Rapid and Sustained Improvement in Itch in Children Aged 6–11 Years With Severe Atopic Dermatitis Treated With Dupilumab: Analysis From the LIBERTY AD PEDS Phase 3 Trial

Gil Yosipovitch[1], Jonathan I. Silverberg[2], Jashin J. Wu[3], Zhen Chen[4], Randy Prescilla[5], Ana B. Rossi[5], Dimittri Delevry[4]

[1]University of Miami, Miami, FL; [2]George Washington University School of Medicine and Health Sciences, Washington, DC; [3]Dermatology Research and Education Foundation, Irvine, CA; [4]Regeneron Pharmaceuticals, Inc, Tarrytown, NY; [5]Sanofi Genzyme, Cambridge, MA; USA

BACKGROUND

- Severe atopic dermatitis (AD) is a complex, highly symptomatic, multidimensional chronic disease characterized by intense pruritus that negatively impacts a patient's life[1]
- Previously, data from the double-blind, placebo-controlled, 16-week, LIBERTY AD PEDS (NCT03345914) phase 3 trial in children aged 6–11 years with severe AD showed that dupilumab significantly improved AD signs, symptoms, and quality of life, with an acceptable safety profile[2]

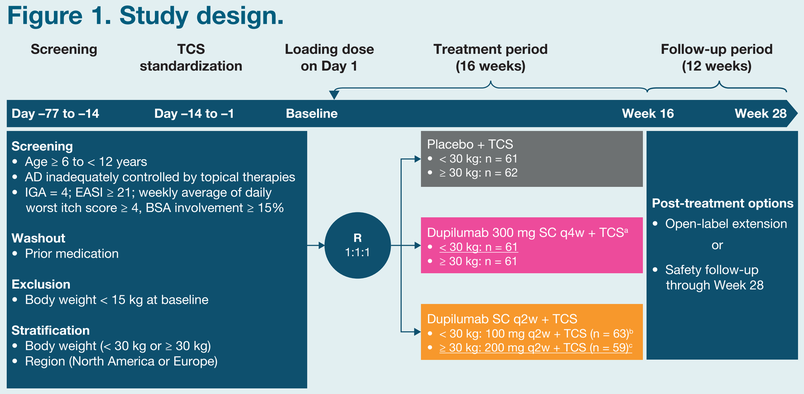
OBJECTIVE

- **To evaluate the time to onset, magnitude, and sustainability of the effect of dupilumab on different measures of itch, using data from a 16-week, phase 3 trial of dupilumab in children aged 6–11 years with severe AD treated with FDA-approved dupilumab doses**

METHODS

Study design

Figure 1. Study design.



The use of TCS was permitted at the discretion of the investigator during the screening period until Day –14. Starting on Day –14, all patients initiated a standardized TCS treatment regimen. FDA-approved doses for children aged 6–11 years are underlined. [a]600 mg loading dose; [b]200 mg loading dose; [c]400 mg loading dose. BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; q2w, every 2 weeks; q4w, every 4 weeks; R, randomization; SC, subcutaneous; TCS, topical corticosteroids.

Outcomes

- Percentage change (least squares mean with standard error [SE]) from baseline in daily worst itch scores from Day 2 to Day 22 and up to Week 16
- Proportion of patients with ≥ 2-point improvement from baseline in daily worst itch score from Day 2 to Day 22 and up to Week 16
- Proportion of patients with ≥ 4-point improvement from baseline in daily worst itch score from Day 2 to Day 22 and up to Week 16
- Proportion of patients reporting the number of days with itchy skin over the previous 7 days by visit, assessed from the "Itch" item of the Patient-Oriented Eczema Measure (POEM) questionnaire through Week 16

RESULTS

Table. Baseline demographics and disease characteristics.[a]

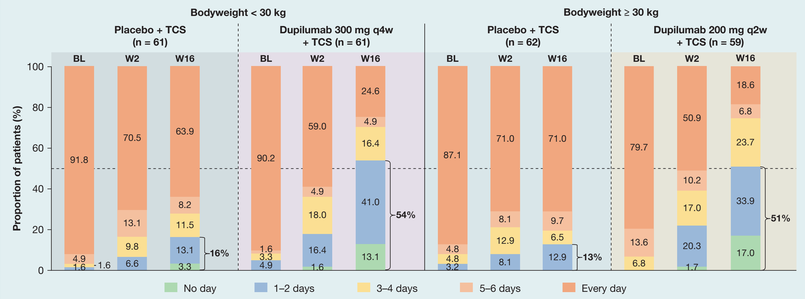
	Placebo + TCS (< 30 kg, n = 61)	Dupilumab 300 mg q4w + TCS (< 30 kg, n = 61)	Placebo + TCS (≥ 30 kg, n = 62)	Dupilumab 200 mg q2w + TCS (≥ 30 kg, n = 59)
Age, mean (SD), years	7.1 (1.3)	7.5 (1.4)	9.5 (1.3)	9.5 (1.4)
Race, n (%)				
White	40 (65.6)	45 (73.8)	37 (59.7)	45 (76.3)
Black/African American	9 (14.8)	9 (14.8)	14 (22.6)	8 (13.6)
Asian	7 (11.5)	4 (6.6)	6 (9.7)	4 (6.8)
Other	4 (6.6)	3 (4.9)	5 (8.1)	1 (1.7)
Not reported/missing	1 (1.6)	0	0	1 (1.7)
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)
BMI, mean (SD), kg/m^2	16.0 (2.5)	15.7 (1.3)	19.8 (4.1)	20.2 (4.0)
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)	38.9 (12.6)	36.9 (12.4)	39.0 (11.5)	37.1 (11.8)
Weekly average of daily worst itch score, mean (SD)	7.6 (1.6)	7.9 (1.5)	7.8 (1.5)	7.6 (1.5)
BSA affected, mean (SD), %	62.0 (20.9)	54.6 (21.9)	58.4 (22.1)	53.9 (20.2)

[a]Only FDA-approved doses of dupilumab are reported. Data for other doses and overall baseline characteristics/severity are similar to the FDA-approved doses. BMI, body mass index; SD, standard deviation.

Efficacy

- Treatment with dupilumab was associated with a significant improvement from baseline in daily worst itch score in children who received the 600 mg loading dose (300 mg q4w + TCS group) by Day 8. In children who received the 400 mg loading dose followed by 200 mg q2w + TCS, significant improvement compared with placebo was seen at Day 16 (**Figure 2A**). These differences in improvement were sustained through Week 16 with continued treatment (**Figure 2B**)

Figure 3. Proportion of patients reporting the number of days with itchy skin over the previous 7 days as assessed from the POEM Itch item question "Over the last week, on how many days has your child's skin been itchy because of their eczema?".



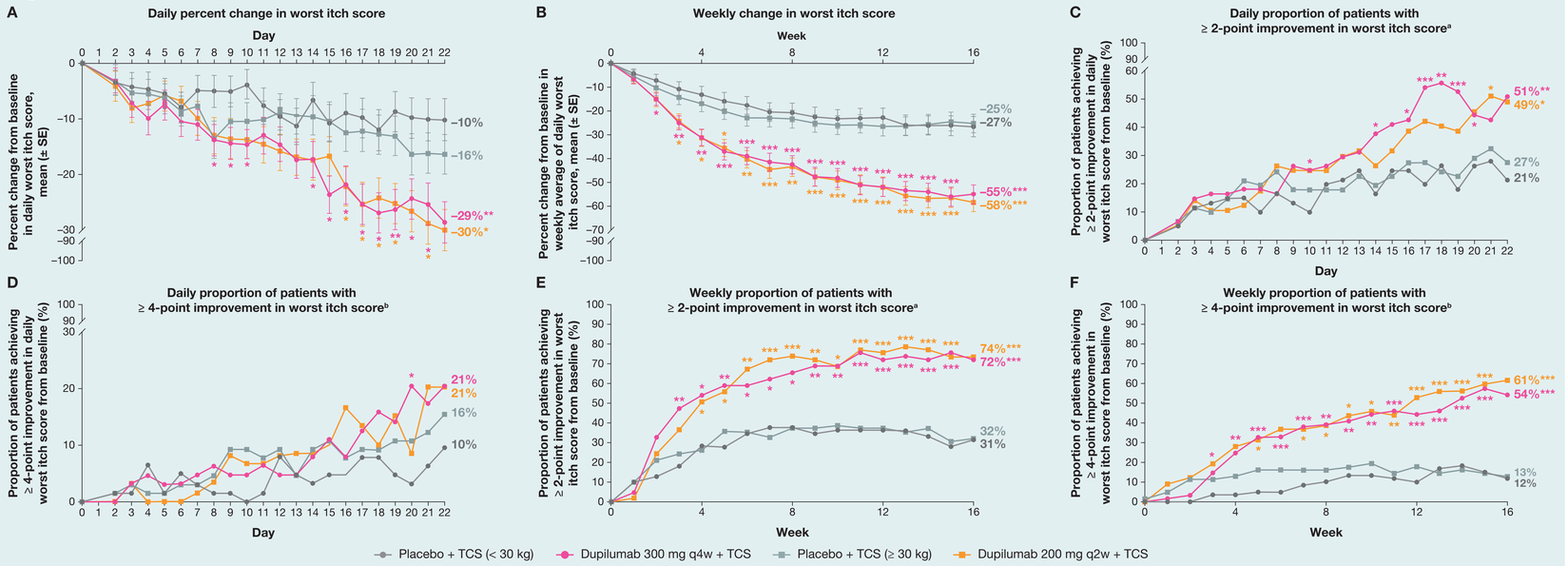
BL, baseline; W, Week.

- The majority of children treated with dupilumab achieved a reduction of days experiencing itch from every day at baseline to ≤ 2 days, with some improving to 0 days/week, by Week 16 (**Figure 3**)

Safety profile

- In the LIBERTY AD PEDS trial,[2] dupilumab + TCS was well tolerated and data were consistent with the known dupilumab safety profile observed in adults and adolescents[3,4]
- Injection-site reactions and conjunctivitis were more common with dupilumab. Infections, and AD exacerbations were more common with placebo[2]

Figure 2. Outcomes related to worst itch scores.



[a]Analysis performed for patients with baseline worst itch score ≥ 2 and non-missing values at each visit. [b]Analysis performed for patients with baseline worst itch score ≥ 4 and non-missing values at each visit.
*$P \leq 0.05$; **$P \leq 0.001$; ***$P \leq 0.0001$ vs placebo + TCS.

CONCLUSION

- **Dupilumab treatment with concomitant TCS provided rapid and sustained improvement in itch intensity and frequency in children aged 6–11 years with severe AD regardless of dosing regimen**

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