A Phase 2 study of BOLD-100 in combination with FOLFOX chemotherapy in patients with advanced gastric cancer: efficacy and safety analysis [BOLD-100-001]

Abstract #4059

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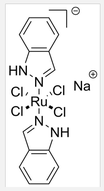
Introduction

- 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.[1]
- 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 interim efficacy and safety data in patients with heavily pre-treated, advanced metastatic gastric cancer (GC) who have received prior treatment with standard therapies.

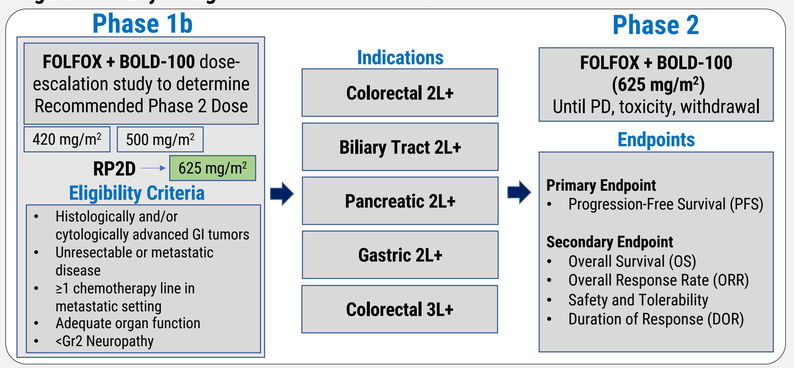


BOLD-100

Methods

Figure 1. Study Design

Study Design



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; 2/3L+. Second or third line and beyond.

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.

Results

- As of the data cut-off date, December 13, 2023, 21 patients with advanced, stage IV (100%) disease were enrolled and treated in the study (**Table 1**).
  - Participants were enrolled from sites in Canada and South Korea.
  - Enrollment is now complete, and follow-up continues.
  - 18 patients were evaluable for efficacy endpoints.

Prior Therapy

- Patients had a median of 4 prior therapies (range: 0 – 7) before enrollment into the study.
- 1 patient had no prior therapies, 2 had 2 prior therapies, 5 with 3 prior therapies, and 13 patients with 4 or more prior therapies.
- Prior therapies consisted of systemic chemotherapy, monoclonal antibodies, immunotherapy, and targeted anti-cancer agents.

Treatment with BOLD-100 and FOLFOX

- Median number of BOLD-100 + FOLFOX cycles was 6 (range: 1 – 27).

Table 1. Demographics and Disease Characteristics

	BOLD-100 + FOLFOX Combination (N = 21)
Median age (range), yrs	61 (35–84)
Male sex, n (%)	15 (71)
Race	
White	2 (10)
Asian	19 (90)
ECOG Performance	
0	10 (48)
1	11 (52)
Stage IV disease	21 (100)
Median prior therapies	4 (0-7)
Time since diagnosis of metastatic disease (months)	29.7 (2.5, 113.7)

Table 2. Prior Treatments in Metastatic Setting

	BOLD-100 + FOLFOX Combination (N = 21)
Type of prior systemic therapy	
Platinum-based chemotherapy	20 (95)
Taxane	19 (90)
Immunotherapy (PD-1/L1)	16 (76)
Targeted therapy (trastuzumab/cetuximab/ramucirumab)	10 (48)
regorafenib and/or trifluridine-tipiracil	4 (19)

SAFETY

Table 4 summarizes the TRAEs related to BOLD-100 + FOLFOX. For all treated patients (n = 21), 19 pts had ≥1 adverse events (AEs), most commonly neutrophil count decreased (n=7, 33%), nausea (n=6, 29%), and peripheral sensory neuropathy (n=4, 19%). Most AEs were grade (G) 1-2.

Table 4. Summary of Treatment-Related Adverse Events ≥10%

	BOLD-100 + FOLFOX Combination (N = 21)	
	Any Grade	Grade ≥ 3
Any TRAE[a], n(%)	19 (90)	13 (62)
Neutrophil count decreased	7 (33)	7 (33)
Nausea	6 (29)	2 (10)
Peripheral sensory neuropathy	4 (19)	0 (0)
Stomatitis	3 (14)	0 (0)
Vomiting	3 (14)	1 (5)
Infusion related reaction	3 (14)	0 (0)
Platelet count decreased	3 (14)	0 (0)
Rash	3 (14)	0 (0)
Urticaria	3 (14)	1 (5)

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 5. Efficacy Results (Intent-to-Treat population)

	BOLD-100 + FOLFOX (n = 18)
Progression-Free Survival (PFS), months	4.3 [2.8, 7.1]
Overall Survival (OS), months	7.9 [4.8, 15.0]
Overall Response Rate (ORR)	11% [2.0, 31.0]
Disease Control Rate (DCR)	72% [49.0, 89.0]

Months in median [95% credible interval]

EFFICACY

- Median Bayesian PFS of 4.3 [2.8, 7.1] months and median Bayesian OS of 7.9 [4.8, 15.0] months.
- Objective response rate was 11% [2.0, 31.0] and Disease control rate was 72% [49.0, 89.0] (**Table 5**)

Figure 2. Median Bayesian Progression-Free Survival (A) and Overall Survival (B) in Metastatic Gastric Cancer

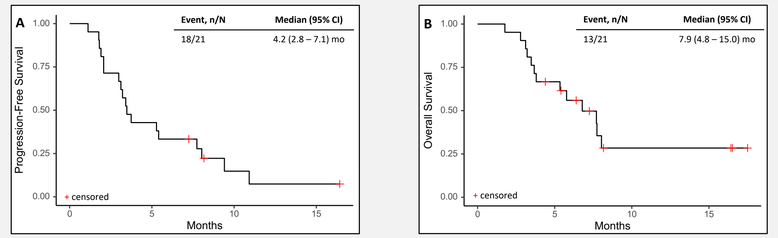


Figure 3. Change in Target Lesion Size Over Time in Response-evaluable Patients

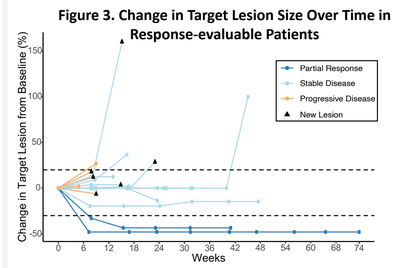
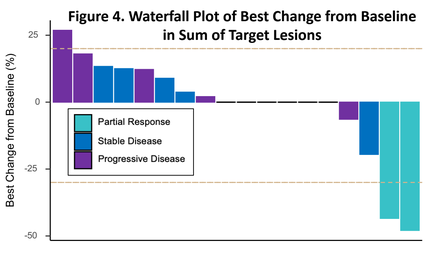


Figure 4. Waterfall Plot of Best Change from Baseline in Sum of Target Lesions



Conclusions

- The combination of BOLD-100 plus FOLFOX is an active and well-tolerated treatment regimen in heavily pre-treated (median of 4 prior therapies) stage IV metastatic gastric cancer patients.
- PFS, OS, ORR and DCR data in this interim analysis demonstrate improvements in this advanced patient population.
- Retreatment with FOLFOX together with BOLD-100 produced partial responses, minor responses, durable stable disease and improvement in median overall survival in this patient population
- All patients had prior oxaliplatin treatment, but fewer than 20% of study patients reported G1/2 peripheral neuropathy or peripheral sensory neuropathy indicating improved tolerability of the BOLD-100 combination.

Selected Case Presentations

Case Presentation #1:
60-yr old female with metastatic gastric cancer

Baseline Characteristics:
- G2 Histopathological grade
- Stage IV

Biomarker Testing:
- HER2-negative
- PD-L1 Combined Positive Score (CPS) <1
- MLH1 (positive), MSH2 (positive)

Prior Treatment:
1L: Cisplatin + 5-FU
2L: Oxaliplatin + 5-FU
3L: Irinotecan + 5-FU
4L: Paclitaxel
5L: Cisplatin
6L: Investigational Agent (NYH817G)
7L: Nivolumab

Treatment:
BOLD-100 + FOLFOX
Cycles: 27 cycles of BOLD-100

Response:
- Partial Response (PR) with 47.9% decrease in target tumor lesions.
- PFS and OS ongoing at 17.7 months at data-cut off date.

Case Presentation #2:
59-yr old male with metastatic gastric cancer

Baseline Characteristics:
- G2 Histopathological grade
- Stage IV

Biomarker Testing:
- HER2-negative
- PD-L1 Combined Positive Score (CPS) ≥ 1
- MLH1 (positive), MSH2 (positive)

Prior Treatment:
BOLD-100 + FOLFOX was administered in the first line (1L) setting.

Treatment:
BOLD-100 + FOLFOX
Cycles: 11 cycles of BOLD-100

Response:
- Partial Response (PR) with 43.4% decrease in target tumor lesions.
- PFS was 9.4 months and OS is ongoing at 20.5 months at data-cut off date.

REFERENCES
1. O'Kane GM, Spratlin JL, Kavan P, et al. BOLD-100-001 (TRIO039): A phase Ib dose-escalation study of BOLD-100 in combination with FOLFOX chemotherapy in patients with advanced gastrointestinal solid tumors. *JCO.* 2021;39(3_suppl):TPS145-TPS145. doi:10.1200/JCO.2021.39.3_suppl.TPS145

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