

Abstract: LB2712

Title: CEVIDOPLLENIB, A SELECTIVE INHIBITOR OF SPLEEN TYROSINE KINASE (SYK), IN PERSISTENT AND CHRONIC IMMUNE THROMBOCYTOPENIA (ITP): EFFICACY AND SAFETY IN A MULTICENTER, PLACEBO CONTROLLED PHASE 2 STUDY

Abstract Type: Oral Presentation

Session Title: Late-Breaking Oral Session

Background:

Immune thrombocytopenia (ITP), an autoimmune disorder is caused by autoantibodies that target platelets, leading to a low platelet count. This can result in bruises and potentially life-threatening internal bleeding. There is an urgent need for a safer and more efficacious treatment option as many ITP patients are refractory to the current standard therapies including thrombopoietin-receptor agonists (TPO-RAs). Cevidoplenib (SKI-O-703) is a highly potent and selective inhibitor of spleen tyrosine kinase (SYK). By inhibiting the signaling downstream of B cell and Fc receptors, SYK inhibitor is expected to be effective in autoantibody-driven pathologies including ITP. In particular, targeting SYK may be an effective way to increase platelet counts by reducing B cell-driven autoantibody production as well as ameliorating macrophage-mediated platelet destruction.

Aims:

To evaluate the efficacy and safety of cevidoplenib in persistent and chronic ITP patients who are refractory to the conventional therapy.

Methods:

The efficacy and safety of oral cevidoplenib (CVP) were evaluated in the Phase II multicenter, randomized, double-blind, placebo (PBO)-controlled, parallel dose trial (NCT04056195) in adults with persistent and chronic ITP who had failed to respond to or relapsed after prior therapy. Stable doses of background medications including corticosteroids and immunosuppressive drugs were permitted but the doses were fixed for at least 2 weeks before Day 1 and remained unchanged throughout the treatment period. Sixty-one participants were randomly assigned to 3 groups using a 2:2:1 ratio to receive 400 mg, 200mg CVP, and PBO twice daily for 12 weeks. The primary endpoint was the proportion of participants with platelet response, defined as platelet count $\geq 30,000/\mu\text{L}$ and doubling the baseline (average of 2 previous counts) without the use of rescue medication. Key secondary endpoints included the proportion of participants achieving pre-specified PLT count.

Results:

Sixty-one participants were randomized (23 in 400mg CVP, 26 in 200 mg CVP, and 12 in PBO, respectively), where 1 was never dosed. Participants had severe ITP (median baseline PLT of $8,500/\mu\text{L}$) and 68.3% of the participants had received ≥ 3 previous lines of therapies. On cevidoplenib, 14 of 22 patients (63.6%) in 400 mg and 12 of 26 patients (46.2%) in 200 mg achieved an overall platelet response, compared with 4 of 12 (33.3%) on placebo group ($P=0.151$ and $P=0.504$ for 400mg and 200mg CVP, respectively, vs PBO). Participants achieving 2 or more consecutive PLT counts $\geq 50,000/\mu\text{L}$ without the use of rescue medication were 40.9% on 400 mg CVP, 19.2% on 200 mg CVP vs. 8.3% on PBO ($P=0.055$ and $P=0.371$ for 400 mg and 200 mg CVP, respectively, vs. PBO). Sustained PLT count (defined retrospectively as PLT counts $\geq 50,000/\mu\text{L}$ at ≥ 4 of the last 6 visits) was reached in 27.3% on 400 mg CVP and 19.2% on 200 mg CVP vs. 0% on PBO. Mean change from baseline in the average of the last 2 available PLT counts (SD) were $41,600/\mu\text{L}$ (46,586) on 400 mg CVP, $36,020/\mu\text{L}$ (50,270) on 200mg CVP and $17,500/\mu\text{L}$ (26,821) on PBO. Platelet responses to cevidoplenib were consistent regardless of prior TPO-RAs use or baseline PLT counts $< 15,000/\mu\text{L}$.

Adverse events (AEs) were reported in 66.7% in the combined CVP groups (32 out of 48 participants treated with cevidoplenib) and 66.7% in the PBO group (8 out of 12 participants). The most frequently reported treatment-

related adverse events were ALT increase (8.3%), AST increase (6.3%) and nausea (4.2%). Most AEs were grade 1 or 2. Serious AEs were reported in 4.2% of the combined CVP group and 25% in the PBO. Treatment related grade 3 or 4 AEs were observed in 6.3% participants in the combined CVP group and resolved spontaneously or with medical management. No death was observed.

Summary/Conclusion:

Cevidoplenib 400 mg twice daily was generally well tolerated and demonstrated robust platelet responses in a significant proportion of participants who had failed multiple prior therapies. It warrants further clinical studies in a larger number of participants for an extended period to confirm durability of the clinical benefits.