Lower incidence of hypereosinophilia with tezepelumab treatment versus placebo in the PATHWAY and NAVIGATOR studies

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Why did we perform this research?

• Biologics for severe asthma that block IL-4 and IL-13 signaling have been consistently linked to hypereosinophilia.1,2
• In the PATHWAY (NCT02054130) and NAVIGATOR (NCT03347279) studies, tezepelumab, an anti-TSLP monoclonal antibody, reduced IL-4, IL-5, and IL-13 activity compared with placebo in patients with severe, uncontrolled asthma, as evidenced by reduced mean TGE levels, BECs, and FeNO levels.4,5
• This post hoc analysis assessed the proportion of patients who experienced hypereosinophilia following tezepelumab treatment using pooled data from the PATHWAY and NAVIGATOR studies.

How did we perform this research?

• This analysis included patients from PATHWAY and NAVIGATOR (12–80 years old) who were randomized 1:1 to receive tezepelumab 210 mg or placebo Q4W subcutaneously for 52 weeks (access via QR code).
• The proportions of patients with ≥ 1 occurrence of hypereosinophilia (BEC > 1500 cells/µL) during the on-treatment and on-study periods were assessed.
  - On-treatment period: the date of the first dose of treatment to the date of the last dose of treatment + 33 days, the date of death or the date of study withdrawal, whichever came first.
  - On-study period: the date of the first dose of treatment to the date of study withdrawal or study completion.

Table 1. Baseline BECs and the proportion of patients with hypereosinophilia were balanced between treatment groups in the pooled PATHWAY and NAVIGATOR population

<table>
<thead>
<tr>
<th>BEC, cells/µL</th>
<th>Tezepelumab 210 mg Q4W (n = 665)</th>
<th>Placebo (n = 669)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQR)</td>
<td>260 (200, 305)</td>
<td>260 (200, 305)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>335 (405)</td>
<td>335 (405)</td>
</tr>
</tbody>
</table>

Figure 1. Fewer tezepelumab versus placebo recipients experienced hypereosinophilic events (BEC ≥ 1500 cells/µL) during the on-treatment period of the PATHWAY and NAVIGATOR studies

How did we perform this research?

The incidence of hypereosinophilia was lower with tezepelumab than with placebo in patients with severe, uncontrolled asthma in the PATHWAY and NAVIGATOR studies.

Abbreviations
BEC, baseline eosinophil count; EME, endogenous mast cell eosinophils; IL-5, interleukin-5; IL-13, interleukin-13; TGE, total granulocyte eosinophils; TEA, TRIM Family Cullin–RING Finger E3 Ligase A

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Disclosures
The authors declare no financial or professional conflicts of interest.

How might this impact current clinical practice?

During both studies, the number of patients with hypereosinophilia was stable in the tezepelumab group, whereas increases were observed with placebo.

The results suggest that TSLP blockade, despite reducing IL-4 and IL-13 activity, is not associated with hypereosinophilia, which is consistent with the ability of tezepelumab to also reduce IL-5 activity and eosinophilic inflammation.

Table 2. Fewer patients in the tezepelumab group versus the placebo group had ≥ 1 occurrence of hypereosinophilia (BEC > 1500 cells/µL) during the on-treatment period in the PATHWAY and NAVIGATOR studies

<table>
<thead>
<tr>
<th>BEC subgroup, cells/µL, n (%)</th>
<th>PATHWAY, n/N (%</th>
<th>NAVIGATOR, n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 150</td>
<td>116 (17.3)</td>
<td>117 (17.3)</td>
</tr>
<tr>
<td>150 to &lt; 300</td>
<td>286 (43.0)</td>
<td>287 (42.9)</td>
</tr>
<tr>
<td>≥ 300</td>
<td>379 (57.3)</td>
<td>382 (57.1)</td>
</tr>
<tr>
<td>300 to &lt; 450</td>
<td>127 (19.1)</td>
<td>116 (17.3)</td>
</tr>
<tr>
<td>≥ 450</td>
<td>150 (23.3)</td>
<td>171 (25.6)</td>
</tr>
<tr>
<td>≥ 1500 (hypereosinophilia)</td>
<td>2 (0.3)</td>
<td>6 (0.9)</td>
</tr>
</tbody>
</table>

The proportion of patients reporting ≥ 1 occurrence of BEC ≥ 3000 cells/µL during the on-treatment period was 0.2% (n = 1) in the PATHWAY and NAVIGATOR population. N: number of patients in the study population; n: number of patients in the BEC subgroup, cells/µL, n (%)

Median (IQR) for baseline eosinophil count for patients with hypereosinophilia during the on-treatment period was 920 (920, 920) cells/µL for patients receiving tezepelumab (n = 1) and 1270 (1270, 1270) cells/µL for patients receiving placebo (n = 1). In the pooled PATHWAY and NAVIGATOR population. N: number of patients in the study population; n: number of patients in the BEC subgroup, cells/µL, n (%)

Figure 2. Time to first hypereosinophilic event (days)

In general, fewer patients in the tezepelumab group than the placebo group had hypereosinophilia at any point during the on-study periods of the PATHWAY and NAVIGATOR studies (Table S2).

References