Dupilumab Reduces the Risk of Severe Exacerbations in Patients With Chronic Obstructive Pulmonary Disease: Results From BOREAS and NOTUS

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Conclusion

Dupilumab treatment was associated with a reduced risk of severe exacerbation events and delayed time-to-first severe exacerbation, with a reduction in ED visits and a reduced need for SCS, suggesting a potential benefit in lowering disease burden and HCRU

Objective

This post hoc analysis assessed the efficacy of dupilumab in reducing the risk of severe exacerbations and its impact on ED visits and SCS use in patients with COPD and type 2 inflammation

Background

- In patients with COPD, severe exacerbations are associated with increased HCRU, morbidity, and mortality risk. Preventing and effectively managing exacerbations is, therefore, key to improving long-term prognosis in patients with COPD[1]
- SCS are often prescribed for management of COPD exacerbations, however long-term SCS use can lead to serious adverse events[2,3]
- In BOREAS and NOTUS, add-on dupilumab reduced moderate or severe exacerbations and improved lung function and quality of life in patients with COPD and type 2 inflammation[4–6]
  - Safety was consistent with the known dupilumab safety profile[4,5]

Methods

Study design

- BOREAS (NCT03930732)[4] and NOTUS (NCT04456673),[5] phase 3, randomized, double-blind, 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 LABA/LAMA/ICS
  - Patients received add-on dupilumab 300 mg or matching placebo q2w for up to 52 weeks
- Endpoints: probability and rate of ≥1 severe exacerbation[b], probability of severe exacerbation and/or ED visit[c], and duration of SCS use

[a]Age criteria for BOREAS: 40 to 80 years; for NOTUS: 40 to 85 years. [b]Severe exacerbations defined as exacerbations requiring hospitalization, emergency department visit >24 hours, or resulting in death. Patients with ≥1 severe exacerbation event were restricted to patients experiencing at least one severe exacerbation event. These patients may have also experienced moderate exacerbations. No deaths occurred due to severe exacerbations. [c]Severe exacerbations and/or ED visits defined as exacerbations requiring hospitalization or an emergency department visit of any duration.

Results

Table 1. Baseline demographics and disease characteristics for patients in the ITT population with ≥1 severe exacerbation during the trial period

	Placebo N = 60	Dupilumab N = 41
Demographics		
Age, mean (SD), years	68.1 (7.0)	66.1 (8.7)
Female, n (%)	18 (30.0)	13 (31.7)
Disease characteristics		
High-dose ICS, n (%)	23 (38.3)	8 (19.5)
Moderate or severe exacerbations in the past year, mean (SD)	2.6 (1.4)	2.7 (1.8)
Pre-bronchodilator FEV_1, mean (SD), L	1.14 (0.36)	1.10 (0.32)
Pre-bronchodilator ppFEV_1, mean (SD), %	41.99 (11.33)	40.55 (11.35)
Patient reported outcomes		
SGRQ total score,[a] mean (SD)	56.6 (17.6)	56.9 (16.5)
E-RS:COPD total score,[b] mean (SD)	16.2 (7.5)	15.3 (7.0)
Biomarkers		
Screening blood eosinophil count, median (Q1–Q3), cells/µL	300 (230–440)	370 (280–500)
FeNO, median (Q1–Q3), ppb	17.0 (10.0–34.0)	15.5 (12.0–24.0)

[a]SGRQ total and domain scores range from 0 to 100, with lower scores indicating a better quality of life. [b]ERS:COPD total scores range from 0 to 40, with a lower score indicating less severe symptoms.

Figure 1. Dupilumab vs placebo significantly reduced the time-to-first severe exacerbation event, with a 39% risk reduction at Week 52

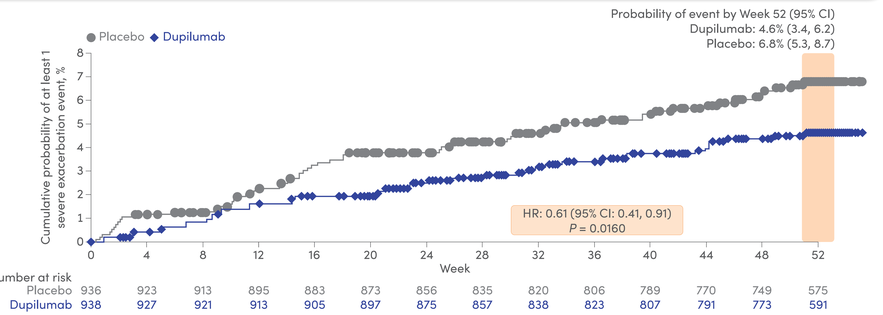


Figure 2. Dupilumab vs placebo significantly reduced the time-to-first severe exacerbation event and/or ED visit, with a 45% risk reduction at Week 52

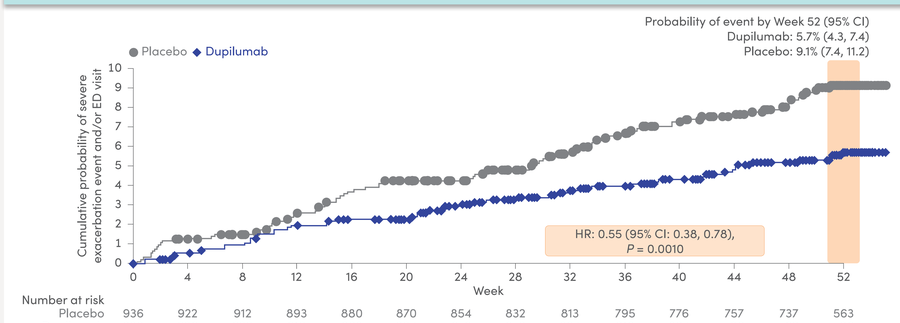


Figure 3. Dupilumab vs placebo significantly reduced severe exacerbation rates and/or ED visits

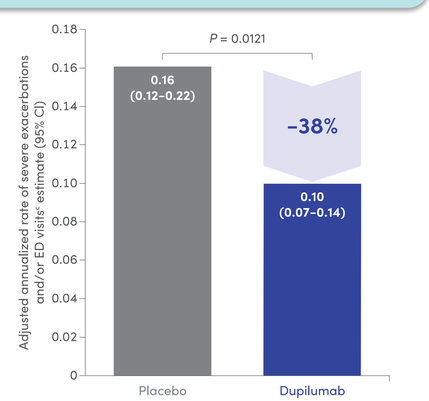
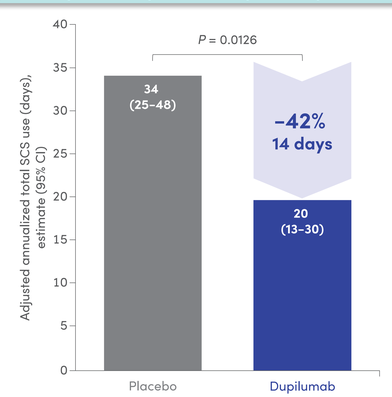


Figure 4. Patients receiving dupilumab who experienced ≥1 severe exacerbation event required SCS use for significantly fewer days when compared to placebo



COPD, chronic obstructive lung disease; ED, emergency department; E-RS:COPD, Evaluating Respiratory Symptoms in COPD; FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; HCRU, health care resource utilization; HR, hazard ratio; ICS, inhaled corticosteroid(s); ITT, intention-to-treat; LABA, long-acting β2-agonist(s); LAMA, long-acting muscarinic antagonist(s); pp, percent predicted; ppb, parts per billion; Q, quartile; q2w, every 2 weeks; SCS, systemic corticosteroid; SD, standard deviation; SGRQ, St. George's Respiratory Questionnaire; UC, urgent care.

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