Background Individualized neoantigen cancer vaccines aim to benefit patients by generating strong, durable neoantigen-specific CD8 T cells. Previous data showed extended overall survival (OS) in patients with metastatic colorectal cancer (CRC) who achieved a molecular response (MR) versus those who did not after individualized neoantigen vaccination in combination with nivolumab and ipilimumab.1 We report updated OS and analysis of clinicopathologic features of patients achieving a MR.

Methods Patients with metastatic CRC, non-small cell lung cancer, or gastroesophageal adenocarcinoma who had received routine chemotherapy were treated in a Phase 1/2 first-in-human study (NCT03639714). The vaccine regimen consisted of sequential administrations of chimpanzee adenovirus and self-amplifying mRNA (samRNA) vectors encoding 20 patient-specific neoantigens in combination with nivolumab (IV 480 mg Q4W) and ipilimumab (SC 30 mg).

Results Thirteen of 29 patients treated had CRC. Six of these 13 had stable disease (SD) and 7 had progressive disease (PD) per RECIST v1.1. Six patients achieved a MR defined as ≥ 30% reduction in ctDNA. Patients with a MR had prolonged overall survival (OS) compared to patients without a MR (see Table 1). MR was not associated with primary tumor location, presence of liver metastases, or RAS mutations and patients with a MR were not enriched for higher tumor mutation burden (TMB), PD-L1, or T cell inflamed gene expression profiles (GEP), and had similar baseline ctDNA values based on variant allele frequency (VAF) (p-value=0.18) (table 1).

Conclusions Patients who achieved MR had extended OS compared with those patients without MR. Patients with a MR were not enriched based on primary or metastatic tumor site or known correlates of response to checkpoint inhibitors. The lower baseline VAF observed in patients with a MR may be reflective of VAF in early metastatic disease. A subsequent, ongoing randomized study is evaluating individualized neoantigen vaccine in the 1L maintenance setting (NCT05141721).

Acknowledgements We thank patients and their families for participating in this clinical study and Bristol-Myers Squibb for supply of nivolumab and ipilimumab.

Trial Registration NCT03639714

REFERENCE

Ethics Approval This study was reviewed and approved by institutional review boards at participating clinical sites and all patients gave informed consent before taking part in this clinical study.

Abstract 660 Table 1 Clinicopathologic features with molecular response.

<table>
<thead>
<tr>
<th>Overall Survival (median in months)</th>
<th>Primary Tumor Location</th>
<th>Presence of liver metastases</th>
<th>Median TMB (mutations per megabase range)</th>
<th>PD-L1</th>
<th>T cell inflamed GEP based on RNaseq (p score)</th>
<th>Baseline ctDNA (mean VAF, range)</th>
<th>OS per RECIST v1.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR (n=6)</td>
<td>Moderate</td>
<td>Colorectal: 3, Breast: 3</td>
<td>4</td>
<td>&lt;1%</td>
<td>&lt;RNaseq-0.4</td>
<td>4.13 (3.3-6.0)</td>
<td>3% (1.0-15.6)</td>
</tr>
<tr>
<td>No MR (n=7)</td>
<td>Low</td>
<td>Colorectal: 5, Breast: 1</td>
<td>6</td>
<td>&lt;1%</td>
<td>&lt;RNaseq-0.3</td>
<td>3.85 (3.3-5.7)</td>
<td>4% (0.7-14.4)</td>
</tr>
</tbody>
</table>