INTRODUCTION

- The RAS oncogene family encodes a pair of protein kinases KRAS and NRAS, which are mutated in approximately 20% of human cancers.
- Sotorasib is a first-in-class and specific irreversible inhibitor of the KRAS G12C protein.
- In the CodeBreaK101 phase 1 trial (NCT03883519), sotorasib monotherapy demonstrated clinical activity in heavily pretreated patients with KRAS G12C-mutated CRC, with an objective response rate (ORR) of 7.1%.

RESULTS (continued)

Treatment-Related Adverse Events (TRAEs)

- No dose-limiting toxicities (DLTs) were observed during the first 28 days (DLT evaluation period).
- The majority of TRAEs were grade 1-2 severity.

RESULTS

- CodeBreaK101 Subprotocol H: Phase 1b Study Evaluating Combination of Sotorasib, a KRASG12C Inhibitor, and Panitumumab (PMab), an EGFR Inhibitor, in Advanced KRASG12C-Mutated Colorectal Cancer (CRC)

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• A minimum of 2 patients must be KRAS G12C-inhibitor naïve and must have progressed after PMab - KRAS G12C-related treatment.

STUDY DESIGN

- CodeBreaK101 Subprotocol H Phase 1b

RESULTS

WBC Dose 80 mg/kg IV Q2W

- Baseline tumor burden
  - Stably disease
  - Progressive disease
  - Stable disease
  - Progression disease

Baseline characteristics and Treatment Exposure

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<tr>
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<tbody>
<tr>
<td>Baseline characteristic</td>
<td>Serum Sotorasib mg/dL</td>
<td>Serum Sotorasib mg/dL</td>
<td>Serum Sotorasib mg/dL</td>
</tr>
<tr>
<td>Median age (yrs)</td>
<td>58 (21-78)</td>
<td>58 (21-78)</td>
<td>58 (21-78)</td>
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<td>Female, n (%)</td>
<td>21 (67.7)</td>
<td>21 (67.7)</td>
<td>21 (67.7)</td>
</tr>
<tr>
<td>Mean time of therapy for metastatic disease (yrs)</td>
<td>2.1 (1.0-6.0)</td>
<td>2.1 (1.0-6.0)</td>
<td>2.1 (1.0-6.0)</td>
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<tr>
<td>Prior chemotherapy, n (%)</td>
<td>5 (16)</td>
<td>5 (16)</td>
<td>5 (16)</td>
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<tr>
<td>Exposure</td>
<td>Median duration of combination, weeks</td>
<td>19 (3.3-48.1)</td>
<td>19 (3.3-48.1)</td>
</tr>
</tbody>
</table>

Tumor Response and Treatment Duration

- The majority of patients had a decrease in target lesion size; this decrease appears to be durable.

Change in Target Lesions Over Time

- Four out of 8 patients who had prior KRASG12C treatment showed tumor shrinkage from 10%–40%.
- The majority of the patients (80%) with prior KRASG12C-related treatment had ≥1 measurable lesions.

RESULTS

- The combination of sotorasib (636 mg daily) and panitumumab (6 mg/kg every 2 weeks) was safe and tolerable in these chemotherapy-naive patients with KRAS G12C-mutated CRC.
- Adverse events were consistent with known adverse events for sotorasib and panitumumab.
- Although follow-up is short in this interim analysis, response rates of the combination of sotorasib and panitumumab were:
  - 15% confirmed ORR
  - 29% ORR (including unconfirmed response avoiding confirmation).
- This ORR were numerically higher than sotorasib monotherapy in KRAS G12C-mutated CRC.
- Sotorasib in combination with panitumumab is associated with signals of early promising efficacy in patients with KRAS G12C-mutated CRC.

CONCLUSIONS

The majority of patients had a decrease in target lesion size; this decrease appears to be durable.

Sotorasib-related toxicities included skin-related toxicities (5); 3 patients were KRAS G12C-inhibitor naïve.

REFERENCES

- Marwan G. Fakhri, Gerald S. Falchook, David S. Hong, Rona Yaeger, Emily Chan, Omar Mather, Panli Cardona, Tian Dai, John H. Strickler.

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