Background

Patients with human papillomavirus negative (HPV-) head and neck squamous cell carcinoma (HNSCC) have poor prognosis with a 5-year survival rate of ~50%, limited durable clinical responses to PD-L1/PD-1 blockade may be due to diminished efficacy of adoptive T cell activation; durable clinical responses with pembrolizumab have been shown in melanoma and mRNA-4157 (V940) is a novel mRNA-based individualized neoantigen therapy that encodes up to 24 neoantigens inducing specific antitumor T cell activation; durable clinical responses with pembrolizumab have been shown in melanoma and mRNA-4157 (V940) is a novel mRNA-based individualized neoantigen therapy that encodes up to 24 neoantigens inducing specific antitumor T cell activation; durable clinical responses with pembrolizumab have been shown in melanoma and mRNA-4157 (V940) is a novel mRNA-based individualized neoantigen therapy that encodes up to 24 neoantigens inducing specific antitumor T cell activation; durable clinical responses with pembrolizumab have been shown in melanoma and mRNA-4157 (V940) is a novel mRNA-based individualized neoantigen therapy that encodes up to 24 neoantigens inducing specific antitumor T cell activation; durable clinical responses with pembrolizumab have been shown in melanoma and mRNA-4157 (V940) is a novel mRNA-based individualized neoantigen therapy that encodes up to 24 neoantigens inducing specific antitumor T cell activation; durable clinical responses with pembrolizumab have been shown in melanoma and mRNA-4157 (V940) is a novel mRNA-based individualized neoantigen therapy that encodes up to 24 neoantigens inducing specific antitumor T cell activation; durable clinical responses with pembrolizumab have been shown in melanoma

Methods

• Part C of this study enrolled patients ~18 years old with checkpoint inhibitor (CT)-naive, recurrent/metastatic HPV-HNSCC

Eligible patients received 200 mg pembrolizumab Q4W following a 3-week lead-in during mRNA-4157 (V940) monotherapy, then combined with 1 mg per kg dose of mRNA-4157 (V940) for up to 3 doses Q3W, followed by pembrolizumab until disease progression, unacceptable toxicity, or 25 total cycles of pembrolizumab (Figure 1)

Safety

• After the clinical cutoff date, the median (range) follow-up was 38.4 (11.7–194.3) weeks

• Kaplan–Meier estimated median (95% CI) progression-free survival and overall survival were 15.0 (11.6–38.6) weeks and 107.1 (42.7–247.6) weeks, respectively

Table 2. Summary of TEOA in n = 2 patients

<table>
<thead>
<tr>
<th>TEOA</th>
<th>Any grade</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>All TEOA (n=0)</td>
<td>22 (96.9)</td>
<td>14 (62.9)</td>
</tr>
<tr>
<td>TEOA (n=2)</td>
<td>mRNA-4157</td>
<td>pembrolizumab</td>
</tr>
<tr>
<td>mRNA-4157 + pembrolizumab (n=2)</td>
<td>22 (96.9)</td>
<td>14 (62.9)</td>
</tr>
</tbody>
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Biomarkers

• Differential gene expression from pretreatment tumor samples suggests increased baseline infiltrated T cell–associated gene expression in patients with disease control (Figure 5A)

Conclusions

• mRNA-4157 (V940) pembrolizumab was associated with preliminary positive clinical responses and disease control in patients with HPV-HNSCC including two complete responses

• mRNA-4157 (V940) pembrolizumab was well tolerated, with an mRNA-4157 safety profile consistent with mRNA-4157 monotherapy

• mRNA-4157 (V940) pembrolizumab showed evidence of activation of immune responses

• Patients with the disease control subgroup demonstrated baseline infiltrated T cell–associated gene expression with decreased mRNA-4157 levels post initiation of pembrolizumab

• Randomized assessment of the mRNA-4157 (V940) pembrolizumab treatment effect in the advanced disease setting may be warranted

References