(PB3439) OB756, A NOVEL SELECTIVE JAK2 INHIBITOR, IN PATIENTS WITH MYELOFIBROSIS AND BASELINE THROMBOCYTOPENIA (<100×10⁹/L), ANEMIA (<100 G/L), AND MASSIVE SPLENOMEGALY: AN EXPLORATORY ANALYSIS

Topic: 16. Myeloproliferative neoplasms - Clinical

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Background

Myelofibrosis (MF) patients frequently develop thrombocytopenia during disease diagnosis or treatment, with approximately 25% of MF patients presenting with moderate to severe thrombocytopenia at diagnosis. For patients with poor baseline characteristics such as severe cytopenia (thrombocytopenia, anemia), high-risk mutations, or massive splenomegaly, treatment options are extremely limited and clinical prognosis is poor. Existing JAK inhibitors generally require platelet counts ≥100×10⁹/L, failing to meet the clinical needs of this population.

Aims

This study aims to evaluate the efficacy and safety of novel JAK2 inhibitor OB756 in myelofibrosis patients with severe baseline cytopenia and massive splenomegaly who are ineligible for existing JAK inhibitors due to platelet count restrictions.

Methods

This study aimed to evaluate the safety and efficacy of OB756 in intermediate- to high-risk MF patients with platelet counts <100×10⁹/L, hemoglobin <100 g/L, or spleen volume >1500 cm³. This project integrated CTR20211396 and CTR2500105524, enrolling patients with primary MF (PMF), post-polycythemia vera MF (Post-PV-MF), or post-essential thrombocythemia MF (Post-ET-MF). Inclusion criteria included: Dynamic International Prognostic Scoring System (DIPSS) intermediate-2 or high risk, spleen volume >1500 cm³, platelet count <100×10⁹/L, and hemoglobin <100 g/L. The primary endpoint was the proportion of patients achieving ≥35% reduction in spleen volume from baseline at Week 24 (SVR35, assessed by Independent Review Committee [IRC]). Key secondary endpoints included: proportion of patients achieving ≥50% reduction in Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score (MPN-SAF TSS) from baseline; safety.

Results

A total of 12 patients receiving OB756 20 mg twice daily (BID) were enrolled across the two trials. Baseline characteristics were as follows: median age 58 years (range 51-74), 8 females (66.7%); ECOG performance status score 1 in 2 patients (16.7%), 2 in 8 patients (66.7%), and 3 in 2 patients (16.7%). Among enrolled patients, anemia was Grade 2 in 7 patients, Grade 3 in 3 patients, and Grade 4 in 1 patient; thrombocytopenia was Grade 1 in 9 patients and Grade 2 in 3 patients. Efficacy results showed: IRC-assessed SVR35 rate at Week 24 was 66.7% (8/12). Hematologic monitoring demonstrated relatively stable platelet counts, hemoglobin, and white blood cell counts during treatment without significant further decline; additionally, 4 patients achieved normalized platelet counts at Week 24. Regarding symptom improvement, 58.3% (7/12) of patients achieved ≥50% reduction in MPN-SAF TSS at Week 24.Safety analysis showed no obvious worsening of hematologic toxicity beyond the existing baseline thrombocytopenia and anemia. For non-hematologic toxicities, Grade 3 or higher infection occurred in 8.3% (1/12).

Summary/Conclusion

Conclusion: In summary, OB756 demonstrated favorable tolerability and significant clinical efficacy in intermediate- to high-risk MF patients with severe cytopenia and massive splenomegaly, particularly showing outstanding efficacy in rapidly reducing spleen volume, with low incidence of non-hematologic toxicities. This study provides a new treatment option for MF patients with poor baseline characteristics.

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