Dupilumab in Adolescents With Moderate-to-Severe Atopic Dermatitis and a History of Allergic Rhinitis: 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[1]
- As previously reported, patients with AD have a high prevalence of comorbid atopic conditions, including allergic rhinitis (AR)[2]
- 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 AR[3]
- In dupilumab trials, > 80% of adult patients have reported ≥ 1 comorbid condition, and as many as 50% have reported comorbid AR[4]

OBJECTIVE

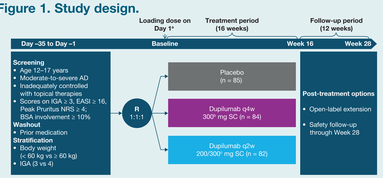
- **To determine if a history of AR impacts the efficacy of dupilumab treatment in adolescent patients with moderate-to-severe AD enrolled in a phase 3 trial**

METHODS

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**)[5]

Figure 1. Study design.



Topical therapy and other systemic AD therapies were prohibited but allowed as rescue treatment for intolerable symptoms. *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. †In 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; q2w, every 2 weeks; q4w, every 4 weeks; R, randomization; SC, subcutaneous.

METHODS (CONT.)

Analysis

- This analysis includes the subpopulation of patients who reported a history of AR at baseline and the complementary subpopulation without a history of AR
- Efficacy outcomes were analyzed among randomized patients (full analysis set) among the 2 subgroups
- Safety was assessed among patients who received ≥ 1 dose of any study drug

RESULTS

Patients

- Of the 251 patients randomized, 166 had a history of AR and 85 did not have a history of AR
- Baseline disease characteristics were similar among treatment groups and between subgroups with a history of AR and no history of AR (**Table 1**)

Table 1. Baseline disease characteristics by history of AR.

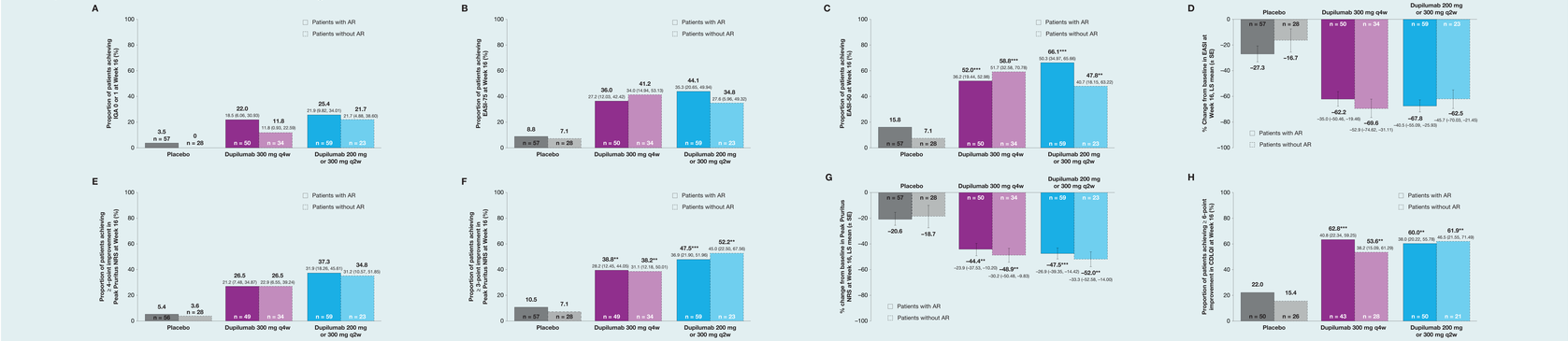
	Patients with a history of AR			Patients without a history of AR		
	Placebo (n = 57)	Dupilumab 300 mg q4w (n = 50)	Dupilumab 200 mg or 300 mg q2w (n = 59)	Placebo (n = 28)	Dupilumab 300 mg q4w (n = 34)	Dupilumab 200 mg or 300 mg q2w (n = 23)
Duration of AD, mean (SD), years	12.4 (3.37)	12.2 (3.08)	12.3 (3.06)	12.0 (3.64)	11.6 (3.32)	12.9 (2.76)
IGA score 4, n (%)	33 (57.9)	28 (56.0)	32 (54.2)	13 (46.4)	18 (52.9)	11 (47.8)
EASI, mean (SD)	37.3 (14.00)	36.2 (15.05)	35.4 (12.68)	32.0 (13.46)	35.1 (14.68)	34.9 (16.75)
SCORAD total score, mean (SD)	71.8 (13.48)	69.7 (13.27)	71.4 (13.12)	67.7 (12.56)	70.0 (15.49)	68.5 (15.80)
BSA involvement of AD, mean (SD), %	58.9 (24.34)	58.1 (22.68)	57.1 (19.99)	51.3 (23.28)	55.2 (24.93)	53.0 (24.91)
Peak Pruritus NRS, mean (SD)	7.6 (1.65)	7.3 (2.06)	7.5 (1.45)	7.9 (1.58)	7.8 (1.44)	7.7 (1.70)
CDLQI, mean (SD)	13.1 (6.69)	15.2 (6.97)	12.4 (5.93)	13.2 (6.90)	14.2 (8.00)	14.5 (6.81)

CDLQI, Children's Dermatology Life Quality Index; SCORAD, SCORing Atopic Dermatitis; SD, standard deviation.

RESULTS (CONT.)

Efficacy

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 scores; (H) Proportion of patients with ≥ 6-point reduction from baseline in CDLQI through Week 16.



Difference vs placebo (95% confidence interval (CI)) are shown below percent values on top of bar graphs. **$P < 0.01$; ***$P < 0.0001$. LS, least squares; SE, standard error.

Safety

Table 2. Safety outcomes in adolescent patients.

Patients with, n (%)	Placebo (n = 85)	Dupilumab 300 mg q4w (n = 83)	Dupilumab 200 mg/300 mg q2w (n = 82)
TEAE	59 (69.4)	53 (63.9)	59 (72.0)
TEAE leading to permanent study discontinuation	1 (1.2)	0	0
Serious TEAE	1 (1.2)	0	0
Death	0	0	0
Most common TEAEs[a]			
Dermatitis atopic (PT)	21 (24.7)	15 (18.1)	15 (18.3)
Skin infection (adjudicated)	17 (20.0)	11 (13.3)	9 (11.0)
Upper respiratory tract infection (PT)	15 (17.6)	6 (7.2)	10 (12.2)
Headache (PT)	9 (10.6)	4 (4.8)	9 (11.0)
Conjunctivitis[b]	4 (4.7)	9 (10.8)	8 (9.8)
Nasopharyngitis (PT)	4 (4.7)	9 (10.8)	3 (3.7)
Infection and infestation (SOC)	37 (43.5)	38 (45.8)	34 (41.5)
Injection-site reaction (HLT)	3 (3.5)	5 (6.0)	7 (8.5)
Herpes viral infection (HLT)	3 (3.5)	4 (4.8)	1 (1.2)

[a]By PT, in ≥ 5% of patients in any treatment group. [b]Includes the PTs atopic keratoconjunctivitis, conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral. HLT, MedDRA High Level Term; MedDRA, 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,[5,6] dupilumab improved signs and symptoms of AD in adolescent patients with moderate-to-severe AD regardless of history of AR, indicating that a potentially increased type 2 burden does not impact dupilumab efficacy**

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Acknowledgments: Data first presented at the 2020 Annual Meeting of the American Academy of Allergy, Asthma & Immunology (AAAAI); Philadelphia, PA, USA; March 13–16, 2020.

Research sponsored by Sanofi and Regeneron Pharmaceuticals, Inc. ClinicalTrials.gov Identifier: NCT03054428 (LIBERTY AD ADOL). Medical writing/editorial assistance provided by Luke Shelton, PhD, of Excerpta Medica, funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.

Disclosures: Sher L: Aimmune, Optinose, Regeneron Pharmaceuticals, Inc., Sanofi Genzyme – advisory board member; Regeneron Pharmaceuticals, Inc., Sanofi Genzyme – speaker fees; Aimmune, Amgen, AstraZeneca, Circassia, DBV, Galderma, GSK, Lupin, Merck, Mylan, Novartis, Novo Nordisk, Optinose, Pearl, Pfizer, Pulmagen, Roxane, Sanofi, Spirometrix, Teva, Vectura, Watson – clinical trial funding. **Soong W:** AstraZeneca, Regeneron Pharmaceuticals, Inc. – speaker, advisory board member, investigator; AbbVie, Regeneron Pharmaceuticals, Inc. – consultant; AbbVie – investigator; Aimmune, GSK, LEO Pharma, Novartis, Pfizer, Teva, Vanda Pharmaceuticals – investigator grants; Genentech – investigator grants, honorarium, advisory board member; Stallergenes Greer – advisory board member. **Chen Z, Bansal A:** Regeneron Pharmaceuticals, Inc. – employees and shareholders. **Prescilla R:** Sanofi Genzyme – employee, may hold stock and/or stock options in the company.

Presented at the 5th Fall Clinical Dermatology Conference for PAs & NPs (FCPANP).