

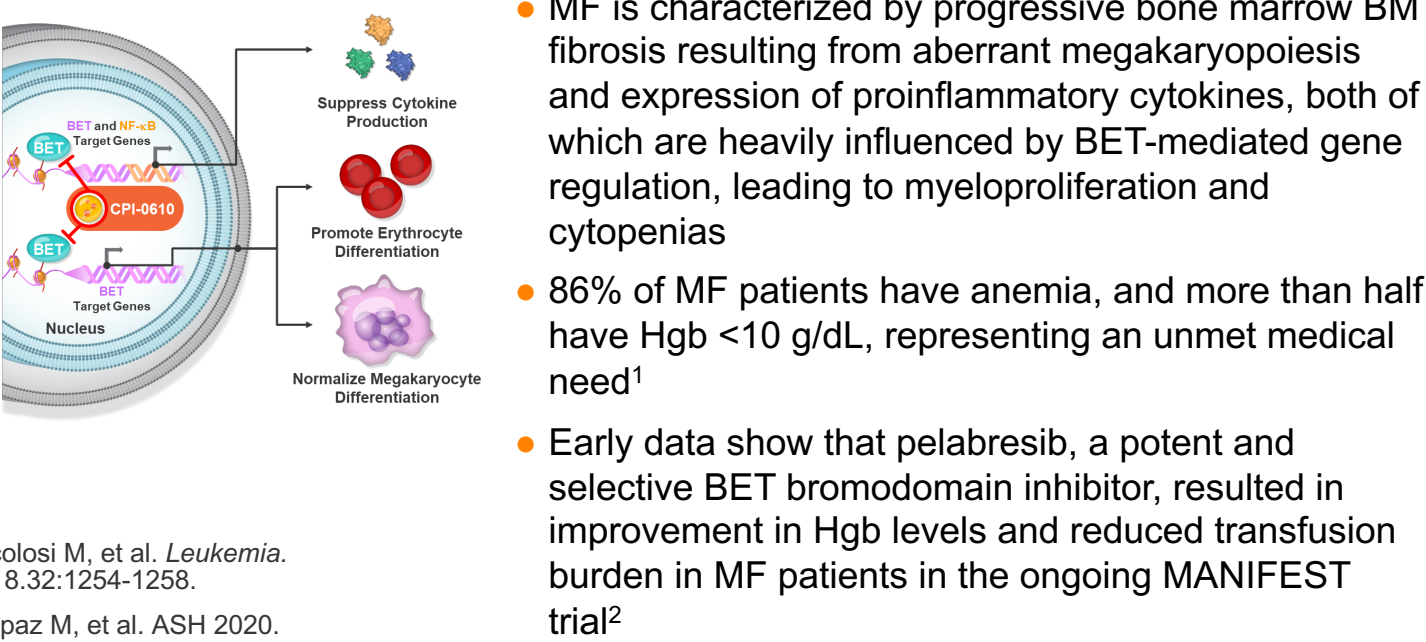
Pelabresib (CPI-0610) Improved Anemia Associated With Myelofibrosis: Interim Results From Ongoing MANIFEST Phase 2 Study

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on behalf of the MANIFEST investigators.

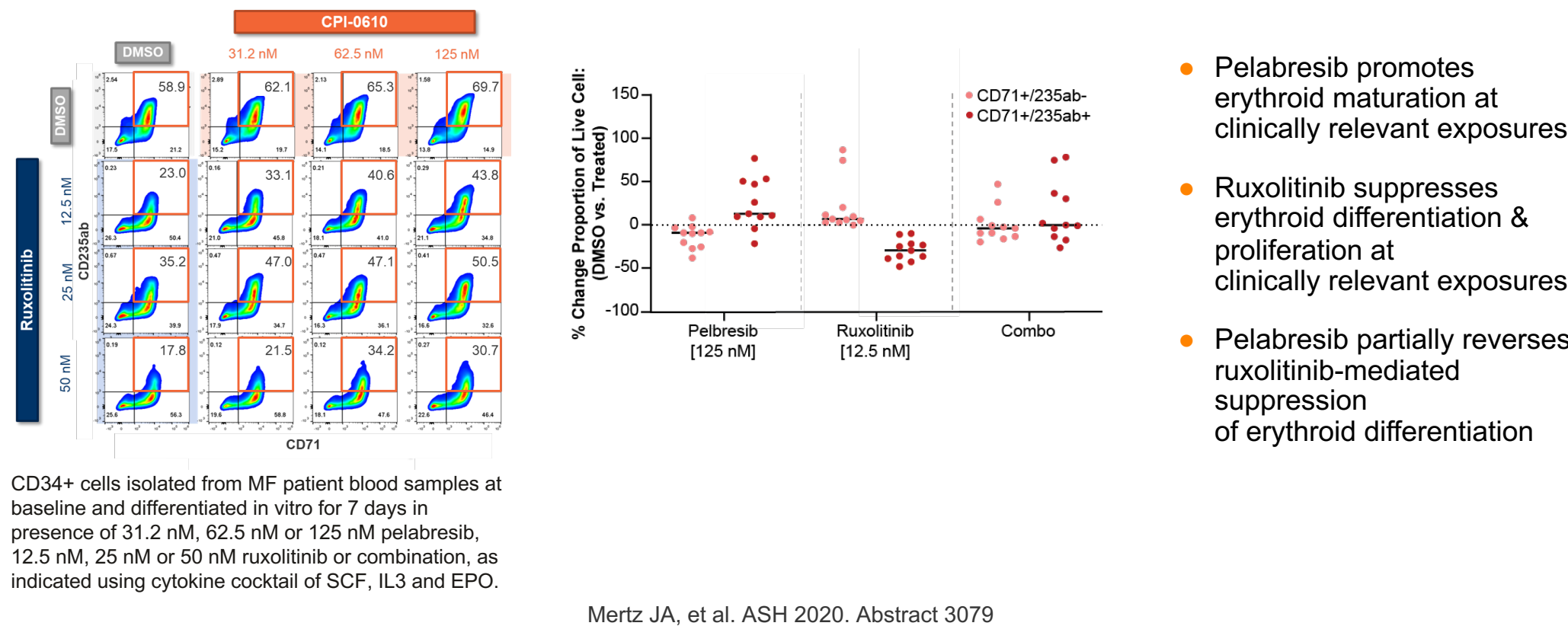
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Background

Pelabresib Improves Hemoglobin Levels and Reduces Transfusion Burden in MF Patients



Pelabresib Partially Reverses Ruxolitinib-Mediated Suppression of Erythroid Differentiation Ex Vivo



Disposition, Demographics and Patient Characteristics

Patient Disposition

	Arm 1	Arm 2	Overall
Enrolled (n)	46	78	124
Ongoing (n [%])	23 (50)	40 (51)	63 (51)
Discontinued (n [%])	23 (50)	38 (49)	61 (49)
Reason for treatment discontinuation(n [%])			
Progressive disease	7 (15)	9 (12)	16 (13)
AE or lab abnormality	2 (4)	5 (6)	7 (6)
Withdrew consent	4 (9)	10 (13)	14 (11)
PI decision	7 (15)	7 (9)	14 (11)
Alternate therapy	2 (4)	0 (0)	2 (2)
Eligible for stem cell transplant	1 (2)	4 (5)	5 (4)
Requiring multiple transfusions	0 (0)	1 (1)	1 (1)
Death	0 (0)	2 (3)	2 (2)
Treatment duration as of Sep 29, 2020 (week)			
Median (min, max)	49 (2, 147)	45 (1, 166)	47 (1, 166)

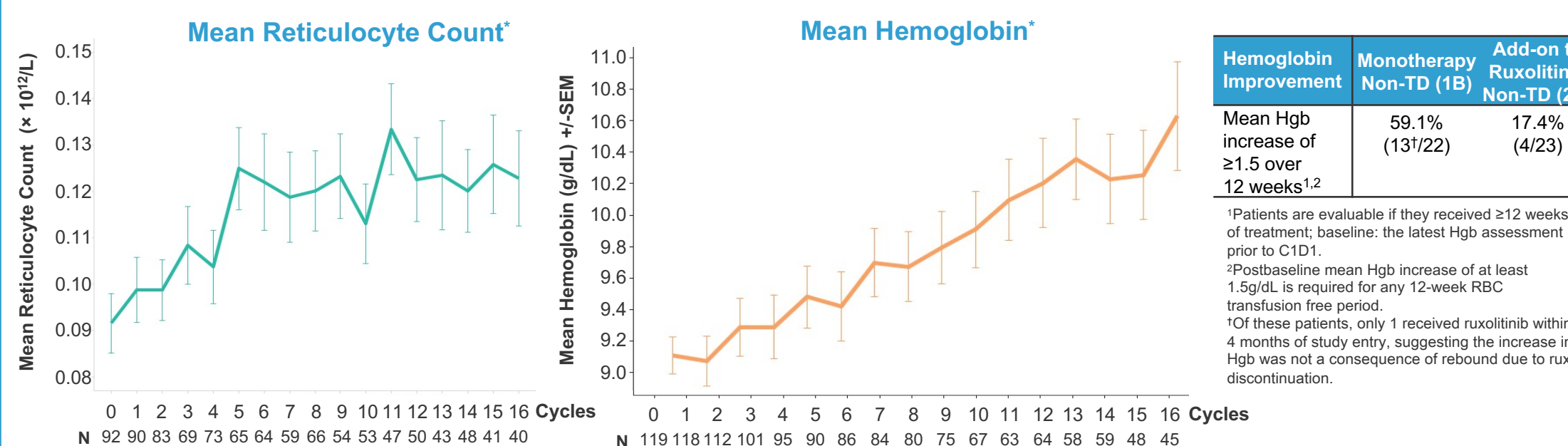
Baseline Demographics and Disease Characteristics

	Arm 1 N=46	Arm 2 N=78	Overall N=124
Age (years)	Mean (SD) 70 (9)	68 (9)	69 (9)
Gender	Male, n (%) 26 (57)	48 (62)	74 (60)
	Int-1, n (%) 8 (17)	7 (9)	15 (12)
	Int-2, n (%) 26 (57)	48 (62)	74 (60)
	High, n (%) 12 (26)	23 (30)	35 (28)
MF subtype	Primary MF, n (%) 30 (65)	55 (71)	85 (69)
	Post-PV MF, n (%) 8 (17)	9 (12)	17 (14)
	Post-ET MF, n (%) 5 (11)	12 (15)	17 (14)
	Missing, n (%) 3 (7)	2 (3)	5 (4)
	≥6 months, n (%) 27 (59)	59 (76)	86 (70)
	<6 months, n (%) 10 (22)	13 (17)	23 (19)
Prior JAK1 therapy ¹	Ruxolitinib naïve, n (%) 7 (15)	-	7 (6)
	Missing, ² n (%) 2 (4)	6 (8)	8 (7)
Prior lines of therapy	Median (Min-Max) 2 (1-6)	1 (1-5)	1 (1-5)
	≥3 mutations, ³ n (%) 19 (41)	43 (55)	62 (50)
Mutations	HMR, ⁴ n (%) 22 (48)	48 (62)	70 (57)
	ASXL1, n (%) 18 (39)	41 (53)	59 (48)
	JAK2 V617F, n (%) 28 (61)	44 (56)	72 (58)
Hemoglobin (g/dL)	Median (Min-Max) 8.9 (6.1, 15.3)	8.9 (5.7, 13.0)	8.9 (5.7, 15.3)
	<10 g/dL, n (%) 35 (76)	59 (76)	94 (76)
Platelet (× 10 ⁹ /L)	Median (Min-Max) 181 (68, 1262)	179 (70, 1114)	179 (68, 1262)
Spleen volume (cc)	Median (Min-Max) 2000 (281, 9155)	2069 (121, 8489)	2046 (121, 9154)
TSS	Median (Min-Max) 21 (1, 56)	20 (1, 62)	21 (1, 62)

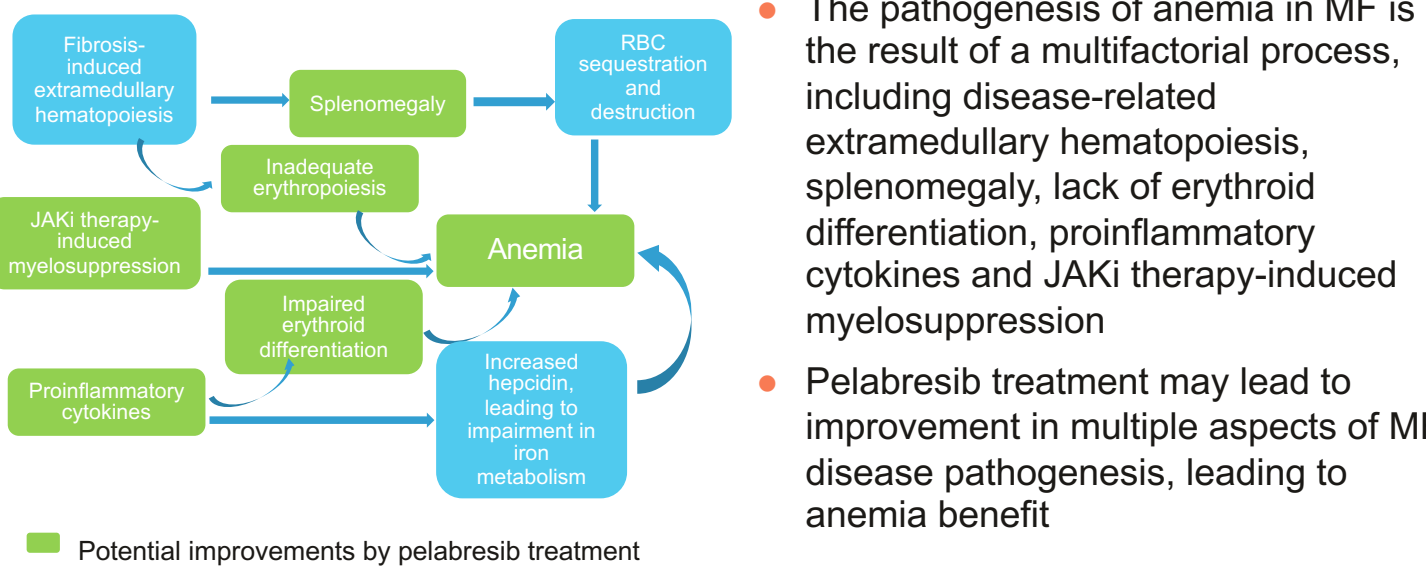
¹All prior JAK1 therapy includes ruxolitinib; ²Data entry pending; ³Mutations: ASXL1, CALR, CBL, CUX1, DNMT3A, EED, ETV6, EZH2, GATA2, GNAS, IDH1/2, JAK2, KRAS, MPL, NRAS, PHF6, PTPN11, SETBP1, SF3B1, SRSF2, TET2, TP53, U2AF1, ZRSR2; ⁴HMR: High-molecular risk mutations: ASXL1, EZH2, IDH1/2, SRSF2, U2AF1.

Results

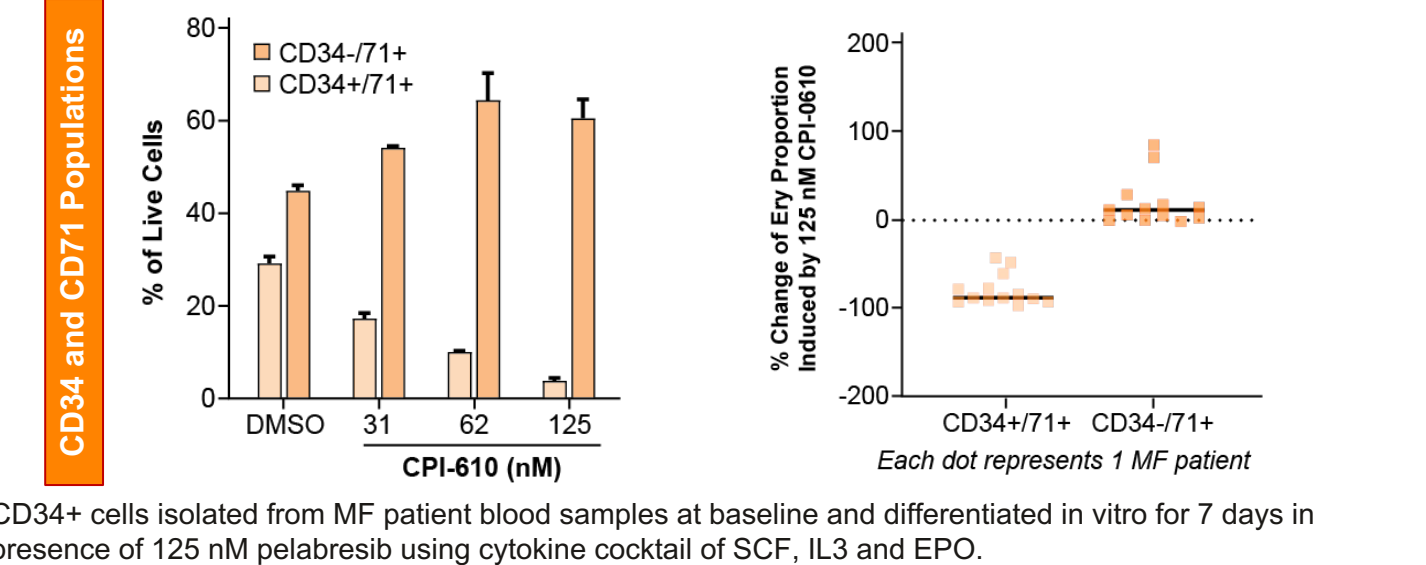
Pelabresib Treatment Resulted in Reticulocyte Increase and Hemoglobin Improvement



The Pathogenesis of Anemia is Multifactorial in MF



Pelabresib Promotes Maturation of Erythroid Progenitors Ex Vivo

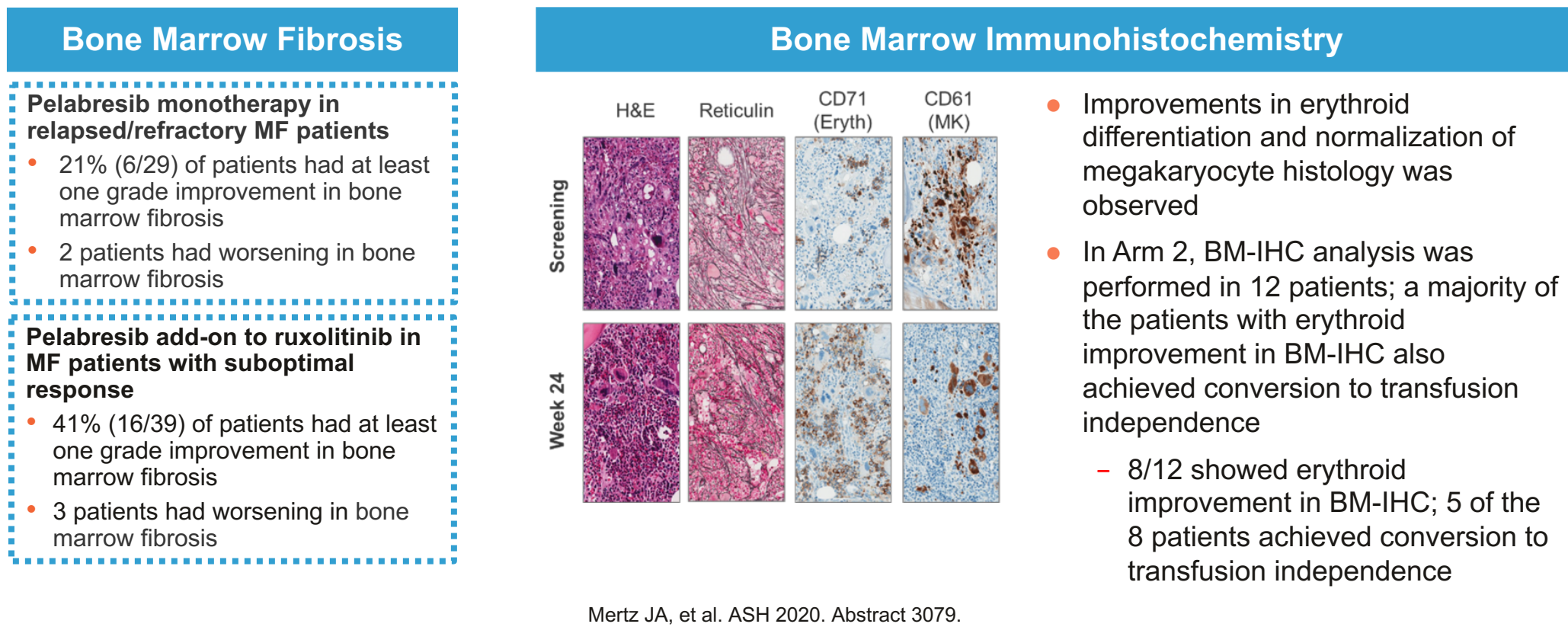


- Pelabresib promotes erythroid maturation of CD34+ cells by:
 - Inducing maturation from CD34+/CD71+ to CD34-/CD71+ populations or
 - Increasing the proportion of the CD71+/CD235ab+ population

Mertz JA, et al. ASH 2020. Abstract 3079.

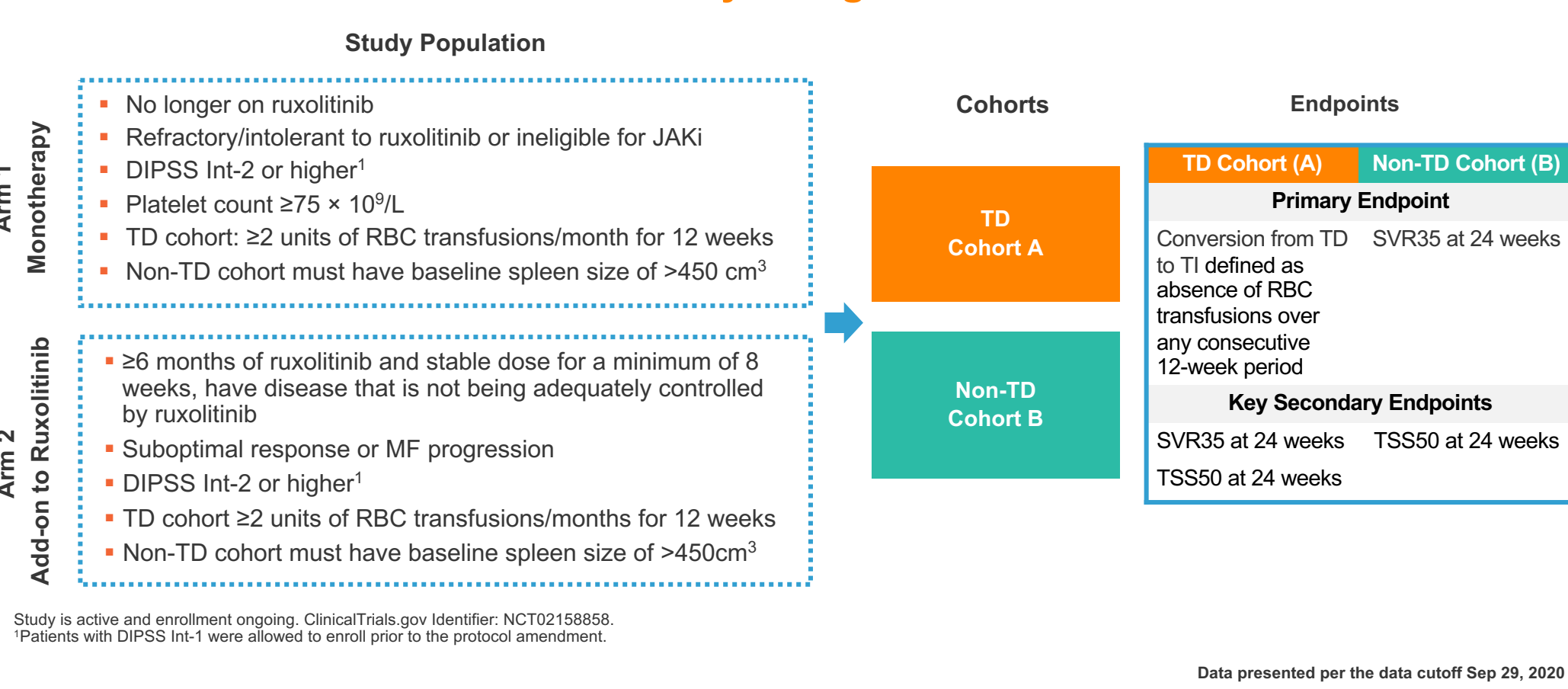
Adapted from Varga E, et al. Erythropoiesis and Megakaryopoiesis in a Dish. In: Mahana RA, ed. *Cell Culture: InterOpen*. 2018. Available at: <https://www.interopen.com/chapters/5327>. Accessed July 2021.

Bone Marrow Improvement Is Observed After 24 Weeks of Treatment

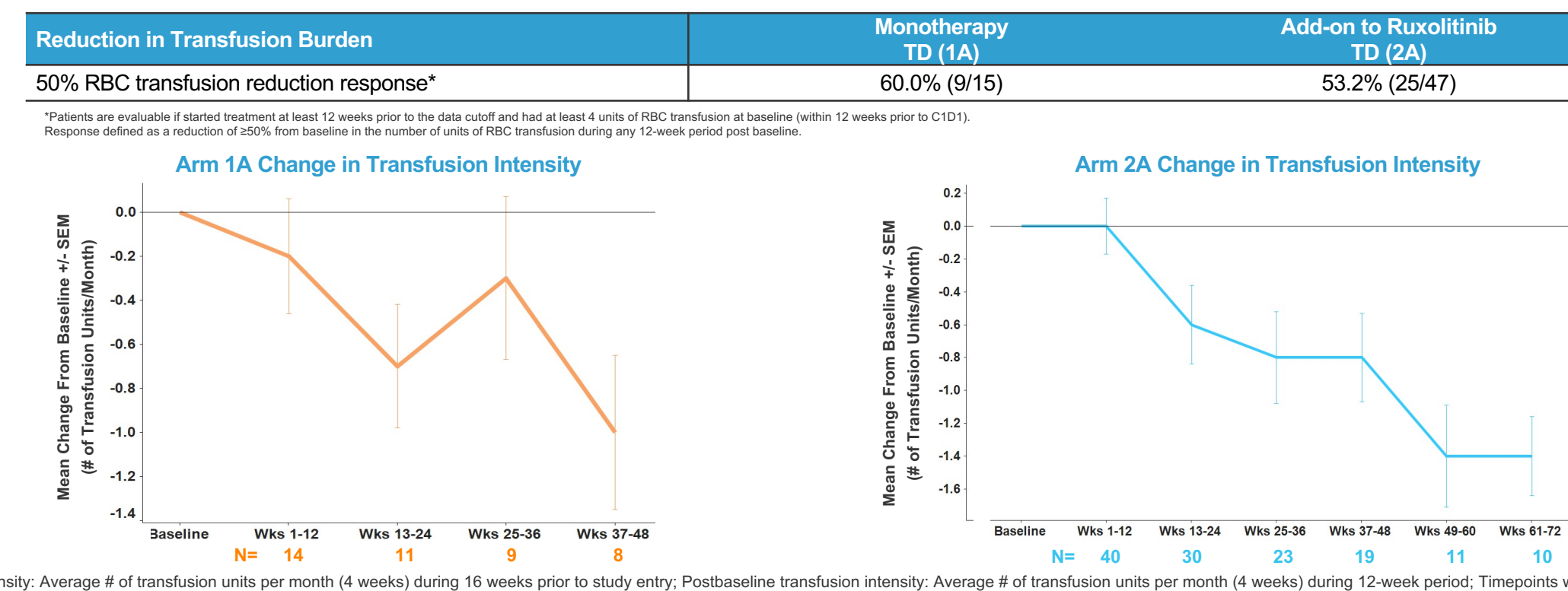


Materials & Methods

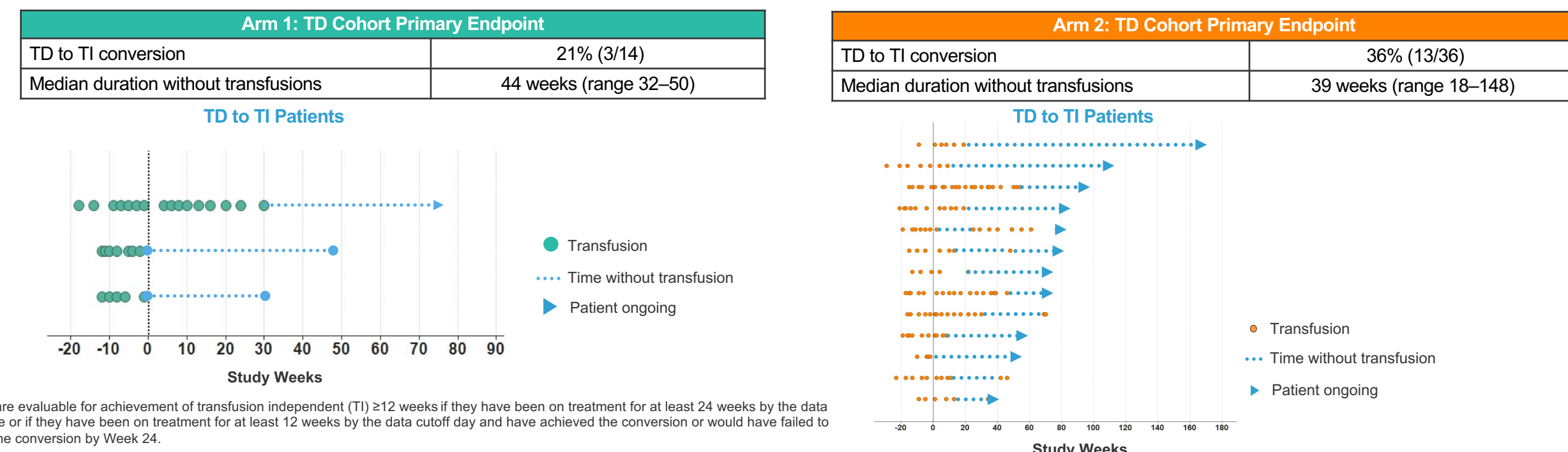
MANIFEST Study Design: Arms 1 and 2



Pelabresib Treatment Results in Reduction in Overall Transfusion Burden



Pelabresib Results in Transfusion Independence ≥12 Weeks



Safety Summary

	Arm 1- Monotherapy	Arm 2- Add-on to Rux
Treatment-Emergent Adverse Events ¹	All Grade N=46 ² n (%)	All Grade N=78 ² n (%)
Hematologic Events		
Thrombocytopenia ³	14 (30)	7 (15)
Anemia	7 (15)	6 (13)
Nonhematologic Events		
Gastrointestinal Events		
Nausea	18 (39)	0
Diarrhea	17 (37)	2 (4)
Constipation	10 (22)	1 (2)
Other Nonhematologic Events		
Dysgeusia	14 (30)	0
Asthenic conditions ⁴	14 (30)	0
Respiratory tract infection ⁵	13 (28)	1 (2)
Cough	12 (26)	0
Weight decreased	10 (22)	1 (2)

¹TEAEs of all grade that occurred in ≥20% of patients and TEAEs of special interest.
²Safety evaluable population: Received at least one dose of study drug as of the data cut.
³Includes TEAE Platelet count decrease.
⁴Includes TEAEs of fatigue and malaise.
⁵Includes TEAEs of upper respiratory tract infection, lower respiratory tract infection, influenza, laryngitis, bronchitis, sinusitis, nasopharyngitis and pneumonia.
⁶Includes TEAEs of asthenia, fatigue, lethargy and malaise.

Conclusions

- Pelabresib treatment resulted in hemoglobin improvement and reduction in transfusion burden
 - Pelabresib monotherapy in heavily pretreated MF pts in Arm 1:
 - 59% of non-TD pts had a 12-week mean hemoglobin increase ≥1.5 g/dL
 - 60% of TD pts had ≥50% reduction in transfusion burden; one-fifth of TD pts achieved conversion to TI
 - Addition of pelabresib to stable doses of ruxolitinib in pts with suboptimal ruxolitinib response in Arm 2:
 - 17% of non-TD pts had a 12-week mean hemoglobin increase ≥1.5 g/dL
 - 53% of TD pts had ≥50% reduction in transfusion burden; 36% of TD pts achieved conversion to TI
- TD to TI conversion is frequently associated with increased erythroid progenitor cells in the bone marrow, suggesting an improvement in bone marrow function that may provide a potential explanation for the pelabresib effect on hemoglobin levels