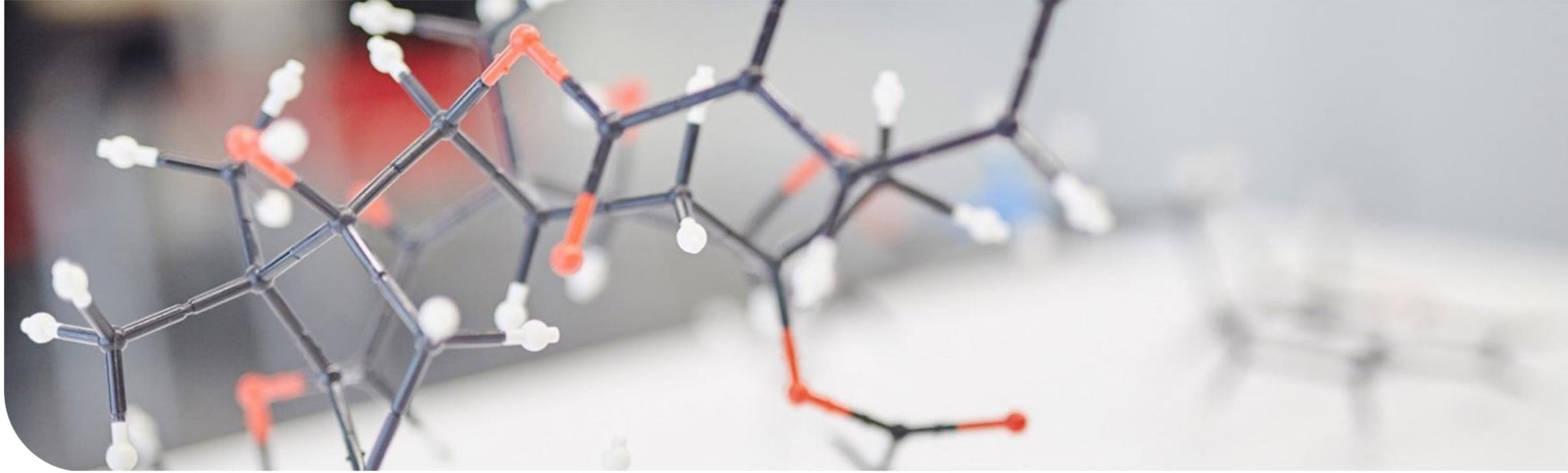

Rusfertide 2025
Post-Congress Reactive Deck

VV-MEDMAT-122737 | June 2025
Global/US Medical

ONCOLOGY

Disclaimers

- Diese Folien wurden zur reaktiven Nutzung durch das Medical-Team im wissenschaftlichen Austausch mit HCPs erstellt, als Antwort auf nicht angeforderte Informationsanfragen zu den hierin enthaltenen Themen.
- Antworten müssen gezielt auf die nicht angeforderte Anfrage zugeschnitten sein und den entsprechenden Kontext vollständig enthalten.
- Das Medical-Team sollte seine professionelle Einschätzung nutzen, um passende Folien in einer Reihenfolge zu präsentieren, die am besten dazu geeignet ist, die nicht angeforderte Anfrage gezielt zu beantworten.
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- Dieses Deck darf nicht vom Vertrieb oder für Vertriebs-Training verwendet werden.
- Rusfertide (TAK-121) ist für die hier beschriebenen Anwendungen nicht zugelassen und eine Zulassung dafür ist derzeit ungewiss.

Company-Sponsored Research

Results From VERIFY, a Phase 3, Double-Blind, Placebo-Controlled Study of Rusfertide for Treatment of Polycythemia Vera (PV)

ASCO 2025
Kuykendall *et al.*

Company-Sponsored Research

Results From VERIFY, a Phase 3, Double-Blind, Placebo-Controlled Study of Rusfertide for Treatment of Polycythemia Vera (PV)

Andrew T. Kuykendall[1], Naveen Pemmaraju[2], Kristen Pettit[3], Joseph Shatzel[4], Alessandro Lucchesi[5], Valentín García-Guitérrez[6], Jiri Mayer[7], Abdulraheem Yacoub[8], Harinder Gill[9], Antonin Hlusi[10], Daniel Sasca[11], Joseph M. Scandura[12], Marina Kremyanskaya[13], Phil Dinh[14], Sarita Khanna[14], Suneel Gupta[14], Arturo Molina[14], Aniket Bankar[15] on behalf of the VERIFY Investigators

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Authors' Conclusions

1. Phase 3 VERIFY study compared the hepcidin mimetic rusfertide to placebo (each added to current standard-of-care) in patients with polycythemia vera

2. Rusfertide met its primary endpoint, all key secondary endpoints, and had a manageable safety profile consistent with prior studies

3. Rusfertide led to statistically significant improvements in several patient reported outcome measures

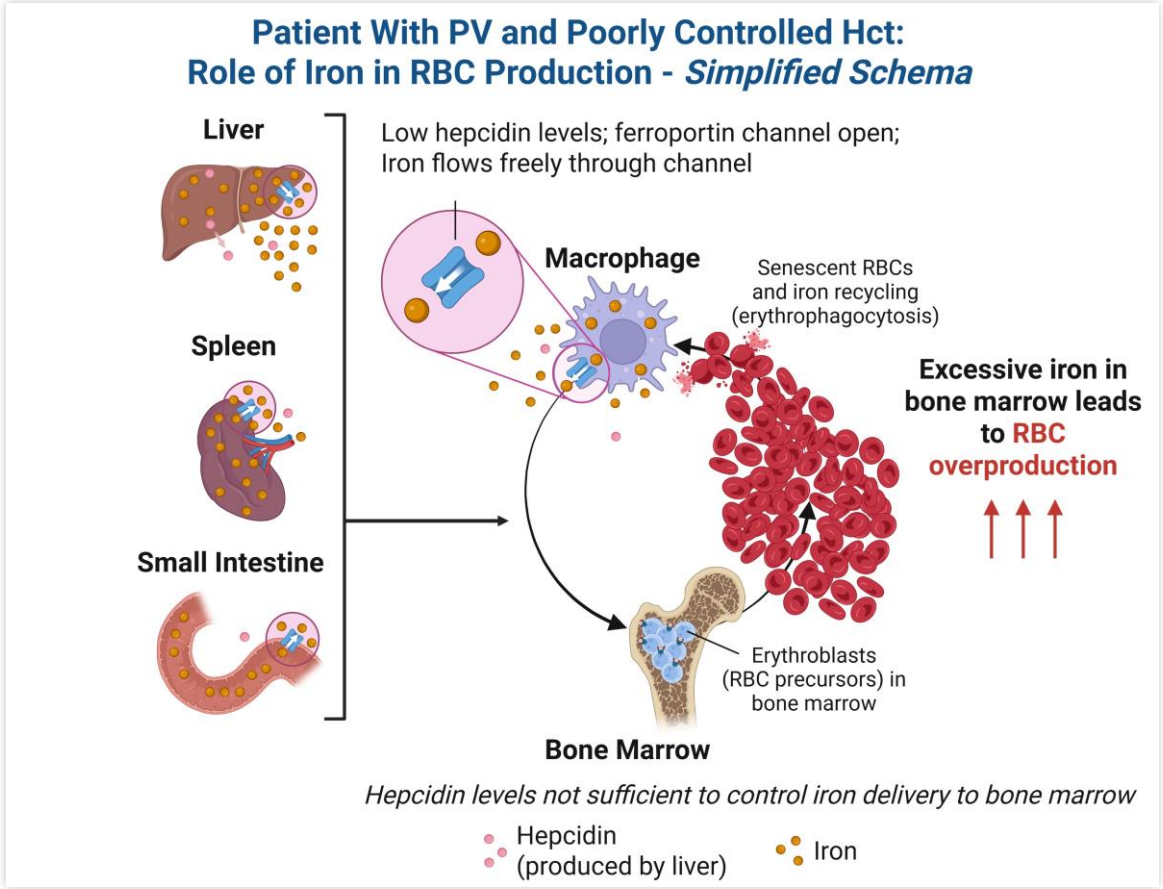
Background

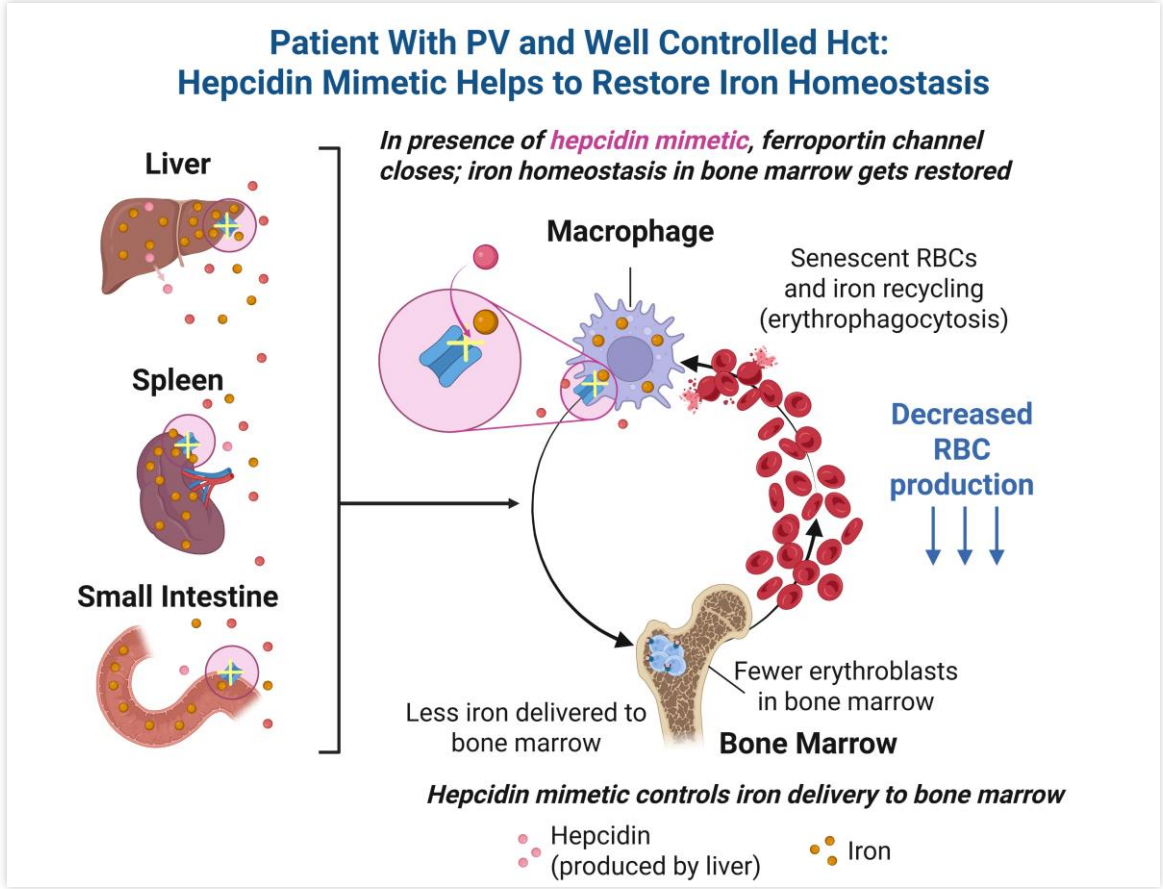
- Polycythemia vera (PV) is a myeloproliferative neoplasm driven by acquired JAK2 mutations[1-3]
- PV is characterized by excessive production of blood cells which contributes to an increased risk of cardiovascular and thrombotic events[2]
- Primary goal of PV treatment aims to reduce thrombotic risk by achieving and maintaining Hct <45%[2,3]
- Current standard-of-care for PV: phlebotomy ± cytoreductive therapy[3]
- Frequent phlebotomy is burdensome and often insufficient for durable Hct control <45%[4-6]

HCT, hematocrit; **PHL**, phlebotomy; **PV**, polycythemia vera.

1. Mora B, Passamonti F. Clin Lymphoma Myeloma Leuk. 2023;23(2):79-85; 2. Marchioli R, et al. N Engl J Med. 2013;368(1):22-33; 3. Tremblay D, et al. JAMA. 2025;333(2):153-60; 4. Alvarez-Larrán A, et al. Haematologica. 2016;102(1):103-9 5. Verstovsek S, et al. Ann Hematol. 2023;102(3):571-81. 6. Ginzburg YZ, Leukemia. 2018;32(10):2105-16.

Polycythemia Vera and the Role of Iron and Hepcidin in Red Blood Cell Production





Images created in BioRender. (2025) https://BioRender.com/y23e071

HCT, hematocrit; **PV**, polycythemia vera; **RBC**, red blood cells.

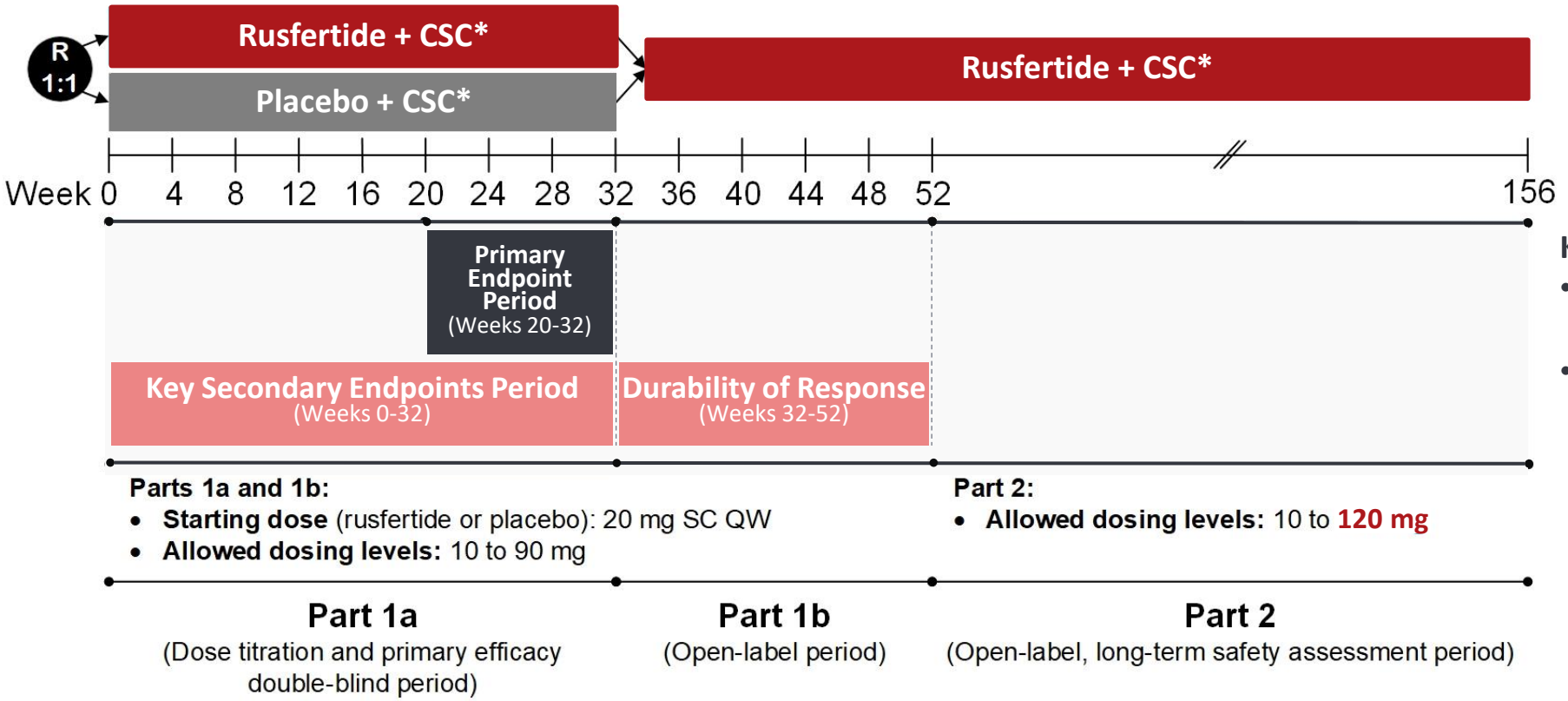
Rusfertide in Polycythemia Vera (PV)

- Rusfertide is a first-in-class subcutaneous peptide mimetic of the endogenous hormone hepcidin, the principal regulator of iron homeostasis[1]
- In the phase 2 REVIVE study (NCT04057040), rusfertide met the primary endpoint for response (i.e., HCT control and absence of PHL eligibility) in patients with PV[1]
- VERIFY (NCT05210790) is a global, ongoing phase 3 study designed to confirm the benefit of adding rusfertide to current standard-of-care (CSC) therapy vs placebo with CSC in patients with PV who require frequent phlebotomies[2]

CSC, current standard of care; **PV**, polycythemia vera

1. Kremyanskaya M, et al. N Engl J Med. 2024;390(8):723-35. 2. A Phase 3 Study of the Hepcidin Mimetic Rusfertide (PTG-300) in Patients With Polycythemia Vera. National Library of Medicine (US). https://clinicaltrials.gov/study/NCT05210790 Last accessed May 2025

Phase 3 VERIFY Study (NCT05210790) Design in PV[1]



Key Inclusion Criteria:

- ≥3 phlebotomies (28 wks prior), OR
- ≥5 phlebotomies (1 year prior)

Stratified by CSC* at randomization (1:1)

*Phlebotomy ± cytroreductive therapy

CSC, current standard of care; **PV**, polycythemia vera

1. A Phase 3 Study of the Hepcidin Mimetic Rusfertide (PTG-300) in Patients with Polycythemia Vera. Protocol Number: PTG-300-11. Protocol Amendment 5.1 dated 09 January 2025

Phase 3 VERIFY Study (NCT05210790) in PV[1]: Prespecified Primary and Key Secondary Endpoints

Rusfertide with CSC vs. placebo with CSC:

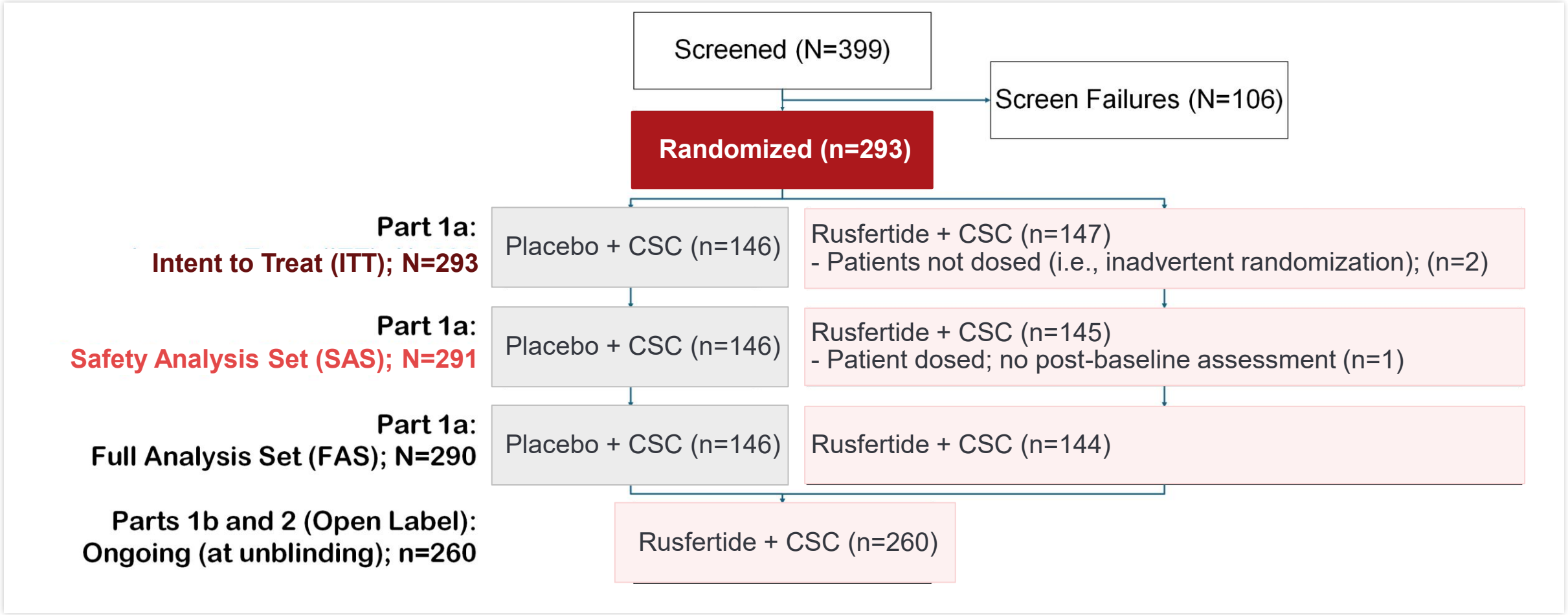
- **Primary Endpoint (US FDA)**: Weeks 20-32
  - Clinical response (absence of phlebotomy eligibility, i.e., confirmed HCT ≥45% and ≥3% higher than baseline HCT OR HCT ≥48%)

- **Key Secondary Endpoints**: Weeks 0-32
  - Mean number of phlebotomies **(EU EMA)**
  - Proportion of patients with HCT <45%
  - Mean change from baseline in PROMIS Fatigue SF-8a Total T-Score
  - Mean change from baseline in MFSAF TSS7

CSC, current standard of care; **EMA**, European Medicines Agency; **EU**, European Union; **FDA**, Food and Drug Administration; Hct, hematocrit; **MFSAF TSS**, Myelofibrosis Symptom Assessment Form version 4.0 Total Symptom Score; **PROMIS**, Patient-Reported Outcomes Measurement Information System; **SF**, short form.

1. A Phase 3 Study of the Hepcidin Mimetic Rusfertide (PTG-300) in Patients with Polycythemia Vera. Protocol Number: PTG-300-11. Protocol Amendment 5.1 dated 09 January 2025

VERIFY Patient Disposition and Analysis Sets: Part 1a[1]



Data cutoff: 7 January 2025

FAS, all randomized patients according to the treatment assigned at randomization (ITT principle) who received at least one dose of study drug and had a baseline and at least one postbaseline assessment in Part 1a.

CSC, current standard of care

1. A Phase 3 Study of the Hepcidin Mimetic Rusfertide (PTG-300) in Patients with Polycythemia Vera. Protocol Number: PTG-300-11. Protocol Amendment 5.1 dated 09 January 2025

Baseline Demographics and Disease Characteristics

	Placebo + CSC (n=146)	Rusfertide + CSC (n=147)	Total (N=293)
Age, years, median (range)	57 (27-82)	58 (28-86)	57 (27-86)
Gender, n (%)			
Male	108 (74.0)	106 (72.1)	214 (73.0)
Female	38 (26.0)	41 (27.9)	79 (27.0)
Risk Category, n (%)			
High risk (age ≥60 years old and/or prior TE)	70 (47.9)	66 (44.9)	136 (46.4)
Disease Characteristics			
Age at PV diagnosis (years), median (range)	51 (22-81)	53 (17-84)	52 (17-84)
PV duration (years), median (range)	3 (0.2-29.2)	2.8 (0.2-26.4)	2.9 (0.2-29.2)
Phlebotomy History – 28 Weeks Prior to Study Treatment			
Number of TPs, mean ± SD	4.1 ± 1.4	4.2 ± 1.6	4.2 ± 1.5
Patients requiring ≥7 TPs, n (%)	7 (4.8)	**16 (10.9)**	23 (7.8)

Data cutoff: 7 January 2025

CSC, current standard of care; **PV**, polycythemia vera; **SD**, standard deviation; **TE**, thromboembolic event; **TP**, therapeutic phlebotomy.

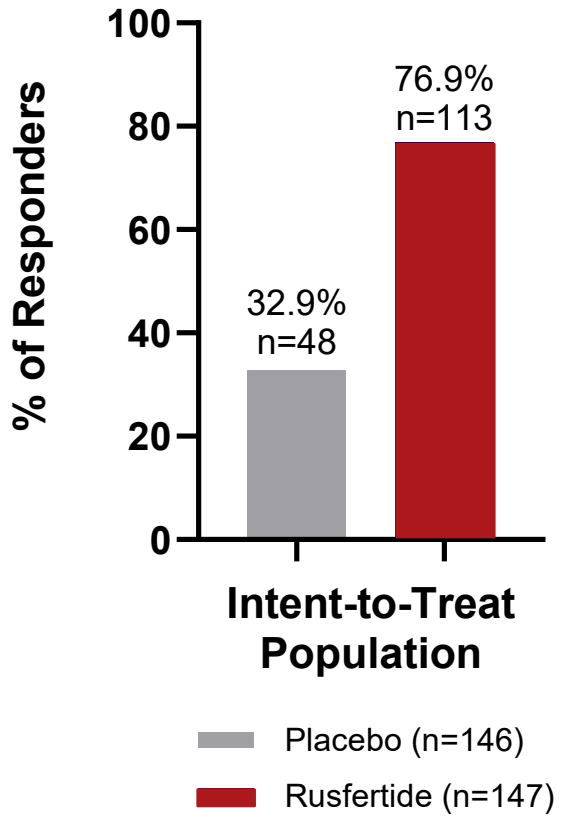
Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract

Concurrent Cytoreductive Therapy During Part 1a

n (%)	Placebo + CSC (n=146)	Rusfertide + CSC (n=147)	Total (N=293)
Patients With Concurrent Cytoreductive Medication	81 (55.5)	83 (56.5)	164 (56.0)
Hydroxyurea	57 (39.0)	58 (39.5)	115 (39.2)
Interferons			
Interferon, peginterferon alpha-2a, or ropeginterferon alfa-2b	20 (13.7)	19 (12.9)	39 (13.3)
JAK Inhibitors			
Ruxolitinib	3 (2.1)	5 (3.4)	8 (2.7)

Data cutoff: 7 January 2025
CSC, current standard of care; **JAK**, Janus Kinase
Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract

VERIFY Study Met Its Primary Endpoint During Weeks 20-32 (Part 1a)



	Placebo + CSC (n=146)	Rusfertide + CSC (n=147)
Responders, n (%)[a]	48 (32.9)	113 (76.9)
p-value*		**<0.0001**
Non-responders, n (%)	98 (67.1)	34 (23.1)

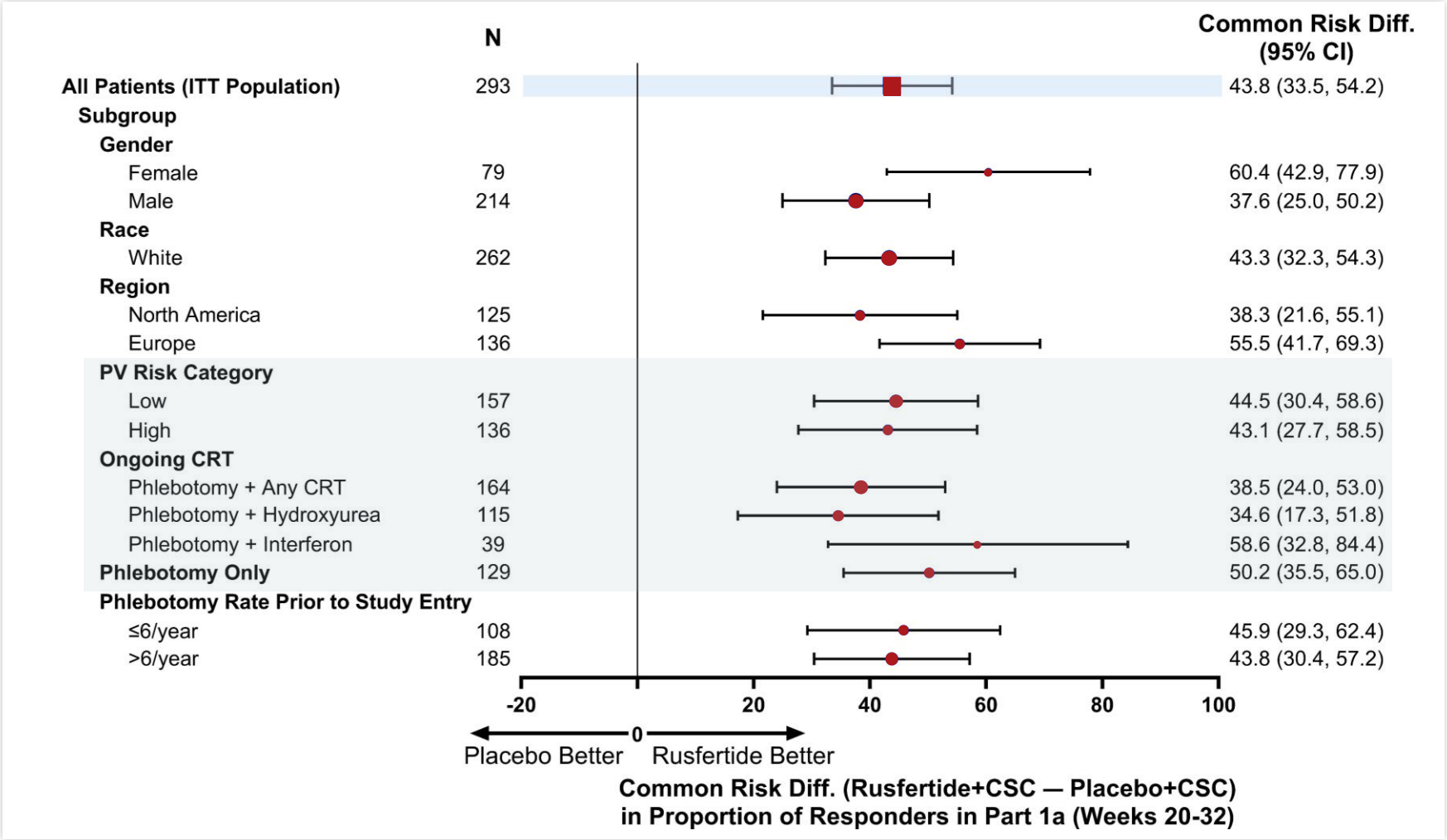
Data cutoff: 7 January 2025

[a]Responder = absence of phlebotomy eligibility (confirmed HCT ≥45% and ≥3% higher than baseline HCT OR HCT ≥48%), no phlebotomies, and completion of Part 1a; *p-value based on Cochran-Mantel-Haenszel test.

CSC, current standard of care; **HCT**, hematocrit.

Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract

Rusfertide + CSC Benefit Maintained vs. Placebo + CSC for Response* Across Subgroups, Including Risk Status and Concurrent Therapy

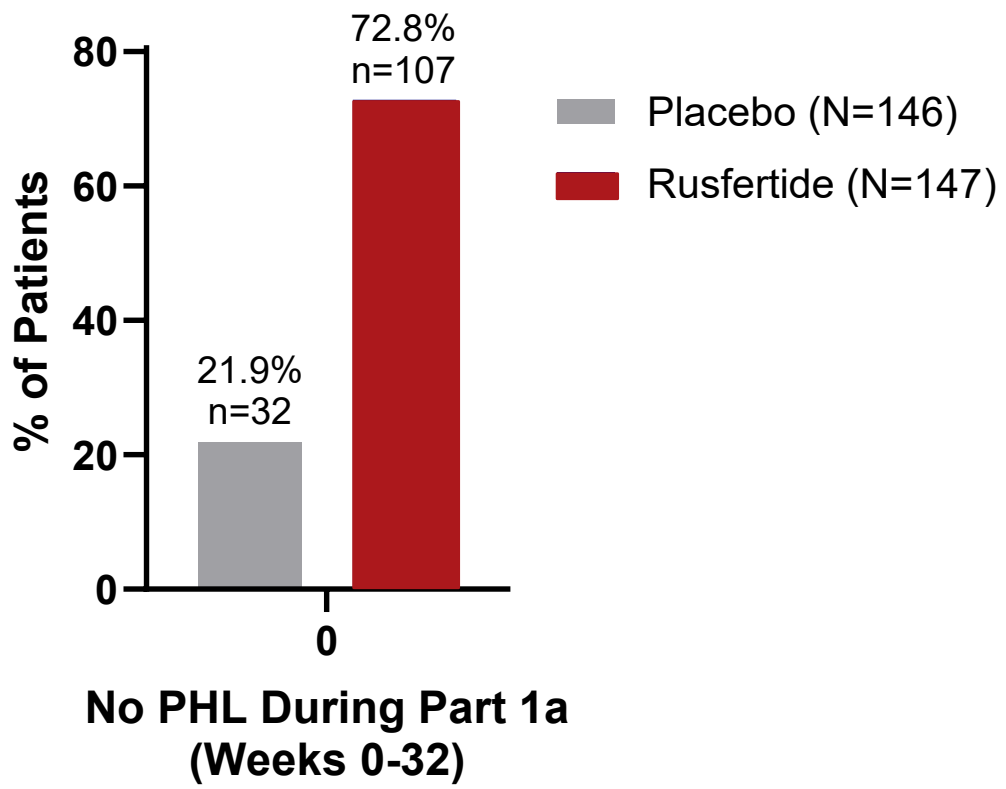


Data cutoff: 7 January 2025 | *Common risk difference for primary endpoint of response.

CRT, cytoreductive therapy**; CSC**, current standard of care; **ITT**, intent to treat

Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract

Rusfertide + CSC Reduced the Mean Number of Phlebotomies (PHL) From Weeks 0-32 vs Placebo + CSC (p<0.0001): Key Secondary Endpoint #1



Number of Phlebotomies	Placebo (n=146)	Rusfertide (n=147)
Mean (SD)	**1.8** (1.5)	**0.5** (1.2)
p-value*	**<0.0001**	

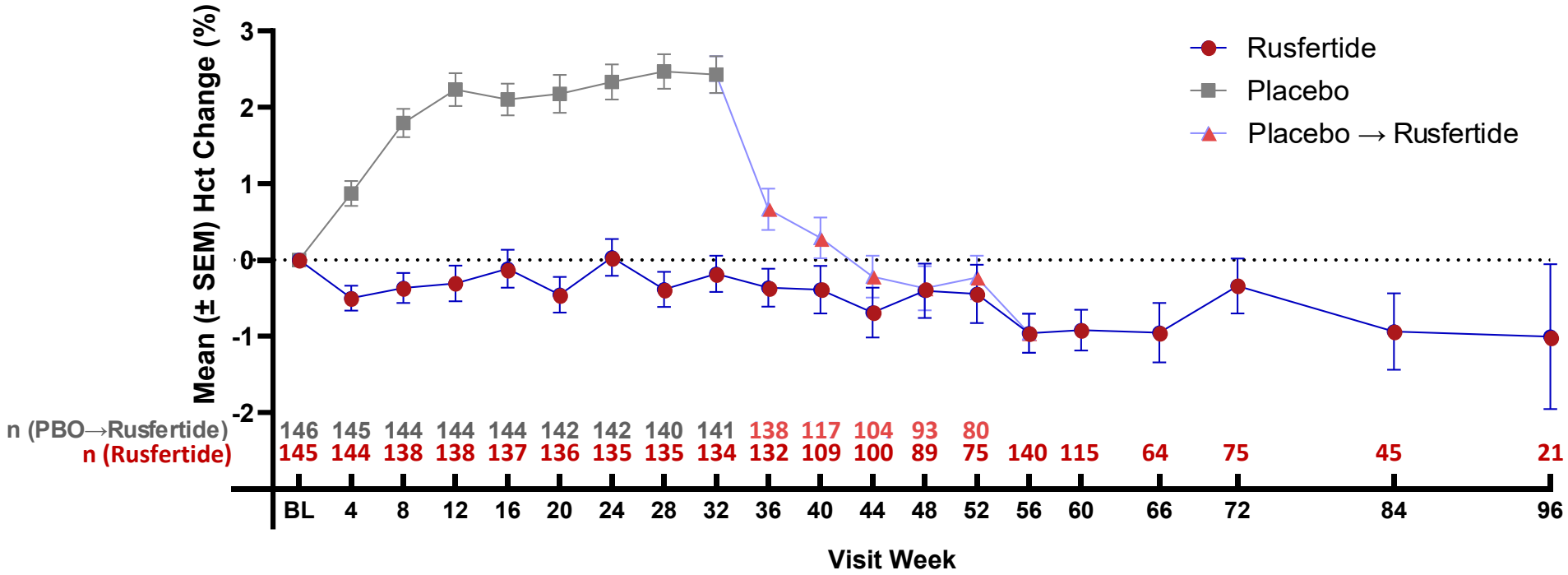
Rusfertide reduced the mean number of PHL (Weeks 0-32) vs. placebo by a statistically significant margin across subgroups, including PV risk category, geographic region, and use of concurrent CRT

Data cutoff: 7 January 2025 | *p-value associated with the LS mean difference.

CRT, cytoreductive therapy; **CSC**, current standard of care; **LS**, least-squares; **PHL**, phlebotomy; **SD**, standard deviation.

Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract

Rusfertide + CSC More Likely to Maintain HCT <45% From Weeks 0-32 vs Placebo + CSC: Key Secondary Endpoint #2



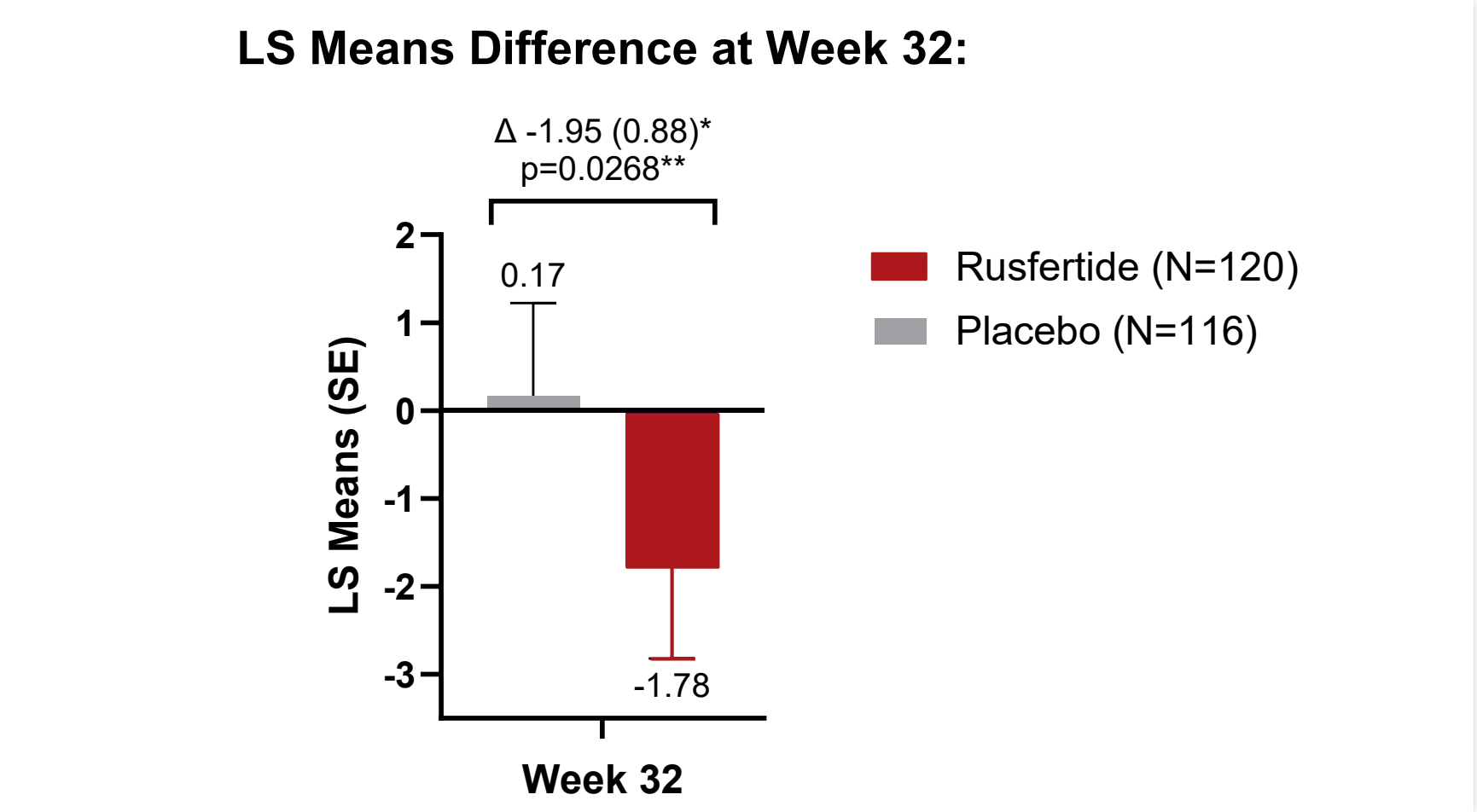
	Placebo + CSC (n=146)	Rusfertide + CSC (n=147)
HCT <45% (Baseline through Week 32), n (%)[a]	21 (14.4)	92 (62.6)
p-value*		**<0.0001**

Data cutoff: 7 January 2025 | [a]HCT <45% from baseline through Week 32 (a single HCT ≥45% was allowed, excluding intercurrent events classified as non-responders); *Cochran-Mantel-Haenszel test.

CSC, current standard of care; **HCT**, hematocrit

Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract

Rusfertide Demonstrated an Improvement in the PROMIS Fatigue SF-8a Total T-Score at Week 32 vs. Placebo: Key Secondary Endpoint #3



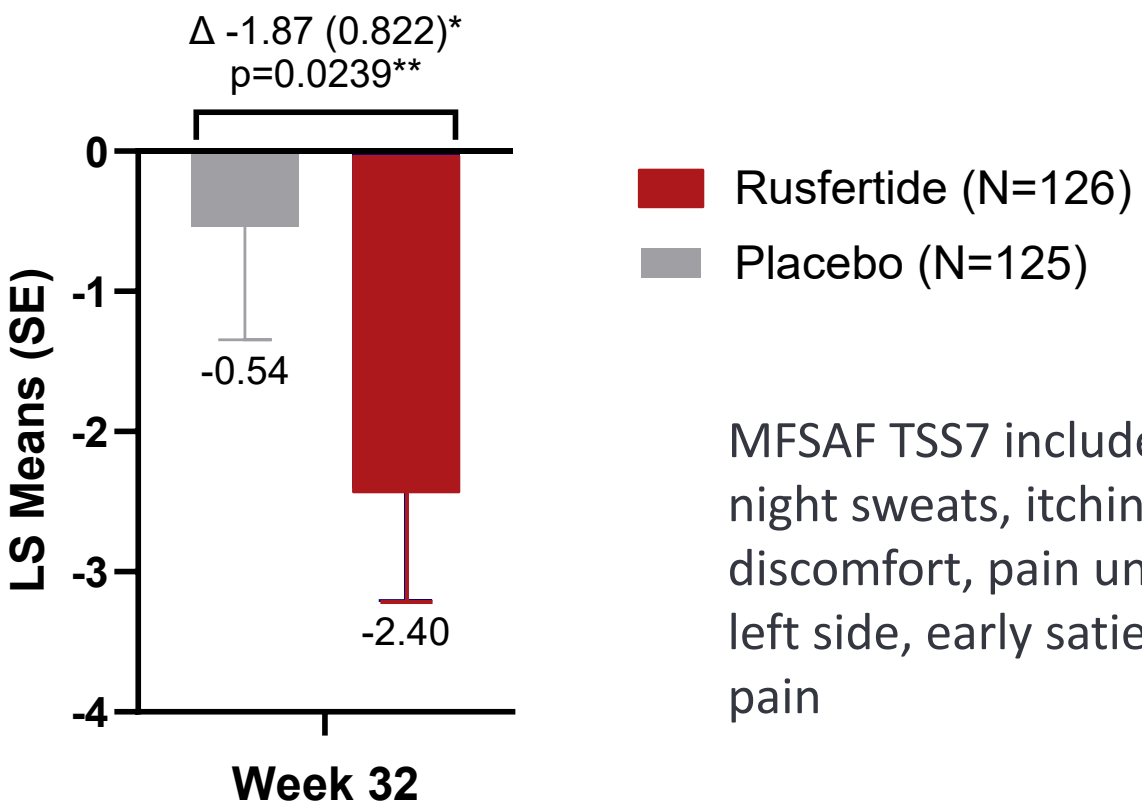
Data cutoff: 7 January 2025

*LS mean (SE) difference (rusfertide – placebo); **p-value associated with the LS mean difference

LS, least-squares; **PROMIS**, Patient-Reported Outcomes Measurement Information System; SF**,** short form

Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract

Rusfertide Demonstrated an Improvement in the MFSAF TSS7 at Week 32 vs. Placebo: Key Secondary Endpoint #4



MFSAF TSS7 includes fatigue, night sweats, itching, abdominal discomfort, pain under ribs on left side, early satiety, and bone pain

Data cutoff: 7 January 2025

*LS mean (SE) difference (rusfertide – placebo); **p-value associated with the LS mean difference

LS, least-squares; **MFSAF TSS7**, Myelofibrosis Symptom Assessment Form version 4.0 Total Symptom Score-7 item

Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract

Exposure and Treatment-Emergent Adverse Events (Part 1a)*

- Median treatment exposure was 32 weeks in both groups
  - Median (min, max) dose was 30 (10, 90) mg in the rusfertide group
- The most common TEAEs in the rusfertide group included localized injection site reactions and anemia
- Discontinuation rates due to TEAEs were 2.7% (placebo) and 5.5% (rusfertide)

Most Frequent TEAEs (≥5% in either group) in Part 1a, n (%)	Placebo + CSC (n=146)	Rusfertide + CSC (n=145)
Patients with at least 1 TEAE	126 (86.3)	129 (89)
Injection site reactions[a]	48 (32.9)	81 (55.9)
Anemia	6 (4.1)	23 (15.9)
Fatigue	23 (15.8)	22 (15.2)
Headache	17 (11.6)	15 (10.3)
COVID-19	16 (11.0)	14 (9.7)
Pruritus	14 (9.6)	14 (9.7)
Diarrhea	8 (5.5)	12 (8.3)
Dizziness	9 (6.2)	12 (8.3)
Arthralgia	12 (8.2)	11 (7.6)
Constipation	11 (7.5)	11 (7.6)
Abdominal distension	8 (5.5)	10 (6.9)
Thrombocytosis	0 (0)	10 (6.9)

[a]Injection site reactions (grouped term); all other TEAEs are preferred terms.

*Safety analysis set
AE, adverse event; **CSC**, current standard of care; **TEAE**, treatment-emergent adverse event
Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract

Cancer Events and Serious TEAEs (Part 1a)*

- 10 skin malignancies (including 1 melanoma) detected prior to randomization
- During Part 1a, non-PV cancer events were reported in 8 patients
- Serious AEs occurred in 3.4% (rusfertide) and 4.8% (placebo) of patients (none related to rusfertide)
- There was 1 TE (acute MI; occurred ~2 weeks after treatment initiation) reported in the rusfertide group and 0 in the placebo group

Cancer Events	Placebo + CSC (n=146)	Rusfertide + CSC (n=145)
Patients with ≥1 Cancer Event, n (%)	7 (4.8)	1 (0.7)
Basal cell carcinoma	3 (2.1)	0
Squamous cell carcinoma	1 (0.7)	1 (0.7)
Malignant melanoma	1 (0.7)	0
Colorectal cancer	1 (0.7)	0
Prostate cancer	1 (0.7)	0

*Safety analysis set
AE, adverse event; **CSC**, current standard of care; **MI**, myocardial infarction; **PV**, polycythemia vera; **TE**, thromboembolic event; **TEAE**, treatment-emergent adverse event
Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract

Limitations

- Heterogeneous patient population that may make interpretability of some of the secondary endpoints (e.g., PROs) challenging
- The placebo-controlled portion of VERIFY (Part 1a) was only 32 weeks long[1]
  - Long-term assessment of safety, thrombotic events, and disease transformation or progression is therefore limited and will continue for up to three years (Parts 1b and 2)

PRO, patient-reported outcome

1. A Phase 3 Study of the Hepcidin Mimetic Rusfertide (PTG-300) in Patients with Polycythemia Vera. Protocol Number: PTG-300-11. Protocol Amendment 5.1 dated 09 January 2025
Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract

Conclusions

- Rusfertide is an investigational weekly subcutaneous injection for PV
- In the phase 3 VERIFY study that included patients with PV who were receiving CSC, rusfertide met its primary endpoint and all four key secondary endpoints vs. placebo
  - In VERIFY Part 1a, rusfertide:
    - Significantly reduced the PHL eligibility and improved HCT vs. placebo
    - Demonstrated a statistically significant improvement in symptoms (assessed using two PRO instruments)
- Rusfertide demonstrated a manageable safety profile consistent with prior studies
- **Rusfertide represents a potential new treatment option for PV**
  - These data will be used to file marketing authorizations throughout the world

CSC, current standard of care; **HCT**, hematocrit; **PRO**, patient-reported outcome; **PV**, polycythemia vera

Kuykendall AT, et al. ASCO 2025 [Abstract LBA3]; see the abstract