Dupilumab for Adolescents With Moderate-to-Severe Atopic Dermatitis: Results From a Phase 3, Randomized, Double-Blinded Trial (LIBERTY AD ADOL)

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BACKGROUND

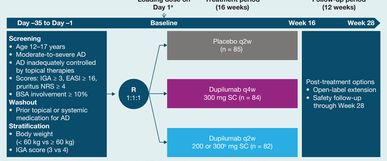
- Interleukin (IL)-4 and IL-13 are type 2 cytokines that are integral to AD pathogenesis[1]
- Dupilumab, a fully human, monoclonal antibody, blocks the shared receptor subunit for IL-4 and IL-13, thus inhibiting signaling of both IL-4 and IL-13[1]
- Dupilumab is approved for subcutaneous administration every 2 weeks (q2w) for the treatment of patients aged 12 and older in the USA with moderate-to-severe AD inadequately controlled with topical prescription therapies or when those therapies are not advisable[2], for the treatment of adult AD patients not adequately controlled with existing therapies in Japan, and for use in adults with moderate-to-severe AD who are candidates for systemic therapy in the EU[3]

OBJECTIVE

- **To evaluate the efficacy and safety of dupilumab monotherapy vs placebo in adolescents with moderate-to-severe AD inadequately controlled by topical therapies**

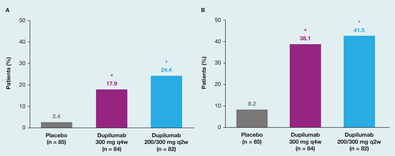
METHODS

Figure 1. Study design (NCT03054428).



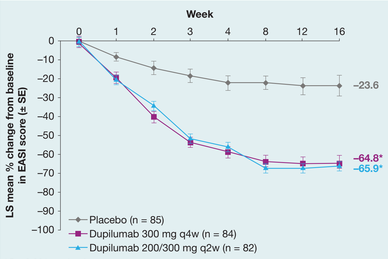
Topical therapy and other systemic AD therapies were prohibited but allowed as rescue treatment for intolerable symptoms.
[a]600 mg on Day 1. [b]Patients with body weight < 60 kg at baseline received 200 mg after a loading dose of 400 mg on Day 1.
BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NRS, Numerical Rating Scale; q4w, every 4 weeks; R, randomization; SC, subcutaneous.

Figure 2. Patients achieving IGA 0 or 1 (A) and EASI-75 at week 16 (B).



*$P < 0.001$ vs placebo.
Patients considered non-responders after rescue medication use.

Figure 3. EASI score at Week 16.



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

RESULTS

Patient disposition

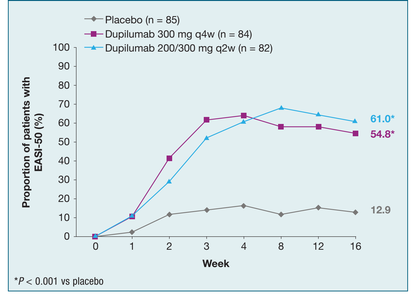
- In total, 251 patients were randomized to either dupilumab q2w (n = 82; 43 received 200 mg, 39 received 300 mg), dupilumab q4w (n = 84), or placebo q2w (n = 85)
  - 1 patient in the dupilumab q4w group was randomized but did not receive study treatment

Table 1. Baseline demographics and disease characteristics.

	Placebo (n = 85)	Dupilumab 300 mg q4w (n = 84)	Dupilumab 200/300 mg q2w (n = 82)
Age, years	14.5 (1.8)	14.4 (1.6)	14.5 (1.7)
Male, n (%)	53 (62.4)	52 (61.9)	43 (52.4)
Disease duration, years	12.3 (3.4)	11.9 (3.2)	12.5 (3.0)
EASI	35.5 (14.0)	35.8 (14.8)	35.3 (13.8)
Patients with IGA score 4, n (%)	46 (54.1)	46 (54.8)	43 (52.4)
Peak Pruritus NRS score	7.7 (1.6)	7.5 (1.8)	7.5 (1.5)
BSA involvement, %	56.4 (24.1)	56.9 (23.5)	56.0 (21.4)
SCORAD score	70.4 (13.3)	69.8 (14.1)	70.6 (13.9)
CDLQI score	13.1 (6.7)	14.8 (7.4)	13.0 (6.2)
POEM score	21.1 (5.4)	21.1 (5.5)	21.0 (5.0)
HADS score	11.6 (7.8)	13.3 (8.2)	12.6 (8.0)
Patients with ≥ 1 concurrent allergic condition, n (%)	78 (91.8)	73 (88)	79 (96.3)
Allergic rhinitis	57 (67.1)	48 (57.8)	59 (72.0)
Asthma	46 (54.1)	42 (50.6)	46 (56.1)
Food allergy	48 (56.5)	52 (62.7)	52 (63.4)
Allergic conjunctivitis	16 (18.8)	21 (25.3)	20 (24.4)
Hives	22 (25.9)	28 (33.7)	22 (26.8)
Chronic rhinosinusitis	7 (8.2)	6 (7.2)	6 (7.3)
Nasal polyps	2 (2.4)	1 (1.2)	2 (2.4)
Eosinophilic esophagitis	0	0	1 (1.2)
Other allergies[a]	62 (72.9)	53 (63.9)	58 (70.7)
Patients with prior systemic medication, n (%)	33 (38.8)	38 (45.8)	35 (42.7)
Corticosteroids	21 (24.7)	27 (32.5)	21 (25.6)
Non-steroidal immunosuppressants	17 (20.0)	15 (18.1)	20 (24.4)
Azathioprine	1 (1.2)	1 (1.2)	0
Cyclosporine	12 (14.1)	6 (7.2)	14 (17.1)
Methotrexate	6 (7.1)	10 (12.0)	10 (12.2)
Mycophenolate	0	1 (1.2)	2 (2.4)

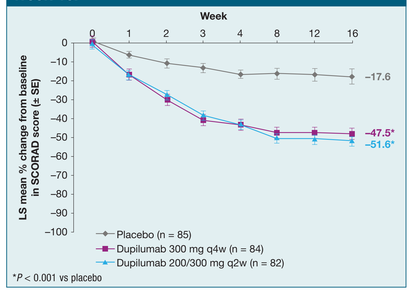
Data are shown as mean (standard deviation) unless otherwise specified.
[a]Includes allergies to medications, animals, plants, mold, dust mites, etc.
CDLQI, Children's Dermatology Life Quality Index; SCORAD, SCORing Atopic Dermatitis; POEM, Patient-Oriented Eczema Measure; HADS, Hospital Anxiety and Depression Scale.

Figure 4. Proportion of patients achieving EASI-50 from baseline through Week 16.



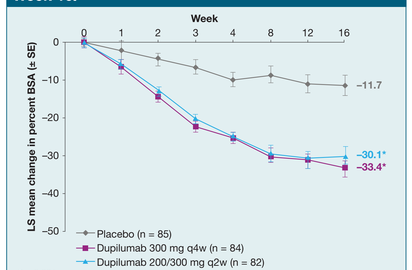
*$P < 0.001$ vs placebo

Figure 5. SCORAD score from baseline through Week 16.



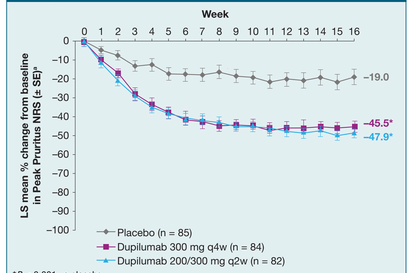
*$P < 0.001$ vs placebo

Figure 6. BSA affected by AD from baseline through Week 16.



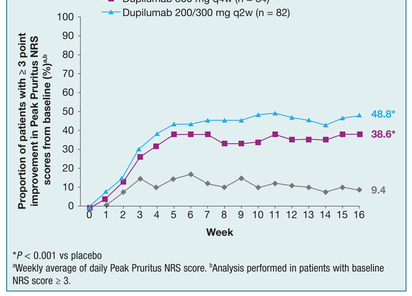
*$P < 0.001$ vs placebo

Figure 7. Peak Pruritus NRS scores from baseline through Week 16.



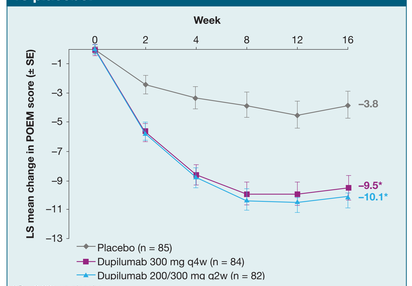
*$P < 0.001$ vs placebo
[a]Weekly average of daily Peak Pruritus NRS score.

Figure 8. Patients achieving a reduction of ≥ 3 points in Peak Pruritus NRS score from baseline through Week 16.



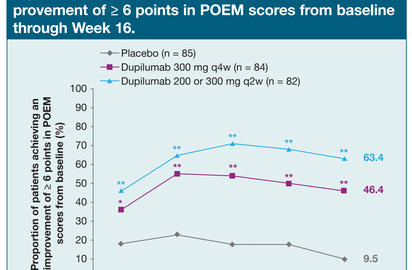
*$P < 0.001$ vs placebo
[a]Weekly average of daily Peak Pruritus NRS score. [b]Analysis performed in patients with baseline NRS score ≥ 3.

Figure 9. POEM scores from baseline through Week 16 vs placebo.



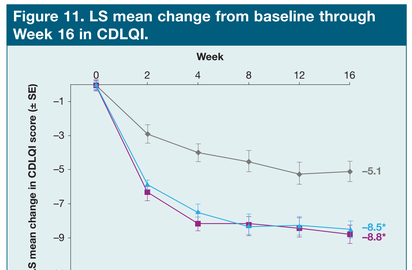
*$P < 0.001$ vs placebo

Figure 10. Proportion of patients achieving an improvement of ≥ 6 points in POEM scores from baseline through Week 16.



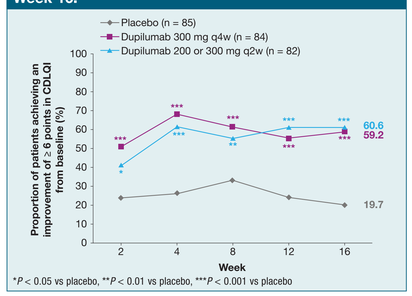
*$P < 0.05$ vs placebo, **$P < 0.01$ vs placebo, ***$P < 0.001$ vs placebo

Figure 11. LS mean change from baseline through Week 16 in CDLQI.



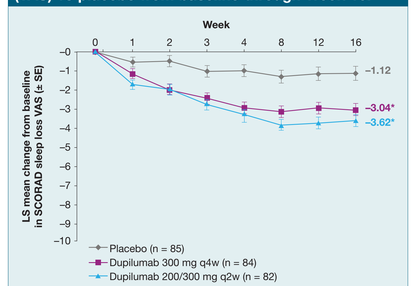
*$P < 0.001$ vs placebo

Figure 12. Proportion of patients achieving an improvement of ≥ 6 points in CDLQI from baseline Week 16.



*$P < 0.05$ vs placebo, **$P < 0.01$ vs placebo, ***$P < 0.001$ vs placebo

Figure 13. SCORAD sleep Visual Analogue Scale (VAS) vs placebo from baseline through Week 16.



*$P < 0.001$ vs placebo

Figure 14. Rescue medications requirement.

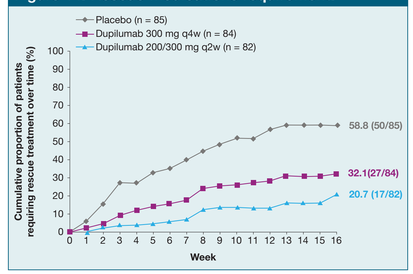
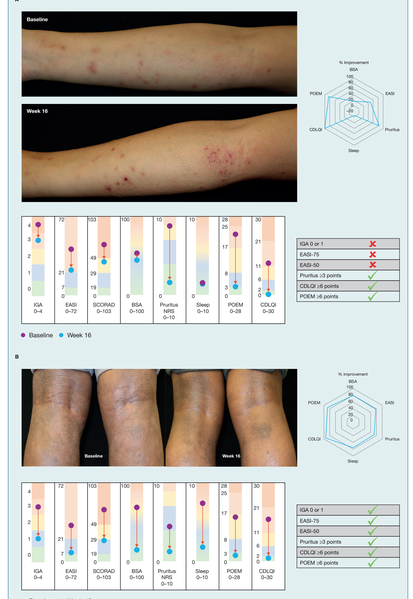


Figure 15. Patient cases.



These are individual cases and not representative of results from all patients.
Examples of patients achieving clinically meaningful improvement in one, two or three domains. The table indicates whether the patient's response met the defined threshold of clinical significance for each outcome. The spider graphic shows percentage of improvement in each outcome. The color scale graphic displays change in absolute values from baseline (purple dot) to Week 16 (blue dot) for each outcome.

Table 2. Adverse events during the 16-week treatment period.

Patients with adverse event, n (%)	Placebo (n = 85)	Dupilumab 300 mg q4w (n = 83)	Dupilumab 200 or 300 mg q2w (n = 82)
TEAEs	59 (69.4)	53 (63.9)	59 (72.0)
TEAEs leading to permanent discontinuation of study drug	1 (1.2)	0	0
Serious TEAEs	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)
Skin infections excluding herpetic skin infections (adjudicated)	16 (18.8)	8 (9.6)	8 (9.8)
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)
Infections and infestations (SOC)	37 (43.5)	38 (45.8)	34 (41.5)
Injection-site reactions (HLT)	3 (3.5)	5 (6.0)	7 (8.5)
Herpes viral infections (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, and conjunctivitis viral.
TEAE,Treatment-Emergent Adverse Events; HLT, MedDRA High Level Term; MedDRA, Medical Dictionary for Regulatory Activities; PT, MedDRA Preferred Term; SOC, system organ class.

CONCLUSIONS

- **In adolescents with moderate-to-severe AD, dupilumab treatment resulted in statistically significant and clinically meaningful improvements in AD signs and symptoms (including pruritus) and quality of life**
- **For most categorical endpoints, the q2w regimen was numerically superior to the q4w regimen**
- **Dupilumab had an acceptable safety profile, similar to that observed in the adult AD population; rates of conjunctivitis and injection-site reactions were higher with dupilumab, and rates of AD exacerbation and non-herpetic skin infections were higher with placebo**
- **Both the placebo-corrected efficacy and safety of dupilumab in adolescents were similar to those observed in adults**

References

1. Gandhi NA, et al. Nat Rev Drug Discov. 2016;15:35–50. 2. DUPIXENT® (dupilumab). Highlights of Prescribing Information. US Food and Drug Administration 2019. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761055s012lbl.pdf. Accessed March 2019. 3. DUPIXENT® (dupilumab). Summary of Product Characteristics. EuropeanMedicines Agency 2017. Available from: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR__Product_Information/human/004390/WC500236507.pdf. Accessed March 2019.

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Disclosures

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