Long-Term Efficacy and Safety of Dupilumab in Adolescents With Atopic Dermatitis: Results From an Open-Label Extension Trial (LIBERTY AD PED-OLE)

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BACKGROUND

- The prevalence of AD among adolescents worldwide is estimated at 14.8%[1]
- In the USA, 4.5%/3.9%/0.8% of adolescents report mild/moderate/severe AD[1]
- Until recently, adolescents with AD inadequately controlled by topical therapies had limited treatment options, with the use of systemic corticosteroids strongly discouraged[2]
- Dupilumab is a fully human[3,4] monoclonal antibody that blocks the shared receptor component 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[5,6]
- In the randomized, double-blinded, placebo-controlled, phase 3 LIBERTY AD ADOL study in adolescent patients (aged ≥ 12 to < 18 years) with moderate-to-severe AD, 16-week treatment with dupilumab resulted in significant improvement in AD signs, symptoms, and quality of life compared with placebo, with an acceptable safety profile[7]

OBJECTIVE

- **To investigate the efficacy and safety of dupilumab in adolescent patients (aged ≥ 12 to < 18 years) with moderate-to-severe AD who had previously participated in dupilumab trials and were subsequently enrolled in an open-label extension (OLE) study**

METHODS

Study design

- This is an ongoing, OLE study (LIBERTY AD PED-OLE, NCT02612454) in patients aged ≥ 6 months to < 18 years with moderate-to-severe AD who participated in previous dupilumab studies
- Here, we present results for the age cohort of ≥ 12 to < 18 years of the study, with a data cutoff date of December 15, 2018
- Previous studies (called parent studies from this point onwards) for this age cohort included the single-dose phase 2a study AD-1412 (NCT02407756),[8] LIBERTY AD ADOL (NCT03054428),[7] and the phase 1b AD-1607 study (NCT03050151)
- Main inclusion criteria were participation in a previous dupilumab trial and completing all visits/assessments (AD-1412) or at least 50% of visits and assessments (AD ADOL and AD-1607)
  - Patients from the placebo arm of the AD ADOL trial could participate in the OLE

Treatment

- Per the original protocol of the OLE study, the dose regimen was 2 mg/kg or 4 mg/kg every week
- Once the pharmacokinetic data were available, the dosing regimen was changed from weight-based dosing (2 mg/kg or 4 mg/kg) to a fixed-dose regimen of 300 mg every 4 weeks (Protocol Amendment 1); the dose was up-titrated at the discretion of the investigators in case of inadequate clinical response at Week 16 as follows
  - Patients weighing < 60 kg: 200 mg every 2 weeks (q2w)
  - Patients weighing ≥ 60 kg: 300 mg (q2w)

METHODS (CONT.)

- Concomitant topical corticosteroids and topical calcineurin inhibitors were allowed without restriction; topical crisaborole was also permitted if approved locally for treatment of AD
  - Systemic medications for AD, including systemic corticosteroids and systemic nonsteroidal immunosuppressants, were not permitted except as rescue treatment

Analysis

- Efficacy outcomes were analyzed descriptively in the safety analysis set among patients with available values at each visit, with no imputation for missing values (all observed values)
- Safety outcomes were analyzed in patients who received ≥ 1 dose of study drug (safety analysis set)

RESULTS

Patients

- At the time of the data cutoff of this analysis, 299 OLE patients were included in the analysis
  - Of these, 36 patients previously participated in the AD-1412 study, 225 in the AD ADOL trial, and 38 in the AD-1607 trial
  - At the cutoff date, 241 (80.6%) patients were still enrolled in the study, 12 (4%) patients had completed the study, and 46 (15.4%) had discontinued the study prematurely
    - The most common reasons for study discontinuation were withdrawal by patient (18 [6.0%]), lack of efficacy (11 [3.7%]), and patient turning 18 years of age (11 [3.7%])
  - 105 (35.1%) patients reached the Week 52 visit
- Demographics and characteristics both at the parent study baseline (PSBL) and current study baseline (BL) for these patients are shown in **Table 1**

Table 1. Baseline demographics and clinical characteristics.

	N = 299	
Age, mean (SD), years	14.7 (1.68)	
Sex, male, n (%)	169 (56.5)	
Race		
White	208 (69.6)	
Black or African American	30 (10.0)	
Asian	42 (14.0)	
Other	15 (5.0)	
BMI, mean (SD), kg/m^2	24.1 (5.99)	
Baseline weight group, n (%)		
< 60 kg	147 (49.2)	
≥ 60 kg	152 (50.8)	
	Parent study	**Current study**
Duration of AD, mean (SD), years	–	12.5 (3.18)
IGA score, n (%)		
0	0	4 (1.3)
1	0	23 (7.7)
2	0	56 (18.7)
3	139 (46.5)	143 (47.8)
4	160 (53.5)	73 (24.4)
EASI, mean (SD)	34.4 (14.3)	19.8 (15.5)
BSA affected, mean (SD), %	54.3 (23.3)	34.0 (25.2)
SCORAD score, mean (SD)	69.6 (13.6)	46.5 (21.2)
CDLQI total score, mean (SD)	13.5 (6.7)	7.1 (6.1)

BMI, body mass index; BSA, body surface area; CDLQI, Children's Dermatology Life Quality Index; IGA, Investigator's Global Assessment; EASI, Eczema Area and Severity Index; SCORAD, SCORing Atopic Dermatitis; SD, standard deviation.

RESULTS (CONT.)

Efficacy outcomes

Figure 1. Proportion of patients with IGA 0 or 1 over time.

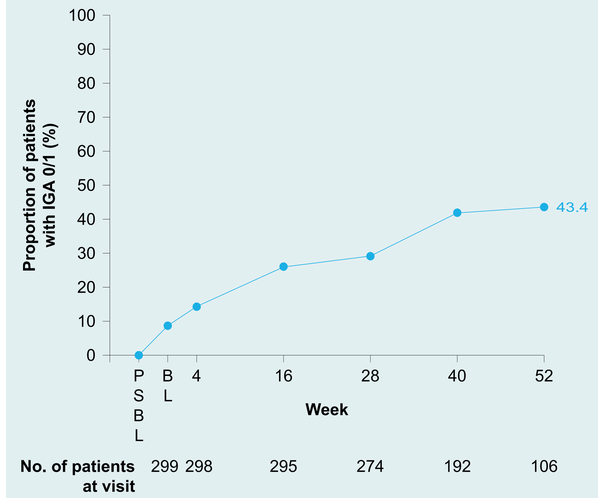


Figure 2. Percent change in EASI from PSBL over time.

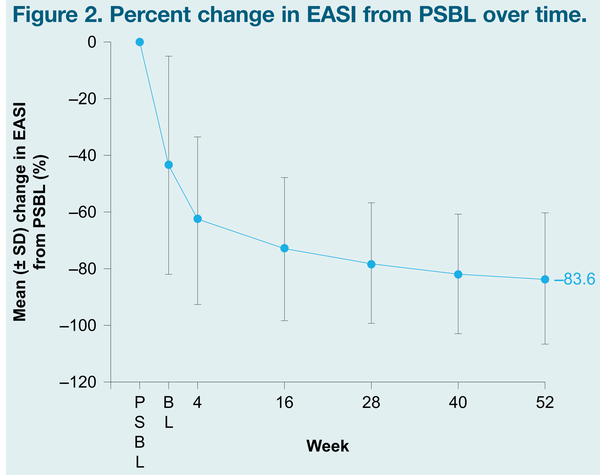


Figure 3. Proportion of patients with EASI-75 calculated from PSBL over time.

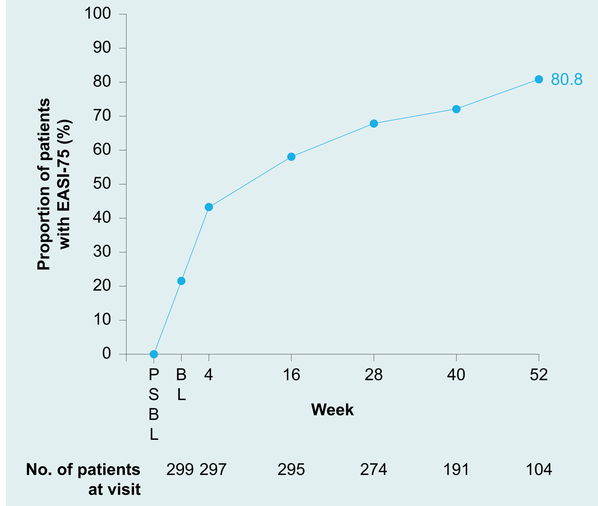
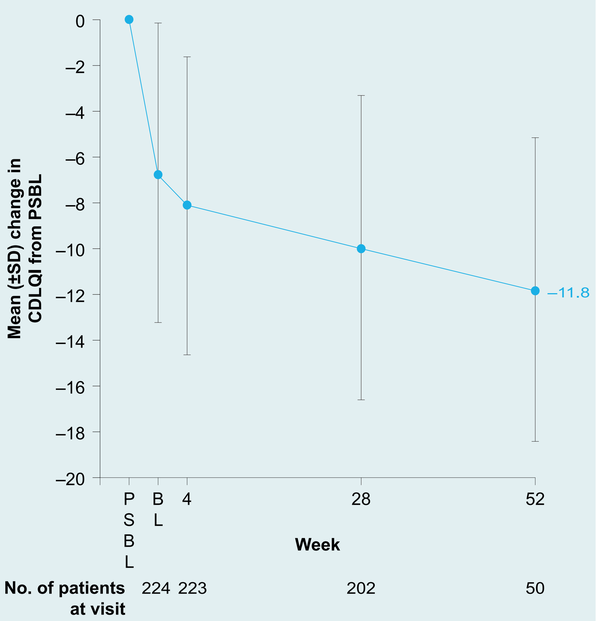


Figure 4. Change in CDLQI from PSBL over time.



Safety outcomes

Table 2. Safety assessment.

	N = 299	
Patients with	**n (%)**	**nP/100PY**
≥ 1 TEAE	222 (74.2)	198.5
≥ 1 treatment-related TEAE	54 (18.1)	20.1
TEAE leading to permanent study treatment discontinuation	2 (0.7)	0.6
Death	0	0
Any serious TEAE	5 (1.7)	1.6
Adverse events reported in ≥ 5% of patients by PT		
Nasopharyngitis	63 (21.1)	24.3
Dermatitis atopic	58 (19.4)	21.7
Upper respiratory tract infection	37 (12.4)	12.9
Headache	28 (9.4)	9.8
Oropharyngeal pain	17 (5.7)	5.7
Conjunctivitis[a]	26 (8.7)	9.0
Injection-site reactions (HLT)	20 (6.7)	6.8

[a]Includes the following PTs: conjunctivitis, conjunctivitis bacterial, conjunctivitis viral, conjunctivitis allergic, and atopic keratoconjunctivitis. HLT, MedDRA High Level Term; MedDRA, Medical Dictionary for Regulatory Activities; nP, number of patients with event; PT, MedDRA Preferred Term.
TEAE, treatment-emergent adverse event; 100PY, 100 patient years.

CONCLUSION

- **Data from this OLE trial of dupilumab support the long-term efficacy and safety of dupilumab in adolescents with AD**

References: 1. Silverberg JI, et al. Data to be presented at the 2020 Annual Meeting of the European Academy of Allergy and Clinical Immunology; London, UK; June 6-10. Abstract 1068. 2. Drucker AM, et al. Br J Dermatol. 2018;178:768-75. 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. Gandhi NA, et al. Nat Rev Drug Discov. 2016;15:35-50. 7. Simpson EL, et al. JAMA Derm. 2019 Nov 6 [Epub ahead of print]. doi: https://doi.org/10.1001/jamadermatol.2019.3336. 8. Cork MJ, et al. Br J Dermatol. 2019 Oct 8 [Epub ahead of print]. doi: https://doi.org/10.1111/bjd.18476

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