Dupilumab demonstrates higher likelihood of maintaining efficacy outcomes compared with lebrikizumab in monotherapy at week 52: results from a placebo-adjusted indirect comparison analysis

Patricia Guyot¹, Yingxin Xu², Amy Praestgaard³, Nick Freemantle⁴, Ana B. Rossi³, Brad Shumel², Gaëlle Bégo-Le-Bagousse¹, Zhixiao Wang², Kerry Noonan³, Mike Bastian⁵

¹Sanofi, Gentilly, France; ²Regeneron Pharmaceuticals Inc., Tarrytown, NY, USA; ³Sanofi, Cambridge, MA, USA; ⁴Institute for Clinical Trials and Methodology, University College London, London, UK; ⁵Sanofi, Frankfurt, Germany

Introduction/Background: The monoclonal antibodies dupilumab (fully human) and lebrikizumab (humanized) have both demonstrated efficacy and safety in clinical trials of atopic dermatitis (AD). In the absence of direct head-to-head comparisons between dupilumab and lebrikizumab, Bucher indirect treatment comparisons (ITCs), in which treatment effects are anchored to a common comparator (e.g. placebo), provide a robust and widely accepted method of evaluating the relative efficacy of drugs, and can offer a useful framework for decision-making.

Objectives: To report the results of a placebo-adjusted Bucher ITC comparing maintenance of efficacy outcomes between dupilumab and lebrikizumab monotherapy at Week 52 in patients with moderate-to-severe AD who had achieved ≥75% improvement from baseline in Eczema Area and Severity Index (EASI-75), or Investigator’s Global Assessment (IGA) score 0/1 (clear/almost clear) at Week 16.

Methods: Placebo-adjusted Bucher ITC utilized phase 3 trial data from SOLO-CONTINUE (dupilumab; NCT02395133) and ADVOCATE 1 and 2 (lebrikizumab; NCT04146363 and
NCT04178967) maintenance phase were used. Data at Week 52 was used with the following doses: 300mg dupilumab every 2 weeks (q2w) or placebo, and 250mg lebrikizumab q2w or every 4 weeks (q4w) or placebo. No adjustments were made for baseline characteristics, and missing data were imputed using non-responder imputation (NRI), excluding patients who had received topical corticosteroids during the maintenance phase of ADVOCATE 1 and 2. Outcomes included proportion of patients maintaining IGA 0/1, EASI-75, EASI-90, and 4-point improvement in peak pruritus Numerical Rating Scale score (PP-NRS ≥4) at Week 52 from SOLO-CONTINUE and ADVOCATE 1 and 2 maintenance phase baseline (Week 16). Odds ratio (OR) with 95% confidence interval (CI) are reported.

**Results:** Comparison of baseline disease characteristics indicated that the patient populations enrolled in ADVOCATE 1 and 2 maintenance phase baseline presented with lower disease severity compared with SOLO-CONTINUE, based on percentage body surface area affected. However, mean EASI and pruritus NRS baseline scores were similar in the compared trials. This analysis favored dupilumab for all outcomes evaluated at Week 52. Comparing q2w dosing, dupilumab had significantly higher ORs for EASI-75 (OR=4.15, 95%CI 1.41–12.18); EASI-90 (OR=3.72, 95%CI 1.09–12.76); IGA 0/1 (OR=4.62, 95%CI 1.02–20.92); PP-NRS ≥4 (OR=11.96, 95%CI 1.24–115.34). Compared with lebrikizumab q4w, dupilumab q2w maintained significantly higher EASI-75 OR (OR=3.53, 95%CI 1.18–10.53), while OR for the other 3 outcomes favored dupilumab, but did not reach statistical significance: EASI-90 (OR=3.31, 95%CI 0.97–11.33), IGA 0/1 (OR=3.31, 95%CI 0.73–15.08), and PP-NRS ≥4 (OR=8.79, 95%CI 0.91–84.81).
**Conclusions:** Based on a Bucher ITC utilizing data from trials with similar designs, patients treated with dupilumab q2w demonstrated higher likelihood of maintaining improvements in signs and symptoms at Week 52 compared with patients treated with lebrikizumab q2w or q4w.

**Keywords:** atopic dermatitis, dupilumab, lebrikizumab, indirect treatment comparison

**Acknowledgments:** Research was funded by Sanofi and Regeneron Pharmaceuticals Inc. Medical writing/editorial assistance was provided by Rosie Morland, PhD, CMPP, of Excerpta Medica, and was funded by Sanofi and Regeneron Pharmaceuticals Inc., according to the Good Publication Practice guidelines.

**Disclosures:** NF: European Union, Cure Parkinson's Trust, Medical Research Council, National Institute for Health and Care Research – (grants); Abbott, Aimmune Therapeutics, ALK, AstraZeneca, Galderma, Gedeon Richter, Ipsen, Novo Nordisk, sanofi-aventis, Théa Pharma, Vertex Pharmaceuticals – (consultancy fees); Abbott Singapore – (honorarium); Patricia Guyot, Amy Praestgaard, Ana B. Rossi, Gaëlle Bégo-Le-Bagousse, Kerry Noonan, Mike Bastian – Sanofi – employees, may hold stock and/or stock options in the company; Yingxin Xu, Brad Shumel, Zhixiao Wang – Regeneron Pharmaceuticals Inc. – employees and shareholders.