Amit Dang, Spandana Bhavanasi, Vipani Cholleti, Fawaz Hussain, Nagarani Vullengala, Rafia Jan, Udhayasri R, Vallish BN, Dimple Dang

Metabolic Healthcare Communications, Hyderabad, India

Clinical and Humanistic Outcomes of BRAF Inhibitors in BRAF Mutant Metastatic Colorectal Cancer

Background
- Around 60–90% of patients with metastatic colorectal cancer (mCRC) are known to harbor mutations in the BRAF gene.
- This mutation is recognized as a poor prognostic factor for mCRC, with a median overall survival of ~ 20 months.1,2
- True, treatment of mCRC with BRAF inhibitors is limited or uncertain.
- Several potential treatment options have been investigated for this subset of patients, including immune checkpoint inhibitors, VEGF inhibitors, MEK inhibitors, and several other small molecules.
- We aimed to evaluate the treatment outcomes and humanistic aspects of BRAF inhibitors used alone or in combination with other agents in the management of patients with mCRC harboring BRAF V600E mutations.

Objective
- To evaluate the safety, efficacy, and humanistic outcomes of BRAF inhibitors when used to manage mCRC with BRAF V600E mutations.

Methodology

Eligibility Criteria

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Retrospective cohort (RWE): 3 studies</th>
<th>Phase I trial: 1 study</th>
<th>Retrospective cohort (RWE): 2 studies</th>
</tr>
</thead>
</table>

Main Characteristics of the Included Studies

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Number of studies</th>
<th>Sample Size</th>
<th>BRAF Inhibitor</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>RWE</td>
<td>3</td>
<td>307</td>
<td>Encorafenib</td>
<td>Panitumumab</td>
</tr>
<tr>
<td>Phase I</td>
<td>1</td>
<td>70</td>
<td>Vemurafenib</td>
<td>Panitumumab</td>
</tr>
</tbody>
</table>

Publication Information

<table>
<thead>
<tr>
<th>Study Design</th>
<th>RCT: 3 studies (SAINT study, SAINTX in analysis, DOX6214)</th>
<th>Phase I: 1 study</th>
<th>Retrospective cohort (RWE): 2 studies</th>
</tr>
</thead>
</table>

Results

- Overall response rate (ORR) of 65% was observed with Dabrafenib + Panitumumab combination.
- Stable Disease (SD) was observed in 56% of patients treated with Dabrafenib + Panitumumab + Trametinib.
- Median survival (OS) and progression-free survival (PFS) were 14.6 and 6.0 months, respectively, with Dabrafenib + Panitumumab + Trametinib.

Intervention and Comparator

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dabrafenib</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>65%</td>
<td>Panitumumab</td>
</tr>
<tr>
<td>SD</td>
<td>56%</td>
<td>Trametinib</td>
</tr>
</tbody>
</table>

Clinical Outcomes: Efficacy

- Compared to no treatment (ITB: 31), doxorubicin chemotherapy (ET 1: 22, 25), Vemurafenib (ET 1: 6, 10) or other treatments.
- Median OS and PFS: 12.7 (9.1-23.9) months and 6.0 (4.0-9.0) months, respectively.
- Higher OS and PFS with Dabrafenib + Panitumumab + Trametinib compared to other treatments.

Side Effects

- Most common side effects were diarrhea, rash, fatigue, and nausea.
- Severe side effects included skin toxicity, liver dysfunction, and hypothyroidism.

Discussion

- Dabrafenib and Panitumumab combination showed promising efficacy in patients with mCRC harboring BRAF V600E mutations.
- Future studies are needed to further evaluate the long-term efficacy and safety of this combination.

Conclusion

- Use of BRAF inhibitors in combination with drugs acting through other mechanisms appears to improve survival (OS, PFS) and treatment response (ORR, PR, SD). Further studies are needed to determine the optimal treatment strategy for patients with BRAF V600E mCRC.

References


Poster presented at Access 2023 Annual Meeting, 3-5 April 2023, Florida, Miami