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BL-M07D1, a HER2 antibody-drug conjugate (ADC), in subjects with locally advanced or metastatic HER2 expressing breast cancer (BC) and other solid tumors: A phase I, multicenter, open-label study

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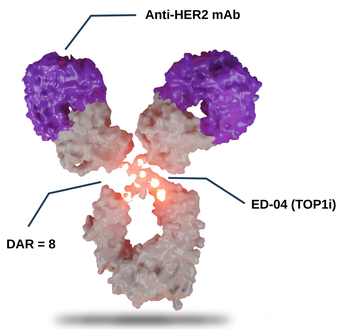
Background



- BL-M07D1, a HER2 antibody-drug conjugate
- Currently, 5 phase I or phase Ib/II clinical studies of BL-M07D1 are being conducted in different carcinomas. The indication in this study (BL-M07D1-101) is HER2 expressing breast cancer and other solid tumors
- Clinical trial information: NCT05461768

Objectives

- Phase Ia: To observe the safety and tolerability of BL-M07D1 in patients with locally advanced or metastatic HER2-positive/low-expressing breast cancer and other solid tumors in order to determine the maximum tolerated dose (MTD) and dose-limiting toxicity (DLT) of BL-M07D1.
- Phase Ib: To observe the safety and tolerability of BL-M07D1 at the recommended dose of Phase Ia and determine the recommended Phase II dose (RP2D).

Methods

- This phase I study enrolled patients with locally advanced or metastatic HER2-positive/low-expressing breast cancer and other solid tumors.
- This open-label, two cohorts Phase I study is designed to evaluate BL-M07D1 safety, tolerability, pharmacokinetic characteristics, and initial efficacy in patients with locally advanced or metastatic HER2 expressing breast cancer and other solid tumors. Dose-escalation and dose-expansion phases are being investigated. During dose-escalation, subjects will receive BL-M07D1 in 2 different schedule (Cohort A: 1.0mg/kg D1/D8 Q3W; Cohort B: 2.6~7.4mg/kg D1 Q3W). In the dose-expansion phase, one or several dosages will be chosen for further evaluation .
- The primary endpoints of the study are dose limiting toxicities (DLT), maximum tolerated dose(MTD), and recommended phase 2 dose(RP2D). Secondary endpoints are treatment emergent adverse events(TEAE), pharmacokinetics parameters, objective response rate(ORR), disease control rate(DCR), overall survival(OS), progression free survival(PFS), duration of response(DOR). Exploratory endpoints are biomarker assessment, and neutralizing antibodies.

Declaration of interest

E.Song has nothing to declare.

Acknowledgments

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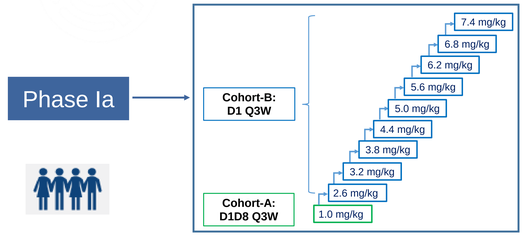
Study Design

Eligibility criteria

- Locally advanced or metastatic HER2-positive/low-expressing breast cancer and other solid tumors
- Previously treated with at least one line of therapy
- Eastern Cooperative Oncology Group performance status of 0-1
- At least one measurable lesion per RECIST v1.1
- Adequate organ and marrow function
- Either no brain metastases or stable brain metastases at screening



Primary endpoints: DLT, MTD, RP2D
Secondary endpoints: ORR, DCR, OS, PFS, DOR, safety

Enrollment

- As of August 15, A total of 107 patients were treated with at least one dose, with 22 patients in the Dose-Escalation (D-ESC) phase and 85 in the Dose-Expansion (D-EXP) phase. Among the 107 patients, 1 patient received 1.0 mg/kg D1D8 Q3W and 106 patients were treated with 2.6~6.2 mg/kg on the D1Q3W schedule.

Table 1. Patient demographics

	ALL (N=107)
Age (Median, Range)	54.0 (31.0 - 75.0)
Sex (Male)	10/107 (9%)
Weight (Mean, Range)	58.7 (33.5 - 85.0)
BMI (Mean, Range)	23.5 (15.3 - 32.8)
BSA (Mean, Range)	1.6 (1.2 - 2.0)
ECOG	
0	16/107 (15%)
1	89/107 (82%)
UNK	2/107 (2%)
Treatment line	
1	16/107 (15%)
2	30/107 (28%)
≥3	61/107 (57%)

Safety

- The most common Grade ≥3 treatment-related adverse events (TRAEs) were neutrophil count decreased (40%), white blood cell count decreased (28%), and anemia (18%).
- No drug-related death was observed.

Table 2. TRAE Summary (freq ≥ 10%)

	BL-M07D1-101 (N=107)				
PT Term	G1	G2	G3	G4	All
White blood cell count decreased	10 (9%)	35 (33%)	28 (26%)	2 (2%)	75 (70%)
Anaemia	18 (17%)	33 (31%)	19 (18%)		70 (65%)
Neutrophil count decreased	4 (4%)	21 (20%)	31 (29%)	12 (11%)	68 (64%)
Nausea	16 (15%)	39 (36%)	2 (2%)		57 (53%)
Platelet count decreased	23 (21%)	12 (11%)	8 (7%)	5 (5%)	48 (45%)
Decreased appetite	16 (15%)	24 (22%)			40 (37%)
Vomiting	17 (16%)	17 (16%)	4 (4%)		38 (36%)
Lymphocyte count decreased	9 (8%)	10 (9%)	8 (7%)		27 (25%)
Alopecia	11 (10%)	14 (13%)			25 (23%)
Asthenia	18 (17%)	7 (7%)			25 (23%)
Gamma-glutamyltransferase increased	15 (14%)	1 (<1%)			16 (15%)
Aspartate aminotransferase increased	14 (13%)	1 (<1%)			15 (14%)
Diarrhoea	10 (9%)	5 (5%)			15 (14%)
Blood alkaline phosphatase increased	13 (12%)	1 (<1%)			14 (13%)
Constipation	9 (8%)	5 (5%)			14 (13%)
Hypokalaemia	10 (9%)	2 (2%)	1 (<1%)	1 (<1%)	14 (13%)
Occult blood positive	13 (12%)				13 (12%)
Alanine aminotransferase increased	11 (10%)	1 (<1%)			12 (11%)
Weight decreased	8 (7%)	3 (3%)	1 (<1%)		12 (11%)

Efficacy

- Among the 107 enrolled patients, 80 were evaluable for efficacy The ORR (n/N, [95%CI]) was 55% (44/80, [43.5, 66.2]), DCR was 95% (76/80, [87.7, 98.6]) (Table 3). The median PFS has not reached.
- In HER2+BC, 38 patients were evaluable for efficacy. The ORR was 78.9% (30/38, [62.7, 90.4]) and the DCR was 100% (38/38) (Table 3).

Table 3. Efficacy by Tumor subtype

BOR, n	HER2+BC (N=38)	HR+HER2-Low (N=25)	TNBC (N=3)	NSCLC (N=3)	Other (N=11)	All (N=80)
Prior treatment line median (range)	3 (1-13)	4 (1-10)	4 (2-5)	2 (1-2)	2 (1-8)	3 (1-13)
cCR	1	0	0	0	0	1
PR	9	3	0	0	1	13
PR→Onging	8	2	/	/	1	
PR→PD	/	1	/	/	/	
PR→Death	/	/	/	/	/	
PR→Other	1	/	/	/	/	
cPR	20	7	0	1	2	30
SD	8	12	3	2	7	32
SD-(ongoing and target lesions shrinkage)	7	10	2	2	5	
PD	0	3	0	0	1	4
ORR, % (95% CI)	78.9% (62.7-90.4)	40.0% (21.1-61.3)	/	33.3% (0.8-90.6)	27.3% (6.0-70.0)	55% (43.5-66.2)
cORR, % (95% CI)	55.3% (38.3-71.4)	28.0% (12.1-49.4)	/	33.3% (0.8-90.6)	18.2% (2.3-51.8)	38.8% (28.1-50.3)
DCR, % (95% CI)	100%	88.0% (68.8-97.5)	100%	100%	90.9% (58.7-99.8)	95% (87.7-98.6)
DoR (m) (median, range)	NR (1.8+~9.7+)	NR (1.8+~3.2+)	/	NR (3.2+)	NR (1.6+~3.9+)	NR (1.6+~9.7+)

Figure 1. Change in Tumor Size

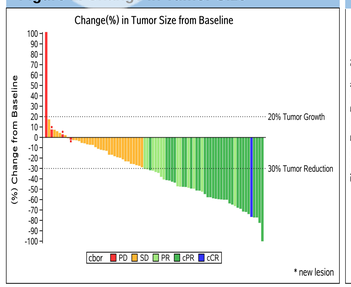


Figure 2. Tumor Response by Months

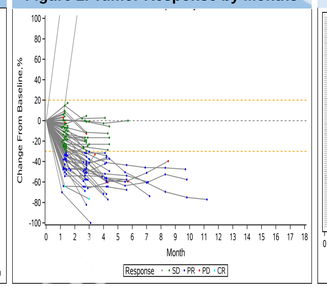
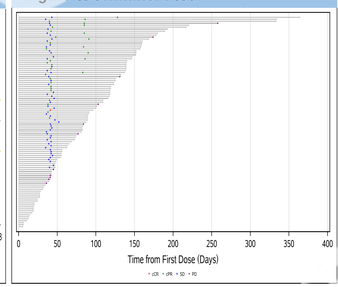


Figure 3. Swimmer Plot



Conclusions

- BL-M07D1 exhibited promising preliminary antitumor activity in patients with both breast cancer and non-small cell lung cancer.
- The maximum tolerated dose for BL-M07D1 was not reached. The observed toxicities were predominantly hematologic, with the important finding that no cases of interstitial lung disease (ILD) were identified.
- Further investigations and clinical trials are warranted to fully assess the efficacy and safety profile of BL-M07D1 in a larger and more diverse patient population.

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