Biparatopic anti-HER2 antibody drug conjugate (ADC) JSKN003 in the treatment of primary platinum-refractory ovarian cancer (OC)

X. Wu[1], J. Li[1], Y. Chen[2], Q. Rao[3], A. Lin[4], G. Weng[5], Z. Zhang[6], B. Liu[7], C. Lan[8], Q. Li[9], D. Tang[10], J.Dai[11], Y. Jing[12], W. Li[12], J. Yang[12], T. Xu[12]

1 Gynecologic Oncology II, Fudan University Shanghai Cancer Center, Shanghai, China, 2 Gynecologic Oncology Surgery, Zhejiang Cancer Hospital, Hangzhou, China, 3 Gynecologic Oncology,Sun Yat-Sen Memorial Hospital, Guangzhou, China, 4 Gynecologic Oncology Surgery, Fujian Provincial Cancer Hospital, Fuzhou, China, 5 Clinical Pharmacology Research Unit, Linyi People's Hospital, Linyi,China, 6 Tumor Center, Linyi People's Hospital, Linyi, China, 7 Oncology, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, Jinan, China, 8 Gynecologic Oncology, Sun Yat-Sen University Cancer Center, Guangzhou, China, 9 Oncology, Shanghai East Hospital, Shanghai, China, 10 Gynecologic Oncology, Hunan Cancer Hospital, Changsha, China, 11 Radiation and Medical Oncology, Zhongnan Hospital of Wuhan University, Wuhan, China,12 President's Office, Jiangsu Alphamab Biopharmaceuticals Co., Ltd., Suzhou, China

FPN: 1079P

BACKGROUND

- Therapies represented by ADCs have made certain progress in treating platinum-resistant ovarian cancer (PROC)[1,2], but not for primary platinum-refractory disease (defined as disease that progressed within 3 months after the last dose of first-line platinum-containing therapy) that were excluded from most of trials. Novel therapeutic options are urgently needed for this patient population with poorer prognosis compared to those who are not primary platinum-refractory.
- JSKN003, a biparatopic HER2-targeting ADC linked to a topoisomerase I inhibitor (TOPIi) with an average drug-to-antibody ratio (DAR) of 4(**Figure 1**), has shown encouraging efficacy and manageable toxicity in early phase studies for PROC regardless of HER2 expression[3].
- Here, we particularly present the findings of JSKN003 in treating patients with primary platinum-refractory OC.

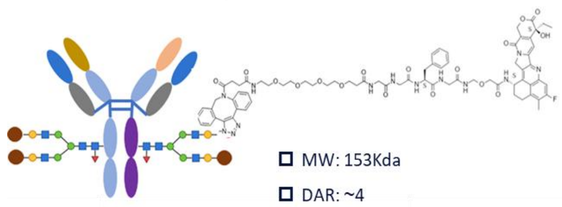

Figure 1. JSKN003 Structure Diagram

METHODS

- JSKN003-102 (NCT05744427) is a phase I/II trial conducted in China, enrolling patients with advanced solid tumors to receive JSKN003 monotherapy.
- Tumor tissue specimens were obtained for central laboratory evaluation of HER2-expression.

RESULTS

Baseline Characteristics

- As of June 13, 2025, a total of 26 patients with primary platinum-refractory OC received JSKN003 at 6.3 mg/kg every three weeks. Demographics and baseline characteristics are summarized in **Table 1**.

Table 1 Demographics & Baseline characteristics

Characteristics	Total (N=26)
Age, median (Q1, Q3)	54.0 (48.0, 60.0)
ECOG, n (%)	
PS 0	5 (19.2)
PS 1	21 (80.8)
Tumor diagnosis, n (%)	
Ovarian cancer	26 (100)
HER2 expression*, n (%)	
IHC 0	15 (57.7)
IHC 1+	5 (19.2)
IHC 2+	2 (7.7)
IHC 3+	1 (3.8)
Unknown	3 (11.5)
Prior lines of anti-cancer therapy, n (%)	
1	11 (42.3)
2	8 (30.8)
3	5 (19.2)
4	2 (7.7)
Site of metastasis, n (%)	
Lung	7 (26.9)
Liver	10 (38.5)
Prior bevacizumab, n (%)	22 (84.6)
Prior PARP inhibitor, n (%)	7 (26.9)

* HER2 status was tested by the central lab; 3 patients had no tumor sample for assessment.

Efficacy

- As of June 13, 2025, 25 patients were efficacy-evaluable. The overall response rate (ORR), disease control rate (DCR), best overall response (BOR), median PFS and 9-month OS rate by HER2 expression are summarized in **Table 2**. The Spider diagram and the Waterfall plot based on HER2 expression are shown in **Figure 2** and **3**.
  - The ORR was 32.0%, the DCR was 72.0%, the median PFS was 4.1 months, and the 9-month OS rate was 65.4%;
  - Efficacy was observed across different HER2 expression subgroups.

Table 2 Efficacy summary

	HER2 IHC			Total (n=25)
	0 (n=15)	1+/2+/3+ (n=8)	Unknown (n=2)	
ORR, % (95% CI)	40.0 (16.3, 67.7)	12.5 (0.3, 52.7)	50.0 (1.3, 98.7)	32.0 (14.9, 53.5)
DCR, % (95% CI)	66.7 (38.4, 88.2)	87.5 (47.3, 99.7)	50.0 (1.3, 98.7)	72.0 (50.6, 87.9)
BOR, n (%)				
CR	0	0	0	0
PR	6 (40.0)	1 (12.5)	1 (50.0)	8 (32.0)
SD	4 (26.7)	6 (75.0)	0	10 (40.0)
PD	5 (33.3)	1 (12.5)	1 (50.0)	7 (28.0)
PFS				
median, month (95% CI)	4.1 (1.3, 9.6)	4.1 (0.8, NE)	NE (1.4, NE)	4.1 (2.7, 4.4)
OS				
9-month rate, % (95% CI)	68.8 (16.3, 92.6)	46.7 (7.1, 80.3)	100 (100, 100)	65.4 (32.0, 85.4)

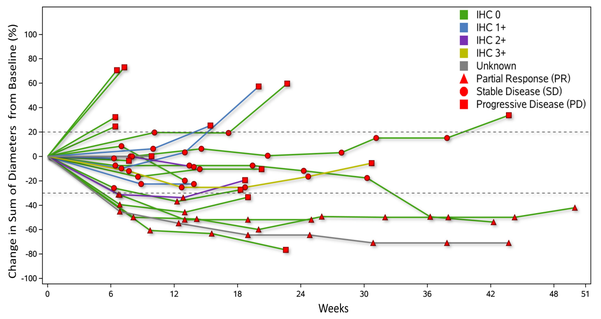

Figure 2. Spider diagram

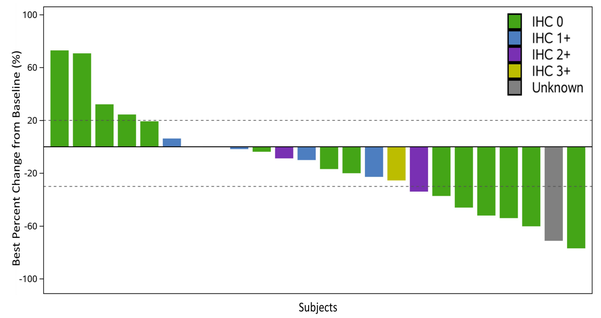

Figure 3. Waterfall plot

Safety

- 92.3% (24/26) patients experienced treatment-related adverse events (TRAEs).
  - Grade 3-4 TRAEs occurred in 15.4% (4/26) of patients.
  - Serious TRAEs were reported in 3.8% (1/26) of patients.
  - No TRAEs leading to death.
  - Interstitial lung disease was observed in 2 patients; all were grade 1.
- Common TRAEs were listed in **Table 3**.

Table 3 TRAEs occurring in > 15% of patients

Preferred Term, n (%)	Any Grade	Grade 3-4
Anaemia	14 (53.8)	1 (3.8)
Nausea	11 (42.3)	0
Hypoalbuminaemia	9 (34.6)	0
Lymphocyte count decreased	8 (30.8)	0
Aspartate aminotransferase increased	7 (26.9)	0
Vomiting	7 (26.9)	1 (3.8)
Platelet count decreased	6 (23.1)	0
Gamma-glutamyltransferase increased	6 (23.1)	0
Diarrhoea	5 (19.2)	0
Blood alkaline phosphatase increased	5 (19.2)	0
Asthenia	4 (15.4)	0
White blood cell count decreased	4 (15.4)	0
Alanine aminotransferase increased	4 (15.4)	0
Decreased appetite	4 (15.4)	0

CONCLUSIONS

JSKN003 demonstrated promising efficacy and tolerability in primary platinum-refractory OC, a patient population with limited treatment options.

DISCLOSURES

The authors declare that they have no conflict of interest.

REFERENCE

1. Kathleen N Moore, et al. N Engl J Med. 2023 Dec 7;389(23):2162-2174.
2. D. Lee, et al. Annals of Oncology Volume 35 Issue S2 2024.
3. Xiaohua Wu, et al. 2025 ASCO.

*The study is sponsored by Alphamab Oncology. Correspondence: Ting Xu; Email: tingxu@alphamabonc.com