Dupilumab Demonstrates Higher Likelihood of Maintaining Efficacy Outcomes Compared with Lebrikizumab in Monotherapy at Week 52: Results from a Placebo-adjusted Indirect Comparison Analysis

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Background

- Monoclonal antibodies, dupilumab and lebrikizumab have demonstrated safety and efficacy in clinical trials.² ⁶
- However, there are no direct head-to-head comparisons of dupilumab and lebrikizumab
- In the absence of direct head-to-head comparisons between dupilumab and lebrikizumab, Bisher indirect treatment comparisons (ITCs), in which treatment effects are anchored to a common comparator (e.g. placebo), provide a robust and widely accepted method of evaluating the relative efficacy of drugs, and can offer a useful framework for decision making.

Methods

- A placebo-adjusted Bisher ITC utilized phase 2 trial data of dupilumab-treated patients from SOLO-CONTINUE² (NCT02109513) and lebrikizumab-treated patients from ADVOCATE 1 and 2² maintenance phase (NCT03443303 and NCT01419067¹)
- Data at Week 52 was used for the following doses:
  - 250 mg dupilumab q2w or placebo
  - 300 mg dupilumab q2w or placebo
  - 250 mg lebrikizumab q2w or q4w or placebo
- No adjustments were made for baseline characteristics, and missing data were imputed using non-responder imputation (NRI)
- The comparison between Dupilumab and Lebrikizumab was made at Week 52 (maintenance phase) for the proportion of patients who maintained an IGA score of 0/1, EASI-75, and 4-point or greater improvement in the peak pruritus numerical rating scale (PP-NRS ≥ 4) from Week 16 (baseline).
- For EASI-50, the patients evaluated at Week 52 were those who had achieved EASI-75 at Week 16 (baseline).
- OR with 95% CI are reported.

Objective

- To report a placebo-adjusted Bisher ITC comparing maintenance of efficacy outcomes in dupilumab- and lebrikizumab-treated patients with moderate-to-severe AD

Conclusion

- A placebo-adjusted Bisher ITC analysis showed that the likelihood of maintaining responses in clinical signs and symptoms was higher in patients treated with dupilumab q2w vs lebrikizumab q2w or q4w

Table 1. Inclusion criteria and study design details for the source studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Inclusion criteria</th>
<th>Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADVOCATE 1 &amp; 2 (NCT04146363 and NCT04178967): Adults (aged ≥18 years), moderate-to-severe AD, dupilumab 300 mg qw, q2w, or placebo, for 16 weeks.</td>
<td>Prospective, open-label, randomized, multicenter phase 3 study.</td>
<td></td>
</tr>
<tr>
<td>LIBERTY AD SOLO-1 &amp; SOLO-2 (NCT02109513): Adults (aged ≥18 years), moderate-to-severe AD, lebrikizumab 250 mg q4w, q2w, or placebo, for 16 weeks.</td>
<td>Prospective, open-label, randomized, multicenter phase 3 study.</td>
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</tbody>
</table>

Table 2. Baseline characteristics.

<table>
<thead>
<tr>
<th>Item</th>
<th>SOLO-CONTINUE (n=80)</th>
<th>Lebrikizumab 250 mg q4w (n=55)</th>
<th>Lebrikizumab 250 mg q2w (n=51)</th>
<th>Lebrikizumab 250 mg q2w (n=32)</th>
<th>Placebo (n=39)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean EASI and PP-NRS baseline scores were similar between the trial populations</td>
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</tbody>
</table>

Table 3. Efficacy outcomes at Week 52.

<table>
<thead>
<tr>
<th>Item</th>
<th>SOLO-CONTINUE</th>
<th>Lebrikizumab 250 mg q4w</th>
<th>Lebrikizumab 250 mg q2w</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>EASI-75</td>
<td>3.31</td>
<td>3.53*</td>
<td>3.72*</td>
<td>4.15*</td>
</tr>
<tr>
<td>EASI-90</td>
<td>3.53</td>
<td>3.72*</td>
<td>3.93</td>
<td>4.32*</td>
</tr>
<tr>
<td>IGA 0/1</td>
<td>7.82</td>
<td>9.74</td>
<td>11.49</td>
<td>13.35</td>
</tr>
<tr>
<td>PP-NRS ≥4</td>
<td>8.76</td>
<td>10.93</td>
<td>12.86</td>
<td>14.96</td>
</tr>
</tbody>
</table>

Results

- Compared with lebrikizumab q2w dosing, dupilumab q2w had significantly higher ORs for EASI-75 (OR=4.13, 95% CI 1.38–12.53), EASI-90 (OR=5.57, 95% CI 1.99–15.53), and PP-NRS ≥4 (OR=3.33, 95% CI 1.09–10.06), which were not statistically significant compared with placebo (EASI-75: OR=1.57, 95% CI 0.98–2.55; EASI-90: OR=2.00, 95% CI 0.98–4.03; PP-NRS ≥4: OR=1.86, 95% CI 0.97–3.55).

References


Figure 1. Bisher ITC results of efficacy outcomes at Week 52.