

# Efficacy of Rademikibart in COPD-like Patients: Sub-analyses from the Phase 2b Trial in Patients with Moderate-to-Severe Asthma

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## Introduction

### COPD in the USA

- An estimated 6% of the US adult population (~16 million people) has received a COPD diagnosis and ~8% of Americans of any age (>26 million people) are burdened by asthma.<sup>1-4</sup>
- According to CDC data, people with COPD have an increased likelihood of a past asthma diagnosis (odds ratio = 3.6).<sup>5</sup>
- CDC data also demonstrate that COPD is a leading cause of mortality and morbidity in the USA, with greater proportions unable to work (24.3% vs 5.3%) and have difficulty walking/climbing stairs (38.4% vs 11.3%), relative to adults without COPD.<sup>1-3</sup>

### Rademikibart demonstrates efficacy for asthma – could patients with COPD benefit too?

- Rademikibart, a mAb and next-generation IL-4R $\alpha$  inhibitor, blocks both IL-4 and IL-13 signaling.<sup>5</sup>
- In a published global phase 2b trial (CBP-201-WW002; NCT04773678), rademikibart demonstrated rapid and significant improvement in lung function in the first week, which was sustained through 24-weeks of treatment, in adults with moderate-to-severe uncontrolled asthma.<sup>6</sup>
- Recent evidence suggests that IL-4R $\alpha$  inhibition may be a therapeutic option for eosinophilic-driven COPD.<sup>7-9</sup>

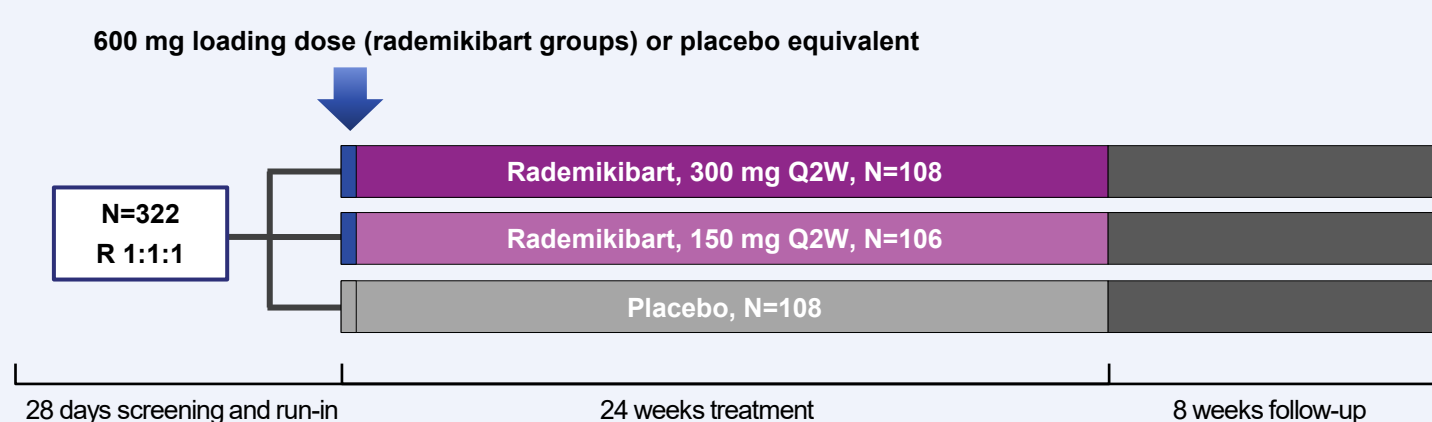
## Objective

Using data from the phase 2b trial of rademikibart therapy for uncontrolled moderate-to-severe asthma (CBP-201-WW002; NCT04773678), we conducted *post hoc* analyses to assess rademikibart's efficacy in a subset of COPD-like patients.

## Methodology

The parent phase 2b trial was a global study conducted with 322 adults with moderate-to-severe uncontrolled asthma (Figure 1). Patients were enrolled in the USA (67%), Europe (19%), or Asia (14%) from April 2021 and completed the study by September 2023.

**Figure 1. Prespecified study design for the parent phase 2b trial of rademikibart therapy, showing randomization of the overall trial population of adults with moderate-to-severe asthma (N=322)**



For the current *post hoc* subgroup analyses, 68 out of the 322 patients were classified as COPD-like patients, defined as having asthma onset after 40 years of age and post-bronchodilator FEV<sub>1</sub>/FVC ratio <0.7 during screening (Figure 2).

**Figure 2. Post hoc selection of the COPD-like patient subgroup (N=68) from the parent phase 2b trial of rademikibart therapy in patients with moderate-to-severe asthma (N=322)**

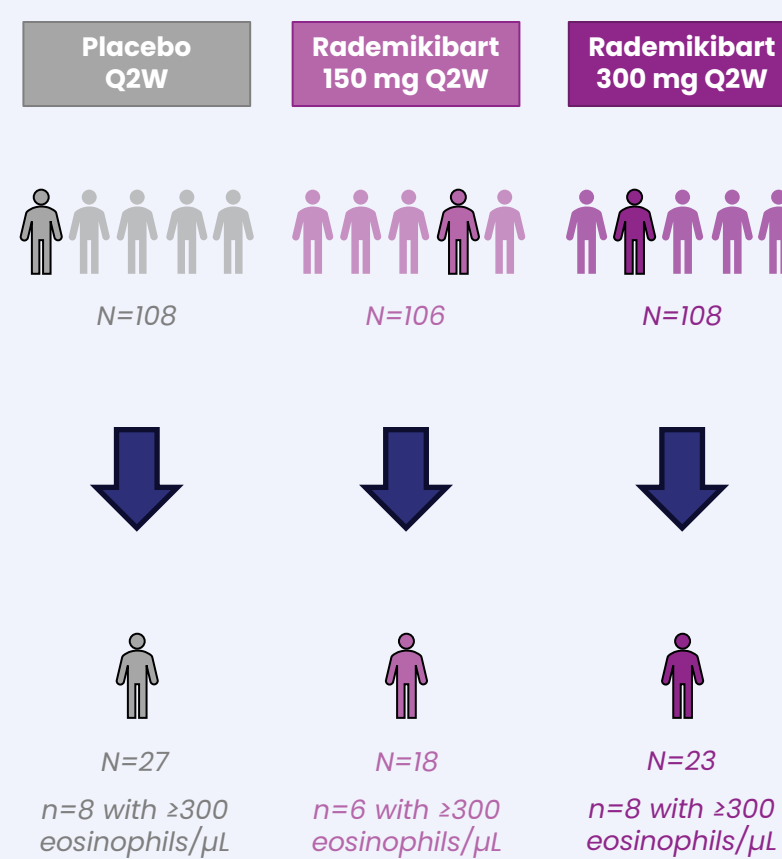
### Adults with moderate-to-severe asthma (N=322)

#### Key inclusion criteria:

- ACQ-6  $\geq 1.5$  and prebronchodilator FEV<sub>1</sub> 40–85% of predicted normal, at screening and baseline
- Medium-to-high dose ICS and reliever/controller for  $\geq 90$  days (stable dose  $\geq 28$  days) at screening, maintained in the study without dose adjustment
- $\geq 1$  asthma exacerbation in the past year (requiring systemic CS,  $\sim 4\times$  baseline ICS dose, or hospitalization/emergency care)
- Patients were initially required to have a screening blood eosinophil count  $\geq 150$  cells/ $\mu$ L; this inclusion criterion was amended in the study protocol to enrich the patient population with  $\geq 300$  cells/ $\mu$ L

### COPD-like patient subgroup (N=68)

- 21% of the 322 patients with moderate-to-severe asthma were classified as COPD-like patients
- 'COPD-like' was defined as asthma onset after 40 years of age and post-bronchodilator FEV<sub>1</sub>/FVC ratio <0.7 during screening



## Results

### Baseline characteristics and disposition for COPD-like patients

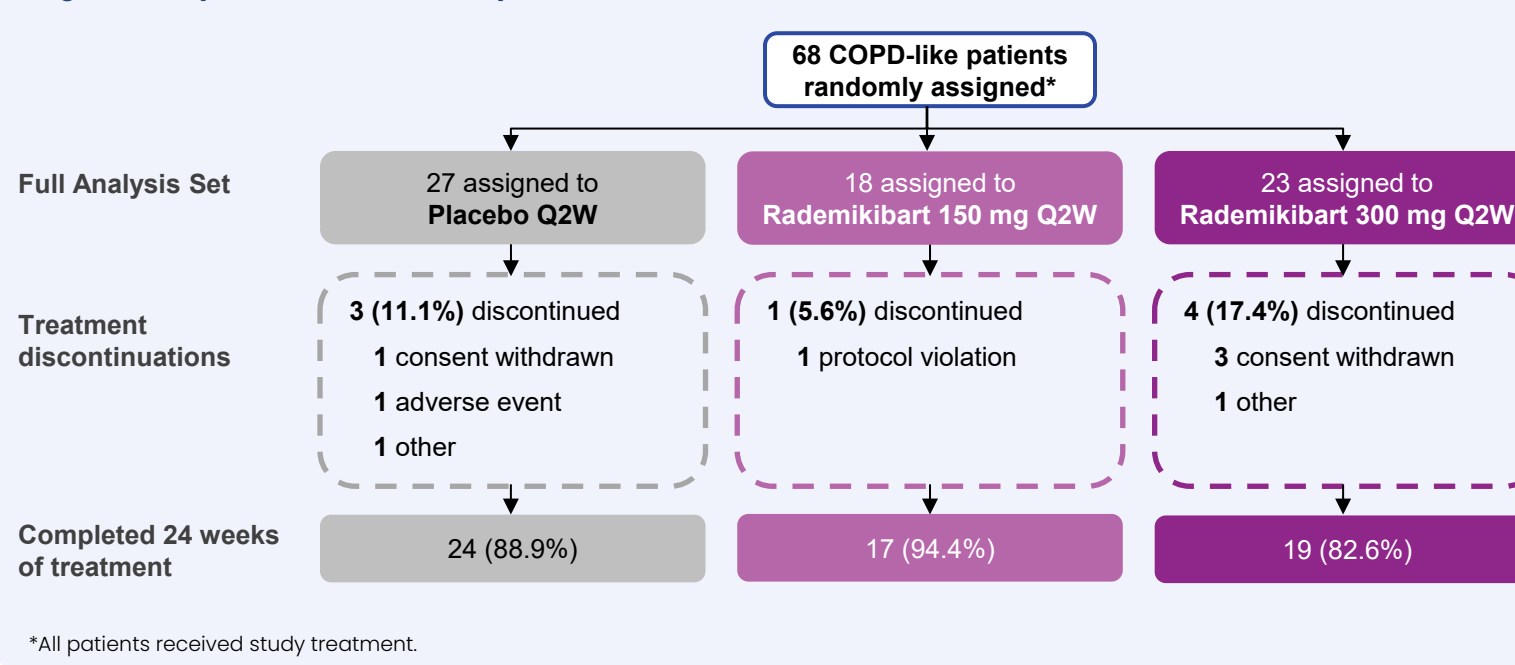
In COPD-like patients (N=68), baseline characteristics were generally comparable across the rademikibart and placebo groups (Table 1). The proportion of patients in the COPD-like subgroup that completed treatment at Week 24 (88%) (Figure 3) was the same as in the overall population (N=322) of patients with moderate-to-severe asthma in the parent phase 2b trial.

**Table 1. Baseline characteristics for COPD-like patients (N=68)**

Characteristic*	Placebo (N=27)	Rademikibart 150 mg Q2W (N=18)	Rademikibart 300 mg Q2W (N=23)
Age (years)	61.3 (6.1)	60.1 (6.1)	60.0 (7.4)
Female, n (%)	14 (51.9)	10 (55.6)	9 (39.1)
Body mass index (kg/m <sup>2</sup> )	28.5 (7.9)	26.8 (3.0)	27.1 (4.5)
Prebronchodilator FEV <sub>1</sub> (mL)	1,581 (428)	1,663 (444)	1,551 (314)
Percent predicted FEV <sub>1</sub>	58.9 (10.4)	60.2 (10.1)	56.4 (9.8)
Eosinophil counts (cells/ $\mu$ L)			
Mean (standard deviation)	278 (188)	265 (219)	325 (307)
Median (min – max)	240 (30 – 890)	220 (20 – 790)	240 (10 – 1370)
Eosinophil counts, n (%)			
< 150 cells/ $\mu$ L	4 (14.8)	6 (33.3)	6 (26.1)
150 < 300 cells/ $\mu$ L	15 (55.6)	6 (33.3)	9 (39.1)
< 300 cells/ $\mu$ L	19 (70.4)	12 (66.7)	15 (65.2)
$\geq 300$ cells/ $\mu$ L	8 (29.6)	6 (33.3)	8 (34.8)
Fractional exhaled nitric oxide (ppb)			
Mean (standard deviation)	27.8 (23.1)	44.6 (39.5)	32.1 (30.1)
Median (min – max)	19 (7.0 – 96.0)	30.5 (9.0 – 146.0)	21.0 (6.0 – 124.0)
Presence of atopic medical condition	12 (44.4)	7 (38.9)	6 (26.1)
Use of maintenance oral/systemic corticosteroids at randomization	6 (22.2)	0	2 (8.7)
Number of asthma exacerbations during 12 months before screening	1.1 (0.4)	1.2 (0.5)	1.1 (0.3)

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

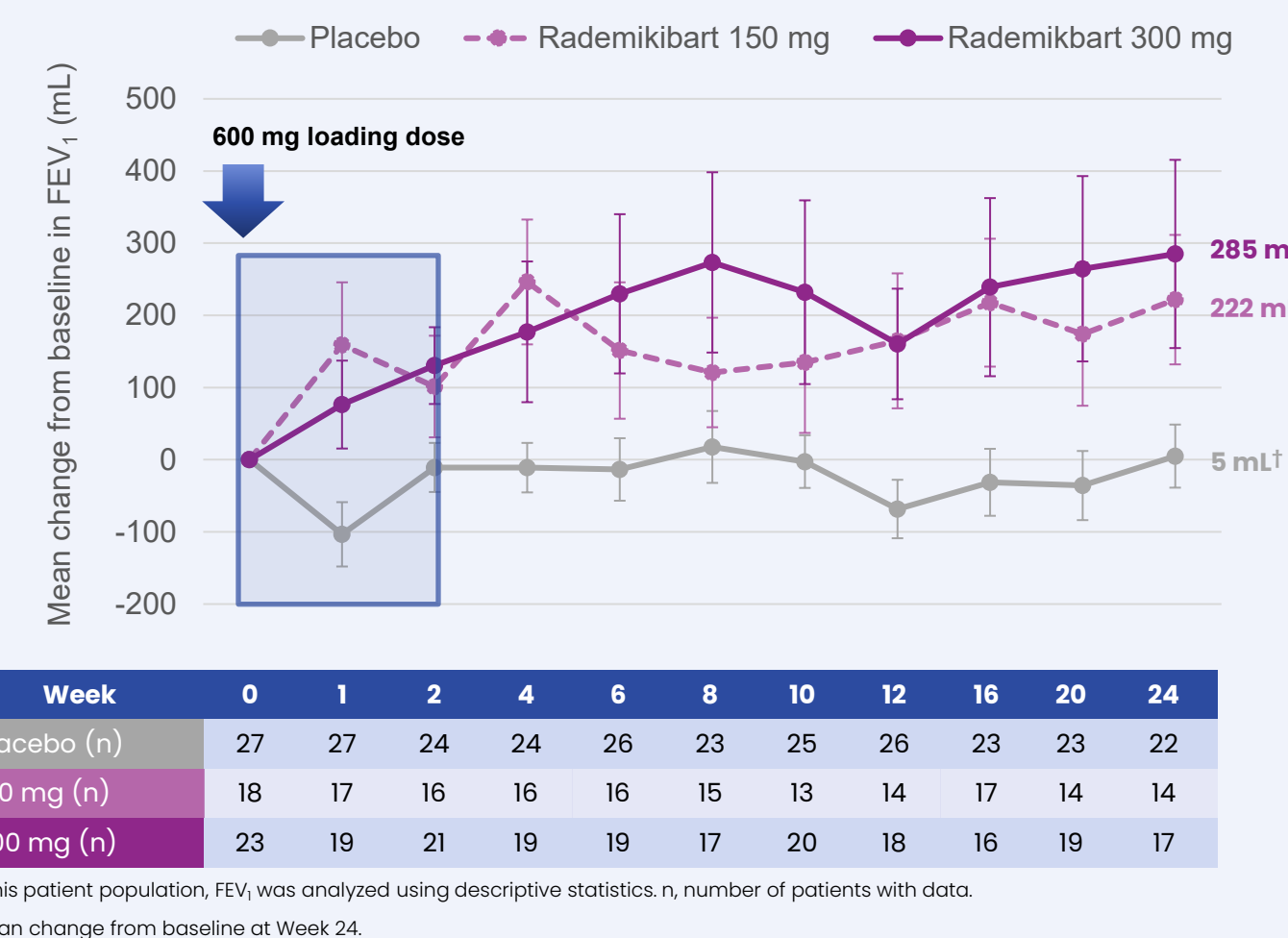
**Figure 3. Disposition of COPD-like patients (N=68) across 24 weeks of treatment**



### Rademikibart resulted in lung function improvements in COPD-like patients

- In COPD-like patients (N=68), prebronchodilator FEV<sub>1</sub> improved from first assessment, at Week 1, and was sustained through 24 weeks of treatment with rademikibart 150 mg Q2W or 300 mg Q2W (Figure 4).
- At Week 1, after a 600 mg rademikibart loading dose, mean FEV<sub>1</sub> (95% CI) improved from baseline by:
  - 159 mL (-25, 343) in the rademikibart 150 mg Q2W arm.
  - 76 mL (-52, 204) in the rademikibart 300 mg Q2W arm.
- At Week 24, after rademikibart Q2W dosing, mean FEV<sub>1</sub> (95% CI) improved further from baseline by:
  - 222 mL (28, 416) in the rademikibart 150 mg Q2W arm.
  - 285 mL (87, 562) in the rademikibart 300 mg Q2W arm.

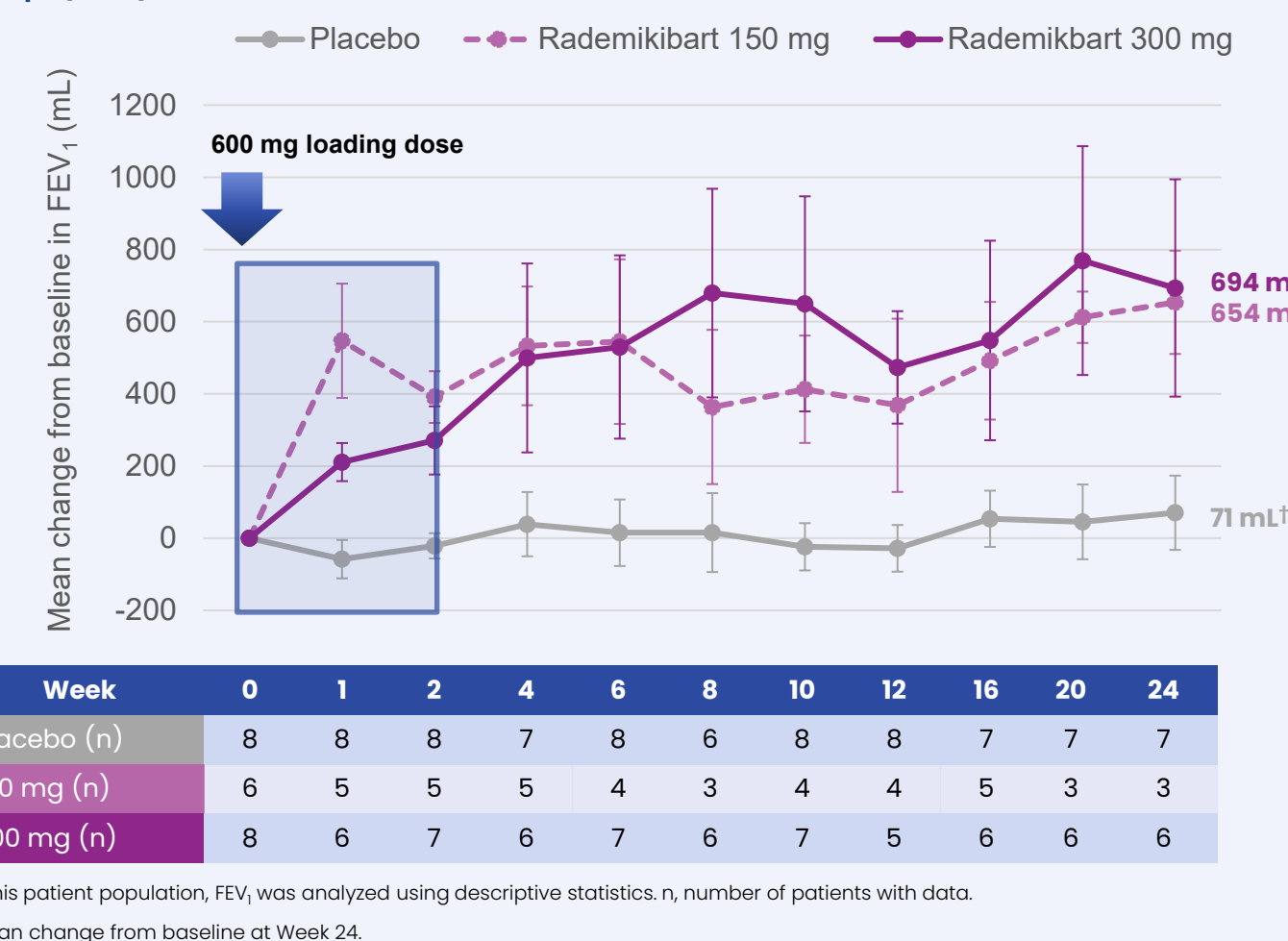
**Figure 4. Change from baseline in prebronchodilator FEV<sub>1</sub> in COPD-like patients (N=68)**



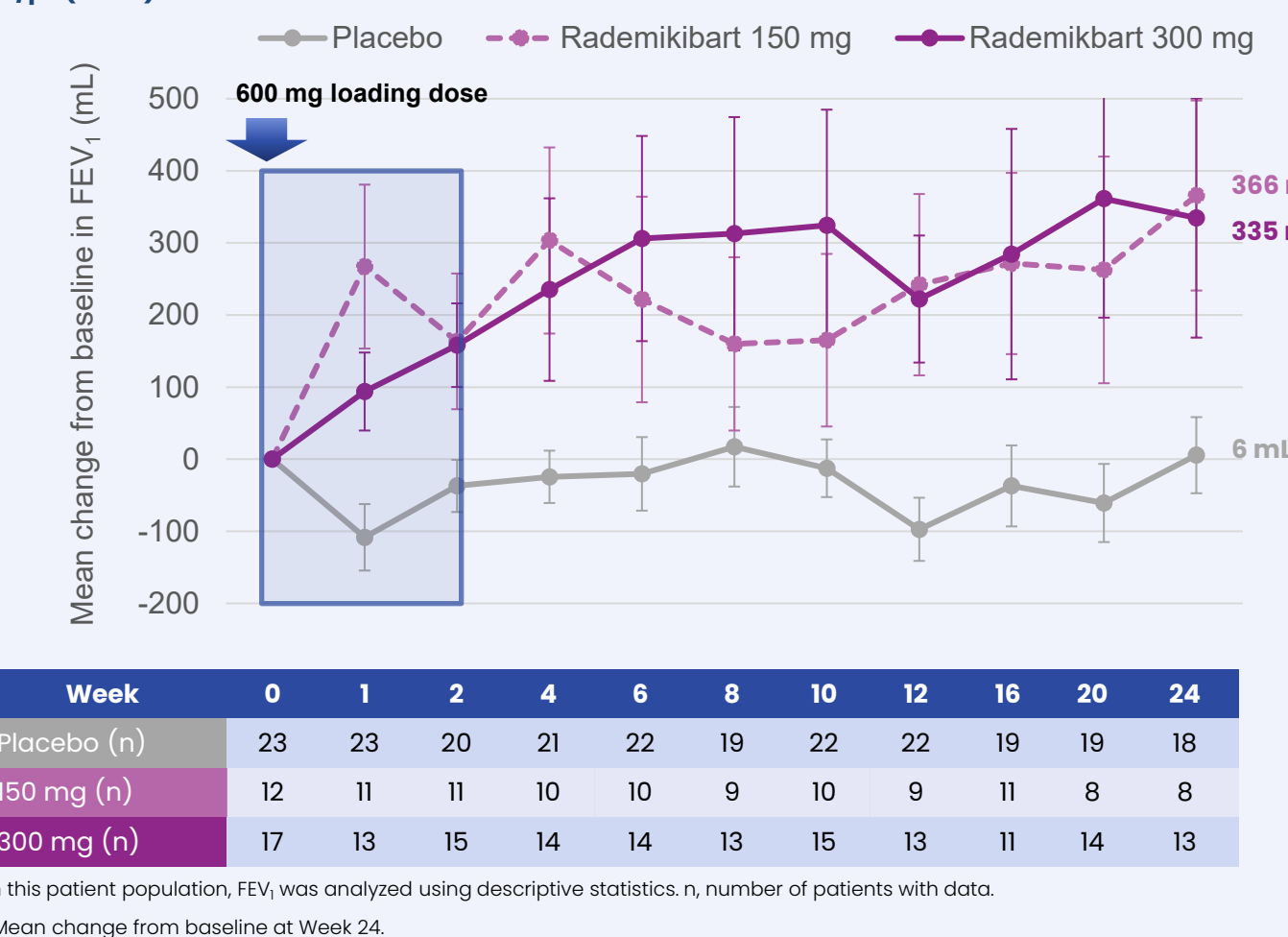
### Greatest improvements occurred in patients with elevated baseline eosinophils

- Throughout 24 weeks of treatment with rademikibart, COPD-like patients with elevated baseline eosinophil counts experienced the greatest improvements in prebronchodilator FEV<sub>1</sub> (Figures 5 and 6), potentially with ACQ-6 score improvement (Figure 7).
- At Week 24, mean FEV<sub>1</sub> (95% CI) improved from baseline, in patients with eosinophil counts  $\geq 300$  cells/ $\mu$ L (Figure 5), by:
  - 654 mL (38, 1269) in the rademikibart 150 mg Q2W arm.
  - 694 mL (-81, 1468) in the rademikibart 300 mg Q2W arm.
- At Week 24, mean FEV<sub>1</sub> (95% CI) improved from baseline, in patients with eosinophil counts  $\geq 150$  cells/ $\mu$ L (Figure 6), by:
  - 366 mL (54, 678) in the rademikibart 150 mg Q2W arm.
  - 335 mL (-27, 696) in the rademikibart 300 mg Q2W arm.

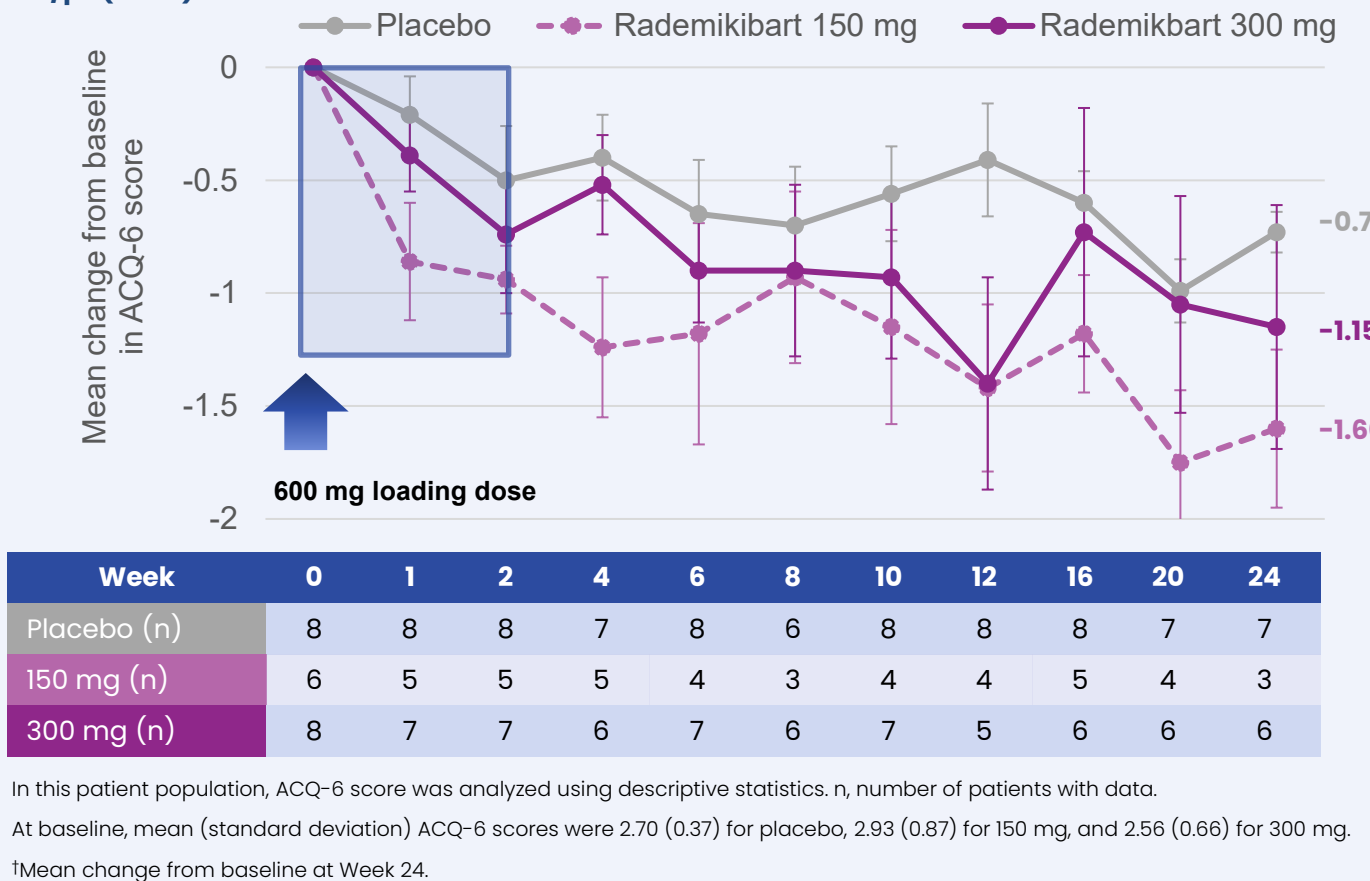
**Figure 5. Change from baseline in prebronchodilator FEV<sub>1</sub> in COPD-like patients with baseline eosinophil counts  $\geq 300$  cells/ $\mu$ L (N=22)**



**Figure 6. Change from baseline in prebronchodilator FEV<sub>1</sub> in COPD-like patients with baseline eosinophil counts  $\geq 150$  cells/ $\mu$ L (N=52)**



**Figure 7. Change from baseline in ACQ-6 score in COPD-like patients with baseline eosinophil counts  $\geq 300$  cells/ $\mu$ L (N=22)**



## Conclusions

- Rademikibart has previously shown statistically significant and clinically meaningful efficacy in patients with moderate-to-severe asthma, in prespecified analyses of the published phase 2b trial.<sup>6</sup>
- In the prespecified analyses, patients with asthma benefited from rapid and sustained improvements in lung function (prebronchodilator FEV<sub>1</sub>) and asthma control (ACQ-6 scores).<sup>6</sup>
- Here, we reported *post hoc* analyses in COPD-like patients from the phase 2b trial.
- Although patient numbers were limited, these *post hoc* analyses suggest that rademikibart may also have the potential to improve outcomes for patients with COPD, with greatest improvements in patients with elevated baseline eosinophil counts.
- These observations, combined with other recently published clinical evidence with IL-4R $\alpha$  inhibition,<sup>7-9</sup> support further examination of rademikibart in the treatment of patients with COPD, particularly in those with eosinophilic-driven COPD.