JSKN016, a First-in-Class anti-TROP2/HER3 Bispecific Antibody-Drug Conjugate(ADC) in Patients(pts) with HER2-Negative Locally Advanced or Metastatic Breast Caner: Results from a Phase I Study

中山大学 孙逸仙纪念医院 SUN YAT-SEN MEMORIAL HOSPITAL,SUN YAT-SEN UNIVERSITY

Abstract #1123

Herui Yao[1], Zhangzhou Huang[2], Hong Zong[3], Min Yan[4], Yanxia Zhao[5], Zhongsheng Tong[6],Jieqiong Liu[1], Jing Wang[7], Yu Cao[7], Qingyuan Zhang[8], Xinghua Han[9], Li Sun[10], Xinhong Wu[11], Jianhua Shi[12], Jianjun Tang[13], Jinhua Wen[13], Haijun Yu[14], Fang Su[15], Huan Zhou[15], Qi Dang[16]

1. Sun Yat-sen Memorial Hospital, Sun Yat-Sen University, Guangzhou, China; 2.Fujian Cancer Hospital, Fujian Medical University Cancer Hospital, Fujian, China, Fuzhou, China; 3.The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; 4.Henan Breast Cancer Center, The Affiliated Cancer Hospital of Zhengzhou University & Henan Cancer Hospital, Zhengzhou, China; 5.Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; 6.Department of Breast Oncology, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; 7.The Affiliated Hospital of Qingdao University, Qingdao, China; 8.Department of Oncology, Harbin Medical University Cancer Hospital, Harbin, China; 9.Department of Oncology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, China; 10.Xuzhou Central Hospital, Xuzhou, China; 11.Hubei Cancer Hospital, Wuhan, China; 12.Department of Medical Oncology, Linyi Cancer Hospital, Linyi, China; 13.The First Affiliated Hospital of Nanchang University, Nanchang, China; 14.Departmentof Radiation and Medical Oncology, Zhongnan Hospital of Wuhan University, Wuhan, China; 15.The First Affiliated Hospital of Bengbu Medical College, Bengbu, China; 16.Phase I Clinical Trial Ward, Cancer Hospital of Shandong First Medical University, Jinan, China

Background

- TROP2 and HER3 are frequently overexpressed in HER2-negative breast cancer and are associated with poor prognosis and treatment resistance.
- JSKN016 is a first-in-class **bispecific** ADC targeting TROP2/HER3, site specifically conjugated to **topoisomerase I inhibitor** (TOP1i) via a cleavable linker (**DAR4**). Glycan conjugation provides high stability and minimizes the off-target toxicity (**Figure 1**).
- This analysis reports the efficacy and safety results of JSKN016 monotherapy in HER2-negative breast cancer.

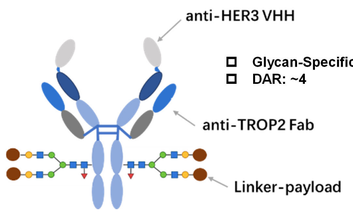

Figure 1 JSKN016 Structure Diagram

Methods

- JSKN016-101 (NCT06592417) is a first-in-human, dose-escalation and expansion study conducted in China, enrolled pts with advanced solid tumors to received JSKN016 monotherapy.
- Dose-escalation explored levels were 0.5, 1, 2, 4, 6, 8 mg/kg Q3W, without reaching maximum tolerated dose (MTD). The recommended phase II dose (RP2D) was established at 6 mg/kg Q3W in breast cancer.
- As of December 22, 2025, a total of 82 HER2-negative breast cancer were enrolled, comprising 50 pts with TNBC and 32 with HR+/HER2- BC, treated at 4 mg/kg (n=14), 6 mg/kg (the recommended phase II dose [RP2D]; n=65), and 8 mg/kg (n=3).
- 98.8% pts presented with stage IV disease, including 13.4% with brain metastases at baseline. The median age was 50 years in TNBC and 52 in HR+/HER2- BC subgroup, with **ECOG PS 1** reported in **78.7% and 76.7%** of pts, respectively.

Results

- All TNBC pts had received prior taxane-based chemotherapy, all HR+/HER2- BC pts had progressed following ae least one line of endocrine therapy combined with CDK4/6 inhibition and at least one line of chemotherapy (**Table 1&2**).

Table 1 Baseline Characteristics in TNBC

	Total (N=50)
Age, median(range), years	50 (40, 60)
Female, n (%)	50 (100)
ECOG PS 0/1, n(%)	11 (22.0) / 39 (78.0)
Brain metastases, n (%)	3 (6.0)
Visceral metastases, n (%)	42 (84.0)
Prior anti-cancer therapy lines ≥3L, n (%)	14 (28.0)
Prior taxane-based chemotherapy, n (%)	50 (100)

Visceral metastasis is defined as metastasis to sites other than bone, soft tissue, lymph node, skin and chest wall.

Table 2 Baseline Characteristics in HR+/HER2- BC

	Total (N=32)
Age, median(range), years	52 (45, 58)
Female, n (%)	32 (100)
ECOG PS 0/1, n(%)	8 (25.0) / 24 (75.0)
Brain metastases, n (%)	3 (9.4)
Visceral metastases, n (%)	30 (93.8)
Prior anti-cancer therapy lines ≥2L, n (%)	17 (53.1)
Prior endocrine therapy, n (%)	32 (100)
Prior CDK4/6i therapy, n (%)	32 (100)

Visceral metastasis is defined as metastasis to sites other than bone, soft tissue, lymph node, skin and chest wall.

Efficacy

- Among the 31 efficacy-evaluable **TNBC** pts who received the RP2D of 6 mg/kg Q3W, the **ORR** was **64.5%** (INV) and **61.3%** (IRC), the median **PFS** was **7.6 m** (INV) **and 7.9 m** (IRC).
- Among the 29 efficacy-evaluable **HR+/HER2- BC** pts who received the RP2D , the **ORR** was **51.7%** (INV) and **55.2%** (IRC), the median **PFS** by IRC was **11.1 m**, with a 6-month PFS rate of 84.5%.

- ✓ With an extended data cutoff of March 17, 2026, the investigator-assessed **ORR** in TNBC pts at RP2D was **64.5%** and **DCR was 83.9%**. The median **PFS was 8.5 m** (95%CI: 4.11, 10.02) (**Figure 2&3**). Among HR+/HER2- BC, the **ORR** was **51.7%** and **DCR was 100%.** The mPFS wasn't mature and 12-month PFS rate was 61.7% (**Figure 4&5**) (**Table 3**).
- ✓ Representing with longer follow-up and data mature, further improvement in efficacy is anticipated.

Figure 2 Waterfall of Plot Best Percentage Change from Baseline in Target Lesions in TNBC

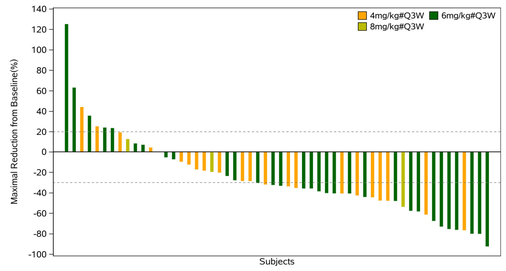

Figure 3 Spider Plot Evaluated by INV in TNBC

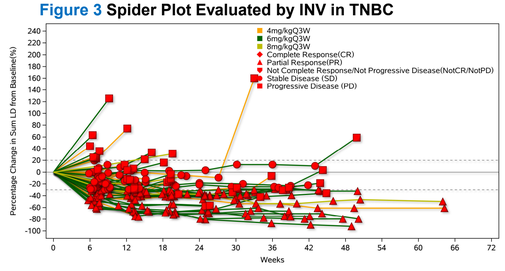

Figure 4 Waterfall of Plot Best Percentage Change from Baseline in Target Lesions in HR+/HER2-BC

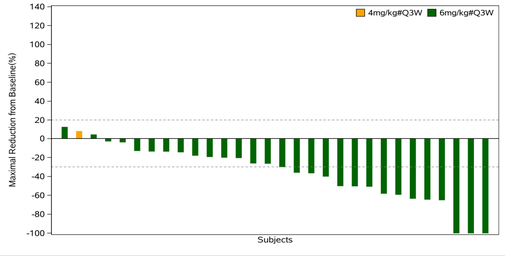

Figure 5 Spider Plot Evaluated by INV in HR+/HER2-BC

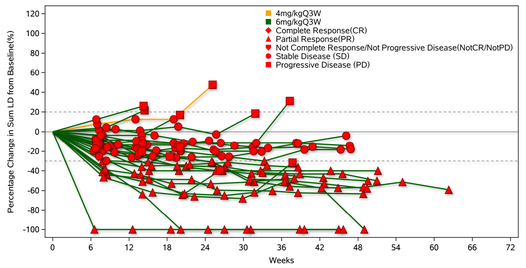

Table 3 Summary of Efficacy in HER2-negative BC Patients

	TNBC 6 mg/kg Q3W N=31	HR+/HER2- BC 6 mg/kg Q3W N=29
uORR, % (95% CI)	**64.5 (45.4, 80.8)**	**51.7 (32.5, 70.6)**
cORR, % (95% CI)	**58.1 (39.1, 75.5)**	**48.3 (29.4, 67.5)**
DCR, % (95% CI)	**83.9 (66.3, 94.5)**	**100 (88.1, 100)**
PFS follow-up time, mos	**10.84**	**10.38**
mPFS, mos (95% CI)	**8.5 (4.1, 10.0)**	**NR (7.0, NE)**
6-month PFS rate, % (95% CI)	**57.7 (38.5, 72.9)**	**74.0 (53.0, 86.7)**
9-month PFS rate, % (95% CI)	**44.1 (26.3, 60.6)**	**61.7 (40.3, 77.3)**
DoR, mos (95% CI)	**8.3 (5.8, NE)**	**NR (6.9, NE)**
12-month OS rate, % (95% CI)	**73.0 (53.1, 85.5)**	**92.4 (72.8, 98.1)**

NR: not reached, NE: not evaluable.

Safety

As of March 17, 2026, with a median follow-up time of 7.8 months,

- TRAEs occurred in 100% of patients, grade ≥3 TRAEs were reported in 24.6% (16/65), with no grade 4/5 events. SAEs occurred in 15.4%, and 12.3% were treatment-related (**Table 4**).
- Dose reduction due to TRAEs occurred in 46.2% at RP2D.
- Permanent treatment discontinuation due to a TRAE occurred in one patient (1.2%), which was a grade 3 conjunctivitis.
- No TRAEs led to death.
- No Interstitial lung disease (ILD) was reported.

Table 4 Overall Safety Summary

AEs, n (%)	RP2D (n=65)	Total (n=91)
TEAEs	65 (100)	91 (100)
TRAEs	65 (100)	91 (100)
Grade ≥3 TEAEs	18 (27.7)	26 (28.6)
Grade ≥3 TRAEs	16 (24.6)	24 (26.4)
SAEs	10 (15.4)	13 (14.3)
TRSAEs	8 (12.3)	11 (12.1)
TRAEs Leading to Dose Reduction	30 (46.2)	32 (35.2)
TRAEs Leading to Discontinuation	1 (1.5)	1 (1.1)
TRAEs Leading to Death	0	0
ILD	0	0

- The most common grade 3 TRAEs were neutrophil count decreased (7.7%), white blood cell count decreased (6.2%), amylase (4.6%), stomatitis (4.6%), asthenia (1.5%), lymphocyte count decreased (1.5%), weight decreased (1.5%), abdominal pain (1.5%), anemia (1.5%) and conjunctivitis (1.5%).

Conclusions

- JSKN016 demonstrated robust antitumor activity with good safety profile in pts with HER2-negative breast cancer. The results support further development of JSKN016 as mono therapy or in combination.
- The favorable benefit-risk profile supports the dual-targeting mechanism for enhanced efficacy while leveraging the glycan-conjugation platform minimizes severe myelosuppression, offering a distinct safety advantage.

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