Dupilumab Treatment Improves Health-Related Quality of Life in Children Aged ≥ 6 to < 12 Years With Severe Atopic Dermatitis

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BACKGROUND

- In children with moderate-to-severe atopic dermatitis (AD), skin lesions often involve a large body surface area (BSA), and patients frequently experience pruritus and sleep deprivation, which significantly impacts quality of life for both patients and their caregivers[1]
- The Children's Dermatology Life Quality Index (CDLQI) is a validated 10-item questionnaire, which assesses patient-reported impact of AD on health-related quality of life (HRQoL) in 6 domains (symptoms and feelings, leisure, school or holidays, personal relationships, sleep, and treatment)[2]
- Dupilumab is a fully human monoclonal antibody[3,4] that selectively inhibits signaling of interleukin-4 and interleukin-13, key and central drivers of type 2 inflammation in AD and other diseases[5]
- Dupilumab provides significant clinical improvement with an acceptable safety profile in adults[6] and adolescents[7] with moderate-to-severe AD and in children aged ≥ 6 to < 12 years with severe AD inadequatelly controlled with topical medications[8]

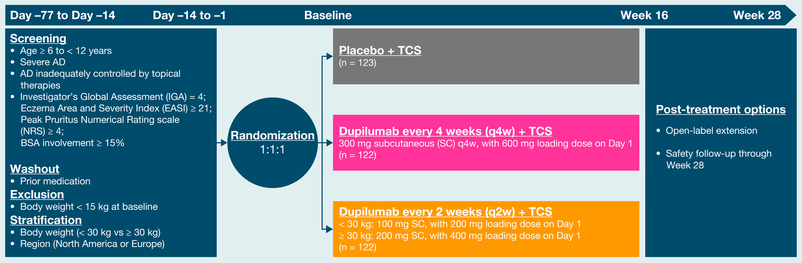
OBJECTIVE

- **To report the improvement in quality of life measured by CDLQI in children aged ≥ 6 to < 12 years with severe AD treated with dupilumab in combination with standardized treatment of medium-potency topical corticosteroids (TCS) from the phase 3 study LIBERTY AD PEDS study (NCT03345914)**

METHODS

Study design

Figure 1. LIBERTY AD PEDS (NCT03345914) study design.[8]



[a]Starting on Day –14, all patients initiated standardized treatment with medium-potency TCS; TCS could be tapered depending on the patient's clinical outcome.

Analysis

- This analysis reports on results from patients treated with FDA-approved doses only (dupilumab 300 mg q4w if baseline weight <30kg; dupilumab 200 mg q2w if baseline weight ≥ 30kg) and weight-matched placebo groups; all patients received concomitant medium-potency TCS
- Data are reported as least squares (LS) mean or mean percentage change at indicated timepoints, proportion of patients achieving ≥ 6-point improvement in CDLQI, categorical change in total CDLQI (CDLQI 0–1 = no effect on HRQoL; 2–6 = small effect; 7–12 = moderate effect; 13–18 = very large effect; 19–30 = extremely large effect) at indicated timepoints, with nominal *P*-values compared with the corresponding placebo group
- LS mean or mean percentage change and P-values are based on ANCOVA model with baseline measurement as covariate and the treatment with respective weight group, randomization stratum region (North America vs Europe) as fixed factors
- Missing data, except for categorical changes in CDLQI, were imputed using the multiple imputation method

RESULTS

Safety

- Safety in children with severe AD was consistent with the known dupilumab safety profile[8]
- Most common adverse events were conjunctivitis and injection site reactions[8]

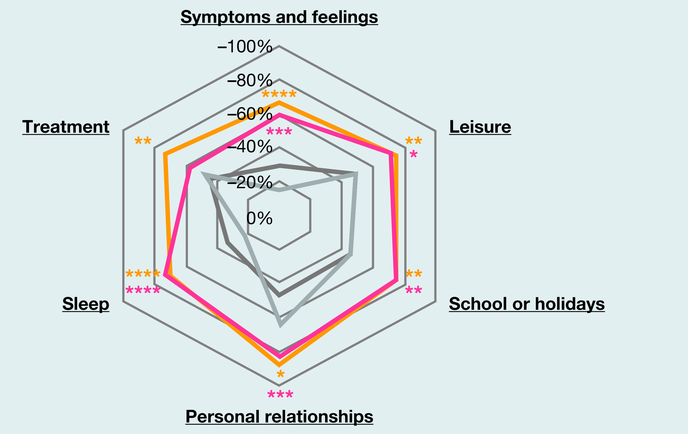
RESULTS (CONT.)

Table. Baseline demographics and disease characteristics.

		Baseline weight < 30 kg		Baseline weight ≥ 30 kg	
	Score range	Placebo + TCS (n = 61)	Dupilumab 300 mg q4w+ TCS (n = 61)	Placebo + TCS (n = 62)	Dupilumab 200 mg q2w+ TCS (n = 59)
Age, mean (SD), years		7.1 (1.3)	7.5 (1.4)	9.5 (1.3)	9.5 (1.4)
Male sex, n (%)		30 (49.2)	27 (44.3)	31 (50.0)	33 (55.9)
Weight, mean (SD), kg		23.3 (3.4)	23.8 (3.0)	39.5 (9.5)	40.2 (10.0)
Duration of AD, mean (SD), years		6.3 (1.7)	6.8 (1.7)	8.0 (2.2)	8.1 (2.3)
EASI, mean (SD)	0–72	38.9 (12.6)	36.9 (12.4)	39.0 (11.5)	37.1 (11.8)
Peak Pruritus NRS score, mean (SD)	0–10	7.6 (1.6)	7.9 (1.5)	7.8 (1.5)	7.6 (1.5)
CDLQI total score, mean (SD)	0–30	16.1 (6.9)	16.9 (8.1)	13.2 (7.7)	13.0 (6.3)
CDLQI domain scores, mean (SD)					
Symptoms and feelings		3.9 (1.5)	4.3 (1.5)	3.4 (1.7)	3.5 (1.3)
Leisure		4.9 (2.6)	4.9 (3.2)	3.7 (2.8)	3.8 (2.8)
School or holidays		1.8 (1.0)	1.8 (1.1)	1.4 (1.1)	1.3 (1.0)
Personal relationships		1.7 (1.8)	2.1 (2.0)	1.4 (1.7)	1.3 (1.5)
Sleep		2.2 (0.8)	2.2 (0.8)	1.8 (0.9)	1.8 (0.9)
Treatment		1.7 (1.0)	1.6 (1.0)	1.6 (1.0)	1.3 (1.0)

SD, standard deviation

Figure 3. Dupilumab consistently and significantly improved all patient-reported outcomes in the 6 CDLQI domains in children with severe AD.



*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$; ****$P < 0.0001$ vs weight-matched placebo + TCS.

Figure 2. Dupilumab resulted in rapid and sustained clinically meaningful improvements in HRQoL.

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$; ****$P < 0.0001$ vs weight-matched placebo + TCS.

[a]From subset of patients with a baseline CDLQI score of ≥ 6. BL, baseline; n1, number of patients with non-missing CDLQI category within each treatment arm and timepoint; SE, standard error; Wk, Week.

CONCLUSIONS

- **Dupilumab + TCS significantly improved HRQoL measured by CDLQI when compared with placebo + TCS and resulted in clinically meaningful responses as early as after the first dose**
- **Rapid and consistent improvements with dupilumab therapy were observed in all 6 individual domains of CDLQI (symptoms and feelings, leisure, school or holidays, personal relationships, sleep, and treatment)**
- **Most patients had at least "moderate" impact of AD on life at baseline, and over three-fourths of patients treated with dupilumab had "no" or "small" impact of AD on life after ~4 months of treatment**

References: 1. Beattie PE, Lewis-Jones MS. Br J Dermatol. 2006;155:145-51. 2. Lewis-Jones MS, Finlay AY. Br J Dermatol. 1995;132:942-9. 3. Macdonald LE, et al. Proc Natl Acad Sci U S A. 2014;111:5147-52. 4. Murphy AJ, et al. Proc Natl Acad Sci U S A. 2014;111:5153-8. 5. Gandhi NA, et al. Expert Rev Clin Immunol. 2017;13:425-37. 6. Beck LA, et al. Am J Clin Dermatol. 2020;21:567-77. 7. Simpson EL, et al. JAMA Dermatol. 2020;156:44-56. 8. Paller A, et al. J Am Acad Dermatol. In press 2020.

Acknowledgments: Data first presented at 2020 Pediatric Dermatology Research Alliance (PeDRA) Digital Conference, October 22–23, 2020. Research sponsored by Sanofi and Regeneron Pharmaceuticals, Inc. ClinicalTrials.gov Identifier: NCT03345914. Medical writing/editorial assistance provided by Julian J. Freen–van Heeren, PhD, of Excerpta Medica, funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc. Spider gram developed by Ana B. Rossi and Marthe Vuillet of Sanofi Genzyme.

Disclosures: Irvine AD: AbbVie, Arena Pharmaceuticals, BenevolentAI, Chugai Pharma, Dermavant, Eli Lilly, Genentech, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi, UCB – consultant; AbbVie, Eli Lilly, LEO Pharma, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Sanofi – speaker; AbbVie, DS Biopharma, Inflazome, Novartis, Sanofi–Regeneron Pharmaceuticals, Inc.– investigator. **Deleuran M:** AbbVie, Almirall, Eli Lilly, LEO Pharma, Pfizer, Pierre Fabre, Regeneron Pharmaceuticals, Inc., Sanofi Genzyme – research support, consulting/advisory board agreements, and/or honoraria for lectures. **Praestgaard A, Rossi AB:** Sanofi Genzyme – employees, may hold stock and/or stock options in the company. **Delevry D:** Regeneron Pharmaceuticals, Inc. – employee and shareholder.

Presented at the Revolutionizing Atopic Dermatitis Conference (RAD 2020); Virtual Conference; December 13–14, 2020.