The Number Needed to Treat With Dupilumab To Prevent Moderate or Severe Chronic Obstructive Pulmonary Disease Exacerbations And Improve Symptoms: BOREAS And NOTUS Post Hoc Analysis

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Conclusion

Treating patients with COPD and type 2 inflammation with add-on dupilumab for 52 weeks was effective in preventing moderate or severe exacerbations, improving lung function, and symptoms, and reducing the need for SCS courses

Objective

To determine the NNT for dupilumab to prevent exacerbation, to have 1 extra responder of E-RS:COPD score improvement, to have 1 extra responder in FEV_1 improvement, and to reduce 1 SCS course

Background

- The NNT is a simple yet intuitive statistical measure to quantify treatment benefits for individual patients[1]
  - It describes the average number of patients who need to receive specific treatment (e.g. dupilumab) for one beneficial outcome (e.g. lung function improvement) to be achieved or one negative outcome (e.g. exacerbation event) to be prevented compared to placebo
- In the BOREAS and NOTUS trials, add-on dupilumab vs placebo reduced exacerbations, increased lung function, and improved quality of life in patients with COPD and type 2 inflammation receiving background triple therapy[2–4]
  - Safety was consistent with the known dupilumab safety profile[2,3]

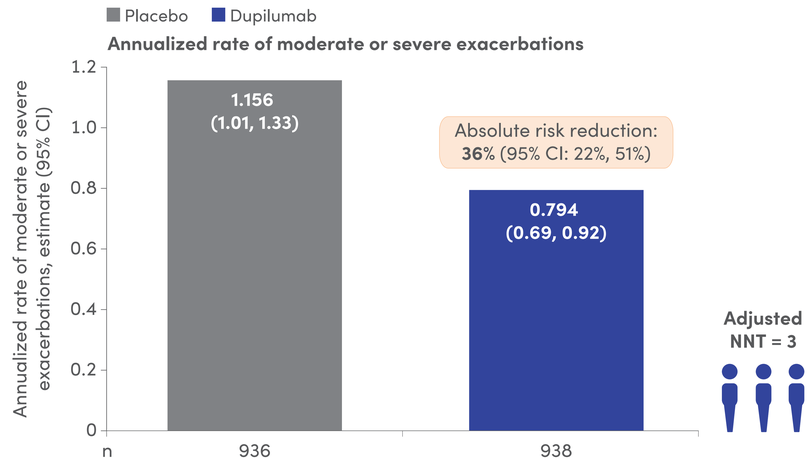
Methods

- BOREAS (NCT03930732) and NOTUS (NCT04456673), phase 3, randomized, placebo-controlled trials, enrolled patients (40 to 85 years[a]) with COPD, moderate-to-severe airflow limitation, and type 2 inflammation (screening blood eosinophils ≥300 cells/µL) on dual or triple therapy
  - Patients received add-on subcutaneous dupilumab 300 mg q2w or matched placebo for 52 weeks
- Endpoints analyzing NNT included adjusted annualized rate of moderate or severe COPD exacerbations, proportion of lung function responders (pre- or post-bronchodilator FEV_1 improvement ≥100 mL) at Week 12, the proportion of patients with an E-RS:COPD total score improvement of ≥2 points at Week 52 and the adjusted annualized number of SCS courses

[a]Age criteria for BOREAS: 40 to 80 years; for NOTUS: 40 to 85 years.

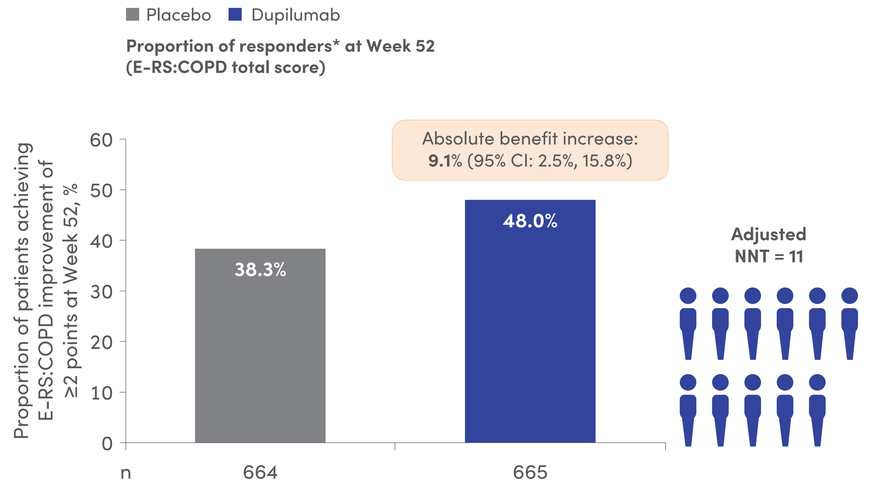
Results

Dupilumab vs placebo was effective in preventing moderate or severe exacerbations



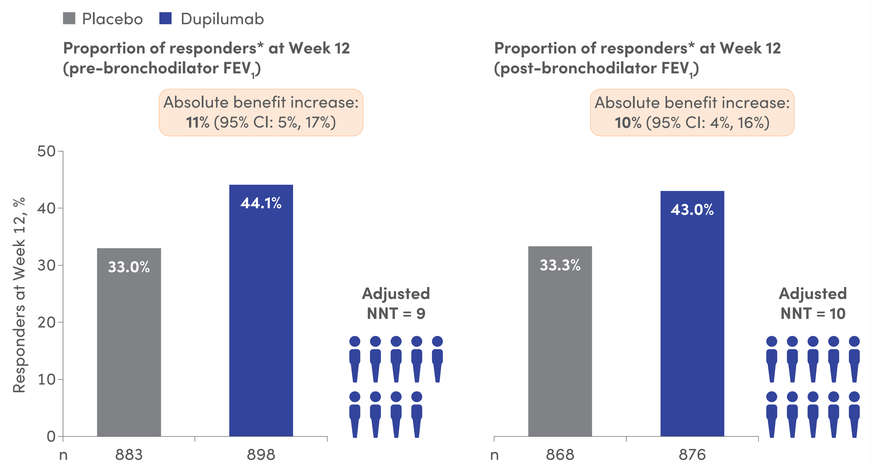
Derived using negative binomial model with the total number of the events occurring during the 52-week treatment period as the response variable, and treatment group, study (if pooled), region (pooled country), ICS dose, smoking status at screening, baseline disease severity, and number of moderate or severe COPD exacerbation events within one year prior to the study as covariates, and log-transformed treatment duration as an offset variable.

Dupilumab vs placebo was effective in improving symptom severity



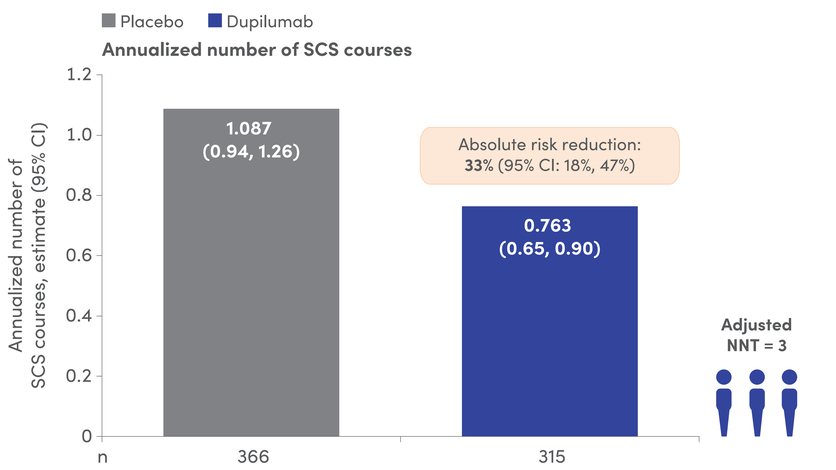
A responder is defined as a participant with improvement from baseline in E-RS: COPD total score at Week 52 by ≥ 2 points.
Adjusted proportion of responders derived from logistic regression model which includes treatment group, study (if pooled), region (pooled country), ICS dose, smoking status at screening, and baseline SGRQ total score or E-RS:COPD total score as covariates.

Dupilumab vs placebo was effective in improving lung function



*Patients with data at baseline and Week 12. Responders defined as an improvement ≥100 mL.
Adjusted proportion of responders derived from logistic regression model which includes treatment group, study, age, sex, height, region (pooled country), ICS dose, smoking status at screening, and baseline pre- or post-bronchodilator FEV_1 as covariates, for subjects with values at both visits

Dupilumab vs placebo was effective in reducing the need for systemic steroid treatment



Derived using negative binomial model with the total number of SCS courses during the 52-week treatment period as the response variable, study (if pooled), treatment group, region (pooled country), ICS dose at baseline, smoking status at screening, baseline disease severity, and number of moderate or severe COPD exacerbation events within one year prior to the study as covariates, and log-transformed treatment duration as an offset variable.

95% CI excluding 0 indicates nominal statistical significance.

CI, confidence interval; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; ICS, inhaled corticosteroid(s); IL, interleukin; ITT, intention-to-treat; LABA, long-acting β_2-agonist(s); LAMA, long-acting muscarinic antagonist(s); NNT, number needed to treat; q2w, every 2 weeks; SCS: systemic corticosteroid(s); SGRQ: St. George's Respiratory Questionnaire.

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