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Primary Efficacy and Safety of BL-M07D1 in Patients with Previously Treated HER2-positive Advanced Gastric Cancer or Gastroesophageal Junction Adenocarcinoma (GC/GEJ)

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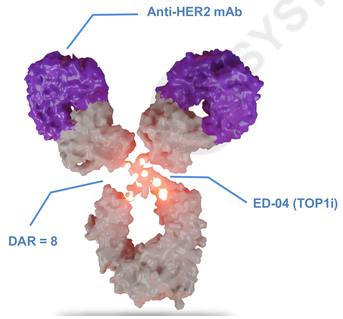
Background



- BL-M07D1 (T-Bren, Trastuzumab Brengitecan) is an anti-HER2 antibody-drug conjugate (ADC) comprised of a humanized anti-HER2 antibody, a cathepsin B cleavable linker, and a novel topoisomerase I inhibitor (Ed-04).
- Here we present results of BL-M07D1 in patients with previously treated HER2+ (IHC 3+ or IHC 2+/ISH+) advanced gastric or gastroesophageal junction (GC/GEJ) cancer from three phase I/II studies (BL-M07D1-101/102/202).
- Clinical trial information: NCT05461768, NCT05631964, NCT06031584

Objectives

- **BL-M07D1-101/102 (Phase I)**:
  - The primary objective is to assess safety and tolerability and determine maximum tolerated dose (MTD), dose-limiting toxicity (DLT) and recommended phase II dose (RP2D).
  - The secondary objectives include evaluating preliminary efficacy and pharmacokinetic (PK) profile.
- **BL-M07D1-202 (Phase Ib/II)**:
  - The primary objective is to further evaluate safety and tolerability of dose 5.0 and 5.6 mg/kg D1 Q3W, to determine RP2D , and to evaluate the preliminary efficacy in HER2 positive/low-expressing advanced gastric or gastroesophageal junction (GC/GEJ) cancer patients.
  - The secondary objectives include characterizing pharmacokinetic (PK) profile and immunogenicity.

Methods

- Three phase I-II studies (BL-M07D1-101/102/202) enrolled patients with previously treated HER2 positive/low-expressing advanced GC/GEJ cancer.
- All enrolled patients were treated with BL-M07D1 at doses of 2.6~7.4 mg/kg Q3W regimens.

Study Endpoints

BL-M07D1-101/102

- Primary: DLT, MTD, RP2D
- Secondary: safety, objective response rate (ORR), disease control rate (DCR), duration of response (DoR), pharmacokinetics (PK), progression-free survival (PFS), overall survival (OS), immunogenicity

BL-M07D1-202

- Primary: RP2D, ORR
- Secondary: safety, DCR, DoR, PFS, PK profile, immunogenicity

Study Design

Eligibility Criteria

- Inoperable locally advanced or metastatic HER2-positive/low-expressing GC/GEJ cancer and other gastrointestinal tumors
- Previously failed in standard therapy or inaccessible to or not suitable for standard therapy before enrollment
- Eastern Cooperative Oncology Group performance status (ECOG PS) 0-1
- At least one measurable lesion per RECIST v1.1
- Adequate organ and marrow function

Dosing Schedule

Escalation

- 7.4 mg/kg D1Q3W
- 6.8 mg/kg D1Q3W
- 6.2 mg/kg D1Q3W
- 5.6 mg/kg D1Q3W
- 5.0 mg/kg D1Q3W
- 4.4 mg/kg D1Q3W
- 3.8 mg/kg D1Q3W
- 3.2 mg/kg D1Q3W
- 2.6 mg/kg D1Q3W

Expansion

In the dose-expansion phase, patients were treated at doses of 3.8, 4.4, 5.0, and 5.6 mg/kg D1 Q3W regimens.

Endpoint

DLT, MTD, RP2D, ORR, DCR, DoR, PFS, OS, safety

Enrollment

- As of July 31, 2025, a total of 76 HER2 + GC/GEJ patients were enrolled and treated with at least one dose of BL-M07D1 across various dose levels (Table 1).
- Among the 76 patients, 5 patients were treated at dose levels<5.0mg/kg, 66 patients were treated at 5.0 mg/kg, and 5 patients were treated at dose levels>5.0 mg/kg.

Table 1. Patient Characteristics

	Total (N=76)	5.0 mg/kg D1Q3W		
		Total (N=66)	Prior 1L (N = 31)	Prior ≥2L (N = 35)
Median (range) age, years	60.5 (26.0, 74.0)	61.0 (26.0, 74.0)	61.0 (43, 74)	59.0 (26, 74)
Male, n (%)	57 (75.0)	51 (77.3)	25 (80.6)	26 (74.3)
Median (range) weight, kg	57.8 (34.2, 99.7)	58.0 (36.0, 99.7)	58.5 (44.8, 99.7)	56.1 (36.0, 80.9)
ECOG PS of 1, n (%)	70 (92.1)	60 (90.9)	29 (93.5)	31 (88.6)
HER2 status, n (%)				
IHC 2+/FISH positive	18 (23.7)	17 (25.8)	8 (25.8)	9 (25.7)
IHC 3+	58 (76.3)	49 (74.2)	23 (74.2)	26 (74.3)
Primary tumor site, n (%)				
Gastric	55 (72.4)	48 (72.7)	22 (71.0)	26 (74.3)
Esophagogastric junction	21 (27.6)	18 (27.3)	9 (29.0)	9 (25.7)
Presence of prior imaging peritoneal metastasis, n(%)	18 (23.7)	17 (25.8)	8 (25.8)	9 (25.7)
Liver metastases, n(%)	43 (56.6)	37 (56.1)	17 (54.8)	20 (57.1)
Number of metastatic organs, n(%)				
0	2 (2.6)	2 (3.0)	1 (3.2)	1 (2.9)
1	16 (21.1)	12 (18.2)	5 (16.1)	7 (20.0)
≥2	58 (76.3)	52 (78.8)	25 (80.6)	27 (77.1)
Prior line of therapy, n (%)				
1	32 (42.1)	31 (47.0)	NA	NA
≥2	44 (57.9)	35 (53.0)	NA	NA
Prior immune therapy, n (%)	32 (42.1)	29 (43.9)	17 (54.8)	12 (34.3)
Prior anti-HER2 therapy*, n(%)	75 (98.7)	65 (98.5)	30 (96.8)	35 (100)

* Including trastuzumab, HER2-ADC, etc.

Safety

- Treatment-related adverse events (TRAEs) occurred in 98.7% of all patients, and grade≥3 TRAEs occurred in 86.8% of patients (Table 2). The median time to resolution of grade 3 or 4 neutropenia was 5-6 days. Most only had 1 episode.
- Two cases of treatment-related ILD (1 G2 from 5.0 mg/kg D1Q3W, 1 G2 from 6.2 mg/kg D1Q3W) were reported.
- At 5.0mg/kg D1Q3W, 2 (3.0%) patients discontinued BL-M07D1 treatment due to TRAEs. No treatment related death was observed.

Table 2. Treatment-related Adverse Events (>20%)

Preferred terms, n (%)	Total (N=76)		5.0 mg/kg D1Q3W (N=66)	
	All Grade	Grade≥3	All Grade	Grade≥3
Anemia	68 (89.5)	41 (53.9)	60 (90.9)	35 (53.0)
Leukopenia	66 (86.8)	36 (47.4)	57 (86.4)	32 (48.5)
Thrombocytopenia	61 (80.3)	32 (42.1)	55 (83.3)	31 (47.0)
Neutropenia	60 (78.9)	39 (51.3)	52 (78.8)	36 (54.5)
Asthenia	36 (47.4)	11 (14.5)	33 (50.0)	9 (13.6)
Decreased appetite	35 (46.1)	1 (1.3)	33 (50.0)	1 (1.5)
Nausea	32 (42.1)	3 (3.9)	28 (42.4)	3 (4.5)
Alopecia	26 (34.2)	1 (1.3)	22 (33.3)	1 (1.5)
Hypokalemia	24 (31.6)	4 (5.3)	20 (30.3)	4 (6.1)
Hypoalbuminemia	23 (30.3)	0	22 (33.3)	0
AST increased	21 (27.6)	0	18 (27.3)	0
Weight decreased	17 (22.4)	0	17 (25.8)	0
ALT increased	16 (21.1)	0	14 (21.2)	0

Efficacy

- All patients treated with BL-M07D1 were included in the analysis.
- Among the 76 enrolled patients, median prior line of therapy was 2 (range, 1-6). The ORR was 55.3%, confirmed ORR was 47.4%. Median DoR was 7.4 months. Median PFS was 8.4 months with 9.0 months follow-up.
- For dose 5.0 mg/kg D1Q3W, the ORR was 57.6%, confirmed ORR was 48.5%. Tumor shrinkage occurred in 89.4% (59/66) of patients and the median (range) shrinkage (%) was -44.5 (-100.0, -1.0). Median DoR was 7.4 months. Median PFS was 8.4 months with 9.0 months follow-up.
- For all patients, median follow-up for OS was 10.4 months and median OS had not been reached.

Table 3. Summary of Efficacy Results

	Total (N=76)	5.0 mg/kg D1Q3W		
		Total (N=66)	1 prior line of therapy (N=31)	≥2 prior lines of therapy (N=35)
Median (range) prior line of therapy	2 (1-6)	2 (1-5)	1 (1-1)	2 (2-5)
Best overall response, n (%)				
CR	1 (1.3)	1 (1.5)	0	1 (2.9)
PR	41 (53.9)	37 (56.1)	18 (58.1)	19 (54.3)
Confirmed	35 (46.1)	31 (47.0)	14 (45.2)	17 (48.6)
PR Pending Confirmation	2 (2.6)	2 (3.0)	1 (3.2)	1 (2.9)
SD	28 (36.8)	23 (34.8)	10 (32.3)	13 (37.1)
PD	4 (5.3)	3 (4.5)	2 (6.5)	1 (2.9)
NE	2 (2.6)	2 (3.0)	1 (3.2)	1 (2.9)
ORR, % (95% CI)	55.3 (43.4, 66.7)	57.6 (44.8, 69.7)	58.1 (39.1, 75.5)	57.1 (39.4, 73.7)
Confirmed ORR, % (95% CI)	47.4 (35.8, 59.2)	48.5 (36.0, 61.1)	45.2 (27.3, 64.0)	51.4 (34.0, 68.6)
DCR, % (95% CI)	92.1 (83.6, 97.0)	92.4 (83.2, 97.5)	90.3 (74.2, 98.0)	94.3 (80.8, 99.3)
CBR (6m), % (95% CI)	72.4 (60.9, 82.0)	74.2 (62.0, 84.2)	77.4 (58.9, 90.4)	71.4 (53.7, 85.4)
Median DoR, months, (95% CI)	7.4 (5.5, NR)	7.4 (5.9, NR)	4.5 (2.9, NR)	NR (6.3, NR)
Median duration of follow-up for PFS, months, (95% CI)	9.0 (7.6, 11.3)	9.0 (8.1, 11.3)	8.2 (5.5, 12.3)	9.9 (7.6, 15.2)
Median PFS, months, (95% CI)	8.4 (6.4, 10.2)	8.4 (6.8, 11.3)	8.4 (5.6, 11.3)	10.2 (6.8, NR)
6-month PFS rate, % (95% CI)	66.5 (53.6, 76.6)	68.7 (54.9, 79.1)	61.8 (40.0, 77.6)	74.4 (55.1, 86.3)
Median duration of follow-up for OS, months, (95% CI)	10.4 (8.5,11.3)	9.6 (8.5, 11.3)	8.4 (5.8, 9.2)	11.3 (9.0, 12.1)
Median OS, months, (95% CI)	NR (10.3, NR)	NR (10.0,NR)	NR (9.5, NR)	NR (10.0, NR)
9-month OS rate, % (95% CI)	73.0 (59.9, 82.4)	75.4 (61.1, 85.0)	81.5 (56.7, 92.9)	71.8 (52.7, 84.3)
12-month OS rate, % (95% CI)	62.7 (47.9, 74.5)	66.2 (49.9, 78.3)	61.2 (29.2, 82.2)	67.3 (47.3, 81.2)

Figure 1. Waterfall Plot (5.0 mg/kg D1 Q3W)

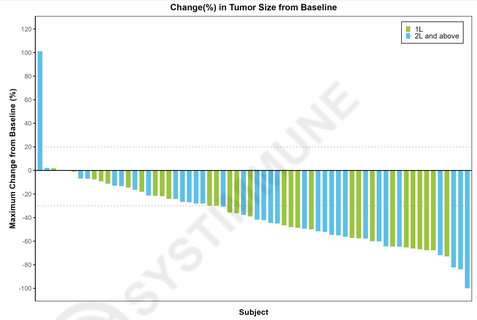
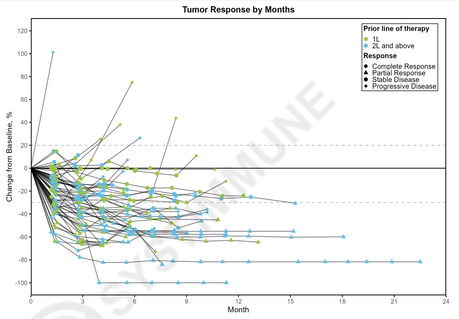


Figure 2. Spider Plot (5.0 mg/kg D1 Q3W)



Conclusions

- BL-M07D1 demonstrated encouraging efficacy with a manageable safety profile in previously treated HER2+ advanced GC/GEJ patients.
- Phase III study of BL-M07D1 in previously treated HER2-positive GC/GEJ patients is on-going (NCT07152405).

Declaration of interest

- Prof. Shuqin Ni has no conflict of interest to declare.

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