Neutralizing interleukin-13 with tralokinumab shifts the molecular phenotype of lesional skin towards that of non-lesional skin and restores skin barrier abnormalities

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Background. Interleukin (IL)-13 is a key driver of skin inflammation and barrier abnormalities in atopic dermatitis (AD) patients. Tralokinumab is a fully human monoclonal antibody that specifically binds the IL-13 cytokine with high affinity, thereby preventing its interaction with the IL-13Rα1/IL-4Rα receptor complex and IL-13 signaling. Tralokinumab demonstrated efficacy and safety in three pivotal phase 3 trials. We measured the impact of IL-13 neutralization using transcriptomic analysis of biopsies taken at baseline (Week 0) and Week 16 from patients enrolled in the ECZTRA 1 trial.
Methods. Gene expression levels of biomarkers related to inflammation and skin barrier were assessed by RNA sequencing and qPCR. Treatment differences were estimated by linear mixed effect models with treatment and time as fixed effects and random effect for each patient.
Results. Biopsies taken at baseline (Week 0) and Week 16 from 46 patients enrolled in the ECZTRA 1 trial were analyzed. A statistically significant change ($P<0.05$) in AD biomarkers related to inflammation through the Th2 (CCL-11 and -17), and the Th17/Th22 pathways (IL-22, S100As, DEFB4, and IL36G) were observed. Tralokinumab treatment also altered the expression levels of epidermal skin barrier components (eg, KRT16 and CLDN23) as well as key lipid metabolism enzymes (eg, ELOVL3 and ELOVL5). Interestingly, expression profiles of biomarkers linked to atherosclerosis (eg, SELE, IL-6, and MMP1) were also changed by tralokinumab treatment. Changes in biomarkers correlated with clinical improvement.
Conclusion. Our analysis showed that treatment with tralokinumab shifted the transcriptome of lesional skin towards that of non-lesional skin, demonstrating that specific neutralization of the IL-13 cytokine is able to reverse key AD skin abnormalities.
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