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
Eric L. Simpson¹, Abhijit Gadkari², Lisa A. Beck³, H. Chih-ho Hong⁴, Ashish Bansal², Zhen Chen², Paola Mina-Osorio², Randy Prescilla⁵
¹Oregon Health & Science University, Portland, OR, USA; ²Regeneron Pharmaceuticals Inc., Tarrytown, NY, USA; ³University of Rochester Medical Center, Rochester, NY, USA; ⁴University of British Columbia and Probity Medical Research, Surrey, BC, Canada; ⁵Sanofi Genzyme, Cambridge, MA, USA;

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.

Acknowledgments and funding sources:
Data first presented at the 28th Annual Meeting of the European Academy of Dermatology and Venereology, October 9-13; 2019; Madrid, Spain.
Research sponsored by Sanofi and Regeneron Pharmaceuticals, Inc. ClinicalTrials.gov identifier: NCT03054428. Medical writing/editorial assistance provided by Ekaterina Semenova, PhD, of Excerpta Medica, funded by Sanofi Genzyme and Regeneron Pharmaceuticals, Inc.
Disclosures

**Simpson EL**: AbbVie, Eli Lilly, Galderma, Kyowa Hakko Kirin, LEO Pharma, Merck, Pfizer, Regeneron Pharmaceuticals, Inc. – investigator; AbbVie, Boehringer-Ingelheim, Dermavant, Eli Lilly, Forte Bio, Incyte, LEO Pharma, Menlo Therapeutics, Pfizer, Pierre Fabre Dermo Cosmétique, Regeneron Pharmaceuticals, Inc., Sanofi Genzyme, Valeant – consultants honorarium.

**Gadkari A, Bansal A, Chen Z, Mina-Osorio P**: Regeneron Pharmaceuticals, Inc. – employees and shareholders.

**Beck LA**: Regeneron Pharmaceuticals Inc. – investigator and consultant; AbbVie, Array Biopharma, Celgene, Genentech Ironwood, Janssen, LEO Pharma, MedImmune, Novartis, Regeneron Pharmaceuticals, Inc., Unilever – consulting fees and/or honoraria.

**Hong HCH**: Centocor, Cutanea, Dermavant, GlaxoSmithKline, MedImmune – investigator; sanofi-aventis – consultant; Boehringer Ingelheim – investigator, consultant; Cipher – speaker; Bausch Health, Roche – speaker, consultant; AbbVie, Amgen, Celgene, Eli Lilly, Galderma, Janssen, LEO Pharma, Novartis, Regeneron Pharmaceuticals, Inc. – speaker, investigator, consultant.

**Prescilla R**: Sanofi Genzyme – employee, may hold stock and/or stock options in the company.