# Pharmacokinetics, Safety, and Efficacy of Dupilumab in Children Aged ≥ 2 to < 6 Years With Severe, Uncontrolled Atopic Dermatitis (LIBERTY AD PRE-SCHOOL)

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## BACKGROUND

- Atopic dermatitis (AD) has an estimated US prevalence of 15–38% in children aged < 5 years[1]
- AD markedly affects the quality of life of both patients[2] and family members,[3] and is associated with an increased risk of hospitalization[4]
- Currently, there is a high unmet medical need in children with AD inadequately controlled by topical therapies, as limited treatment options are available, and systemic corticosteroids are strongly discouraged[5]
- As children have a developing and potentially immature immune system, it is important to assess the safety and efficacy of an immunomodulator in dedicated clinical trials
- Dupilumab is a fully human[6,7] 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.[8,9]

## OBJECTIVE

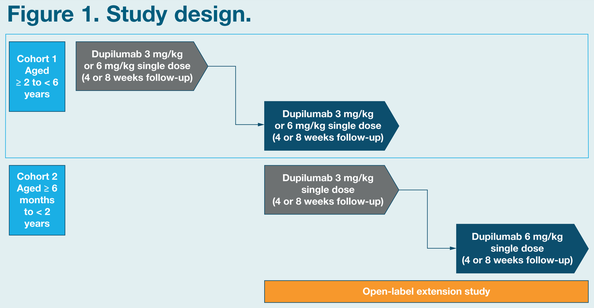
- **To report the pharmacokinetics (PK), safety, and efficacy of dupilumab in a phase 2, open-label, single-dose, sequential cohort study in children aged ≥ 2 to < 6 years with severe AD inadequately controlled with topical therapies**

## METHODS

### Study design

- LIBERTY AD PRE-SCHOOL (NCT03346434) is a phase 2/3, two-part study aimed at assessing PK, safety, and efficacy of dupilumab in children aged ≥ 6 months to < 6 years with severe AD
  - Part A (**Figure 1**) is an open-label, single ascending dose, sequential-cohort, multi-center, global, phase 2 study investigating the PK, safety, and efficacy of dupilumab; Part A is divided into 2 age cohorts
    - Cohort 1: ≥ 2- to < 6-year-old patients (reported here)
    - Cohort 2: ≥ 6 months to < 2-year-old patients (not reported here)
  - Part B (LIBERTY AD INFANT) is planned to be a randomized, double-blinded, parallel-group, placebo-controlled, phase 3 study to evaluate the efficacy and safety of dupilumab (not reported here)

**Figure 1. Study design.**




The additional 4-week follow-up period was only for patients who declined, or were ineligible to participate in a subsequent open-label extension [OLE] study, R668-AD-1434 LIBERTY AD PED-OLE, NCT02612454.

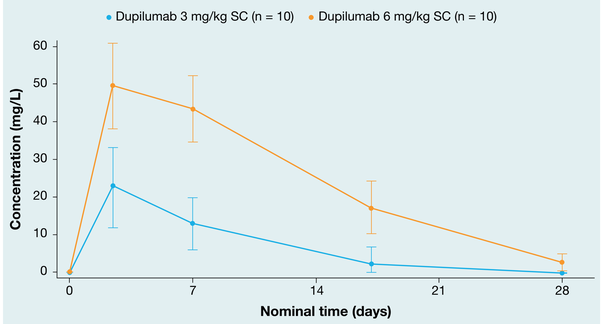
## RESULTS

**Table 1. Baseline demographics and clinical characteristics.**

| | Dupilumab 3 mg/kg (n = 10) | Dupilumab 6 mg/kg (n = 10) |
|---|---|---|
| Age, mean (SD), months | 45.8 (16.1) | 53.2 (11.2) |
| Male, n (%) | 6 (60) | 7 (70) |
| Race, n (%) | | |
| White | 7 (70) | 8 (80) |
| Black or African American | 3 (30) | 1 (10) |
| Asian | 0 | 1 (10) |
| Weight, mean (SD), kg | 16.6 (3.8) | 17.6 (3.6) |
| BMI, mean (SD), kg/m$^2$ | 16.2 (1.9) | 16.3 (1.7) |
| Duration of AD, mean (SD), months | 40.9 (14.3) | 50.6 (10.7) |
| Use of TCS for AD, n (%) | 9 (90) | 8 (80) |
| TCS group I (mild potency), n (%) | 1 (10) | 1 (10) |
| TCS group II (moderate potency), n (%) | 7 (70) | 7 (70) |
| TCS group III (potent), n (%) | 3 (30) | 4 (40) |
| TCS group IV (very potent), n (%) | 0 | 0 |
| Prior systemic immunosuppressant use, n (%) | 1 (10) | 4 (40) |
| Patients with allergic disease other than AD, n (%) | 10 (100) | 10 (100) |
| Food allergy, n (%) | 10 (100) | 8 (80) |
| Allergic rhinitis, n (%) | 7 (70) | 6 (60) |
| Other allergies, n (%) | 6 (60) | 4 (40) |
| Asthma, n (%) | 3 (30) | 3 (30) |
| Hives, n (%) | 3 (30) | 2 (20) |
| Allergic conjunctivitis (keratoconjunctivitis), n (%) | 0 | 2 (20) |
| Patients with IGA score 4, n (%) | 10 (100) | 10 (100) |
| EASI, mean (SD) | 35.2 (9.2) | 40.2 (11.8) |
| Caregiver-reported Peak Pruritus NRS score, mean (SD) | 8.4 (1.2) | 8.1 (1.5) |
| Percentage BSA involvement, mean (SD) | 58.1 (11.1) | 67.5 (16.1) |
| SCORAD score, mean (SD) | 73.5 (10.2) | 75.1 (8.1) |

BMI, body mass index; BSA, body surface area; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NRS, Numerical Rating Scale; SCORAD, SCORing Atopic Dermatitis; SD, standard deviation; TCS, Concomitant topical corticosteroid.

**Figure 2. Mean (± SD) concentration of dupilumab in serum over time.**



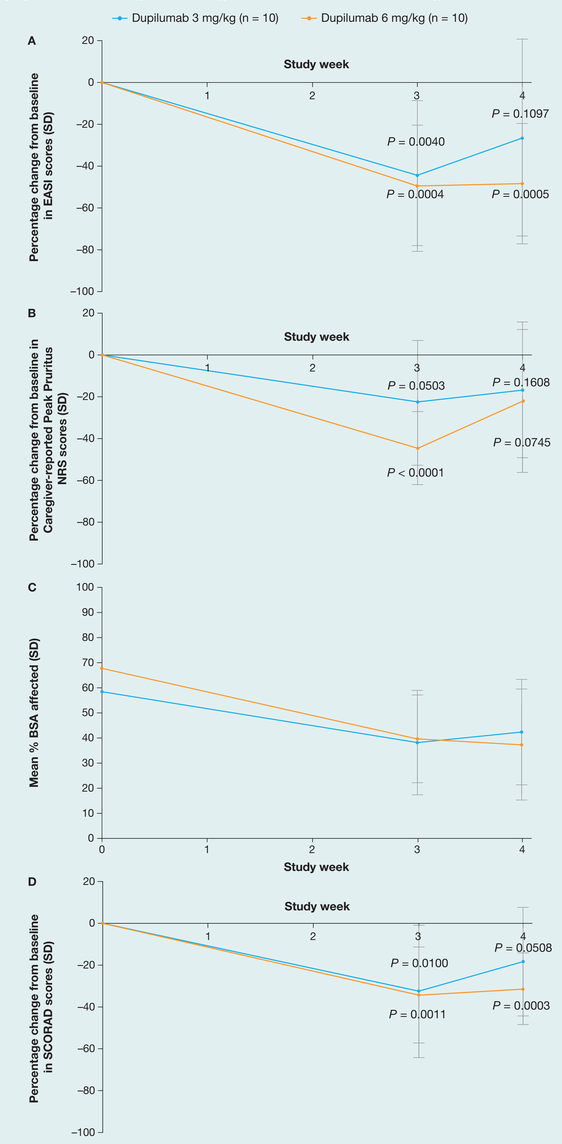

All treated patients who received any study drug and who had at least 1 non-missing functional dupilumab measurement following administration of the first dose of study drug. Exposure derived by determining area under the serum concentration-time curve from time zero to time of last measurable concentration ($AUC_{last}$).

**Table 2. Safety assessment.**

| | Dupilumab 3 mg/kg (n = 10) | Dupilumab 6 mg/kg (n = 10) |
|---|---|---|
| TEAEs, n | | |
| Total TEAEs | 5 | 3 |
| Total serious TEAEs | 1 | 0 |
| Total TEAEs related to treatment | 0 | 0 |
| Total TEAEs related to permanent treatment discontinuation | N/A | N/A |
| Patients with TEAEs, n (%) | | |
| ≥ 1 TEAE | 3 (30) | 2 (20) |
| ≥ 1 serious TEAE[a] | 1 (10) | 0 |
| ≥ 1 TEAE leading to treatment discontinuation | N/A | N/A |
| ≥ 1 severe TEAE | 0 | 0 |
| Any infection (SOC) | 2 (20) | 1 (10) |
| Skin infection | 1 (10) | 0 |
| Non-herpetic skin infections[b] | 1 (10) | 0 |
| Impetigo (PT) | 1 (10) | 0 |
| Herpes viral infections (HLT) | 0 | 0 |
| Injection-site reaction (HLT) | 0 | 0 |
| TEAEs (PT), n (%) | | |
| Nasopharyngitis | 1 (10) | 1 (10) |
| Pyrexia | 1 (10) | 0 |
| Anaphylactic reaction[a] | 1 (10) | 0 |
| Skin abrasion | 0 | 1 (10) |
| Cough | 0 | 1 (10) |
| Dermatitis atopic | 1 (10) | 0 |
| Conjunctivitis | 0 | 0 |
| Herpes simplex | 0 | 0 |

[a]1 serious TEAE of anaphylactic reaction was reported; this event was deemed as not related to dupilumab, as an alternate cause for the event was present: the patient had a history of allergy to nuts and an event of consumption of nuts just prior to onset of this anaphylactic reaction event. [b]Adjudicated. HLT, MedDRA High Level Term; MedDRA, Medical Dictionary for Regulatory Activities; N/A, not applicable; PT, MedDRA Preferred Term; SOC, MedDRA System Organ Class; TEAE, treatment-mergent adverse events.

**Figure 3. Dupilumab efficacy: (A) Percentage change in EASI through Week 4; (B) Percentage change in Caregiver-reported Peak Pruritus NRS through Week 4; (C) Mean change in % BSA affected through Week 4; (D) Percentage change in SCORAD through Week 4.**




Nominal *P* values are reported for the difference versus baseline.

## CONCLUSIONS

- **Single doses of 3 mg/kg or 6 mg/kg of dupilumab in children aged ≥ 2 to < 6 years showed a greater than dose-proportional increase in exposure, as determined by $AUC_{last}$**
- **Both doses of dupilumab resulted in improvement in signs and symptoms of AD**
- **Dupilumab was generally well tolerated, and safety was generally consistent with previous findings in children**

**References:** 1. Al-Naqeeb J, et al. J Am Board Fam Med. 2019;32:191-200. 2. Ramirez FD, et al. JAMA Pediatr. 2019;173:e190025. 3. Ramirez FD, et al. JAMA Dermatol. 2019;155:556-63. 4. Hua T, Silverberg JL, J Am Acad Dermatol. 2019;81:862-5. 5. Drucker AM, et al. Br J Dermatol. 2018;178:768-75. 6. Macdonald LE, et al. Proc Natl Acad Sci USA. 2014;111:5147-52. 7. Murphy AJ, et al. Proc Natl Acad Sci USA. 2014;111:5153-8. 8. Gandhi NA, et al. Expert Rev Clin Immunol. 2017;13:425-37. 9. Gandhi NA, et al. Nat Rev Drug Discov. 2016;15:35-50.

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