for patients with locally advanced or metastatic UC who have not progressed after ≥1 previous line of platinum-based chemotherapy and as maintenance treatment for those who have not progressed with platinum-based chemotherapy. JAVELIN Medley VEGF (NCT03472560) evaluated avelumab + axitinib in metastatic UC who have not progressed with platinum-based chemotherapy and are subject to change due to COVID-19. Data have not undergone standard quality checks and are assessed in baseline tumor samples (Ventana SP263 assay).

Methods Eligible patients with NSCLC had received ≥1 prior platinum-containing therapy and ≤2 prior lines of systemic therapy for locally advanced or metastatic disease; patients with UC were treatment naive in the locally advanced or metastatic setting and ineligible for cisplatin-containing chemotherapy. Patients were immune checkpoint inhibitor naïve and received avelumab 800 mg intravenously every 2 weeks + axitinib 5 mg orally twice daily. The primary endpoint was confirmed objective response (OR) per investigator assessment (RECIST 1.1). Secondary endpoints included progression-free survival (PFS) and safety. PD-L1 expression was assessed in baseline tumor samples (Ventana SP263 assay).

Results A total of 41 patients with NSCLC and 20 with UC received avelumab + axitinib. The confirmed OR rate was 31.7% (95% CI, 18.1–48.1) in the NSCLC cohort and 10% (95% CI, 1.2–31.7) in the UC cohort (all partial responses); 16 patients (39.0%) and 5 (25.0%) had stable disease, respectively. Responses were observed regardless of PD-L1 expression status. Median PFS was 5.3 months (95% CI, 2.5–7.0) in the NSCLC cohort and 2.3 months (95% CI, 1.8–5.6) in the UC cohort. Grade ≥3 treatment-related adverse events (TRAES) occurred in 24 patients (58.5%) in the NSCLC cohort; the most common was hypertension (n=7 [17.1%]). Grade ≥3 TRAEs occurred in 9 patients (45.0%) in the UC cohort; the most common were amylase increased, asthenia, decreased appetite, and palmar-plantar erythrodysesthesia syndrome (n=2 [10%] each). One patient in each cohort experienced a TRAE that led to death (gastric perforation and urinary bladder hemorrhage).

Conclusions Avelumab + axitinib showed antitumor activity and a manageable safety profile in patients with advanced or metastatic NSCLC or UC consistent with findings from studies of each drug alone and in combination.

Trial Registration NCT03472560

Ethics Approval The study was approved by each site’s independent ethics committee.

Consent N/A

REFERENCES


Abstract 282 Table 1 Response Rates and Sensitivity at Individual CPS Cutopts for Pembrolizumab-Treated Patients

<table>
<thead>
<tr>
<th>Population</th>
<th>Prevalence, %</th>
<th>ORR, %</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>100</td>
<td>17.6</td>
<td>1</td>
</tr>
<tr>
<td>CPS = 0</td>
<td>34.8</td>
<td>11.1</td>
<td>0.22</td>
</tr>
<tr>
<td>CPS ≥1</td>
<td>65.2</td>
<td>21</td>
<td>0.78</td>
</tr>
<tr>
<td>CPS ≥10</td>
<td>28.6</td>
<td>27.7</td>
<td>0.45</td>
</tr>
<tr>
<td>CPS ≥20</td>
<td>19.3</td>
<td>30.4</td>
<td>0.33</td>
</tr>
<tr>
<td>CPS ≥50</td>
<td>10</td>
<td>33.1</td>
<td>0.19</td>
</tr>
</tbody>
</table>

CPS, combined positive score; ORR, objective response rate.
Background MRx0518 is a novel, human gut microbiome-derived, single-strain, live biotherapeutic in clinical development for treatment of solid tumors. Preclinically, MRx0518 induced broad immunostimulatory activity and demonstrated anti-tumorigenic effects in a range of murine tumor models. MRx0518 increased CD4+ and CD8+ T cell and NK cell tumor infiltration and decreased Tregs. Activation of tumor TLR5 was observed and linked to the bacterial flagellin moiety, which was shown to strongly induce NFκB, cytokine responses and IFNγ+ CD4+ and CD8+ T cells.

Methods Heavily pre-treated patients refractory to ICIs were enrolled from March 2019 to March 2020. Patients had experienced at least SD from previous ICI (monotherapy or combination) but eventually progressed as confirmed by two radiological scans ≥4 weeks apart in the absence of rapid clinical progression and within 12 weeks of last dose of ICI. Patients were treated with 1 capsule of MRx0518 (1 × 10^{10} to 1 × 10^{11} CFU) BID and pembrolizumab (200 mg every 3 weeks) for up to 35 cycles or disease progression. Tumor response was assessed every 9 weeks per RECIST 1.1. The primary objective was to evaluate safety of the combination by monitoring toxicities in the first cycle of treatment. Secondary objectives were to evaluate efficacy via ORR, DOR, DCR and PFS.

Results In Part A, patients with mRCC (n=9) and mNSCLC (n=3) were recruited. At data cut-off (21 Aug 20), 5 patients remain on study treatment. 83% of patients were male and 17% were female. Median number of prior lines of therapy was 3. 10 patients received nivolumab previously (83%), one received avelumab (8%) and one received pembrolizumab and nivolumab (8%). 83% of patients had experienced SD as best response to prior ICI and 17% had PR as best response. Of 6 patients with available PD-L1 results, 5 had a positive CPS/TPS (>1) and 1 negative (<1). The combination shows a positive safety profile with no treatment-related SAEs or toxicity-related drug discontinuations. No increase in irAEs has been reported. On study treatment, 2 RCC patients and 1 NSCLC patient experienced a PR, with an additional 2 RCC patients experiencing durable SD (6 and 13 months), a protocol defined DCR of 42%. Median PFS is 2.14 months at data cut-off (table 1).

Conclusions This data represents first-in-class proof of concept for a live biotherapeutic in an oncology setting. The combination was tolerable and there were preliminary signals of efficacy. Part B (phase II) in NSCLC, RCC and bladder cancer is ongoing.

Trial Registration www.clinicaltrials.gov NCT03637803

Ethics Approval This study was approved by University of Texas MD Anderson’s Institutional Review Board; approval ref. 2018-0290

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0283