INTRODUCTION

Patients with polycythemia vera (PV) are treated with periodic therapeutic phlebotomy (TP) to maintain hematocrit levels <45% to reduce the incidence of thrombotic events. Since many PV patients are seen irregularly, they may experience periods of time with hematocrit >45%, potentially increasing thrombotic risk, especially in patients with high TP requirements. Hepcidin is the body’s main iron homeostasis regulatory hormone and elevated hepcidin levels are expected to reduce iron availability and control excessive erythropoiesis. We hypothesized rusfertide (PTG-300), a potent hepcidin mimetic, could decrease erythropoiesis and phlebotomy requirements in PV patients, thereby alleviating PV-related symptoms.

OBJECTIVE

To examine the impact of rusfertide therapy on TP and patient reported symptoms in PV.

METHODS

• PTG-300-04 (REVIVE study, NCT04057040) is a phase 2 study consisting of three parts: (1) a 28-week dose-finding; (2) a 12-week blinded randomized withdrawal rusfertide vs placebo (2:1); and (3) a 52-week open-label extension (Fig 1).
• Eligibility criteria include PV diagnosis (by 2016 WHO criteria) and ≥3 phlebotomies with or without concurrent cytoreductive therapy to maintain hematocrit <45% in the 28 weeks prior to enrollment.
• Rusfertide was administered subcutaneously weekly and was added to each subject’s pre-randomization therapy for PV; rusfertide dose was adjusted to maintain hematocrit <45%.
• Patients completed the 10 question Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score 10 (MPN-SAF TSS 10) at protocol-specific visits.
• Symptoms relating to fatigue, early satiety, abdominal discomfort, inactivity, problems with concentration, night sweats, itching, bone pain, fever and unintentional weight loss were assessed.
• Each question has a range of 0-10.
• Higher scores indicate higher severity.

RESULTS

• 70 subjects were enrolled, 61 subjects completed the dose titration phase through week 28 and 9 subjects discontinued. 53 subjects completed Part 2 of the study.
• Rusfertide met the primary efficacy endpoint of reduction in therapeutic phlebotomies during the randomized withdrawal (weeks 29-41) (Fig 2).
• Rusfertide significantly delays time to event on the outcomes of absence of phlebotomy eligibility and hematocrit <45% compared to placebo (Fig 3).
• Consistency of effect on being phlebotomy-free can be seen in the open-label as well as the double-blind parts of the study (Fig 4).
• In subjects with moderate or severe symptoms at baseline, statistically significant improvement in symptoms of Fatigue, Problems with concentration, itching and Inactivity was seen (Fig 5).

CONCLUSION

Rusfertide is a hepcidin mimetic under clinical investigation for the treatment of PV. These results demonstrate that rusfertide was well tolerated and highly effective in maintaining hematocrit <45%, obviating the need for phlebotomy in most patients, reverting iron deficiency, and improving PV-related symptoms.

CONTACT INFORMATION

Andrew T Kuykendall, H. Lee Moffitt Cancer Center, Tampa, FL, USA. Andrew.Kuykendall@moffitt.org
SuneeL Gupta, Protagonist Therapeutics, Inc, Newark CA, USA. S.Gupta@ptgx-inc.com