Abstract: S297

Title: SOVLEPLENIB FOR THE TREATMENT OF WARM ANTIBODY AUTOIMMUNE HEMOLYTIC ANEMIA (WAIHA): RESULTS FROM THE RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE 2 PART OF THE STUDY

Abstract Type: Oral Presentation

Session Title: Thalassemias and rare anemias

Background:

wAIHA is an acquired hemolysis caused by the accelerated destruction of red blood cells due to autoantibody reactions on erythrocytes.

Sovleplenib (HMPL-523) is a novel, potent and highly selective spleen tyrosine kinase (Syk) inhibitor that has shown significant improvement in efficacy in patients with primary immune thrombocytopenia (ITP).

Aims:

A randomized, double-blind, placebo-controlled phase 2/3 study (NCT05535933) was conducted to evaluate the efficacy and safety of sovleplenib in adult wAIHA patients in China. Here we report the final results from the phase 2 portion of the study.

Methods:

Patients with primary or secondary wAIHA who had a hemoglobin (Hb) level <100 g/L, positive direct antiglobulin test (IgG+, with or without C3+) and failed at least one prior line of corticosteroid therapy, were eligible.

In the phase2 study, eligible patients were randomized (3:1) to receive sovleplenib or placebo, 300 mg once daily (QD), for 8 weeks, followed by open-label treatment for at least 16 weeks. The primary endpoint was overall Hb response (at least one Hb ≥100 g/L with an increase of at least ≥20 g/L from baseline, not impacted by rescue therapy) within 24 weeks. And the key secondary endpoint was durable Hb response (Hb ≥100 g/L in 3 consecutive available evaluations with an interval of at least 7 days, and with an increase of ≥20 g/L from baseline, not impacted by rescue therapy).

Results:

As of 19 Dec 2023, 21 patients (16:5) were randomized to receive the study treatment or placebo. All 21 patients completed 8 week double-blind treatment and ended the open-label treatment phase. The key baseline characteristics are shown in Table 1. The median age was 45 years, and the median baseline Hb level was 87.0 g/L. Patients received a median of 3.0 lines of prior anti-wAIHA therapies, and 38% of the patients previously received anti-CD20 therapy.

Efficacy results are shown in Table 2. During the 0-8 weeks double-blind period, the overall Hb response (OR) rate was 43.8% (7/16) in sovleplenib, which was higher than that in placebo (0%). The durable Hb response (DR) rate was 18.8% (3/16) in sovleplenib vs. 0% in placebo. The median time to response (Hb increased ≥15 g/L from baseline) was 1.3 weeks. 25.0% (4/16) vs. 60.0% (3/5) of the patients in sovleplenib vs. placebo received rescue therapies.

During the 0-24 weeks of sovleplenib treatment, the OR rate and DR rate was 66.7% (14/21) and 47.6% (10/21), respectively. 28.6% (6/21) of patients had received rescue therapies. For those patients previously-treated with anti-CD20 therapy, the OR rate and DR rate was 62.5% (5/8) and 37.5% (3/8), respectively.

During the double-blind treatment, 13 (81.3%) patients in sovleplenib vs. 5 (100%) patients in placebo

reported treatment-emergent adverse events (TEAEs), and 4 (25.0%) patients vs. 4 (80.0%) patients reported grade 3 TEAEs. No grade 4 or 5 TEAEs occurred in any group. The most common TEAEs are presented in Table 3.

The PK profile of sovleplenib was similar in wAIHA patients compared to ITP population. The steady-state of sovleplenib at 300 mg QD can cover the EC50 (47.7 ng/mL, ex vivo anti IgE induced CD63+ basophil activation assay) for at least 16 hours.

Summary/Conclusion:

Sovleplenib demonstrated a favourable safety profile and an encouraging Hb benefit compared with placebo. The randomized phase 3 study (ESLIM-02) will further investigate the efficacy and safety of sovleplenib 300 mg QD for the treatment of wAIHA.

Table 1 Key Baseline Characteristics in the Intent-to-Treat Population

	Sovleplenib (N=16)	Placebo (N=5)	Total (N=21)
Age, median (range), years	**48.5 (28, 69)**	**37.0 (28, 53)**	**45.0 (28, 69)**
Gender, n (%)			
Male	3 (18.8)	1 (20.0)	4 (19.0)
Female	13 (81.3)	4 (80.0)	17 (81.0)
ECOG performance status, n (%)			
0	3 (18.8)	1 (20.0)	4 (19.0)
1	13 (81.3)	4 (80.0)	17 (81.0)
Baseline Hb level, median (range), g/L	**84.0 (52.0, 99.0)**	**96.0 (71.0, 99.0)**	**87.0 (52.0, 99.0)**
≥70 g/L, n (%)	12 (75.0)	5 (100.0)	17 (81.0)
<70 g/L, n (%)	4 (25.0)	0	4 (19.0)
Concomitant anti-wAIHA therapy at baseline, n (%)			
Yes	**10 (62.5)**	**4 (80.0)**	14 (66.7)
No	6 (37.5)	1 (20.0)	7 (33.3)
Prior anti-CD20 therapy, n (%)	**6 (37.5)**	**2 (40.0)**	**8 (38.1)**
wAIHA type, n (%)			
Primary wAIHA	14 (87.5)	5 (100.0)	19 (90.5)
Secondary wAIHA	2 (12.5)	0	2 (9.5)
Time from diagnosis of wAIHA to randomization, median (range), months	**26.20 (3.6, 90.4)**	**9.56 (1.5, 92.9)**	**19.19 (1.5, 92.9)**
Lines of prior anti-wAIHA therapies, median (range)	**3.0 (1, 11)**	**2.0 (1, 4)**	**3.0 (1, 11)**

ECOG = Eastern Cooperative Oncology Group; Hb = hemoglobin; wAIHA = warm antibody autoimmune hemolytic anemia.

Table 2 Efficacy Results

Efficacy endpoints	Double-blind phase (0-8 weeks)		0-24 weeks
	Sovleplenib (N=16)	Placebo (N=5)	Overall* (N=21)
Overall response rate, n (%)	7 (43.8)	0 (0)	14 (66.7)
Durable response rate, n (%)	3 (18.8)	0 (0)	10 (47.6)
Rescue therapy, n (%)	4 (25.0)	3 (60.0)	6 (28.6)
Time to response with Hb increase of at least 15 g/L from baseline , weeks, median (range)	1.3 (0.9, 5.9)	NA	4.1 (0.9, 22.1)

NA=not available.

*include 5 patients crossed over from placebo.

Table 3 The Most Common TEAEs in the Double-Blind Phase and 0-24 weeks by Preferred Term

	0-8 weeks				0-24 weeks	
	Sovleplenib (N=16)		Placebo (N=5)		Sovleplenib (N=21)	
	All grades	Grade 3*	All grades	Grade 3*	All grades	Grade 3*
At least one TEAE, n (%)	13 (81.3)	4 (25.0)	5 (100.0)	4 (80.0)	21 (100.0)	7 (33.3)
Gamma-glutamyltransferase increased	2 (12.5)	0	1 (20.0)	0	5 (23.8)	0
Anaemia	3 (18.8)	3 (18.8)	2 (40.0)	2 (40.0)	4 (19.0)	4 (19.0)
Abdominal pain upper	2 (12.5)	0	0	0	4 (19.0)	0
Alanine aminotransferase increased	2 (12.5)	0	0	0	4 (19.0)	0
Aspartate aminotransferase increased	1 (6.3)	0	0	0	4 (19.0)	0
Constipation	1 (6.3)	0	0	0	4 (19.0)	0
Hyperuricaemia	1 (6.3)	0	1 (20.0)	0	4 (19.0)	0
Hypokalaemia	2 (12.5)	0	2 (40.0)	0	4 (19.0)	0
Nausea	1 (6.3)	0	2 (40.0)	0	2 (9.5)	0
Hepatic function abnormal	0	0	1 (20.0)	1 (20.0)	2 (9.5)	0
Thoracic vertebral fracture	1 (6.3)	1 (6.3)	0	0	1 (4.8)	1 (4.8)
Respiratory tract infection	0	0	1 (20.0)	1 (20.0)	1 (4.8)	1 (4.8)
Lymphocyte count decreased	0	0	1 (20.0)	1 (20.0)	0	0

TEAE: treatment-emergent adverse event. TEAEs were presented with incidence >20% of all grade or with all grade ≥3 events in any group in 0-8weeks, or with incidence >15% of any grade in 0-24 weeks.
*, No grade 4 or 5 TEAEs were reported in the study.

Keywords: Anemia, Autoimmune hemolytic anemia (AIHA), SYK