Dupilumab Improved Asthma Control in Patients With Uncontrolled, Modifier-Free, Asthma Regardless of Exacerbations in the Previous Year

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BACKGROUND
• Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin (IL)-4 and IL-13, thus inhibiting signaling of both IL-4 and IL-13, which are key drivers of type 2 inflammation
• Dupilumab is approved in the USA for patients aged ≥ 12 years with moderate-to-severe eosinophilic or oral corticosteroid-dependent asthma and in several countries for the treatment of adults with inadequately controlled moderate-to-severe atopic dermatitis

In the phase 3 LIBERTY ASThma QUEST study (NCT02414845), add-on dupilumab 200 mg administered every 2 weeks in patients with 2 or more prior exacerbations in the previous year significantly reduced severe exacerbations during the 52-week treatment period by 48% and 46%, respectively (both P < 0.001), improved pre-bronchodilator forced expiratory volume in 1 second (FEV1) at Week 12 by 0.14 L and 0.13 L, respectively (both P < 0.001), improved quality-of-life measures, and suppressed biomarkers of type 2 inflammation in patients with uncontrolled, moderate-to-severe asthma.

– Greater therapy effects were observed in patients with elevated baseline blood eosinophilia and fractional exhaled nitric oxide (FeNO)

OBJECTIVE
– The post hoc analysis of the phase 3 QUEST study assessed the effect of dupilumab on asthma control, using the 5-item Asthma Control Questionnaire (ACQ-5), in the subgroup of patients who had ≥ 1, ≥ 2, and ≥ 3 prior severe exacerbations in the previous year

METHODS

Study assessments
• Change from baseline in ACQ-5 score during the 52-week treatment period in patients with ≥ 1, ≥ 2, and ≥ 3 prior severe exacerbation events
• ACQ-5 is a patient-reported outcomes questionnaire. It includes 5 items that measure asthma symptoms and assess the adequacy of control in asthma control in the previous 7 days (global scale 0–6)

RESULTS

Patient characteristics
– Baseline demographics and clinical characteristics were generally similar across the treatment groups (Table 1)
– There was a trend of higher blood eosinophil counts in patients with more exacerbations in the previous year
– Baseline ACQ-5 scores were comparable across subgroups based on previous exacerbation history

Change from baseline in ACQ-5 scores in patients with ≥ 1, ≥ 2, and ≥ 3 prior severe exacerbation events
• Dupilumab 200 mg / 300 mg q2w vs placebo significantly reduced ACQ-5 scores during the 52-week treatment period in patients with ≥ 1, ≥ 2, and ≥ 3 prior severe exacerbation events, respectively (P ≤ 0.001)

CONCLUSIONS
• Dupilumab significantly reduced ACQ-5 scores vs placebo, indicating better asthma control, regardless of number of severe asthma exacerbations in the previous year

– A clinically meaningful change from baseline in ACQ-5 scores was observed as early as Week 2
– Improvement in asthma control was rapid and maintained for up to 52 weeks
• Dupilumab was generally well tolerated

Table 1. Baseline demographics and clinical characteristics among patients with ≥ 1, ≥ 2, and ≥ 3 prior severe exacerbation events.

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<th>Group</th>
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<th>Dupilumab 300 mg q2w</th>
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Table 2. Overview of TEAEs and injection-site reactions in the safety population.

<table>
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<th>Placebo 1.14 mL q2w</th>
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Disclosures
Data presented at the 2018 Annual Scientific Meeting of the American College of Allergy, Asthma & Immunology (ACAAI); Seattle, Washington; November 15–19, 2018.

References

Figure 1. Change from baseline in ACQ-5 scores for dupilumab 200 mg and 300 mg regimens during the 52-week treatment period in patients with ≥ 1, ≥ 2, and ≥ 3 severe exacerbation events, respectively (ITT population). (A) ≥ 1 severe exacerbation event, (B) ≥ 2 severe exacerbation events, and (C) ≥ 3 severe exacerbation events.

Figure 2. Change from baseline in ACQ-5 scores for dupilumab 200 mg and 300 mg regimens during the 52-week treatment period in patients with ≥ 1, ≥ 2, and ≥ 3 severe exacerbation events, respectively (ITT population).