On-treatment clinical remission with tezepelumab in patients with severe, uncontrolled asthma in the phase 3 DESTINATION study


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 abstract

Purpose

To investigate the proportion of patients with severe asthma who achieved on-treatment clinical remission with tezepelumab in the phase 3 DESTINATION study.

Methods

The DESTINATION study is a double-blind, placebo-controlled phase 3 trial that investigated the efficacy and safety of tezepelumab in patients with severe asthma, defined as having at least four exacerbations in the previous year and a postbronchodilator FEV1 < 70% of predicted value. Patients were randomized to tezepelumab 150 mg subcutaneously every 4 weeks or placebo. Clinical remission was defined as the achievement of all four criteria: no oral corticosteroid use, no exacerbations, no use of rescue medication, and no pre-BD FEV1 < 95% of predicted value at the end of the study period. The study included a 2-year extension.

Results

A modified Delphi survey was conducted among experts to establish on-treatment remission as the gold-standard treatment goal for clinical practice. This post hoc exploratory analysis assessed the proportion of tezepelumab recipients in DESTINATION (NCT03706079) who achieved on-treatment clinical remission during the 2-year extension study.

• A modified Delphi survey was conducted among experts in asthma care to develop a consensus framework for asthma remission.
• Two statistical approaches for clinical remission analyses were taken.
  - For patients who completed treatment with data missing at week 104, the last available off-treatment measurement for ACQ-6 score or pre-BD FEV1 was input to replace missing values (Figures 2, 3, and Table S2).
  - Patients who completed treatment but with data missing were assumed not to have achieved clinical remission (Figure S3 and Table S2).

See supplementary material for further details of the study design, endpoints and statistical analyses.

Abbreviations

ACQ-6, Asthma Control Questionnaire-6; BD, bronchodilator; CI, confidence interval; EPOC, European Pulmonary O2 Commentary; FEV1, forced expiratory volume in 1 second; NCT, National Clinical Trial; OCS, oral corticosteroid; QR, quick response; REM, respiratory exacerbation management; REM, respiratory exacerbation management; RQLQ, Respiratory Quality of Life Questionnaire; SABA, short-acting β2-agonist; SMD, standard mean difference; UVIC, University of Victoria; VR, visual representation; WAGR, Wisconsin Airway Group of Renalologists; WOB, Work of Breathing; WQOL, Work-Quality-of-Life Questionnaire; ZEQ, Zeitschrift für Ernährungswissenschaft.

Disclosures

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Conclusion

These findings support the benefits of tezepelumab in a broad assessment of patients with severe asthma and contribute towards the goal of clinical remission.

Why did we perform this research?

• Asthma remission is characterized by long-term disease stabilization and control with or without ongoing treatment.
• A modified Delphi survey was conducted among experts in asthma care to develop a consensus framework for asthma remission.
• Two statistical approaches for clinical remission analyses were taken.
  - For patients who completed treatment with data missing at week 104, the last available off-treatment measurement for ACQ-6 score or pre-BD FEV1 was input to replace missing values (Figures 2, 3, and Table S2).
  - Patients who completed treatment but with data missing were assumed not to have achieved clinical remission (Figure S3 and Table S2).

See supplementary material for further details of the study design, endpoints and statistical analyses.

What did we find?

Figure 1. On-treatment clinical remission was defined as meeting all of the following criteria

| Baseline demographics and clinical characteristics are shown in Table S1. |

<table>
<thead>
<tr>
<th>Week 104</th>
<th>NCT03706079</th>
<th>NCT03347279</th>
</tr>
</thead>
<tbody>
<tr>
<td>No asthma exacerbations</td>
<td>97%</td>
<td>96%</td>
</tr>
<tr>
<td>No oral corticosteroid use</td>
<td>69%</td>
<td>72%</td>
</tr>
<tr>
<td>ACQ-6 score ≤ 1.5</td>
<td>31%</td>
<td>28%</td>
</tr>
<tr>
<td>pre-BD FEV1 &gt; 95%</td>
<td>81%</td>
<td>84%</td>
</tr>
</tbody>
</table>

Table S2. Clinical remission criteria used post hoc

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<table>
<thead>
<tr>
<th>Week 0 to 104</th>
<th>Tezepelumab</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achieved clinical remission</td>
<td>28.5%</td>
<td>21.9%</td>
</tr>
<tr>
<td>Did not achieve clinical remission</td>
<td>33.5%</td>
<td>26.7%</td>
</tr>
</tbody>
</table>

Figure 2. A higher proportion of patients receiving tezepelumab than placebo achieved on-treatment clinical remission during the time periods assessed.

Table S3. Odds ratios for reaching clinical remission criteria and post hoc exploratory analysis assessed the proportion of tezepelumab recipients in DESTINATION (NCT03706079) who achieved on-treatment clinical remission during the 2-year extension study.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Weeks 0 to 52</th>
<th>Weeks &gt; 52 to 104</th>
</tr>
</thead>
<tbody>
<tr>
<td>No asthma exacerbations</td>
<td>1.44 (0.95–2.19)</td>
<td>1.44 (0.97–2.14)</td>
</tr>
<tr>
<td>No oral corticosteroid use</td>
<td>1.44 (0.95–2.19)</td>
<td>1.44 (0.97–2.14)</td>
</tr>
</tbody>
</table>

Figure 3. The proportion of patients receiving tezepelumab who achieved on-treatment clinical remission was 37% in weeks 24–52 and 34% in weeks 52–104.

How did we perform this research?

• Patients (12–80 years) who completed NAVIGATOR (NCT03347279) could enrol in DESTINATION (Figure S1, access via QR code).
• Two statistical approaches for clinical remission analyses were taken.
  - For patients who completed treatment with data missing at week 104, the last available off-treatment measurement for ACQ-6 score or pre-BD FEV1 was input to replace missing values (Figures 2, 3, and Table S2).
  - Patients who completed treatment but with data missing were assumed not to have achieved clinical remission (Figure S3 and Table S2).

See supplementary material for further details of the study design, endpoints and statistical analyses.

How might this impact current clinical practice?

• Achieving and maintaining disease remission is becoming the ultimate goal for asthma treatment.
• A higher proportion of patients who received tezepelumab than placebo achieved on-treatment clinical remission during the time periods assessed.
• These findings support the benefits of tezepelumab in a broad assessment of patients with severe asthma and contribute towards the goal of clinical remission.

E-poster

Supplementary material

Audio/video

References

Supplementary material

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