Dupilumab increases levels of bone growth biomarker irrespective of prior use of systemic corticosteroids in children with moderate-to-severe atopic dermatitis

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Introduction/Background: Children with moderate-to-severe atopic dermatitis (AD) are at increased risk of lower bone mineral density (BMD) and fractures. Peak bone mass achieved during prepubescence is a major determinant of lifetime risk of fractures and osteoporosis. Bone alkaline phosphatase (BALP) promotes bone mineralization and contributes to density and linear growth in children. Systemic corticosteroids (SCS) negatively impact growth and bone health.

Objectives: To describe the impact of dupilumab treatment on BALP in children aged 6–11 years with moderate-to-severe AD and prior history of SCS use.

Methods: BALP levels in sera from participants receiving dupilumab 300 mg every 4 weeks (q4w) or placebo in LIBERTY AD PEDS (NCT03345914) and dupilumab 300 mg q4w in LIBERTY AD PED-OLE (NCT02612454) were analyzed at baseline and at 8, 12, 16 (PEDS), and 52 weeks (PED-OLE). Serum BALP levels (mcg/L) were stratified by prior use (with SCS; n = 42) or with no prior use of SCS (without SCS; n = 203), as captured in PEDS patient history at baseline.
**Results:** Regardless of prior SCS use, dupilumab treatment led to significant increase in BALP levels in children with moderate-to-severe AD at Week 16 compared with the placebo group (with SCS: 300 mg q4w [n = 25] vs placebo [n = 17], mean change [standard deviation] in BALP levels of 15.1 mcg/L [16.5] vs -5.5 mcg/L [16.0], \( P = 0.0099 \); without SCS: 300 mg q4w [n = 97] vs placebo [n = 106], 11.8 mcg/L [18.8] vs 2.2 mcg/L [16.3], \( P = 0.0074 \)). By Week 52, BALP levels further increased vs baseline regardless of prior SCS use and were comparable with reference intervals (with SCS: 24.5 mcg/L [16.8], \( P = 0.0044 \); without SCS: 13.4 mcg/L [19.4], \( P = 0.0002 \)). Patients in the placebo group who switched to dupilumab in PED-OLE had improved to levels similar to those of patients continuing treatment by Week 52 (with SCS: 23.3 mcg/L [19.3], \( P = 0.0067 \) [vs baseline]; without SCS: 18.4 mcg/L [20.4], \( P < 0.0001 \) [vs baseline]).

**Conclusions:** Dupilumab treatment increased BALP levels in children aged 6-11 years with moderate-to-severe AD irrespective of prior history of SCS use. These results add to the body of evidence that moderate-to-severe AD can negatively impact BALP levels, and that this effect may be improved with dupilumab in this age group, regardless of history of SCS use. The increase in BALP levels suggests that dupilumab may help improve bone mineralization in children with moderate-to-severe AD when treated during prepubescence.

**Keywords:** atopic dermatitis, pediatric, bone alkaline phosphatase, dupilumab

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