

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

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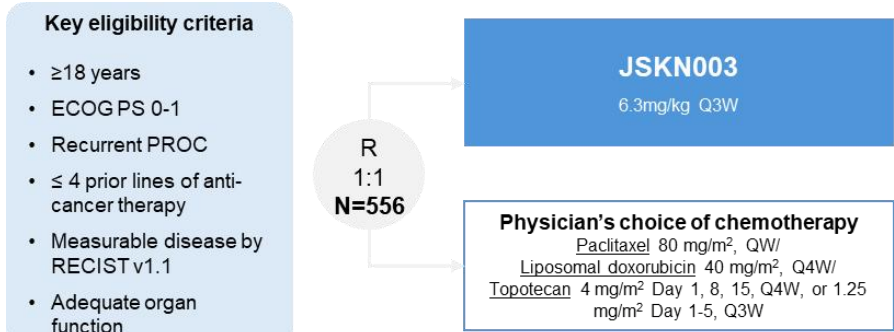
INTRODUCTION

- 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 expression⁶:
 - 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



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.

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