

Efficacy and Safety of Obuprazine (HS-10380) in Patients with Schizophrenia: A Phase 2b Randomized Placebo- and Active-Controlled Trial

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- ✓ Over 6-week treatment period, HS-10380 demonstrated promising efficacy in Chinese patients with acute schizophrenia, with marked improvements in PANSS total, positive, negative and cognitive symptoms.
- ✓ HS-10380 exhibited a favorable overall safety and tolerability profile.
- ✓ These findings collectively demonstrated that HS-10380 produced rapid and clinically meaningful improvements in symptoms of schizophrenia, with efficacy that exceeded both placebo and aripiprazole across multiple endpoints.

Background

- Substantial unmet clinical needs persist in managing all aspects of schizophrenia.
- Obuprazine (HS-10380) is an oral multi-target agent acting on dopamine and serotonin pathways, designed to address the broad symptom domains of schizophrenia.
- Previous studies (NCT05480592, NCT05964790) demonstrated promising efficacy signals of HS-10380 with a favorable safety profile.

Methods

- This was a randomized, double-blind, placebo- and active-controlled phase 2 study conducted across 24 centers in China (NCT07550387).

Key Eligibility Criteria	Treatment*	Endpoint
- Acute episode of schizophrenia requiring hospitalization within 2 months prior to screening - Aged 18–65 years - Positive and Negative Syndrome Scale (PANSS) total score 80–120 - Clinical Global Impression-Severity (CGI-S) score ≥4	HS-10380 1.5–3 mg (n=80)	Primary efficacy endpoints - Change from baseline in PANSS total score on Day 42 Key secondary endpoints - PANSS response rate - PANSS subscales - Marder 5 factors - Adverse events (AEs)
	HS-10380 4.5–6 mg (n=80)	
	HS-10380 6–9 mg (n=80)	
	Aripiprazole 10–20 mg (n=40)	
	Placebo (n=80)	
*Fixed-flexible dosing regimen for 42 days, followed by a 1-week taper period.		

Results

Demographics and Disease Characteristics

- A total of 363 participants were randomized to HS-10380 1.5–3 mg, HS-10380 4.5–6 mg, HS-10380 6–9 mg, aripiprazole, or placebo group.
- Demographics and baseline characteristics were well balanced across groups (Table 1).

Table 1. Demographics and baseline characteristics

	Placebo (N=81)	HS-10380			Aripiprazole (N=40)
		1.5–3 mg (N=79)	4.5–6 mg (N=80)	6–9 mg (N=79)	
Age (years), mean (SD)	38.5 (11.80)	37.3 (9.97)	38.5 (11.04)	38.2 (10.09)	34.4 (9.62)
Male, n (%)	36 (44.4)	34 (43.0)	38 (47.5)	37 (46.8)	22 (55.0)
BMI (kg/m ²), mean (SD)	24.0 (3.89)	24.3 (4.56)	24.2 (4.25)	24.6 (4.67)	24.0 (4.11)
CGI-S score, mean (SD)	5.3 (0.62)	5.3 (0.70)	5.2 (0.68)	5.2 (0.60)	5.2 (0.66)

Analyses were based on the full analysis set (FAS), comprising all randomized participants who received ≥1 dose of investigational product and had both baseline and ≥1 post-baseline PANSS assessment. Abbreviations: BMI, body mass index; CGI-S, Clinical Global Impression-Severity; SD, standard deviation.

Efficacy

- All HS-10380 dose groups demonstrated **greater improvements in PANSS total score compared with placebo** (Table 2). The PANSS response rate (≥50% reduction) in the HS-10380 1.5–3 mg and 4.5–6 mg groups demonstrated a notable increase compared to both the placebo and aripiprazole from as early as Day 14 (Figure 1).
- HS-10380 **outperformed placebo in negative symptoms and disorganized thought (cognitive factor) dimensions with clinically meaningful improvements** (Table 2).
- HS 10380 also showed favorable efficacy trends compared to aripiprazole across multiple endpoints.

Table 2. Efficacy measures at Day 42

	Placebo (N=81)	HS-10380			Aripiprazole (N=40)
		1.5–3 mg (N=79)	4.5–6 mg (N=80)	6–9 mg (N=79)	
PANSS total score					
Baseline, mean (SD)	95.8 (10.75)	94.6 (9.83)	92.9 (9.14)	97.6 (8.72)	96.5 (10.84)
Change from baseline, LSM (SEM)	-11.9 (2.11)	-28.6 (2.07)	-25.1 (2.02)	-26.6 (2.08)	-24.0 (2.87)
LSMD (95% CI)		-16.7 (-22.5, -10.9)	-13.2 (-18.9, -7.4)	-14.7 (-20.5, -8.8)	-12.1 (-19.1, -5.1)
P value		<0.0001	<0.0001	<0.0001	0.0007
PANSS positive subscale					
Baseline, mean (SD)	23.9 (4.09)	24.0 (3.95)	23.3 (3.23)	25.0 (4.36)	23.6 (4.24)
Change from baseline, LSM (SEM)	-5.0 (0.66)	-10.3 (0.64)	-10.0 (0.63)	-10.5 (0.65)	-7.3 (0.89)
LSMD (95% CI)		-5.3 (-7.1, -3.4)	-5.0 (-6.8, -3.2)	-5.5 (-7.3, -3.7)	-2.3 (-4.5, -0.1)
P value		<0.0001	<0.0001	<0.0001	0.0393
PANSS negative subscale					
Baseline, mean (SD)	25.7 (5.34)	24.6 (5.11)	23.8 (4.48)	25.1 (4.40)	25.3 (5.89)
Change from baseline, LSM (SEM)	-1.7 (0.67)	-6.2 (0.66)	-5.0 (0.64)	-4.8 (0.66)	-5.0 (0.91)
LSMD (95% CI)		-4.4 (-6.3, -2.6)	-3.3 (-5.1, -1.4)	-3.1 (-4.9, -1.2)	-3.3 (-5.5, -1.1)
P value		<0.0001	0.0005	0.0011	0.0037
PANSS Marder's cognitive factor					
Baseline, mean (SD)	24.8 (5.09)	23.0 (5.92)	23.2 (5.04)	24.6 (4.97)	24.8 (6.03)
Change from baseline, LSM (SEM)	-2.5 (0.64)	-5.6 (0.62)	-6.0 (0.60)	-5.9 (0.62)	-5.0 (0.86)
LSMD (95% CI)		-3.2 (-4.9, -1.4)	-3.6 (-5.3, -1.8)	-3.5 (-5.2, -1.7)	-2.5 (-4.6, -0.4)
P value		0.0004	<0.0001	0.0001	0.0182

Efficacy analyses were based on the FAS. All differences were compared with placebo and all p values were nominal. Endpoints were analyzed with a mixed-effects model for repeated measures. Abbreviations: CI, confidence interval; LSM, least squares mean; LSMD, least squares mean difference; PANSS, Positive and Negative Syndrome Scale; SD, standard deviation; SEM, standard error of the mean.

Safety

- Most TEAEs were mild to moderate in severity (Table 3).
- TEAEs occurring in ≥10% in the combined HS-10380 dose groups, and at an incidence at least twice that observed in the placebo group were extrapyramidal disorder, akathisia, vomiting, hyperprolactinemia, dizziness and nausea.

Table 3. Adverse events

AE, n (%)	Placebo (N=81)	1.5–3 mg (N=81)	4.5–6 mg (N=80)	6–9 mg (N=81)	Aripiprazole (N=40)
Any TEAE	64 (79.0)	75 (92.6)	78 (97.5)	80 (98.8)	36 (90.0)
Any TRAE	48 (59.3)	70 (86.4)	77 (96.3)	76 (93.8)	33 (82.5)
SAE	0	0	0	1 (1.2)	0
Severe TEAE	0	0	0	1 (1.2)	0
TEAE leading to study discontinuation	2 (2.5)	1 (1.2)	1 (1.3)	3 (3.7)	0

Analyses were based on the safety set (SS), comprising all randomized participants who received ≥1 dose of investigational product. Abbreviations: SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Conclusions

- The 6-week treatment with HS-10380 showed a favorable benefit-risk profile in Chinese adults with acute schizophrenia, with both efficacy and overall tolerability clearly demonstrated, providing robust foundational evidence for further clinical development in schizophrenia and other central nervous system indications.