AIRCULES

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Lunsekimig for patients with moderate-to-severe asthma: Results from the AIRCULES trial

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Conflict of interest disclosure

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Affiliation / Financial interest	Commercial company
Grants/research support:	Her institution received research support from Amgen, AstraZeneca, Avillion, Bellus, Evidera, Gossamer Bio, Genentech, GSK, Janssen, Pfizer, Regeneron, Roche, Sanofi, Novartis and Teva
Honoraria or consultation fees:	Received consulting fees from AbbVie, Amgen, Apogee, AstraZeneca, Avillion, Chiesi, Foresee, Genentech, GSK, Incyte, Johnson & Johnson, Niox, Novartis, Pfizer, Pharmosa, Regeneron, Sanofi, and Teva; and Honoraria for non-speakers bureau presentations from GSK, TEVA, Sanofi/Regeneron and Astra Zeneca
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Other support / potential conflict of interest:	Received travel support from Astra Zeneca, Sanofi, TEVA, Regeneron and GSK; and she is an honorary faculty member of Observational and Pragmatic Research Institute (OPRI) but does not receive compensation for this role

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Aims / Learning objectives

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To evaluate the efficacy and safety of lunsekimig, a novel pentavalent, bispecific NANOBODY® molecule that blocks TSLP and IL-13, in adults with moderate-to-severe asthma

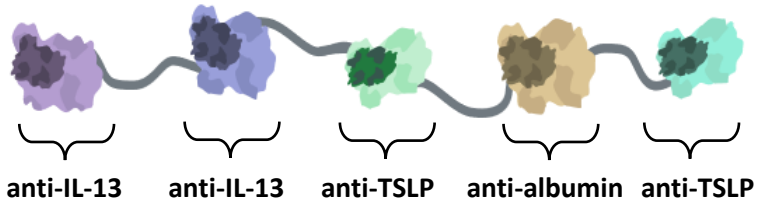
IL-13, interleukin-13; TSLP, thymic stromal lymphopoietin.

Lunsekimig is a novel pentavalent, bispecific NANOBODY® molecule that blocks TSLP and IL-13

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NANOBODY® molecule

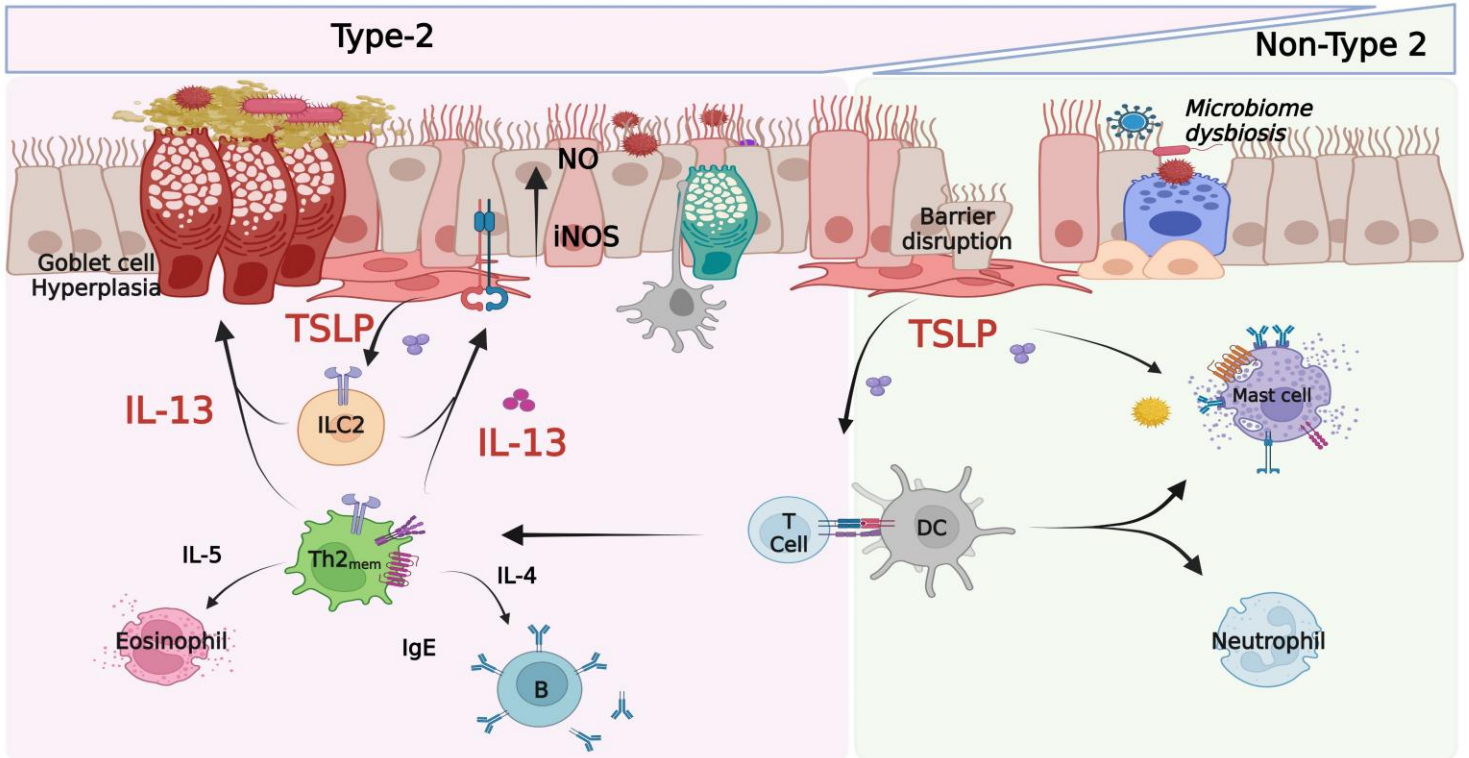
Lunsekimig:



NANOBODY® molecules are derived from *Camelid* heavy-chain only monoclonal antibodies:

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

Lunsekimig addresses key and complementary drivers of airway inflammation in asthma



1. Parnes JR, et al. *J Asthma Allergy* 2022;15:749–765; 2. Schleich F, et al. Eur Respir Rev. 2023;32(168):220193; 3.Deiteren A, et al. *Eur Respir J* 2025;65(4):2401461.
DC, dendritic cell; IgE, immunoglobulin E; IL, interleukin; ILC2, group 2 innate lymphoid cell; iNOS, inducible nitric oxide synthase; NO, nitric oxide; Th2mem, memory T helper 2 cell; TSLP, thymic stromal lymphopoietin.

AIRCULES a phase 2, randomized, double-blind, placebo-controlled, parallel group, dose-ranging study (NCT06102005)

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Key inclusion criteria

- Aged 18 to 80 years
- Asthma GINA 4-5
- Medium-to-high dose ICS
- ≥1 asthma exacerbation in past year
- ACQ-5 ≥1.5
- FEV_1 40-80%

Stratification factors:

- Screening FeNO (<25 or ≥25 ppb)
- Prior exacerbations in past year (1 or ≥2)
- Region†

There were no biomarker restrictions for study inclusion

Randomized **2:1:2:2:2**

Study design

- **Placebo** (n=152) Q4W
- **Lunsekimig** (n=75) 60 mg Q8W‡ *(Not statistically tested)*
- **Lunsekimig** (n=154) 60 mg Q4W
- **Lunsekimig** (n=151) 300 mg Q8W
- **Lunsekimig** (n=153) 300 mg Q4W

Endpoints & multiple testing procedure

60 mg Q4W	300 mg Q8W	300 mg Q4W

Primary Endpoint*:
Annualized asthma exacerbation rate (AAER) over 48 weeks

Key Secondary Endpoint*:
Change in pre-BD FEV_1 at Week 48

Secondary Endpoint:
Time to first asthma exacerbation

Overall, 1-sided α = 0.025 maintained across endpoints and dose groups versus placebo

Other Secondary Endpoints:
Change in ACQ-5 and AQLQ at Week 48

*Subgroup analyses of the primary and key secondary endpoints in participants with ≥2 prior exacerbations in the last 12 months, in those with FeNO <25 or ≥25 ppb and eosinophils <300 or ≥300 cells/µL were pre-specified. †Regions included Western: US, Canada, UK, Israel, South Africa; Latin America: Argentina, Brazil, Chile, Mexico; Asia: China, India, Japan, South Korea; Eastern Europe: Turkey. ‡60mg Q8W was included to characterize exposure-response relationship and was not statistically tested. AAER, annualized asthma exacerbation rate; ACQ-5, 5-item Asthma Control Questionnaire; AQLQ, asthma quality of life questionnaire; FeNO, fractional exhaled nitric oxide; GINA, Global Initiative for Asthma; ICS, inhaled corticosteroids; OCS, oral corticosteroids; Pre-BD FEV_1, pre-bronchodilator forced expiratory volume in 1 second; QXW, every X weeks.

Baseline disease characteristics were representative of a population with moderate-to-severe asthma

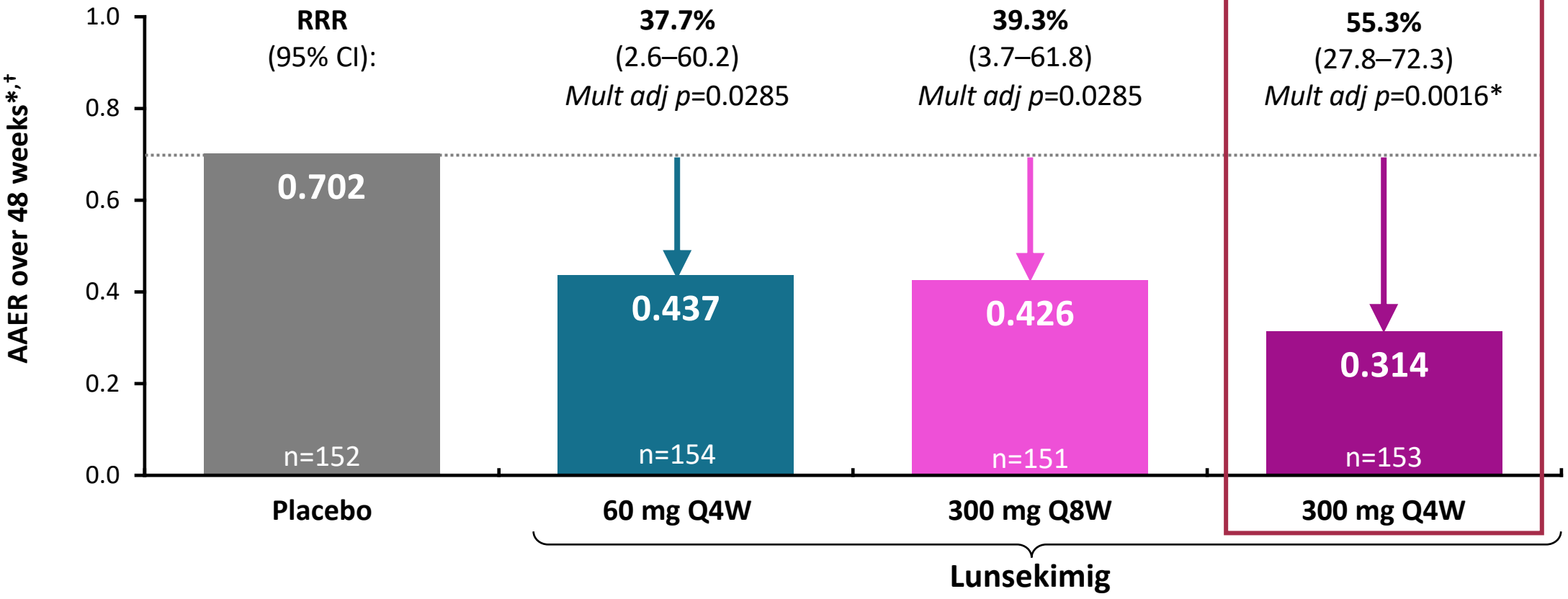
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	Characteristics	Placebo N=152	60 mg Q4W N=154	300 mg Q8W N=151	300 mg Q4W N=153	All* N=685
Demographics	**Age, mean ± SD (years)**	52.3 ± 12.1	52.5 ± 14.1	51.4 ± 13.8	53.1 ± 14.6	52.3 ± 13.7
	Male, n (%)	58 (38.2)	61 (39.6)	46 (30.5)	50 (32.7)	240 (35.0)
	White race, n (%)	102 (67.1)	106 (68.8)	106 (70.2)	107 (69.9)	470 (68.6)
	BMI, mean ± SD (kg/m2)	29.14 ± 5.45	29.40 ± 5.53	28.97 ± 5.23	28.20 ± 5.02	28.85 ± 5.32
	Region†, n (%)					
	Western countries + others	55 (36.2)	56 (36.4)	57 (37.7)	55 (35.9)	250 (36.5)
	Latin America	54 (35.5)	55 (35.7)	53 (35.1)	55 (35.9)	244 (35.6)
	Asia	34 (22.4)	36 (23.4)	34 (22.5)	35 (22.9)	156 (22.8)
	Eastern Europe	9 (5.9)	7 (4.5)	7 (4.6)	8 (5.2)	35 (5.1)
Disease Characteristics	**Number of prior exacerbations (past year), n (%)**					
	1	58 (38.2)	58 (37.7)	55 (36.4)	53 (34.6)	252 (36.8)
	2	75 (49.3)	76 (49.4)	68 (45.0)	78 (51.0)	338 (49.3)
	≥3	19 (12.5)	20 (13.0)	28 (18.5)	22 (14.4)	95 (13.9)
	Baseline FeNO, mean ± SD (ppb)	37.1 ± 31.7	37.7 ± 35.7	34.5 ± 27.3	37.7 ± 37.0	37.0 ± 32.9
	Baseline Eosinophils, mean ± SD (10^9/L)	0.360 ± 0.312	0.408 ± 0.433	0.377 ± 0.439	0.329 ± 0.384	0.377 ± 0.433
	Pre-BD percent predicted FEV_1, mean ± SD (%)	61.6 ± 15.0	60.2 ± 12.8	61.4 ± 14.6	61.7 ± 13.8	60.8 ± 14.2
	ACQ-5 score, mean ± SD	2.8 ± 0.9	2.6 ± 0.8	2.7 ± 0.7	2.9 ± 0.9	2.8 ± 0.8
	AQLQ(S)+12 score, mean ± SD	4.0 ± 1.2	4.2 ± 1.0	4.2 ± 1.1	4.0 ± 1.1	4.1 ± 1.1

*All includes participants from the lunsekimig 60 mg Q8W arm (N=75). †Prespecified stratification factor; Western countries: US, Canada, UK, Israel, South Africa; Latin America: Argentina, Brazil, Chile, Mexico; Asia: China, India, Japan, South Korea; Eastern Europe: Turkey. ACQ-5, 5-item Asthma Control Questionnaire; AQLQ(S)+12, Standardized Asthma Quality of Life Questionnaire for 12 years and older; BMI, body mass index; FeNO, fractional exhaled nitric oxide; Pre-BD FEV1, pre-bronchodilator forced expiratory volume in 1 second; Q4W, every 4 weeks; Q8W, every 8 weeks; SD, standard deviation.

Lunsekimig 300 mg Q4W demonstrated a statistically significant and clinically meaningful reduction in annualized asthma exacerbation rate (AAER)

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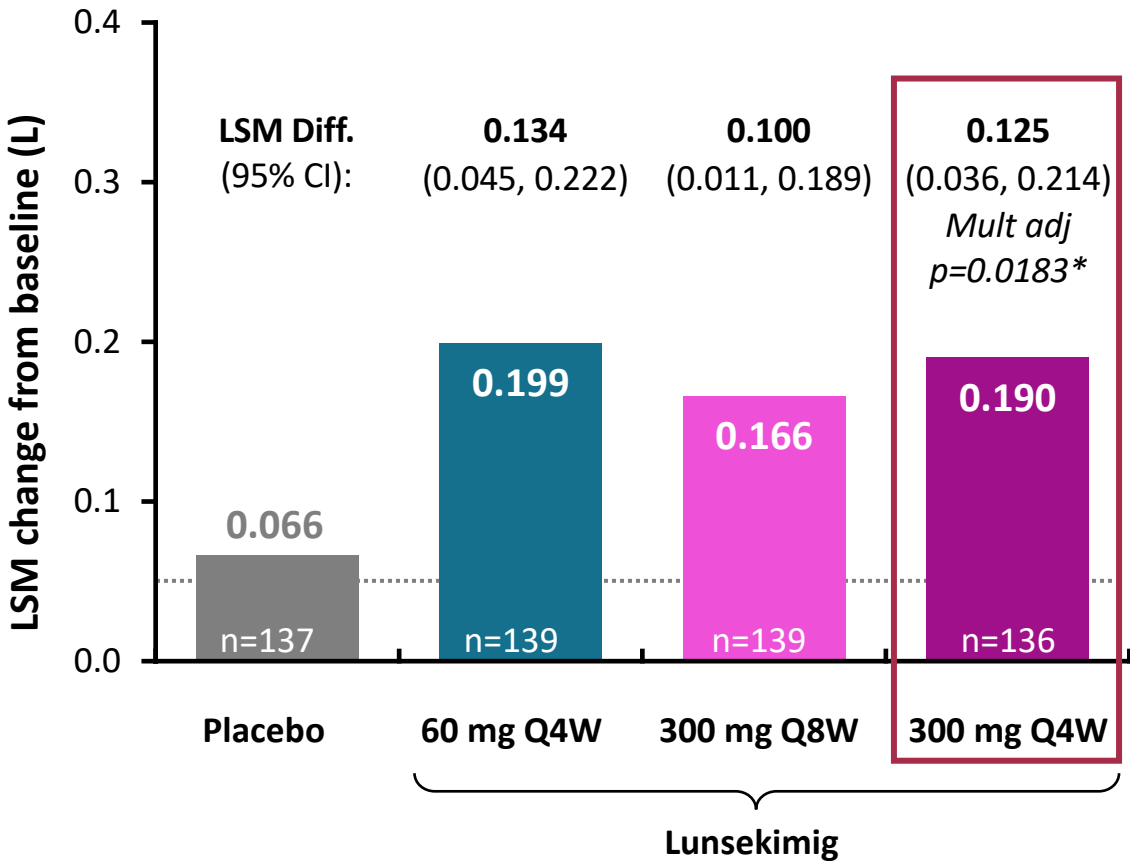
Other lunsekimig doses showed **clinically meaningful improvements**, but were not statistically significant by multiple testing procedure

One-sided multiplicity-adjusted p-values are presented and based on pre-specified multiple testing procedure.
*Statistically significant at one-sided α=0.025 after multiplicity adjustment; †Step 1 in multiple testing procedure.
AAER, annualized asthma exacerbation rate; CI, confidence interval; Q4W, every 4 weeks; Q8W, every 8 weeks; RRR, relative risk reduction.

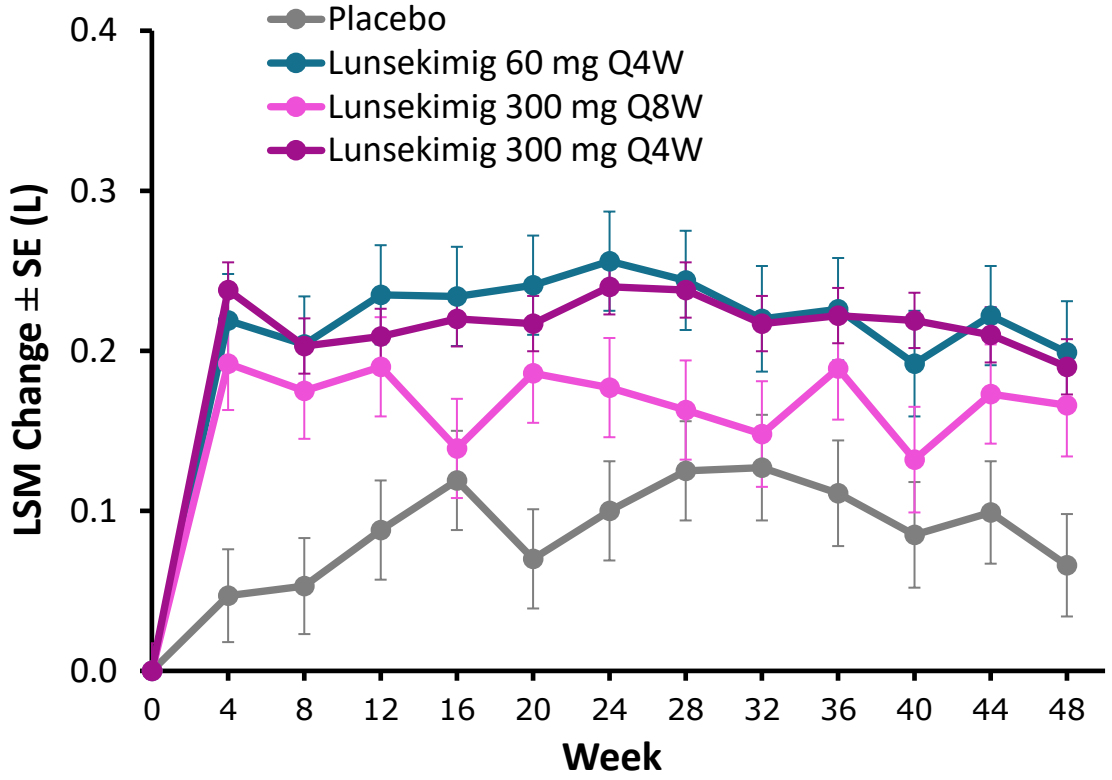
Lunsekimig 300 mg Q4W demonstrated a statistically significant and clinically meaningful improvement in Pre-BD FEV_1 which was rapid and sustained

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Change in Pre-BD FEV_1 at Week 48*,†



Change in Pre-BD FEV_1 Over Time



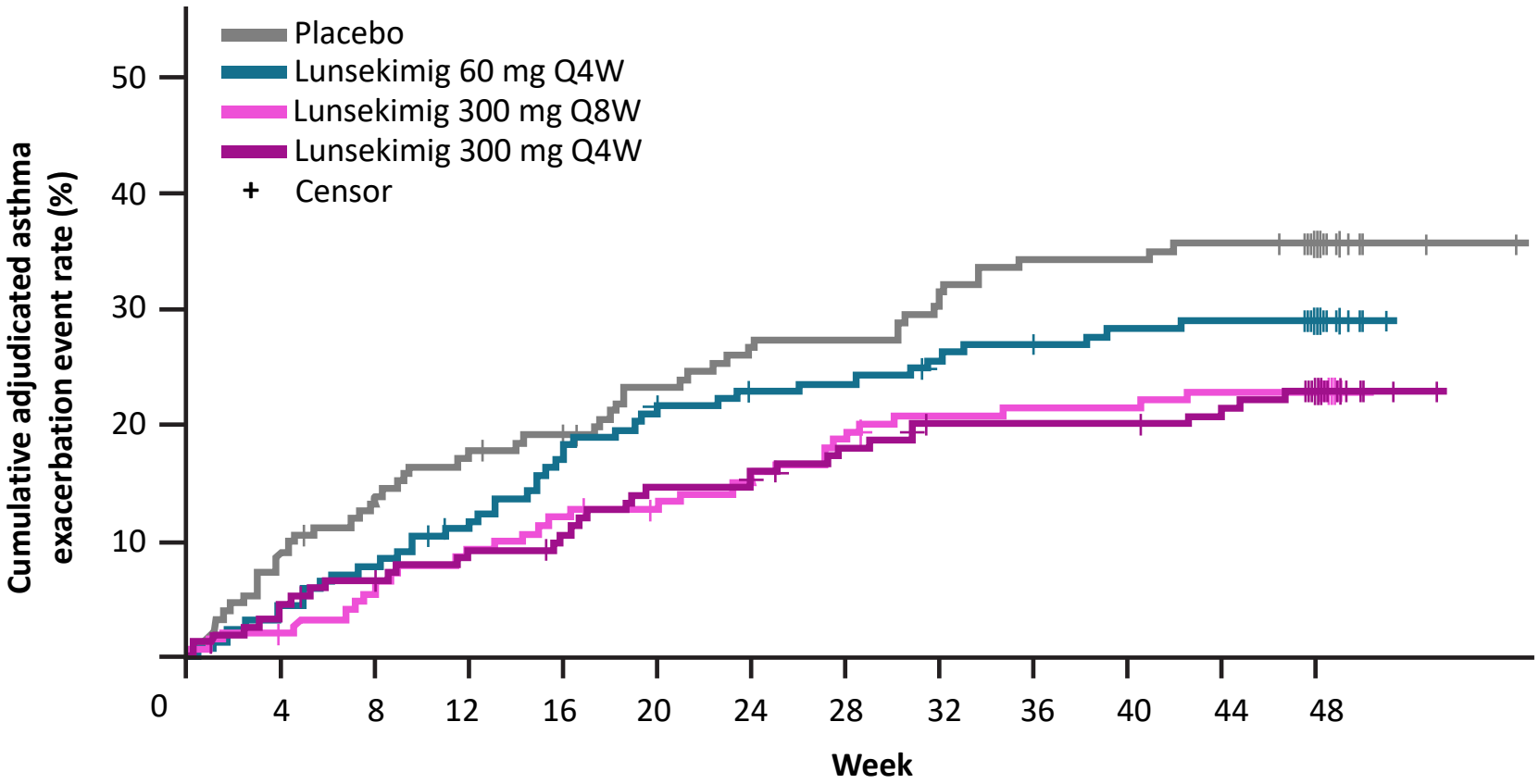
One-sided multiplicity-adjusted p-value is presented and based on pre-specified multiple testing procedure. P-values for 60 mg Q4W and 300 mg Q8W are not presented as statistical testing stopped after Step 1 due to lack of statistical significance.*Statistically significant at one-sided α=0.025 after multiplicity adjustment; †Step 2 in multiple testing procedure.

CI, confidence interval; LSM, least squares mean; Pre-BD FEV_1, pre-bronchodilator forced expiratory volume in 1 second; Q4W, every 4 weeks; Q8W, every 8 weeks; SE, standard error.

Lunsekimig 300 mg Q4W reduced the risk of first asthma exacerbation

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Time-to-first asthma exacerbation*



60 mg Q4W	
HR (95% CI):	**Risk Reduction:**
0.802 (0.520, 1.235)	19.8%

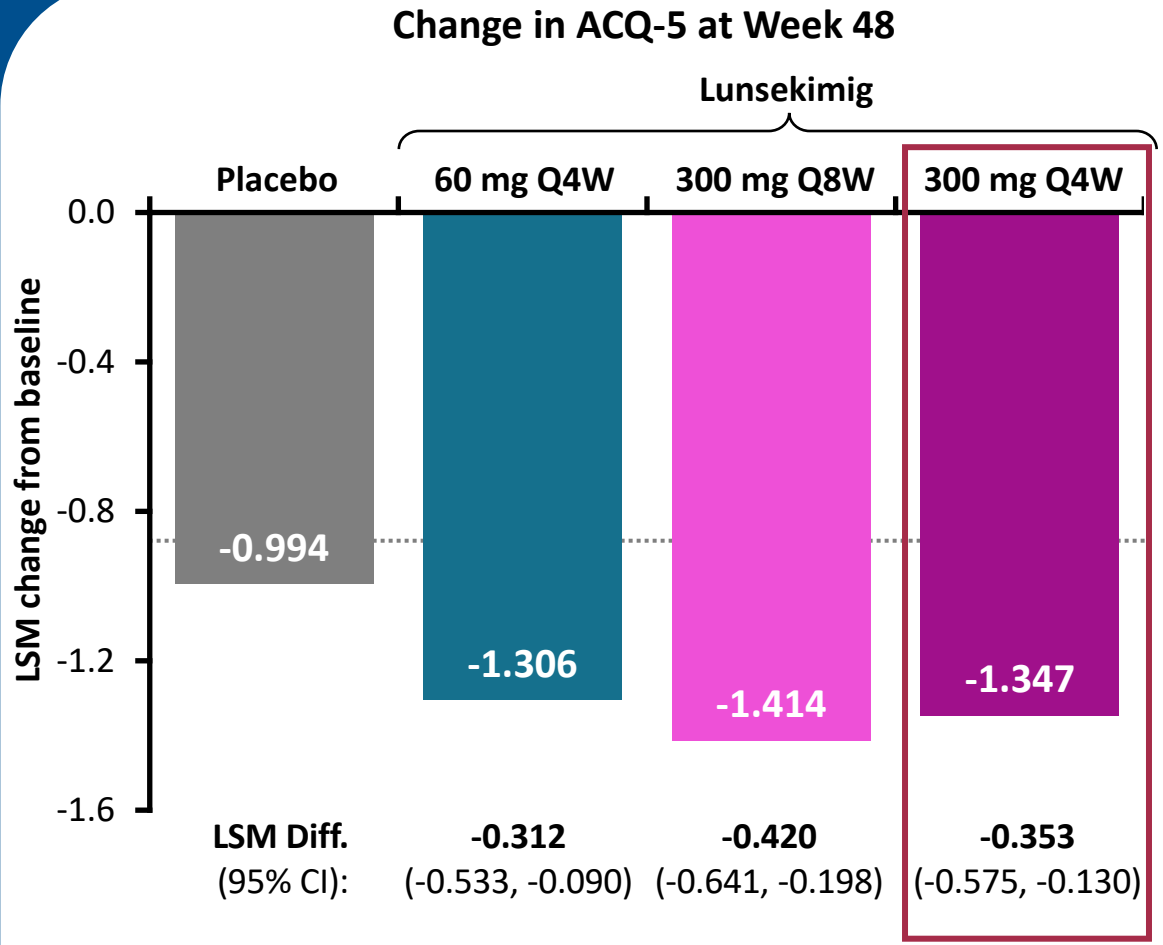
300 mg Q8W	
HR (95% CI):	**Risk Reduction:**
0.592 (0.378, 0.928)	40.8%

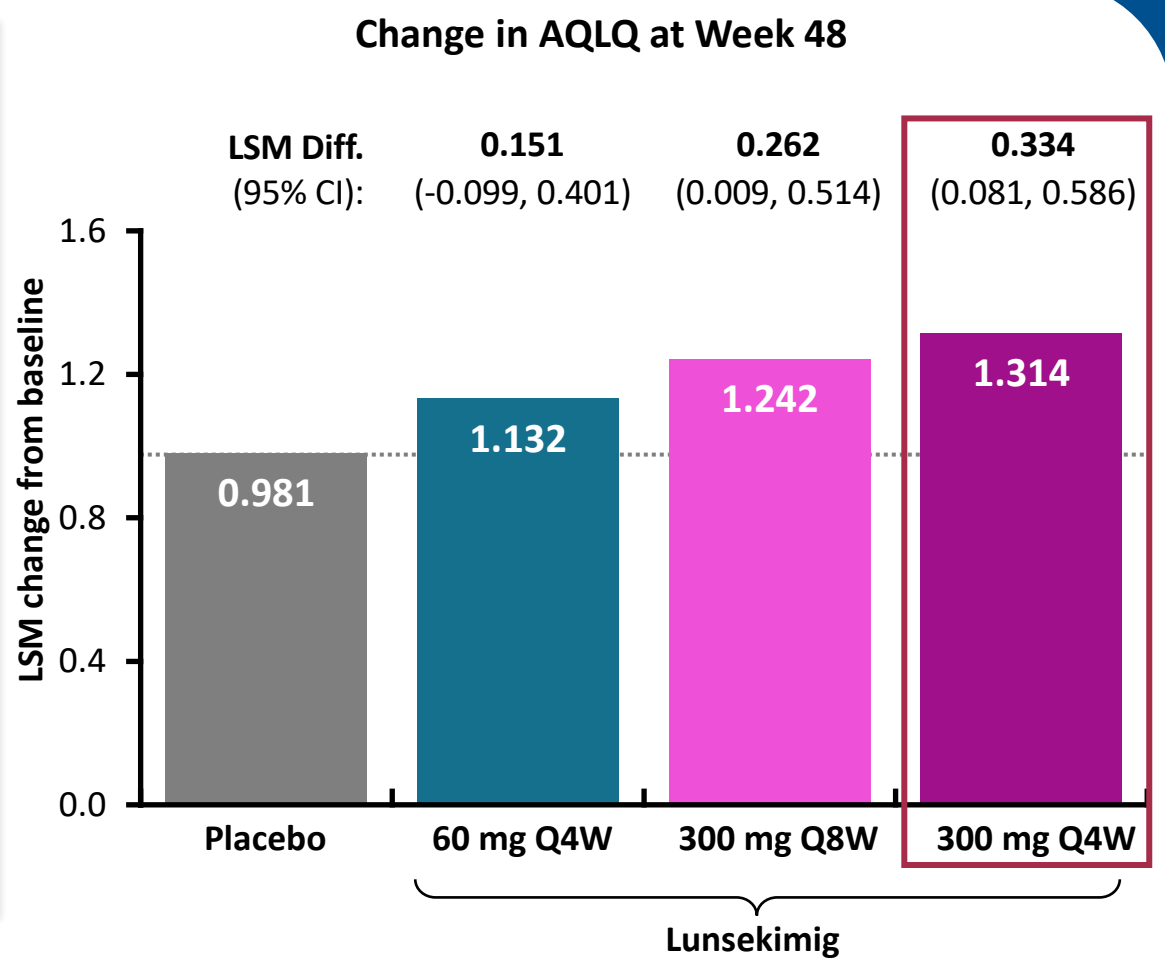
300 mg Q4W	
HR (95% CI):	**Risk Reduction:**
0.601 (0.382, 0.944) Mult adj p=0.0483	39.9%

One-sided multiplicity-adjusted p-value is presented and based on pre-specified multiple testing procedure. *Step 3 in multiple testing procedure.
CI, confidence interval; HR, hazard ratio; Q4W, every 4 weeks; Q8W, every 8 weeks.

Lunsekimig improved asthma symptom control (ACQ-5) and asthma quality of life (AQLQ)

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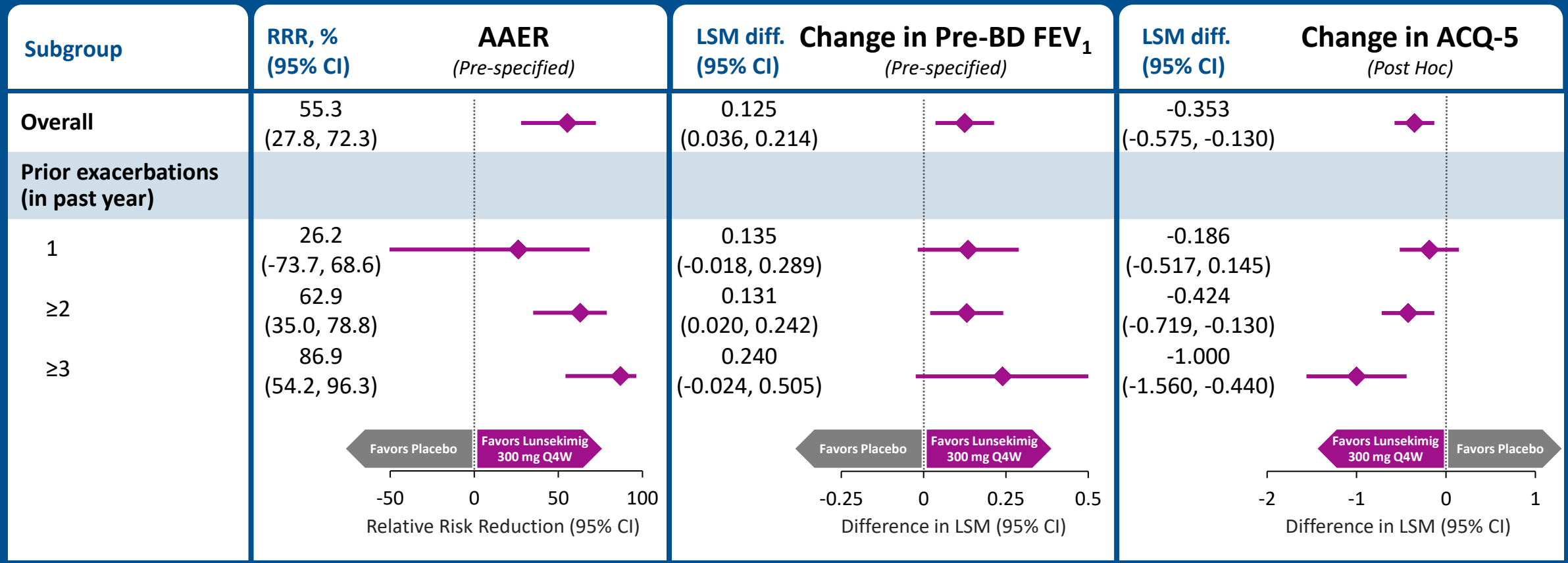




ACQ-5 and AQLQ were not included in the multiple testing procedure.
ACQ-5, asthma control questionnaire-5; AQLQ, asthma quality of life questionnaire; CI, confidence interval; LSM, least squares mean; Q4W, every 4 weeks; Q8W, every 8 weeks.

A greater magnitude of response to lunsekimig was observed among frequent exacerbators, with improvements seen across all subgroups

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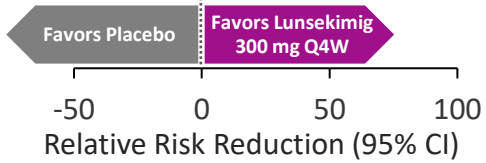
Time to first exacerbations showed a similarly increasing magnitude of response in those with ≥2 prior exacerbations
[Hazard Ratio (95%CI): 0.494 (0.292, 0.835)]

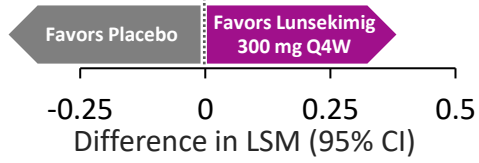
Ns (300mg Q4W / Placebo): **AAER**: Overall: 153/152; Exacerbations in past year 1: 53/58, ≥2: 100/94, ≥3: 22/19. **FEV1**: Overall: 136/137; Exacerbations in past year 1: 47/53, ≥2: 89/84, ≥3: 22/17. **ACQ-5**: Overall: 134/138; Exacerbations in past year 1: 47/53, ≥2: 87/85, ≥3: 20/17. AAER, annualized asthma exacerbation rate; ACQ-5, 5-item Asthma Control Questionnaire; CI, confidence interval; LSM, least squares mean; Pre-BD FEV_1, pre-bronchodilator forced expiratory volume in 1 second; Q4W, every 4 weeks; RRR, relative risk reduction.

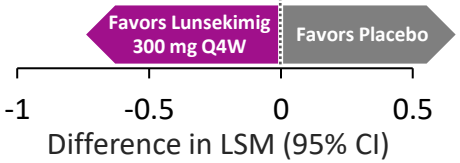
A greater magnitude of response to lunsekimig was observed in those with high Type-2 inflammation, with consistent benefit across biomarker subgroups

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Subgroup	RRR, % (95% CI)	AAER (Pre-specified)	LSM diff. (95% CI)	Change in Pre-BD FEV_1 (Pre-specified)	LSM diff. (95% CI)	Change in ACQ-5 (Post Hoc)
Overall	55.3 (27.8, 72.3)		0.125 (0.036, 0.214)		-0.353 (-0.575, -0.130)	
Baseline FeNO level (ppb)						
<25	39.5 (-19.6, 69.4)		-0.040 (-0.173, 0.094)		-0.044 (-0.386, 0.298)	
≥25	65.1 (30.5, 82.5)		0.263 (0.146, 0.379)		-0.613 (-0.908, -0.317)	
Baseline eosinophil level (cells/µL)						
<300	34.8 (-26.3, 66.3)		0.092 (-0.016, 0.200)		-0.246 (-0.533, 0.042)	
≥300	70.6 (40.5, 85.5)		0.176 (0.025, 0.327)		-0.484 (-0.843, -0.126)	







Ns (300mg Q4W / Placebo): **AAER**: Overall: 153/152; FeNO <25: 66/66, ≥25: 86/86; Eos <300: 92/86, ≥300: 60/66. **FEV1**: Overall: 136/137; FeNO <25: 59/61, ≥25: 76/76; Eos <300: 80/77, ≥300: 55/60. **ACQ-5**: Overall: 134/138; FeNO <25: 57/60, ≥25: 75/78; Eos <300: 79/77, ≥300: 54/61. AAER, annualized asthma exacerbation rate; ACQ-5, 5-item Asthma Control Questionnaire; CI, confidence interval; Eos, eosinophil; FeNO, fractional exhaled nitric oxide; LSM, least squares mean; Pre-BD FEV_1, pre-bronchodilator forced expiratory volume in 1 second; Q4W, every 4 weeks; RRR, relative risk reduction.

Lunsekimig was generally well tolerated

n (%)	Placebo N=152	60 mg Q4W N=154	300 mg Q8W N=151	300 mg Q4W N=153	All lunsekimig* N=533
Any TEAE	102 (67.1)	121 (78.6)	110 (72.8)	112 (73.2)	385 (72.2)
Any severe TEAE	11 (7.2)	8 (5.2)	6 (4.0)	9 (5.9)	27 (5.1)
Any treatment-emergent SAE†	11 (7.2)	11 (7.1)	9 (6.0)	10 (6.5)	34 (6.4)
Any TEAE leading to death	0	0	0	0	0
Any TEAE leading to permanent intervention discontinuation‡	1 (0.7)	5 (3.2)	0	6 (3.9)	13 (2.4)
Any TEAE related to treatment§	12 (7.9)	20 (13.0)	28 (18.5)	31 (20.3)	87 (16.3)

Anti-Drug Antibodies (ADA)

ADA titers were generally low and had no apparent impact on PK, efficacy or safety of lunsekimig

*All includes participants from the lunsekimig 60 mg Q8W arm (N=75). †The most frequent treatment-emergent SAEs were pneumonia (1.3%), asthma (1.1%) and prostate cancer (0.6%). ‡The most frequent TEAEs leading to permanent discontinuation were prostate cancer (0.6%) and pregnancy (0.6%). §Per investigator assessment. Q4W, every 4 weeks; Q8W, every 8 weeks; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Lunsekimig was generally well tolerated

n (%)	Placebo N=152	60 mg Q4W N=154	300 mg Q8W N=151	300 mg Q4W N=153	All lunsekimig* N=533
Most frequent TEAEs (≥5% in any arm)					
Nasopharyngitis	12 (7.9)	11 (7.1)	18 (11.9)	17 (11.1)	51 (9.6)
Upper respiratory tract infection	19 (12.5)	24 (15.6)	21 (13.9)	16 (10.5)	65 (12.2)
Influenza	7 (4.6)	5 (3.2)	4 (2.6)	9 (5.9)	22 (4.1)
Urinary tract infection	5 (3.3)	14 (9.1)	4 (2.6)	6 (3.9)	25 (4.7)
Headache	5 (3.3)	8 (5.2)	8 (5.3)	6 (3.9)	27 (5.1)
Injection site reaction†	7 (4.6)	12 (7.8)	21 (13.9)	11 (7.2)	48 (9.0)
Dose scheduling errors‡	11 (7.2)	15 (9.7)	12 (7.9)	16 (10.5)	48 (9.0)

*All includes participants from the lunsekimig 60 mg Q8W arm (N=75. †The high-level term 'Injection site reaction' is presented, which includes the following preferred terms: injection site erythema, injection site induration, injection site pain, injection site papule, injection site plaque, injection site pruritus, injection site rash, injection site reaction, injection site swelling; ‡No cases of symptomatic overdose were observed.
Q4W, every 4 weeks; Q8W, every 8 weeks; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

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Conclusions

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The AIRCULES trial evaluating lunsekimig, a first-in-class NANOBODY® molecule, demonstrated:

Lunsekimig 300 mg Q4W achieved a **statistically significant** and **clinically meaningful reduction** in **asthma exacerbation**

Lunsekimig 300 mg Q4W resulted in **statistically significant** and **clinically meaningful improvement** in **lung function, which was rapid and sustained**

Patient-centric outcomes, including **asthma symptom control** and **quality of life** were also improved with lunsekimig

Improvements were observed across subgroups, with greater magnitude of response in participants with **greater disease severity, including frequent exacerbators**

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

Results from this phase 2 study support dual TSLP and IL-13 targeting to address unmet needs in individuals with moderate-to-severe asthma

IL-13, interleukin-13; Q4W, every 4 weeks; TSLP, thymic stromal lymphopoietin.



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1. Parnes JR, et al. *J Asthma Allergy* 2022;15:749–765.

2. Schleich F, et al. Eur Respir Rev. 2023;32(168):220193

3. Deiteren A, et al. *Eur Respir J* 2025;65(4):2401461.