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

Abstract #4115

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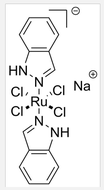
Introduction

- 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 pretreated, advanced metastatic biliary tract cancer (BTC) who have progressed on standard-of-care gemcitabine-cisplatin (GEM-CIS) based treatment regimens.



BOLD-100

Methods

Figure 1. Study Design

Study Design

Phase 1b

FOLFOX + BOLD-100 dose-escalation study to determine Recommended Phase 2 Dose

420 mg/m² | 500 mg/m²

RP2D → 625 mg/m²

Eligibility Criteria

- Histologically and/or cytologically advanced GI tumors
- Unresectable or metastatic disease
- ≥1 chemotherapy line in metastatic setting
- Adequate organ function
- <Gr2 Neuropathy

Indications

- **Colorectal 2L+**
- **Biliary Tract 2L+**
- **Pancreatic 2L+**
- **Gastric 2L+**
- **Colorectal 3L+**

Phase 2

FOLFOX + BOLD-100 (625 mg/m²) Until PD, toxicity, withdrawal

Endpoints

Primary Endpoint
- Progression-Free Survival (PFS)

Secondary Endpoint
- Overall Survival (OS)
- Overall Response Rate (ORR)
- Safety and Tolerability
- Duration of Response (DOR)

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, 22 patients with advanced metastatic BTC (5 gall bladder, 5 intrahepatic, 8 distal, 1 perihilar, and 3 unknown) were enrolled and treated in the study (**Table 1**).
  - Participants were enrolled from sites in the USA, Canada, and South Korea.
  - Enrollment is complete, and follow-up continues for efficacy endpoints.

Prior Therapy

- Patients had a median of 2 prior therapies (range: 1 – 5) before enrollment into the BOLD-100-001 trial.
- 21 (95%) patients received prior GEM/CIS, 8 (36%) pts had 5-FU based treatment, and 6 (27%) had prior immunotherapy (either durvalumab or pembrolizumab).

Treatment with BOLD-100 and FOLFOX

- Median number of BOLD-100 + FOLFOX cycles was 4 (range: 1 – 41).

Table 1. Demographics and Disease Characteristics

	BOLD-100 + FOLFOX Combination (N = 22)
Median age (range), yrs	61 (33–81)
Male sex, n (%)	12 (55)
Race	
White	8 (36)
Asian	14 (64)
ECOG Performance	
0	10 (45)
1	12 (55)
Stage IV disease	22 (100)
Median prior therapies	2 (1-5)
Time since diagnosis of metastatic disease (months), median (range)	10.9 (2.1, 65.0)

Table 2. Prior Treatments in Metastatic Setting

	BOLD-100 + FOLFOX Combination (N = 22)
Type of prior systemic therapy, n(%)	
Gemcitabine-cisplatin chemotherapy	22 (100)
Targeted therapy	8 (36)
Immunotherapy (durvalumab or pembrolizumab)	6 (27)
Taxane	3 (14)
oxaliplatin and/or capecitabine	3 (14)

Targeted therapy include investigational BRCA-, FGFR2-, ERK- and HER2-targeted therapies.

SAFETY

Table 4 summarizes the TRAEs related to BOLD-100 + FOLFOX. For all treated patients, 21 reported 1 or more treatment-related adverse events (AEs), most commonly neutrophil count decreased (n=10, 46%), nausea (n=8, 36%), fatigue (n=7, 32%), peripheral sensory neuropathy (n=6, 27%), and pyrexia (n=6, 27%). Nine patients (41%) reported G3/4 neutrophil count decreased.

Table 4. Summary of Treatment Related Adverse Events (TRAEs) ≥10%

	BOLD-100 + FOLFOX Combination (N = 22)	
	Any Grade	Grade ≥ 3
Any TRAE[a], n(%)	21 (96)	16 (73)
Neutrophil count decreased	10 (46)	9 (41)
Nausea	8 (36)	0 (0)
Fatigue	7 (32)	0 (0)
Peripheral sensory neuropathy	6 (27)	0 (0)
Pyrexia	6 (27)	1 (5)
Anaemia	5 (23)	4 (18)
Diarrhoea	5 (23)	0 (0)
Platelet count decreased	5 (23)	1 (5)
Neutropenia	4 (18)	4 (18)
Vomiting	4 (18)	0 (0)
Thrombocytopenia	3 (14)	2 (9)
Chills	3 (14)	0 (0)
Decreased appetite	3 (14)	0 (0)

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 (Evaluable-population)

	BOLD-100 + FOLFOX (n = 18)	Landmark[2]
Progression-Free Survival (PFS), months	6.0 [3.8, 10.0]	4.0
Overall Survival (OS), months	7.3 [4.5, 13.0]	6.2
Overall Response Rate (ORR)	6% [1.0, 23.0]	5%
Disease Control Rate (DCR)	83% [62.0, 95.0]	44%

Months in median [95% credible interval]

EFFICACY

- Median Bayesian PFS of 6.0 [3.8, 10.0] months and median Bayesian OS of 7.3 [4.5, 13.0] months
- Objective response rate was 6% [1.0, 23.0] and disease control rate was 83% [62.0, 95.0] (**Table 5**)

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

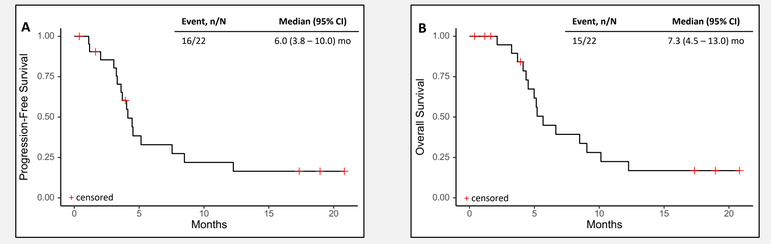


Figure 3. Change in Target Lesion Size Over Time in Response-evaluable Patients

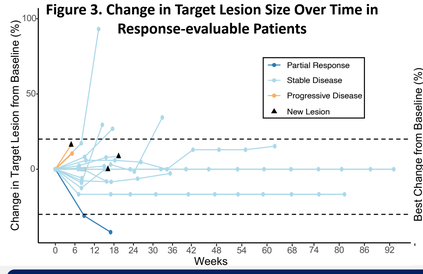
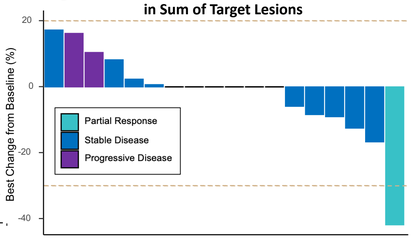


Figure 4. Waterfall Plot of Best Change from Baseline in Sum of Target Lesions



Conclusions

- The combination of BOLD-100 plus FOLFOX is an active and well-tolerated treatment regimen in pretreated, advanced metastatic biliary tract cancer.
- Treatment with FOLFOX together with BOLD-100 produced one partial response and several minor responses, durable stable disease and improvement in median overall survival in this patient population.
- This active treatment combination is worthy of further study in this patient population.

Selected Case Presentations

Case Presentation #1: 60-yr old female with metastatic biliary tract cancer	Metastatic Sites: Soft tissue infiltration around celiac axis	Case Presentation #2: 60-yr old female with metastatic biliary tract cancer	Metastatic Sites: Liver and Lung
Baseline Characteristics: ▪ Distal CCA ▪ G2 histopathological grade ▪ Stage IV **Biomarker Testing:** ▪ HER2-negative ▪ PD-L1 Combined Positive Score (CPS) <1 ▪ Microsatellite Stable (MSS)	**Prior Treatment:** 1L Treatment: Cisplatin + Gemcitabine + Investigational agent; treatment was administered for 5.8 months until progressive disease.	**Baseline Characteristics:** ▪ Distal CCA ▪ G2 histopathological grade ▪ Stage IV **Biomarker Testing:** ▪ HER2-negative ▪ PD-L1 Combined Positive Score (CPS) <1 ▪ MLH1 (no loss), MSH2 (no loss)	**Prior Treatment: Adjuvant:** Cisplatin + 5-FU **1L:** 5-FU + Radiation **2L:** Cisplatin + Gemcitabine **3L:** Cisplatin + Gemcitabine + Nab-Paclitaxel
Treatment: BOLD-100 + FOLFOX Cycles: 32 cycles of BOLD-100 **Response:** ▪ Minor Response with 16.8% decrease in target tumor lesions. ▪ PFS and OS ongoing at 21.7 months at data-cut off date.		**Treatment: BOLD-100 + FOLFOX Cycles:** 46 cycles of BOLD-100 **Response:** ▪ Prolonged stable disease (0% tumor growth) ▪ PFS and OS ongoing at 23.1 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
2. Lamarca A, Palmer DH, Wasan HS, et al. Second-line FOLFOX chemotherapy versus active symptom control for advanced biliary tract cancer (ABC-06): a phase 3, open-label, randomised, controlled trial. *The Lancet Oncology*. 2021;22(5):690-701. doi:10.1016/S1470-2045(21)00027-9

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