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

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Introduction

- The interleukin (IL)-13 cytokine is a key driver of the skin inflammation seen in patients with atopic dermatitis (AD).
- By binding to the IL-13 cytokine with high affinity, tralokinumab prevents the receptor interaction and IL-13 signaling.
- Tralokinumab demonstrated efficacy and safety in three Phase 3 trials for the treatment of AD.

Methods

- Skin biopsy samples were taken at Baseline, Week 4, and Week 16 from patients (n=12) enrolled in the ECZTRA 1 trial.
- Gene expression levels of biomarkers related to inflammation and skin barrier were assessed by RNA sequencing and validated by quantitative polymerase chain reaction (qPCR).

Results

- Baseline characteristics were similar between the two treatment arms (Table 1).
- Tralokinumab treatment led to a greater shift towards a non-lesional profile at 16 Weeks relative to placebo (Figure 2).

Table 1. Baseline demographics and clinical characteristics for randomized subjects in parent study (ECZTRA 1) and in the transcriptomic subgroup

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All randomized subjects</th>
<th>Non-randomized subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>39 (15–65)</td>
<td>38 (15–65)</td>
</tr>
<tr>
<td>Sex, %</td>
<td>52.0%</td>
<td>50.0%</td>
</tr>
<tr>
<td>Race, %</td>
<td>65.0%</td>
<td>60.0%</td>
</tr>
<tr>
<td>Disease stage</td>
<td>42.5%</td>
<td>42.5%</td>
</tr>
</tbody>
</table>

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

Conclusions

- Treatment with tralokinumab shifted the AD transcriptome towards that of non-lesional skin.
- Neutralization of the IL-13 cytokine significantly modulated key AD immune and barrier abnormalities in skin lesions.

References


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Figure 2. Transcriptome analyses depicting A. Direction of dysregulation in AD
B. Improvements towards non-lesional transcriptomic profiles for tralokinumab and placebo groups

Figure 3. Levels of skin biomarkers in the following immune pathways were reduced over 16 Weeks of tralokinumab treatment: A. Th2, B. Th1, C. Th17, and D. Th1-specific

Figure 4. Levels of key AD-related immune and barrier genes over 16 Weeks measured by A. Transcripts of IL-13, validated by qPCR

Figure 5. Immunohistochemistry images of the epidermal barrier with quantification at baseline, Week 4, and Week 16.