

VERIFY: A PHASE 3 STUDY OF THE HEPCIDIN MIMETIC RUSFERTIDE (PTG-300) IN PATIENTS WITH POLYCYTHEMIA VERA

Srdan Verstovsek, MD PhD¹, Andrew Kuykendall, MD², Ronald Hoffman, MD³, Steffen Koschmieder, MD⁴, Francesco Passamonti, MD⁵, Frank Valone MD⁶, Nishit B Modi PhD⁶, Sarita Khanna PhD⁶, Paula O'Connor MD, Suneel K Gupta PhD⁶, Jean-Jacques Kiladjian MD, PhD⁷

¹Department of Leukemia, M.D. Anderson Cancer Center, Houston, TX, ²Department of Malignant Hematology, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL ³Division of Hematology Oncology, Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY; ⁴Department of Hematology, Oncology, Hemostaseology and Stem Cell Transplantation, Faculty of Medicine, University Hospital of Aachen, Aachen, Germany; ⁵Hematology, Department of Medicine and Surgery, University of Insubria, Varese, Italy; ⁶Protagonist Therapeutics, Newark, CA; ⁷Hôpital Saint-Louis; Université de Paris, INSERM, Paris, France



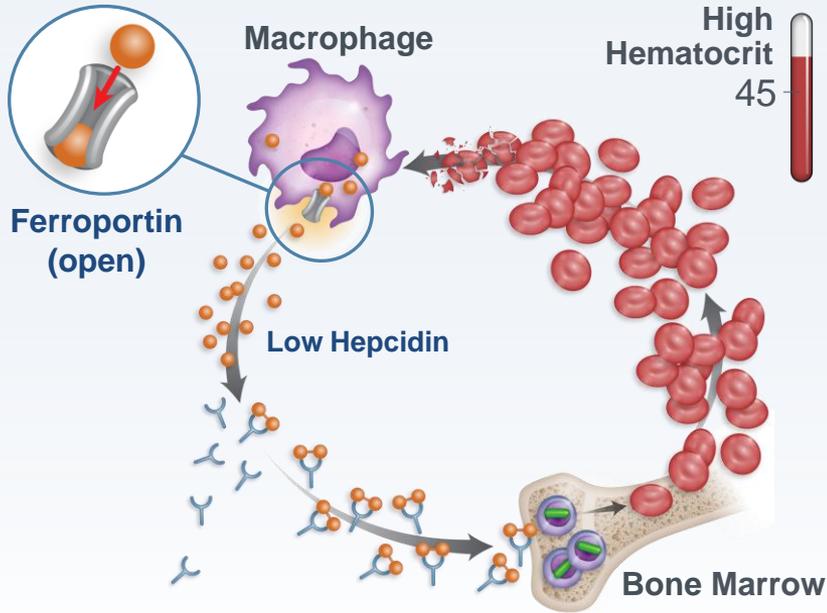
I Introduction

- Polycythemia Vera (PV) is characterized by increased red blood cell production
- PV patients likely spend significant time with hematocrit (HCT) > 45% thereby increasing their risk of thrombosis.
- PV patients are treated with periodic therapeutic phlebotomy (TP) to maintain hematocrit levels < 45% to reduce the incidence of thrombotic events.
- Symptomatic iron deficiency represents a challenge in PV as it is commonly present at diagnosis and worsens after repeated and/or frequent TP.
- Rusfertide, a hepcidin mimetic, presents an alternate mechanism of action to limit erythrocytosis, maintaining HCT <45%, essentially eliminating phlebotomies and reducing PV-related symptom burden.



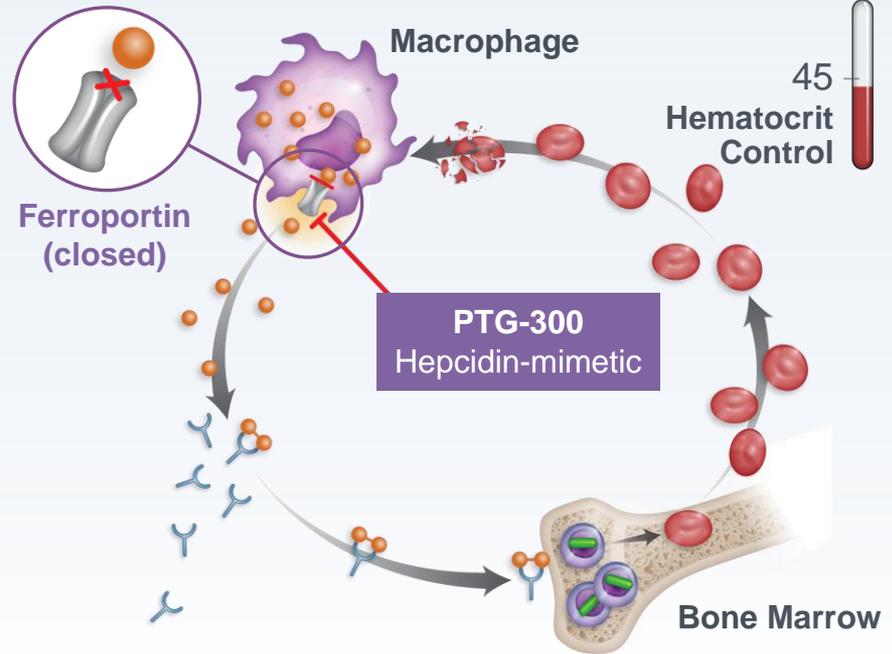
Rusfertide Mechanism of Action

Polycythemia Vera



Transferrin (TF) Iron (Fe) TF-Fe

PTG-300 Reduces Erythrocytosis



Erythroblast JAK2 Red Blood Cell

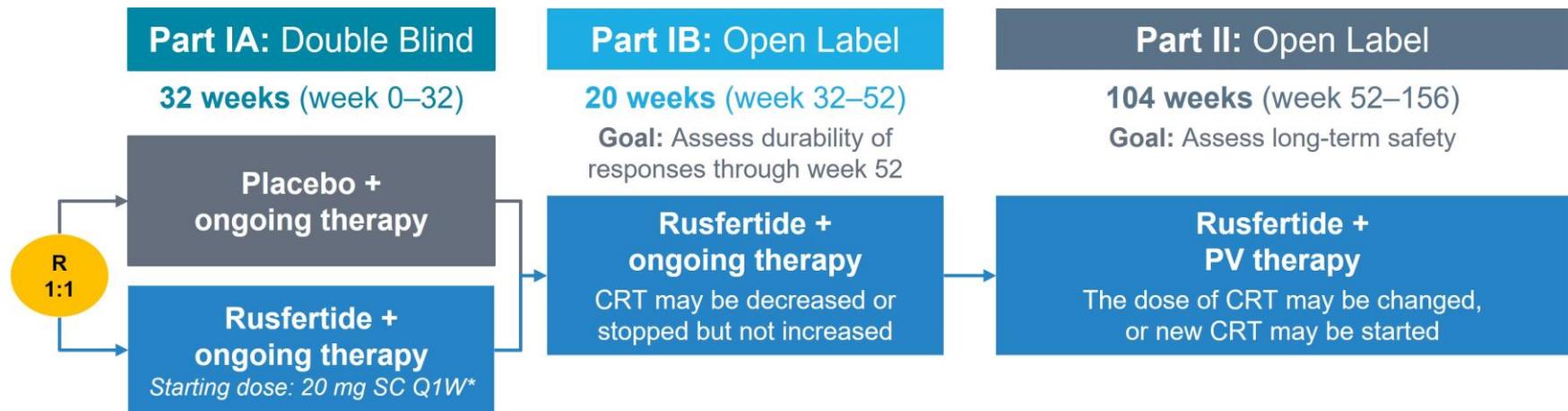


| Phase 2 Data

- Two ongoing Phase 2 studies in PV subjects suggest that rusfertide could be an effective agent for treatment of PV, reversing iron deficiency and eliminating the need for TP in PV patients.
- Elimination of TP requirements for 6-8 months in TP-dependent PV subjects is significant. The effect of PTG-300 on PV-related symptoms is also being evaluated.
- Rusfertide maintains HCT < 45% and essentially eliminates TP in both low and high-risk PV patients.
- Rusfertide induction therapy with twice weekly dosing was also effective in rapidly achieving target hematocrit below 45% in PV patients with elevated hematocrit.



Study Schematic



Approximately 250 subjects to be randomized
Trial currently recruiting globally



Key Inclusion Criteria

- Age ≥ 18 years
- Meet revised 2016 World Health Organization (WHO) criteria for the diagnosis of polycythemia vera.
- Phlebotomy requiring defined as: (a) ≥ 3 phlebotomies due to inadequate hematocrit control in 6 months before randomization or at least 5 phlebotomies due to inadequate hematocrit control in 1 year before randomization, **and** (b) last phlebotomy due to inadequate hematocrit control within 3 months before randomization, **and** (c) no phlebotomy within 6 days prior to randomization
- Subjects may on stable regimen with Phlebotomy alone or in combination with cytoreductive agents (Hydroxyurea, Interferon and Ruxolitinib).



| Key Exclusion Criteria

- Subjects requiring phlebotomy at hematocrit levels lower than 45%
- History of invasive malignancies within the last 5 years, except localized cured prostate cancer and cervical cancer
- Subjects with non-invasive non-melanomatous skin cancer during screening unless adequately treated before randomization



End Points

Primary:

- Proportion of subjects achieving a response starting at Week 20 through Week 32 (inclusive) who receive rusfertide compared to placebo. Response is defined as absence of phlebotomy eligibility. Phlebotomy eligibility is defined as
 - **either** a confirmed hematocrit $\geq 45\%$ and that is at least 3% higher than the baseline hematocrit (value immediately prior to randomization at Week 0); confirmation required within 1 to 7 days
 - Hemoglobin $\geq 48\%$

Key Secondary:

- Mean number of phlebotomies between Weeks 0 to 32 (inclusive)
- Proportion of subjects with all hematocrit values $< 45\%$ between Weeks 0 and 32 (inclusive)
- Mean change from baseline in total fatigue score based on PROMIS Short Form 8a at Week 32
- Mean change from baseline in total score based on MFSAF v4.0 at Week 32

