Poster
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BOLD-100-001: A Phase 2 Study of BOLD-100 in Combination with FOLFOX in Advanced mCRC Patients that have Failed at Least Two Prior Lines of Therapy

Grainne O'Kane MD[1]; Jennifer Spratlin MD[2]; Do-Youn Oh MD[3]; Sun Young Rha MD[4]; Elaine McWhirter, MD[5]; Elena Elimova MD[6]; Petr Kavan, MD[7]; Moon Ki Choi MD[8]; Dae Won Kim MD[9]; Rachel Goodwin MD[10]; J Randolph Hecht MD[11]; Dong-Hoe Koo MD[12]; Khalif Halani[13]; E Russell McAllister[14]; Michelle Jones[14]; Malcolm Snow[14]; Yasmin Lemmerick[15]; Gonzalo Spera MD[16]; Jim Pankovich[14]

[1]Cross Cancer Institute, University of Alberta, Edmonton, Canada; [2]Trinity St. James Cancer Institute, Dublin, Ireland; [3]Seoul National University Hospital, Seoul, South Korea; [4]Yonsei Cancer Center, Yonsei University Health System, Seoul, South Korea; [5]Hamilton Health Sciences Centre, Ontario, Canada; [6]Princess Margaret Cancer Centre-UHN, Toronto, Canada; [7]Sir Mortimer B. Davis Jewish General Hospital, Montreal, Canada; [8]National Cancer Center, Goyang, Korea; [9]Moffitt Cancer Center, Tampa, FL USA; [10]The Ottawa Cancer Center, Ottawa, Canada; [11] David Geffen School of Medicine at UCLA, Santa Monica, CA USA; [12]Kangbuk Samsung Hospital, Seoul, South Korea; [13]EMMES, Burnaby, Canada; [14]Bold Therapeutics, Inc., Vancouver, Canada; [15]Translational Research in Oncology, Edmonton, Canada; [16]Translational Research in Oncology, Montevideo, Uruguay

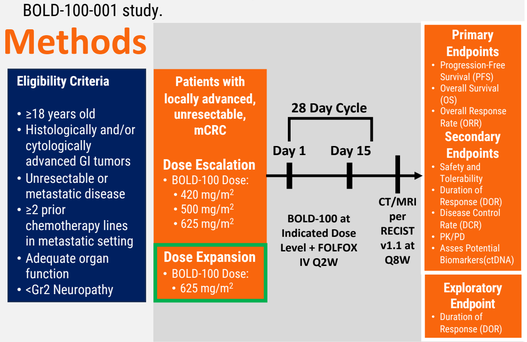
Background

- Metastatic colorectal cancer (mCRC) is the second leading cause of cancer related deaths worldwide, with median overall survival ranging from 6–10 months after progressing on standard first and second-line therapy.[1,2]
- BOLD-100 is a first-in-class ruthenium-based anticancer agent in development for the treatment of gastrointestinal (GI) cancers.
- BOLD-100 is currently being tested in a Phase 2 clinical trial in combination with standard-of-care FOLFOX in patients with advanced GI cancers (NCT04421820) and has potential in a range of solid and liquid cancer indications.[3]
- BOLD-100 exerts its function via the modulation of the unfolded protein response via GRP78 downregulation, with secondary mechanistic pathways including generation of reactive oxygen species, DNA damage, modulation of lipid metabolism, and interactions with ribosomal proteins.
- Here, we present efficacy and safety data in patients with heavily pre-treated, advanced metastatic colorectal cancer (mCRC) who have received prior treatment in the metastatic setting.

Objective

- To assess the safety, and efficacy, including progression-free survival (PFS), overall survival (OS) and overall response rate (ORR) of BOLD-100 in combination with FOLFOX in patients with mCRC enrolled into the BOLD-100-001 study.

Methods



FOLFOX regimen: oxaliplatin 85 mg/m² IV Q2W; leucovorin 400 mg/m² IV Q2W; and 5-FU 2400 mg/m² (continuous 46-hour infusion). 5-FU, 5-fluorouracil; IV, intravenously; Q2W, once every 2 weeks; Gr, Grade; RP2D, Recommended phase 2 dose; ≥2, Second-line and beyond; PK/PD: pharmacokinetic/pharmacodynamic.

STATISTICAL ANALYSIS

- Safety analyses included all patients who received ≥1 dose of any study drug
- Efficacy analyses included all 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 RECIST v1.1 criteria
  - Disease control rate (DCR) was defined as the percentage of patients with a best overall response of complete response (CR), partial response (PR), or stable disease (SD)
  - A Bayesian statistical approach was used in this study.

AUTHOR CONTACT: Grainne.O'Kane@uhn.ca
CORRESPONDING AUTHOR: jp@bold-therapeutics.com
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Results

- As of the data cut-off date, March 14, 2024, 1 participant with stage III (3%) and 37 participants with stage IV (97%) disease were enrolled and treated in the third-line and beyond study
- Baseline demographic and disease characteristics are reported in **Table 1**
- The median (range) number of cycles of BOLD-100 + FOLFOX cycles was 6 (range: 1 – 18).
- Participants had a median (range) of 4 (2, 8) prior therapies before enrollment into the BOLD-100-001 trial
- All participants had microsatellite stable disease (MSS)

Table 1. Demographics and Disease Characteristics

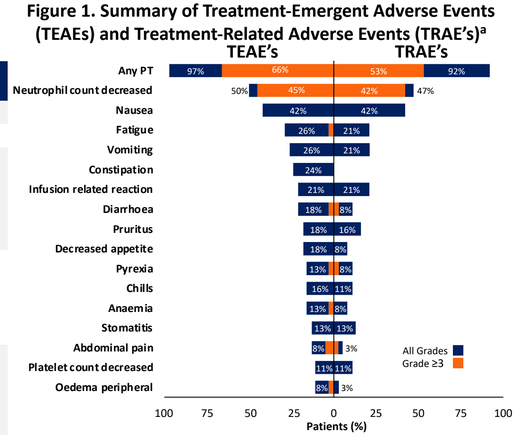
Characteristic	(N = 38)
Age, median (range)	62 (40–78)
Male, n (%)	18 (47)
Race, n (%)	
White	10 (26)
Asian	27 (71)
American Indian or Alaska Native	1 (3)
ECOG PS, n (%)	
0	10 (26)
1	28 (74)
Tumor Sidedness, n (%)	
Left	23 (61)
Right	10 (26)
Unknown	5 (13)
Lines of prior therapy for metastatic or locally advanced disease, median (range)	4 (2-8)
Previous systemic therapy, n (%)	
Fluoropyrimidine-based	38 (100)
Oxaliplatin-based	38 (100)
Anti-VEGF	30 (80)
Anti-EGFR	12 (32)
Regorafenib and/or TAS-102	17 (45)
PD-1/PD-L1 inhibitor	12 (32)
Stage IV disease, n (%)	37 (97)
Time since diagnosis of metastatic disease, median (range)	31.9 (7.5, 123.2)

PS: performance score; PD-1/PD-L1: programmed cell death protein 1/programmed death-ligand 1; anti-VEGF inhibitor: vascular endothelial growth factor; EGFR: epidermal growth factor receptor; TAS-102: trifluridine/tipiracil; Time represented in months

SAFETY

Figure 1 includes safety information from the treatment combination. Treatment was well tolerated. Of the 38 treated pts, 35 had 1 or more treatment-related adverse events (TRAEs), most common neutropenia (n=18, 47%), nausea (n=16, 42%), vomiting (n=8, 21%), fatigue (n=8, 21%), infusion related reaction (n=8, 21%), and pruritus (n=6, 16%). Most related AEs were grade (G) 1-2. Sixteen pts (42%) had G3/4 neutrophil count decrease. Despite previous oxaliplatin treatment, fewer than 5% of pts reported peripheral neuropathy; those reported were G1/2.

Figure 1. Summary of Treatment-Emergent Adverse Events (TEAEs) and Treatment-Related Adverse Events (TRAE's)[a]



Data are reported as number of patients, n (%). **a.** All AEs were recorded using the Medical Dictionary for Regulatory Activities (MedDRA) with severity graded by investigators according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0.

Table 2. Safety Profile

	(N = 38)	
Any TEAE, n (%)	37 (97)	
Any TRAE, n (%)		
Grade 1-2	35 (92)	
Grade 3-4	20 (53)	
Grade 5	0 (0)	
Any Serious Adverse Event, n (%)	7 (18)	
	All Grades	**Grade ≥3**
Most common TRAEs,[b] n (%)		
Neutrophil count decrease	18 (47)	16 (42)
Nausea	16 (42)	0 (0)
Fatigue	8 (21)	0 (0)
Vomiting	8 (21)	0 (0)
Infusion-related reaction	8 (21)	0 (0)

[b]TRAE's were most common if prevalence was n, (%) ≥20%

EFFICACY

Table 3 and **Figures 2–6** summarize the efficacy findings from the BOLD-100 and FOLFOX treatment combination.

Table 3. Disease Response (Efficacy-Evaluable)

Disease Response Endpoints	(N = 31)
ORR, n (%) [95% CI]	3 (10) [3, 24]
Partial Response, n (%)	3 (10)
Stable Disease, n (%)	21 (67)
Progressive Disease, n (%)	7 (23)
DCR, n (%)	24 (77)
Progression-Free Survival (median), [95% CI]	4.2 [3.0, 6.0]
Overall Survival (median), [95% CI]	8.3 [5.7, 13.0]

ORR: investigator-assessed Overall Response Rate by RECIST criteria v1.1; CI: credible interval; DCR: Disease Control Rate (partial response + stable disease)

Figure 2. Median Bayesian Progression-Free Survival (A)

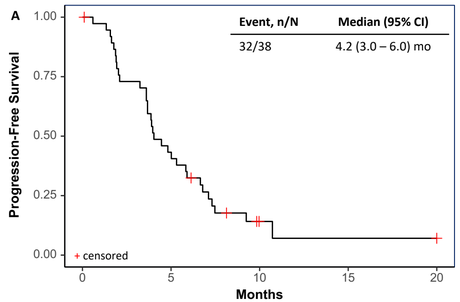


Figure 3. Median Bayesian Overall Survival (B)

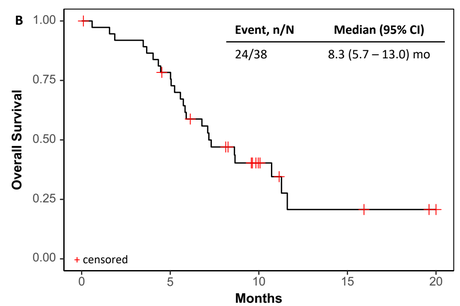


Figure 4. Summary of Overall Survival (Intent-to-treat)

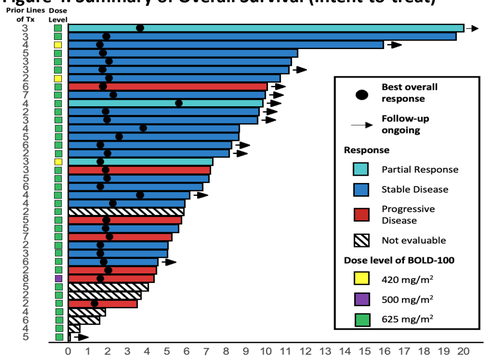


Figure 5. Waterfall Plot of Best Change from Baseline in Sum of Target Lesions

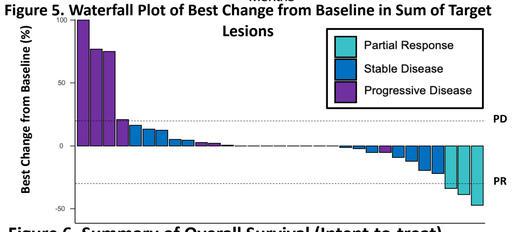
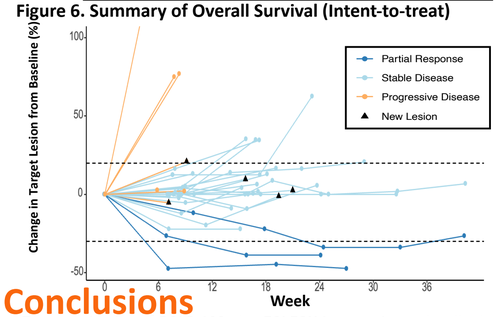


Figure 6. Summary of Overall Survival (Intent-to-treat)



Conclusions

- The combination of BOLD-100 plus FOLFOX is an active and well-tolerated treatment regimen in heavily pre-treated stage IV metastatic colorectal cancer patients in the third-line and beyond treatment setting.
- The mPFS, mOS, ORR and DCR data in this analysis demonstrate clinical benefit with minimal neuropathy or significant toxicities.
- All patients had prior oxaliplatin treatment, but fewer than 5% of study patients reported G1/2 peripheral neuropathy or peripheral sensory neuropathy indicating improved tolerability of the BOLD-100 combination.

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