

Efficacy of Mepolizumab Stratified by Baseline Blood Eosinophil Count

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Aims

Mepolizumab is approved as an add-on maintenance treatment for patients with severe eosinophilic asthma.¹ Among these patients, it reduces blood eosinophil counts and the rate of clinically significant exacerbations, and improves lung function and health-related quality of life compared with placebo.²⁻⁵

Evidence suggests that baseline blood eosinophil counts are predictive of response to mepolizumab treatment.²⁻⁶

Using data from the previous mepolizumab clinical trials, we performed a meta-analysis to assess the relationship between baseline eosinophil counts and mepolizumab efficacy in patients with severe eosinophilic asthma.

Methods

DREAM², MENSA³, & MUSCA⁴

Studies

- Randomized
- Double-blind
- Placebo-controlled
- Multicenter

Phase IIb/III (DREAM [NCT01000506])

Phase III (MENSA [NCT01691521] & MUSCA [NCT02281318])

Patients

- 616 (DREAM)
- 576 (MENSA)
- 551 (MUSCA)

≥12 years of age
Severe eosinophilic asthma:
High-dose ICS plus ≥1 other controller therapy
≥2 exacerbations in previous year
Eosinophilic inflammation

Treatments

Study	Standard of care therapy, plus:	Duration
DREAM	Placebo	52 weeks
DREAM	Mepolizumab 75 mg IV	52 weeks
MENSA	Placebo	32 weeks
MENSA	Mepolizumab 75 mg IV	32 weeks
MUSCA	Placebo	24 weeks
MUSCA	Mepolizumab 100 mg SC	24 weeks
MUSCA	Mepolizumab 250 mg IV	24 weeks
MUSCA	Mepolizumab 750 mg IV	24 weeks

Post hoc meta-analysis

Endpoints

- Annualized rate of clinically significant exacerbations*
- Change from baseline in SGRQ total score at study end
- Change from baseline in ACQ-5 score at Week 24
- Change from baseline in pre-bronchodilator FEV₁ at Week 24

Analyses†

Stratified by baseline blood eosinophil count

Blood eosinophil thresholds:

- ≥150 cells/μL
- ≥300 cells/μL
- ≥500 cells/μL

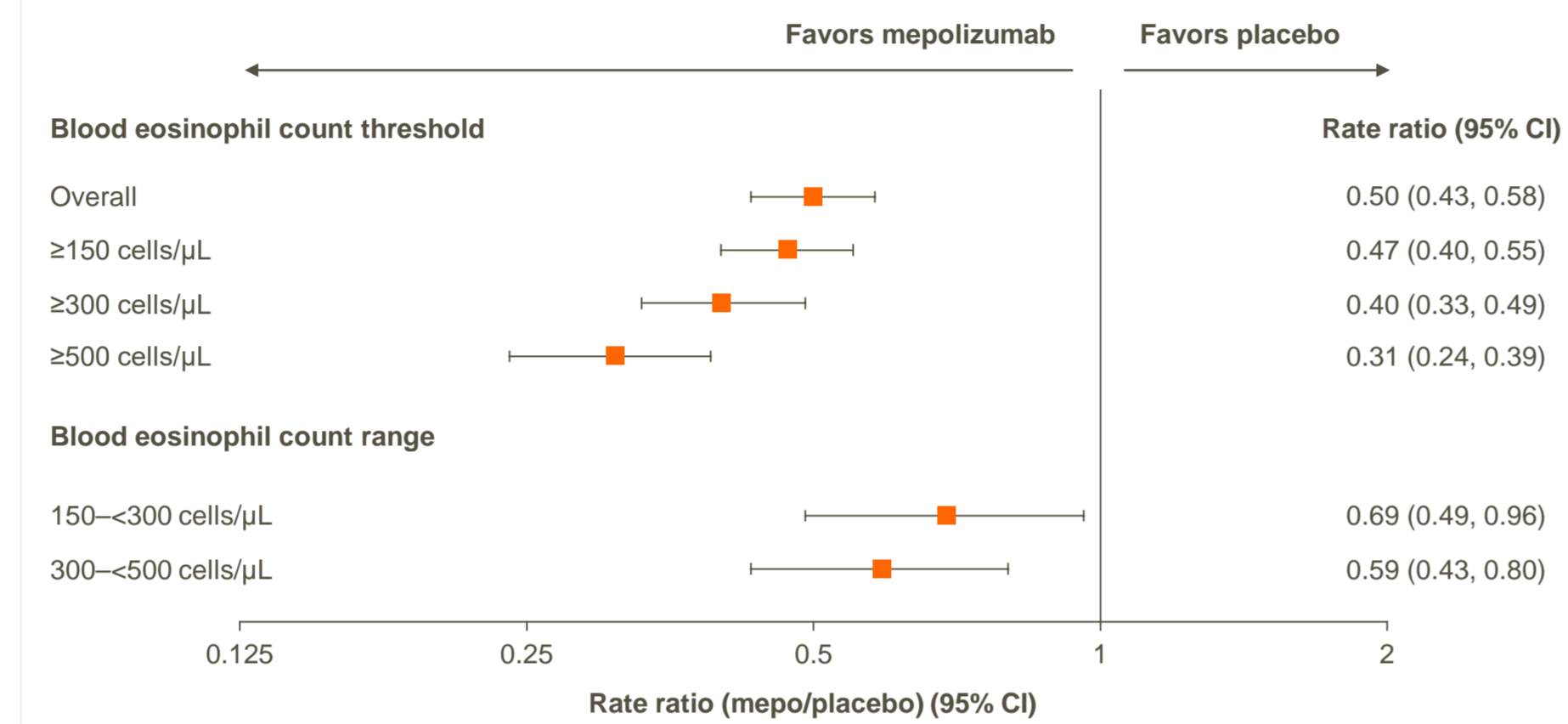
Blood eosinophil ranges:

- ≥150–<300 cells/μL
- ≥300–<500 cells/μL

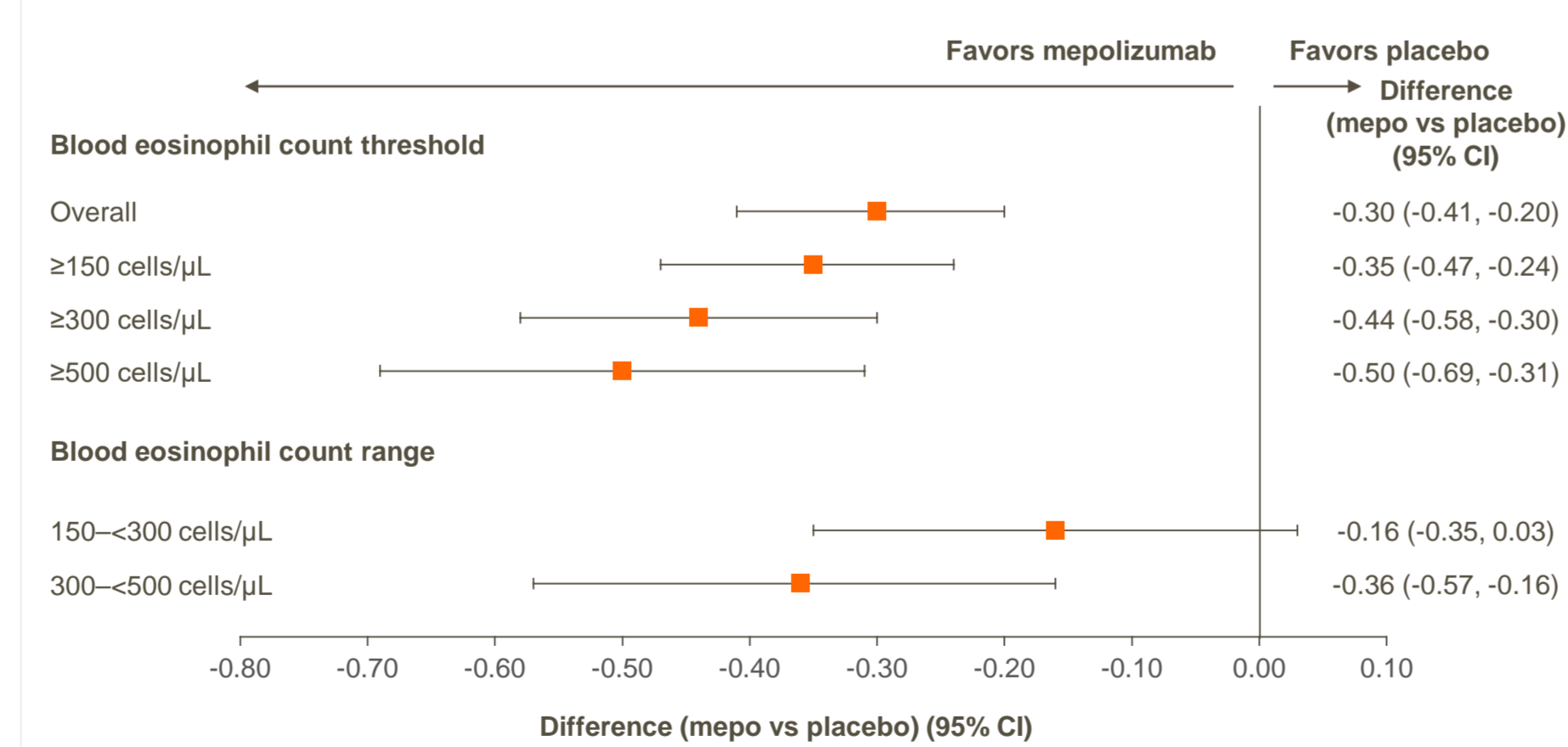
*Worsening of asthma requiring OCS or systemic corticosteroids for ≥3 days and/or hospitalization and/or an ER visit; †performed separately for each subgroup using a negative binomial regression model (exacerbations) or mixed model repeated measures (SGRQ, ACQ-5, FEV₁) with adjustment for covariates. Note: SGRQ not collected in DREAM study. ACQ-5, Asthma Control Questionnaire; ER, emergency room; FEV₁, forced expiratory volume in 1 second; ICS, inhaled corticosteroids; IV, intravenous; OCS, oral corticosteroids; SC, subcutaneous; SGRQ, St George's Respiratory Questionnaire

Results

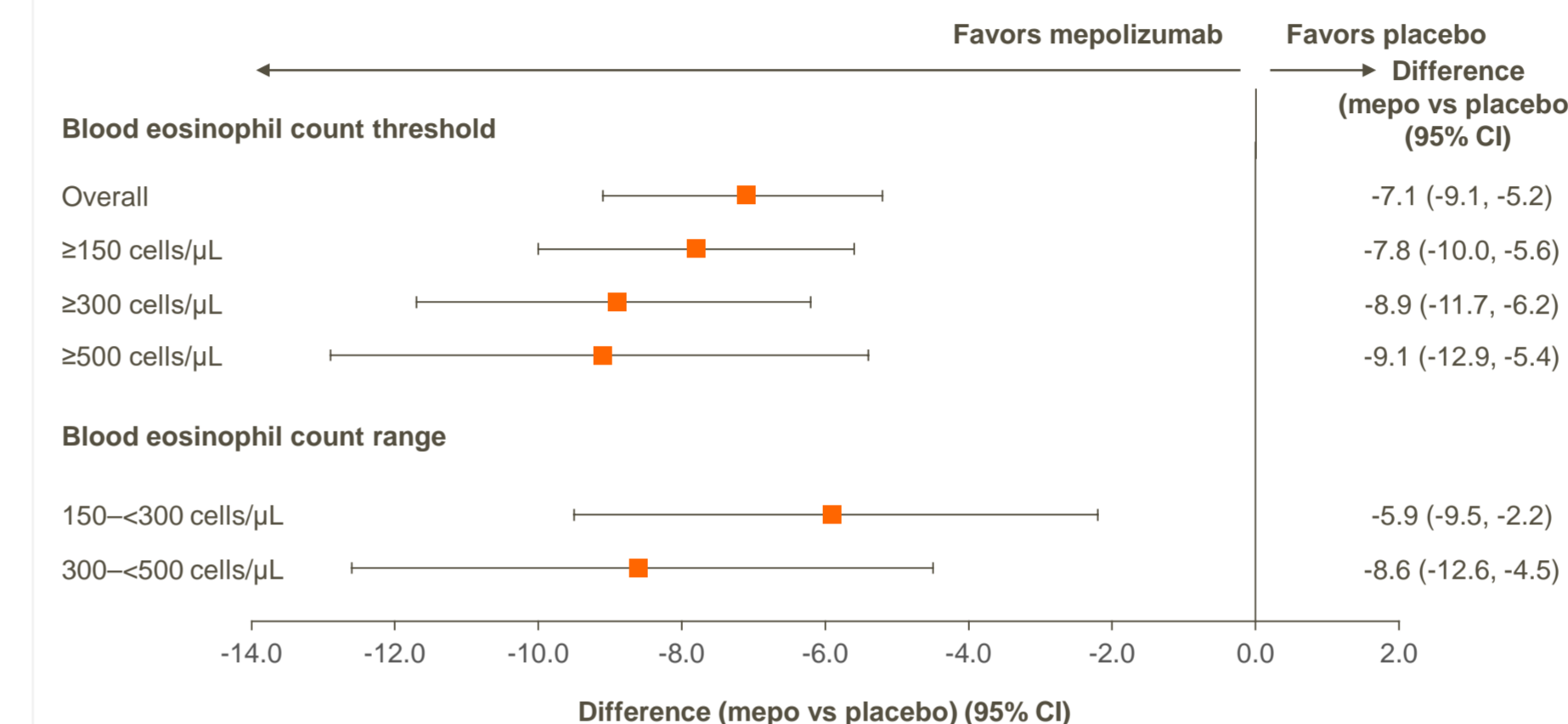
Patients receiving mepolizumab experienced fewer clinically significant exacerbations than those receiving placebo, with a trend towards greater improvements with increasing baseline blood eosinophil count



Mepolizumab was associated with an improvement from baseline at Week 24 in ACQ-5 score compared with placebo, with a trend towards greater improvements with increasing baseline blood eosinophil count

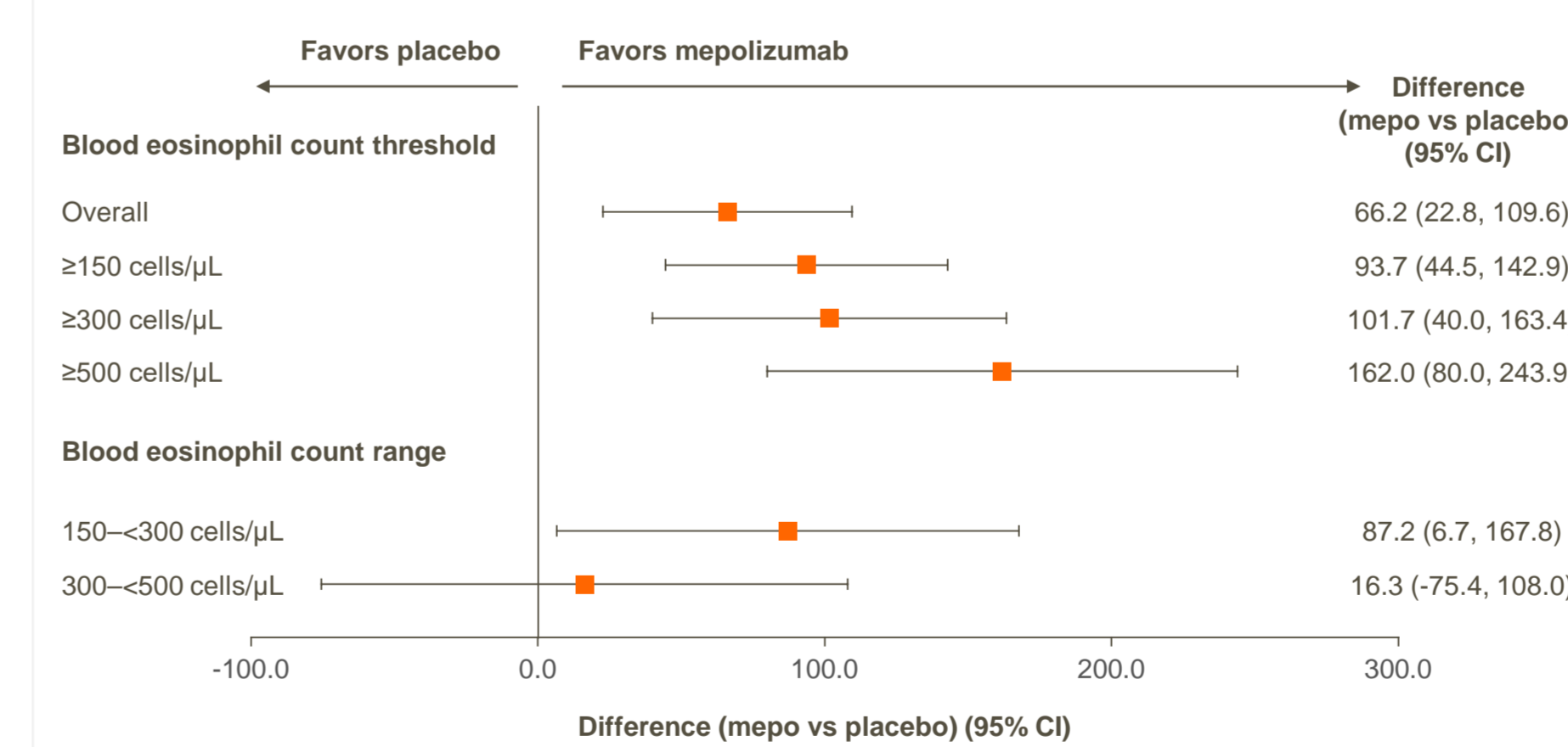


Mepolizumab was associated with an improvement from baseline at study end in SGRQ total score compared with placebo, with a trend towards greater improvements with increasing baseline blood eosinophil count



Note: SGRQ not collected in DREAM study.

Mepolizumab was associated with an improvement from baseline at Week 24 in FEV₁ compared with placebo, with a trend towards greater improvements with increasing baseline blood eosinophil count



Conclusions

- In this post hoc meta-analysis of the DREAM, MENSA, and MUSCA studies, clinically relevant reductions in exacerbation frequency, and improvements in SGRQ, ACQ-5, and lung function were seen with mepolizumab versus placebo across patient subgroups with differing baseline blood eosinophil counts.
- A positive relationship exists between baseline blood eosinophil count and the clinical efficacy of mepolizumab treatment.
- These data confirm the utility of the ≥150 cells/μL blood eosinophil count threshold for identifying patients with a consistent response to mepolizumab treatment.

Baseline demographics and clinical characteristics	Placebo N=624	Mepolizumab (all doses) N=1119
Age, years	50 (13)	50 (13)
Female, n (%)	381 (61)	659 (59)
BMI, kg/m ²	28.0 (6.0)	28.2 (6.1)
Duration of asthma, years	19 (15)	20 (14)
Exacerbations in previous year, n (%)		
2	340 (54)	549 (49)
3	146 (23)	245 (22)
≥4	138 (22)	325 (29)
Receiving maintenance OCS therapy, n (%)	156 (25)	307 (27)
% predicted pre-bronchodilator FEV ₁	59.8 (16.6)	59.8 (16.8)
SGRQ total score	46.6 (19.3)	46.6 (18.9)
ACQ-5 score	2.3 (1.2)	2.2 (1.1)
Blood eosinophil count, cells/μL*	320 (0.94)	280 (0.96)
Blood eosinophil count, n (%)		
Thresholds: ≥150 cells/μL	515 (83)	863 (77)
≥300 cells/μL	359 (58)	573 (51)
≥500 cells/μL	211 (34)	330 (30)
Ranges: 150–<300 cells/μL	156 (25)	290 (26)
300–<500 cells/μL	148 (24)	243 (22)

*Values are presented as mean (SD) unless otherwise stated. †Data are presented as geometric mean (SD on log-transformed eosinophil count). Note: SGRQ not collected in DREAM study. BMI, body mass index; SD, standard deviation

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Disclosures

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