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# RUSFERTIDE (PTG-300) ELIMINATES THE NEED FOR THERAPEUTIC PHLEBOTOMY IN BOTH LOW AND HIGH-RISK POLYCYTHEMIA VERA (PV) PATIENTS

Topic: 16. Myeloproliferative neoplasms - Clinical

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**Background:** Polycythemia vera (PV) patients are treated with periodic therapeutic phlebotomy (TP) to maintain hematocrit levels <45% in an effort to reduce the incidence of thrombotic events. PV patients likely spend significant time with hematocrit levels >45%, between TP and increase the risk of thrombosis. Hepcidin is the body's main negative regulator of iron metabolism such that elevated hepcidin levels are expected to reduce iron availability and decrease erythropoiesis. Rusfertide (PTG-300) is a hepcidin-mimetic. We hypothesized that rusfertide would decrease erythropoiesis and phlebotomy requirement in PV patients.

**Aims:** The current study aims to compare the iron status and phlebotomy requirements in high TP-requiring PV patients before and during treatment with rusfertide.

**Methods:** PTG-300-04 is a Phase 2 trial consisting of 3 parts: (1) a 28-week dose-finding; (2) a 12-week blinded randomized withdrawal (1:1) rusfertide vs placebo; and (3) a 52-week open label extension (**NCT04057040**). Eligibility criteria include PV diagnosis and ≥3 phlebotomies with or without concurrent cytoreductive therapy to maintain hematocrit <45% in the 24 weeks prior to enrollment. Rusfertide doses of 10, 20, 40, 60 and 80 mg administered subcutaneously weekly were added on to each subject's pre-study treatment for PV and the dose of rusfertide was adjusted to maintain hematocrit <45%.

**Results:** Thirty-five patients were enrolled to date: 16/35 with low-risk PV, age rangd between 31-75yrs. Prior to enrollment all patients received TP range of TP 3-9; median time between TP = 36 days. In addition, out of 35 patients; 8 patients received concurrently hydroxyurea, 3 patients received concurrently interferon, and 1 patient received concurrently ruxolitinib. The rate of TP after starting rusfertide decreased significantly compared to the rate of TP before starting rusfertide ($p< 0.0001$). Four subjects required one TP early in the dose-finding period (within 12 weeks) and 3 have subsequently been TP-free after increasing the dose of rusfertide. Thirteen patients have completed 28 weeks of dosing in Part 1. Ten patients were TP-free for 28 weeks; 2 patients required 1 TP each and 1 required 2 compared to >3 TP each over 28 weeks pre-study. Hematocrit was <45% at study entry and remained continuously <45% during the study. Prior to treatment, mean ferritin levels were consistent with systemic iron deficiency while serum ferritin increased progressively toward normal range during the study. Furthermore, both MCV and MCH values increased suggesting a redistribution of iron within erythropoiesis. The most frequent adverse events (AE) were injection site reactions (ISR) reported by 9 patients. Most of the ISR were grade 1 and there were no drug related SAE.

**Summary/Conclusion:** The current results indicate that rusfertide is an effective agent for the treatment of PV, reversing iron deficiency and eliminating the need for TP in PV patients. Elimination of TP requirements for 7 months in TP-dependent PV patients is significant and unexpected. The effect of rusfertide on PV-related symptoms is also being evaluated. Continued patient enrollment will enable more definitive conclusions regarding the efficacy and safety of rusfertide in PV patients. Rusfertide looks very promising in maintaining hematocrit <45% and in eliminating the therapeutic phlebotomies in both low and high-risk PV patients.

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