Abstract 1027: A Phase Ib/IIa study of BAT8010 (an anti - HER2 antibody - exatecan conjugate) + BAT1006 (an ADCC - enhanced HER2 mAb) in advanced solid tumor patients

NCT06376136

Shusen Wang[1], Jiajia Huang[1], Wen Xia[1], Dan-yun Ruan[1], Fei Xu[1], Furong Liu[1],Yuping Sun[2], Yuxiang Ma[1], Qiufan Zheng[1], Zuoxing Niu[2], Lixin Wan[3], Ruoxi Hong[1], Xin Wang[4], Ning Li[4], Xin An[1], Chuanqi Chao[5], Shuqiang Song[5], Shengfeng Li[5],Ruihua Xu[1]*

*Corresponding author

1. Sun Yat-sen University Cancer Center, Guangzhou, China, 2. Shandong Cancer Hospital, Jinan, China, 3. Nanyang Central Hospital, Nanyang, China, 4. Shanxi Cancer Hospital, Taiyuan, China, 5. Bio-Thera Solutions, Ltd., Guangzhou, China

BACKGROUND

- BAT8010 is a HER2 - targeted antibody - drug conjugate (ADC), was developed adopting a novel ADC platform technology with Exatecan as the payload tethered to a cleavable linker. The drug-to-antibody ratio (DAR) stands 7~8.
- BAT1006 is a humanized monoclonal antibody. Unlike BAT8010, it targets a non-overlapping HER2 epitope. Its fucose - free nature enhances ADCC. Binding to HER2's extracellular domain II, it blocks HER2 heterodimerization with EGFR/HER3/HER4, inhibiting tumor cell growth and survival.
- This compares data of BAT1006 (n = 31) and Perjeta (n = 29, BO17929 study) in Her2+ breast cancer patients. BAT1006 patients had 1-6 prior treatment lines (87.5% ≥ 3L), versus Perjeta patients with only 1 prior line. BAT1006's ORR was 12.9%, DCR 64.5%, mPFS 4.1m; Perjeta's were 3.4%, 10.3%, 1.7m respectively. It is not a head - to - head study.

OBJECTIVE

Primary Objective

- To assess the safety and tolerability of BAT8010+BAT1006 in patients with advanced solid tumors, explore the maximum tolerated dose (MTD) and provide the recommended dose for subsequent studies.

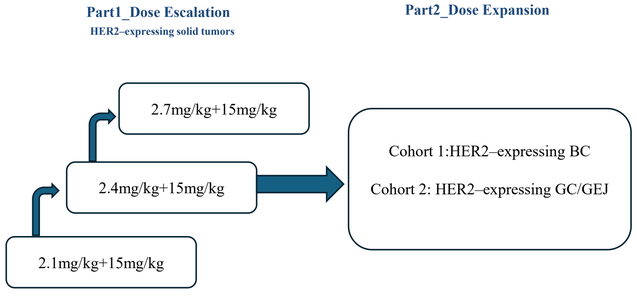
Secondary Objectives

- To evaluate the pharmacokinetic (PK) profiles and immunogenicity;
- To evaluate the preliminary anti-tumor efficacy;
- To explore the relationship between efficacy of BAT8010+BAT1006 and the expression of HER2 in tumor tissues and serum.

METHODS

Study design

•This is a multicenter, open-label Phase Ib/IIa dose escalation and dose expansion study with an accelerated titration and "3 + 3" dose escalation design. BAT8010 (2.4 mg/kg) + BAT1006 (15 mg/kg) dose was selected in the dose expansion study and patients are recruiting.



KEY INCLUSION & EXCLUSION CRITERIA

Inclusion:

- Histologically or cytologically confirmed advanced or metastatic solid tumors, unresponsive to standard treatments, intolerant to or declining standard therapies;
- At least one measurable target lesion according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1);

• i. Cohort A: Standard treatment failure/absence/unsuitability, HER2 ADC-treated, histo/cytopathologically-confirmed HER-2 (≥IHC1+) mBC patients.

ii. Cohort B: Histo/cytopathologically-confirmed metastatic/unresectable locally advanced/metastatic HER-2 (≥IHC1+) GC/GEJ patients with post-standard treatment progression or intolerance.

SAFETY & TOLERABILITY

- As of May 7, 2025, 36 subjects with advanced solid tumor were recruited. Two DLT (Grade 4 thrombocytopenia/neutropenia) were reported in BAT8010 (2.7 mg/kg) + BAT1006 (15 mg/kg) dose cohort during dose escalation study.
- In all dose optimal/expansion cohorts (including all advanced solid tumor subjects), 8.3%（3/36）subject experienced dose reduction, and 2.7%（1/36） subject experienced study drug interruption. One subject terminated the study treatment due to TEAE in BAT8010 (2.7 mg/kg) + BAT1006 (15 mg/kg) cohort. No treatment related death. No ILD/pneumonitis was reported in dose escalation and dose expansion study.
- In mBC and GC/GEJ optimal/expansion cohorts ,the major TRAEs were hematological toxicity. The incidences of ≥ Grade 3 thrombocytopenia and neutropenia were 19% vs 23.5% and 44% vs 41%, respectively.

The Most Common TEAEs in Dose Optimal/Expansion Study in Advanced Solid Tumor Subject (N=36)

	Breast Cancer (n = 17)		Gastric Cancer (n = 19)	
	All grade	≥Grade 3	All grade	≥Grade 3
Leukopenia	11 (69%)	7 (44%)	7 (65%)	11 (29%)
Neutropenia	10 (62%)	7 (44%)	11 (65%)	7 (41%)
Nausea	4 (25%)	4 (25%)	3 (18%)	-
Thrombocytopenia	7 (44%)	3 (19%)	6 (35%)	4 (23.5%)
Anemia	10 (62%)	3 (19%)	6 (35%)	3 (18%)
Febrile Neutropenia	1(6%)	1(6%)	4 (23.5%)	4 (23.5%)
Lymphopenia			2 (12%)	2 (12%)
Myelosuppression	7 (44%)		3 (18%)	
Elevated alanine aminotransferase	6 (37.5%)		4 (23.5%)	
Elevated Aspartate aminotransferase	7 (12%)		8 (16%)	
Infusion - related Reaction	7 (44%)		8 (47%)	1 (6%)
Anorexia	3 (19%)		4 (23.5%)	
Vomiting	2 (12.5%)		2 (12.5%)	

EFFICACY

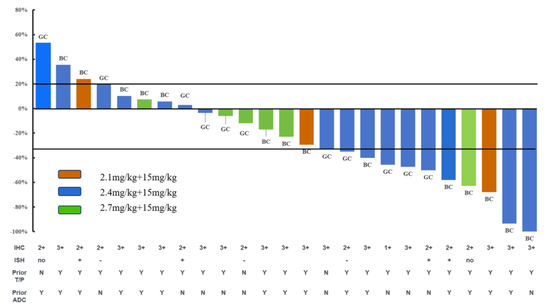
• To the date of data cut-off May 7, 2025, 36 subjects with breast cancer or gastric cancer were treated with BAT8010+BAT1006 doses of 2.1~2.7 mg/kg + 15mg/kg and have received at least one tumor assessment. 92.8% (13/14) of breast cancer patients had received any HER2-ADC treatment, and 54.5% (6/11) of gastric cancer patients had received ≥ 3 lines of prior treatment.

The ORR in mBC/GC Patients (N=25)

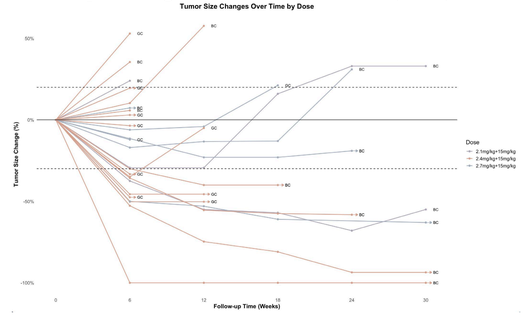
	ALL (n=25)	Breast Cancer (n=14)	Gastric Cancer (n=11)
ORR	11 (44.0%)	6* (42.8%)	5# (45.4%)
DCR	21 (84%)	11 (78.5%)	10 (91%)
CR	1(4%)	1*(4%)	0
PR	10 (40%)	5* (35.7%)	5# (45.4%)
SD	10 (40%)	5 (35.7%)	5 (45.5%)
PD	4 (16%)	3 (21.5%)	1 (9%)

*Including 5 confirmed PR and 1 CR, # including 2 confirmed PR

Maximum Target Lesions Reduction in mBC/GC Patients (N=25）



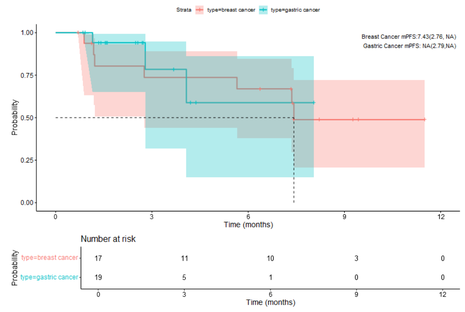
Spider diagram of mBC/GC Patients (N=25)



- With a median follow up of 4.4 months (1.6, 8.0), the median duration of response (mDOR) was 2.8 months

  The majority of PR subjects remain on study treatment.
- The Kaplan-Meier curve indicated that the mBC mPFS is 7.43 months（2.76~NA）.
- The breast cancer OS rate in 6 months and 1 year were 87.0%, 87.0%.
- The gastric cancer OS rate in 6 months and 1 year were 100%, 100%.

➢ **mPFS**



CONCLUSION

Safety aspect: The combination of BAT8010 and BAT1006 has favorable safety. The main adverse events are hematological toxicities, which can be predicted and managed, and there is no reported interstitial lung disease (ILD).

Efficacy aspect: The preliminary efficacy of BAT8010 + BAT1006 is remarkable. It shows effectiveness even in breast cancer patients resistant to HER2-ADC and gastric cancer patients with HER2-low status.

Ongoing research: Currently, dose expansion studies are being carried out on gastric cancer with IHC ≥ 1 and HER2-positive breast cancer in the first-line treatment. The combination also demonstrates good potential efficacy in these tumor types.

CONTACT: *Shusen Wang (wangshs@sysucc.org.cn) Rui-hua Xu *(xurh@sysucc.org.cn)*