# Efficacy of Dupilumab in Adolescents With Moderate-to-Severe Atopic Dermatitis With and Without Comorbid Asthma: Subgroup Analysis From a Phase 3 Trial (LIBERTY AD ADOL)

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# BACKGROUND

- Atopic dermatitis (AD) is a chronic inflammatory skin disease often associated with atopic comorbidities
- As previously reported, patients with AD have a high prevalence of comorbid atopic conditions, including asthma<sup>2</sup>
- Dupilumab, a fully human monoclonal antibody, blocks the shared receptor subunit for interleukin (IL)-4 and IL-13, inhibiting signaling of both IL-4 and IL-13, which are key drivers of type 2-mediated inflammation in multiple diseases, such as AD and asthma<sup>3</sup>
- In dupilumab trials, > 80% of adult patients have reported ≥ 1 comorbid condition, and as many as 45% have reported comorbid asthma<sup>4</sup>

### OBJECTIVE

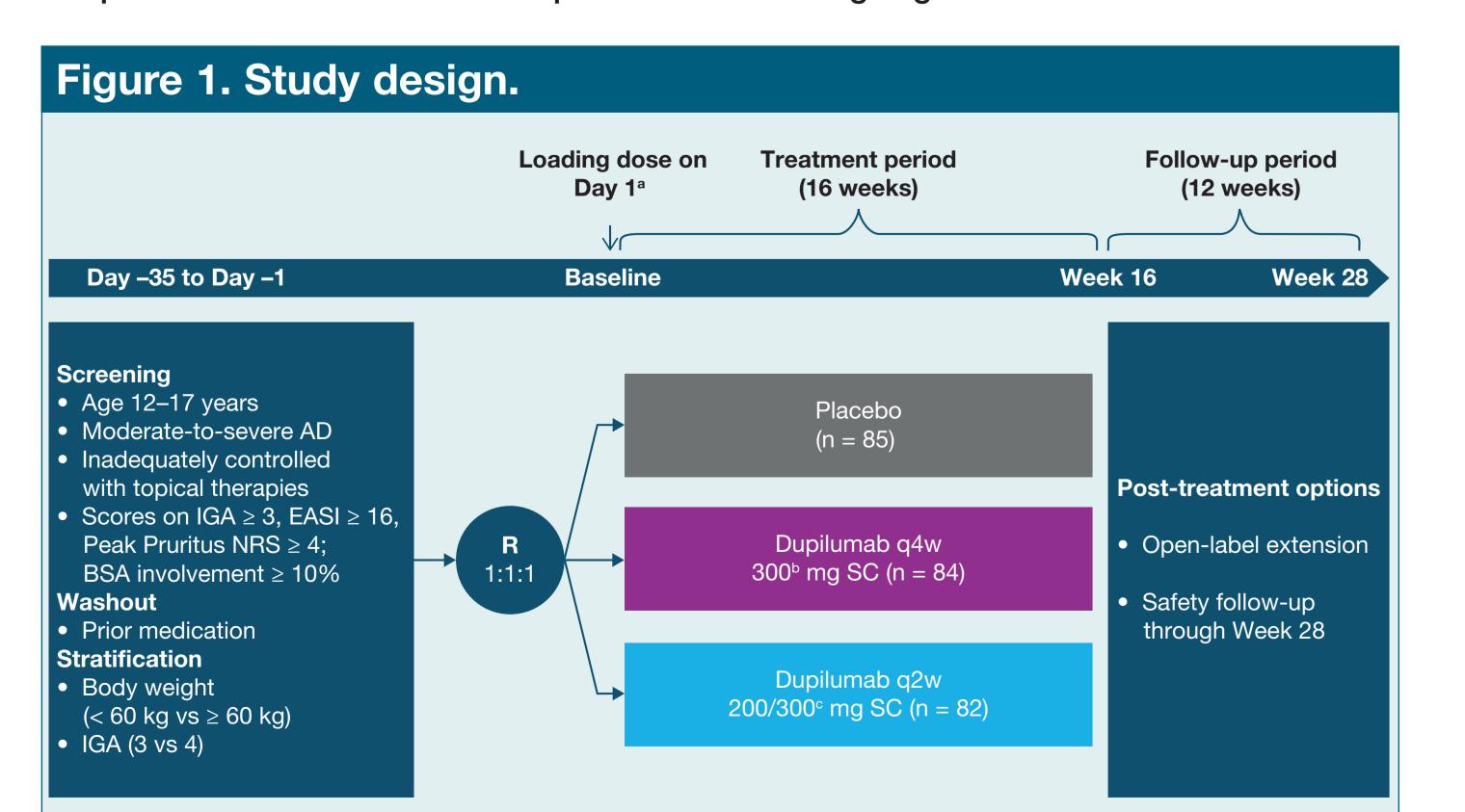
 To determine if a history of asthma impacts the efficacy of dupiluma treatment in adolescent patients with moderate-to-severe AD enrolled in a phase 3 trial

### METHODS

R, randomization; SC, subcutaneous.

### Study design

- This was a randomized, double-blinded, placebo-controlled, parallel-group, phase 3 trial of dupilumab in adolescents with moderate-to-severe AD (LIBERTY AD ADOL, NCT03054428, Figure 1)<sup>5</sup>
- Patients were randomized (1:1:1) to 200 or 300 mg dupilumab every 2 weeks (q2w) (patients with body weight < 60 kg received 200 mg of dupilumab; patients with body weight ≥ 60 kg received 300 mg), 300 mg dupilumab every 4 weeks (q4w), or placebo for 16 weeks
- The study was conducted in accordance with the provisions of the Declaration of Helsinki, the International Conference on Harmonisation Good Clinical Practice guideline, and applicable regulatory requirements; the protocol was reviewed and approved by institutional review boards/ethics committees at all study sites
- For all patients, written informed consent was obtained prior to any study procedure either from the patient or their legal guardian



Topical therapy and other systemic AD therapies were prohibited but allowed as rescue treatment for ntolerable symptoms. <sup>a</sup>All patients receiving q4w, regardless of weight, received a 600 mg loading dose. For q2w, patients with body weight < 60 kg at baseline received a loading dose of 400 mg on Day 1, while patients with body weight ≥ 60 kg received a 600 mg loading dose. bIn the q4w group, patients received 300 mg regardless of body weight. In the q2w group, patients with body weight < 60 kg received 200 mg of the study drug; patients with body weight ≥ 60 kg received 300 mg. BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NRS, Numerical Rating Scale;

# **Endpoints**

- The following endpoints were evaluated in patients with and without a history
- Proportion of patients with IGA 0 or 1
- Proportion of patients with ≥ 75% improvement from baseline in EASI
- Proportion of patients with  $\geq 50\%$  improvement from baseline in EASI
- Percent change from baseline in EASI
- Proportion of patients with  $\geq$  4-point improvement from baseline in Peak Pruritus NRS score (among patients with baseline Peak Pruritus NRS ≥ 4)
- Proportion of patients with  $\geq$  3-point improvement from baseline in Peak Pruritus NRS score (among patients with baseline Peak Pruritus NRS ≥ 3)
- Percent change from baseline in Peak Pruritus NRS score
- Proportion of patients with  $\geq$  6-point improvement from baseline in Children's Dermatology Life Quality Index (CDLQI)

- This analysis includes the subpopulation of patients who reported a history f asthma at baseline and the complementary subpopulation without a history of asthma
- Efficacy outcomes were analyzed among randomized patients (full analysis set) among the 2 subgroups
- For categorical endpoints, values are given at the Week 16 time point together with 95% confidence intervals (CIs) of the difference between dupilumab and placebo, calculated using normal approximation; patients who dropped out or received rescue medication were counted as non-responders from the time of dropout/rescue medication, while patients with missing values at Week 16 were considered non-responders at Week 16
- P values were derived by Cochran–Mantel–Haenszel test, stratified by baseline disease severity (IGA = 3 vs IGA = 4) and baseline weight group  $(< 60 \text{ kg vs} \ge 60 \text{ kg})$
- Continuous endpoints were analyzed using an analysis of covariance (ANCOVA) model with baseline measurement as covariate and the treatment randomization strata (baseline disease severity and body weight < 60 kg vs ≥ 60 kg) as fixed factors; missing data were imputed using the multiple imputation methods with data set to missing after first rescue treatment use
- Safaty was accessed among nationts who recoived 1 does of any study drug

 The CI with P value is based on treatment difference (dupilumab group vs placebo) in the least squares (LS) mean percent change, using the above-described model

# RESULTS

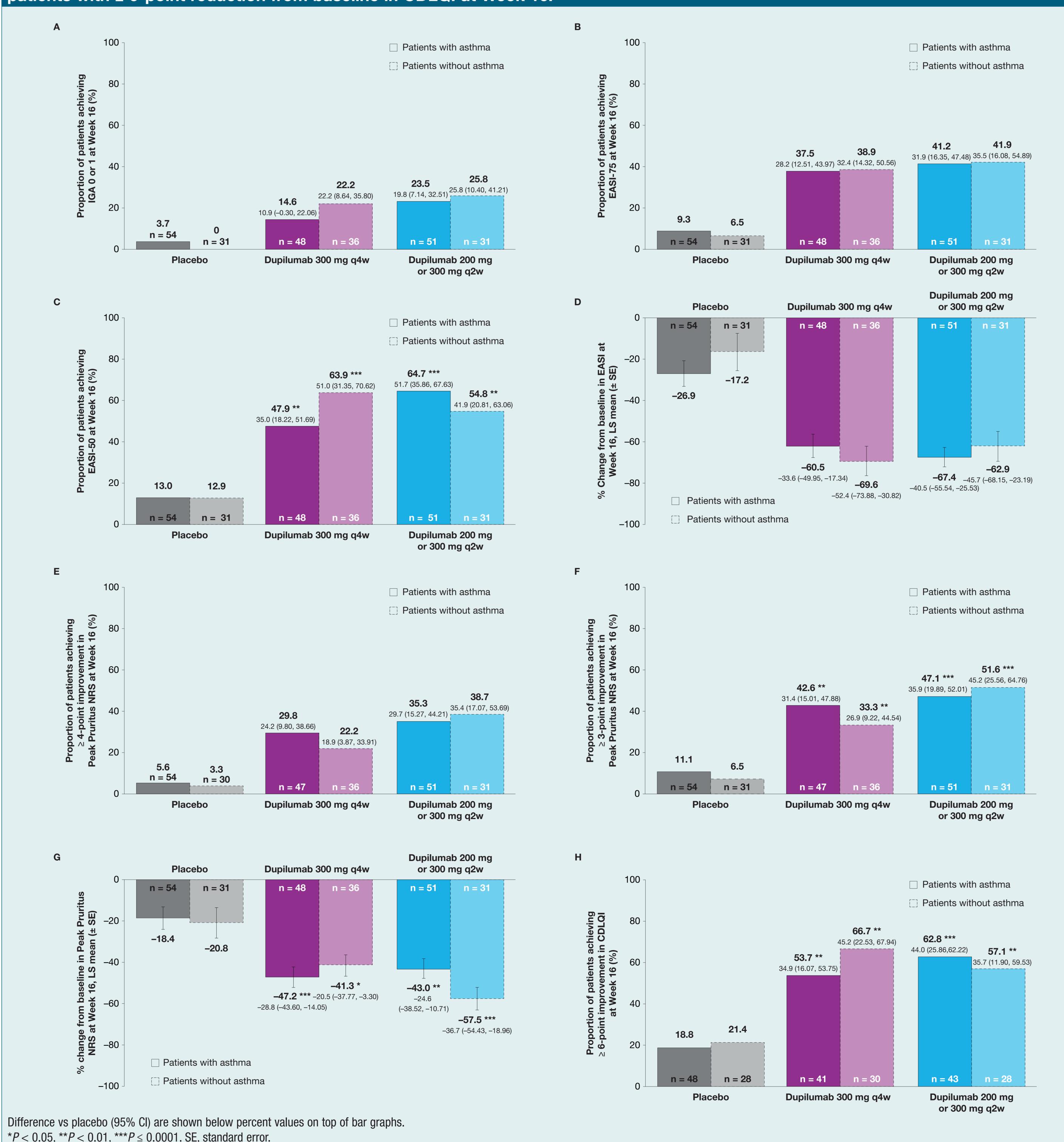
- Of the 251 patients randomized, 153 had a history of asthma and 98 did not have a history of asthma
- Baseline demographics and disease characteristics were similar among treatment groups and between the subgroups with a history of asthma and no history of asthma (**Table 1**)

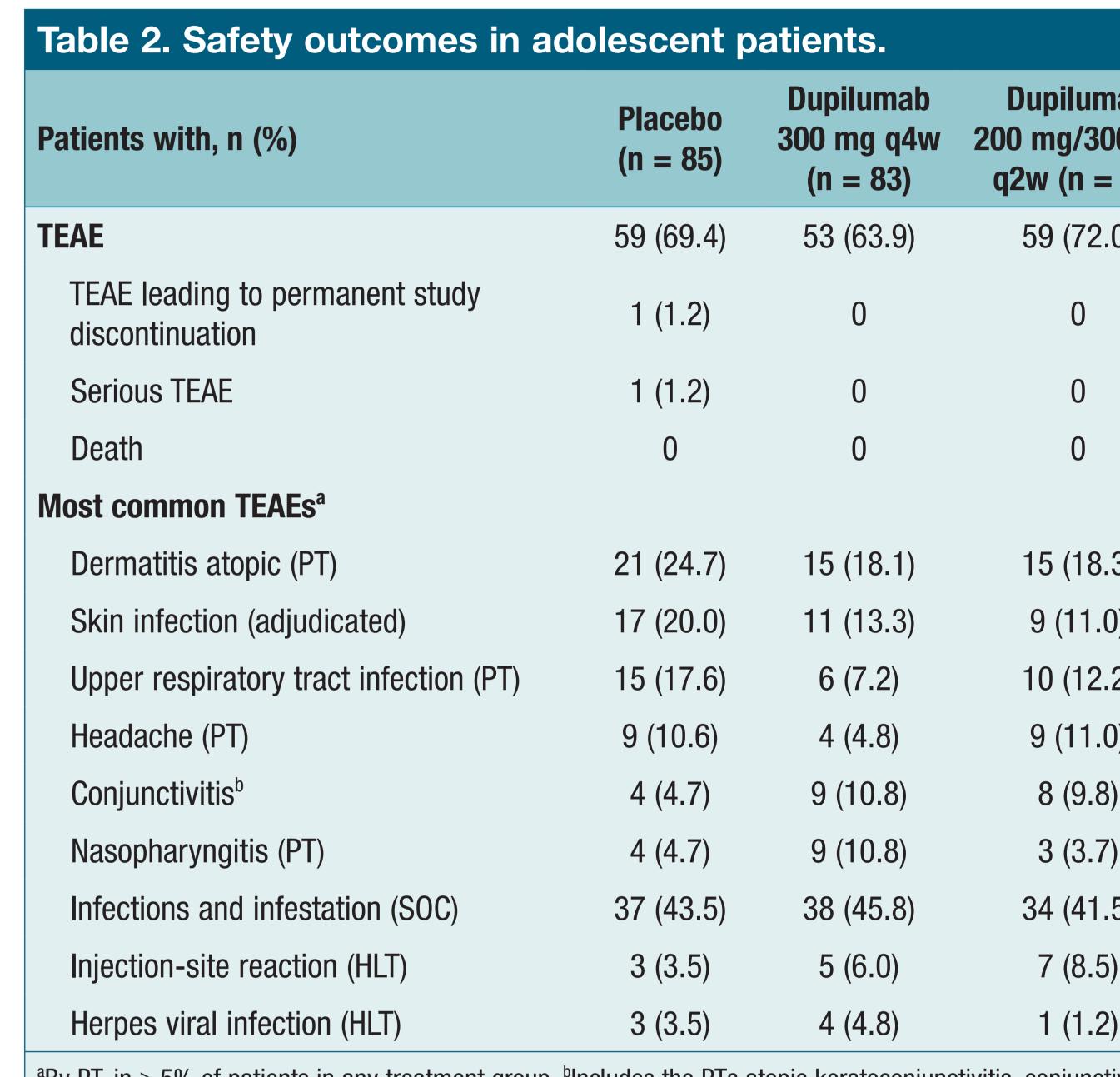
- At Week 16 of the trial, more patients on dupilumab achieved an IGA score of 0 or 1 vs placebo in both the subgroup of patients with a history of asthma and the subgroup of patients without a history of asthma (Figure 2A)
- A higher proportion of patients achieved EASI-75 (Figure 2B) or EASI-50 (Figure 2C) at Week 16 with both dupilumab regimens compared with placebo, regardless of asthma history
- At Week 16 of the trial, both dupilumab regimens showed higher reduction in EASI compared with placebo, with similar results seen in the subgroup of patients with a history of asthma and without a history of asthma (Figure 2D)
- Compared with placebo, a higher proportion of patients receiving either dupilumab regimen achieved ≥ 4-point improvement in Peak Pruritus NRS and ≥ 3-point improvement in Peak Pruritus NRS at Week 16, regardless of asthma history (Figure 2E and 2F, respectively); furthermore, both dupilumab regimens vs placebo led to higher percent reductions in Peak Pruritus NRS from baseline to Week 16 (Figure 2G), regardless of asthma
- Finally, in patients with and without a history of asthma, both dupilumab regimens improved patient quality of life, as shown by a higher proportion of patients achieving  $\geq$  6-point improvement in CDLQI from baseline to Week 16 (Figure 2H)

- Safety in adolescents was consistent with that seen in adults, and data were consistent with the known dupilumab safety profile (Table 2)
- There were more cases of conjunctivitis and injection-site reaction with dunilumah compared with placeho (Table 2)

	Patients with a history of asthma			Patients without a history of asthma		
	Placebo (n = 54)	Dupilumab 300 mg q4w (n = 48)	Dupilumab 200 mg or 300 mg q2w (n = 51)	Placebo (n = 31)	Dupilumab 300 mg q4w (n = 36)	Dupilumab 200 mg or 300 mg q2w (n = 31)
Duration of AD, mean (SD), years	12.5 (3.36)	12.7 (2.72)	12.5 (2.68)	11.8 (3.58)	10.9 (3.47)	12.4 (3.45)
IGA score 4, n (%)	31 (57.4)	28 (58.3)	28 (54.9)	15 (48.4)	18 (50.0)	15 (48.4)
EASI, mean (SD)	37.6 (13.84)	37.3 (15.59)	35.5 (12.97)	32.0 (13.70)	33.8 (13.69)	34.9 (15.38)
SCORAD total score, mean (SD)	72.5 (12.69)	70.2 (14.79)	70.4 (12.67)	66.8 (13.60)	69.4 (13.36)	71.0 (15.91)
BSA involvement of AD, mean (SD), %	60.3 (23.54)	57.9 (24.53)	57.7 (20.65)	49.6 (23.97)	55.6 (22.34)	53.2 (22.66)
Peak Pruritus NRS, mean (SD)	7.7 (1.53)	7.6 (1.86)	7.4 (1.51)	7.7 (1.80)	7.4 (1.81)	7.7 (1.54)
CDLQI, mean (SD)	13.4 (6.99)	15.2 (7.35)	12.5 (6.04)	12.6 (6.30)	14.3 (7.48)	13.8 (6.50)

Figure 2. (A) Proportion of patients achieving IGA 0 or 1 at Week 16; (B) Proportion of patients achieving EASI-75 at Week 16; (C) Proportion of patients achieving EASI-50 at Week 16; (D) Percent change from baseline to Week 16 in EASI; (E) Proportion of patients with ≥ 4-point reduction from baseline in Peak Pruritus NRS at Week 16; (F) Proportion of patients with ≥ 3-point reduction from baseline in Peak Pruritus NRS at Week 16; (G) Percent change from baseline to Week 16 in Peak Pruritus NRS; (H) Proportion of patients with ≥ 6-point reduction from baseline in CDLQI at Week 16.





Medical Dictionary for Regulatory Activities; PT, MedDRA Preferred Term; SOC, MedDRA System Organ Class; TEAE, treatment-emergent adverse event.

### CONCLUSIONS

 Similar to previous findings in the adult population,<sup>5,6</sup> dupilumab improved signs and symptoms of AD in adolescent patients with and without a history of asthma, suggesting that, in adolescent patients with moderate-to-severe AD, the efficacy of dupilumab is not affected by comorbid atopic diseases such as asthma

### References

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### **Disclosures**

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