

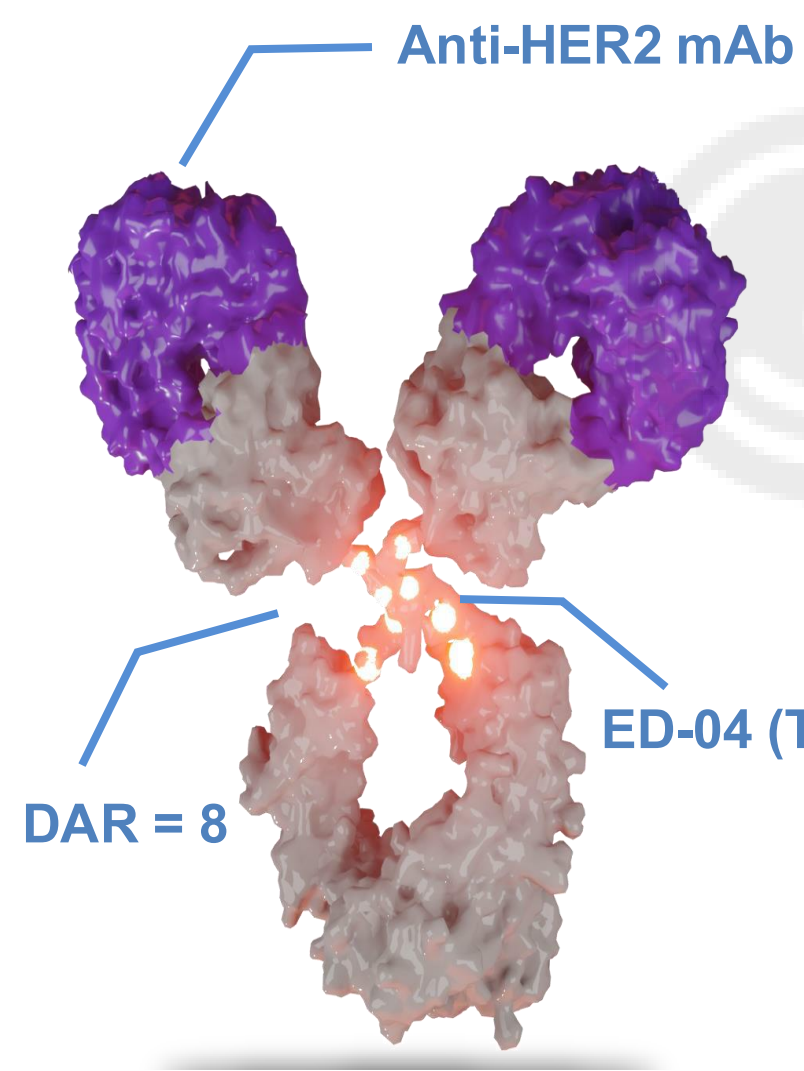
BL-M07D1, a Novel HER2 Antibody-drug Conjugate, in Subjects with Locally Advanced or Metastatic Breast Cancer and Other Solid Tumors: Results from a Phase 1 Study

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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).
- Currently, 7 phase I or phase Ib/II clinical studies of BL-M07D1 are being conducted across different carcinomas. The indication of this study (BL-M07D1-101) is HER2-positive/negative 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/negative breast cancer and other solid tumors and 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 open-label, two-cohort phase I study is designed to evaluate the safety, tolerability, pharmacokinetic characteristics, and initial efficacy of BL-M07D1 in patients with locally advanced or metastatic HER2-positive/negative breast cancer and other solid tumors.
- During dose-escalation, subjects will be treated with BL-M07D1 in 2 different schedules (Cohort A:1.0 mg/kg D1D8 Q3W; Cohort B: 2.6~7.4 mg/kg D1Q3W). Multiple dose levels will be selected for further evaluation in the dose-expansion phase, including both dose-expansion and indication-expansion cohorts, to characterize safety, tolerability, and preliminary antitumor activity.
- Study endpoints
 - Primary: dose limiting toxicities (DLT), maximum tolerated dose (MTD), and recommended phase II dose (RP2D).
 - Secondary: treatment-emergent adverse events (TEAE), pharmacokinetics parameters, objective response rate (ORR), disease control rate (DCR), duration of response (DoR).
 - Exploratory: progression free survival (PFS), overall survival (OS), biomarkers, and neutralizing antibodies.

Declaration of interest

- Prof. Hong Zong has no conflict of interest to declare.

Acknowledgements

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Study Design

Eligibility Criteria

- Locally advanced or metastatic HER2-positive/negative breast cancer and other solid tumors*
- Previously failed in standard therapy or inaccessible to or not suitable for standard therapy before enrollment
- ECOG PS 0-1
- Measurable lesion per RECIST v1.1
- Adequate organ and marrow function
- Either no brain metastases or stable brain metastases at screening

*HER2-positive: IHC 3+, or IHC 2+ and ISH positive;
HER2-negative: IHC 2+ and ISH negative, IHC 1+ or IHC 0

Primary endpoints: DLT, MTD, RP2D
Secondary endpoints: ORR, DCR, DoR, safety

Enrollment

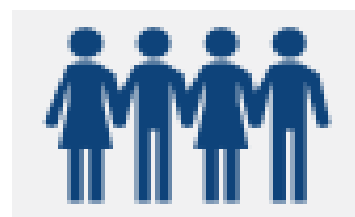
- As of July 31, 2025, a total of 199 breast cancer patients have been treated with at least one dose of BL-M07D1 (Table 1).
- Among these patients, 32 patients were treated at lower dose (<4.4mg/kg), 137 patients were treated at 4.4 mg/kg, and 30 patients were treated at higher dose (>4.4 mg/kg).

Table 1. Patient Characteristics

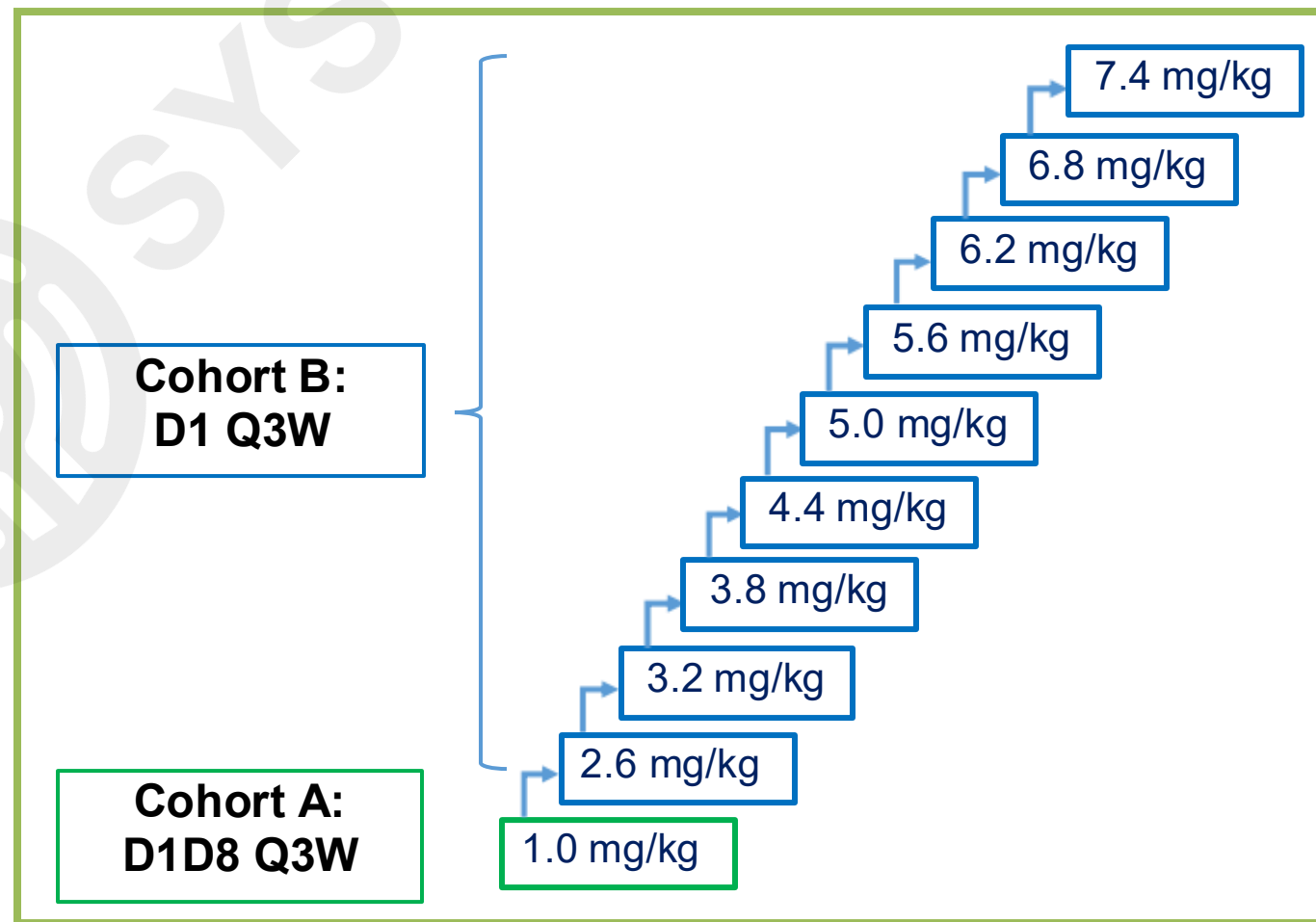
Characteristics	Total (N=199)	4.4 mg/kg D1Q3W					
		HER2+ (N=45)	HR+HER2- (N=60)	TNBC (N=27)	HER2 low (IHC 1+ or 2+) HR+HER2 low (N=58)	HR-HER2 low (N=20)	
Age (Median, Range), years	54.0 (24.0-75.0)	55.0 (33-69)	54.5 (24-72)	56.0 (33-68)	54.0 (24-72)	55.0 (33-66)	
Female, n (%)	196 (98.5)	44 (97.8)	59 (98.3)	27 (100)	57 (98.3)	20 (100)	
Weight (Mean, Range), kg	59.5 (32.7-85.3)	59.9 (42.5-79.0)	58.4 (36.5-84.3)	60.7 (42.0-85.3)	58.3 (36.5-84.3)	60.5 (42.0-85.3)	
ECOG PS score 1, n (%)	162 (81.4)	38 (84.4)	50 (83.3)	21 (77.8)	48 (82.8)	14 (70.0)	
Molecular subtyping, n (%)							
HER 2+	79 (39.7)	NA	NA	NA	NA	NA	
HR+/HER 2-	84 (42.2)	NA	NA	NA	NA	NA	
TNBC	30 (15.1)	NA	NA	NA	NA	NA	
HER 2 status, n (%)							
IHC 0	10 (5.0)	0	2 (3.3)	7 (25.9)	0	0	
IHC 1+	47 (23.6)	0	24 (40.0)	10 (37.0)	24 (41.4)	10 (50.0)	
IHC 2+ and ISH -	57 (28.6)	0	34 (56.7)	10 (37.0)	34 (58.6)	10 (50.0)	
IHC 2+ and ISH+	19 (9.5)	10 (22.2)	0	0	0	0	
IHC 2+*	5 (2.5)	0	0	0	0	0	
IHC 3+	60 (30.2)	35 (77.8)	0	0	0	0	
Missing#	1 (0.5)	0	0	0	0	0	
HR status, n (%)							
Negative	59 (29.6)	17 (37.8)	0	27 (100)	0	20 (100)	
Positive	138 (69.3)	27 (60.0)	60 (100)	0	58 (100)	0	
Missing	2 (1.0)	1 (2.2)	0	0	0	0	
Visceral Metastases, n(%)							
Brain metastases, n (%)	168 (84.4)	36 (80.0)	57 (95.0)	18 (66.7)	55 (94.8)	12 (60.0)	
Liver metastases, n (%)	22 (11.1)	9 (20.0)	6 (10.0)	2 (7.4)	6 (10.3)	1 (5.0)	
Lung metastases, n (%)	97 (48.7)	16 (35.6)	41 (68.3)	9 (33.3)	40 (69.0)	6 (30.0)	
Prior line of therapy, n (%)	106 (53.3)	27 (60.0)	33 (55.0)	10 (37.0)	31 (53.4)	6 (30.0)	
Prior line of therapy, n (%)							
1L	38 (19.1)	12 (26.7)	7 (11.7)	8 (29.6)	7 (12.1)	7 (35.0)	
2L	59 (29.6)	8 (17.8)	21 (35.0)	13 (48.1)	20 (34.5)	8 (40.0)	
≥3L	102 (51.3)	25 (55.6)	32 (53.3)	6 (22.2)	31 (53.4)	5 (25.0)	
Prior chemotherapy, n (%)							
Prior line of chemotherapy, n (%)	192 (96.5)	45 (100)	53 (88.3)	27 (100)	51 (87.9)	20 (100)	
Prior line of chemotherapy, n (%)							
0L	20 (10.1)	0	15 (25.0)	0	13 (22.4)	0	
1L	65 (32.7)	17 (37.8)	18 (30.0)	9 (33.3)	18 (31.0)	7 (35.0)	
2L	59 (29.6)	9 (20.0)	24 (40.0)	15 (55.6)	24 (41.4)	10 (50.0)	
≥3L	55 (27.6)	19 (42.2)	3 (5.0)	3 (11.1)	3 (5.2)	3 (15.0)	
Prior anti-HER2 therapy ^Δ , n (%)							
Prior CDK4/6, n (%)	94 (47.2)	44 (97.8)	7 (11.7)	3 (11.1)	7 (12.1)	1 (5.0)	
Prior Endocrine, n (%)	77 (38.7)	4 (8.9)	47 (78.3)	4 (14.8)	45 (77.6)	2 (10.0)	
Prior Endocrine, n (%)	124 (62.3)	19 (42.2)	54 (90.0)	8 (29.6)	53 (91.4)	6 (30.0)	

^a: HER2 status were 2+ with FISH data missing; ^b: due to missing HER2 data; ^c: Including trastuzumab, pertuzumab, HER2 TKI, HER2-ADC, etc.

Phase Ia



Phase Ib



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

Safety

- The most common grade ≥3 TRAEs were hematologic toxicities, including anemia (50.8%), leukopenia (39.7%), neutropenia (49.2%), and thrombocytopenia (35.2%) (Table 2). Median time to resolution of grade 3 or 4 neutropenia was 3-5 days. Most only had 2 episodes.
- ILD occurred in 6/199 (3%) patients (grade 1-2, 4/199 patients; grade 3, 2/199 patients). 2/137 patients (one with HER2+ breast cancer and one with HR+/HER2- breast cancer in 4.4 mg Q3W group had ILD (one case of grade 3 and one case of grade 1).
- Two (1.0%) patients died due to TRAEs (one was at 4.4 mg/kg D1Q3W dose level). 14 (7.0%) patients discontinued treatment due to TRAEs.
- The MTD was 5.6 mg/kg D1 Q3W, and the RP2D for breast cancer was set to be 4.4 mg/kg D1 Q3W.

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

Preferred terms, n (%)	Total (N=199)	
	All grade	Grade≥3
Any treatment-related AE	199 (100)	156 (78.4)
Anemia	181 (91.0)	101 (50.8)
Leukopenia	173 (86.9)	79 (39.7)
Neutropenia	162 (81.4)	98 (49.2)
Thrombocytopenia	148 (74.4)	70 (35.2)
Nausea	129 (64.8)	4 (2.0)
Decreased appetite	92 (46.2)	2 (1.0)
AST increased	82 (41.2)	1 (0.5)
Vomiting	79 (39.7)	7 (3.5)
Asthenia	76 (38.2)	5 (2.5)
Lymphocyte count decreased	70 (35.2)	31 (15.6)
Alopecia	69 (34.7)	0
Gamma GT increased	64 (32.2)	6 (3.0)
ALT increased	62 (31.2)	0
Stomatitis	62 (31.2)	4 (2.0)
Weight decreased	61 (30.7)	2 (1.0)
Blood ALP increased	57 (28.6)	0
Constipation	54 (27.1)	0
Hypoalbuminemia	49 (24.6)	0
Diarrhea	45 (22.6)	2 (1.0)
Hypokalemia	44 (22.1)	7 (3.5)

Efficacy

- All patients (except one who were still on treatment with insufficient follow-up) were included in the efficacy analysis.
- Among the 198 patients, the ORR was 71.2%, confirmed ORR was 68.2%. Median DoR was 13.8 months. Median PFS was 14.8 months.
- In 4.4 mg/kg D1 Q3W dose level, the ORR was 72.8%, confirmed ORR was 71.3%. Tumor shrinkage occurred in 91.9% (125/136) of patients and the median (range) shrinkage (%) was -56.0 (-100.0, -0.7). Median DoR was 13.9 months. Median PFS was 14.1 months.
 - For HER 2+ patients, the ORR was 86.7%, confirmed ORR was 82.2%. Median DoR was 19.4 months. Median PFS was 18.0 months. The 12 and 18-month OS rate was 93.1% and 85.5%, respectively.
 - For HR+ HER 2- patients, the ORR was 70.0%, confirmed ORR was 70.0%. Median DoR was 13.7 months. Median PFS was 15.2 months. The 12 and 18-month OS rate was 85.9% and 72.6%, respectively.
 - For TNBC patients, the ORR was 55.6%, confirmed ORR was 55.6%. Median DoR was 5.8 months. Median PFS was 7.2 months. The 12 and 18-month OS rate was 83.9% and 75.5%, respectively.

Table 3. Summary of Efficacy Results

	Total (N=198)	4.4 mg/kg D1Q3W				
		HER 2+ (N=45)	HR+ HER 2- (N=60)	TNBC (N=27)	HER2 low (IHC 1+ or 2+) (N=58)	HR-HER2low (N=20)
Prior line of therapy, median (range)	3 (1-13)	3 (1-9)	3 (1-7)	2 (1-5)	3 (1-7)	2 (1-5)
Best overall response, n (%)						
CR	8 (4.0)	2 (4.4)	0	3 (11.1)	0	3 (15.0)
PR	133 (67.2)	37 (82.2)	42 (70.0)	12 (44.4)	42 (72.4)	9 (45.0)
Confirmed	127 (64.1)	35 (77.8)	42 (70.0)	12 (44.4)	42 (72.4)	9 (45.0)
SD	42 (21.2)	5 (11.1)	15 (25.0)	6 (22.2)	13 (22.4)	5 (25.0)
PD	8 (4.0)	0	2 (3.3)	3 (11.1)	2 (3.4)	1 (5.0)
NE ¹	7 (3.5)	1 (2.2)	1 (1.7)	3 (11.1)	1 (1.7)	2 (10.0)
ORR, % (95% CI)	71.2 (64.4, 77.4)	86.7 (73.2, 94.9)	70.0 (56.8, 81.2)	55.6 (35.3, 74.5)	72.4 (59.1, 83.3)	60.0 (36.1, 80.9)
Confirmed ORR, % (95% CI)	68.2 (61.2, 74.6)	82.2 (67.9, 92.0)	70.0 (56.8, 81.2)	55.6 (35.3, 74.5)	72.4 (59.1, 83.3)	60.0 (36.1, 80.9)
DCR, % (95% CI)	92.4 (87.8, 95.7)	97.8 (88.2, 99.9)	95.0 (86.1, 99.0)	77.8 (57.7, 91.4)	94.8 (85.6, 98.9)	85.0 (62.1, 96.8)
CBR (6m), % (95% CI)	83.8 (78.0, 88.7)	93.3 (81.7, 98.6)	85.0 (73.4, 92.9)	70.4 (49.8, 86.2)	86.2 (74.6, 93.9)	80 (56.3, 94.3)
Median (range) time to response, months	1.5 (1.2-18.1)	1.4 (1.2-4.2)	1.6 (1.2-18.1)	1.5 (1.2-4.3)	1.6 (1.2-18.1)	2.1 (1.2-4.3)
Median DoR, months, (95% CI)	13.8 (11.3, 16.5)	19.4 (13.0, NR)	13.7 (6.8, 16.5)	5.8 (3.7, 7.1)	13.7 (6.8, 16.5)	6.3 (2.8, 7.5)
Median follow-up for PFS, months, (95% CI)	19.4 (17.8, 20.6)	20.6 (18.1, 20.9)	11.3 (8.5, 17.8)	17.8 (11.3, NR)	12.0 (8.5, 17.8)	17.8 (11.3, NR)
Median PFS, months, (95% CI)	14.8 (10.0, 17.9)	18.0 (11.0, NR)	15.2 (8.3, 18.2)	7.2 (5.4, 8.4)	15.2 (8.3, 18.2)	8.3 (5.3, 9.5)
Median duration of follow-up for OS, months, (95% CI)	19.8 (18.2, 20.8)	22.6 (21.1, 23.1)	14.6 (11.3, 17.8)	12.3 (8.4, 15.6)	14.6 (11.5, 18.2)	14.1 (9.6, 18.0)
Median OS, months, (95% CI)	NR (27.3, NR)	NR (24.9, NR)	22.5 (18.8, NR)	NR (12.7, NR)	22.5 (18.8, NR)	NR (12.7, NR)
12-month OS rate, % (95% CI)	89.0 (83.3, 92.9)	93.1 (80.2, 97.7)	85.9 (72.3, 93.1)	83.9 (57.5, 94.6)	85.8 (72.1, 93.0)	87.5 (58.6, 96.7)
18-month OS rate, % (95% CI)	77.5 (70.0, 83.4)	85.5 (70.5, 93.3)	72.6 (54.7, 84.4)	75.5 (45.6, 90.4)	72.5 (54.6, 84.3)	78.8 (46.6, 92.8)

1. Including patients without post-baseline tumor assessment.

Figure 1. Waterfall Plot (4.4 mg/kg D1Q3W)

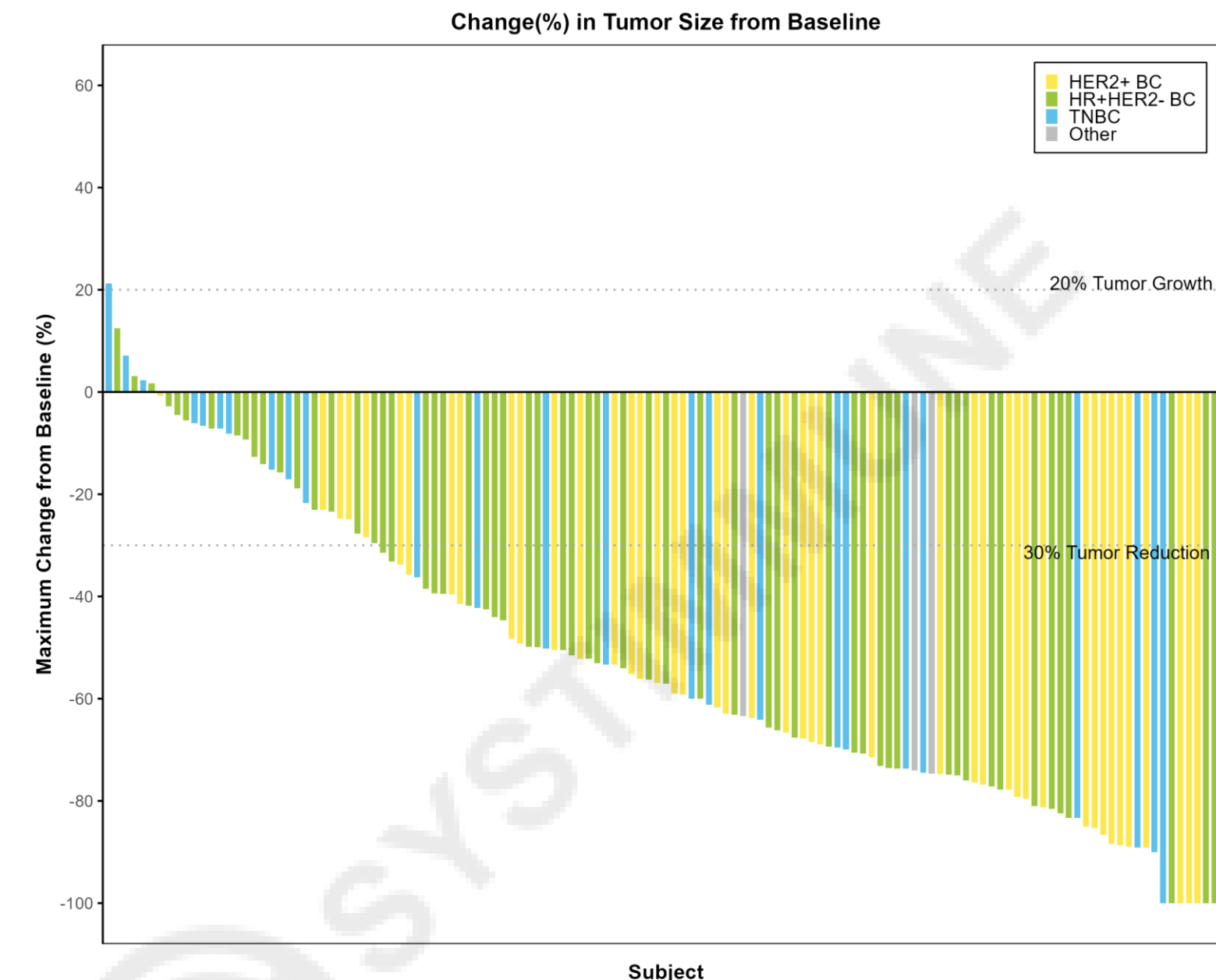
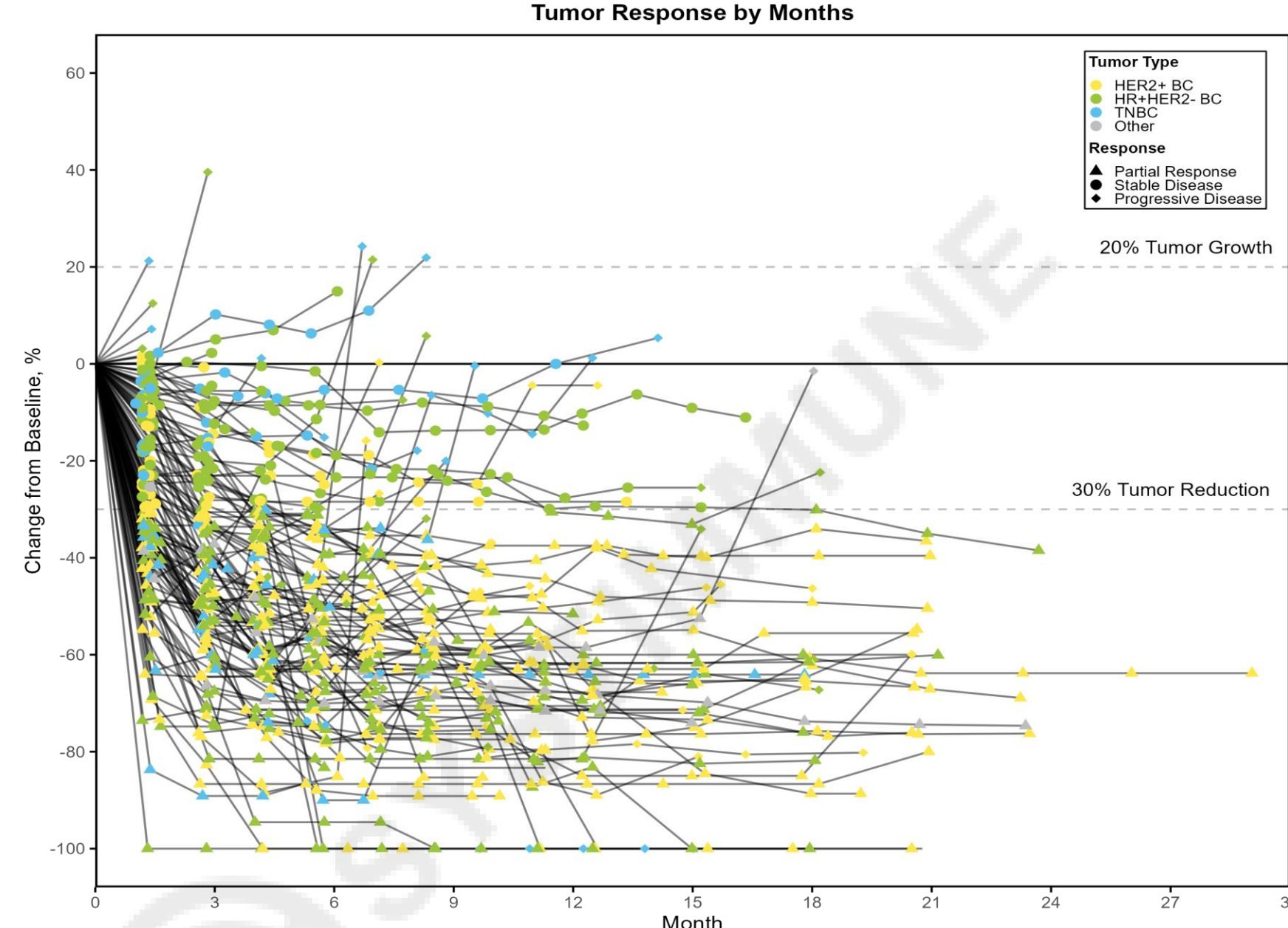


Figure 2. Spider Plot (4.4 mg/kg D1Q3W)



Conclusions

- BL-M07D1 demonstrated encouraging efficacy in patients with heavily pretreated breast cancers, especially in HER2-positive breast cancer.
- BL-M07D1 was well tolerated, and safety profile was manageable.