

Rapid Improvement in Lung Function Observed with Rademikibart in Patients with Moderate-to-Severe Uncontrolled Asthma

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Introduction

Asthma in the USA

- More than 26 million Americans are estimated to be burdened with asthma symptoms.¹
- Approximately 40% of people with asthma experience acute attacks per year in the USA, with severe cases requiring urgent intervention to prevent hospitalization and death.^{1,3}
- In an observational study of US adults with asthma, 36% (based on Asthma Control Test) and 56% (based on ACO-6) had inadequately controlled disease when treated with fixed-dose ICS/LABA, which was associated with greater HCRU.⁴
- Asthma directly costs the USA >\$50 billion annually, with up to 37.5% attributable to uncontrolled severe asthma.⁵⁻⁷

Rademikibart results in sustained relief from asthma – how rapid is the onset?

- Rademikibart, a mAb and next-generation IL-4R α inhibitor, blocks both IL-4 and IL-13 signaling.⁸
- In a global phase 2b trial of rademikibart therapy for moderate-to-severe uncontrolled asthma (CBP-201-WW002; NCT04773678), in-clinic spirometry demonstrated significant lung function improvements at first assessment (Week 1), sustained across 24 weeks of treatment.⁹
- During the phase 2b trial, at-home spirometry readings were also collected, notably at timepoints before the first in-clinic spirometry reading at Week 1, thus allowing assessment of how rapidly rademikibart exerts its effects on lung function.

Objective

Using self-administered at-home spirometry at timepoints during Week 1, we examined rademikibart's ability to rapidly improve lung function, when administered as a single 600 mg loading dose in patients with uncontrolled moderate-to-severe asthma in the phase 2b trial (CBP-201-WW002; NCT04773678). We thereby investigated the potential of rademikibart as a fast-acting therapy for acute exacerbations.

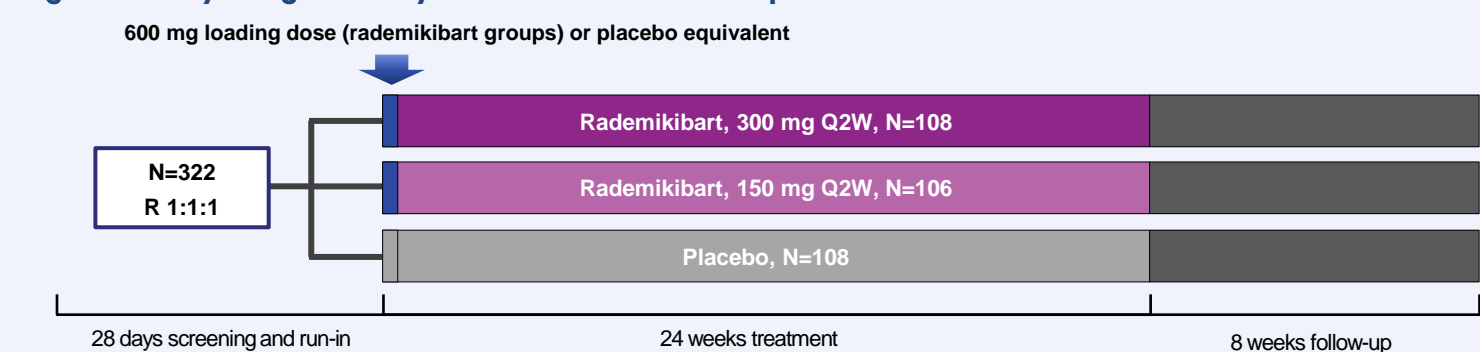
For comparison, prespecified in-clinic prebronchodilator FEV₁ at Week 12 (primary endpoint) and other timepoints (secondary endpoints) are also reported.

Methodology

This global phase 2b trial was conducted with 322 patients, randomized 1:1:1 to rademikibart 150 mg Q2W or 300 mg Q2W or placebo, subcutaneously administered. Patients initially received a 600 mg loading dose of rademikibart or equivalent for placebo (Figure 1). Patients were enrolled from April 2021 and completed the study by September 2023.

The *post hoc* endpoint of interest was absolute change from baseline (CFB) in the prebronchodilator FEV₁ from self-administered at-home spirometry during the first week of treatment (particularly in the first two days) in the overall population and by baseline eosinophil count subgroup.

Figure 1. Study design and key inclusion criteria for the phase 2b trial of rademikibart



Adults with moderate-to-severe uncontrolled asthma

- ACO-6 ≥ 15 and prebronchodilator FEV₁ 40–85% of predicted normal, at screening and baseline.
- Medium-to-high dose ICS 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, $\geq 4x$ baseline ICS dose, or hospitalization/emergency care).
- Patients were also initially required to have a screening blood eosinophil count of ≥ 150 cells/ μ L, with this inclusion criterion amended in the study protocol to enrich the population of patients with ≥ 300 cells/ μ L.

Results

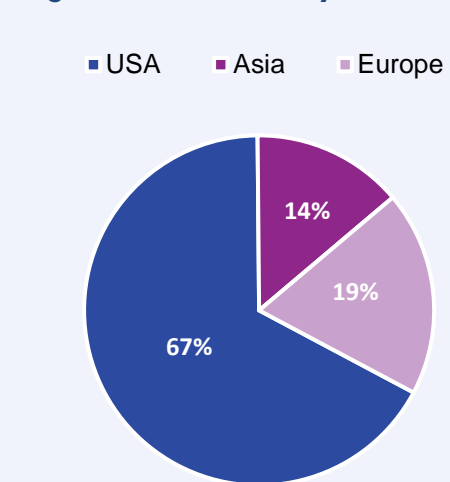
Baseline characteristics, including eosinophil counts, and patient disposition

In the phase 2b trial, baseline disease characteristics and demographics were generally comparable across the rademikibart and placebo groups (Table 1). Of 322 patients enrolled, 67% were in the USA (Figure 2). Overall, 88% of patients completed treatment at Week 24 (Figure 3).

Table 1. Baseline characteristics, including eosinophil counts

Characteristic*	Placebo (N=108)	Rademikibart 150 mg Q2W (N=106)	Rademikibart 300 mg Q2W (N=108)
In-clinic prebronchodilator FEV ₁ (mL)	1,836 (578)	1,908 (647)	1,902 (590)
At-home prebronchodilator FEV ₁ (mL)	1,783 (671)	1,845 (690)	1,928 (592)
Eosinophil counts (cells/ μ L)	299 (229)	268 (179)	320 (220)
Eosinophil counts, n (%)			
< 150 cells/ μ L	26 (24.1)	26 (24.5)	23 (21.3)
150 < 300 cells/ μ L	41 (38.0)	42 (39.6)	35 (32.4)
≥ 300 cells/ μ L	41 (38.0)	38 (35.8)	50 (46.3)
FeNO (ppb)	31.6 (31.5)	35.8 (35.1)	33.8 (32.7)
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)
Race, n (%)			
American Indian or Alaska Native	1 (0.9)	0	0
Asian	17 (15.7)	18 (17.0)	14 (13.0)
Black or African American	10 (9.3)	6 (5.7)	5 (4.6)
Native Hawaiian or other Pacific Islander	0	0	1 (0.9)
White	79 (73.1)	82 (77.4)	88 (81.5)
Other	1 (0.9)	0	0

Figure 2. Enrollment by location

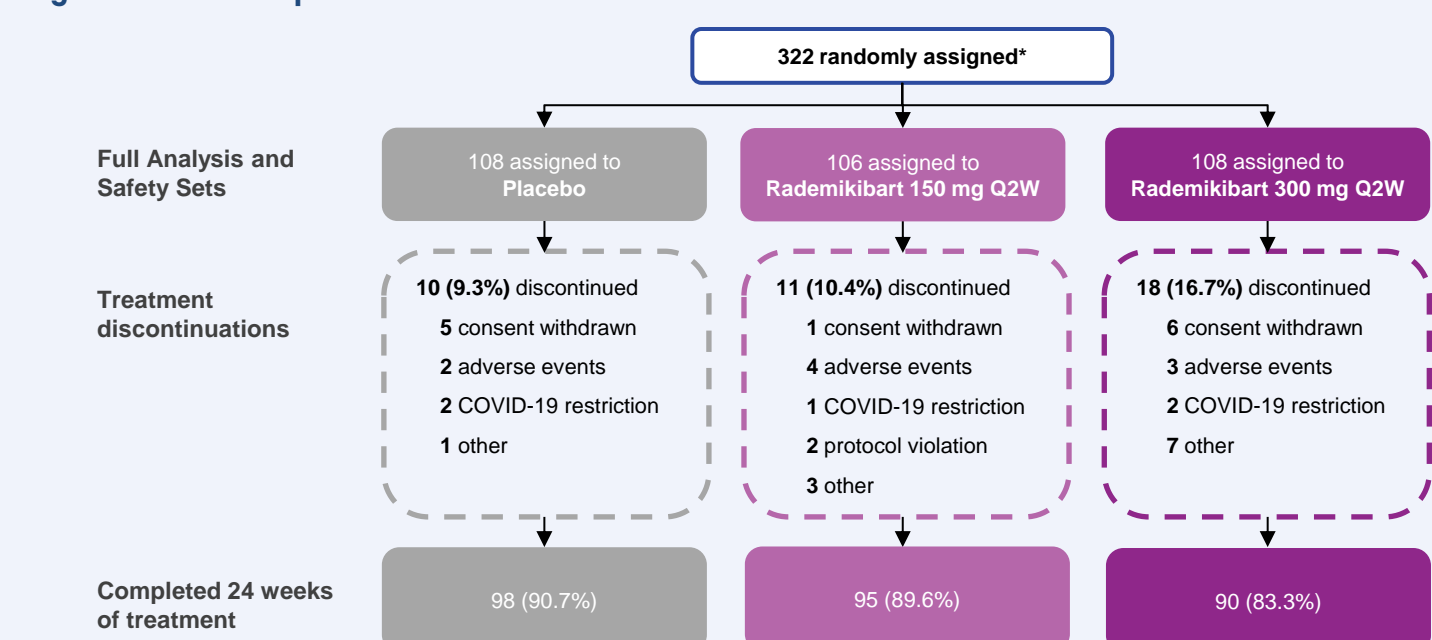


Patients were enrolled at 78 centers in five countries:

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

*Mean (standard deviation) at baseline, unless otherwise noted.

Figure 3. Patient disposition across 24 weeks of treatment

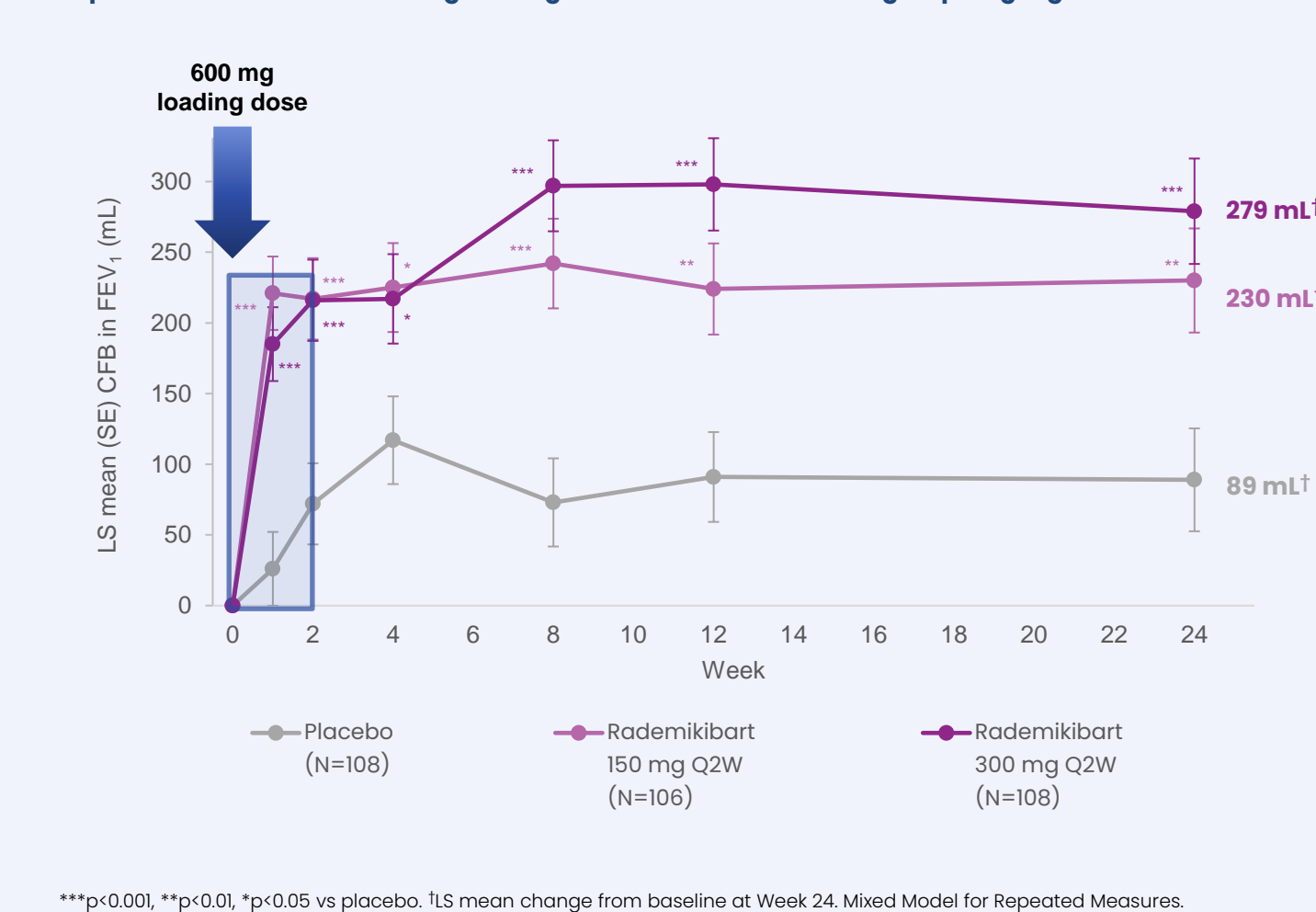


*All patients received at least one dose of study treatment.

Rademikibart resulted in rapid and substantial improvements in lung function, when assessed at 24 hours

- In-clinic spirometry demonstrated that most prebronchodilator FEV₁ improvement occurred by Week 1 of the 24-week treatment period (Figure 4).
 - At Week 1, FEV₁ improved by approximately 200 mL after single 600 mg loading doses in the two rademikibart groups.
 - At Week 24, FEV₁ improvement was sustained in the 150 mg Q2W and 300 mg Q2W groups, at 230 mL and 279 mL, respectively.
- In patients with EOS ≥ 300 cells/ μ L (entry criteria for on-going Phase 2 trials), lung function improved rapidly after administration of the 600mg loading dose (Figure 5), based on *post hoc* analysis of self-assessed prebronchodilator FEV₁.
 - FEV₁ improvements at 24 hr, 48 hr, and Week 1 (i.e. 168 hr) were 93 mL, 102 mL, and 121 mL, respectively; placebo adjusted FEV₁ improvements were 194 mL, 135 mL, and 162 mL, respectively (Figure 5a).
 - 77% and 84% of Week 1 benefit occurred by first and second assessments (24 hr and 48 hr, respectively) (Figure 4b).
- Of note, these self-administered at-home spirometry readings (Figure 5a) were lower than in prespecified analyses of in-clinic readings (Figure 4), possibly due to a lack of coaching by medical personnel.

Figure 4. In-clinic prebronchodilator FEV₁ change from baseline (CFB) across 24 weeks of treatment, with the time period after the initial 600 mg loading dose in the rademikibart groups highlighted blue



***p<0.001, **p<0.01, *p<0.05 vs placebo. †LS mean change from baseline at Week 24. Mixed Model for Repeated Measures.

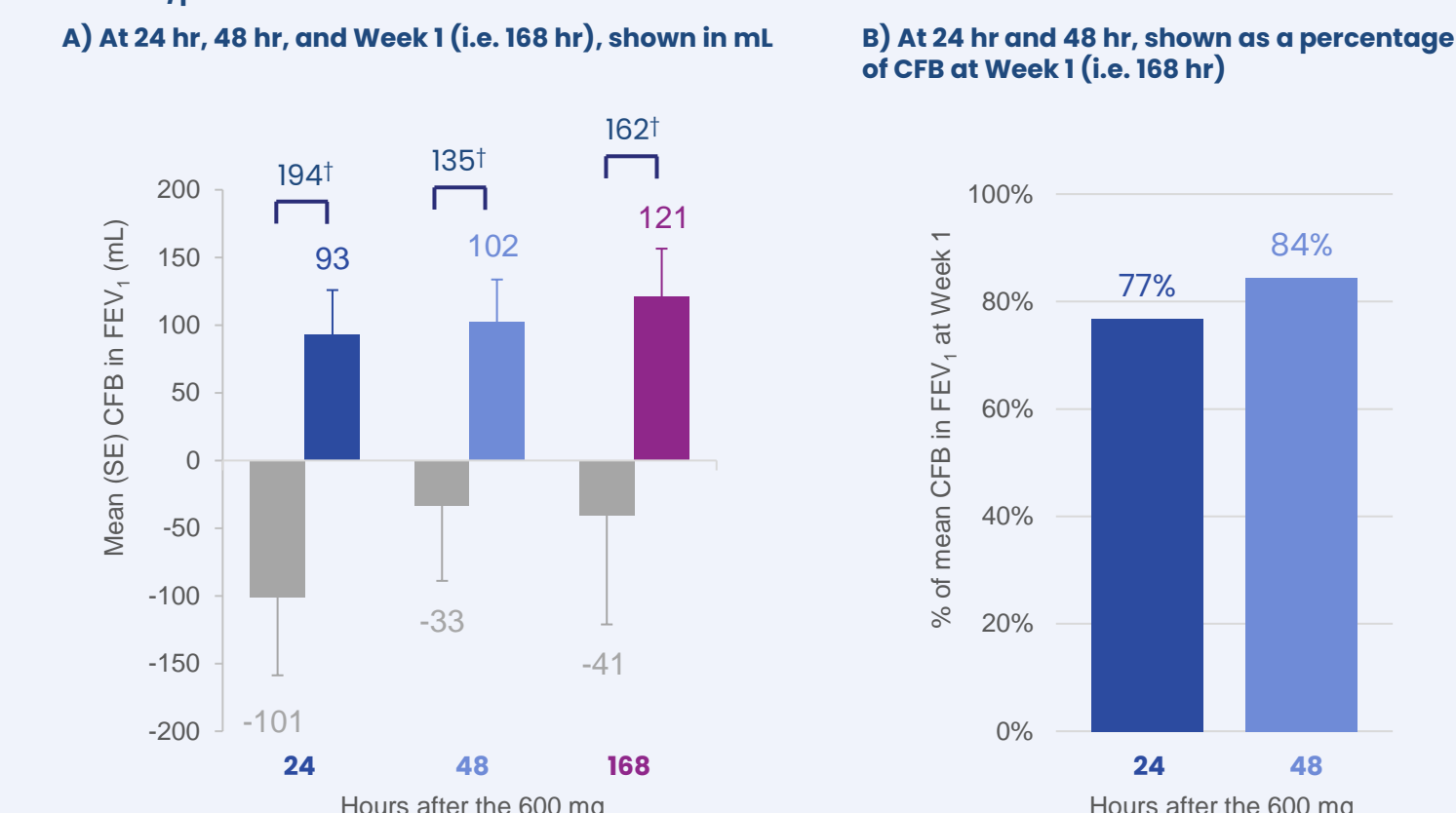
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Abbreviations: ACO-6, Six-Item Asthma Control Questionnaire (ACO-6 was measured as a validated ACO incorporating patient-reported questions and FEV₁, without an albuterol component); CFB, change from baseline; CS, corticosteroid; EOS, eosinophils; FeNO, fractional exhaled nitric oxide; FEV₁, Forced Expiratory Volume in one second; HCRU, healthcare resource use; ICS, inhaled corticosteroid; IL, interleukin; IL-4R α , IL-4 receptor alpha; LABA, long-acting β_2 -agonist; LS, least squares; mAb, monoclonal antibody; Q2W, every 2 weeks; R, randomized; SE, standard error; SOC, System Organ Class; TEAE, treatment-emergent adverse event.

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Figure 5. Self-assessed prebronchodilator FEV₁ change from baseline (CFB) after the 600 mg load dose of rademikibart (colored bars) or equivalent placebo (gray bars) in patients with baseline eosinophil counts ≥ 300 cells/ μ L

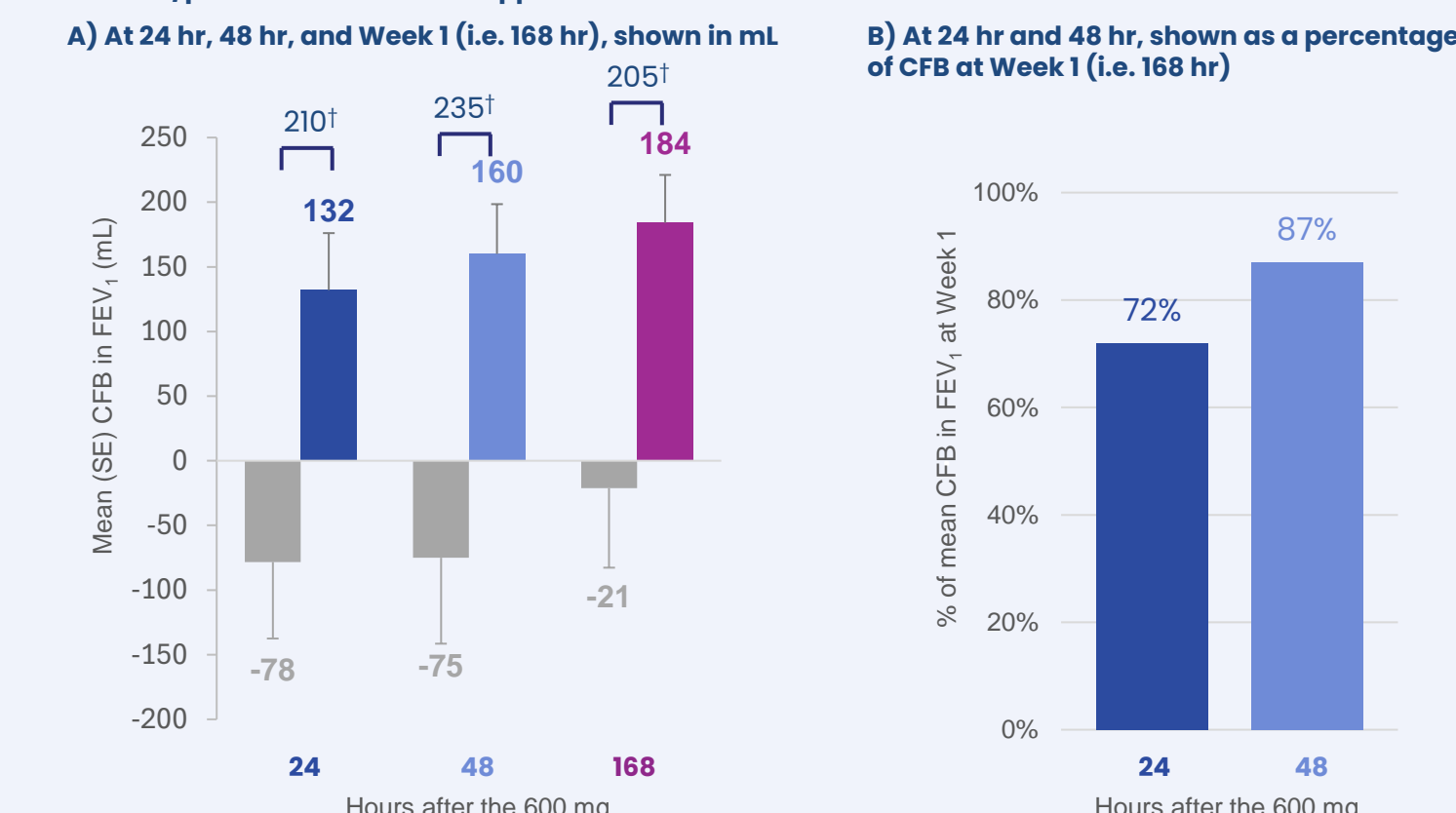


- At baseline, mean (standard deviation) self-assessed FEV₁ = 1773 mL (660 mL) for placebo (N=41) and 1873 mL (616 mL) for rademikibart (N=88).
- †At 24 hr, 48 hr, and 168 hr, p=0.001, p=0.0094, and p=0.018, respectively. P-values are based on LS means and obtained from ANCOVA which is adjusted by treatment, blood eosinophil stratification factor from RTSM (≥ 300 cells/ μ L or < 300 cells/ μ L), baseline weight, baseline height, baseline FeNO, and baseline measure of Morning Pre-bronchodilator (trough) FEV₁.

Greater improvements in lung function were observed in patients with elevated baseline eosinophil counts and increased FeNO levels, markers of type 2 inflammation

- Improvements in self-assessed prebronchodilator FEV₁ were greater in patients with elevated eosinophil counts ≥ 300 cells/ μ L and a FeNO level ≥ 25 ppb (high EOS/high FeNO) (Figure 6a), compared with the analysis of the population with EOS < 300 cells/ μ L (Figure 5a).
- In the high EOS/high FeNO subgroup (N=77), at 24 hr, 48 hr, and Week 1 (i.e. 168 hr) were 132 mL, 160 mL, and 184 mL, respectively; placebo adjusted improvements in FEV₁ were 210 mL, 235 mL, and 205 mL, respectively (Figures 6a).
- Also, in the high EOS/high FeNO subgroup, most self-assessed FEV₁ improvement at Week 1 occurred at first assessment, 72% at 24 hr and 87% at 48 hr (Figure 6b), which was consistent with observations with the analysis of the population with EOS ≥ 300 cells/ μ L (Figure 5b).
- In these patients, the exacerbation rate was reduced by 63% (p=0.02) to 73% (p=0.04) with the 150 mg and 300 mg doses respectively.

Figure 6. Self-assessed prebronchodilator FEV₁ change from baseline (CFB) after the 600 mg load dose of rademikibart (colored bars) or equivalent placebo (gray bars) in patients with baseline eosinophil counts ≥ 300 cells/ μ L and a FeNO level ≥ 25 ppb



- At baseline, mean (standard deviation) self-assessed FEV₁ = 1540 mL (483 mL) for placebo (N=23) and 1702 mL (547 mL) for rademikibart (N=57).
- †At 24 hr, 48 hr, and 168 hr, p=0.0009, p=0.0002, and p=0.0012, respectively. P-values are based on LS means and obtained from ANCOVA which is adjusted by treatment, blood eosinophil stratification factor from RTSM (≥ 300 cells/ μ L or < 300 cells/ μ L), baseline weight, baseline height, baseline FeNO, and baseline measure of Morning Pre-bronchodilator (trough) FEV₁.

Rademikibart was generally well tolerated

- Treatment-emergent adverse events (TEAEs) were comparable per treatment group.
- Most TEAEs were Grade 1 (mild) or Grade 2 (moderate) in intensity (Table 2).
- No eosinophilia TEAEs (Preferred Term) were observed. Two patients (300 mg group) experienced non-serious Grade 1 'eosinophil count increased' (n=2) and 'eosinophil percentage increased' (n=1) and did not discontinue treatment.
- Of 322 patients, 86% completed 24 weeks of either dose of rademikibart treatment, compared with 91% for placebo (Figure 3), and few patients discontinued due to TEAEs (n=9) (Table 2 and Figure 3).
 - All TEAEs resulting in discontinuation resolved, except for a resolving case of hepatomegaly (300 mg group) that was not related to treatment.
 - All TEAEs resulting in discontinuation were Grade 2, except for Grade 1 transaminases increased (150 mg group) and Grade 3 asthma (placebo group), neither of which was related to treatment.
- No treatment-related serious TEAEs were reported in the rademikibart groups, and the proportions of patients experiencing serious TEAEs (1.9–2.8% were comparable per treatment group) (Table 2).
- In the 'General Disorders and Administration Site Conditions' SOC, an imbalance was observed in TEAEs related to treatment, due to the occurrence of mostly Grade 1 (mild) injection site reactions. In the SOC, all TEAEs were Grade ≤ 2 .
- Two patients experienced conjunctivitis (one per rademikibart group), which were Grade 2 (moderate) and did not lead to treatment discontinuation.

Table 2. Adverse events per treatment group

n (%) patients	Placebo (N=108)	Rademikibart 150 mg Q2W (N=106)	Rademikibart 300 mg Q2W (N=108)
At least one TEAE	64 (59.3)	77 (72.6)	76 (70.4)
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)
Eosinophilia (Preferred Term)	0	0	0
TEAEs (preferred terms) occurring in $\geq 5\%$ 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)
Serious TEAEs (none were related to treatment with rademikibart)			
Any serious TEAE	3 (2.8)	2 (1.9)	3 (2.8)
Asthma	2 (1.9)	1 (0.9)	1 (0.9)
Acute respiratory failure	0	1 (0.9)	0
COVID-19 pneumonia	0	1 (0.9)	0
Otitis media acute	1 (0.9)	0	0
Pancreatic mass	0	0	1 (0.9)
Bile duct stone	0	0	1 (0.9)
Anxiety disorder	0	1 (0.9)	0
TEAEs of particular interest			
Injection site reactions (lasting >24 hr)*	0	14 (13.2)	8 (7.4)
Injection site erythema	0	5 (4.7)	4 (3.7)
Injection site pruritus	0	4 (3.8)	3 (2.8)
Injection site reaction	0	4 (3.8)	4 (3.8)
Conjunctivitis	0	1 (0.9)	1 (0.9)

*Injection site reactions were mostly Grade 1 (mild) – the three most common injection site reaction preferred terms are shown.

Conclusions

- Rademikibart rapidly improved lung function (FEV₁) during the initial week of treatment, and most FEV₁ increase was observed within 24 hours, as demonstrated in *post hoc* analyses of self-administered spirometry data.
- These rapid improvements in at-home, self-administered FEV₁ readings during the first 24 hours of treatment are compatible with prespecified observations of FEV₁ improvements at first in-clinic assessment (Week 1) that were subsequently sustained throughout the treatment period (Week 24).
- Self-administered at-home spirometry readings were lower than the in-clinic readings, possibly due to a lack of coaching by medical personnel.
- These findings support rademikibart's potential as an effective therapy for patients with type 2 inflammation-driven asthma, providing both fast-acting and sustained improvements in lung function.
- Thus, these results indicate a possible use for rademikibart in the early treatment setting following an acute exacerbation and support two ongoing Phase 2 studies examining rademikibart treatment immediately following an exacerbation of asthma (NCT06940154) or COPD (NCT06940154).
- Visit Booth CT-2 (ATS 2025) for more information

