DUPILUMAB OFFERS A RAPID IMPROVEMENT IN PRURITUS IN ADOLESCENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS VS PLACEBO: A POST-HOC ANALYSIS OF A PHASE 3 TRIAL

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Introduction: Atopic dermatitis (AD) is a complex, highly symptomatic, chronic disease characterized by intense pruritus/itch that negatively impacts multiple dimensions of a patient's life, including sleep. Dupilumab is a fully human monoclonal antibody that blocks the shared receptor component for interleukin (IL)-4 and IL-13, thus inhibiting signaling of both IL-4 and IL-13, key drivers of type 2 inflammation in multiple diseases. In a double-blind, placebo-controlled, phase 3 trial in adolescents with moderate-to-severe AD (NCT03054428), dupilumab vs placebo significantly improved measures of pruritus. We assess the time to onset of improvement in pruritus in dupilumab- vs placebo-treated adolescent AD patients.

Methods: Adolescent patients (aged ≥12 to <18 years) were randomized 1:1:1 to 16-week subcutaneous dupilumab every 2 weeks (q2w, 200mg if baseline weight <60kg [400mg loading dose on Day1], 300mg if ≥60kg, [600mg loading dose]); every 4 weeks (q4w, 300mg, [600mg loading dose]); or placebo. This post-hoc analysis evaluated daily change from baseline through Day15 in the Peak Pruritus Numerical Rating Scale (PP-NRS) scores, and the proportion of patients who achieved ≥3-point improvement in daily PP-NRS score from baseline through Day15.

Results: The trial included 251 patients (q2w n=82, q4w n=84, placebo n=85). Baseline demographics and disease characteristics were similar among groups. Mean (standard deviation) values for weekly average of daily PP-NRS at baseline for q2w/ q4w/placebo groups were 7.5(1.52)/7.5(1.84)/7.7(1.62), respectively, consistent with severe pruritus. Significant improvement in pruritus with dupilumab vs placebo was seen as early as Day 5 for q2w and Day 6 for q4w. At Day 5, least squares mean percentage change from baseline (standard error) in daily PP-NRS score for dupilumab q2w/q4w vs placebo was −12.5(2.43)/−8.8(2.41) vs −4.9(2.39); $P<0.05$/not significant. Day 6 values were: −13.0(2.28)/−12.9(2.27) vs 4.5(2.24); $P<0.01$ for both. The improvement in pruritus scores continued to Day 15: −25.3(2.68)/−21.8(2.69) vs −5.7(2.64); $P<0.0001$ for both. A higher proportion of q2w patients showed clinically meaningful response (≥3-point improvement) in daily PP-NRS score vs placebo as early as Day 13 ($P<0.05$). By Day 15, significantly higher proportions of patients in both dupilumab groups achieved clinically meaningful improvement from baseline: 25.6%/25.3% vs 9.4% for q2w/q4w vs placebo, respectively; $P<0.01$ for both. No new safety signals were observed in adolescents compared with adults.

Conclusions: Dupilumab treatment vs placebo demonstrated rapid improvement in pruritus in adolescents with moderate-to-severe AD as early as Day5 and clinically meaningful improvement by Day 13.

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