Abstract 5550: Phase 1b/2a Study of BAT8006, a Folate Receptor α Antibody Drug Conjugate with Strong Bystander Effect, in Subjects with Advanced Solid Tumors

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BACKGROUND

- Folate receptor α (FRα) exhibits an increased expression on cell surfaces in multiple solid tumors, including ovarian, lung, breast and endometrial cancer, while demonstrating limited expression in normal tissues.
- BAT8006 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. Upon binding to FRα, BAT8006 undergoes receptor-mediated internalization. Subsequent proteolytic cleavage releases the cytotoxic payload Exatecan, leading to DNA strand breaks and consequently disrupting DNA replication and transcription.

OBJECTIVE

Primary Objective

- To assess the safety and tolerability of BAT8006 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 BAT8006 and the expression of FRα in tumor tissues and serum.

METHODS

Study design

- This is a multicenter, open-label dose escalation and dose expansion study with an accelerated titration and "3 + 3" dose escalation design. Two doses were selected in the dose optimal/expansion study and patients are recruiting.

Procedures

- BAT8006 was administrated once every 3 weeks. The study incorporated 6 escalation dose groups: 1.2mg/kg, 1.8mg/kg, 2.1mg/kg, 2.4mg/kg, 84mg/m^2, and 93mg/m^2. The 1.2mg/kg group followed an accelerated titration dose escalation design, while the other groups are escalated following the conventional "3+3" rule. The dose of 84mg/m^2 and 93mg/m^2 were selected in the dose optimal and expansion study after an exposure-response analysis and further evaluation in a series of tumor is ongoing.

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);
- No FRα expression was required in dose escalation study and FRα expression ≥1% in dose expansion study.

Exclusion:

- Presence of >Grade 1 adverse events (AEs as per CTCAE 5.0) resulting from prior antitumor treatment;
- With primary central nervous system tumors, symptomatic CNS metastasis, meningeal metastasis;
- History of non-infectious pneumonitis/pneumonitis requiring glucocorticoid therapy, or current interstitial lung diseases (ILD), or where suspected ILD/pneumonitis cannot be ruled out.

SAFETY & TOLERABILITY

- As of May 8, 2024, 156 subjects with advanced solid tumor were recruited. One DLT (Grade 4 thrombocytopenia) was reported in 2.4 mg/kg dose cohort during dose escalation study. The maximum tolerated dose was not established.
- In 84 and 93mg/m^2 dose optimal/expansion cohorts (including all advanced solid tumor subjects), 3.5%（2/57）and 3.9% (2/51) subjects experienced dose reduction, and 5.3% (3/57) and 13.7%(7/51) subjects experienced study drug interruption, respectively. One subject terminated the study treatment due to TEAE in 93mg/m^2 cohort. No treatment related death. No ILD/pneumonitis and keratitis, uveitis, decreased vision was reported in dose escalation and dose expansion study.
- The major TRAEs were hematological toxicity. The incidences of ≥ Grade 3 thrombocytopenia and neutropenia were 9% vs 28% and 19% vs 37%, respectively.

The Most Common TEAEs (incidence≥10%)in Dose Optimal/Expansion Study in Advanced Solid Tumor Subject (N=108)

	84mg/m^2 (n=57)		93mg/m^2 (n=51)	
	All grade	≥Grade 3	All grade	≥Grade 3
Leukopenia	39 (68%)	7 (12%)	44 (86%)	19 (37%)
Anemia	37 (65%)	6 (11%)	43 (84%)	13 (26%)
Thrombocytopenia	24 (42%)	5 (9%)	31 (61%)	14 (28%)
Neutropenia	36 (63%)	11 (19%)	37 (73%)	19 (37%)
Constipation	12 (21%)		12 (24%)	
Nausea	25 (44%)		27 (53%)	
Vomiting	29 (51%)		37 (73%)	
Loss of appetite	7 (12%)		10 (20%)	
Elevated alanine aminotransferase	7 (12%)		6 (12%)	
Elevated Aspartate aminotransferase	7 (12%)		8 (16%)	
Headache	10 (18%)		10 (20%)	
Fever	18 (32%)		22 (43%)	
Fatigue	13 (23%)		10 (20%)	

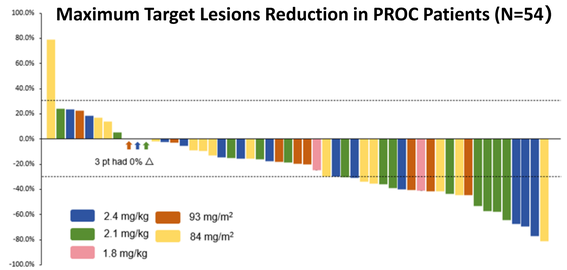
EFFICACY

- To the date of data cut-off May 8, 2024, 54 subjects with platinum refractory or platinum-resistant epithelial ovarian, fallopian tube or primary peritoneal cancer (PROC) were treated with BAT8006 doses of 1.8~2.4 mg/kg and 84/93mg/m^2 and have received at least one tumor assessment. All of them received prior bevacizumab treatment and 38.9% of them (21/54) had undergone > 3 lines prior systemic treatment.

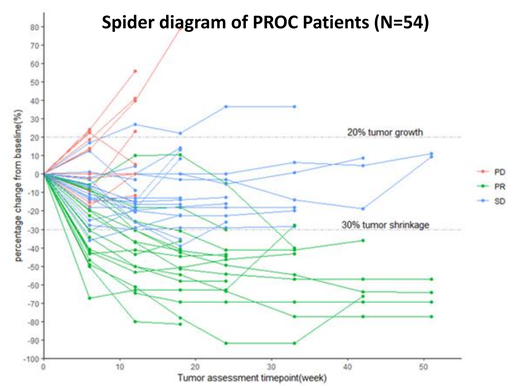
	ALL (n=54)	FRα < 50% (n=21)	FRα≥50% (n=33)	FRα≥75% (n=15)
ORR	20 (37.0%)	7* (33.3%)	13# (39.4%)	7 (46.7%)
DCR	42 (77.8%)	15 (71.4%)	27 (81.8%)	14 (93.3%)
CR	0	0	0	0
PR	20 (37%)	7* (33.3%)	13# (39.4%)	7 (46.7%)
SD	22 (40.7%)	8 (38.1%)	14 (42.4%)	7 (46.7%)
PD	12 (22.2%)	6 (28.6%)	7 (21.2%)	1 (6.7%)

*Including 3 unconfirmed PR, # including 2 unconfirmed PR

Maximum Target Lesions Reduction in PROC Patients (N=54)

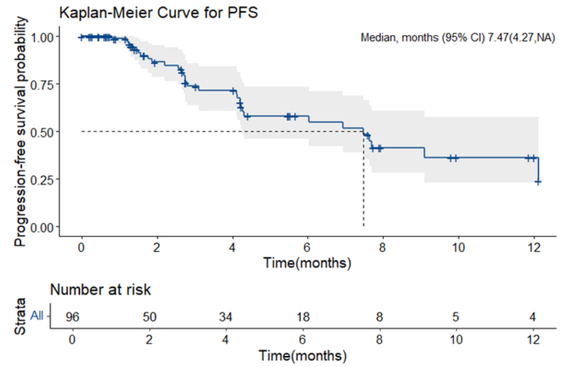


Spider diagram of PROC Patients (N=54)

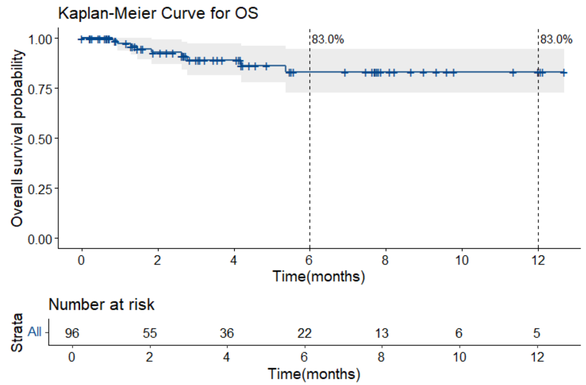


- With a median follow up of 6.5 months (1.3, 18.0), the median duration of response (mDOR) was 6.3 months (1.8-16.5 months). The majority of PR subjects remain on study treatment.
- The Kaplan-Meier curve indicated that the mPFS is 7.47 months（4.27~NA）.
- The OS rate in 6 months and 1 year were 83.0%, 83.0%.

➢ **mPFS**



➢ **mOS**



CONCLUSION

The safety of BAT8006 is favorable. The major adverse events were hematological toxicity and were predictable and manageable. No ILD and notable ocular toxicity was reported. The preliminary efficacy of BAT8006 was superior even in all PROC patients regardless of the FRα expression. BAT8006 may benefit broad patient population while providing a promising efficacy. An exploration on endometrial carcinoma, breast cancer and NSCLC in dose expansion study is ongoing, the efficacy was demonstrated in these tumor type as well.

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