Efficacy and safety of Albumin-Bound Paclitaxel (SYHX2011) in Patients with Advanced Breast Cancer: A Multicenter, Randomized, Double-blind Phase III study

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Background

- Paclitaxel is a highly active chemotherapy agent as the standard treatment for advanced breast cancer.
- Albumin-bound paclitaxel is SPARC mediated enhanced paclitaxel distribution in tumor by high binding affinity to albumin, with high incidence of rash after treatment.
- SYHX2011 is a novel albumin-bound paclitaxel, with most non-particular human albumin replaced with mannitol and sucrose.
- This study aimed to compare SYHX2011 and paclitaxel for injection (albumin-bound) (PAB) outcomes in the patients with breast cancer.

Methods

This is a multicenter, randomized, double-blind, phase III trial conducted at 56 centers (NCT05753865) in China.

Eligibility criteria

- Unresectable locally advanced or metastatic breast cancer
- Be suitable for single-agent albumin-bound paclitaxel therapy
- Aged 18 years and older
- Had at least a measurable lesion
- ECOG performance status of 0-1

R → SYHX2011 260 mg/m^2, Q3W

R → PAB 260 mg/m^2, Q3W

Stratified factor:
- Previous taxanes use and rash occurrence
- Previous chemotherapy for advanced disease

Primary endpoint:
- Confirmed ORR assessed by IRC

Second endpoints:
- Incidence of rash
- Other efficacy outcomes
- Safety

Outcomes

Primary endpoint:
- Confirmed objective response rate (ORR) assessed by independent review committee (IRC) per RECIST version 1.1.

Key secondary endpoint:
- Incidence of rash during the first two administration cycles and the whole cycles.

Other secondary endpoints:
- Confirmed ORR assessed by investigator, progression-free survival (PFS), time to progression (TTP), overall survival (OS)
- Safety
- Investigational drug admixture time (completeness of dissolution).

Statistical consideration

- The primary endpoint of IRC assessed ORR was first tested for non-inferiority, then for superiority.
- Noninferiority was verified if the lower confidence bound of 95% confidence interval (CI) in rate ratio (RR) was higher than 0.75; and superiority would subsequently be evaluated and considered to be confirmed if it was higher than 1.

Results

- Data cut-off date: September 21, 2024
- 459 patients were enrolled
- The demographics and baseline characteristics of the patients are summarized in Table 1.

Table 1. Demographic and disease characteristics at baseline

	SYHX2011 (*n*=229)	PAB (*n*=230)
Age, median(range), years	57.0 (27, 84)	56.0 (28, 84)
< 65 years	183 (79.9)	187 (81.3)
≥ 65 years	46 (20.1)	43 (18.7)
Female, *n* (%)	227 (99.1)	230 (100.0)
ECOG PS, *n* (%)		
0	85 (37.1)	95 (41.3)
1	144 (62.9)	135 (58.7)
Breast cancer molecule subtype, *n* (%)		
HR positive breast cancer	173 (75.5)	166 (72.2)
Triple negative breast cancer	56 (24.5)	64 (27.8)
Clinical stage, *n* (%)		
Stage IV at diagnosis	138 (60.3)	126 (54.8)
Relapsed and metastatic	46 (20.1)	61 (26.5)
Unknown or others	45 (19.6)	43 (18.7)
Previous chemotherapy for advanced disease, *n* (%)		
0	165 (72.1)	167 (72.6)
≥1	64 (27.9)	63 (27.4)
Previous taxanes use and rash occurrance, *n* (%)		
Previous taxanes with rash	3 (1.3)	1 (0.4)
Previous taxanes with no rash	158 (69.0)	159 (69.1)
No previous taxanes	68 (29.7)	70 (30.4)

*2 patients in the SYHX2011 group were male.
ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hormone receptor.

- The confirmed ORR assessed by IRC were 35.8% with SYHX2011 and 25.8% with PAB (RR=1.38, 95%CI 1.04-1.84; P=0.0124), indicating that SYHX2011 was noninferior to PAB.
- The superiority of SYHX2011 over PAB was also confirmed (Table 2).

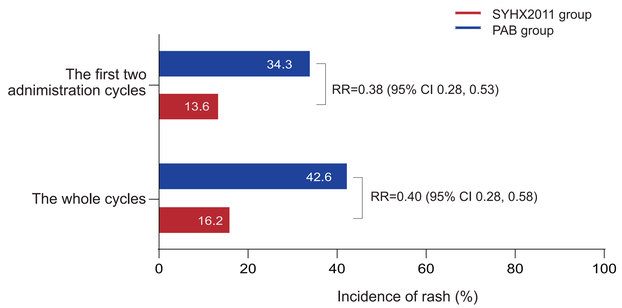
Table 2. Summary of best overall reponse assessed by IRC and investigator

	SYHX2011 (*n*=215*)		PAB (*n*=221*)	
	IRC assessed	INV assessed	IRC assessed	INV assessed
Best overall response, *n* (%)				
Complete response	0	3 (1.4)	2 (0.9)	3 (1.4)
Partial response	77 (35.8)	78 (36.3)	55 (24.9)	59 (26.7)
Stable disease	106 (49.3)	104 (48.4)	122 (55.2)	120 (54.3)
Progressive disease	28 (13.0)	28 (13.0)	37 (16.7)	34 (15.4)
Not evaluable	4 (1.9)	2 (0.9)	5 (2.3)	5 (2.3)
ORR, %, 95% CI	35.8 (29.4, 42.6)	37.7 (31.2, 44.5)	25.8 (20.2, 32.1)	28.1 (22.2, 34.5)
DCR, %, 95% CI	85.1 (79.6, 89.6)	86.0 (80.7, 90.4)	81.0 (75.2, 86.0)	82.4 (76.7, 87.1)

*Efficacy was evaluated in all the randomized population who received at least one dose of the study drug and had baseline and post-baseline efficacy assessments.
CI, confidence interval; DCR, disease control rate; INV, investigator; IRC, independent review committee; ORR, objective response rate

- The incidence of rash during the first two administration cycles in the SYHX2011 group was lower compared with those in the PAB group.
- Similar results on the incidence of rash during the whole cycles were also observed (Figure 1).

Figure 1. Incidence of rash during the first two cycles and whole cycles



- Treatment-related adverse events (TRAEs) occurred in 98.2% of patients receiving SYHX2011, and 98.3% of patients receiving PAB.
- Summary of TRAEs were shown in Table 3.

Table 3. Summary of TRAEs (occurring ≥ 10% of patients)

	SYHX2011 (*n*=228*)		PAB (*n*=230)	
	All grades	Grade ≥ 3	All grades	Grade ≥ 3
Common TRAEs				
Anemia	131 (57.5)	14 (6.1)	138 (60.0)	15 (6.5)
Leukopenia	109 (47.8)	32 (14.0)	93 (40.4)	27 (11.7)
Thrombocytopenia	100 (43.9)	12 (5.3)	88 (38.3)	10 (4.3)
Peripheral sensory neuropathy	93 (40.8)	24 (10.5)	90 (39.1)	24 (10.4)
Alopecia	87 (38.2)	0	99 (43.0)	0
Increased ALT	85 (37.3)	3 (1.3)	89 (38.7)	3 (1.3)
Neutropenia	85 (37.3)	36 (15.8)	72 (31.3)	26 (11.3)
Increased AST	82 (36.0)	5 (2.2)	85 (37.0)	3 (1.3)
Pruritus	59 (25.9)	1 (0.4)	54 (23.5)	0
Fatigue	54 (23.7)	4 (1.8)	62 (27.0)	4 (1.7)
γ-GGT elevation	47 (20.6)	5 (2.2)	41 (17.8)	2 (0.9)
Nausea	47 (20.6)	0	40 (17.4)	0
Lymphopenia	44 (19.3)	21 (9.2)	47 (20.4)	23 (10.0)
Weight loss	42 (18.4)	0	55 (23.9)	1 (0.4)
Hyperuricemia	41 (18.0)	0	37 (16.1)	1 (0.4)
Peripheral neuropathy	35 (15.4)	6 (2.6)	32 (13.9)	4 (1.7)
Increased ALP	35 (15.4)	0	41 (17.8)	0
Vomiting	31 (13.6)	2 (0.9)	35 (15.2)	0
Pruritic rash	29 (12.7)	1 (0.4)	86 (37.4)	9 (3.9)

* One patient didn't receive SYHX2011 after randomazition. ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, glutamyl transferase; TRAEs, treatment related adverse events.

Conclusion

- SYHX2011 not only demonstrated noninferiority vs PAB in efficacy but also showed statistically superior efficacy compared to PAB.
- SYHX2011 significantly reduced the incidence of rash compared with PAB.
- SYHX2011 might be a more effective and safe treatment option for patients with advanced breast cancer.

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