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Pelabresib in combination with ruxolitinib for Janus kinase inhibitor-naive patients with myelofibrosis: 72-week follow-up with long-term efficacy outcomes of the Phase III MANIFEST-2 study

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Pelabresib (CPI-0610/DAK539) is an investigational new drug and has not been approved by any regulatory authority.

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Oral S223 presented at: European Hematology Association (EHA) Annual Congress; June 12-15, 2025; Milan, Italy

Disclosures

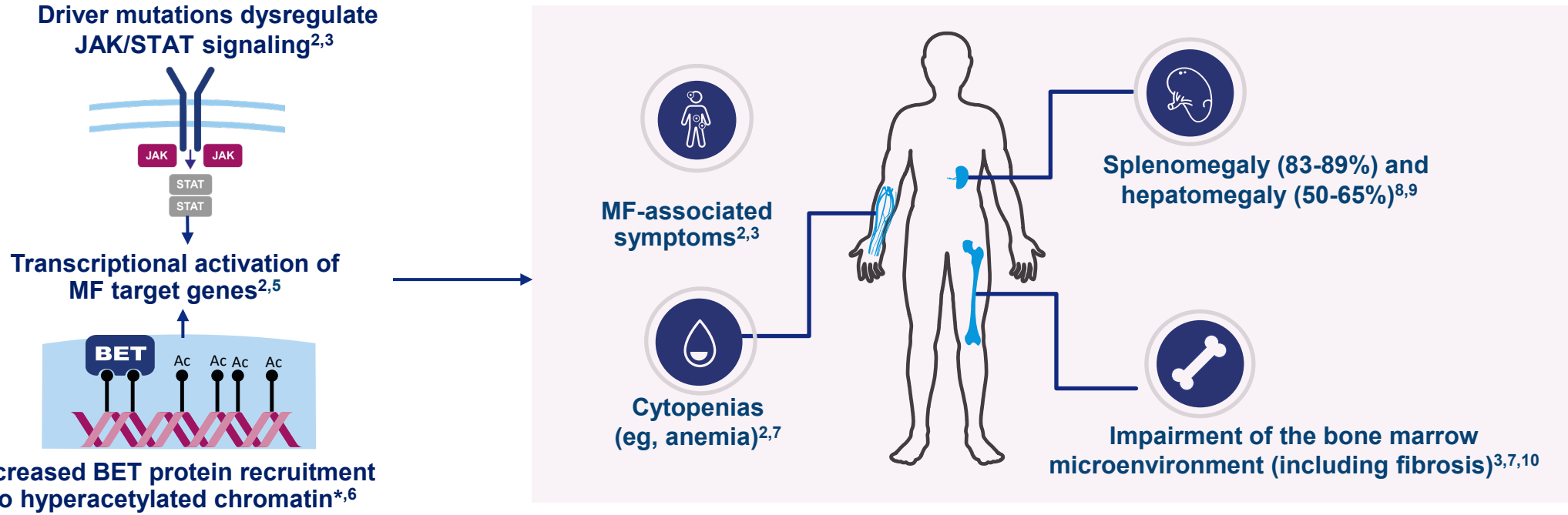
Professor Alessandro M. Vannucchi

- Consulting or advisory activities: AOP, Blueprint, Bristol Myers Squibb, GSK, Incyte, Novartis
- Speakers' bureau: AOP, Blueprint, Bristol Myers Squibb, GSK, Incyte, Novartis

Oral S223 presented at: European Hematology Association (EHA) Annual Congress; June 12-15, 2025; Milan, Italy

Dysregulation of the JAK/STAT pathway and BET-mediated gene modulation are associated with MF pathophysiology[1,2]

- **MF is a progressive and life-threatening disease, characterized by debilitating symptoms, cytopenias (eg, anemia), splenomegaly, and impairment of the bone marrow microenvironment (including fibrosis).[3] Reduction in spleen size has been associated with improved OS[4]**



- JAK inhibitor monotherapy is the standard of care in intermediate- and high-risk MF.[11] However, unmet medical need persists due to suboptimal depth and durability of response and treatment-emergent adverse events in a proportion of patients[11,12]
- Pelabresib (CPI-0610/DAK539) is an investigational, oral, small molecule drug that inhibits BET proteins and alters BET-mediated expression of genes that contribute to the pathology of MF[13]

Figure modified with permission from Springer Nature Customer Service Centre GmbH: Springer Nature, *Leukemia*, Paradigm shift: combination BET and JAK inhibition in myelofibrosis, J Mascarenhas et al. Copyright ©2021.
*Based on BET activity in neoplasms, not specifically in MF.[6]
Ac, histone acetylation; BET, bromodomain and extraterminal domain; JAK, Janus kinase; MF, myelofibrosis; OS, overall survival; STAT, signal transducer and activator of transcription.
1. Kleppe M, et al. *Cancer Cell*. 2018;33(1):29-43; 2. Mughal TI, et al. *Int J Gen Med*. 2014;7:89-101; 3. Tefferi A. *Am J Hematol*. 2021;96(1):145-162; 4. Vannucchi A, et al. *Haematologica*. 2015;100(9):1139-1145; 5. Schieber M, et al. *Blood Cancer J*. 2019;9(9):74; 6. Shorstova T, et al. *Br J Cancer*. 2021;124(9):1478-1490; 7. Naymagon L, Mascarenhas J. *Hemasphere*. 2017;1(1):e1; 8. Cervantes F, et al. *Blood*. 2009;113(13):2895-2901; 9. Passamonti F, et al. *Blood*. 2010;116(15):2857-2858; 10. Gangat N, et al. *Br J Haematol*. 2020;191(2):152-170; 11. Bose P, Verstovsek S. *Hemasphere*. 2020;4(4):e424; 12. Harrison CN, et al. *Future Oncol*. 2022;18(27):2987-2997; 13. Mascarenhas J, et al. *J Clin Oncol*. 2023;41(32):4993-5004.

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The MANIFEST-2 study is a global, randomized, double-blind, Phase III trial

The MANIFEST-2 study is investigating the efficacy and safety of the combination therapy of PELA+RUX versus PBO+RUX in JAKi-naive patients with MF[1,2]

Study population

JAKi-naive patients with MF (N=430)
(primary or post-ET/PV)

- DIPSS Int-1 risk or higher
- Spleen volume (≥450 cm^3)
- Platelet count ≥100 × 10^9/L
- TSS ≥10 (≥3 for two symptoms, MFSAF v4.0)
- Peripheral blast count <5%
- ECOG PS ≤2

Double-blind randomization (1:1)

Treatment arms

PELA 125 mg* PO QD Day 1-14 + **RUX** Per label with a 5 mg BID lower starting dose† Day 1-21

21-day cycles

PBO PO QD Day 1-14 + **RUX** Per label with a 5 mg BID lower starting dose† Day 1-21

Primary endpoint

- SVR35 response at Week 24

Key secondary endpoints

- Absolute change in TSS from baseline at Week 24
- TSS50 response at Week 24

Safety

- AEs of all grades and serious AEs

- The MANIFEST-2 study met its primary endpoint, showing a statistically significant improvement in SVR35 response at Week 24 with PELA+RUX compared with PBO+RUX in JAKi-naive patients with MF[1]
- Here, we present follow-up efficacy and safety outcomes at Week 72; in addition, longer-term analyses were conducted for PFS,‡ OS, and LFS, although the study was not powered for survival outcomes

*The starting dose for pelabresib was 125 mg QD and protocol-defined dose modifications based on AEs and treatment response allowed a dose range between 50 mg and 175 mg QD. †RUX was started at 10 mg BID (baseline platelet count 100-200 × 10^9/L) or 15 mg BID (baseline platelet count >200 × 10^9/L) with a mandatory dose increase by 5 mg BID after 1 cycle and a maximum dose of 25 mg BID as per the label. ‡Defined as the time from randomization to documented progression, or death from any cause.
AE, adverse event; BID, twice daily; DIPSS, Dynamic International Prognostic Scoring System; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, essential thrombocythemia; Int, intermediate; JAKi, Janus kinase inhibitor; LFS, leukemia-free survival; MF, myelofibrosis; MFSAF, Myelofibrosis Symptom Assessment Form; OS, overall survival; PBO, placebo; PELA, pelabresib; PFS, progression-free survival; PO, orally; PV, polycythemia vera; QD, once daily; RUX, ruxolitinib; SVR35, ≥35% reduction in spleen volume from baseline; TSS, total symptom score; TSS50, ≥50% reduction in total symptom score from baseline.
1. Rampal R, et al. *Nat Med*. 2025;31(5):1531-1538; 2. Rampal R, et al. Presented at EHA 2024 [Oral S221].

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Comparable patient disposition across treatment arms at Week 72 data cutoff

	PELA+RUX	PBO+RUX
Randomized	214 (100%)	216 (100%)
Treated	212 (99.1%)	214 (99.1%)
Ongoing for study follow-up*	145 (67.8%)	157 (72.3%)
Ongoing on double-blind treatment	114 (53.3%)	120 (55.6%)
Discontinued double-blind treatment†	98 (45.8%)	94 (43.5%)
Reasons for discontinuation:		
Adverse event	38 (17.8%)	23 (10.6%)
Physician decision (including lack of benefit)	16 (7.5%)	30 (13.9%)
Disease progression	11 (5.1%)	11 (5.1%)
Eligible for transplant	10 (4.7%)	14 (6.5%)
Other‡	23 (10.7%)	15 (6.9%)

Data cutoff date: August 30, 2024. The study opened for enrollment in November 2020; the first patient received their initial treatment on April 22, 2021, and the last patient received their first treatment on March 2, 2023.
Percentages reported are based on the number of patients randomized (intent-to-treat set), and based on a minimum treatment duration of 72 weeks for the last patient enrolled.
*Includes patients on double-blind treatment, patients who are no longer on treatment but being monitored for PFS/OS, and patients on open-label treatment (2 patients on PBO+RUX who crossed over to PELA+RUX).
†One patient in the PBO+RUX arm did not report reason for treatment discontinuation. ‡Other: non-compliance, withdrawal of consent.
OS, overall survival; PBO, placebo; PELA, pelabresib; PFS, progression-free survival; RUX, ruxolitinib.

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Patient and disease characteristics were balanced across treatment arms

Characteristic[1]		PELA+RUX (N=214)	PBO+RUX (N=216)
Age — years	Median (min, max)	66 (19, 84)	66 (26, 88)
Sex — n (%)	Female / male	85 (39.7) / 129 (60.3)	94 (43.5) / 122 (56.5)
Race — n (%)	White / Asian / Black	160 (74.8) / 35 (16.4) / 2 (0.9)	163 (75.5) / 42 (19.4) / 0
	American Indian or Alaska Native	1 (0.5)	0
	Not reported / Unknown	15 (7.0) / 1 (0.5)	11 (5.1) / 0
Myelofibrosis subtype — n (%)	Primary myelofibrosis	107 (50.0)	110 (50.9)
	Post-polycythemia vera myelofibrosis	45 (21.0)	53 (24.5)
	Post-essential thrombocytopenia myelofibrosis	62 (29.0)	53 (24.5)
Dynamic International Prognostic Scoring System — n (%)	Intermediate-1	128 (59.8)	127 (58.8)
	Intermediate-2	75 (35.0)	74 (34.3)
	High-risk	11 (5.1)	15 (6.9)
Mutations — n (%)	*JAK2* V617F	124 (57.9)	122 (56.5)
	CALR	45 (21.0)	50 (23.2)
	MPL	11 (5.1)	13 (6.0)
	Triple negative*	8 (3.7)	8 (3.7)
	High molecular risk mutations†	91 (42.1)	79 (36.9)
Hemoglobin — g/dL	Median (range)	10.9 (5.8-18.0)	11.0 (6.7-17.9)
	≤10 — n (%)	70 (32.7)	76 (35.2)
Platelets — × 10^9/L	Median (min, max)	285 (99, 1303)	287 (66, 1084)
	>200 × 10^9/L — n (%)	154 (72)	157 (72.7)
Peripheral blasts	Mean (SD)	0.8 (1.18)‡	0.8 (1.25)§
RBC transfusions¶ — patient n (%)	Requiring RBC transfusion at baseline	22 (10.3)	21 (9.7)
Transfusion dependent at enrollment‖,1 — patient n (%)		8 (3.7)	2 (0.9)
ECOG performance status — n (%)	0	107 (50.0)	109 (50.5)
	1	97 (45.3)	95 (44.0)
	≥2	10 (4.7)	10 (4.6)
	Missing	0	2 (0.9)
Spleen volume (central read)#	Median spleen volume (range) — cc	1308.89 (200.24-7117.03)	1382.97 (277.87-5540.45)
Total symptom score**	Median total symptom score (range)	26.6 (7.3-66.4)	24.7 (9.0-68.4)
Bone marrow fibrosis grade — n (%)	0	6 (2.8)	3 (1.4)
	1	32 (15.0)	35 (16.2)
	2	58 (27.1)	67 (31.0)
	3	81 (37.9)	82 (38.0)
	Missing	37 (17.3)	29 (13.4)

*Triple-negative status was missing for 55 patients (28 in the PELA+RUX arm and 27 in the PBO+RUX arm). †High molecular risk mutations include *ASXL1*, *EZH2*, *IDH1*, *IDH2*, *SRSF2*, and *U2AF1* mutations. ‡n=208. §n=207.
¶RBC transfusions refer to number of patients who received any RBC transfusion during the 12-week baseline period prior to dosing. ‖Transfusion dependent at enrollment is defined as having received ≥6 units of RBC transfusions during the 12-week baseline period prior to dosing. #Randomization of patients was based on local read. **Patients with baseline TSS values of <10 have ≥2 individual symptoms score ≥3 at baseline.
ASXL1, ASXL transcriptional regulator 1; *CALR*, calreticulin; ECOG, Eastern Cooperative Oncology Group; *EZH2*, enhancer of zeste 2 polycomb repressive complex 2 subunit; *IDH1/2*, isocitrate dehydrogenase 1/2; *JAK2*, Janus kinase 2; max, maximum; min, minimum; *MPL*, MPL proto-oncogene, thrombopoietin receptor; PBO, placebo; PELA, pelabresib; RBC, red blood cell; RUX, ruxolitinib; SD, standard deviation; *SRSF2*, serine and arginine rich splicing factor; TSS, total symptom score; *U2AF1*, U2 small nuclear RNA auxiliary factor 1.
1. Rampal R, et al. Presented at EHA 2024 [Oral S221].

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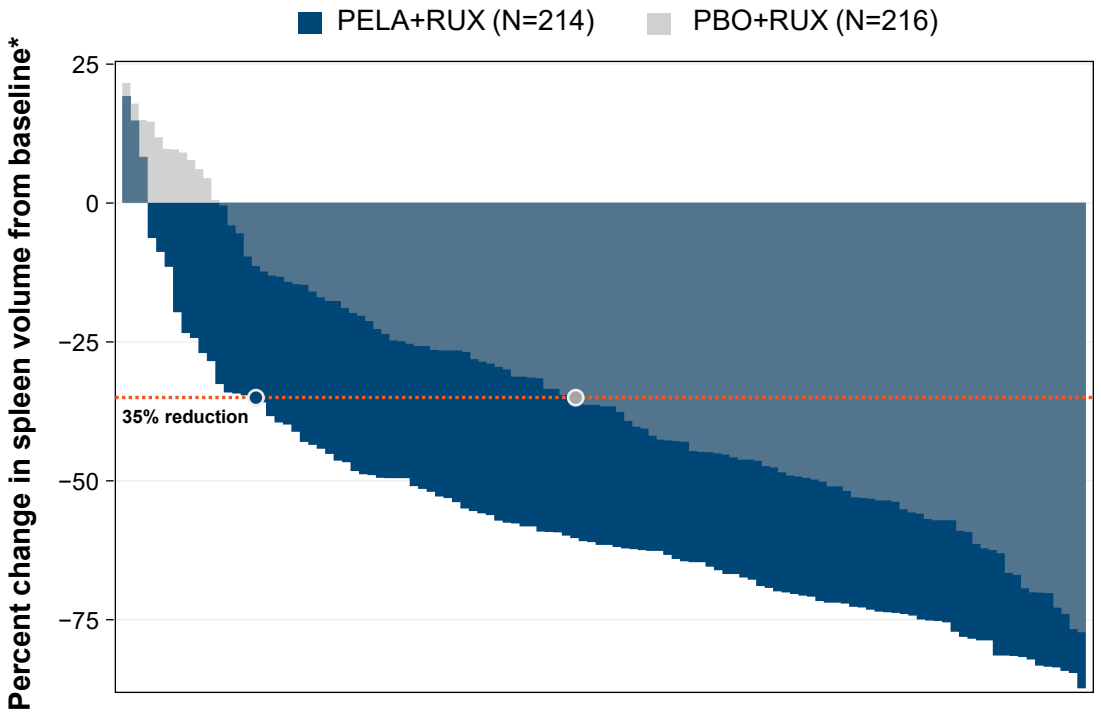
Splenic response rates continued to be greater at Week 72 with PELA+RUX versus PBO+RUX

Sustained improvements in spleen volume with PELA+RUX versus PBO+RUX at Week 72



ITT population

	PELA+RUX (N=214)	PBO+RUX (N=216)
SVR35 response at Week 72	46.3	29.2
Difference† (95% CI)	16.7 (7.9-25.4)	

Mean % change in spleen volume at Week 72‡	−57.2 (n=114)	−34.9 (n=119)
95% CI	−61.0, −53.3	−39.0, −30.7

Data cutoff date: August 30, 2024.
Spleen volume assessed by central read.
*Waterfall plots represent patients who have baseline and Week 72 data. †Calculated by stratified Cochran-Mantel-Haenszel test. ‡Patients without Week 72 assessment are considered non-responders.
CI, confidence interval; ITT, intent-to-treat; PBO, placebo; PELA, pelabresib; RUX, ruxolitinib; SVR35, ≥35% reduction in spleen volume from baseline.

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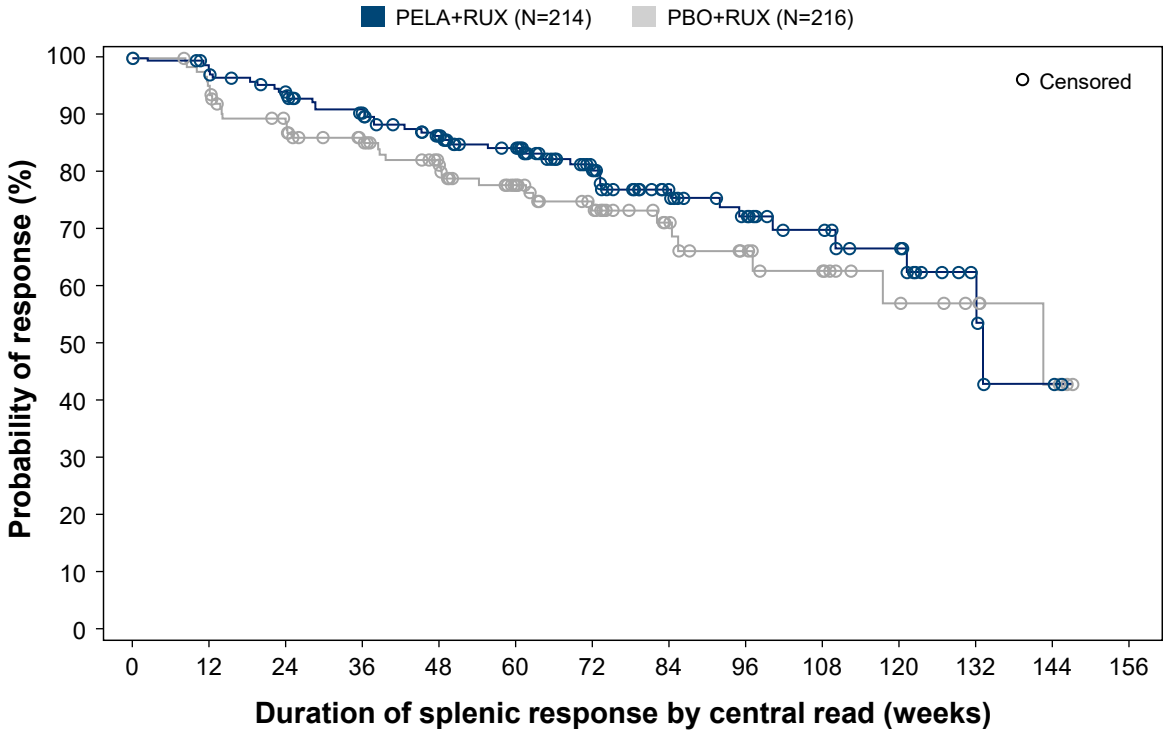
A greater number of patients maintained SVR35 responses with PELA+RUX versus PBO+RUX at Week 72 data cutoff

Durable splenic response persists with PELA+RUX versus PBO+RUX at Week 72 data cutoff



Number of at-risk patients

PELA+RUX	176	168	155	139	124	111	77	55	42	27	18	7	3	0
PBO+RUX	132	118	104	91	78	60	46	30	23	16	10	6	3	0

ITT population

	PELA+RUX (N=214)	PBO+RUX (N=216)
Loss of SVR35 response and >25% increase in spleen volume from nadir, % (n/N)*	**22.7** (40/176)	**25.8** (34/132)

80% of responders in the PELA+RUX arm maintained their response for 72 weeks compared with 73% in the PBO+RUX arm

Data cutoff date: August 30, 2024. Based on a minimum treatment duration of 72 weeks for the last patient enrolled.
Spleen volume assessed by central read.
*Among anytime SVR35 responders. Duration of the splenic response is defined as the time from when the criterion for splenic response is first met (ie, a ≥35% reduction from baseline spleen volume) until the time at which there is a <35% reduction in spleen volume from baseline and also an increase of >25% from nadir as measured by MRI or CT is first documented.
CT, computed tomography; ITT, intent-to-treat; MRI, magnetic resonance imaging; PBO, placebo; PELA, pelabresib; RUX, ruxolitinib; SVR35, ≥35% reduction in spleen volume from baseline.

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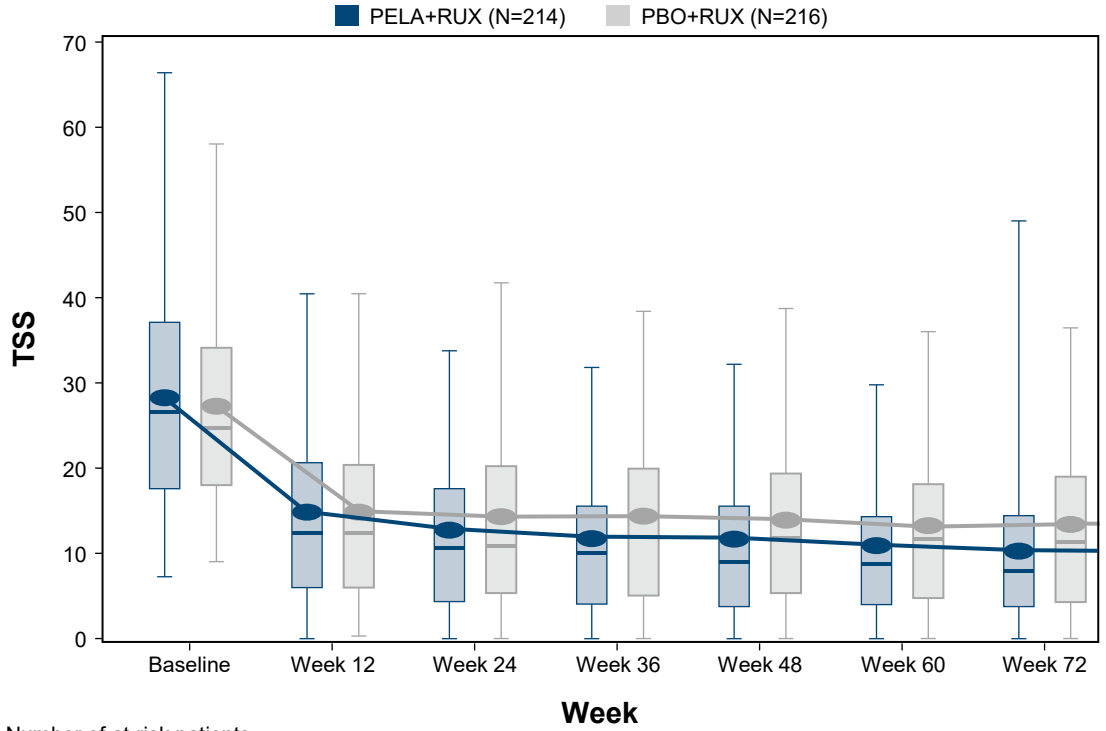
Numerically greater improvements in TSS at Week 72 were observed in patients treated with PELA+RUX versus PBO+RUX

Sustained improvements in TSS with PELA+RUX versus PBO+RUX at Week 72



Number of at-risk patients

PELA+RUX	214	191	184	165	154	141	129
PBO+RUX	216	199	193	169	157	151	133

ITT population

	PELA+RUX (N=214)	PBO+RUX (N=216)
Absolute change in TSS* at Week 72, LSM	−15.42	−13.19
LSM difference (95% CI) at Week 72	−2.23 (−4.73, 0.27)	
TSS50 response at Week 72, %	42.1	35.2
Difference† (95% CI) at Week 72	6.3 (−2.6, 15.3)	

Data cutoff date: August 30, 2024.
Spleen volume assessed by central read.
*TSS assessed by MFSAF v4.0 and using an MMRM analysis of absolute change from baseline in TSS. †Difference in treatment groups analyzed by stratified Cochran-Mantel-Haenszel test (weighted 95% CI adjusted across strata).
CI, confidence interval; ITT, intent-to-treat; LSM, least squares mean; MFSAF, Myelofibrosis Symptom Assessment Form; MMRM, mixed model for repeated measures; PBO, placebo; PELA, pelabresib; RUX, ruxolitinib; TSS, total symptom score; TSS50, ≥50% reduction in total symptom score from baseline.

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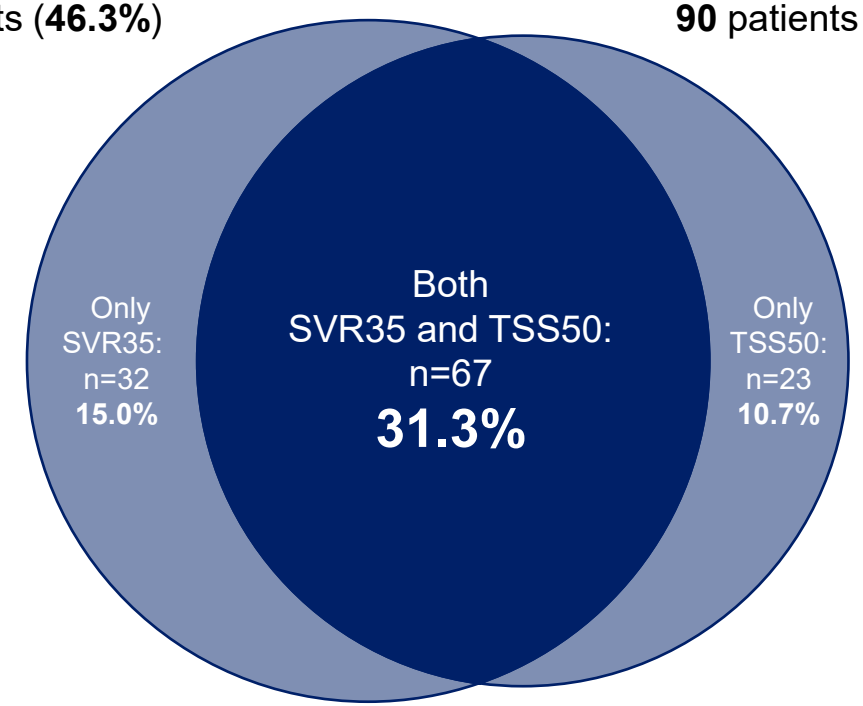
Nearly twice as many patients achieved both SVR35 and TSS50 responses with PELA+RUX versus PBO+RUX at Week 72

PELA+RUX (N=214)

SVR35 response:
99 patients (**46.3%**)

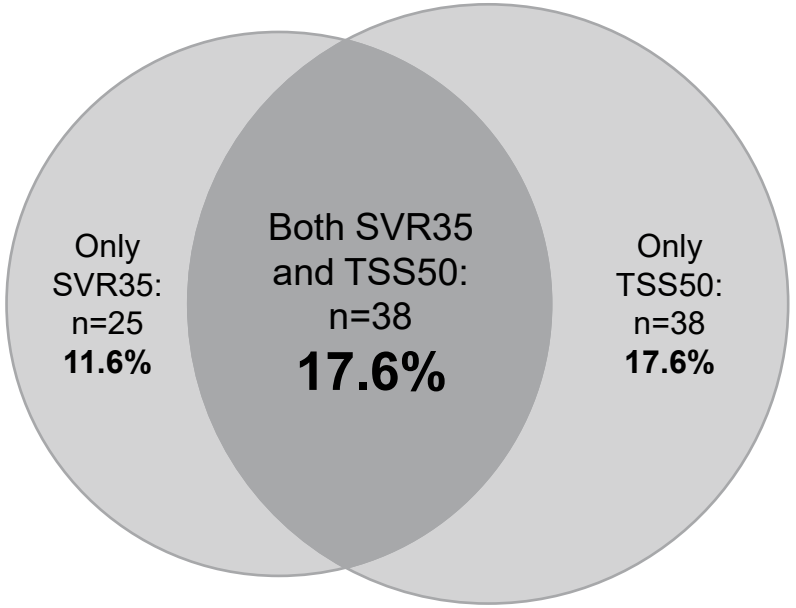
TSS50 response:
90 patients (**42.1%**)



PBO+RUX (N=216)

SVR35 response:
63 patients (**29.2%**)

TSS50 response:
76 patients (**35.2%**)



Dual SVR35 / TSS50 responders at Week 72

Data cutoff date: August 30, 2024.
PBO, placebo; PELA, pelabresib; RUX, ruxolitinib; SVR35, ≥35% reduction in spleen volume from baseline; TSS50, ≥50% reduction in total symptom score from baseline.

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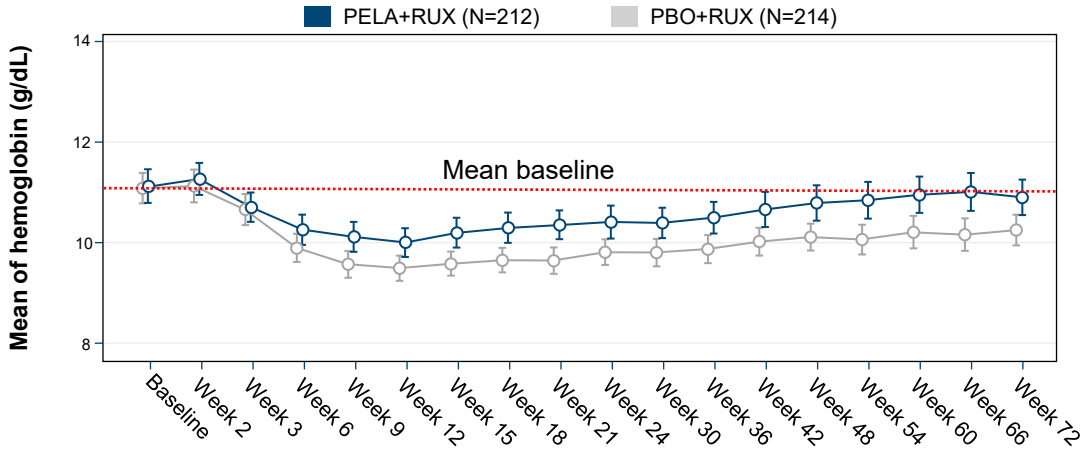
A numerically greater proportion of patients had a hemoglobin response, and fewer patients required RBC transfusions with PELA+RUX versus PBO+RUX

Hemoglobin levels in the PELA+RUX arm continued to rise, approaching baseline levels at Week 72 (safety population*)



Number of at-risk patients

PELA+RUX	212	204	209	199	193	189	186	185	184	181	171	168	162	156	148	144	139	136
PBO+RUX	214	206	211	209	207	205	204	199	196	195	185	179	175	170	161	152	145	139

ITT population

	PELA+RUX (N=214)	PBO+RUX (N=216)
Hemoglobin response,†,‡ % (n/N) (95% CI)	**16.4** (35/214) (11.4-21.31)	**9.3** (20/216) (5.39-13.12)
Hemoglobin response,†,‡ in patients with anemia (baseline <10 g/dL), % (n/n) (95% CI)	**20.9** (14/67) (11.16-30.63)	**16.9** (12/71) (8.18-25.62)

Fewer patients in the PELA+RUX arm versus the PBO+RUX arm required RBC transfusions§ over 72 weeks:

- Weeks 0 to 24: 24.1% (35/145) versus 36.4% (59/162)
- Weeks 25 to 48: 19.3% (28/145) versus 30.9% (50/162)
- Weeks 49 to 72: 19.3% (28/145) versus 25.3% (41/162)

Data cutoff date: August 30, 2024. *Safety population received ≥1 dose of study drug. †Hemoglobin response is defined as a ≥1.5 g/dL mean increase in hemoglobin from baseline in the absence of transfusions during the prior 12 weeks in the ITT population. ‡Baseline hemoglobin defined as the last assessment prior to or on Cycle 1 Day 1, regardless of blood transfusions. §RBC transfusions refer to number of patients who received any RBC transfusion during the first 24 weeks after Cycle 1 Day 1, during the 25-48 weeks after Cycle 1 Day 1 or during the 49-72 weeks after Cycle 1 Day.
CI, confidence interval; ITT, intent-to-treat; PBO, placebo; PELA, pelabresib; RBC, red blood cell; RUX, ruxolitinib.

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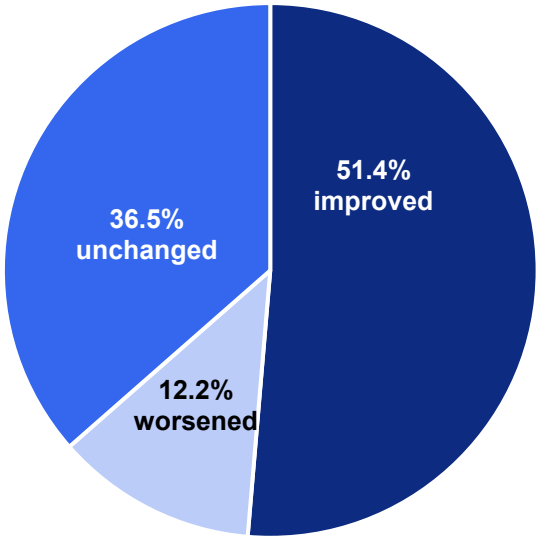
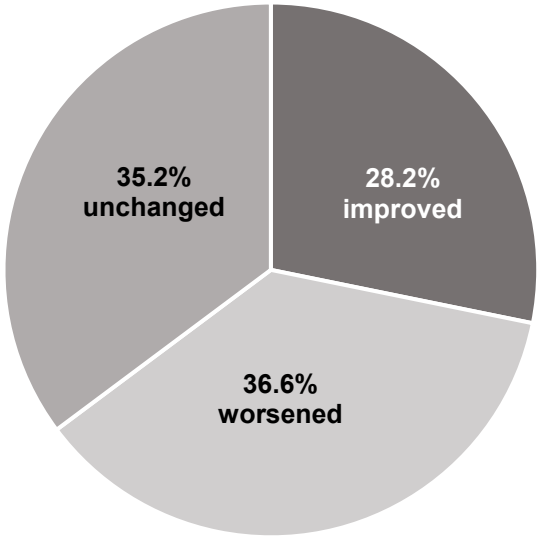
A greater proportion of patients had improvements in bone marrow fibrosis at Week 72 with PELA+RUX versus PBO+RUX

Improvement of reticulin fibrosis grade* with PELA+RUX versus PBO+RUX at Week 72

PELA+RUX (n=74†)



PBO+RUX (n=71†)



	PELA+RUX (N=74†)	PBO+RUX (N=71†)
Improved by ≥1 grade at Week 72, %	51.4	28.2
Worsened by ≥1 grade at Week 72, %	12.2	36.6

- BMF improvement of ≥1 grade in evaluable patients was reported in 51.4% versus 28.2% of patients in the PELA+RUX versus PBO+RUX arms, respectively, at Week 72 (difference: 25.33%; 95% CI: 9.77-40.88)

Data cutoff date: August 30, 2024.
*By central read. †n=145 evaluable patients (patients with non-missing baseline and non-missing Week 72 BMF data); n=74 in the PELA+RUX arm and n=71 in the PBO+RUX arm. n=285 (66%) missing data.
BMF, bone marrow fibrosis; CI, confidence interval; PBO, placebo; PELA, pelabresib; RUX, ruxolitinib.

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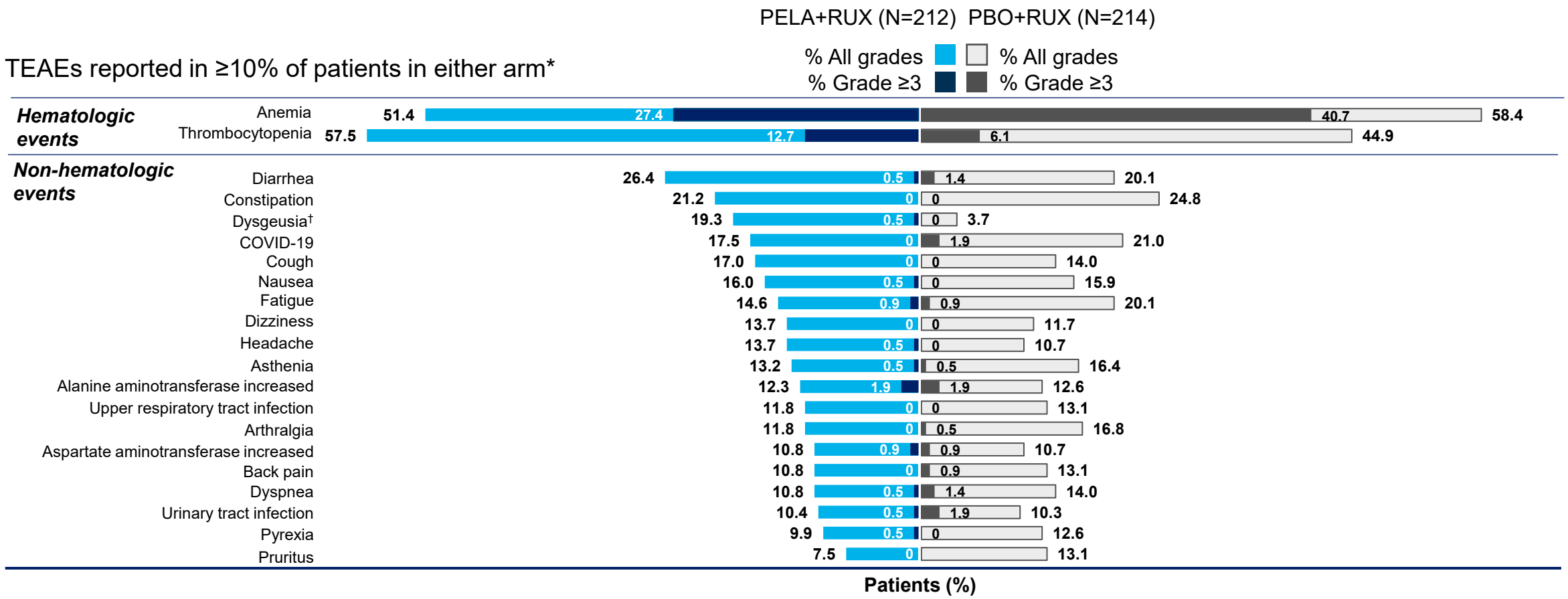
Treatment-emergent adverse events were similar between treatment arms at Week 72 data cutoff

The most frequent TEAEs in both treatment arms were low grade (Grade <3)



Data cutoff date: August 30, 2024.
*Safety population: received ≥1 dose of study drug. TEAEs are regardless of relationship to study drug. A TEAE for the double-blind treatment period is defined as an adverse event that has a start date on or after the first dose of PELA/PBO and before 30 days after the last dose of PELA/PBO or before the start of alternative (off-study) treatment for MF, whichever occurs first. †Dysgeusia was successfully managed in most patients by dose reductions of pelabresib.
COVID-19, coronavirus disease 2019; MF, myelofibrosis; PBO, placebo; PELA, pelabresib; RUX, ruxolitinib; TEAE, treatment-emergent adverse event.

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Leukemic transformation

Accelerated- and blast-phase progression*

	PELA+RUX			PBO+RUX		
	Accelerated and blast phase*	Accelerated phase	Blast phase	Accelerated and blast phase*	Accelerated phase	Blast phase
As of March 29, 2024, (Week 48) data cutoff, % (n/N)†,‡	**6.1** (13/213)	**0.9** (2/213)	**5.2** (11/213)	**2.3** (5/214)	**1.4** (3/214)	**0.9** (2/214)
As of August 30, 2024, (Week 72) data cutoff, % (n/N)§,¶	**6.1** (13/214)	**0.9** (2/214)	**5.1** (11/214)	**4.2** (9/214)	**1.4** (3/214)	**2.8** (6/214)

- As of August 30, 2024, accelerated- and blast-phase progression, adjudicated independently by external experts, was reported in 6.1% (13/214) of patients on PELA+RUX and in 4.2% (9/214) of patients on PBO+RUX

- An early imbalance in cases of leukemic transformation was observed with PELA+RUX compared with PBO+RUX. Over time, the imbalance in proportion of patients with transformation to blast phase decreased. Overall, the observed frequency was in line with what is typically seen in MF

*Assessment based on local laboratory results, adverse events, and documented disease progression. Leukemic transformation confirmed by a bone marrow blast count of ≥20% or a peripheral blood blast content of ≥20% associated with an absolute blast count of ≥1 × 10^9/L that lasts for at least 2 weeks. †Minimum of 48 weeks of leukemia-free survival follow-up; median follow-up 17.1 months. ‡The denominator of 213 includes 1 patient who crossed over from placebo + ruxolitinib. §Minimum of 72 weeks of leukemia-free survival follow-up. The last adjudication in March 2025, with the cutoff as of August 30, 2024, showed a ratio of 11:6. ¶The denominator of 214 for PELA+RUX includes 2 patients who crossed over from PBO+RUX.
MF, myelofibrosis; PBO, placebo; PELA, pelabresib; RUX, ruxolitinib.

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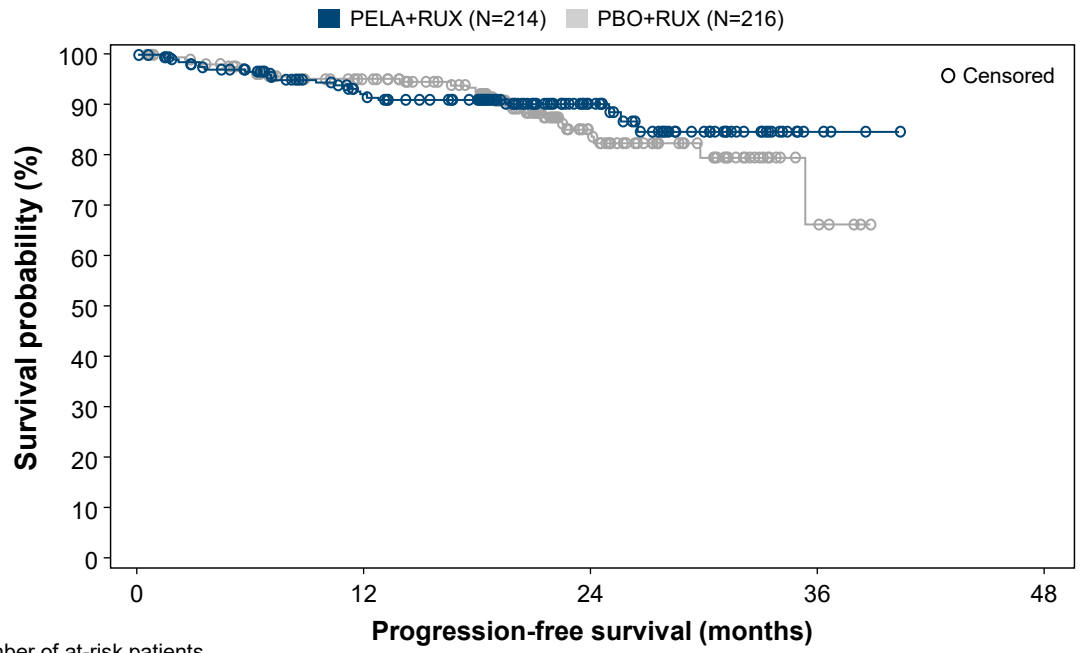
Progression-free survival and leukemia-free survival (ITT population)

Longer-term follow-up (Week 72 data cutoff) showed fewer PFS events in the PELA+RUX arm compared with the PBO+RUX arm; LFS outcomes were similar between the two arms

Progression-free survival*

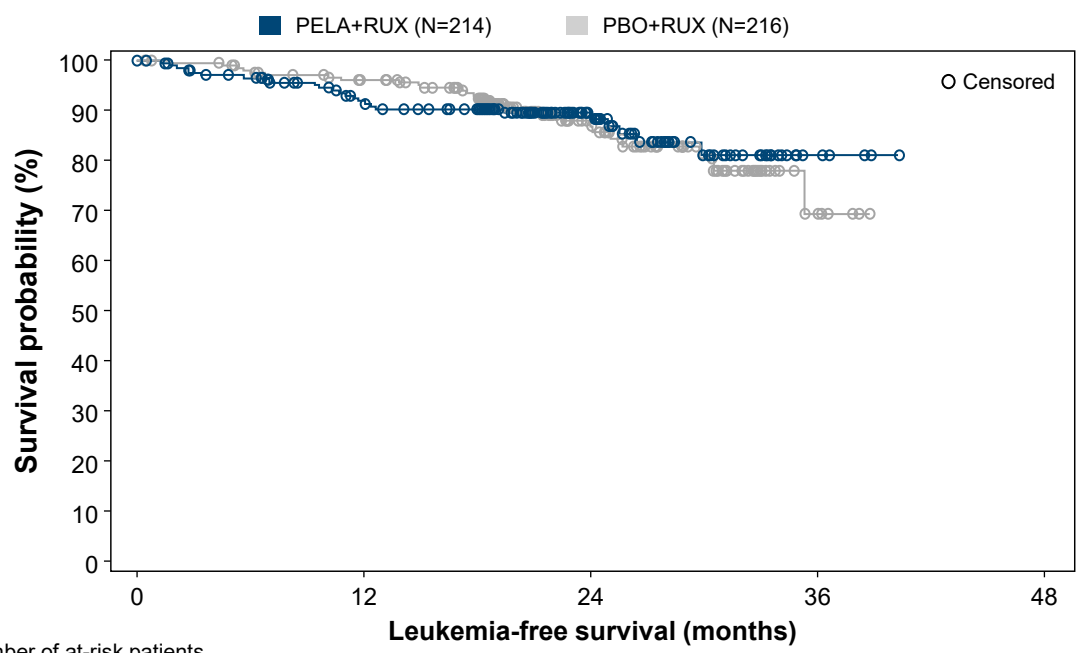


Number of at-risk patients

PELA+RUX	214	159	60	4	0
PBO+RUX	216	176	62	5	0

	PELA+RUX (N=214)	PBO+RUX (N=216)
Total events, n (%)	**21** (9.8)	**27** (12.5)
Hazard ratio (95% CI)	0.87 (0.49-1.56)	

Leukemia-free survival



Number of at-risk patients

PELA+RUX	214	172	72	5	0
PBO+RUX	216	194	76	7	0

	PELA+RUX (N=214)	PBO+RUX (N=216)
Total events, n (%)	**25** (11.7)	**28** (13.0)
Hazard ratio (95% CI)	0.99 (0.57-1.72)	

Data cutoff date: August 30, 2024. Median follow-up of 92 weeks. ***Defined as time from randomization until documented progression or until death from any cause for patients without documented progression, whichever comes first. Progression was defined as progressive splenomegaly (enlargement of spleen volume by MRI or CT of ≥25% vs baseline by central radiology review) or leukemic transformation (confirmed by blast of ≥20%), whichever comes first.
CI, confidence interval; CT, computed tomography; ITT, intent-to-treat; LFS, leukemia-free survival; MRI, magnetic resonance imaging; PBO, placebo; PELA, pelabresib; PFS, progression-free survival; RUX, ruxolitinib.

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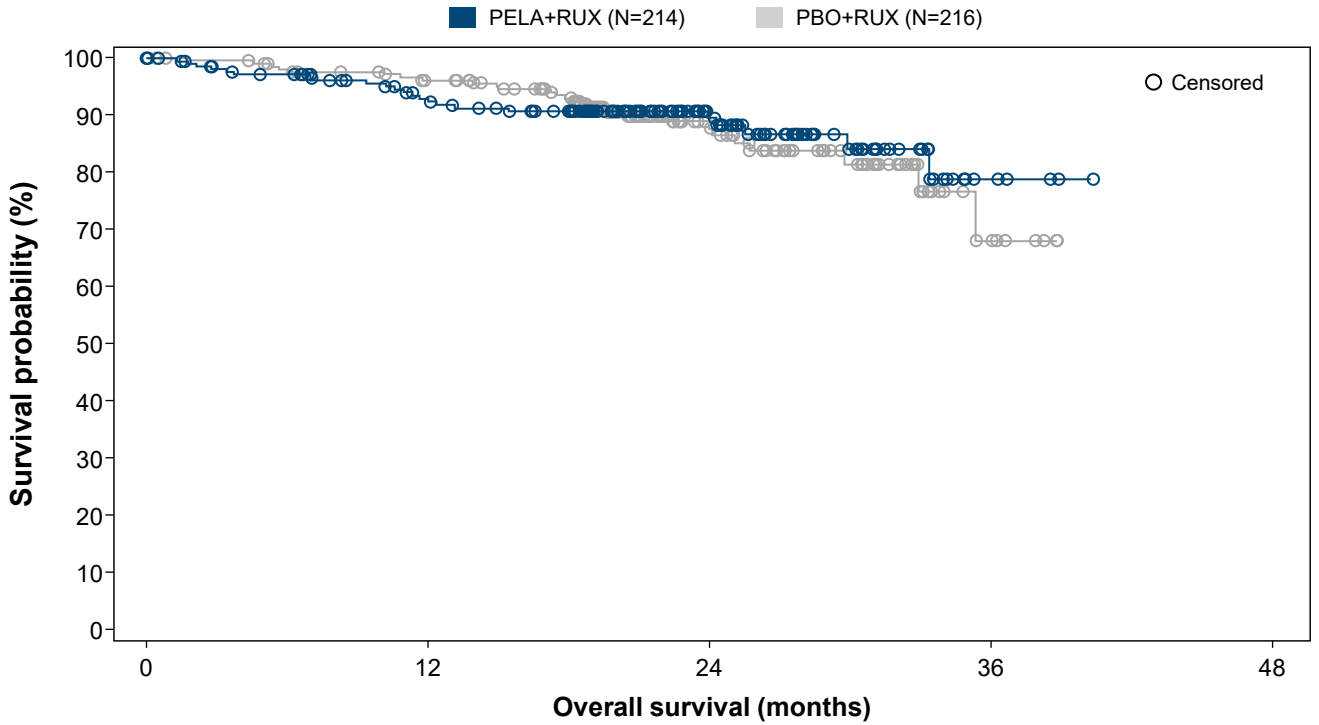
Overall survival (ITT population)

Longer-term follow-up (Week 72 data cutoff) showed fewer deaths in the PELA+RUX arm compared with the PBO+RUX arm



Number of at-risk patients

PELA+RUX	214	174	73	7	0
PBO+RUX	216	194	77	5	0

	PELA+RUX (N=214)	PBO+RUX (N=216)
Total events, n (%)	**23** (10.7)	**27** (12.5)
Hazard ratio (95% CI)	0.93 (0.53-1.66)	

Data cutoff date: August 30, 2024. Median follow-up of 92 weeks.
CI, confidence interval; ITT, intent-to-treat; PBO, placebo; PELA, pelabresib; RUX, ruxolitinib.

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Conclusions

- In JAKi-naive patients with MF, PELA+RUX compared with PBO+RUX at Week 72 data cutoff continues to demonstrate meaningful clinical benefits, with correlative biomarkers supporting potential evidence of ongoing disease modification, specifically:
  - Deep and sustained spleen reduction, with a higher proportion of patients maintaining response
  - Sustained numerical improvements in absolute change in TSS from baseline and TSS50 response
  - Nearly double the percentage of patients with dual SVR35 / TSS50 response
  - Higher rates of hemoglobin responses, fewer patients with transfusion requirement, and fewer anemia AEs
  - Continued improvement in bone marrow fibrosis
- The most frequent TEAEs in both treatment arms were low grade (Grade <3)
- An early imbalance in cases of leukemic transformation was observed with PELA+RUX compared with PBO+RUX. Over time, the imbalance in proportion of patients with transformation to blast phase decreased. Overall, the observed frequency was in line with what is typically seen in MF
- Longer-term follow-up (Week 72 data cutoff) showed fewer deaths in the PELA+RUX arm compared with the PBO+RUX arm

AE, adverse event; JAKi, Janus kinase inhibitor; MF, myelofibrosis; PBO, placebo; PELA, pelabresib; RUX, ruxolitinib; SVR35, ≥35% reduction in spleen volume from baseline; TEAE, treatment-emergent adverse event; TSS, total symptom score; TSS50, ≥50% reduction in total symptom score from baseline.

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Acknowledgments

- We thank the patients and their families, investigators, and staff at participating study sites
- This study is sponsored by Constellation Pharmaceuticals, Inc., a Novartis Company
- The development of pelabresib was funded, in part, by the Leukemia & Lymphoma Society (LLS)
- Editorial and writing support was provided by Laura Travers, PhD, of LiNK Health Group, funded by MorphoSys, a Novartis Company

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