BOLD-100-001 (TRIO039): A Phase 1b/2a Dose-Escalation Study of BOLD-100 in Combination with FOLFOX Chemotherapy in Patients with Pre-Treated Advanced Colorectal Cancer: Interim Efficacy, Safety and Tolerability Analyses

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Methods

**STUDY DESIGN**

**Phase 1**
- Dose escalation study to determine RP2D
- Colorectal 2L+
- Biliary Tract 3L+
- Pancreatic 2L+
- Gastric 2L+
- FOLFOX + BOLD-100 (62 mg/m²) used PO, toxicity withdrawal (n = 12 in total)
- Primary Endpoint: Progression-Free Survival (PFS)
- Secondary Endpoint: Overall Survival (OS)
- Safety and Tolerability
- Duration of Response (ORR) Function

**Phase 2**
- FOLFOX + BOLD-100 (62 mg/m²) used PO, toxicity withdrawn (n = 12 in total)
- Efficacy analyses included patients who had a baseline and ≥1 post-baseline assessment or discontinued study treatment due to progressive disease or death
- Clinical activity was assessed via ROC (receiver operating characteristic) curve
- Disease control rate (DCR) was defined as the percentage of patients with a best overall response or complete response (CR), partial response (PR), or stable disease (SD)
- A Bayesian approach was used to calculate the posterior probability that each endpoint is greater than the landmark historic value and 95% credible intervals were calculated.
- It is recommended that the posterior probability of superiority to the landmark exceed at least 70% for at least one endpoint.

**STATISTICAL ANALYSIS**
- Safety analyses included all 3L+ patients who received ≥1 dose of any study drug
- Efficacy analyses included all 3L+ patients who had a baseline and ≥1 post-baseline assessment or discontinued study treatment due to progressive disease or death
- Clinical activity was assessed via ROC (receiver operating characteristic) curve
- Disease control rate (DCR) was defined as the percentage of patients with a best overall response or complete response (CR), partial response (PR), or stable disease (SD)
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**EFFICACY**
- Median Bayesian PFS was 4.7 [2.9, 8.6] months with a median Bayesian OS of 9.8 [5.2, 22.0] months (Table 3, Figure 2), which compares favourably with current SOC in late-line mCRC (median PFS 2.0 months; median OS 7.1 months for trifluridine/tipiracil).
- Median number of cycles was 7 (range 1-12)

**RESULTS**

<table>
<thead>
<tr>
<th>Table 1. Demographics and Disease Characteristics</th>
<th>All Patients (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range), years</td>
<td>62 (47-78)</td>
</tr>
<tr>
<td>Male ratio, n (%)</td>
<td>8 (47)</td>
</tr>
<tr>
<td>Race</td>
<td>0</td>
</tr>
<tr>
<td>White</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Asian</td>
<td>9 (53)</td>
</tr>
<tr>
<td>American Indian</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>

**Table 2. Summary of Treatment Emergent Adverse Events (TEAEs) Related to BOLD-100 + FOLFOX 220%**

**SAFETY**

**Table 3. Summary of Efficacy Data**

**Figure 3. Overall Survival and Time of Best Clinical Response**

**Figure 4. Waterfall Plot of Best Change from Baseline in Sum of Target Lesions**

**Conclusions**

- In the 3L+ setting, PFS were observed in 2/15 patients (ORR: 13%) and 11 patients had disease control rate (DCR) of ≥70% for at least one endpoint would be significant

**BEST OVERALL RESPONSE**

- In the 3L+ setting, PFS were observed in 2/15 patients (ORR: 13%) and 11 patients had disease control rate (DCR) of ≥70% for at least one endpoint would be significant

- For all 3L+ patients, investigator-assessed disease control rate was 87%, 2 patients were ineligible for assessment of tumour response.

**Figure 1. Study Design**

**Figure 2. Median Bayesian Progression Free Survival (A) and Overall Survival (B)**

**Figure 3. Overall Survival and Time of Best Clinical Response**

**Figure 4. Waterfall Plot of Best Change from Baseline in Sum of Target Lesions**

**Table 3. Summary of Efficacy Data**

- Progression-Free Survival (PFS), months
- Overall Survival (OS), months
- Overall Response Rate (ORR)
- Disease Control Rate (DCR)

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