Apremilast Efficacy in Patients With Early Oligoarticular Psoriatic Arthritis (PsA) Affecting Weight-bearing Joints by Body Mass Index (BMI): Results From the Randomized, Double-blind, Placebo-controlled FOREMOST Study

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BACKGROUND

- Despite limited joint involvement, oligoarticular (oligo; ≤4 active joints) psoriatic arthritis (PsA) can significantly impact quality of life and physical functioning[1-3]
- In FOREMOST (NCT03747939), patients were randomized (2:1) to apremilast or placebo for 24 weeks (early escape at Week 16), followed by an extension phase, during which all patients could receive apremilast through Week 48[4]
- As previously reported, fewer patients receiving apremilast vs placebo progressed from ≤4 to >4 active (swollen and/or tender) joints at Week 16[4]

OBJECTIVE

- To evaluate the effect of apremilast on weight-bearing joints in patients with early oligo PsA enrolled in FOREMOST through Week 48

Weight-bearing Joint Analysis (post hoc)

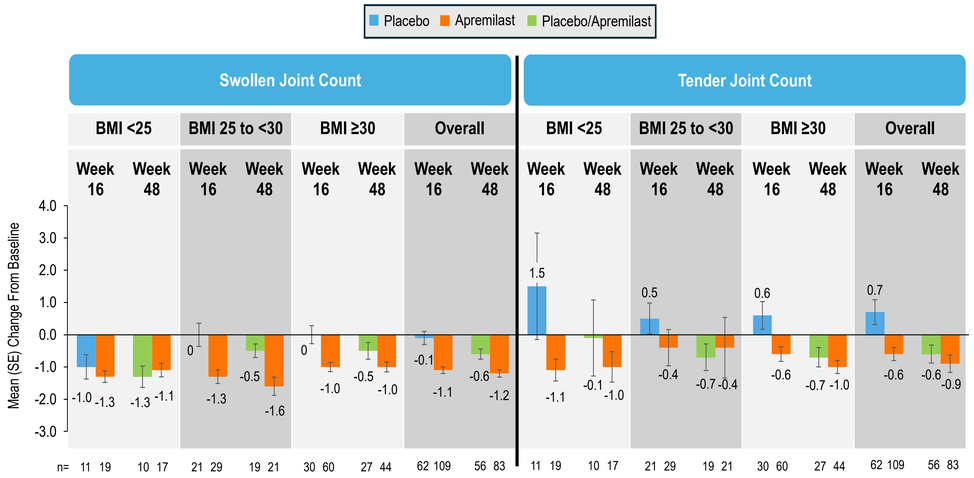
- N=187 patients with **active weight-bearing joints** at baseline who **received ≥1 dose of apremilast (as randomized or transitioned)**; patient characteristics are summarized below and were consistent across BMI subgroups (*scan QR code for baseline data by BMI subgroup*)
- **Weight-bearing joints** defined as hip, knee, ankles, midfoot, metatarsophalangeal, and proximal interphalangeal joint for foot[5]
- **Outcomes assessed through Week 48**: Swollen joint count (SJC), tender joint count (TJC), Health Assessment Questionnaire–Disability Index (HAQ-DI), 36-Item Short-Form Health Survey (SF-36) physical component score (PCS), and 12-item PsA Impact of Disease (PsAID-12) fatigue score
- **Subgroup analysis** by baseline BMI: <25, 25 to <30, ≥30kg/m^2
- **HAQ-DI**: Patient-reported ability to function; range, 0–3, higher scores indicate worse function; HAQ-DI <0.5 considered normal function

Baseline characteristics	Placebo (n=62)	Apremilast (n=125)
BMI, mean (SD), kg/m^2	31.0 (7.4)	30.8 (6.9)
SJC (0–26), mean (SD)	1.2 (0.9)	1.5 (0.9)
TJC (0–28), mean (SD)	1.8 (0.9)	1.9 (1.0)
Active joint count, mean (SD)	1.9 (1.0)	2.1 (1.0)
HAQ-DI (0–3)*, mean (SD)	1.24 (0.41)	1.26 (0.42)

*Summarized for patients with baseline HAQ-DI >0.5 (placebo, n=46; apremilast, n=92).

RESULTS

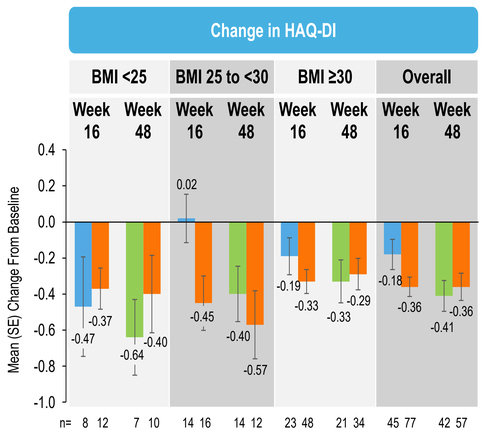
Across weight-bearing joints, larger reductions in SJC and TJC were observed for apremilast vs placebo at Week 16, regardless of BMI, and sustained through Week 48

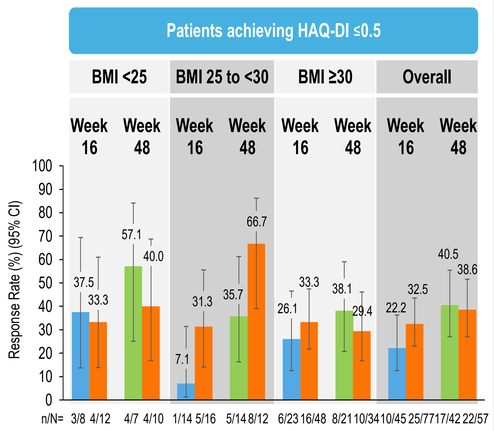


Data as observed for weight-bearing joints in patients with active weight-bearing joints at baseline who received ≥1 dose of apremilast (randomized or transitioned); active joint defined as swollen and/or tender; n=number of patients with non-missing data; SJC based on 26 weight-bearing joints; TJC based on 28 weight-bearing joints. BMI, body mass index (kg/m^2); SE, standard error; SJC, swollen joint count; TJC, tender joint count.

Patients with BMI <25 reported similar changes in HAQ-DI for apremilast and placebo at Week 16

Across most BMI categories, patients with active weight-bearing joints reported larger improvements in HAQ-DI for apremilast vs placebo at Week 16; improvements were sustained through Week 48



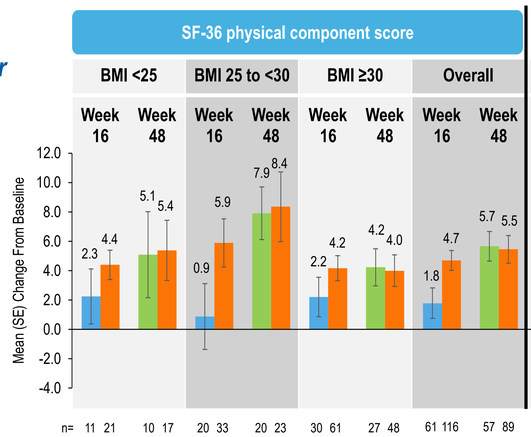


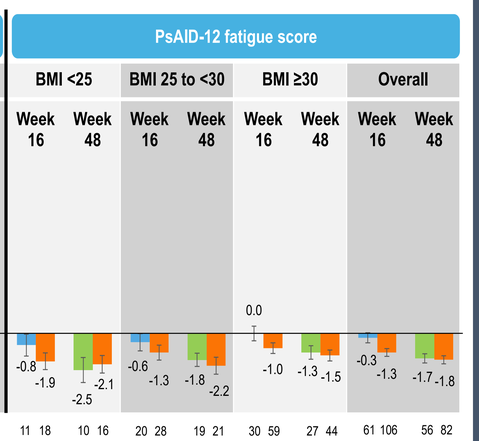
Data as observed for patients with active weight-bearing joints and HAQ-DI >0.5 at baseline who received ≥1 dose of apremilast (randomized or transitioned); active joint defined as swollen and/or tender.

Left: n=number of patients with non-missing data. Right: n=number of patient achieving outcome; N=number with non-missing data.

BMI, body mass index (kg/m2); HAQ-DI, Health Assessment Questionnaire–Disability Index; SE, standard error.

Patients with active weight-bearing joints reported larger improvements in SF-36 and PsAID-12 fatigue score at Week 16 for apremilast vs placebo, regardless of BMI, and sustained through Week 48





Data as observed for patients with active weight-bearing joints at baseline who received ≥1 dose of apremilast (randomized or transitioned); active joint defined as swollen and/or tender; n=number of patients with non-missing data.

BMI, body mass index; PCS, physical component summary; PsAID, Psoriatic Arthritis Impact of Disease; SE, standard error; SF-36, 36-Item Short-Form Health Survey.

Key Takeaways

- **Apremilast improved clinical and patient-reported outcomes at Week 16 in patients with early oligoarticular PsA involving weight-bearing joints at baseline**
- **Greater reductions in swollen and tender joint counts were seen at Week 16 with apremilast vs placebo, regardless of baseline BMI**
- **Patients reported greater improvements in physical function with apremilast vs placebo at Week 16, with consistent results across most BMI categories**
- **Improvements were maintained for up to 48 weeks**

Scan QR code for study design, additional analyses (including active joint count, MCID in HAQ-DI, and PsAID-12 fatigue score ≤1 or 2), and references

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The 31-GEP stratifies risk of death in patients with stage I-IIA cutaneous melanoma: A SEER real-world evidence study

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Background

- Current American Joint Committee on Cancer (AJCC 8th edition) staging stratifies patients with cutaneous melanoma (CM) by their risk of dying from their disease.[1]
- Patients with early-stage I-IIA CM are considered at low risk of poor outcomes; however, recent evidence suggests that many of these patients have a higher risk of death than AJCC suggests.[2]
- Identifying patients who have a higher risk of poor outcomes than suggested by their cancer stage can help clinicians recommend more personalized, risk-appropriate surveillance and treatment management options.[2,3]
- The 31-gene expression profile (31-GEP) is prospectively validated to stratify the risk of death in patients with CM.[4-6]

Objective

Validate 31-GEP MSS and OS risk stratification in patients with stage I-IIA CM in a real-world setting.

Methods

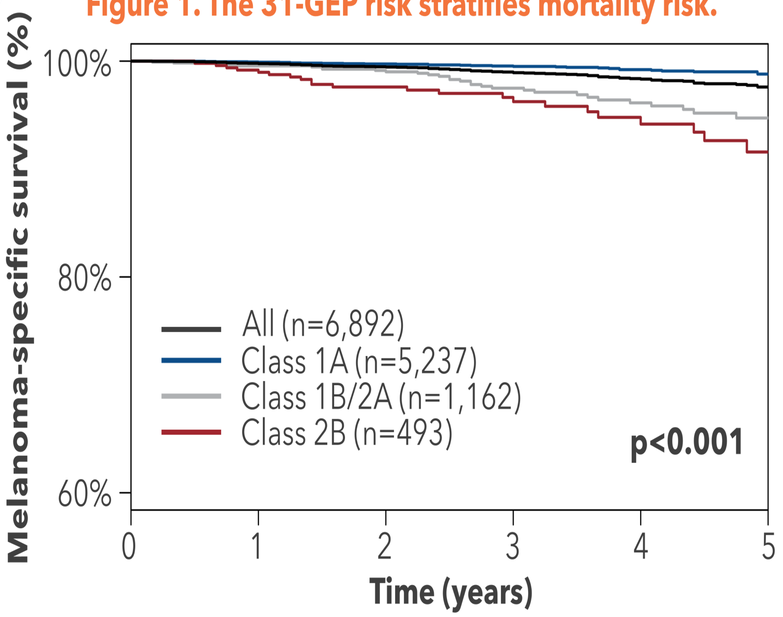
- Registry data from the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) program were linked to data from patients with stage I-IIA CM clinically tested with the 31-GEP (n=6,892). Survival was estimated using Kaplan-Meier analysis, and differences between groups were compared using the log-rank test. Multivariable Cox regression was used to identify predictors of melanoma-specific and all-cause mortality.[4]

Table 1. Patient Demographics

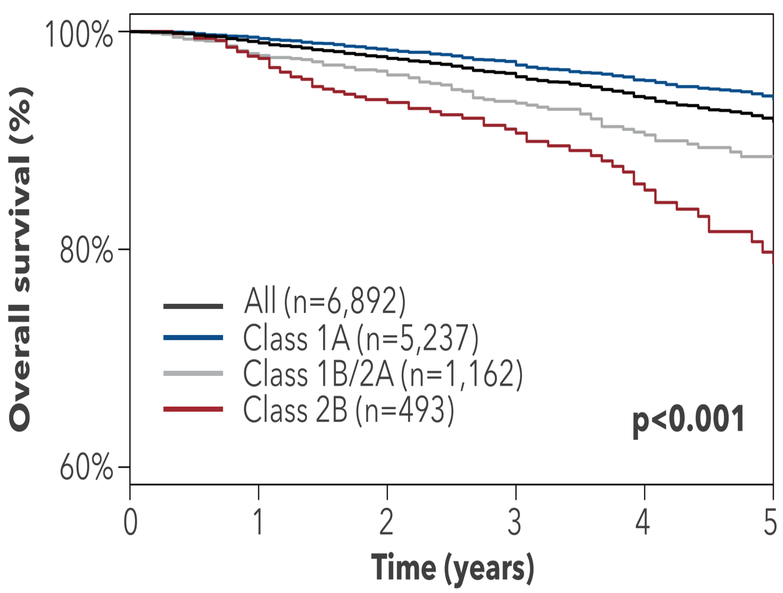
Descriptor	Class 1A (n=5,237)	Class 1B/2A (n=1,162)	Class 2B (n=493)	Combined (n=6,892)
Age				
Median (Range)	60 (18-89+)	65 (18-89+)	67 (22-89+)	62 (18-89+)
Gender				
Female	2448 (46.7%)	465 (40.0%)	185 (37.5%)	3098 (45.0%)
Male	2789 (53.3%)	697 (60.0%)	308 (62.5%)	3794 (55.1%)
AJCCv8 Stage				
Stage IA	4267 (81.5%)	443 (38.1%)	130 (26.4%)	4840 (70.2%)
Stage IB	766 (14.6%)	419 (36.1%)	126 (25.6%)	1311 (19.0%)
Stage IIA	204 (3.9%)	300 (25.8%)	237 (48.1%)	741 (10.8%)
Breslow thickness				
Median (Range)	0.6 (0-4)	1.2 (0.05-4)	1.5 (0.05-4)	0.7 (0-4)
Ulceration				
Absent	4934 (94.2%)	975 (83.9%)	352 (71.4%)	6261 (90.8%)
Unknown	163 (3.1%)	23 (2.0%)	13 (2.6%)	199 (2.9%)
Present	140 (2.7%)	164 (14.1%)	128 (26.0%)	432 (6.3%)

Results

Figure 1. The 31-GEP risk stratifies mortality risk.



Patients with Class 1A results had higher 5-year MSS than patients with Class 1B/2A or Class 2B results (98.8%, 94.7%, vs. 91.6%, p<0.001).



Patients with Class 1A results had higher 5-year OS than patients with Class 1B/2A or Class 2B results (93.8%, 88.5%, vs. 78.7%, p<0.001).

Table 2. Multivariable analysis identifies the 31-GEP as the strongest predictor of melanoma-specific and all-cause mortality

Factor	Melanoma-specific mortality		All-cause mortality	
	Hazard ratio	P-value	Hazard ratio	P-value
Class 1A	Reference	--	Reference	--
Class 1B/2A	**2.81**	**<0.001***	**1.46**	**0.015**
Class 2B	**3.34**	**<0.001***	**1.91**	**<0.001***
Breslow thickness	1.14	0.392	1.13	0.124
Ulceration (absent)*	Reference	--	Reference	--
Ulceration (present)	1.49	0.207	1.05	0.805
Age	**1.05**	**<0.001***	**1.09**	**<0.001***
Mitotic rate	1.06	0.144	1.04	0.174

Bold indicates statistical significance (p<0.05).
*Ulceration unknown HR was ~0 (p>0.99).

Clinical Impact

- In a real-world cohort of patients considered low risk by AJCC staging, the 31-GEP identified patients at higher risk of mortality who may benefit from increased surveillance and management to improve outcomes.

Conclusions

- In a large, real-world cohort of patients with stage I-IIA CM, the 31-GEP stratified MSS and OS.
- The 31-GEP was the strongest predictor of melanoma-specific and all-cause mortality in multivariable analysis.

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Matching-adjusted Indirect Comparison of Efficacy in Patients With Moderate-to-Severe Atopic Dermatitis Treated With Lebrikizumab Plus Topical Corticosteroids Versus Dupilumab Plus Topical Corticosteroids

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BACKGROUND

- Lebrikizumab and dupilumab are monoclonal antibodies (biologic therapies) for treating patients with moderate-to-severe atopic dermatitis (AD).[1] Lebrikizumab is approved in Europe, Japan, Korea, and other countries, and it is under FDA review in the US.
- Without head-to-head clinical trials, indirect treatment comparisons (ITCs) can be used to evaluate relative efficacy.[1]
- A recent study compared the week-16 efficacy of lebrikizumab plus topical corticosteroids (TCS) in the ADhere trial (NCT04250337) versus dupilumab plus TCS in the CHRONOS trial (NCT02260986) using Bucher's ITC, which anchored on the placebo arm while not adjusting for between-trial population difference.[2] Bucher's ITC method compares absolute trial outcomes and can lead to biased conclusions when patient characteristics that affect treatment response (i.e., effect modifiers) are not balanced between trials. The TCS approach also differed in the ADhere and CHRONOS trials, which may lead to different outcomes.
- A matching-adjusted indirect comparison (MAIC),[3] a population-adjusted ITC, is a more suitable ITC method to compare the efficacy of lebrikizumab versus dupilumab because it adjusts for population differences between trials that may impact treatment effect.

OBJECTIVE

- This study compared the efficacy of lebrikizumab every 2 weeks plus TCS (Q2W+TCS) versus dupilumab Q2W+TCS at week 16 in patients with moderate-to-severe AD using an anchored MAIC.

CONCLUSION

- When using an anchored MAIC, a population-adjusted ITC, lebrikizumab Q2W+TCS and dupilumab Q2W+TCS showed similar efficacy at week 16 across multiple endpoints in patients with moderate-to-severe AD.

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RESULTS AND DISCUSSION

- The baseline characteristics of ADhere patients were well-matched to those of CHRONOS patients after study-level matching (i.e., after population-adjustment; **Table 1**).
- When patients from ADhere were re-weighted to match the CHRONOS population, lebrikizumab Q2W+TCS and dupilumab Q2W+TCS showed similar efficacy at week 16 across endpoints **(Table 2; Figure 1)**.
- Although odds ratios (ORs) for EASI 75 (≥75% improvement in Eczema Area and Severity Index score from baseline) and IGA0/1 (Investigator Global Assessment score of 0/1) endpoints showed numerical superiority of lebrikizumab Q2W+TCS versus dupilumab Q2W+TCS, these ORs were not statistically different **(Figure 1)**. The ORs for PNRS≥4 (Pruritus Numerical Rating Scale score ≥4-point improvement from baseline) and DLQI≥4 (Dermatology Life Quality Index score ≥4-point improvement from baseline) favoured dupilumab Q2W+TCS versus lebrikizumab Q2W+TCS, but they were also not statistically different **(Figure 1)**.
- A MAIC is an appropriate method for comparing the efficacy of lebrikizumab Q2W+TCS versus dupilumab Q2W+TCS as it accounts for population heterogeneity between trials, which potentially impacts relative treatment effect.

Table 1. Baseline participant characteristics in ADhere before and after matching

	CHRONOS (dupilumab trial; target)	ADhere (lebrikizumab trial; before matching)	ADhere (lebrikizumab trial; after matching)
Age in years, mean (SD)	37.4 (13.3)	43.6 (17.0)	37.4 (13.4)
Proportion male	0.61	0.52	0.61
Proportion of white ethnicity	0.67	0.58	0.67
EASI, mean (SD)	32.9 (13.0)	27.1 (11.2)	32.9 (13.1)
Proportion with IGA=4	0.48	0.33	0.48
n/effective sample size	421	165	98

Data based on the weights when the whole ADhere adult population was used in the analysis. IGA=4 indicates severe atopic dermatitis. Abbreviations: EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; SD, standard deviation.

Table 2. Efficacy at week 16 for lebrikizumab Q2W+TCS versus dupilumab Q2W+TCS when using a MAIC

	CHRONOS (dupilumab trial; target; response rate)		ADhere (lebrikizumab trial; pre-matching response rate)		ADhere (lebrikizumab trial; post-matching response rate)		MAIC risk ratio (95% CI)	MAIC odds ratio (95% CI)
	Placebo	Dupi	Placebo	Lebri	Placebo	Lebri		
EASI 75 [a]	0.23	0.69	0.35	0.62	0.24	0.72	1.04 (0.57–1.92)	1.14 (0.42–3.09)
IGA0/1 [a]	0.12	0.39	0.17	0.35	0.11	0.42	1.29 (0.48–3.42)	1.39 (0.42–4.60)
PNRS≥4 [b]	0.20	0.59	0.30	0.46	0.26	0.49	0.64 (0.32–1.28)	0.48 (0.17–1.37)
DLQI≥4 [c]	0.43	0.81	0.51	0.76	0.47	0.83	0.91 (0.59–1.40)	0.89 (0.29–2.70)

[a] In CHRONOS, N=315 in the placebo group and N=106 in the dupi group. In ADhere, N=52 in the placebo group and N=113 in the lebri group (pre-matching); ESS=33 in the placebo group and ESS=65 in the lebri group (post-matching). [b] In CHRONOS, N=299 in the placebo group and N=102 in the dupi group. In ADhere, N=46 in the placebo group and N=106 in the lebri group (pre-matching); ESS=30 in the placebo group and ESS=63 in the lebri group (post-matching). [c] In CHRONOS, N=300 in the placebo group and N=100 in the dupi group. In ADhere, N=47 in the placebo group and N=104 in the lebri group (pre-matching); ESS=30 in the placebo group and ESS=64 in the lebri group (post-matching). For [b] and [c], available patients with baseline values ≥4 points from the two trials were used in the analysis. The analysis populations in the target trial were assumed to have the same baseline characteristics as the whole CHRONOS population. The background therapy of "plus topical corticosteroids" was omitted in the labelling of arms in both trials. Abbreviations: CI, confidence interval; DLQI≥4, Dermatology Life Quality Index score ≥4-point improvement from baseline; dupi, dupilumab; EASI 75, ≥75% improvement in Eczema Area and Severity Index score from baseline; ESS, effective sample size; IGA0/1, Investigator Global Assessment score of 0/1; lebri, lebrikizumab; MAIC, matching-adjusted indirect comparison; PNRS≥4, Pruritus Numerical Rating Scale score ≥4-point improvement from baseline; Q2W+TCS, every 2 weeks plus topical corticosteroids.

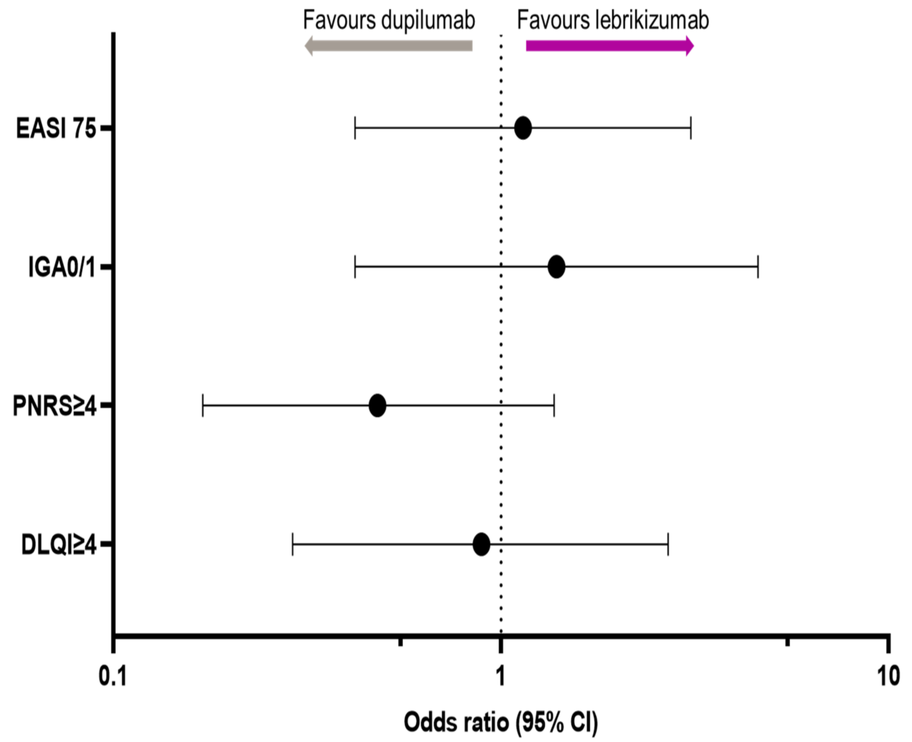

Figure 1. Efficacy at week 16 for lebrikizumab Q2W+TCS versus dupilumab Q2W+TCS when using a MAIC

Abbreviations: CI, confidence interval; DLQI≥4, Dermatology Life Quality Index score ≥4-point improvement from baseline; EASI 75, ≥75% improvement in Eczema Area and Severity Index score from baseline; IGA0/1, Investigator Global Assessment score of 0/1; MAIC, matching-adjusted indirect comparison; PNRS≥4, Pruritus Numerical Rating Scale score ≥4-point improvement from baseline; Q2W+TCS, every 2 weeks plus topical corticosteroids.

METHODS

- **Data sources:** The efficacy of lebrikizumab Q2W+TCS was assessed using individual patient data from the placebo-controlled ADhere trial (NCT04250337). The efficacy of dupilumab Q2W+TCS was assessed using aggregate patient data (N=421) from the placebo-controlled CHRONOS trial (NCT02260986). Week-16 data from both trials were included.
- **Statistical methods:** An anchored MAIC was used where the respective placebo+TCS arm was used as the common comparator. ADhere patients (N=165) were re-weighted to align with reported aggregate statistics for effect modifiers of patients in the CHRONOS trial. Study-level matching was performed, and matching covariates included age, sex, race, and baseline scores on the Eczema Area and Severity Index (EASI; mean) and the Investigator Global Assessment (IGA; proportion with IGA=4).
- **Endpoints:** Efficacy endpoints evaluated at week 16 were EASI 75, IGA0/1, PNRS≥4, and DLQI≥4. Missing data for efficacy endpoints in both trials were handled using non-responder imputation. Relative treatment effects were quantified using ORs and risk ratios (RRs) with 95% confidence intervals (CIs).

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Efficacy and safety of oral deucravacitinib in patients with cutaneous manifestations of lupus erythematosus: results from PAISLEY CLE, a global, randomized, placebo-controlled, phase 2 trial

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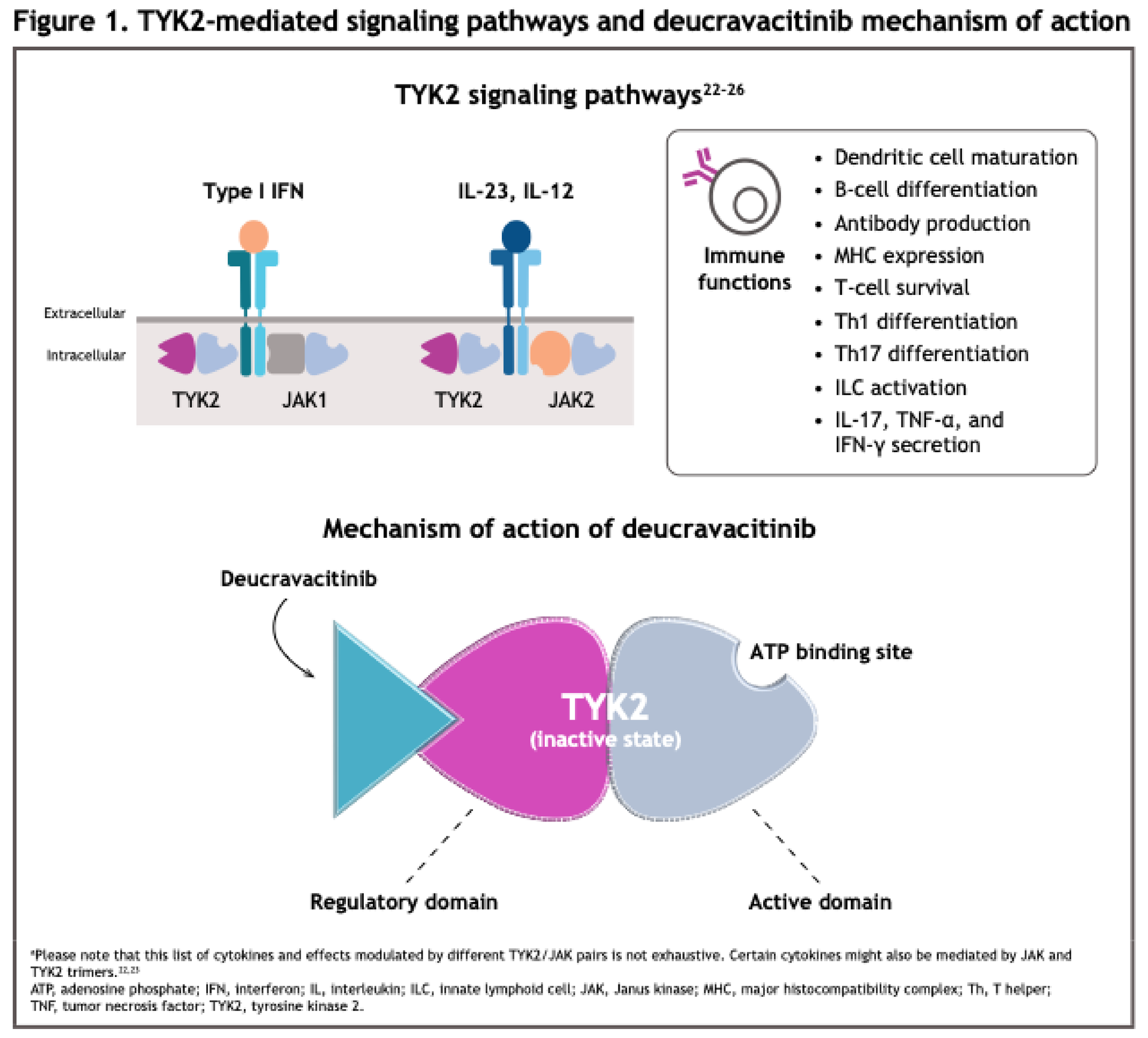
Introduction

- Cutaneous lupus erythematosus (CLE) is an autoimmune disease with a broad range of dermatologic manifestations and a high unmet need for novel treatments[1-3]
- CLE may be associated with systemic lupus erythematosus (SLE) and is classified into 4 main subtypes: acute (ACLE), subacute (SCLE), chronic (the most common manifestation is discoid [DLE]), and intermittent (ICLE) cutaneous lupus erythematosus, according to European guidelines[4,5]
  - DLE and SCLE are the most common forms of CLE, accounting for approximately 80% and 16% of cases, respectively[4]
- Tyrosine kinase 2 (TYK2) is an important mediator of cytokine signaling (eg, type I and III interferons [IFNs], interleukin [IL]-23, and IL-12) involved in immune-specific responses (**Figure 1**)[6,7]
- TYK2 and type I and III IFNs are known to be involved in CLE pathophysiology[8-10]
- Genetic polymorphisms in *TYK2*, interferon regulatory factor 5 (*IRF5*), and signal transducer and activator of transcription 4 (*STAT4*) are associated with an increased risk of SLE[11-13] as well as DLE and SCLE[9]
- Levels of IFN-regulated gene expression correlate with cutaneous disease activity in patients with SLE[8]
- Increases in cytokines, including type I and III IFNs, have been characterized in DLE lesions from patients with SLE[10,14]
- Deucravacitinib is a first-in-class, oral, selective TYK2 inhibitor[15] (**Figure 1**) with an established clinical profile in moderate to severe plaque psoriasis[16-18]
  - Deucravacitinib is approved in multiple countries for this indication[19,20]
- Deucravacitinib uniquely binds the distinct TYK2 regulatory domain, locking the enzyme in an inactive state and inhibiting downstream cytokine signaling, whereas Janus kinase (JAK)1,2,3 inhibitors bind to the adenosine triphosphate (ATP) binding site on the active domain[6,21]

Figure 1. TYK2-mediated signaling pathways and deucravacitinib mechanism of action



[a]Please note that this list of cytokines and effects modulated by different TYK2/JAK pairs is not exhaustive. Certain cytokines might also be mediated by JAK and TYK2 trimers.[22,23]
ATP, adenosine phosphate; IFN, interferon; IL, interleukin; ILC, innate lymphoid cell; JAK, Janus kinase; MHC, major histocompatibility complex; Th, T helper; TNF, tumor necrosis factor; TYK2, tyrosine kinase 2.

- Deucravacitinib is currently under investigation in five POETYK phase 3 trials in SLE (NCT05617677 and NCT05620407), Sjögren's disease (NCT05946941), and psoriatic arthritis (PsA; NCT04908202 and NCT04908189), with primary analysis results from 1 PsA study recently reported[27]
- In the phase 2 PAISLEY SLE trial, deucravacitinib showed higher rates of achieving a ≥ 50% reduction from baseline in the Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity (CLASI-A) score (CLASI-50) at week 48 in the overall SLE population[15]
  - CLASI-50 rates in patients with SLE who received deucravacitinib 3 mg twice daily (BID), 6 mg BID, and 12 mg once daily (QD) vs placebo were 69.6%, 56.0%, and 62.1% vs 16.7%, respectively
- Subgroup analyses from PAISLEY also showed higher rates of CLASI-50 response with deucravacitinib 3 mg BID, 6 mg BID, and 12 mg QD vs placebo, although the patient numbers per group were small[28]
  - Patients with SLE and ACLE: 68.4%, 54.2%, and 60.0% vs 15.0%, respectively
  - Patients with SLE and SCLE: 100%, 33.3%, and 80.0% vs 0%, respectively
  - Patients with SLE and DLE: 71.4%, 45.5%, and 66.7% vs 25.0%, respectively

Objective

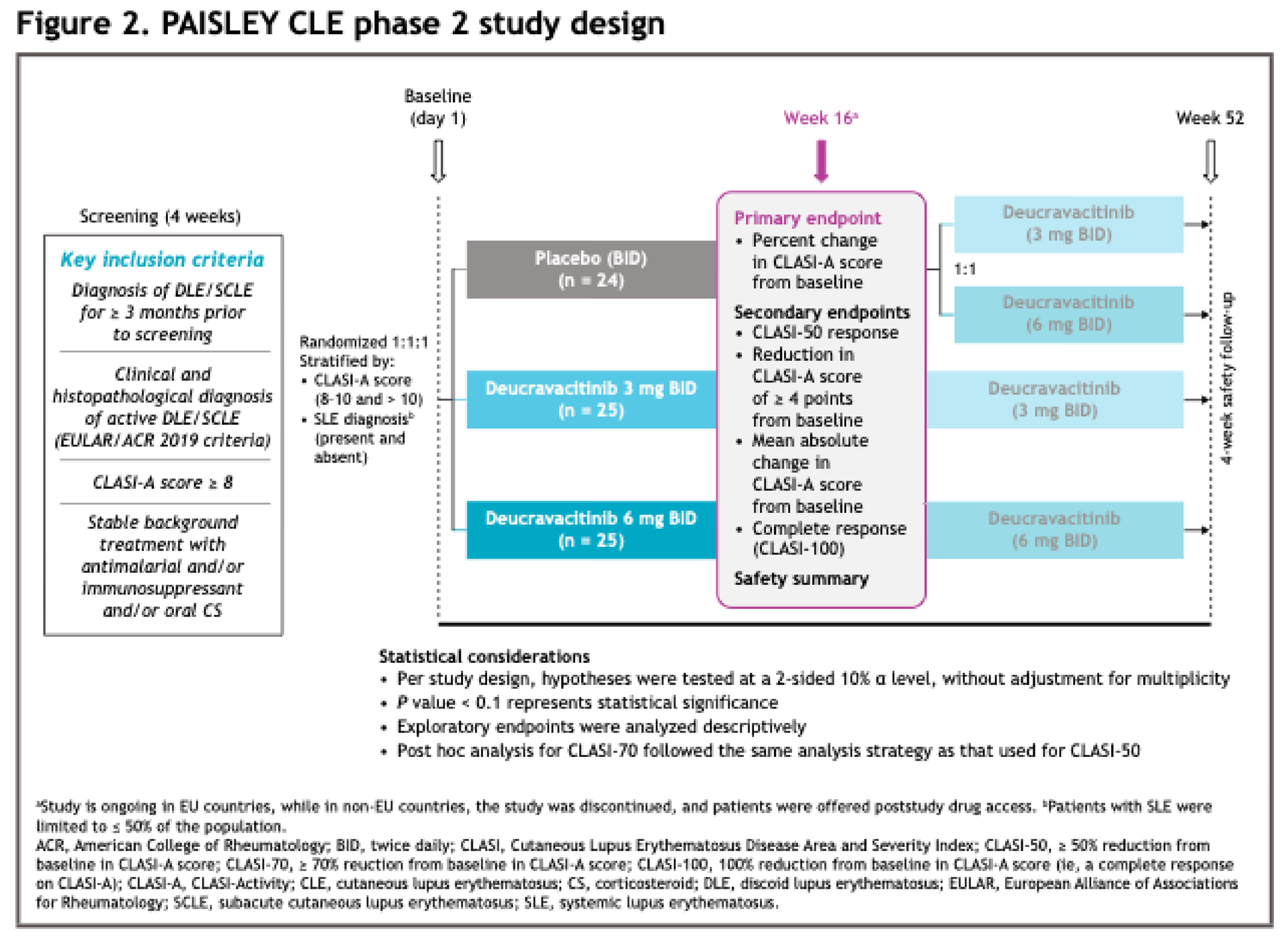
- The phase 2 PAISLEY CLE study was initiated to evaluate the efficacy and safety of deucravacitinib (3 mg and 6 mg BID) vs placebo in patients with DLE and/or SCLE with or without SLE

Methods

Study design

- Adults with a histologically confirmed clinical diagnosis of DLE and/or SCLE with active, moderate to severe cutaneous disease (CLASI-A score ≥ 8) were enrolled in this global, randomized, double-blind, placebo-controlled, phase 2 trial (NCT04857034) (**Figure 2**)
- Patients with SLE, according to the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria, were limited to ≤ 50% of the study population
- Patients were randomized 1:1:1 to receive placebo or deucravacitinib (3 mg BID or 6 mg BID) for 16 weeks
  - At week 16, patients receiving placebo were rerandomized to deucravacitinib 3 mg BID or 6 mg BID until week 52; patients originally randomized to deucravacitinib continued the same treatment until week 52
  - The study is ongoing in EU countries; in non-EU countries, the study was discontinued, and patients were offered treatment through a poststudy drug access program
- The study primary endpoint was mean percent change from baseline (CFB) in CLASI-A score at week 16
  - CLASI-50 and mean absolute CFB in CLASI-A score at week 16 were among the secondary endpoints evaluated
  - Exploratory endpoints included mean percent CFB in CLASI-A score by visit to week 52, reduction of CLASI-A score of at least 7 points at week 16, and CFB in the patient-reported outcome of skin pain at week 16, as measured by the skin pain visual analog scale (VAS)
  - Achievement of ≥ 70% reduction from baseline in CLASI-A score (CLASI-70) at week 16, achievement of a CLASI-A score of ≤ 3 points at week 16, and time to CLASI-50 response were post hoc analyses
- Hypotheses were tested at a 2-sided 10% α level, with a *P* value of < 0.1 representing statistical significance
  - No adjustments for multiplicity were made in this phase 2 study; exploratory endpoints were analyzed descriptively

Figure 2. PAISLEY CLE phase 2 study design



[a]Study is ongoing in EU countries, while in non-EU countries, the study was discontinued, and patients were offered poststudy drug access. [b]Patients with SLE were limited to ≤ 50% of the population.
ACR, American College of Rheumatology; BID, twice daily; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-50, ≥ 50% reduction from baseline in CLASI-A score; CLASI-70, ≥ 70% reuction from baseline in CLASI-A score; CLASI-100, 100% reduction from baseline in CLASI-A score (ie, a complete response on CLASI-A); CLASI-A, CLASI-Activity; CLE, cutaneous lupus erythematosus; CS, corticosteroid; DLE, discoid lupus erythematosus; EULAR, European Alliance of Associations for Rheumatology; SCLE, subacute cutaneous lupus erythematosus; SLE, systemic lupus erythematosus.

Results

Patients

- Patients (N = 74) were randomized to placebo (n = 24), deucravacitinib 3 mg BID (n = 25), or deucravacitinib 6 mg BID (n = 25) (**Table 1**)
- Most patients in all arms completed treatment (63/74; 85.1%); no patients withdrew from the study due to adverse events or lack of efficacy (**Table 1**)
- Baseline patient demographics and disease characteristics were generally balanced across arms (**Tables 2 and 3**)
  - At screening, 41.7%, 32.0%, and 52.0% of patients in the placebo, deucravacitinib 3 mg BID, and deucravacitinib 6 mg BID groups, respectively, had SLE

Table 1. Patient disposition through week 16

Disposition	Placebo	Deucravacitinib 3 mg BID	Deucravacitinib 6 mg BID
Randomized, n	24	25	25
Completed through week 16, n (%)	22 (91.7)	21 (84.0)	20 (80.0)
Ongoing treatment, n (%)	0	0	1 (4)[a]
Discontinued treatment, n (%)	2 (8.3)	4 (16.0)	4 (16.0)
Reasons for discontinuation, n (%)			
Patient withdrew consent	2 (8.3)	1 (4.0)	1 (4.0)
Patient requested treatment discontinuation	0	2 (8.0)	2 (8.0)
Pregnancy	0	1 (4.0)	1 (4.0)
Adverse event	0	0	0
Death	0	0	0

[a]The safety follow-up visit for this patient occurred after the cutoff for the database lock; therefore, this patient has ongoing treatment status for the purpose of this analysis.
BID, twice daily.

Table 2. Baseline patient demographics

Demographics	Placebo (n = 24)	Deucravacitinib 3 mg BID (n = 25)	Deucravacitinib 6 mg BID (n = 25)
Age, median (range), years	46 (25-72)	48 (20-74)	42 (21-62)
Weight, median (range), kg	69.85 (51.3-93.0)	73.50 (43.2-129.0)	74.80 (51.0-119.0)
BMI, median (range), kg/m²	25.6 (19.0-30.9)	24.7 (18.0-42.5)	27.7 (18.5-43.7)
Female, n (%)	18 (75.0)	17 (68.0)	19 (76.0)
Race, n (%)			
American Indian or Alaska Native	3 (12.5)	1 (4.0)	0
Asian	2 (8.3)	2 (8.0)	3 (12.0)
Black or African American	2 (8.3)	4 (16.0)	6 (24.0)
White	13 (54.2)	17 (68.0)	13 (52.0)
Other	4 (16.7)	1 (4.0)	3 (12.0)
Ethnicity, n (%)			
Hispanic or Latino	13 (54.2)	9 (36.0)	5 (20.0)
Not Hispanic or Latino	11 (45.8)	16 (64.0)	20 (80.0)
Geographic region, n (%)			
Asia	2 (8.3)	1 (4.0)	2 (8.0)
Europe	6 (25.0)	8 (32.0)	11 (44.0)
North America	5 (20.8)	8 (32.0)	8 (32.0)
South America/Latin America	11 (45.8)	7 (28.0)	3 (12.0)
Rest of world	0	1 (4.0)	1 (4.0)

BID, twice daily; BMI, body mass index.

Table 3. Baseline disease characteristics

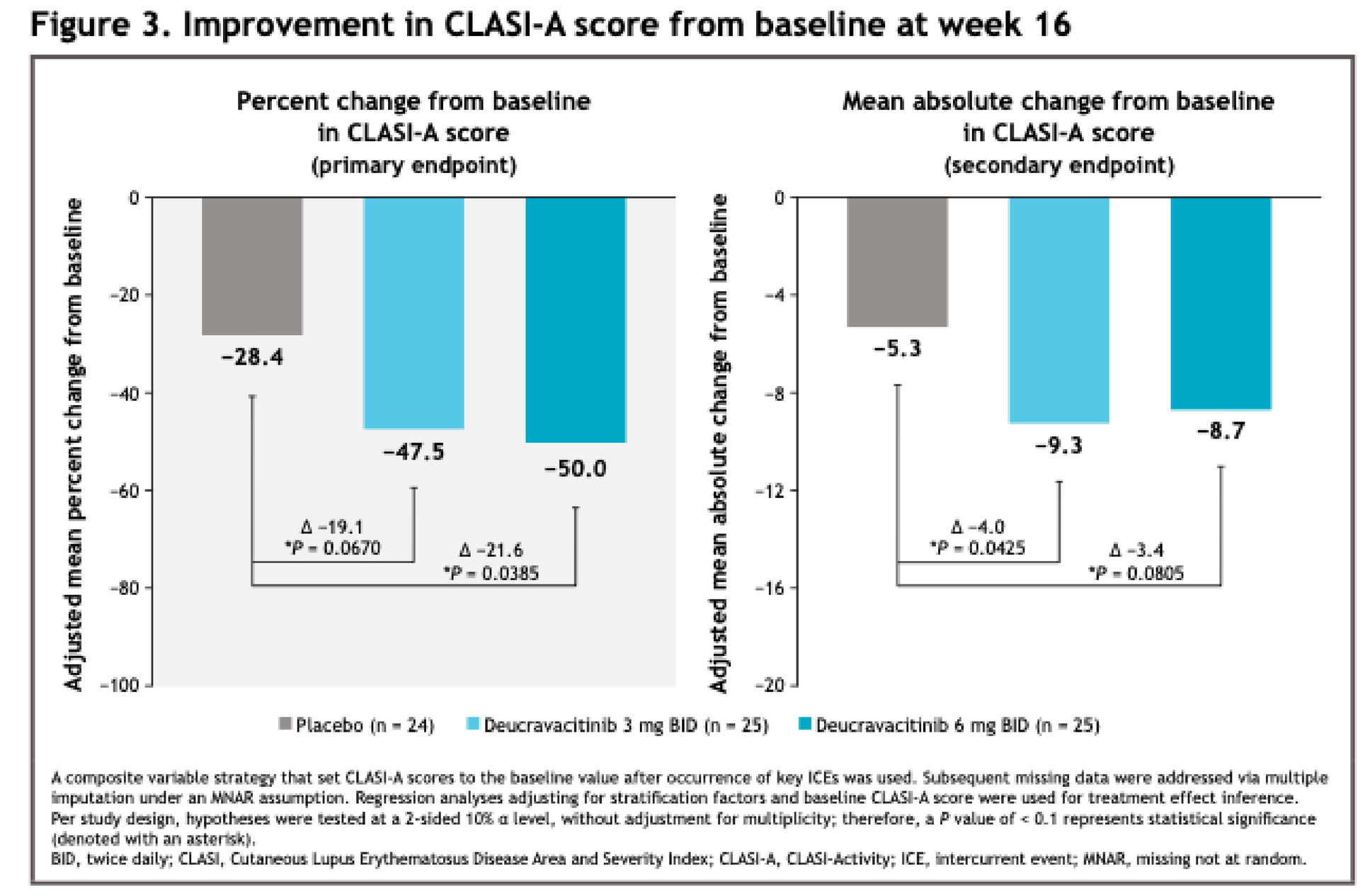
Disease characteristics	Placebo (n = 24)	Deucravacitinib 3 mg BID (n = 25)	Deucravacitinib 6 mg BID (n = 25)
Baseline total CLASI-A score			
Mean (SD)	16.0 (6.1)	18.1 (10.6)	14.8 (5.2)
Median (range)	16.0 (8-33)	14.0 (8-44)	14.0 (8-29)
Baseline CLASI-A severity, n (%)[a]			
8-10	5 (20.8)	5 (20.0)	7 (28.0)
> 10	19 (79.2)	20 (80.0)	18 (72.0)
Duration of disease, median (range), years	4.5 (0.3-39.2)	6.3 (0.4-42.1)	6.9 (0.6-35.1)
SLE diagnosis at screening, n (%)[a]	10 (41.7)	8 (32.0)	13 (52.0)
Disease subtype(s), n (%)			
DLE	13 (54.2)	15 (60.0)	19 (76.0)
SCLE	5 (20.8)	5 (20.0)	5 (20.0)
Both DLE and SCLE	6 (25.0)	5 (20.0)	1 (4.0)
Baseline therapies of interest, n (%)			
Oral corticosteroids	13 (54.2)	8 (32.0)	5 (20.0)
Topical corticosteroids	2 (8.3)	2 (8.0)	1 (4.0)
Immunosuppressants	8 (33.3)	7 (28.0)	3 (12.0)
Antimalarials	20 (83.3)	24 (96.0)	20 (80.0)
Prior therapies, n (%)			
Oral corticosteroids	6 (25.0)	5 (20.0)	0
Topical corticosteroids	12 (50.0)	14 (56.0)	13 (52.0)
Immunosuppressants	12 (50.0)	8 (32.0)	11 (44.0)
Antimalarials	8 (33.3)	3 (12.0)	5 (20.0)

[a]As reported on the patient's case report form.
BID, twice daily; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-A, CLASI-Activity; DLE, discoid lupus erythematosus; SCLE, subacute cutaneous lupus erythematosus; SD, standard deviation; SLE, systemic lupus erythematosus.

Efficacy

- The primary endpoint was met; patients treated with deucravacitinib achieved significantly greater improvements in CLASI-A score vs placebo (**Figure 3**)
  - Deucravacitinib 3 mg BID vs placebo: −47.5% vs −28.4%; *P* = 0.0670
  - Deucravacitinib 6 mg BID vs placebo: −50.0% vs −28.4%; *P* = 0.0385

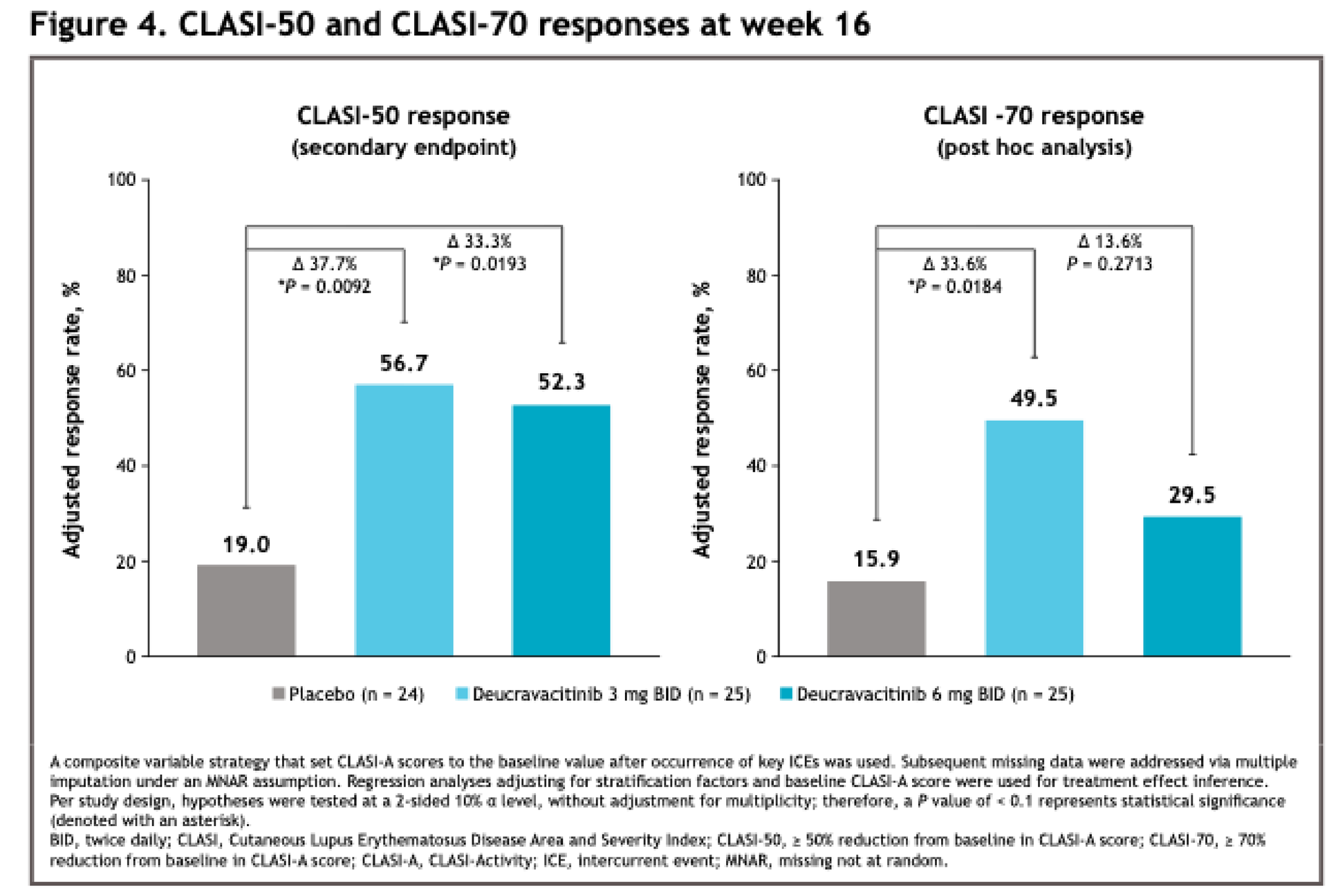
Figure 3. Improvement in CLASI-A score from baseline at week 16



A composite variable strategy that set CLASI-A scores to the baseline value after occurrence of key ICEs was used. Subsequent missing data were addressed via multiple imputation under an MNAR assumption. Regression analyses adjusting for stratification factors and baseline CLASI-A score were used for treatment effect inference. Per study design, hypotheses were tested at a 2-sided 10% α level, without adjustment for multiplicity; therefore, a *P* value of < 0.1 represents statistical significance (denoted with an asterisk).
BID, twice daily; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-A, CLASI-Activity; ICE, intercurrent event; MNAR, missing not at random.

- More patients treated with deucravacitinib achieved CLASI-50 and CLASI-70 vs placebo (**Figure 4**)

Figure 4. CLASI-50 and CLASI-70 responses at week 16



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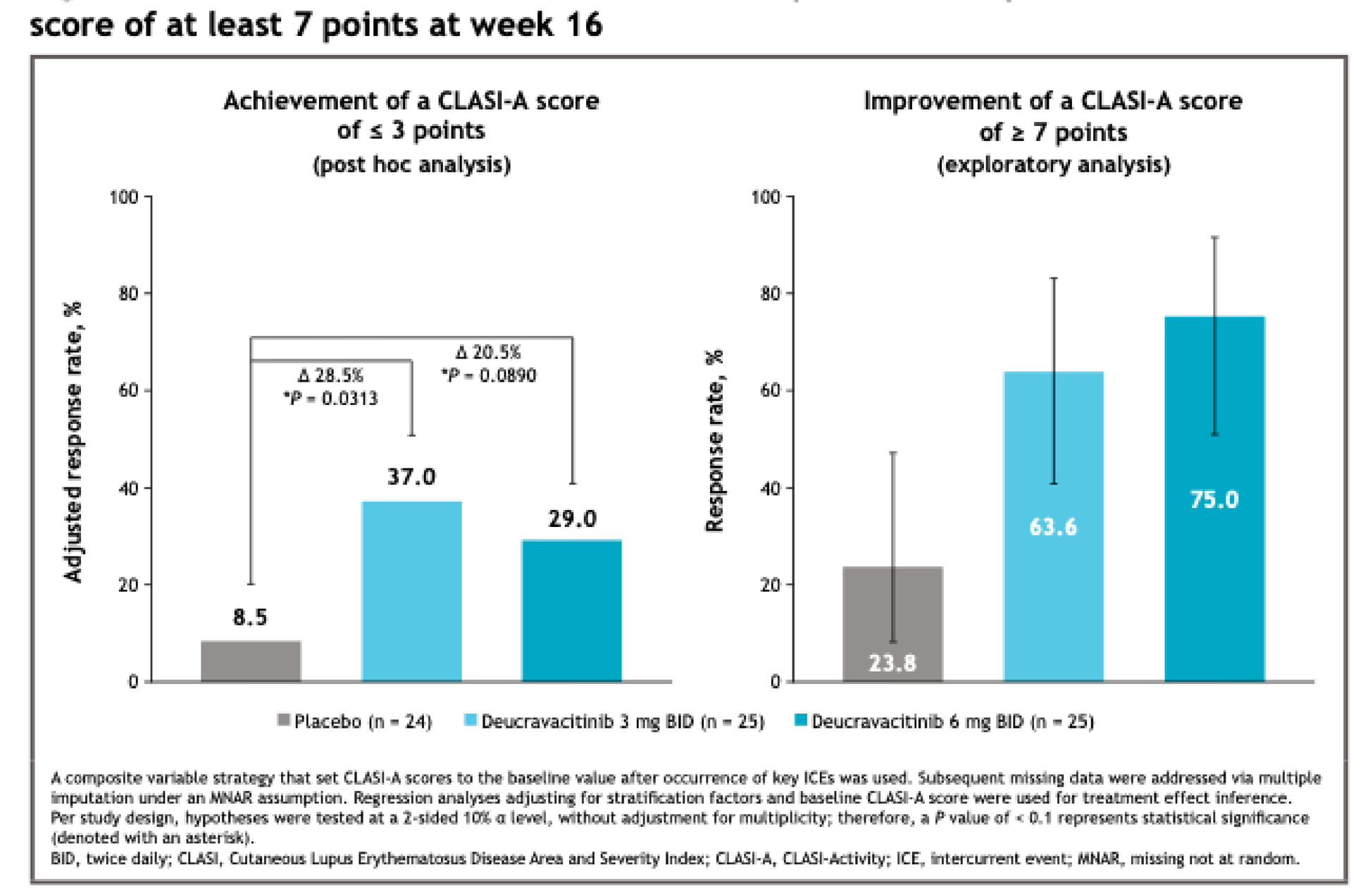
BID, twice daily; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-50, ≥ 50% reduction from baseline in CLASI-A score; CLASI-70, ≥ 70% reduction from baseline in CLASI-A score; CLASI-A, CLASI-Activity; ICE, intercurrent event; MNAR, missing not at random.

- A complete response on CLASI-A (100% reduction from baseline in CLASI-A score), which represents a complete resolution of symptoms, was achieved by 4 patients treated with deucravacitinib (3 mg BID, n = 3; 6 mg BID, n = 1) and no patients who received placebo
- More patients treated with deucravacitinib vs placebo achieved a CLASI-A score of ≤ 3points or showed at least a 7-point improvement in CLASI-A score (**Figure 5**)

Figure 5. Achievement of a CLASI-A score of ≤ 3 points and improvement in CLASI-A score of at least 7 points at week 16



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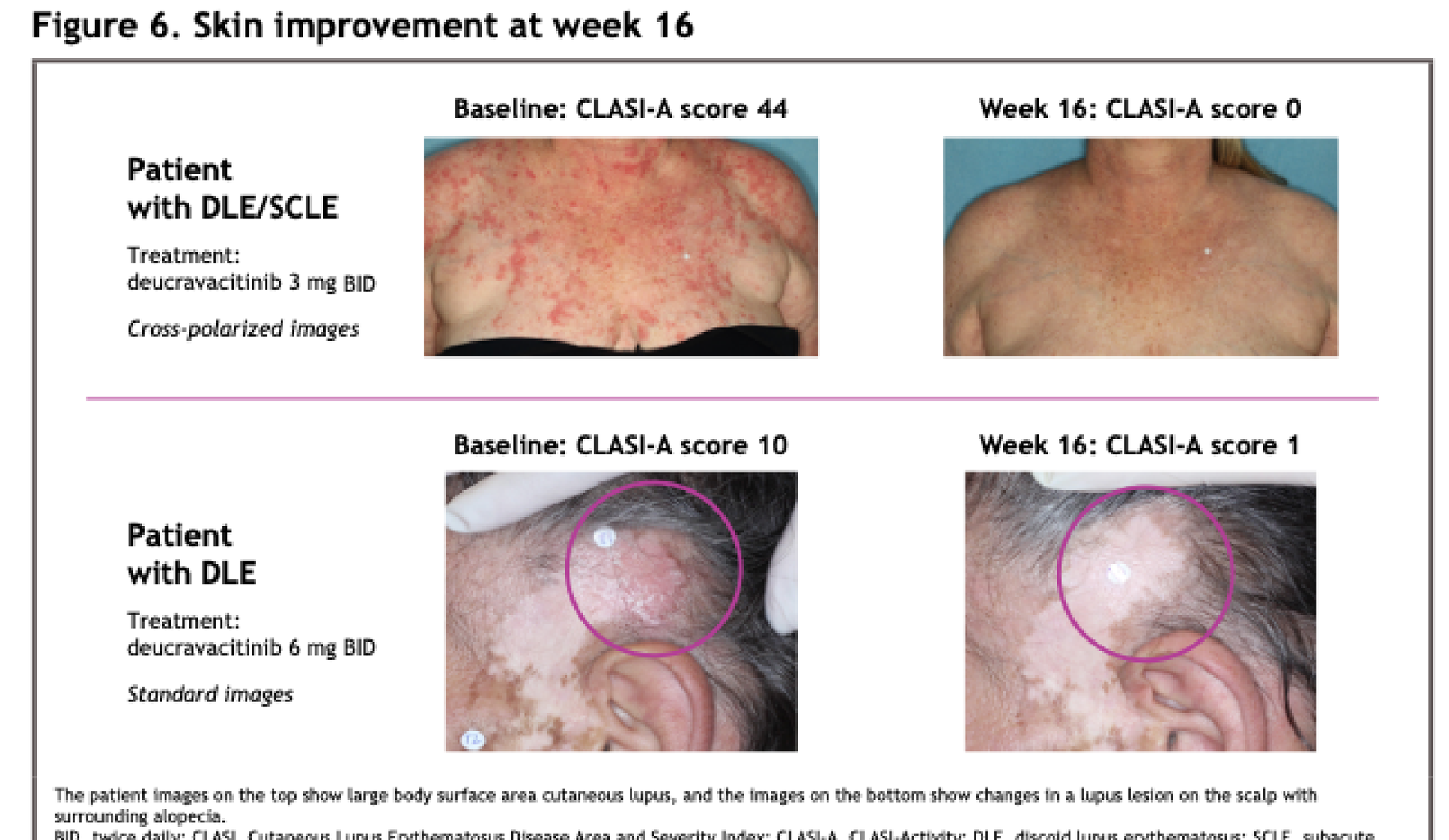
BID, twice daily; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-A, CLASI-Activity; ICE, intercurrent event; MNAR, missing not at random.

- Patient images captured at week 16 show improvement in the cutaneous manifestations of 2 patients who achieved CLASI-A scores of 0 and 1, respectively (**Figure 6**)

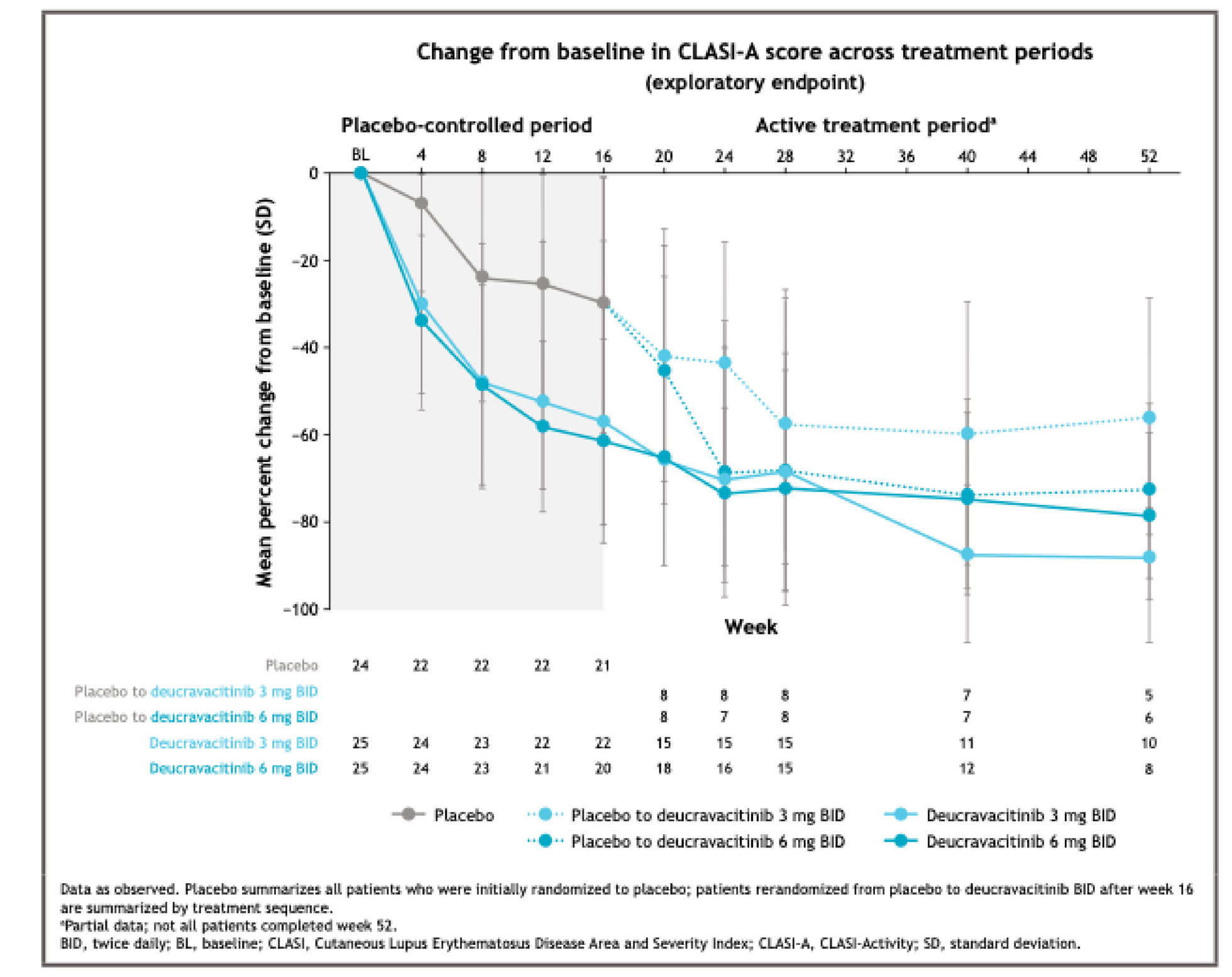
Figure 6. Skin improvement at week 16



The patient images on the top show large body surface area cutaneous lupus, and the images on the bottom show changes in a lupus lesion on the scalp with surrounding alopecia.
BID, twice daily; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-A, CLASI-Activity; DLE, discoid lupus erythematosus; SCLE, subacute cutaneous lupus erythematosus.

- Analysis of CLASI-A score over time showed numerical improvements in CLASI-A score with both deucravacitinib doses as early as 4 weeks, with a trend toward continued improvement throughout the study (**Figure 7**)
  - Response to deucravacitinib (separation of the curves) was seen as early as 4 weeks

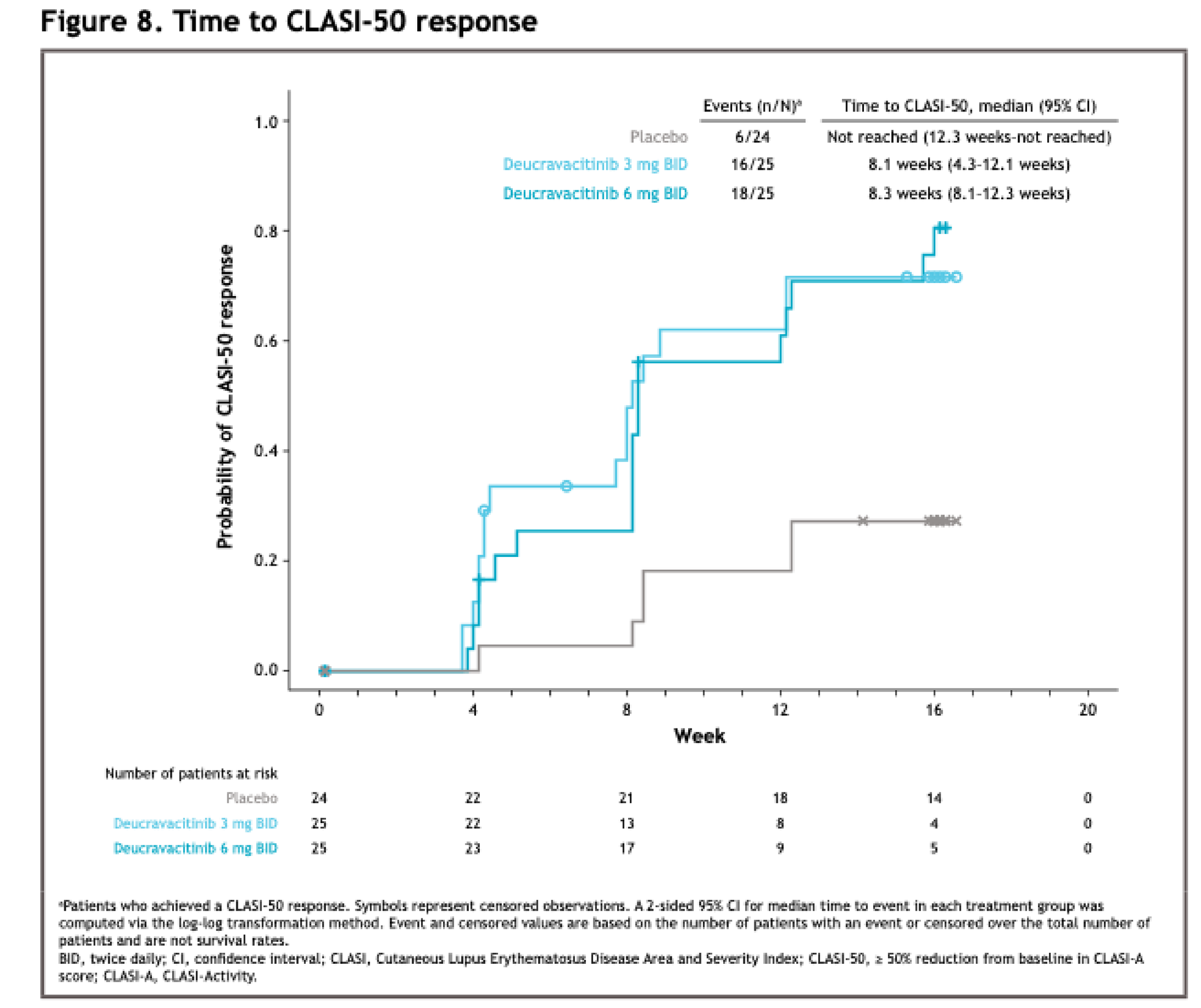
Figure 7. Improvement in CLASI-A score from baseline by visit



Data as observed. Placebo summarizes all patients who were initially randomized to placebo; patients rerandomized from placebo to deucravacitinib BID after week 16 are summarized by treatment sequence.
[a]Partial data; not all patients completed week 52.
BID, twice daily; BL, baseline; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-A, CLASI-Activity; SD, standard deviation.

- Median time to CLASI-50 response was 8.1 weeks with deucravacitinib 3 mg BID, 8.3 weeks with deucravacitinib 6 mg BID, and not reached with placebo (**Figure 8**)

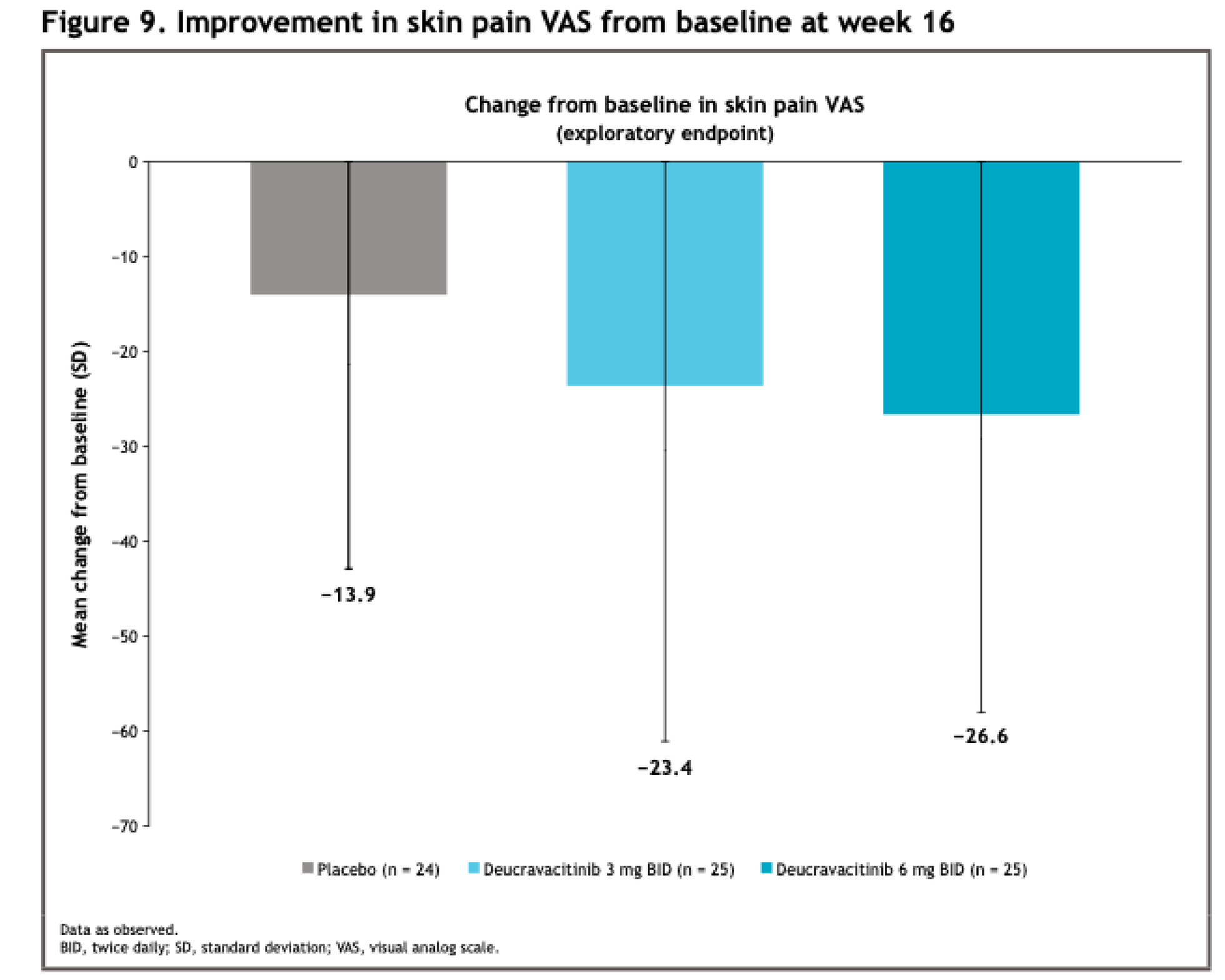
Figure 8. Time to CLASI-50 response



[a]Patients who achieved a CLASI-50 response. Symbols represent censored observations. A 2-sided 95% CI for median time to event in each treatment group was computed via the log-log transformation method. Event and censored values are based on the number of patients with an event or censored over the total number of patients and are not survival rates.
BID, twice daily; CI, confidence interval; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-50, ≥ 50% reduction from baseline in CLASI-A score; CLASI-A, CLASI-Activity.

- The patient-reported outcome of skin pain was numerically improved with both deucravacitinib doses vs placebo at week 16 (**Figure 9**)

Figure 9. Improvement in skin pain VAS from baseline at week 16



Data as observed.
BID, twice daily; SD, standard deviation; VAS, visual analog scale.

Safety

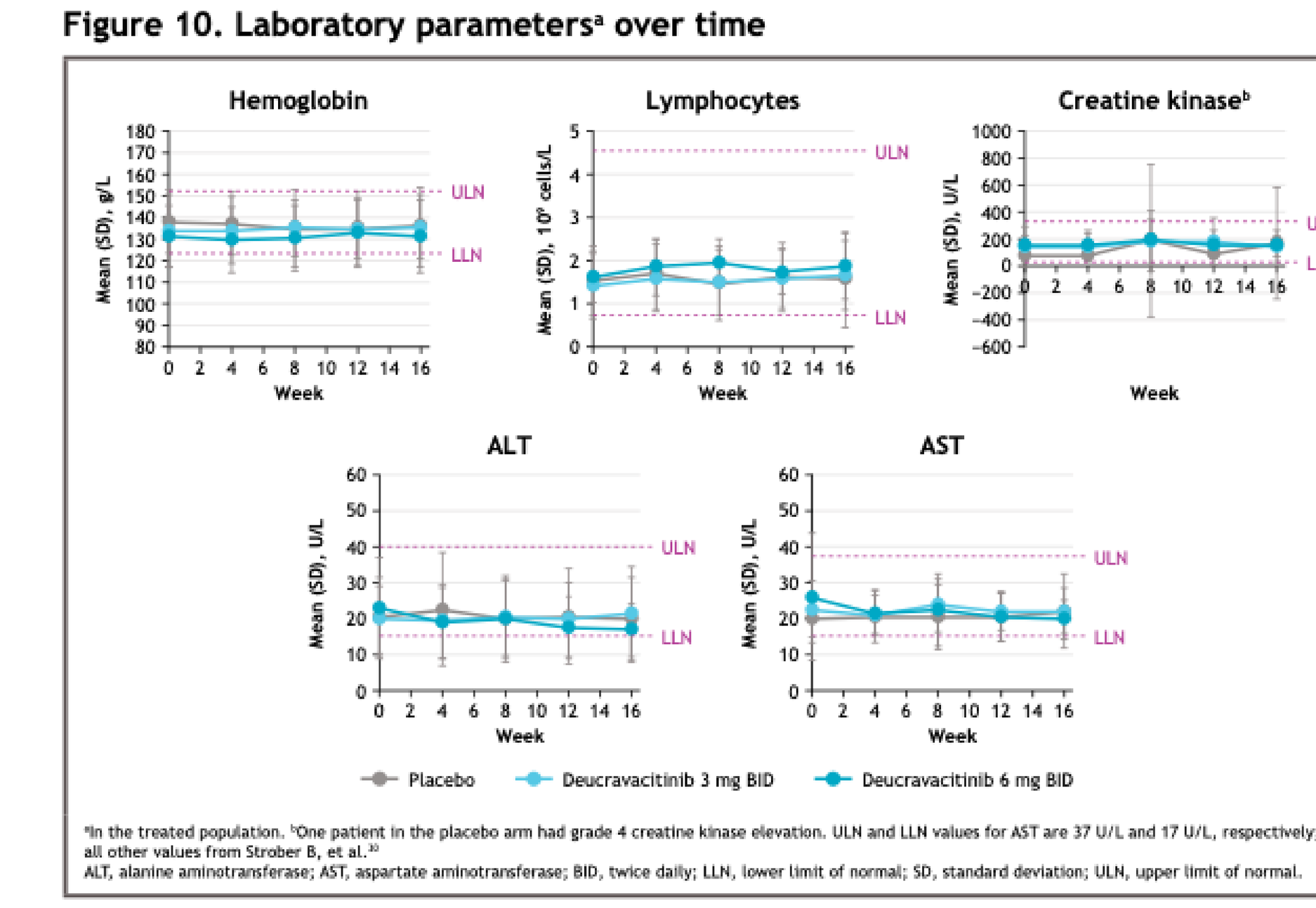
- The reported adverse events (AEs) (**Table 4**) are consistent with the known safety profile of deucravacitinib[15-17,29]
- The most common AEs with deucravacitinib 3 mg and 6 mg BID at week 16 included headache, dermatitis acneiform, and upper respiratory tract infection (**Table 4**)
- Most AEs were mild to moderate in severity; no discontinuations due to AEs were observed (**Table 4**)
- No cases of herpes zoster, major adverse cardiac events (MACE), venous thromboembolism (VTE), malignancy, or opportunistic infections occurred with deucravacitinib, and no deaths were reported (**Table 4**)
- No significant changes in laboratory parameters were observed (**Figure 10**)

Table 4. Safety summary: weeks 0-16[a]

Patients with an AE, n (%)	Placebo (n = 24)	Deucravacitinib 3 mg BID (n = 25)	Deucravacitinib 6 mg BID (n = 25)
Deaths	0	0	0
AEs	12 (50.0)	17 (68.0)	19 (79.2)
Serious AEs	1 (4.2)[b]	2 (8.0)[c]	2 (8.3)[d]
Serious infections/infestations	0	1 (4.0)	1 (4.2)
AEs leading to discontinuation	0	0	0
Most frequent AEs (≥ 2 patients)			
Headache	0	3 (12.0)	1 (4.2)
Dermatitis acneiform	0	2 (8.0)	5 (20.8)
Upper respiratory tract infection	1 (4.2)	2 (8.0)	3 (12.5)
Other AEs of interest			
Overall infections/infestations			
Influenza	0	1 (4.0)	0
COVID-19	0	1 (4.0)	1 (4.2)
Oral herpes	0	1 (4.0)	0
Herpes zoster	1 (4.2)	0	0
Skin-related AEs			
Rash	0	1 (4.0)	2 (8.3)
Folliculitis	0	2 (8.0)	2 (8.3)
Malignancy events	1 (4.2)	0	0
MACE or VTE	0	0	0
Opportunistic infections	0	0	0

AEs per CTCAE version 5.0 and MedDRA version 27.0. Includes events reported between the first treatment dose and 30 days after the last treatment dose.
[a]In the treated population. [b]Stress urinary incontinence. [c]Oral herpes and spontaneous abortion. [d]Pyrexia and pneumonia.
AE, adverse event; BID, twice daily; CTCAE, Common Terminology Criteria for Adverse Events; MACE, major adverse cardiac events; MedDRA, Medical Dictionary for Regulatory Activities; VTE, venous thromboembolism.

Figure 10. Laboratory parameters[a] over time



[a]In the treated population. [b]One patient in the placebo arm had grade 4 creatine kinase elevation. ULN and LLN values for AST are 37 U/L and 17 U/L, respectively; all other values from Strober B, et al.[30]
ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; LLN, lower limit of normal; SD, standard deviation; ULN, upper limit of normal.

Conclusions

- In the PAISLEY CLE study, the primary endpoint was met, with statistically significant improvements in percent change in CLASI-A score with deucravacitinib 3 mg BID and 6 mg BID vs placebo at week 16 in patients with DLE and/or SCLE, with or without SLE
- Other measures of CLASI-A were also improved with deucravacitinib, including CLASI-50 and CLASI-70 responses, achievement of CLASI-A score of ≤ 3 points, and improvement of CLASI-A score of at least 7 points
  - An early clinical response was seen, which continued over time
- Skin pain was generally improved with deucravacitinib vs placebo
- Deucravacitinib was well tolerated, and AEs were consistent with the known safety profile[15-17,29]
  - No opportunistic infections, MACE, VTE, AEs leading to treatment discontinuation, or deaths were observed
  - No clinically meaningful trends in laboratory parameters were observed
- These data support the further evaluation of deucravacitinib for the treatment of cutaneous manifestations of lupus, including in patients with SLE in the ongoing phase 3 POETYK SLE trials (NCT05617677, NCT05620407)

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Efficacy and safety of deucravacitinib in patients with active psoriatic arthritis who are naive to biologic disease-modifying antirheumatic drugs (bDMARDs) or previously received TNF-α inhibitor treatment: week 16 results from POETYK PsA-2, a multicenter, randomized, double-blind, placebo-controlled, phase 3 study

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Introduction

- Psoriatic arthritis (PsA) is a heterogeneous disease with multiple core symptom domains, including joint and skin manifestations[1,2]
  - Proinflammatory cytokine signaling contributes to PsA pathophysiology[1,2]
- Tyrosine kinase 2 (TYK2) is an important mediator of cytokine signaling (eg, interleukin [IL]-23, IL-12, type I interferon) involved in immune-specific responses[3]
- Deucravacitinib is a first-in-class, oral, selective TYK2 inhibitor with an established clinical profile in moderate to severe plaque psoriasis (PsO)
  - Peak efficacy was demonstrated at 24 weeks with a durable response through 5 years[4-6]
  - Deucravacitinib is approved in multiple countries worldwide for this indication[7,8]
- Deucravacitinib uniquely binds to the distinct TYK2 regulatory domain, locking the enzyme in an inactive state and inhibiting downstream cytokine signaling, whereas Janus kinase 1,2,3 inhibitors bind to the adenosine triphosphate binding site on the active domain[3,9]
- Positive efficacy and safety data were reported with deucravacitinib in a phase 2 PsA study[10]
- Deucravacitinib is currently under investigation in two phase 3 trials in PsA (POETYK PsA-1 [NCT04908202] and POETYK PsA-2 [NCT04908189]) as well as in systemic lupus erythematosus (NCT05617677; NCT05620407) and Sjögren's disease (NCT05946941)

Objective

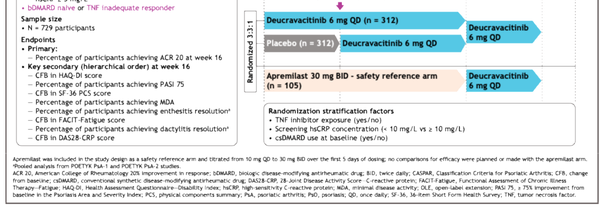
- To report the efficacy and safety of deucravacitinib through week 16 in patients with active PsA who participated in the POETYK PsA-2 trial

Methods

Study design

- In the POETYK PsA-2 trial, participants with active PsA (≥ 3 swollen joints; ≥ 3 tender joints; high-sensitivity C-reactive protein [hsCRP] ≥ 3 mg/L) were randomized 3:3:1 to oral placebo, deucravacitinib 6 mg once daily (QD), or apremilast 30 mg twice daily (BID) (**Figure 1**)
- Patients randomized to placebo crossed over to deucravacitinib at week 16
- Patients randomized to apremilast were included as a safety reference arm
- The primary endpoint was the proportion of patients who achieved an American College of Rheumatology 20% improvement in response (ACR 20) with deucravacitinib vs placebo at week 16

Figure 1. POETYK PsA-2 study design



Apremilast was included in the study design as a safety reference arm and titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing; no comparisons for efficacy were planned or made with the apremilast arm.
*Pooled analysis from POETYK PsA-1 and POETYK PsA-2 studies.
ACR 20, American College of Rheumatology 20% improvement in response; bDMARD, biologic disease-modifying antirheumatic drug; BID, twice daily; CASPAR, Classification Criteria for Psoriatic Arthritis; CFB, change from baseline; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28-CRP, 28-Joint Disease Activity Score–C-reactive protein; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy–Fatigue; HAQ-DI, Health Assessment Questionnaire–Disability Index; hsCRP, high-sensitivity C-reactive protein; MDA, minimal disease activity; OLE, open-label extension; PASI 75, ≥ 75% improvement from baseline in the Psoriasis Area and Severity Index; PCS, physical components summary; PsA, psoriatic arthritis; PsO, psoriasis; QD, once daily; SF-36, 36-Item Short Form Health Survey; TNF, tumor necrosis factor.

Outcomes

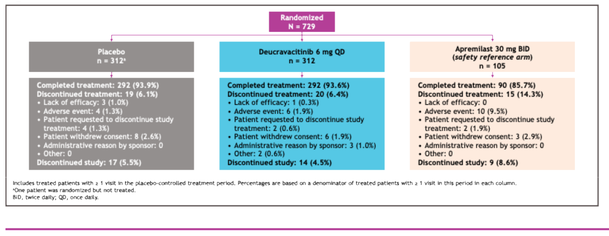
- The primary outcome at week 16 was an ACR 20, defined as:
  - ≥ 20% improvement from baseline in swollen (66 joints) and tender (68 joints) joint counts
  - ≥ 20% improvement in 3 of 5 other core measures, including Patient Global Assessment of Disease Activity, Patient Global Assessment of Pain, Health Assessment Questionnaire-Disability Index (HAQ-DI), Physician Global Assessment of PsA, and hsCRP level
- Other efficacy outcomes at week 16 included:
  - ACR 50/70
  - ACR 20/50/70 over time (through week 24)
  - ≥ 75% improvement from baseline in the Psoriasis Area and Severity Index (PASI 75)
  - Improvement on the HAQ-DI
  - Achievement of minimal disease activity (MDA)
  - Change from baseline in Disease Activity Score 28—CRP score (DAS28-CRP)
- Patient-reported outcomes at week 16 included:
  - Change from baseline in the 36-item Short Form Health Survey physical components summary (SF-36 PCS)
  - Change from baseline in the Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-Fatigue) score
- Extra-articular manifestations of PsA outcomes included:
  - Enthesitis: Leeds Enthesitis Index (LEI) and Spondyloarthritis Research Consortium of Canada (SPARCC) resolution
  - Dactylitis resolution
- Safety was evaluated throughout the trial

Results

Patients

- Patients (n = 729) were randomized to placebo (n = 312), deucravacitinib 6 mg QD (n = 312), or apremilast 30 mg BID (n = 105) (**Figure 2**)
  - Over 90% of patients receiving deucravacitinib and placebo completed treatment
  - A lower proportion of patients receiving deucravacitinib and placebo vs apremilast discontinued due to safety reasons during the placebo-controlled period

Figure 2. Patient disposition at week 16



Includes treated patients with ≥ 1 visit in the placebo-controlled treatment period. Percentages are based on a denominator of treated patients with ≥ 1 visit in this period in each column.
*One patient was randomized but not treated.
BID, twice daily; QD, once daily.

- Baseline patient demographics and disease characteristics were similar between the 3 treatment groups (**Table 1** and **Table 2**)
  - About two-thirds of patients were using conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) at baseline
  - Approximately 13% of patients with prior tumor necrosis factor inhibitor (TNFi) use were included

Table 1. Baseline patient demographics

Demographics	Placebo (n = 312)	Deucravacitinib 6 mg QD (n = 312)	Apremilast 30 mg BID (*safety reference arm*) (n = 105)
Age, median (range), years	50 (22-78)	49 (21-80)	48 (18-83)
Weight, median (range), kg	83.00 (47.0-171.0)	82.10 (44.5-172.4)	81.30 (45.1-151.6)
BMI, median (range), kg/m²	29.18 (17.7-51.6)	29.05 (15.2-65.2)	29.23 (18.7-59.6)
Female, n (%)	168 (53.8)	153 (49.0)	56 (53.3)
Race, n (%)			
American Indian or Alaska Native	7 (2.2)	13 (4.2)	4 (3.8)
Asian	45 (14.4)	54 (17.3)	28 (26.7)
Native Hawaiian or other Pacific Islander	1 (0.3)	0	0
White	240 (76.9)	223 (71.5)	65 (61.9)
Other	19 (6.1)	22 (7.1)	8 (7.6)
Ethnicity, n (%)			
Hispanic or Latino	50 (16.0)	54 (17.3)	16 (15.2)
Not Hispanic or Latino	200 (64.1)	195 (62.5)	64 (61.0)
Not reported	62 (19.9)	63 (20.2)	25 (23.8)
Geographic region, n (%)			
Asia	42 (13.5)	48 (15.4)	27 (25.7)
Europe	171 (54.8)	163 (52.2)	51 (48.6)
North America	58 (18.6)	47 (15.1)	12 (11.4)
South America/Latin America	32 (10.3)	43 (13.8)	11 (10.5)
Rest of world	9 (2.9)	11 (3.5)	4 (3.8)

BID, twice daily; BMI, body mass index; QD, once daily.

Table 2. Baseline disease characteristics

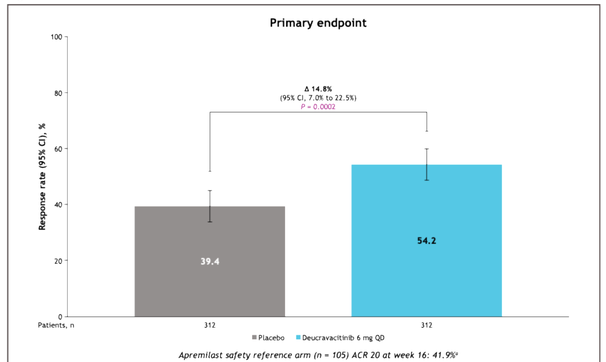
Disease characteristics	Placebo (n = 312)	Deucravacitinib 6 mg QD (n = 312)	Apremilast 30 mg BID (*safety reference arm*) (n = 105)
Prior TNFi use, n (%)	45 (14.4)	39 (12.5)	14 (13.3)
Baseline csDMARD use, n (%)	196 (62.8)	194 (62.2)	68 (64.8)
Duration of disease, mean (SD), years	5.90 (6.94)	5.03 (5.99)	4.70 (6.45)
hsCRP, mean (SD), mg/L	12.20 (15.53)	11.71 (17.88)	10.33 (13.93)
DAS28-CRP, mean (SD)	4.90 (0.91)	4.71 (0.96)	4.82 (1.00)
Swollen joint count (66), mean (SD)	9.6 (7.53)	9.2 (6.53)	10.6 (7.10)
Tender joint count (68), mean (SD)	16.6 (11.53)	15.2 (10.91)	16.8 (11.92)
HAQ-DI score, mean (SD)	1.18 (0.64)	1.10 (0.63)	1.18 (0.59)
BSA involvement > 3%, n (%)	157 (50.3)	164 (52.6)	46 (43.8)
PASI > 1, n (%)	244 (78.2)	260 (83.3)	75 (71.4)
PASI, mean (SD)[a,b]	8.48 (6.85)	9.13 (7.14)	8.82 (7.78)
Tender entheseal points ≥ 1, n (%)	150 (48.1)	140 (44.9)	49 (46.7)
Enthesitis, LEI, mean (SD)[c,d]	2.3 (1.4)	2.1 (1.3)	2.4 (1.4)
Enthesitis, SPARCC, mean (SD)[e,f]	4.0 (3.0)	3.7 (3.0)	4.1 (3.5)
Tender dactylitis count ≥ 1, n (%)	80 (25.6)	78 (25.0)	33 (31.4)
Dactylitis, LDI, mean (SD)[d,h]	76.36 (233.65)	45.06 (83.44)	82.55 (125.34)
FACIT-Fatigue score, mean (SD)	33.0 (11.88)	33.6 (10.70)	32.9 (11.13)
SF-36 PCS score, mean (SD)	35.86 (9.24)	36.34 (8.42)	35.89 (8.20)

[a]n 346 evaluable patients. [b]Subset of patients with ≥ 3% BSA involvement and an sPGA score ≥ 2 at baseline. [c]n 339 evaluable patients. [d]Baseline enthesitis (LEI) was calculated for patients with enthesitis present at baseline by LEI. [e]n 45 evaluable patients. [f]Baseline enthesitis (SPARCC) was calculated for patients with enthesitis present at baseline by SPARCC. [g]n 148 evaluable patients. [h]Baseline dactylitis index (LDI) was calculated for patients with dactylitis present at baseline.
BID, twice daily; BSA, body surface area; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28-CRP, Disease Activity Score 28–C-reactive protein; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy–Fatigue; HAQ-DI, Health Assessment Questionnaire–Disability Index; hsCRP, high-sensitivity C-reactive protein; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; PASI, Psoriasis Area and Severity Index; PCS, physical components summary; QD, once daily; SD, standard deviation; SF-36, 36-Item Short Form Health Survey; SPARCC, Spondyloarthritis Research Consortium of Canada; sPGA, static Physician Global Assessment; TNFi, tumor necrosis factor inhibitor.

Efficacy

- The primary endpoint of ACR 20 at week 16 was met (**Figure 3**)
- A significantly higher proportion of patients treated with deucravacitinib (54.2%) vs placebo (39.4%) achieved ACR 20 ($P = 0.0002$)

Figure 3. ACR 20 at week 16

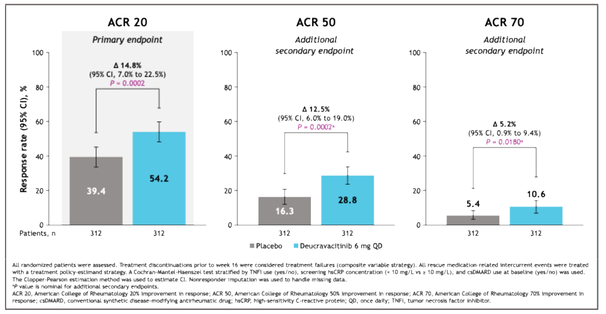


Apremilast safety reference arm (n = 105) ACR 20 at week 16: 41.9%‡

An ACR 20 response was defined as a ≥ 20% improvement from baseline in swollen (66 joints) and tender (68 joints) joint counts as well as a ≥ 20% improvement in 3 of 5 other core measures, including Patient Global Assessment of Disease Activity, Patient Global Assessment of Pain, HAQ-DI, Physician Global Assessment of PsA, and hsCRP level. All randomized patients were assessed. Treatment discontinuations prior to week 16 were considered treatment failures (composite variable strategy). All rescue medication related intercurrent events were treated with a treatment policy-estimand strategy. A Cochran-Mantel-Haenszel test stratified by TNFi use (yes/no), screening hsCRP concentration (< 10 mg/L vs ≥ 10 mg/L), and csDMARD use at baseline (yes/no) was used. The Clopper-Pearson estimation method was used to estimate CI. Nonresponder imputation was used to handle missing data.
‡No formal comparative statistical analyses for efficacy were planned for the apremilast safety reference arm.
ACR 20, American College of Rheumatology 20% improvement in response; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire–Disability Index; hsCRP, high-sensitivity C-reactive protein; PsA, psoriatic arthritis; QD, once daily; TNFi, tumor necrosis factor inhibitor.

- ACR 50 and ACR 70 response rates were also higher with deucravacitinib vs placebo (**Figure 4**)

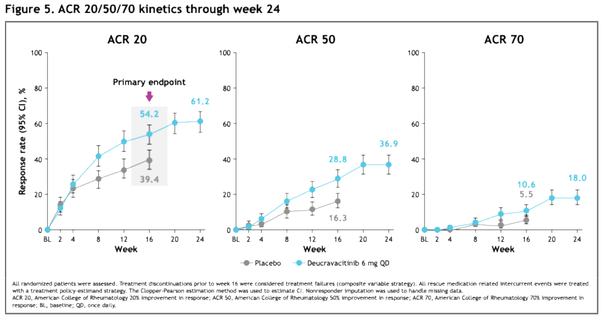
Figure 4. ACR 20/50/70 at week 16



All randomized patients were assessed. Treatment discontinuations prior to week 16 were considered treatment failures (composite variable strategy). All rescue medication-related intercurrent events were treated with a treatment policy-estimand strategy. A Cochran-Mantel-Haenszel test stratified by TNFi use (yes/no), screening hsCRP concentration (< 10 mg/L vs ≥ 10 mg/L), and csDMARD use at baseline (yes/no) was used. The Clopper-Pearson estimation method was used to estimate CI. Nonresponder imputation was used to handle missing data.
*P value is nominal for additional secondary endpoints.
ACR 20, American College of Rheumatology 20% improvement in response; ACR 50, American College of Rheumatology 50% improvement in response; ACR 70, American College of Rheumatology 70% improvement in response; csDMARD, conventional synthetic disease-modifying antirheumatic drug; hsCRP, high-sensitivity C-reactive protein; QD, once daily; TNFi, tumor necrosis factor inhibitor.

- The proportion of patients with ACR responses continued to increase up to week 24, similar to the time course observed for the primary endpoints evaluated in the POETYK PsO clinical studies[4,5] (**Figure 5**)

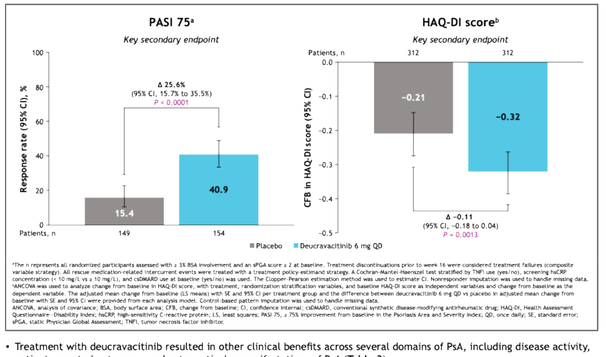
Figure 5. ACR 20/50/70 kinetics through week 24



All randomized patients were assessed. Treatment discontinuations prior to week 16 were considered treatment failures (composite variable strategy). All rescue medication related intercurrent events were treated with a treatment policy-estimand strategy. The Clopper-Pearson estimation method was used to estimate CI. Nonresponder imputation was used to handle missing data.
ACR 20, American College of Rheumatology 20% improvement in response; ACR 50, American College of Rheumatology 50% improvement in response; ACR 70, American College of Rheumatology 70% improvement in response; BL, baseline; QD, once daily.

- Significantly more patients receiving deucravacitinib vs placebo achieved PASI 75 (40.9% vs 15.4%, respectively; $P < 0.0001$) (**Figure 6**)
- Statistically significant improvement was also achieved with deucravacitinib vs placebo for patient-reported functional ability (HAQ-DI)

Figure 6. PASI 75 and HAQ-DI at week 16



*The n represents all randomized participants assessed with ≥ 3% BSA involvement and an sPGA score ≥ 2 at baseline. Treatment discontinuations prior to week 16 were considered treatment failures (composite variable strategy). All rescue medication-related intercurrent events were treated with a treatment policy-estimand strategy. A Cochran-Mantel-Haenszel test stratified by TNFi use (yes/no), screening hsCRP concentration (< 10 mg/L vs ≥ 10 mg/L), and csDMARD use at baseline (yes/no) was used. The Clopper-Pearson estimation method was used to estimate CI. Nonresponder imputation was used to handle missing data. †ANCOVA was used to analyze change from baseline in HAQ-DI score, with treatment, randomization stratification variables, and baseline HAQ-DI score as independent variables and change from baseline as the dependent variable. The adjusted mean change from baseline (LS means) with SE and 95% CI per treatment group and the difference between deucravacitinib 6 mg QD vs placebo in adjusted mean change from baseline with SE and 95% CI were provided from each analysis model. Control-based pattern imputation was used to handle missing data.
ANCOVA, analysis of covariance; BSA, body surface area; CFB, change from baseline; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire–Disability Index; hsCRP, high-sensitivity C-reactive protein; LS, least squares; PASI 75, ≥ 75% improvement from baseline in the Psoriasis Area and Severity Index; QD, once daily; SE, standard error; sPGA, static Physician Global Assessment; TNFi, tumor necrosis factor inhibitor.

- Treatment with deucravacitinib resulted in other clinical benefits across several domains of PsA, including disease activity, patient-reported outcomes, and extra-articular manifestations of PsA (**Table 3**)

Table 3. Other efficacy endpoints at week 16

Endpoint at week 16		Placebo	Deucravacitinib 6 mg QD	*P* value Δ (95% CI)
Composite clinical efficacy	**MDA, %**	14.7	25.6	0.0007 10.9 (4.6 to 17.1)
	CFB DAS28-CRP score, mean (SE)	−0.80 (0.08)	−1.28 (0.08)	< 0.0001* −0.48 (−0.65 to −0.31)
Patient-reported outcomes	**CFB SF-36 PCS score, mean (SE)**	3.80 (0.50)	5.84 (0.49)	0.0002 2.04 (0.98 to 3.11)
	CFB FACIT-Fatigue score, mean (SE)	1.8 (0.56)	2.5 (0.56)	0.2017 0.8 (−0.4 to 2.0)
Extra-articular manifestations of PsA (pooled analyses)	**Enthesitis (LEI) resolution,† %**	45.1	50.3	0.1781 5.3 (−2.4 to 12.9)
	Enthesitis (SPARCC) resolution,‡ %	36.1	47.1	0.0018* 10.8 (4.1 to 17.6)
	Dactylitis resolution,§ %	44.1	57.6	0.0100* 12.8 (3.2 to 22.4)

Response rate is the proportion of responders to total number of participants in the randomized population and in the participant subset for the endpoint, where applicable. A Cochran-Mantel-Haenszel test stratified by TNFi use (yes/no), screening hsCRP concentration (< 10 mg/L vs ≥ 10 mg/L), and csDMARD use at baseline (yes/no) was used to compare the response rates with deucravacitinib 6 mg QD vs placebo. CFB was analyzed using ANCOVA with treatment, randomization stratification variables, and baseline value as independent variables.
*P value is nominal. †Pooled analysis from POETYK PsA-1 and POETYK PsA-2 in patients with enthesitis by LEI at baseline; patients with enthesitis by SPARCC criteria at baseline; or patients with a tender dactylitis count ≥ 1 at baseline.
ANCOVA, analysis of covariance; CFB, change from baseline; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAS28-CRP, 28-Joint Disease Activity Score–C-reactive protein; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy–Fatigue Scale; hsCRP, high-sensitivity C-reactive protein; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; PCS, physical components summary; PsA, psoriatic arthritis; QD, once daily; SF-36, 36-Item Short Form Health Survey; SPARCC, Spondyloarthritis Research Consortium of Canada; TNFi, tumor necrosis factor inhibitor.

Safety

- The frequency of serious adverse events (AEs) and discontinuations due to AEs was lower with deucravacitinib vs apremilast (**Table 4**)
- No deaths were reported
- The most frequent AEs that occurred with deucravacitinib vs placebo were related to infections and events affecting the skin
- The most frequent AEs that occurred with apremilast were gastrointestinal related

Table 4. Safety summary: weeks 0-16

Patients with an AE, n (%)	Placebo (n = 311)	Deucravacitinib 6 mg QD (n = 312)	Apremilast 30 mg BID (*safety reference arm*) (n = 105)
Any AEs	170 (54.7)	196 (62.8)	77 (73.3)
Serious AEs	3 (1.0)	6 (1.9)	4 (3.8)
AEs leading to discontinuation	4 (1.3)	7 (2.2)	11 (10.5)
Deaths	0	0	0
Most frequent AEs (≥ 5%) in any arm by PT			
COVID-19	17 (5.5)	22 (7.1)	7 (6.7)
Upper respiratory tract infection	13 (4.2)	19 (6.1)	4 (3.8)
Nasopharyngitis	21 (6.8)	14 (4.5)	4 (3.8)
Headache	11 (3.5)	13 (4.2)	8 (7.6)
Nausea	6 (1.9)	7 (2.2)	7 (6.7)
Diarrhea	15 (4.8)	11 (3.5)	11 (10.5)
Hypertension	8 (2.6)	8 (2.6)	7 (6.7)

Analyzed in the treated population. AEs are defined as treatment-emergent AEs with an onset date on or after the first dose date of study treatment up to 30 days after the last dose date of treatment in the study. MedDRA v27.1 was used to define PTs.
AE, adverse event; BID, twice daily; MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term; QD, once daily.

- The most commonly observed AEs of special interest were infections and skin-related events, consistent with the known safety profile of deucravacitinib (**Table 5**)
- No major adverse cardiovascular events, venous thromboembolism/arterial thromboembolism events, malignancies, or opportunistic infections occurred in the deucravacitinib arm

Table 5. AEs of special interest to deucravacitinib occurring in ≥ 2 patients: weeks 0-16

Patients with an AE of special interest by PT, n (%)	Placebo (n = 311)	Deucravacitinib 6 mg QD (n = 312)	Apremilast 30 mg BID (*safety reference arm*) (n = 105)
Total patients with an event	37 (11.9)	70 (22.4)	17 (16.2)
COVID-19	17 (5.5)	22 (7.1)	7 (6.7)
Suspected COVID-19	2 (0.6)	1 (0.3)	0
Influenza	1 (0.3)	5 (1.6)	1 (1.0)
Oral herpes	0	2 (0.6)	2 (1.9)
Herpes simplex	2 (0.6)	1 (0.3)	0
Herpes zoster	2 (0.6)	1 (0.3)	0
Rash	3 (1.0)	12 (3.8)	1 (1.0)
Acne	0	10 (3.2)	1 (1.0)
Eczema	2 (0.6)	4 (1.3)	1 (1.0)
Folliculitis	0	4 (1.3)	0
Urticaria	1 (0.3)	4 (1.3)	0
Dermatitis	0	2 (0.6)	0
Dermatitis acneiform	2 (0.6)	2 (0.6)	0
Pruritus	4 (1.3)	2 (0.6)	1 (1.0)
Pustule	0	2 (0.6)	0

Analyzed in the treated population. AEs are defined as treatment-emergent AEs with an onset date on or after the first dose date of study treatment up to 30 days after the last dose date of treatment in the study. The following AEs were considered AEs of special interest: skin-related AEs, select infections (influenza, opportunistic infections, herpes infections, tuberculosis, and COVID-19), malignancies, and cardiovascular events. MedDRA v27.1 was used to define PTs.
AE, adverse event; BID, twice daily; MedDRA, Medical Dictionary for Regulatory Activities; PT, preferred term; QD, once daily.

Conclusions

- In the POETYK PsA-2 study, deucravacitinib met the primary endpoint of ACR 20 at week 16 and showed superior clinical benefit vs placebo across multiple core PsA domains, including joint and skin manifestations, in patients with active PsA
- Deucravacitinib was well tolerated through 16 weeks when compared with placebo and apremilast
  - The safety profile of deucravacitinib in this study was consistent with that established in the phase 2 PsA study and the phase 3 PsO clinical program, with no new safety signals[4-6,10]
- These results support the potential of deucravacitinib, the first oral TYK2 inhibitor evaluated in a phase 3 study of PsA, to become an efficacious and well-tolerated treatment for patients with active PsA

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Deucravacitinib in moderate to severe plaque psoriasis: 5-year, long-term safety and efficacy results from 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 1,2,3 inhibitors bind,[1,7] driving its selectivity for TYK2 and representing the first in a new class of oral drugs
- The global, 52-week, phase 3 POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) trials demonstrated that deucravacitinib 6 mg once daily (QD) 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 previously reported to be well maintained through 4 years, with no new safety signals compared with Year 3, in deucravacitinib-treated patients in the ongoing POETYK LTE trial[10,11]

Objective

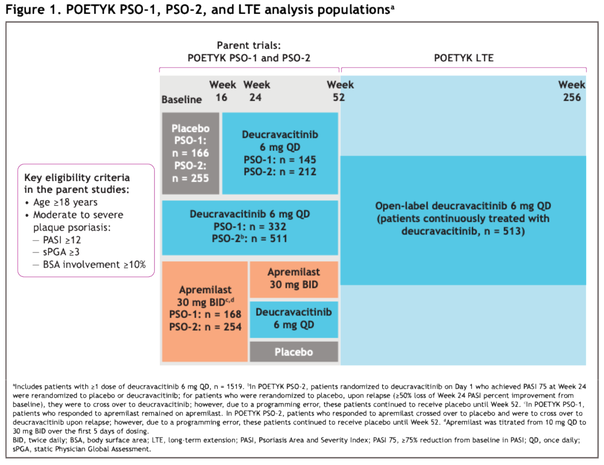
- To report the safety and efficacy of deucravacitinib treatment through 5 years (Week 256; data cutoff, September 2, 2024) in patients with moderate to severe plaque psoriasis who participated in the POETYK PSO-1, PSO-2, and LTE trials

Methods

Study designs

- In the POETYK PSO-1 and PSO-2 trials, adults with moderate to severe plaque psoriasis (Psoriasis Area and Severity Index [PASI] ≥12, static Physician Global Assessment [sPGA] ≥3, and body surface area [BSA] involvement ≥10% at baseline) were randomized 1:2:1 to oral placebo, deucravacitinib 6 mg QD, or apremilast 30 mg twice daily (BID) (**Figure 1**)
- At Week 52, eligible patients were allowed to enroll in the POETYK LTE trial and receive open-label deucravacitinib 6 mg QD

Figure 1. POETYK PSO-1, PSO-2, and LTE analysis populations[a]



[a]Includes patients with ≥1 dose of deucravacitinib 6 mg QD, n = 1519. [b]In POETYK PSO-2, patients randomized to deucravacitinib on Day 1 who achieved PASI 75 at Week 24 were rerandomized to placebo or deucravacitinib; for patients who were rerandomized to placebo, upon relapse (≥50% loss of Week 24 PASI percent improvement from baseline), they were to cross over to deucravacitinib; however, due to a programming error, these patients continued to receive placebo until Week 52. [c]In POETYK PSO-1, patients who responded to apremilast remained on apremilast. In POETYK PSO-2, patients who responded to apremilast crossed over to placebo and were to cross over to deucravacitinib upon relapse; however, due to a programming error, these patients continued to receive placebo until Week 52. [d]Apremilast was titrated from 10 mg QD to 30 mg BID over the first 5 days of dosing.
BID, twice daily; BSA, body surface area; LTE, long-term extension; PASI, Psoriasis Area and Severity Index; PASI 75, ≥75% reduction from baseline in PASI; QD, once daily; sPGA, static Physician Global Assessment.

Analysis populations

- **Safety population:** patients receiving ≥1 dose of deucravacitinib at any time in the pooled parent (POETYK PSO-1 and PSO-2) and POETYK LTE trials over 5 years in the as-treated population
- **Efficacy population:** patients from the pooled parent trials (POETYK PSO-1 and PSO-2) who received continuous deucravacitinib treatment from Day 1 of the parent trials through 5 years (Week 256)

Outcomes

- Safety outcomes:
  - Adverse events (AEs), serious AEs, deaths, and AEs leading to treatment discontinuation through the last data cutoff (September 2, 2024)
- Efficacy outcomes:
  - Achievement of ≥75%/≥90% reduction from baseline in PASI (PASI 75/90)
  - An sPGA score of 0 (clear) or 1 (almost clear) (sPGA 0/1)
  - A scalp-specific PGA score of 0 (clear) or 1 (almost clear) (ss-PGA 0/1) in patients with a baseline ss-PGA ≥3
  - A PGA-Fingernail score of 0 (clear) or 1 (almost clear) (PGA-F 0/1) in patients with a baseline PGA-F ≥3

Statistical analysis

- Safety and efficacy were analyzed through the data cutoff (September 2, 2024; Week 256, 5 years)
- AEs were ascribed to the assigned treatment at the time of the event
  - When a patient had multiple events of the same type, the patient was counted only once
- Safety data were reported as exposure-adjusted incidence rate (EAIR)/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])
- In addition to observed values, two additional methods of imputation for missing data were used as sensitivity analyses for efficacy
  - **Treatment failure rules (TFR)[12]:** patients who discontinued treatment due to lack of efficacy or worsening of psoriasis were imputed as nonresponders; all other missing data were not imputed
  - **Modified nonresponder imputation (mNRI)[13]:** patients who either discontinued prior to Week 256 or reached Week 256 were included; patients with missing data who discontinued treatment due to worsening of psoriasis were imputed as nonresponders; all other missing data were imputed by multiple imputation

Results

Patients

- Baseline patient demographics and clinical characteristics for the safety and efficacy populations are presented in **Table 1**

Table 1. Baseline patient demographics and clinical characteristics

Parameter	Patients who received ≥1 dose of deucravacitinib (safety population, n = 1519)	Patients who received continuous deucravacitinib (efficacy population, n = 513)
Age, mean (SD), y	46.6 (13.4)	46.9 (13.3)
Weight, mean (SD), kg	90.6 (21.6)	89.9 (22.2)
Body mass index, mean (SD), kg/m²	30.5 (6.8)	30.3 (7.0)
Female, n (%)	493 (32.5)	159 (31.0)
Race, n (%)		
White	1325 (87.2)	440 (85.8)
Asian	153 (10.1)	64 (12.5)
Black or African American	23 (1.5)	5 (1.0)
Other	18 (1.2)	4 (0.8)
Disease duration, mean (SD), y	18.7 (12.7)	18.8 (12.6)
PASI, mean (SD)	21.1 (8.1)	21.1 (7.9)
sPGA score, n (%)		
3 (moderate)	1211 (79.7)	401 (78.2)
4 (severe)	308 (20.3)	112 (21.8)
BSA involvement, mean (SD), %	26.2 (15.8)	26.9 (15.8)
PSSD total score, mean (SD)	-	52.9 (23.5)
DLQI, mean (SD)	-	11.8 (6.6)

BSA, body surface area; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PSSD, Psoriasis Symptoms and Signs Diary; SD, standard deviation; sPGA, static Physician Global Assessment.

Overall safety

- A cumulative safety summary is presented in **Table 2**
- Incidence rates of AEs (EAIR = n/100 PY) decreased from 1 year to 5 years
  - The most common AEs continued to be nasopharyngitis and upper respiratory tract infections
  - The data cutoffs for Year 1 of the POETYK PSO-1 and PSO-2 trials were October 15, 2020, and December 22, 2020, respectively; the peak of the global COVID-19 pandemic occurred during the first 2 years of the POETYK LTE trial, contributing to the higher COVID-19 rate seen through Year 5 compared with Year 1
  - COVID-19 rates with deucravacitinib treatment did not reflect an increased risk when compared with contemporaneous reference populations[14]

Table 2. Cumulative safety summary through 1 year and 5 years (as-treated population)

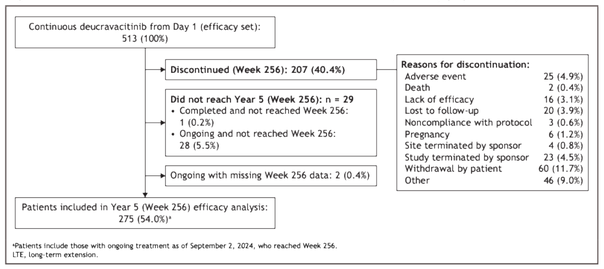
	Cumulative through 1 year[a] (POETYK PSO-1 + PSO-2)		Cumulative through 5 years[b] (POETYK PSO-1 + PSO-2 + LTE)	
	Deucravacitinib (n = 1364) Total PY = 969.0		Deucravacitinib (n = 1519) Total PY = 5046.7	
AE category	**1-Year cumulative n (%)**	**EAIR/100 PY (95% CI)**	**5-Year cumulative n (%)**	**EAIR/100 PY (95% CI)**
AEs	995 (72.9)	229.2 (215.4-243.9)	1315 (86.6)	127.4 (120.6-134.5)
Serious AEs	55 (4.0)	5.7 (4.4-7.4)	235 (15.5)	5.1 (4.4-5.8)
Discontinued treatment due to AEs	43 (3.2)	4.4 (3.3-5.9)	106 (7.0)	2.1 (1.7-2.5)
Deaths	2 (0.1)[c]	0.2 (0.1-0.8)	11 (0.7)[d]	0.2 (0.1-0.4)
Most common AEs (EAIR ≥5/100 PY)				
Nasopharyngitis	229 (16.8)	26.1 (23.0-29.8)	363 (23.9)	9.1 (8.2-10.1)
Upper respiratory tract infection	124 (9.1)	13.4 (11.3-16.0)	258 (17.0)	5.8 (5.1-6.6)
Headache	80 (5.9)	8.5 (6.8-10.5)	124 (8.2)	2.6 (2.2-3.1)
Diarrhea	69 (5.1)	7.3 (5.7-9.2)	102 (6.7)	2.1 (1.7-2.6)
Arthralgia	55 (4.0)	5.7 (4.4-7.4)	126 (8.3)	2.7 (2.2-3.2)
COVID-19[e]	5 (0.4)	0.5 (0.2-1.2)	352 (23.2)	8.2 (7.4-9.1)

Not all patients were receiving deucravacitinib 6 mg QD continuously throughout this period. Total PY corresponds to the total exposure time to deucravacitinib during the indicated time period. [a]This represents the pooled patient population of POETYK PSO-1 and PSO-2 (Weeks 0-52). [b]This represents the pooled POETYK PSO-1, PSO-2, and LTE population through the data cutoff (September 2, 2024). [c]In POETYK PSO-1 and PSO-2 through 1 year, 1 patient discontinued deucravacitinib after 4 days of treatment due to prohibited medication (leflunomide) and died 9 days later reportedly due to heart failure and sepsis, with no medical records available. Another death occurred between Weeks 16 and 52 and was due to hepatocellular carcinoma in a patient with a history of hepatitis C virus infection and liver cirrhosis. Both deaths were considered unrelated to treatment by the investigator. [d]After Week 52, 7 deaths were due to COVID-19 (all in patients with risk factors for severe disease; 2 deaths were considered related to treatment and the other 5 deaths were considered unrelated to treatment by the investigator). One patient with cardiovascular risk factors died due to a ruptured aortic aneurysm, which was considered not related to treatment by the investigator. One patient with a history of type 2 diabetes mellitus with neuropathy, hypertension, and hypercholesterolemia died due to sudden death of unknown cause, which was not considered related to treatment by the investigator. [e]POETYK PSO-1, PSO-2, and LTE trials were conducted during the COVID-19 pandemic.
AE, adverse event; CI, confidence interval; EAIR, exposure-adjusted incidence rate; LTE, long-term extension; PY, person-years; QD, once daily.

Patient population: efficacy

- Of the 513 patients in the efficacy population who received deucravacitinib from Day 1 and entered the POETYK LTE trial, 207 (40.4%) discontinued before Week 256 (**Figure 2**):
  - 16 (3.1%) due to lack of efficacy and 25 (4.9%) due to AEs
  - Common reasons for discontinuation were: withdrawal by patient (60 [11.7%]); "other" miscellaneous causes as described by patients (46 [9.0%]); and site/study terminated by the sponsor (27 [5.3%])
- As of the data cutoff date, 28 (5.5%) patients were receiving deucravacitinib in the POETYK LTE trial but had not yet reached Week 256 (**Figure 2**)

Figure 2. End of treatment summary in the POETYK LTE trial (efficacy population)

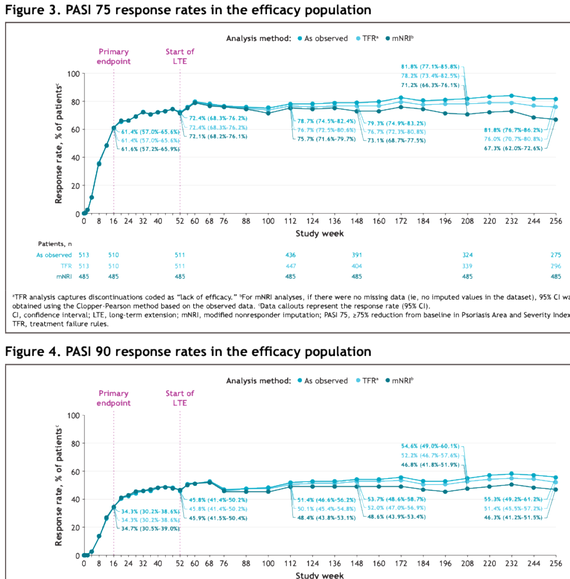


[a]Patients include those with ongoing treatment as of September 2, 2024, who reached Week 256.
LTE, long-term extension.

Efficacy

- PASI 75 (**Figure 3**), PASI 90 (**Figure 4**), and sPGA 0/1 (**Figure 5**) response rates were maintained from Week 52 (beginning of the POETYK LTE trial) through 5 years

Figure 3. PASI 75 response rates in the efficacy population

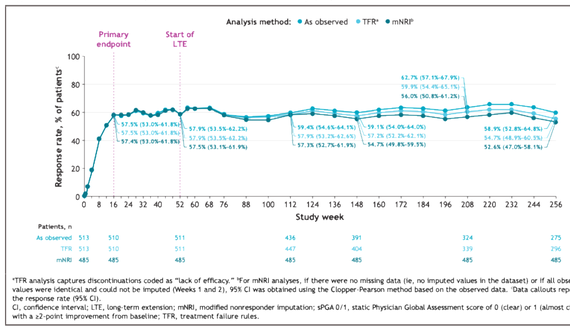


[a]TFR analysis captures discontinuations coded as "lack of efficacy." [b]For mNRI analyses, if there were no missing data (ie, no imputed values in the dataset), 95% CI was obtained using the Clopper-Pearson method based on the observed data. [c]Data callouts represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 75, ≥75% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

Figure 4. PASI 90 response rates in the efficacy population

[a]TFR analysis captures discontinuations coded as "lack of efficacy." [b]For mNRI analyses, if there were no missing data (ie, no imputed values in the dataset) or if all observed values were identical and could not be imputed (Weeks 1 and 2), 95% CI was obtained using the Clopper-Pearson method based on the observed data. [c]Data callouts represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PASI 90, ≥90% reduction from baseline in Psoriasis Area and Severity Index; TFR, treatment failure rules.

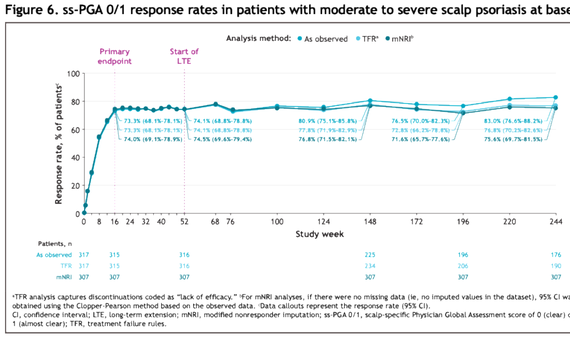
Figure 5. sPGA 0/1 response rates in the efficacy population



[a]TFR analysis captures discontinuations coded as "lack of efficacy." [b]For mNRI analyses, if there were no missing data (ie, no imputed values in the dataset) or if all observed values were identical and could not be imputed (Weeks 1 and 2), 95% CI was obtained using the Clopper-Pearson method based on the observed data. [c]Data callouts represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; sPGA 0/1, static Physician Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline; TFR, treatment failure rules.

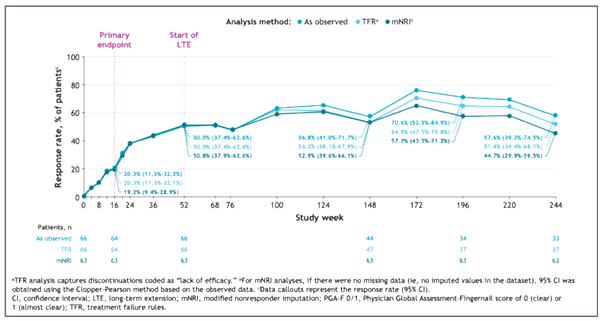
- In patients with moderate to severe psoriasis in hard-to-treat areas (scalp and fingernail) at baseline, improvements in scalp psoriasis, assessed by achievement of ss-PGA 0/1 (**Figure 6**), and in fingernail psoriasis, assessed by achievement of PGA-F 0/1 (**Figure 7**), were maintained from Week 52 through 5 years

Figure 6. ss-PGA 0/1 response rates in patients with moderate to severe scalp psoriasis at baseline



[a]TFR analysis captures discontinuations coded as "lack of efficacy." [b]For mNRI analyses, if there were no missing data (ie, no imputed values in the dataset), 95% CI was obtained using the Clopper-Pearson method based on the observed data. Data callouts represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; ss-PGA 0/1, scalp-specific Physician Global Assessment score of 0 (clear) or 1 (almost clear); TFR, treatment failure rules.

Figure 7. PGA-F 0/1 response rates in patients with moderate to severe fingernail psoriasis at baseline



[a]TFR analysis captures discontinuations coded as "lack of efficacy." [b]For mNRI analyses, if there were no missing data (ie, no imputed values in the dataset), 95% CI was obtained using the Clopper-Pearson method based on the observed data. [c]Data callouts represent the response rate (95% CI).
CI, confidence interval; LTE, long-term extension; mNRI, modified nonresponder imputation; PGA-F 0/1, Physician Global Assessment-Fingernail score of 0 (clear) or 1 (almost clear); TFR, treatment failure rules.

Conclusions

- Deucravacitinib demonstrated a consistent safety profile through 5 years with >5000 PY of exposure and no increases in AE or serious AE rates over time or emergence of any new safety signals
- PASI 75, PASI 90, and sPGA 0/1 response rates were maintained through 5 years in over 500 patients treated continuously with deucravacitinib from Day 1 in the parent trials
  - Efficacy results were consistent regardless of imputation method, indicating the robustness of the results
- Deucravacitinib improved psoriasis disease burden in the hard-to-treat areas of scalp and fingernail psoriasis in patients with moderate to severe psoriasis in these areas at baseline; improvement was maintained through 5 years of treatment
- These data support the long-term safety and durable efficacy profile through 5 years of treatment with deucravacitinib, the first-in-class, allosteric TYK2 inhibitor treatment for psoriasis

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Presented at the Elevate-Derm Summer Conference; July 23-27, 2025; Park City, UT
This is an encore of the 2025 Diversity in Dermatology Conference poster

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Early and Sustained Effects of Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel

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SYNOPSIS

- Treatments that lead to fast and substantial acne clearance with minimal tolerability issues are highly desirable and can increase patient adherence[1]
- A three-pronged approach using a topical antibiotic, topical retinoid, and benzoyl peroxide (BPO) has been shown to be one of the most effective treatments for acne, with greater efficacy compared with monotherapy or dual-combination products[2]; however, it is unknown if triple-combination provides more rapid improvement
- Clindamycin phosphate 1.2%/adapalene 0.15%/BPO 3.1% (CAB) gel (Cabtreo®, Ortho Dermatologics) is the only fixed-dose, triple-combination topical approved for acne
- CAB gel has demonstrated efficacy and favorable tolerability in phase 2 and phase 3 clinical trials[3-6]

OBJECTIVE

- To evaluate the efficacy and safety of CAB gel following 4 and 12 weeks of treatment vs vehicle gel

METHODS

- Data were pooled from 4 double-blind, 12-week trials of participants with moderate to severe acne (phase 2, NCT03170388 and NCT04892706; phase 3, NCT04214639 and NCT04214652)
  - Participants were aged ≥9 years (≥12 years in NCT04892706)
  - CeraVe® hydrating cleanser and CeraVe® moisturizing lotion (L'Oréal, NY) were provided as needed for optimal skin moisturization/cleaning
- Pooled, post hoc analyses of all 4 studies were conducted in participants randomized to receive CAB or vehicle gel once daily
- Endpoints included least-squares (LS) mean percent change from baseline in inflammatory and noninflammatory lesion counts and treatment success, defined as the percentage of participants achieving ≥2-grade reduction from baseline in the Evaluator's Global Severity Score (EGSS) and a score of 0 (clear) or 1 (almost clear)
- Treatment-emergent adverse events (TEAEs) and cutaneous safety/tolerability were also assessed

RESULTS

Participants

- A total of 1115 participants were included in this analysis (CAB, n=618; vehicle, n=497)
- The mean age in both groups was 20 years; most participants were female (CAB, 61%; vehicle, 58%) and White (CAB, 72%; vehicle, 71%)
- At baseline, most participants had moderate acne (EGSS=3; 88% and 90%)

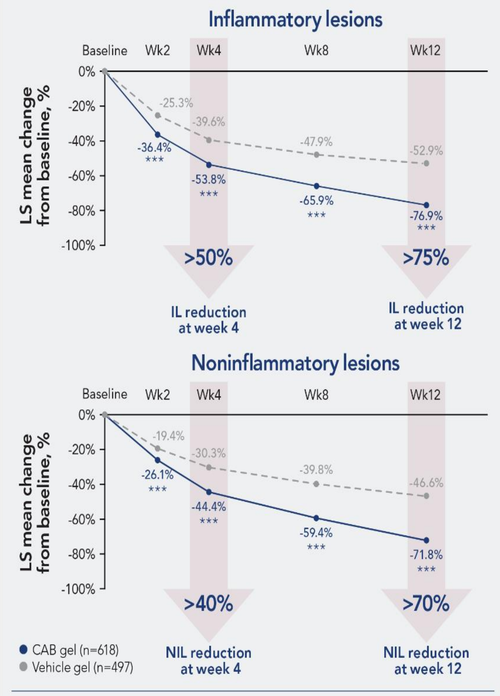
Efficacy

- At week 4, inflammatory lesions were reduced by >50% in CAB-treated participants, with continued improvements to >75% reduction at week 12, which was significantly greater than vehicle (*P*<0.001, both; **Figure 1**)
  - Significance vs vehicle was seen as early as week 2
  - Similar trends were observed for noninflammatory lesions (*P*<0.001, all)
- At week 12, over half (51.0%) of CAB-treated participants achieved treatment success vs 18.3% of vehicle-treated participants (*P*<0.001); significant differences with CAB vs vehicle were seen at week 4 (**Figure 2**)
- Representative images depicting acne improvement in CAB-treated participants are shown in **Figure 3**

Safety and Tolerability

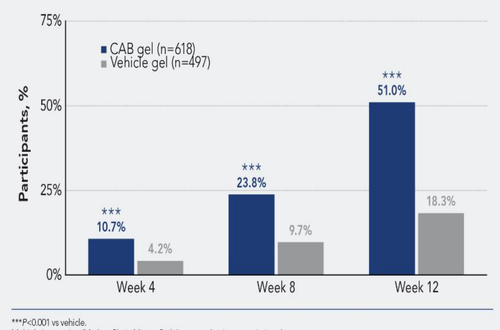
- TEAEs were reported in 33% and 14% of participants treated with CAB and vehicle, respectively (19% and 2% deemed related to treatment); most were deemed mild/moderate
  - Discontinuations due to TEAEs were in 2.8% and 0.4% of participants, respectively
- Application site pain was the only TEAE in ≥5% of CAB-treated participants (11%) vs 0.4% with vehicle
- Transient increases in mean safety/tolerability scores for scaling, erythema, itching, stinging, and burning with CAB generally resolved at/near baseline levels by week 4; most instances were mild to moderate in severity (**Figure 4**)

FIGURE 1. **Lesion Reductions (ITT Population, Pooled)**



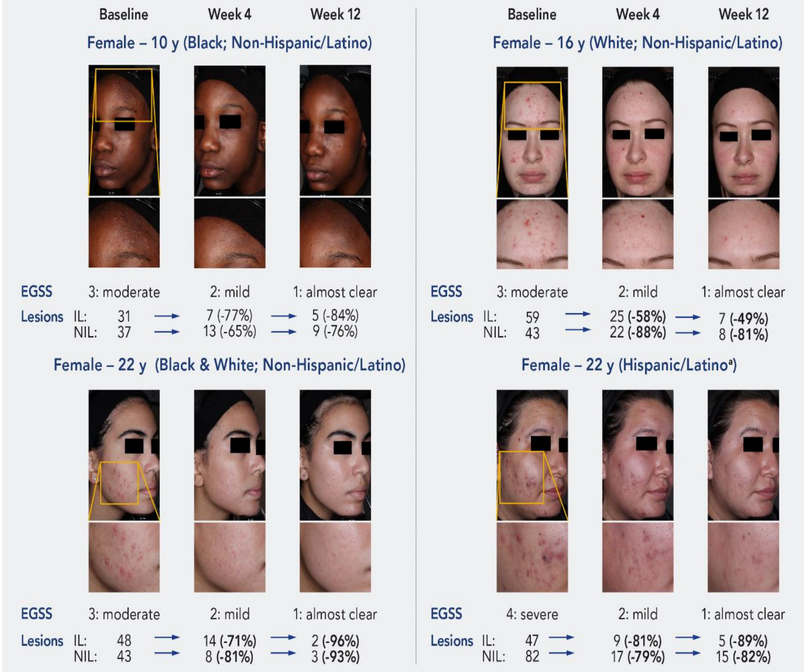
***P<0.001 vs vehicle.
Multiple imputation (Markov Chain Monte Carlo) was used to impute missing data.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; IL, inflammatory lesion; ITT, intent to treat; LS, least-squares; NIL, noninflammatory lesion.

FIGURE 2. **Treatment Success[a] (ITT Population, Pooled)**



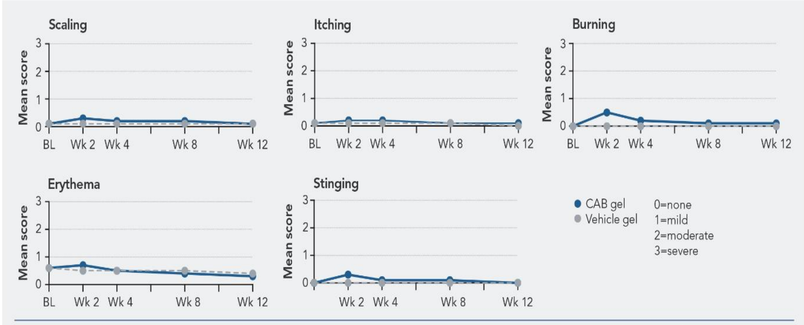
***P<0.001 vs vehicle.
Multiple imputation (Markov Chain Monte Carlo) was used to impute missing data.
[a]Defined as the percentage of participants achieving ≥2-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 (clear) or 1 (almost clear).
CAB, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%; ITT, intent to treat.

FIGURE 3. **Acne Improvements With CAB Gel**



Individual results may vary.
Photographic images © 2025. Courtesy of Ortho Dermatologics Study Investigators.
*Race unknown.
CAB, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15%; EGSS, Evaluator's Global Severity Score; IL, inflammatory lesions; NIL, noninflammatory lesions.

FIGURE 4. **Cutaneous Safety and Tolerability (Safety Population, Pooled)**



Assessments were scored using a 4-point scale (0=none, 1=mild, 2=moderate, and 3=severe). Investigators assessed scaling, erythema, hypopigmentation, and hyperpigmentation; there were no increases in mean score for hypopigmentation or hyperpigmentation, so these data are not shown. Participants assessed itching, burning, and stinging.
N values: CAB at baseline, n=613; CAB at week 12, n=540 or 541; vehicle at baseline, n=495; vehicle at week 12, n=436 or 437.
BL, baseline; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%.

CONCLUSIONS

- Fixed-dose, triple-combination CAB gel was well tolerated, with rapid therapeutic effects
  - Inflammatory acne lesion reductions with CAB were >50% by week 4 and >75% by week 12
  - Over half of participants (51%) achieved treatment success by week 12, with 11% achieving success by week 4
- While extended topical acne treatment is often needed to achieve clear skin, the fast-acting efficacy of the only approved triple-combination product for acne—coupled with its once-daily dosing and tolerability—may positively impact patient satisfaction and treatment adherence

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5. Kircik LH, et al. *Dermatol Ther (Heidelb)*. 2024;14(5):1211-1227.
6. Kircik L, et al. *J of Skin*. 2024;8(4):S416.

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A Case Report of Clindamycin Phosphate 1.2%/Adapalene 0.15%/Benzoyl Peroxide 3.1% Gel to Treat Acne Induced by Janus Kinase Inhibitor Treatment

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SYNOPSIS

- Janus kinase inhibitors (JAKi)—developed to treat inflammatory and immune-mediated diseases—have shown an increased risk of acne development, especially when used to treat dermatologic conditions[1-4]
- While JAKi-induced acne has similar clinical characteristics to both acne vulgaris (AV) and acneiform lesions, with predominantly inflammatory lesions, there are no treatment guidelines[1,5]
- Some of the most efficacious treatments for AV are oral isotretinoin monotherapy and triple combinations that include benzoyl peroxide (BPO), a topical retinoid, and an oral/topical antibiotic[6]
- Fixed-dose, triple-combination clindamycin phosphate 1.2%/adapalene 0.15%/BPO 3.1% (CAB; Cabtreo®; Ortho Dermatologics) gel has demonstrated good efficacy, safety, and tolerability in phase 2 and 3 clinical trials of participants with moderate to severe AV[7-9]

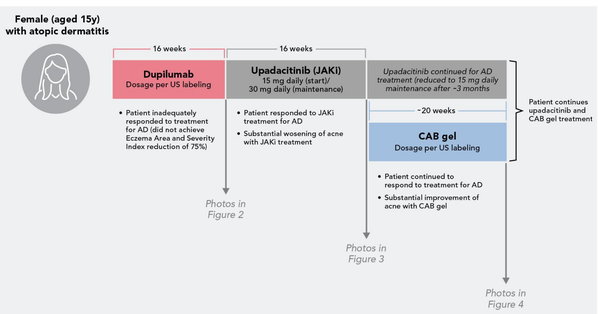
OBJECTIVE

- To show a case report that highlights the possible utility of once-daily CAB gel treatment for JAKi-induced acne

RESULTS

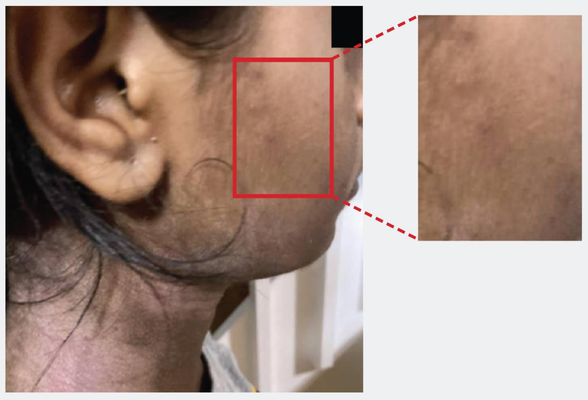
- A 15-year-old female patient was administered the oral JAKi upadacitinib (15 mg daily, titrated up to 30 mg daily) for 16 weeks to treat atopic dermatitis (AD)
  - The patient's AD had inadequately responded to prior treatment with dupilumab for 16 weeks (dosage per US labeling; **Figure 1**)

FIGURE 1. Patient Treatment Timeline



AD, atopic dermatitis; CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; JAKi, Janus kinase inhibitor.

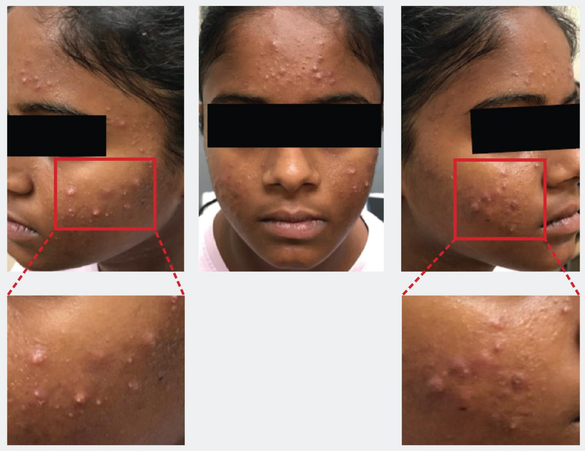
FIGURE 2. Atopic Dermatitis of the Neck and Mild Facial Acne Prior to JAKi Treatment



Scaling atopic dermatitis rash on the right neck and mild acne comedones on the right cheek prior to upadacitinib treatment.
JAKi, Janus kinase inhibitor.

- Prior to JAKi treatment, the patient had mild preexisting comedonal and inflammatory facial AV, with a few 1- to 2-mm closed comedones or pink papules, primarily on the cheeks and forehead (**Figure 2**)
- Her acne worsened over the first few months of JAKi treatment to moderate/severe inflammatory acne (**Figure 3**)
  - Larger 2- to 9-mm, pink to red inflammatory papules were observed on the forehead and cheeks, many with prominent pustule formation
  - The patient also had acne-induced erythema and postinflammatory hyperpigmentation

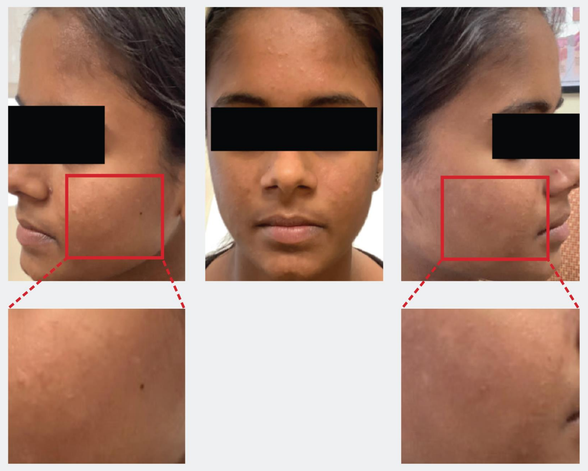
FIGURE 3. Moderate to Severe Facial Acne Following JAKi Treatment



Facial acne lesions following 16 weeks of treatment with oral upadacitinib 15 mg or 30 mg once daily (prior to initiation of CAB gel).
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%; JAKi, Janus kinase inhibitor.

- The patient applied CAB gel to the face once daily for approximately 20 weeks without any other acne treatments
- CAB treatment provided substantial improvements in acne, without adverse effects (**Figure 4**)
  - The patient's acne severity went from moderate/severe to mild/almost clear, with no significant acne-induced sequelae (scarring, postinflammatory hyperpigmentation, or erythema)

FIGURE 4. Following CAB Gel Treatment: Mild to Almost Clear Facial Acne



Facial acne lesions following 5 months of once-daily treatment with CAB gel while maintaining upadacitinib therapy.
CAB, clindamycin phosphate 1.2%/adapalene 0.15%/benzoyl peroxide 3.1%

- The patient continues treatment with both CAB and a reduced dose of upadacitinib (15 mg) once daily

CONCLUSIONS

- JAKi treatment was highly effective in controlling this patient's AD when dupilumab could not, making successful acne treatment important for sustaining effective AD therapy
- Treatment guidelines for the management of AV often recommend oral drugs, such as isotretinoin, for patients with moderate to severe acne[10]
  - Similar recommendations for oral isotretinoin were suggested in a letter to the editor on the management of severe JAKi-induced acne[2]
- This case presented here, however, demonstrates that topical CAB gel can treat moderate to severe JAKi-induced inflammatory acne

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AUTHOR DISCLOSURES

Nicole Olszewski has served as a Clinical Research Coordinator for AbbVie's LEVEL-UP clinical trial. Christopher G. Bunick has served as an investigator and/or consultant for AbbVie, Almirall, Amgen, Apogee, Arcutis, Botanix, Connect BioPharma, Daiichi Sankyo, Dermavant, Eli Lilly, EPI Health/Novan, Incyte, LEO Pharma, Novartis, Ortho Dermatologics, Palvella, Pfizer, Regeneron, Sanofi, Sun Pharma, Takeda, Timber, Teladoc, and UCB.

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Roflumilast Foam 0.3% in Patients With Psoriasis of the Scalp and Body: Improvements in Patient-Reported Outcomes in the ARRECTOR Trial

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INTRODUCTION

- Plaque psoriasis is a chronic inflammatory skin condition with a substantial burden of disease[1]
- Commonly used topical therapies for psoriasis (eg, corticosteroids and calcineurin inhibitors) may have side effects, limitations on duration of use, and restrictions for use in thin-skinned areas, depending on potency[2,3]
  - There may also be difficulties with application that decrease adherence for some individuals[3]
- Topical roflumilast is a PDE4 inhibitor formulated as a water-based foam or cream, which do not contain ethanol, propylene glycol, or fragrances that can irritate skin[4]
- In the phase 3 ARRECTOR (NCT05038683) trial, roflumilast foam 0.3% demonstrated significant improvements in disease signs and symptoms compared with vehicle in patients aged ≥12 years with psoriasis of the scalp and body[5]
  - Safety and application-site tolerability profiles were favorable
  - Patients reported improvements in symptoms and aggregated PROs[6]
- Detailed results of PROs from the ARRECTOR trial are reported here

METHODS

- ARRECTOR was a randomized, parallel-group, double-blind, vehicle-controlled, multicenter, phase 3 trial of roflumilast foam 0.3% applied once daily for 8 weeks in adolescent and adult patients with psoriasis of the scalp and body
- Assessments through 8 weeks of study treatment included the following:
  - S-IGA success (co-primary endpoint): clear (0) or almost clear (1) plus ≥2-grade improvement from baseline when rated from clear (0) to severe (4)
  - B-IGA success (co-primary endpoint): 0/1 plus ≥2-grade improvement from baseline when rated from clear (0) to severe (4)
  - SI/WI-NRS: proportion of patients with 0/1, on a scale from 0 (no itch) to 10 (worst itch imaginable)
  - PSSI-75 and PSSI-100: ≥75% and 100% reduction in PSSI, respectively
  - PSD: a validated 16-item questionnaire assessing various psoriasis symptoms, including itch, pain, and scaling
  - Scalpdex: a validated 23-item survey assessing quality of life in patients with scalp dermatitis
  - Safety and application-site tolerability

Study Design

RESULTS

- Demographics and baseline disease characteristics were similar across treatment groups
  - Most patients (81.9%) had previously used topical corticosteroids for treatment of their psoriasis of the scalp and body
- Roflumilast foam 0.3% was well tolerated, consistent with safety outcomes reported in previous trials of roflumilast cream 0.3% in patients with psoriasis[7]
  - Most TEAEs were mild or moderate in both the roflumilast (96.0%) and vehicle (93.0%) groups, and 5.7% and 3.0% were considered related to study treatment, respectively
  - Discontinuations of the study due to TEAEs were limited and similar between the roflumilast (n=5 [1.8%]) and vehicle (n=3 [1.3%]) groups
- At Week 8, significantly greater (P≤0.0001) proportions of patients in the roflumilast group achieved S-IGA success, B-IGA success, SI-NRS/WI-NRS 0/1, PSSI-75/100, and improvement in PROs, compared with patients in the vehicle group
  - Improvements in patient-reported Scalpdex and PSD component scores were observed with roflumilast as early as Week 2 and continued through Week 8

Patient Demographics and Baseline Disease Characteristics

ITT[a]	Roflumilast foam 0.3% (n=281)	Vehicle foam (n=151)
Age, years, mean (SD) [range]	48.6 (14.9) [12–87]	48.0 (14.3) [13–86]
Female sex at birth, n (%)	152 (54.1)	91 (60.3)
S-IGA, mean (SD)	3.1 (0.36)	3.1 (0.34)
3 (moderate), n (%)	239 (85.1)	131 (86.8)
4 (severe), n (%)	42 (14.9)	20 (13.2)
B-IGA, mean (SD)	2.8 (0.52)	2.8 (0.54)
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)
BSA, %, mean (SD)	6.1 (4.3)	6.0 (4.3)
PSSI, mean (SD)	21.4 (11.1)	22.2 (11.0)
Scalpdex, mean (SD)	47.2 (22.9)	50.5 (20.4)
PSD total, mean (SD)	73.4 (40.2)	75.2 (36.9)
PSD itch/pain/scaling aggregate score, mean (SD)	15.7 (7.3)	16.2 (6.7)

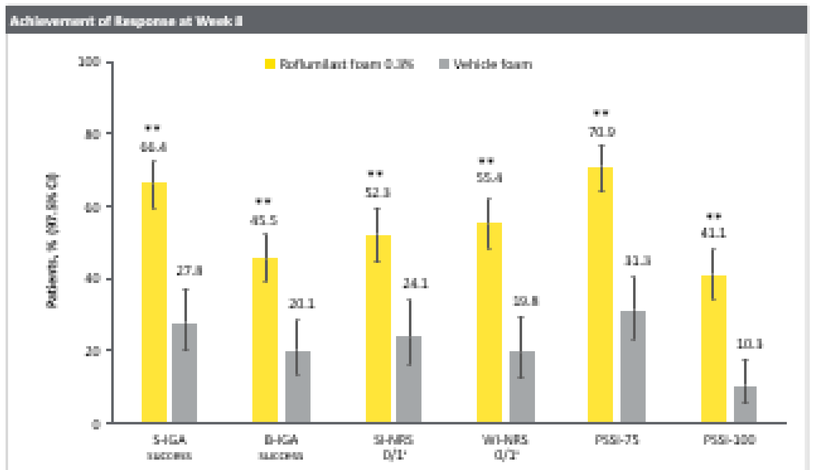
[a]All randomized patients.

Summary of Adverse Events

n (%)[a]	Roflumilast foam 0.3% (n=281)	Vehicle foam (n=151)
Patients with any TEAE	75 (26.7)	25 (16.6)
Patients with any treatment-related TEAE	16 (5.7)	3 (2.0)
Patients with any SAE[b]	2 (0.7)	1 (0.7)
Patients with any treatment-related SAE	1 (0.4)	0
Most common TEAEs by preferred term, ≥2% in either group		
Headache	13 (4.6)	3 (2.0)
Diarrhea	9 (3.2)	4 (2.6)
COVID-19	8 (2.8)	4 (2.6)
Nausea	6 (2.1)	0

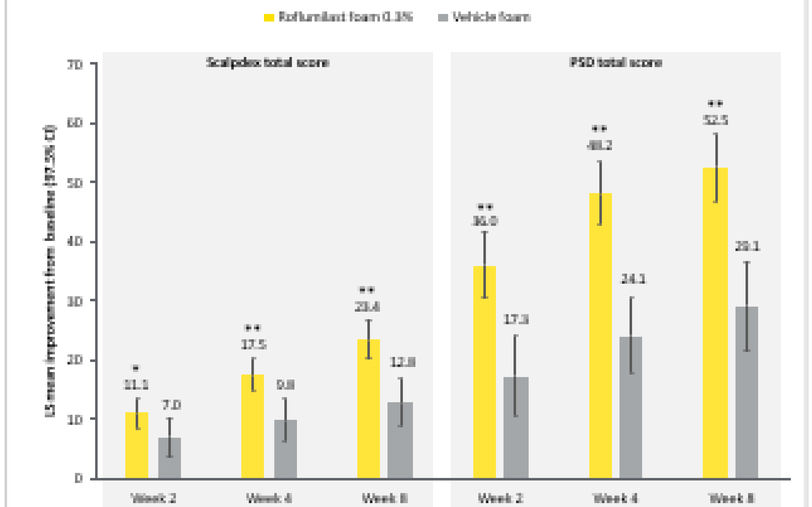
[a]Safety population (all patients who enrolled and received ≥1 confirmed dose of trial medication). [b]All in the roflumilast group were gastritis and bipolar disorder and in the vehicle group were skin ulceration and ovarian fracture.

Achievement of Response at Week 8



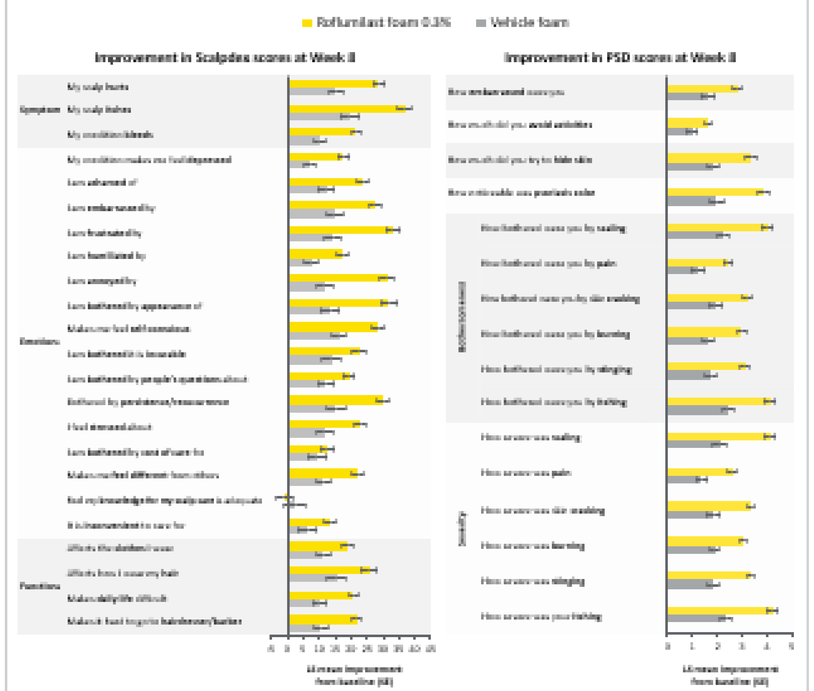
[a]P<0.0001. ITT population. Multiple imputation. [b]Patients with baseline daily SI-NRS (roflumilast, n=253; vehicle, n=133) or WI-NRS (roflumilast, n=253; vehicle, n=131) ≥3.

Improvement in PROs Over Time



[a]P≤0.01; [b]P<0.0001. ITT population. Observed data.

Patient-Reported Outcome Components



ITT population. Observed data. Symptom and Function statements are related to impact of scalp condition.

CONCLUSIONS

Once-daily roflumilast foam 0.3% was effective and well tolerated throughout 8 weeks of treatment in patients with psoriasis of the scalp and body.

- Roflumilast demonstrated improvements in psoriasis signs and symptoms across efficacy measures
- Improvements were observed as early as the first assessment at 2 weeks and were maintained or improved through 8 weeks
  - This is also in line with significant improvement (P<0.05) in scalp itch (SI-NRS) and worst itch (WI-NRS) previously observed within 24 hours after the first application of roflumilast foam 0.3%[8]
- Safety and efficacy are consistent with previous trials of roflumilast foam 0.3%[7] and roflumilast cream 0.3%[7,13] in patients with psoriasis

Roflumilast foam 0.3% significantly improved quality of life and other PROs throughout study treatment.

- Patients reported improvements in symptoms, as well as a reduction in how psoriasis symptoms impacted daily life
- Improvements with roflumilast were observed across areas of the 23-component Scalpdex assessment, including psoriasis symptoms and mental and emotional state

ABBREVIATIONS

BSA, Body surface area affected; DLQI, Dermatology Life Quality Index; ITT, intent-to-treat; QD, once-a-day; PASI, Psoriasis Area and Severity Index; PSSI, ghosphodiesterase 4; PRO, patient-reported outcome; PSD, Psoriasis Symptom Diary; PSSI, Psoriasis Scalp Severity Index; QD, once daily; S-IGA, Scalp Investigator Global Assessment; SAE, serious adverse event; SI-NRS, Scalp Itch Numeric Rating Scale; TEAE, treatment-emergent adverse event; WI-NRS, Worst Itch Numeric Rating Scale.

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DISCLOSURES

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Long-Term Efficacy and Safety of Lebrikizumab is Maintained in Patients With Moderate-to-Severe Atopic Dermatitis: Results Up to 3 Years From ADjoin

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Sponsored by Eli Lilly and Company

OBJECTIVE

- To evaluate the long-term efficacy and safety of 3 years of continuous treatment of lebrikizumab, with or without TCS, in responders[a] from ADvocate1&2 (NCT04146363; NCT04178967)[1] and ADhere (NCT04250337)[2] enrolled into the extension study ADjoin (NCT04392154)[3]

[a]Responders in ADvocate1&2 and ADhere were defined as those patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of LEBRI 250 mg Q2W treatment without use of rescue therapy.

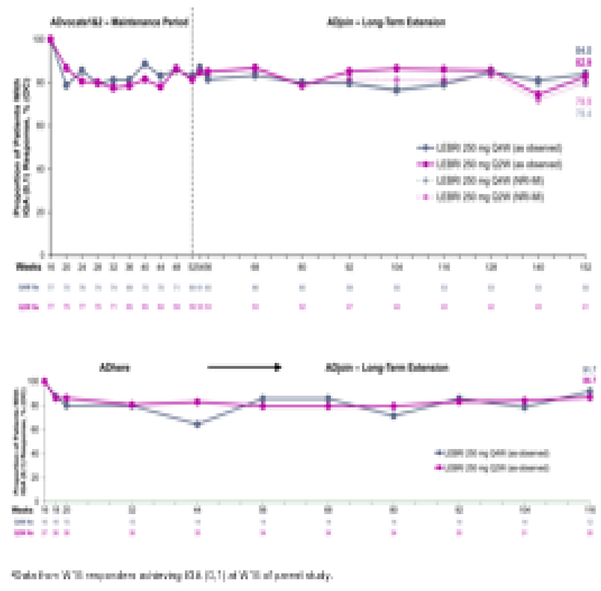
CONCLUSIONS

- Efficacy outcomes were maintained through 3 years of continuous lebrikizumab treatment, with or without TCS, in Week 16 responders in both the lebrikizumab 250 mg Q4W and Q2W dose regimens, with most patients maintaining clear or almost clear skin as assessed by IGA (0,1)
  - Additionally, most patients maintained EASI 75 and EASI 90 through 3 years of continuous lebrikizumab for both dose regimens
- Most patients did not require rescue therapy with continuous lebrikizumab treatment
- The safety profile of lebrikizumab in ADjoin was consistent with that observed in ADvocate1&2, ADhere, and other lebrikizumab studies in patients with moderate-to-severe AD
  - Rates of adverse events did not increase over time
- These long-term 3-year data demonstrate that lebrikizumab provides disease control over time, and helps inform clinical practice in a chronic and relapsing disease

Elevate-Derm Summer Conference, Park City, Utah, USA; July 23 - 27, 2025

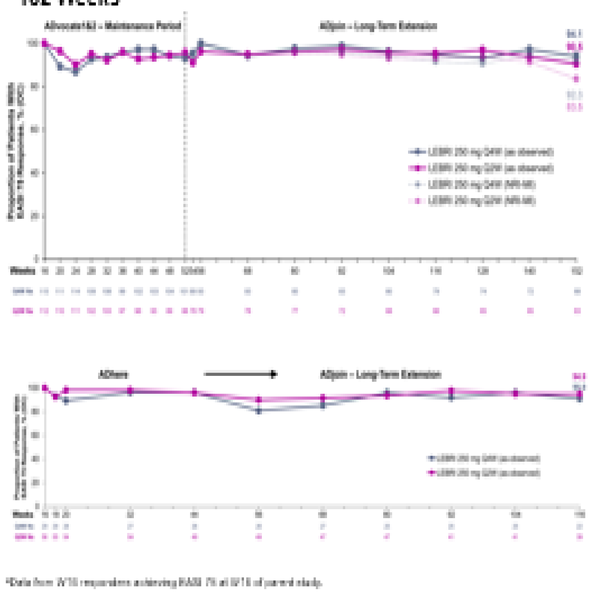
KEY RESULTS

IGA (0,1) Response Rates[a] Were Maintained in Patients Receiving Lebrikizumab Q4W and Q2W Through 152 Weeks



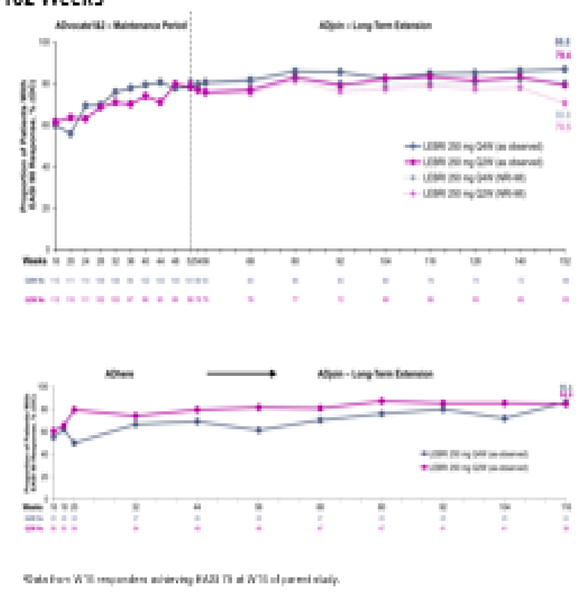
[a]Data from W16 responders achieving IGA (0,1) at W16 of parent study.

EASI 75 Response Rates[a] Were Maintained in Patients Receiving Lebrikizumab Q4W and Q2W Through 152 Weeks



[a]Data from W16 responders achieving EASI 75 at W16 of parent study.

EASI 90 Response Rates[a] Were Maintained and Improved in Patients Receiving Lebrikizumab Q4W and Q2W Through 152 Weeks



[a]Data from W16 responders achieving EASI 75 at W16 of parent study.

Methods

Outcomes

- Maintenance of response for:
  - IGA (0,1) (in Week 16 responders achieving IGA [0,1] at Week 16 of parent study)
  - EASI 75 (in Week 16 responders achieving EASI 75 at Week 16 of parent study)
  - EASI 90 (in Week 16 responders achieving EASI 75 at Week 16 of parent study

Note: Responders in ADvocate1&2 and ADhere were defined as those patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of LEBRI 250 mg Q2W treatment without use of rescue therapy.

Statistical Analyses and Assessment

- Analysis population
  - *Modified intent-to-treat population*[a]: ADvocate1&2 → ADjoin: Lebrikizumab responders[b] who were randomized to lebrikizumab 250 mg Q4W or lebrikizumab 250 mg Q2W at Week 16, and enrolled into ADjoin with the same dose regimen at Week 52
  - *Modified intent-to-treat population*[a]: ADhere → ADjoin: Lebrikizumab responders[b] in ADhere who were randomized to lebrikizumab 250 mg Q4W or lebrikizumab 250 mg Q2W and enrolled into ADjoin at Week 16
- Efficacy analysis
  - As-observed (OC) analyses used all collected data regardless of rescue medication use
  - In addition to as-observed analyses, the non-responder imputation-multiple imputation[c] method was implemented to handle missing data. For each imputation process, 25 datasets with imputations were calculated using SAS® software version 9.4
  - ADvocate1&2 → ADjoin: Efficacy outcomes were assessed during the maintenance period of ADvocate1&2 (Weeks 16-52) and then for 100 weeks in ADjoin (Weeks 52-152)
  - ADhere → ADjoin: Efficacy outcomes were assessed up to 100 weeks in ADjoin (Weeks 16-116)
- Safety data were reported from ADjoin enrollment up to the data cut-off April 24, 2024

[a]Patients from one site participating in ADvocate1 and ADhere not included in the modified intended-to-treat populations due to site audit findings. [b]Responders in ADvocate1&2 and ADhere were defined as those who achieved either EASI 75 or IGA (0,1) following 16 weeks of lebrikizumab 250 mg Q2W treatment without use of rescue therapy. [c]Patients who discontinued treatment due to lack of efficacy had values set to their parent study baseline value (carryforward) for this trial. Observations after discontinuing treatment due to other reasons are set as missing and handled with multiple imputation.[4,5,6,7]

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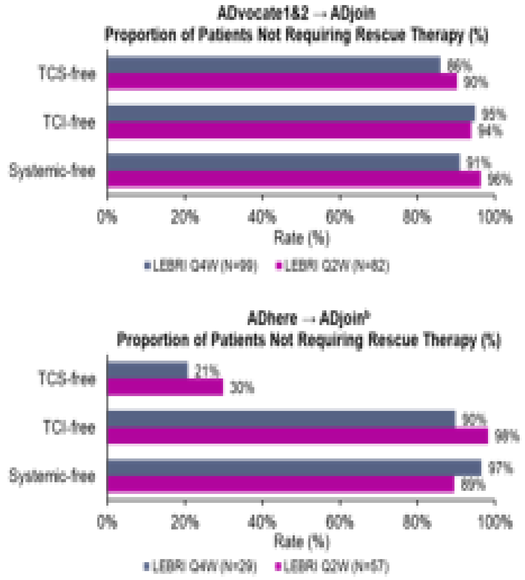
Results

Most Patients Receiving Lebrikizumab Q4W and Q2W Through 152 Weeks Did Not Require Rescue Therapy[a]



[a]Rescue therapy included any topical or systemic therapy during the treatment period. [b]Patients enrolling into ADjoin from ADhere, continued or stopped TCS use, as needed.

Notes: Topical rescue therapy included TCS and TCI; systemic rescue therapy included systemic corticosteroids, immunosuppressants, biologics, phototherapy, and photochemotherapy. Majority of systemic rescue use was used to treat TRAEs.

Abbreviations: AD=atopic dermatitis; AE=adverse event; BAI=body mass index; BSA=body surface area; DLQI=Dermatology Life Quality Index; EASI 75=at least 75% improvement from baseline in EASI; EASI 90=at least 90% improvement from baseline in EASI; IGA=Investigator's Global Assessment; IGA (0,1)=IGA response of clear or almost clear; LEBRI=lebrikizumab; NMSC=non-melanoma skin cancer; NRS=Numeric Rating Scale; n=number of patients with event/study group; OC=observed case; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; PI=preferred term; SAE=serious adverse event; SC=subcutaneous injection; TCI=topical calcineurin inhibitor; TCS=topical corticosteroid; TRAE=treatment-emergent AE; W=Week.

Safety Summary for Patients Entering ADjoin From ADvocate1&2 and ADhere

	ADvocate1&2 → ADjoin[a]		ADhere → ADjoin[a]	
	LEBRI 250 mg Q4W (N=99)	LEBRI 250 mg Q2W (N=82)	LEBRI 250 mg Q4W (N=29)	LEBRI 250 mg Q2W (N=57)
Patients with ≥1 TEAE	67 (67.7)	59 (72.0)	17 (58.6)	35 (61.4)
Mild	25 (25.3)	28 (34.1)	12 (41.4)	13 (22.8)
Moderate	36 (36.4)	28 (34.1)	4 (13.8)	21 (36.8)
Severe	6 (6.1)	3 (3.7)	1 (3.4)	1 (1.8)
Serious AE	3 (3.0)	3 (3.7)	2 (6.9)	2 (3.5)
Death	0	0	0	1 (1.8)[b]
Discontinuation from study treatment due to AE	3 (3.0)	2 (2.4)	0	2 (3.5)
TEAEs of Special Interest				
Conjunctivitis cluster[c]	5 (5.1)	3 (3.7)	3 (10.3)	8 (14.0)
Keratitis cluster[c]	1 (1.0)	0	0	0
Infections[d]	45 (45.5)	38 (46.3)	11 (37.9)	24 (42.1)
Potential opportunistic infections[e]	1 (1.0)	4 (4.9)	1 (3.4)	0
Skin infections	3 (3.0)	1 (1.2)	1 (3.4)	2 (3.5)
Herpes infections	3 (3.0)	6 (7.3)	1 (3.4)	2 (3.5)
Parasitic infections	0	0	1 (3.4)	0
Injection site reactions[f]	0	1 (1.2)	1 (3.4)	1 (1.8)
Malignancies[g]	0	0	0	0
Hypersensitivity	1 (1.0)	2 (2.4)	1 (3.4)	1 (1.8)
Eosinophilia[h]	1 (1.0)	1 (1.2)	0	0

[a]Modified safety population from Week 0 of ADjoin through to data cutoff of April 24, 2024. [b]As reported by the investigator, a 65-year-old male patient died of natural causes on Study Day 602 and the event was assessed to be unrelated to study treatment; the patient had a medical history of hypertension, cardiac arrhythmia, AD, insomnia, and gastroesophageal reflux. [c]Conjunctivitis cluster includes MedDRA preferred terms of conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, giant papillary conjunctivitis. [d]Keratitis cluster includes MedDRA preferred terms of keratitis, atopic keratoconjunctivitis, allergic keratitis, ulcerative keratitis, and corneal keratoconjunctivitis. [e]Infections are defined using the MedDRA preferred terms from the Infections and Infestations System Organ Class. [f]All potential opportunistic infections were assessed as not opportunistic based on the Worldwide criteria. [g]Injection site reactions are defined using MedDRA High Level Term of injection site reactions, excluding administration preferred terms. [h]Excludes both NMSC and malignancies excluding NMSC. [i]Eosinophilia is defined as 3 preferred terms of eosinophilia and allergic eosinophilia and the following preferred terms under the high level term blood and lymphatic system disorders: eosinophil count abnormal, eosinophil count increased, and eosinophil percentage increased. No eosinophilia-related disorders were reported.

Notes: Data are presented as n (%). A TEAE is defined as an event that first occurred or worsened in severity after baseline and on or prior to the date of the last visit within the specified treatment period. Patients with multiple occurrences of these categories are counted once for each category. Patients may be counted in >1 category. Deaths are also included as serious AEs and discontinuations due to AEs. MedDRA Version 27.0.

Supplemental Materials

Scan the QR code for additional Supplemental Materials

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Icotrokinra, a Targeted Oral Peptide That Selectively Blocks the Interleukin-23–Receptor, for the Treatment of Moderate-to-Severe Plaque Psoriasis: Results Through Week 24 of the Phase 3, Randomized, Double-blind, Placebo-Controlled ICONIC-LEAD Trial

Robert Bissonnette,[1] Jennifer Soung,[2] Adelaide Hebert,[3] Andrew E. Pink,[4] Andreas Pinter,[5] Yuling Shi,[6] Megan Miller,[7] Joseph Cafone,[7] Jing Zhi (Gigi) Jiang,[8] Cynthia DeKlotz,[7] Mark G. Lebwohl[9]

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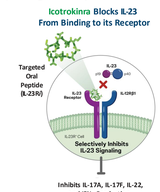
Background

Patients with moderate-to-severe plaque psoriasis (PsO) are generally limited to injectable therapies to achieve high-level efficacy with a favorable safety profile

Icotrokinra (ICO) is a first-in-class, targeted oral peptide that:

- Selectively binds the interleukin (IL)-23 receptor and inhibits IL-23 pathway signaling[1]
- Demonstrated significant skin clearance and no safety signals through 1 year in Phase 2 PsO studies[2,3]
- Is being evaluated in Phase 3 studies in adults and adolescents with moderate-to-severe plaque PsO (ICONIC-LEAD)



IFN=interferon, **IL-12Rβ1**=Interleukin-12 receptor beta 1, **IL-17A**=Interleukin-17A, **IL-17F**=Interleukin-17F, **IL-22**=Interleukin-22, **IL-23**=Interleukin-23, **IL-23R**=Interleukin-23 receptor, **IL-23Ri**=Interleukin-23 receptor inhibitor

Objectives

Here we report key clinical and patient-reported outcomes (PROs) and safety-related findings from the pivotal ICONIC-LEAD study through Week (W) 24

ICONIC-LEAD study design

Moderate-to-severe plaque PsO (N=684)

Key inclusion criteria

- ≥12 years
- Plaque PsO for ≥26 weeks
- Body surface area (BSA) ≥10%, Psoriasis Area and Severity Index (PASI) score ≥12, and Investigator's Global Assessment (IGA) score ≥3
- Candidate for phototherapy or systemic treatment for plaque PsO

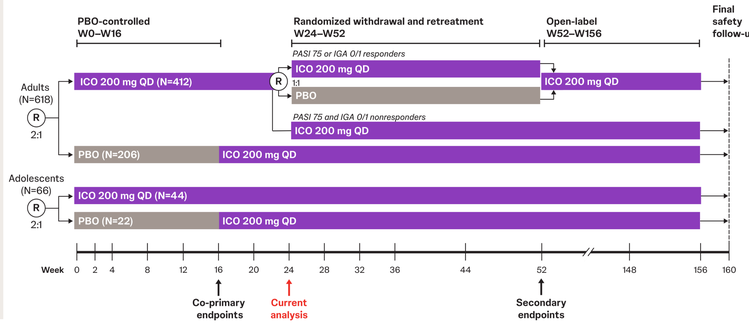
Endpoints

Co-primary endpoints:

- IGA 0/1 at W16
- PASI 90 at W16

Key secondary endpoints:

- **Clinical outcomes** (PASI 75/90/100, IGA 0) at W4, W8, and/or W16
- **PROs** (≥4-point improvement from baseline in Psoriasis Symptom and Sign Diary [PSSD] Itch, PSSD Symptom 0) at W4, W8, and/or W16
- **Scalp PsO** (scalp-specific [ss]-IGA 0/1) at W16



Participants with the following intercurrent events were considered as nonresponders: discontinued study drug due to a lack of efficacy or AE of worsening PsO or initiated prohibited medication that could impact PsO. After accounting for these intercurrent events, nonresponder imputation was applied to participants with missing data. **AE**=Adverse event, **ICO**=Icotrokinra, **IGA 0/1**=Investigator's Global Assessment score of 0 (clear)/1 (almost-clear) and a ≥2-grade improvement, **PASI 75/90/100**=Reduction from baseline of 75%/90%/100% in the Psoriasis Area and Severity Index score, **PBO**=Placebo, **PsO**=Psoriasis, **PSSD**=Psoriasis Symptom and Sign Diary, **QD**=Once daily, **R**=Randomization, **ss-IGA**=Scalp-specific Investigator's Global Assessment, **ss-IGA 0/1**=ss-IGA score of 0 (clear)/1 (almost clear) and a ≥2-grade improvement from baseline, **W**=Week

Key Takeaways

In ICONIC-LEAD, among the first pivotal trials evaluating the novel targeted oral peptide ICO in adults and adolescents with moderate-to-severe plaque PsO:

- ✓ **ICO demonstrated *significantly higher rates of clear/almost clear skin and scalp* disease and *PsO symptom relief* than PBO at W16**
- ✓ **ICO demonstrated *separation from PBO as early as W4,* with *increasing response rates through W24***
- ✓ ***Rates of AEs were similar* between the ICO and PBO groups**
- ✓ ***No safety signal* was identified through W24**

Results

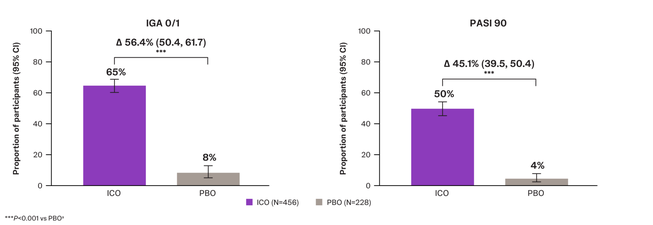
Baseline characteristics were similar between groups

- Overall, 5% of participants (ICO: 4%; placebo [PBO]: 6%) discontinued prior to W16[a]

Baseline characteristics	ICO 200 mg QD (N=456)	PBO (N=228)
Demographic characteristics		
Age, year, mean (SD)	42.4 (16.3)	43.2 (16.6)
Adolescent cohort, year	15.0 (1.8)	15.0 (1.5)
Male	64%	68%
White	72%	72%
BMI, kg/m^2, mean (SD)[b]	29.2 (6.9)	29.3 (7.0)
Disease characteristics		
Psoriasis disease duration, year, mean (SD)	17.3 (13.9)	16.6 (12.7)
% BSA with PsO, mean (SD)	24.6 (14.3)	27.1 (16.2)
IGA score		
Moderate (3)	75%	76%
Severe (4)	25%	24%
PASI (0–72), mean (SD)	19.4 (7.1)	20.8 (8.1)
PsO involving the scalp area		
ss-IGA score[c]		
Moderate (3)	59%	51%
Severe (4)	17%	22%
Prior treatment for PsO		
Phototherapy (PUVA and UVB)	30%	29%
Systemic therapy[d]	72%	71%
Biologic therapy[e]	32%	37%

[a]Among the participants who discontinued prior to W16 (ICO: n=19 [4%]; PBO: n=14 [6%]), the most common reasons for discontinuation were withdrawal by participant in the ICO group (n=8 [2%]) and lack of efficacy in the PBO group (n=8 [4%]). [b]ICO: N=455; PBO: N=227. [c]ICO: N=451; PBO: N=227. [d]Conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics. [e]Adalimumab, alefacept, briakinumab, brodalumab, certolizumab pegol, efalizumab, etanercept, guselkumab, infliximab, ixekizumab, natalizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab. **BMI**=Body mass index, **BSA**=Body surface area, **ICO**=Icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=Placebo, **PsO**=Psoriasis, **PUVA**=Psoralen plus ultraviolet A, **QD**=Once daily, **SD**=Standard deviation, **ss-IGA**=Scalp-specific Investigator's Global Assessment, **UVB**=Ultraviolet B, **W**=Week

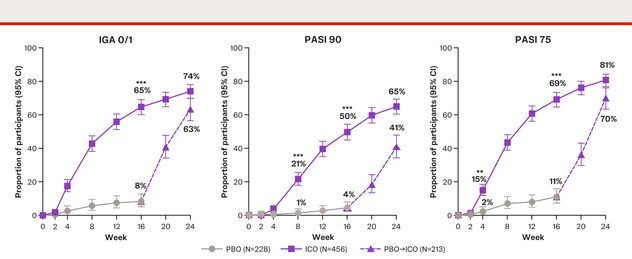
ICO demonstrated *significantly higher rates of IGA 0/1 and PASI 90* vs PBO at W16 (co-primary endpoints)



***P<0.001 vs PBO[a]

[a]*P* values were calculated based on Cochran-Mantel-Haenszel chi-square test stratified by age group, baseline weight category (adults only), and geographic region. **CI**=Confidence interval, **ICO**=Icotrokinra, **IGA**=Investigator's Global Assessment, **IGA 0/1**=IGA score of 0 (clear)/1 (almost clear) and a ≥2-grade improvement, **PASI**=Psoriasis Area Severity Index, **PASI 90**=Reduction from baseline of 90% in the PASI score, **PBO**=Placebo

ICO demonstrated *early separation* from PBO; rates of clear/almost clear skin increased through W24

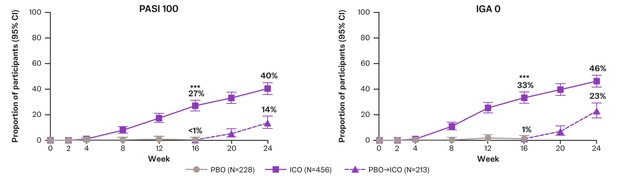


**, ***Multiplicity-adjusted *P*<0.01, *P*<0.001 vs PBO[a]

[a]*P* values were calculated based on Cochran-Mantel-Haenszel chi-square test stratified by age group, baseline weight category (adults only), and geographic region, if applicable. **CI**=Confidence interval, **ICO**=Icotrokinra, **IGA**=Investigator's Global Assessment, **IGA 0/1**=IGA score of 0 (clear)/1 (almost clear) and a ≥2-grade improvement, **PASI**=Psoriasis Area Severity Index, **PASI 75/90**=Reduction from baseline of 75%/90% in the PASI score, **PBO**=Placebo

ICO demonstrated significantly higher rates of *complete skin clearance* vs PBO

- ICO showed separation from PBO as early as W8; rates of complete skin clearance increased through W24

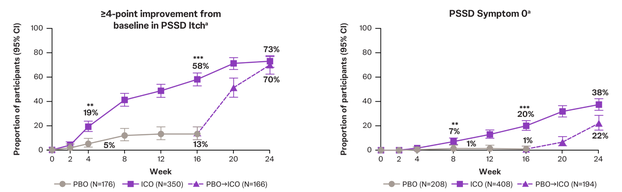


***Multiplicity-adjusted *P*<0.001 vs PBO[a]

[a]*P* values were calculated based on Cochran-Mantel-Haenszel chi-square test stratified by age group, baseline weight category (adults only), and geographic region. **CI**=Confidence interval, **ICO**=Icotrokinra, **IGA**=Investigator's Global Assessment, **IGA 0**=IGA score of 0 (clear) and a ≥2-grade improvement, **PASI**=Psoriasis Area Severity Index, **PASI 100**=Reduction from baseline of 100% in the PASI score, **PBO**=Placebo

Significantly higher proportions of ICO- vs PBO-treated participants reported *meaningful improvements in PsO itch*

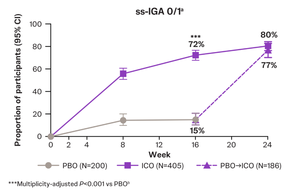
- ICO demonstrated early separation from PBO on improving itch and resolving symptoms; response rates increased through W24



**, ***Multiplicity-adjusted *P*<0.01, *P*<0.001 vs PBO[a]

[a]Among participants with a baseline PSSD Itch score ≥4 or PSSD Symptom score >0. [b]*P* values were calculated based on Cochran-Mantel-Haenszel chi-square test stratified by age group, baseline weight category (adults only), and geographic region, if applicable. Fisher's exact test was used for PSSD Symptom 0 at Week 8. **CI**=Confidence interval, **ICO**=Icotrokinra, **PSSD**=Psoriasis Symptom and Sign Diary, **PBO**=Placebo

ICO demonstrated significantly higher rates of *clear/almost clear scalp PsO* vs PBO



***Multiplicity-adjusted *P*<0.001 vs PBO[a]

[a]Among participants with a baseline ss-IGA score ≥2. [b]*P* values were calculated based on Cochran-Mantel-Haenszel chi-square test stratified by age group, baseline weight category (adults only), and geographic region. **CI**=Confidence interval, **ICO**=Icotrokinra, **PBO**=Placebo, **ss-IGA**=Scalp-specific Investigator's Global Assessment

Adverse event (AE) rates were generally similar between groups through W16

- Through W24 of ICO treatment, the most commonly reported AEs were similar to those observed through W16 and no safety signal emerged

	ICO 200 mg QD (N=456)	PBO (N=228)
Safety through W16		
Mean weeks of follow-up	15.9	15.8
Any AE	225 (49%)	112 (49%)
Most common AEs (≥5%)		
Nasopharyngitis	31 (7%)	15 (7%)
Upper respiratory tract infection	30 (7%)	16 (7%)
SAE[a]	6 (1%)	6 (3%)
Infection	107 (23%)	51 (22%)
Serious infection	1 (<1%)	0
AE leading to discontinuation[b]	6 (1%)	1 (<1%)
Gastrointestinal AE	26 (6%)	13 (6%)
Active TB	0	0
Malignancy[c]	2 (<1%)	0

[a]SAEs through W16 included acute cholecystitis, concussion, craniofacial fracture, pelvic fracture, psoriasis, and hypertensive urgency in the PBO group; and adenocarcinoma of the colon, prostate cancer, pancreatitis, bacterial gastroenteritis (serious infection), arthralgia, and subarachnoid hemorrhage in the ICO group. [b]AEs leading to discontinuation through W16 included blood glucose increased in the PBO group; and adenocarcinoma of the colon, prostate cancer, hypertriglyceridemia, subarachnoid hemorrhage, erectile dysfunction, and psoriasis in the ICO group. [c]Malignancies reported were adenocarcinoma of the colon (n=1 in a participant who had a history of smoking; the participant reported mild gastroenteritis during screening, and severe colitis starting on study day 7, and severe ileus on day 14 leading up to the diagnosis of grade 3 adenocarcinoma of the colon on day 19) and prostate cancer (n=1 in a 62-year-old male, former smoker [30 pack years], with a family history [brother] of prostate cancer, and an elevated prostate-specific antigen level prior to baseline was diagnosed with grade 1 prostate cancer on study day 48 following a positive biopsy). **AE**=Adverse event, **ICO**=Icotrokinra, **PBO**=Placebo, **QD**=Once daily, **SAE**=Serious adverse event, **TB**=Tuberculosis, **W**=Week

PRESENTED AT: Elevate-Derm Summer Conference 2025; Park City, UT, USA; July 23-27, 2025. **REFERENCES: 1.** Fourie AM, et al. *Sci Rep.* 2024;14:17515. **2.** Bissonnette R, et al. *N Engl J Med*. 2024;390:510–21. **3.** Ferris LK, et al. *J Am Acad Dermatol*. Published online November 14, 2024. doi: 10.1016/j.jaad.2024.10.076. **ACKNOWLEDGMENTS:** Medical writing support was provided by Lumanity Communications, Inc. under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med*. 2022;175:1298–1304). Layout design and reformatting for this encore presentation was provided by Sandeep Chavan of SIRO Medical Writing Pvt. Ltd., Thane, Maharashtra, India (funded by Johnson & Johnson). This study was sponsored by Johnson & Johnson. **DISCLOSURES: RB:** serves as advisory board member, consultant, speaker and/or investigator for and received honoraria and/or grants from AbbVie, Alumis, Amgen, Arcutis, Bausch Health, Boston Pharma, Bristol Myers Squibb/Celgene, Dermavant, Eli Lilly, Janssen, LEO Pharma, Nimbus, Novartis, Pfizer, Regeneron, UCB, VentyxBio, and Xencor; and is an employee and shareholder of Innovaderm Research. **JS:** served as a speaker, consultant and/or investigator for AbbVie, Amgen, Arcutis, Bristol Myers Squibb, Covalí Biopharma, Dermavant, Eli Lilly, Janssen, KoBio Labs, LEO Pharma, National Psoriasis Foundation, Novartis, Pfizer, Regeneron, Sanofi, and UCB. **AH:** had research grants paid to the medical school from Amgen, Arcutis, Dermavant, Janssen, LEO Pharma, Eli Lilly, Pfizer, Takeda; received honoraria from Arcutis, Dermavant, Galderma, Incyte, Janssen, Ortho Dermatologics, Pfizer, Sun Pharma, Verrica; and served on a data safety monitoring board for Ortho Dermatologics and Sanofi Regeneron. **AEP:** served as an investigator, advisor and/or speaker and/or received educational support from AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Galderma, Janssen, LEO Pharma, Novartis, Pfizer, Sanofi, and UCB. **AP:** served as an advisor and/or received speaker's honoraria and/or received grants and/or participated in clinical trials for AbbVie, Almirall Hermal, Amgen, Biogen Idec, BioNTech, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Galderma, GSK, Hexal, Janssen-Cilag GmbH, Klinge Pharma, LEO Pharma, MC2, Medac, Merch Serono, Mitsubishi, MSD, Novartis, Pascoe, Pfizer, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi Genzyme, Schering-Plough, Tigercat Pharma, UCB, and Zuellig Pharma. **YS:** reports no conflicts of interest. **MM, JC, JZ,** and **CD:** are employees of Johnson & Johnson and may own company stock/stock options. **MGL:** is an employee of Mount Sinai and receives research funds from AbbVie, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Clexio, Dermavant Sciences, Eli Lilly, Incyte, Inozyme, Janssen, Pfizer,Sanofi-Regeneron, and UCB; and is a consultant for Almirall, AltruBio Inc., Apogee, Arcutis, AstraZeneca, Atomwise, Avotres, Boehringer Ingelheim, Bristol Myers Squibb, Castle Biosciences, Celltrion, CorEvitas, Dermavant, Dermsquared, Evommune, Inc., Facilitation of International Dermatology Education, Forte Biosciences, Galderma, Genentech, Incyte, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Sanofi-Regeneron, Seanergy, Strata, Takeda, Trevi, and Verrica. **PREVIOUSLY PRESENTED AT:** American Academy of Dermatology (AAD) Annual Meeting; Orlando, FL, USA; March 7–11, 2025.

Inhibition of Structural Damage Progression With Guselkumab, a Selective IL-23i, in Participants With Active PsA: Results Through Week 24 of the Phase 3b, Randomized, Double-Blind, Placebo-Controlled APEX Study

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Background

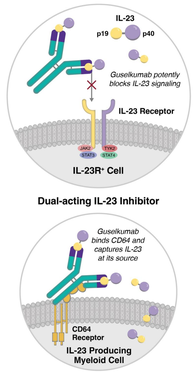
Psoriatic arthritis (PsA), a chronic, heterogeneous, inflammatory disease affecting joints and skin, can substantially impact health-related quality of life[1,2]

- Structural damage resulting from chronic inflammation leads to poorer outcomes[3]

Guselkumab (GUS) is a fully human, dual-acting, monoclonal antibody that selectively inhibits the interleukin (IL)-23p19 subunit[4]

- Indicated to treat moderate-to-severe plaque psoriasis (PsO), active PsA, and moderately-to-severely active Crohn's disease and ulcerative colitis[5]

In DISCOVER-2, biologic-naïve participants (pts) with active PsA receiving GUS every 4 weeks (Q4W) exhibited significantly less radiographic progression vs placebo (PBO); the lower rate of radiographic progression seen with GUS every 8 weeks (Q8W) vs PBO did not reach statistical significance[6]



Objectives

Report findings through Week (W) 24 of the ongoing Phase 3b, randomized, double-blind, placebo-controlled APEX study (NCT04882098), intended to further evaluate GUS effects on clinical and radiographic progression outcomes in pts with active PsA

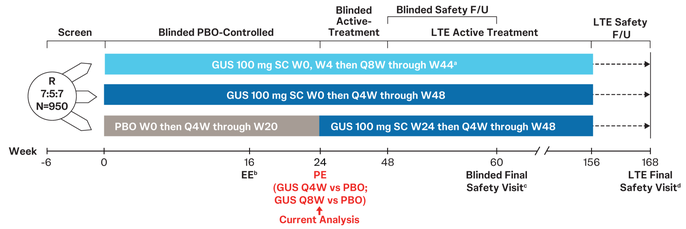
APEX Study Design

Inclusion Criteria

- ✓ Biologic-naive
- ✓ Age ≥18 years
- ✓ Active PsA ≥6 months (despite prior csDMARD, apremilast, NSAID); CASPAR criteria met
- ✓ ≥3 SJC; ≥3 TJC; CRP ≥0.3 mg/dL
- ✓ **≥2 erosive joints on hand/foot radiographs**
- ✓ Active plaque PsO (≥1 PsO plaque ≥2 cm and/or nail PsO)

Multiplicity-Controlled Endpoints

- **Primary:** ACR20 response at W24
- **Major Secondary:** Mean change in total PsA-modified vdH-S score at W24



- **Modified full analysis set (mFAS):** All randomized pts excluding those from Ukraine sites rendered unable to support key study operations due to major disruptions; employed as the main efficacy analysis set (N=1020)
- **Safety analysis set:** All pts who received ≥1 administration of any study intervention (N=1054)

[a]PBO SC W8 then Q8W through W48 administered to maintain blinding. [b]EE if <20% improvement from BL in both TJC and SJC at W16. EE pts may initiate/increase dose permitted medication up to the maximum dose, at the investigator's discretion. [c]Final safety visit for those who do not enter LTE. [d]Final safety visit for those who entered LTE. **ACR**=American College of Rheumatology, **BL**=Baseline, **CASPAR**=CASsification criteria for Psoriatic ARthritis, **CRP**=C-reactive protein, **csDMARD**=Conventional synthetic disease-modifying antirheumatic drug, **EE**=Early escape, **F/U**=Follow-up, **GUS**=Guselkumab, **LTE**=Long-term extension, **NSAID**=Nonsteroidal anti-inflammatory drug, **PBO**=Placebo, **PE**=Primary endpoint, **PsA**=Psoriatic arthritis, **PsO**=Plaque psoriasis, **Pts**=Participants, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **R**=Randomization, **SC**=Subcutaneous, **SJC**=Swollen joint count, **TJC**=Tender joint count, **vdH-S**=van der Heijde-Sharp, **W**=Week

Key Takeaways

At W24 of the ongoing Phase 3b APEX study of GUS, a dual-acting selective IL-23i for PsA, the Q4W & Q8W regimens demonstrated:

- ✓ **Significantly higher ACR20 response rates vs PBO**
- ✓ **Significantly lower rates of radiographic progression (Δ GUS vs PBO = -0.80)**
- ✓ **Consistent effects on erosion & JSN scores**
- ✓ **Higher proportion of pts with no progression of structural damage vs PBO**
- ✓ **Higher rates of ACR50, ACR70, PASI 90 & greater improvement in physical function vs PBO; Simila AE profile for GUS and PBO; No new GUS safety signal**

GUS is the only selective IL-23i to demonstrate significant inhibition of structural damage progression

Results

Characteristics of APEX pts with active and erosive PsA were comparable across groups

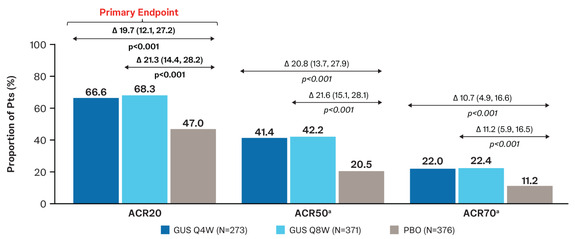
- **Background PsA medication use and treatment completion through W24 (96–97%) were consistent across treatment groups**

	GUS Q4W (N=273)	GUS Q8W (N=371)	PBO (N=376)	Total (N=1020)
Baseline Demographics				
Age, years	52.2 (13.2)	53.2 (12.9)	53.5 (13.0)	53.0 (13.0)
Male	55%	54%	57%	55%
Weight, kg	85.6 (20.1)	83.2 (17.4)	83.1 (18.2)	83.8 (18.5)
BMI, kg/m^2	29.4 (6.0)	29.0 (5.6)	28.9 (5.7)	29.1 (5.7)
PsA Characteristics				
PsA disease duration, years	7.5 (7.1)	7.2 (7.6)	7.2 (6.9)	7.3 (7.2)
SJC [0–66][a]	9.0 (6.0; 14.0)	10.0 (6.0; 14.0)	9.0 (6.0; 15.0)	9.0 (6.0; 14.0)
TJC [0–68][a]	16.0 (10.0; 27.0)	17.0 (11.0; 26.0)	16.6 (10.0; 25.5)	16.1 (10.0; 26.0)
HAQ-DI [0–3]	1.2 (0.7)	1.2 (0.6)	1.2 (0.6)	1.2 (0.7)
CRP, mg/dL[a]	0.7 (0.4; 1.5)	0.8 (0.4; 1.6)	0.8 (0.4; 1.8)	0.8 (0.4; 1.6)
Enthesitis / Dactylitis	58% / 44%	59% / 39%	59% / 45%	58% / 43%
Mean LEI [1–6] / DSS [1–60]	3.2 / 10.8	3.0 / 11.0	3.0 / 10.2	3.1 / 10.6
PsO Characteristics				
% BSA	15.0 (19.2)	16.5 (21.9)	16.3 (21.5)	16.0 (21.0)
PASI [0–72]	7.6 (8.3)	8.3 (10.1)	8.2 (9.5)	8.1 (9.4)
Radiographic Characteristics				
PsA-modified vdH-S score [0–528]	27.7 (47.6)	26.7 (43.4)	26.8 (42.2)	27.0 (44.1)
Erosion score [0–320]	13.7 (24.3)	13.4 (21.9)	13.4 (20.7)	13.5 (22.1)
JSN score [0–208]	14.0 (24.2)	13.3 (22.8)	13.4 (22.4)	13.5 (23.0)

Values are reported as mean (SD) unless otherwise noted. [a]Values are median (IQR). **BMI**=Body mass index, **BSA**=Body surface area, **CRP**=C-reactive protein, **DSS**=Dactylitis Severity Score, **GUS**=Guselkumab, **HAQ-DI**=Health Assessment Questionnaire-Disability Index, **IQR**=Interquartile range, **JSN**=Joint space narrowing, **LEI**=Leeds Enthesitis Index, **PASI**=Psoriasis Area and Severity Index, **PBO**=Placebo, **PsA**=Psoriatic arthritis, **PsO**=Plaque psoriasis, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **SD**=Standard deviation, **SJC**=Swollen joint count, **TJC**=Tender joint count, **vdH-S**=van der Heijde-Sharp

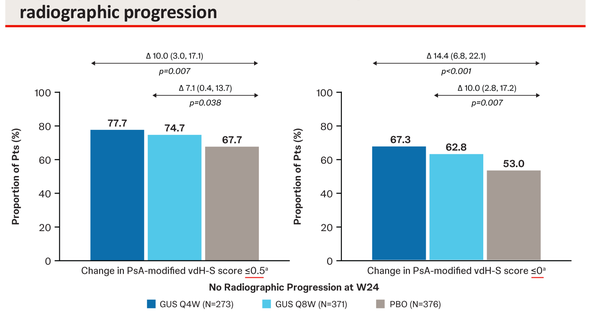
GUS demonstrated significantly higher ACR20 response rates vs PBO at W24

- **GUS demonstrated higher rates of ACR50 and ACR70 vs PBO at W24**



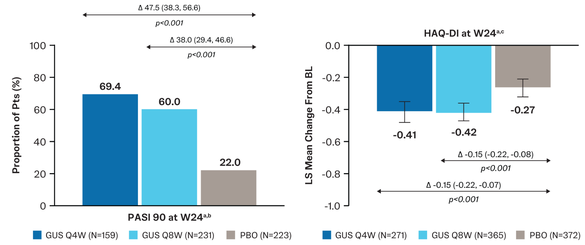
Primary Endpoint p-values are multiplicity controlled using a fixed sequence testing procedure and can be used to determine statistical significance. Statistics are based on Cochran-Mantel-Haenszel across multiply imputed datasets. [a]Italicized p-values are nominal. Δ=treatment difference (95% CI). **ACR**=American College of Rheumatology, **CI**=Confidence interval, **GUS**=Guselkumab, **PBO**=Placebo, **Pts**=Participants, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks

Higher proportions of GUS vs PBO-treated pts showed no radiographic progression



[a]Italicized p-values are nominal. Δ=treatment difference (95% CI). **CI**=Confidence interval, **GUS**=Guselkumab, **PBO**=Placebo, **PsA**=Psoriatic arthritis, **Pts**=Participants, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **vdH-S**=van der Heijde-Sharp, **W**=Week

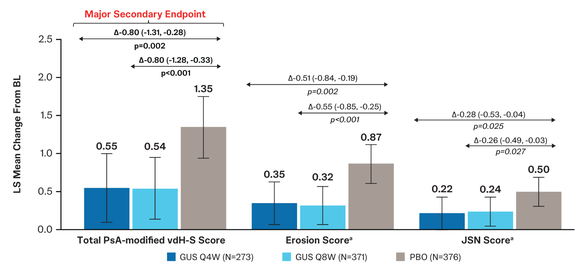
Higher skin clearance rates and greater improvement in physical function with GUS vs PBO



[a]Italicized p-values are nominal. [b]Among pts who had ≥3% BSA psoriatic involvement and an IGA score of ≥2 (mild) at BL. PASI 90 response: ≥90% improvement from baseline in PASI score. [c]HAQ-DI score is the average of the computed categories scores (dressing, arising, eating, walking, hygiene, gripping and daily living). Lower scores indicate better functioning. Δ=treatment difference (95% CI). **BL**=Baseline, **BSA**=Body surface area, **CI**=Confidence interval, **GUS**=Guselkumab, **HAQ-DI**=Health Assessment Questionnaire-Disability Index, **IGA**=Investigator's Global Assessment, **LS**=Least squares, **PASI**=Psoriasis Area and Severity Index, **PBO**=Placebo, **Pts**=Participants, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **W**=Week

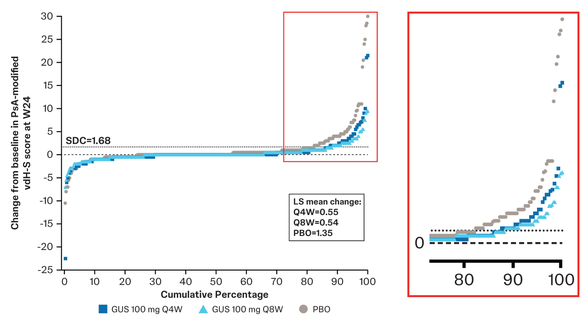
GUS exhibited significantly lower rates of radiographic progression vs PBO at W24

- **GUS exhibited consistent treatment effects for both erosion and joint space narrowing (JSN) scores**



Major secondary endpoint (PsA-modified vdH-S score) p-values are multiplicity controlled using a fixed sequence testing procedure and can be used to determine statistical significance. Statistics are based on analysis of covariance across multiply imputed datasets. [a]Italicized p-values are nominal. Δ=treatment difference (95% CI). BL=Baseline, **CI**=Confidence interval, **GUS**=Guselkumab, **JSN**=Joint space narrowing, **LS**=Least squares, **PsA**=Psoriatic arthritis, **PBO**=Placebo, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **vdH-S**=van der Heijde-Sharp

Pt-level data also showed clear separation between GUS and PBO



GUS=Guselkumab, **LS**=Least squares, **PBO**=Placebo, **PsA**=Psoriatic arthritis, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **SDC**=Smallest detectable change, **vdH-S**=van der Heijde-Sharp, **W**=Week

GUS AE profile through W24 was similar to PBO

Safety Through W24	GUS Q4W (N=280)	GUS Q8W (N=388)	PBO (N=386)
Mean weeks of follow up	24.0	23.9	23.8
Pts with ≥1:			
AE	107 (38.2%)	165 (42.5%)	144 (37.3%)
SAE	5 (1.8%)	12 (3.1%)	10 (2.6%)
AE leading to study agent d/c	2 (0.7%)	6 (1.5%)	1 (0.3%)
Infection	52 (18.6%)	91 (23.5%)	81 (21.0%)
Serious infection	2 (0.7%)	5 (1.3%)	1 (0.3%)
Active tuberculosis	0	0	0
Opportunistic infection	0	0	0
Venous thromboembolism event	1 (0.4%)	1 (0.3%)	1 (0.3%)
Anaphylactic or serum sickness reaction	0	0	0
Clinically important hepatic disorder[a]	0	0	0

Safety analysis set. AEs are coded using MedDRA Version 27.0. Data are n (%) unless otherwise noted. [a]Clinically important hepatic disorders were prespecified as AE terms within the MedDRA category of Drug-Related Hepatic Disorders that met the criteria for an SAE or led to study agent d/c. **AE**=Adverse event, **d/c**=Discontinuation, **GUS**=Guselkumab, **MedDRA**=Medical Dictionary for Regulatory Activities, **PBO**=Placebo, **Pts**=Participants, **Q4W**=Every 4 weeks, **Q8W**=Every 8 weeks, **SAE**=Serious AE, **W**=Week

- **Study remains blinded through W48**
- **2 pts with malignancy (prostate, renal); 1 major adverse cardiovascular event (myocardial infarction); 1 COVID-19 death in unvaccinated elderly pt**
- **No new-onset inflammatory bowel disease**

PRESENTED AT: Elevate-Derm Summer Conference 2025; Park City, UT, USA; July 23–27, 2025. **REFERENCES: 1.** Gladman DD, et al. *J Rheumatol.* 1987;62:127–41. **2.** Ritchlin CT. *J Rheumatol.* 2008;35:1434–7. **3.** van der Heijde D, et al. *Arthritis Res Ther.* 2020;22:18. **4.** Sachen KL, et al. *Front Immunol.* 2025;16:1532852. **5.** Janssen Biotech, Inc. *US FDA website.* Revised March 2025. **6.** Mease PJ, et al. *Lancet.* 2020;395:1126–36. **ACKNOWLEDGMENTS:** Medical writing support was provided by Mona Patel, PharmD, under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med.* 2022;175:1298–1304). This study was sponsored by Johnson & Johnson. Layout design and reformatting for this encore presentation was provided by Samita Warang of SIRO Medical Writing Pvt Ltd, Thane, India (funded by Johnson & Johnson). **DISCLOSURES: PJM:** received grants from AbbVie, Acelyrin, Amgen, Bristol Myers Squibb, Eli Lilly, Johnson & Johnson, Novartis, and UCB; consulting fees from AbbVie, Acelyrin, Amgen, Bristol Myers Squibb, Eli Lilly, Immagene, Johnson & Johnson, Novartis, Pfizer, UCB, and Ventyx; Speaker fees from AbbVie, Amgen, Eli Lilly, Johnson & Johnson, Novartis, Pfizer, and UCB. **CTR:** received grant/research support from AbbVie, Amgen, and UCB; consulting fees from AbbVie, Amgen, Eli Lilly, Gilead, Johnson & Johnson, Novartis, Pfizer, and UCB. **LCC:** Has received grants/research support from AbbVie, Amgen, Celgene, Eli Lilly, Johnson & Johnson, Novartis, Pfizer and UCB; worked as a paid consultant for AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Galapagos, Johnson & Johnson, Moonlake, Novartis, Pfizer, and UCB; and has been paid as a speaker for AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Johnson & Johnson, Medac, Novartis, Pfizer, and UCB. **APK, BZ, YJ, KB, KV, RB, and SDC:** are employees of Johnson & Johnson; may own stock/stock options in Johnson & Johnson. **PR:** received consulting fees from AbbVie, Amgen, Bristol Myers Squibb; Celgene, Eli Lilly, Johnson & Johnson, Merck, Novartis, Pfizer, and UCB; meeting attendance/travel support from Johnson & Johnson; and research grants from Johnson & Johnson, and Novartis. **DvdH:** received consulting fees from AbbVie, Alfasigma, argenx, Bristol Myers Squibb, Eli Lilly, Grey-Wolf Therapeutics, Janssen, Novartis, Pfizer, Takeda, and UCB; serves as the Associate Editor of Annals of Rheumatic Diseases; on the editorial board of Journal of Rheumatology, and as the director of Imaging Rheumatology BV. **PREVIOUSLY PRESENTED AT:** European Alliance of Associations for Rheumatology (EULAR) 2025, Barcelona, Spain; June 11–14, 2025.

Phase 3 Results From an Innovative Trial Design of Treating Plaque Psoriasis Involving Difficult-to-Treat, High-Impact Sites With Icotrokinra, a Targeted Oral Peptide That Selectively Inhibits the IL-23–Receptor

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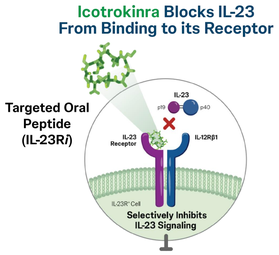
Key Takeaways

- **In ICONIC-TOTAL, a pivotal phase 3 study evaluating ICO in a diverse cohort of pts with plaque PsO and difficult-to-treat, high-impact site involvement:**
  - ✓ **ICO demonstrated significantly higher rates of clear/almost clear skin, including in the scalp and genital areas, than PBO at W16**
  - ✓ **ICO-treated pts achieved significantly higher PRO response rates, including meaningful improvements in the scalp and genital areas, vs PBO at W16**
  - ✓ **Rates of adverse events were generally similar in the ICO and PBO groups; no safety signal was identified through W16**
- **ICONIC-TOTAL results complement those of the ongoing phase 3 ICONIC-LEAD study evaluating ICO in adults & adolescents with moderate-to-severe plaque PsO[4]**

Background

Icotrokinra for plaque psoriasis

- Patients with moderate-to-severe plaque psoriasis (PsO) are generally limited to injectable therapies to achieve high-level efficacy with a favorable safety profile
- Icotrokinra (ICO) is a first-in-class targeted oral peptide that:
  - Selectively binds the interleukin (IL)-23 receptor and inhibits IL-23 pathway signaling[1]
  - Demonstrated significant skin clearance and no safety signals through 1 year in phase 2 PsO studies[2,3] and through Week (W)24 in adults & adolescents with moderate-to-severe plaque PsO in the phase 3 ICONIC-LEAD study[4]



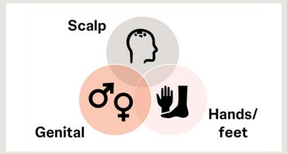
IFN=Interferon, **IL-12Rβ1**=Interleukin-12 receptor beta 1, **IL-17A**=Interleukin-17A, **IL-17F**=Interleukin-17F, **IL-22**=Interleukin-22, **IL-23**=Interleukin-23, **IL-23R**=Interleukin-23 receptor, **IL-23Ri**=Interleukin-23 receptor inhibition

Objectives

The pivotal, phase 3 ICONIC-TOTAL study evaluated ICO in adults & adolescents with plaque PsO involving difficult-to-treat, high-impact sites, by employing a novel basket-like design; key clinical/patient-reported outcomes (PROs) and safety-related findings are reported through W16

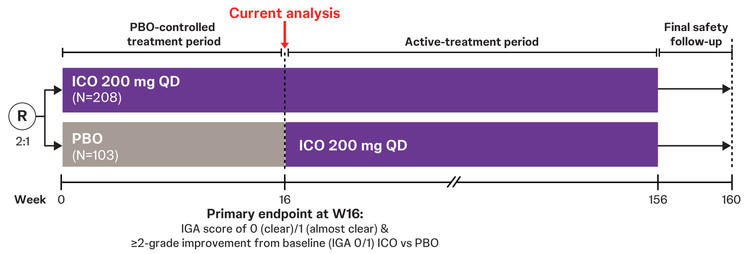
ICONIC-TOTAL: a novel basket-like design

Adults & adolescents with plaque PsO involving high-impact sites evaluated using a basket-like study design (N=311)



Key inclusion criteria

- ≥12 years
- Plaque PsO for ≥26 weeks
- Body surface area (BSA) ≥1% and Investigator's Global Assessment (IGA) score ≥2
- At least moderate high-impact PsO involving ≥1 site:
  - **Scalp PsO:** scalp-specific IGA (ss-IGA) score ≥3
  - **Genital PsO:** static Physician's Global Assessment of Genitalia (sPGA-G) score ≥3
  - **Hand/foot PsO:** Physician's Global Assessment of hands and feet (hf-PGA) score ≥3
- Candidate for phototherapy or systemic treatment for plaque PsO and failed ≥1 topical



Participants (pts) with the following intercurrent events were considered as nonresponders: discontinued study drug due to a lack of efficacy or AE of worsening PsO or initiated prohibited medication that could impact PsO. After accounting for these intercurrent events, nonresponder imputation was applied to pts with missing data. **AE**=Adverse event, **ICO**=Icotrokinra, **IGA**=Investigator's Global Assessment, **PBO**=Placebo, **QD**=Once daily, **R**=Randomization, **W**=Week

Results

Baseline characteristics were generally similar between groups

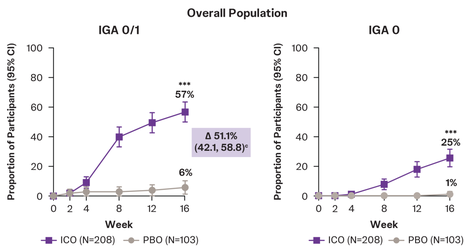
- Overall, 5% of participants [pts] (ICO: 4%; placebo [PBO]: 9%) discontinued treatment through W16[d]

Baseline characteristics		ICO 200 mg QD (N=208)	PBO (N=103)
Demographics			
	Age, years	45.3 (14.6)	43.5 (13.8)
	Male	66%	61%
	White	77%	80%
	BMI, kg/m^2	29.0 (6.6)[a]	29.4 (8.1)[a]
Disease characteristics			
	PsO disease duration, years	16.8 (13.3)	15.2 (10.5)
	% BSA with PsO	16.6 (13.5)	14.8 (11.7)
	<10%	36%	37%
	≥10%	64%	63%
	IGA score		
	Moderate (3)	74%	71%
	Severe (4)	22%	21%
	PASI (0–72)	14.6 (7.6)	14.0 (7.0)
Prior treatment for PsO			
	Phototherapy (PUVA and UVB)	43%	31%
	Systemic therapy[b]	73%	73%
	Biologic therapy[c]	34%	31%

Data shown are mean (SD), unless otherwise indicated. [a]ICO: N=203; PBO: N=101. [b]Conventional nonbiologic systemics, novel nonbiologic systemics, 1,25-vitamin D3 and analogues, phototherapy, and biologics. [c]Adalimumab, alefacept, briakinumab, brodalumab, certolizumab pegol, efalizumab, etanercept, guselkumab, infliximab, ixekizumab, natalizumab, risankizumab, secukinumab, tildrakizumab, and ustekinumab. [d]Among the pts who discontinued treatment through W16 (ICO: n=8 [4%]; PBO: n=9 [9%]), the most common reasons for discontinuation were lack of efficacy and AEs in the ICO group (n=3 [1%] for each) and lack of efficacy in the PBO group (n=5 [5%]). **AEs**=Adverse events, **BMI**=Body mass index, **BSA**=Body surface area, **ICO**=Icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=Placebo, **Pts**=Participants, **PsO**=Psoriasis, **PUVA**=Psoralen plus ultraviolet A, **QD**=Once daily, **SD**=Standard deviation, **UVB**=Ultraviolet B, **W**=Week

ICO demonstrated significantly higher rates of IGA 0/1 vs PBO at W16 (primary endpoint)

- Significantly higher proportions of ICO-treated pts reported meaningful improvement in itch (Clinically meaningful improvement [CMI] Psoriasis Symptom and Sign Diary [PSSD] Itch,[a,b] 60% vs 14%; *P*<0.001) and symptom resolution at W16 (PSSD Symptom 0,[a,b] 16% vs 3%; *P*<0.01)

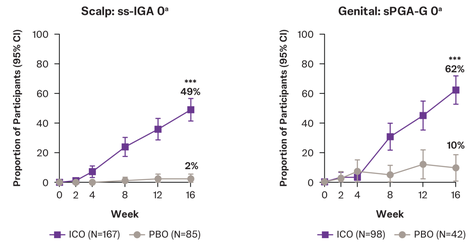


***Multiplicity-adjusted *P*<0.001 vs PBO[b]

[a]Among pts with a baseline PSSD Itch score ≥4 or PSSD Symptom score >0. [b]*P* values were based on Cochran-Mantel-Haenszel chi-square test stratified by high-impact site involvement and BSA category, if applicable. [c]Treatment difference and 95% CI (using Miettinen-Nurminen method) were calculated adjusting for high-impact site involvement and BSA category using Mantel-Haenszel weights. **BSA**=Body surface area, **CI**=Confidence interval, **ICO**=Icotrokinra, **IGA**=Investigator's Global Assessment, **PBO**=Placebo, **PSSD**=Psoriasis Symptom and Sign Diary, **Pts**=Participants

ICO demonstrated higher rates of completely clear scalp and genital PsO vs PBO

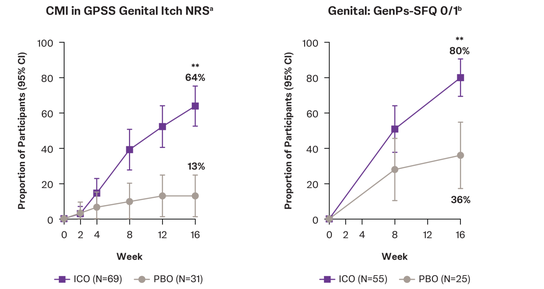
- A numerically greater proportion of ICO-treated pts achieved hf-PGA 0[a] vs PBO at W16 (25% vs 13%)



***Nominal *P*<0.001 vs PBO[b]

[a]Among pts with a baseline ss-IGA score, sPGA-G score, or hf-PGA score ≥3. [b]*P* values were based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region and/or BSA category. **BSA**=Body surface area, **CI**=Confidence interval, **ICO**=Icotrokinra, **hf-PGA**=Physician's Global Assessment of hands and feet, **ss-IGA**=Scalp-specific Investigator's Global Assessment, **sPGA-G**=Static Physician's Global Assessment of Genitalia, **PBO**=Placebo, **Pts**=Participants

ICO significantly improved pt-reported genital PsO itch & impact of PsO on sexual activity vs PBO



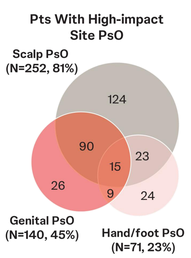
**Multiplicity-adjusted *P*<0.01 vs PBO[c]

[a]Among pts with a baseline GPSS Genital Itch NRS score (Item 1) ≥4 and a sPGA-G score ≥3. [b]Among pts with a baseline GenPs-SFQ score (Item 2) ≥2 and a sPGA-G score ≥3. [c]*P* values were based on Cochran-Mantel-Haenszel chi-square test stratified by BSA category. **BSA**=Body surface area, **CI**=Confidence interval, **CMI**=Clinically meaningful improvement (≥4-point improvement from baseline), **GenPs-SFQ**=Genital Psoriasis Sexual Frequency Questionnaire, **GPSS**=Genital Psoriasis Symptoms Score, **ICO**=Icotrokinra, **NRS**=Numeric rating scale, **PBO**=Placebo, **Pts**=Participants, **sPGA-G**=Static Physician's Global Assessment of Genitalia

Scalp and genital PsO severity at baseline was generally similar between groups

- Among the limited subset of pts with hf-PGA score ≥3, a higher proportion in the ICO group had severe involvement vs PBO
- 44% of pts had >1 high-impact site involved

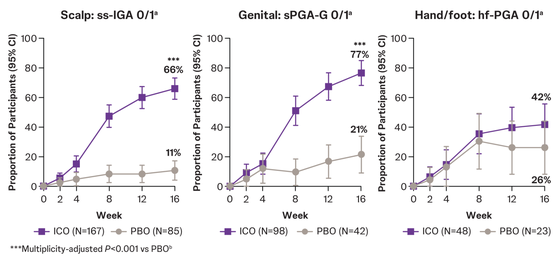
High-impact Site PsO Severity[a]		ICO 200 mg QD (N=208)	PBO (N=103)
ss-IGA score ≥3		167 (80%)	85 (83%)
	Moderate (3)	80%	75%
	Severe (4)	20%	25%
sPGA-G score ≥3		98 (47%)	42 (41%)
	Moderate (3)	77%	69%
	Severe (4)	22%	29%
	Very severe (5)	1%	2%
hf-PGA score ≥3		48 (23%)	23 (22%)
	Moderate (3)	65%	83%
	Severe (4)	35%	17%



Data shown are n (%), unless otherwise indicated. [a]PsO involving high-impact sites was not mutually exclusive. **hf-PGA**=Physician's Global Assessment of hands and feet, **ICO**=Icotrokinra, **PBO**=Placebo, **PsO**=Psoriasis, **Pts**=Participants, **QD**=Once daily, **ss-IGA**=Scalp-specific Investigator's Global Assessment, **sPGA-G**=Static Physician's Global Assessment of Genitalia

ICO demonstrated significantly higher rates of clear/almost clear scalp and genital PsO vs PBO

- A numerically greater proportion of ICO-treated pts achieved hf-PGA 0/1 vs PBO at W16

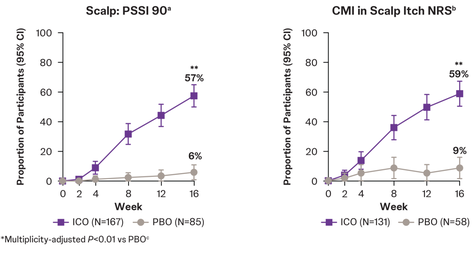


***Multiplicity-adjusted *P*<0.001 vs PBO[b]

[a]Among pts with a baseline ss-IGA score, sPGA-G score, or hf-PGA score ≥3. [b]*P* values were based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region and/or BSA category. **BSA**=Body surface area, **CI**=Confidence interval, **hf-PGA**=Physician's Global Assessment of hands and feet, **ICO**=Icotrokinra, **ss-IGA**=Scalp-specific Investigator's Global Assessment, **sPGA-G**=Static Physician's Global Assessment of Genitalia, **PBO**=Placebo, **Pts**=Participants

ICO demonstrated significantly higher rates of scalp clearance and meaningful improvement in scalp itch vs PBO

- ICO demonstrated early separation from PBO



**Multiplicity-adjusted *P*<0.01 vs PBO[c]

[a]Among pts with a baseline ss-IGA score ≥3. [b]Among pts with a baseline Scalp Itch NRS score ≥4 and a ss-IGA score ≥3. [c]*P* values were based on Cochran-Mantel-Haenszel chi-square test stratified by geographic region and BSA category. **BSA**=Body surface area, **CMI**=Clinically meaningful improvement (≥4-point improvement from baseline), **CI**=Confidence interval, **ICO**=Icotrokinra, **NRS**=Numeric rating scale, **PBO**=Placebo, **PSSI**=Psoriasis Scalp Severity Index, **PSSI 90**=Reduction from baseline of ≥90% in the PSSI score, **Pts**=Participants, **ss-IGA**=Scalp-specific Investigator's Global Assessment

Adverse event rates were generally similar between groups through W16

	ICO 200 mg QD (N=208)	PBO (N=103)
Safety through W16		
Mean weeks of follow-up	16.0	15.7
Any AE	104 (50%)	43 (42%)
Most common AEs (≥5%)		
Nasopharyngitis	26 (12%)	11 (11%)
Upper respiratory tract infection	9 (4%)	5 (5%)
Headache	6 (3%)	6 (6%)
SAE[a]	1 (<1%)	2 (2%)
Infection	59 (28%)	22 (21%)
Serious infection	0	1 (1%)
AE leading to discontinuation[b]	4 (2%)	3 (3%)
Gastrointestinal AEs	15 (7%)	8 (8%)
Active TB	0	0
Malignancy[c]	1 (<1%)	0

[a]SAEs through W16 included COVID-19 pneumonia, sepsis, sciatica, and acute respiratory failure in the PBO group; and hepatitis in the ICO group. [b]AEs leading to discontinuation through W16 included COVID-19 pneumonia, psoriatic arthropathy, and psoriasis in the PBO group; and vision blurred, visual field defect, laryngitis fungal, malignant melanoma in situ, and headache in the ICO group. [c]Malignancy reported in the ICO group was malignant melanoma in situ in a pt with a recent personal history of melanoma (in 2021). **AE**=Adverse event, **COVID-19**=Coronavirus disease 2019, **ICO**=Icotrokinra, **PBO**=Placebo, **Pt**=Participant, **QD**=Once daily, **SAE**=Serious adverse event, **TB**=Tuberculosis, **W**=Week

PRESENTED AT: Elevate-Derm Summer Conference 2025; Park City, UT, USA; July 23–27, 2025. **REFERENCES: 1.** Fourie AM, et al. *Sci Rep*. 2024;14:17515. **2.** Bissonnette R, et al. *N Engl J Med*. 2024;390:510-21. **3.** Ferris LK, et al. *J Am Acad Dermatol*. 2025;92:495-502. **4.** Bissonnette R, et al. Presented at: AAD Annual Meeting; March 8, 2025; Orlando, FL, USA. **ACKNOWLEDGMENTS:** Medical writing support was provided by R. Contento, PharmD of Johnson & Johnson, under the direction of the authors in accordance with Good Publication Practice guidelines (*Ann Intern Med*. 2022;175:1298-1304). Layout design and reformatting for this encore presentation was provided by Ganesh Karpe SIRO Medical Writing Pvt Ltd, Thane, Maharashtra, India (funded by Johnson & Johnson). This presentation was sponsored by Johnson & Johnson. **DISCLOSURES: MJG:** served as a speaker, investigator, or advisory board member for AbbVie, Acelyrin, Akros, Alumis, Amgen, AnaptysBio, Apogee, Arcutis, Arena, Aslan, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Coherus, Dermavant, Dermira, Eli Lilly, Galderma, GlaxoSmithKline, Incyte, Inmagene, JAMP Pharma, Johnson & Johnson, Kyowa Kirin, LEO Pharma, Medimmune, Merck, Moonlake, Nimbus, Novartis, Pfizer, Regeneron, Reistone, Sanofi Genzyme, Sun Pharma, Takeda, Tarsus, UCB, Union, and Vyne. **EL:** served as a speaker, consultant, advisory board member, or principal investigator for AbbVie, Aslan, Biofrontera, Caliway, Cassiopeia, Castle Biosciences, Concert, Celldex, Eli Lilly, Evommune, Galderma, Incyte, Johnson & Johnson, L'Oreal, Nielsen BioSciences, Peregrine Ophthalmic, Pfizer, Regeneron, RegenX Science, Sanofi, Symatese, Takeda, Teoxane, UCB, Verademics, and Vyne. **RB:** served as an advisory board member, consultant, speaker, and/or investigator for and received honoraria and/or grants from AbbVie, Alumis, Amgen, AnaptysBio, Arcutis, BMS/Celgene, Dermavant, Eli Lilly, Johnson & Johnson, LEO Pharma, Nimbus, Takeda, UCB, VentyxBio, Vyne, Xencor, Zai Lab, and Zurabio; and is an employee and shareholder of Innovaderm Research. **Y-HH:** served as an investigator and/or consultant for AbbVie, Bristol Myers Squibb, Celgene, Johnson & Johnson, Novartis, and Pfizer. **CL:** served as a speaker and/or consultant and/or principal investigator for AbbVie, Acelyrin, Akros, Altius, Amgen, Apogee, Aralez, Arcutis, Avillion, Bausch Health, Bayer, Bioderma, BioJAMP, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celldex, Celltrion, CeraVe, Cipher, Concert, Dermavant, Dermira, Devonian, DICE, Eli Lilly, Evelo, Fresnius Kabi, Galderma, GlaxoSmithKline, Incyte, Innovaderm, Intega Skin, Johnson & Johnson, Kyowa Kirin, La Roche Posay, LEO Pharma, L'Oreal, Medexus, MedX, Merck, MoonLake, Naos, Nektar, Nimbus, Novartis, Organon, Orukai, P&G, Pediapharm, Pfizer, Regeneron, Roche, Sandoz, Sanofi Genzyme, Searchlight Pharma, Sentrex, SkinCeuticals, Sun Pharma, Takeda, UCB, Viatris, Volo Health, and Vyne. **MH:** served as an advisory board member, consultant, speaker, and/or investigator for and/or received honoraria and/or grants from AbbVie, Almirall, Biofrontera, Bristol Myers Squibb, Dermapharm, Dermasence, Forward, Galderma, Incyte, Johnson & Johnson, Kiniksa, LEO Pharma, Eli Lilly, L'Oréal, MSD, Nektar, Novartis, Pierre Fabre, Pfizer, Sanofi, Schering-Plough, Smerud Medical Research, Stallergenes Greer, Viatris, and UCB. **EJS:** served as an investigator, consultant, and/or speaker for AbbVie, Acelyrin, Alphyn, Alumis, Amgen, Apogee, Arcutis, Aslan, Boehringer Ingelheim, Bristol Myers Squibb, CorEvitas, Dermavant, DermBiont, Eli Lilly, Galderma, Incyte, Johnson & Johnson, LEO Pharma, Moonlake, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, TARGET PharmaSolutions, TIMBER, and UCB. **JHB, AMD,** and **M-CH:** employees of Johnson & Johnson; employees may own stock/stock options in Johnson & Johnson. **RBW:** served as a consultant and/or speaker for AbbVie, Almirall, Alumis, Amgen, Apogee, Arena, Astellas, Avillion, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, DICE Therapeutics, Eli Lilly, Galderma, GlaxoSmithKline, Johnson & Johnson, LEO Pharma, Meiji Pharma, Nektar, Novartis, Pfizer, RAPT Pharmaceuticals, Sanofi, Sitryx, Sun Pharma, UCB, and UNION; and has received research grants from AbbVie, Almirall, Amgen, Celgene, Eli Lilly, Johnson & Johnson, LEO Pharma, Novartis, Pfizer, and UCB. **PREVIOUSLY PRESENTED AT:** SID Annual Meeting; San Diego, CA, USA; May 7–10, 2025.

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CSU Disease Activity Band Shift after Long-Term Treatment With Remibrutinib in the Phase 3 REMIX-1 and REMIX-2 Studies

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KEY FINDINGS & CONCLUSIONS

- Remibrutinib **reduced CSU disease activity** as early as **week 1** in patients with CSU, and the **fast response** was **sustained** over **long-term** treatment for **52 weeks**
- Of note, treatment transition from placebo to remibrutinib resulted in **similar fast improvements, with well-controlled and complete response levels being comparable to remibrutinib patients** at **week 52**
- Remibrutinib has the potential to become a novel oral treatment option that provides **fast (as early as week 1)** and **sustained improvements** in disease activity in patients with **CSU**

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Originally presented as a poster presentation at the European Academy of Dermatology and Venereology (EADV 2024), September 25–28, 2024, Amsterdam, Netherlands.

Poster presented at the Elevate-Derm Summer Conference, July 23–27, 2025, Park City, UT.

INTRODUCTION

- Remibrutinib, a novel, highly selective, oral, Bruton's tyrosine kinase inhibitor, has previously shown superior efficacy versus placebo at week 12 and a favorable safety profile in the 24-week double-blind period of the pivotal phase 3 REMIX-1 and REMIX-2 studies in patients with chronic spontaneous urticaria (CSU) who remained symptomatic despite treatment with second-generation H1-antihistamines[1]
- In a previously presented REMIX analysis up to week 24, a reduction in CSU disease activity was observed as early as week 1 with remibrutinib, sustained up to 24 weeks of treatment in the target population of patients with moderate to severe CSU disease activity at baseline[2]

OBJECTIVE

- The objective of this analysis was to explore the shift in weekly Urticaria Activity Score (UAS7) bands after treatment with remibrutinib versus placebo up to week 52 on a patient level in the REMIX studies

METHODS

Study Design

- REMIX-1 and REMIX-2 are two identical, global, double-blind, placebo-controlled phase 3 studies of remibrutinib 25 mg twice daily (bid) administered orally
- Adult patients with CSU who remained symptomatic despite treatment with second-generation antihistamines were randomized 2:1 to oral remibrutinib 25 mg bid or placebo for 24 weeks, followed by an open-label treatment with remibrutinib 25 mg bid for 28 weeks (patients on placebo transitioned to remibrutinib at week 24)[1]

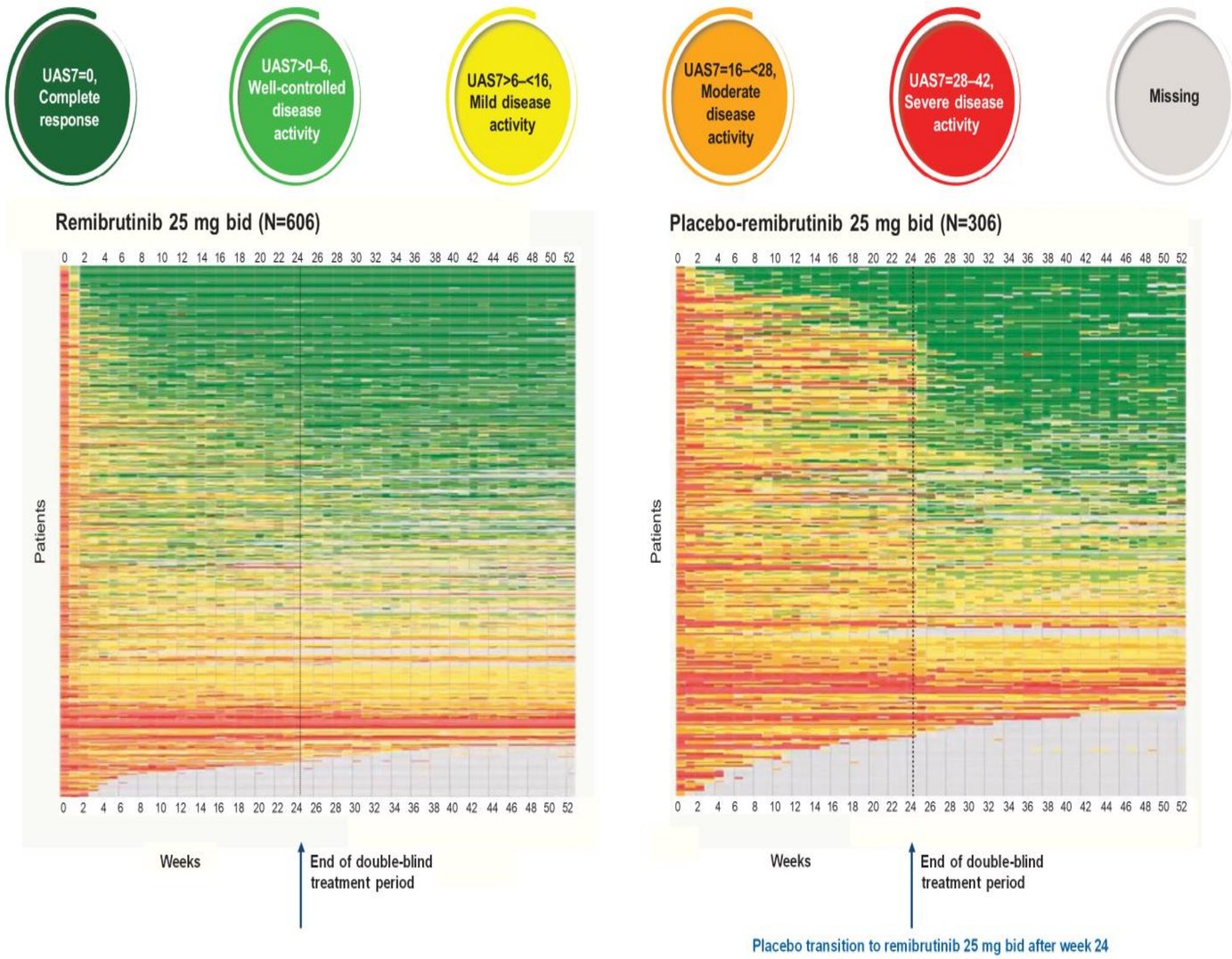
Study Assessments and Data Analysis

- CSU disease activity was categorized into five bands, based on UAS7 (**Figure**)
- This post hoc analysis assessed the proportion of patients who experienced a shift in CSU disease activity from baseline to week 52 after treatment
- In addition, patients' individual UAS7 band shifts per week, up to week 52, were visualized in swimmer plots. Each patient is represented by a horizontal line, with each UAS7 band achievement represented by a color, as indicated in the **Figure**

RESULTS

- This pooled analysis included randomized patients who received at least one dose of **remibrutinib 25 mg bid** (**N=606**) or **placebo** for 24 weeks (**N=306**) in the **REMIX-1 and REMIX-2 studies**
- Disease severity at baseline was similar among patients in the remibrutinib and placebo treatment arms; **215** (**35.5%**) and **386** (**63.7%**) patients from the **remibrutinib** arm and **122** (**39.9%**) and **181** (**59.2%**) from the **placebo** arm had **moderate** and **severe** CSU disease activity, respectively
- Overall, patients treated with **remibrutinib** vs **placebo** experienced substantial improvements in CSU disease activity and moved to a **lower disease activity band** as early as **week 1,** with more patients remaining in lower disease activity bands up to **week 24** (**Figure**)
  - Patients on placebo **transitioned** to **remibrutinib 25 mg bid** after **week 24** and moved to a **lower disease activity band** as early as **week 1** after the transition and remained in the lower disease activity bands up to week 52, in line with patients who were on remibrutinib throughout (**Figure**)
- In the remibrutinib treatment arm, while **63.7% of patients** were in the **severe band** at baseline, the number dropped to **24.9%, 17.2%, 9.1%, 7.8%** and **8.1%** at **weeks 1, 2, 12, 24** and **52,** respectively
- Similarly, of the **35.5%** of patients in the **moderate** band at baseline, the number dropped to **30.7%, 24.1%, 10.6%, 7.9%** and **7.3%** at **weeks 1, 2, 12, 24** and **52**, respectively
- There were no patients in the **well-controlled** and **complete response** disease bands at baseline; however, the numbers for the **well-controlled** (UAS7≤6) and **complete response** (UAS7=0) groups combined increased with remibrutinib vs placebo to **11.7%** (71/606) **vs 0.7%** (2/306) and **31.5%** (191/606) vs **4.2%** (13/606) at **weeks 1** and **2**, consistently improving up to **week 24** (**48.5%** [294/606] vs **28.4%** [87/306])
  - Notably, the proportion of patients receiving remibrutinib who **showed complete response increased** from **0.3%** at **week 1** to **16.2%** at **week 2**, with continued improvements up to **week 52** (**35.1%**)
  - By the **end of week 52**, patients who had **transitioned to remibrutinib** from placebo, after **week 24**, had achieved similar band shifts as patients who had been on remibrutinib for 52 weeks

Figure. Swimmer plot of the disease activity band shift based on UAS7 scores from baseline to week 52 (pooled full analysis set; observed data)



Each patient is represented by a horizontal line. bid, twice daily; N, number of patients; UAS7, weekly Urticaria Activity Score.

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REMIX-1/-2: Early Symptom Improvements With Remibrutinib in Chronic Spontaneous Urticaria From Week 1

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KEY FINDINGS & CONCLUSIONS

- In REMIX-1 and REMIX-2, fast and significant improvements in CSU symptoms of itch and hives vs placebo were observed as early as week 1, with further improvements through week 24
- Likewise, ≥50% of patients with CSU achieved MID for UAS7, ISS7, and HSS7, by weeks 1 to 2 of treatment with remibrutinib
- A limitation of the study is that post hoc analyses were used which may introduce biases from selective data analysis
- Overall, remibrutinib has the potential to become a novel oral treatment option with an early onset of response in patients with CSU inadequately controlled by H_1-AH

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Originally presented as a poster presentation at American College of Allergy, Asthma & Immunology (ACAAI) Annual Scientific Meeting, November 9–13, 2023, Anaheim, CA.
Poster presented at the Elevate-Derm Summer Conference, July 23–27, 2025, Park City, UT.

INTRODUCTION

- CSU is a disease which is characterized by the spontaneous appearance of itchy wheals, angioedema, or both, lasting ≥6 weeks and can substantially impact patients' well-being[1–3]
- First-line treatment involves second-generation H_1-AHs; however over 50% of patients do not achieve symptom control with H_1-AHs alone[1,5,6]
- Remibrutinib is a novel, oral, highly selective BTK inhibitor that prevents mast cell–mediated release of histamine and other proinflammatory mediators[4,7,8]
  - Remibrutinib has shown superior efficacy vs placebo in symptom improvement after 12 weeks of treatment in patients with CSU[4]
- A UAS7 decrease of 9.5–10.5 points is commonly considered to indicate the MID[9]
- The objective of this analysis was to assess early treatment responses with remibrutinib vs placebo in the phase 3 REMIX-1 (NCT05030311) and REMIX-2 (NCT05032157) studies

METHODS

- REMIX-1 and REMIX-2 are multicenter, randomized, double-blind, parallel-arm, placebo-controlled phase 3 studies investigating the safety and efficacy of remibrutinib administered orally
- Patients were randomized 2:1 to remibrutinib 25 mg twice daily, or to placebo, for 24 weeks (**Figure 1**)
- In this analysis, LS mean CFB in weekly UAS7, ISS7, and HSS7 was assessed at weeks 1, 2, 4, 12, and 24 (weeks 1, 2, and 4 were post hoc analyses)
  - A higher score reflects higher disease activity
- The onset of action of remibrutinib was explored post hoc in terms of early achievement of MID in CSU disease activity, defined as a change in score of ≥10.5 for UAS7, ≥5.0 for ISS7, and ≥5.5 for HSS7[9]
- Data were analyzed using summary statistics, and MMRM was used for the analysis of CFB

Figure 1. Study Design for REMIX-1 and REMIX-2 Studies

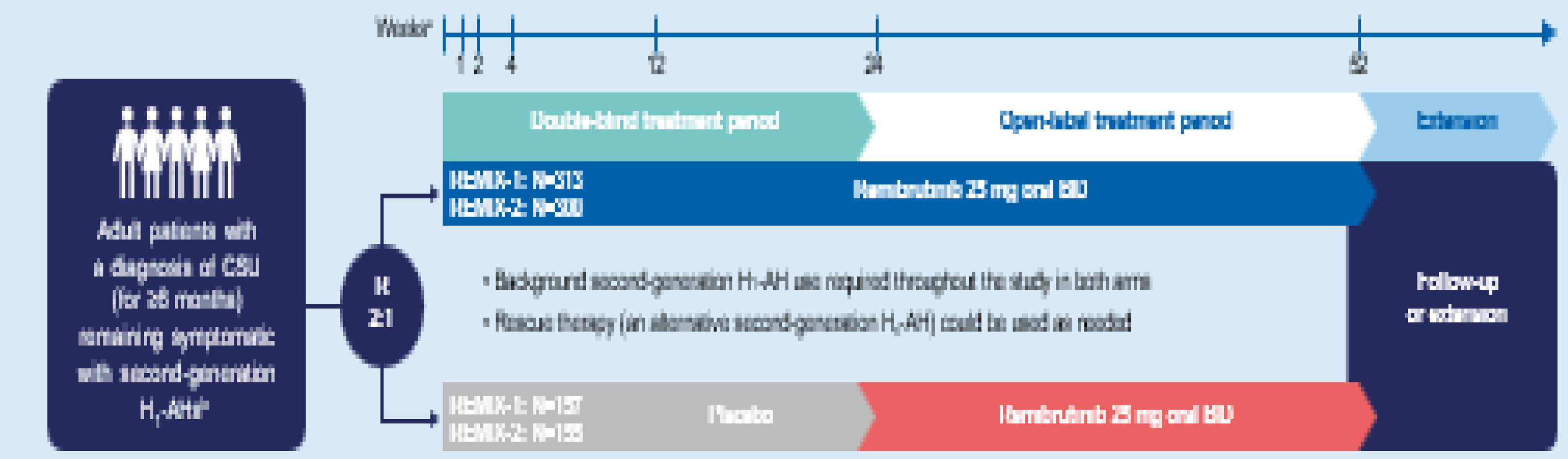


Figure originally presented at the American College of Allergy, Asthma & Immunology (ACAAI) Annual Scientific Meeting 2023.
[a]UAS7, ISS7, and HSS7 scores were collected weekly and analyzed at weeks 1, 2, 4, 12, and 24.
[b]Presence of itch and hives for ≥6 consecutive weeks prior to screening despite the use of a second-generation H_1-AH; UAS7 score ≥16, ISS7 score ≥6, and HSS7 score ≥6 during the 7 days prior to randomization (day 1).
BID, twice daily; CSU, chronic spontaneous urticaria; H_1-AH, histamine 1-antihistamine; HSS7, weekly hives severity score; ISS7, weekly itch severity score; R, randomized; UAS7, weekly urticaria activity score.

RESULTS

- Overall, 470 patients were randomized in REMIX-1 (remibrutinib, n=313; placebo, n=157) and 455 patients in REMIX-2 (remibrutinib, n=300; placebo, n=155) (**Table 1**)

Demographics and Clinical Characteristics

- Patient demographics and baseline characteristics were well balanced between treatment arms in REMIX-1 and REMIX-2 (**Table 1**)
  - Baseline weekly UAS7, ISS7, and HSS7 were similar between remibrutinib and placebo in REMIX-1 and REMIX-2

Table 1. Patient Disposition and Baseline Characteristics (Randomized Set)[10]

	REMIX-1			REMIX-2		
	Remibrutinib 25 mg BID (n=313)	Placebo (n=157)	Total (N=470)	Remibrutinib 25 mg BID (n=300)	Placebo (n=155)	Total (N=455)
Patient disposition, n (%)						
Completed double-blind treatment period (24 weeks)	270 (86.3)	134 (85.4)	404 (86.0)	259 (86.3)	129 (83.2)	388 (85.3)
Baseline characteristics						
Age (years), mean ± SD	44.6 ± 14.3	45.9 ± 13.4	45.0 ± 14.0	41.9 ± 14.5	41.3 ± 14.6	41.7 ± 14.5
Gender (female), n (%)	212 (67.7)	109 (69.4)	321 (68.3)	197 (65.7)	100 (64.5)	297 (65.3)
BMI (kg/m²), mean ± SD	27.8 ± 6.4	28.3 ± 6.5	28.0 ± 6.4	27.0 ± 6.5	27.0 ± 5.9	27.0 ± 6.3
Duration of CSU (years), mean ± SD	6.9 ± 9.3	6.1 ± 7.1	6.6 ± 8.6	5.5 ± 7.6	4.6 ± 6.2	5.2 ± 7.2
Baseline disease severity						
UAS7, mean ± SD	30.6 ± 7.9	29.6 ± 7.7	30.3 ± 7.9	30.2 ± 8.0	29.5 ± 7.6	30.0 ± 7.9
ISS7, mean ± SD	14.7 ± 4.2	14.3 ± 4.0	14.6 ± 4.2	14.3 ± 4.4	13.9 ± 4.1	14.2 ± 4.3
HSS7, mean ± SD	15.9 ± 4.6	15.3 ± 4.6	15.7 ± 4.6	15.9 ± 4.6	15.7 ± 4.5	15.8 ± 4.6

BID, twice daily; BMI, body mass index; CSU, chronic spontaneous urticaria; HSS7, weekly hives severity score; ISS7, weekly itch severity score; UAS7, weekly urticaria activity score; SD, standard deviation.

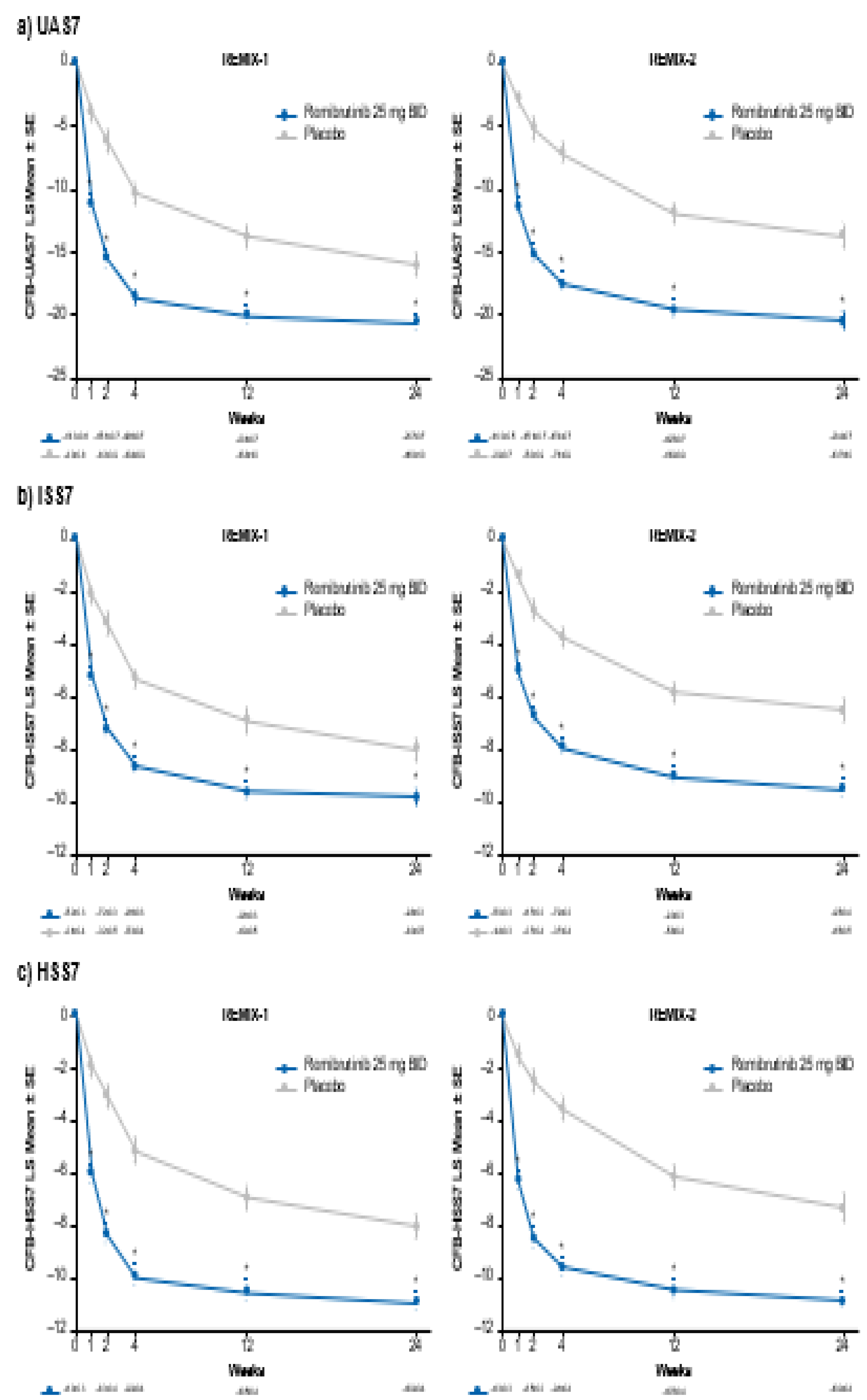
Change From Baseline in UAS7, ISS7, and HSS7, Week 1 to Week 24

- The full analysis set included 462 and 450 patients randomized in REMIX-1 and REMIX-2, respectively
- Remibrutinib showed significant improvements vs placebo in LS mean (±SE) CFB-UAS7 as early as week 1 (**Figure 2**)
  - REMIX-1: −11.3 ± 0.6 vs −4.0 ± 0.8 (P<0.001)
  - REMIX-2: −11.3 ± 0.5 vs −2.9 ± 0.7 (P<0.001)
- Significant improvements were also shown in LS mean (±SE) CFB-ISS7 and CFB-HSS7 from week 1 (**Figure 2**)
  - CFB-ISS7:
    - REMIX-1: −5.2 ± 0.3 vs −2.1 ± 0.4 (P<0.001)
    - REMIX-2: −5.0 ± 0.3 vs −1.4 ± 0.3 (P<0.001)
  - CFB-HSS7:
    - REMIX-1: −6.0 ± 0.3 vs −1.9 ± 0.4 (P<0.001)
    - REMIX-2: −6.3 ± 0.3 vs −1.5 ± 0.4 (P<0.001)
- Improvements in LS mean (±SE) UAS7, ISS7, and HSS7 were further improved and maintained to week 24 with remibrutinib (**Figure 2**)

MID of UAS7, ISS7, and HSS7 at Week 1

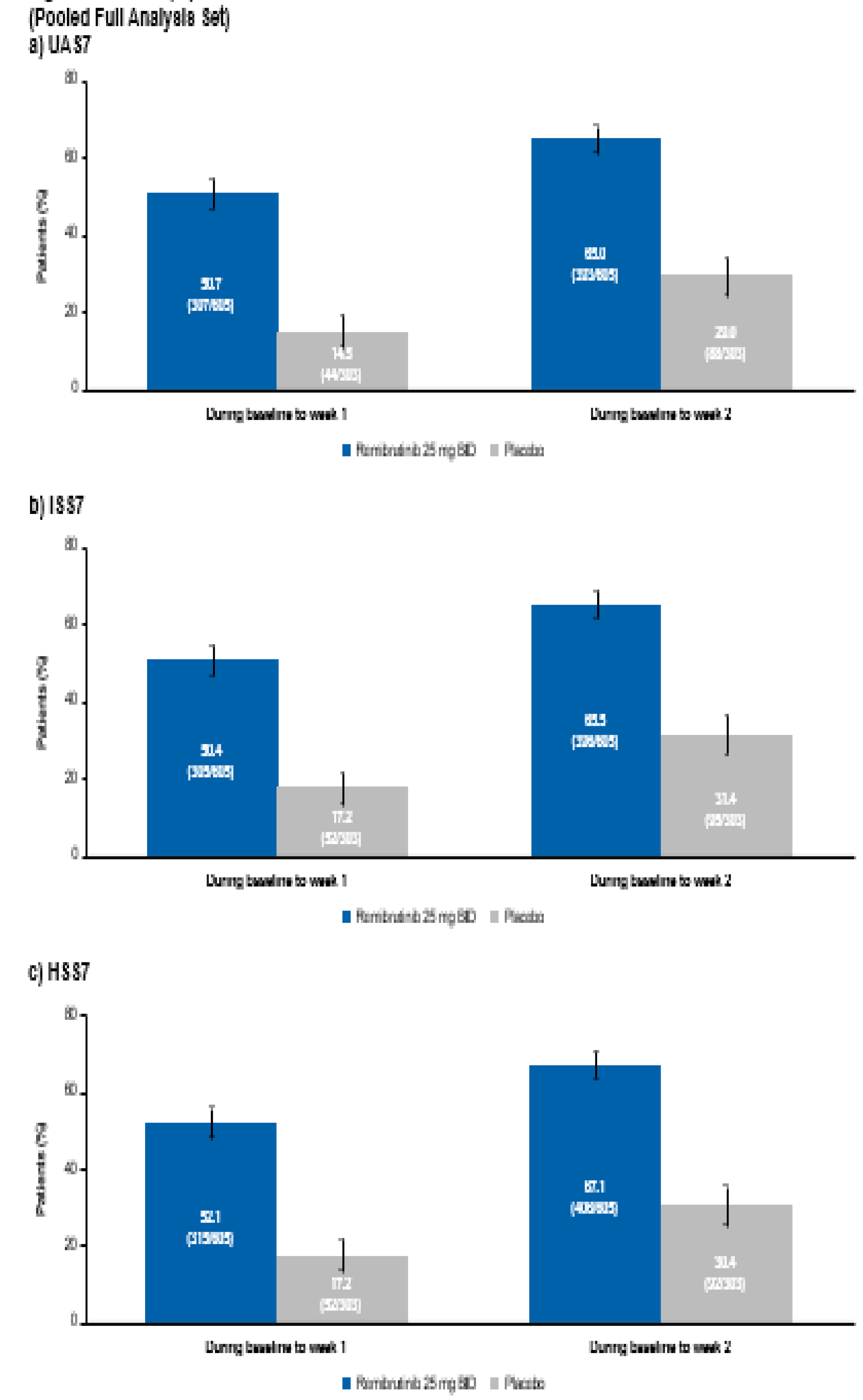
- The number of patients who achieved MID in disease activity for UAS7, ISS7, and HSS7 is displayed in **Figure 3**
- A higher proportion of patients on remibrutinib compared with placebo achieved improvements in UAS7, ISS7, and HSS7 by week 1 (50.7% vs 14.5%; 50.4% vs 17.2%; 52.1% vs 17.2%), indicating early onset of action of remibrutinib

Figure 2. Improvement Over Time in UAS7, ISS7, and HSS7 Change From Baseline (Full Analysis Set)



Imputed data.
*There was a statistically significant difference in LS mean CFB between remibrutinib and placebo at weeks 1, 2, 4, 12, and 24 (P<0.001).
BID, twice daily; CFB, change from baseline; HSS7, weekly hives severity score; ISS7, weekly itch severity score; LS, least squares; SE, standard error; UAS7, weekly urticaria activity score.

Figure 3. Number (%) of Patients Who Achieved MID for UAS7, ISS7, and HSS7 at Week 1 and Week 2 (Pooled Full Analysis Set)



Observed data. MID was defined as a change in score of ≥10.5 for UAS7, ≥5.0 for ISS7, and ≥5.5 for HSS7; only the first occurrence was considered here. Error bars represent 95% CI.
BID, twice daily; CI, confidence interval; HSS7, weekly hives severity score; ISS7, weekly itch severity score; MID, minimum important difference; UAS7, weekly urticaria activity score.

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Abbreviations

BID, twice daily; BMI, body mass index; BTK, Bruton's tyrosine kinase; CFB, change from baseline; CI, confidence interval; CSU, chronic spontaneous urticaria; H_1-AH, histamine 1-antihistamine; HSS7, weekly hives severity score; ISS7, weekly itch severity score; LS, least squares; MID, minimum important difference; MMRM, mixed models for repeated measures; R, randomized; SD, standard deviation; SE, standard error; UAS7, weekly urticaria activity score.

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Impact of Chronic Spontaneous Urticaria on Health-Related Quality of Life Domains: Country-Specific Data from Patients Participating in the Urticaria Voices Study

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KEY FINDINGS & CONCLUSIONS

- The majority of patients report ongoing symptomatic disease despite treatment
- Most patients received H1-AH therapy, of whom 84% reported inadequate CSU control, measured by UCT score
- Across countries, patients with CSU report high levels of negative impact across HRQoL domains, with mental and emotional well-being were most consistently ranked as being negatively impacted
- Patients in most countries (except Japan) sought additional services (e.g. dietetics, psychology and homeopathy) in an effort to manage their disease
- New treatments effectively alleviating the burden of CSU symptoms are required to support patients, general and mental well-being

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This study was sponsored by Novartis Pharma AG, Basel, Switzerland.

Originally presented as a poster presentation at the European Academy of Dermatology and Venereology (EADV 2024), September 25–28, 2024, Amsterdam, Netherlands.

Poster presented at the Elevate-Derm Summer Conference, July 23–27, 2025, Park City, UT.

INTRODUCTION

- Chronic spontaneous urticaria (CSU) is characterized by itch, hives and/or angioedema for more than 6 weeks[1] and can significantly impact health-related quality of life (HRQoL)[2]
- The Urticaria Voices study aimed to assess perceptions of patients with CSU and physicians treating CSU on various aspects of disease management
- We previously reported pooled data on the unmet needs of patients with CSU, burden of disease on HRQoL and worldwide patients' experiences on living with CSU from the Urticaria Voices study[3,4]

OBJECTIVE

- Herein, we report country-specific data on the impact of CSU on HRQoL domains. We also report additional services (e.g. dietician or psychological support) adopted by patients for relief from their CSU symptoms

METHODS

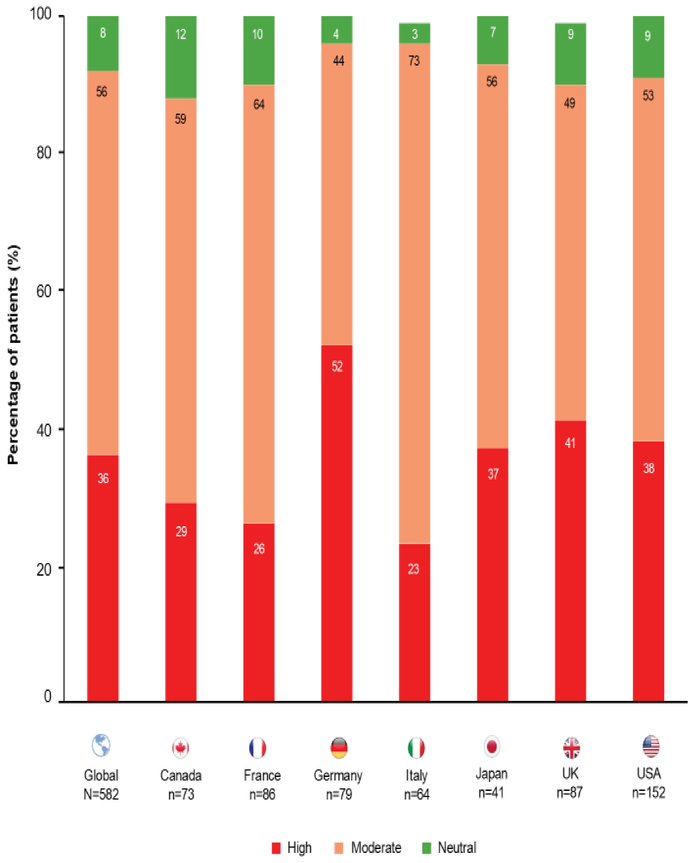
Study Design

- Urticaria Voices was designed as a global (Canada, France, Germany, Italy, Japan, the UK and USA), cross-sectional, online survey of anonymized patients with CSU and physicians treating CSU, conducted between February 2022 and September 2022
- Eligible adult patients had a self-reported clinician-provided diagnosis of CSU and were currently following a physician-prescribed treatment
- Patients provided an electronically signed informed consent before completing a 40-minute online survey, which comprised questions on socio-demographics, Urticaria Control Test (UCT) and treatments received (duration of treatment was not recorded); no patient identifiers were collected
- Patients who were recruited from the general population panel were remunerated according to fair market value, while those recruited via patient advocacy groups were not
- Data were analysed descriptively, and results are reported as % (n/N) or in terms of top 3 box, middle 4 box and bottom 3 box scores, pooled and by country

RESULTS

- Overall, 582 patients with CSU (62% female, mean [SD] age: 42 [11.9] years) participated in the study
- Of these, 79% (460/582) reported being on H1 anti-histamine (H1-AH) therapy, of whom 84% (386/460) reported inadequate control (UCT<12)
- Globally, 36% of patients reported a high negative impact of CSU on their daily life, 56% reported moderate negative impact and 8% were neutral (**Figure 1**)

Figure 1. Percentage of patients with CSU, per country, ranking a high, moderate and neutral* negative impact of CSU on their daily life



Data are presented as n (%), unless specified otherwise. Data are based on response to survey questions.

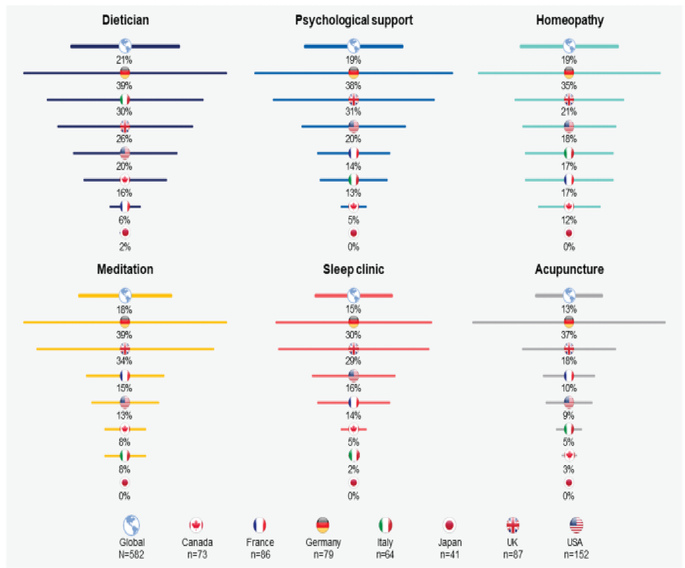
*'Top 3 box' scores refer to the percentage of patients assigning a high score of 8, 9 and 10. The 'middle 4 box' refers to the percentage of patients assigning a moderate score of 4, 5, 6 and 7 and the 'bottom 3 box' refers to the percentage of patients assigning a neutral score of 1, 2 and 3.

CSU, chronic spontaneous urticaria; N, total number of patients; n, number of patients in each subgroup.

- Globally, the negative impact of CSU (at its worst symptoms) on the mental and emotional well-being was 36%, social life and intimate relationships was 31%, activities of daily living was 29%, professional and academic life was 23%, family life and fulfilling responsibilities to others was 22%, and financial life was 20%
- At the country-level, the percentage of patients reporting negative impact of CSU (at its worst symptoms) on the HRQoL domains was evident
  - Mental and emotional well-being (ranging from 44% in Canada to 23% in Germany)
  - Social life and intimate relationships (ranging from 40% in Canada to 16% in Germany)
  - Activities of daily living (ranging from 37% in the UK to 14% in Germany)
  - Professional and academic life (ranging from 28% in the UK to 14% in Germany)
  - Family life and fulfilling responsibilities to others (ranging from 30% in the US to 9% in Germany), and
  - Financial life (ranging from 28% in Italy to 11% in Canada)
- Patients were asked questions on the several HRQoL domains, the factors that were considered to have the highest negative impact are presented in **Figure 2A**
- Globally, patients reported being negatively impacted by stress due to the spontaneous nature of CSU (37%), avoiding social interactions (31%), not being able to be intimate with their partners as frequently as they desired (24%) and being stared at in public or asked whether they were contagious (33% each; **Figure 2A**)
- Country-level data on the top concerns are presented in **Figure 2A**
- In addition to their prescribed treatments for CSU, currently, 21% (122/582) of patients consulted a dietician, 19% (111/582) reported using psychological support, 19% (108/582) reported using homeopathic therapy, 18% (104/582) reported practising meditation, 15% (90/582) consulted a sleep clinic and 13% (73/582) reported using acupuncture for relief from their CSU symptoms (**Figure 2B**)
- At the country-level, Germany reported using these additional services more frequently compared to other countries, while these reported uptake was extremely low (e.g. Japan; **Figure 2B**)

Figure 2A. Negative impact of CSU on mental and emotional well-being, social and family life, intimate relationships and discrimination and stigma – Country-specific data

Figure 2B. Percentage of patients, per country, who reported using additional services to manage their CSU in addition to their prescribed treatments



Data are presented as n (%), unless specified otherwise. Data are based on response to survey questions. CSU, chronic spontaneous urticaria; N, total number of patients; n, number of patients in each subgroup.

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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, an oral phosphodiesterase 4 inhibitor approved for the treatment of plaque psoriasis, psoriatic arthritis, and oral ulcers associated with Behçet's disease, has demonstrated significant efficacy in Japanese patients with moderate to severe PPP, and has recently been approved in the treatment of these patients in Japan[2,3]
- In a phase 3 trial (NCT05174065), apremilast 30 mg twice daily (BID) was superior to placebo, with statistically significant improvements in primary and secondary endpoints achieved at Week 16[3]

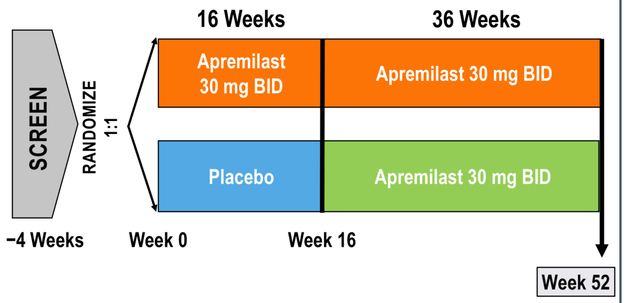
OBJECTIVE

- We report 52-week efficacy and safety from a phase 3 trial of apremilast in Japanese patients with moderate to severe PPP

METHODS

Study Schema

- **Inclusion criteria:** adults with PPP Area and Severity Index (PPPASI) total score ≥12, PPPASI pustules/vesicles severity score ≥2, and inadequate response to topicals

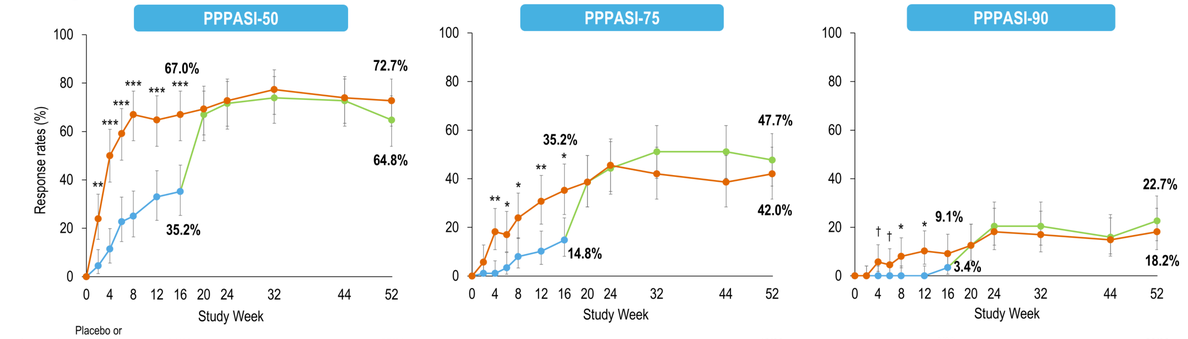


- Among 176 patients randomized (apremilast, n=88; placebo, n=88), 164 (93.2%) completed Week 52 (apremilast/apremilast, n=84 [95.5%]; placebo/apremilast, n=80 [90.9%])

RESULTS

Placebo — Apremilast — Placebo/Apremilast

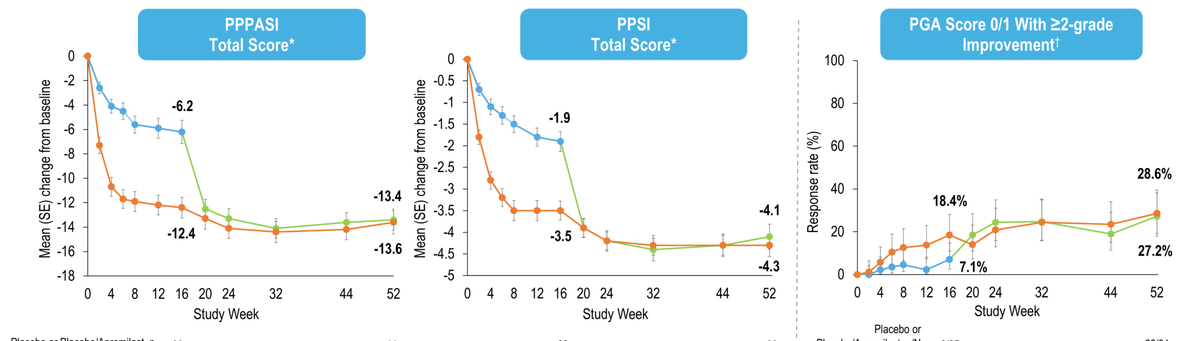
PPPASI-50, PPPASI-75, and PPPASI-90 responses at Week 16 were maintained or further improved through Week 52



Placebo or Placebo/Apremilast, n/N	31/88	57/88	13/88	42/88	3/88	20/88
Apremilast, n/N	59/88	64/88	31/88	37/88	8/88	16/88

*Nominal $P<0.01$. **Nominal $P<0.001$. ***Nominal $P\leq0.0001$. †Nominal $P<0.05$.
ITT population. Error bars 95% CI. NRI used for missing data; for patients who discontinued study drug due to lack of efficacy/adverse event or use of protocol-prohibited medication (defined as IEs) were considered nonresponders at time of IE through end of study, regardless of observed data.
n=the number of patients achieving a response; N=the number of patients analyzed.
CI, confidence interval; IE, intercurrent event; ITT, intent-to-treat; NRI, nonresponder imputation; PPPASI, Palmoplantar Pustulosis Area and Severity Index; PPPASI-50/75/90, ≥50/75/90% reduction in PPPASI total score.

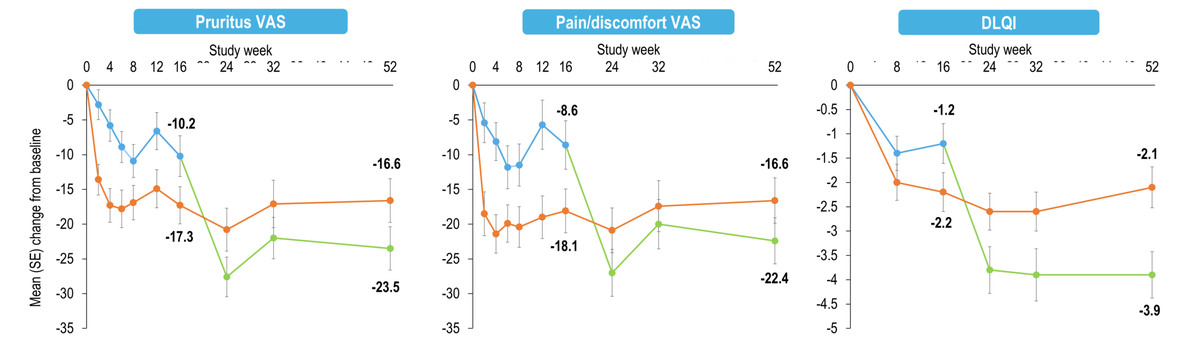
Improvements in PPPASI total score, PPSI total score, and PGA responses were maintained from Week 16 to Week 52



Placebo or Placebo/Apremilast, n/N	88	88	88	88	6/85	22/81
Apremilast, n/N	88	88	88	88	16/87	24/84

*ITT population. LOCF used for missing data; for patients who discontinued the study drug due to lack of efficacy/adverse event or use of protocol-prohibited medication (defined IEs), data from time of IE through end of study were imputed from the baseline value, regardless of observed data.
†ITT population with PGA score >1 at baseline. DAO. Error bars are 95% CI.
Left: n=the number of patients assessed. **Right**: n=the number of patients achieving a response; N=the number of patients with non-missing data.
CI, confidence interval; DAO, data as observed; IE, intercurrent event; ITT, intent-to-treat; LOCF, last observation carried forward; PGA, Physician's Global Assessment; PPPASI, Palmoplantar Pustulosis Area and Severity Index; PPSI, Palmoplantar Pustulosis Severity Index; SE, standard error.

Improvements in pruritus, pain/discomfort, and DLQI were maintained from Week 16 to Week 52



ITT population. LOCF used for missing data; for patients who discontinued the study drug due to lack of efficacy/adverse event or use of protocol-prohibited medication (defined IEs), data from time of IE through end of study were imputed from the baseline value, regardless of observed data.
DLQI, Dermatology Life Quality Index; IE, intercurrent event; ITT, intent-to-treat; LOCF, last observation carried forward; SE, standard error; VAS, visual analog scale.

Key Takeaways

- **Improvements in PPP observed with apremilast treatment at Week 16 were maintained or further improved through Week 52**
  - **These included improvements in 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**
  - **Patients who transitioned achieved response rates similar to the apremilast group by Week 20 for PPPASI and PPSI, and by Week 24 for patient-reported outcomes (the first assessment for each respective outcome after transitioning from placebo)**
- **No new safety signals were observed**

Scan the QR code for additional information on eligibility criteria and outcome measures

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Elevate-Derm Summer 2025; Park City, UT; July 23–27, 2025

The TCS/TCI-Free Rate Remains High and Stable While on Lebrikizumab for Treatment of Moderate-to-Severe Atopic Dermatitis Over 1 Year

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Sponsored by Eli Lilly and Company

OBJECTIVE

- To summarize the proportion of patients without TCS or TCI usage across the maintenance period from Week 16 to Week 52
- To assess the proportion of patients without TCS or TCI usage by study visit during the maintenance period

CONCLUSION

- Pooled ADvocate1&2 data show that 9 out of 10 Week 16 lebrikizumab respondersa did not use TCS nor TCI during the maintenance period from Week 16 to Week 52
- The proportion of patients[a] who did not use TCS nor TCI remained high and stable over the course of the maintenance period

[a] Responders achieved EASI 75 or IGA (0,1) with ≥2-point improvement at Week 16 without rescue medication use

Elevate-Derm Summer Conference, Park City, Utah, USA; July 23 - 27, 2025

BACKGROUND

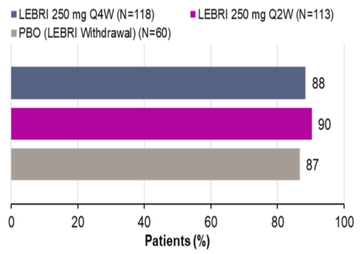
- Lebrikizumab is a novel monoclonal antibody that binds with high affinity and slow off-rate to IL-13, thereby blocking the downstream effects of IL-13 with high potency[1,2]
- ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) were 2 identically designed Phase 3, randomized, double-blind, placebo-controlled trials in patients with moderate-to-severe AD in which lebrikizumab demonstrated efficacy and safety[3,4]
  - Lebrikizumab has demonstrated clinical benefit in patients with moderate-to-severe AD after 16 and 52 weeks of treatment[3,4]
- TCS and TCI are commonly used as concomitant treatments for AD[a]
- Long-term use of TCS or TCI has challenges with large areas of BSA involvement or more diffuse involvement, and may lead to side effects[5] and increased burden[6]

[a] Intermittent TCS or TCI use was permitted in the ADvocate1&2 maintenance period

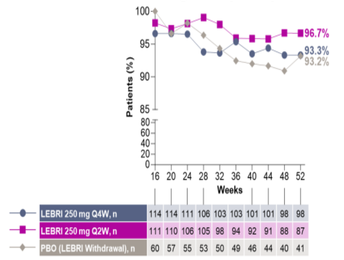
RESULTS

Most Patients[a,b] Did Not Use TCS or TCI During the Maintenance Period

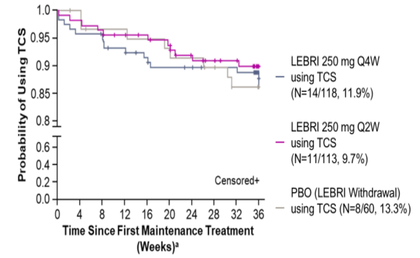
Patients[a,b] Not Using TCS Across the 36 Weeks of the Maintenance Period (Week 16 to Week 52)



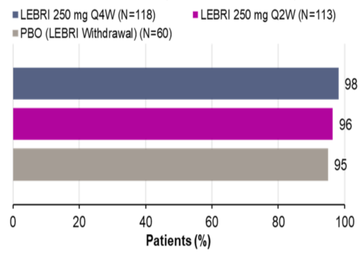
Patients[a,b] Not Using TCS by Study Visit



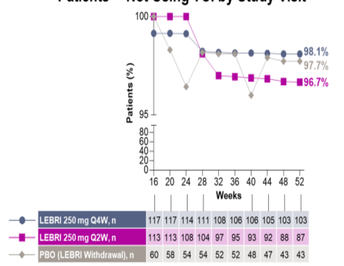
Time to First Use of TCS



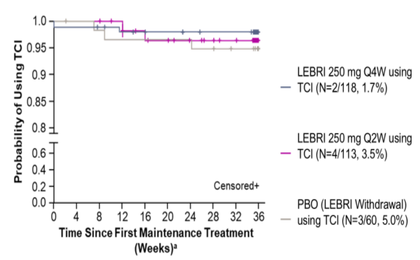
Patients[a,b] Not Using TCI Across the 36 Weeks of the Maintenance Period (Week 16 to Week 52)



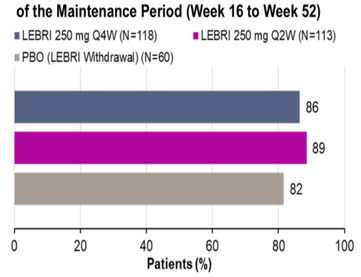
Patients[a,b] Not Using TCI by Study Visit



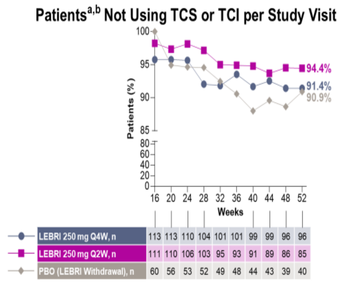
Time to First Use of TCI



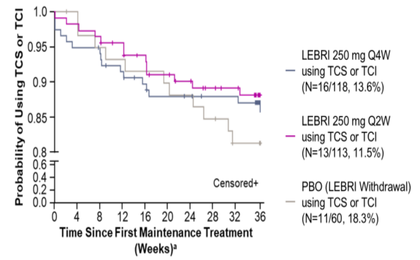
Patients[a,b] Not Using TCS or TCI Across the 36 Weeks of the Maintenance Period (Week 16 to Week 52)



Patients[a,b] Not Using TCS or TCI per Study Visit



Time to First Use of TCS or TCI

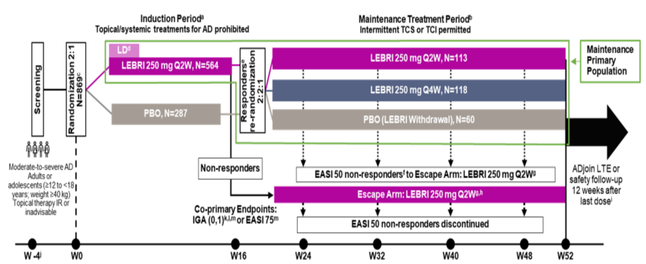


[a] In the pooled mMPP of ADvocate1&2; [b] Lebrikizumab responders who achieved EASI 75 or IGA (0,1) with ≥2-point improvement at Week 16 without rescue medication use

[a] Week 0 of the maintenance period is equivalent to Week 16 of the ADvocate 1&2 trials

METHODS

Study Design: ADvocate1 and ADvocate2



[a] Use of topical/systemic treatments for AD prohibited; [b] Use of intermittent topical rescue medications for AD permitted. Responders who received PBO during induction who were re-randomized to LEBRI received an LD of either 500 mg given at W16 or 500 mg given at W16 and W18; [c] 424 patients (ADvocate1) and 445 patients (ADvocate2) with moderate-to-severe AD; [d] 500 mg LD at W0 and W2; [e] Responders achieving EASI 75 or IGA (0,1) with ≥2-point improvement at W16, without rescue medication use; [f] Patients who did not maintain ≥EASI 50 were assigned to the Escape Arm; [g] Maintenance of response assessed by EASI 50 at W24, W32, W40, and W48, respectively. Patients who received systemic rescue medication were required to washout for 5 half-lives prior to initiating treatment in the Escape Arm.; [h] Participants who were eligible for the Escape Arm at W16 received blinded LD at W16 and W18, based on their prior treatment assignment.; [i] Patients completing ADvocate1/2 were offered treatment in ADjoin; otherwise, patients participated in a safety follow-up 12 weeks after their last dose; [j] ≤30-day Screening Period; [k] IGA (0,1) with ≥2-point improvement from baseline; [l] FDA primary endpoint; [m] EMA co-primary endpoint

Key Eligibility Criteria

- Adults or adolescents (≥12 to <18 years; weight ≥40 kg)
- Diagnosis of AD, as defined by the American Academy of Dermatology Consensus Criteria, for ≥1 year before screening
- Moderate-to-severe AD, defined as having all of the following at the baseline visit:
  - EASI ≥16
  - IGA ≥3
  - BSA involvement ≥10%
- Candidate for systemic therapy
- Biologic naïve

Analysis Population

- Pooled mMPP of ADvocate1&2[a] (lebrikizumab responders at Week 16[b]) who entered the maintenance period through Week 52
- ADvocate2 efficacy and safety analyses were performed on a modified population, excluding 17 patients who entered the maintenance period (from a single study site) whose eligibility could not be confirmed

Statistical Methodology

- The proportions of patients summarized across the maintenance period or by study visit from Week 16 to Week 52 were based on descriptive analyses of observed data, reported for patients not using TCS, TCI, or either TCS or TCI
- The time to the first use of TCS, TCI, or either TCS or TCI was analyzed using the Kaplan-Meier method, and the survival time across groups was compared with the log-rank test

[a] All patients randomly assigned to receive lebrikizumab 250 mg Q2W at baseline visit (Week 0) and also met protocol defined response criteria were re-randomized to receive lebrikizumab or placebo at Week 16; [b] Protocol-defined response was defined as achieving EASI 75 or IGA (0,1) with ≥2-point improvement at Week 16 without rescue medication use

Baseline Demographics and Disease Characteristics

	Pooled mMPP of ADvocate1&2[a]		
	LEBRI Q4W (N=118)	LEBRI Q2W (N=113)	PBO (LEBRI Withdrawal) (N=60)
Age, years	35.8 (17.3)	36.1 (17.0)	33.8 (16.6)
Adolescent (≥12 to <18 years), n (%)	17 (14.4)	13 (11.5)	8 (13.3)
Adult (≥18 years), n (%)	101 (85.6)	100 (88.5)	52 (86.7)
Female, n (%)	69 (58.5)	53 (46.9)	36 (60.0)
Region, n (%)			
USA	51 (43.2)	44 (38.9)	22 (36.7)
Europe	38 (32.2)	40 (35.4)	18 (30.0)
Rest of the world	29 (24.6)	29 (25.7)	20 (33.3)
BMI, kg/m^2	26.2 (5.9)	26.3 (6.9)	25.3 (4.8)
Disease duration,[b] years	22.6 (14.8)	21.7 (14.2)	20.4 (14.9)
IGA, n (%)			
3 (Moderate)	78 (66.1)	70 (61.9)	37 (61.7)
4 (Severe)	40 (33.9)	43 (38.1)	23 (38.3)
EASI	28.8 (12.6)	29.5 (10.8)	28.9 (11.2)
Pruritus NRS[c]	7.0 (1.8)	7.2 (1.7)	7.5 (1.8)
POEM	19.9 (5.8)	21.0 (5.0)	21.1 (5.3)
Sleep loss[d] due to pruritus	2.1 (1.0)	2.3 (0.9)	2.3 (1.1)
AD treatment used in the past, n (%)			
TCS	118 (100)	108 (95.6)	59 (98.3)
TCI	46 (39.0)	47 (41.6)	23 (38.3)
Immunosuppressive/immunomodulating drugs	60 (50.8)	42 (37.2)	24 (40.0)
Systemic corticosteroids	52 (44.1)	36 (31.9)	22 (36.7)
Cyclosporine	5 (4.2)	9 (8.0)	8 (13.3)
Methotrexate	6 (5.1)	7 (6.2)	5 (8.3)

[a] Protocol-defined response was defined as achieving EASI 75 or IGA (0,1) with ≥2-point improvement at Week 16 without rescue medication use; [b] Since AD onset; [c] Pruritus NRS was assessed by the patient based on an 11-point scale to rate itch severity, with 0 indicating "No itch" and 10 indicating "Worst itch imaginable"; [d] Sleep loss due to pruritus was assessed by the patient based on a 5-point Likert scale, with 0 indicating "not at all" and 4 indicating "unable to sleep at all"
Data are mean (SD) unless stated otherwise

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ABBREVIATIONS

AD=atopic dermatitis; BSA=body surface area; BMI=body mass index; EASI=Eczema Area and Severity Index; EASI 50/75=50/75% improvement from baseline in EASI; EMA=European Medicines Agency; FDA=US Food and Drug Administration; IGA=Investigator's Global Assessment; IGA (0,1)=IGA response of clear or almost clear; IL=interleukin; IR=inadequate responder; LD=loading dose; LEBRI=lebrikizumab; LTE=long-term extension; mMPP=modified Maintenance Primary Population; n=number of patients in the specified category; NRS=Numeric Rating Scale; PBO=placebo; POEM=Patient-Oriented Eczema Measure; Q2W=every 2 weeks; Q4W=every 4 weeks; SD=standard deviation; TCI=topical calcineurin inhibitors; TCS=topical corticosteroids; W=Week

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Maintenance of **Optimal Response** Over **2 Years** in Patients With **Atopic Dermatitis** Treated With **Dupilumab**

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AD

Conclusions

- Long-term dupilumab treatment in adults with AD demonstrated maintenance of an optimal response over 2 years with sustained improvement in clinical signs
  - These and other recent findings[1–7] suggest that increased dosing intervals may be appropriate for some individuals
- Efficacy was rapidly regained after 36 weeks of withdrawal in patients re-randomized to placebo in SOLO-CONTINUE who then received dupilumab in the OLE
- Safety was consistent with the known dupilumab safety profile

Objective

To report maintenance of optimal response in patients treated with dupilumab for over 2 years

Background

- Sustained disease control is an important goal of long-term therapies for AD[1]
- Dupilumab for up to 5 years in a phase 3, OLE study demonstrated long-term efficacy with an acceptable safety profile in adults with moderate-to-severe AD[2]
- Real-world data on dupilumab treatment for up to 5 years have confirmed the long-term effectiveness of dupilumab in clinical practice[3]

Methods

- Adults with moderate-to-severe AD who received dupilumab 300 mg q2w in SOLO 1/2 (NCT02277743/NCT02277769) and achieved optimal response of IGA 0/1 and/or EASI-75 at Week 16 were re-randomized in SOLO-CONTINUE (NCT02395133) for an additional 36 weeks to dupilumab 300 mg monotherapy q2w, q4w, q8w, or placebo, followed by 60 weeks of dupilumab 300 mg qw in an OLE study (NCT01949311)
- Concomitant treatments for AD, including TCS/TCI, were permitted in the OLE
- The proportion of patients maintaining IGA 0/1 and/or EASI-75 and absolute EASI are reported
- This analysis is based on a modified non-responder imputation method
  - Patients discontinuing due to lack of efficacy (all studies) or receiving systemic rescue treatment (SOLO 1/2; SOLO-CONTINUE) were considered non-responders

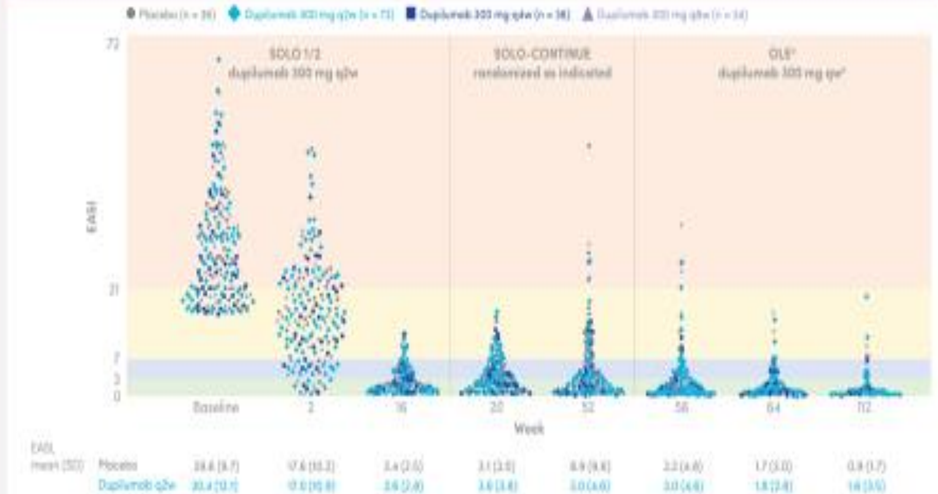
Results

Demographics and baseline disease characteristics

	Placebo[a] (n = 36)	Dupilumab 300 mg q2w[a] (n = 73)	Dupilumab 300 mg q4w[a] (n = 36)	Dupilumab 300 mg q8w[a] (n = 34)
Age, mean (SD), years[b]	39.2 (15.4)	36.3 (14.0)	39.0 (16.1)	35.6 (14.3)
Sex, male, n (%)[b]	18 (50.0)	36 (49.3)	20 (55.6)	22 (64.7)
Duration of AD, mean (SD), years[b]	27.1 (16.1)	27.3 (14.9)	27.9 (16.2)	23.2 (11.0)
IGA 0/1, n (%)				
SOLO 1/2 baseline (Week 0)	0	0	0	0
SOLO-CONTINUE baseline (Week 16)	29 (80.6)	60 (82.2)	29 (80.6)	26 (76.5)
EASI, mean (SD)				
SOLO 1/2 baseline (Week 0)	29.6 (9.7)	30.4 (12.1)	27.2 (10.6)	27.6 (10.8)
SOLO-CONTINUE baseline (Week 16)	2.4 (2.5)	2.6 (2.7)	2.5 (2.8)	2.4 (2.2)
EASI-75, n (%)[b]	35 (97.2)	68 (93.2)	35 (97.2)	32 (94.1)

[a]All patients received dupilumab 300 mg q2w in SOLO 1/2 and were then randomized to treatment in SOLO-CONTINUE as indicated before receiving dupilumab 300 mg qw in the OLE study. [b]At SOLO-CONTINUE baseline (Week 16).

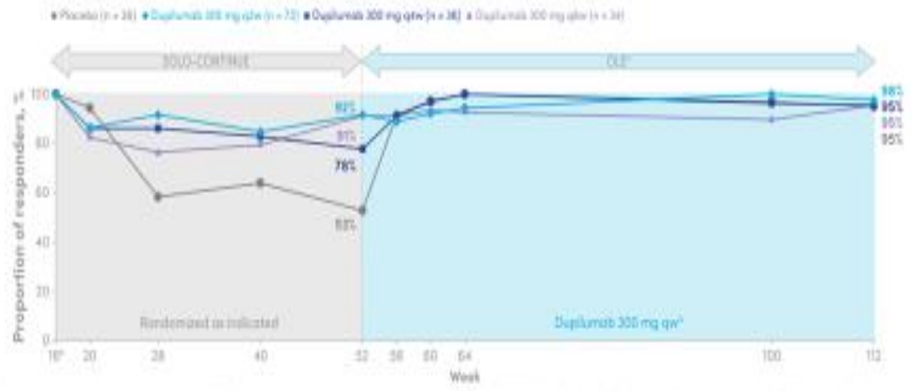
Absolute EASI score was consistent across dupilumab dose regimens during the study period



EASI									
mean (SD)	Placebo	29.6 (9.7)	17.6 (10.2)	8.4 (7.5)	7.1 (5.9)	6.9 (6.8)	7.2 (6.8)	7.7 (5.0)	6.8 (5.7)
	Dupilumab q2w	30.4 (12.1)	17.9 (10.9)	8.6 (7.8)	7.6 (7.4)	8.0 (6.6)	8.0 (6.6)	8.8 (7.8)	8.6 (8.5)
	Dupilumab q4w	27.2 (10.6)	15.5 (9.4)	7.5 (7.8)	7.2 (7.5)	6.1 (5.7)	7.2 (7.0)	7.5 (7.9)	6.9 (7.6)
	Dupilumab q8w	27.6 (10.8)	16.3 (8.8)	8.4 (7.2)	7.7 (7.5)	6.6 (6.3)	7.2 (7.2)	7.0 (5.8)	7.2 (7.1)

All patients received dupilumab 300 mg q2w in SOLO 1/2 and were then randomized to treatment in SOLO-CONTINUE as indicated before receiving 300 mg qw in the OLE study. [a]Concomitant treatments for AD, including TCS/TCI, were permitted in the OLE; note, 300 mg qw is not the approved dose of dupilumab.

Most dupilumab-treated patients achieving IGA 0/1 and/or EASI-75 at Week 16 maintained response over 2 years



All patients received dupilumab 300 mg q2w in SOLO 1/2 and were then randomized to treatment in SOLO-CONTINUE as indicated before receiving 300 mg qw in the OLE study. All observed values are presented regardless of rescue treatment use with modified non-responder imputation method, where a patient is considered a non-responder if rescue treatment is systemic (SOLO 1/2 and SOLO-CONTINUE) or if they discontinue treatment due to lack of efficacy. [a]Concomitant treatments for AD, including TCS/TCI, were permitted in the OLE; note, 300 mg qw is not the approved dose of dupilumab. [b]Week 16 of SOLO 1/2 is SOLO-CONTINUE baseline. Only optimal responders were eligible to continue treatment for an additional 36 weeks in SOLO-CONTINUE.

Summary of safety indicators from SOLO 1/2 baseline through SOLO-CONTINUE and OLE

Patients with ≥1 event, n (%)	Placebo[a] (n = 36)	Dupilumab 300 mg q2w[a] (n = 73)	Dupilumab 300 mg q4w[a] (n = 36)	Dupilumab 300 mg q8w[a] (n = 34)
TEAE	21 (58.3)	45 (61.6)	28 (77.8)	24 (70.6)
Serious TEAE	2 (5.6)	5 (6.9)	2 (5.6)	2 (5.9)
Severe TEAE	0	4 (5.5)	0	1 (2.9)
TEAE leading to discontinuation	2 (5.6)	2 (2.7)	0	1 (2.9)
TEAE leading to death	0	0	0	0

[a]Treatment arm in SOLO-CONTINUE. All patients in this analysis received dupilumab 300 mg q2w in SOLO 1/2 and dupilumab 300 mg qw in the OLE.

AD, atopic dermatitis; EASI, Eczema Area and Severity Index; EASI-75, ≥75% improvement from SOLO 1/2 baseline in EASI; IGA, Investigator's Global Assessment; OLE, open-label extension; q2w, every 2 weeks; qw, every week; q4w, every 4 weeks; q8w, every 8 weeks; qw, weekly; SD, standard deviation; TCI, topical calcineurin inhibitor(s); TCS, topical corticosteroid(s); TEAE, treatment-emergent adverse event.

References: 1. Silverberg JI, et al. J Eur Acad Dermatol Venereol. 2024 Jul 11 [Epub ahead of print]. 2. Blauvelt A, et al. JAMA Dermatol. 2016;152:eS5. 3. Bissonnette R, et al. JAMA Dermatol. 2021;157:1047. 4. Simpson EL, et al. J Eur Acad Dermatol Venereol. 2020;34:2717. 5. Wollenberg A, et al. J Eur Acad Dermatol Venereol. 2021;35:1187. 6. Jonstrup AT, et al. Br J Dermatol. 2020 Oct;183:740. 7. Valenta C, et al. J Eur Acad Dermatol Venereol. 2024;38:e780.

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Dupilumab Monotherapy Prevents Flares and Provides Sustained Control of Atopic Dermatitis Over 1 Year Across Various Dose Regimens

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Conclusions

AD

- Dupilumab monotherapy over 1 year prevented flares in 8 out of 10 patients regardless of the maintenance dose regimen (q2w, q4w, q8w)
- Safety was consistent with the known dupilumab safety profile

Objective

To report the efficacy of dupilumab monotherapy to prevent flares and maintain disease control in adults treated with various dose regimens during the maintenance phase

Background

- Disease control in AD can be defined as absence of flares, an important goal for physicians and patients; flare is a worsening of disease requiring escalation of treatment[1]
- Dupilumab with concomitant TCS was shown to prevent flares in 84% of adults with moderate-to-severe AD in a 1-year, randomized, placebo-controlled clinical trial[2,3]

Methods

- Adults with moderate-to-severe AD who received dupilumab 300 mg q2w in SOLO 1/2 (NCT02277743/ NCT02277769) and achieved optimal response of IGA 0/1 and/or EASI-75 at Week 16 were rerandomized in SOLO-CONTINUE (NCT02395133) for an additional 36 weeks to dupilumab 300 mg monotherapy q2w, q4w, q8w, or placebo
- Patients who received rescue treatment in SOLO 1/2 (including TCS/TCI) were considered non-responders
- This analysis reports the proportion of patients with no flares by visit and time to first flare during SOLO-CONTINUE (Kaplan–Meier statistics); data are presented as observed
- Flare defined per protocol as worsening of disease requiring initiation or escalation of rescue treatment (including starting topical treatment)

Results

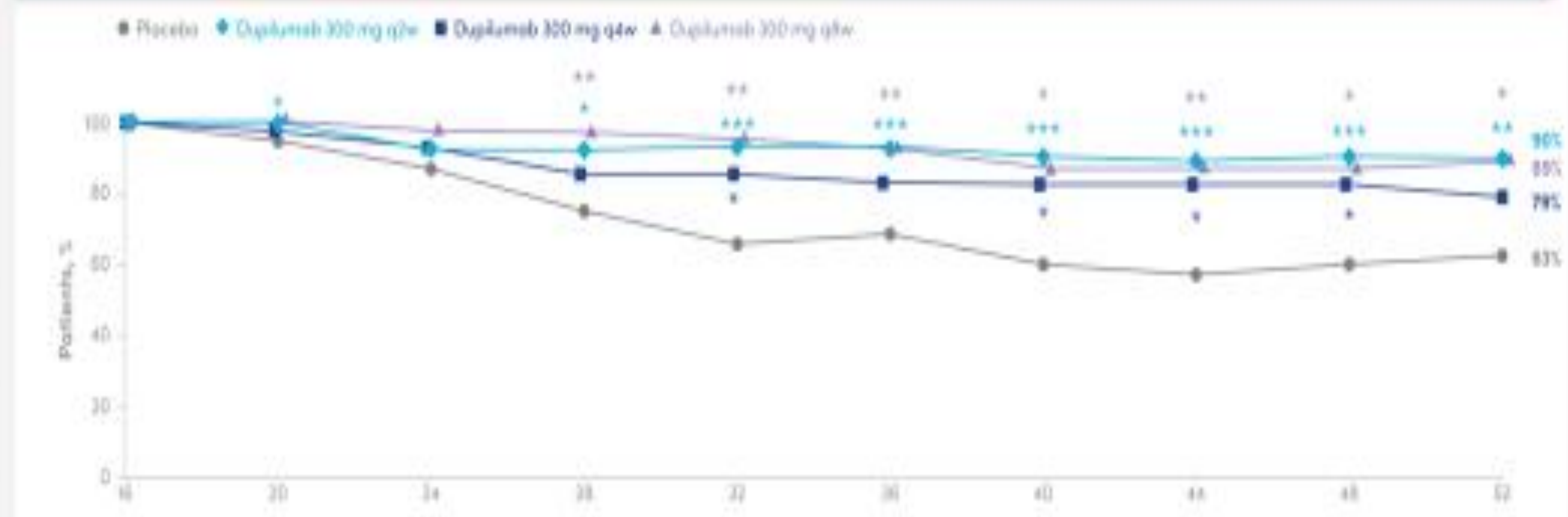
Demographics and baseline disease characteristics

	SOLO 1/2 baseline (Week 0)				SOLO-CONTINUE baseline (Week 16)			
	Placebo* n = 38	Dupilumab 300 mg q2w* n = 80	Dupilumab 300 mg q4w* n = 41	Dupilumab 300 mg q8w* n = 39	Placebo* n = 38	Dupilumab 300 mg q2w* n = 80	Dupilumab 300 mg q4w* n = 41	Dupilumab 300 mg q8w* n = 39
Age, mean (SD), years	38.9 (15.0)	38.8 (14.8)	37.7 (17.8)	34.3 (13.8)	38.9 (15.0)	38.8 (14.8)	38.2 (17.6)	34.8 (13.8)
Sex, male, n (%)	18 (46.2)	38 (47.5)	23 (56.1)	22 (56.4)	18 (46.2)	38 (47.5)	23 (56.1)	22 (56.4)
Duration of AD, mean (SD), years	26.8 (15.8)	28.2 (16.2)	26.4 (16.1)	23.9 (10.8)	26.8 (15.8)	28.2 (16.2)	26.4 (16.1)	23.9 (10.8)
Body surface area, mean % (SD)	48.8 (17.3)	48.3 (21.1)	47.1 (20.7)	47.3 (20.3)	14.9 (14.2)	8.4 (10.7)	13.0 (14.6)	15.4 (15.3)
Patients with ≥1 AD flare in 12 months before screening visit, n (%)	33 (84.7)	66 (82.5)	37 (90.2)	35 (89.7)				
Number of flares in 12 months before treatment period, median	3.0	3.0	3.0	4.0				

Summary of safety indicators from SOLO 1/2 baseline through SOLO-CONTINUE

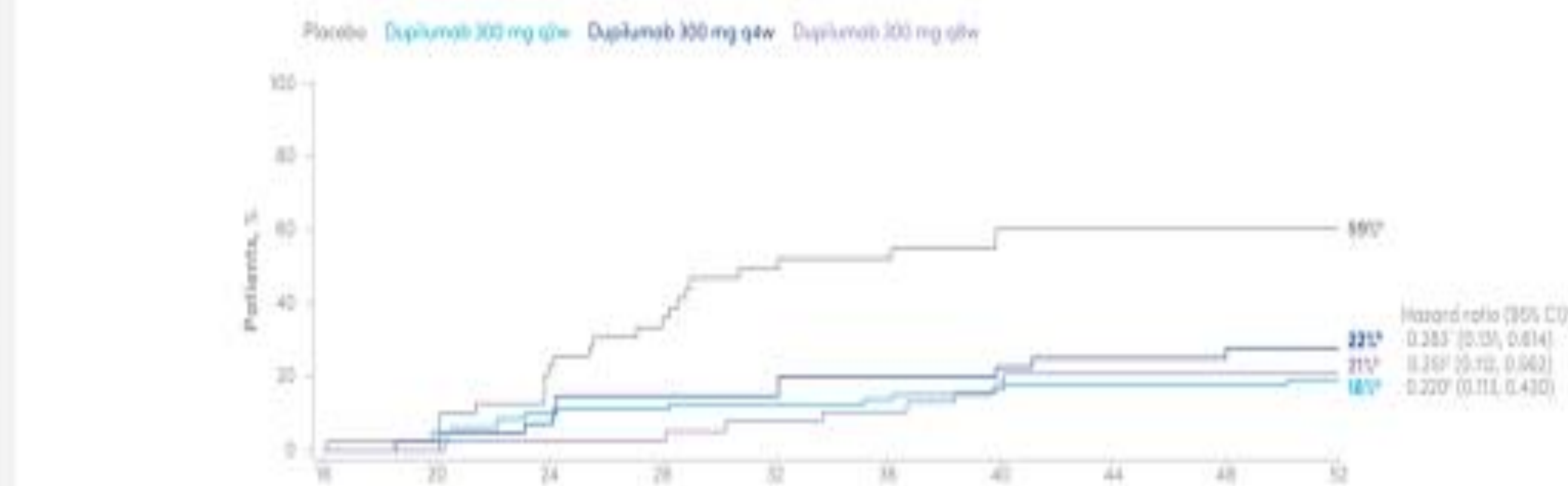
Patients with ≥1 event, n (%)	Placebo* n = 38	Dupilumab 300 mg q2w* n = 80	Dupilumab 300 mg q4w* n = 41	Dupilumab 300 mg q8w* n = 39
TEAE	34 (87.2)	59 (73.8)	29 (70.7)	29 (74.4)
Serious TEAE	1 (2.6)	4 (5.0)	1 (2.4)	0
Severe TEAE	3 (7.7)	4 (5.0)	2 (4.9)	2 (5.1)
TEAE leading to discontinuation	2 (5.1)	0	0	0
TEAE leading to death	0	0	0	0

Most patients had no flares* over 1 year with continued dupilumab monotherapy



n/N	20	24	28	32	36	40	44	48	52
Placebo	38/38	33/38	27/38	23/38	24/38	21/38	20/39	21/38	20/33
Dupilumab q2w	78/78	71/77	75/76	68/71	68/73	66/73	65/73	66/73	62/69
Dupilumab q4w	42/43	38/42	35/41	35/41	34/41	33/40	33/40	33/40	30/38
Dupilumab q8w	40/40	39/40	38/40	38/39	37/40	34/39	34/39	34/39	32/36

The proportion of patients who experienced a flare* remained low across dupilumab dose regimens



Number at risk	16	20	24	28	32	36	40	44	48	52
Placebo	38	37	31	25	19	18	15	15	12	14
Dupilumab q2w	80	80	71	69	66	65	63	62	60	57
Dupilumab q4w	41	40	37	33	33	31	30	29	28	28
Dupilumab q8w	39	38	37	37	35	34	31	30	29	29

Sustained **Disease Control** Among Adults With Moderate-to-Severe Atopic Dermatitis in Clinical Practice: **5-Year** Follow-Up Results From the RELIEVE-AD Study

Zhixiao Wang[1], Bruno Martins[2], Jingdong Chao[1], Min Yang[3], Kerry Noonan[1], Brad Shumel[1], Debra Sierka[1]

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AD

Conclusion

In this long-term, real-world study, the majority of patients with moderate-to-severe AD who remained in the study reported rapid and sustained disease control for 5 years after initiating dupilumab treatment

Objective

To report 5-year data from RELIEVE-AD on AD disease control

Background

- AD often requires long-term therapy, which highlights the importance of assessing long-term effectiveness

Methods

Study design and population

- RELIEVE-AD is a single-arm, prospective, observational study of adults with moderate-to-severe AD receiving dupilumab who participated in surveys at BL (before dupilumab initiation) and M1, M2, M3, M6, M9, M12, M33, M48, and M60

Study outcomes

- Disease control was assessed with the Atopic Dermatitis Control Tool (ADCT, range 0–24, score <7 indicating controlled disease; mean ADCT score, with items scored on a 5-point scale ranging from 0 to 4, and 0 being none/no effect)

Statistical analysis

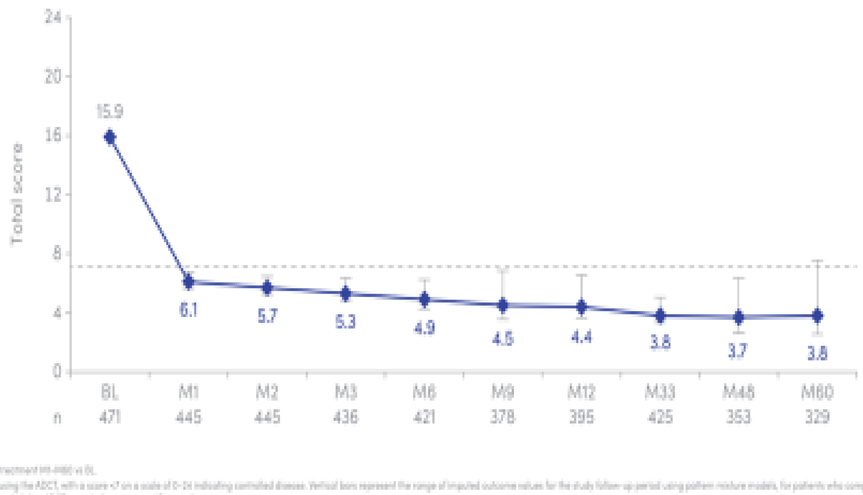
- Statistical significance, comparing each time point to BL, was determined using GEE to account for correlated data from the same patients over time; only patients who responded to at least one of the M33 or M48 surveys were contacted for the M60 survey, to decrease the burden of outreach to patients who had not participated in recent surveys

Limitations

- 69.9% of patients who were contacted responded to the survey at Month 60, which could have led to survivor bias

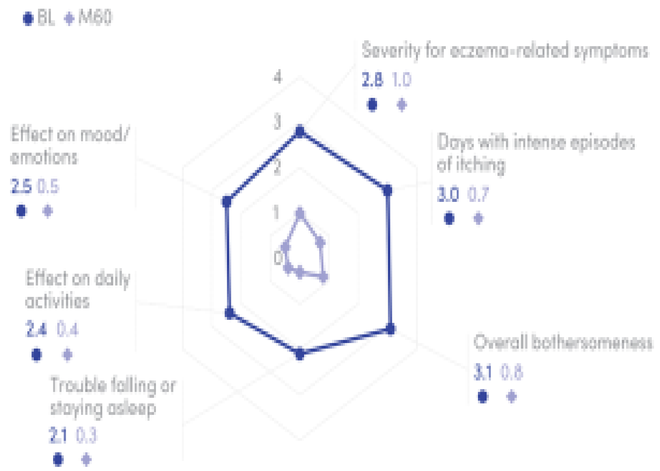
Results

Mean Total ADCT Score[a,b] (range 0-24)*



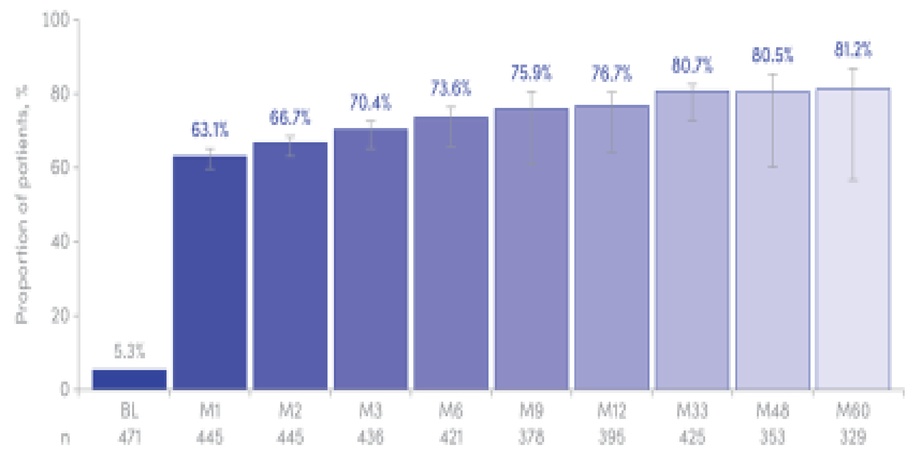
*P < 0.001 treatment M1-M60 vs BL.
[a]Assessed using the ADCT, with a score <7 on a scale of 0–24 indicating controlled disease. Vertical bars represent the range of imputed outcome values for the study follow-up period using pattern mixture models, for patients who completed the BL survey. [b]Higher ADCT score indicates worse AD control.

Mean ADCT Items[a] (range 0-4)*



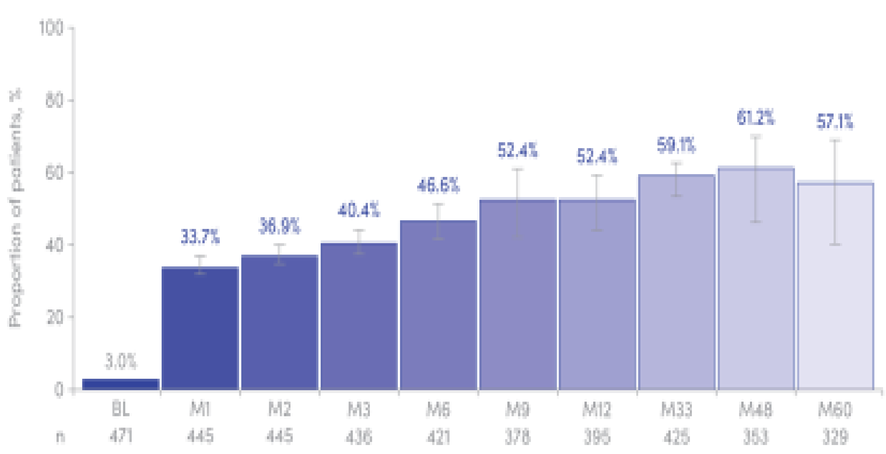
*P < 0.001 treatment M1-M60 vs BL.
[a]Items were scored on a 5-point scale ranging from 0 to 4, with 0 being none/no effect.

Disease control status assessed by ADCT[a] (total score <7)*



*P < 0.001 treatment M1-M60 vs BL.
[a]Assessed using the ADCT, with a score <7 on a scale of 0–24 indicating controlled disease. Vertical bars represent the range of imputed outcome values for the study follow-up period using pattern mixture models, for patients who completed the BL survey.

No intense episodes of itching over the last week*[a]



*P < 0.001 treatment M1-M60 vs BL.
[a]Vertical bars represent the range of imputed outcome values for the study follow-up period using pattern mixture models for patients who completed the baseline survey.

AD, atopic dermatitis; ADCT, Atopic Dermatitis Control Tool; BL, baseline; GEE, generalized estimating equations; MCID, minimal clinically important difference; M, month.

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Presented at the Elevate Derm Summer Conference 2025; Park City, Utah, USA; July 23 – 27, 2025.

Patients Maintain Stable Response With No or Minimal Fluctuations During 3 Years of Continuous Treatment With Lebrikizumab During Long-Term Extension Trial

Jonathan I. Silverberg[1], Linda Stein Gold[2], Peter Lio[3], James Del Rosso[4], Andreas Wollenberg[5], Jose Manuel Carrascosa[6], Gaia Gallo[7], Yuxin Ding[7], Helena Agell[8], Christian Vestergaard[9]

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Sponsored by Eli Lilly and Company

OBJECTIVE

- To assess the stability of response after 3 years of lebrikizumab treatment using data from ADvocate 1&2 and ADjoin

CONCLUSION

- Most patients treated continuously with lebrikizumab for 3 years experienced stable improvements in skin and itch with no or minimal fluctuations in the ADjoin long-term extension trial

Elevate-Derm Summer Conference, Park City, Utah, USA; July 23 - 27, 2025

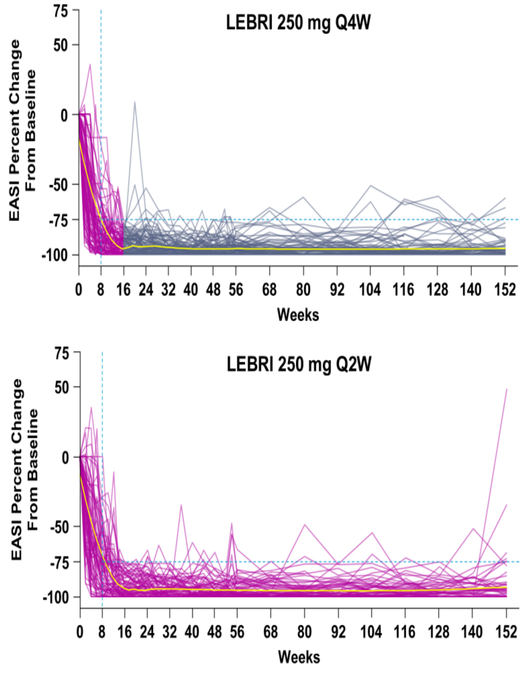
BACKGROUND

- Lebrikizumab is a monoclonal antibody that binds with high affinity and slow off-rate to IL-13, thereby blocking the downstream effects of IL-13 with high potency[1]
- Lebrikizumab demonstrated safety and efficacy as monotherapy through 3 years of treatment in adults and adolescents (≥40 kg) with moderate-to-severe AD in recent Phase 3 trials (ADvocate 1, NCT04146363; ADvocate 2, NCT04178967; ADjoin, NCT04392154)[2-4]
- Most patients treated with monotherapy lebrikizumab Q2W or Q4W maintained a stable response with no or minimal fluctuations of efficacy up to 2 years[5]

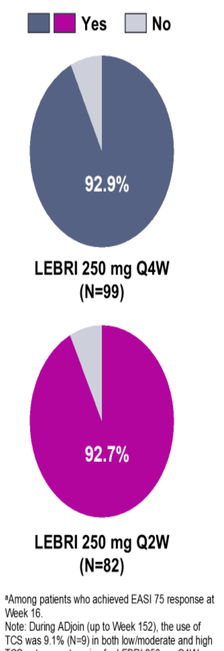
SUMMARY OF KEY FINDINGS

93% of Week 16 EASI 75 Responders Maintained Stable EASI 75 Response for 3 Years of Lebrikizumab Treatment

Patients With Stable EASI 75 Response Up to Week 152



Proportion of Patients With Stable EASI 75 Response[a]

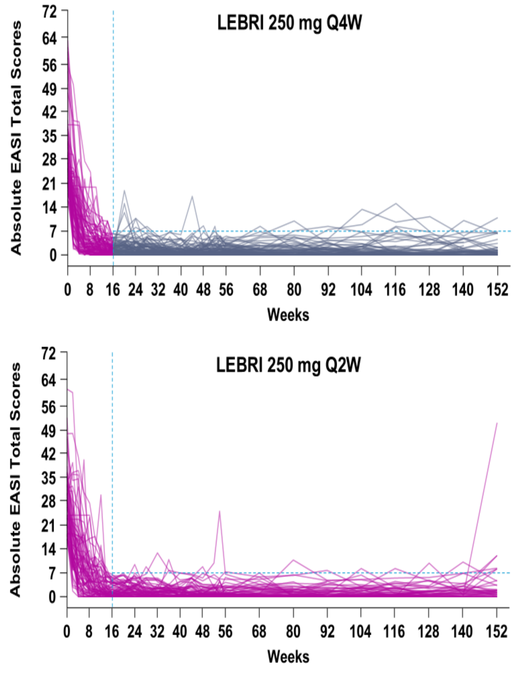


[a]Among patients who achieved EASI 75 response at Week 16.
Note: During ADjoin (up to Week 152), the use of TCS was 9.1% (N=9) in both low/moderate and high TCS potency categories for LEBRI 250 mg Q4W, whereas it was 4.9% (N=4) and 6.1% (N=5) in low/moderate and high TCS potency categories for LEBRI 250 mg Q2W, respectively.

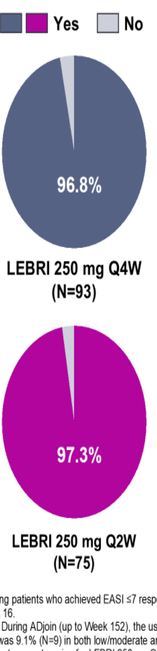
Notes: Responder patients at Week 16 after the induction with LEBRI Q2W were re-randomized to LEBRI Q2W or Q4W for 36 weeks of Maintenance Period in ADvocate 1&2, and continued the same treatment in ADjoin up to Week 152. Each line represents data of an individual patient over time. Lines represent patients who achieved EASI 75 response during ≥80% of attended visits of between Week 16 and Week 152. The yellow lines are the smoothing lines fitted by locally estimated scatterplot smoothing.

97% of Week 16 EASI ≤7 Responders Maintained Stable EASI ≤7 Response for 3 Years of Lebrikizumab Treatment

Patients With Stable EASI ≤7 Response Up to Week 152



Proportion of Patients With Stable EASI ≤7 Response[a]



[a]Among patients who achieved EASI ≤7 response at Week 16.
Note: During ADjoin (up to Week 152), the use of TCS was 9.1% (N=9) in both low/moderate and high TCS potency categories for LEBRI 250 mg Q4W, whereas it was 4.9% (N=4) and 6.1% (N=5) in low/moderate and high TCS potency categories for LEBRI 250 mg Q2W, respectively.

Notes: Responder patients at Week 16 after the induction with LEBRI Q2W were re-randomized to LEBRI Q2W or Q4W for 36 weeks of Maintenance Period in ADvocate 1&2, and continued the same treatment in ADjoin up to Week 152. Each line represents data of an individual patient over time. Lines represent patients who achieved EASI ≤7 response during ≥80% of attended visits between Week 16 and Week 152.

Methods

Analysis Population

- The analysis population consisted of patients treated with lebrikizumab in the pooled modified Maintenance Primary Population of ADvocate 1&2 who were EASI 75, or EASI ≤7, or Pruritus Numeric Rating Scale (NRS)[a] ≥3-point improvement responders at Week 16 and who subsequently enrolled into ADjoin[b] with the same lebrikizumab treatment regimen; Pruritus NRS score was not collected beyond Week 104 in ADjoin

Stability of Response

- Stability of response was defined as patients' maintenance of:
  - EASI[c] 75 response at ≥80% of attended visits
  - EASI ≤7 response at ≥80% of attended visits
  - Pruritus NRS improvement ≥3 points from baseline (the minimum clinically important difference[6]) at ≥80% of attended visits[d]

Outcome Measures (Up to Week 152)

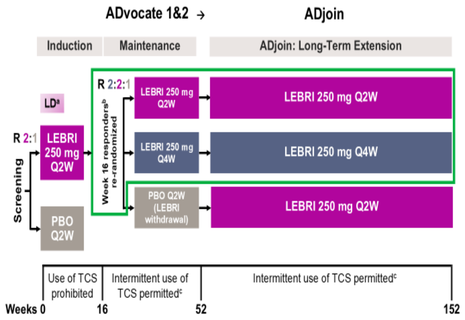
- EASI percent change from baseline
- Absolute EASI total score
- Pruritus NRS change from baseline

Statistical Analyses

- All observed data were used in the analyses, regardless of rescue medication use
- The number of total attended visits varied for different patients

[a]A patient-reported, single-item, 11-point scale that is used daily by participants to rate their worst itch severity over the past 24 hours (0 indicating "no itch", 10 indicating "worst itch imaginable")[5]; [b]The pooled modified Maintenance Primary Population of ADvocate 1&2 consisted of Week 16 responders (patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of lebrikizumab 250 mg Q2W treatment without use of rescue therapy) and excluded 17 patients from the ADvocate 2 trial (from a single study site) whose eligibility could not be confirmed; [c]A composite index with scores ranging from 0 to 72, with the higher values indicating more severe and/or extensive disease and with EASI 75 representing an improvement of ≥75% from baseline in EASI; [d]In patients with baseline Pruritus NRS ≥3.

Study Design



[a]Patients treated with LEBRI received a 500-mg LD at Weeks 0 and 2; [b]Responders in ADvocate 1&2 were defined as those patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of LEBRI 250 mg Q2W treatment, without use of rescue therapy; [c]Patients who required short-term systemic treatment for AD in the Maintenance Period were assessed on a case-by-case basis.

Key Eligibility Criteria

Parent Studies (ADvocate 1&2)

- Adults (≥18 years) and adolescents (≥12 to <18 years; weight ≥40 kg)
- Diagnosis of AD, as defined by the American Academy of Dermatology Consensus Criteria, for ≥1 year before screening
- Moderate-to-severe AD, defined as having all the following at the baseline visit:
  - EASI ≥16
  - IGA ≥3
  - Body surface area involvement ≥10%

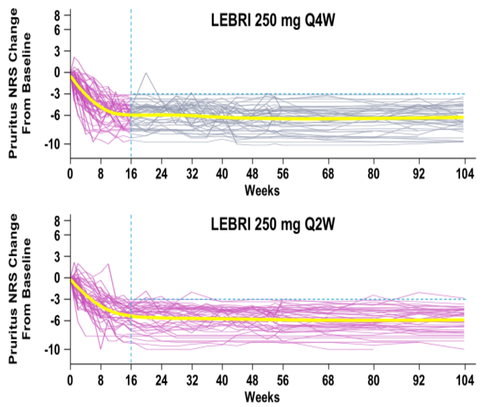
ADjoin

- Patients could choose to enroll if they had completed the study treatments and last patient visit of the parent trial

Results

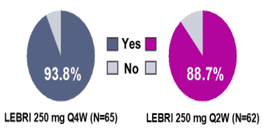
94% of Week 16 Pruritus NRS Improvement ≥3 Achievers Maintained Pruritus NRS Improvement ≥3 for 2 Years of Lebrikizumab Treatment

Patients with Stable Pruritus NRS Improvement ≥3[a] Response Up to Week 104



[a]Week 16 responders enrolling into ADjoin who achieved Pruritus NRS improvement ≥3 at Week 16 with baseline Pruritus NRS ≥3.
Notes: Responder patients at Week 16 after the induction with LEBRI Q2W were re-randomized to LEBRI Q2W or Q4W for 36 weeks of Maintenance Period in ADvocate 1&2, and continued the same treatment in ADjoin up to Week 104. Each line represents data of an individual patient over time. Lines represent patients who achieved Pruritus NRS improvement ≥3 during ≥80% of attended visits between Week 16 and Week 104. The yellow lines are the smoothing lines fitted by locally estimated scatterplot smoothing.

Proportion of Patients With Stable Pruritus Improvement ≥3[a]



[a]Week 16 responders enrolling into Adjoin who achieved Pruritus NRS improvement ≥3 at Week 16 with baseline Pruritus NRS ≥3.
Note: During ADjoin (up to Week 152), the use of TCS was 9.1% (N=9) in both low/moderate and high TCS potency categories for LEBRI 250 mg Q4W, whereas it was 4.9% (N=4) and 6.1% (N=5) in low/moderate and high TCS potency categories for LEBRI 250 mg Q2W, respectively.

References: 1. Okragly AJ, et al. *Dermatol Ther (Heidelb).* 2023;13:1535-1547. 2. Silverberg JI, et al. *N Engl J Med.* 2023;388:1080-1091. 3. Blauvelt A, et al. *Br J Dermatol.* 2023;188:740-748. 4. Thaçi D, et al. Oral presentation at: *EADV 2024.* Abstract #7829. 5. Silverberg JI, et al. Poster presentation at: *AAD 2024.* Poster #52792. 6. Yosipovitch G, et al. Poster presentation at: *RAD 2022.* Poster #628.

Abbreviations: *AD=atopic dermatitis; EASI=Eczema Area and Severity Index; EASI 75=≥75% improvement from baseline in EASI; IGA=Investigator's Global Assessment; IGA (0,1)=IGA response of clear or almost clear; IL=interleukin; LD=loading dose; LEBRI=lebrikizumab; NRS=Numeric Rating Scale; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; R=randomization; TCS=topical corticosteroids*

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Tapinarof Cream 1% Once Daily: Maintenance of Low Disease Activity Including Pruritus Through End of the Treatment-free Interval in a Long-term Extension Trial in Patients Down to 2 Years of Age with Atopic Dermatitis

Jonathan I. Silverberg,[1] Robert Bissonnette,[2] Linda Stein Gold,[3] Philip M. Brown,[4] Mark Boguniewicz,[5] David Rosmarin,[6] Autumn F. Burnette,[7] Wendy Cantrell,[8] Matthew J. Bruno,[9] Anna M. Tallman[4]

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OBJECTIVE

- To characterize disease activity at the end of treatment-free (remittive) intervals in the ADORING 3 long-term trial

CONCLUSIONS

- **In ADORING 3, after first achieving complete disease clearance (vIGA-AD™=0) and discontinuing treatment, a high proportion of patients demonstrated low disease activity, including itch, after ~80 consecutive days off treatment**
  - **Mean EASI scores at the end of treatment-free intervals were <4, indicating mild disease**
- **Tapinarof monotherapy induced complete disease clearance followed by prolonged treatment-free (remittive) intervals and low disease activity in adults and children down to 2 years of age with AD**
  - **Slow re-emergence of mild symptoms during treatment-free intervals is unlike most topicals, where a rapid disease rebound is often observed[1]**
- **Tapinarof is a once-daily, non-steroidal cream without restrictions on duration, extent, or location of use, and without the need for long-term maintenance therapy**

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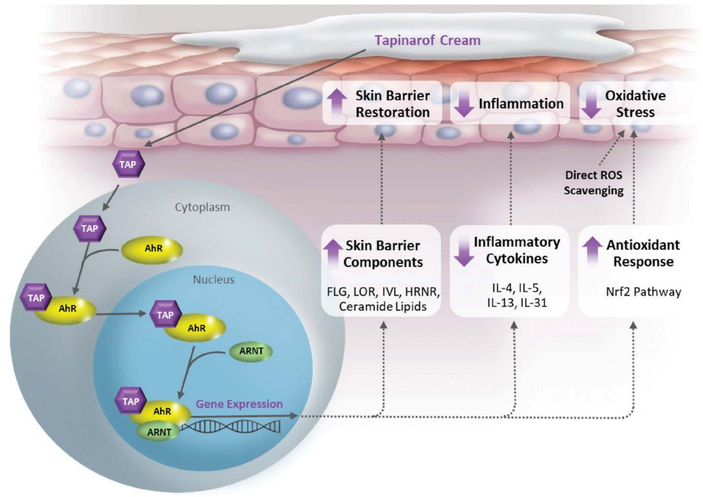
INTRODUCTION

- Tapinarof (VTAMA®, Dermavant Sciences, an Organon Company) is a non-steroidal, topical aryl hydrocarbon receptor (AhR) agonist approved by the FDA for the treatment of atopic dermatitis (AD) in adults and children down to 2 years of age, and for the treatment of plaque psoriasis in adults[2]
- Tapinarof binds to and activates AhR to restore the skin barrier by upregulating key barrier components, downregulating pro-inflammatory cytokines associated with AD, and reducing oxidative stress (**Figure 1**)[1]
- Discontinuation of topical therapy for AD may be associated with rapid return of disease[1]
- Preventative maintenance with topicals may be a significant treatment burden for patients and caregivers[1,3,4]
- In the ADORING 3 long-term trial, adults and children with AD received tapinarof cream 1% once daily (QD)[5]
  - Patients entered with or achieved complete disease clearance (51.9%; Validated Investigator Global Assessment for Atopic Dermatitis™ [vIGA-AD™]=0) and clear or almost clear skin (81.6%; vIGA-AD™=0 or 1)[5]
  - After discontinuing tapinarof per protocol, patients maintained clear or almost clear skin for 79.8 (mean) consecutive days (first treatment-free interval)[5]

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



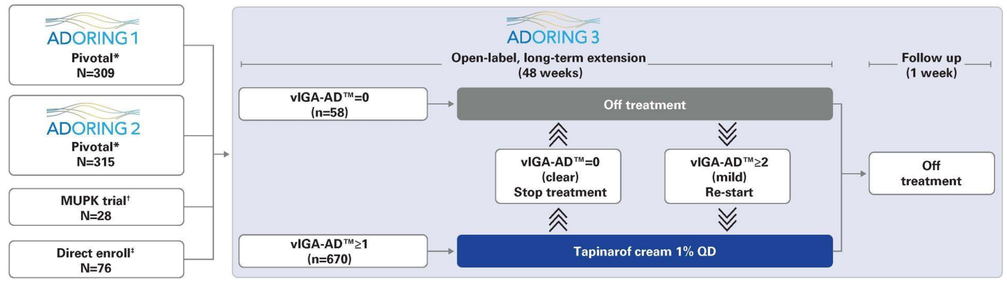
AhR, aryl hydrocarbon receptor; ARNT, aryl hydrocarbon receptor nuclear translocator; FLG, filaggrin; HRNR, hornerin; IL, interleukin; IVL, involucrin; LOR, loricrin; Nrf2, nuclear factor erythroid 2-related factor 2; ROS, reactive oxygen species; TAP, tapinarof.

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 (remittive effect, i.e., 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,[6] 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,[6] 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™.

Endpoints

- Treatment-free interval is 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
- Endpoints assessed at the end of treatment-free intervals:
  - Proportion of patients with vIGA-AD™ scores of 0 (clear) to 4 (severe)
  - Mean Eczema Area and Severity Index (EASI) score and mean weekly Peak Pruritus Numerical Rating Scale (PP-NRS) score
- Patients could experience more than one treatment-free interval during ADORING 3
- Safety assessments included the incidence and frequency of treatment-emergent adverse events (TEAEs), including adverse events of special interest (AESI); and investigator- and patient- or parent/caregiver-assessed Local Tolerability Scale (LTS) scores

RESULTS

ADORING 3 Baseline Patient Demographics and Disease Characteristics

- 728 patients enrolled in ADORING 3 (**Table 1**)
  - Pediatric patients (aged 2–17 years) comprised 83.0% of the trial population, including 76 children who enrolled directly
  - ~47% patients were non-white (White, 52.6%; Black/African American, 30.1%; Asian, 11.1%; other races, 4.4%)
- Patients entered with vIGA-AD™ scores ranging from 0 (clear) to 4 (severe) depending on their entry route
  - In the parent pivotal trials, most patients had moderate or severe AD at baseline

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 naive (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)
PP-NRS, mean (SD)	2.5 (2.3)	4.2 (2.8)	3.0 (2.2)	6.2 (2.8)	3.4 (2.8)

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

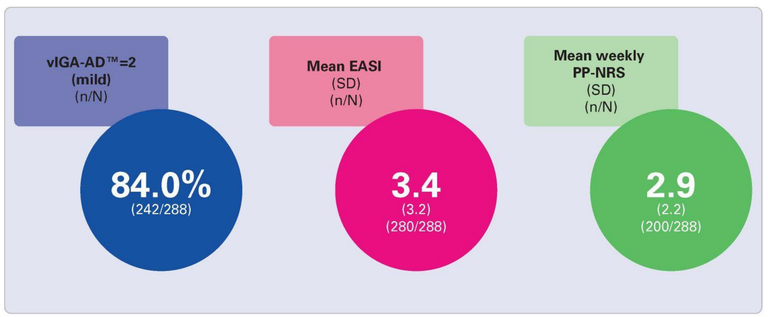
Maintenance of Low Disease Activity at the End of the First Treatment-free Interval

- After achieving complete disease clearance and discontinuing tapinarof, the mean duration of the first treatment-free interval was ~80 consecutive days off therapy
- Low disease activity was maintained at the end of the first treatment-free interval: 84.0% had vIGA-AD™=2; mean EASI=3.4 (standard deviation [SD]±3.2); mean weekly PP-NRS=2.9 (SD±2.2) (**Figure 3**)

Maintenance of Low Disease Activity at the End of all Treatment-free Intervals

- The overall mean duration of all treatment-free intervals was ~75 consecutive days (SD 76.0), demonstrating consistent ability to achieve complete clearance and maintain clear or almost clear skin
  - The mean duration of all treatment-free intervals may be an underestimate, due to the duration of some intervals being truncated prematurely by trial end (right censoring) and not by the need to restart treatment
- Similar low disease activity was seen at the end of subsequent treatment-free intervals

Figure 3. Low Disease Activity at the End of the First Treatment-free Interval with Tapinarof Cream 1% QD



EASI, Eczema Area and Severity Index; PP-NRS, Peak Pruritus Numerical Rating Scale; QD, once daily; SD, standard deviation; vIGA-AD™, Validated Investigator Global Assessment for Atopic Dermatitis™.

Tolerability

- Tapinarof cream was well tolerated; the majority of patients or parents/caregivers reported no or minimal burning/stinging and itching with long-term treatment for 48 weeks, even with intermittent treatment[5]
- Investigators assessed that most 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 baseline[5]
- Tapinarof was well tolerated locally, even when applied on sensitive skin across all evaluations for 48 weeks[5]

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%)[5]
- 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)[5]

Raising the Bar of Efficacy in Atopic Dermatitis: Lebrikizumab Maintains Depth of Response Over 3 Years in Week 16 Responders

Eric Simpson[1], Tilo Biedermann[2], Leon Kircik[3], Raj Chovatiya[4,5], Ignasi Figueras-Nart[6], Marta Casillas[7], Gaia Gallo[7], Yuxin Ding[7], Evangeline Pierce[7], Helena Agell[8], Christian Vestergaard[9]

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Sponsored by Eli Lilly and Company

OBJECTIVE

- To report maintenance of deep response and quality of life with 3 years of continuous treatment of lebrikizumab in responders[a] from ADvocate1&2 (NCT04146363; NCT04178967)[1] enrolled into the extension study ADjoin (NCT04392154)[2]

[a]Responders in ADvocate1&2 were defined as those patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of LEBRI 250 mg Q2W treatment without use of rescue therapy.

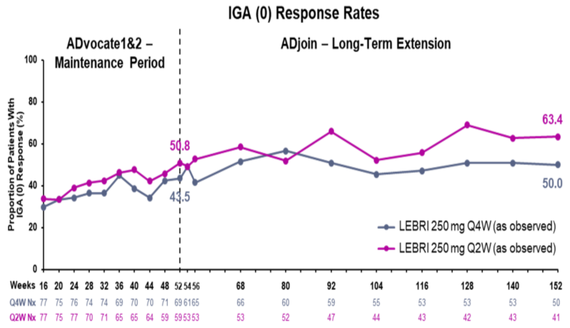
CONCLUSIONS

- Under lebrikizumab maintenance treatment in Week 16 responders, approximately 8 out of 10 achieved almost clear skin (as indicated by EASI 90) up to 3 years; additionally, over 50% of patients experienced total skin clearance, as assessed by EASI 100 or IGA (0)
- Quality of life was maintained through 3 years of continuous lebrikizumab treatment in Week 16 responders; approximately 1 out of 3 patients reported minimal to no AD-specific symptoms, as assessed by POEM (0,1), at Week 152
- Most patients did not require use of rescue therapy (TCS, TCI, or systemic treatment) with continuous lebrikizumab treatment
- These 3-year data suggest that long-term maintenance of total skin clearance is an achievable treatment goal for at least half of lebrikizumab Week 16 monotherapy responders

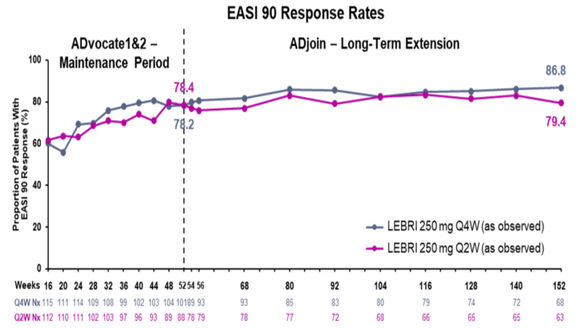
Elevate-Derm Summer Conference, Park City, Utah, USA; July 23 - 27, 2025

KEY RESULTS

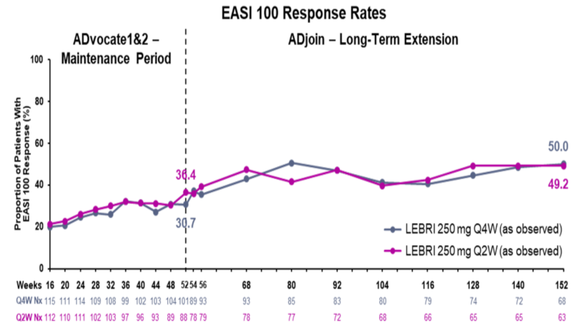
Deep Responses Were Maintained and Improved in Lebrikizumab Week 16 Responders Up to Week 152 for Both Q4W and Q2W Dosing



Notes: Data from Week 16 responders achieving IGA (0,1) at Week 16 of parent study. Not all patients completing ADvocate1 and ADvocate2 were enrolled to ADjoin; Week 52 data are from ADvocate1&2 parent studies.



Notes: Data from Week 16 responders achieving EASI 75 at Week 16 of parent study. Not all patients completing ADvocate1 and ADvocate2 were enrolled to ADjoin; Week 52 data are from ADvocate1&2 parent studies.



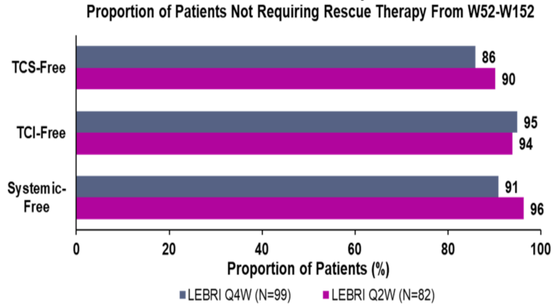
Notes: Data from Week 16 responders achieving EASI 75 at Week 16 of parent study. Not all patients completing ADvocate1 and ADvocate2 were enrolled to ADjoin; Week 52 data are from ADvocate1&2 parent studies.

Baseline Demographics and Disease Characteristics

	ADvocate1&2 → ADjoin[a]	
	LEBRI 250 mg Q4W (N=99)	LEBRI 250 mg Q2W (N=82)
Mean age, years (SD)	35.8 (17.2)	35.5 (16.2)
Adolescent (≥12 to <18), n (%)	14 (14.1)	11 (13.4)
Female, n (%)	60 (60.6)	42 (51.2)
Region, n (%)		
USA	41 (41.4)	32 (39.0)
Europe	33 (33.3)	32 (39.0)
Rest of the world	25 (25.3)	18 (22.0)
Mean BMI, kg/m^2 (SD)	26.4 (6.3)	26.4 (6.2)
Mean duration of disease since AD onset, years (SD)	22.4 (14.2)	23.6 (14.7)
IGA, n (%)		
3 (Moderate)	63 (63.6)	50 (61.0)
4 (Severe)	36 (36.4)	32 (39.0)
Mean EASI score (SD)	28.9 (12.2)	29.2 (11.2)
Mean POEM score (SD)	20.1 (5.8)	21.0 (5.1)

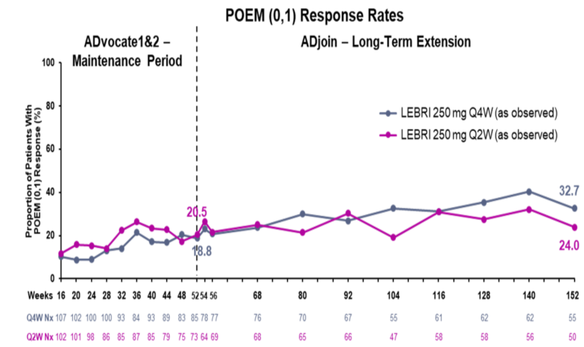
[a]Data at Week 0 of ADvocate1&2 are reported here as baseline data.

Most Patients Receiving Lebrikizumab Q4W and Q2W Through 152 Weeks Did Not Require Rescue Therapy[a]



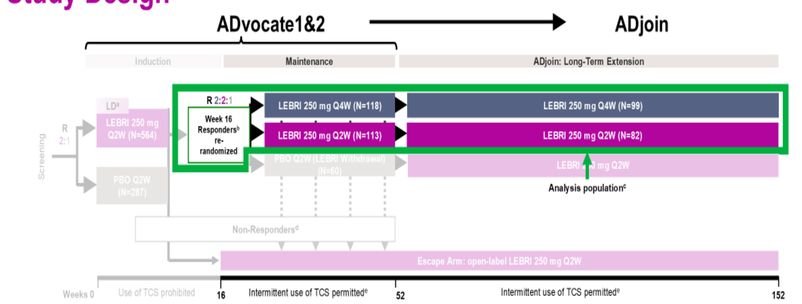
[a]Rescue therapy included any topical or systemic therapy during the treatment period.
Notes: Topical rescue therapy included TCS and TCIs. Systemic rescue therapy included systemic corticosteroids, immunosuppressants, biologics, phototherapy, and photochemotherapy. The majority of systemic rescue was used to treat TEAEs. Patients may have received more than 1 form of rescue therapy.

POEM (0,1) Response Was Maintained and Improved Through 152 Weeks for Both Q4W and Q2W Dosing



Note: Data from Week 16 responders of parent study. Not all patients completing ADvocate1 and ADvocate2 were enrolled to ADjoin; Week 52 data are from ADvocate1&2 parent studies.

Study Design



[a]LEBRI-treated patients received a 500-mg LD at Weeks 0 and 2; [b]Responders in ADvocate1&2 were defined as those patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of LEBRI 250 mg Q2W treatment without use of rescue therapy; [c]LEBRI responders randomized to LEBRI 250 mg Q2W or LEBRI 250 mg Q4W at Week 16 (ADvocate1&2), and enrolled into ADjoin at Week 52 with the same dosage regimen; [d]Patients who required short-term systemic treatment for AD in the Maintenance and Long-Term Extension Periods were assessed on a case-by-case basis.

Note: This analysis did not include per-protocol non-responders, defined as patients who used rescue therapy (including topical) during the 16-week Induction Period and assigned to receive open-label LEBRI 250 mg Q2W as part of the Escape Arm; additionally, during the 36-week Maintenance Period, patients who did not maintain EASI 50 (assessed at Weeks 24, 32, 40, 48) were also assigned to the Escape Arm. Once in the Escape Arm, patients who did not achieve EASI 50 after at least 8 weeks of treatment were terminated from the study. Non-responders receiving systemic rescue medication were required to washout for 5 half-lives prior to initiating treatment in the Escape Arm. In the Long-Term Extension Period, patients who did not achieving an EASI-50, from parent study baseline, by Week 16, maintaining an EASI-50 response, or not achieving clinical benefit were terminated from study. Additionally, in the Escape Arm, intermittent use of TCS for patients who required short-term systemic treatment for AD (assessed on a case-by-case basis) was permitted, but patients requiring long-term systemic treatment (eg, non-responders) were discontinued from the study.

Parent Studies (ADvocate1&2)

- Adults (≥18 years) and adolescents (≥12 to <18 years; weight ≥40 kg)
- Diagnosis of AD, as defined by the American Academy of Dermatology Consensus Criteria, for ≥1 year before screening
- Moderate-to-severe AD, defined as having all the following at the baseline visit:
  - EASI ≥16
  - IGA ≥3
  - BSA involvement ≥10%

ADjoin

- Patients could be included if they completed the study treatment and the last patient visit of the parent trial
- Patients were excluded if in the parent trial they:
  - Developed an SAE related to lebrikizumab or an AE related to lebrikizumab that led to treatment discontinuation, which indicated that continued treatment with lebrikizumab could present an unreasonable risk for the patient
  - Met conditions in the previous parent study consistent with protocol-defined criteria for permanent study drug discontinuation, if deemed related to lebrikizumab or if led to investigator- or sponsor-initiated withdrawal of patient from the study (eg, non-compliance, inability to complete study assessments)

Outcomes

- Deep response was assessed using:
  - IGA (0) (in Week 16 responders achieving IGA [0,1] at Week 16 of parent study)
  - EASI 90 (in Week 16 responders achieving EASI 75 at Week 16 of parent study)
  - EASI 100 (in Week 16 responders achieving EASI 75 at Week 16 of parent study)
- Quality of life was assessed using:
  - Total score POEM[3] (0,1) in Week 16 responders
    - POEM is a validated, patient-reported, 7-item questionnaire that assesses AD-specific symptoms over the past week
      - Patients respond to questions about the frequency of itch, sleep disturbance, bleeding, weeping/oozing, cracking, flaking, and dryness/roughness, with each symptom scored from 0 to 4 (*0=no days; 1=1 to 2 days; 2=3 to 4 days; 3=5 to 6 days; and 4=every day*)
      - Total scores range from 0 to 28, with lower total score indicating better quality of life

Note: Responders in ADvocate1&2 were defined as those patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of LEBRI 250 mg Q2W treatment without use of rescue therapy.

Statistical Analyses and Assessment

- Analysis populations:
  - **Parent studies (ADvocate1&2):** Week 16 lebrikizumab responders[a] randomized to lebrikizumab 250 mg Q4W or lebrikizumab 250 mg Q2W
  - **ADjoin:** Lebrikizumab responders[a] randomized to lebrikizumab 250 mg Q4W or lebrikizumab 250 mg Q2W at Week 16 (ADvocate1&2), and enrolled into ADjoin at Week 52 with the same dosage regimen
- Efficacy analyses:
  - Descriptive statistics were reported using all collected as-observed data, regardless of rescue medication use

[a]Responders were defined as those patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of LEBRI 250 mg Q2W treatment without use of rescue therapy in ADvocate1&2.

Abbreviations: *AD=atopic dermatitis; AE=adverse event; BMI=body mass index; BSA=body surface area; EASI=Eczema Area and Severity Index; EASI 75/90/100=≥75%/≥90%/100% improvement from baseline in EASI; IGA=Investigator's Global Assessment; IGA (0)=IGA response of clear; IGA (0,1)=IGA response of clear or almost clear; LD=loading dose; LEBRI=lebrikizumab; Nx=number of patients with non-missing values; PBO=placebo; POEM=Patient-Oriented Eczema Measure; Q2W=every 2 weeks; Q4W=every 4 weeks; R=randomization; SAE=serious AE; SD=standard deviation; TCI=topical calcineurin inhibitor; TCS=topical corticosteroid; TEAE=treatment-emergent AE*

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