Phase Ⅲ study of JSKN003, a biparatopic anti-HER2 antibody-drug conjugate (ADC), versus physician's choice of chemotherapy in platinum-resistant ovarian cancer (PROC): JSKN003-306

Authors: L. Wu[1], G. Yuan[1], K. Wang[2], X. Lu[3], Y. Chen[4], L. Chen[5], Z. Yang[6], Q. Rao[7], Y. Shen[8], G. Li[9], J. Yao[10], G. Lou[11], X. Chen[12], X. Yan[13], Y. Ji[14], K. Tu[15], L. Zhou[16], Z. Hu[17], Z. Qiao[18], X. Chen[19], T. Wang[20], R. Yin[21], Y. Huang[22], H. Yang[23], H. Liang[24], X. Li[25], L. Lin[26], L. Han[27], W. Fang[28], Y. Zhou[29], D, Wang[30], Y Shen[31], T. Wu[32], G. Weng[33], Z. Zhang[34], Y. Jing[35], W. Li[35], J. Yang[35], T. Xu[35]

1 Gynecology Ward, Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China, 2 Gynecological Oncology, Tianjin Medical University Cancer Institute & Hospital, Tianjin, China, 3, Gynecological Oncology, Obstetrics and Gynecology Hospital of Fudan University, Shanghai, China, 4 Gynecologic Oncology Surgery, Zhejiang Cancer Hospital, Hangzhou, China, 5 Ovarian Tumor Ward, Cancer Hospital of Shandong First Medical University (Shandong Cancer Institute, Shandong Cancer Hospital), Jinan, China, 6 Gynecology Ward, Guangxi Medical University Affiliated Cancer Hospital, Nanning, China, 7 Gynecologic Tumor, Department of Gynecologic Oncology, Sun Yat-Sen Memorial Hospital, Sun Yat-sen University, Guangdong Provincial Clinical Research Center for Obstetrical and Gynecological Diseases, Guangzhou, China, 8 Gynecological Oncology, Women's Hospital School of Medicine Zhejiang University, Hangzhou, China, 9 Gynecological Oncology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, 10 Oncology, The First Affiliated Hospital of Henan University of Science& Technology, Luoyang, China, 11 Gynecology Department, Area I, Harbin Medical University Cancel Hospital, Harbin, China, 12 Gynecological Oncology, Fudan University Shanghai Cancer Center, Shanghai, China, 13 Gynecology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China, 14 Oncology, The First Affiliated Hospital of Xinxiang Medical University, Xinxiang, China, 15 Gynecology Oncology, Jiangxi Maternal and Child Health Hospital, Nanchang, China, 16 Gynecology, Cancer Hospital of Shantou University Medical College, Shantou, China, 17 Gynecological Oncology, Zhongnan Hospital of Wuhan University, Wuhan, China, 18 Oncology, The Hospital affiliated with Jining Medical College, Jining, China, 19 Gynecology, The Second Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China, 20 Radiation Oncology, The Second Norman Bethune Hospital of Jilin University, Changchun, China, 21 Radiation Therapy and Chemotherapy for Gynecological Cancer, West China Second University Hospital, Sichuan University/West China Women's and Children's Hospital, Chengdu, China, 22 Gynaecological Oncology, Hubei Cancer Hospital, Wuhan, China, 23 Department of Radiotherapy, Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University, Taizhou, China, 24 First Department of Medical Oncology, Qingdao Central Hospital, University of Health and Rehabilitation Sciences, Qingdao, China, 25 Gynecology, Linyi Cancer Hospital, Linyi, China, 26 Gynecology, Anyang Cancer Hospital, Anyang, China,

FPN: 1219TiP

INTRODUCTION

- Platinum-resistant ovarian cancer (PROC) is known for low efficacy to non-platinum single-agent chemotherapy±bevacizumab, the standard-of-care (SOC)[1, 2], with an overall response rate (ORR) of 15%, a median progression-free survival (PFS) of 3 months, and a median overall survival (OS) of 12 months[2, 3, 4].
- Other approved treatments for PROC include mirvetuximab soravtansine (a FRα-ADC), but it is only applicable to patients with high FRα expression (accounting for only 30%)[4], and trastuzumab deruxtecan (a HER2-ADC) (accelerated approved by the FDA, but only for those with high HER2 expression (IHC 3+), accounting for less than 10%)[5], remaining a high unmet clinical need for PROC.
- JSKN003, a biparatopic HER2-targeting ADC linked to a topoisomerase I inhibitor (TOPIi) with an average drug-to-antibody ratio (DAR) of 4, has shown encouraging efficacy and manageable toxicity in early phase studies for PROC regardless of HER2 expression[6]:
  - ***In 46 efficacy-evaluable patients, 45.7% were HER2 no-expressing (IHC 0);***
  - ***91.3% of 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%;***
  - ***In HER2 expressing (IHC 1+/2+/3+) patients, the ORR and median PFS were 72.2% and 9.4 months, respectively;***
  - ***JSKN003 monotherapy has been granted Breakthrough-Therapy Designation for the treatment of PROC by the National Medical Products Administration (NMPA) of China. So far, JSKN003 is the only anti-HER2-ADC to receive this designation without HER2 expression restrictions.***
- The aim of the present study, JSKN003-306, is to investigate the efficacy and safety of JSKN003 monotherapy compared to physician's choice of chemotherapy in PROC.

METHODS

- JSKN003-306 is a phase Ⅲ, multi-center, open-label, randomized controlled study, enrolling 556 patients with recurrent platinum-resistant epithelial ovarian, primary peritoneal or fallopian tube cancer, irrespective of HER2 expression.
- Patients are randomized 1:1 to receive either JSKN003 or physician's choice of chemotherapy. Treatment continues until disease progression or intolerable toxicity.

Study design

Key eligibility criteria

- ≥18 years
- ECOG PS 0-1
- Recurrent PROC
- ≤ 4 prior lines of anti-cancer therapy
- Measurable disease by RECIST v1.1
- Adequate organ function

R
1:1
N=556

JSKN003
6.3mg/kg Q3W

Physician's choice of chemotherapy
Paclitaxel 80 mg/m², QW/
Liposomal doxorubicin 40 mg/m², Q4W/
Topotecan 4 mg/m² Day 1, 8, 15, Q4W, or 1.25 mg/m² Day 1-5, Q3W

ECOG, Eastern Cooperative Oncology Group; PS, Performance Status; PROC, Platinum-Resistant Ovarian Cancer; RECIST v 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; R, Randomization; Q3W, every three weeks; QW, every week; Q4W, every four weeks

Stratification

- Platinum-free interval (≤3 vs. 3-6 months)
- Number of prior lines of anti-cancer therapy (1/2 vs. 3/4)
- Central lab-assessed HER2 expression (expressing vs. no-expressing)

Endpoints

- **Primary endpoints**: PFS by blind independent central review (BICR) as per RECIST v1.1 and OS.
- **Secondary endpoints**: BICR-assessed ORR, duration of response (DoR), disease control rate (DCR), PFS-2; investigator-assessed PFS, ORR, DoR and DCR; CA-125 response as per Gynecologic Cancer Inter Group (GCIG) criteria, adverse events (AEs), patient-reported quality of life (QoL), pharmacokinetics (PKs), and immunogenicity.
- **Exploratory endpoint**: The relationship between HER2 expression and the efficacy of JSKN003.

Eligibility

Inclusion criteria

- ≥18 years
- ECOG PS 0-1
- Recurrent PROC, irrespective of HER2 expression
- ≤ 4 prior lines of anti-cancer therapy
- Prior anti-VEGF, PARPi, mirvetuximab soravtansine permitted
- Disease progression within 6 months after the last dose of platinum-base chemotherapy
- Eligible to receive either paclitaxel, liposomal doxorubicin or topotecan
- Measurable disease by RECIST v1.1
- Mandatory biopsy and/or archival tissues for HER2 examination

Exclusion criteria

- Prior TOPIi or TOPIi-containing ADC, such as T-Dxd
- Active central nervous system metastases
- History or current status of interstitial lung disease (ILD) or non-infectious pneumonitis requiring systemic glucocorticoid therapy, or suspected ILD or non-infectious pneumonitis
- Uncontrollable comorbidities

SUMMARY

- JSKN003 is an investigational biparatopic anti-HER2 ADC in development for PROC, which preliminarily showed promising anti-tumor activity and controllable safety.
- JSKN003-306, the confirmatory study, evaluates JSKN003 vs. physician's choice of chemotherapy in patients with PROC. It is actively enrolling, targeting 556 patients across 80 sites in China.
- JSKN003-306 is registered with Clinicaltrials.gov (NCT06751485).

DISCLOSURES

The authors declare that they have no conflict of interest.

REFERENCES

1. 2025 v1 NCCN Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer.
2. 2024 GUIDELINES OF CSCO OVARIAN CANCER.
3. Guangwen Yuan, et al. SCORES. 2024 ASCO.
4. Kathleen N Moore, et al. N Engl J Med . 2023 Dec 7;389(23):2162-2174.
5. D. Lee, et al. Annals of Oncology Volume 35 Issue S2 2024.
6. Xiaohua Wu, et al. 2025 ASCO

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