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

Jennifer L. Spratlin MD[1], Grainne M. O'Kane MD[2], Rachel Anne Goodwin MD[3], Elaine McWhirter MD[4], Darby Thompson[5], Khalif Halani[5], Michelle Jones[6], Malcolm Snow[6], E. Russell McAllister[6], Andres Machado MD[7], Yasmin Lemmerick[8], Jim Pankovich[6]

bold therapeutics

1. Alberta Health Services, Edmonton, AB; 2. Princess Margaret Cancer Centre, Toronto, ON; 3. National Cancer Institute of Canada Clinical Trials Group, The Ottawa Hospital, Ottawa, ON; 4. Juravinski Cancer Centre, McMaster University, Hamilton, ON; 5. Emmes Canada, Vancouver, BC; 6. Bold Therapeutics Inc., Vancouver, BC; 7. Translational Research in Oncology, Uruguay; 8. Translational Research in Oncology, Canada

TRIO Translational Research In Oncology — A global network, bringing tomorrow's treatments to the world today.

1 Background

- BOLD-100 is a first-in-class ruthenium-based anticancer agent in Phase 1b/2 clinical development for the treatment of advanced gastrointestinal (GI) cancers in combination with FOLFOX
- 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 anticancer 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-expansion (Part B) study of BOLD-100 in combination with FOLFOX for the treatment of colorectal, pancreatic, gastric and biliary tract cancers, with patients receiving both BOLD-100 and FOLFOX via IV on Day 1 of each 14-day cycle

- 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

3 Study Design

Phase 1b Dose-Escalation (n=19; Completed Feb 2022) ✓

Primary Endpoints: safety, tolerability and maximum tolerated dose (MTD)

Eligibility Criteria

- Histologically and/or cytologically gastrointestinal cancers
- Unresectable or metastatic disease
- ≥ 1 chemotherapy line in metastatic setting

Study Design

FOLFOX + BOLD-100 to determine dose level for dose-expansion phase

- Dose 420 mg/m2
- Dose 500 mg/m2
- Dose 625 mg/m2

MTD

Phase 2 Dose-Expansion (n=~80; 20 per arm)

Primary Endpoints: efficacy via progression-free survival (PFS), overall survival (OS), response rate

- Arm I: 2L+ Gastric
- Arm II: 2L+ Pancreatic
- Arm III: 2L+ Colorectal ✓
- Arm IV: 2L+ Bile Duct

FOLFOX + BOLD-100 (625 mg/m2) until progressive disease (PD), toxicity, and/or withdrawal

4 Results

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

	420 mg/m2 (n=6)	500 mg/m2 (n=7)	625 mg/m2 (n=6)	Total
Age				
Median (Min-Max)	58 (48,77)	61 (54,72)	76 (57,84)	64 (48,84)
Sex, n (%)				
Female Male	5 (83) 1 (17)	3 (43) 4 (57)	3 (50) 3 (50)	11 (58) 8 (42)
Indication, n (%)				
Cholangiocarcinoma Colorectal Pancreatic Gastric	1 (17) 4 (67) 1 (17) 0 (0)	3 (43) 2 (29) 2 (29) 0 (0)	1 (17) 3 (50) 1 (17) 1 (0)	5 (26) 9 (41) 4 (17) 1 (5)
Prior systemic therapies				
Median (Min-Max)	3 (1-4)	4 (2-8)	2 (1-6)	3 (1-8)
Time since diagnosis of unresectable / metastatic disease				
Median (Min-Max)	15.3 (7.5, 36.2)	22.8 (6.7, 72.2)	19.6 (8.5, 46.1)	17.6 (6.7, 72.2)
ECOG, n (%)				
1 0	4 (67) 2 (33)	5 (71) 2 (29)	6 (100) 0 (0)	15 (79) 4 (21)
Disease status at enrollment, n (%)				
Stage III Stage IV	1 (17) 5 (83)	0 (0) 7 (100)	0 (0) 6 (100)	1 (95) 18 (5)

Table 1 – Selected baseline characteristics

Safety

- 18 patients reported ≥1 treatment-emergent adverse events (AEs), majority grade (G) 1-2
- Most common treatment-related (per Investigator) AEs were fatigue (n= 10, 53%), nausea (n= 9, 47%) and stomatitis (n= 7, 37%)
- Seven G4 AEs (all neutropenia), and 1 unrelated G5 AE of pulmonary embolism occurred
- No clinically meaningful post-baseline trends were noted in clinical laboratory results for chemistry and hematology

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 AEs (cohort #3)

Efficacy

- 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 11 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

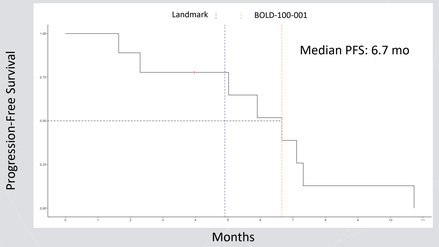

Figure 1 – PFS, colorectal patients

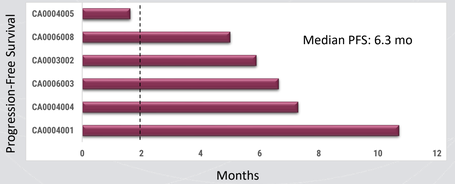

Figure 2 – PFS, 3L+ colorectal patients

5 Conclusions

- BOLD-100 plus FOLFOX is well-tolerated with no clinically significant safety findings
- Dose-escalation data supported a BOLD-100 RP2D of 625 mg/m2 for the dose-expansion phase, which is currently enrolling
- Promising preliminary efficacy data observed for colorectal patients treated at dose-escalation phase, particularly 3L+ patients

Disclosures and Acknowledgements: This study is sponsored by Bold Therapeutics Inc. Please contact Jennifer Spratlin at Jennifer.Spratlin@albertahealthservices.ca for questions or comments

Abstract #377283: Presented at ASCO 2022 Annual Meeting, June 3-7, 2022