PS5-03-03: TROP2-directed antibody-drug conjugate SHR-A1921 combined with PD-L1 inhibitor adebrelimab for patients with advanced triple negative breast cancer: Results from a phase 2, multi-cohort, open-label, non-controlled trial.

Tao Wang, MD[1]; Wei Zhao, PhD[2]; Jinyi Xiao, MD[1]; Jinmei Zhou, MD[1]; Xiaoying Shi, MD[2]; Qingshan Li, MD[2]; Zefei Jiang, MD[1];
[1]The Fifth Medical Center of Chinese PLA General Hospital, Beijing, CHINA, [2]Beijing Gobroad Hospital, Beijing, CHINA

Background

- The advent of novel antibody-drug conjugates (ADCs) has greatly changed the treatment landscape of advanced HER2-negative breast cancer. Preclinical studies have showed potential synergistic effect between ADCs and immunotherapies, while the clinical evidence remains limited.
- Our phase 2, multi-cohort, open-label, non-controlled trial (NCT06433609), was designed to evaluate the efficacy and safety of ADCs with distinct targets combined with PD-L1 inhibitor adebrelimab in patients (pts) with pretreated advanced HER2-negative breast cancer.
- Here, we present the preliminary results of TROP2-ADC SHR-A1921 combined with adebrelimab in pts with advanced triple negative breast cancer (aTNBC).

Methods

- Pts with HER2-negative advanced breast cancer who had experienced disease recurrence or progression on or after at least one line of systematic therapy were eligible for this trial. Prior PD-1/L1 inhibitors were allowed. Eligible pts with aTNBC enrolled in Cohort 2 received SHR-A1921 (3 mg/kg IV on day 1, Q3W) and adebrelimab (1200mg IV on day 1, Q3W).
- The primary endpoint was objective response rate (ORR) per investigator based on RECIST v1.1. Secondary endpoints included disease control rate (DCR), clinical benefit rate (CBR), duration of response (DoR), progression-free survival (PFS), overall survival (OS) and safety.

Results

- Between Sept. 6th, 2024 and Dec. 31st, 2024, 15 pts were enrolled in the intention-to-treat (ITT) group of Cohort 2.
- Baseline Characteristics were shown in **Table 1.**
- With a median follow-up of 9.7 months (range, 4.0-12.6) at the date cut-off (Oct. 28th, 2025), all pts had received at least one cycle of SHR-A1921 + adebrelimab and at least one efficacy assessment.

- The ORR was 60.0% (95% confidence interval [CI], 32.3-83.7) with a median DoR of 4.9 months (95% CI, 4.5-NR). DCR was 86.7% (95%CI, 59.5-98.3) and CBR was 60.0% (95% CI,32.3-83.7) **(Figure 1).**

Table 1. Clinical Characteristics of Enrolled Pts

	N=15
Median age (range, years)	52 (29-70)
ECOG PS	
0	2 (13.3%)
1	13 (86.7%)
PD-L1 CPS	
≥1 (PD-L1 positive, PD-L1+)	8 (53.3%)
<1 (PD-L1 negative, PD-L1-)	6 (40.0%)
Unknown	1 (6.7%)
Median metastatic sites (range)	3 (1-6)
Metastatic sites	
Visceral metastases	13 (86.7%)
Lung	6 (40.0%)
Liver	8 (53.3%)
Brian	2 (13.3%)
No visceral metastases	2 (13.3%)
Prior systematic therapy	
Chemotherapy	15 (100.0%)
Endocrine therapy	6 (40.0%)
CDK4/6 inhibitor	1 (6.7%)
ADC*	1 (6.7%)
PD-1/PD-L1 inhibitor	2 (13.3%)
Other targeted therapies**	6 (40.0%)
Median lines of prior therapy (range)***	2 (1-8)
1 line	7 (46.7%)
2 lines	6 (40.0%)
≥3 lines	2 (13.3%)

*One pt received T-DXd therapy.
**Other targeted therapies include bevacizumab, olaparib, everolimus, trastuzumab and pertuzumab.
***For (neo)adjuvant therapy, if progression/recurrence/metastasis occurred during therapy or within 6 months after treatment completion, it would be considered as one line of prior therapy.

- Ten PFS events were observed, and the median PFS was 5.1 months (95%CI 3.1-NR). **(Figure 2)**
- Antitumor efficacy was observed in both PD-L1+ and PD-L1- subgroups. **(Figures 1-2)**
- Three pts died after disease progression, and the median OS was unmatured.

Figure 1. Treatment exposure and duration of tumor response.

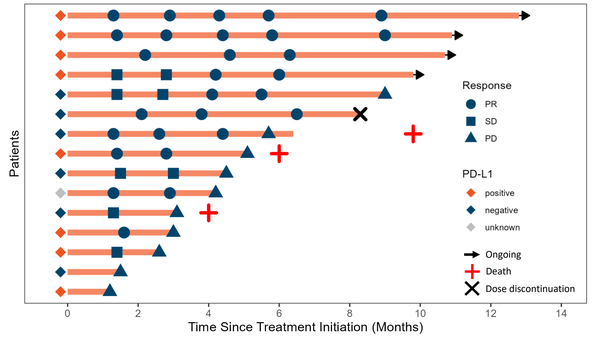
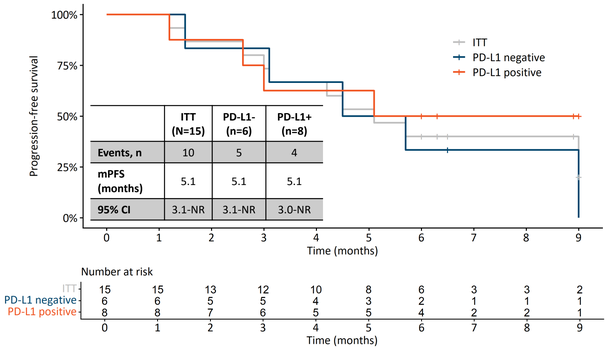


Figure 2. KM plot of PFS in ITT group, PD-L1- and PD-L1+ subgroups.



- Treatment-related adverse events (TRAEs) occurred in all pts, and mostly were of grade 1-2. Grade ≥3 TRAEs occurred in 2 pts (13.3%), including one (6.7%) grade 3 stomatitis and one (6.7%) grade 3 lymphocyte decreased. **(Table 2)**
- Eight pts experienced dose reduction of SHR-A1921 due to TRAEs. No dose discontinuation and no death due to AE was reported.

Table 2. TRAEs occurring in ≥25% of patients

	SHR-A1921+Adebrelimab (N=15)	
	Any grade	Grade ≥3
TRAEs	15 (100.0)	2 (13.3)
Stomatitis	14 (93.3)	1 (6.7)
Nausea	10 (66.7)	/
Fatigue	10 (66.7)	/
Epistaxis	6 (40.0)	/
White blood cell count decreased	5 (33.3)	/
Hypercholesterolaemia	5 (33.3)	/
Cough	5 (33.3)	/
Dyspnoea	5 (33.3)	/
Decreased appetite	5 (33.3)	/
Alanine aminotransferase increased	4 (26.7)	/
Abdominal discomfort	4 (26.7)	/
Vomiting	4 (26.7)	/
Dizziness	4 (26.7)	/
Neutrophil count decreased	4 (26.7)	/
Constipation	4 (26.7)	/

Conclusions

The combination of SHR-A1921 and adebrelimab demonstrated promising anti-tumor efficacy and manageable safety in pretreated TNBC pts regardless of PD-L1 status, warranting further investigations in this population. Our exploration of ADCs combined with adebrelimab in HER2-negative advanced breast cancer is still ongoing.

Contact
Tao Wang, The Fifth Medical Center of Chinese PLA General Hospital, Beijing, CHINA

This presentation is the intellectual property of the author/presenter. Contact them at tao.wang.1234@outlook.com for permission to reprint and/or distribute.