Efficacy and Safety of Dupilumab in Children Aged ≥ 6 Months to < 6 Years With Moderate-to-Severe Atopic Dermatitis

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BACKGROUND

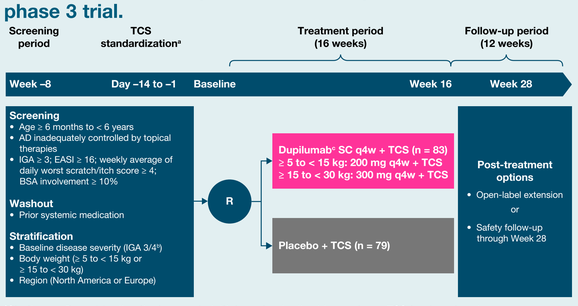
- There is currently a high unmet medical need in patients aged 6 months to < 6 years with moderate-to-severe pediatric atopic dermatitis (AD), with a lack of approved systemic treatments
- Previous phase 3 studies showed that dupilumab substantially improved AD-associated signs, symptoms, and quality of life, with a favorable safety profile in adults, adolescents, and children aged 6 to < 12 years[1–3]

OBJECTIVE

- **To evaluate the efficacy and safety of 16-week dupilumab treatment with concomitant low-potency topical corticosteroids (TCS) in children aged 6 months to < 6 years with moderate-to-severe AD inadequately controlled with topical therapies**

METHODS

Figure 1. Study design LIBERTY AD INFANT/PRE-SCHOOL Part B (NCT03346434), a double-blind, placebo-controlled, phase 3 trial.



[a]Starting on Day –14, all patients were to initiate a standardized low-potency TCS treatment regimen (hydrocortisone acetate 1% cream).
[b]Number of patients with IGA 3 was capped to 40.
[c]No loading dose. Weight-tiered doses were assigned by baseline body weight for the duration of the study.
BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; q4w, every 4 weeks; R, randomization; SC, subcutaneous.

CONCLUSIONS

- **In children aged 6 months to < 6 years with moderate-to-severe AD, dupilumab q4w + low-potency TCS rapidly and significantly improved AD signs and symptoms**
- **Dupilumab was well tolerated and demonstrated a favorable safety profile similar to that observed in adults and older children**

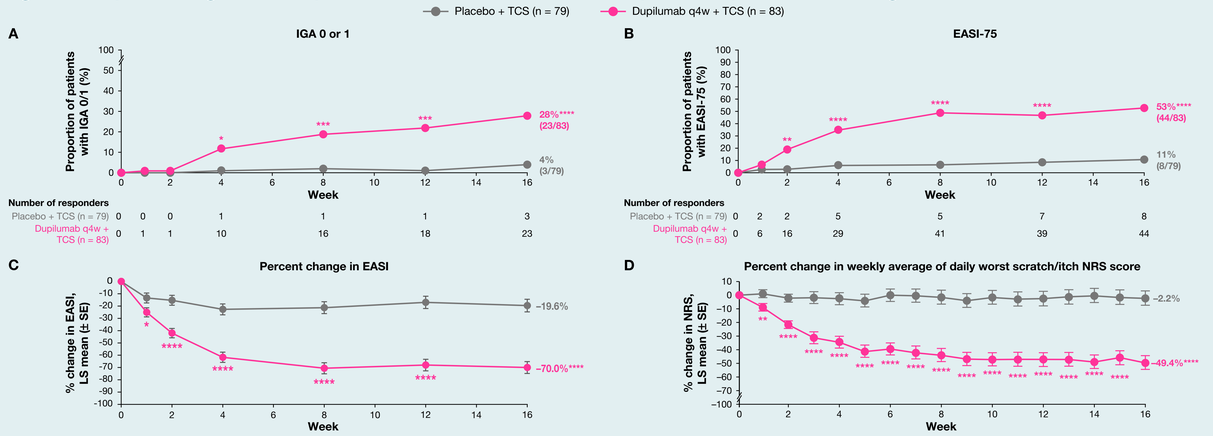
RESULTS

Table 1. Baseline demographics and disease characteristics.

	Placebo + TCS (n = 79)	Dupilumab + TCS (n = 83)	Overall (N = 162)
Age, mean (SD), years	3.8 (1.3)	3.9 (1.2)	3.8 (1.2)
≥ 6 months to < 2 years, n (%)	5 (6.3)	6 (7.2)	11 (6.8)
≥ 2 years to < 6 years, n (%)	74 (93.7)	77 (92.8)	151 (93.2)
Male sex, n (%)	55 (69.6)	44 (53.0)	99 (61.1)
Race, n (%)			
White	53 (67.1)	58 (69.9)	111 (68.5)
Black or African American	16 (20.3)	14 (16.9)	30 (18.5)
Asian	4 (5.1)	6 (7.2)	10 (6.2)
Other	4 (5.1)	3 (3.6)	7 (4.3)
Weight, mean (SD), kg	16.7 (3.6)	17.1 (4.4)	16.9 (4.0)
5 to < 15 kg, n (%)	25 (31.6)	26 (31.3)	51 (31.5)
15 to < 30 kg, n (%)	54 (68.4)	57 (68.7)	111 (68.5)
Duration of AD, mean (SD), years	3.4 (1.3)	3.4 (1.3)	3.4 (1.3)
Age at onset < 6 months, n (%)	57 (72.2)	50 (60.2)	107 (66.0)
Age at onset ≥ 6 months, n (%)	22 (27.8)	33 (39.8)	55 (34.0)
EASI (range 0–72), mean (SD)	33.1 (12.2)	35.1 (13.9)	34.1 (13.1)
IGA score (range 0–4), n (%)			
3	17 (21.5)	20 (24.1)	37 (22.8)
4	62 (78.5)	63 (75.9)	125 (77.2)
Weekly averaged worst scratch/itch NRS score (range 0–10), mean (SD)	7.6 (1.5)	7.5 (1.3)	7.6 (1.4)
BSA affected (range 0–100), mean (SD), %	57.4 (20.9)	59.3 (22.5)	58.4 (21.7)
SCORAD score (range 0–103), mean (SD)	72.2 (11.4)	72.7 (13.0)	72.4 (12.2)
CDLQI[a] (range 0–30), mean (SD)	17.7 (6.3; n = 38)	17.5 (5.4; n = 48)	17.6 (5.8)
IDQoL[a] (range 0–30), mean (SD)	17.1 (5.4; n = 41)	17.4 (5.4; n = 35)	17.2 (5.4)
DFI score[a] (range 0–30), mean (SD)	17.6 (7.2)	17.2 (6.0)	17.4 (6.6)
Peak skin pain NRS score (range 0–10), mean (SD)	7.2 (1.8)	6.8 (1.8)	7.0 (1.8)
Patient sleep quality NRS score (range 0–10), mean (SD)	4.6 (2.1)	4.9 (1.9)	4.8 (2.0)
Current history of atopic comorbidities,[b] n (%)	65 (83.3)	66 (79.5)	131 (81.4)
Prior use of systemic medications for AD,[b] n (%)	22 (28.2)	24 (28.9)	46 (28.6)
Prior use of systemic corticosteroids,[b] n (%)	14 (17.9)	16 (19.3)	30 (18.6)
Prior use of systemic non-steroidal immunosuppressants,[b] n (%)	12 (15.4)	13 (15.7)	25 (15.5)

Higher score indicates worse disease/larger impact, except for Patient sleep quality NRS, where a higher score indicates better sleep quality.
[a]CDLQI assesses QoL in pediatric patients ≥ 4 to < 18 years, IDQoL in patients < 4 years, and DFI in caregivers.
[b]Assessed in safety analysis set.
CDLQI, Children's Dermatology Life Quality Index; DFI, Dermatitis Family Impact; IDQoL, Infant's Dermatitis Quality of Life; NRS, Numerical Rating Scale; QoL, quality of life; SCORAD, SCORing Atopic Dermatitis; SD, standard deviation.

Figure 2. Rapid and significant improvements in lesional burden and patient-reported itch through Week 16.



Values after first rescue treatment use were set to missing.
(A, B) Patients with missing values at Week 16 due to rescue treatment, withdrawn consent, AE, and lack of efficacy were considered as non-responders. Patients with missing values due to other reasons including COVID-19 were imputed by MI.
(C, D) Patients with missing values at Week 16 due to rescue treatment, withdrawn consent, AE, and lack of efficacy were imputed by WOCF. Patients with missing values due to other reasons including COVID-19 were imputed by MI. All non-missing data before imputation of WOCF was used for MI.
*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$; ****$P < 0.0001$ vs placebo.
AE, adverse event; EASI-75, 75% improvement from baseline in EASI; LS, least squares; MI, multiple imputation; SE, standard error; WOCF, worst observation carried forward.

Table 2. Key safety data.

n (%)	Placebo + TCS (n = 78)	Dupilumab + TCS (n = 83)
Patients with ≥ 1 TEAE	58 (74.4)	53 (63.9)
Patients with ≥ 1 serious TEAE	4 (5.1)[a]	0
Patients with AE leading to treatment discontinuation	1 (1.3)[b]	1 (1.2)[c]
Deaths	0	0
TEAE of special interest	0	1 (1.2)[d]
Conjunctivitis (narrow[e])	0	4 (4.8)
Skin infection (excluding herpes infection)	19 (24.4)	10 (12.0)
Injection-site reactions (HLT)	2 (2.6)	2 (2.4)
Herpes viral infections (HLT)	4 (5.1)[f]	5 (6.0)[g]

[a]Serious TEAEs were atopic dermatitis, hypersensitivity, staphylococcal bacteremia, and staphylococcal cellulitis. All occurred in the placebo + TCS group and none led to study drug discontinuation. [b]Patient discontinued due to AE of nightmares due to blood draws. [c]Patient discontinued due to AE of AD flare. [d]AE of special interest of blepharitis. [e]Standardized MedDRA query containing conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, and atopic keratoconjunctivitis. [f]Oral herpes (2), eczema herpeticum, herpes simplex. [g]Herpes virus infection (2), varicella (2), oral herpes.
HLT, MedDRA High Level Term; MedDRA, Medical Dictionary for Regulatory Activities (version 23.1); TEAE, treatment-emergent adverse event.

Table 3. TEAEs reported in ≥ 5% of patients by Preferred Term.

n (%) System Organ Class Preferred Term	Placebo + TCS (n = 78)	Dupilumab + TCS (n = 83)
Infections and infestations	40 (51.3)	35 (42.2)
Nasopharyngitis	7 (9.0)	7 (8.4)
Upper respiratory tract infection	6 (7.7)	5 (6.0)
Impetigo	6 (7.7)	3 (3.6)
Skin and subcutaneous tissue disorders	28 (35.9)	17 (20.5)
Dermatitis atopic	25 (32.1)	11 (13.3)
Urticaria	4 (5.1)	1 (1.2)
Respiratory, thoracic, and mediastinal disorders	15 (19.2)	9 (10.8)
Asthma	5 (6.4)	3 (3.6)
Cough	5 (6.4)	0
Blood and lymphatic system disorders	7 (9.0)	6 (7.2)
Lymphadenopathy	6 (7.7)	3 (3.6)
General disorders and administration site conditions	9 (11.5)	5 (6.0)
Pyrexia	7 (9.0)	1 (1.2)

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