2025 ESMO BREAST CANCER
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PHASE I STUDY OF IZA-BREN (BL-B01D1), AN EGFR & HER3 BISPECIFIC ANTIBODY-DRUG CONJUGATE (ADC), IN PATIENTS WITH LOCALLY ADVANCED OR METASTATIC BREAST CANCER (BC)

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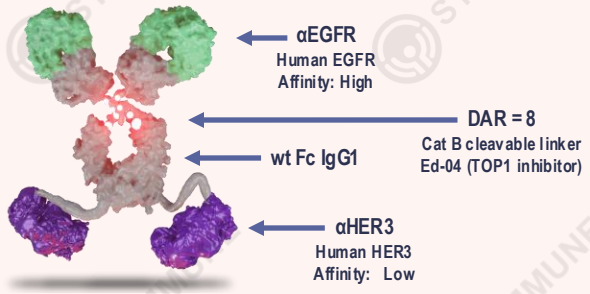
DECLARATION OF INTERESTS

The author declares no financial or non-financial conflicts of interest related to this presentation.

PROJECT OVERVIEW

iza-bren, an EGFR × HER3 bispecific ADC



- iza-bren is a potential first-in-class (FIC) ADC consisting of an EGFR x HER3 bispecific antibody conjugated to a novel topoisomerase I inhibitor payload (Ed-04) via a stable tetrapeptide-based cleavable linker.
- Results for safety, tolerability and preliminary efficacy in previously treated patients with Her2-negative† (HER2-) breast cancer in phase I study (BL-B01D1-104) are presented.
- Clinical trial information: NCT05470348.

Study Design

Eligibility criteria

- Locally advanced or metastatic breast cancer and other solid tumors
- Previously treated with standard therapy
- ECOG PS 0-1
- Measurable disease per RECIST v1.1
- Adequate organ and marrow function

Phase Ia (referred to BL-B01D1-101)

- **Cohort A** D1D8 Q3W: 2.5 mg/kg → 3.0 mg/kg → 3.5 mg/kg
- **Cohort B** D1 Q3W: 5.0 mg/kg → 6.0 mg/kg → 7.0 mg/kg

Phase Ib

In the dose-expansion phase, subjects received iza-bren in 2.5 mg/kg D1D8 Q3W.

Primary endpoints: DLT, MTD (or MAD), RP2D
Secondary endpoints: ORR, DCR, DOR, Safety
Exploratory endpoints: PFS, OS, Biomarker, NAb

† **HER2-** defined as IHC 0, 1+, or 2+/ISH-.

wt: wild type; **Cat B:** cathepsin B; **TOPI:** Topoisomerase I; **ECOG PS:** Eastern Cooperative Oncology Group performance status; **RECIST:** Response Evaluation Criteria in Solid Tumors; **DLT:** Dose Limiting Toxicity; **MTD:** Maximum Tolerated Dose; **MAD:** Maximum Administered Dose; **RP2D:** Recommended Phase 2 Dose; **ORR:** Overall Response Rate; **DCR:** Disease Control Rate; **DOR:** Duration of Response; **PFS:** Progression Free Survival; **OS:** Overall Survival; **Nab:** Neutralizing antibody

BASELINE CHARACTERISTICS

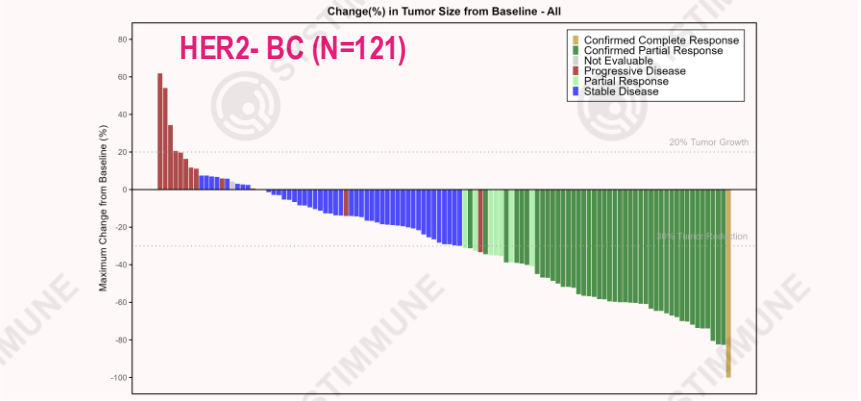
	HER2- BC patients at 2.5 mg/kg D1D8 Q3W		
	HER2 zero (N = 55)	HER2 1+/2+ (N = 66)	Total (N=121)
Age, median (range)	51.0 (26.0, 71.0)	54.5 (30.0, 75.0)	54.0 (26.0, 75.0)
ECOG-PS Score, n (%)			
0	9 (16.4)	5 (7.6)	14 (11.6)
1	46 (83.6)	61 (92.4)	107 (88.4)
Brain metastasis at baseline (Y), n (%)	3 (5.5)	7 (10.6)	10 (8.3)
Prior lines of therapy, n (%)			
0L	0	1 (1.5)	1 (0.8)
1L	9 (16.4)	9 (13.6)	18 (14.9)
2L	13 (23.6)	10 (15.2)	23 (19.0)
≥ 3L	33 (60.0)	46 (69.7)	79 (65.3)
Prior lines of chemotherapy, n (%)			
0L	7 (12.7)	6 (9.1)	13 (10.7)
1L	17 (30.9)	23 (34.8)	40 (33.1)
2L	16 (29.1)	16 (24.2)	32 (26.4)
≥ 3L	15 (27.3)	21 (31.8)	36 (29.8)
Prior PBC, n (%)	21 (38.2)	26 (39.4)	47 (38.8)
Prior paclitaxel, n (%)	49 (89.1)	62 (93.9)	111 (91.7)
Prior anti-PD(L)-1, n (%)	11 (20.0)	16 (24.2)	27 (22.3)
Prior CDK4/6 inhibitors, n (%)	20 (36.4)	33 (50.0)	53 (43.8)
Prior ADC, n (%)	1 (1.8)	10 (15.2)	11 (9.1)
HER2 Status, n (%)			
0	55 (100.0)	0	55 (45.5)
1+	0	35 (53.0)	35 (28.9)
2+/ISH-	0	31 (47.0)	31 (25.6)
HR Positive, n (%)	29 (52.7)	48 (72.7)	77 (63.6)

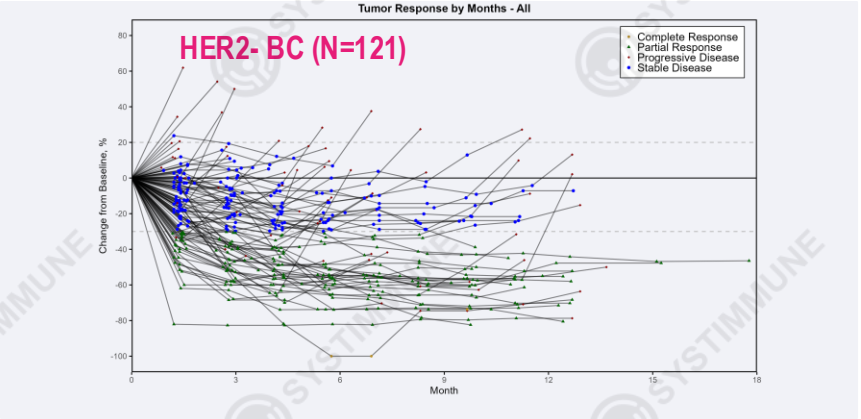
Data cutoff: September 30, 2024

PRELIMINARY EFFICACY IN HER2- BC

	HER2 zero (N = 55)	HER2 1+/2+ (N = 66)	Total (N = 121)
Prior lines of therapy, median (range)	3 (1-11)	3 (0* -13)	3 (0*-13)
BOR, n			
CR/PR	23	28	51
confirmed	20	24	44
SD	21	25	46
PD	8	5	13
NE	3	8	11
ORR, %	41.8	42.4	42.1
cORR, %	36.4	36.4	36.4
DCR, %	80.0	80.3	80.2
mPFS (mo) (95% CI)	8.3 (4.8,12.7)	6.3 (5.1, 8.3)	6.9 (5.5, 8.4)
mDOR (mo) (95% CI)	11.5 (5.4, NR)	9.7 (5.5, NR)	9.7 (5.8, 11.7)

Efficacy analysis was conducted based on HER2- BC patients who received at least one dose of iza-bren (N=121).
The median follow-up is 11.7 months.
*: 1 patient without standard treatment due to poor economic condition.





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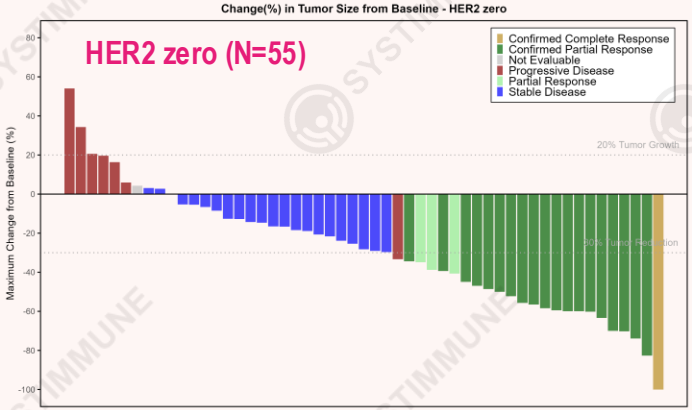
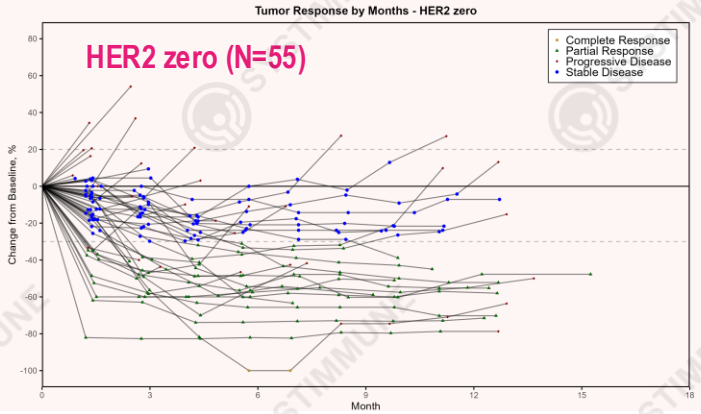
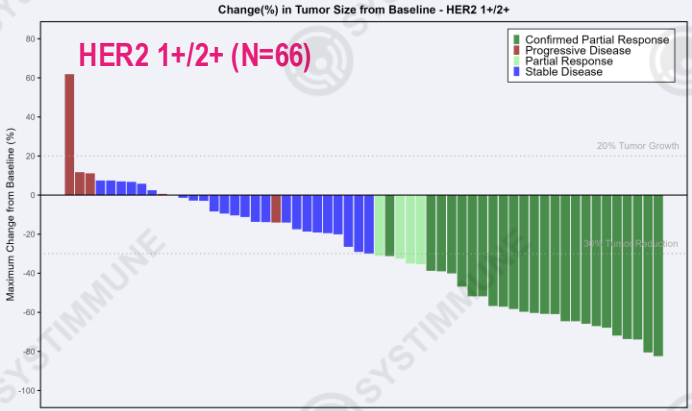
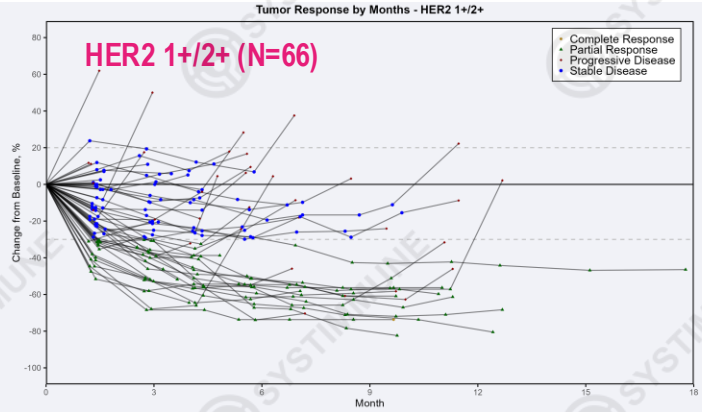
PRELIMINARY EFFICACY









Data cutoff: September 30, 2024

MOST COMMON TRAE IN HER2- BC PATIENTS

	Total (N = 121)	
Preferred Term (PT), n (%)	All Grade	Grade ≥3
Hematological AE		
Anemia	109 (90.1)	53 (43.8)
Leukopenia	109 (90.1)	55 (45.5)
Neutropenia	105 (86.8)	66 (54.5)
Thrombocytopenia	87 (71.9)	37 (30.6)
Non-Hematological AE		
Nausea	74 (61.2)	6 (5.0)
Stomatitis	64 (52.9)	4 (3.3)
Vomiting	58 (47.9)	1 (0.8)
Asthenia	57 (47.1)	13 (10.7)
AST increased	56 (46.3)	0
ALT increased	54 (44.6)	0
Hypertriglyceridemia	45 (37.2)	2 (1.7)
Hypokalemia	45 (37.2)	6 (5.0)
Alopecia	44 (36.4)	0
Decreased appetite	43 (35.5)	1 (0.8)

TRAE: treatment related adverse event

- The most common TRAEs were hematological toxicities.
- The non-hematological toxicities were mostly Grade 1 or 2.
- One treatment related death due to febrile neutropenia.
- No ILD was observed. No new safety signals were observed.
- Grade 3 and above TRAEs were able to be effectively managed with standard supportive measures, as demonstrated by the low rate (5.0%) of TRAE leading to drug discontinuation.

Data cutoff: September 30, 2024

CONCLUSIONS

- In heavily pre-treated locally advanced or metastatic HER2- BC, iza-bren has demonstrated encouraging efficacy with a manageable safety profile regardless of HER2 expression.
- Phase III studies of iza-bren in TNBC and HR+HER2-BC are ongoing (NCT06382142 & NCT06343948).
- Global phase II/III study of iza-bren in BC is ongoing (NCT06926868).

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