

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

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**Introduction:** Atopic dermatitis (AD), with an estimated US prevalence of 15–38% in children, markedly affects the quality of life (QoL) of both patients and family members. Limited treatment options are available currently for children with AD inadequately controlled by topical therapies. 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 monoclonal antibody blocking the shared receptor component for interleukin (IL)-4 and IL-13, key drivers of type 2 inflammation in multiple diseases, thus inhibiting their signaling. In multiple phase 3 trials, dupilumab significantly improved signs, symptoms, and QoL in patients aged  $\geq 12$  years with moderate-to-severe AD, with an acceptable safety profile. We report the pharmacokinetics (PK), safety, and efficacy of dupilumab in a phase 2, open-label, single-ascending dose, sequential cohort study in children aged  $\geq 2$  to  $< 6$  years with severe AD inadequately controlled with topical therapies (LIBERTY AD PRE-SCHOOL: NCT03346434).

**Methods:** In the trial, patients aged  $\geq 6$  months to  $< 6$  years (N=40) were randomized 1:1 to subcutaneous dupilumab 3mg/kg or 6mg/kg, followed by a 4-week pharmacokinetic sampling and monitoring period.

**Results:** Twenty patients aged  $\geq 2$  to  $< 6$  years were included. Single-dose dupilumab resulted in a slightly greater than dose-proportional increase in exposure, as measured by  $AUC_{last}$  (similar pharmacokinetic profiles were reported for adults). The incidence of adverse events (AEs) was similar across both treatment groups (AEs reported in single patients). One serious AE (anaphylactic reaction due to existing peanut allergy) was reported with dupilumab 3mg/kg. Efficacy was assessed as mean percentage change from baseline at Week 4: Eczema Area and Severity Index (SD)  $-26.6(47.4)/-48.7(28.9)$  (nominal  $P=0.1097/P=0.0005$ ); SCORing AD  $-18.6(26.2)/-31.9(17.5)$  (nominal  $P=0.0508/P=0.0003$ ); Peak Pruritus Numerical Rating Scale:  $-16.7(32.5)/-22.0(34.5)$  (nominal  $P=0.1608/P=0.0745$ ) for dupilumab 3mg/kg and 6mg/kg. One patient receiving dupilumab 3mg/kg had Investigator's Global Assessment 0/1 at Week 4.

**Conclusions:** Single doses of dupilumab in children aged  $\geq 2$  to  $< 6$  years showed a slightly greater than dose-proportional increase in exposure. Dupilumab was generally well tolerated, and no new safety signals were observed with single-dose treatment. There was no event of serious infection or systemic hypersensitivity related to dupilumab. Both dupilumab doses were clinically beneficial against signs and symptoms of AD.

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