## (PS1990) A NOVEL JAK2 INHIBITOR OB756 FOR POLYCYTHEMIA VERA WITH SPLENOMEGALY: A PHASE IB/II, MULTICENTER STUDY

**Topic:** 16. Myeloproliferative neoplasms - Clinical

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### Background

OB756, is a novel oral, small molecule Janus kinase2（JAK2）inhibitor, was shown to have a clinical benefit in patients with myeloproliferative neoplasm (MPN) in phase 1 study. Here we conducted a phase Ib/II multicenter study to evaluate the safety and efficacy of OB756 in polycythemia vera (PV) patients with splenomegaly.

### Aims

We conducted a phase Ib/II multicenter study to evaluate the safety and efficacy of OB756 in polycythemia vera (PV) patients with splenomegaly.

### Methods

A multicenter, phase Ib/II trial (CTR20201950) was conducted at 11 sites in China. Eligible patients aged ≥18 years with polycythemia vera (PV) with splenomegaly intolerant or resistant to hydroxyurea or interferon were enrolled in this study. Patients were required to have Eastern Cooperative Oncology Group (ECOG) performance status ≤2. Patients were treated with OB756 16 mg or 20 mg twice daily in continuous 28-day cycles until lack of efficacy, intolerance, or disease progression. The primary endpoint was complete haematologic response (CHR) rate at 24 week. The secondary key endpoints included spleen volume reduction ≥35% (SVR35), haematologic response (HR), molecular response, and safety.

## Results

Between November 3, 2020 and January 20, 2026, 51 patients of PV with splenomegaly were enrolled and treated with either OB756 16 mg BID or 20 mg BID. Median treatment duration was 508 (range, 29~1066) days. At baseline, median age was 63 (range, 34-73) years, and 26/51 (52.0%) patients were men. Baseline median spleen volume was 633.8 (rang, 400~4015)$cm^3$. The percentages of intermediate and high risks based on survival risk status in PV patients were 35.3% (18/51) and 52.9% (27/51), respectively **(Figure A)**. A total of 42/51 (82.4%) evaluable patients met the primary endpoint of CHR at week 24. 26.2% (11/42) of patients achieved CHR at week 24, and 26.3% (10/38) of patients achieved CHR at week 48. In addition, 20/49 (40.8%), and 14/32 (43.8%) patients achieved CHR at EOC3, EOC9, respectively **(Figure B)**. High percentage of hematocrit control was achieved with 81.4% (35/43) at week 24. Similarly, HR rates was achieved with 41/50(82.0%), 37/46(80.4%), 28/30(93.3), and 37/39 (94.8%) at EOC3, EOC6, EOC9, and EOC12, respectively **(Figure C)**. Patients with splenomegaly at baseline achieved SVR35 was 65.9% (29/44) at week 24 **(Figure D)**. The median spleen reduction was -40.3% (-83.7% to -0.05%), -39.6% (-83.7% to -0.06%) at EOC6, and EOC12, respectively. MPN-TSS decreased ≥ 50% were recorded with 76.7% (23/30) at week 24 **(Figure F)**. The mean change in the JAK2-V617F allele burden from baseline to 48 week was –9.0% **(Figure E)**. The most common treatment-emergent adverse events (TEAEs) were 1~2 grade, and only 1/51 (2.0%) patients were observed with thrombocytopenia. No death was reported with related to disease progression of PV or OB756. TEAEs were generally manageable.

## Summary/Conclusion

OB756 was well tolerated and showed meaningful clinical benefits in PV patients with splenomegaly, especially for quick spleen reduction. OB756 may be a new treatment option for PV patients with splenomegaly. Furthermore, a randomized double-blind phase 3 study is ongoing, aiming to assess the efficacy and safety of OB756 compared to hydroxyurea in patients with PV in China (CTR20240873).

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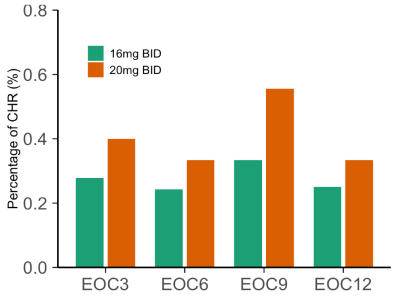
**A**

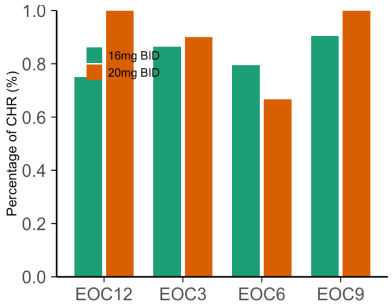
Table 1. Baseline Demographic and Clinical Characteristics of PV Patients with Splenomegaly.

| Characteristic | 16mg BID (N=41) | 20mg BID (N=10) | Total (N=51) |
|---|---|---|---|
| Age(y), median (range) | 63(34-79) | 64(53-73) | 63(34-73) |
| Sex, n(%) | | | |
| Male | 19 | 7 | 26(51.0) |
| Female | 22 | 3 | 25(49.0) |
| Diease duration (months), median (range) | 55(0-219) | 54(0-160) | 55(0-219) |
| Thrombosis risk status in PV | | | |
| Low | 35 | 7 | 42(82.4) |
| High | 6 | 3 | 9(17.6) |
| Survival risk status in PV | | | |
| Low | 5 | 1 | 6(11.8) |
| Intermediate | 15 | 3 | 18(35.3) |
| High | 21 | 6 | 27(52.9) |
| *JAK2* mutational profile, n(%) | | | |
| *JAK2 V617F* | 41 | 10 | 51(100.0) |
| *JAK2 Exon12* | 0 | 0 | 0(0.0) |
| Frequency of *JAK2 V617F* mutation(%), median (range) | 50.0(4.0-100) | 48.0(25.0-91.9) | 51.0(4.0-100) |
| History of thrombosis, n (%) | 7(1.9) | 3(7.6) | 10(19.2) |
| WBC ($x10^9$/L), median (range) | 13.6(3.4-43.9) | 10.9(3.7-32.0) | 13.2(3.4-43.9) |
| Platelets ($x10^9$/L), median (range) | 478(100-1456) | 571 (282-922) | 536(100-1456) |
| Hemstocrit (%), median (range) | 51.5(37.8-62.5) | 47.5(36.9-63.7) | 51.2(36.9-63.7) |
| MPN-SAF TSS | 8(0-31) | 7(0-30) | 8(0-31) |
| Spleen volume, $cm^3$ (range) | 637(400-4015) | 546(443-2099) | 633.8(400-4015) |

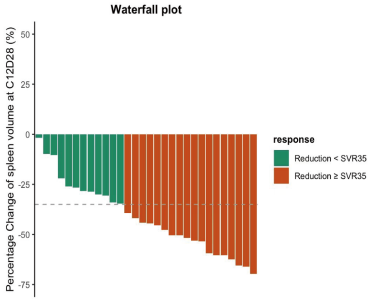
**B**



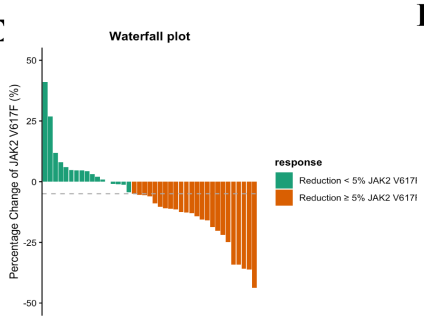

**C**




**D**




**E**




**F**