Dupilumab Long-Term Safety and Efficacy in Patients With Asthma: LIBERTY ASTHMA TRAVERSE


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I have the following real or perceived conflicts of interest that relate to this presentation:

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<tbody>
<tr>
<td>Grants / research support:</td>
<td>GSK, Sanofi</td>
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<td>Honoraria or consultation fees:</td>
<td>AstraZeneca, Boehringer Ingelheim, Equillium, Gala Therapeutics, Genentech, Genzyme, GSK, Mylan, Novartis, Pulmatrix, ResTORBio, Regeneron Pharmaceuticals, Inc., Sanofi, Sentien Biotechnologies, Teva</td>
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• Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for IL-4 and IL-13, key and central drivers of type 2 inflammation in multiple diseases\textsuperscript{1–4}

• The efficacy and safety of dupilumab up to 1 year have been demonstrated
  – In the phase 2b DRI (P2b; NCT01854047)\textsuperscript{5} and phase 3 QUEST (NCT02414854)\textsuperscript{6} studies, add-on dupilumab 200 mg and 300 mg q2w, vs placebo, significantly reduced severe asthma exacerbations and improved pre-BD FEV\textsubscript{1} in patients with uncontrolled, moderate-to-severe asthma with greater treatment effects in patients with elevated type 2 biomarkers at baseline

**Aim**

• To evaluate the long-term safety, tolerability, and efficacy of dupilumab in an open-label extension study (NCT02134028) of patients with asthma who completed a previous dupilumab asthma clinical study (P2b, phase 3 QUEST, phase 2a EXPEDITION [NCT02573233], or phase 3 VENTURE [NCT02528214])
Patient numbers presented for parent studies represent the number of patients who enrolled into and were exposed to treatment in the OLE. Total number of patients enrolled and exposed to treatment in the OLE. Total number of patients who continued to be exposed to treatment beyond 48 weeks. OCS, oral corticosteroid; OLE, open-label extension; q4w, every 4 weeks; SC, subcutaneous.
Rates of TEAEs in the OLE were similar to those observed in the parent studies\textsuperscript{5–7} with no new safety signals identified

- Rates of TEAEs in the overall ITT populations of the parent studies, P2b, QUEST, and VENTURE, were 75–83%, 81–83%, and 62–64%, respectively\textsuperscript{5–7}

<table>
<thead>
<tr>
<th>OLE outcomes</th>
<th>Patients from P2b</th>
<th>Patients from QUEST</th>
<th>Patients from VENTURE</th>
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<tbody>
<tr>
<td></td>
<td>Placebo/dupilumab\textsuperscript{a} (n = 111)</td>
<td>Dupilumab/dupilumab\textsuperscript{b} (n = 421)</td>
<td>Placebo/dupilumab\textsuperscript{a} (n = 517)</td>
</tr>
<tr>
<td>Patients with any TEAE</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>n (%)</td>
<td>88 (79.3)</td>
<td>369 (87.6)</td>
<td>414 (80.1)</td>
</tr>
<tr>
<td>n/PY (nP/100 PY)\textsuperscript{c}</td>
<td>88/72.5 (121.4)</td>
<td>369/228.7 (161.4)</td>
<td>414/293.6 (141.0)</td>
</tr>
<tr>
<td>Patients with any treatment-emergent SAE</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>n (%)</td>
<td>14 (12.6)</td>
<td>42 (10.0)</td>
<td>48 (9.3)</td>
</tr>
<tr>
<td>n/PY (nP/100 PY)\textsuperscript{c}</td>
<td>14/207.0 (6.8)</td>
<td>42/794.2 (5.3)</td>
<td>48/747.9 (6.4)</td>
</tr>
<tr>
<td>Patients with any TEAE leading to death</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>n (%)</td>
<td>0</td>
<td>3 (0.7)</td>
<td>0</td>
</tr>
<tr>
<td>n/PY (nP/100 PY)\textsuperscript{c}</td>
<td>0/222.3</td>
<td>3/827.6 (0.4)</td>
<td>0/780.5</td>
</tr>
<tr>
<td>Patients with any TEAE leading to permanent treatment discontinuation</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>n (%)</td>
<td>3 (2.7)</td>
<td>19 (4.5)</td>
<td>12 (2.3)</td>
</tr>
<tr>
<td>n/PY (nP/100 PY)\textsuperscript{c}</td>
<td>3/221.5 (1.4)</td>
<td>19/822.4 (2.3)</td>
<td>12/777.1 (1.5)</td>
</tr>
</tbody>
</table>

- The most common TEAEs occurring in any treatment group during OLE were nasopharyngitis and injection-site erythema, 9–13% of patients experienced SAEs, the number of patients with TEAE leading to permanent discontinuation was low and 4 deaths occurred (metastatic lung cancer, adenocarcinoma gastric, craniocerebral injury, and respiratory failure)

\textsuperscript{a}Patients who had been in the placebo arms of the parent studies and then exposed to dupilumab 300 mg q2w in the OLE. \textsuperscript{b}Patients who had been in the dupilumab arms of the parent studies and exposed to dupilumab 300 mg q2w in the OLE.

\textsuperscript{5}For patients with event, PY are calculated up to the date of the first incidence; for patients without event, PY correspond to the length of study observation period.

\textsuperscript{6}ITT, intent-to-treat; MedDRA, Medical Dictionary for Regulatory Activities; n (%), number and percentage of patients with ≥ 1 TEAE; nP, number of patients with any event; nP/100 PY, number of patients with ≥ 1 event per 100 patient-years; PY, patient-years; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
In non-OCS dependent patients, the low unadjusted annualized exacerbation rate observed in the parent studies\(^5\)\(^-\)\(^7\) were sustained during the OLE.

- At parent study baseline for P2b and QUEST, mean number of exacerbations in the past year across treatment groups in the overall ITT populations were 1.85–2.37 and 2.02–2.31, respectively\(^5\),\(^6\)

- At end of parent study treatment, unadjusted AER for placebo- and dupilumab-treated patients were 1.07 and 0.31–0.69 for P2b and 0.98–1.09 and 0.48–0.56 for QUEST, respectively

- During the OLE, unadjusted AER ranged from 0.31–0.35 in the non-OCS dependent population

\[^a\]\(^*\)The total number of events that occurred during the treatment period divided by the total number of patient-years followed in the treatment period. AER, Annualized severe exacerbation rate.
In non-OCS dependent patients, improvements in FEV$_1$ observed in the parent studies$^{5–7}$ were sustained during the OLE.

- At parent study baseline for P2b and QUEST, mean FEV$_1$ across treatment groups in the overall ITT populations was 1.79–1.86 and 1.75–1.78 L, respectively$^{5,6}$

- At end of parent study treatment, mean FEV$_1$ for placebo- and dupilumab-treated patients was 1.99 and 2.11–2.15 L for P2b and 1.89–1.94 and 2.13 L for QUEST, respectively$^{5,6}$

- At Week 96 of the OLE, mean FEV$_1$ was 2.02–2.12 L (13%–22% mean percent change from parent study baseline) in the non-OCS dependent population.
Conclusions

- Long-term treatment of adult and adolescent moderate-to-severe asthma patients with dupilumab 300 mg q2w was generally well tolerated, with a long-term safety profile that was consistent with that seen in the shorter duration parent studies, P2b, QUEST and VENTURE\textsuperscript{5–7}

- Long-term treatment of adult and adolescent, non-OCS dependent, moderate-to-severe asthma patients with dupilumab demonstrated maintenance of the clinical efficacy that was observed in the parent studies, P2b and QUEST,\textsuperscript{5,6} including a persistently low exacerbation rate and sustained improvements in lung function up to 96 weeks
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