

Dupilumab Improves Lung Function and Asthma Control While Reducing Systemic Corticosteroid Use in Patients With Allergic Bronchopulmonary Aspergillosis: The Phase 2 LIBERTY ABPA AIRED Study

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Asthma

Conclusion

Dupilumab treatment vs placebo significantly improved lung function, substantially reduced severe respiratory exacerbations and SCS use, and improved quality of life in patients with asthma and ABPA during the 24- to 52-week treatment period

Objectives

The phase 2 LIBERTY ABPA AIRED study (NCT04442269) evaluated the efficacy and safety of dupilumab in patients with asthma and ABPA

Background

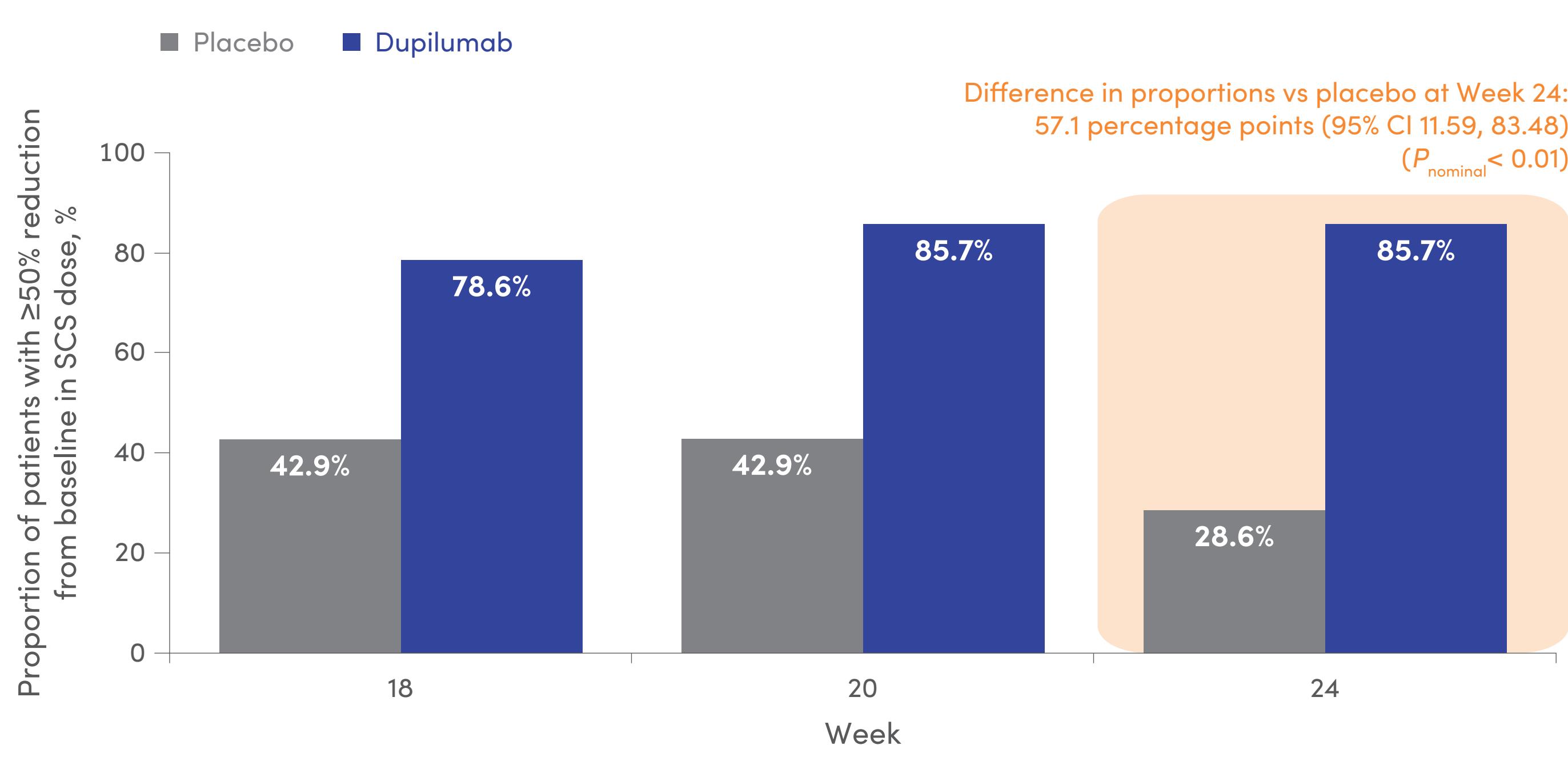
- Allergic bronchopulmonary aspergillosis (ABPA) is a rare progressive lung disease that affects 2.5% of patients with asthma globally¹
- ABPA is characterized primarily by hypersensitivity to, and airway colonization with, *Aspergillus fumigatus* in patients with asthma and a robust type 2 inflammatory response, as well as increased IgE levels, and elevated blood eosinophil counts²⁻⁴
- Patients with asthma and ABPA often receive SCS and experience more severe clinical outcomes than those without ABPA, highlighting the need for treatments that address the immunological basis of ABPA^{3,5,6}

Results

Key baseline characteristics

Characteristic	Placebo N = 27	Dupilumab N = 35	Total N = 62
Age, mean (SD), years	57.1 (14.38)	61.2 (8.62)	59.4 (11.56)
Female, n (%)	17 (63.0)	22 (62.9)	39 (62.9)
Pre-bronchodilator FEV ₁ , mean (SD), L	1.83 (0.58)	1.95 (0.68)	1.90 (0.63)
Pre-bronchodilator ppFEV ₁ , mean (SD), %	64.4 (18.5)	71.4 (25.7)	68.3 (22.9)
Severe respiratory exacerbations requiring SCS in the 12 months prior to screening, n (%)			
≤1	20 (74.1)	23 (65.7)	43 (69.4)
2	6 (22.2)	5 (14.3)	11 (17.7)
>2	1 (3.7)	7 (20.0)	8 (12.9)
SGRQ total score, mean (SD)	51.3 (17.2)	52.4 (15.3)	51.9 (16.0)
Biomarkers, median (Q1–Q3)			
Blood eosinophil count, cells/µL	600 (230–1,260)	560 (180–800)	575 (230–890)
Total IgE, IU/mL	2,051 (693–4,206)	1,969 (1,005–3,475)	2,010 (1,005–3,475)
A. fumigatus-specific IgE, kU/L	52.5 (4.7–108.6)	39.9 (1.1–91.5)	44.4 (3.8–91.5)
FeNO, ppb	47.0 (18.0–63.0)	33.5 (19.0–54.0)	35.0 (18.5–60.0)
Medical history events			
Bronchiectasis, n (%)	3 (11.1)	3 (8.6)	6 (9.7)

Figure 3. Dupilumab vs placebo was associated with a higher proportion of patients with SCS dose reduction by ≥50% from baseline



FeNO, fractional exhaled nitric oxide; FEV₁, forced expiratory volume in 1 second; IgE, immunoglobulin E; LS, least squares; OCS, oral corticosteroid(s); ppb, parts per billion; ppFEV₁, percent predicted FEV₁; Q, quartile; q2w, every 2 weeks; RR, rate ratio; SCS, systemic corticosteroid(s); SD, standard deviation; SE, standard error; SGRQ, St. George's Respiratory Questionnaire.

Disclosures: Bourdin A: GSK – non-financial support during the conduct of the study; Acceleron Pharma, Actelion, Galapagos, Merck Sharp & Dohme, Novartis, Pulmonix, United Therapeutics, Vertex Pharmaceuticals – other; Boehringer Ingelheim – grants, personal fees; AstraZeneca, Chiesi, GSK, Regeneron Pharmaceuticals Inc., Sanofi – personal fees. Shah A: AstraZeneca, Gilead, Pfizer, Vertex Pharmaceuticals – grants; Gilead, Inamed, Pfizer – speaker fees; AstraZeneca, Mundipharma – advisory board member. Baxter CG: Nob Hill Therapeutics Ltd – strategic advisory board member. Davidescu L: AstraZeneca, Boehringer Ingelheim, Chiesi, Novartis, Sanofi – speaker fees. Paleczny H, Chiarappa JA, Fontenot A, Dakin P, Maloney J, Radin A: Regeneron Pharmaceuticals Inc. – employees and shareholders. Laws E, Robinson LB: Sanofi – employees, may hold stock and/or stock options in the company. Corren J: AstraZeneca, Genentech, Novartis, Regeneron Pharmaceuticals Inc., Sanofi – research grants, consultant; AstraZeneca, Genentech, Novartis – speaker fees.

Methods

- Patients aged ≥12 years^a with uncontrolled asthma^a (≥1 severe respiratory exacerbation requiring treatment with SCS, or hospitalization, or treatment in emergency department/urgent care within the past 12 months; or receiving long-term low-dose OCS) meeting clinical criteria for ABPA^b received dupilumab 300 mg or placebo q2w for 24–52 weeks
- The primary endpoint was change from baseline in pre-bronchodilator FEV₁ at Week 24, assessed through formal hypothesis testing
- Select secondary and exploratory endpoints included annualized rate of severe respiratory exacerbations, change from baseline in SGRQ score, and proportion of patients with ≥50% reduction in SCS dose, assessed through within-group, descriptive statistics

^aNo adolescents were enrolled in the trial.

Figure 1. Dupilumab vs placebo improved pre-bronchodilator FEV₁ over the 24- to 52-week treatment period

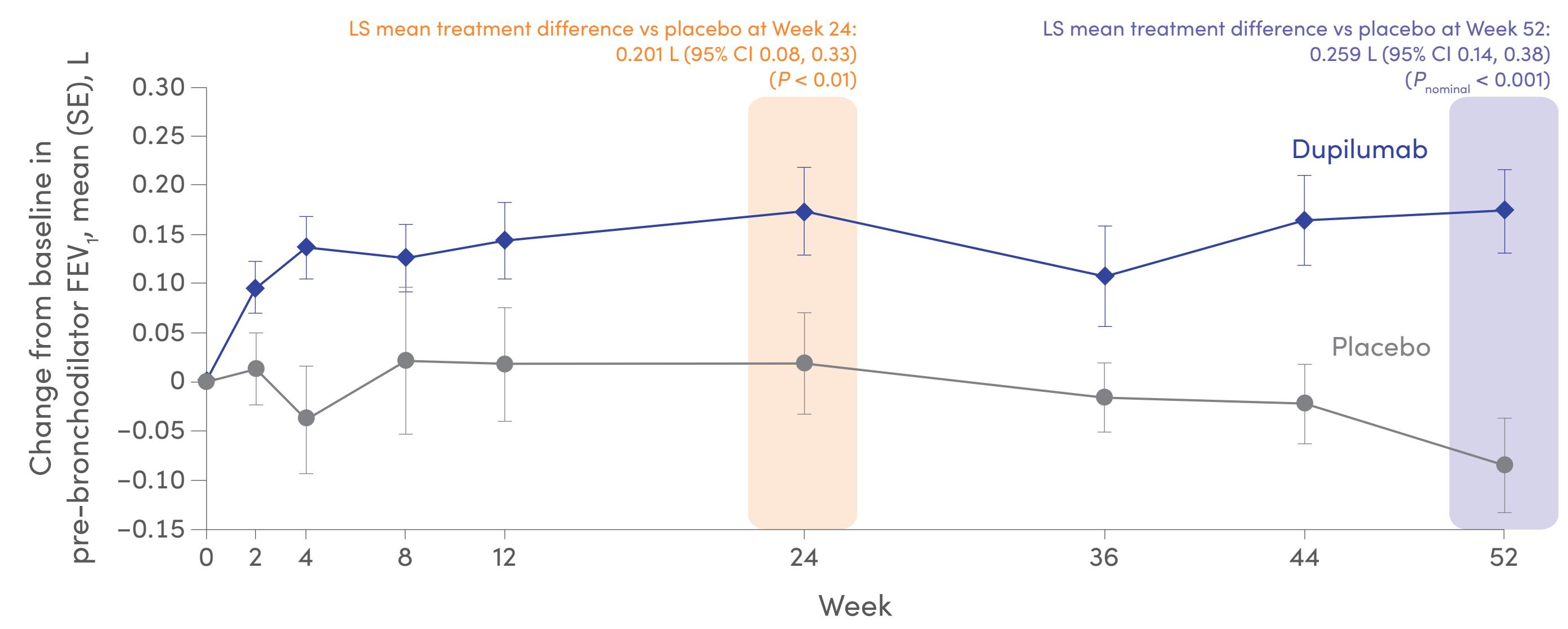
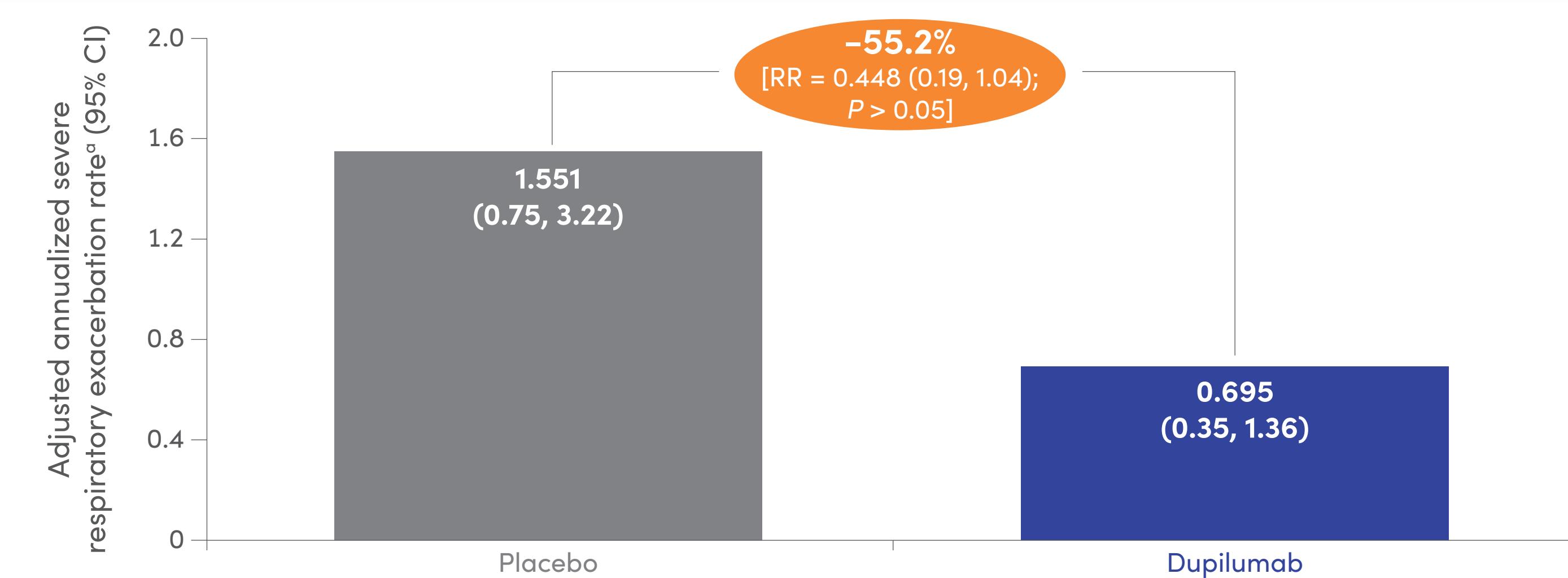
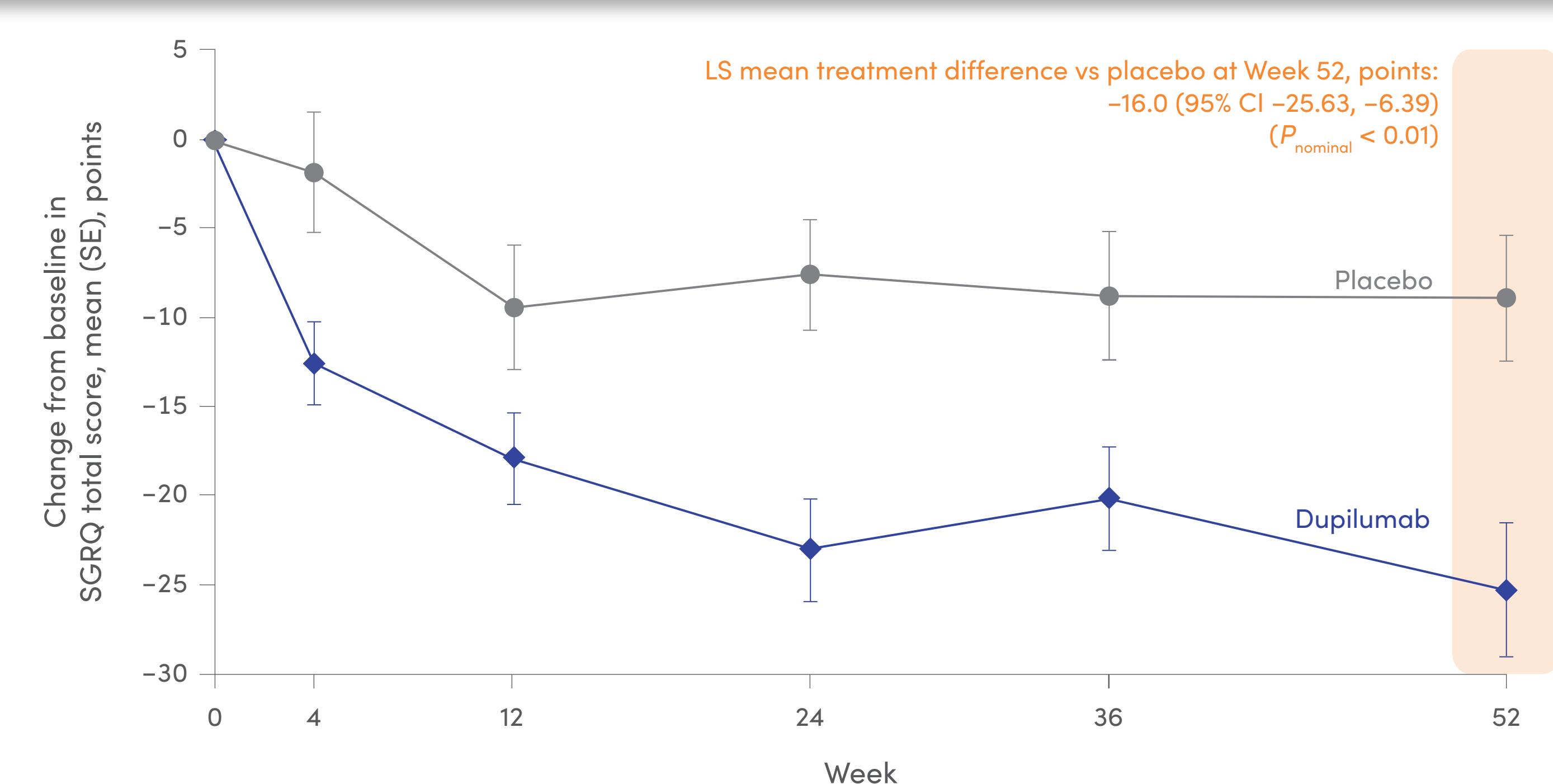


Figure 2. Treatment with dupilumab vs placebo reduced the annualized rate of severe respiratory exacerbations during the 24- to 52-week treatment period



^aSevere respiratory exacerbations are defined as new onset symptoms or clinical worsening that require systemic corticosteroid treatment for ≥3 consecutive days, and, for patients who are on maintenance systemic corticosteroids, at least double the dose of maintenance systemic corticosteroids for ≥3 consecutive days plus antibiotic therapy if indicated.

Figure 4. Dupilumab vs placebo improved the SGRQ total score during the 24- to 52-week treatment period



Lower scores indicate better quality of life, and a change of 4 points is the minimal clinically important difference.