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IN-PERSON AND LIVE STREAMED

Updated Long-Term Results from the Phase 2 REVIVE Study Investigating the Hepcidin Mimetic Rusfertide in Polycythemia Vera Patients: Hematocrit Control and Therapeutic Phlebotomy Frequency

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Background

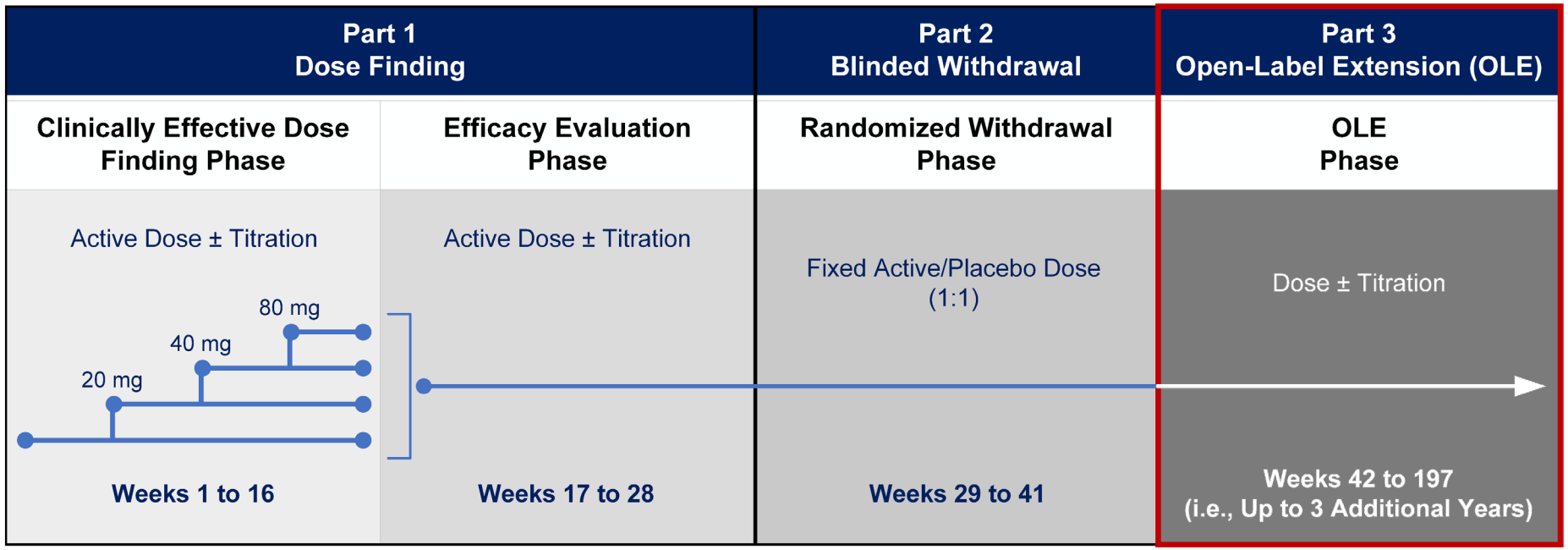
- PV is an MPN leading to excessive RBC production; this condition can also increase leukocyte and platelet counts[1]
- Patients with PV have an increased risk of thrombosis due to elevated Hct levels[2]
- Current treatments (eg, therapeutic PHL and CRT) aim to reduce Hct <45%[3-6]
  - Existing treatments (including frequent PHL) cause iron deficiency and worsening PV symptoms such as fatigue[2,7,8]; PHL can also be time consuming
- Rusfertide (PTG-300) is a weekly subcutaneous injectable peptide mimetic of the natural hormone hepcidin that restricts the availability of iron for RBC production[9-11]

CRT, cytoreductive therapy; Hct, hematocrit; PHL, phlebotomy; MPN, myeloproliferative neoplasm; PV, polycythemia vera; RBC, red blood cells.

1. Mora B, Passamonti F. *Clin Lymphoma Myeloma Leuk*. 2023;23(2):79-85. 2. McMullin MFF, et al. *Br J Haematol*. 2019;184(2):161-175. 3. Gisslinger H, et al. *Lancet Haematol*. 2020;7(3):e196-e208. 4. Mascarenhas J, et al. *Blood*. 2022;139(19):2931-41. 5. Passamonti F, et al. *Lancet Oncol*. 2017;18(1):88-99. 6. Vannucchi AM. *N Engl J Med*. 2015;372(17):1670-1. 7. Verstovsek S, et al. *Leuk Res*. 2017;56:52-9. 8. Handa S, et al. *Curr Opin Hematol*. 2023;30(2):45-52. 9. Kremyanskaya M, et al. EHA 2023, June 11, 2023, Frankfurt, Germany, and Virtual. 10. Kremyanskaya M, et al. *N Engl J Med*. 2024;390(8):723-35. 11. Ritchie EK, et al. *Blood*. 2023;142(Suppl 1):745.

Phase 2 REVIVE Study Design With Randomized Withdrawal Phase

- As reported previously in REVIVE (PTG-300-04; NCT04057040), rusfertide was superior to placebo in helping patients with PV who are dependent on therapeutic PHL (with or without concurrent CRT) achieve mean Hct levels <45% during a 12-week randomized withdrawal period (Part 2)[1,2] and provided durable Hct control[3,4]



- The primary objective of this presentation is to provide updated, long-term results from REVIVE, including data from patients who have received rusfertide for 3+ years

CRT, cytoreductive therapy; Hct, hematocrit; OLE, open-label extension; PHL, phlebotomy; PV, polycythemia vera. Figure adapted from Kremyanskaya M, et al. EHA2023. (Abstract LB2710).

1. Kremyanskaya M, et al. *N Engl J Med*. 2024;390(8):723-35. 2. Kremyanskaya M, et al. EHA 2023, June 11, 2023, Frankfurt, Germany, and Virtual. 3. Ritchie EK, et al. ASH Annual Meeting, December 9-12, 2023, San Diego, California. 4. Ritchie EK, et al. *Blood*. 2023;142(Suppl 1):745.

REVIVE Part 3: Demographics and Disease Characteristics

- In REVIVE, 58 of 70 patients who enrolled in Part 1 continued to Part 3 (OLE)
  - Part 2 (n=59) was the randomized withdrawal phase; these data were reported previously[1,2]
- In Part 3[3,4], median (range) patient age was 57 (27-77); the majority were male (70.7%) and had high-risk disease (51.7%)
  - In Part 3, 55.2% and 44.8% of patients were treated with therapeutic PHL alone or therapeutic PHL with CRT, respectively

	Part 1	Part 3
	Rusfertide	Rusfertide
	N=70	N=58
Age (years), median (range)	58 (27-77)	57 (27-77)
Gender, n (%)		
Male	49 (70.0)	41 (70.7)
Female	21 (30.0)	17 (29.3)
Risk Category, n (%)		
High Risk	40 (57.1)	30 (51.7)
Low Risk	30 (42.9)	28 (48.3)
Disease Characteristics		
Age at PV diagnosis (years), median (range)	55 (5-74)	55 (26-74)
PV duration (years), median (range)	2.5 (0-35)	2.3 (0-22)
Phlebotomy History – 28 weeks Prior to Rusfertide Treatment		
Number of phlebotomies, mean ± SD	4.7 ± 1.6	4.7 ± 1.6
Requiring ≥5 phlebotomies, n (%)	30 (42.9)	26 (44.8)
Concurrent Therapy, n (%)		
Phlebotomy only	37 (52.9)	32 (55.2)
Phlebotomy + Cytoreductive therapy	33 (47.1)	26 (44.8)

Data cutoff: 9 April 2024

CRT, cytoreductive therapy; OLE, open-label extension; PHL, phlebotomy; PV, polycythemia vera; SD, standard deviation.

1. Kremyanskaya M, et al. *N Engl J Med*. 2024;390(8):723-35. 2. Kremyanskaya M, et al. EHA 2023, June 11, 2023, Frankfurt, Germany, and Virtual. 3. Ritchie EK, et al. ASH Annual Meeting, December 9-12, 2023, San Diego, California. 4. Ritchie EK, et al. *Blood*. 2023;142(Suppl 1):745.

REVIVE: Rusfertide Exposure and Treatment Duration

- In Part 3, the median weekly average dose of rusfertide was 40.6 mg (range, 5-95)

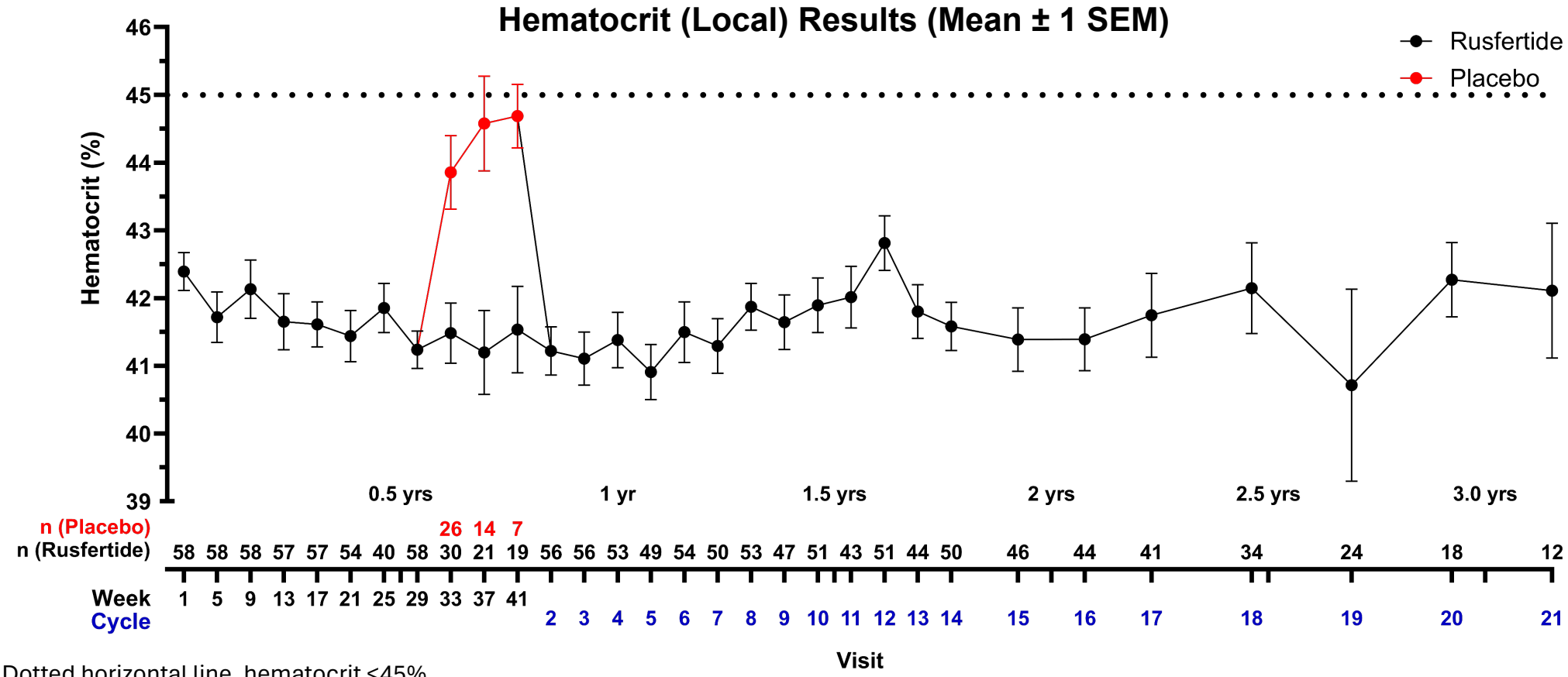
Part 3: Weekly Average Rusfertide Dose, mg	Patients Receiving Weekly Average Dose, n (%) N=58
<40	26 (44.8)
40 to <80	30 (51.7)
80 to <100	2 (3.4)

- Overall, median duration of exposure to rusfertide was 124.3 weeks (range, 3-205)
  - 48 patients (68.6%) have received rusfertide for ≥2 years

Parts 1-3: Cumulative Duration	Patients, n (%) N=70
≥52 weeks (≥1 year)	57 (81.4)
≥104 weeks (≥2 years)	48 (68.6)
≥130 weeks (≥2.5 years)	32 (45.7)
≥156 weeks (≥3 years)	10 (14.3)

Data cutoff: 9 April 2024

Rusfertide Provided Durable Control of Hematocrit Through 3 Years

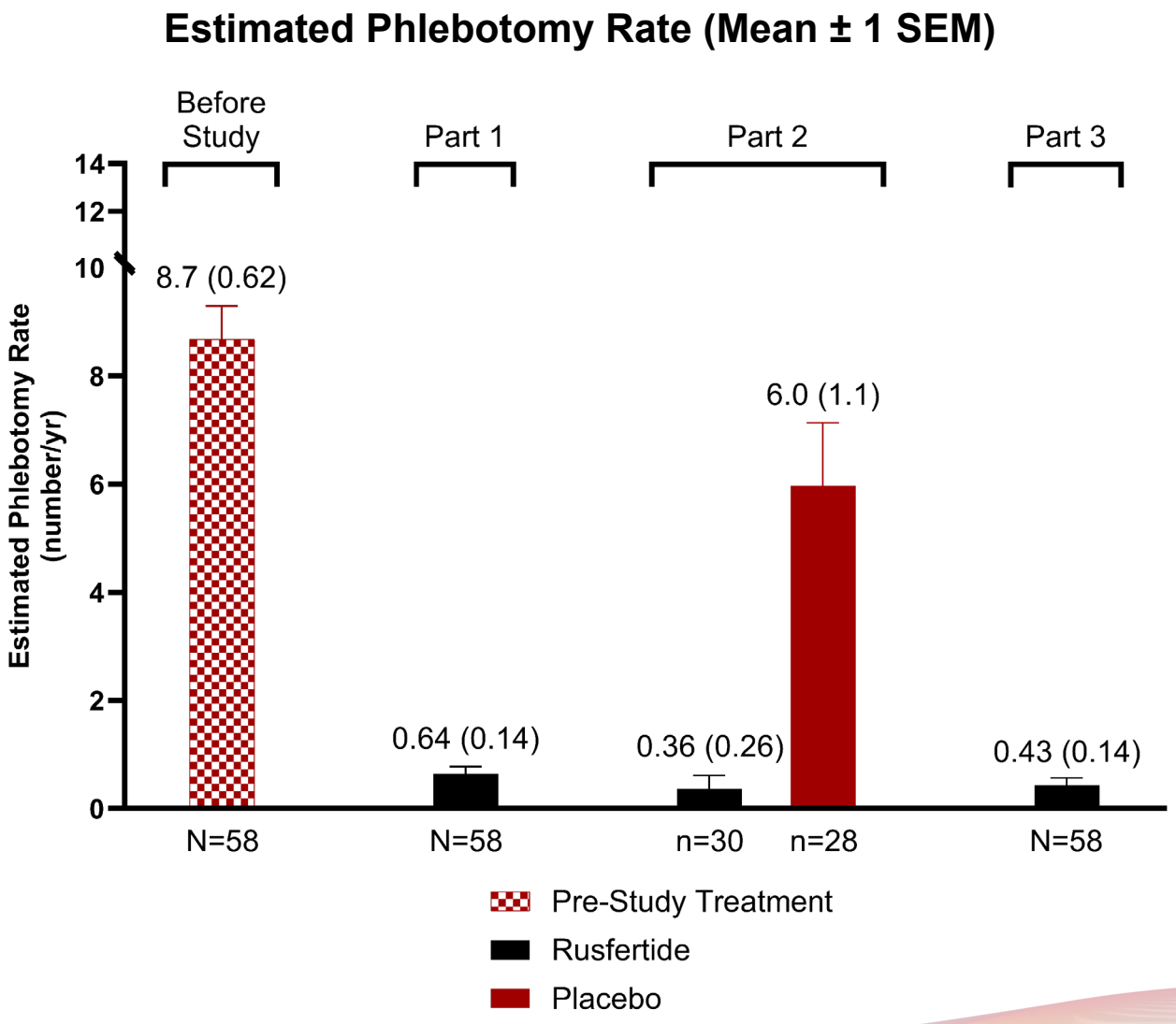


Dotted horizontal line, hematocrit <45%.
Hct, hematocrit; SEM, standard error of the mean; yr, year.

Data cutoff: 9 April 2024

- Starting within 4 weeks of treatment initiation, rusfertide consistently maintained Hct <45%, including in patients who were on therapy for 3+ years

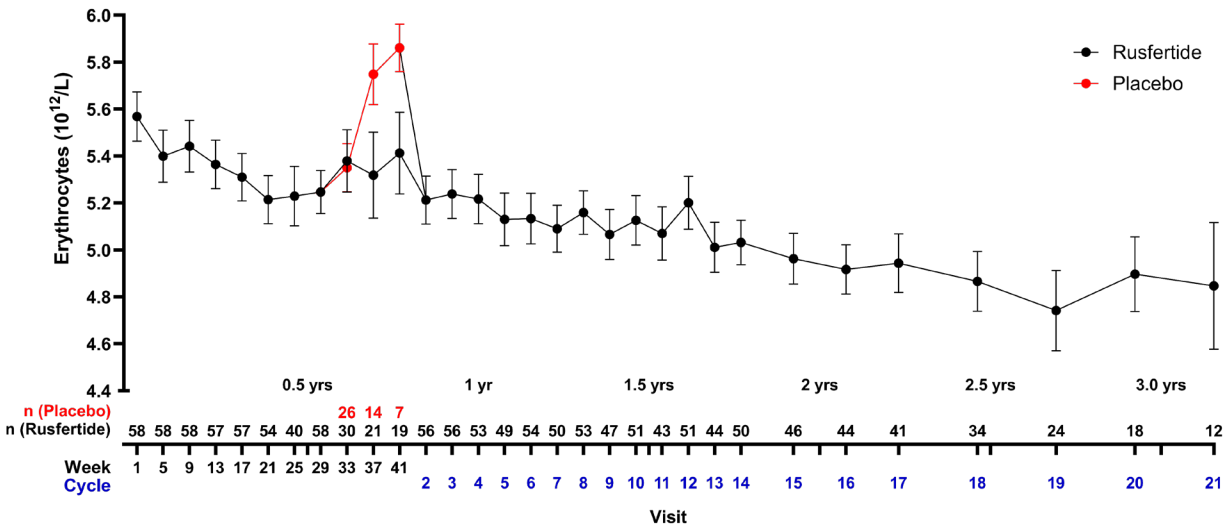
Rusfertide Reduced the Estimated Average Phlebotomy Rate



SEM, standard error of the mean; yr, year.
Data cutoff: 9 April 2024

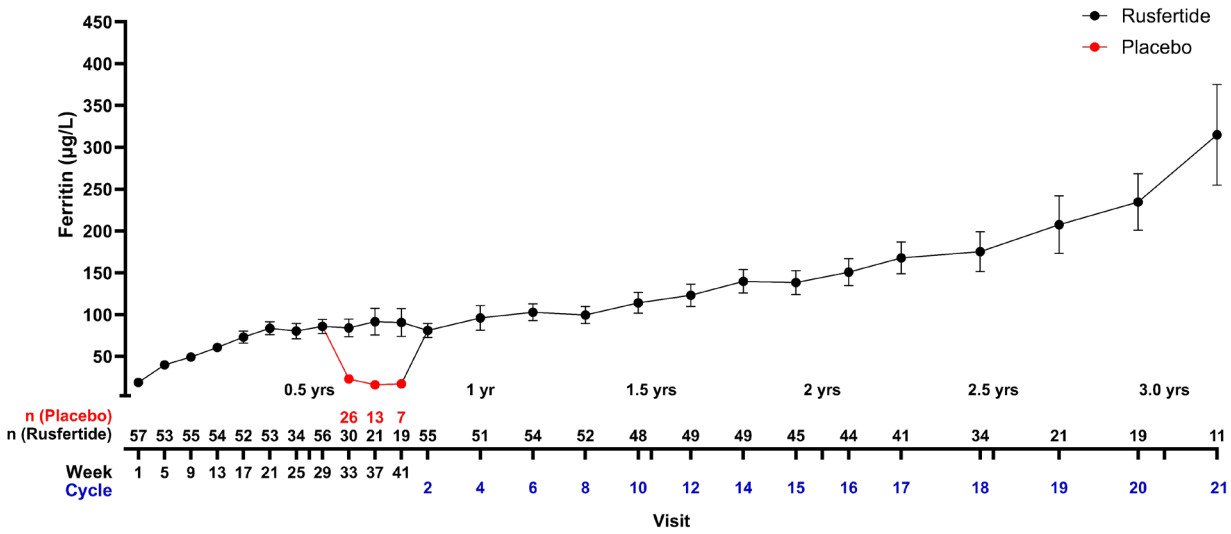
Erythrocytes Decreased Over Time; Serum Ferritin Increased Over Time

Erythrocyte (Local) Results (Mean ± 1 SEM)



- Erythrocyte counts decreased and stabilized over time

Serum Ferritin (Central) Data (Mean ± 1 SEM)



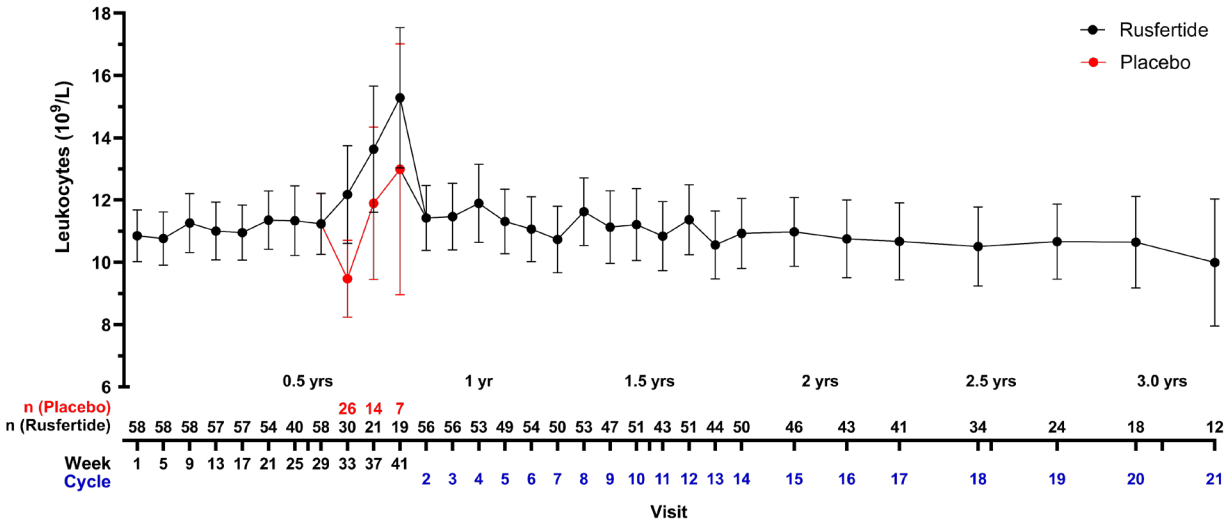
- Rusfertide increased serum ferritin levels over time

SEM, standard error of the mean; yr, year.

Data cutoff: 9 April 2024

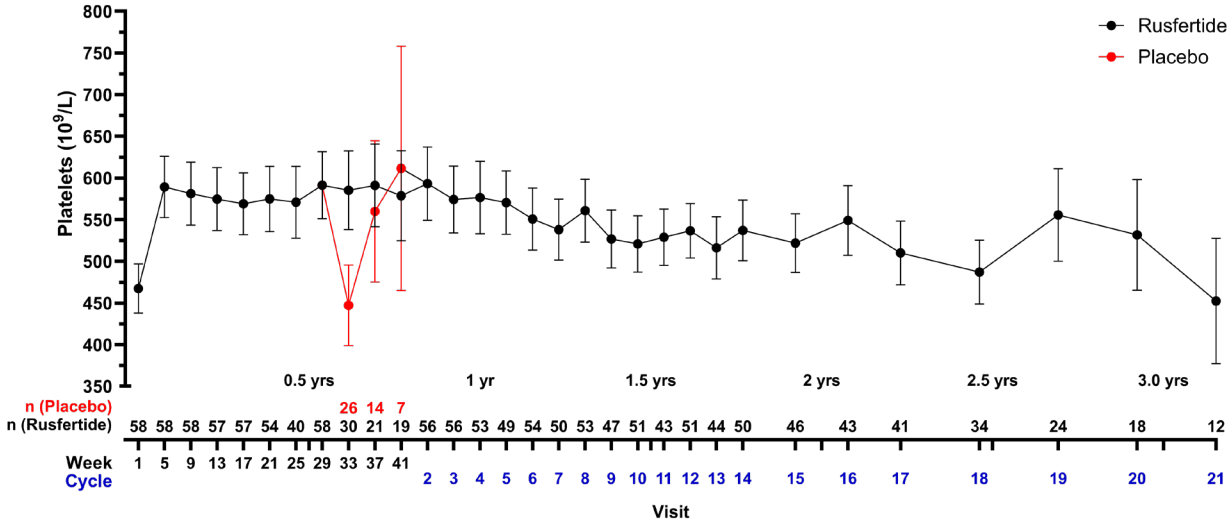
Leukocytes and Platelet Values Stabilized Over Time

Leukocyte (Local) Results (Mean ± 1 SEM)



- Mean leukocyte counts remained stable throughout the study

Platelet (Local) Results (Mean ± 1 SEM)



- Platelets increased post-baseline without significant clinical sequelae and stabilized over time

SEM, standard error of the mean; yr, year.

Data cutoff: 9 April 2024

REVIVE: Long-Term Safety Profile of Rusfertide

- The most common (≥20%) TEAEs were injection site reactions, fatigue, COVID-19, pruritus, arthralgia, dizziness, nausea, anemia, and headache
  - Grade 3 TEAEs occurred in 25.7% of patients
  - There were no Grade 4 or 5 TEAEs
- No TEs occurred in low-risk patients
- 40 patients entered the study with high-risk PV
  - 14 patients had a TE prior to study entry
- 5 patients with high-risk PV developed 6 TEs on study
  - 2 of these patients had a TE prior to study entry
    - One patient with a portal vein thrombosis prior to study entry had an MI (Part 1; Week 10) and developed a recurrent MI (Part 3; Week 95); this patient remains ongoing on study (Week 108+)

Reported TEAEs (Any Grade) in ≥10 Patients	Overall, n (%)
Patients with at least 1 TEAE	70 (100.0)
Injection site erythema	**46 (65.7)**
Injection site pain	30 (42.9)
Injection site pruritus	27 (38.6)
Fatigue	25 (35.7)
COVID-19	22 (31.4)
Injection site mass	21 (30.0)
Pruritus	21 (30.0)
Arthralgia	19 (27.1)
Dizziness	19 (27.1)
Injection site swelling	17 (24.3)
Nausea	17 (24.3)
Anemia	16 (22.9)
Headache	16 (22.9)
Injection site irritation	14 (20.0)
Diarrhea	12 (17.1)
Injection site bruising	11 (15.7)
Dyspnea	10 (14.3)
Hyperhidrosis	10 (14.3)
Injection site warmth	10 (14.3)
Myalgia	10 (14.3)
Paresthesia	10 (14.3)
Upper respiratory tract infection	10 (14.3)

Data cutoff: 9 April 2024

COVID-19, coronavirus disease; MI, myocardial infarction; PV, polycythemia vera; TE, thromboembolic event; TEAE, treatment-emergent adverse event.

Serious Adverse Events (SAEs)

- Overall, 15 patients (21.4%) experienced SAEs
  - Most SAEs were unrelated and likely associated with underlying disease
  - 1 SAE was assessed as treatment-related by the investigator

Reported SAEs (Any Grade)	Overall, n (%)
Patients with at least 1 SAE	15 (21.4)
Basal cell carcinoma	3 (4.3)
Malignant melanoma	2 (2.9)
Acute myeloid leukemia	1 (1.4)
Acute myocardial infarction	1 (1.4)
Anogenital dysplasia	1 (1.4)
Atrial fibrillation	1 (1.4)
Bladder transitional cell carcinoma	1 (1.4)
Constipation	1 (1.4)
Gastroenteritis	1 (1.4)
Hematoma	1 (1.4)
Ischemic stroke	1 (1.4)
Lung adenocarcinoma	1 (1.4)
Non-cardiac chest pain	1 (1.4)
Peripheral artery aneurysm	1 (1.4)
Peripheral vascular disorder	1 (1.4)
Sepsis	1 (1.4)
Squamous cell carcinoma	1 (1.4)
Syncope	1 (1.4)
Transient ischemic attack	1 (1.4)

Data cutoff: 9 April 2024

Prior Cancer History and Malignancies Reported on Study

- 3 New Cases Shown in **Yellow**; 11 of 70 Patients (15.7%) Reported Malignancy on Study[§]

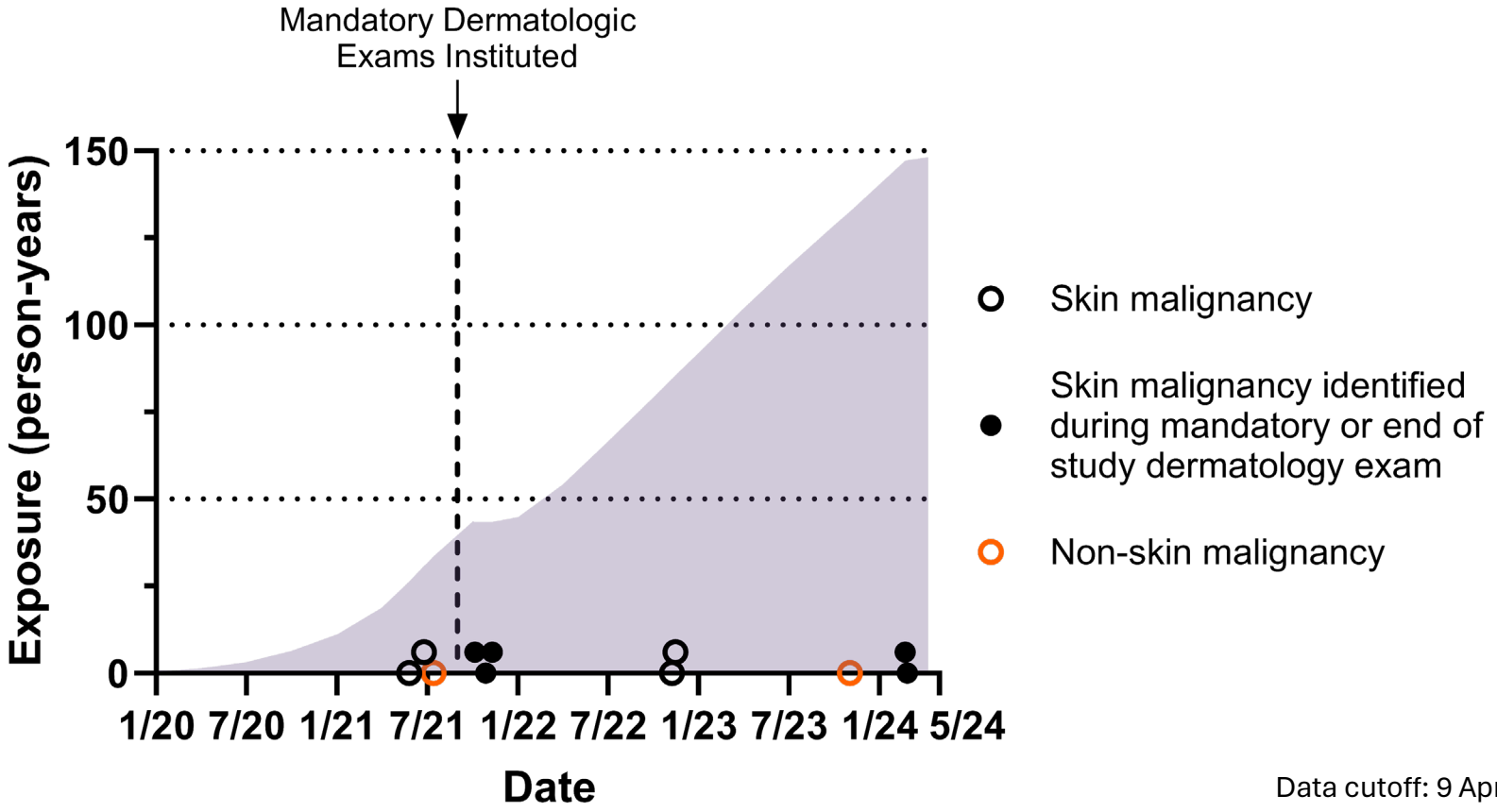
Malignancy #	Age/ Gender	Medical History, Including Prior Therapy (Risk Factors)	Concurrent Therapy	Cancer Type	Relatedness (investigator assessment)	Week Identified on Study	Patient Status
1	72/F	SCC, melanoma; HU	PHL+HU	SCC	No	7.1	Remains on rusfertide
2	64/M	BCC, melanoma (in situ), thyroid cancer (I^{131}); HU	PHL+HU	Bowen's Disease, AML	No	32.3, 36.1	Off study (35.1 weeks)
3	57/F	Cervix cancer, COPD; HU, JAK	PHL	Lung	No	32.3	Off study (130.3 weeks)
4	64/M	BCC; JAK	PHL+IFN+JAK	BCC, Melanoma	No	24.4*	Remains on rusfertide
5	55/M	Preexisting skin lesion (papule) at cancer site	PHL	BCC	No	33.4	Off study (67.4 weeks)
6	70/F	SCC, BCC; JAK	PHL	SCC, BCC	No	43.9, 116.3	Off study (138.0 weeks)
7	68/M	BCC; HU	PHL+HU	BCC	No	114.0	Remains on rusfertide
8	51/M	Preexisting pigmented skin lesion at melanoma site	PHL	Melanoma	Possibly Related	80.3	Remains on rusfertide
9	**74/M**	**Prostate cancer (XRT)**	**PHL**	**Non-invasive Bladder TCC**	**No**	**133.3**	**Remains on rusfertide**
10	**64/M**	**BCC; HU**	**PHL+HU**	**BCC**	**No**	**215.3**	**Remains on rusfertide**
11	**52/M**	**Fitzpatrick type 2 skin**	**PHL**	**Melanoma**	**No**	**212.7**	**Remains on rusfertide**

[§]3 new cases reported since 17 October 2023; 8 cases presented previously at the 2023 ASH Meeting and Exposition (Ritchie EK, et al. *Blood*. 2023;142(Suppl 1):745.) Data cutoff: 9 April 2024

*BCC and melanoma were identified simultaneously; Malignancy #, patient with malignancy in order of occurrence on study; Week, time from first dose of rusfertide to diagnosis of malignancy on study.

AML, acute myeloid leukemia; BCC, basal cell carcinoma; COPD, chronic obstructive pulmonary disease; F, female; HU, hydroxyurea; IFN, interferon; JAK, JAK2 inhibitor; M, male; PHL, phlebotomy; SCC, squamous cell carcinoma; TCC, transitional cell carcinoma; XRT, radiotherapy.

No Apparent Increase in Malignancies on Study With Increasing Exposure to Rusfertide

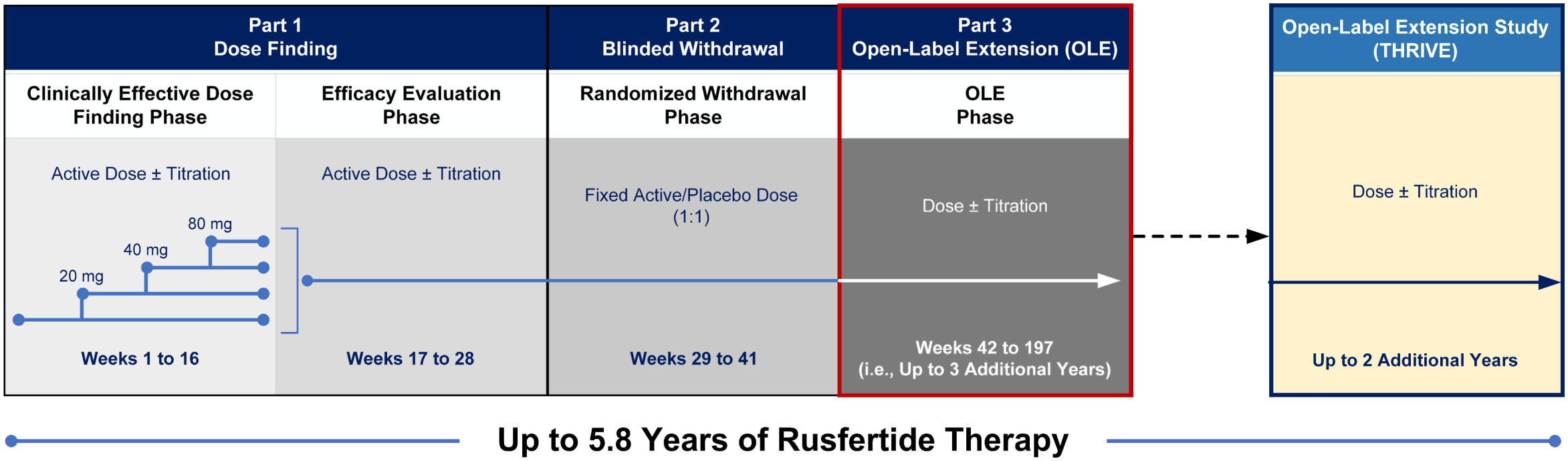


Data cutoff: 9 April 2024

- 5 of 7 skin cancers were identified during mandatory dermatology exams that were implemented in September 2021

Patients in REVIVE Part 3 (OLE) Are Transitioning to THRIVE

- Patients in THRIVE are eligible to continue receiving rusfertide for up to 2 years, or a total of 5.8 years of rusfertide therapy
- Of the 58 patients who enrolled in the OLE portion of REVIVE, 47 patients (81.0%) remain on rusfertide therapy



OLE, open-label extension; PV, polycythemia vera.

Conclusions

- In REVIVE, rusfertide added to PHL with or without CRT provided long-term durable control of Hct
- Patients generally maintained durability of response and freedom from PHL in REVIVE Part 3 (OLE)
- Changes in leukocytes and platelets were asymptomatic and stabilized over time
- Rusfertide was well-tolerated; the most common adverse events were Grade 1 or 2 injection site reactions, fatigue, pruritus, COVID-19, arthralgia, dizziness, headache, nausea, and anemia
  - Grade 3 TEAEs occurred in 25.7% of patients; there were no Grade 4 or 5 TEAEs
  - Non-PV malignancies were reported in 11 patients
    - Prior malignancies, prior lesions, and/or the patient's medical history may have contributed to the development of these malignancies
  - TEs were reported in 5 patients

CRT, cytoreductive therapy; Hct, hematocrit; OLE, open-label extension; PHL, phlebotomy; PV, polycythemia vera; TE, thromboembolic event; TEAE, treatment-emergent adverse event.

Conclusions (continued)

- 47 (81.0%) of the patients who enrolled in the OLE portion of REVIVE remain on rusfertide therapy
  - Patients in REVIVE are eligible to roll over to the open-label extension THRIVE study (NCT06033586), which will continue to assess the long-term safety and efficacy of rusfertide
  - Patients participating in THRIVE are eligible to continue receiving rusfertide for 2 additional years (i.e., up to 5.8 years of rusfertide therapy in REVIVE and THRIVE)
- The randomized phase 3 VERIFY study (NCT05210790) is evaluating rusfertide + PHL ± CRT vs. placebo + PHL ± CRT in patients with PV and has reached its randomization target (~250 patients)
  - Top-line data from VERIFY are anticipated during Q1 2025

CRT, cytoreductive therapy; OLE, open-label extension; PHL, phlebotomy; PV, polycythemia vera.

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