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

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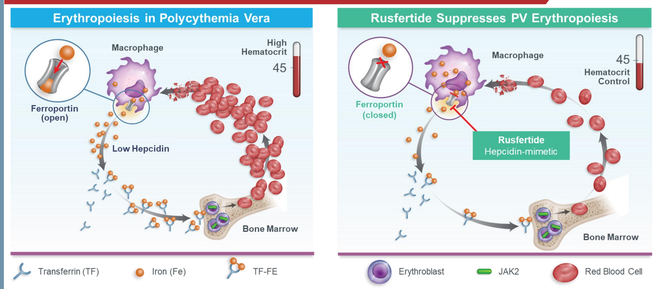
BACKGROUND AND RATIONALE

- 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

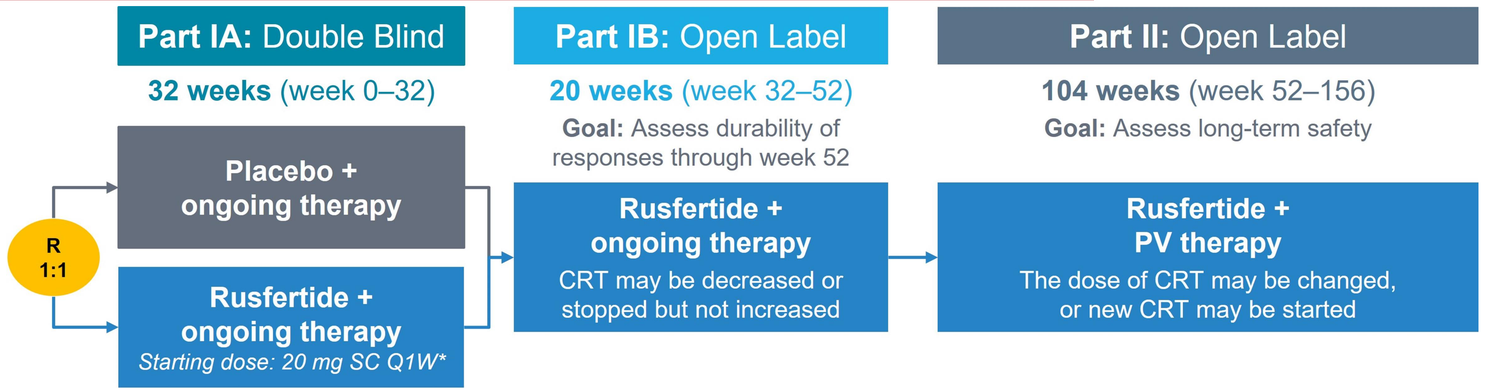
RUSFERTIDE MECHANISM OF ACTION



RUSFERTIDE DATA IN PHASE 2 PV STUDIES

- 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.

TRIAL DESIGN



Approximately 250 subjects to be randomized
Trial currently recruiting globally

OBJECTIVES

Primary Objective:

To evaluate the safety and efficacy of rusfertide in subjects with polycythemia vera in maintaining hematocrit control.

PRIMARY AND KEY SECONDARY OBJECTIVES

Primary Efficacy Endpoint:

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 ≥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, **or** a hematocrit ≥48%.

Key Secondary Efficacy Endpoints: Rusfertide vs Placebo

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

KEY ELIGIBILITY CRITERIA

Inclusion Criteria:

1. Age ≥18 years
2. Meet revised 2016 World Health Organization (WHO) criteria for the diagnosis of polycythemia vera.
3. 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
4. Subjects may on stable regimen with Phlebotomy alone or in combination with cytoreductive agents (Hydroxyurea, Interferon and Ruxolitinib).

Exclusion Criteria:

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