**Impact of targeting interleukin-13 on *Staphylococcus aureus* colonization: results from a Phase 3, randomized, double-blind, placebo-controlled trial with tralokinumab in adult patients with atopic dermatitis**

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**Background.** Atopic dermatitis is a chronic, inflammatory skin disease with a high disease burden. Pathogenesis is multifactorial, characterized mainly by increased levels of type 2 cytokines including interleukin (IL)-13, and skin barrier dysfunction, which collectively lead to microbial dysbiosis and *Staphylococcus aureus* colonization. This dysbiosis is associated with greater atopic dermatitis severity and correlates with atopic dermatitis flares. Tralokinumab is a fully human monoclonal antibody that specifically neutralizes IL-13. In the ECZTRA 1 Phase 3 trial (NCT03131648), tralokinumab led to significant improvements in Investigator Global Assessment (IGA) and Eczema Area and Severity Index (EASI) scores compared with placebo. The objective of this exploratory analysis was to characterize the effect of tralokinumab treatment on eliminating *S. aureus* colonization.
**Methods.** Patients with moderate-to-severe atopic dermatitis were randomized 3:1 to subcutaneous tralokinumab 300 mg or placebo every 2 weeks for an initial 16 weeks. Changes in skin colonization by *S. aureus* at week 16 in patients was an exploratory endpoint. Absolute abundance of *S. aureus* on lesional skin was assessed by rotation of sterile swabs on the skin, followed by quantitative polymerase chain reaction analysis of extracted DNA. Association of *S. aureus* colonization with disease severity and select serum or skin biomarkers was assessed. The ratio between treatment groups in relative reduction cutaneous *S. aureus* from baseline to week 16 was assessed by a t-test of changes in log-transformed values.
**Results.** 802 patients were randomized to tralokinumab (n=603) or placebo (n=199); 50.7% had severe atopic dermatitis (IGA 4; 5-point scale) at baseline; mean EASI score was 32.4. *S. aureus* colonisation correlated with disease severity (EASI score) at baseline and week 16. *S. aureus* colonisation further correlated significantly with serum levels of biomarkers, including IL-13, IL-22, and human beta-defensin-2 at baseline and week 16. Median *S. aureus* abundance was reduced more from baseline to week 16 in patients receiving tralokinumab (n=555; from 969 to 22 gene copies/cm$^2$) vs placebo (n=184; from 649 to 238 gene copies/cm$^2$), with a 10-fold greater reduction in tralokinumab-treated patients compared with those who received placebo (ratio=0.09; $P$<0.0001).
**Discussion.** Treatment with tralokinumab was associated with significant reduction in *S. aureus* colonization in lesional skin compared with placebo in adult patients with moderate-to-severe atopic dermatitis. This supports previous studies (Guttman-Yassky E, et al. Presented at: EADV, Paris, France; Poster P0283; 2018) and suggests that reduction of *S. aureus* colonization by neutralization of IL-13 contributes to the efficacy of tralokinumab in improving the hallmarks of atopic dermatitis and breaking the cycle of itching, scratching, skin barrier dysfunction, and immune-mediated inflammation.
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