JSKN003, a biparatopic anti-HER2 antibody drug conjugate (ADC), in the treatment of platinum-resistant ovarian cancer (PROC): Updated findings from two clinical trials

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BACKGROUND

- Patients with PROC have limited treatment options, with non-platinum chemotherapy showing low response rates of 10%-15%, short median progression-free survival (PFS) of 3-4 months, and short overall survival (OS) of 12 months[1, 2].
- Recent advancements include ADCs like Mirvetuximab soravtansine and Trastuzumab deruxtecan, which can improve prognosis in FRα-positive and HER2-positive patients, respectively[1, 3].
- However, challenges in patients without appropriate biomarkers persist, necessitating new therapies.
- JSKN003 is a biparatopic HER2-targeting ADC conjugated to a topoisomerase Ⅰ inhibitor with an average drug-to-antibody ratio (DAR) of 4 (Figure 1). It showed encouraging efficacy and safety in PROC regardless of HER2 expression[4].
- This update presents the latest findings for non-primary platinum-refractory patients at a longer follow-up time.

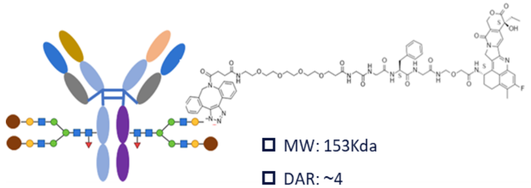

Figure 1. JSKN003 Structure Diagram

METHODS

- A pooled analysis of patients with PROC was performed from phase Ⅰ JSKN003-101 trial conducted in Australia (NCT05494918) and phase Ⅰ/Ⅱ JSKN003-102 trial conducted in China (NCT05744427). Both trials enrolled patients with advanced solid tumors and who were to receive JSKN003 monotherapy at various dose levels.
- Tumor tissue samples were collected for central lab assessment of HER2 expression status.

RESULTS

Baseline Characteristics

- As of February 28, 2025, 46 PROC patients were enrolled. They received JSKN003 at doses of 4.2 mg/kg (n=2), 5.2 mg/kg (n=2), 6.3 mg/kg (n=40, RP2D), 7.3 mg/kg (n=1), and 8.4 mg/kg (n=1), every three weeks. Demographics and baseline characteristics are summarized in Table 1.

Table 1 Demographics & Baseline characteristics

Characteristics	RP2D 6.3 mg/kg (N=40)	Total (N=46)
Age, median (Q1, Q3)	58.5 (52.5, 62.5)	59.0 (53.0, 63.0)
Race, n (%)		
Asian	36 (90.0)	39 (84.8)
White	3 (7.5)	6 (13.0)
Other	1 (2.5)	1 (2.2)
ECOG, n (%)		
PS 0	17 (42.5)	19 (41.3)
PS 1	23 (57.5)	26 (56.5)
Tumor diagnosis, n (%)		
Ovarian cancer	37 (92.5)	42 (91.3)
Primary peritoneal cancer	1 (2.5)	2 (4.3)
Fallopian tube cancer	2 (5.0)	2 (4.3)
HER2 expression*, n (%)		
IHC 0	21 (52.5)	21 (45.7)
IHC 1+	10 (25.0)	10 (21.7)
IHC 2+	4 (10.0)	5 (10.9)
IHC 3+	3 (7.5)	3 (6.5)
Platinum-free interval (PFI)#, n (%)		
≤ 3 months	13 (32.5)	14 (30.4)
> 3 months	23 (57.5)	23 (50.0)
Prior lines of anti-cancer therapy, n (%)		
1-2	16 (40.0)	16 (34.8)
≥ 3	24 (60.0)	30 (65.2)
Prior bevacizumab, n (%)	33 (82.5)	37 (80.4)
Prior PARP inhibitor, n (%)	26 (65.0)	29 (63.0)

* HER2 status was tested by the central lab; 7 patients had no tumor sample for assessment.
# Specific PFIs for 9 patients from JSKN003-101 study were not detailed.

Efficacy

- With a median follow-up time of 9.3 months, 46 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 and the Kaplan-Meier curve of PFS are shown in Figure 2, 3, and 4.
  - 91.3% (42/46) patients exhibited tumor shrinkage;
  - The ORR was 63.0%, the median PFS was 7.7 months, and the 9-month OS rate was 89.9%;
  - Efficacy was observed across different HER2 expression subgroups.

Table 2 Efficacy summary

Response	HER2 IHC* 0 (n = 21)	HER2 IHC* 1+/2+/3+ (n = 18)	Total (n = 46)
ORR, % (95% CI)	52.4 (29.8, 74.3)	72.2 (46.5, 90.3)	63.0 (47.5, 76.8)
DCR, % (95% CI)	90.5 (69.6, 98.8)	94.4 (72.7, 99.9)	93.5 (82.1, 98.6)
BOR, n (%)			
Complete Response	0	2 (11.1)	2 (4.3)
Partial Response	11 (52.4)	11 (61.1)	27 (58.7)
Stable Disease	8 (38.1)	4 (22.2)	14 (30.4)
Progressive Disease	1 (4.8)	1 (5.6)	2 (4.3)
PFS			
median, month (95% CI)	6.6 (4.1, 8.3)	9.4 (5.7, NE)	7.7 (5.7, 9.7)
OS			
9-month rate, % (95% CI)	100 (100, 100)	82.5 (54.9, 94.0)	89.9 (75.0, 96.1)

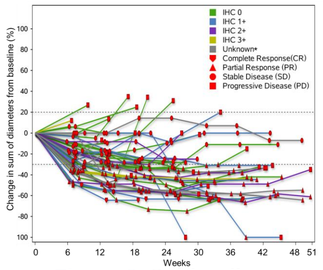

Figure 2. Spider diagram

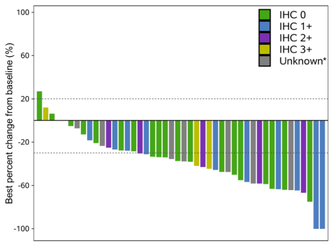

Figure 3. Waterfall plot

* HER2 was tested by the central lab; 7 patients had no tumor sample for assessment.

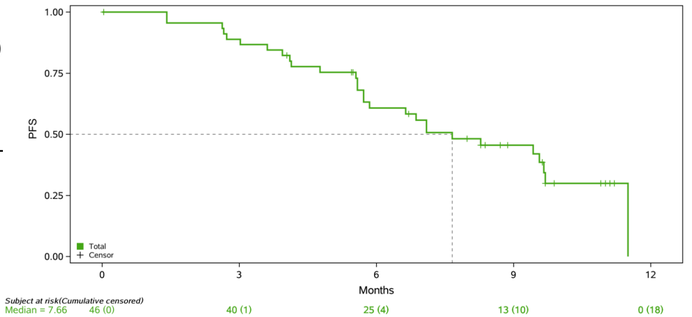

Figure 4. Kaplan-Meier curve of PFS

Safety

- 95.7% (44/46) patients experienced treatment-related adverse events (TRAEs).
  - Grade 3-4 TRAEs occurred in 19.6% (9/46) of patients.
  - Serious TRAEs were reported in 13.0% (6/46) of patients.
  - No TRAEs leading to death.
  - Interstitial lung disease was observed in 5 (10.9%) patients, all were Grade 1/2.
- Common TRAEs were listed in Table 3.

Table 3 TRAEs occurring in > 15% of patients

Preferred Term, n (%)	Any Grade	Grade 3-4
Anaemia	18 (39.1)	3 (6.5)
Aspartate aminotransferase increased	18 (39.1)	0
Diarrhoea	17 (37.0)	0
Nausea	17 (37.0)	0
Asthenia	16 (34.8)	1 (2.2)
Vomiting	13 (28.3)	0
White blood cell count decreased	13 (28.3)	0
Hypoalbuminaemia	12 (26.1)	0
Alanine aminotransferase increased	11 (23.9)	0
Decreased appetite	11 (23.9)	0
Weight decreased	11 (23.9)	0
Lymphocyte count decreased	9 (19.6)	2 (4.3)
Neutrophil count decreased	9 (19.6)	0
Platelet count decreased	9 (19.6)	1 (2.2)
Blood alkaline phosphatase increased	8 (17.4)	0
Blood creatinine increased	7 (15.2)	0

CONCLUSIONS

- With extended follow-up, JSKN003 demonstrated robust PFS improvement in PROC, along with early signals of OS benefit.
- A confirmatory trial (NCT06751485) is currently enrolling all comers regardless of HER2 expression to validate JSKN003 as a treatment option for this patient population.

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