Efficacy and Safety of Once-Daily Roflumilast Cream 0.05% in Pediatric Patients Aged 2– 5 Years With Mild-to-Moderate Atopic Dermatitis: A Phase 3 Randomized Controlled Trial (INTEGUMENT-PED)

Poster 2

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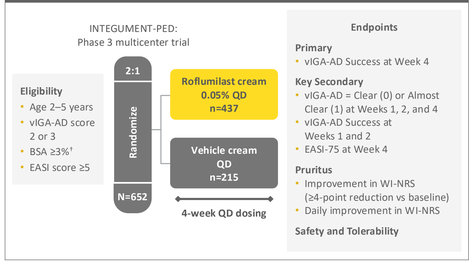
INTRODUCTION

- Current topical atopic dermatitis (AD) treatments are limited by dosing frequency, local tolerability issues, and restrictions on application to the face/eyelids, large body surface areas, and long-term use
- Roflumilast cream 0.05% is a once-daily nonsteroidal topical formulation of roflumilast, a potent phosphodiesterase 4 (PDE4) inhibitor
  - Demonstrated safety and efficacy in Phase 3 trials in patients with psoriasis (≥2 years of age)[1] and seborrheic dermatitis (≥9 years of age)[2]
  - Roflumilast potency is ~25 to >300-fold higher than apremilast and crisaborole,[3] with roflumilast more closely mimicking cyclic adenosine monophosphate (cAMP) binding to PDE4[4]
  - Does not contain ethanol, propylene glycol, or fragrances that can irritate skin
- In two Phase 3 trials (INTEGUMENT-1 and 2; NCT04773587, NCT04773600) and in the Phase 3 open-label extension trial (INGETUMENT-OLE; NCT04804605), roflumilast cream 0.15% was well tolerated and demonstrated efficacy in patients aged ≥6 years with AD[5,6]; assessment of safety and efficacy in patients 2–5 years of age in INTEGUMENT-OLE is complete
  - Continued improvement in efficacy over 56 weeks of treatment with roflumilast cream 0.15% in patients ≥6 years of age was observed in INTEGUMENT-OLE, with 61.5% and 66.2% of patients achieving ≥75% improvement in Eczema Area and Severity Index (EASI-75) after 28 and 56 weeks, respectively
  - Here, we present results of a Phase 3 trial (INTEGUMENT-PED; NCT04845620) of roflumilast cream 0.05% in patients aged 2–5 years with AD

METHODS

- Children aged 2–5 years with mild-to-moderate AD were treated with roflumilast cream 0.05% or vehicle once daily for 4 weeks (**Figure 1**)
- The primary efficacy endpoint was Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) Success (defined as a score of 0 [clear] or 1 [almost clear] plus ≥2-grade improvement from baseline) at Week 4

Figure 1. Study Design



†No upper limit on BSA restriction.
vIGA-AD Success = Clear or Almost Clear vIGA-AD status plus ≥2-grade improvement from baseline.
BSA: body surface area; EASI: Eczema Area and Severity Index; EASI-75: ≥75% reduction in EASI score from baseline; QD: once daily; vIGA-AD: Validated Investigator Global Assessment for Atopic Dermatitis; WI-NRS: Worst Itch Numerical Rating Scale.

RESULTS

- Demographics and baseline disease characteristics were similar between the groups (**Table 1–2**)
- At Week 4, significantly more roflumilast-treated than vehicle-treated patients achieved vIGA-AD Success (25.4% vs 10.7%; *P*<0.0001; **Figure 2**), vIGA-AD Clear or Almost Clear (35.4% vs 14.6%; *P*<0.0001; **Figure 3**), EASI-75 (39.4% vs 20.6%; *P*<0.0001; **Figure 4**), and Worst Itch-Numeric Rating Scale (WI-NRS) Success (≥4-point improvement in patients with baseline score ≥4) (35.3% vs 18.0%; nominal *P*=0.0002; **Figure 5**); significantly greater improvements in daily WI-NRS scores were observed for roflumilast versus vehicle starting at 24 hours after the first application (*P*=0.0014; **Figure 6**)

Table 1. Demographics: ITT Population

	Roflumilast 0.05% (n=436)	Vehicle (n=215)
Age, years, mean (SD)	3.3 (1.1)	3.2 (1.1)
Male, n (%)	225 (51.6)	116 (54.0)
Race, n (%)		
Asian	37 (8.5)	17 (7.9)
Black or African American	68 (15.6)	32 (14.9)
White	294 (67.4)	156 (72.6)
Other or >1 race	37 (8.5)	10 (4.7)
Ethnicity, n (%)		
Hispanic or Latino	82 (18.8)	31 (14.4)
Not Hispanic or Latino	351 (80.5)	184 (85.6)
Not reported	3 (0.7)	0
Fitzpatrick skin type, n (%)†		
I–III	279 (64.0)	148 (68.8)
IV–VI	157 (36.0)	66 (30.7)
Key body areas involved, n (%)		
Face	226 (51.8)	119 (55.3)
Eyelids	90 (20.6)	51 (23.7)
Prior inadequate response, intolerance, or contraindication to:		
Topical corticosteroids	226 (51.8)	114 (53.0)
Topical calcineurin inhibitors	74 (17.0)	35 (16.3)
Crisaborole	40 (9.2)	18 (8.4)

†Fitzpatrick skin type data was missing for 1 patient in the vehicle group.
ITT: intent-to-treat; SD: standard deviation.

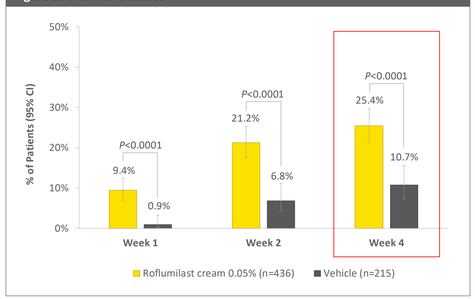
Table 2. Baseline Disease Characteristics: ITT Population

	Roflumilast 0.05% (n=436)	Vehicle (n=215)
Baseline vIGA-AD, n (%)		
2 (mild)	99 (22.7)	43 (20.0)
3 (moderate)	337 (77.3)	172 (80.0)
EASI		
Mean (SD)	12.2 (6.9)	11.6 (6.2)
Median (min, max)	10.3 (4.6, 42.0)	9.5 (5.0, 32.9)
BSA		
Mean (SD)	22.5 (16.4)	21.2 (15.7)
Median (min, max)	17.3 (3.0, 82.0)	16.5 (4.0, 78.8)
Average weekly baseline WI-NRS		
Mean (SD)	6.2 (2.3)	5.9 (2.2)
Median (min, max)	6.6 (0, 10)	6.3 (0, 10)
Average weekly baseline WI-NRS ≥4, n (%)	347 (79.6)	160 (74.4)

max: maximum; min: minimum.

Overall, 519 (79.7%) patients had a baseline BSA ≥10%

Figure 2. vIGA-AD Success



Box indicates primary endpoint. CI: confidence interval.

Figure 3. vIGA-AD Clear or Almost Clear

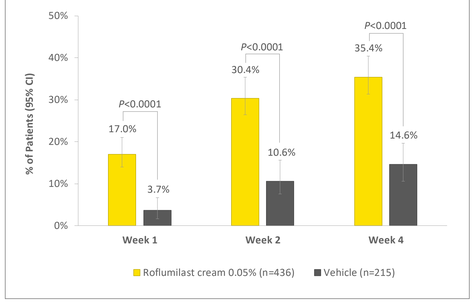


Figure 4. EASI-75

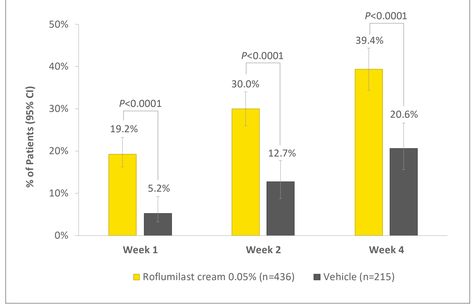
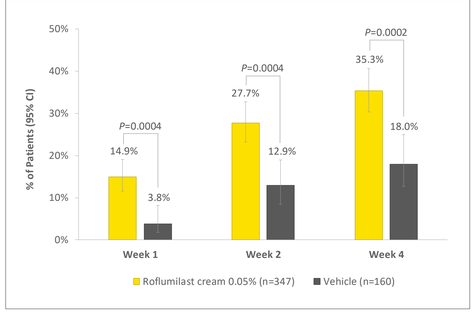
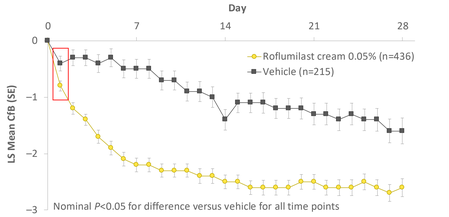


Figure 5. WI-NRS Success



WI-NRS Success = ≥4-point improvement in patients with baseline score ≥4.

Figure 6. LS Mean Change From Baseline in Daily WI-NRS Score

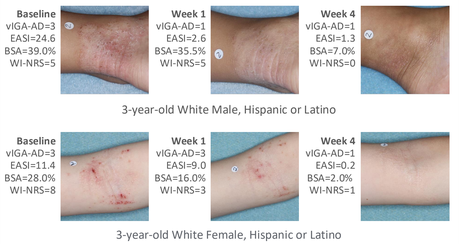


Improvement in itch with roflumilast cream 0.05% was observed at 24 hours after first application (indicated by box; *P*=0.0014 vs vehicle)

Evaluated in all patients, not just those with baseline WI-NRS ≥4.
CfB: change from baseline; LS: least squares; SE: standard error.

- A series of photographs of patients with improvement in AD following treatment is shown in **Figure 7**
- AEs occurring in >2% of patients and greater in the roflumilast-treated group were upper respiratory tract infection, diarrhea, and vomiting (**Table 3**)
- For local tolerability, >92% of roflumilast-treated patients reported no or mild sensation across treatment groups at any time point (**Figure 8**)

Figure 7. Treatment With Roflumilast Cream 0.05% Once Daily



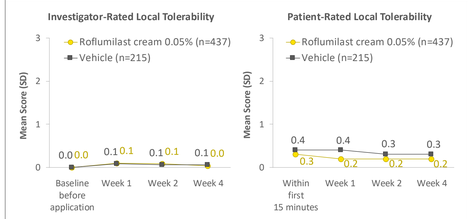
Values represent global assessments. vIGA-AD, EASI, BSA, and WI-NRS are global assessments.

Table 3. Safety

n (%)	Roflumilast 0.05% (n=437)	Vehicle (n=215)
Patients with at any TEAE	130 (29.7)	47 (21.9)
Patients with any treatment-related TEAE	15 (3.4)	6 (2.8)
Patients with at least one treatment-emergent SAE†	1 (0.2)	0
Patients with at least one TEAE leading to IP discontinuation††	5 (1.1)	5 (2.3)
Patients with at least one TEAE on an application site	23 (5.3)	13 (6.0)
Most common TEAEs by preferred term, >2 in either group and greater in the roflumilast-treated group		
Upper respiratory tract infection	18 (4.1)	3 (1.4)
Diarrhea	11 (2.5)	1 (0.5)
Vomiting	9 (2.1)	0

†SAE: 2-year-old female, cellulitis of right leg on non-eczematous skin, hospitalized 3 days for antibiotics. IP held for 5 days; SAE deemed unlikely related to study drug; event resolved.
††Roflumilast: application site pain, dermatitis atopic, impetigo, neurodermatitis, varicella; Vehicle: application site pain, dermatitis atopic, upper respiratory tract infection, urticaria.
AE: adverse event; IP, investigational product; SAE: serious adverse event; TEAE: treatment-emergent adverse event.

Figure 8. Investigator- and Patient-Rated Local Tolerability



Scale for investigator-rated local tolerability (0–7)
0 = no evidence of irritation; 1 = minimal erythema, barely perceptible; 2 = definite erythema, readily visible; minimal edema or minimal papular response; 3 = erythema and papules; 4 = definite edema; 5 = erythema, edema, and papules; 6 = vesicular eruption; 7 = strong reaction spreading beyond application site

Scale for patient-rated local tolerability (0–3)
0 (none) = no sensation; 1 (mild) = slight warm, tingling sensation; not really bothersome; 2 (moderate) = definite warm, tingling sensation that is somewhat bothersome; 3 (severe) = hot, tingling/stinging sensation that has caused definite discomfort

59 (9%) patients reported prior inadequate response, intolerance, or contraindication to crisaborole
35 of the 59 patients reported stinging, burning, and/or poor tolerability as a reason for stopping crisaborole
Among these 35 patients, 2 of 21 roflumilast-treated and 1 of 14 vehicle-treated patients reported any application site TEAE

CONCLUSION

- Once-daily, nonsteroidal roflumilast cream 0.05% significantly improved AD in children 2–5 years of age
  - Significant improvement in AD was observed as early as 1 week after treatment initiation
  - Reduction in pruritus was observed 24 hours (*P*=0.0014) following the first application
- No adverse event occurred in >4.1% of patients in either treatment group
- Efficacy and safety were consistent with previous trials of roflumilast cream 0.15% in patients ≥6 years of age with AD (INTEGUMENT-1/2[5] and INTEGUMENT-OLE[6])

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ACKNOWLEDGMENTS

Thank you to the investigators and their staff for their participation in the trials. We are grateful to the study participants and their families for their time and commitment. Writing support was provided by Lauren Ramsey, PharmD, Alligent Biopharm Consulting LLC, and funded by Arcutis Biotherapeutics, Inc.

DISCLOSURES

LE, JB, TF, MEG, AAH, ML, VHP, RS, and LS are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; RH and DB are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.

ID #1

Associations between atopic dermatitis flares and treatments: Advanced practice providers' reports from a real-world study in the United States

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OBJECTIVE

This study examined the association between flare experiences and treatment use in patients with a history of moderate-to-severe AD.

CONCLUSION

Despite current treatments, AD flares were common in patients with a history of moderate-to-severe AD.

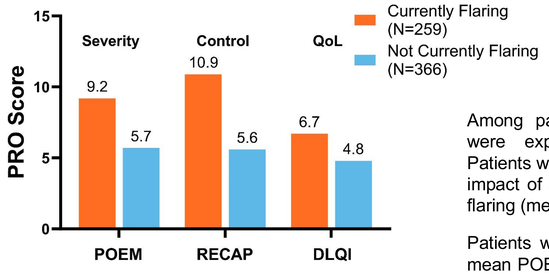
Patients who were currently flaring were less likely to be receiving systemic/biologic (dupilumab) or topical (crisaborole) treatments approved for AD than those who were not currently flaring.

RELEVANCE TO THE DERMATOLOGY PRACTITIONER

Flares appear to be managed reactively with corticosteroids. Future research should explore if flares can be managed proactively, reducing the severity and incidence of flares, with systemic or AD-indicated therapies and which therapies improve disease control.

2025 SDNP National Conference; Indian Wells, CA; April 30 - May 3, 2025

Patient Reported Measures

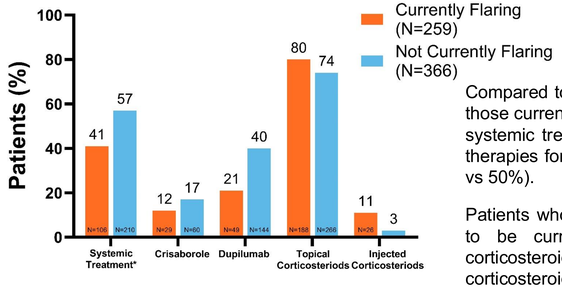


POEM scores: Clear or almost clear = 0 to 2; Mild eczema = 3 to 7; Moderate eczema = 8 to 16; Severe eczema = 17 to 24; Very severe = 25 to 28. RECAP scores: 0–1 (completely controlled), 2–5 (mostly controlled), 6–11 (moderately controlled), 12–19 (a little controlled), 20–28 (not at all controlled). DLQI scores: 0-1 = no effect at all on patient's life, 2-5 = small effect on patient's life, 6-10 = moderate effect on patient's life, 11-20 = very large effect on patient's life, 21-30 = extremely large effect on patient's life.

Among patients who were currently flaring, 85% were experiencing a moderate-to-severe flare. Patients who were currently flaring reported a greater impact of AD on their QoL than those not currently flaring (mean DLQI score 6.7 vs 4.8).

Patients who were currently flaring reported higher mean POEM scores (9.2 vs 5.7) and RECAP scores (10.9 vs 5.6) at the time of the flare.

Current Treatments



Compared to patients who were not currently flaring, those currently flaring were less likely to be using any systemic treatment (41% vs 57%) or FDA approved therapies for AD (crisaborole and/or dupilumab; 29% vs 50%).

Patients who were currently flaring were more likely to be currently prescribed very potent topical corticosteroids (80% vs 74%) or injected corticosteroids (11% vs 3%).

*Systemic treatment included Oral corticosteroid, Injected corticosteroid, Cyclosporine, Azathioprine, Methotrexate, Mycophenolate mofetil, and dupilumab

Patient Demographics

Characteristic	Currently Flaring* N=259	Not Currently Flaring N=366
Age-years, mean (SD)	42.2 (18.64)	41.2 (18.4)
Female sex n (%)	144 (56%)	209 (57%)
Race, n (%)		
White/Caucasian	177 (68%)	235 (64%)
African American	45 (17%)	69 (19%)
Native American	1 (0%)	3 (1%)
Asian	14 (6%)	19 (5%)
Hispanic / Latino	13 (5%)	24 (7%)
Middle Eastern	2 (1%)	5 (1%)
Mixed race	3 (1%)	5 (1%)
South-East Asian	4 (2%)	4 (1%)
Other	0 (0%)	2 (1%)

Disease Characteristics

Characteristic	Currently Flaring* N=259	Not Currently Flaring N=366
Days since first diagnosis, mean (SD)	1437.6 (2726.29)	1916.3 (2365.6)
Level of severity at first diagnosis, n (%)		
Mild	26 (10%)	49 (13%)
Moderate	146 (57%)	152 (42%)
Severe	50 (19%)	131 (36%)
Don't know	37(14%)	34 (9%)
EASI Score, mean (SD)	8.1 (8.12)	5.6 (6.04)
BSA, mean % (SD)	17.6 (16.85)	10.6 (13.28)
RECAP Score, mean (SD)	10.9 (8.16)	5.6 (5.56)
Under Control (<6 RECAP Score), n %	12 (31%)	49 (60%)

*Flares were not defined and were left to the interpretation of the APP.

Methods

- Data were drawn from the Adelphi AD Disease Specific Programme[1], a cross-sectional real-world study conducted in the United States between February 2021 and February 2022.
- For each patient, the NP/PA completed a patient record form including demographics, subjective HCP assessment of overall current AD severity (mild, moderate or severe), body areas affected, assessment of disease progression (improving, stable, changeable or deteriorating), level of satisfaction with disease control on current treatment (satisfied/neither/dissatisfied).
- Patients filled out a questionnaire including their subjective assessment of current AD severity, disease progression, level of satisfaction with current treatment.
- Patients also completed validated patient reported outcome (PRO) tools including the Dermatology Life Quality Index (DLQI)[2], Patient Oriented Eczema Measure (POEM)[3], RECAP of Atopic Eczema[4].
- Patients were grouped according to flare status: whether they were currently flaring or not currently flaring at the time of the study, flares were not defined and left to the interpretation of the APP.

Acknowledgments: The authors would like to thank Conor McVeigh, employee of Eli Lilly and Company, for their writing and editorial contributions.

Key Eligibility Criteria

- **Healthcare professional (HCP) inclusion criteria:**
  - Nurse practitioners/physician assistants (NPs/PAs)
  - Affiliated with a dermatologist or allergist
  - Involved in drug management of adult patients with atopic dermatitis
- **Patient inclusion criteria:**
  - Next 10 consenting adult (18 years or older) patients
  - Currently moderate-to-severe or with a history of moderate-to-severe AD
  - Involved in drug management of adult patients with atopic dermatitis

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Flare* Characteristics

What is the severity of this patient's current acute episode (flare)? (n, %)	Currently Flaring	Not Currently Flaring
	n=259	n=NA
Mild	40 (15%)	NA
Moderate	163 (63%)	NA
Severe	56 (22%)	NA
What is the typical duration of an acute episode for this patient? (day)	**Currently Flaring**	**Not Currently Flaring**
	n=243	n=363
Mean	14.0	11.4
Min	1	1
Max	60	60
Std dev	10.59	8.64
Over the last 12 months, has the number of flares this patient experiences: n (%)	**Currently Flaring**	**Not Currently Flaring**
	n=389	n=148
Increased	67 (17%)	43 (29%)
Stayed the same	177 (46%)	86 (58%)
Decreased	145 (37%)	19 (13%)

*Flares and flare severity were not defined and were left to the interpretation of the APP. Flare severity was not assessed in patients not currently flaring.

Disclosures: LM is a consultant for Abbvie, Amgen, BMS, Castle, Dermavant, Galderma,Ferndale, Sanofi, J&J, Lilly, Boehringer Ingelheim, UCB and receives honorarium. She is a speaker for Abbvie, Amgen, BMS, Dermavant, Sanofi, Lilly, UCB and receives honorarium. ZD and EP are employees and shareholders of Eli Lilly and Company. JL is a speaker/consultant for Regeneron/Sanofi, Arcutis, Abbvie, Lilly, Galderma, Leo Pharma, J&J, UCB, Organon/Dermavant. PA,JP and SM are employees of Adelphi Group, which was contracted by Incyte Corporation to perform this analysis. MY has received investigator fees, speaker fees, clinical research grants, and/or honoraria from AbbVie, Amgen, Arcutis, Lilly, Johnson and Johnson, Sun, Dermavant, Sanofi, Novartis, Takeda, Alumis, Anaptys, Aslan, Pfizer, Caratherapeutics, Boehinger Ingelheim, Leo, and UCB.

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Patient-Reported Outcomes and Family Impact With Roflumilast Cream in Atopic Dermatitis: Pooled Results From the Phase 3 INTEGUMENT-1 and INTEGUMENT-2 Trials

Poster 3

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INTRODUCTION

- Atopic dermatitis (AD) is a chronic inflammatory skin disease that has a substantial impact on patients' quality of life[1,2]; families/parents/caregivers of children and adolescents with AD are also negatively impacted[2,3]
- Roflumilast, a potent phosphodiesterase 4 inhibitor (PDE4), is formulated as a water-based cream and foam
  - Roflumilast potency is ~25 to >300-fold higher than other PDE4 inhibitors apremilast and crisaborole, with roflumilast more closely mimicking cyclic adenosine monophosphate binding[4,5]
  - Roflumilast cream 0.15% was recently approved by the US Food and Drug Association for treatment of mild-to-moderate AD in patients aged ≥6 years
- The safety, efficacy, and patient-reported outcomes from two identically designed phase 3 trials (INTEGUMENT-1/INTEGUMENT-2) of once-daily roflumilast cream 0.15% in patients aged ≥6 years with AD have been published[6,7]; here, we present the overall improvement in AD signs and symptoms as well as the impact on families and caregivers

METHODS

Study Design

Identically designed, parallel, phase 3 multicenter trials (NCT04773587, NCT04773600)

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

Randomize 2:1

- Roflumilast Cream 0.15% QD
- Vehicle Cream QD

4 weeks dosing[a]

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

- The primary endpoint was Validated Investigator Global Assessment for AD (vIGA-AD) Success (0 [Clear] or 1 [Almost Clear] plus ≥2-grade improvement from baseline) at Week 4
- Other outcome measures included Worst Itch-Numeric Rating Scale (WI-NRS), SCORing AD (SCORAD) total score, Patient-Oriented Eczema Measure (POEM), and Dermatitis Family Impact (DFI; patients aged ≤17 years)
- Safety and local tolerability were also assessed

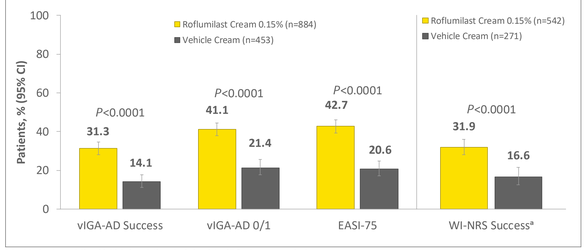
RESULTS

Patient Demographics and Baseline Disease Characteristics

		Roflumilast Cream 0.15% (n=884)	Vehicle Cream (n=453)
Age, years, mean (SD)		27.9 (19.4)	27.3 (19.0)
Age group, n (%)	6–11 years	214 (24.2)	103 (22.7)
	12–17 years	192 (21.7)	106 (23.4)
	18–64 years	434 (49.1)	223 (49.2)
	≥65 years	44 (5.0)	21 (4.6)
Female at birth, n (%)		489 (55.3)	272 (60.0)
Hispanic or Latino, n (%)		150 (17.0)	72 (15.9)
Race, n (%)	White	529 (59.8)	267 (58.9)
	Asian	114 (12.9)	62 (13.7)
	Black/African American	176 (19.9)	96 (21.2)
	American Indian/Alaskan Native	7 (0.8)	1 (0.2)
	Native Hawaiian/Other Pacific Islander	1 (0.1)	0
	>1 race	24 (2.7)	14 (3.1)
	Other	33 (3.7)	13 (2.9)
Fitzpatrick skin type, n (%)	I–III	481 (54.4)	238 (52.5)
	IV–VI	403 (45.6)	215 (47.5)
vIGA-AD,[a] n (%)	2 (mild)	211 (23.9)	112 (24.7)
	3 (moderate)	673 (76.1)	341 (75.3)
BSA, mean (median) [range]		13.5 (9.7) [3.0–88.0]	13.9 (10.0) [3.0–86.0]
WI-NRS[b]	Mean (median)	6.1 (6.3)	5.9 (6.0)
	Average weekly baseline score ≥4, n (%)	542 (61.3)	271 (59.8)
SCORAD,[c] mean (median) [range]		45.5 (45.3) [18.2–81.5]	45.1 (43.9) [20.9–83.5]
POEM,[d] mean (median) [range]		15.8 (16) [0–28]	15.3 (15) [0–28]
DFI,[e] mean (median) [range]		6.5 (5) [0–27]	6.5 (5) [0–30]

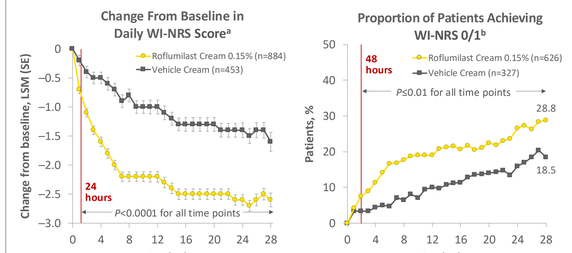
[a]5-point scale ranging from 0 (Clear) to 4 (Severe) assessing inflammatory signs of AD. [b]11-point scale ranging from 0 (no itch) to 10 (worst itch imaginable) assessed only in patients aged ≥12 years. [c]Scored up to 103 based on extent of involvement, disease intensity, and subjective symptoms. [d]Scale ranging from 0–2 (Clear/Almost Clear) to 28 (Very Severe) measuring disease severity per patient reports of signs and symptoms. [e]Scored up to 30 evaluating the effect of AD on patients' family life and relationships for patients aged ≤17 years.

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



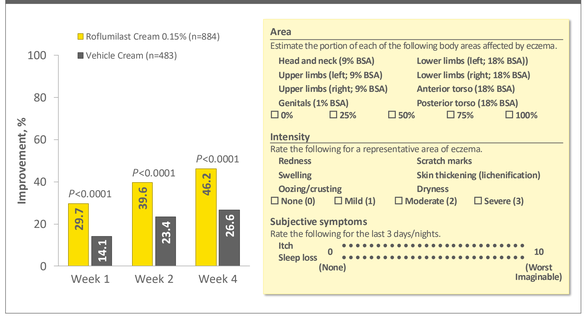
Intent-to-treat population. Multiple imputation of missing data. All *P* values are nominal.
[a]WI-NRS success was evaluated in patients aged >12 years with baseline WI-NRS ≥4.
vIGA-AD Success = 0 (Clear) or 1 (Almost Clear) plus ≥2-grade improvement from baseline. EASI-75 = ≥75% reduction from baseline. WI-NRS Success = ≥4-point improvement in patients with baseline WI-NRS score ≥4.

Improvements in Pruritus



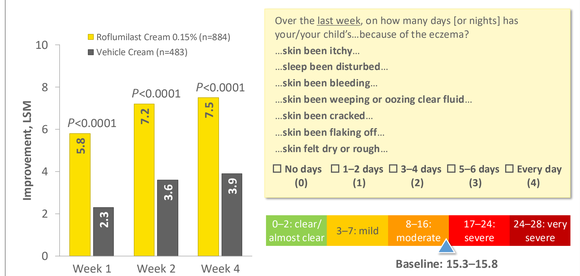
All *P* values are nominal.
[a]Evaluated in all patients, not just those with baseline WI-NRS ≥4. [b]Evaluated in patients aged >12 years with baseline WI-NRS ≥2.
LSM: least squares mean.

Improvements in SCORing AD (SCORAD) Total Score



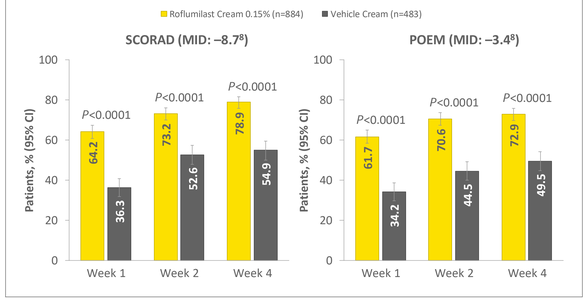
All *P* values are nominal.

Improvements in Patient-Oriented Eczema Measure (POEM)



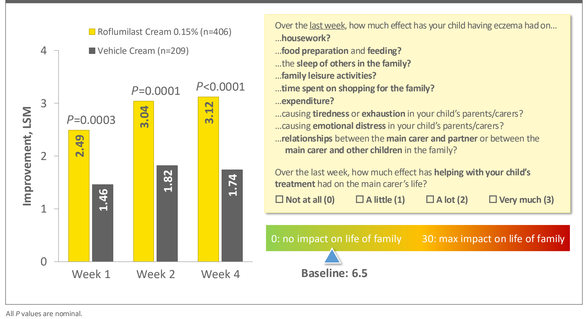
All *P* values are nominal.

Proportions of Patients Achieving Minimally Important Differences (MIDs)



All *P* values are nominal.

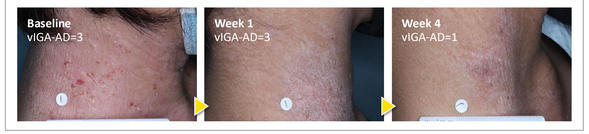
Improvements in Dermatitis Family Impact (DFI)



All *P* values are nominal.
DFI was evaluated in patients aged ≤17 years.

Neck of an 11-Year-Old Female With AD Treated With Roflumilast Cream 0.15%

Asian, Not Hispanic/Latino
Fitzpatrick skin type V
Duration of AD: 6 years
Prior intolerance, inadequate response, or contraindication to TCS



vIGA-AD is a global assessment.

Safety and Local Tolerability

- Incidence of TEAEs was low in both treatment groups

Patients, n (%)	Roflumilast Cream 0.15% (n=885)	Vehicle Cream (n=451)
Patients with any treatment-related TEAE	53 (6.0)	12 (2.7)
Patients with any treatment-emergent SAE[a]	8 (0.9)	0
Patients with any TEAE leading to discontinuation of trial/trial drug	14 (1.6)	5 (1.1)
Patients with any TEAE[b]	194 (21.9)	65 (14.4)

[a]SAEs were: atopic dermatitis, cutaneous nerve entrapment, depression, diverticulitis, general physical health deterioration, pulmonary embolism, staphylococcal scalded skin syndrome, suicidal ideation. [b]Most frequently reported TEAEs (≥1% in either group) were (roflumilast/vehicle): headache (2.9%/0.9%), nausea (1.9%/0.4%), application site pain (1.5% 0.7%), diarrhea (1.5%/0.4%), vomiting (1.5%/0.4%), and COVID-19 (0.8%/1.8%).

- Local tolerability was similar for roflumilast and vehicle. Across both treatment groups at all time points:

>95% of patients showed **no signs of irritation** on investigator-rated local tolerability assessments

>90% of patients reported **no or mild (slight warm tingling that was not really bothersome)** sensation

CONCLUSIONS

- Once-daily nonsteroidal roflumilast cream 0.15% provided meaningful improvements in signs and symptoms of AD, including improvement in pruritus within 24 hours of application
- Roflumilast cream also improved the impact of AD on patients' families and patient-reported measures
- Roflumilast cream was well tolerated, with low rates of discontinuations because of AEs occurring in both groups
- Local tolerability with roflumilast was generally similar to that of patients treated with vehicle

ABBREVIATIONS

AD: atopic dermatitis; BSA: body surface area; DFI: Dermatitis Family Impact Questionnaire; EASI: Eczema Area and Severity Index; LSM: least squares mean; MID: minimal important difference; PED4: phosphodiesterase 4 inhibitor; POEM: Patient-Oriented Eczema Measure; QD: once daily; SCORAD: SCORing Atopic Dermatitis; TCS: topical corticosteroids; vIGA-AD: Validated Investigator Global Assessment for Atopic Dermatitis; WI-NRS: Worst Itch-Numeric Rating Scale.

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ACKNOWLEDGMENTS

Thank you to the investigators and their staff for their participation in the trial. We are grateful to the study participants and their families for their time and commitment. Writing support was provided by Lauren Ramsey, PharmD, and Christina McManus, PhD, Alligent Biopharm Consulting LLC, and funded by Arcutis Biotherapeutics, Inc.

DISCLOSURES

ELS, MB, LFE, BG, VHP, and SFF are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; DRB and DHC are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.

Clinical Efficacy and Patient-Reported Impacts of Roflumilast Foam 0.3% in Seborrheic Dermatitis: An Analysis of STRATUM Data for Patients Unresponsive or Intolerant to Topical Corticosteroids

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[1]Arcutis Biotherapeutics, Inc., Westlake Village, CA; [2]Lumanity Inc., Bethesda, MD; [3]DOCS Dermatology, Probity Medical Research, and Ohio University, Bexley, OH

INTRODUCTION

- Seborrheic dermatitis (SD) is a chronic, inflammatory, dermatologic condition that causes flaking scales and persistent itching.[1] Treatment options include topical corticosteroids (TCS), which present challenges such as limited efficacy and adverse effects[1]
- In the Phase 3 STRATUM trial, roflumilast foam 0.3% demonstrated efficacy and tolerability in the treatment of moderate-to-severe SD (**Table 1**)[2]
- This subgroup analysis supports that roflumilast foam 0.3% provides meaningful efficacy and quality-of-life (QOL) improvements in patients with SD who report an inadequate response, intolerance, or contraindication to TCS prior to enrollment in STRATUM

METHODS

- Patients aged ≥ 9 years with at least moderate SD (Investigator Global Assessment [IGA] ≥ 3) who reported a previous inadequate response, intolerance, or contraindication to TCS were randomized 2:1 to roflumilast foam 0.3% or vehicle for 8 weeks
- Efficacy was assessed using a 5-point physician-evaluated IGA – a common clinical endpoint used in dermatology trials. The primary efficacy endpoint was IGA success (Clear or Almost Clear with at least a 2-grade improvement) at Week 8
- QOL was evaluated in patients aged ≥ 17 years using the Dermatology Life Quality Index (DLQI) – a validated patient-reported questionnaire (score range of 0–30), with higher scores indicating greater QOL effects. Endpoints included percentage change from baseline in DLQI score, achievement of a minimal important difference (MID; defined as at least a 4-point reduction in baseline DLQI score), and achievement of a DLQI score of 0 or 1 (indicating no disease effect at all) by treatment group at Weeks 2, 4, and 8
- Differences in change from baseline DLQI scores were assessed using the Kruskal-Wallis test. The Cochran–Mantel–Haenszel test was used to assess differences in the proportion of patients achieving binary endpoints between treatment groups

RESULTS

- 189 patients at baseline were included in the subgroup analysis (129 roflumilast foam 0.3%; 60 vehicle). At Week 8, 78.8% of roflumilast foam 0.3% patients achieved IGA success versus 48.3% of vehicle patients (odds ratio [OR]: 3.45; 95% confidence interval [CI]: 1.62, 7.36; p < 0.001) (**Figure 1**)
- At all time points, percentage change from baseline in DLQI score was significantly greater for roflumilast foam 0.3%-treated patients relative to vehicle (**Figure 2**)
- Treatment with roflumilast foam 0.3% significantly increased the odds of achieving an MID in DLQI score from baseline to Weeks 2, 4, and 8 compared with vehicle (OR: 6.97; 95% CI: 3.97, 12.24; p < 0.001) (**Figure 3**)
- Relative to vehicle, the odds of achieving a DLQI score of 0 or 1 from baseline to Weeks 2, 4, and 8 was significantly higher for patients treated with roflumilast foam 0.3% (OR: 2.46; 95% CI: 1.58, 3.81; p < 0.001) (**Figure 4**)

Table 1. STRATUM study design[2]

Phase 3, parallel group, double-blind, vehicle-controlled study (N = 457)

Eligibility criteria
- Adults and adolescents (≥ 9 years of age) who had a clinical diagnosis of seborrheic dermatitis for at least 3 months
- Stable disease for at least 4 weeks before the baseline assessment
- IGA score of at least 3 on a 5-point scale
- Involvement of up to 20% BSA

Randomize 2:1

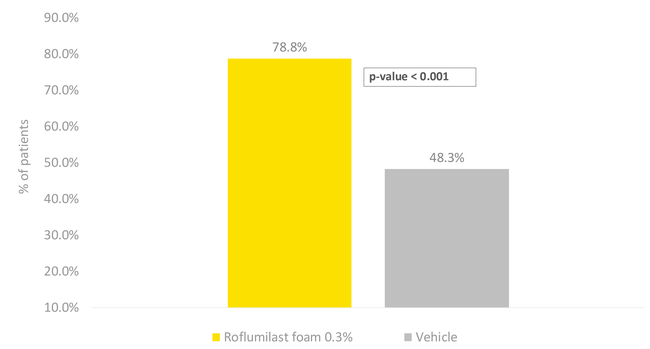
- **Roflumilast foam 0.3% QD**
- **Vehicle foam QD**

8 weeks dosing
Visits: Weeks 2, 4, 8

Baseline patient characteristics		
Age (years), mean (SD): 42.7 (17.03)	Male, n (%): 228 (49.9)	BSA (%), mean (SD): 2.92 (2.24)
IGA 3, n (%): 428 (93.7)	IGA 4, n (%): 29 (6.3)	WI-NRS, mean (SD): 4.95 (2.32)[a]

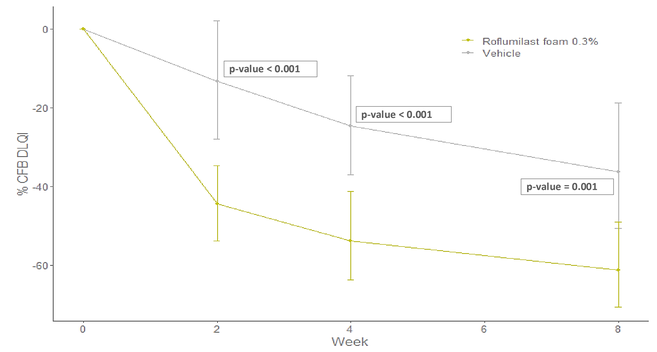
Key: BSA, body surface area; IGA, Investigator Global Assessment; QD, once daily; SD, standard deviation; WI-NRS, Worst Itch Numeric Rating Scale.

Figure 1. Patients achieving IGA success by treatment group at Week 8



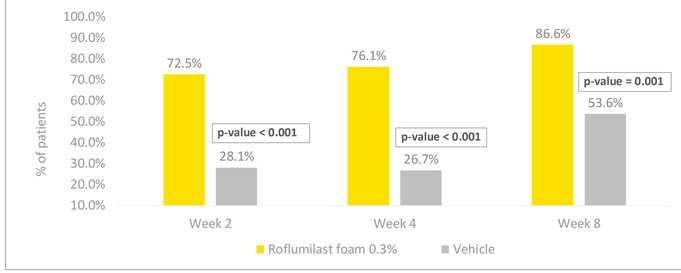
Key: IGA, Investigator Global Assessment.

Figure 2. Percentage change in baseline DLQI score by treatment group



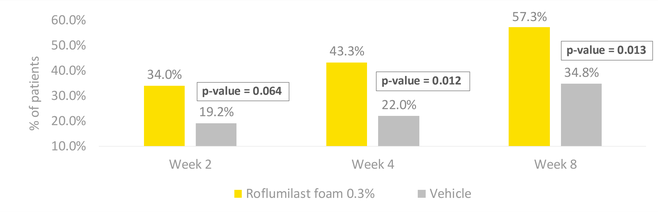
Key: CFB, change from baseline; DLQI, Dermatology Life Quality Index.

Figure 3. Patients achieving an MID in DLQI score by treatment group



Note: Patients were required to have a baseline DLQI score >4 for this analysis.
Key: DLQI, Dermatology Life Quality Index; MID, minimally important difference.

Figure 4. Patients achieving a DLQI score of 0 or 1 by treatment group



Key: DLQI, Dermatology Life Quality Index.

LIMITATIONS

- The limited follow-up period of 8 weeks in STRATUM may not allow for the assessment of long-term QOL impacts associated with roflumilast foam 0.3%
- Although the DLQI is a commonly used endpoint in dermatology clinical trials, it is not specific to SD and may not reflect the full impact of SD
- Patients with IGA scores below 3 were not included in the analysis; therefore, conclusions may not be applicable to those with SD classified as Mild (2)
- QOL was not assessed in participants from STRATUM aged 9 to < 17 years. QOL results may need to be confirmed in younger patients

CONCLUSIONS

- Patients with SD and an inadequate response, intolerance, or contraindication to TCS had approximately 3.5 times greater odds of achieving IGA success with roflumilast foam 0.3% treatment compared with vehicle
- Roflumilast foam 0.3% was associated with a rapid and significant improvement in DLQI scores relative to vehicle in this patient population. Furthermore, roflumilast foam 0.3%-treated patients had six times greater odds of achieving a clinically meaningful difference in DLQI score and twice as likely to achieve a score of 0 or 1
- Roflumilast foam 0.3% may offer important benefits for patients with SD when treatment with TCS is unsuccessful or contraindicated. This should be considered by providers and healthcare decision-makers when assessing treatment options for these patients

DISCLOSURES

This study was funded by Arcutis Biotherapeutics, Inc. DC and BS are employees of Arcutis Biotherapeutics, Inc. JL, BB, CH, RB, and TW are employees of Lumanity, Inc., a consulting company that provides paid consulting services to Arcutis Biotherapeutics, Inc. MZ is an employee of DOCS Dermatology.

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

Poster 5

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INTRODUCTION

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

OBJECTIVE

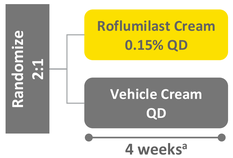
- Assess the efficacy of roflumilast cream 0.15% in patients with AD based on race (White, Black or African American, Asian, or other race), ethnicity (Hispanic or Latino, or Not Hispanic or Latino), and Fitzpatrick skin type (I–III or IV–VI) using pooled data from Phase 3 randomized controlled trials

METHODS

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

Study Design

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



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

ABBREVIATIONS

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

RESULTS

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

Patient Demographics

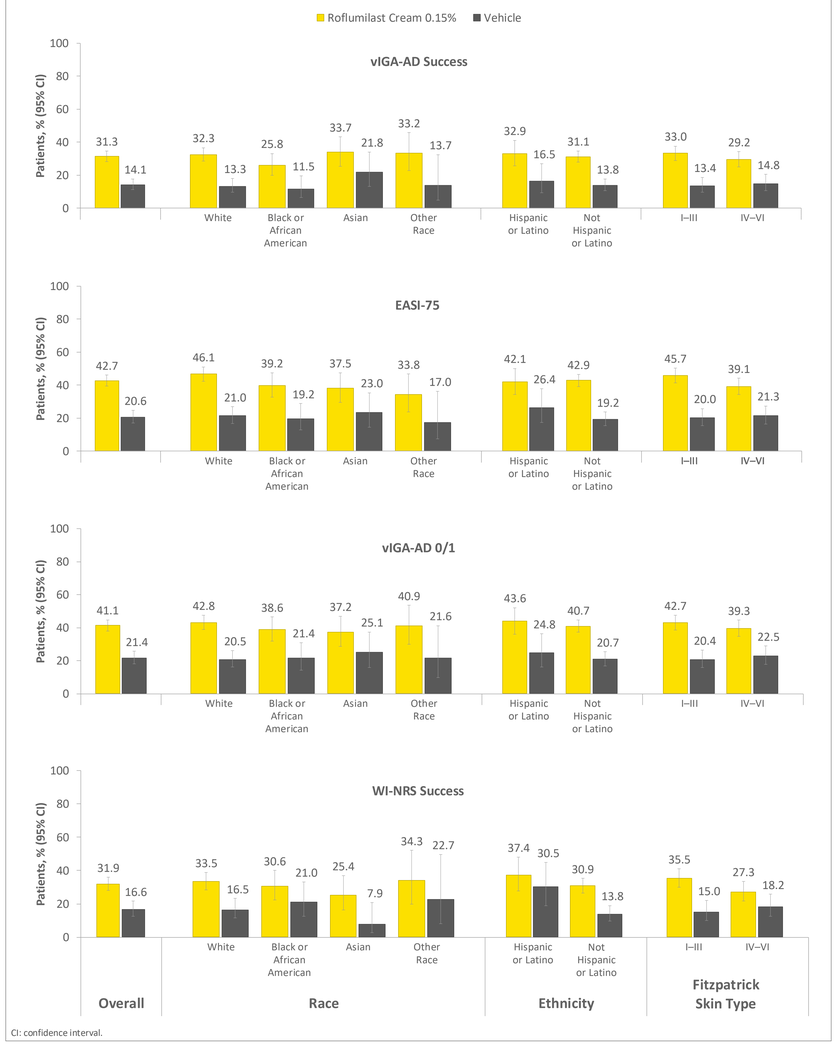
		Roflumilast Cream 0.15% (n=884)	Vehicle Cream (n=453)
Age, years, mean (SD) [range]		27.9 (19.4) [6–91]	27.3 (19.0) [6–84]
Female at birth, n (%)		489 (55.3)	272 (60.0)
Ethnicity, n (%)	Hispanic or Latino	150 (17.0)	72 (15.9)
	Not Hispanic or Latino	730 (82.6)	377 (83.2)
	Not reported[a]	4 (0.5)	4 (0.9)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

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

Baseline Disease Characteristics

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

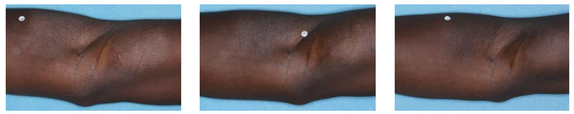
Proportion of Patients Achieving vIGA-AD Success, vIGA-AD 0/1, EASI-75, and WI-NRS Success at Week 4



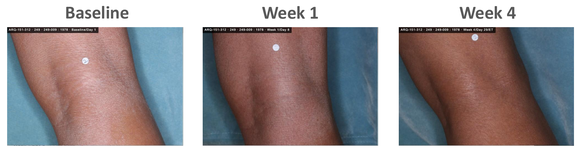
CI: confidence interval.

Improvement in Patients With AD Treated With Roflumilast Cream 0.15%

Antecubital fossa of a Black/African American non-Hispanic/Latino male, aged 15 years, Fitzpatrick skin type V, duration of disease 10 years, 2 flares in the previous 12 months



Popliteal fossa of an Asian non-Hispanic/Latino female, aged 43 years, Fitzpatrick skin type III, duration of disease 10 months, 10 flares in the previous 12 months



vIGA-AD and EASI are global measures.

Safety

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

CONCLUSIONS

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

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ACKNOWLEDGMENTS

This work was supported by Arcutis Biotherapeutics, Inc. Thank you to the investigators and their staff for their participation in the trial. We are grateful to the study participants and their families for their time and commitment. Writing support was provided by Christina McManus, PhD, CMPP, Lauren Ramsey, PharmD, and Ashley Oney, MD, Alligent Biopharm Consulting LLC, and funded by Arcutis Biotherapeutics, Inc.

DISCLOSURES

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

Comparative Efficacy of Lebrikizumab, Dupilumab, and Tralokinumab in Maintaining Treatment Response in Atopic Dermatitis at Varying Treatment Continuance Rates

Jonathan I. Silverberg[1], Alan Irvine[2], Peter Foley[3], James Del Rosso[4], Luis Puig[5], Linda Stein Gold[6], Martin Dossenbach[7], Marta Casillas[7], Gaia Gallo[7], Buelent Akmaz[8], Kim Rand[9], Louise Deluca Carter[7] (Non-author presenter)

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Sponsored by Eli Lilly and Company

OBJECTIVE

- This study aims to understand whether the durability of treatment effect is a critical factor to consider when managing a chronic disease such as atopic dermatitis (AD) whose symptoms can fluctuate over time.
  - In real-world settings, patients with AD may need to pause treatment or may not be completely compliant with treatment[1]
  - Recent phase 3 monotherapy trials indicate that the impact of treatment pauses may vary for dupilumab, tralokinumab, and lebrikizumab[2-4]
  - We developed the "durability index" (DI), a novel estimate of drug performance that captures a drug's ability to maintain efficacy whether on-therapy or off-therapy at the population level

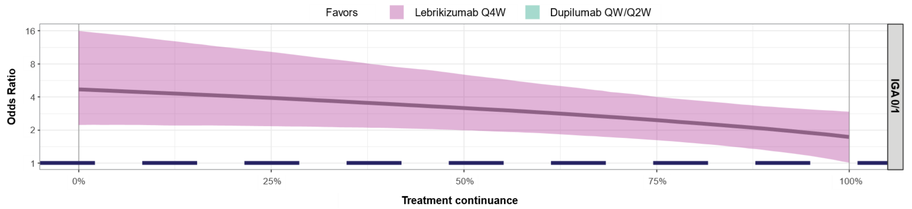
CONCLUSIONS

- This indirect comparative analysis demonstrates that biologics differ in their maintenance of population-level efficacy at varying treatment continuance rates
- Treatment responses were significantly higher for lebrikizumab than dupilumab or tralokinumab at most continuance rates, especially lower rates
- This finding suggests that lebrikizumab may have better maintenance of response in real-life settings where treatment pauses may occur, and continuance rates may be below 100%

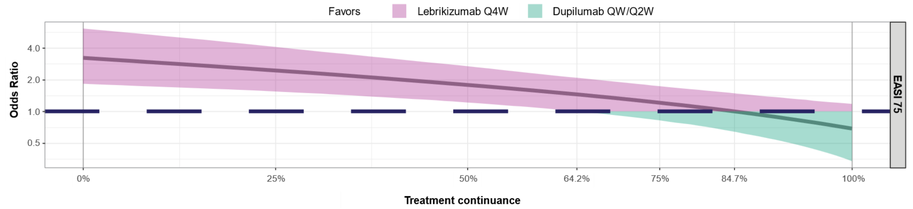
Society of Dermatology Nurse Practitioners (SDNP) National Conference 2025, Indian Wells, CA, USA; April 30 - May 3 2025

KEY RESULTS

Durability index odds ratios for lebrikizumab and dupilumab for IGA 0/1 and EASI 75 from 0% to 100% treatment continuance

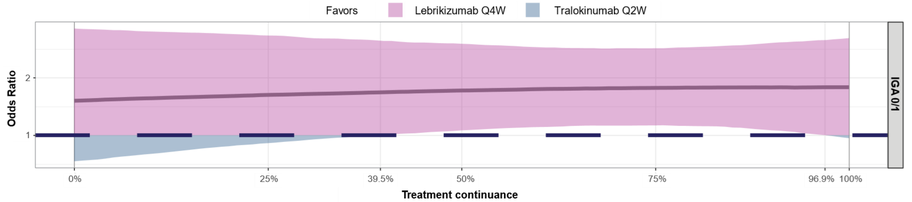


- IGA 0/1: Lebrikizumab had statistically significantly better odds of durability at week 52 than dupilumab for continuance rates from 0% (OR 4.69, 95% CrI: 2.23–15.96) to 100% (1.73, 1.01–2.94)

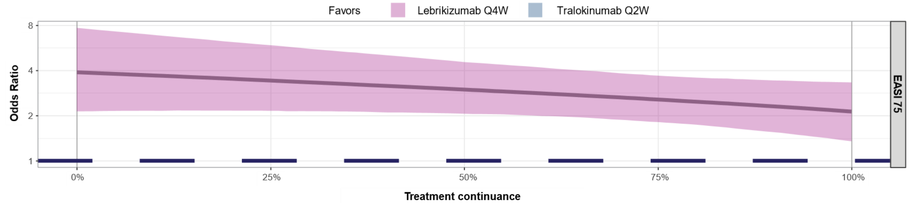


- EASI 75: Lebrikizumab had significantly better odds of durability than dupilumab at continuance rates from 0% (OR 3.24, 1.83–6.12) to 64.2% (1.45, 1.00–2.08). Lebrikizumab also had numerically better odds from 64.2% to 84.7%, while dupilumab had numerically better odds from 84.7% to 100%.

Durability index odds ratios for lebrikizumab and tralokinumab for IGA 0/1 and EASI 75 from 0% to 100% treatment continuance



- IGA 0/1: Lebrikizumab had significantly better odds of durability than tralokinumab at continuance rates between 39.5% (OR 1.68, 95% CrI: 1.00–3.12) and 96.9% (1.79, 1.00–3.14). Lebrikizumab also had numerically better odds at continuance rates <39.5% and >96.9%.



- EASI 75: Lebrikizumab had statistically significantly better odds of durability at week 52 than tralokinumab at continuance rates from 0% (OR 3.89, 2.13–7.66) to 100% (2.13, 1.35–3.32)

Solid line represents the point estimate for ORs. **Upper and lower bands** represent 95% CrIs. **Dashed line** represents the point of equivalence (i.e., no difference between drugs).

Abbreviations: CrI, credible interval; EASI 75, ≥75% improvement in Eczema Area Severity Index; IGA 0/1, Investigator's Global Assessment of 0 (clear) or 1 (almost clear), with a ≥2 point reduction from baseline; OR, odds ratio; Q2W, every 2 weeks; Q4W, every 4 weeks

METHODS

Durability index development

- A population-adjusted indirect comparison was conducted of placebo-controlled phase 3 monotherapy trials with similar designs in post-induction periods
  - Lebrikizumab 250 mg Q4W (ADvocate1 and ADvocate2)[2]
  - Tralokinumab 300 mg Q2W (ECZTRA1 and ECZTRA 2)[3]
  - Dupilumab 300 mg QW/Q2W (SOLO 1, SOLO 2, and SOLO CONTINUE)[4]
- Patients were eligible for these trials if they had responded to biologics at week 16
  - Responders were re-randomized at week 16 to continue treatment or switch to treatment withdrawal until week 52
  - Data from these trials cannot be connected in a network meta-analysis using the withdrawal arm as a common comparator because patients in this arm received treatment during the 16-week induction period
  - The withdrawal arm, however, can be used to evaluate a drug's effect after treatment discontinuation as a population-level measure of long-term durability of response (**Table 1**)
  - For the DI analysis, patients who used rescue medication after week 16 were considered non-responders

Table 1: Proportion of week-16 responders maintaining response at week 52 in phase 3 trials

	Treatment withdrawal	Treatment continuation
IGA 0/1		
Lebrikizumab 250 mg Q4W[2*]	40.1%	69.4%
Tralokinumab 300 mg Q2W[3]	34.0%	55.9%
Dupilumab 300 mg QW/Q2W[4]	14.3%	54.0%
EASI 75		
Lebrikizumab 250 mg Q4W[2*]	59.2%	68.7%
Tralokinumab 300 mg Q2W[3]	26.4%	57.3%
Dupilumab 300 mg QW/Q2W[4]	30.4%	71.6%

Abbreviations: EASI 75, ≥75% improvement in Eczema Area Severity Index; IGA 0/1, Investigator's Global Assessment of 0 (clear) or 1 (almost clear), with a ≥2 point reduction from baseline; Q2W, every 2 weeks; Q4W, every 4 weeks.
* Analysis included the ADvocate 1 and 2 adult population.

Durability index definition

- The DI was developed as a novel estimate of the population-level efficacy of biologics when different proportions of patients who respond to treatment either continue or suspend treatment
- The DI can be based on varying rates of treatment continuance, from 0% to 100% continuing therapy
- The durability index was calculated as the proportion of predicted week-52 responders out of week-16 responders at varying continuance rates from 0% to 100%

Statistical analysis

- Unanchored simulated treatment comparison (STC) was used to estimate odds ratios (OR) adjusting for baseline covariates
  - STC regresses outcomes on baseline covariates, treating them as prognostic factors and including interaction terms for effect modifiers
  - Two STC logistic regression models were generated: one for week-16 outcomes and one for week 52 outcomes
- Uncertainty was handled using non-parametric bootstrapping, with 5000 resamples drawn from the active induction treatment population
- All comparisons remained consistent even when the target population and the covariates used for adjustment were varied

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Acknowledgments: This analysis was funded by Eli Lilly and Company. Medical writing support was provided by Michael Franklin (PPD, a Thermo Fisher company) in accordance with Good Publication Practice (GPP3) guidelines and funded by Eli Lilly and Company.

Disclosures: JIS has served as advisor, speaker, or consultant for AbbVie, Asana Biosciences, Dermavant Sciences, Galderma, GlaxoSmithKline, Glenmark, Kiniksa, LEO Pharma, Lilly, Menlo Therapeutics, Novartis, Pfizer, Realm Pharma, and Regeneron-Sanofi; and is a researcher for GlaxoSmithKline. **AID** has received research funding or served as an advisor, speaker, or consultant for AbbVie, Arena Pharmaceuticals, BeneviolentAI, Eli Lilly and Company, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi, Pfizer, and the International Eczema Council. **PF** has received research funding or served as an advisor, speaker, or consultant received grants from AbbVie, Amgen, Argenx, Arcutis, Aslan, AstraZeneca, Boehringer Ingelheim, Botanix, Bristol-Myers Squibb, Celgene, Celtaxsys, CSL, Cutanea, Dermira, Celgene, Eli Lilly and Company, Evelo, Galderma, Genentech, Geneseq, GenesisCare, GlaxoSmithKline, Hexima, Incyte, Janssen, Kymab, LEO Pharma, Mayne Pharma, Merck, MedImmune, Novartis, Pfizer, Regeneron Pharmaceuticals, Roche, Sanofi, Sun Pharma, Teva, UCB Pharma, and Valeant. **JDL** has received grants as an investigator, honoraria for lecturing, and/or consulting fees from AbbVie, Amgen (Celgene), AOBiome, Aslan, Arbonne, Arcutis, Bausch Health (Ortho Derm), Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, Exeltis, Ferndale, Galderma, Incyte, IntraDerm, Johnson & Johnson, La Roche-Posay/L'Oréal, LEO Pharma, Menlo Therapeutics, Nektar, Pfizer, Pierre Fabre, Regeneron/Sanofi Genzyme, Sun Pharma, Theraplex, UCB Pharma, Unilever, and Verrica Pharmaceuticals. **LP** has received consultancy/speaker's honoraria from and/or participated in clinical trials sponsored by Abbvie, Almirall, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Fresenius-Kabi, J&J Innovative Medicine, Leo-Pharma, Lilly, Novartis, Pfizer, STADA, Sun-Pharma, and UCB. **KR** is an employee of Maths In Health B.V., which was funded by Eli Lilly and Company to provide analytical services for this publication. **MD**, **GG**, and **MC** are employees and minor shareholders of Eli Lilly and Company. **BA** is an employee of Almirall. **LSG** is an investigator and/or consultant and/or speaker for: AbbVie, Amgen, Arcutis, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, and UCB Pharma.

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

Scan the QR code for a list of all Lilly content presented at the congress.

Scan the QR code for supplemental results showing comparisons between dupilumab and tralokinumab.

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Clinical Remission and **Off-Treatment Remission** in **Infants and Preschoolers** With Moderate-to-Severe **Atopic Dermatitis** Treated With **Dupilumab:** Preliminary Data From an **Open-Label Extension Study**

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Conclusions

- Over one-third of pediatric patients aged 6 months to 5 years with moderate-to-severe AD treated with dupilumab experienced clinical remission on therapy during the first year of treatment with dupilumab
- Of these patients, about half maintained remission off treatment for 3 months and one-third for 6 months after dupilumab was discontinued
- Most patients (80%) who did not maintain remission had mild AD
- Longer term observations will elucidate whether these findings are durable, suggesting disease course modification

Objective

To report rates of pediatric patients aged 6 months to 5 years treated with dupilumab achieving clinical remission on dupilumab treatment and maintaining the remission off treatment

Background

- Pediatric patients with moderate-to-severe AD have a high burden of disease that often requires long-term management
- Higher severity and earlier onset of AD are predictive factors for disease persistence
- Despite the approval of dupilumab in patients as young as 6 months with severe AD, and the favorable long-term safety, physicians and caregivers question if treatment could be interrupted in patients achieving disease remission

Methods

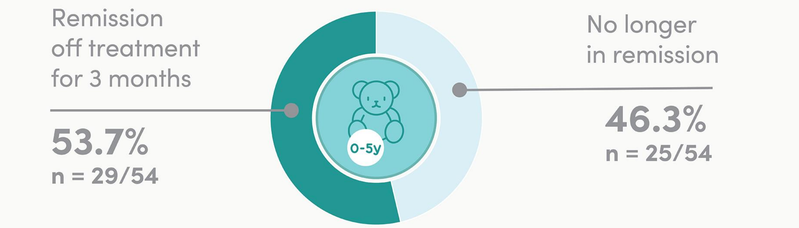
- This study analyzed patients aged 6 months to 5 years with moderate-to-severe AD (n = 163) enrolled in the ongoing open-label extension LIBERTY AD PED-OLE study (NCT02612454) treated with dupilumab every 4 weeks based on weight:
  - 5 to <15 kg: 200 mg
  - 15 to <30 kg: 300 mg
  - Concomitant use of topical corticosteroids was not standardized
- Clinical remission was defined as maintaining an IGA score of 0/1 (clear or almost clear skin) for ≥12 weeks after 40 weeks on dupilumab
- Patients reaching clinical remission discontinued dupilumab (remission off treatment) and were monitored for recurrent AD (IGA score ≥2 at any one visit), at which point dupilumab was restarted

Results

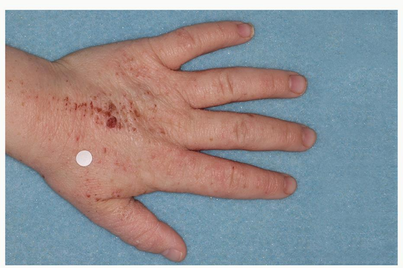
Proportion of patients aged 6 months to 5 years achieving clinical remission.

	6 months to 5 years (N = 163)
Patients who achieved clinical remission, N1 (%)	54 (33.1)
Patients who maintained remission off treatment for at least 3 months, n/N1 (%)	29/54 (53.7)
Patients who maintained remission off treatment for at least 6 months, n/N1 (%)	16/54 (29.6)

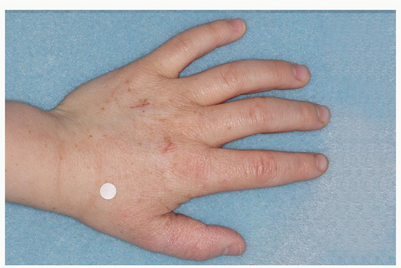
Proportion of patients aged 6 months to 5 years achieving clinical remission.



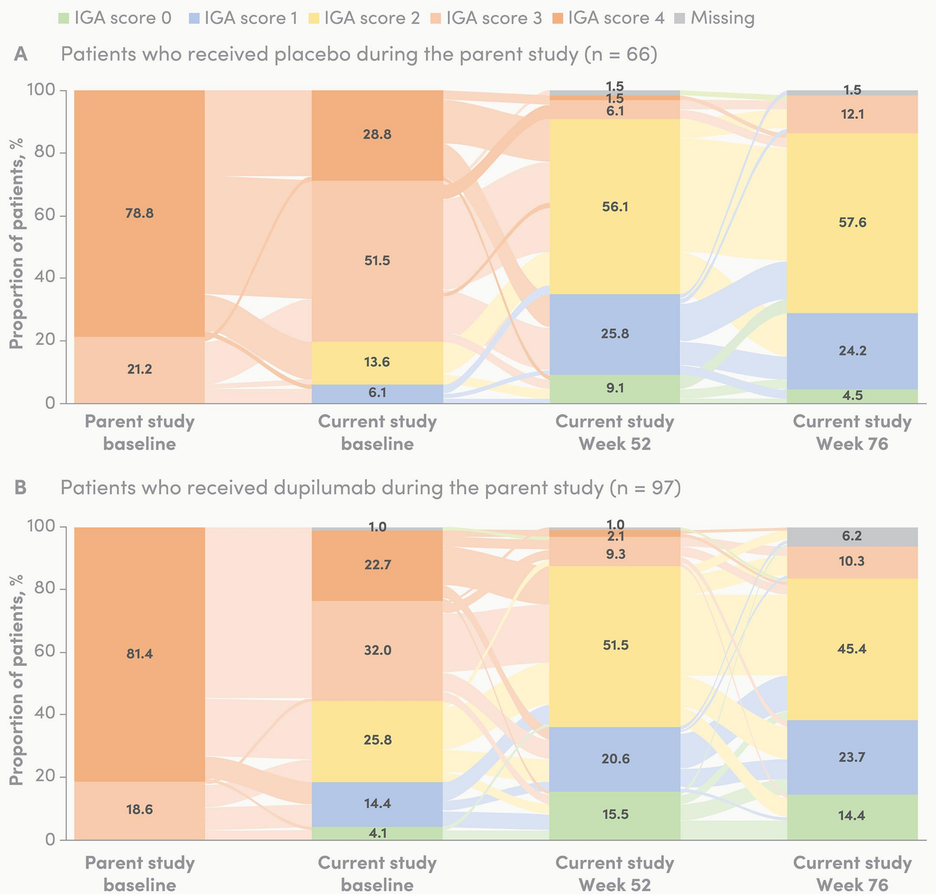
4-year-old patient at baseline (severe AD)



After 4 months of dupilumab treatment (mild AD)



Percentage distribution of IGA over time for patients aged 6 months to 5 years.



AD, atopic dermatitis; IGA, Investigator's Global Assessment.

Acknowledgments: Data first presented at the 10th Congress of the European Academy of Paediatric Societies; Vienna, Austria; October 17-20, 2024. Research sponsored by Sanofi and Regeneron Pharmaceuticals Inc. ClinicalTrials.gov Identifier: NCT02612454. Medical writing/editorial assistance was provided by Alyssa DiLeo, PhD, of Excerpta Medica, and was funded by Sanofi and Regeneron Pharmaceuticals Inc., according to the Good Publication Practice guidelines.

Disclosures: ECS: Dermavant, Eli Lilly, Pfizer, Regeneron Pharmaceuticals Inc., Verrica Pharmaceuticals – consultant; GSK, LEO Pharma, Novan – data and safety monitoring board; Eli Lilly, Janssen, Regeneron Pharmaceuticals Inc., Stiefel, Verrica Pharmaceuticals – Principal Investigator in clinical trials. TB: AbbVie, AnaptysBio, Asana BioSciences, Astellas Pharma, BioVersys, BMS, Daiichi Sankyo, Dermavant, Eli Lilly, Galapagos/MorphoSys, Galderma, Glenmark, GSK, Kymab, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi – speaker fees. ASP: AbbVie, Biomendics, Dermavant, Eli Lilly, Incyte, Johnson & Johnson Innovative Medicine, Regeneron, UCB– investigator; Abeona, Arcutis, BioCryst, Boehringer-Ingelheim, Castle Creek, Chiesi, Dermavant, Johnson & Johnson Innovative Medicine, Krystal, LEO, Lilly, L'Oreal, MoonLake Immunotherapeutics, Pelthos, Quoin, Regeneron, and Sanofi – consultant; AbbVie, Abeona, Biocryst, Daiichi Sankyo, and Galderma– data and safety monitoring board. ELS: AbbVie, Eli Lilly, Galderma, Kyowa Hakko Kirin, LEO Pharma, Merck, Pfizer, Regeneron Pharmaceuticals Inc. – investigator; AbbVie, Boehringer Ingelheim, Dermavant, Eli Lilly, Forte, Incyte, LEO Pharma, Menlo Therapeutics, Pfizer, Pierre Fabre Derma-Cosmetics, Regeneron Pharmaceuticals Inc., Sanofi, Valeant – consultant. MJC: AbbVie, Astellas Pharma, Beats, Dermavant, Galapagos, Galderma, Hyphens Pharma, Johnson & Johnson, LEO Pharma, L'Oreal, Menlo Therapeutics, Novartis, Oxagen, Pfizer, Procter & Gamble, Reckitt Benckiser, Regeneron Pharmaceuticals Inc., Sanofi – investigator and/or consultant. SW: Treatment of Atopic Eczema (TREAT) Registry Taskforce Germany – co-principal investigator; LEO Pharma, L'Oreal, Pfizer, Sanofi – institutional research grants; AbbVie, Almirall, Boehringer Ingelheim, Galderma, Incyte, Kymab, LEO Pharma, Lilly, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi – consultancies; AbbVie, Almirall, LEO Pharma, Lilly, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi – lectured at educational events; clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of psoriasis and atopic eczema. LFE: AbbVie, Amgen, Arcutis, BMS, Castle Biosciences, Dermavant, Eli Lilly, Forte, Galderma, Incyte, LEO Pharma, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi, Valeant/Ortho Dermatologics – honoraria for consulting services; AbbVie, Amgen, Arcutis, Dermavant, Eli Lilly, Galderma, Incyte, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi, Valeant – study support (to institution). PL: AbbVie, Amgen, Arcutis, Bausch Health, Boehringer Ingelheim, BMS, Celgene, Eli Lilly, Galderma, Incyte, LEO Pharma, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi, Sun Pharma, UCB – speaker and consultant. ZC, AB, HY: Regeneron Pharmaceuticals Inc. – employees and shareholders. ABR: Sanofi – employee; may hold stock and/or stock options in the company.

Presented at the Society of Dermatology Nurse Practitioners National Conference (SDNP 2025); Indian Wells, CA, USA; April 30 - May 3, 2025.

Treatment **Outcomes of Systemic Treatments** for Moderate-to-Severe **Atopic Dermatitis in Children** Under 12 Years of Age: **4-Year Results From the PEDISTAD** Registry

Alan D. Irvine[1], Michele Ramien[2,3], Lin Ma[4], Danielle Marcoux[5,6], Eulalia Baselga[7], Marlies de Graaf[8], Martti A. Antila[9], Nelson A. Rosario Filho[10], Lara Wine Lee[11], Joel C. Joyce[12], Rajan Gupta[13], Marius Ardeleanu[14], Annie Zhang[13]

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Conclusion

Patients aged <12 years treated with dupilumab had a greater improvement in AD signs, lower cumulative discontinuation rates, and a slightly lower percentage of AEs compared with patients treated with methotrexate or cyclosporine

Objective

To report the efficacy and safety of dupilumab in treating moderate-to-severe AD vs cyclosporine and methotrexate after 4 years of treatment in children <12 years old

Background

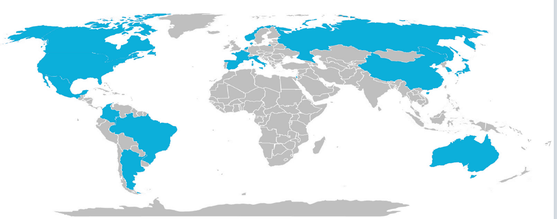
- Dupilumab significantly improves AD signs and symptoms in children enrolled in phase 3 clinical trials
- Understanding the long-term, real-world treatment outcomes, safety, and discontinuations for patients receiving systemic therapies is important for the continued management of AD in children

Methods

PEDISTAD (NCT03687359) 4-year interim analysis
N = 535

- Phase 4, global, 10-year, observational registry[1]
- Children aged <12 years from 20 countries
- Patients received dupilumab, methotrexate, or cyclosporine
- All analyses are descriptive

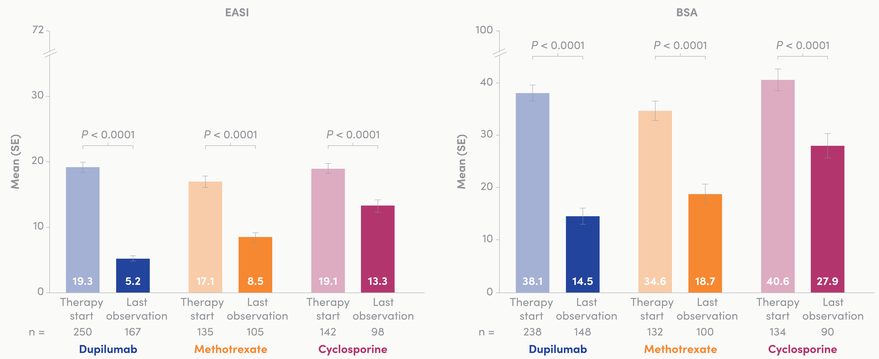
Countries of enrolment



- Participating countries include Argentina, Australia, Brazil, Canada, China, Colombia, Denmark, France, Greece, Israel, Italy, Japan, Mexico, the Netherlands, Norway, Portugal, Russia, South Korea, Spain, and the United States of America

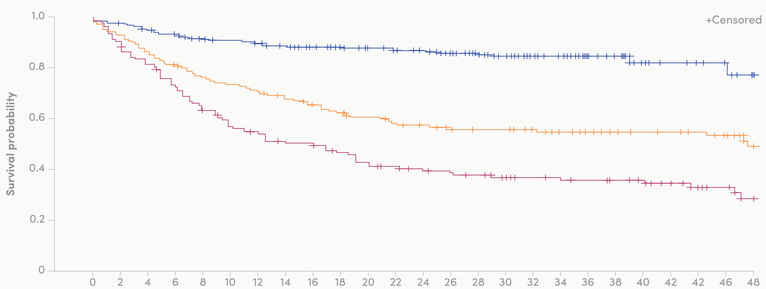
Results

Patients treated with dupilumab had a greater improvement in EASI and BSA compared with patients treated with methotrexate or cyclosporine.



Mean (SE) treatment duration was 27.3 (0.9) months for dupilumab, 28.1 (1.6) for methotrexate, and 19.5 (1.4) for cyclosporine

Patients treated with dupilumab had a lower discontinuation rate compared with patients treated with methotrexate or cyclosporine.



No. at risk																								
Dupilumab	255	247	239	233	221	216	212	204	194	187	179	174	169	152	138	106	80	69	51	41	28	25	22	17	11
Methotrexate	140	130	120	113	105	101	97	90	85	84	76	72	68	64	62	62	57	53	49	46	43	42	40	34	21
Cyclosporine	146	129	118	104	90	78	74	69	68	60	55	50	47	45	43	39	36	34	33	31	27	23	18	16	11

4 year cumulative discontinuation rate (%)
14.9
45.7
63.7

Censored, patients lost to follow-up.

Patients treated with dupilumab had fewer treatment-emergent AEs compared with patients treated with methotrexate or cyclosporine.

Dupilumab			Methotrexate			Cyclosporine		
	AEs by PT with an incidence of ≥1%, n (%)[a]	EAER per 100 patient-years[b]		AEs by PT with an incidence of ≥1%, n (%)	EAER per 100 patient-years[b]		AEs by PT with an incidence of ≥1%, n (%)	EAER per 100 patient-years[b]
Any AE	**72 (28.3%)**		**Any AE**	**44 (31.4%)**		**Any AE**	**46 (31.5%)**	
COVID-19	12 (4.7%)	2.45	Atopic dermatitis	10 (7.1%)	3.71	Atopic dermatitis	21 (14.4%)	11.89
Conjunctivitis	7 (2.8%)	1.22	Abdominal pain	4 (2.9%)	2.16	Impetigo	5 (3.4%)	2.05
Upper respiratory tract infection	5 (2.0%)	1.57	Molluscum contagiosum	4 (2.9%)	1.85	Allergic conjunctivitis	4 (2.7%)	1.64
Allergic conjunctivitis	4 (1.6%)	0.70	Upper respiratory tract infection	4 (2.9%)	1.24	Influenza	4 (2.7%)	1.64
Atopic dermatitis	4 (1.6%)	0.87	Asthenia	2 (1.4%)	0.62	Fatigue	3 (2.1%)	1.23
Asthma	3 (1.2%)	0.52	Diarrhea	2 (1.4%)	0.62	Anxiety	2 (1.4%)	1.23
Ear infection	3 (1.2%)	0.87	Impetigo	2 (1.4%)	0.62	Abdominal pain	2 (1.4%)	0.82
Viral gastroenteritis	3 (1.2%)	0.52	Nasopharyngitis	2 (1.4%)	0.62	Asthma	2 (1.4%)	0.82
Headache	3 (1.2%)	0.52	Nausea	2 (1.4%)	0.62	Eczema herpeticum	2 (1.4%)	0.82
Influenza	3 (1.2%)	0.52	Streptococcal pharyngitis	2 (1.4%)	0.93	Insomnia	2 (1.4%)	0.82
Limb injury	3 (1.2%)	0.52	Skin papilloma	2 (1.4%)	0.62	Pyrexia	2 (1.4%)	0.82
Pyrexia	3 (1.2%)	0.52				Superinfection	2 (1.4%)	1.23

[a]Calculated as the number of patients who reported an AE.
[b]Calculated as number of new adverse events occurring in exposure periods between the first dose and up to and including 30 days after the last dose of a specific therapy for AD divided by total patient years (number of AEs/drug exposure time (100 patient-years)).

Safety

- Safety was consistent with the known dupilumab safety profile

AD, atopic dermatitis; AE, adverse event; BSA, body surface area; EAER, exposure-adjusted event rate; EASI, Eczema Area and Severity Index; PT, Preferred Term; SD, standard deviation; SE, standard error.

Reference: 1. Paller AS, et al. BMJ Open. 2020;10:e033507.

Acknowledgements: Data first presented at the 14th Georg RAJKA Symposium on Atopic Dermatitis (ISAD); Doha, Qatar; October 24–26, 2024. Research sponsored by Sanofi and Regeneron Pharmaceuticals Inc. ClinicalTrials.gov Identifier: NCT03687359. Medical writing/editorial assistance was provided by Benjamin Crane, PhD, of Excerpta Medica, and was funded by Sanofi and Regeneron Pharmaceuticals Inc., according to the Good Publication Practice guidelines.

Disclosures: ADI: AbbVie, Arena Pharmaceuticals, BenevolentAI, Chugai Pharmaceutical, Dermavant, Eli Lilly, Genentech, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi, UCB – consultant; AbbVie, Eli Lilly, LEO Pharma, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi – speaker; AbbVie, DS Biopharma, Inflazome, Novartis, Sanofi-Regeneron Pharmaceuticals Inc. – investigator. MR: AbbVie, LEO Pharma, Pfizer, Sanofi – consultant; Sanofi – registry study. LM: Pfizer – consultant. DM: AbbVie, Amgen, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi – investigator; AbbVie, Amgen, BMS, Eli Lilly, Janssen, LEO Pharma, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi, UCB – consultant; AbbVie, Amgen, BMS, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi – speaker. EB: AbbVie, LEO Pharma, Novartis, Pfizer, Pierre Fabre Dermo-Cosmetics – investigator; Pierre Fabre Dermo-Cosmetics, Regeneron Pharmaceuticals Inc., Sanofi – consultant. MDG: AbbVie, Eli Lilly, LEO Pharma, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi – investigator; AbbVie, Almirall, Eli Lilly, LEO Pharma, Regeneron Pharmaceuticals Inc., Sanofi – consultant; AbbVie, ALK, Eli Lilly, LEO Pharma, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi – speaker. MAA: AbbVie AstraZeneca, EMS, Eurofarma, GSK, Humanigen, Janssen, Novartis, Sanofi, Veru – participation in clinical studies; Abbott, Aché, AstraZeneca, Chiesi, EuroPharma, IPI ASAC, Sanofi – conferences and consultancy activities. NARF: AbbVie, AstraZeneca, Boehringer Ingelheim, Chiesi, Sanofi, Viatris – investigator, consultant, and/or speaker. LWL: Castle Creek Biosciences, Eli Lilly, Pfizer, Regeneron Pharmaceuticals Inc. – advisory board; AbbVie, Amryt Pharma, Krystal Biotech, Novartis, Pyramid Biosciences – consultant; AbbVie, Amgen, Amryt Pharma, Arcutis Biotherapeutics, Castle Creek Biosciences, Celgene, Eli Lilly, Galderma, Incyte, Mayne Pharmaceuticals, Novartis, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi, Target Pharma, Trevi Therapeutics, UCB – investigator; MoonLake Immunotherapeutics, Timer – research funding; Amryt Pharma – speaker. JCJ: Pfizer, Regeneron, Sanofi – consultant fees; AbbVie, Sanofi – speaker fees; AbbVie, Aclaris Therapeutics, Amgen, Apogee Therapeutics, AstraZeneca, Bayer, BMS, CorEvitas, Eli Lilly, Galderma, Incyte, Janssen, Novartis, Pfizer, Regeneron, Sanofi, UCB – study investigator. RG: Sanofi – consultant. MA: Regeneron Pharmaceuticals Inc. – employee and shareholder. AZ: Sanofi – employee, may hold stock and/or stock options in the company.

Presented at the Society of Dermatology Nurse Practitioners National Conference (SDNP 2025); Indian Wells, CA, USA; April 30 - May 3, 2025.

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

Eric L. Simpson[1], Margitta Worm[2], Robert Bissonnette[3], Servando E. Marron[4,5], Hiroshi Mitsui[6], Stefan Beissert[7], H. Chih-ho Hong[8,9], Andreas Pinter[10], Amy Praestgaard[11], Deborah Griffis[12], Ana B. Rossi[11]

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Conclusions

- **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)

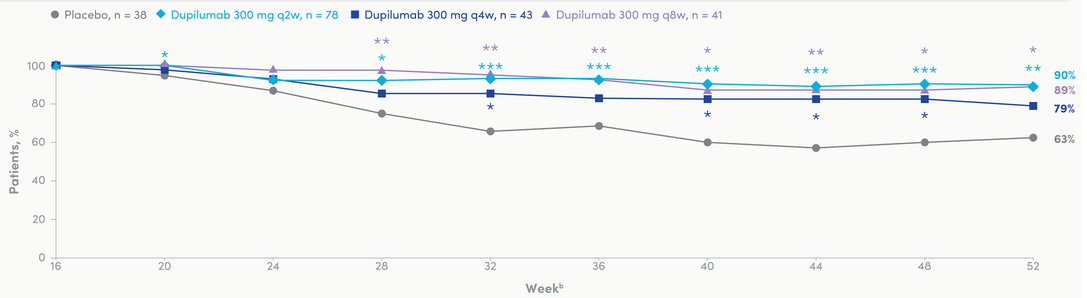
Results

Demographics and baseline disease characteristics.

	SOLO 1/2 baseline (Week 0)				SOLO-CONTINUE baseline (Week 16)			
	Placebo[a] n = 39	Dupilumab 300 mg q2w[a] n = 80	Dupilumab 300 mg q4w[a] n = 41	Dupilumab 300 mg q8w[a] n = 39	Placebo[a] n = 39	Dupilumab 300 mg q2w[a] n = 80	Dupilumab 300 mg q4w[a] n = 41	Dupilumab 300 mg q8w[a] n = 39
Age, mean (SD), years	38.5 (15.0)	38.6 (14.8)	37.7 (17.6)	34.3 (13.8)	38.9 (15.0)	38.9 (14.8)	38.2 (17.5)	34.6 (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 (15.9)	28.2 (16.2)	26.4 (16.1)	22.9 (10.5)	26.8 (15.9)	28.2 (16.2)	26.4 (16.1)	22.9 (10.5)
Body surface area, mean % (SD)	48.6 (17.5)	48.3 (21.1)	47.1 (20.7)	47.3 (20.2)	14.9 (14.2)	8.4 (10.7)	13.0 (14.4)	12.4 (15.3)
Patients with ≥1 AD flare in 12 months before screening visit, n (%)	36 (94.7)	66 (83.5)	37 (90.2)	35 (89.7)				
Number of flares in 12 months before treatment period, median	3.0	3.0	3.0	4.0				

[a]All patients received dupilumab 300 mg q2w in SOLO 1/2 and were then randomized to treatment in SOLO-CONTINUE as indicated.

Most patients had no flares[a] over 1 year with continued dupilumab monotherapy.



n/N									
Placebo	36/38	33/38	27/36	23/35	24/35	21/35	20/35	21/35	20/32
Dupilumab q2w	78/78	71/77	70/76	68/73	68/73	66/73	65/73	66/73	62/69
Dupilumab q4w	42/43	39/42	35/41	35/41	34/41	33/40	33/40	33/40	30/38
Dupilumab q8w	40/40	39/40	39/40	38/40	37/40	34/39	34/39	34/39	32/36

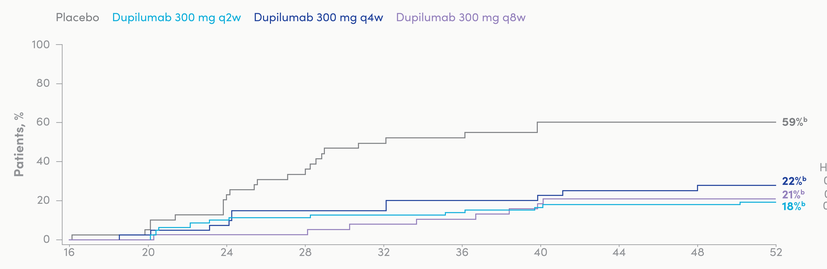
All patients received dupilumab 300 mg q2w in SOLO 1/2 and were then randomized to treatment in SOLO-CONTINUE as indicated.
P values were derived by Cochran–Mantel–Haenszel test stratified by region, and baseline IGA strata (0, 1, >1) as fixed factors. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$ vs placebo.
[a]No rescue treatment use. [b]Weeks correspond to SOLO-CONTINUE study, in continuation of SOLO 1/2. Patients who received rescue treatment in SOLO 1/2 (including TCS/TCI) were considered non-responders.

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

Patients with ≥1 event, n (%)	Placebo[a] n = 39	Dupilumab 300 mg q2w[a] n = 80	Dupilumab 300 mg q4w[a] n = 41	Dupilumab 300 mg q8w[a] 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

[a]Treatment arm in SOLO-CONTINUE. All patients in this analysis received dupilumab 300 mg q2w in SOLO 1/2 and were then randomized to treatment in SOLO-CONTINUE as indicated.

The proportion of patients who experienced a flare[a] remained low across dupilumab dose regimens.



Number at risk										
Placebo	39	37	31	25	19	18	15	15	15	14
Dupilumab q2w	80	80	71	69	66	65	63	62	62	57
Dupilumab q4w	41	40	37	33	33	31	30	29	29	26
Dupilumab q8w	39	38	37	37	35	34	31	30	29	25

Kaplan–Meier curves present time to flare[a] in SOLO-CONTINUE. All patients received dupilumab 300 mg q2w in SOLO 1/2 and were then randomized to treatment in SOLO-CONTINUE as indicated.
$^{*}P = 0.0014$; $^{\dagger}P = 0.0008$; $^{\ddagger}P < 0.0001$ vs placebo.
[a]First rescue treatment use. [b]Proportion of patients with flare. [c]Based on Cox proportional hazard model with treatment as effect. [d]Weeks correspond to SOLO-CONTINUE study, in continuation of SOLO 1/2.

AD, atopic dermatitis; EASI-75, ≥75% improvement from baseline in Eczema Area and Severity Index; IGA, Investigator's Global Assessment; n, number of patients with no flares; N, number of patients with data available; q2w, every 2 weeks; q4w, every 4 weeks; q8w, every 8 weeks; SD, standard deviation; TCI, topical calcineurin inhibitor(s); TCS, topical corticosteroid(s); TEAE, treatment-emergent adverse event.

References: 1. Thomas KS, et al. PLoS ONE. 2015;10:e0124770. 2. Merola JF, et al. J Am Acad Dermatol. 2021;84:495–97. 3. Blauvelt A, et al. Lancet. 2017;389:2287–303.

Acknowledgments: Data first presented at the 14th Georg Rajka Symposium on Atopic Dermatitis (ISAD); Doha, Qatar; October 24–26, 2024. Research sponsored by Sanofi and Regeneron Pharmaceuticals Inc. ClinicalTrials.gov Identifiers: NCT02277743, NCT02277769, and NCT02395133. The authors would like to thank Dr. Diamart Thapi for his contribution to abstract development. Medical writing/editorial assistance was provided by Jamie Church, PhD, of *Excerpta Medica*, and was funded by Sanofi and Regeneron Pharmaceuticals Inc., according to the Good Publication Practice guidelines.

Disclosures: ELS: AbbVie, Amgen, Arcutis, Arteleo Therapeutics, BMS, CorEvitas, Corvus, Dermira, Eli Lilly, Evelo Biosciences, FIDE, Forte Bio RX, Galderma, Gilead Sciences, GSK, Impetus Healthcare, Incyte, Innovaderm Reche, Janssen, Johnson & Johnson, Kyowa Kirin Pharmaceutical Development, LEO Pharma, Merck, NUMAB Therapeutics AG, Pfizer, Physicians World LLC, PRIMÉ, Recludix Pharma, Regeneron Pharmaceuticals Inc., Roivant, Sanofi, Sitryx Therapeutics, Trevi Therapeutics, Valeant – personal fees; AbbVie, Acrotech, Amgen, Arcutis, Aslan, Castle, CorEvitas, Dermavant, Dermira, Incyte, Lilly, Kymab, Kyowa Kirin, National Jewish Health, LEO Pharma, Pfizer, Regeneron Pharmaceuticals Inc., Sanofi, Target, VeriSkin – grants/serves as principal investigator. MW: AbbVie, Eli Lilly, LEO Pharma, Novartis, Regeneron Pharmaceuticals Inc., Sanofi – advisory board member, consulting fees. RB: AbbVie, Aclaris, Alumis, Amgen, Apogee, Arcutis Biotherapeutics, Arteleo, Asana BioSciences, Bellus, Biomedicine, BioMimetix, Bluefin, Boehringer Ingelheim, Boston Pharma, CARA Therapeutics, Dermavant, Eli Lilly, Excient, Evidera, Fresh Tracks (Brickell), Galderma, GSK, Incyte, Inmagene Bio, Janssen, LEO Pharma, Merck, Novartis, Opsidio, Pfizer, RAPT Therapeutics, Sanofi, Sitryx, Target RWE, Vyne Therapeutics, Zencor – consultant and/or grants/research support; Innovaderm Research – shareholder. SEM: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Eli Lilly, Galderma, Janssen, LEO Pharma, Novartis, Regeneron Pharmaceuticals Inc., Roche, Sanofi – advisory board member, consultant, research support; honoraria. HM: AbbVie, Eli Lilly, LEO Pharma, Otsuka Pharmaceutical, Pfizer, Sanofi, Torii Pharmaceutical – speaker fees. SB: Actelion, Amgen, Biogen, Celgene, Galderma, Janssen-Cilag, Lilly, Menlo Therapeutics, MSD, Novartis, Pfizer, Sanofi, UCB Pharma – advisory board member; AbbVie, Actelion, BMS, Celgene, Galderma, GSK, Hexal, Janssen-Cilag, La Roche-Posay, MSD, Novartis, Pfizer – speaker honoraria; Regeneron Pharmaceuticals Inc. – investigator. HC–hH: Centocor, Cutanea, Dermavant, GSK, MedImmune – investigator; Sanofi – consultant; Boehringer Ingelheim – investigator, consultant; Cipher Pharmaceuticals – speaker; Bausch Health, Roche – speaker, consultant; AbbVie, Amgen, BMS, Eli Lilly, Galderma, Janssen, LEO Pharma, Novartis, Regeneron Pharmaceuticals Inc. – speaker, investigator, consultant. AP: AbbVie, Almirall Hermal, Amgen, Biogen Idec, BioNtech, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Galderma, GSK, Hexal, Janssen, Klinge Pharma, LEO Pharma, MC2 Pharma, Medac, Merck Serono, Mitsubishi Tanabe Pharma, MSD, Novartis, Pascoe, Pfizer, Regeneron Pharmaceuticals Inc., Roche, Sandoz, Sanofi, Schering-Plough, Tigercat Pharma – clinical trials; AbbVie, Almirall Hermal, Amgen, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Galderma, Janssen, Klinge Pharma, LEO Pharma, Medac, Novartis, Pfizer, Sanofi, UCB Pharma, Zuellig Pharma – speaker fees; AbbVie, Almirall – grants. AP, ABR: Sanofi – employees, may hold stock and/or stock options in the company. DG: Regeneron Pharmaceuticals Inc. – employee and shareholder.

Presented at the Society of Dermatology Nurse Practitioners National Conference (SDNP 2025); Indian Wells, CA, USA; April 30 - May 3, 2025.

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

Emma Guttman-Yassky[1], Alan Irvine[2], Eric Simpson[3], Melinda Gooderham[4], Stephan Weidinger[5], Lynda Spelman[6], Jonathan Silverberg[7], Heidi Crane[8], Hany Elmaraghy[8], Louise DeLuca-Carter[8] (Presenter), Maria Lucia Buziqui Piruzeli[8], Chaoran Hu[8], Evangeline Pierce[8], Helena Agell[9], Diamant Thaçi[10]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Children's Health Ireland, Dublin, Ireland; [3]Oregon Health & Science University, Portland, OR, USA; [4]SKiN for Dermatology, Probity Medical Research and Queen's University, Peterborough, Canada; [5]University Hospital Schleswig-Holstein, Kiel, Germany; [6]Veracity Clinical Research, Queensland, Australia; [7]George Washington University, Washington, DC, USA; [8]Eli Lilly and Company, Indianapolis, IN, USA; [9]Almirall S.A., Barcelona, Spain; [10]University of Lübeck, Lübeck, Germany

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.

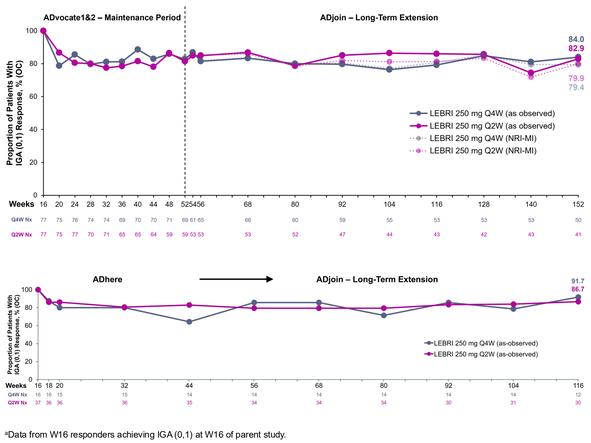
CONCLUSIONS

- 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

Society of Dermatology Nurse Practitioners (SDNP) National Conference 2025, Indian Wells, CA, USA; April 30 - May 3 2025

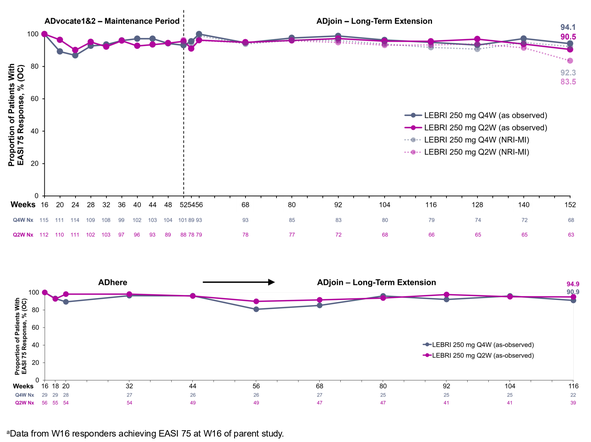
KEY RESULTS

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



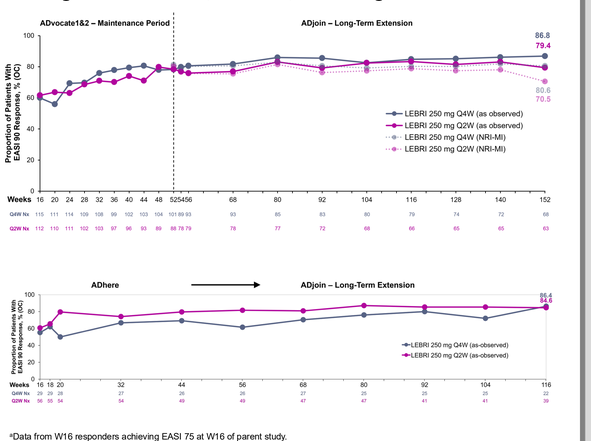
[a]Data from W16 responders achieving IGA (0,1) at W16 of parent study.

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.

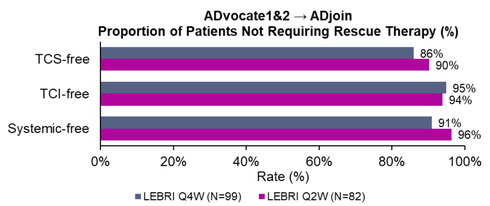
Statistical Analyses and Assessment

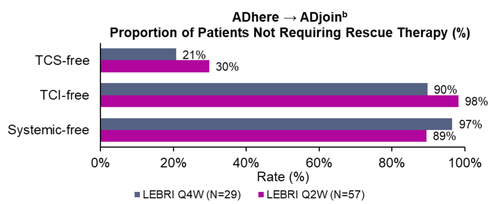
- Analysis population
  - *Modified intent-to-treat population*[a]: ADvocate1&2 → ADjoin: Lebrikizumab responders[b] who were randomized to lebrikizumab 250 mg Q4W or lebrikizumab 250 mg Q2W at Week 16, and enrolled into ADjoin with the same dose regimen at Week 52
  - *Modified intent-to-treat population*[a]: 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 ADvocate2 and ADhere not included in the modified intent-to-treat population 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 subsequent to this time. Observations after discontinuing treatment due to other reasons are set as missing and handled with multiple imputation.

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 was used to treat TEAEs.

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[d]	1 (1.0)	0	0	0
Infections[e]	45 (45.5)	38 (46.3)	11 (37.9)	24 (42.1)
Potential opportunistic infections[f]	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[g]	0	1 (1.2)	1 (3.4)	1 (1.8)
Malignancies[h]	0	0	0	0
Hypersensitivity	1 (1.0)	2 (2.4)	1 (3.4)	1 (1.8)
Eosinophilia[i]	1 (1.0)	1 (1.2)	0	0

[a]Modified safety population from Week 0 of ADjoin through to data cut-off of April 24, 2024; [b]As reported by the investigator, a 55-year-old male patient died of natural causes on Study Day 462 and the event was assessed to be unrelated to study treatment; the patient had a medical history of hypertension, cardiac ablation, 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 vernal 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 Winthrop criteria; [g]Injection site reactions are defined using MedDRA High Level Term of injection site reactions, excluding joint-related preferred terms; [h]Includes both NMSC and malignancies excluding NMSC; [i]Eosinophilia is defined as 2 preferred terms of eosinophilia and allergic eosinophilia and the following preferred terms under the high-level term of white blood cell analysis: eosinophil count abnormal eosinophil count increased, and eosinophil percentage increased. No eosinophilic-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.

References: 1. Blauvelt A, et al. *Br J Dermatol*. 2023;188:740-748. 2. Simpson E, et al. *JAMA Dermatol*. 2023;159:182-191. 3. Guttman-Yassky E, et al. Poster presented at: *Fall CDC 2023*. Abstract 494.

Abbreviations: *AD=atopic dermatitis; AE=adverse event; BMI=body mass index; BSA=body surface area; EASI=Eczema Area and Severity Index; EASI 75=at least 75% improvement from baseline in EASI; EASI 90=at least 90% improvement from baseline in EASI; 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 non-missing values; OC=observed case; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; R=randomization; SAE=serious adverse event; SD=standard deviation; TCI=topical calcineurin inhibitor; TCS=topical corticosteroid; TEAE=treatment-emergent AE; W=Week.*

Disclosures: E. Guttman-Yassky is an employee of: Mount Sinai; and has received research funds (grants paid to institution) from and/or been a consultant for: AbbVie, Almirall, Amgen, AnaptysBio, Asana BioSciences, ASLAN Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Connect Biopharma, Eli Lilly and Company, EMD Serono, Evidera, Galderma, Incyte Corporation, Innovaderm Research, Janssen, Kiniksa, Kyowa Kirin, LEO Pharma, Novartis, Pfizer, RAPT Therapeutics, Regeneron, Sanofi, Sato Pharmaceutical, TARGET PharmaSolutions, UCB Pharma, and Ventyx Biosciences; **A. Irvine** is a speaker, advisory board member, and/or investigator for: AbbVie, Almirall, Connect BioPharma, Eli Lilly and Company, LEO Pharma, OM Pharma, Pfizer, RAPT Therapeutics, Regeneron, and Sanofi. **E. Simpson** has received grants (or serves as principal investigator role) for: AbbVie, Acrotech, Amgen, Arcutis, ASLAN Pharmaceuticals, Castle Biosciences, CorEvitas, Dermavant, Dermira, Eli Lilly and Company, Incyte Corporation, Kymab, Kyowa Kirin, LEO Pharma, National Jewish Health, Pfizer, Regeneron, Sanofi, TARGET PharmaSolutions, VentiSkin; and personal fees from: AbbVie, Amgen, Arcutis, Arteleia Therapeutics, Bristol Myers Squibb, CorEvitas, Corvus Pharmaceuticals, Dermira, Eli Lilly and Company, Evelo Biosciences, FIDE, Forte Biosciences, Galderma, GlaxoSmithKline, Gilead Sciences, Impetus Healthcare, Incyte Corporation, Innovaderm Reche, Janssen, Johnson & Johnson, Kyowa Kirin Pharmaceutical Development, LEO Pharma, Merck, NUMAB Therapeutics AG, Pfizer, Physicians World LLC, PRIImE, Recludix Pharma, Regeneron, Roivant Sciences, Sanofi Genzyme, Sitryx Therapeutics, Trevi Therapeutics, and Valeant Pharmaceuticals; **M. Gooderham** has been an investigator, speaker, and/or advisor for: AbbVie, Akros Pharma, Alumis, Amgen, Arcutis, Aristea Therapeutics, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Incyte Corporation, Janssen, Kyowa Kirin, LEO Pharma, Medimmune, Merck, MoonLake Immunotherapeutics, Nimbus Therapeutics, Novartis, Pfizer, Regeneron, Reistone Biopharma, Roche, Sanofi Genzyme, Sun Pharma, UCB Pharma, and Vyne Therapeutics; **S. Weidinger** is a speaker; advisory board member, and/or investigator for: AbbVie, Almirall, Eli Lilly and Company, Kymab, LEO Pharma, Novartis, Pfizer, Regeneron, and Sanofi; and has received research grants from: La Roche-Posay, Pfizer, and Sanofi; **L. Spelman** has been a consultant, and/or scientific advisor, and/or investigator, and/or scientific officer, and/or speaker for: AbbVie, Akeso Biopharma, Alphyn Biologics, Amgen, Anacor, Ascend, ASLAN Pharmaceuticals, Astellas, AstraZeneca, Blaze Bioscience, Bristol Myers Squibb, Boehringer Ingelheim, Botanix, Celgene, Connect Biopharmaceuticals Australia, Dermira, Eli Lilly and Company, Evelo Biosciences, Galderma, Genentech, GlaxoSmithKline, Hexima, Immunic Therapeutics, Invion, Janssen, Kiniksa Pharmaceuticals, Kobiolab, LEO Pharma, Lipidio Pharma, Mayne Pharma, Medimmune, Merck Sharp & Dohme, Merck Serono, Novartis, Otsuka, Pfizer, Phosphagenics, Photon MD, Regeneron, Reistone Biopharma, Roche, Samumed, Sanofi Genzyme, SHR, Sun Pharma ANZ, Trius, UCB Pharma, Vyne Therapeutics, and Zai Lab; **J. Silverberg** has received grants and/or personal fees from: AbbVie, AFYX Therapeutics, Arena Pharmaceuticals, Asana BioSciences, Bluefin Biomedicine, Boehringer Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Incyte Corporation, Kiniksa, LEO Pharma, Luna Pharma, Menlo Therapeutics, Novartis, Pfizer, RAPT Therapeutics, Regeneron, and Sanofi; **H. Crane**, **H. Elmaraghy**, **L. DeLuca-Carter**, **M. L. Buziqui Piruzeli**, **C. Hu**, and **E. Pierce** are employees and stockholders of: Eli Lilly and Company; **H. Agell** is an employee of: Almirall; **D. Thaçi** has received personal fees from: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Janssen Cilag, Kyowa Kirin, LEO Pharma, NewBridge Pharmaceuticals, Novartis, Pfizer, Regeneron, Sandoz, Sanofi Genzyme, and UCB Pharma; and has received grants from: AbbVie, LEO Pharma, and Novartis.
Medical writing assistance was provided by Thai Cao, MS, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company
Previously Presented at the Fall Clinical 2024; Las Vegas, USA; 24-27 October 2024

These studies were funded by Dermira, a wholly owned subsidiary of Eli Lilly and Company. Almirall, S.A. has licensed the rights to develop and commercialize lebrikizumab for the treatment of dermatology indications, including atopic dermatitis, in Europe. Lilly has exclusive rights for development and commercialization of lebrikizumab in the United States and the rest of the world outside of Europe.

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

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OBJECTIVES

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

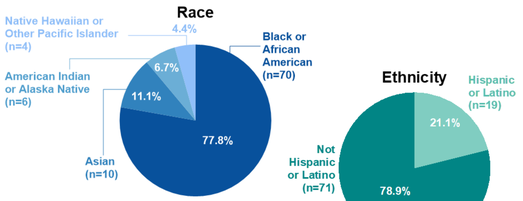
CONCLUSIONS

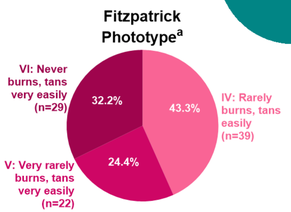
- ADmirable is the first clinical trial to report data from patients with moderate-to-severe AD and skin of color (78% Black or African American patients) using novel tools and scales to evaluate signs and symptoms that matter to patients
- Lebrikizumab improved AD signs and symptoms after 16 weeks of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

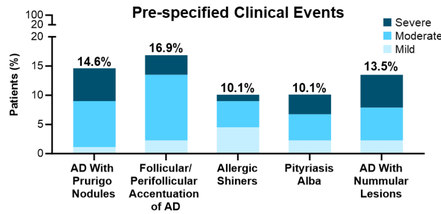
Society of Dermatology Nurse Practitioners (SDNP) National Conference 2025, Indian Wells, CA, USA; April 30 - May 3 2025

Baseline Demographics and Disease Characteristics

	LEBRI 250 mg Q2W (N=90)
Age, years	40.7 (19.6)
Adult (≥18 years), n (%)	76 (84.4)
Adolescent (≥12 to <18 years), n (%)	14 (15.6)
Female, n (%)	39 (43.3)
BMI, kg/m²	30.1 (7.7)
BMI category, n (%)	
Underweight (<18.5 kg/m²)	3 (3.3)
Normal (≥18.5 and <25 kg/m²)	19 (21.1)
Overweight (≥25 and <30 kg/m²)	30 (33.3)
Obese (≥30 and <40 kg/m²)	26 (28.9)
Extreme obese (≥40 kg/m²)	12 (13.3)
Duration since AD onset, years	19.7 (16.1)
IGA[b]	
3 (Moderate), n (%)	62 (68.9)
4 (Severe), n (%)	27 (30.0)
EASI	26.4 (12.2)
BSA % affected	37.8 (20.5)
POEM	17.3 (6.5)
Pruritus NRS[c]	7.0 (2.2)
≥3, n (%)	73 (93.6)
≥4, n (%)	70 (89.7)
Sleep-Loss scale[c]	2.0 (1.1)
DLQI[d]	13.2 (7.4)
cDLQI[d]	12.2 (8.2)
PO-SCORAD[e]	57.1 (17.8)
PDCA-Derm™[,f]	
Hypopigmented lesion(s), n (%)	16 (17.8)
Hyperpigmented lesion(s), n (%)	52 (57.8)

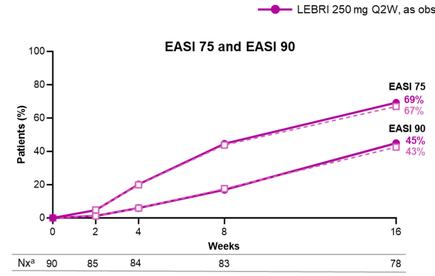






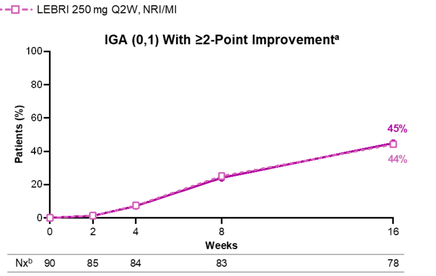
[a]Based on the patient's reported cutaneous reaction to sun exposure; [b]1 patient inadvertently enrolled with IGA=2 and discontinued when discovered they did not meet enrollment criteria; [c]Nx=78; [d]Patients <16 years of age at baseline completed cDLQI [Nx=10]; others completed DLQI [Nx=77]; [e]Nx=87;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

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



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

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



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

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

At Week 16:

33% — Improved hypopigmented lesions[a]

17% — Hypopigmented lesions improved to normal skin tone[a]

20% — Hyperpigmented lesions improved to normal skin tone[b]

63% — Improved hyperpigmented lesions[b]

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

Results

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

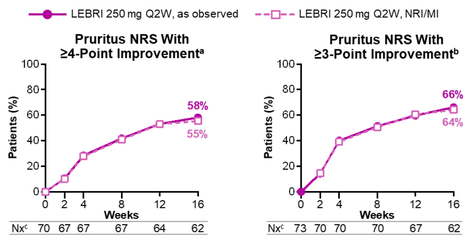
50-year-old Black/African American, non-Hispanic female

Baseline	
IGA	EASI
3	19.35

Week 16		
IGA	EASI	EASI % CFB
1	2.4	88%

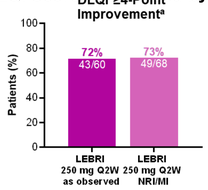
- Information on the ADmirable Study Design, Key Eligibility Criteria, Methods, and Use of Concomitant Topical and Systemic Therapy are described in **Supplemental Materials**

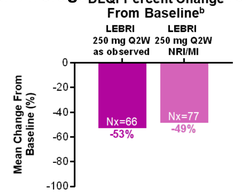
58% of Patients Achieved ≥4-Point Improvement, and 66% Achieved ≥3-Point Improvement in Pruritus NRS at Week 16



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

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





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

Adverse Events

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

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

Abbreviations: *AAD=American Academy of Dermatology; AD=atopic dermatitis; AE=adverse event; BMI=body mass index; BSA=body surface area; cDLQI=Children's DLQI; CFB=change from baseline; DLQI=Dermatology Life Quality Index; EASI=Eczema Area and Severity Index; EASI 75/90=≥75/90% improvement from baseline in EASI; IGA=Investigator's Global Assessment: IGA (0,1)=IGA response of clear or almost clear; ITT=intent-to-treat; IP=investigational product; JAK=Janus kinase; LD=loading dose; LEBRI=lebrikizumab; MedDRA=Medical Dictionary for Regulatory Activities; MI=multiple imputation; NMSC=non-melanoma skin cancer; NRI=non-responder imputation; NRS=Numeric Rating Scale; Nx=number of patients with non-missing values; PDE4=phosphodiesterase 4; PGIM=Patient-Oriented Eczema Measure; PO-SCORAD=Patient-Oriented SCORing of Atopic Dermatitis; Q2W=every 2 weeks; Q4W=every 4 weeks; QoL=quality of life; SAE=severe adverse event; SD=standard deviation; TCI=topical calcineurin inhibitor; TCS=topical corticosteroids; TEAE=treatment-emergent adverse event*

References:
1. Alexis A, et al. Oral presentation at: *AAD 2024*. Presentation number LEBPT3.
2. Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;70:338-351.
3. Blauvelt A, et al. *Br J Dermatol*. 2023;188:740-748.
4. Paller AS, et al. *Dermatol Ther (Heidelb)*. 2023;13:1517-1534.
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Disclosures: A. Alexis has received grant support from: AbbVie, Amgen, Arcutis, Castle Biosciences, Dermavant, Galderma, and LEO Pharma; has served as a consultant and/or advisor for: AbbVie, Allergan, Almirall, Alphyn Biologics, Amgen, Apogee Therapeutics, Arcutis, Avita Medical, Bausch Health, Beiersdorf, Bristol Myers Squibb, Canfield Scientific, Cara Therapeutics, Castle Biosciences, Cutera, Dermavant, Eli Lilly and Company, EPI Health, Galderma, Genentech, Incyte Corporation, Janssen, LEO Pharma, L'Oréal, Ortho Dermatologics, Pfizer, Sanofi Genzyme, Sanofi Regeneron, Swiss American CDMO, UCB Pharma, and VisualDx; has served as a speaker for: Bristol Myers Squibb, Janssen, Johnson & Johnson, L'Oréal, Regeneron, and Sanofi Genzyme; has received royalties from: Springer Science+Business Media, Wiley Blackwell, and Wolters Kluwer Health; and has received equipment from: Aerolase. **A. Moiin** has received reimbursement for travel costs from and conducted clinical trials for: Eli Lilly and Company. **J. Waibel** has served as a consultant and/or investigator and/or on scientific advisory boards for: Allergan, Amgen, argenx, BellaMa Technologies, Bristol Myers Squibb, Candela Healthcare, Cytrellis, Eli Lilly and Company, Embalion, Galderma, Horizon Therapeutics, Janssen/Johnson & Johnson, Lumenis, Neuronetics, Pfizer, Procter & Gamble, REGENXBIO, Sanofi, SkinCeuticals, Shanghi Biopharma, and Port Wine Birthmark; and is a recipient of a: VA Merit Grant for Amputated Veterans. **P. Wallace** has served as a principal investigator, advisor, and/or speaker for: AbbVie, Amgen, Arcutis, Biogen, Bristol Myers Squibb, Celgene, Centocor, Cynosure, Eli Lilly and Company, Genentech, GlaxoSmithKline, Merck, Novartis, Pfizer, Sanofi-Aventis, and UCB Pharma; and has received equipment (loan to institution) from: Cynosure. **D. Cohen** reports no financial conflicts of interest. **V. Laquer** has served as a researcher for: AbbVie, ACELYRIN, Acotech Bioharma, Amgen, Arcutis, argenx, ASLAN Pharmaceuticals, Biofrontera, Bristol Myers Squibb, Cara Therapeutics, Dermavant, Eli Lilly and Company, Galderma, Horizon Therapeutics, Incyte Corporation, Janssen, LEO Pharma, Novartis, Padagis, Pfizer, Q32 Bio, Rapt Therapeutics, Sun Pharma, UCB Pharma, and Ventyx Biosciences. **P. Kwong** is a principal investigator for: AbbVie, Amgen, Arcutis, Castle Creek Biosciences, Dermavant, Eli Lilly and Company, Galderma, Incyte Corporation, Novartis, Pfizer, and UCB Pharma; a consultant/advisor for: Bristol Myers Squibb, Eli Lilly and Company, EPI Health, Galderma, Incyte Corporation, LEO Pharma, Novan, Ortho Pharmaceutical, Pfizer, Sanofi Regeneron, UCB Pharma, and Verrica Pharmaceuticals; and a speaker for: AbbVie, Arcutis, EPI Health, Incyte Corporation, L'Oréal, Ortho Pharmaceutical, Sanofi Regeneron, Sun Pharma, and Verrica Pharmaceuticals; **A. Reck Atwater** is a former employee of: Eli Lilly and Company; **J. Proper**, **M. Silk**, **E. Pierce**, **S. Pillai**, and **M. J. Rueda** are employees and shareholders of: Eli Lilly and Company; **A. Moore** has received research grants or honoraria from: AbbVie, Acrotech, Arcutis, Bristol Myers Squibb, Cara Therapeutics, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, Johnson & Johnson, Pfizer, Rapt Therapeutics, and Sanofi Regeneron
Medical writing assistance was provided by Heidi Tran, PhD, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company
Previously presented at Fall Clinical 2024; Las Vegas, USA; 24-27 October 2024

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Almirall, S.A. has licensed the rights to develop and commercialize lebrikizumab for the treatment of dermatology indications, including atopic dermatitis, in Europe. Lilly has exclusive rights for development and commercialization of lebrikizumab in the United States and the rest of the world outside of Europe.

Lebrikizumab Confirms a Consistent Safety Profile in Adults and Adolescents With Moderate-to-Severe Atopic Dermatitis: Data From 11 Trials With Over 3000 Patient-Years of Exposure

Linda Stein Gold[1], Eric Simpson[2], Diamant Thaçi[3], Alan Irvine[4], Marjolein de Bruin-Weller[5], Gaia Gallo[6], Maria Lucia Buziqui Piruzeli[6], Hany Elmaraghy[6], Jinglin Zhong[7], Sonia Montmayeur[6], Ruth Coll[8], Mark G. Lebwohl[9], Louise Deluca Carter[6] (Non-author Presenter)

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Sponsored by Eli Lilly and Company

OBJECTIVE

- To provide updated long-term safety data for lebrikizumab treatment in adults and adolescents with moderate-to-severe AD, using data from 11 Phase 2/3 clinical trials

CONCLUSIONS

- This study confirms a safety profile for lebrikizumab that is consistent with previously reported data from the lebrikizumab clinical trial program in adolescents and adults with AD[1]
- Overall, TEAEs did not increase with longer duration of exposure to lebrikizumab
- No new safety signals were detected

Society of Dermatology Nurse Practitioners (SDNP) National Conference 2025, Indian Wells, CA, USA; April 30 - May 3 2025

KEY RESULTS

Most TEAEs Were Mild or Moderate in Severity and Did Not Lead to Treatment Discontinuations

	PBO (N=719) PYE=205.9	LEBRI 250 mg Q2W (N=1251) PYE=375.8	ALL LEBRI (N=2415) PYE=3167.8
	n (adj%) [adj IR]	n (adj%) [adj IR]	n (adj%) [adj IR]
Patients with ≥1 TEAE	368 (51.9) [284.2]	661 (52.7) [276.4]	1681 (69.6) [133.2]
Mild	198 (27.6)	366 (29.3)	778 (32.2)
Moderate	144 (20.7)	268 (21.3)	784 (32.5)
Severe	26 (3.6)	27 (2.2)	119 (4.9)
Death[a]	1 (0.1)	0	4 (0.2)
Serious AE	12 (1.7) [5.9]	15 (1.2) [3.9]	90 (3.7) [2.9]
AE leading to treatment discontinuation	12 (1.5) [5.4]	25 (2.0) [6.8]	100 (4.1) [3.2]

[a]1 death due to myocardial infarction in a 56-year-old male in the PBO group during the 16-week induction of ADvocate2 and 4 deaths in participants treated with LEBRI 250 mg Q2W (a 74-year-old male due to pancreatic cancer, a 64-year-old male due to metastatic pancreatic cancer, a 56-year-old male due to natural causes, and a 13-year-old male due to cardiac arrest). No deaths were considered related to study drug by investigators.

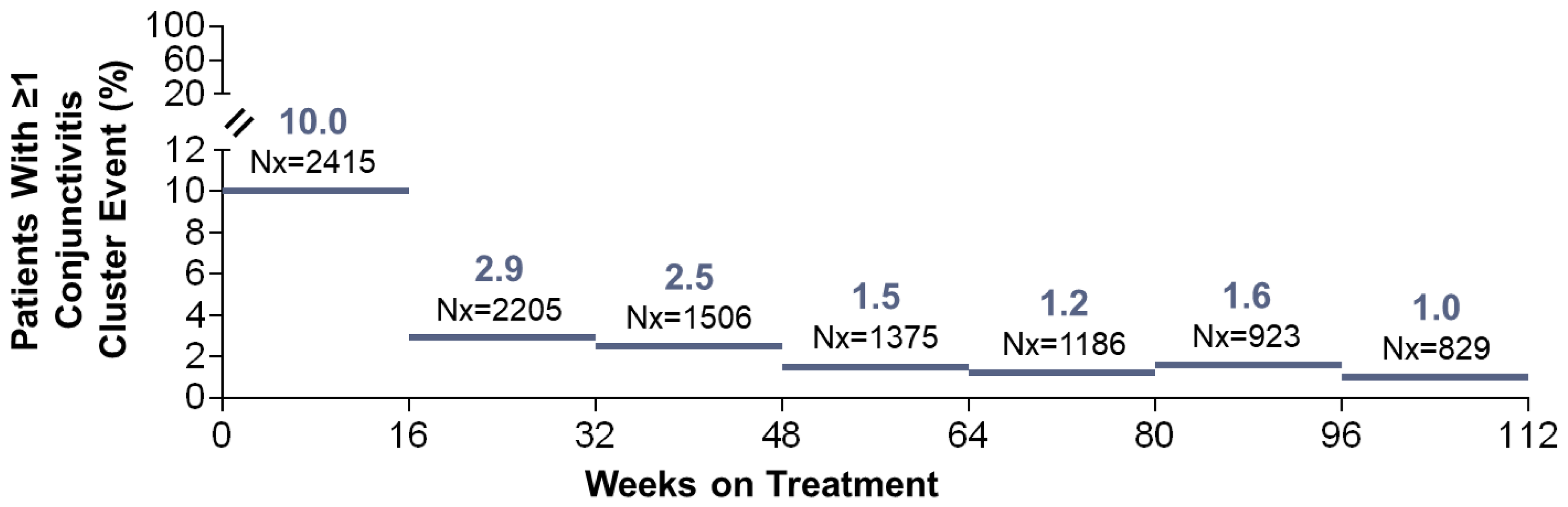
- In the PBO-Controlled dataset, the frequency of TEAEs was similar between treatment groups
- Frequency of serious AEs were low in the PBO-Controlled dataset and IR decreased with longer lebrikizumab exposure

AEs of Special Interest Did Not Increase With Longer Duration of Exposure

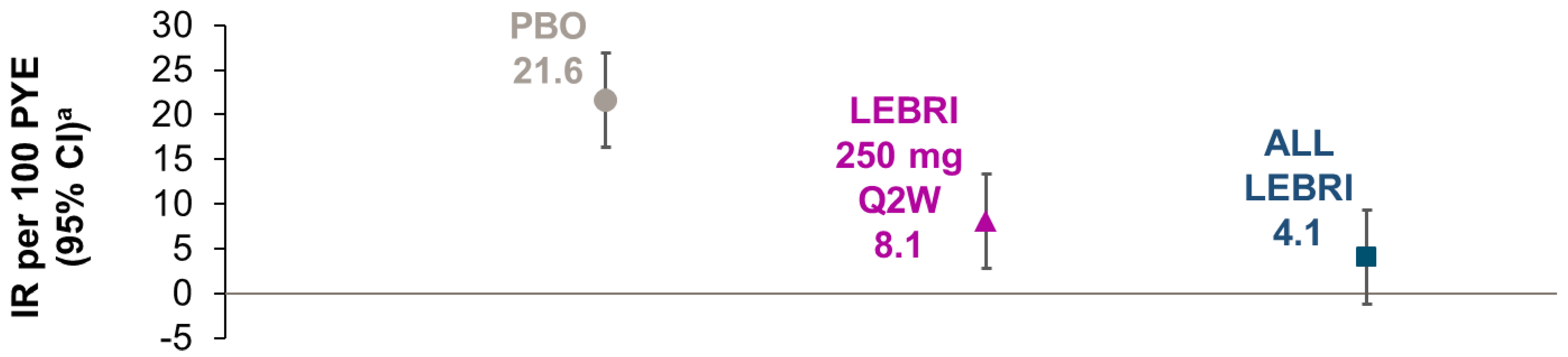
	PBO (N=719) PYE=205.9	LEBRI 250 mg Q2W (N=1251) PYE=375.8	ALL LEBRI (N=2415) PYE=3167.8
	n (adj%) [adj IR]	n (adj%) [adj IR]	n (adj%) [adj IR]
Conjunctivitis cluster[a]	21 (3.0) [10.7]	148 (11.7) [43.1]	345 (14.3) [12.3]
Mild	15 (2.1)	81 (6.4)	187 (7.7)
Moderate	6 (0.9)	67 (5.3)	151 (6.3)
Severe	0	0	7 (0.3)
Injection site reactions[b]	12 (1.6) [5.7]	35 (2.9) [9.7]	87 (3.6) [2.8]
Herpes zoster	1 (0.1) [0.4]	5 (0.4) [1.3]	25 (1.0) [0.8]

- None of the herpes zoster events were severe and none led to discontinuation.
- No eosinophilic-related disorders were reported

Conjunctivitis Cluster: Frequency Decreased With Longer Duration of Lebrikizumab Exposure



Skin Infections: IR Was Lower in the Lebrikizumab Q2W Group Than in the Placebo Group and Decreased With Longer Duration of Lebrikizumab Exposure (ALL LEBRI Dataset)

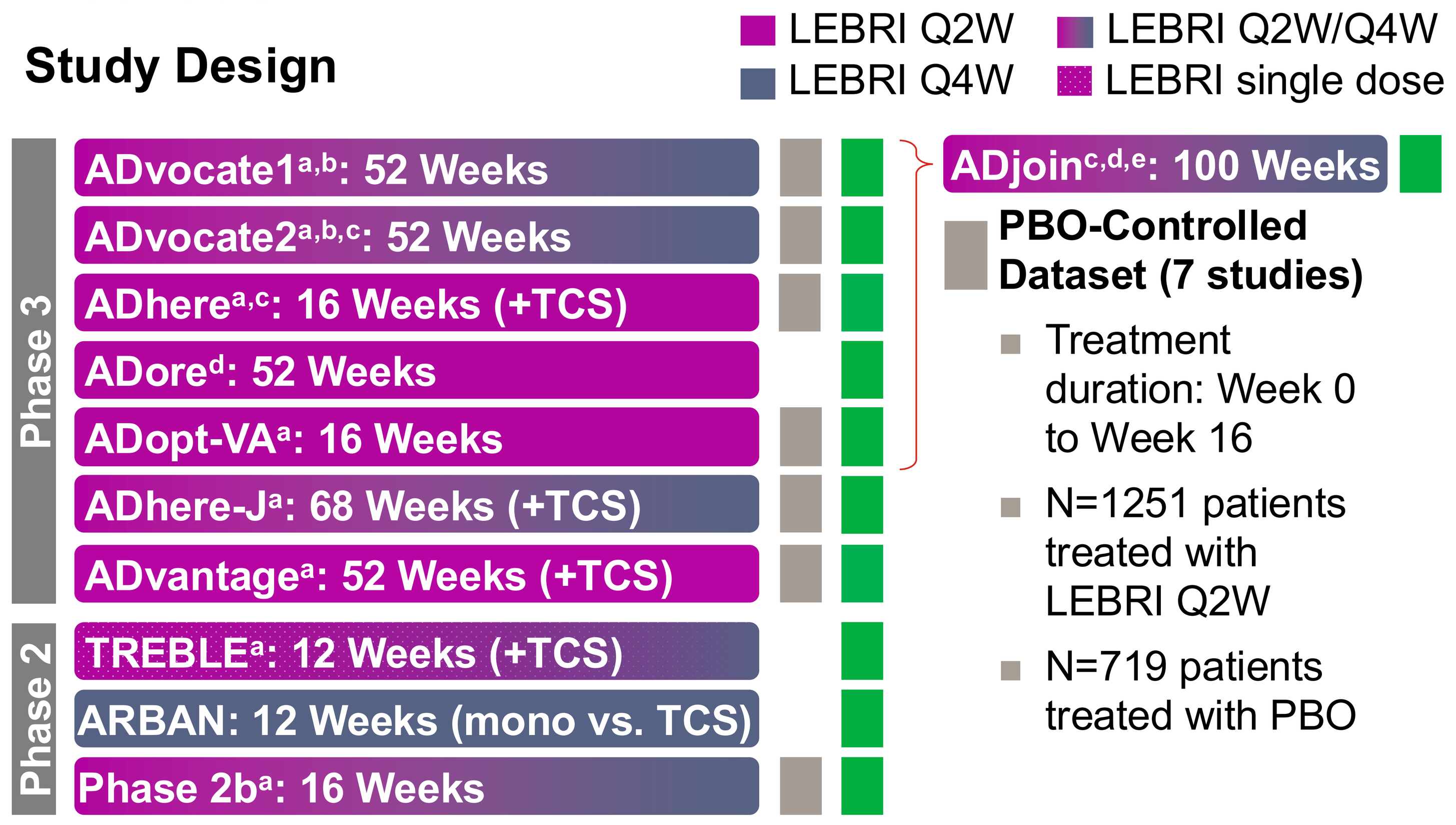


	PBO (N=719; PYE=205.9)	LEBRI 250 mg Q2W (N=1251; PYE=375.8)	Any LEBRI (N=2415; PYE=3167.8)
Patients with ≥1 event, n (%)	43 (6.0)	30 (2.4)	124 (5.1)
PYR	199.1	370.0	3051.1

[a]IR and 95% CI (not adjusted by study size).
Note: Skin infections were defined using the MedDRA high-level term of "skin structures and soft tissue infections" and included the following preferred terms: cellulitis, eczema impetiginous, folliculitis, staphylococcal skin infection, cellulitis staphylococcal, furuncle, erysipelas, and fungal skin infection; IR was defined as the number of patients experiencing the adverse event divided by the event-specific exposure to treatment (exposure time up to the event for patients with the event and exposure time up to the end of the period for patients without the event) multiplied by 100, in years.

Methods

Study Design



[a]PBO-Controlled; [b]TCS/TCI use was permitted during the Maintenance Period of ADvocate1 and 2; [c]Modified safety population, defined as patients who received ≥1 dose of study treatment, excluding 45 patients from 2 study sites (17 patients in ADhere who continued in ADjoin [site 1], 18 patients in ADvocate2 who continued in ADjoin [site 1], 3 patients in ADjoin [site 1], 7 patients in ADopt-VA [2 patients from site 1 and 5 patients from site 2]), as the patient eligibility criteria could not be confirmed; [d]TCS/TCI use was permitted; [e]This study has direct entry patients too.
Note: Database lock date was 31 October 2023.

ALL LEBRI Dataset (11 studies)

- Treatment duration: Any time from any of the 11 studies
- N=2415 patients who received ≥1 dose of LEBRI (any LEBRI dose)

Assessments and Statistical Analyses

- Integrated data from 11 Phase 2/3 clinical trials are presented
- The safety assessment for lebrikizumab treatment in adults and adolescents with moderate-to-severe AD was based on patients who received ≥1 dose of study treatment, excluding 45 patients from 2 study sites,[a] as the patient eligibility criteria could not be confirmed
- Percentage and exposure adjusted IR[b] are provided for the PBO-Controlled and ALL LEBRI datasets, with study-size adjusted values provided for the PBO-Controlled dataset, as studies had different randomization ratios

[a]17 patients in ADhere who continued in ADjoin (site 1), 18 patients in ADvocate2 who continued in ADjoin (site 1), 3 patients in ADjoin (site 1), and 7 patients in ADopt-VA (2 patients from site 1 and 5 patients from site 2); [b]IR is defined as the number of patients experiencing the adverse event divided by the event-specific exposure to treatment (exposure time up to the event for patients with the event and exposure time up to the end of the period for patients without the event) multiplied by 100, in years.

Results

- This analysis provides data for a total of 2415 patients and 3168 patient-years in the ALL LEBRI dataset
  - Median exposure: 391.0 days
  - Maximum exposure: 1138 days (3.12 years)
- Compared with the previous integrated data analysis[1] that reported data from 10 trials[a], this analysis includes data from:
  - 1 additional study: ADvantage[b]
  - Approximately 1 additional year from ADjoin
  - Additional data from the now-completed ADhere-J and ADopt-VA

[a]ADvocate1, ADvocate2, ADhere, ADore, ADopt-VA, ADhere-J, ADjoin, TREBLE, ARBAN, and Phase 2b; [b]European study.

Disclosures: **L. Stein Gold** is an investigator and/or consultant and/or speaker for: AbbVie, Amgen, Arcutis, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, and UCB Pharma; **E. Simpson** reports personal fees from: AbbVie, Advances in Cosmetic Medical Dermatology Hawaii, Amgen, AOBiome, Arcutis, Arena Pharmaceuticals, ASLAN Pharmaceuticals, Bristol Myers Squibb, CorEvitas, Dermira, Eli Lilly and Company, Evelo Biosciences, Excerpta Medica, FIDE, Forte Biosciences, Galderma, GlaxoSmithKline, Impetus Healthcare, Incyte Corporation, Innovaderm Research, Janssen, Johnson & Johnson, Kyowa Kirin, LEO Pharma, Maui Derm, Medscape, Merck, MJH Holding, MLG Operating, Pfizer, Physicians World, PRImE, Recludix Pharma, Regeneron, Revolutionizing Atopic Dermatitis, Roivant Sciences, Sanofi, Trevi Therapeutics, Valeant Pharmaceuticals, Vindico Medical Education, and WebMD; and has received grants or serves as principal investigator for: AbbVie, Acrotech, Amgen, Arcutis, ASLAN Pharmaceuticals, Castle, CorEvitas, Dermira, Dermavant, Eli Lilly and Company, Incyte Corporation, Kymab, Kyowa Kirin, National Jewish Health, LEO Pharma, Pfizer, Regeneron, Sanofi, Target, and VeriSkin. These potential conflicts of interest have been reviewed and managed by Oregon Health & Science University; **D. Thaçi** has received personal fees from: AbbVie, Almirall, Amgen, Boehringer Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Janssen Cilag, Kyowa Kirin, LEO Pharma, NewBridge Pharmaceuticals, Novartis, Pfizer, Regeneron, Sandoz, Sanofi, and UCB Pharma; and has received grants from: AbbVie, LEO Pharma, and Novartis; **A. Irvine** is a speaker, advisory board member, and/or investigator for: AbbVie, Almirall, Connect Biopharma, Eli Lilly and Company, LEO Pharma, OM Pharma, Pfizer, RAPT Therapeutics, Regeneron, and Sanofi; **M. de Bruin-Weller** has served as a consultant, speaker, advisor, and/or advisory board member for: AbbVie, Almirall, Amgen, ASLAN Pharmaceuticals, Eli Lilly and Company, Galderma, LEO Pharma, Pfizer, Regeneron, and Sanofi; **M. L. Buziqui Piruzeli**, **H. Elmaraghy**, **S. Montmayeur**, and **G. Gallo** are employees and shareholders of: Eli Lilly and Company; **J. Zhong** is an employee of: IQVIA; **R. Coll** is an employee of: Almirall; **M. G. Lebwohl** is an employee of: Mount Sinai and receives research funds from: AbbVie, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Clexio Biosciences, Dermavant Sciences, Eli Lilly and Company, Incyte Corporation, Inozyme, Janssen, Pfizer, Sanofi Regeneron, and UCB Pharma; and is a consultant for Almirall, AltruBio, Apogee, Arcutis, AstraZeneca, Atomwise, Avotres Therapeutics, Boehringer Ingelheim, Bristol Myers Squibb, Castle Biosciences, Celltrion, CorEvitas, Dermavant, Dermsquared, Evommune, FIDE, Forte Biosciences, Galderma, Genentech, Incyte Corporation, LEO Pharma, Meiji Seika Pharma, Mindera, Pfizer, Sanofi Regeneron, Seanergy, STRATA Skin Sciences, Takeda, Trevi Therapeutics, and Verrica Pharmaceuticals

Medical writing assistance was provided by Loredana Spoerri, PhD, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company.
Previously presented at Fall Clinical Dermatology Conference - 44th Anniversary, October 24 - 27, 2024, Las Vegas, NV, USA

These studies, with the exception of ADhere-J, were funded by Dermira, a wholly owned subsidiary of Eli Lilly and Company. ADhere-J was funded by Eli Lilly and Company. Almirall, S.A. has licensed the rights to develop and commercialize lebrikizumab for the treatment of dermatology indications, including atopic dermatitis, in Europe. Lilly has exclusive rights for development and commercialization of lebrikizumab in the United States and the rest of the world outside of Europe.

Reference: 1. Stein Gold L, et al. Poster presented at *AAD 2024*. Presentation 52041.

Abbreviations: *AD=atopic dermatitis; adj %=study size-adjusted percentage; adj IR=study size-adjusted IR; AE=adverse event; CI=confidence interval; IR=incidence rate; LEBRI=lebrikizumab; MedDRA=Medical Dictionary for Regulatory Activities; mono=monotherapy; N=number of patients in the analysis set; Nx=number of patients at risk in the specified category; PBO=placebo; PYE=patient-years of exposure; PYR=patient-years at risk; Q2W=every 2 weeks; Q4W=every 4 weeks; TCI=topical calcineurin inhibitor; TCS=topical corticosteroid; TEAE=treatment-emergent AE*

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Attributes of Treatment and Factors Influencing Patient Preference and Satisfaction in Atopic Dermatitis: Literature Review

Magdalena Bebrysz[1], Efstathios Zikos[2], Laurence Lucats[2], Cori Gray[3], Ana Maria Rodriguez-Leboeuf[1], Ella Brookes[4]

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Key Conclusions

1 Efficacy and safety are key drivers of patient preferences

2 Mode and frequency of administration are important to patients and key to reducing treatment burden

3 Communication with HCPs regarding treatment can influence treatment perceptions and subsequent compliance

Introduction

- Atopic dermatitis (AD) is the most common type of eczema, affecting more than 9.6 million children and about 16.5 million adults in the United States with over one-third of cases classified as moderate-to-severe in intensity[1]. Worldwide prevalence is around 3% and it affects up to 10% of adults in certain countries
- As many AD treatments and care options become available to a wider number of patients, there is a growing need for more information about willingness and preference from those that are living with moderate-to-severe AD to engage with these treatments
- Stated patient preference research methods help predict factors that influence health behaviors in the future
- This study is a literature review of findings from stated preference and qualitative studies regarding the unmet needs and preferences of people living with AD when considering their treatment to deliver a Conceptual Model (CM) of attributes impacting treatment choice, satisfaction and adherence

Objective

- To identify a list of AD treatments' attributes/factors influencing preferences and experience of patients with AD
- To develop a preliminary CM capturing relevant attributes of AD treatments that may influence patients' preferences
- The research questions to be answered in this literature review were:
  - What are the drivers of patient preferences towards AD treatments?
  - What are the most burdensome symptoms and impacts of AD from patients' and caregivers' perspectives?

Methods

- A Targeted Literature Review (TLR) of papers published from 1st Jan 2013–14th Feb 2023 was performed to identify concepts relevant to patients with moderate-to-severe AD and their caregivers when managing AD, and to identify key wording and terminologies used by patients and caregivers to describe these treatment products and preferences
- The searches were conducted on Medline through PubMed. The initial search strategy identified 346 records using the search string as detailed below

Table 1. Literature Review Scope

	Inclusion Criteria	Exclusion Criteria
Population of Interest	Patients with atopic dermatitis (any age) or their caregivers	Not applicable
Interventions of Interest	Any drug or no drug	
Comparators of Interest	Any comparator or no comparator	
Outcomes of Interest	Patient or caregiver assessment of burdensomeness of signs, symptoms, and impacts of the disease, disease experience, disease burden Treatment qualities preferences, overall preference for treatments, treatment satisfaction, treatment impact, reasons for treatment selection, non-adherence and discontinuation	Not applicable
Study Design of Interest	Preference study Interview/focus group Other qualitative study (including exit interviews) Cross-sectional survey Case report Mixed-methods study	Editorial Guideline Epidemiology study

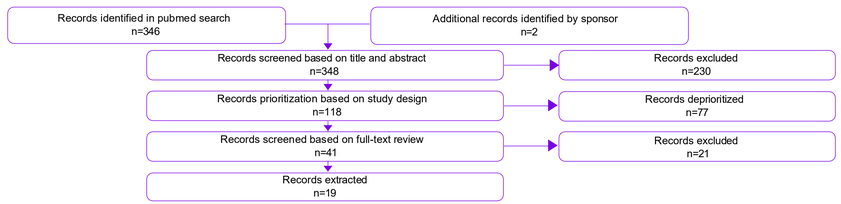
Table 2. Search String

Category	ID	Search String	# Hits
Disease	1	"atopic dermatitis" OR "eczema" [Title/Abstract]	42,320
Outcomes	2	"patient perspective*" OR "caregiver perspective*" OR "perception" OR "health perception*" OR "patient opinion" OR "caregiver opinion" OR "valuation*" OR "patient experience" OR "impact" OR "functioning" OR "burden" OR "work" OR "everyday" OR "patient needs" OR "caregiver needs" OR "satisfaction" OR "expectation*" OR "patient choice*" OR "caregiver choice*" OR "treatment choice" OR "treatment adherence" OR "treatment discontinuation" OR "attributes" OR "preference*" [Title/Abstract]	3,491,032
Study Design	3	"qualitative" OR "interview*" OR "focus group*" OR "grounded" OR "phenomenological" OR "thematic" OR "conceptual model" OR "ethnograph*" OR "survey*" OR "Delphi" OR "preference elicitation" OR "preference score*" OR "preference based" OR "preference-based" OR "discrete choice" OR "discrete-choice" OR "conjoint" OR "best-worst scaling" OR "time trade-off" OR "DCE" OR "BWS" OR "TTO" OR "swing-weighting" OR "threshold technique" [Title/Abstract]	1,449,285
Total	4	#1 AND #2 AND #3	525
	5	Filters: in the last 10 years, Humans, English	346

Results

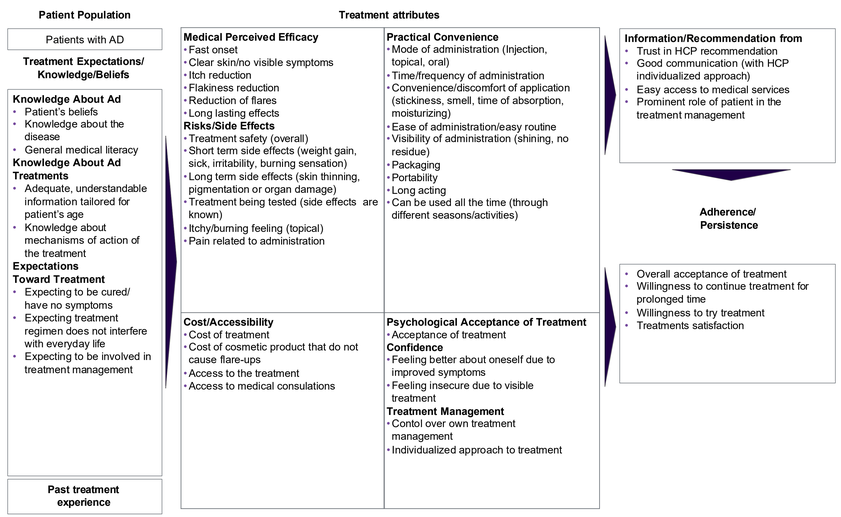
- 346 records were screened for inclusion, 19 articles identified were selected for full text extraction (**Figure 1**)
  - 5 articles reporting attributes impacting patient or caregiver preferences toward AD treatment were identified
  - 3 articles describing patient and caregiver experience with various AD treatments were included and 3 articles exploring patient adherence to AD treatment were identified
  - 2 manuscripts exploring preferences toward topical AD treatment and 4 exploring experiences with topical treatment were identified
  - 1 article reporting AD symptoms and 1 article exploring impacts of AD in Asia were included
- For the included studies; 10 qualitative studies, 4 Discrete choice experiments (DCEs), 4 surveys, and 1 mixed-method study
- Each DCE tested 6 to 9 treatment attributes classified as 'perceived efficacy', 'risk of side effects', 'practicality' and 'cost'
- 'Perceived efficacy' was defined as itch reduction, skin lesions, prevention of progression and speed of onset
- 'Risk of side effects' overall was tested, as well as risk of VTE, serious infection, malignancy, injection site reaction and eye inflammation
- 'Practicality' was tested through oral vs. injectable modes of administrations, frequency of administration, frequency of check-ups, administration settings, flare adaptability or interrelationship to topicals
- 'Efficacy' and 'risk of side effects' were the most valued by DCE participants
- Efficacy and onset of action positively influenced treatment satisfaction, while side effects, injection, high cost, low access, frequency, burdensome routine and duration of administration impacted treatment satisfaction and potentially adherence
- Communication with HCPs including recommendations or information on treatment and access to medical consultation influenced treatment perception and subsequent compliance
- Lastly, patient medical literacy about AD or treatment, forgetfulness and busyness were also factors of treatment satisfaction and adherence

Figure 1. Article Screening Results



Reasons for exclusion: Not focused on AD, patient or caregiver perspective, disease symptoms, impacts, treatment experience or treatment preference.
Reasons for deprioritisation: Not qualitative or preference study design and not Japanese or Chinese population.

Figure 2. Conceptual Model of AD Treatment Attributes and their Relevance to Treatment Satisfaction and Compliance[2–9]



Only qualitative studies were included.

- These findings informed a CM for AD treatment attributes and their relevance to satisfaction and compliance **(Figure 2)**
- This literature review highlights efficacy and safety as paramount to treatment satisfaction and use, but other treatment attributes, including personal and environmental factors are important as well
- Further preference research is needed to better understand the drivers of patient preferences among a heterogenous population, to gain a deeper understanding of the influences on treatment satisfaction and adherence and to evaluate a more comprehensive or alternative list of attributes across countries to improve shared decision making

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Abbreviations

AD, Atopic dermatitis; CM, Conceptual model; DCE, Discrete choice experiment; HCP, Health care practitioner; TLR, Targeted literature review; VTE, Venous thrombo-embolism.

Acknowledgments and Funding

The data in this poster was originally presented at the European Academy of Dermatology and Venereology (EADV) 2024; Amsterdam, Netherlands; September 25–28, 2024. The data will be presented by Lindsay Billings (Medical Science Liaison, NA Medical Immunology Non-Alliance Central, Genzyme Corporation)

Disclosures

LL, EB, EZ and **CG** are employees of Sanofi and may hold stock or stock options. **BM** and **AMR** are employees of IQVIA and may hold stock or stock options.

Presented at the Society of Dermatology Nurse Practitioners National conference (SDNP); Indian Wells, CA; April 30–May 3, 2025

Avapritinib Improved Skin Findings in Patients With Indolent Systemic Mastocytosis (ISM) in the Registrational, Double-Blind, Placebo-Controlled PIONEER Study

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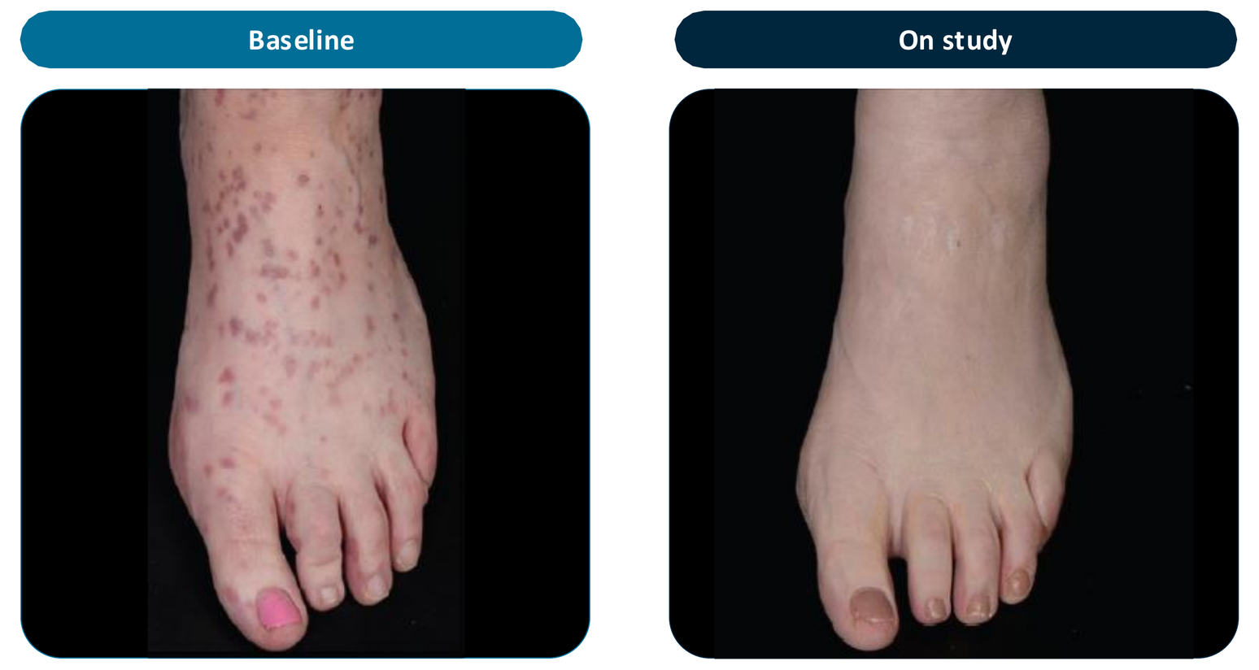
Rationale

- Indolent systemic mastocytosis (ISM) is the most common form of systemic mastocytosis (SM); driven by the *KIT* D816V mutation in approximately 95% of cases[1–4]
- Patients with ISM can have lifelong debilitating symptoms across multiple organ systems[4,5]
- The vast majority of patients with ISM have highly heterogeneous maculopapular skin lesions[5–10]
  - Lesions may be localized or diffuse, typically on the thighs and torso
  - Patients also experience Darier's sign, pruritus, and flushing
- Avapritinib has previously demonstrated improvements in multiple SM symptoms including skin manifestations and quality of life (QoL) measurements (**Figure 1**)[11–15]
- In Part 1 of PIONEER, avapritinib significantly reduced total mast cell burden and abnormal CD30+ mast cells in skin lesions[11]
- Avapritinib is approved in the USA and Europe to treat adults with ISM, in the USA for adults with advanced systemic mastocytosis (AdvSM), and in Europe for adults with AdvSM after ≥1 prior systemic therapy[16,17]

Figure 1: Skin improvements with avapritinib in patients with AdvSM from the EXPLORER study[15]



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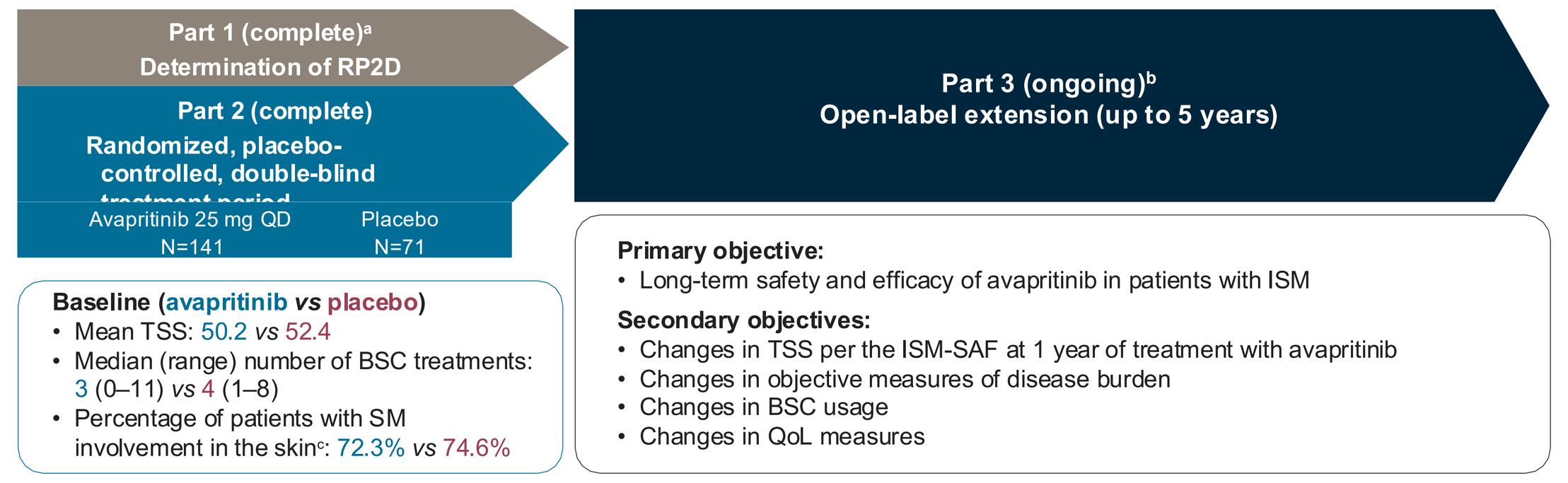
Methods

- PIONEER, a global, randomized, double-blind, placebo-controlled trial, evaluated the safety, efficacy, and QoL in patients with ISM receiving avapritinib + best supportive care (BSC; avapritinib) compared with patients receiving placebo + BSC (placebo)
  - In Part 2, there were 212 patients randomly assigned in a 2:1 ratio to receive avapritinib 25 mg orally once daily (QD) or placebo for 24 weeks
  - After 24 weeks of treatment was completed, patients were eligible to receive avapritinib 25 mg QD for up to 5 years in Part 3

Overall, 226 patients were exposed to avapritinib 25 mg across Parts 1, 2, and 3



[a]The RP2D of avapritinib was identified based on efficacy and safety results from Part 1 that included four cohorts: 25 mg avapritinib (n=10), 50 mg avapritinib (n=10), 100 mg avapritinib (n=10), and placebo (n=9). [b]As of April 7, 2023. [c]By principal investigator assessment.
BSC, best supportive care; ISM, indolent systemic mastocytosis; ISM-SAF, Indolent Systemic Mastocytosis Symptom Assessment Form; QD, once daily; QoL, quality of life; RP2D, recommended Part 2 dose; SM, systemic mastocytosis; TSS, total symptom score.

- Adult patients with centrally confirmed ISM with uncontrolled moderate to severe symptoms (total symptom score [TSS] of ≥28 at screening), despite treatment with ≥2 BSC, were eligible for the study
- The ISM Symptom Assessment Form (ISM-SAF[a]) is a validated symptom assessment tool specifically developed for evaluation of ISM symptomology[18–20]
  - TSS is based on the severity of 11 ISM symptoms
  - The ISM-SAF was developed over the past 8 years with input from patients, disease experts, and global regulatory agencies[10]
- The primary endpoint of PIONEER Part 2 was the mean change in ISM-SAF TSS from baseline to Week 24 in avapritinib-treated patients compared with placebo, and in Part 3 the primary endpoint is to assess the long-term efficacy and safety of avapritinib
- Here, we present Part 2 data at a cut-off of June 23, 2022

Figure 2: Comprehensive assessment of skin changes from baseline to Week 24

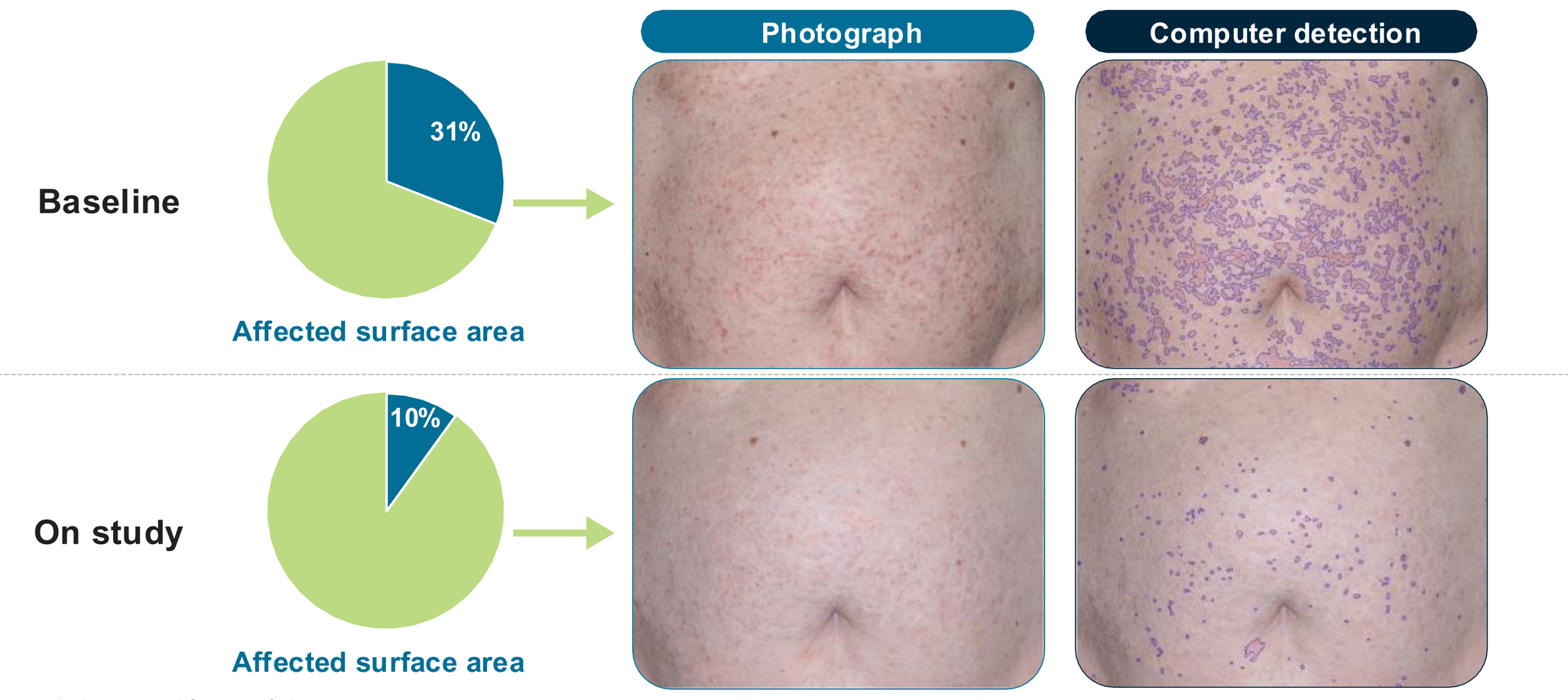
ISM-SAF (completed by all patients)
- Daily PRO assessment of 11 ISM-related symptoms
- Each evaluated on a 0–10 scale (no symptoms – worst imaginable)
- Skin domain is comprised of spot, flushing, and itching for a total scale of 0–30

Skin photographs (avapritinib n=74, placebo n=37)
- Optional, taken at baseline and every 12 weeks
- Photographs assessed by:
  – *Computer-generated algorithm* - calculated affected surface area
  – *Blinded SAC*

Skin biopsies (avapritinib n=107, placebo n=60)
- Performed in patients with mastocytosis in the skin at baseline and at Week 24
- Quantification of mast cell infiltrates was performed by central pathology
- Mast cell number and immunophenotype in skin biopsies were assessed via light microscopy and immunohistochemistry

PRO, patient-reported outcome; SAC, skin assessment committee.

Figure 3: Blinded SAC evaluation of skin photographs



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- The blinded skin assessment committee (SAC) determined the most affected region at baseline and color change over time (**Figure 3**)
- The affected surface area was followed with a computer-generated detection method and the number of lesions, fractional area, and percent fractional area were determined (**Figure 3**)

Results

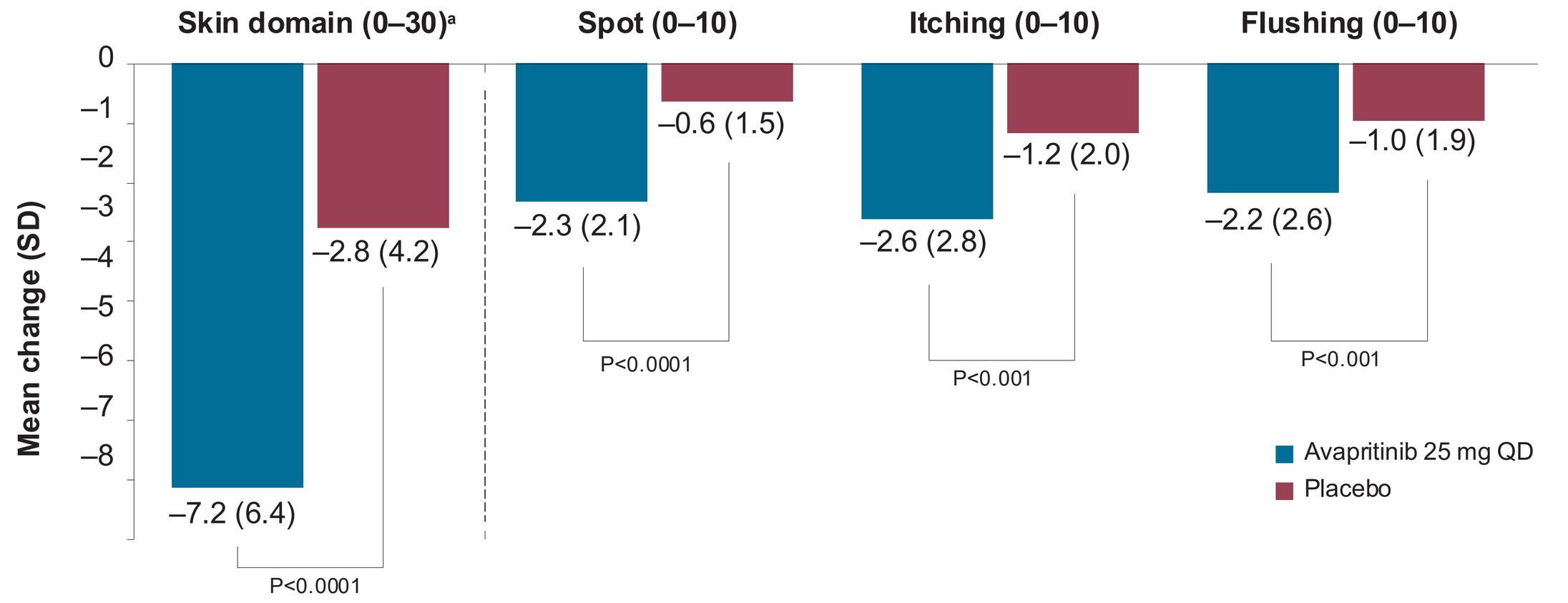
Table 1: Baseline patient demographics and characteristics

Patient demographics	Skin biopsy (n=167) Avapritinib 25 mg QD (n=107)	Skin biopsy (n=167) Placebo (n=60)	ITT population (N=212) Avapritinib 25 mg QD (n=141)	ITT population (N=212) Placebo (n=71)
Age (years), median (range)	49 (18–77)	55 (26–79)	50.0 (18–77)	54.0 (26–79)
Female, n (%)	78 (73)	45 (75)	100 (71)	54 (76)
TSS baseline, mean (SD)[a,b]	50.8 (19.1)	53.9 (18.8)	50.2 (19.1)	52.4 (19.8)
Most severe symptom score, mean (SD)	7.7 (1.7)	8.1 (1.6)	7.7 (1.7)	7.9 (1.7)
Mast cell burden				
Median serum tryptase (central), ng/mL (range)	39.5 (3.6–256.0)	49.6 (5.7–501.6)	38.4 (3.6–256.0)	43.7 (5.7–501.6)
Median bone marrow biopsy mast cells (central), % (range)	7.0 (1.0–50.0)	7.0 (1.0–70.0)	7.0 (1.0–50.0)	7.0 (1.0–70.0)
Mast cell aggregates present, n (%)	84 (79)	50 (83)	106 (75.2)	57 (80.3)
Median *KIT* D816V VAF in peripheral blood, % (range)[c]	0.5 (Undetectable –41.3)	0.4 (Undetectable –36.7)	0.4 (Undetectable –41.3)	0.3 (Undetectable –36.7)
SM therapy				
Prior cytoreductive therapy, n (%)[d]	15 (14)	6 (10)	19 (13)	7 (10)
Prior TKI therapy, n (%)	8 (7)	4 (7)	10 (7)	4 (6)
Number of BSC treatments, median (range)[e]	3 (0–11)	3 (1–8)	3 (0–11)	4 (1–8)

[a]Eligibility for enrollment was based on TSS ≥28 at screening; patients may have a score <28 at baseline. [b]Two patients in the avapritinib group had missing baseline TSS values, therefore the denominator was based on patients with available data at baseline (n=139). [c]The limit of detection was 0.02%. [d]Cytoreductive therapies included dasatinib, imatinib, masitinib, nilotinib, midostaurin, brentuximab vedotin, cladribine, hydroxyurea, rapamycin, and interferon alpha. Includes treatments received by patients at baseline; patients may have received BSC treatments previously discontinued at the time of enrollment/baseline. [e]All patients had at least two BSC treatments prior to or at screening.
A total of 10 (7%) patients treated with avapritinib and five (7%) patients treated with placebo had <2 BSC treatments at the start of the study. In patients with skin biopsies, a total of nine (8%) patients treated with avapritinib and four (7%) patients treated with placebo had <2 BSC treatments at the start of the study.
ITT, intent to treat; SD, standard deviation; TKI, tyrosine kinase inhibitor; VAF, variant allele frequency.

- More than 70% of PIONEER patients had skin involvement; baseline characteristics were comparable to the intent to treat (ITT) population (**Table 1**)
  - A subset of patients with skin biopsies agreed to optional skin photographs; baseline characteristics were similar to patients with skin biopsies and the ITT population
- At Week 24, avapritinib significantly improved TSS (–15.6 *vs* –9.2; P=0.003) *versus* placebo (both with BSC)

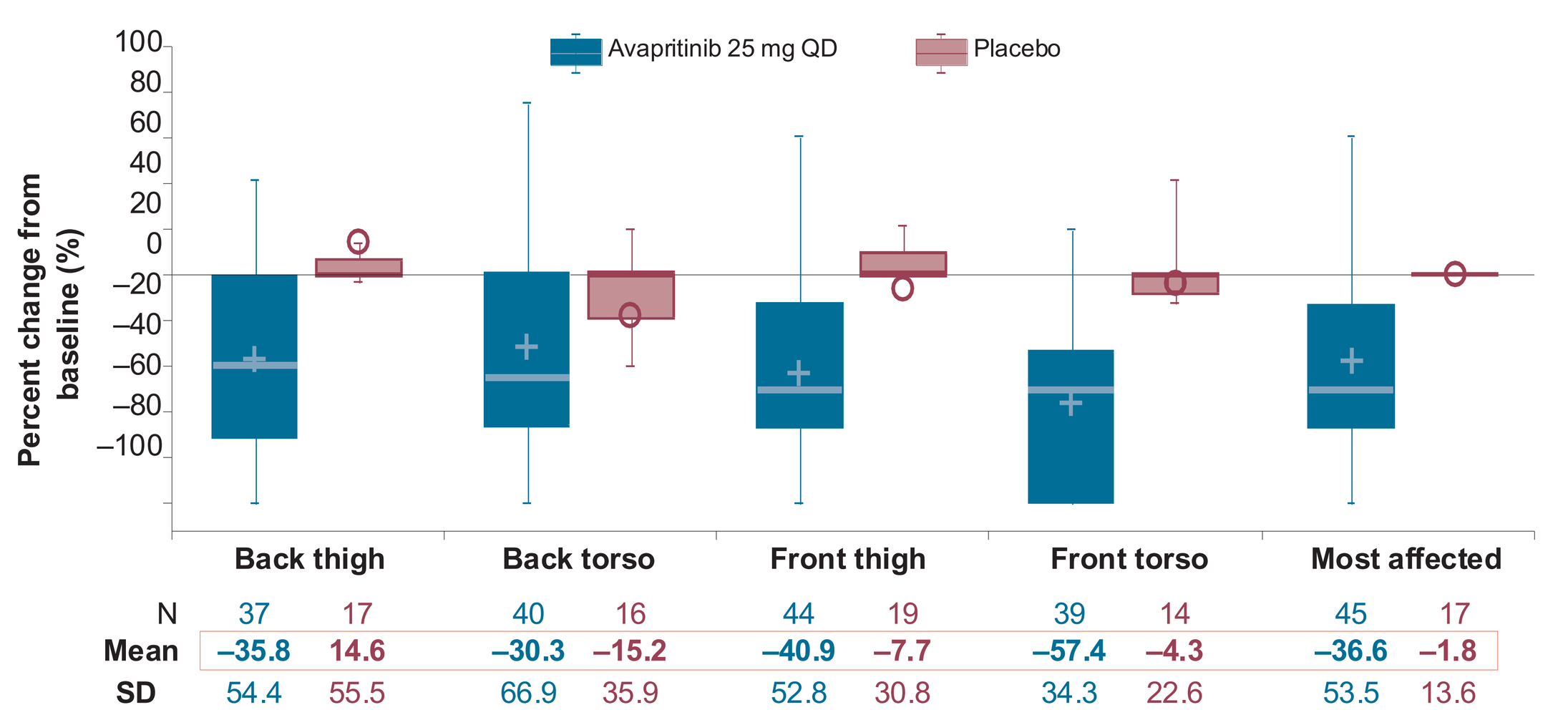
Figure 4: ISM-SAF skin symptoms in patients with skin biopsies



[a]Skin domain scores include the total score for spot, itching, and flushing severity.

- Significant improvements in ISM-SAF patient-reported skin domain, individual skin symptoms, and QoL in avapritinib-treated patients (**Figure 4**)
  - In the majority of patients, the most severe symptom domain at baseline was the skin domain
  - A correlation was observed between ISM-SAF skin domain score change from baseline and mastocytosis-QoL total score change from baseline

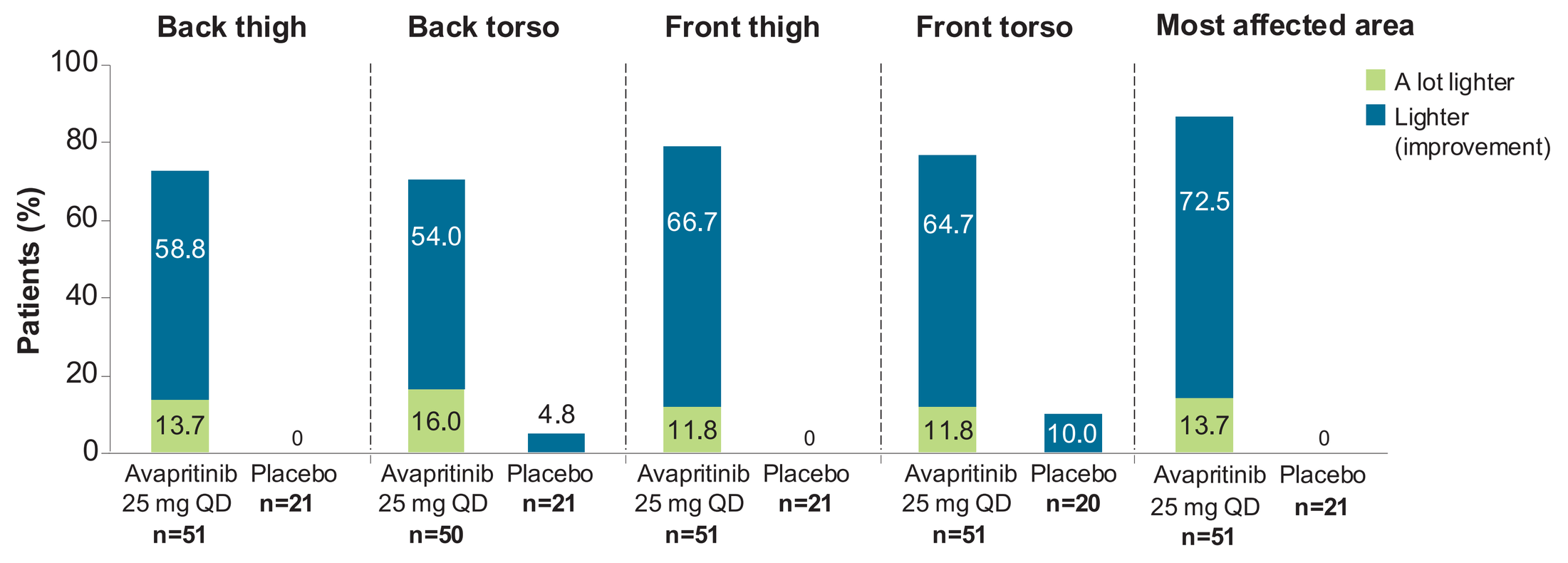
Figure 5: Fractional area estimate determined by computer-generated algorithm



Outliers are removed for visual presentation. The box represents the first and third quartile of the data. The symbol represents the mean, the line within the box represents the median, and the whiskers represent the upper 75th to 90th percentiles and lower 10th to 25th percentiles.

- Surface area of skin lesions was reduced at Week 24 in avapritinib-treated patients (**Figure 5**)
  - In patients with paired photographs (baseline and Week 24), mean percent reduction (SD) in lesion surface area was −36.6% (53.5) with avapritinib *versus* −1.8% (13.6) with placebo in the most affected skin region

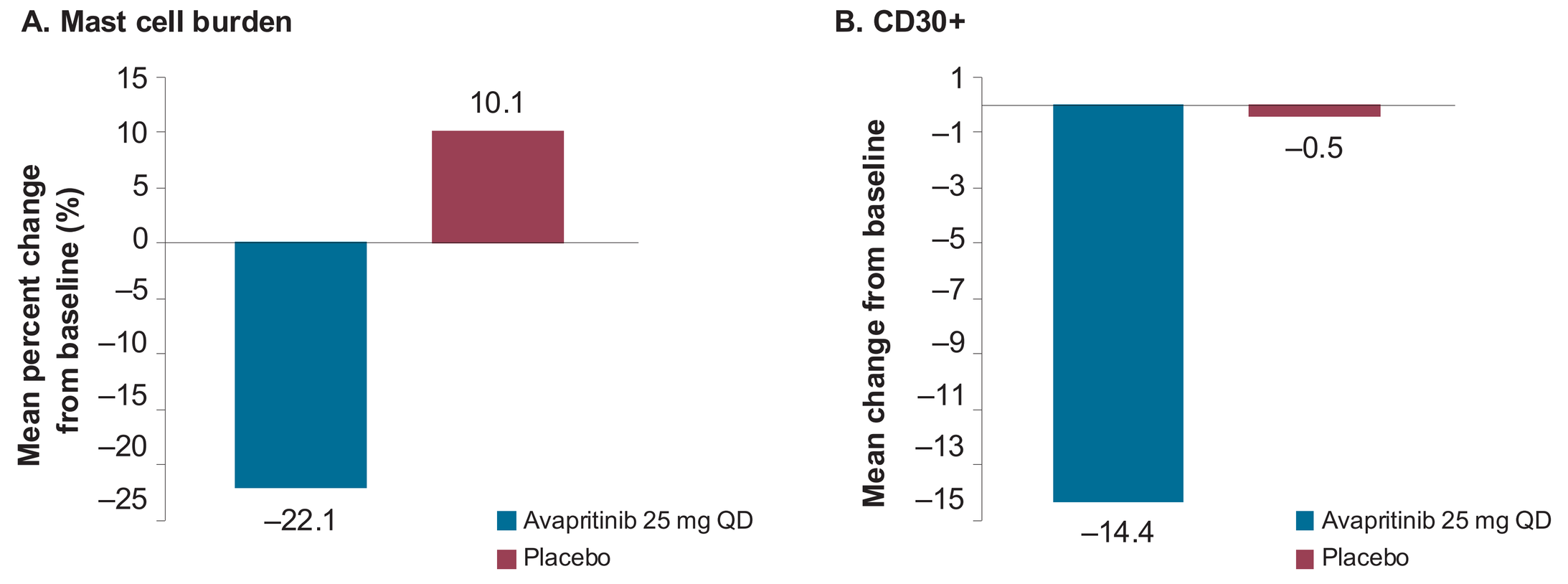
Figure 6: Skin lesion color change



Patients with no change or darkening of skin lesion color have not been included in the figure.

- Avapritinib treatment improved skin lesion color at Week 24 as assessed by a blinded SAC (**Figure 6**)
  - In patients with paired photographs, 86% of avapritinib-treated patients *versus* 0% of placebo patients had improved skin lesion color in the most affected skin region at Week 24
  - Rapid improvement in skin lesion color with avapritinib *versus* placebo was observed
  - At Week 12, 57% *versus* 4% of patients, respectively, had improved skin lesion color in the most affected area

Figure 7: Skin lesional tissue pathology



- Marked reduction of mast cell burden and CD30+ in skin lesions with avapritinib treatment (**Figure 7**)
  - Mean percent change (SD) of mast cell burden decreased at Week 24 with avapritinib (−22.1% [106], n=87) but increased with placebo (10.1% [121], n=49; **Figure 7A**)
  - Avapritinib significantly decreased CD30+ mast cell proportion in skin lesions at Week 24 *versus* placebo (−14.4% *vs* −0.5%; P=0.0015; **Figure 7B**)

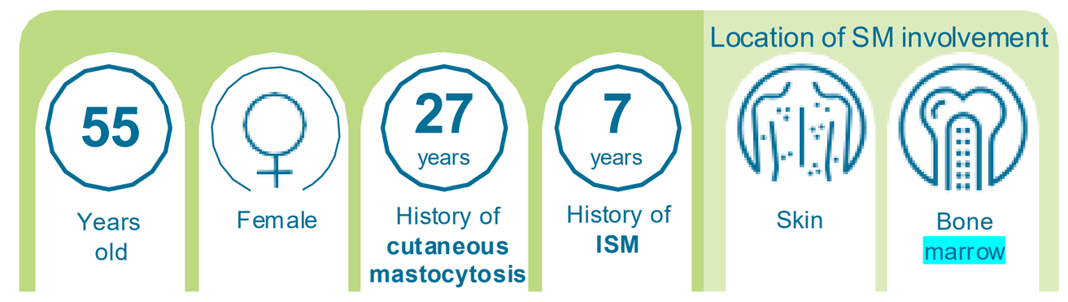
Table 2: Summary of AEs

	Avapritinib 25 mg QD (N=141)	Placebo (n=71)
Any AEs[a,b], n (%)	128 (91)	66 (93)
Grade 1–2 AEs	98 (70)	51 (72)
Grade 1–2 related AEs	74 (52)	30 (42)
Grade ≥3 AEs	30 (21)	15 (21)
Grade ≥3 related AEs	3 (2)	2 (3)
SAEs, n (%)	7 (5)	8 (11)
Any grade TRAEs	77 (55)	32 (45)
Most frequently reported TRAEs (≥5% of patients)		
Headache	11 (8)	7 (10)
Nausea	9 (6)	6 (8)
Peripheral edema	9 (6)	1 (1)
Periorbital edema	9 (6)	2 (3)
Dizziness	4 (3)	5 (7)
TRAEs leading to discontinuation	2 (1)	1 (1)

[a]AEs refer to TEAEs, defined as any AE that occurred between Day 1 of Part 2 through to a day prior to Day 1 of Part 3 if the patient crossed over to Part 3; if the patient did not cross over, then through 30 days after the last dose of study drug.
[b]There were too few events (≤5 per group) to assess the impact of avapritinib on anaphylaxis.
AEs, adverse events; SAEs, serious adverse events; TEAEs, treatment-emergent adverse events; TRAEs, treatment-related adverse events.

- Avapritinib 25 mg QD was well tolerated, with a similar safety profile to placebo (**Table 2**)
- Majority of adverse events (AEs) were Grade 1 or 2 with a low rate of discontinuation
- Serious AEs (SAEs) were reported more frequently in the placebo group (no treatment-related SAEs in either group)
- Edema AEs were higher in the avapritinib group (majority Grade 1, and did not result in discontinuation)

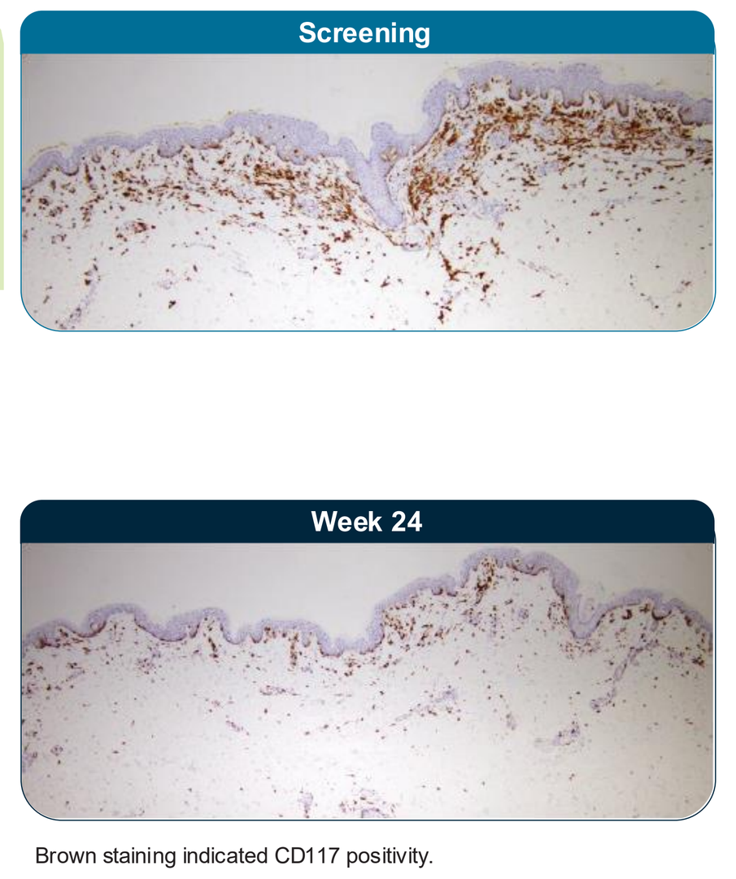
Case study



BSC: **fexofenadine, montelukast, famotidine, omalizumab** (all ongoing)
levocetirizine, hydroxyzine (discontinued after ~3 months)

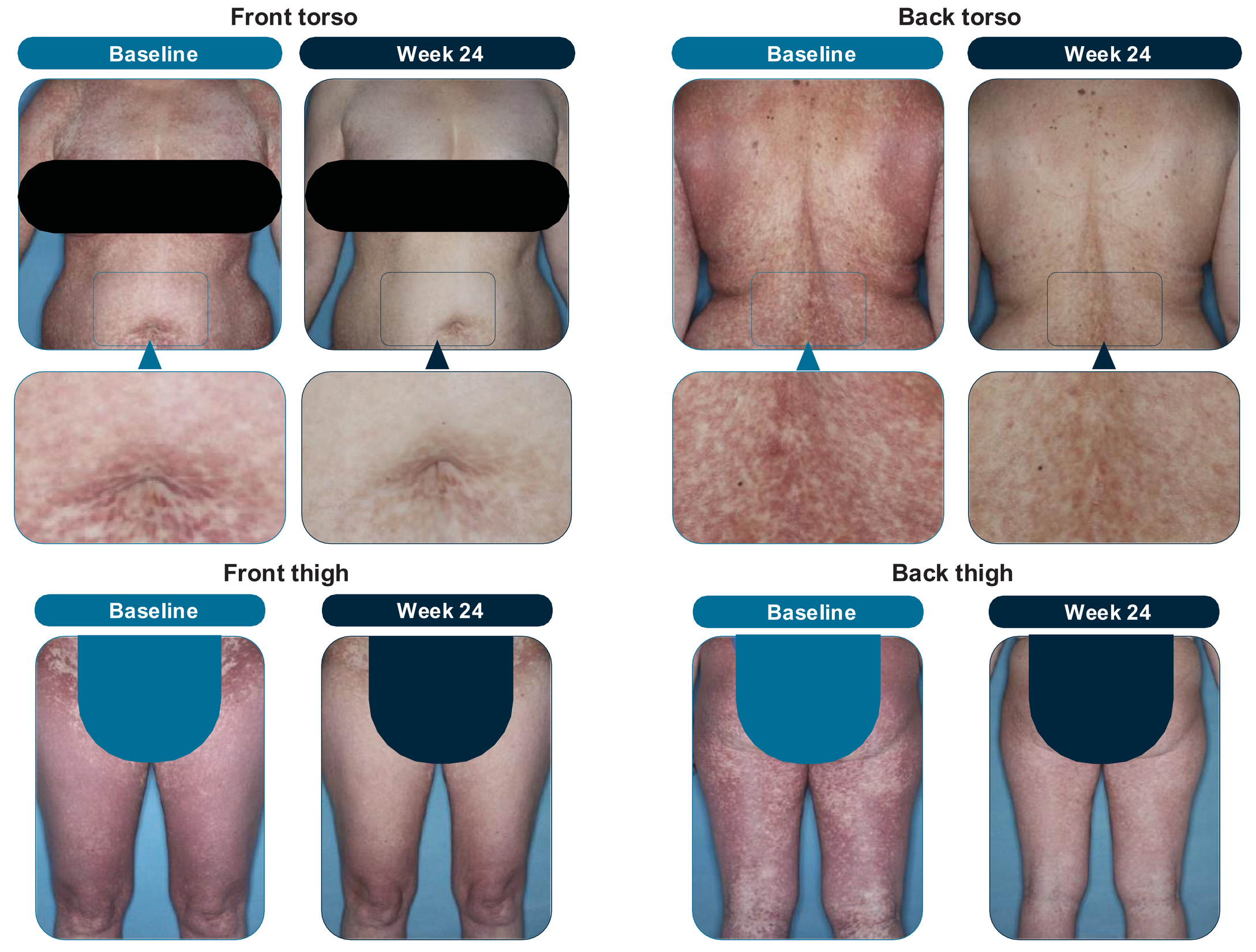
	% change from baseline to Week 24
ISM-SAF TSS	**–23.3**
Skin domain score	–44.4
MC-QoL total score	**–54.7**
Skin domain score	–77.3
Serum tryptase	**–26.3**
KIT D816V	**Central lab:** –63.2
BM mast cells	**No sample collected at Week 24**

BM, bone marrow; MC-QoL, mastocytosis quality of life.



Brown staining indicated CD117 positivity.

Case study (continued)



Patient permission granted for use of photos.

- Area and color of skin lesions improved at Week 24 with avapritinib treatment

Summary

- Avapritinib demonstrated statistically significant and clinically meaningful improvement *versus* placebo (both with BSC) in symptoms in the primary analysis, as measured with the TSS and biomarkers of mast cell burden
  - Of the patients with skin involvement, those treated with avapritinib experienced marked reductions in skin symptoms, skin color, surface area of skin lesions, and pathologic mast cell burden
  - Results confirmed the findings from Part 1, CD30 may be the most relevant biomarker of aberrant mast cells in skin lesions and further research is warranted
  - Improvements in skin symptoms were correlated with improvements in QoL
- Avapritinib was well tolerated and demonstrated a similar safety profile to placebo

Conclusion

- Avapritinib substantially impacted ISM-related skin symptoms, and skin lesion area, and color in addition to providing overall disease improvement in mast cell burden, symptoms, and QoL for patients with ISM

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Acknowledgements

We would like to dedicate this work to the memory of our dear colleague, Dr Marcus Maurer, whose passion, expertise, and contribution to the field of allergology and systemic mastocytosis have had a profound impact on patients and colleagues alike. The authors would like to thank the patients and their families for making this trial possible. The authors also thank the investigators and clinical trial teams who participated in the trial. Medical writing support was provided by Hannah Boyd, PhD, and editorial support was provided by Travis Taylor, BA, all of Paragon (a division of Prime, Knutsford, UK), supported by Blueprint Medicines Corporation, Cambridge, MA, according to Good Publication Practice guidelines.

Disclosures

Dr Siebenhaar has received honoraria (advisory board, speaker) and/or institutional grant/research support from Allakos, Aralez, Biocryst, Blueprint Medicines Corporation, Glenmark, Hyphens, Moxie, Novartis, Pediapharm, Sanofi, Sun Pharma, and Uriach. For all author disclosures, please contact medinfo@blueprintmedicines.com.

Treatment outcomes and management of generalized pustular psoriasis with spesolimab

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Background

- Spesolimab is a humanized anti-IL-36 monoclonal antibody approved in the US to treat GPP in adults and adolescents ≥12 years and weighing ≥40 kg as an IV dosage to treat flares and a SC dosage to treat GPP when patients are not experiencing a flare[1]
- Here, we describe the outcomes in 10 patients with GPP flare who received IV spesolimab at hospital and outpatient clinical practices across the US

Conclusions

- Access to targeted treatment is crucial to improve outcomes in patients experiencing GPP flare
- These 10 cases demonstrate the safety and efficacy of spesolimab in providing rapid improvement in GPP symptoms and patient QoL

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Case presentations

Figure 1. Summary of patient cases

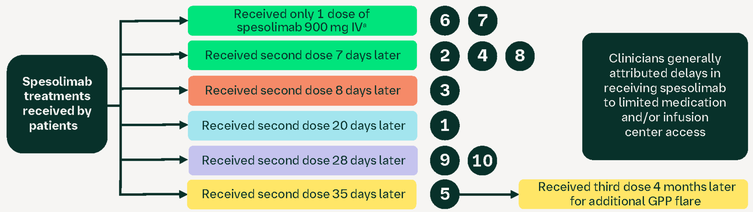
Case Report	Patient Demographics	GPP Presentation	GPP History	Hospitalized	MisDx	Skin Presentation: Before	Skin Presentation: After[a]
1	36-year-old American Indian male	Severe GPP presentation with systemic symptoms		✓			
2	58-year-old White female	Moderate to severe flare of sterile pustules that progressed to whole body, with no systemic symptoms			✓		
3	40-year-old White female	Pustular plaques on the extremities and trunk with systemic symptoms		✓	✓		
4	18-year-old Asian male	Plaques studded with pustules of moderate skin severity affecting 15–20% of BSA	✓		✓		
5	73-year-old White male	Numerous annular and arcuate erythematous plaques studded with pustules, and with trailing scale			✓		
6	62-year-old White female	Severe, diffuse erythematous rash with sheets of desquamation and sensation of heat in skin, fever, and chills	✓	✓			
7	92-year-old White female	Erythematous, scaly papules coalescing into plaques on trunk and extremities; fever, arthralgias, and altered mental status		✓			
8	72-year-old Black female	Severe erythroderma and widespread pustules, skin pain, fever, and chills	✓	✓			
9	47-year-old Black female	Erythema, swelling, and pustules on trunk and extremities; severe joint pain and muscle aches	✓		✓		
10	39-year-old White male	Localized erythematous eczematous rash to anterior neck and trunk, with no systemic symptoms			✓	Not available	Not available

[a]After 1 dose of 900 mg IV spesolimab

Results

- All 10 patients received FDA-approved IV spesolimab 900 mg over a 90-minute infusion for the treatment of their GPP flare (**Figure 2**)
  - Initiation of spesolimab was delayed in 8 patients (5 patients by 3–4 weeks, 2 patients by 4 months, and 1 patient by 20 months)
- 2 patients did not receive a second dose of IV spesolimab; 1 elderly patient achieved skin clearance after the first dose, while another developed diffuse HSV-1 infection attributed to either spesolimab or concurrent cyclosporine
- All other patients received a second infusion of spesolimab 7–35 days following the first infusion to facilitate further skin clearance
- 1 patient had an additional GPP flare requiring a third infusion of spesolimab

Figure 2. Summary of spesolimab 900 mg IV doses received by 10 patients

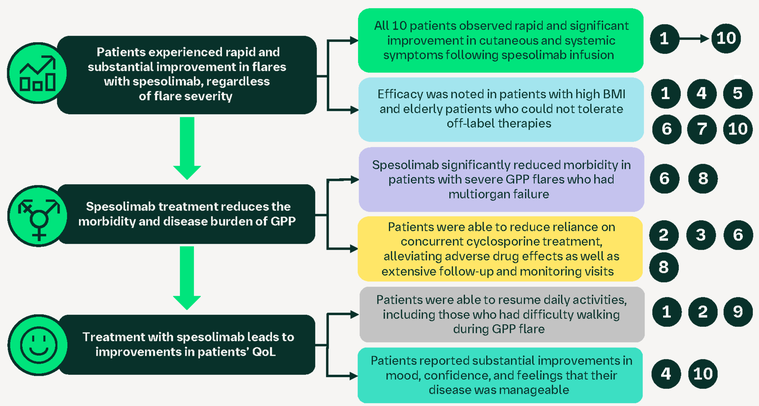


[a]FDA-approved dosing regimen of spesolimab

- Across all patients, treatment with IV spesolimab resulted in rapid and significant improvements in cutaneous and systemic symptoms (**Figure 3**)
- 7 patients had significant skin improvement within 1 week after the first IV spesolimab dose, while the remaining 3 patients achieved significant improvement in their skin following their second spesolimab infusion

Figure 3. Outcomes following treatment with spesolimab[a]

[a]The listed cases reported these as salient outcomes, and are not necessarily the only cases experiencing the outcomes



- The severity and morbidity of GPP flares in these patients highlight the need for immediate diagnosis and treatment
- Multiorgan failure and impaired QoL can also be profoundly debilitating for patients with GPP, and necessitates consideration of long-term management strategies for GPP

Presented at: 2025 Society of Dermatology Nurse Practitioners (SDNP) National Conference, Indian Wells, CA, USA; April 30–May 3, 2025

Originally presented at: Maui Derm Caribbean, St. Thomas, USVI; January 8–11, 2025

Poster ID: 25

Abbreviations
BMI, body mass index; BSA, body surface area; FDA, Food and Drug Administration; GPP, generalized pustular psoriasis; HSV-1, herpes simplex virus 1; IV, intravenous; MisDx, misdiagnoses; PsO, psoriasis; QoL, quality of life; SC, subcutaneous

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Disclosures
JKT, AC, JD, and **LES** have served on an advisory board for Boehringer Ingelheim. **MA** has received research funding from UCB, participated on an advisory board for Novartis, and has been a consultant for Santa Ana Bio. **TS, LR, BW, ES,** and **BJW** declare no competing interests.

Acknowledgments
The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors did not receive payment related to the development of this poster. Jia Gao, PharmD, of Elevate Scientific Solutions provided medical writing, editorial support, and formatting support, which were contracted and funded by Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI). BIPI was given the opportunity to review the poster for medical and scientific accuracy, as well as intellectual property considerations.

Boehringer Ingelheim

The chronicity and disease burden of generalized pustular psoriasis

Joe K. Tung,[1] Maria Aleshin,[2] Angad Chadha,[3] Jacquelyn Dosal,[4] Thomas Selby,[5] Laura Rezac,[6] Brooke Walterscheid,[7] Ella Solomon,[8] Lauren E. Stephens,[9] Benjamin Workman[10]

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Background

- GPP is a rare, inflammatory skin disease characterized by sudden, widespread eruption or flares of small sterile pustules, often with systemic symptoms[1]
- Many patients experience chronic symptoms between flares and may require continuous management[2]
- Here, we describe the long-term burden of GPP and its effects on QoL in 10 patients who presented to US hospitals or outpatient clinical practices with GPP flare

Conclusions

- GPP is associated with both recurrent flares and chronic symptoms between flares, leading to decreased patient QoL, increased morbidity, and risk of complications
- Safe and effective long-term treatment options for GPP are needed to mitigate disease burden

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Key themes

- Patients experience recurrent flares even after treatment
- Patients experience chronic symptoms even when not having a GPP flare
- GPP flares can lead to severe complications and high morbidity
- GPP is often misdiagnosed, and living with GPP can have a substantial impact on patient QoL
- Patients require long-term and continuous treatment to manage GPP

Case presentations

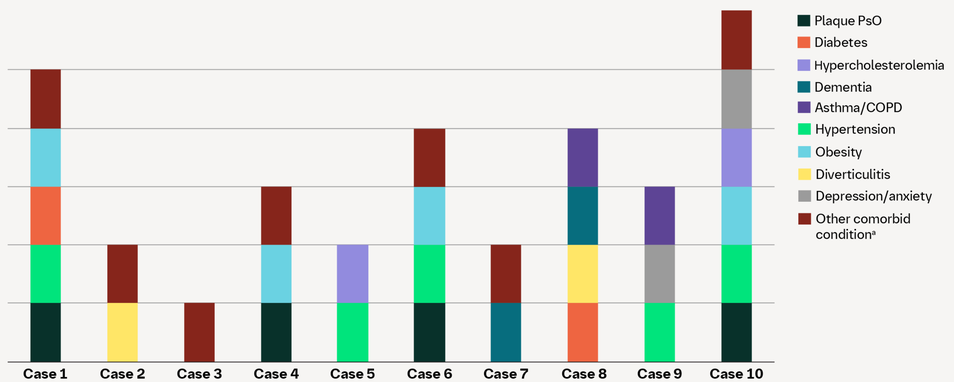
- 10 patients aged 18–92 years had heterogeneous presentations of GPP flare in addition to several comorbid conditions (**Table 1**, **Figure 1**)
- All patients experienced negative QoL burden related to GPP (**Figure 2**)

Table 1. Summary of patient cases

Case Report	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Patient demographics	36-year-old American Indian male	58-year-old White female	40-year-old White female	18-year-old Asian male	73-year-old White male	62-year-old White female	92-year-old White female	72-year-old Black female	47-year-old Black female	39-year-old White male
GPP presentation	Severe GPP presentation with systemic symptoms	Moderate to severe flare of sterile pustules that progressed to whole body, with no systemic symptoms	Pustular plaques on the extremities and trunk with systemic symptoms	Plaques studded with pustules of moderate skin severity affecting 15–20% of BSA	Numerous annular and arcuate erythematous plaques studded with pustules, and with trailing scale	Severe, diffuse erythematous rash with sheets of desquamation and sensation of heat in skin; fever, and chills	Erythematous, scaly papules coalescing into plaques on trunk and extremities; fever, arthralgias, and altered mental status	Severe erythroderma and widespread pustules, skin pain, fever, and chills	Erythema, swelling, and pustules on trunk and extremities; severe joint pain and muscle aches	Localized erythematous eczematous rash to anterior neck and trunk, with no systemic symptoms
Flare trigger	IV and PO corticosteroid	HCQ	HCQ	Possibly COVID	HCQ, corticosteroid withdrawal	Possibly COVID	Corticosteroid withdrawal	Stress	Unknown	Stress
Hospitalized?	Yes	No	Yes	No	No	Yes	Yes	Yes	No	No
Initial diagnosis	GPP	AGEP	AGEP	Guttate PsO	Nummular dermatitis	GPP	GPP	GPP	RA and lupus	Contact dermatitis

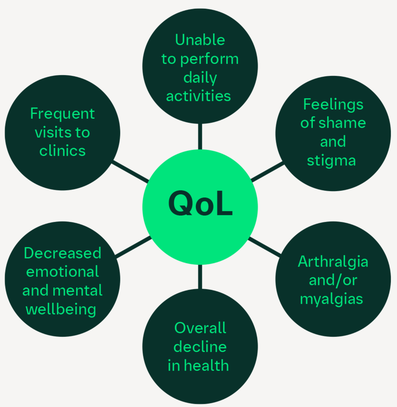
- All patients had comorbid conditions; hypertension was the most common, followed by plaque PsO (**Figure 1**)
- 4 patients had a history of GPP
- 6 patients were initially misdiagnosed, leading to delays in treatment
- 5 patients were hospitalized due to the severity of their GPP flare, and multiorgan failure was reported in 2 patients
- Patients reported GPP decreased their QoL, with impaired confidence, mood, and ability to carry out activities of daily living (**Figure 2**)
  - Some patients had limited mobility; Case 1 required a wheelchair, and Case 9 was initially bedridden and then required a walker
  - Case 4 reported being bullied due to the appearance of his skin, while Case 10 felt that his disease was difficult to manage after failing multiple therapies
- After failure of off-label therapies, all 10 patients received targeted GPP therapy with IV spesolimab

Figure 1. Burden of GPP and comorbid conditions



[a]Others included obstructive sleep apnea, non-specific arthritis, Raynaud's, granuloma annulare, autoimmune hepatitis, autism, SHOX gene duplication, tachycardia, colorectal cancer, ostomy, history of allergic contact dermatitis, and history of cerebral vascular accident

Figure 2. Burden of GPP on patient QoL



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Poster ID: 26

Abbreviations
BSA, body surface area; COPD, chronic obstructive pulmonary disease; COVID, coronavirus disease; GPP, generalized pustular psoriasis; HCQ, hydroxychloroquine; IV, intravenous; PO, by mouth; PsO, psoriasis; QoL, quality of life; RA, rheumatoid arthritis

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Impact Of Amlitelimab (an Anti-OX40 Ligand Antibody) on Atopic Dermatitis of the Head And Neck: Post Hoc Results From the STREAM-AD Phase 2b Study of Moderate-to-Severe Atopic Dermatitis

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Key Conclusions

1 Amlitelimab demonstrated nominally significant reduction in head and neck EASI vs placebo at Week 24

2 Amlitelimab was effective across all 4 signs (erythema, oedema/papulation, excoriation, lichenification) relevant for head and neck AD

3 All doses of amlitelimab were effective at reducing head and neck EASI and subscores, especially excoriation and lichenification, with the highest response observed in the 250 mg+LD arm

4 Amlitelimab may be an effective future treatment option for patients with AD affecting the head and neck, a hard-to-treat location

Introduction

- Amlitelimab is a fully human non-depleting anti-OX40L monoclonal antibody[1,2]
  - Blocks upstream OX40L on antigen-presenting cells
  - Inhibits T-cell-dependent inflammation without T-cell depletion
- Phase 2a and 2b STREAM-AD trials demonstrated efficacy and safety of amlitelimab in patients with moderate-to-severe atopic dermatitis (AD)[3,4]
  - STREAM-AD met primary (Week 16) and key secondary (Week 24) endpoints of reduction in percentage change in EASI
  - Improvements observed with other lesional and pruritic secondary endpoints
- AD lesions on the head and neck are often difficult to treat[5]
  - Head and neck regions experience constant exposure to external factors
- Head and neck lesions have a high impact on patients' quality of life[5]
  - Localisation of AD to head and neck linked to social embarrassment and stigmatisation

Objective

- Evaluate the 24-week efficacy of amlitelimab in patients with moderate-to-severe AD with inadequate response to/inadvisability of AD topical treatments in the STREAM-AD trial (post hoc analysis) on
  - Head and neck EASI body region score
  - Head and neck EASI body region subscores of erythema, oedema/papulation, excoriation, and lichenification

Methods

EASI Calculations

- STREAM-AD is a 2-part, randomised, double-blind, placebo-controlled, Phase 2b trial
  - Part 1: 24-week treatment period
  - Part 2: 28-week randomised maintenance/withdrawal phase
- Adults (18 to <75 years; N=390) with moderate-to-severe AD (EASI≥16) randomised 1:1:1:1:1 to receive placebo every 4 weeks (Q4W; n=79) or subcutaneous amlitelimab Q4W:
  - 250 mg+500 mg loading dose (LD), N=77
  - 125 mg without LD, N=77
  - 250 mg without LD, N=78
  - 62.5 mg without LD, N=79
- EASI was measured at baseline, Week 2, Week 4, and every 4 weeks thereafter. For this analysis, up to Week 24 data were included
- No multiplicity adjustments were performed in this post hoc analysis

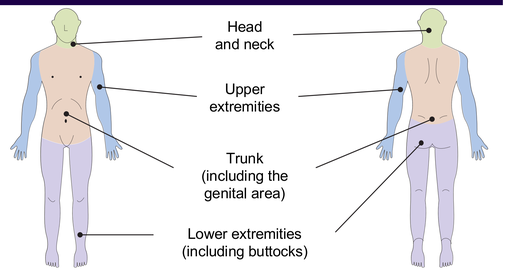
EASI Calculations

- EASI was calculated by clinicians at each timepoint (**Figure 1**)
- Maximum head and neck EASI region score is 7.2

Figure 1. EASI scoring system[6]

Severity Score

Grade each sign on a scale of 0–3:
0, clear/none
1, mild
2, moderate
3, severe



Area Score

% Involvement	0	1–9%	10–29%	30–49%	50–69%	70–89%	90–100%
Area Score	0	1	2	3	4	5	6

EASI Calculator (Adults)

Body Region	Erythema (0–3)	Oedema/ papulation (0–3)	Excoriation (0–3)	Lichenification (0–3)	Area Score (0–6)	Multiplier	Score
Head/neck	(+	+	+	)	×	× 0.1	
Trunk	(+	+	+	)	×	× 0.3	
Upper extremities	(+	+	+	)	×	× 0.2	
Lower extremities	(+	+	+	)	×	× 0.4	

Final EASI score is sum of the 4 region scores (0–72): _____

Results

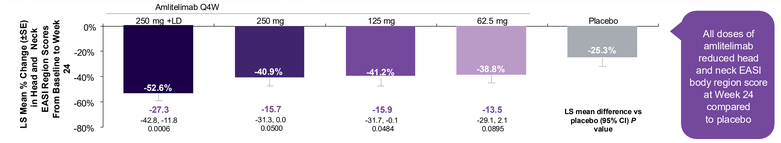
Baseline Demographics and Disease Characteristics

- 390 patients were screened and enrolled; 388 were treated (2 determined to not be eligible after randomisation); 333 of the treated patients completed through Week 24 (85.8%)
- Baseline demographics and disease characteristics were generally balanced across treatment groups
  - IGA, mean (SD): 3.3 (0.45); IGA 3 (moderate), n (%): 280 (71.8); IGA 4 (severe): 110 (28.2)
  - EASI, mean (SD): 28.9 (10.7); EASI≥16–21 (moderate), n (%): 111 (28.5); EASI>21 (severe): 279 (71.5)
  - Head and neck EASI, mean (SD): Amlitelimab 250 mg+LD: 3.29 (1.32); 250 mg: 3.18 (1.45); 125 mg: 3.35 (1.23); 62.5 mg: 3.27 (1.33); placebo: 3.13 (1.20)

Changes From Baseline in Head and Neck EASI Body Region Score

Similar to the effect on total EASI at Week 24, a reduction was observed in head and neck EASI region score at Week 24 with amlitelimab treatment vs placebo, with the greatest reduction observed in the amlitelimab 250 mg +LD arm (**Figure 2**)

Figure 2. Head and neck EASI body region score is reduced at Week 24 with amlitelimab vs placebo



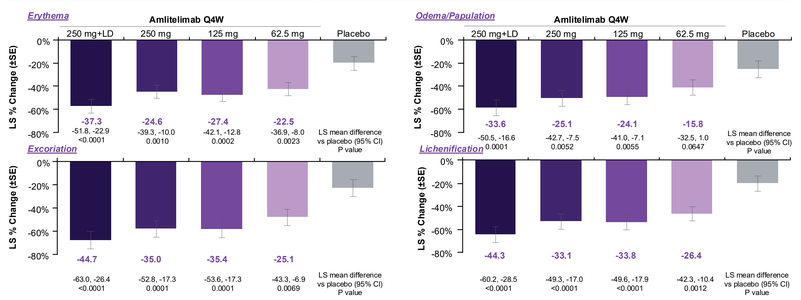
All doses of amlitelimab reduced head and neck EASI body region score at Week 24 compared to placebo

Any data on or after treatment discontinuation or use of rescue/prohibited medications impacting efficacy, whichever earlier, are set to missing and imputed by WOCF.

Changes From Baseline in Head and Neck EASI Body Region Subscores

- All 4 signs of head and neck EASI (erythema, oedema/papulation, excoriation, and lichenification) were reduced from baseline with all amlitelimab doses at Week 24 vs placebo, with the greatest improvements seen in the amlitelimab 250 mg+LD arm (**Figure 3**)

Figure 3. Head and neck EASI body region score is reduced at Week 24 with amlitelimab vs placebo



Any data on or after treatment discontinuation or use of rescue/prohibited medications impacting efficacy, whichever earlier, are set to missing and imputed by WOCF.

All doses of amlitelimab reduced head and neck EASI body region subscores of erythema, oedema, excoriation, and lichenification at Week 24 compared to placebo

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1. Weidinger S, et al. *Br J Dermatol.* 2023;189(5):531–539.
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Abbreviations

AD, atopic dermatitis; CI, confidence interval; EASI, Eczema Area And Severity Index; IGA, Investigator's Global Assessment; LD, loading dose; LS, least squares; OX40L, OX40 ligand; Q4W, every 4 weeks; SD, standard deviation; SE, standard error; WOCF, worst observation carried forward.

Acknowledgments and Funding

The authors thank the study patients, trial staff, and investigators for their participation; Dr Ben Porter-Brown for his help on the conception/design of the trial, and all of the study team for their support throughout the trial. Medical writing assistance, was provided by Sierra Swords, PhD, of IMPRINT Science (New York, NY, USA). The data in this poster was originally presented at the European Academy of Dermatology and Venereology (EADV) 2024; Amsterdam, Netherlands; September 25–28, 2024. Lindsay Billings (Medical Science Liaison, NA Medical Immunology Non-Alliance Central, Genzyme Corporation) is the non-author presenter for this poster. This study was funded by Kymab Ltd, a Sanofi company.

Disclosures

Adam Reich: AbbVie, Bioderma, Celgene, Chema-Elektromet, Drug Delivery Solutions, Eli Lilly, Galderma, Genentech, Janssen Pharmaceuticals, Kymab (a Sanofi company), LEO Pharma, Medac, Menlo Therapeutics, Merck Sharpe & Dohme, MetrioPharm, Novartis, Pfizer, Pierre Fabre, Sandoz, Trevi Therapeutics.
Stephan Weidinger: AbbVie, Almirall, AstraZeneca, Eli Lilly, Galderma, Janssen, Kymab (a Sanofi company), La Roche-Posay, LEO Pharma, Pfizer, Regeneron Pharmaceuticals, Sanofi.
Vivian Y Shi: On board of directors for the Hidradenitis Suppurativa Foundation; adviser for the National Eczema Association; stock shareholder of LearnHealth; has served as an advisory board member, an investigator, speaker for and/or has received research funding from AbbVie, Almirall, Altus Lab/CQuell, Alumis, Aristea Therapeutics, Bain Capital, Boehringer Ingelheim, Burt's Bees, Dermira, Eli Lilly, Galderma, Genentech, Genzyme (a Sanofi company), GPSKIN, Incyte, Kiniksa Pharmaceuticals, LEO Pharma, Menlo Therapeutics, MyOr Diagnostics, Novartis, Pfizer, Polyfins Technology, Regeneron Pharmaceuticals, Skin Actives Scientific, Sun Pharma, Target PharmaSolutions, UCB.
Norito Katoh: Speaker/consultant for AbbVie, Ely Lilly Japan, Maruho, Otsuka Pharmaceutical, Sanofi; received grants as an investigator from LEO Pharma, Maruho, Sun Pharmaceutical Industries.
Cori Gray, Charlotte Bernigaud, and Kassim Rahawi: Employees of Sanofi – may hold stock and/or stock options in the company.

Presented at the Society of Dermatology Nurse Practitioners (SDNP); April 30–May 3, 2025, Indian Wells, CA, USA

68-week safety results of amlitelimab (an anti-OX40 Ligand antibody) in participants with moderate-to-severe atopic dermatitis from STREAM-AD Phase 2b dose-ranging and withdrawal study

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Introduction

Amlitelimab: a fully human, **nondepleting, anti-OX40L monoclonal antibody**[1,2]

- Blocks upstream OX40L on antigen-presenting cells
- Inhibits T-cell-dependent inflammation without T-cell depletion

Phase 2b STREAM-AD trial[3]

- **Part 1 (24 weeks) – primary endpoint met** (percent change in EASI at Week 16); **efficacy and acceptable safety profile** of amlitelimab demonstrated at Week 24
- **Part 2 (28 weeks) – durability** of clinical response (efficacy) and acceptable **safety** profile on- and off-treatment at Week 52
- **16-week** safety follow-up period **through Week 68**

Figure 1. OX40L-OX40 axis: a secondary co-stimulatory pathway

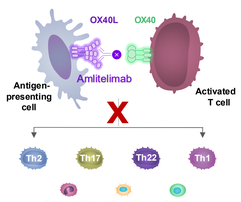


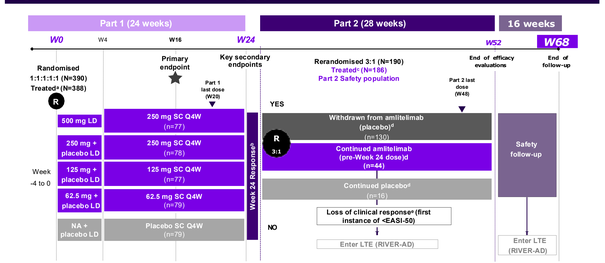
Figure adapted from Fu Y, et al. *Acta Pharm Sin B*. 2020;10(3):414-433; and Haddad EB, et al. *Dermatol Ther (Heidelb)*. 2022;12(7):1501-1533.

Obective

Present the safety profile of amlitelimab from the participants who completed 68 weeks of the Phase 2b STREAM-AD trial

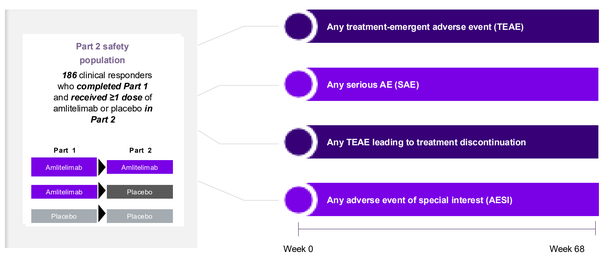
Methods

Figure 2. STREAM-AD Phase 2b trial design (NCT05131477)



[a]Two patients found to be ineligible after randomisation; [b]Met IGA 0/1 and/or EASI-75 randomised to Withdrawal (placebo) or pre-Week 24 dose groups; did not meet EASI-75 or IGA 0/1 entered into LTE or Safety follow-up; [c]Four patients were rerandomised but not treated; [d]Patients demonstrating loss of clinical response during Part 2 were entered into the LTE or Safety follow-up; [e]Loss of clinical response was defined as the first instance of <EASI-50 during Part 2 where rescue therapy was no longer permitted.

Figure 3. Safety endpoints through Week 68



Key Conclusions

1. The ***efficacy of amlitelimab*** in patients with moderateto-severe AD was ***demonstrated over 52 weeks*** in the STREAMAD Phase 2b trial [4,5]
2. Amlitelimab demonstrated an ***acceptable safety profile over 68 weeks***
   - Most ***TEAEs were mild or moderate*** and considered ***not related*** to treatment
   - ***Low incidence of SAEs and treatment discontinuation*** reported across all treatment arms with both 24 and 52 weeks of amlitelimab exposure
3. ***No clear dose dependent response*** was observed
4. ***Ongoing trials*** will provide additional ***robust safety data***
   - OCEANA Phase 3 trials
   - Long-term extension studies (ATLANTIS, RIVER-AD, ESTUARY)

Results

Table 1. Amlitelimab demonstrated an acceptable safety profile from Week 0-24 across all dose groups

n (%) of unique participants with ≥1 TEAE	Week 0-24 Part 1 Safety Population (N=390)[a]					
Part 1 Treatment Group:	**Amlitelimab 250 mg +LD (N=77)**	**Amlitelimab 250 mg (N=78)**	**Amlitelimab 125 mg (N=77)**	**Amlitelimab 62.5 mg (N=78)**	**Amlitelimab Total N=310**	**Placebo N=78**
Any TEAE	51 (66.2)	52 (66.7)	52 (67.5)	53 (67.9)	208 (67.1)	47 (60.3)
Any SAE[b]	2 (2.6)	0	1 (1.3)	5 (6.4)	8 (2.6)	1 (1.3)
Any TEAE leading to treatment discontinuation	3 (3.9)	5 (6.4)	1 (1.3)	5 (6.4)	14 (4.5)	5 (6.4)
Any AESI[c]	3 (3.9)	0	2 (2.6)	1 (1.3)	6 (1.9)	1 (1.3)

[a]Part 1 safety population comprised all randomised patients who received ≥1 dose of study treatment (including placebo) up to Week 24; [b]SAEs included: amlitelimab 250 mg +LD: metabolic acidosis, alcohol withdrawal syndrome, and supraventricular tachycardia [all 3 events in same participant], and tension headache; amlitelimab 125 mg: dermatitis bullous; amlitelimab 62.5 mg: appendicitis, pharyngitis, hemorrhoidal hemorrhage, osteoarthritis, and forearm fracture; placebo: atrial fibrillation; dermatitis bullous was deemed related to amlitelimab or placebo by investigator; [c]Adverse events defined as AESIs were systemic or localised allergic reactions that required immediate treatment; severe injection-site reactions that lasted longer than 24 hours; severe or opportunistic viral, bacterial, or fungal infection and/or any uncommon, unanticipated, or persistent infection (viral, parasitic, bacterial, or fungal); malignancy; increase in ALT >3x ULN AESIs included: amlitelimab 250 mg +LD: 2 cases of ALT increase, and (in same patient) 1 case of conjunctivitis allergic and 1 case of face edema; amlitelimab 125 mg: 1 ALT increase, 1 case of dermatitis bullous; amlitelimab 62.5 mg: 1 ALT increase; placebo: 1 ALT increase. One AESI (dermatitis bullous) was considered related to study treatment by investigator.

- During Part 1, rates of TEAEs were generally similar between amlitelimab groups, with ***no observed dose effect*** on TEAE incidence
  - Majority of all reported TEAEs were mild or moderate:
    - *96.2% of all TEAEs in the amlitelimab groups (pooled) were mild or moderate*
    - *95.9% of all TEAEs in the placebo group were mild or moderate*
- Incidence of SAEs in the pooled amlitelimab groups ranged from 1.3% to 6.4% vs. 1.3% in the placebo group

Table 2. Amlitelimab demonstrated an acceptable safety profile from Week 0-68 in all pooled dose groups

n (%) of unique participants with ≥1 TEAE	Week 0-68 Part 2 Safety Population (N=186[a]		
Part 1 Treatment Group:	**Pooled Amlitelimab**	**Pooled Amlitelimab**	**Placebo**
Part 2 Treatment Group:	**Pooled Amlitelimab (N=43)[b]**	**Pooled Withdrawal (Placebo) (N=128)[c]**	**Placebo (N=15)[d]**
Any TEAE	36 (83.7)	118 (92.2)	14 (93.3)
Any SAE[e]	2 (4.7)	3 (2.3)	0
Any TEAE leading to treatment discontinuation	1 (2.3)	0	0
Any AESI[f]	1 (2.3)	1 (0.8)	0

[a]Part 2 safety population includes only participants who were deemed "responders" at Week 24 and continued into Part 2, receiving ≥1 injection of amlitelimab or placebo in Part 2; [b]Treatment with amlitelimab was given through Week 52 (last dose at Week 48) with safety follow-up through Week 68; [c]Participants received amlitelimab in Part 1 (last dose at Week 20), and there was a period of continued exposure to amlitelimab (based on half-life) during transition to placebo in Part 2; [d]Participants never received amlitelimab; [e]SAEs included: 250 mg +LD continue: umbilical hernia; 250 mg +LD withdraw: tendon rupture; 250 mg withdraw: abnormal weight loss and spinal osteoarthritis [both events in same participant], rotator cuff syndrome; 125 mg continue: ankle fracture; only weight loss was considered related to amlitelimab or placebo by investigator; [f]Adverse events defined as AESIs were systemic or localised allergic reactions that required immediate treatment; severe injection-site reactions that lasted longer than 24 hours; severe or opportunistic viral, bacterial, or fungal infection and/or any uncommon, unanticipated, or persistent infection (viral, parasitic, bacterial, or fungal); malignancy; increase in ALT >3x ULN.

- Of all TEAEs reported in the Part 2 safety population in the study, the majority were **mild or moderate in severity:**
  - ***96.3%*** *of TEAEs in the groups who continued amlitelimab in Part 2 were mild or moderate*
  - ***99.1%*** *of TEAEs in the groups who withdrew from amlitelimab in Part 2 were mild or moderate*
- ***No deaths*** occurred in the study

Table 3. Similar safety profile was observed across each individual treatment arm

n (%) of unique participants with ≥1 TEAE	Week 0-68 Part 2 Safety Population (N=186)[a]								
Part 1 Treatment Group:	**Amlitelimab 250 mg (500 mg LD)**		**Amlitelimab 250 mg (no LD)**		**Amlitelimab 125 mg**		**Amlitelimab 62.5 mg**		**Placebo**
Part 1 Treatment Group:	**250 mg (N=13)[b]**	**Placebo (N=34)[c]**	**250 mg (N=11)[b]**	**Placebo (N=28)[c]**	**125 mg (N=12)[b]**	**Placebo (N=32)[c]**	**62.5 mg (N=7)[b]**	**Placebo (N=34)[c]**	**Placebo (N=15)[c]**
Any TEAE	11 (84.6)	30 (88.2)	9 (81.8)	27 (96.4)	11 (91.7)	30 (93.8)	5 (71.4)	31 (91.2)	14 (93.3)
Any SAE	1 (7.7)	1 (2.9)	0	2 (7.1)	1 (8.3)	0	0	0	0
Any TEAE leading to treatment discontinuation	0	0	0	0	1 (8.3)	0	0	0	0
Any AESI[e]	0	0	0	0	1 (8.3)	0	0	1 (2.9)	0

[a]Part 2 safety population includes only participants who were deemed "responders" at Week 24 and continued into Part 2, receiving ≥1 injection of amlitelimab or placebo in Part 2; [b]Treatment with amlitelimab was given through Week 52 (last dose at Week 48) with safety follow-up through Week 68; [c]Participants received amlitelimab in Part 1 (last dose at Week 20), and there was a period of continued exposure to amlitelimab (based on half-life) during transition to placebo in Part 2; [d]Participants never received amlitelimab; [e]Adverse events defined as AESIs were systemic or localised allergic reactions that required immediate treatment; severe injection-site reactions that lasted longer than 24 hours; severe or opportunistic viral, bacterial, or fungal infection and/or any uncommon, unanticipated, or persistent infection (viral, parasitic, bacterial, or fungal); malignancy; increase in ALT >3x ULN:

- ***No obvious dose dependency*** in TEAE incidence was observed across dose arms

One SAE and no AESIs were considered related to amlitelimab or placebo
Week 0-68 Part 2 Safety Population (N=186)[a]

SAEs

- ***6 SAEs occurred*** in 5 participants from Week 0-68, all during Part 2

Part 1: amlitelimab/ Part 2: amlitelimab
- Umbilical hernia
- Ankle fracture

Part 1: amlitelimab/ Part 2: placebo
- Tendon rupture
- Rotator cuff syndrome related[b])
- Abnormal weight loss and spinal osteoarthritis
  - (occurred in same patient, not temporally related[b])
- **Only 1 SAE considered related** to amlitelimab or placebo by blinded investigator:
  - **Abnormal weight loss;** in 250 mg (no LD) amlitelimab withdrawal arm; not resolved
- **Occurred** on study **day 400; last dose** of amlitelimab was study **day 141**

AESIs[c]

- ***2 participants experienced ALT increase;*** both events considered by investigator as ***not related*** to amlitelimab or placebo; ***both resolved***
- 1 event in continued 125 mg amlitelimab armd (severe[e])
  - Considered by the investigator as **due to recent acetaminophen use**
  - Led to treatment discontinuation
- 1 event in 62.5 mg amlitelimab-to-withdrawal arm (moderate[e])
  - Considered by the investigator as **due to recent alcohol intake**

[a]Part 2 safety population includes only participants who were deemed "responders" at Week 24 and continued into Part 2, receiving ≥1 injection of amlitelimab or placebo in Part 2; [b]Spinal osteoarthritis (on study day 196, resolved on day 233, history of spinal osteoarthritis prior to enrolment), abnormal weight loss (on study day 400); [c]Adverse events defined as AESIs were systemic or localised allergic reactions that required immediate treatment; severe injection-site reactions that lasted longer than 24 hours; severe or opportunistic viral, bacterial, or fungal infection and/or any uncommon, unanticipated, or persistent infection (viral, parasitic, bacterial, or fungal); malignancy; increase in ALT >3x ULN; [d]Event was associated with 3 other liver laboratory abnormalities (increased AST, blood alkaline phosphatase, and gamma-glutamyltransferase); [e]Based on Common Terminology Criteria for Adverse Events v5.0.

Table 4. The most frequent TEAEs (≥5% in the pooled continuing amlitelimab group in Part 2 and more common than in amlitelimab/placebo or placebo/placebo groups)

n (%) of unique participants with ≥1 TEAE	Most Frequent TEAEs: Week 0-68 Part 2 Safety Population (N=186)[a] (≥5% in continuing amlitelimab group and more frequent than in either the amlitelimab/placebo or the placebo/placebo group)		
Part 1 Treatment Group:	**Pooled Amlitelimab**	**Pooled Amlitelimab**	**Placebo**
Part 2 Treatment Group:	**Pooled Amlitelimab (N=43)[b]**	**Pooled Withdrawal (Placebo) (N=128)[c]**	**Placebo (N=15)[d]**
Upper respiratory tract infection[e]	7 (16.3)	18 (14.1)	3 (20.0)
Headache	7 (16.3)	14 (10.9)	2 (13.3)
Nasopharyngitis	6 (14.0)	24 (18.8)	2 (13.3)
Accidental overdose[f]	4 (9.3)	5 (3.9)	1 (6.7)
COVID-19	4 (9.3)	13 (10.2)	0
Dizziness	3 (7.0)	1 (0.8)	1 (6.7)

[a]Part 2 safety population includes only participants who were deemed "responders" at Week 24 and continued into Part 2, receiving ≥1 injection of amlitelimab or placebo in Part 2; [b]Treatment with amlitelimab was given through Week 52 (last dose at Week 48) with safety follow-up through Week 68; [c]Participants received amlitelimab in Part 1 (last dose at Week 20), and there was a period of continued exposure to amlitelimab (based on half-life) during transition to placebo in Part 2; [d]Participants never received amlitelimab; e)Includes preferred terms "Upper Respiratory Tract Infection," "Viral Upper Respiratory Tract Infection," and "Upper Respiratory Tract Infection Bacterial"; f)Accidental overdoses: less than 21 days between 2 injections – all asymptomatic.

- ***All of the most frequent TEAEs were mild or moderate***, and none resulted in treatment discontinuation
- All patients with COVID-19 recovered

Amlitelimab demonstrated an acceptable safety profile from Week 0-68
Week 0-68 Part 2 Safety Population (N=186)[a]

Any treatment-emergent adverse event (TEAE)

From Week 0-68, there were ***low reported proportions of patients experiencing TEAEs of***

- Nausea: continued amlitelimab, pooled: 0 (0%); withdrawn, pooled: 1 (0.8%); placebo: 0 (0%)
- Conjunctivitisb: continued amlitelimab, pooled: 1 (2.3%); withdrawn, pooled: 2 (1.6%); placebo: 0 (0%)
- Herpes[c] : continued amlitelimab, pooled: 2 (4.7%); withdrawn, pooled: 6 (4.7%); placebo: 1 (6.7%)

From Week 0-68, there were ***no reported TEAEs of:***

- Treatment-related anaphylactic reactions
- Malignancy
- Serious injection-site reactionsd
- Opportunistic infectionse
- Pyrexia/chills within 72 hours of injection
- Aphthous ulcers

[a]Part 2 safety population includes only participants who were deemed "responders" at Week 24 and continued into Part 2, receiving ≥1 injection of amlitelimab or placebo in Part 2; [b]Includes preferred terms of 'conjunctivitis allergic', and 'conjunctivitis bacterial'; [c]Includes preferred terms of 'oral herpes', 'herpes simplex', 'herpes dermatitis', and 'eczema herpeticum'; [d]One patient had "severe" pain after injection associated with a moderate nonserious TEAE of "pre-syncope"; [e]MedDRA SMQ Opportunistic Infections (Narrow).

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ACKNOWLEDGMENTS AND FUNDING

The authors thank the study patients, trial staff, and the investigators for their participation. The authors also thank Dr. Ben Porter-Brown for his help in the conception and design of the STREAM-AD trial, and the study team for their support throughout the trial.
This with poster was originally submitted at European Academy of Dermatology and Venereology (EADV) 2024. Medical writing support was provided by Sierra Swords, PhD, from IMPRINT Science (New York, NY, USA). The authors would like to thank Lindsay Billings (Sanofi, NJ, USA) for presenting the data at the Society of Dermatology Nurse Practitioners (SDNP): April 30 - May 3, 2025, Indian Wells, CA, USA. This study was funded by Kymab Ltd, a Sanofi Company.

ABBREVIATIONS

AD, atopic dermatitis; AESI, adverse event of special interest; ALT, alanine aminotransferase; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; LD, loading dose; LTE, long-term extension; MedDRA, Medical Dictionary for Regulatory Activities; NA, not applicable; OX40L, OX40 Ligand; Q4W, every 4 weeks; R, randomisation; SAE, serious adverse event; SC, subcutaneous; SMQ, standardised MedDRA query; TEAE, treatment-emergent adverse event; Th, helper T cell; ULN, upper limit of normal; W, week.

DISCLOSURES

Stephan Weidinger: AbbVie, Almirall, Boehringer Ingelheim, Eli Lilly, Galderma, GlaxoSmithKline, Kymab Ltd (a Sanofi company), LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi, Sanofi Deutschland GmbH, Sanofi Genzyme
Linda Stein Gold: AbbVie, Amgen, Arcutis Biotherapeutics, Dermavant Sciences, Eli Lilly, Incyte, LEO Pharma, Pfizer, Regeneron, Sanofi
Yoko Kataoka: AbbVie, Eli Lilly, LEO Pharma, Maruho, Novartis, Otsuka, Pfizer, Sanofi, Taiho Pharmaceutical
Yanzhen Wu, John T. O'Malley, Charlotte Bernigaud, and Samuel Adelman: Employees of Sanofi – may hold stock and/or stock options in the company

Presented at Society of Dermatology Nurse Practitioners (SDNP); April 30 - May 3, 2025, Indian Wells, CA, USA.