Abstract 46289

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Improved lung function and asthma control observed with rademikibart in patients with moderate-to-severe asthma

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Conflict of interest disclosure

Raúl Collazo is an employee of the study sponsor, Connect Biopharma

Background

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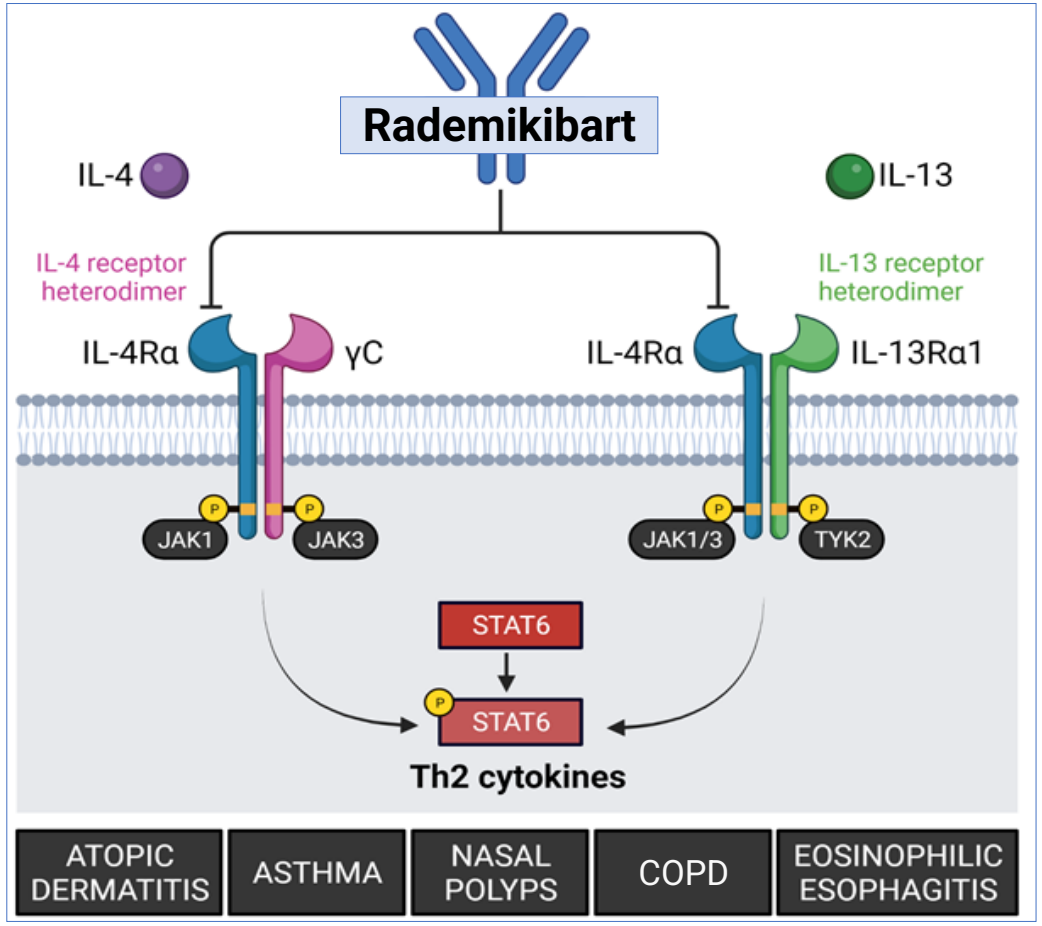
Burden of uncontrolled asthma

- >25 million Americans were burdened by asthma in 2020;[1] 5–10% have severe asthma[2,3]
- Severe exacerbations require urgent intervention to prevent hospitalization & death[4,5]
- Of direct costs (>$50 billion annually in the USA), up to 37.5% is attributable to uncontrolled severe asthma[2,3,6]

Rademikibart (formerly CBP-201)

- Rademikibart, a next-generation monoclonal antibody, binds with higher affinity to IL-4Rα than dupilumab, & blocks IL-4 and IL-13 signaling.[7]
- Patients with atopic dermatitis (a T2 inflammatory disease) benefit from rademikibart therapy.[8,9]
- Thus, rademikibart has great potential to benefit patients with asthma & other T2 inflammatory diseases



References: 1. https://www.cdc.gov/asthma/data-visualizations/default.htm. 2. Burnette A, et al. J Manag Care Spec Pharm. 2023;29:825-834. 3. Hankin CS, et al. J Allergy Clin Immunol. 2013;131:AB126. 4. Czira A, et al. Respir Med. 2022;191:106670. 5. Nurmagambetov T, et al. Ann Am Thorac Soc. 2018;15:348-356. 6. Bourdin A, et al. Eur Respir J. 2019;54:1900900. 7. Zhang L, et al. Sci Rep. 2023;13:12411. 8. Wang J, et al. Clin Transl Sci. 2023;16:2614-2627. 9. Silverberg JI, et al. J Allergy Clin Immunol. 2024:153(4):1040-1049.e12.

Global phase 2b asthma trial

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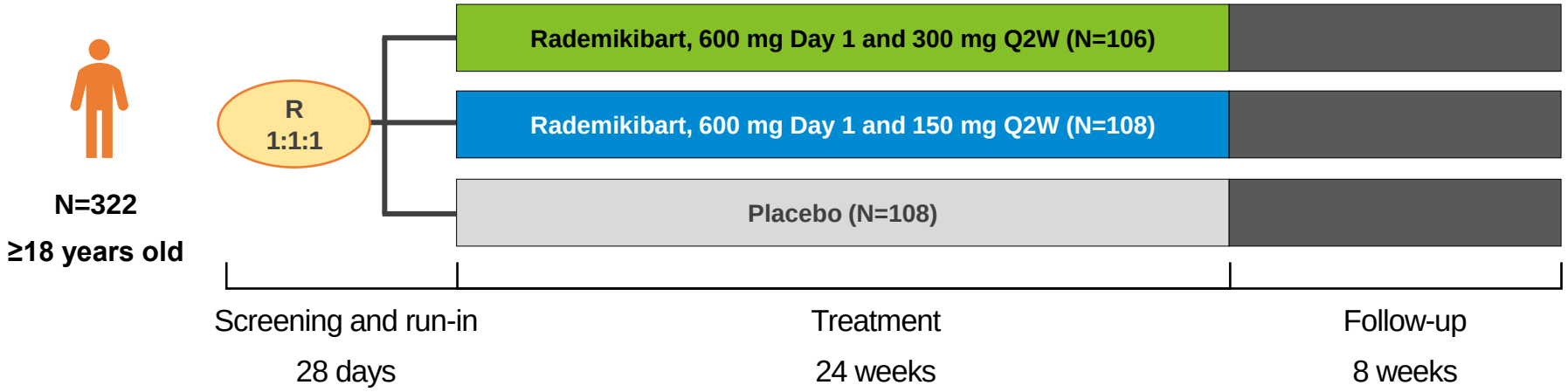

Key inclusion criteria

Moderate-to-severe uncontrolled asthma:

- ACQ-6 ≥1.5 and prebronchodilator FEV_1 40–85% of predicted normal, at screening and baseline
- Medium-to-high dose inhaled CS and reliever/controller for ≥90 days (stable dose ≥28 days) at screening, maintained in the study without dose adjustment
- ≥1 asthma exacerbation in the past year (requiring systemic CS, ~4x baseline inhaled CS dose, or hospitalization/ emergency care)
- ≥150 eosinophils/µL blood (~40% study population enrichment for ≥300 eosinophils/µL); no count required on maintenance oral CS

ACQ, Asthma Control Questionnaire. CS, corticosteroid. FEV_1, Forced expiratory volume in one second. Q2W, every other week.

Baseline characteristics

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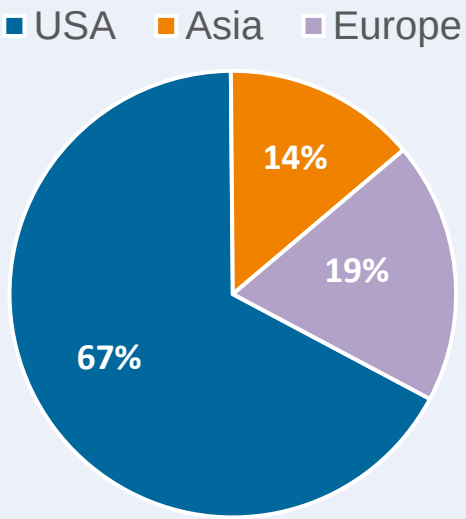
Characteristic*	Placebo (N=108)	Rademikibart 150 mg Q2W (N=106)	Rademikibart 300 mg Q2W (N=108)
Age (years)	54.8 (12.4)	51.6 (12.0)	52.7 (12.9)
Female, n (%)	60 (55.6)	70 (66.0)	68 (63.0)
Body mass index (kg/m^2)	30.5 (7.4)	30.4 (6.8)	30.5 (6.6)
Prebronchodilator FEV_1 (mL)	**1,836 (578)**	**1,908 (647)**	**1,902 (590)**
Percent predicted FEV_1	**61.6 (10.8)**	**63.3 (10.9)**	**64.7 (12.4)**
FEV_1 reversibility (%)†	28.0 (14.9)	24.4 (11.2)	27.5 (15.4)
FeNO (ppb)	31.6 (31.5)	35.8 (35.1)	33.8 (32.7)
ACQ-6 score	**2.72 (0.64)**	**2.71 (0.72)**	**2.68 (0.71)**
Eosinophil counts (cells/µL)	**299 (229)**	**268 (179)**	**320 (220)**
Eosinophil counts, n (%) < 150 cells/µL 150 < 300 cells/µL ≥ 300 cells/µL	 26 (24.1) 41 (38.0) 41 (38.0)	 26 (24.5) 42 (39.6) 38 (35.8)	 23 (21.3) 35 (32.4) 50 (46.3)
Presence of atopic medical condition, n (%)	62 (57.4)	65 (61.3)	63 (58.3)
Maintenance oral/systemic CS, n (%)‡	21 (19.4)	15 (14.1)	10 (9.2)
Exacerbations across the past 12 months†	1.13 (0.39)	1.11 (0.35)	1.10 (0.33)

Enrollment by location



Enrolled in 78 centers:

- USA (42 centers)
- China (22 centers)
- South Korea (4 centers)
- Poland (8 centers)
- Hungary (2 centers)

*Mean (standard deviation) at baseline, unless otherwise noted. †At screening. ‡At randomization.

ACQ, Asthma Control Questionnaire. CS, corticosteroid. FEV_1, Forced expiratory volume in one second. Q2W, every other week.

Improvement in FEV_1 at Week 12
Primary endpoint

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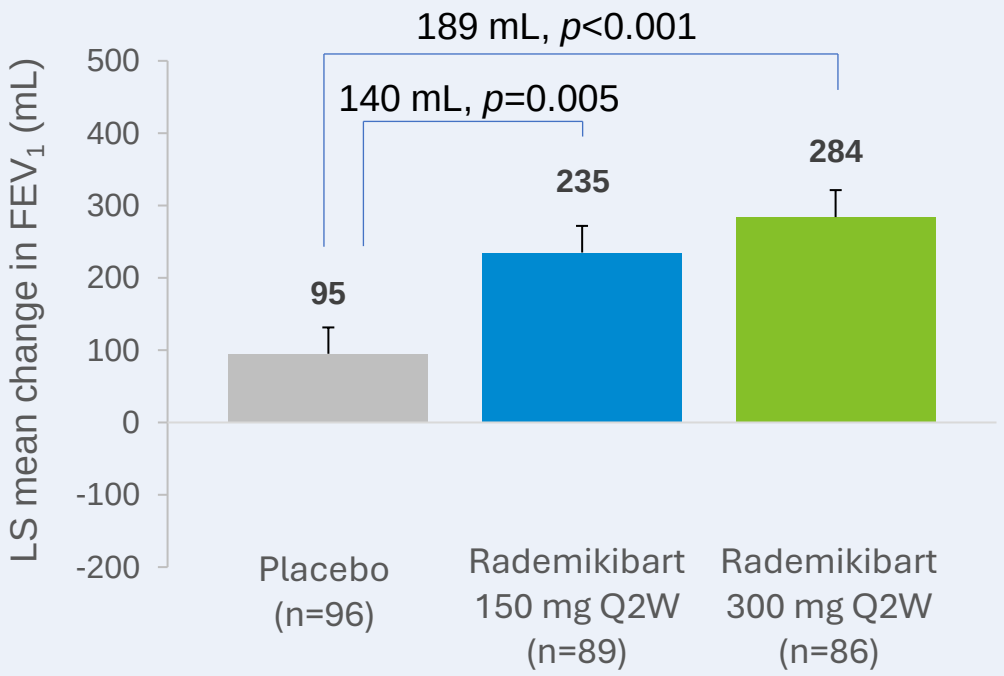
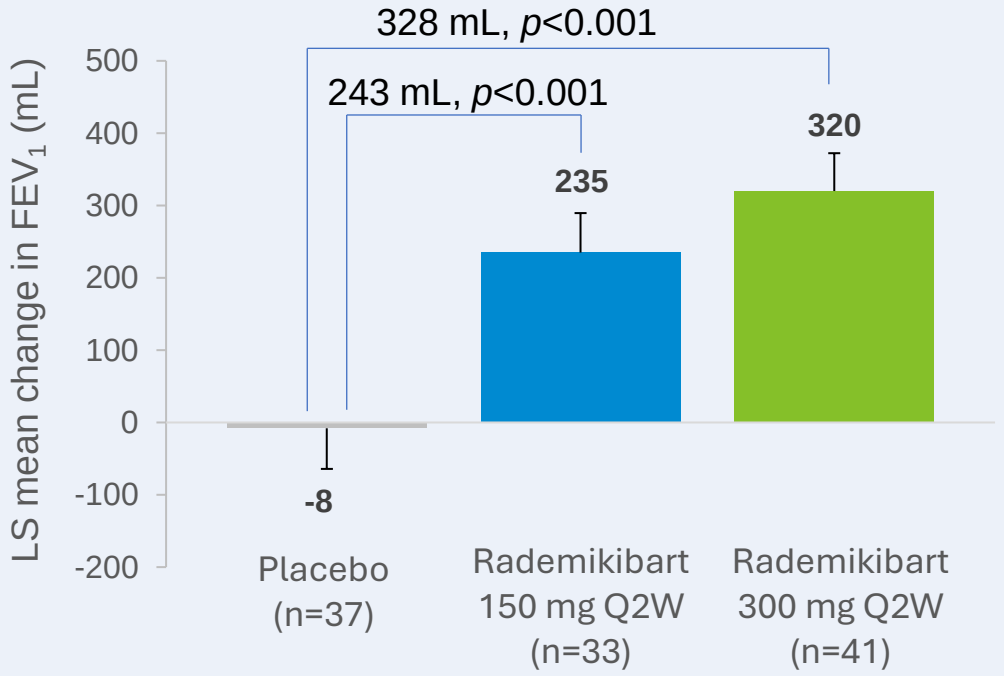
Primary endpoint in the overall population



High blood eosinophil subgroup (baseline ≥300 cells/µL)



Error bars = standard error.

n, number of patients with data at Week 12. FEV_1, Forced expiratory volume in one second. Q2W, every other week.

In the Overall Population and the High Eosinophil subgroup, data were analyzed with ANCOVA and MMRM, respectively, in the Full Analysis Set.

At Week 24, LS mean change in FEV_1 in the placebo, rademikibart 150-mg Q2W and 300-mg Q2W groups, respectively, was: 89 mL, 230 mL, and 279 mL (overall population); -44 mL, 258 mL, and 376 mL (high eosinophil subgroup).

Improvement in FEV_1 through Week 24
Primary and secondary endpoints

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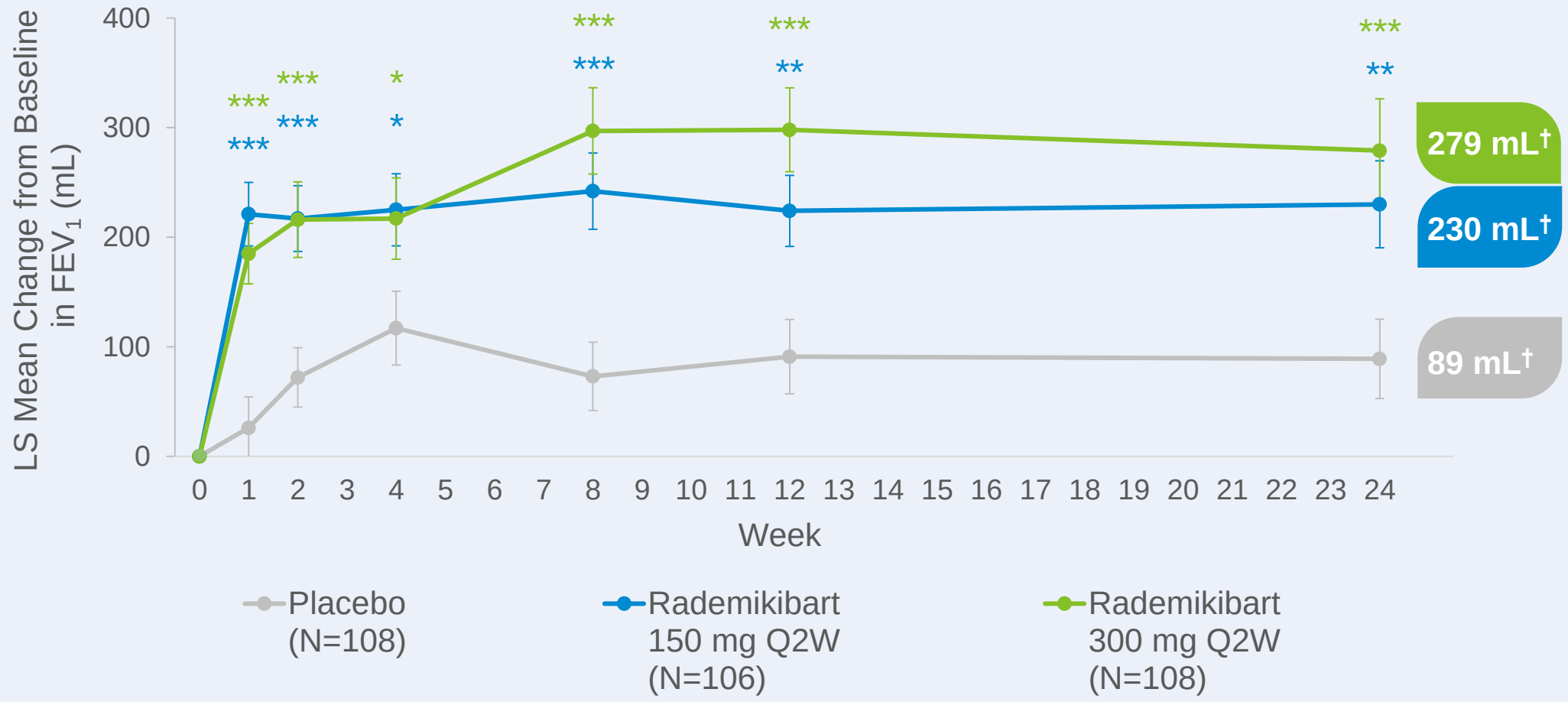

***p<0.001, **p<0.01, *p<0.05 vs placebo. Error bars = standard error.

†LS mean differences from baseline at Week 24. All data points were analyzed with Mixed Model for Repeated Measures in the Full Analysis Set.

FEV_1, Forced expiratory volume in one second. LS, least squares. N, total number of patients with data. Q2W, every other week.

Improvement in FEV_1 at Week 12
Subgroup analyses

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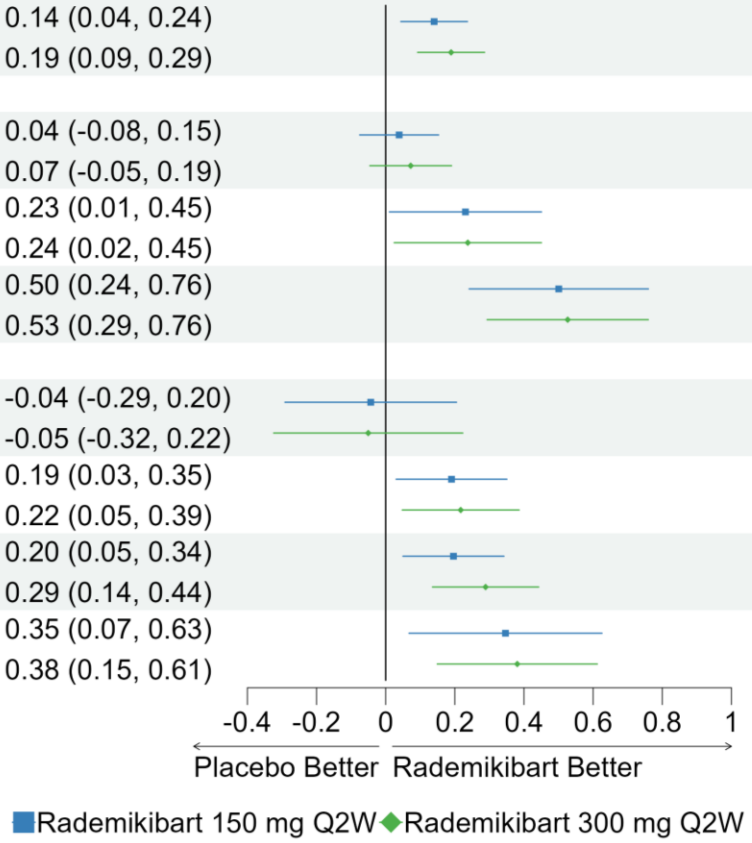
	LS Mean Difference (95% CI)	Placebo	Rademikibart 150 mg Q2W	Rademikibart 300 mg Q2W
Overall	0.14 (0.04, 0.24) 0.19 (0.09, 0.29)	96	89	86
FeNO at Baseline				
< 25 ppb	0.04 (-0.08, 0.15) 0.07 (-0.05, 0.19)	56	50	43
25 - < 50 ppb	0.23 (0.01, 0.45) 0.24 (0.02, 0.45)	21	24	26
≥ 50 ppb	0.50 (0.24, 0.76) 0.53 (0.29, 0.76)	19	15	17
Central Lab Blood Eosinophil at Baseline				
< 150 cells/µL	-0.04 (-0.29, 0.20) -0.05 (-0.32, 0.22)	23	22	17
150 − < 300 cells/µL	0.19 (0.03, 0.35) 0.22 (0.05, 0.39)	36	34	28
300 − < 500 cells/µL	0.20 (0.05, 0.34) 0.29 (0.14, 0.44)	23	25	24
≥ 500 cells/µL	0.35 (0.07, 0.63) 0.38 (0.15, 0.61)	14	8	17



ANCOVA model.

CI, confidence interval. FeNO, fractional exhaled nitric oxide. FEV_1, forced expiratory volume in one second. LS, least squares. n, number of patients with data at Week 12. Q2W, every other week.

Trends toward fewer exacerbations
Secondary and exploratory endpoints

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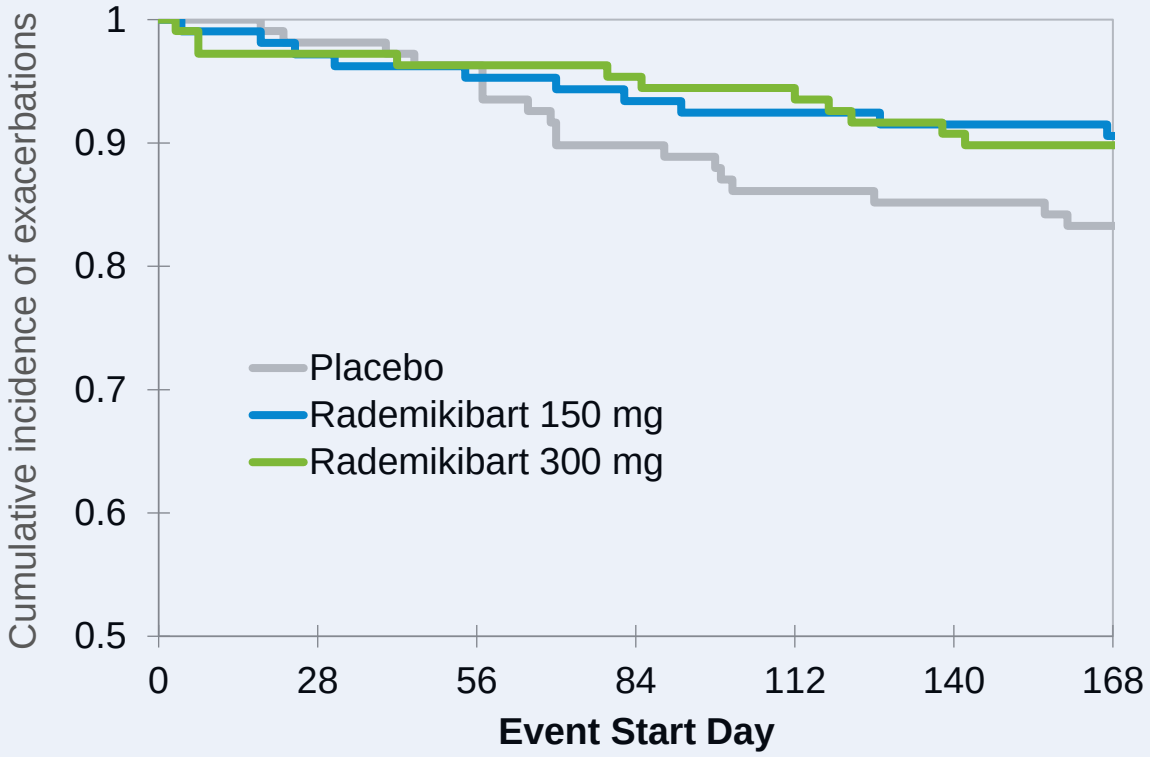
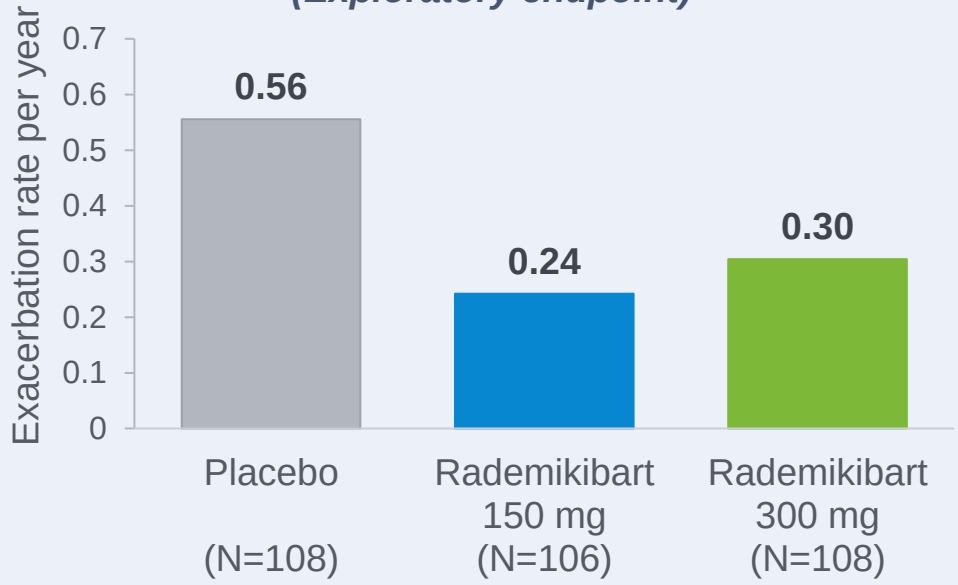
Time to exacerbation
(Secondary endpoint)



Annualized exacerbation rate
(Exploratory endpoint)



	Placebo (N=108)	Rademikibart 150 mg (N=106)	Rademikibart 300 mg (N=108)
Total exacerbations through 24 weeks*	26	11	13
Patients with exacerbation through 24 weeks*	16.7%	7.5%	9.3%

*Secondary endpoints.

Exacerbation defined as hospitalization or urgent medical care due to asthma, treatment with approximately 4 times the patient's normal dose of inhaled corticosteroids, or treatment with systemic steroids. Population asthma exacerbation rate is calculated as total number of asthma exacerbations while subjects were on treatment divided by total duration of treatment in years.

Safety summary

No new safety signals vs previous rademikibart trials

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n (%) patients	Placebo (N = 108)	Rademikibart 150 mg Q2W (N = 106)	Rademikibart 300 mg Q2W (N = 108)
At least one TEAE	64 (59.3)	78 (73.6)	77 (71.3)
Serious	3 (2.8)	2 (1.9)	3 (2.8)
Grade 3 or 4	4 (3.7)	3 (2.8)	3 (2.8)
Leading to death	0	0	0
Leading to discontinuation	2 (1.9)	4 (3.8)	3 (2.8)
TEAEs (preferred terms) occurring in ≥5% of patients in the overall population			
COVID-19	11 (10.2)	10 (9.4)	16 (14.8)
Cough	18 (16.7)	7 (6.6)	14 (13.0)
Dyspnea	13 (12.0)	9 (8.5)	11 (10.2)
Asthma	10 (9.3)	8 (7.5)	8 (7.4)
Wheezing	11 (10.2)	8 (7.5)	7 (6.5)
Nasopharyngitis	5 (4.6)	6 (5.7)	6 (5.6)
Adverse events of particular interest			
Injection site reactions (lasting >24 hr)* Injection site erythema Injection site pruritus Injection site reaction	0 0 0 0	14 (13.2) 5 (4.7) 4 (3.8) 4 (3.8)	8 (7.4) 4 (3.7) 3 (2.8) 3 (2.8)
Conjunctivitis	0	1 (0.9)	1 (0.9)

*Injection site reactions were mainly Grade 1 (mild) – the three most common injection site reaction preferred terms are shown. TEAE, treatment-emergent adverse event.

Conclusions

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Rademikibart improved lung function and asthma control

Significant improvements in lung function with rademikibart

- At Week 12 (**primary endpoint**), placebo-adjusted FEV_1 improved by **+140 mL (150 mg Q2W)** and **+189 mL (300 mg Q2W)** in the overall population
- Placebo-adjusted FEV_1 improved by **+328 mL (300 mg Q2W)** at Week 12 in patients with ≥ 300 eosinophils/μL at baseline
- **Improvement was rapid** (as early as **Week 1**) and **sustained through 24 weeks**

Strong trends in reductions in exacerbations with rademikibart

- Prolonged time to exacerbation
- Reduced the annual exacerbation rate by ~50% vs placebo

Improved asthma control with rademikibart

- ACQ scores numerically separated from placebo at Week 1, with significant differences from Weeks 2–24

Safety

- Rademikibart was generally well tolerated in the 24-week treatment period

ACQ, Asthma Control Questionnaire. FEV_1, Forced expiratory volume in one second. Q2W, every other week.

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