NON-PNEUMONITIS IMMUNE-MEDIATED ADVERSE EVENTS WITH DURVALUMAB IN PATIENTS WITH UNRESECTABLE STAGE III NSCLC (PACIFIC)

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Background
In PACIFIC, a Phase 3 trial of durvalumab versus placebo in patients with unresectable NSCLC with or without progression after concurrent chemoradiotherapy (CCRT), durvalumab significantly prolonged progression-free survival (PFS) (HR: 0.72; 95% CI: 0.60–0.87; p = 0.0003) compared with placebo. A manageable safety profile and no clinically relevant differences in pneumonitis imAE status were observed between treatment arms. In this analysis, we report on the occurrence of non-pneumonitis (np) imAEs occurring on durvalumab and their impact on treatment discontinuation and patient outcomes.

Conclusions
Non-pneumonitis imAEs occurred infrequently, but were more common with durvalumab than placebo (32.4% vs 25.8%, respectively). Thyroid disorders were the most common non-pneumonitis imAEs, followed by rash/dermatitis and gastrointestinal (GI) disorders. Of durvalumab-treated patients who experienced non-pneumonitis imAEs, 11% had grade 3/4 np imAEs and none had fatal non-pneumonitis imAEs. Non-pneumonitis imAEs were generally managed and did not lead to high rates of durvalumab discontinuation.

All-cause pneumonitis incidence with durvalumab was similar regardless of whether patients experienced non-pneumonitis imAEs, and no clinically meaningful relationship was observed between non-pneumonitis imAE status and pneumonitis incidence. Non-clinically relevant associations between the presence or absence of non-pneumonitis imAEs and baseline clinical characteristics were observed. These results indicate that the potential role of non-pneumonitis imAEs should not deter use of the PACIFIC regimen in eligible patients.

Methods
Trial design
PACIFIC was a Phase 3, randomized, double-blind trial of patients with World Health Organization performance status (WHO PS) 0–1 whose disease did not progress following ≥2 cycles of platinum-based cCRT and who were not candidates for surgery. Patients were randomized 2:1 to receive durvalumab (n=404) or placebo (n=234) via intravenous infusion every 2 weeks until disease progression or unacceptable toxicity. The detailed study design has been published elsewhere.

Assessments and analysis
On-study np imAEs (imAEs occurring on study treatment and within 60 days of last on-study drug exposure) were assessed by the investigators, with subsequent review and adjudication by the first author.

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Table 1. Timing of np imAEs on durvalumab-treated patients (categories with ≥5 patients with events)

<table>
<thead>
<tr>
<th>Time to resolution, median (IQR)</th>
<th>Placebo (n=234)</th>
<th>Durvalumab (n=404)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 week</td>
<td>1.0 (0.0–6.0)</td>
<td>1.0 (0.0–6.0)</td>
</tr>
<tr>
<td>≥1 week, ≤6 months</td>
<td>2.0 (1.0–6.0)</td>
<td>2.0 (1.0–6.0)</td>
</tr>
<tr>
<td>&gt;6 months, ≤12 months</td>
<td>3.0 (2.0–6.0)</td>
<td>3.0 (2.0–6.0)</td>
</tr>
<tr>
<td>&gt;12 months</td>
<td>4.0 (3.0–6.0)</td>
<td>4.0 (3.0–6.0)</td>
</tr>
</tbody>
</table>

References

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