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

Alan D. Irvine1, Amy S. Paller2,3, Sara Hamon4, Julie Horowitz4, Annamaria Farrell6, Sarah Hatsell4, Ainara Rodríguez Marco5, Ashish Bansal7, Zhen Chen7, Sonya L. Cyr3

1 Trinity College Dublin, Dublin, Ireland; 2 Northwestern University Feinberg School of Medicine, Chicago, IL, USA; 3 Ann and Robert H. Lurie Children’s Hospital, Chicago, IL, USA; 4 Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; 5 Sanofi, Madrid, Spain

BACKGROUND
• Children with atopic dermatitis (AD) are at risk of 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, chronic inflammation and corticosteroid use may contribute to lower levels of bone alkaline phosphatase (BALP), 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.4
• Low BAP and BMD in children with moderate-to-severe AD could contribute to a higher prevalence of osteopenia and osteoporosis

OBJECTIVE
• To report the impact of dupilumab treatment on markers of bone mineralization in children aged 6 to 11 years with moderate-to-severe AD

METHODS
• The analysis was performed retrospectively on sera from participants in LIBERTY AD PEDS (NCT03343914) and LIBERTY AD PED-OLE (NCT02812454).
• In LIBERTY AD PEDS, a double-blind, 16-week, phase 3 trial, children aged 6 to 11 years were randomized 1:1:1 to 300 mg dupilumab every 4 weeks (q4w), a weight-based regimen of peak bone mass achieved during prepubertal years,4 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 q4w for those with baseline weight > 60 kg); all patients received concomitant medium-potency TCS
• Bone biomarkers including BALP, procollagen type 1 N-terminal procpeptide (P1NP), C-terminal crosslinking telopeptide of type 1 collagen (β-CTX) and osteocalcin (OC), as well as insulin-like growth factor 1 (IGF-1) were analyzed at baseline, 8, 12, and 16 weeks, and BALP only at 52 weeks
• There is a limited number of data points for P1NP, β-CTX, OC and IGF-1 due to insufficient volumes of serum available for analysis

RESULTS
• After the initial 16-week trial were eligible to be enrolled in the open-label extension study LIBERTY AD PED-OLE: patients received dupilumab 300 mg q4w, or 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 q4w for those with baseline weight > 60 kg); all patients received concomitant medium-potency TCS
• Bone biomarkers including BALP, procollagen type 1 N-terminal procpeptide (P1NP), C-terminal crosslinking telopeptide of type 1 collagen (β-CTX) and osteocalcin (OC), as well as insulin-like growth factor 1 (IGF-1) were analyzed at baseline, 8, 12, and 16 weeks, and BALP only at 52 weeks
• There is a limited number of data points for P1NP, β-CTX, OC and IGF-1 due to insufficient volumes of serum available for analysis

CONCLUSIONS
• Dupilumab treatment is associated with a rapid and significant increase in BALP in children aged 6 to 11 years with moderate-to-severe AD; a trend towards increased levels was observed for other bone turnover biomarkers, although data were limited
• Mean baseline BALP levels measured in dupilumab-treated children were lower than those seen in the pediatric healthy control group and in children with moderate-to-severe AD; a trend towards increased levels was observed for other bone turnover biomarkers, although data were limited

References:

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