Dupilumab Treatment of Children with Moderate-to-Severe Atopic Dermatitis Increases Bone Alkaline Phosphatase, a Marker of Bone Mineralization

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Introduction/Background: Children with atopic dermatitis (AD) are at risk for low bone mineral density (BMD), which is associated with increased prevalence of osteopenia, osteoporosis, and fracture risk.[1,2] Factors such as restricted nutrition, vitamin D deficiency, poor sleep and corticosteroid use contribute to lower bone alkaline phosphatase (BALP) levels, a marker of bone mineralization, seen in children with moderate-to-severe AD compared with healthy children.[3] A major determinant for lifetime risk of fractures and osteoporosis is the magnitude of peak bone mass achieved during prepubescent years. Low BALP and BMD in children with moderate-to-severe AD could contribute to a higher prevalence of osteopenia and osteoporosis.

Objective: The objective of this analysis is to report the impact of dupilumab treatment on markers of bone formation in children aged ≥ 6 to < 12 years with moderate-to-severe AD.

Methods: The analysis was performed retrospectively on sera from participants in LIBERTY AD PEDS (NCT03345914) and LIBERTY AD PED-OLE (NCT02612454). In LIBERTY AD PEDS, a double-blind, 16-week, phase 3 trial, children aged 6 to < 12 years were randomized 1:1:1 to 300 mg dupilumab every 4 weeks (300 mg q4w), a weight-based regimen of dupilumab every 2 weeks (100 mg q2w for patients with baseline weight < 30 kg, and 200 mg q2w for those with baseline weight ≥ 30 kg), or placebo; with concomitant medium-potency topical corticosteroids (TCS). After the initial 16-week trial, children aged

6 to < 12 years were enrolled in the open-label extension study LIBERTY AD PED-OLE. Patients received dupilumab 300 mg q4w, which could be titrated up in case of inadequate clinical response at Week 16 (200 mg q2w for patients with baseline weight < 60 kg, and 300 mg q2w for those with baseline weight ≥ 60 kg); with concomitant medium-potency TCS. Bone biomarkers including BALP, procollagen type 1 N-terminal propeptide, C-terminal crosslinking telopeptide of type 1 collagen, osteocalcin, and insulin-like growth factor 1 were analyzed at baseline, 8, 12, 16 and BALP only at 52 weeks.

Results: Dupilumab treatment led to a rapid and significant increase in geometric mean(standard error) levels of BALP in children with moderate-to-severe AD at 16 weeks compared with patients in the placebo group (77.7(1.02) µg/L vs 65.0(1.04) µg/L; P<0.0001). As well as a rapid and significant increase in BALP levels in children from the placebo group once they joined the OLE trial. BALP levels increased over 52 weeks in all treated children, reaching a level of 78–84 µg/L which constitutes a significant improvement compared with baseline, and is comparable to healthy reference intervals. An increasing trend from baseline to 16 weeks of dupilumab treatment was observed for other biomarkers, however there was a limited number of data points due to insufficient volumes of serum available for analysis.

Conclusions: These placebo-controlled results show, for the first time, a rapid and significant increase in BALP, and a possible trend in other biomarkers, in children with AD during treatment with dupilumab. These results suggest increased bone mineralization during the treatment period.

Keywords: dupilumab, bone formation, bone alkaline phosphatase

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