Treatment With Dupilumab Resulted in Early and Sustained Improvement in Sleep in Adolescents With Moderate-to-Severe Atopic Dermatitis

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BACKGROUND

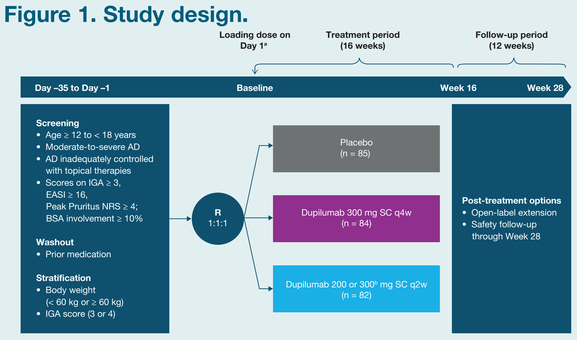
- Atopic dermatitis (AD) is a type 2 inflammatory skin disease[1]
- Adolescent patients with moderate-to-severe AD report reduced quality of life, primarily driven by pruritus and sleep disturbance[2]
- There are limited treatment options for patients with moderate-to-severe AD unresponsive to topical treatment[3]
- Dupilumab is a fully human monoclonal antibody[4–5] that blocks the shared receptor component for interleukin (IL)-4 and IL-13, thus inhibiting signaling of both IL-4 and IL-13, key drivers of type 2 inflammation in multiple diseases.[6]
- In a phase 3 trial in adolescents with moderate-to-severe AD, dupilumab vs placebo significantly improved AD signs, symptoms, and quality of life and showed an acceptable safety profile[7]

OBJECTIVE

- **To report on the effect of dupilumab on sleep, in adolescent patients with moderate-to-severe AD, from a randomized, double-blind, placebo-controlled, phase 3 trial (LIBERTY AD ADOL: NCT03054428)**

METHODS

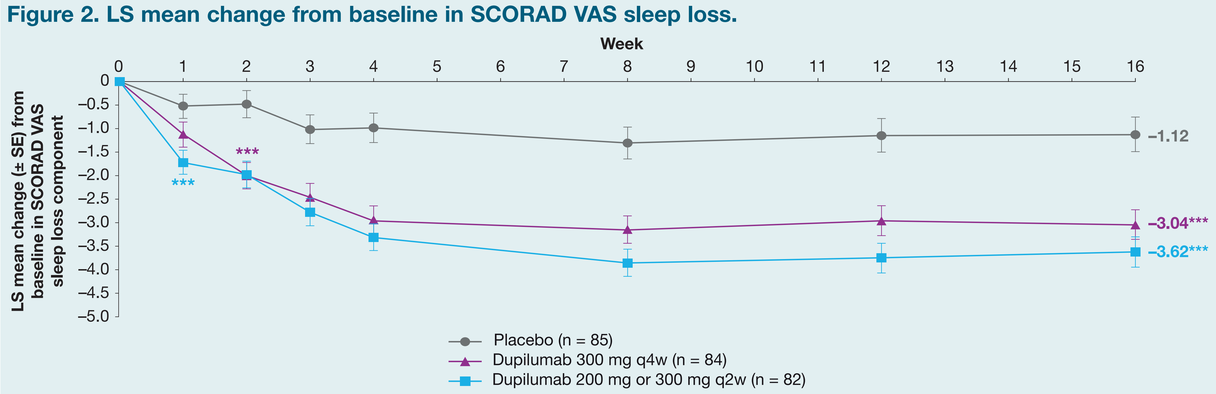
Figure 1. Study design.



[a]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 loading dose of 600 mg. All patients in the q4w group, regardless of weight, received a 600 mg loading dose. [b]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; q4w, every 4 weeks; R, randomization.

RESULTS

Figure 2. LS mean change from baseline in SCORAD VAS sleep loss.



***$P < 0.001$.
LS, least squares; SE, standard error.

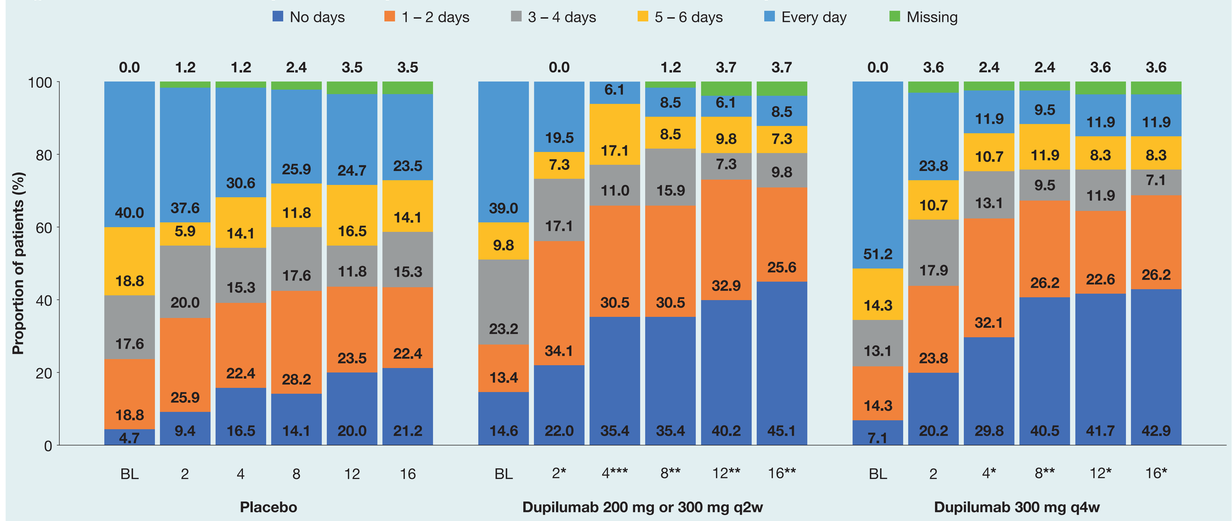
RESULTS (CONT.)

Table 1. Baseline demographics and disease characteristics.

	Range	Placebo (N = 85)	Dupilumab 200 mg or 300 mg q2w (N = 82)	Dupilumab 300 mg q4w (N = 84)
Age, mean (SD), years	–	14.5 (1.8)	14.5 (1.7)	14.4 (1.6)
Male, n (%)	–	53 (62.4)	43 (52.4)	52 (61.9)
Duration of AD, mean (SD), years	–	12.3 (3.4)	12.5 (3.0)	11.9 (3.2)
BSA affected by AD, mean (SD), %	–	56.4 (24.1)	56.0 (21.4)	56.9 (23.5)
Patients with IGA 4, n (%)	0–4	46 (54.1)	43 (52.4)	46 (54.8)
EASI score, mean (SD)	0–72	35.5 (14.0)	35.3 (13.8)	35.8 (14.8)
SCORAD total score, mean (SD)	0–103	70.4 (13.3)	70.6 (13.9)	69.8 (14.1)
Peak Pruritus NRS score, mean (SD)	0–10	7.7 (1.6)	7.5 (1.5)	7.5 (1.8)
SCORAD VAS itch score, mean (SD)	0–10	7.7 (1.8)	7.9 (1.6)	7.9 (1.8)
SCORAD VAS sleep loss score, mean (SD)	0–10	**5.6 (3.1)**	**5.4 (3.3)**	**5.9 (3.2)**
POEM total score, mean (SD)	0–28	21.1 (5.4)	21.0 (5.0)	21.1 (5.5)
POEM disturbed sleep-score, mean (SD)	0–4	2.7 (1.3)	2.5 (1.5)	2.9 (1.4)
POEM disturbed-sleep distribution of patient responses, n (%)				
No days		**4 (4.7)**	**12 (14.6)**	**6 (7.1)**
1–2 days		**16 (18.8)**	**11 (13.4)**	**12 (14.3)**
3–4 days		**15 (17.6)**	**19 (23.2)**	**11 (13.1)**
5–6 days		**16 (18.8)**	**8 (9.8)**	**12 (14.3)**
Every day		**34 (40.0)**	**32 (39.0)**	**43 (51.2)**
CDLQI total score, mean (SD)	0–30	13.1 (6.7)	13.0 (6.2)	14.8 (7.4)
CDLQI affected-sleep score, mean (SD)	0–3	2.0 (1.0)	1.9 (1.0)	2.1 (1.0)
CDLQI affected-sleep distribution of patient responses, n (%)				
Not at all		**5 (5.9)**	**10 (12.2)**	**5 (6.0)**
Only a little		**23 (27.1)**	**20 (24.4)**	**21 (25.0)**
Quite a lot		**23 (27.1)**	**23 (28.0)**	**21 (25.0)**
Very much		**34 (40.0)**	**29 (35.4)**	**37 (44.0)**

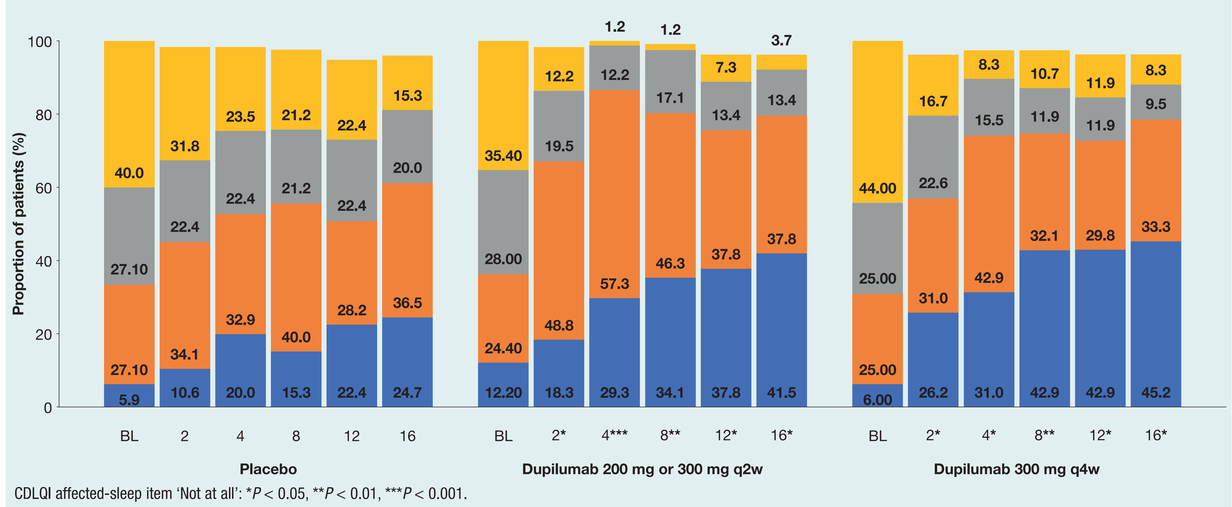
SD, standard deviation; SCORAD, SCORing Atopic Dermatitis; VAS, Visual Analog Scale; POEM, Patient Oriented Eczema Measure; CDLQI; Children's Dermatology Life Quality Index.

Figure 3. Distribution of patient responses in the POEM disturbed-sleep item.



POEM disturbed-sleep item 'no days': *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. BL, baseline.

Figure 4. Distribution of patient responses in the CDLQI affected-sleep item.



CDLQI affected-sleep item 'Not at all': *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Table 2. Safety.

Patients with adverse event	Placebo (N = 85)	Dupilumab 200 mg or 300 mg q2w (N = 82)	Dupilumab 300 mg q4w (N = 83[a])
TEAE, n (%)	59 (69.4)	59 (72.0)	53 (63.9)
TEAE leading to discontinuation of study drug, n (%)	1 (1.2)	0	0
Serious TEAE, n (%)	1 (1.2)	0	0
Death, n (%)	0	0	0

[a]One patient randomized to dupilumab q4w did not receive any study treatment and was excluded from the safety analysis set. TEAE, treatment-emergent adverse event.

CONCLUSIONS

- **Treatment with dupilumab vs placebo resulted in significant improvement in sleep as measured by SCORAD VAS sleep loss, POEM disturbed-sleep, and CDLQI affected-sleep item scores**
- **Treatment with dupilumab showed improvement in sleep as early as Week 2 for q2w**
- **These improvements were sustained through Week 16**
- **No new safety signals were observed in adolescents compared with adults**

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