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 (AD) is a chronic inflammatory skin disease with a high disease burden and a multifactorial pathogenesis, characterized by skin barrier disruption and immune dysregulation.1,2 Atopic dermatitis (AD) is a chronic inflammatory skin disease with a high disease burden and a multifactorial pathogenesis, characterized by skin barrier disruption and immune dysregulation.3
• The epidermal barrier functions as a protective layer that includes skin colonization by Staphylococcus aureus.4
• Staphylococcus aureus is a Gram-positive, facultative anaerobic bacterium that leads to high skin colonization and specifically mediate5
• Staphylococcus aureus, a common co-colonizer with in the Phase 2 trial (ECZTRA 1) and in the Phase 3 ECZTRA 1 trial (ECZTRA 2).

Objective

To characterize the effect of tralokinumab treatment on Staphylococcus aureus colonization correlation with disease severity.

Methods

Study design and patients

ECZTRA 1 (NCT03131648) was a multinational, double-blind, randomized, placebo-controlled, 52-week trial
• Randomized, double-blind, placebo-controlled trial with tralokinumab in adult patients with atopic dermatitis

Microbiome characterization

Changes in skin colonization by S. aureus were analyzed in staphylococcal gene copy number/cm². Absolute abundance of S. aureus microbiota were assayed using ribosomal RNA from skin samples followed by quantitative real-time polymerase chain reaction (PCR) analysis. S. aureus and Staphylococcus epidermidis were the only S. aureus species present. A total of 2-week intervals and week 16 for skin colonization by S. aureus

Statistical analysis

To determine the correlation between S. aureus colonization and disease severity, we used linear regression models with S. aureus colonization as the dependent variable. The correlation was assessed at baseline and week 16.

Results

Patient demographics

Baseline demographic and baseline AD severity at week 16 were compiled in Table 1. EASI-75 responders (ESI-75) were defined as patients who achieved EASI-75 with tralokinumab or placebo treatment for at least 14 weeks.

Correlation of S. aureus and EASI score

Levels of S. aureus colonization correlated with disease severity (Spearman’s rank correlation coefficient (Spearman’s correlation test: rho=0.4340) in week 16.

Correlation of S. aureus and serum biomarkers

In an analysis excluding patients who used rescue medication, there was a significant reduction in S. aureus colonization at week 16 compared with baseline (rho=0.3329, p<0.0001) (Figure 1).

Reduction in S. aureus colonization from baseline to week 16

In an analysis excluding patients who used rescue medication, there was a significant reduction in S. aureus colonization from baseline to week 16 in tralokinumab versus placebo in EASI-75 responders (rho=-0.4340). There was a significant reduction from baseline to week 16 in median count for tralokinumab versus placebo in EASI-75 responders (rho=-0.4340, p<0.0001) (Figure 2).

Levels of S. aureus colonization at week 16

S. aureus colonization levels were lower at week 16 compared with baseline in EASI-75 responders. Though the causal relationship between atopic dermatitis, inflammation, and disease severity remains unclear, the results shown here suggest the reduction of S. aureus colonization is due to specific neutralization of IL-13 with tralokinumab and not due to mainly to atopic dermatitis skin improvement.

Conclusions

• Levels of S. aureus colonization correlated positively with EASI score and serum levels of several atopic dermatitis biomarkers, including IL-13, IL-12, and CCIL7
• Treatment with tralokinumab was associated with a significantly greater reduction in S. aureus colonization in lesional skin compared with placebo in adult patients with moderate-to-severe atopic dermatitis. This supports a previous study demonstrating an S. aureus colonization reduction with tralokinumab.
• Though the causal relationship between atopic dermatitis, inflammation, and disease severity remains unclear, the results shown here suggest the reduction of S. aureus colonization is due to specific neutralization of IL-13 with tralokinumab and not due to mainly to atopic dermatitis skin improvement.

References


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