Matching-adjusted indirect comparison of the efficacy of tralokinumab and dupilumab in the treatment of moderate-to-severe atopic dermatitis beyond week 16

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Objective
- To indirectly compare tralokinumab and dupilumab, both in combination with TCS, for the treatment of moderate-to-severe AD in adult patients, as determined by clinical endpoints and PROs beyond week 16

Results
Clinical outcomes at Week 32
- Tralokinumab and dupilumab showed comparable efficacy across clinical response endpoints at week 32 (Figure 1)
- The matched proportion of patients achieving EASI 75 (49.9%) was numerically higher for tralokinumab (52.1%) compared with dupilumab (47.4%; difference 4.7; 95% CI, 0.5, 8.9; P=0.03) (Figure 2A)
- For EASI-75, the proportion of responders was equivalent for tralokinumab and dupilumab (71.9%; difference 0.6%; 95% CI, -3.1, 4.3; P=0.81)
- The proportion of patients with an EASI-50 response was numerically favourable for tralokinumab (75.3%), compared with dupilumab (77.5%; difference 2.2%; 95% CI, -4.8, 9.2; P=0.56)
- For EASI-90, the proportion of responders was numerically favourable for tralokinumab (56.4%) compared with dupilumab (53.5%; difference 2.9%; 95% CI, -7.8, 14.6; P=0.57)

Patient-reported outcomes at week 32 vs dupilumab at week 52
- PRO results were generally similar for tralokinumab and dupilumab
- Rates of patients experiencing a ≥4-point improvement in worst daily pruritus NRS or POEM were similar for both tralokinumab and dupilumab (Table 1, A), as were mean changes from baseline in these measures
- Comparative proportions of patients achieving EASI benefit for both tralokinumab (73.7%) and dupilumab (72.5%) were similar
- The mean change in DLQI was greater in the tralokinumab arm than in the dupilumab arm (d = 0.12) (Table 1, B)

Background
- Tralokinumab and dupilumab are both licensed for the treatment of moderate-to-severe AD in adult patients who are candidates for systemic treatment
- However, to date no head-to-head or indirect comparisons of their efficacy beyond week 16 have been conducted
- In the absence of head-to-head data, indirect comparison methods adjusting for cross-trial differences are used to compare therapies
- In this study, we use a MAIC approach to compare tralokinumab and dupilumab, both used in combination with TCS, beyond 16 weeks
- Data were taken from the ECZTRA 3 tralokinumab trial and the LIBERTY AD CHRONOS dupilumab trial

Matching-Adjusted Indirect Comparison Methods
- An unanchored MAIC analysis was conducted using IPD from patients randomized to tralokinumab Q2W or Q4W from week 16, in the ECZTRA 3 trial, with aggregate data from patients treated with dupilumab Q2W in the LIBERTY AD CHRONOS trial
- Tralokinumab IPD were selected by applying the inclusion criteria from LIBERTY AD CHRONOS, then weighted to match the baseline characteristics of dupilumab patients
- The baseline characteristics matched were sex, age, BMI, disease duration, DLQI, EASI, IGA and SCORAD
- Outcomes assessed in the MAIC were:
  - Clinical outcomes
    - Patients achieving a ≥ 10-point improvement in EASI
    - Patients achieving a ≥ 75% improvement in EASI (EASI-75, -90, -95)
    - Mean change from baseline in EASI and DLQI
  - PRO outcomes
    - Mean change from baseline in DLQI
- Table 1. Population matching

Conclusions
- This study used a MAIC approach to compare the efficacy of tralokinumab Q2W, and Q4W after week 16, with that of dupilumab Q2W, both in combination with TCS, beyond 16 weeks
- The results were broadly comparable across treatment arms in both clinical and PRO endpoints
- The results of this study confirm similar efficacy for tralokinumab and dupilumab in the treatment of moderate-to-severe AD beyond 16 weeks of therapy

Population Matching
- A total of 250 patients treated with tralokinumab in ECZTRA 3 were compared with 106 patients treated with dupilumab after week 16
- The indirect comparison was conducted using IPD from patients randomized to tralokinumab Q2W or Q4W and dupilumab Q2W
- The results of this analysis confirm similar efficacy for tralokinumab and dupilumab in the treatment of moderate-to-severe AD in adult patients

Table 1. Population matching

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>N=106</th>
<th>N=250</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>17.7</td>
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<td>Sex, % male</td>
<td>56.7</td>
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</tr>
<tr>
<td>BMI, kg/m²</td>
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<tr>
<td>Disease duration, years</td>
<td>13.5</td>
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</tr>
<tr>
<td>Race, % white</td>
<td>86.0</td>
<td>86.0</td>
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<tr>
<td>EASI score</td>
<td>28.7</td>
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<tr>
<td>IGA score</td>
<td>3.5</td>
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</tr>
<tr>
<td>SCORAD score</td>
<td>69.7</td>
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Table 2. Clinical outcomes

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Study Limitations
- For PRO endpoints, the difference in time points may introduce some bias to the analysis
- Results reported after week 16 do not reflect all participants who were randomized to dupilumab Q2W – consequently, the matched tralokinumab population may not be completely representative of the dupilumab population for which outcomes are reported
- Due to differences in the treatment of patients receiving placebo in the two trials, an anchored analysis could not be performed
- As with all indirect comparisons, observed unexplained differences across the trials cannot be ruled out

Abbreviations
AD, atopic dermatitis; BMI, body mass index; CI, confidence interval; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EASI-75, 75% improvement in EASI; EASI-90, 90% improvement in EASI; EASI-95, 95% improvement in EASI; ECZTRA, Eczema: A Direct Comparison of Tocilizumab and Tralokinumab; EVC, Ezcema Validation Committee; IGA, Investigator’s Global Assessment; IPD, individual patient data; MAIC, matching-adjusted indirect comparison; NRS, numerical rating scale; POEM, Patient-Oriented Eczema Measure; PRO, patient-reported outcome; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; SD, standard deviation; SE, standard error; TCS, topical corticosteroids

Disclosure
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