Tralokinumab provides progressive improvements beyond week 16 in patients with atopic dermatitis with an initial partial response

Eric Simpson,[1] Jacob P Thyssen,[2] Carsten Flohr,[3] Norito Katoh,[4] Kim Papp,[5] Louise Abildgaard Steffensen,[6] Bo Bang,[6] Alexandra Kuznetsova,[6] Andrew Blauvelt[7]

[1]Department of Dermatology, Oregon Health & Science University, Portland, OR, USA; [2]Department of Dermatology and Allergy, Copenhagen University Hospital Herlev-Gentofte, Copenhagen, Denmark; [3]St. John's Institute of Dermatology, King's College London and Guy's and St. Thomas' NHS Foundation Trust, London, UK; [4]Department of Dermatology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan; [5]Probity Medical Research, Waterloo, Ontario, Canada; [6]LEO Pharma A/S, Ballerup, Denmark; [7]Oregon Medical Research Center, Portland, OR, USA

Introduction: Tralokinumab is a fully human monoclonal antibody that specifically neutralises interleukin-13, a key driver of the signs and symptoms of atopic dermatitis (AD). In the pivotal Phase 3 ECZTRA 1 (NCT03131648) and 2 (NCT03160885) trials in adults with moderate-to-severe AD, tralokinumab monotherapy provided significant and early improvements in clinically relevant endpoints. In both trials, significantly more patients treated with tralokinumab monotherapy than those who received placebo achieved the primary endpoints of Investigator Global Assessment of 0 or 1 (IGA 0/1) [clear or almost clear skin] and 75% improvement in Eczema Area and Severity Index (EASI-75). Herein, we analyse patients who did not achieve IGA 0/1 or EASI-75 at week 16 and continued to receive tralokinumab open-label plus optional topical corticosteroids (TCS) for an additional 36 weeks.

Methods: ECZTRA 1 and 2 were 52-week, randomized, double-blind, placebo-controlled, international trials of identical design. Adult patients with AD for ≥1 year who were candidates for systemic therapy were initially randomized 3:1 to tralokinumab 300 mg or placebo every 2 weeks (q2w) for 16 weeks. Patients who achieved IGA 0/1 or EASI-75 with tralokinumab at week 16 were re-randomised (2:2:1) to tralokinumab q2w or every 4 weeks, or placebo. Patients who did not achieve IGA 0/1 or EASI-75 transferred to open-label tralokinumab 300 mg q2w plus optional TCS for an additional 36 weeks. This *post hoc* analysis of pooled data from both studies assessed clinical responses during open-label treatment in patients who did not achieve IGA 0/1 or EASI-75 at week 16.

Results: In the pooled analysis, 686 of 1196 (57.4%) tralokinumab-treated patients (360 and 326 from ECZTRA 1 and 2, respectively) were transferred to open-label treatment. The proportion of patients achieving IGA 0/1 or EASI-75 at week 52 with tralokinumab plus optional TCS was 20.1% and 42.9%, respectively. More than half of the responder proportions at week 52 were achieved within 8 weeks of starting open-label treatment; 11.4% and 31.9% achieved IGA 0/1 and EASI-75 by week 24 of the studies. In an alternative analysis, to understand if the increased response over time was due to the addition of optional TCS or to extended tralokinumab treatment alone, patients (49.3%) who used concomitant anti-inflammatory treatment (mainly TCS) were considered non-responders; the response rates were 13.9% and 25.7% for IGA 0/1 and EASI-75 at week 52, respectively. When considering the level of AD disease activity at week 16, 53.2% of the patients who had EASI-50 to -74 at week 16 achieved EASI-75 at week 52, and 36.5% of the patients who had IGA 2 at week 16 achieved IGA 0/1 at week 52. By contrast, 29.3% of the patients with EASI <25 at week 16 achieved EASI-75 at week 52, and 7.6% of patients with IGA 4 at week 16 achieved IGA 0/1 at week 52.

Conclusion: These data show that adult patients who did not achieve IGA 0/1 or EASI-75 at week 16 improved progressively with continued tralokinumab treatment beyond week 16. The clinical response with continued treatment beyond week 16 was driven mainly by continued tralokinumab treatment, and not by the addition of optional TCS. This suggests that a substantial proportion of patients not achieving success endpoints at week 16 continues to experience further disease improvement with continued tralokinumab therapy over the course of 52 weeks.