

Clinical Benefit of Pelabresib (CPI-0610) in Combination With Ruxolitinib in JAK Inhibitor Treatment-Naïve Myelofibrosis

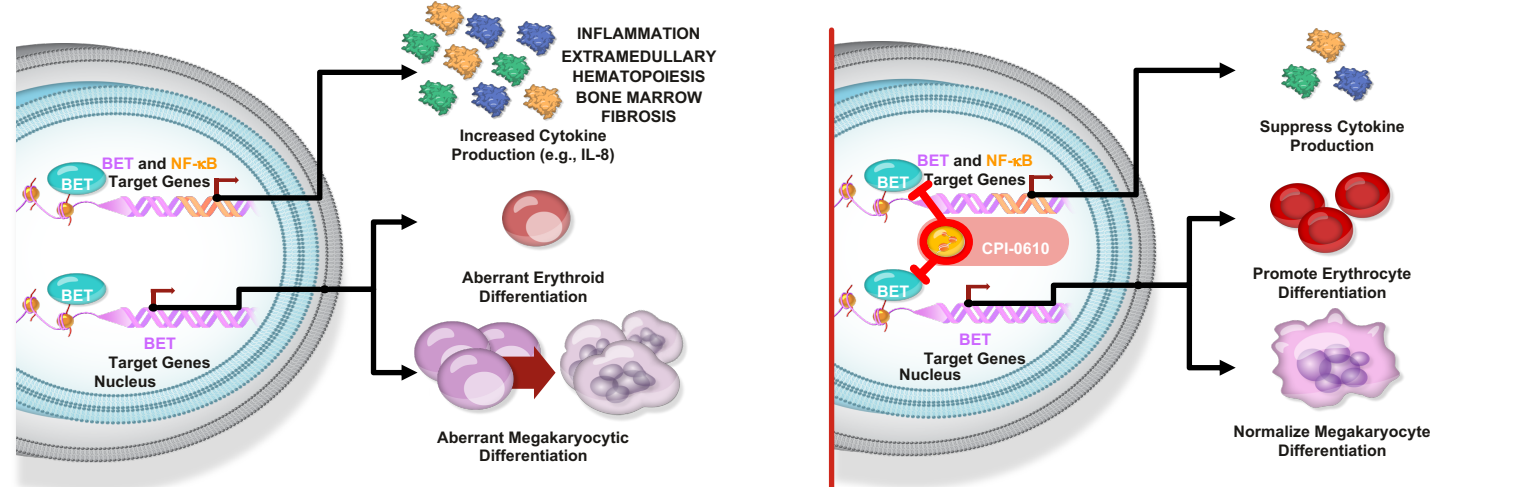
Patients: Interim Efficacy Subgroup Analysis From Arm 3 of MANIFEST Phase 2 Study

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Background

BET Bromodomain Inhibitor Pelabresib in MF



Disposition, Demographics and Patient Characteristics

MANIFEST Arm 3: Patient Disposition

Patient Disposition		
Enrolled (n)	78	
Ongoing (n [%])	66 (85)	
Discontinued (n [%])	12 (15)	
Reason for treatment discontinuation (n [%])		
Progressive disease	0 (0)	
AE or lab abnormality	2 (3)	
Withdrew consent	3 (4)	
PI decision	3 (4)	
Death	2 (3)	
COVID-19	1 (1)	
Stem cell transplant	1 (1)	
Treatment duration as of Sep 29, 2020 (week)		
Median (min, max)	40 (2,79)	

MANIFEST Arm 3: Baseline Demographics and Disease Characteristics

N=78		
Age (years)	Mean (SD)	67 (10)
Gender	Male, n (%)	56 (72)
	Int-1, n (%)	19 (24)
DIPSS	Int-2, n (%)	49 (63)
	High, n (%)	10 (13)
IPSS	Int-1, n (%)	11 (14)
	Int-2, n (%)	26 (33)
MF subtype	High, n (%)	39 (50)
	Missing, n (%)	2 (3)
Mutations	Primary MF, n (%)	42 (54)
	Post-PV MF, n (%)	9 (12)
Hemoglobin (g/dL)	Post-ET MF, n (%)	24 (31)
	Missing, n (%)	3 (4)
Plateletlet (x 10 ⁹ /L)	≥3 mutations, ¹ n (%)	37 (47)
	HMR, ² n (%)	43 (55)
Spleen volume (cc)	ASXL1, n (%)	34 (44)
	JAK2 V617F, n (%)	55 (71)
TSS	Median (Min, Max)	9.1 (7.0, 16.9)
	<10, n (%)	51 (65)
TSS	Median (Min, Max)	294 (100, 1849)
	<200, n (%)	27 (35)
TSS	Median (Min, Max)	1719 (451, 4782)
	Median (Min, Max)	16 (0, 38)

¹Mutations: 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; ²HMR: High-molecular-risk mutations; ASXL1, EZH2, IDH1/2, SRSF2, U2AF1.

Methods

MANIFEST Arm 3: Pelabresib + Ruxolitinib in JAKi-Naïve MF Patients

Study Population

- No prior JAKi
- DIPSS: Int-2 or higher¹

Treatment

Pelabresib + Ruxolitinib

Primary Endpoint

- SVR35: Spleen volume response defined as ≥35% reduction from baseline (MRI or CT) after 24 weeks of treatment

Key Secondary Endpoint

- TSS50: Total symptom score defined as ≥50% reduction in TSS measured by MFSAF v4.0 after 24 weeks of treatment

ClinicalTrials.gov Identifier: NCT02158858.

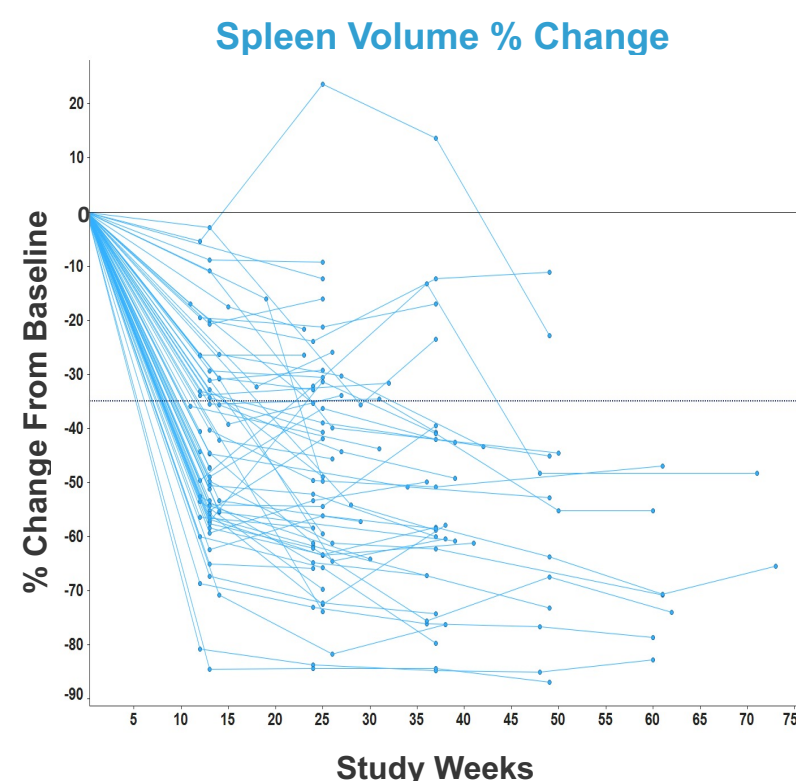
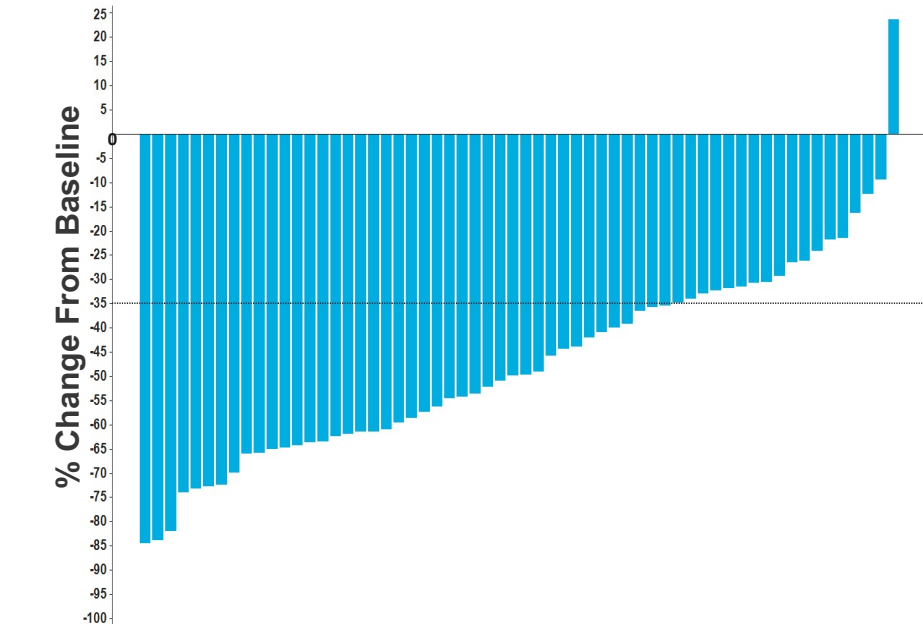
¹Patients with DIPSS Int-1 were allowed to enroll prior to the protocol amendment.

Data presented per the data cutoff Sep 29, 2020

Results

Pelabresib Treatment Resulted in 67% SVR35 Responses at Week 24 in JAKi-Naïve MF Patients

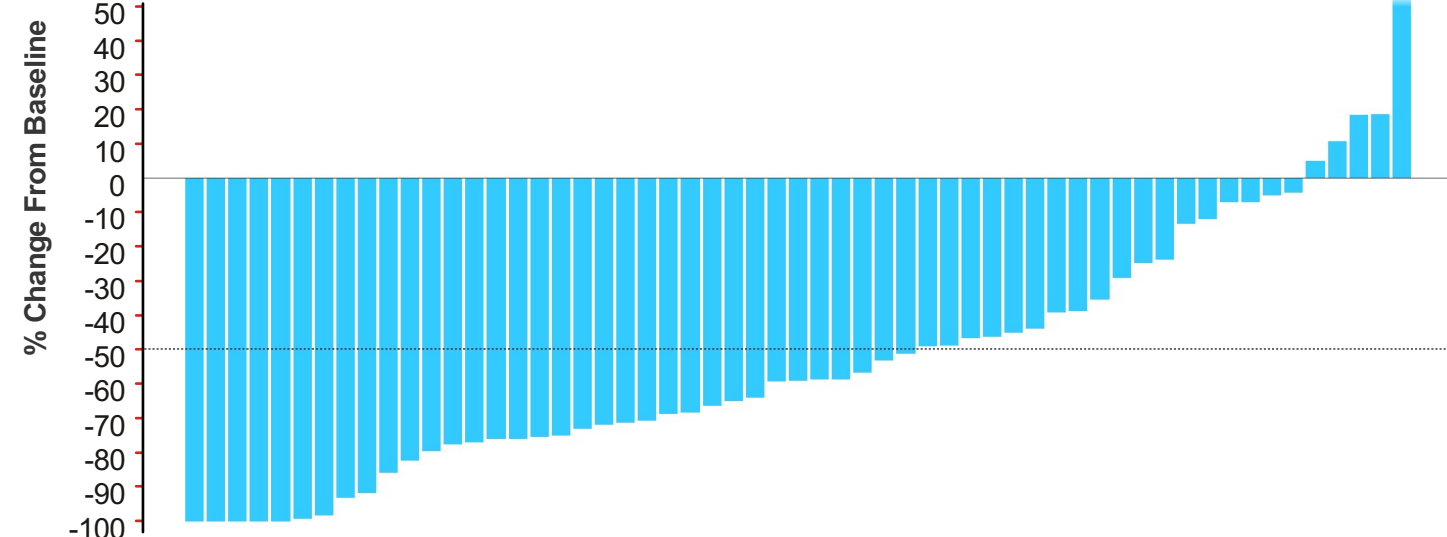
- SVR35 at Week 24: 67% (42/63), 95% CI: [54, 78]
- Median SVR: ~50%



Patients are evaluable for SVR35 at Week 24 if they have had Week 24 or later spleen volume assessment by the data cutoff date or discontinued prior to Week 24 due to any reason. Spleen volume assessments are per local radiologist read.

Majority of Patients Had Symptom Reduction Benefit at Week 24

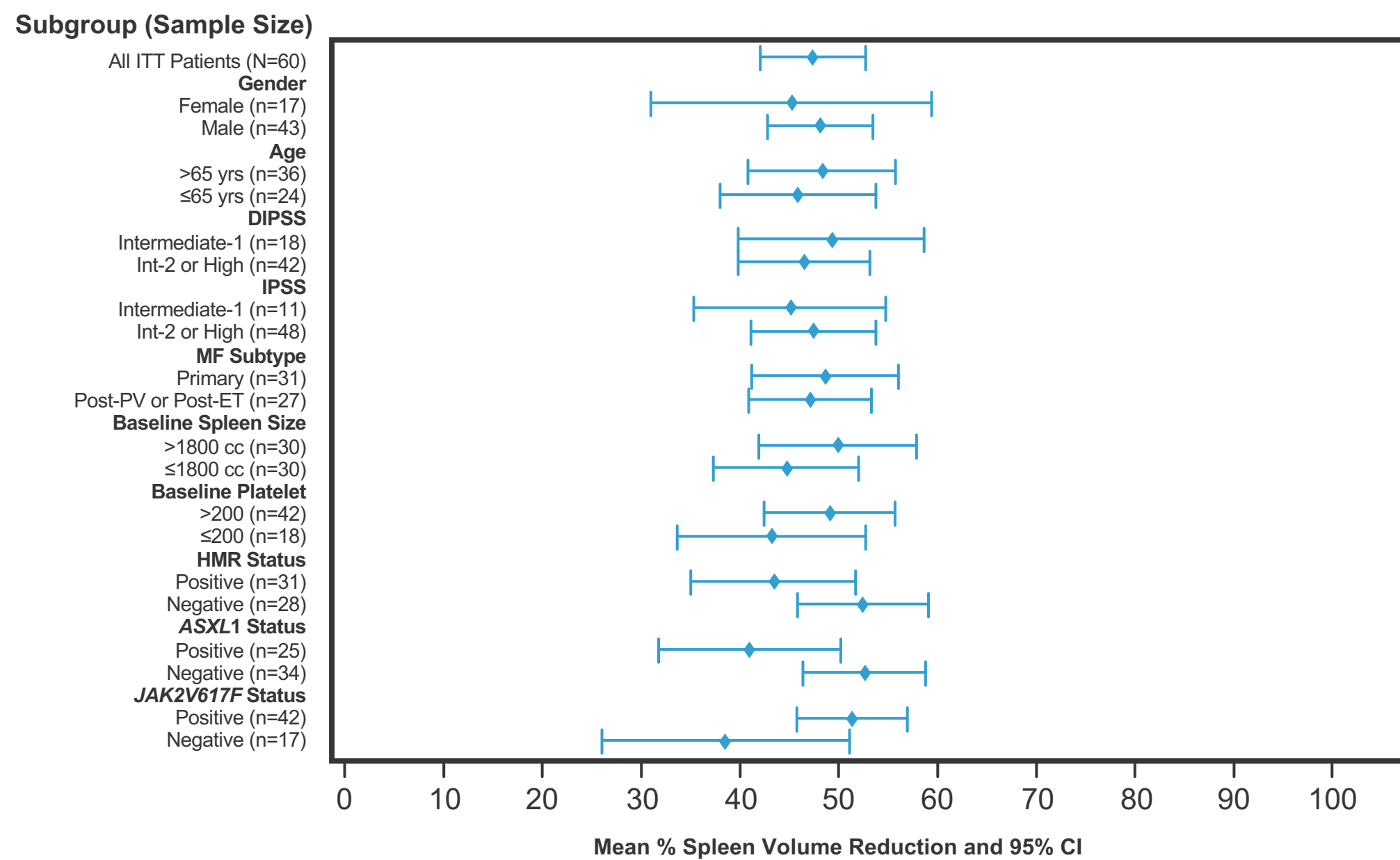
- TSS50 at Week 24: 57% (34/60), 95% CI: [43, 69]
- Median TSS reduction: ~59%



Patients are evaluable for TSS50 at Week 24 if they have had Week 24 TSS assessment by the data cutoff date or discontinued prior to Week 24 due to any reason. One patient with missing baseline TSS and one patient with baseline TSS=0 were excluded from the analysis.

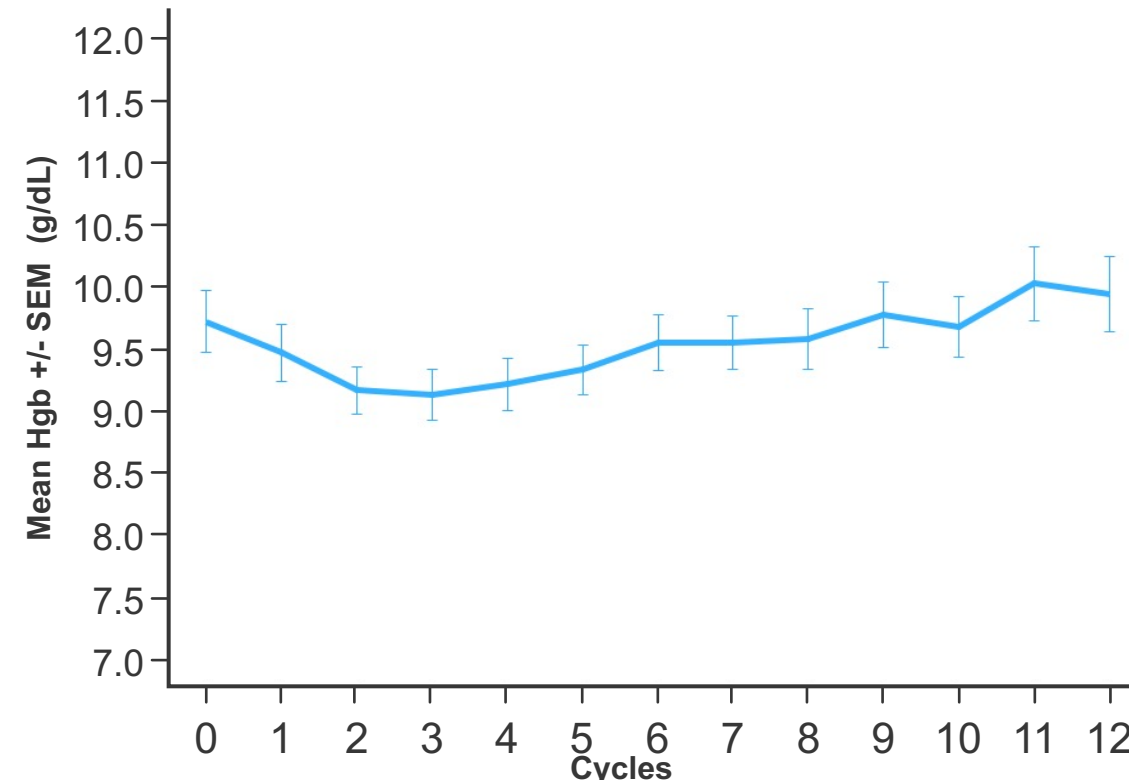
Pelabresib Treatment Resulted in Similar Spleen Volume Reduction at Week 24 Across Patient Subgroups

Subgroup Analysis of Percentage Reduction in Spleen Volume From Baseline to Week 24



Hemoglobin Improvement Observed in Patients With Baseline Hemoglobin <10 g/dL

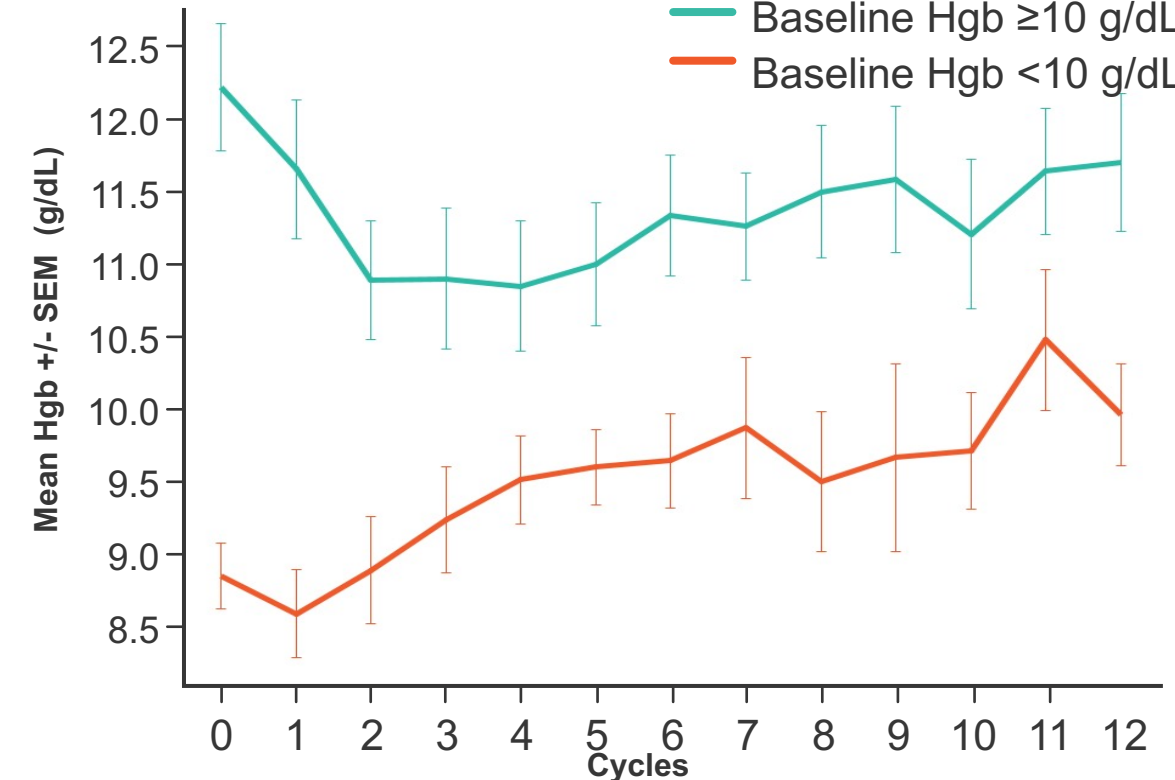
All Patients¹ Mean Hgb Over Time



■ N 69 68 68 69 67 66 61 62 59 49 48 43 42

¹Patients on treatment ≥12 weeks; ²Received no transfusions 12 weeks prior to C101 and during treatment.

Patients Without Transfusions^{1,2} Mean Hgb Over Time



■ N 18 18 17 18 18 18 17 18 17 14 13 14 14
■ N 8 8 8 8 8 8 7 7 6 6 7 5 5

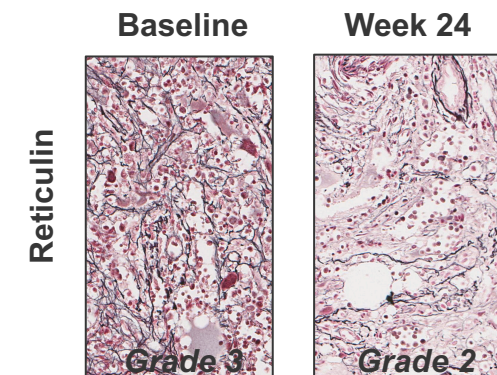
Pelabresib Treatment Results in Bone Marrow Fibrosis Grade Improvement as Assessed by Central Pathology Review

Reticulin Fibrosis Grade	Local Review ¹ (n=48)	Central Review ¹ (n=27)
Improved ≥ -1 grade	33%	33%
Stabilized/No change	52%	59%
Worsened ≥ +1 grade	4%	4%
Discontinuation*	10%	4%

Per the central review:

- 33% of patients had at least one grade improvement in bone marrow fibrosis
- All the improvements were observed within 6 months of treatment
- One patient had worsening in bone marrow fibrosis

Representative Example of Bone Marrow Biopsy at Baseline and 24 Weeks



Patients are evaluable for bone marrow fibrosis assessment if they have had baseline and at least one postbaseline bone marrow biopsy evaluation or discontinued prior to Week 24 for any reason.
*Patients came off study without having postbaseline treatment biopsy.
†Best change in bone marrow fibrosis grade any time during study.

Safety Summary

Treatment-Emergent Adverse Events ¹	All Grade N=78 ² n (%)	Grade 3 N=78 ² n (%)	Grade 4 N=78 ² n (%)
Hematologic Events			
Anemia	26 (33)	22 (28)	1 (1)
Thrombocytopenia ³	25 (32)	4 (5)	2 (3)
Nonhematologic Events			
Gastrointestinal Events			
Diarrhea	23 (30)	0	0
Nausea	13 (17)	0	0
Abdominal pain ⁴	13 (17)	0	0
Other Nonhematologic Events			
Dysgeusia	15 (19)	0	0
Asthenic conditions ⁵	15 (19)	0	0
Musculoskeletal pain ⁶	15 (19)	0	0
Respiratory tract infection ⁷	14 (18)	0	1 (1)
Dizziness ⁸	13 (17)	0	0

¹TEAEs of all grade that occurred in ≥15% of patients; ²Safety-evaluable population: received at least one dose of study drug at the time of the data cut; ³Includes TEAEs platelet count decreases; ⁴Includes TEAEs abdominal pain upper; ⁵Includes TEAEs of asthenia and fatigue; ⁶Includes TEAEs of myalgia, bone pain, arthralgia and back pain; ⁷Includes TEAEs of upper respiratory tract infection, influenza, bronchitis, sinusitis, rhinitis, nasopharyngitis, pneumonia and pulmonary sepsis; ⁸Includes TEAEs vertigo.

Conclusions

- Pelabresib treatment in combination with ruxolitinib in JAKi treatment-naïve MF patients resulted in similar spleen volume reduction at Week 24 across all patient subgroups compared with the overall population
- Improvement in bone marrow findings by central pathology review suggests potential disease modification
- Pelabresib in combination with ruxolitinib was generally well tolerated; thrombocytopenia was generally low grade, manageable and reversible
- Based on these encouraging results, MANIFEST-2, a Phase 3 randomized double-blind trial of pelabresib + ruxolitinib vs placebo + ruxolitinib in a JAKi-naïve patient population, has been initiated and is open for enrollment (NCT04603495)