Background

The TAPUR Study is a phase II basket study that evaluates the anti-tumor activity of commercially available targeted agents used in patients (Pts) with advanced cancers with specific genomic alterations.

Pembrolizumab (P) is an immune checkpoint inhibitor. HTMB is an emerging predictive biomarker for checkpoint inhibitor therapy. Results of a cohort of Pts with metastatic colorectal cancer (mCRC) with HTMB defined as ≥9 mutations/megabase (Muts/Mb) treated with P are reported.

Methods

Study Design:

Eligible pts had advanced mCRC with no remaining standard treatment options, PS 0-1, adequate organ function, and measurable disease. Treatment was assigned according to pre-specified protocol matching rules based on genomic testing performed in CLIA-certified, CAP-accredited labs selected by clinical sites.

Pts received P at 2 mg/kg over 30 minutes (n=8) or 200 mg (n=20) every 3 weeks (wks) until disease progression. Tumor evaluations were performed at wks 8 to 16 (n=26) or approved by the TAPUR Molecular Tumor Board (MTB) (n=2). Tumor MS status was reported stable for 25 pts, ambiguous for 1 pt and not available for 1 pt.

Clinical Outcomes:

DC rate, % (OR or SD at 16+ wks), the cohort is expanded to stage IIIb if ≥2 Pts (N=2). Tumor MS status was reported stable for 25 pts, ambiguous for 1 pt and not available for 1 pt.

Table 1: Demographics and Baseline Characteristics (N=27)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>14 (52%)</td>
</tr>
<tr>
<td>Male</td>
<td>13 (48%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>18 (67%)</td>
</tr>
<tr>
<td>Black</td>
<td>6 (22%)</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Prefer not to answer</td>
<td>2 (7%)</td>
</tr>
</tbody>
</table>

TOC Performance Status

0 | 9 (33%)
1 | 18 (67%)

Prior systemic regimens

1-2 | 6 (22%)
≥3 | 21 (78%)

Genomic test performed

FoundationOne | 26 (93%)
In house laboratory | 1 (7%)

Clinical Outcomes:

DC and OR were observed in 28% and 11% of Pts respectively (Table 2). Median PFS, 1 year OS and mOS are reported in Table 2 and shown in Figure 1.

Figure 1: OS and PFS in Advanced mCRC Pts treated with P (N=27)

Figure 2: Best percent change from baseline in target lesion size (N=27)

Note: Mutational burden is reported above bars in Muts/Mb.

Figure 3: Time on Treatment in Pts with SD at 16 wks or OR (N=8)

Figure 3: Time on Treatment in Pts with SD at 16 wks or OR (N=8)

Statistical Methods:

• Simon’s optimal two-stage design was used to test the null hypothesis of 15% disease control (DC) rate versus the alternative of 35%. Power and one-sided type I error rate were set at 85% and 10%, respectively.

• Design requires 10 pts in stage I and if ≤2 pts have DC (OR or SD at 16+ wks), the cohort is expanded to stage II if ≥28 pts. If 7 of ≥28 pts have DC, the drug is considered worthy of further study.

Conclusions

Monotherapy with P showed anti-tumor activity in heavily pre-treated mCRC patients with HTMB. Additional study is warranted to confirm the efficacy of P in this population.

Acknowledgements

The authors would like to acknowledge the pts who participated in these cohorts as well as the following clinical lead of Merck, a TAPUR supporting pharmaceutical company: Eric Rubin, MD.