BOLD-100-001 (TRIO039): A Phase 1b dose-escalation study of BOLD-100 in combination with FOLFOX chemotherapy in patients with advanced gastrointestinal solid cancers: interim safety and efficacy

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1. Background

- BOLD-100 is a first-in-class ruthenium-based antiangiogenic agent in Phase 1b/2 clinical development for the treatment of advanced gastrointestinal (GI) cancers in combination with FOLFIRI

- Being developed initially as a combinational agent, BOLD-100 induces cellular stress through modulation of the unfolded protein response, production of reactive oxygen species and induction of DNA damage

- BOLD-100 demonstrates synergy in established preclinical models in combination with various antiangiogenic therapies, particularly in resistant cell lines

2. Methods

- BOLD-100-001 / TRIO039 is a prospective, Phase 1b dose-escalation (Part A) and Phase 2 dose-escalation (Part B) study of BOLD-100 in combination with FOLFIRI for the treatment of colorectal, pancreatic, gastric and biliary tract cancers, with patients receiving both BOLD-100 and FOLFIRI via IV on Day 1 of each 14-day cycle

3. Study Design

- Phase 2 Dose-Expansion (n=20; 20 per arm)

- In Part A (completed), patient were enrolled in a 3+3 design to determine the combination Recommended Phase 2 Dose (RP2D). Part B comprises 4 cohorts treated at the RP2D until either progressive disease or unacceptable toxicity

4. Results

- Baseline characteristics from the 19 patients dosed in the Phase 1b dose-escalation portion of the study are as follows:

<table>
<thead>
<tr>
<th>Indication, n (%)</th>
<th>22 (22)</th>
<th>48 (48)</th>
<th>41 (41)</th>
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<tr>
<td>MTD</td>
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<td>560 mg/m²</td>
<td>625 mg/m²</td>
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<td>Median age (y)</td>
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- Two dose-limiting toxicities were observed:

  • G3 neutropenia complicated by fever > 38.5°C or infection (cohort #2)
  • Inability to receive planned doses due to AE (cohort #3)

5. Conclusions

- BOLD-100 plus FOLFIRI is well-tolerated with no clinically significant safety findings

- Dose-escalation data supported a BOLD-100 RP2D of 625 mg/m² for the dose-escalation phase, which is currently enrolling

- Promising preliminary efficacy data observed for colorectal patients treated at dose-escalation phase, particularly L+ patients

- BOLD-100-001 / TRIO039 is a prospective, Phase 1b dose-escalation (Part A) and Phase 2 dose-escalation (Part B) study of BOLD-100 in combination with FOLFIRI for the treatment of colorectal, pancreatic, gastric and biliary tract cancers, with patients receiving both BOLD-100 and FOLFIRI via IV on Day 1 of each 14-day cycle

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- Preliminary results include data from 19 patients enrolled in the Phase 1b dose-escalation portion of the study

  • For evaluable pts (n = 16; colorectal arm n = 9), disease control rate of 75%, 1 partial response (48% target lesion reduction) and 3 stable disease were observed (cut-off date: 14-Apr-22)

  • Figure 1 presents the PFS for all 9 colorectal cancer patients enrolled in Part A.

  • Figure 2 represents the PFS for colorectal cancer patients that had failed at least 2 prior therapies. Benchmark for this patient population is 2 months

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