are not shown here
- Endpoints included percentage of participants achieving treatment success (defined as ≥2-grade reduction from baseline in Evaluator's Global Severity Score [EGSS] and clear/almost clear skin) and least-squares mean percent change from baseline in inflammatory/noninflammatory lesion counts at week 12
- Treatment-emergent adverse events (TEAEs) and cutaneous safety (Investigator-assessed) and tolerability (participant-reported) were also assessed
- Pooled data for participants randomized to CAB or vehicle across all three studies were analyzed for participants categorized by age: 9-24 years (pediatric and adolescent) or ≥25 years (adult)
  - These ages were chosen as acne in patients aged 18-24 years is more similar to adolescents than adults, and age 25 is often used to define "adult acne"[1,5]

RESULTS

Participants

- The pooled population comprised 657 participants in two age group: aged 9-24 years (CAB: n=297; vehicle: n=218) and aged ≥25 years (n=91; n=51)
- The majority of participants were female and White, and most had moderate acne (EGSS 3) at baseline (**Table 1**)

Efficacy

- At week 12, approximately half of CAB-treated participants in both age groups achieved treatment success versus less than one fourth with vehicle ($P<0.01$, both; **Figure 1**)
- Treatment with CAB resulted in >70% reductions from baseline in inflammatory and noninflammatory lesions in both age groups at week 12, versus 45%-62% with vehicle ($P\leq0.001$, all; **Figure 2**)
- The only significant difference between CAB-treated participants in the two age groups across the efficacy endpoints was for treatment success at week 8 ($P<0.05$)
- Images of acne improvements in adolescent and adult participants treated with CAB are shown in **Figure 3**

Safety

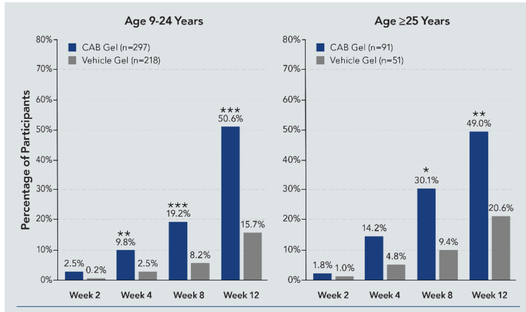
- No notable age-related trends in safety or tolerability were observed (**Table 2**; **Figure 4**)
- Most TEAEs with CAB were of mild-moderate severity, with no age-related trends (**Table 2**)
- Transient increases in the severity of cutaneous safety/tolerability assessments with CAB did not substantially differ between the age groups, with mean scores beginning to normalize by week 4 (**Figure 4**)

TABLE 1. Baseline Demographics and Characteristics (ITT Population, Pooled Participants)

	Age 9-24 Years		Age ≥25 Years	
	CAB Gel (n=297)	Vehicle Gel (n=218)	CAB Gel (n=91)	Vehicle Gel (n=51)
Age, mean (SD), y	16.7 (3.2)	17.2 (3.2)	31.1 (5.3)	32.1 (6.1)
Age, median (range), y	16 (10-24)	17 (11-24)	29 (25-48)	30 (25-47)
Sex, female, n (%)	159 (53.5)	115 (52.8)	79 (86.8)	42 (82.4)
Ethnicity, Hispanic/Latino, n (%)	66 (22.2)	49 (22.5)	24 (26.4)	8 (15.7)
Race, n (%)				
White	218 (73.4)	164 (75.2)	49 (53.8)	29 (56.9)
Black or African American	41 (13.8)	24 (11.0)	23 (25.3)	16 (31.4)
Asian	21 (7.1)	17 (7.8)	10 (11.0)	5 (9.8)
Other[a]	17 (5.7)	13 (6.0)	9 (9.9)	1 (2.0)
Inflammatory lesion count, mean (SD)	38.2 (10.4)	38.8 (9.8)	36.0 (5.7)	34.0 (4.7)
Noninflammatory lesion count, mean (SD)	52.3 (20.1)	50.6 (18.3)	43.8 (9.5)	43.6 (11.0)
Evaluator's Global Severity Score, n (%)				
3 – Moderate	260 (87.5)	192 (88.1)	80 (87.9)	50 (98.0)
4 – Severe	37 (12.5)	26 (11.9)	11 (12.1)	1 (2.0)

[a]American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander, and Multiple/Not Reported/Unknown.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent to treat; SD, standard deviation.

FIGURE 1. Treatment Success[a] Through Week 12 by Age (ITT Population, Pooled Participants)



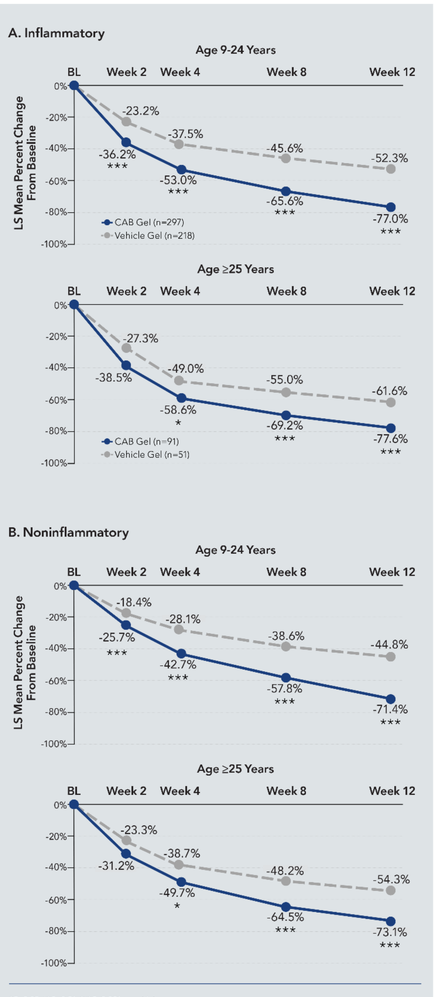
*P<0.05, **P<0.01, ***P<0.001 vs vehicle.
[a]Treatment success defined as ≥2-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 (clear) or 1 (almost clear).
There were no significant differences between active treatment age groups except at week 8 ($P<0.05$).
Values have been adjusted for multiple imputation (MCMC).
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent to treat; MCMC, Markov Chain Monte Carlo.

TABLE 2. Treatment-Emergent Adverse Events Through Week 12 by Age (Safety Population, Pooled Participants)

	Age 9-24 Years		Age ≥25 Years	
Participants, n (%)	CAB Gel (n=293)	Vehicle Gel (n=216)	CAB Gel (n=90)	Vehicle Gel (n=51)
TEAEs	93 (31.7)	30 (13.9)	24 (26.7)	2 (3.9)
Related	56 (19.1)	3 (1.4)	20 (22.2)	1 (2.0)
Serious AEs	1 (0.3)[b]	0	0	0
Discontinued drug or study due to AE	8 (2.7)	2 (0.9)	3 (3.3)	0
Most common treatment-related TEAEs[a]				
AS pain	33 (11.3)	2 (0.9)	9 (10.0)	0
AS dryness	11 (3.8)	0	5 (5.6)	0
Xerosis	0	0	3 (3.3)	1 (2.0)
AS erythema	2 (0.7)	0	3 (3.3)	0
AS pruritus	2 (0.7)	0	3 (3.3)	0

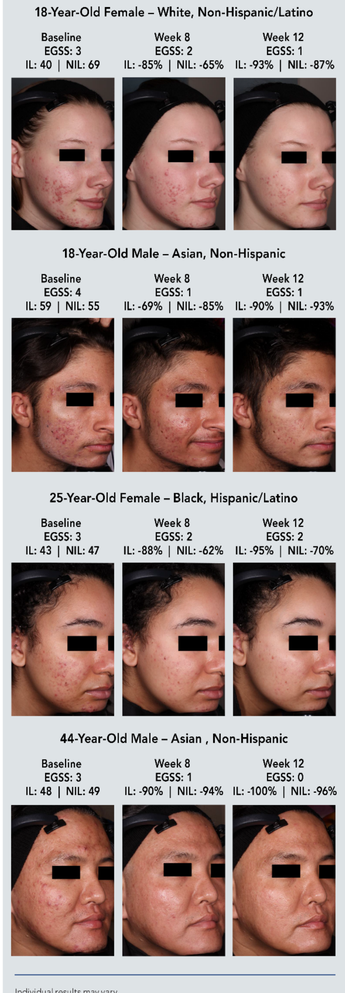
[a]Reported by >3% participants in any treatment group.
[b]Sickle cell anemia with crisis; not considered related to study drug.
AE, adverse event; AS, application site; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

FIGURE 2. Least Squares Mean Percent Reductions in Lesion Counts Through Week 12 by Age (ITT Population, Pooled Participants)



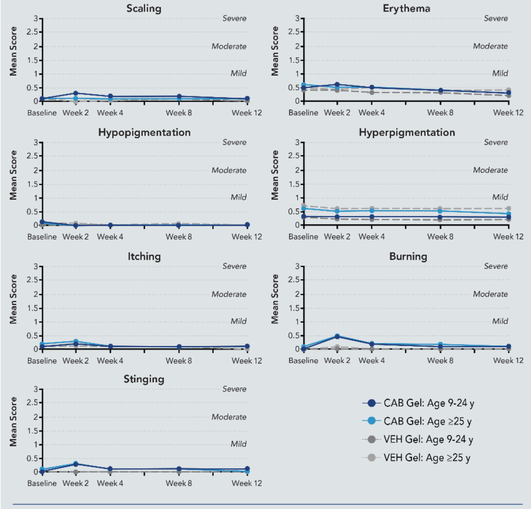
*P<0.05; **P<0.01; ***P<0.001 vs vehicle.
Values have been adjusted for multiple imputation (MCMC).
BL, baseline; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; ITT, intent to treat; LS, least squares; MCMC, Markov Chain Monte Carlo.

FIGURE 3. Acne Improvements with CAB in Participants Aged 9-24 and ≥25 Years



Individual results may vary.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; EGSS, Evaluator's Global Severity Score (0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe); IL, inflammatory lesions; NIL, noninflammatory lesions.

FIGURE 4. Cutaneous Safety and Tolerability Through Week 12 by Age (Safety Population, Pooled Participants)



Investigator-assessed cutaneous safety (scaling, erythema, hypopigmentation, and hyperpigmentation) and participant-reported tolerability (itching, burning, and stinging) were evaluated via a 4-point scale where 0=none and 3=severe.
N values at baseline: CAB age 9-24 y, n=293; VEH age 9-24 y, n=216; CAB age ≥25 y, n=90; VEH age ≥25 y, n=51.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% gel; VEH, vehicle gel.

CONCLUSIONS

- Fixed-dose, triple-combination CAB gel was efficacious and well tolerated in participants with moderate-to-severe acne, regardless of age
- Approximately half of CAB-treated pediatric/adolescent and adult participants achieved clear/almost clear skin, with >70% reductions in lesion counts
- No age-related trends in efficacy or tolerability were observed, suggesting that the innovative CAB gel (approved for use in patients aged ≥12 years) is a valuable treatment option for patients of all ages

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Early Acne Improvements With Fixed-Dose Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel: What to Expect in the First 4 Weeks of Treatment

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SYNOPSIS

- Treatments associated with fast and substantial clearance of acne lesions, as well as those that can cause fewer side effects, can increase patient adherence[1]
- While the term "acne improvement" may vary from person-to-person, a previous study has suggested that a 10-15% reduction in facial acne lesions may be relevant to patients[2]
- A three-pronged approach using once-daily application of an antibiotic, retinoid, and antibacterial may increase treatment efficacy versus monotherapy or dual-combination products,[3] though it is unknown if triple-combination would provide more rapid improvement
- The first triple-combination, fixed-dose topical approved for acne—clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide (BPO) 3.1% gel (CAB; Cabtreo®, Ortho Dermatologics)—was efficacious and well tolerated in three clinical studies, with lesion reductions of >70% after 12 weeks of treatment[4,5]

OBJECTIVE

- To evaluate the efficacy and safety of CAB gel in the first 4 weeks of treatment compared with its dyad components and vehicle gel

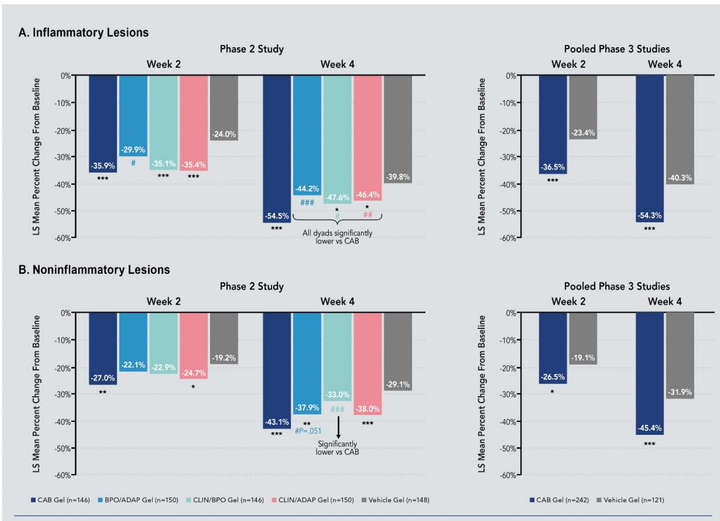
METHODS

- A phase 2 (N=741; NCT03170388) and two phase 3 (N=183; N=180; NCT04214639; NCT04214652), double-blind, 12-week studies enrolled participants aged ≥9 years with moderate-to-severe acne
- Participants were randomized to receive once-daily CAB or vehicle gel; the phase 2 study included three additional dyad gel randomization arms: BPO/adapalene; clindamycin phosphate/BPO; and clindamycin phosphate/adapalene
  - CeraVe® hydrating cleanser and CeraVe® moisturizing lotion (L'Oreal, NY) were provided as needed for optimal moisturization/cleaning of the skin
- Efficacy assessments included least-squares mean percent change from baseline in inflammatory and noninflammatory lesion counts
- Cutaneous safety and tolerability assessments were graded on a 4-point scale (0=none; 3=severe)
- Post hoc analyses included the percentage of participants achieving a one-third and one-half reduction in acne lesions

RESULTS

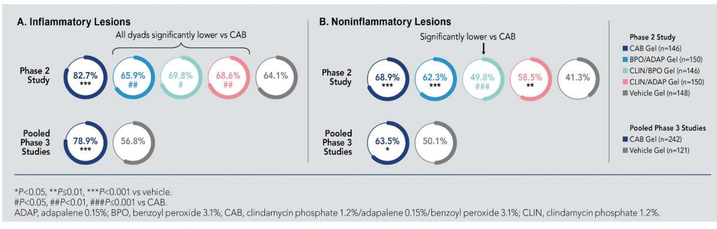
- At week 4, CAB led to ~55% reductions from baseline in inflammatory acne lesions, significantly greater than vehicle and its 3 dyads (range: 39.8%-47.6%; *P*<0.05, all; **Figure 1A**)
  - Improvements with CAB were also greater versus vehicle at week 2 (*P*<0.001), though there was no statistical separation from the dyads at this time point
- The percentage of participants with a one-third reduction of their inflammatory lesions at week 4 was substantial with CAB (~80%), and significantly greater than vehicle and dyads (range: 56.8-69.8%; *P*<0.05, all; **Figure 2A**)
- Overall, one-half reductions in inflammatory lesions were achieved by ~60% of CAB-treated participants at week 4, significantly greater than vehicle and dyads (range: 37.9-47.4%; *P*<0.05, all; **Figure 3A**)
- Generally similar trends were observed for noninflammatory lesions, though reductions were less pronounced than for inflammatory lesions (**Figures 1B, 2B, and 3B**)
- Images of representative CAB-treated participants are shown in **Figure 4**
- Transient increases from baseline to week 2 in scaling, erythema, itching, burning, and stinging were observed for CAB, BPO/adapalene, and clindamycin phosphate/adapalene, with scores beginning to normalize by week 4 (**Figure 5**); this retinization period is expected for retinoids such as adapalene
  - The greatest increases from baseline were observed for scaling, burning, and stinging, though mean scores for all active treatments remained ≤0.6 (1=mild)
  - No trends in dyspigmentation were observed
- Mean scores for all cutaneous assessments in the first 4 weeks of treatment were highest for the dyad BPO/adapalene (**Figure 5**)
- The improved cutaneous profile of CAB compared with BPO/adapalene may be due to the following[4]:
  - The polymeric technology of CAB gel, which provides more uniform distribution of active ingredients, and/or
  - The addition of clindamycin, which may be providing a moderating effect on safety/tolerability through its anti-inflammatory properties

FIGURE 1. **Percent Change From Baseline in Acne Lesion Counts: First Month of Treatment**



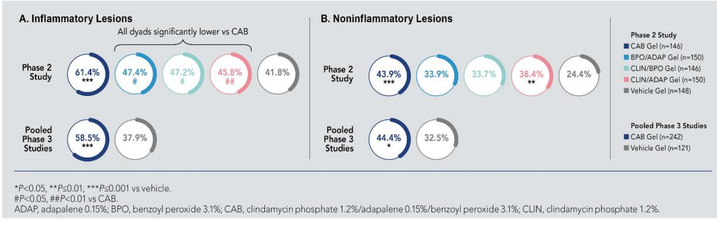
*P<0.05, **P≤0.01, ***P<0.001 vs vehicle.
#P<0.05, ##P<0.01, ###P≤0.001 vs CAB.
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%; LS, least squares.

FIGURE 2. **Percentage of Participants With One-Third Reduction in Acne Lesions at Week 4**



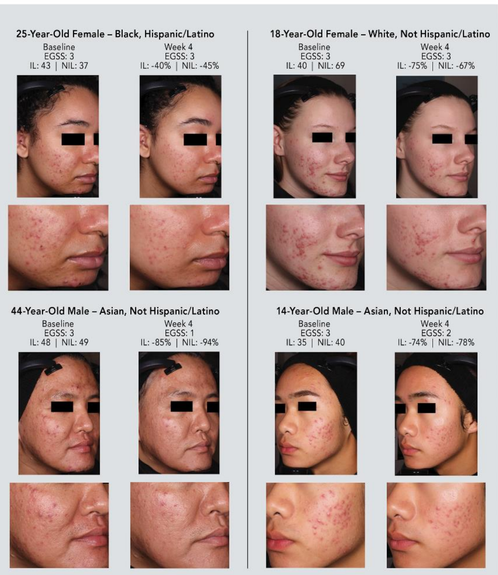
*P<0.05, **P≤0.01, ***P<0.001 vs vehicle.
#P<0.05, ##P<0.01, ###P≤0.001 vs CAB.
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%.

FIGURE 3. **Percentage of Participants With One-Half Reduction in Acne Lesions at Week 4**



*P<0.05, **P≤0.01, ***P≤0.001 vs vehicle.
#P<0.05, ##P<0.01 vs CAB.
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%.

FIGURE 4. **Acne Improvements with CAB Gel From Baseline to Week 4**

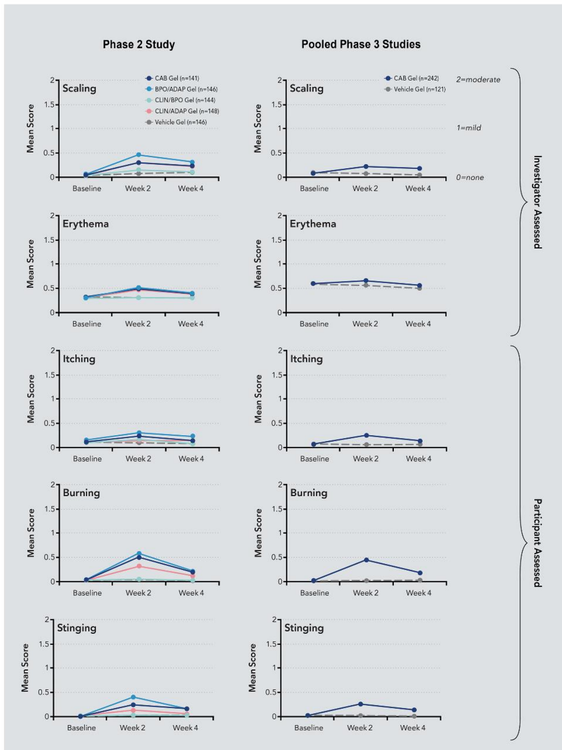


Individual results may vary.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; EGSS, Evaluator's Global Severity Score (0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe); IL, inflammatory lesions; NIL, noninflammatory lesions.

CONCLUSIONS

- Fixed-dose, triple-combination clindamycin phosphate 1.2%/adapalene 0.15%/BPO 3.1% (CAB) gel was well tolerated, with rapid therapeutic effects
  - Acne lesion reductions were significantly greater with triple-combination gel versus its dyads and vehicle gel as early as week 4
  - Cutaneous safety and tolerability assessments with CAB were better than BPO/adapalene, indicating that the additional product in the triple combination did not worsen tolerability
- While extended acne treatment is recommended to achieve clear skin, the faster-acting efficacy of the first triple-combination acne product—coupled with its optimized formulation, once-daily dosing, and tolerability—may positively impact patient satisfaction and treatment adherence

FIGURE 5. **Cutaneous Safety and Tolerability Assessments: First Month of Treatment**



Cutaneous safety and tolerability assessments were graded on a 4-point scale (0=none; 1=mild; 2=moderate; 3=severe). Investigator-assessed hyperpigmentation and hypopigmentation are not shown, as no trends in dyspigmentation were observed.
ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%.

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AUTHOR DISCLOSURES

Julie C. Harper has received honoraria from Aclaris, Almirall, BioPharmX, Cassiopea, Cutanea, Dermira, Foamix, Galderma, LaRoche-Posay, Ortho Dermatologics, and Sun. Leon H. Kircik has served as either a consultant, speaker, advisor or an investigator for Allergan, Almirall, Epi Health, Galderma, Novartis, Ortho Dermatologics, and Sun Pharma. Michael Gold has acted as an investigator, advisor, speaker, and consultant for Ortho Dermatologics. Adelaide A. Hebert has received honoraria from Galderma, LEO Pharma, Almirall, Cassiopea, Ortho Dermatologics, Cutanea, Ferrer, Pfizer, Demira; the UTHealth McGovern Medical School has received research grants from Cassiopea, Demira, Ortho Dermatologics. Jeffrey L. Sugarman is a consultant and speaker for Arcutis, Ortho Dermatologics, Bausch Health, Bristol Myers Squibb, Regeneron, Sanofi, Verrica, Incyte, and Pfizer. Lawrence Green has served as investigator, consultant, or speaker for Almirall, Cassiopea, Galderma, Ortho Dermatologics, Sol Gel, Sun Pharma, and Vyne. Linda Stein Gold has served as investigator/consultant or speaker for Ortho Dermatologics, LEO Pharma, Dermavant, Incyte, Novartis, AbbVie, Pfizer, Sun Pharma, UCB, Arcutis, and Lilly. Hilary Baldwin has served as advisor, investigator, and on speakers' bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. James Q. Del Rosso has served as a consultant, investigator, and/or speaker for Ortho Dermatologics, AbbVie, Almirall, Amgen, Arcutis, Biofrontera, Cassiopea, Cutera, Dermavant, EPI Heath, Evommune, Galderma, Incyte, JEM Health, Journey, La Roche-Posay, LEO Pharma, Lilly, LOreal, MC2 Therapeutics, Novan, Nutrafol, Pfizer, Sente, Strata, Sun Pharma, UCB and Vyne. Eric Guenin is an employee of Ortho Dermatologics and may hold stock and/or stock options in its parent company.

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Efficacy and Safety of Fixed-Dose Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel in Hispanic Participants With Moderate-to-Severe Acne

Valerie D. Callender, MD[1,2]; Hilary Baldwin, MD[3,4]; Linda Stein Gold, MD[5]; Fran E. Cook-Bolden, MD[6,7]; Andrew F. Alexis, MD, MPH[7]; Eric Guenin, PharmD, PhD, MPH[8]

[1]Callender Dermatology and Cosmetic Center, Glenn Dale, MD; [2]Howard University College of Medicine, Washington, DC; [3]The Acne Treatment and Research Center, Brooklyn, NY; [4]Robert Wood Johnson University Hospital, New Brunswick, NJ; [5]Henry Ford Hospital, Detroit, MI; [6]Fran E. Cook-Bolden, MD, PLLC, New York, NY; [7]Weill Cornell Medicine, New York, NY; [8]Ortho Dermatologics*, Bridgewater, NJ
Ortho Dermatologics is a division of Bausch Health US, LLC

SYNOPSIS

- Acne vulgaris is a common dermatologic condition and a leading dermatologic diagnosis among self-identified Black and Hispanic patients[1-3]
- While treatments should be efficacious and rapid, safety and tolerability are also important considerations when treating patients with skin of color, as they are more likely to experience post-inflammatory hyperpigmentation[1,3]
- Topical clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1% (CAB; Cabtreo®, Ortho Dermatologics) gel is the only fixed-dose, triple-combination formulation approved for the treatment of acne
- In three published clinical studies of participants with moderate-to-severe acne, CAB gel demonstrated superior efficacy to vehicle and component dyads, with good safety and tolerability[4-6]

OBJECTIVE

- These post hoc analyses were performed to determine the efficacy, safety, and tolerability of CAB in Hispanic participants

METHODS

- In one phase 2 (NCT03170388) and two phase 3 (NCT04214652, NCT04214639) randomized, double-blind, 12-week studies, participants aged ≥9 years with moderate-to-severe acne were randomized to once-daily CAB or vehicle gel; data for participants randomized to the component dyad gels (phase 2 study) are not shown here
- Endpoints included percentage of participants achieving treatment success (defined as ≥2-grade reduction from baseline in Evaluator's Global Severity Score [EGSS] and clear/almost clear skin) and least-squares mean percent change from baseline in inflammatory/noninflammatory lesion counts at week 12
- Treatment-emergent adverse events (TEAEs) and cutaneous safety (investigator-assessed) and tolerability (participant-assessed) were also evaluated
- Pooled data for participants randomized to CAB or vehicle across all three studies were analyzed based on participants' self-identification of ethnicity, including "Hispanic or Latino" (hereafter referred to as Hispanic)
  - These studies were not powered for statistical analysis of subgroups

RESULTS

Participants

- From the 3 pooled clinical studies, 147 participants self-identified as Hispanic (n=90 CAB; n=57 vehicle gel, intent-to-treat population; **Table 1**)
  - The majority were White, and more than half were female
  - Most had moderate acne (EGSS=3) at baseline

Efficacy

- At week 12, over half of Hispanic participants achieved treatment success with CAB vs less than one-quarter with vehicle gel (56.2% vs 18.4%; *P*<0.001; **Figure 1A**)
- Significantly more Hispanic participants achieved ≥2-grade reduction from baseline in EGSS at weeks 4, 8, and 12 with CAB vs vehicle (*P*<0.05, all; **Figure 1B**)
- CAB treatment provided >75% reductions in inflammatory/noninflammatory lesion counts at week 12 vs 56.4% and 45.0%, respectively, with vehicle (*P*<0.001, both; **Figure 2**)
- Efficacy results were similar to those of the overall study populations[4-6]
- Images showing acne improvement in CAB-treated Hispanic participants are shown in **Figure 3**

TABLE 1. Demographics and Baseline Characteristics of Hispanic Participants (ITT Population, Pooled)

	CAB Gel (n=90)	Vehicle Gel (n=57)
Age, mean (SD), y	21.0 (7.2)	19.1 (5.4)
Sex, female, n (%)	60 (66.7)	32 (56.1)
Race, n (%)		
White	74 (82.2)	50 (87.7)
Black/African American	5 (5.6)	1 (1.8)
Asian	1 (1.1)	0
Other[a]	10 (11.1)	6 (10.5)
Inflammatory lesion count, mean (SD)	37.2 (8.9)	36.8 (8.4)
Noninflammatory lesion count, mean (SD)	48.6 (17.7)	46.6 (14.8)
Evaluator's Global Severity Score, n (%)		
3 – Moderate	80 (88.9)	52 (91.2)
4 – Severe	10 (11.1)	5 (8.8)

[a]American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander, and Multiple/Other/Not Reported/Unknown.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; SD, standard deviation.

Safety

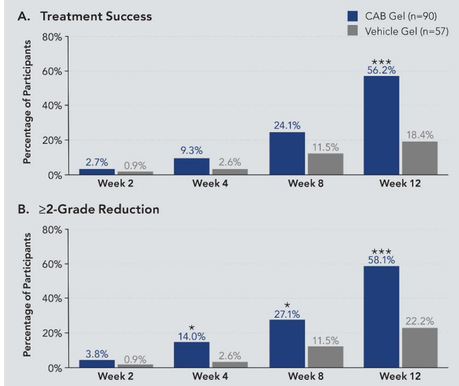
- TEAE rates with CAB in the Hispanic population (**Table 2**) were similar to those in the overall study populations (27% vs 24.6%-36.2%[4-6])
  - Most TEAEs were of mild-to-moderate severity, and discontinuations due to adverse events were low (<4%)
  - The most common (>3% in any treatment group) treatment-related TEAE was application site pain
- Mean cutaneous safety and tolerability scores at all visits with CAB were <1 (mild; **Figure 4**), similar to the overall study populations (<1)[4-6]
  - Hyperpigmentation scores decreased from baseline (0.6) to week 12 (0.3) following CAB treatment

TABLE 2. Summary of Adverse Events Through Week 12 in Hispanic Participants (Safety Population, Pooled)

Participants, n (%)	CAB Gel (n=89)	Vehicle Gel (n=55)
Reporting any TEAE	24 (27.0)	3 (5.5)
Reporting any SAEs	0	0
Discontinued drug or study due to AE	3 (3.4)	0
TEAE Severity		
Mild	10 (11.2)	2 (3.6)
Moderate	10 (11.2)	1 (1.8)
Severe	4 (4.5)	0
Related TEAEs	16 (18.0)	1 (1.8)
Most common treatment-related TEAEs[a]		
AS pain	9 (10.1)	0
AS pruritus	3 (3.4)	0

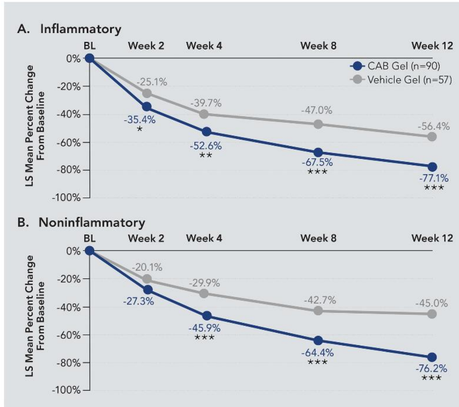
[a]Reported in >3% of participants in any treatment group.
AE, adverse event; AS, application site; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

FIGURE 1. Treatment Success[a] and Reduction in Acne Severity[b] in Hispanic Participants by Visit (ITT Population, Pooled)



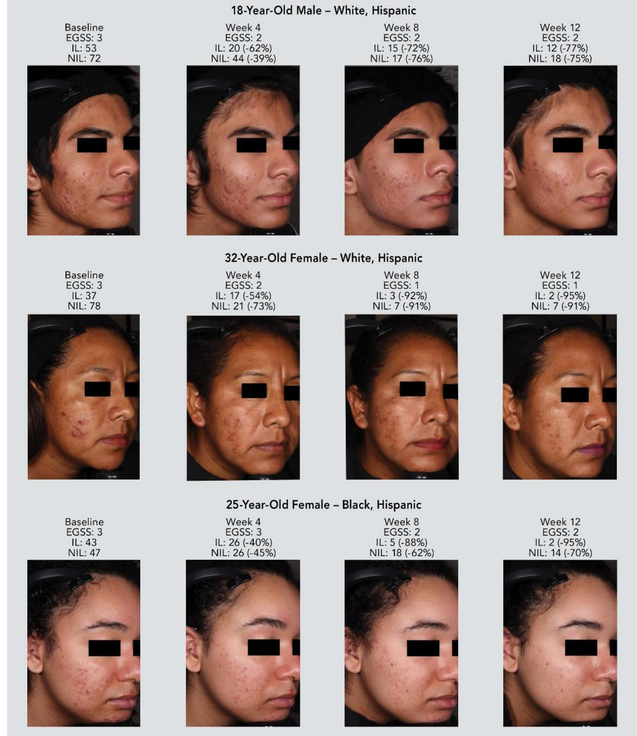
*P<0.05, ***P<0.001 vs vehicle.
[a]≥2-grade reduction from baseline in Evaluator's Global Severity Score (0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe) and clear/almost clear skin.
[b]≥2-grade reduction in Evaluator's Global Severity Score.
Values have been adjusted for multiple imputation (MCMC).
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; MCMC, Markov Chain Monte Carlo.

FIGURE 2. Mean Percent Change From Baseline in Lesion Counts by Visit in Hispanic Participants (ITT Population, Pooled)



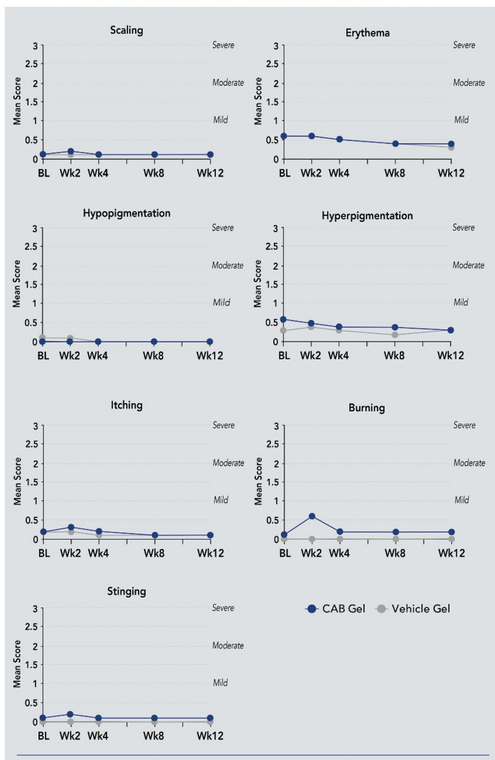
*P<0.05, **P<0.01, ***P≤0.001 vs vehicle.
Values have been adjusted for multiple imputation (MCMC)
BL, baseline; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; ITT, intent to treat; LS, least squares; MCMC, Markov Chain Monte Carlo.

FIGURE 3. Acne Improvements With CAB Gel in Hispanic Participants



Individual results may vary.
Photographic Images Copyright 2024. Courtesy of Ortho Dermatologics Study Investigators.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; EGSS, Evaluator's Global Severity Score (0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe); IL, inflammatory lesions; NIL, noninflammatory lesions.

FIGURE 4. Cutaneous Safety and Tolerability in Hispanic Participants (Safety Population, Pooled)



Investigator-assessed: hyperpigmentation, hypopigmentation, erythema, and scaling; participant-assessed: itching, burning, and stinging.
Scored from 0 (none) to 3 (severe).
N values: CAB: baseline n=89, week 12 n=76; vehicle: baseline n=55, week 12 n=53.
BL, baseline; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%.

CONCLUSIONS

- In Hispanic participants with moderate-to-severe acne treated with CAB, over half achieved treatment success, and acne lesion reductions were reduced by >75% by week 12, without any additional safety signals
- These results, combined with those of previous post hoc analyses in self-identified Black study participants,[7] demonstrate that CAB is an efficacious, safe, and tolerable acne treatment for patients of different racial and ethnic groups

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7. Callender VD, et al. Poster presented at: the 2024 Congress of Clinical Dermatology; May 30-June 2, 2024; Amelia Island, FL

AUTHOR DISCLOSURES

Valerie Callender has served as an investigator, consultant, or speaker for Acne Store, Almirall, Aerolase, AbbVie, Allergan Aesthetics, Avava, Avita Medical, Beiersdorf, Cutera, Dermavant, Erion Therapeutics, Eli Lilly, Galderma, Janssen, Jeune Aesthetics, L'Oréal, Ortho Dermatologics, Pfizer, Prollineum, Regeneron, Scientis, Sente, SkinBetter Science, SkinCeuticals, Symatese, Teoxane, and UpToDate. Hilary Baldwin has served as advisor, served as investigator, and served on speakers bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. Linda Stein Gold has served as investigator/consultant or speaker for Ortho Dermatologics, LEO Pharma, Dermavant, Incyte, Novartis, AbbVie, Pfizer, Sun Pharma, UCB, Arcutis, and Lilly. Fran Cook-Bolden has served as advisor, served as investigator, and served on speakers bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, LEO Pharma, Dermavant, AbbVie, Pfizer, Encore, Foamix, Hovione, Aclaris, and Cutanea. Andrew Alexis has received grants (funds to institution) from LEO Pharma, Amgen, Galderma, Arcutis, Dermavant, AbbVie, and Castle; advisory board/consulting fees from LEO Pharma, Galderma, Pfizer, Sanofi-Regeneron, Dermavant, Beiersdorf, Ortho Dermatologics, L'Oreal, BMS, Bausch Health, UCB, Arcutis, Janssen, Allergan, Almirall, AbbVie, Amgen, VisualDx, Eli Lilly, Swiss American, Cutera, Cara, EPI, Incyte, Castle, Apogee, Canfield, Alphyn, Avita Medical, and Gementech; speaker fees from Regeneron, SANOFI-Genzyme, BMS, L'Oreal, Janssen, and J&J; equipment (loan to institution) from Aerolase; and royalties from Wiley-Blackwell and Wolters Kluwer Health. Eric Guenin is an employee of Ortho Dermatologics and may hold stock and/or stock options in its parent company.

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