Abstract: S316

Title: EFFICACY AND SAFETY OF THE SYK INHIBITOR SOVLEPLENIB (HMPL-523) IN ADULT PATIENTS WITH PRIMARY IMMUNE THROMBOCYTOPENIA IN CHINA (ESLIM-01): A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 3 STUDY

Abstract Type: Oral Presentation

Session Title: Platelet disorders in the spotlight: Clinical and translational

Background:

Sovleplenib is a novel spleen tyrosine kinase inhibitor that demonstrated promising safety and efficacy in patients (pts) with primary immune thrombocytopenia (ITP) in a phase 1b/2 trial.

Aims:

A pivotal trial (ESLIM-01) was conducted to assess the efficacy and safety of sovleplenib for the primary ITP pts in China (NCT05029635).

Methods:

This randomized, double-blind, placebo-controlled phase 3 trial was conducted in pts with primary ITP who had received ≥1 previous anti-ITP treatment.

Pts were randomized (2:1) to receive sovleplenib or placebo, 300 mg orally QD, for 24 weeks (wks), and were stratified by baseline platelet counts (cut-off 15×10^9 platelets/L), prior splenectomy and concomitant anti-ITP therapy at baseline. Pts not responding to study treatment within the first 12 wks could enter an open-label sub-study to receive sovleplenib 300 mg QD.

The primary endpoint was durable response rate (platelet counts ≥50×10^9 platelets/L on at least 4 of 6 scheduled visits during wks 14–24, not impacted by rescue therapy).

Results:

From 2021-09-29 to 2022-12-31, 188 randomized pts received sovleplenib (N=126) or placebo (N=62). At baseline, most patients had ITP for ≥3 years (77.7%), median prior lines of ITP therapy was 4.0 and 134 (71.3%) patients had received prior TPO/TPO TPO-RA treatment. The median treatment duration was 24.1 vs. 12.1 wks with sovleplenib vs. placebo, and 86 (68.3%) vs. 8 (12.9%) pts receiving treatment for 24 wks.

The durable response rate was significantly higher with sovleplenib, than with placebo (48.4% vs. 0%, p <0.0001 in ITT pts; 46.8% vs. 0%, p <0.0001 in pts with prior TPO/TPO-RA treatment). The median platelet counts were higher in sovleplenib group than placebo group at all post-baseline visits and were 90–100×10^9 platelets/L for the durable responders in sovleplenib group. Among the durable responders, 51 of 61 (84%) pts responded at least 5 of 6 clinic visits and 39 of 61 (64%) at all 6 clinic visits within the week 14–24.

In addition, sovleplenib showed a significantly higher overall response rate (at least 1 platelet count ≥50×10^9 platelets/L, not caused by rescue therapy) in wks 0–12 (68.3% vs. 14.5%, p<0.0001) and wks 0–24 (70.6% vs. 16.1%, p<0.0001), decreased rescue medication use during the treatment (22.2% vs. 35.5%, p=0.0451), reduced mean of WHO bleeding scale in wks 0–12 (least squares mean: 0.6 vs. 0.8, p=0.0019) and wks 0–24 (0.6 vs. 0.8, p=0.0002), compared to placebo. The median time to response was 1.1 wks vs. 4.3 wks.

Grade ≥3 treatment-emergent adverse events (TEAEs) were reported in 32 (25.4%) patients with sovleplenib and 15 (24.2%) patients with placebo. The frequent (≥20% with sovleplenib) TEAEs were upper respiratory tract infections (28.6% vs 9.7%), COVID-19 infection (23.8% vs 12.9%), blood lactate dehydrogenase increased (23.8% vs 6.5%). Most events were mild or moderate and resolved spontaneously or with intervention.

Quality of life was significantly improved with sovleplenib in domains of physical functioning and energy/fatigue ($p<0.05$), compared to placebo.

Summary/Conclusion:

Sovleplenib demonstrated a clinically meaningful early and sustained durable platelet response in primary ITP patients, with a tolerable safety profile and improvement in patient quality of life. Sovleplenib could be a potential treatment option for ITP who have received ≥1 prior therapy.

Keywords: Immune thrombocytopenia (ITP), SYK