VELVET

Efficacy and safety of lunsekimig in moderate-to-severe atopic dermatitis: Results from the Phase 2b VELVET trial

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Disclosures

Jordan Talia has served as a consultant for AbbVie, Arcutis Biotherapeutics, Biogen, Bristol-Myers Squibb, Calliditas Therapeutics, Galderma, Incyte, Johnson & Johnson, Leo Pharma, Novartis, Navigator Medicines, Primus Pharmaceuticals, Sanofi Genzyme, Stifel Financial, and UCB. He serves or has served as an investigator for Attovia Therapeutics, LEO Pharma, Priovant Therapeutics, and Sanofi. He is a shareholder of Nektar Therapeutics.

Bartłomiej Kwiek reports serving as a clinical study investigator for AbbVie, Almirall, Amgen Inc, Arcutis Biotherapeutics, Aslan, Bristol Myers Squibb, Celdex Therapeutics, Celltrion, Dermira, Galderma, Glenmark, Incyte, LEO Pharma, Novartis, Pfizer, Regeneron, and Samsung.

Ken Igawa is a speaker and an advisory board member for AbbVie, Eli Lilly, LEO Pharma, Maruho, Pfizer, Otsuka Pharmaceutical, and Sanofi.

Raja K. Sivamani has served as a consultant or speaker for Amgen, Sanofi, Bristol Myers Squibb, Codex Labs, Pfizer, Phothera, Almirall, Nutraceutical Wellness, Lilly, Galderma, Incyte, Novartis, Arcutis, Janssen, Abbvie, Leo, UCB, Sun and Regeneron Pharmaceuticals.

Robert Bissonnette participated as an advisory board member and is a consultant, speaker and/or investigator for and receives honoraria and/or grant from AbbVie, Aclaris, Almirall, Alumis, Amgen, Apogee, Arcutis, Areteia, Artax, Attovia, BioMimetix, Bluefin, CARA Therapeutics, Eli Lilly, Fresh Tracks (Brickell), GSK, Incyte, Inmagene Bio, J&J (Janssen), Khanda Therapeutic, LEO Pharma, Merck, Opsidio, Organon (Dermavant), Pfizer, Q32, Sanofi Genzyme, Sanofi Aventis, Sitryx, Target RWE, T Rex Bio, Triveni, Xencor and Zurabio. He is also an employee and shareholder of Innovaderm Research – Indero.

Fan Wu, Julian Lel, Viktoria Stachanow, Benjamin T. Suratt, Megan Hardin, and ***Maria Plataki*** are employees of Sanofi and may hold stock and/or stock options in the company.

Medical writing support was provided by Andrea Hough, PhD, of IMPRINT Science (New York, NY, USA) and was funded by the study sponsor

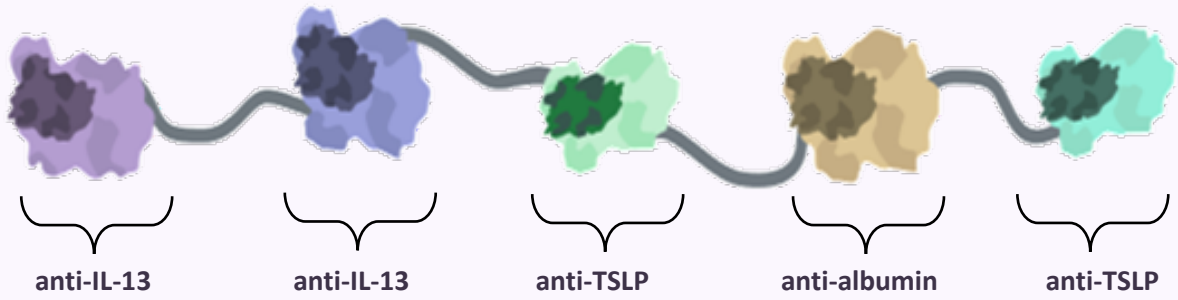
This study was funded by Sanofi

Lunsekimig (SAR443765): a novel, pentavalent, dual-targeting NANOBODY® molecule that blocks TSLP and IL-13

NANOBODY® molecules are derived from *Camelid* heavy-chain–only monoclonal antibodies[1]:

- Small and robust
- Easily linked together
- Nano- to pico-molar affinities

Lunsekimig



Lunsekimig addresses key and complementary drivers of inflammation in atopic dermatitis:

- IL-13 is a major cytokine in atopic dermatitis pathophysiology[2]
- TSLP acts upstream of IL-13 by initiating inflammation in atopic dermatitis pathogenesis[3,4]
- Limited data exist on dual TSLP/IL-13 inhibition, thus, lunsekimig provides a novel strategy to investigate combined pathway blockade in atopic dermatitis.

IL-13, interleukin-13; TSLP, thymic stromal lymphopoietin.

1. Deiteren A, et al. *Eur Respir J* 2025;65(4):2401461. **2.** Moyle M, et al. *Exp Dermatol* 2019;28(7):756-68. **3.** Liu YJ, et al. *Annu Rev Immunol* 2007;25:193-219. **4.** Kolkhir P, et al. *Nat Rev Drug Discov* 2023;22(9):743-67.

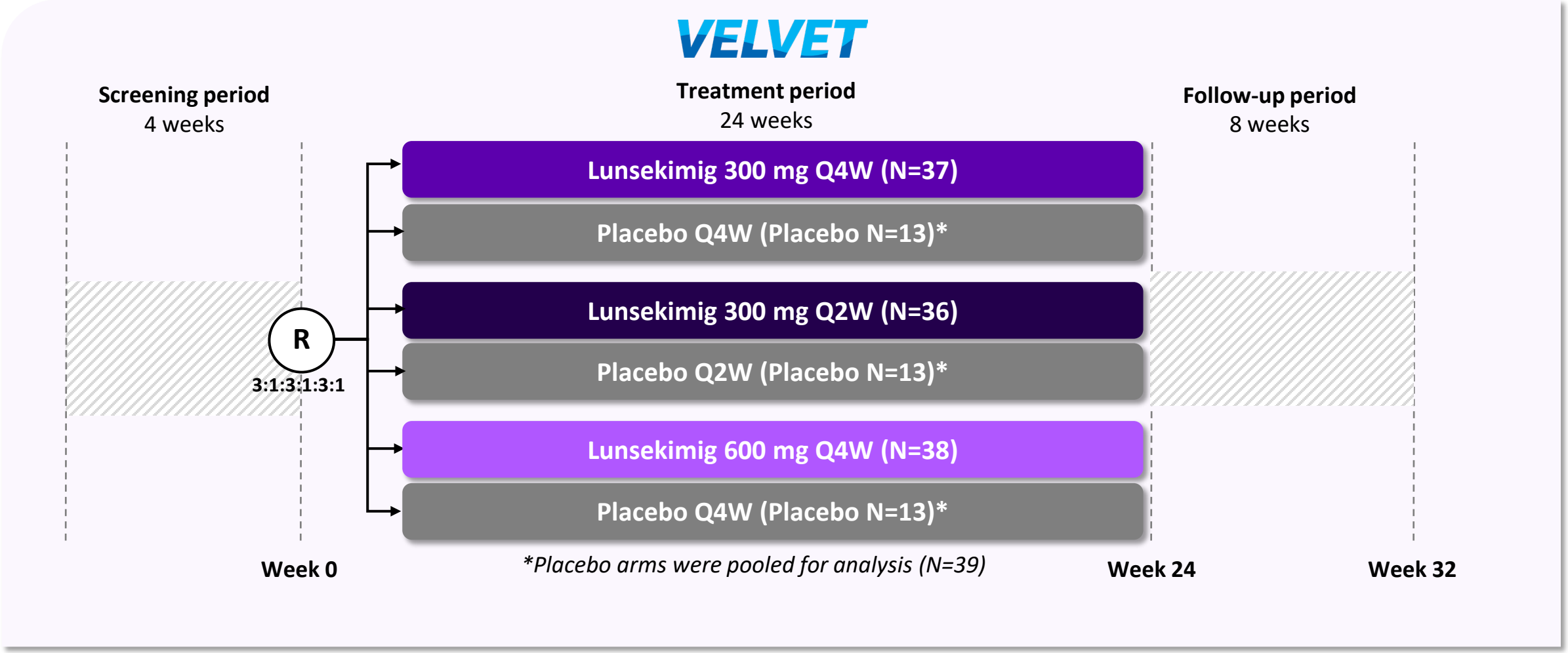
Study Objective

VELVET

To assess the efficacy and safety of lunsekimig in patients with moderate-to-severe atopic dermatitis who have demonstrated inadequate response to topical therapies or for whom topical therapies are not advised

VELVET study design (NCT06790121)

A Phase 2b, multicentre, randomised, double-blind, placebo-controlled, parallel-group, dose-ranging study evaluating the efficacy and safety of lunsekimig in participants with moderate-to-severe atopic dermatitis



The study consisted of 6 arms (3 parallel dosing regimens and matching placebo arms). Participants were randomized in a 3:1:3:1:3:1 ratio to receive: lunsekimig 300 mg (1 SC injection of 2 mL) Q4W or placebo (1 SC injection of 2 mL) Q4W, lunsekimig 300 mg (1 SC injection of 2 mL) Q2W or placebo (1 SC injection of 2 mL) Q2W, lunsekimig 600 mg (2 SC injections of 2 mL) Q4W or placebo (2 SC injections of 2 mL) Q4W. Participants, Investigators, study site personnel, and the study team were blinded to the study intervention (lunsekimig treatment versus placebo) but were not blinded to the dosing regimen.

Q2W, every 2 weeks; Q4W, every 4 weeks; R, randomization; SC, subcutaneous.

Eligibility criteria and endpoints

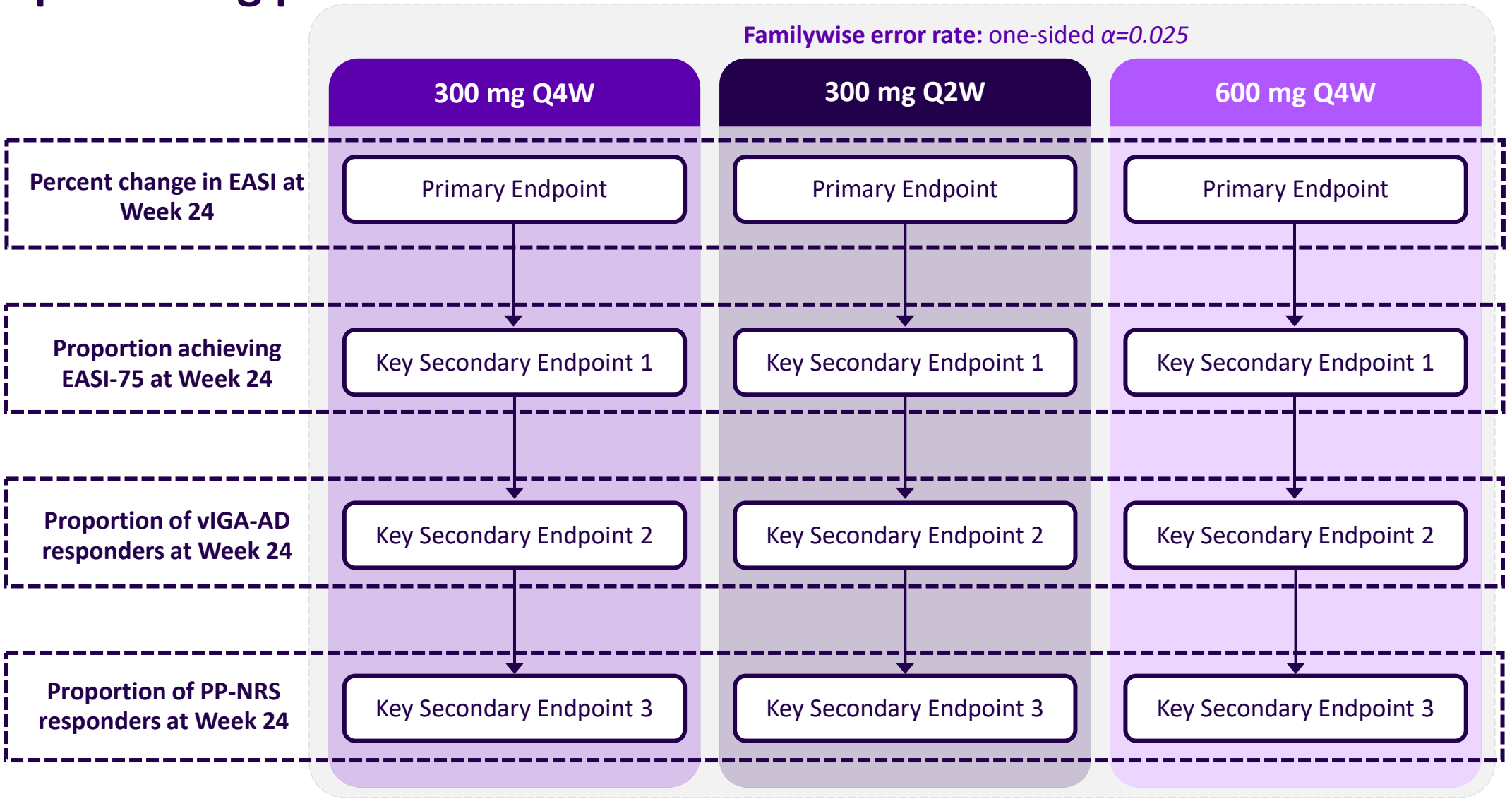
Key Inclusion Criteria

- 18 to 80 years old
- Clinical diagnosis of atopic dermatitis for ≥1 year
- Documented history of inadequate response or inadvisability of topical treatments
- EASI score ≥16 at baseline
- vIGA-AD ≥3 at baseline
- BSA ≥10% at baseline
- PP-NRS ≥4 at baseline

Primary Endpoint	• Percent change in **EASI score** from baseline to Week 24
Key Secondary Endpoints	• Proportion of participants achieving **EASI-75 response** at Week 24 • Proportion of participants with a **vIGA-AD score of 0 or 1** and a reduction from baseline of ≥2 points at Week 24 • Proportion of participants with a **reduction of ≥4 points** in weekly average of daily **PP-NRS score** from baseline at Week 24
Additional Secondary Endpoints	• Proportion of participants achieving **EASI-90 response** at Week 24 • Proportion of participants with a **vIGA-AD score of 0 or 1** with presence of only **barely perceptible erythema** at Week 24
Safety analysis	• Incidence of participants with **TEAEs**, including local reactions, and **SAEs**, throughout the study

BSA, body surface area; EASI, eczema area and severity index; PP-NRS, peak pruritus numerical rating scale; Q2W, every 2 weeks; Q4W, every 4 weeks; SAE, serious adverse event; TEAE, treatment-emergent adverse event; vIGA-AD, validated investigator global assessment for atopic dermatitis.

Multiple testing procedure



An enhanced-mixture gatekeeping procedure was implemented to control the familywise error rate at a one-sided α=0.025 across several dose regimens compared to placebo on multiple endpoints

EASI, eczema area and severity index; PP-NRS, peak pruritus numerical rating scale; Q2W, every 2 weeks; Q4W, every 4 weeks; vIGA-AD, validated investigator global assessment for atopic dermatitis.

Key baseline characteristics were generally balanced across treatment arms

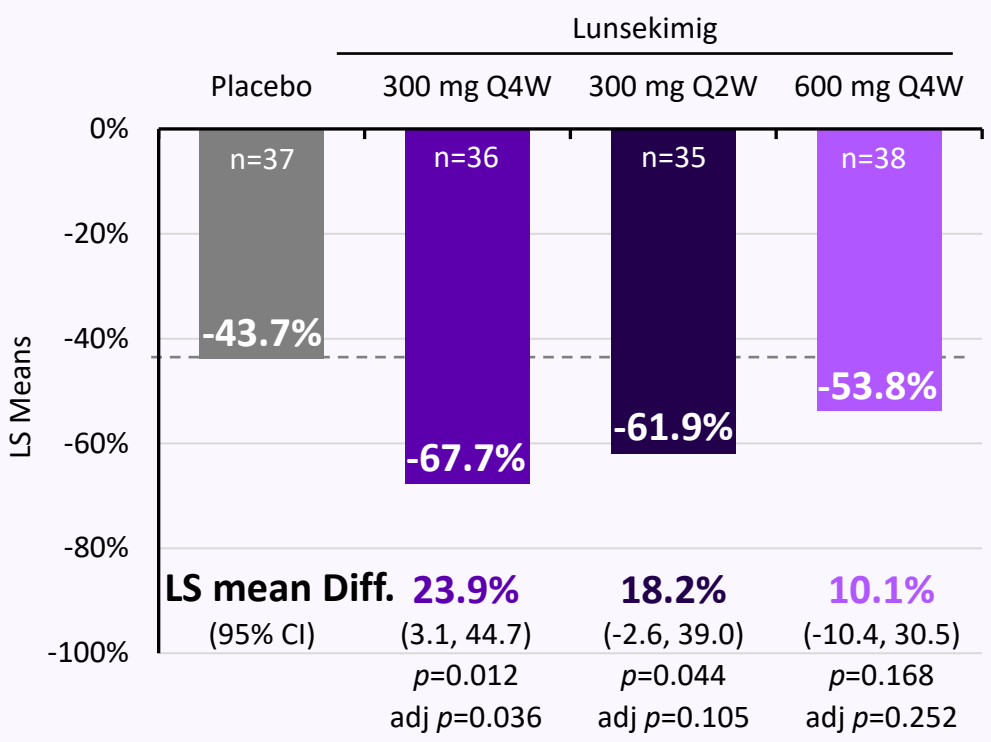
	Placebo (N=39)	Lunsekimig 300 mg Q4W (N=37)	Lunsekimig 300 mg Q2W (N=36)	Lunsekimig 600 mg Q4W (N=38)	All (N=150)
Age (years), mean ± SD	39.5±15.6	37.9±14.7	39.9±15.8	37.7±12.8	38.8±14.6
Male, n (%)	21 (53.8)	23 (62.2)	16 (44.4)	14 (36.8)	74 (49.3)
White, n (%)	27 (69.2)	28 (75.7)	25 (69.4)	23 (60.5)	103 (68.7)
Region, n (%)					
Asia Pacific	3 (7.7)	3 (8.1)	5 (13.9)	5 (13.2)	16 (10.7)
Europe	22 (56.4)	20 (54.1)	18 (50.0)	20 (52.6)	80 (53.3)
North America	14 (35.9)	14 (37.8)	13 (36.1)	13 (34.2)	54 (36.0)
Prior systemic therapy, n (%)	26 (66.7)	22 (59.5)	23 (63.9)	22 (57.9)	93 (62.0)
BSA affected by AD, mean ± SD	39.2±21.0	45.5±22.5	44.6±20.4	40.4±22.3	42.4±21.5
EASI score, mean ± SD	29.0±10.9	30.1±12.7	28.8±10.2	28.1±12.9	29.0±11.6
>21 (Severe), n (%)	26 (66.7)	26 (70.3)	25 (69.4)	22 (57.9)	99 (66.0)
vIGA-AD score, mean ± SD	3.5±0.5	3.4±0.5	3.5±0.5	3.4±0.5	3.4±0.5
4 (Severe), n (%)	18 (46.2)	15 (40.5)	18 (50.0)	16 (42.1)	67 (44.7)
PP-NRS, mean ± SD	7.3±1.8	6.7±1.7	7.5±1.7	7.4±1.8	7.2±1.7

AD, atopic dermatitis; BMI, body mass index; BSA, body surface area; EASI, eczema area and severity index; PP-NRS, peak pruritus numerical rating scale; Q2W, every 2 weeks; Q4W, every 4 weeks; SCORAD, scoring atopic dermatitis; SD, standard deviation; vIGA-AD, validated investigator's global assessment for atopic dermatitis.

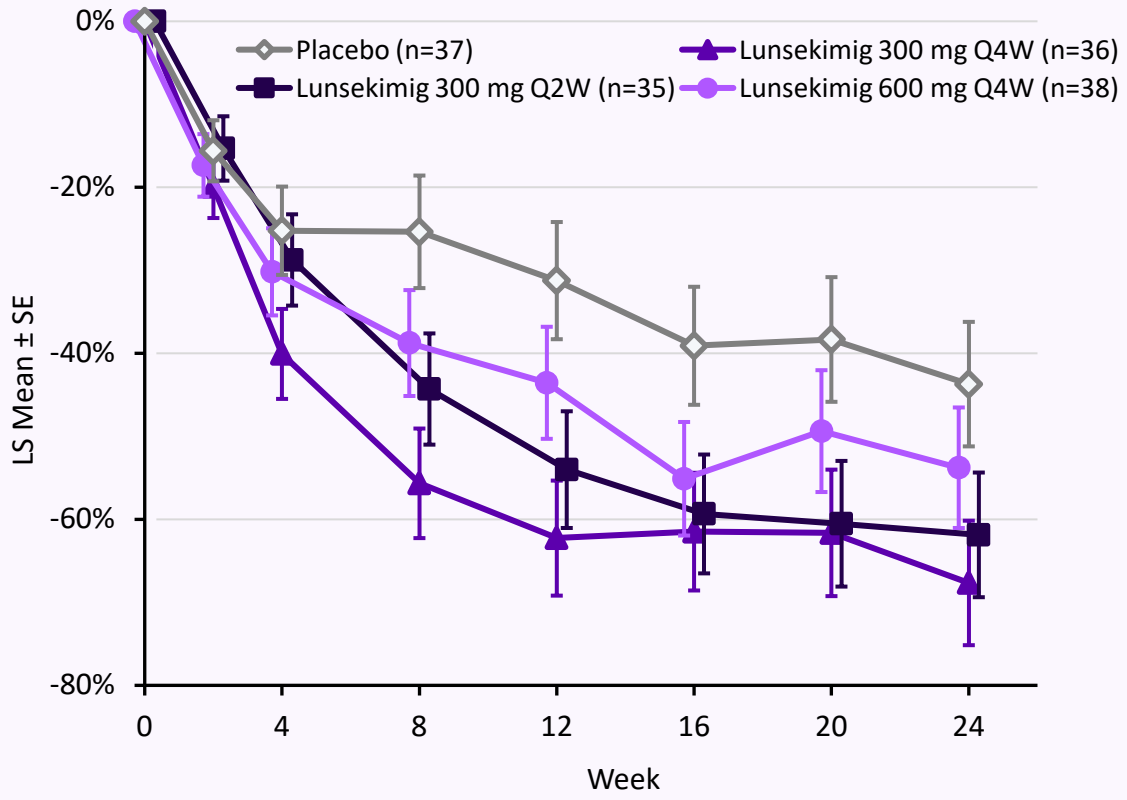
Numeric decrease in EASI were observed across all lunsekimig arms

Statistical significance was not achieved for the primary endpoint at any dose

EASI Percent Change from Baseline at Week 24



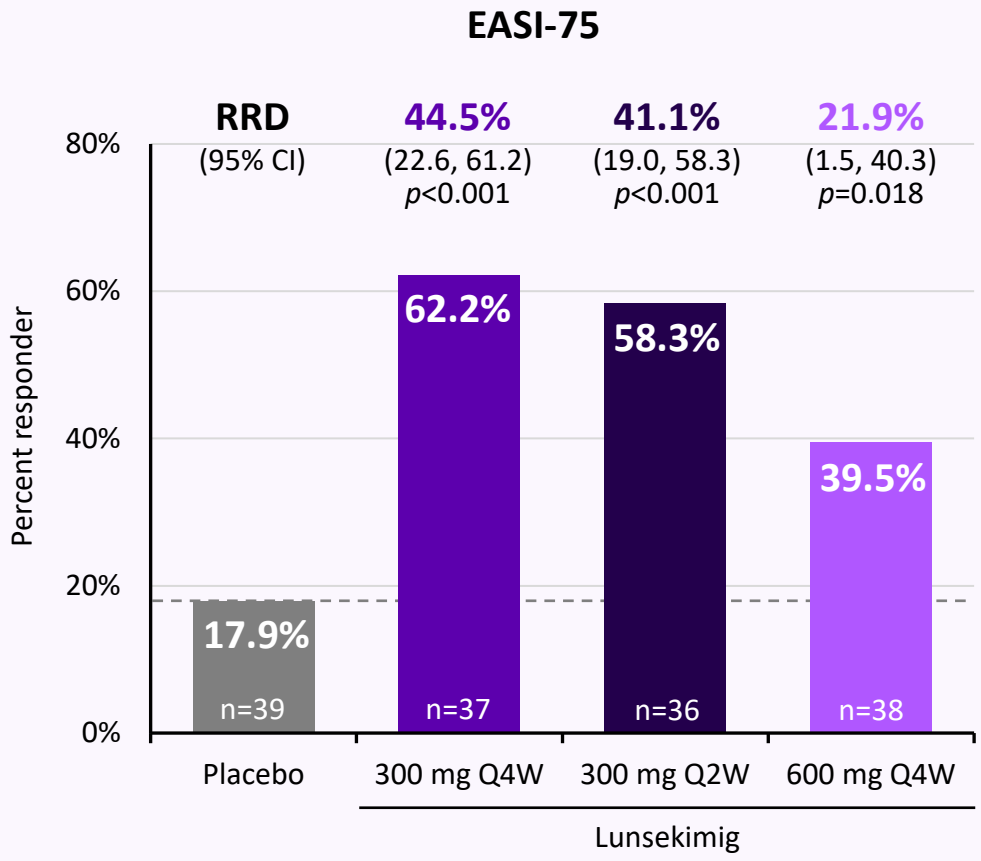
EASI Percent Change from Baseline by Visit

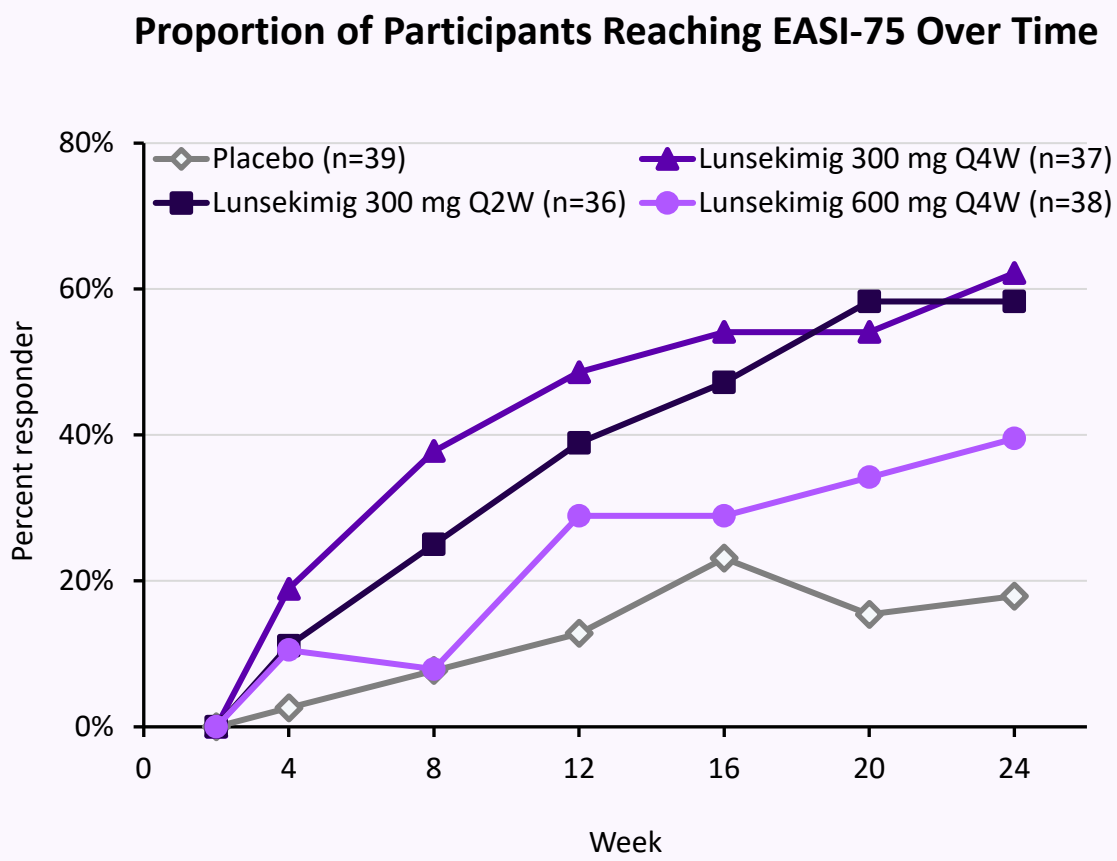


N represents the number of participants in the ANCOVA model/with data assigned by WOCF for intercurrent event handling using composite variable strategy/multiply imputed for missing data. ANCOVA model includes treatment, randomization strata (atopic dermatitis severity, prior systemic medications) as fixed effects, and baseline EASI as covariate. Adjusted *p*-value accounts for the testing hierarchy and adj $p<0.025$ indicates statistical significance of the treatment effect.

ANCOVA, analysis of covariance; CI, confidence interval; EASI, eczema area and severity index; LS, least squares; Q2W, every 2 weeks; Q4W, every 4 weeks; SE, standard error; WOCF, worst observation carried forward.

Lunsekimig showed numerically higher EASI-75 response at Week 24 versus placebo

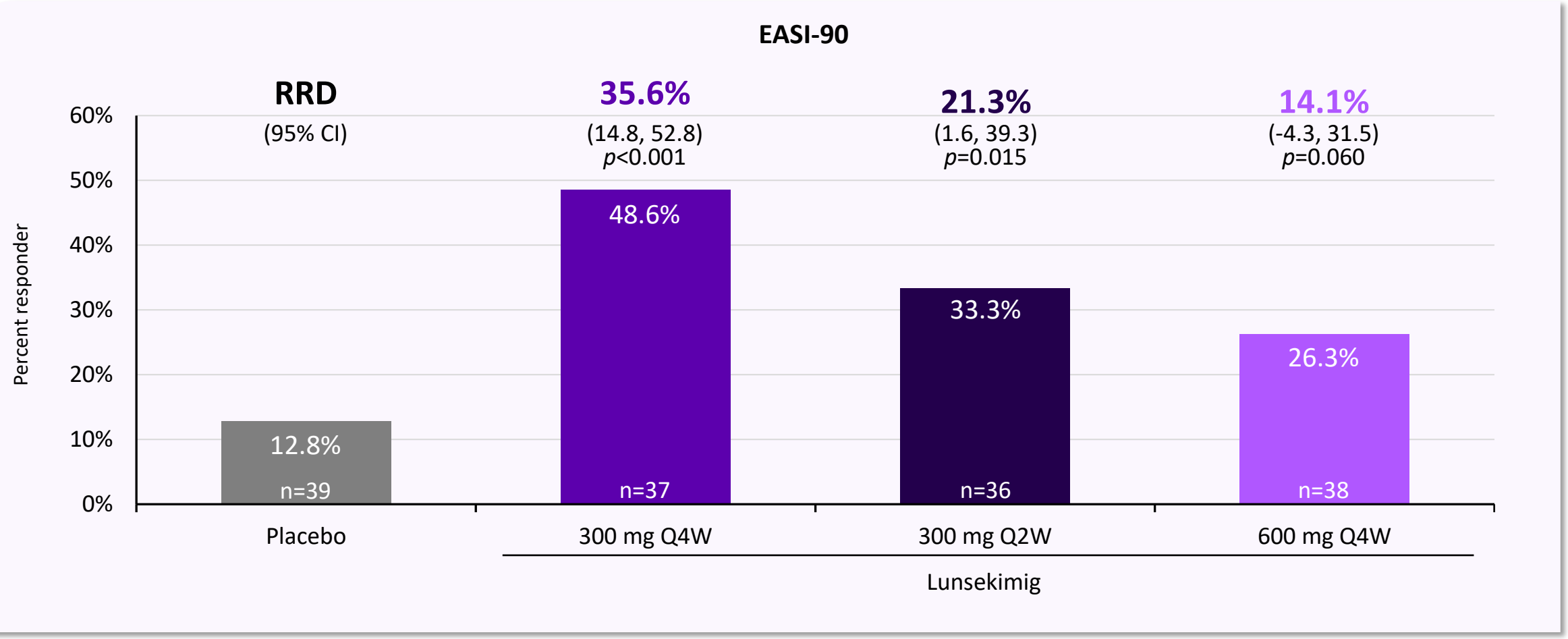




EASI-75 response was observed early with continued improvement to Week 24 with lunsekimig

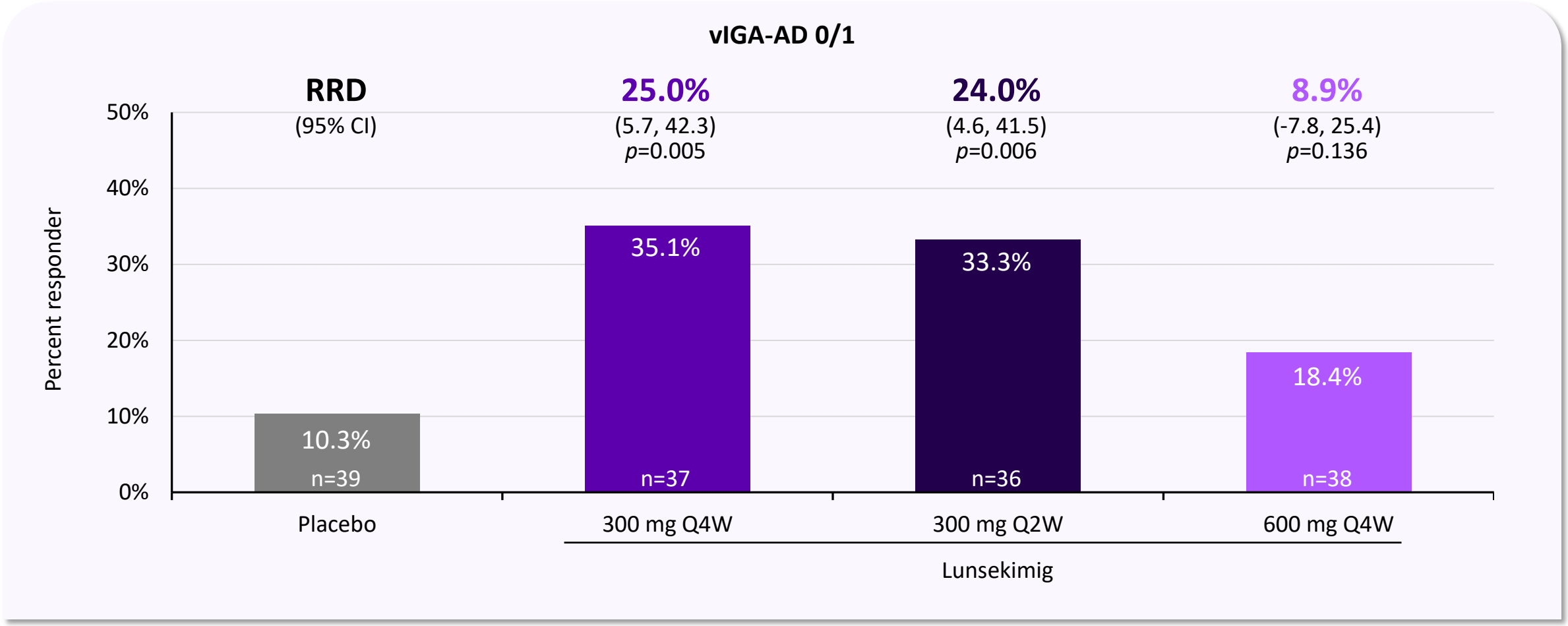
N represents the number of participants included in the model. Response rate difference derived from the Mantel-Haenszel estimator, 95% CI based on Newcombe method. *p*-values are nominal; nominal *p*-value of odds ratio based on Cochran-Mantel-Haenszel (CMH) test. Responders are the participants achieving an EASI-75 at Week 24. CMH test is stratified by stratification factors (AD severity, prior systemic medication).
CI, confidence interval; EASI, eczema area and severity index; RRD, response rate difference versus placebo; Q2W, every 2 weeks; Q4W, every 4 weeks.

Lunsekimig showed numerically higher EASI-90 response at Week 24 versus placebo



N represents the number of participants included in the model. Response rate difference derived from the Mantel-Haenszel estimator, 95% CI based on Newcombe method. *p*-values are nominal; nominal *p*-value of odds ratio based on Cochran-Mantel-Haenszel (CMH) test. Responders are the participants achieving an EASI-90 at Week 24. CMH test is stratified by stratification factors (AD severity, prior systemic medication).
CI, confidence interval; EASI, eczema area and severity index; RRD, response rate difference versus placebo; Q2W, every 2 weeks; Q4W, every 4 weeks.

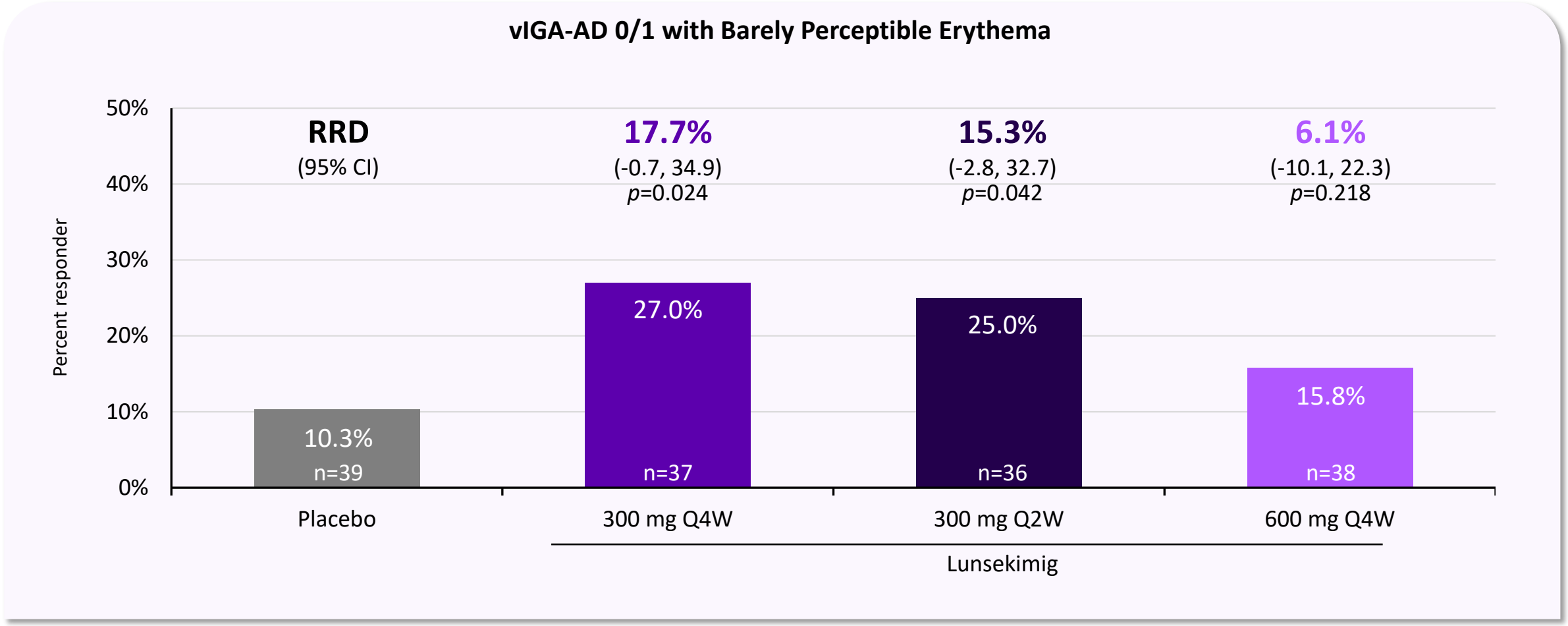
A numerically higher proportion of participants achieved vIGA-AD 0/1 with lunsekimig versus placebo at Week 24



N represents the number of participants included in the model. Response rate difference derived from the Mantel-Haenszel estimator, 95% CI based on Newcombe method. *p*-values are nominal; nominal *p*-value of odds ratio based on Cochran-Mantel-Haenszel (CMH) test. vIGA-AD 0/1 responders are the participants with a vIGA-AD score of 0 or 1 and a reduction from baseline of ≥ 2 points. CMH test is stratified by stratification factors (AD severity, prior systemic medication).

CI, confidence interval; Q2W, every 2 weeks; Q4W, every 4 weeks; RRD, response rate difference versus placebo; vIGA-AD, validated investigator's global assessment for atopic dermatitis.

A trend toward higher vIGA-AD 0/1 response with barely perceptible erythema was observed with lunsekimig versus placebo at Week 24*

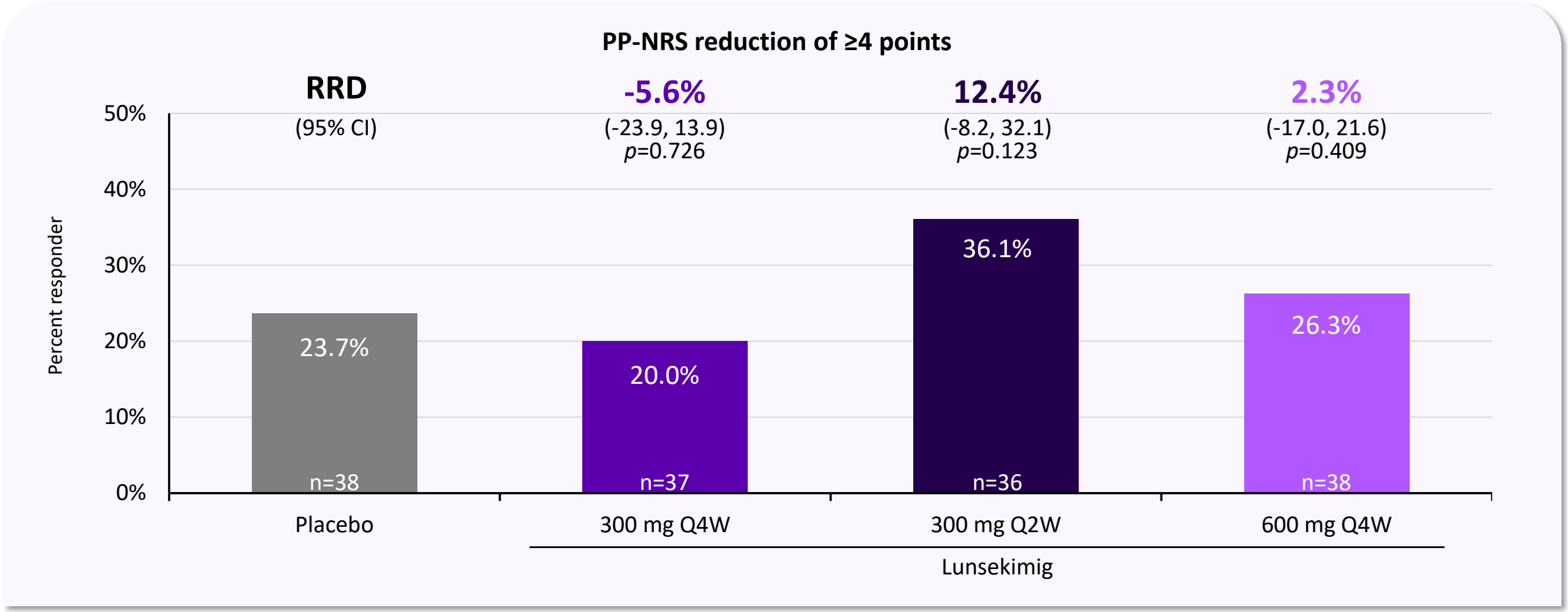


N represents the number of participants included in the model. Response rate difference derived from the Mantel-Haenszel estimator, 95% CI based on Newcombe method. Nominal *p*-value of odds ratio based on Cochran-Mantel-Haenszel (CMH) test. CMH test is stratified by stratification factors (AD severity, prior systemic medication).

*vIGA-AD 0/1 with barely perceptible erythema responders are the participants with a vIGA-AD score of 0 or 1 with presence of only barely perceptible erythema (no induration/papulation, lichenification, oozing, or crusting) at Week 24.

CI, confidence interval; Q2W, every 2 weeks; Q4W, every 4 weeks; RRD, response rate difference versus placebo; vIGA-AD, validated investigator's global assessment for atopic dermatitis.

Lunsekimig did not demonstrate clinically meaningful differences in PP-NRS across all dosing regimens at Week 24 versus placebo



Missing data are more prominent in PP-NRS measurements compared with other responder analyses. Participants without data were imputed as non-responders

N represents the number of participants included in the model. Response rate difference derived from the Mantel-Haenszel estimator, 95% CI based on Newcombe method. *p*-values are nominal; nominal *p*-value of odds ratio based on Cochran-Mantel-Haenszel (CMH) test. Responders are the participants with reduction (improvement) of ≥4 points in the weekly average of daily PP-NRS scores from baseline. Analysis is performed on participants with a baseline weekly average of daily PP-NRS scores of ≥4 points. Treatment effects shown are Mantel-Haenszel estimator common rate differences (point) and 95% CIs (horizontal segment). Given the limited sample size, subgroup analyses should be interpreted with caution.
CI, confidence interval; PP-NRS, peak pruritus numerical rating scale; Q2W, every 2 weeks; Q4W, every 4 weeks; RRD, response rate difference versus placebo.

Lunsekimig was generally well-tolerated at all doses

n (%)	Placebo (N=39)	Lunsekimig 300 mg Q4W (N=36)	Lunsekimig 300 mg Q2W (N=36)	Lunsekimig 600 mg Q4W (N=38)	All lunsekimig (N=110)
Any TEAE	21 (53.8)	24 (66.7)	25 (69.4)	24 (63.2)	73 (66.4)
Any severe TEAE	2 (5.1)	1 (2.8)	2 (5.6)	2 (5.3)	5 (4.5)
Any treatment emergent SAE	1 (2.6)	2 (5.6)	2 (5.6)	1 (2.6)	5 (4.5)
Any TEAE leading to death	0	0	1 (2.8)	0	1 (0.9)*
Any TEAE leading to permanent study intervention discontinuation	1 (2.6)	1 (2.8)	0	3 (7.9)	4 (3.6)

In the combined lunsekimig group, incidence of less than 5% was seen for treatment emergent SAEs, severe TEAEs, and TEAEs leading to discontinuation

*Death due to motor vehicle accident.

Q2W, every 2 weeks; Q4W, every 4 weeks; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Rates of TEAEs were generally similar across arms with the exception of injection site reactions

n (%)	Placebo (N=39)	Lunsekimig 300 mg Q4W (N=36)	Lunsekimig 300 mg Q2W (N=36)	Lunsekimig 600 mg Q4W (N=38)	Lunsekimig All lunsekimig (N=110)
Most common TEAEs (≥5% in any intervention group)					
Upper respiratory tract infection	3 (7.7)	4 (11.1)	2 (5.6)	3 (7.9)	9 (8.2)
Nasopharyngitis	3 (7.7)	2 (5.6)	3 (8.3)	3 (7.9)	8 (7.3)
Urinary tract infection	0	2 (5.6)	1 (2.8)	1 (2.6)	4 (3.6)
Headache	1 (2.6)	2 (5.6)	2 (5.6)	0	4 (3.6)
Hypertension	0	0	2 (5.6)	0	2 (1.8)
Dermatitis atopic	2 (5.1)	0	2 (5.6)	2 (5.3)	4 (3.6)
Back pain	0	0	0	2 (5.3)	2 (1.8)
Osteoarthritis	0	0	2 (5.6)	0	2 (1.8)
Injection site reaction*	2 (5.1)	6 (16.7)	6 (16.7)	7 (18.4)	19 (17.3)

*All injection site reactions in this study were reported by the PT "Injection Site Reaction".
PT, preferred term; Q2W, every 2 weeks; Q4W, every 4 weeks; TEAE, treatment-emergent adverse event.

Conclusions

In the **VELVET Phase 2b** dose-ranging study, the **primary endpoint was not met.** Lunsekimig showed **numerical** improvements across multiple measures of **skin clearance and disease severity** among participants with **moderate-to-severe atopic dermatitis**

Lunsekimig achieved **numerically higher treatment effects** versus placebo in **EASI % change** from baseline, **EASI-75**, **vIGA-AD**, **EASI-90** and **vIGA-AD with barely perceptible erythema** at Week 24

The primary outcome of **percent change in EASI score** may have been impacted by a **high placebo response**

Lunsekimig did not demonstrate clinically meaningful differences in PP-NRS; however, interpretation of PP-NRS may be limited by **small sample size**, **missing data** and **scoring variability**

Lunsekimig was **generally well tolerated** at all doses

These data support **further investigation into the role of dual TSLP/IL-13 inhibition** in moderate-to-severe atopic dermatitis

EASI, eczema area and severity index; IL-13, interleukin-13; TSLP, thymic stromal lymphopoietin; vIGA-AD, validated investigator's global assessment for atopic dermatitis.

THANK YOU