# Key Opinion Leader Investor Event

*Pelabresib in Myeloproliferative Neoplasms*

June 21, 2023

**Gail, L**iving with Myelofibrosis since 2018

# Forward-Looking Statements

**This communication contains certain forward-looking statements concerning the MorphoSys group of companies, including the expectations regarding Monjuvi's ability to treat patients with relapsed or refractory diffuse large B-cell lymphoma, the further clinical development of tafasitamab, including ongoing confirmatory trials, additional interactions with regulatory authorities and expectations regarding future regulatory filings and possible additional approvals for tafasitamab as well as the commercial performance of Monjuvi. The words "anticipate", "believe", "estimate", "expect", "intend", "may", "plan", "predict", "project", "would", "could", "potential", "possible", "hope" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The forward-looking statements contained herein represent the judgment of MorphoSys as of the date of this release and involve known and unknown risks and uncertainties, which might cause the actual results, financial condition and liquidity, performance or achievements of MorphoSys, or industry results, to be materially different from any historic or future results, financial conditions and liquidity, performance or achievements expressed or implied by such forward-looking statements. In addition, even if MorphoSys' results, performance, financial condition and liquidity, and the development of the industry in which it operates are consistent with such forward-looking statements, they may not be predictive of results or developments in future periods. Among the factors that may result in differences are MorphoSys' expectations regarding risks and uncertainties related to the impact of the COVID-19 pandemic to MorphoSys' business, operations, strategy, goals and anticipated milestones, including its ongoing and planned research activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved products, and launching, marketing and selling current or future approved products, the global collaboration and license agreement for tafasitamab, the further clinical development of tafasitamab, including ongoing confirmatory trials, and MorphoSys' ability to obtain and maintain requisite regulatory approvals and to enroll patients in its planned clinical trials, additional interactions with regulatory authorities and expectations regarding future regulatory filings and possible additional approvals for tafasitamab as well as the commercial performance of Monjuvi, MorphoSys' reliance on collaborations with third parties, estimating the commercial potential of its development programs and other risks indicated in the risk factors included in MorphoSys' Annual Report on Form 20-F and other filings with the U.S. Securities and Exchange Commission. Given these uncertainties, the reader is advised not to place any undue reliance on such forward-looking statements. These forward-looking statements speak only as of the date of publication of this document. MorphoSys expressly disclaims any obligation to update any such forward-looking statements in this document to reflect any change in its expectations with regard thereto or any change in events, conditions or circumstances on which any such statement is based or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements, unless specifically required by law or regulation.**

**The compounds discussed in this slide presentation are investigational products being developed by MorphoSys and its partners and are not currently approved by the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA) or any other regulatory authority (except for tafasitamab/Monjuvi® and tafasitamab/Minjuvi®). There is no guarantee any investigational product will be approved by regulatory authorities.**
**Monjuvi® and Minjuvi® are registered trademarks of MorphoSys AG.**

# 01

# Welcome & Opening Remarks

**JEAN-PAUL KRESS, M.D.**
Chief Executive Officer, MorphoSys

# Strategic Focus on Oncology Supported by Strong Financial Position

## OUR AMBITION

*Redefine How Cancer is Treated*

## PELABRESIB

Substantially improve standard of care in myelofibrosis and expand into other myeloid diseases

| | |
|---|---|
| **Monjuvi®** | Drive use in second-line DLBCL, and expand into first-line setting |
| **Tulmimetostat** | Demonstrate potential in different advanced solid tumors and lymphomas |

## STRONG BALANCE SHEET TO FUND STRATEGIC PRIORITIES

Monjuvi® (tafasitamab-cxix) is only approved under accelerated approval by the U.S. FDA in combination with lenalidomide for the treatment of adult patients with relapsed or refractory DLBCL not otherwise specified, including DLBCL arising from low grade lymphoma, and who are not eligible for autologous stem cell transplant (ASCT); DLBCL: diffuse large B-cell lymphoma; Pelabresib and tulmimetostat are investigational medicines that have not yet been evaluated or approved by any regulatory authorities.

# Agenda

**01** **Welcome & Opening Remarks**

Jean-Paul Kress, M.D., MorphoSys Chief Executive Officer

**02** **Myelofibrosis Burden of Disease and Medical Need**

Gabriela Hobbs, M.D., Assistant Professor of Medicine at Harvard Medical School and Clinical Director of Leukemia Service at Massachusetts General Hospital

**03** **Living with Myelofibrosis**

Gail, Living with Myelofibrosis since 2018

**04** **Pelabresib in Myelofibrosis Update**

John Mascarenhas, M.D., Professor of Medicine and Director of the Adult Leukemia Program at The Tisch Cancer Institute at Mount Sinai, New York

**05** **Pelabresib Clinical Development Roadmap**

Tim Demuth, M.D., Ph.D., MorphoSys Chief Research & Development Officer

**06** **Q&A**

Moderated Q&A

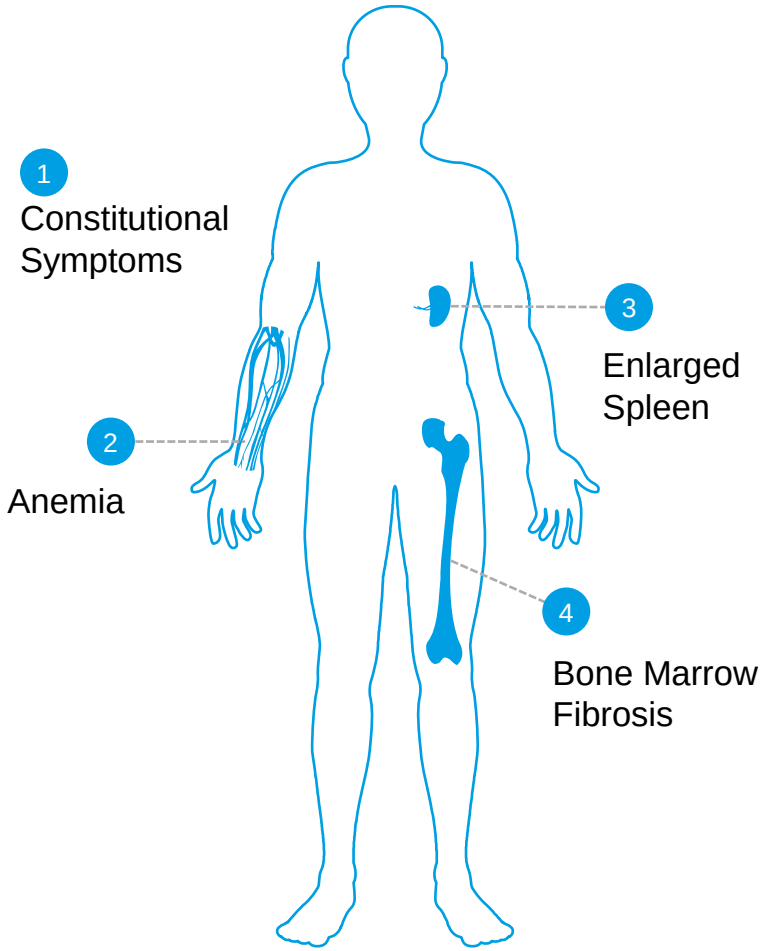
# 02

# Myelofibrosis Burden of Disease and Medical Need

**GABRIELA HOBBS, M.D.**

Assistant Professor of Medicine at Harvard Medical School and Clinical Director of Leukemia Service at Massachusetts General Hospital

# Myelofibrosis is a Debilitating, Progressive and Often Deadly Blood Cancer




**Myeloproliferative neoplasm caused by genetic abnormalities in bone marrow stem cells and characterized by four hallmarks: bone marrow fibrosis, enlarged spleen, anemia, and constitutional symptoms**

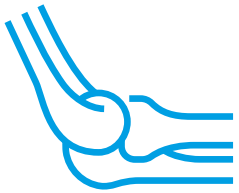
At diagnosis, **~90%** of patients have intermediate- or high-risk disease

Median Overall Survival

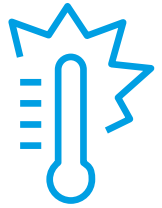
- Intermediate-risk **2.9 – 6.5 years**
- High-risk **~1.3 years**

# Patients with Myelofibrosis Suffer from a Range of Constitutional Symptoms, Severely Impacting Their Quality of Life

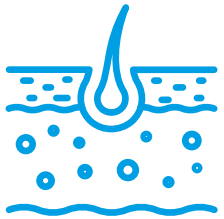
SEVERE FATIGUE



BONE OR JOINT PAIN

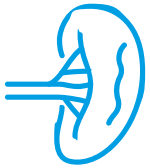


FEVER



ITCHING

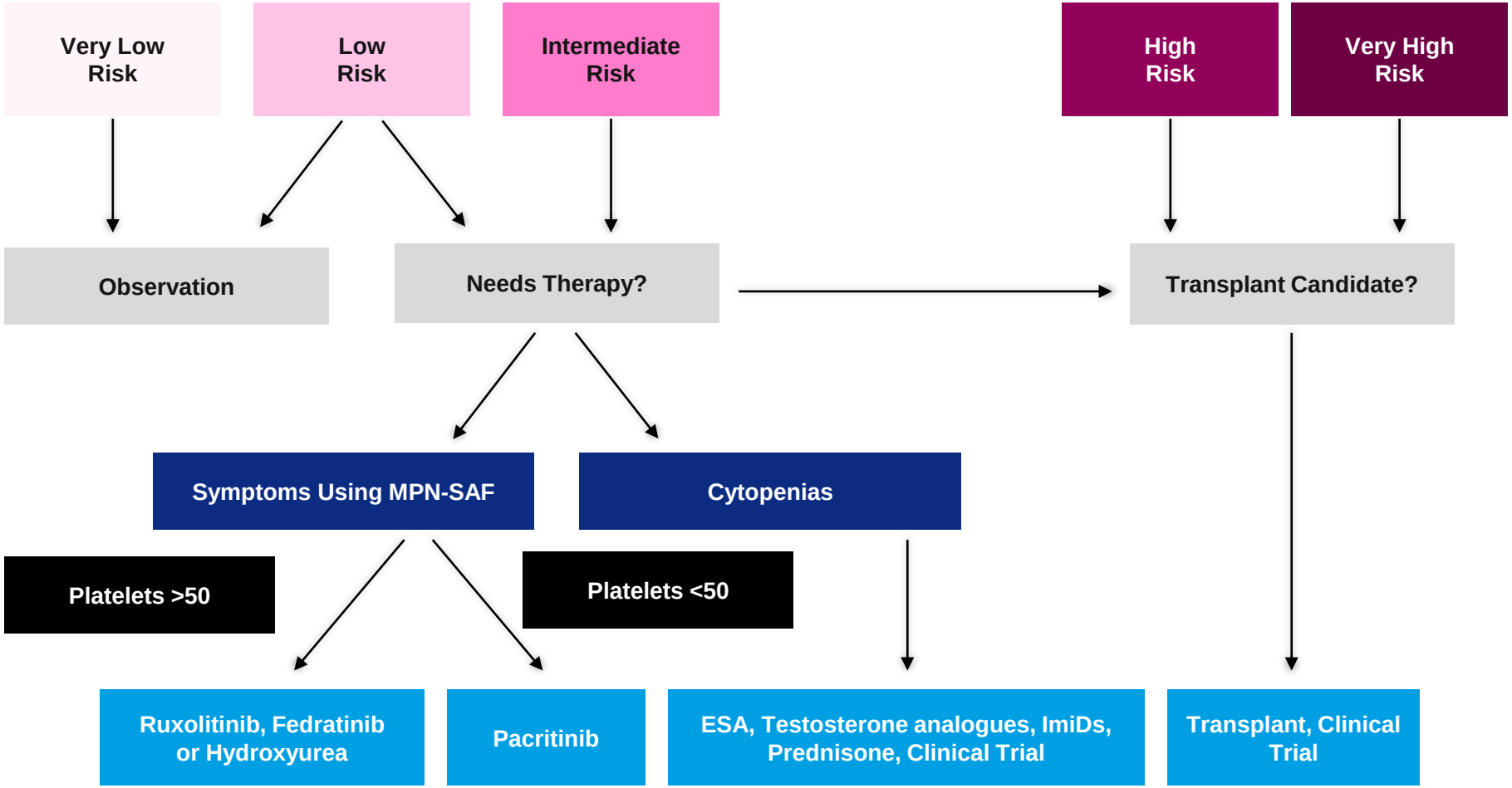
NIGHT SWEATS



SYMPTOMATIC SPLENOMEGALY (ENLARGED SPLEEN)

WEIGHT LOSS

# Current Treatment Approach[1-3]



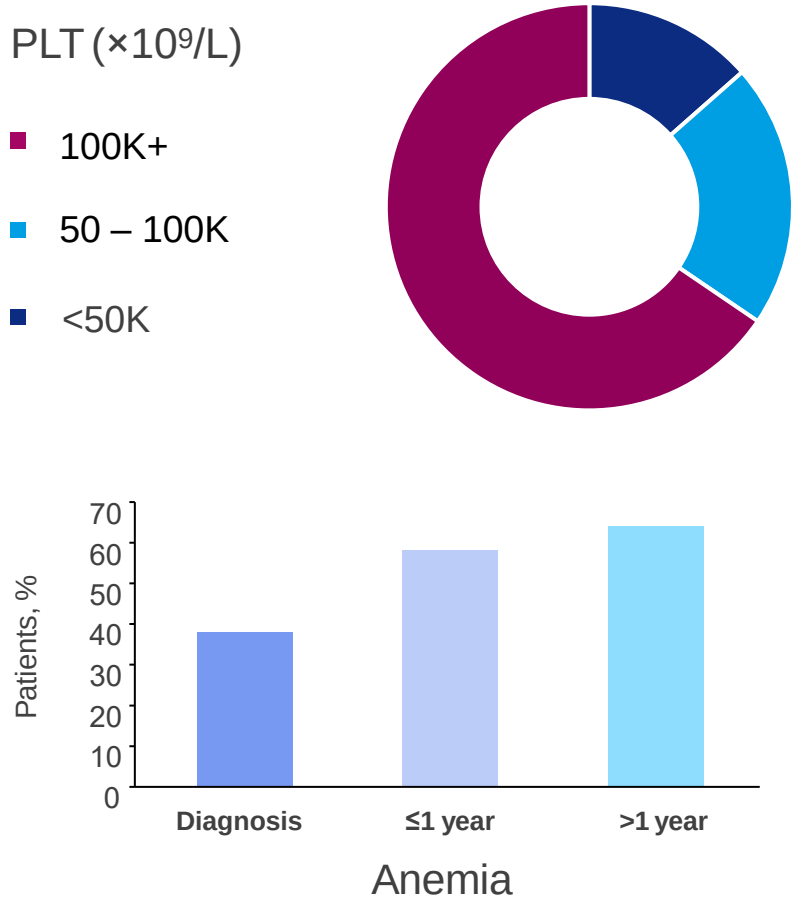

- ESA, erythropoiesis-stimulating agents; IMiD, immunomodulatory drugs; MF, myelofibrosis; MPN-SFA, myeloproliferative neoplasms symptom assessment form; NCCN, National Comprehensive Cancer Network.
- [1] Mesa R. *Leuk Lymphoma*. 2013;54:242-251. [2] Tefferi A. *Am J Hematol*. 2018;93:1551-1560. [3] Vannucchi A, et al. *Ann Oncol*. 2015;26(Suppl 5):v85-v99.
- Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms V.2.2022. 

# Unmet Need # 1: Watch and Wait

1. Lack of drugs that *consistently disease modify* mean we watch and wait for patients to get worse
2. Transplant is the only curative therapy but not generally recommended for low-risk patients
3. Interest in using interferons in this space has not yielded consistent results

# Incidence and Burden of Anemia and Thrombocytopenia

- Prevalence of thrombocytopenia at diagnosis [1]
  - Severe Thrombocytopenia (PTL <50 ×10⁹/L): 11-16%
  - Moderate Thrombocytopenia (PLT 50 – 100 ×10⁹/L): 16-26%
- Other characteristics of cytopenic MF[2]
  - Hgb < 10 g/dL[2]
  - Dependence on RBC transfusions[2]
  - Enlarged spleen[3]
  - Constitutional symptoms [2]
- Both anemia and thrombocytopenia lead to shortened survival[1,2]

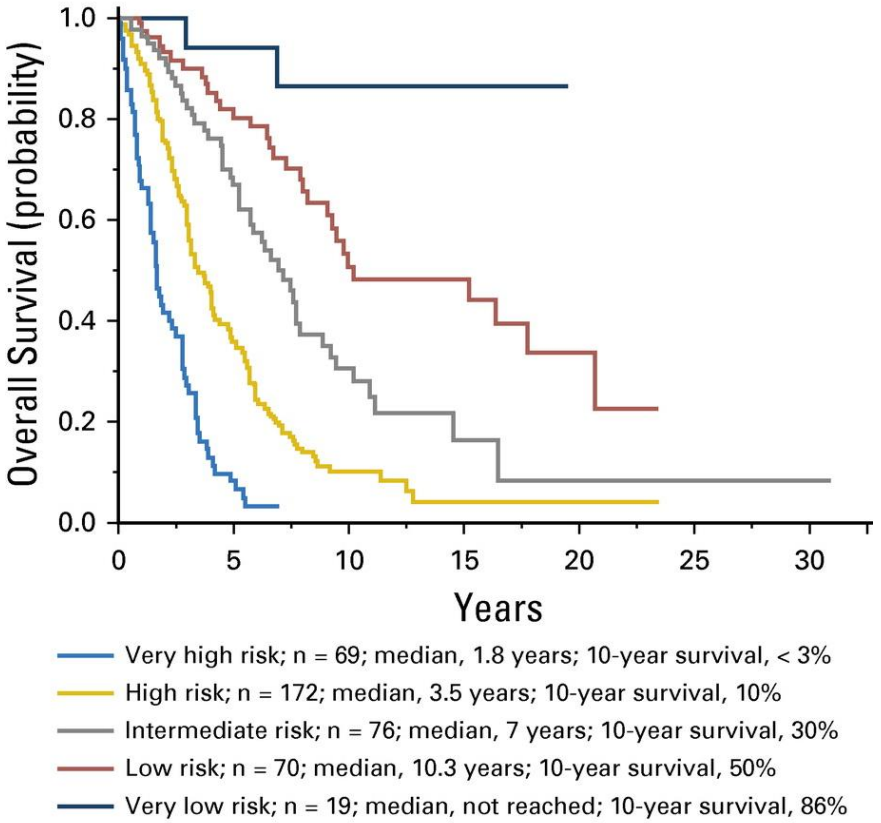



- Hgb, hemoglobin; MF, myelofibrosis; PLT, platelet; RBC, red blood cell.
- [1] Sastow et al. *Clinical Lymphoma Myeloma and Leukemia.* 2022;22:e507-e520. [2] Nicolosi M, et al. *Leukemia.* 2018;32:1254-1258. [3] Song MK, et al. *Int J Mol Sci.* 2018;19(3):898. [4] Passamonti F, et al. *Crit Rev Oncol Hematol.* 2022;180:103862.

# Implications for Patients

- Survival is impacted by cytopenias
- QoL is significantly impacted by cytopenias, transfusion burden

**MIPSS70+V2 Risk Stratification**




*Tefferi, JCO, 2018*

# Unmet Need # 2: Anemia

## This is Starting to be Addressed:

- Pacritinib- JAK2/ACVR1/IRAK1 inhibitor, ~25% of patients experience anemia improvement (and some platelet improvement/stability)
- Luspatercept under investigation (and used off label already)
- Momelotinib is expected to be approved this year ~30% anemia improvement

## Combination Studies that Show Improvement in Anemia:

- Pelabresib (monotherapy and in combination with ruxolitinib)
- Navitoclax

Momelotinib, pelabresib and navitoclax are investigational agents, not approved by regulatory authorities

# Unmet Need # 3: Thrombocytopenia

- Most thrombocytopenic patients are excluded from trials
- Development of thrombocytopenia on trials = dose interruption/ reduction or that patient can’t continue on study
- Pacritinib is the only drug studied/approved in severe thrombocytopenic patients
- Generally, JAK inhibitors worsen cytopenias

# Why Haven’t Cytopenias Been Addressed?

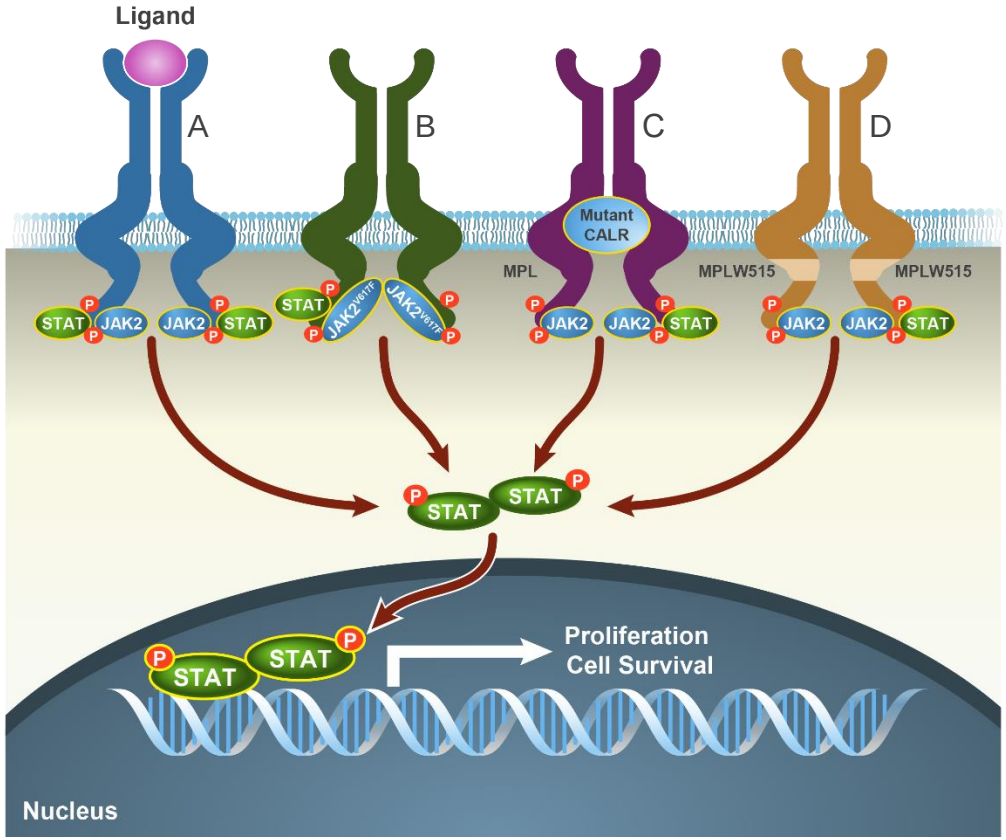
- Endpoints have focused on Spleen/Symptoms
- Patients with cytopenias traditionally excluded from trials
- Drugs are myelosuppressive, further discouraging the inclusion of cytopenic patients (despite this being the norm in other leukemias)

# Unmet Need # 4: Novel Endpoints to Measure Disease Modification

JAK/STAT pathway is at the center of MF pathology → inhibition is a logical target

JAKi improve spleen volume and symptoms, making them standard endpoints

Difficult to define pathological and biological to define MF progression and modification




- (A) Normal JAK-STAT signaling; (B) Constitutive activation via JAK2V617F; (C) CALR; (D) MPLW515.
- JAK, Janus kinase; JAKi, Janus kinase inhibitor; MF, myelofibrosis; STAT, signal transducer and activator of transcription; SVR, spleen volume reduction; TSS, Total Symptom Score.
- Hobbs GS, et al. *Hematol oncol Clin North Am.* 2017;31(4):613-626.

# Novel Endpoints are Needed

- Tension between regulatory requirements vs patient need
- Inhibiting JAK-STAT is a logical target, thus most efforts have focused on TKI drug development in this space
- Most novel compounds are still held to the SVR/TSS endpoints neglecting the marrow failure component
- Improvements in cytopenias, marrow fibrosis, PFS, OS and leukemia free survival should be the goal of novel therapies

# Unmet Need # 5: Education

## Myelofibrosis is a Rare Disease:

- Difficult for general oncologist to have expertise as they see few cases/year

## Education is Needed to Help In:

- Early diagnosis
- Therapy initiation and therapy modification
- Referral to experienced centers/clinicians
- Utilization of current and new therapies

# Summary

- Myelofibrosis is a debilitating, progressive and often deadly blood cancer
- Current treatments are not addressing all patients' needs
- New, novel therapies are needed

# 03

# Living with Myelofibrosis

**GAIL**

Living with Myelofibrosis since 2018

# 04

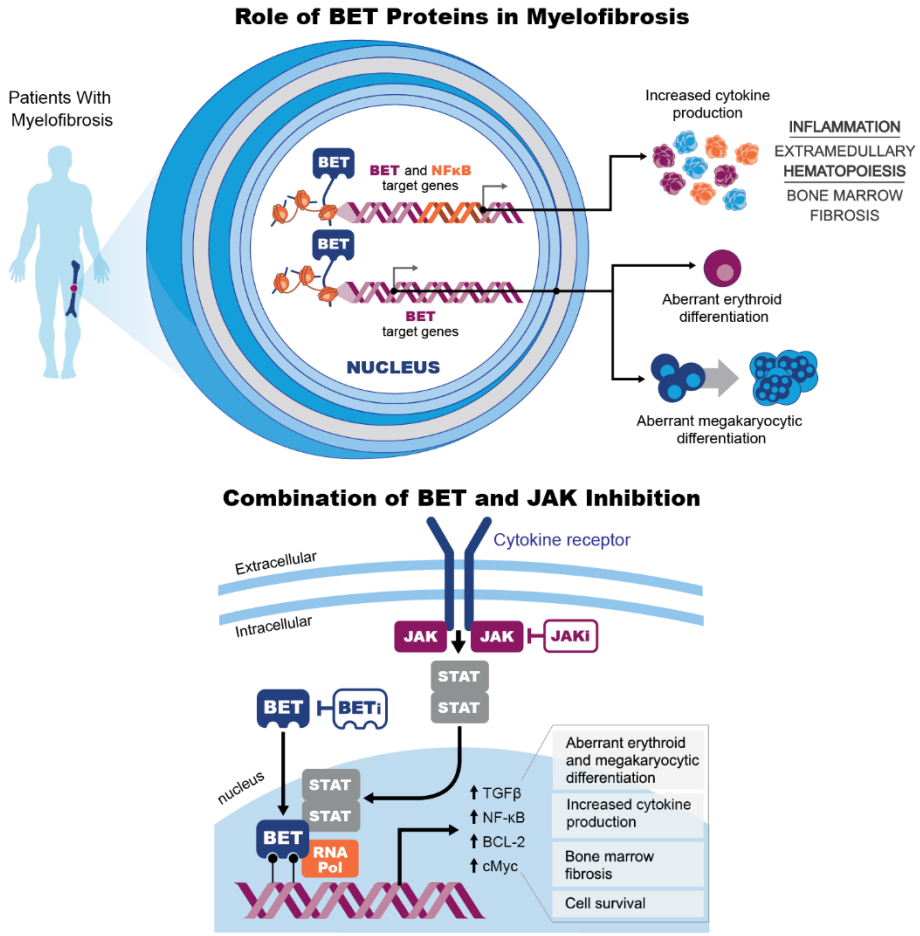
# Pelabresib in Myelofibrosis Update

**JOHN MASCARENHAS, M.D.**

Professor of Medicine and Director of the Adult Leukemia Program
at The Tisch Cancer Institute at Mount Sinai, New York

# Simultaneous inhibition of BET and JAK in Myelofibrosis

A potential therapeutic approach to address heterogenous disease pathology




- JAK inhibition with ruxolitinib is the standard of care in patients with higher risk MF who are ineligible for HSCT[1]
- Unmet medical need persists due to limited efficacy with currently available JAKi monotherapy, high rates of discontinuation and toxicities[1]
- Preclinical data indicated non-overlapping activity of BET and JAK inhibition in MF[2]
- Pelabresib, a BET inhibitor, downregulates the expression of genes that contribute to the heterogenous pathology of MF[3–7]

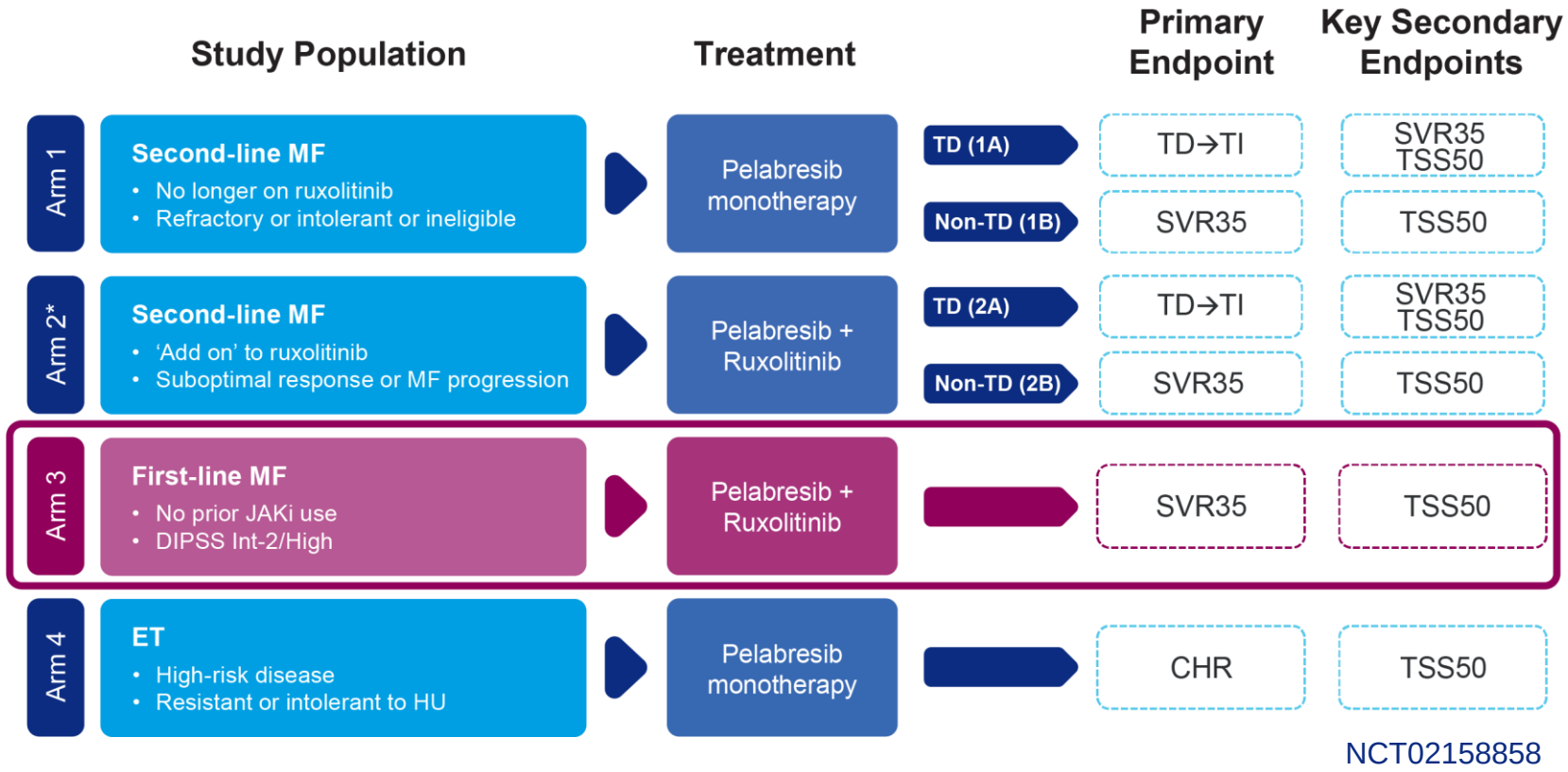


BET, bromodomain and extraterminal domain; JAK, Janus kinase; JAKi, Janus kinase inhibitor; NF-κB, nuclear factor kappa B; STAT, signal transducer and activator of transcription; TGFβ, transforming growth factor β.

1. Verstovsek S, et al. *Haematologica* 2015;100:479–488; 2. Kleppe M, et al. *Cancer Cell* 2018;33:29–43.e7; 3. Stratton MS, et al. *F1000Res* 2017;6:F1000 Faculty Rev–1015; 4. Ding N, et al. *PNAS* 2015;112:15713–15718; 5. Ceribelli M, et al. *PNAS* 2014;111:11365–11370; 6. Tefferi A, et al. *J Clin Oncol* 2011;29:573–582; 7. Keller P, et al. *Hemasphere* 2021;5(Suppl 2):515.

# Arm 3: Combination in JAK Inhibitor Naïve Patients

MANIFEST: Ongoing, global, open-label Phase 2 study investigating pelabresib in myelofibrosis and essential thrombocythemia




CHR, complete hematologic response; DIPSS, Dynamic International Prognostic Scoring System; ET, essential thrombocythemia; HU, hydroxyurea; Int-2, intermediate-2; JAKi, Janus kinase inhibitor; SVR35, ≥35% reduction in spleen volume at Week 24; TD, transfusion dependent; TI, transfusion independent; TSS50, ≥50% reduction in total symptom score at Week 24.
Clinicaltrials.gov. NCT02158858. Available at: https://clinicaltrials.gov/ct2/show/NCT02158858. Accessed April 26, 2023.

Harrison C, et al. EHA 2023. Abstract P1027 | **Pelabresib (CPI-0610) is an investigational new drug and has not been approved by any regulatory authority**

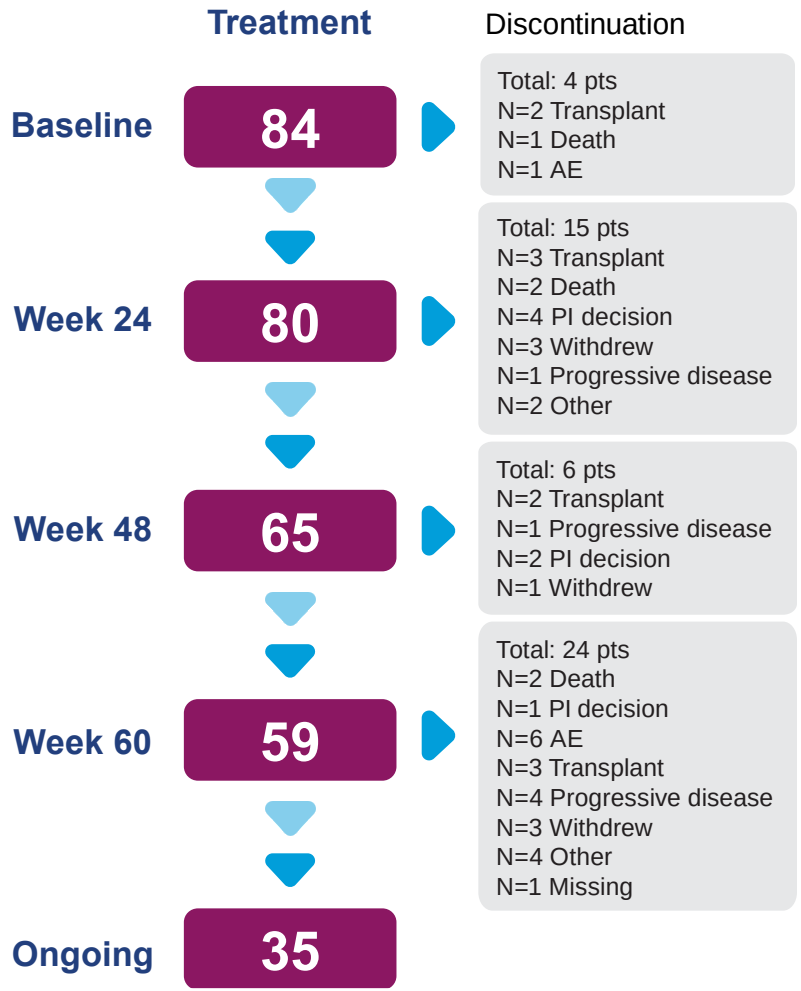
# Recently Presented Durability of Response and Safety in MANIFEST Arm 3: Pelabresib (CPI-0610) Combined With Ruxolitinib for JAK Inhibitor Treatment-Naïve Patients With Myelofibrosis

Claire Harrison,[1] Andrea Patriarca,[2] Vikas Gupta,[3] Francesca Palandri,[4] Timothy Devos,[5] Raajit K Rampal,[6] Moshe Talpaz,[7] Alessandro Vannucchi,[8] Andrew Kuykendall,[9] Jean-Jacques Kiladjian,[10] Srdan Verstovsek,[11] Ruben Mesa,[12] Gozde Colak,[13] Soumik Dutta,[14] Sandra Klein,[13] Jike Cui,[13] Tzuu-Wang Chang,[13]John Mascarenhas[15] on behalf of the MANIFEST study investigators.

[1]Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom; [2]Hematology Unit, Department of Translational Medicine, University of Eastern Piedmont and AOU Maggiore della Carità, Novara, Italy; [3]Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada; [4]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli", Bologna, Italy; [5]University Hospitals Leuven and Laboratory of Molecular Immunology (Rega Institute), KU Leuven, Leuven, Belgium; [6]Memorial Sloan-Kettering Cancer Center, New York, NY, USA; [7]University of Michigan Comprehensive Cancer Center, Ann Arbor, MI, USA; [8]University of Florence, Azienda Ospedaliero-Universitaria Careggi, CRIMM, Florence, Italy; [9]Moffitt Cancer Center, Tampa, FL, USA; [10]Hôpital Saint-Louis, Université de Paris, Paris, France; [11]Leukemia Department, University of Texas MD Anderson Cancer Center, Houston, TX, USA; [12]Mays Cancer Center at UT Health San Antonio MD Anderson Cancer Center, San Antonio, TX, USA; [13]Constellation Pharmaceuticals, Inc., a MorphoSys Company, Boston, MA, USA; [14]MorphoSys US, Inc., Boston, MA, USA; [15]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA.

# Arm 3: Patient Disposition

| | ARM 3 |
|---|---|
| **Enrolled (n)** | 84 |
| Ongoing treatment [n (%)] | 35 (42) |
| Discontinued treatment [n (%)] | 49 (58) |
| **Primary reason for treatment discontinuation [n (%)]** | |
| Progressive disease | 6 (7) |
| AE* or lab abnormality | 7 (8) |
| Withdrew consent | 7 (8) |
| PI decision | 7 (8) |
| Death | 5 (6) |
| Stem cell transplant | 10 (12) |
| Other | 6 (7) |
| Missing† | 1 (1) |
| **Pelabresib dose** (median, range) | 125 mg QD (50, 225) |
| **Ruxolitinib dose** (median, range) | 10 mg BID (5, 25) |




Median treatment duration‡: Median: 26.7 months (95% CI 19.1–30.8) 46% (39/84) of patients were treated ≥2 years
*Two patients were initially discontinued due to AEs that later resulted in death.
†Pending data entry.
‡Kaplan–Meier estimate.

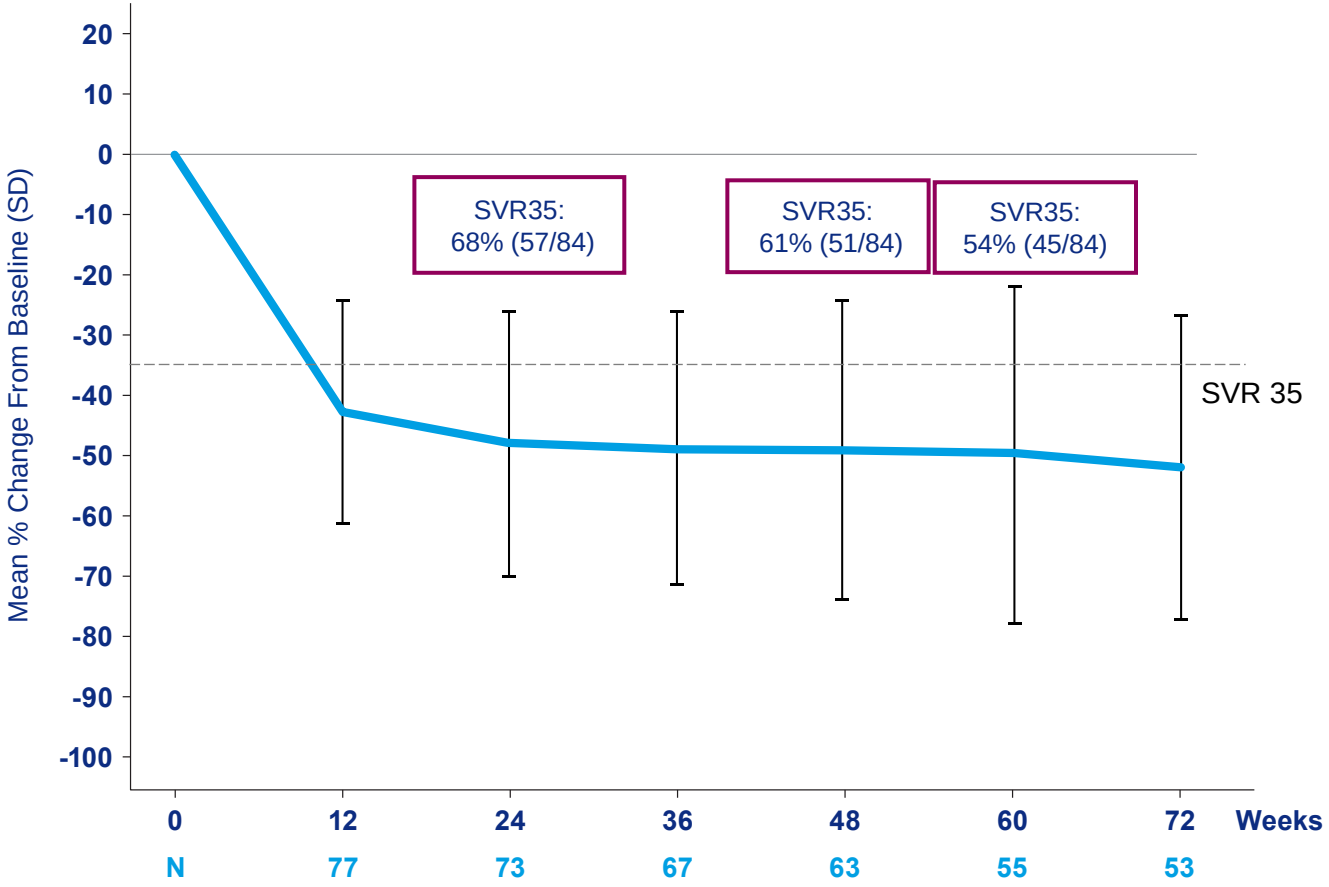
# Arm 3: Patient Baseline Demographics and Disease Characteristics

| CHARACTERISTIC | | N=84 |
|---|---|---|
| **Age (years)** | Mean (SD) | 67 (10) |
| **Gender** | Male, n (%) | 59 (70) |
| **DIPSS** | Int-1, n (%) | 19 (23) |
| | Int-2, n (%) | 52 (62) |
| | High, n (%) | 13 (16) |
| **IPSS** | Int-1, n (%) | 10 (12) |
| | Int-2, n (%) | 29 (35) |
| | High, n (%) | 45 (54) |
| **MF subtype** | Primary MF, n (%) | 46 (55) |
| | Post-PV MF, n (%) | 9 (11) |
| | Post-ET MF, n (%) | 27 (32) |
| | Missing*, n (%) | 2 (2) |
| **Hemoglobin (g/dL)** | Median (min, max) | 9 (7, 17) |
| | <10, n (%) | 55 (66) |
| **Platelet (× $10^9$/L)** | Median (min, max) | 294 (100, 1849) |
| **Spleen volume (cc)** | Median (min, max) | 1698 (458, 4782) |
| **TSS** | Median (min, max) | 16 (0, 38) |
| **Mutations** | HMR†, n (%) | 47 (56) |
| | *ASXL1*, n (%) | 37 (44) |
| | *JAK2 V617F*‡, n (%) | 59 (70) |
| | *CALR*‡, n (%) | 17 (20) |
| | *MPL*, n (%) | 6 (7) |
| | Triple negative, n (%) | 3 (4) |

*Pending data entry; †HMR mutations: *ASXL1, EZH2, IDH1/2, SRSF2, U2AF1*; ‡One patient had both *JAK2 V617F* and *CALR* mutations.
ET, essential thrombocythemia; HMR, high-molecular risk; Int, intermediate; IPSS, International Prognostic Scoring System; PV, polycythemia vera.

# Arm 3: Spleen Response

## Spleen Volume Mean Percentage Change Over Time

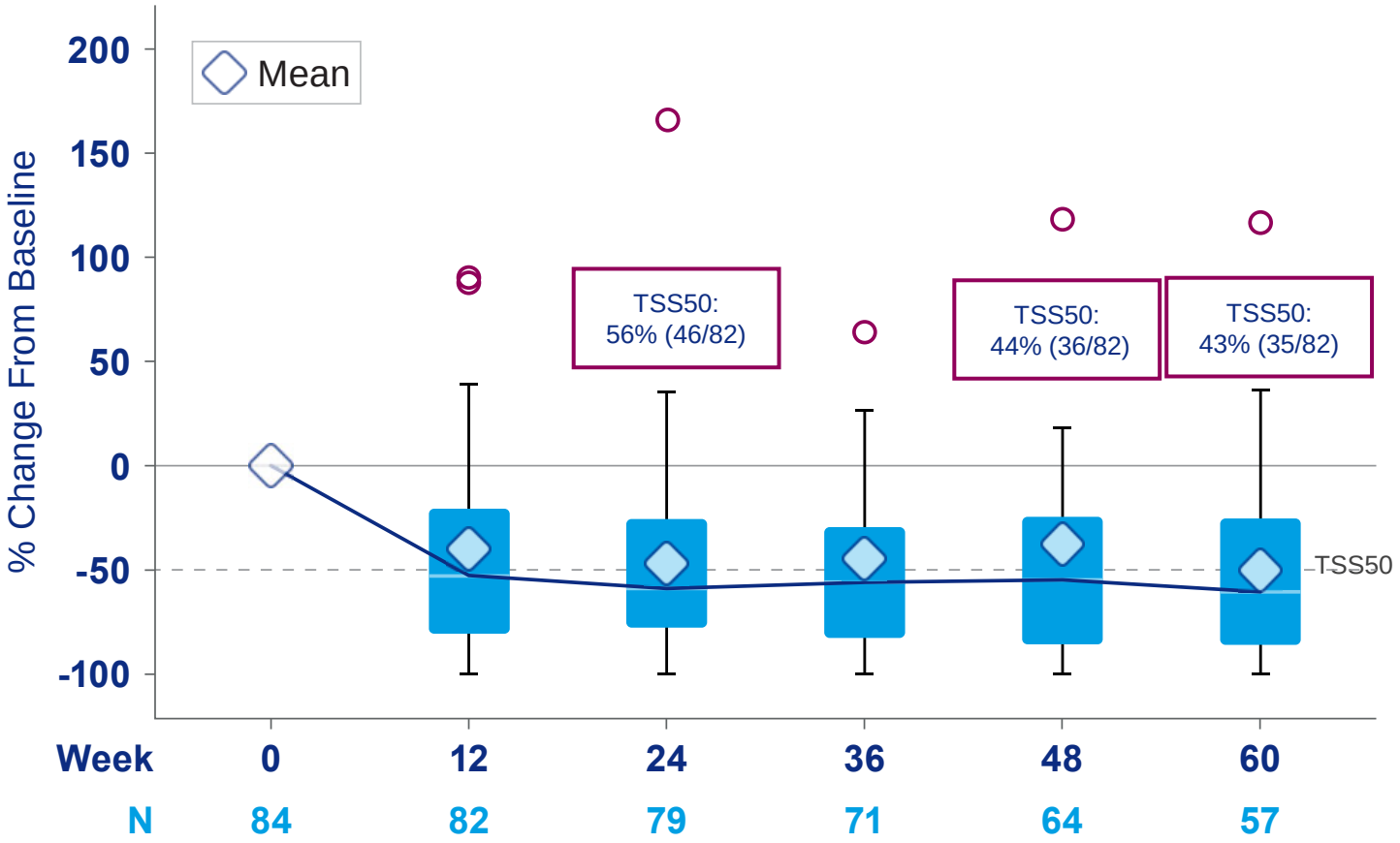



| N=84 | |
|---|---|
| Median time to SVR35 response | 12 wks (range 10–51) |
| **Median follow-up* for SVR35 response** | 84 wks (95% CI 66–90) |
| **Response maintained at data cutoff** | 70% (47/67) |

*Median has not been reached; reverse Kaplan–Meier estimate of median duration of follow-up for SVR35 response.
Spleen volume per local radiology review. Spleen volume mean percentage change: patients with an available spleen volume assessment for the corresponding time points.

# Arm 3: Symptom Response

## TSS Mean Percentage Change Over Time

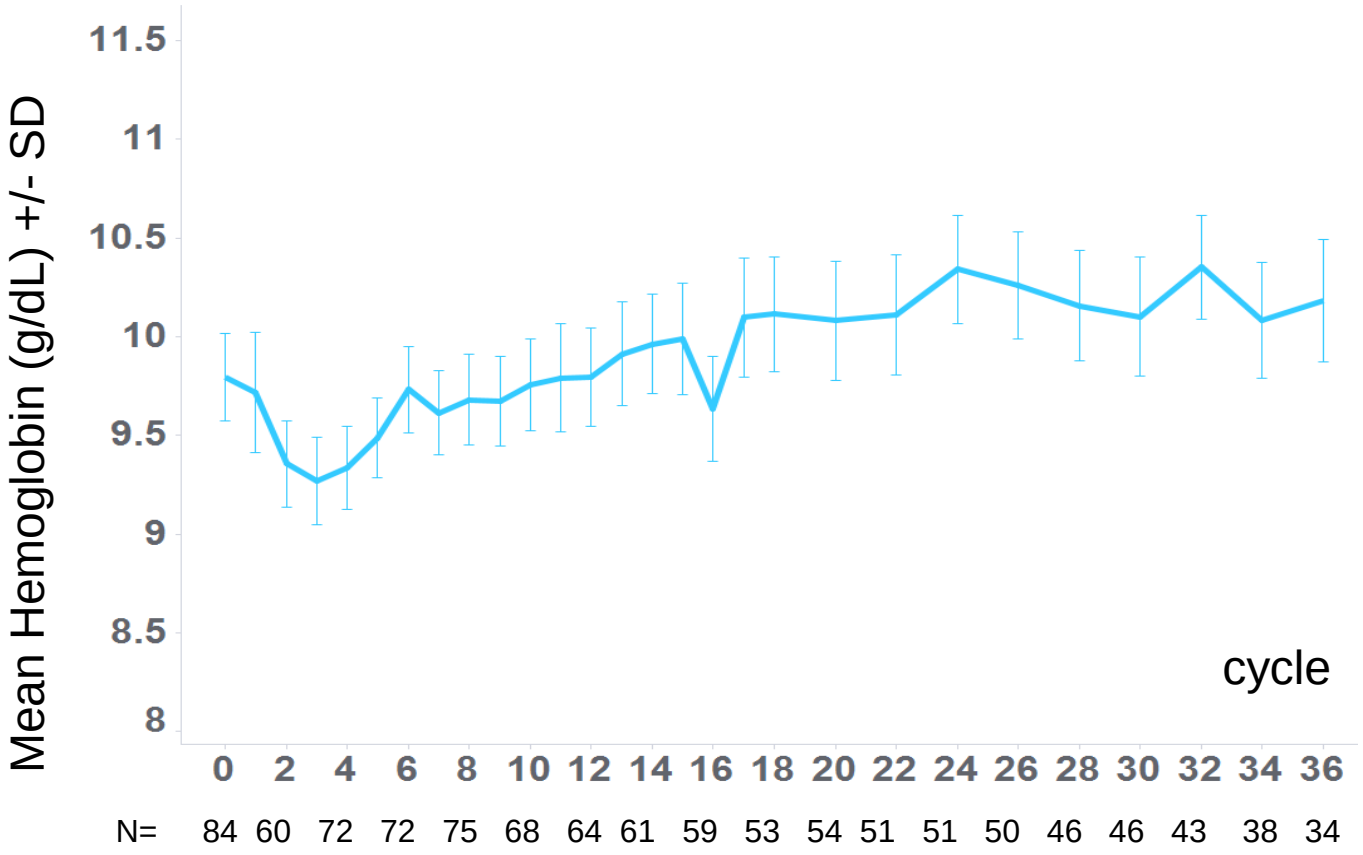



| TSS50 | |
|---|---|
| **At any time** | 83% (68/82*) |

Two ongoing patients were nonevaluable for TSS50; n=1 due to missing baseline, n=1 due to baseline TSS=0.

# Arm 3: Anemia Response

## Hemoglobin improvement over time



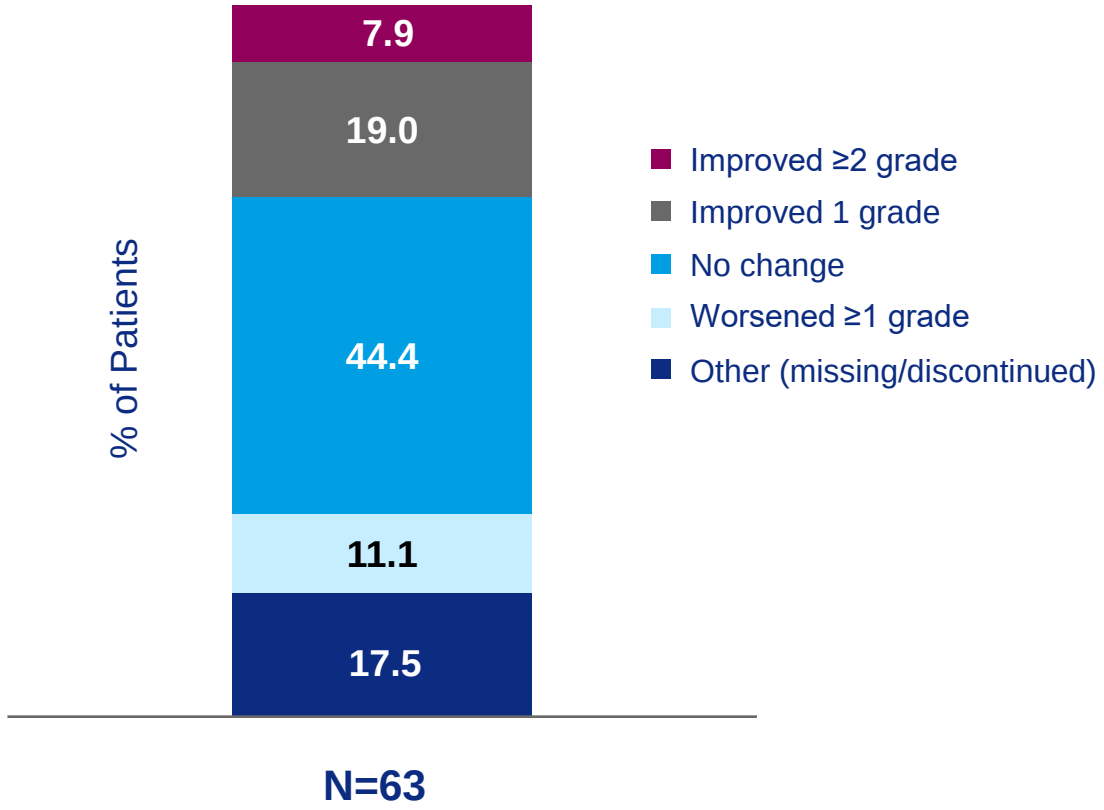

| Non-TD | Hemoglobin Response* |
|---|---|
| **Response Rate** | 27% (21/79) |
| **Time to Response (Median)** | 60 wks (range 2-174) |
| **Duration of Response (Median)** | 28 wks (range 12-135) |

- 50% of patients achieved at least a 50% reduction in transfusion burden†
- Median transfusion requirement during the first 6 months: 0.16 u/month

*Hemoglobin response defined as the proportion of patients who enrolled as non-TD and achieved ≥1.5 g/dL Hgb increase from baseline over any consecutive 12-week period in the absence of RBC transfusions.
†Defined as reduction of ≥50% from baseline in the number of units of RBC transfusion during any 12 wk period post-baseline. Patients are evaluable if receiving ≥4 RBC transfusion units at baseline.
Hgb, hemoglobin; RBC, red blood cell.

# Arm 3: BMF Reduction

## Change in Bone Marrow Fibrosis Grade at Week 24 by Central Pathology Review

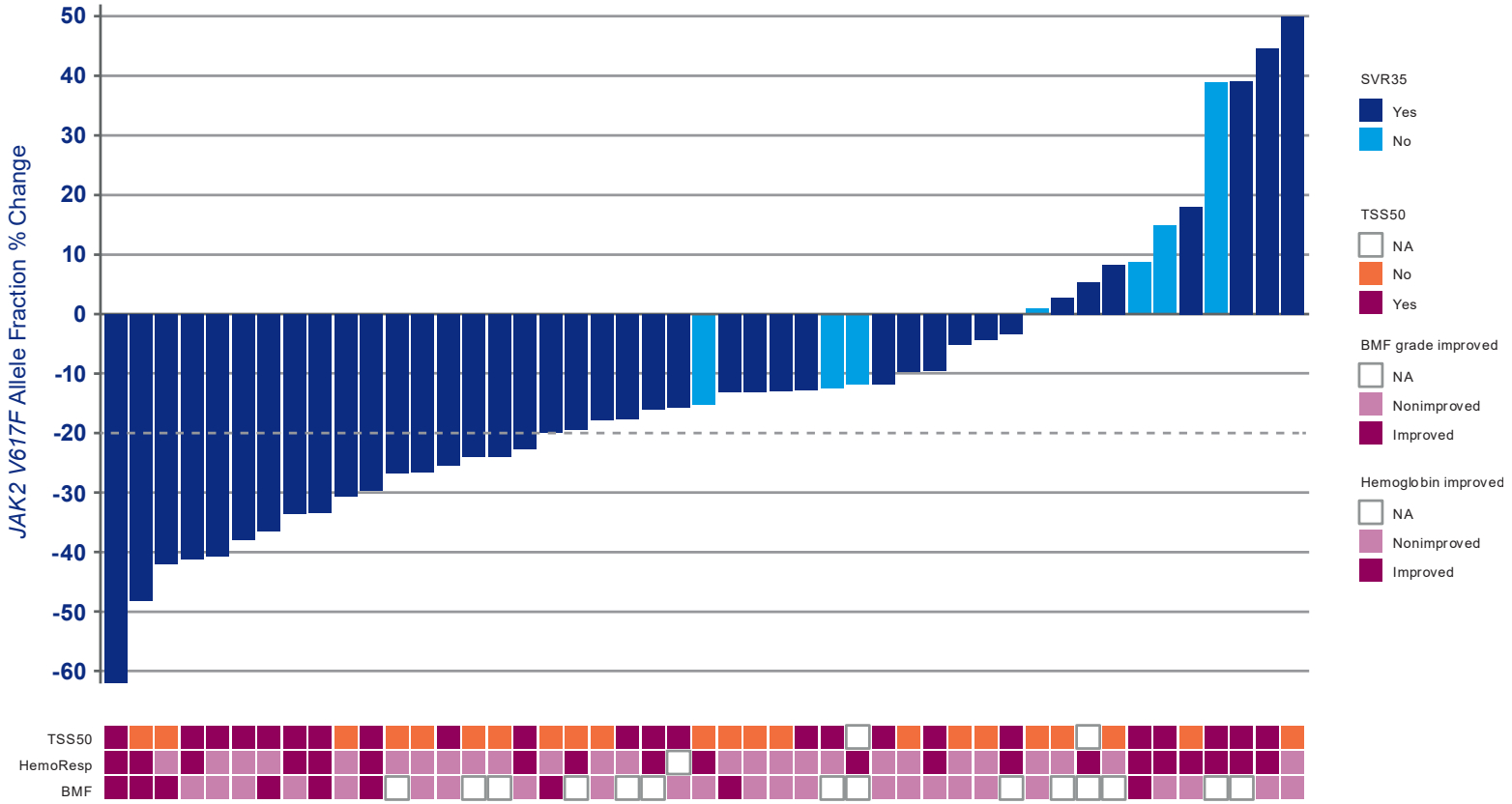



- 27% (17/63) of patients showed ≥1 grade improvement at Week 24
  - This improvement was maintained in 59% (10/17) of patients at the next available assessment or longer
- 40% (25/63) of patients had ≥1 grade improvement at any time
- 59% (16/27) of patients had a ≥15% increase in distance between nuclei of CD61+ cells* in the bone marrow

*Marker of megakaryocytes; an increased distance between CD61+ nuclei cells is indicative of megakaryocyte declustering in the bone marrow.
Patients evaluable if nonmissing baseline or discontinued without a Week 24 bone marrow assessment; bone marrow fibrosis grade assessed by three independent and blinded pathologists per central pathology review, maturing data with central review ongoing.

# Arm 3: Reduction of Driver Mutation as Surrogate for Disease Burden

## Overlapping clinical responses associated with *JAK2 V617F* VAF reduction at Week 24




- 18/47 (38%) patients reached a ≥20% reduction in *JAK2 V617F* VAF
  - \+ Median (min, max) reduction was –14% (–62%, 50%)
- An association of *JAK2 V617F* VAF reductions and bone marrow fibrosis was observed with SVR35 (8 pts), TSS50 (5 pts) and Hgb responses (5 pts)

Hgb assessment within 2 weeks after RBC transfusion was excluded from the analysis; any level of increase from baseline (range: 0.1–3.8 g/dL).
Hgb, hemoglobin; VAF, variant allele frequency; pts, patients

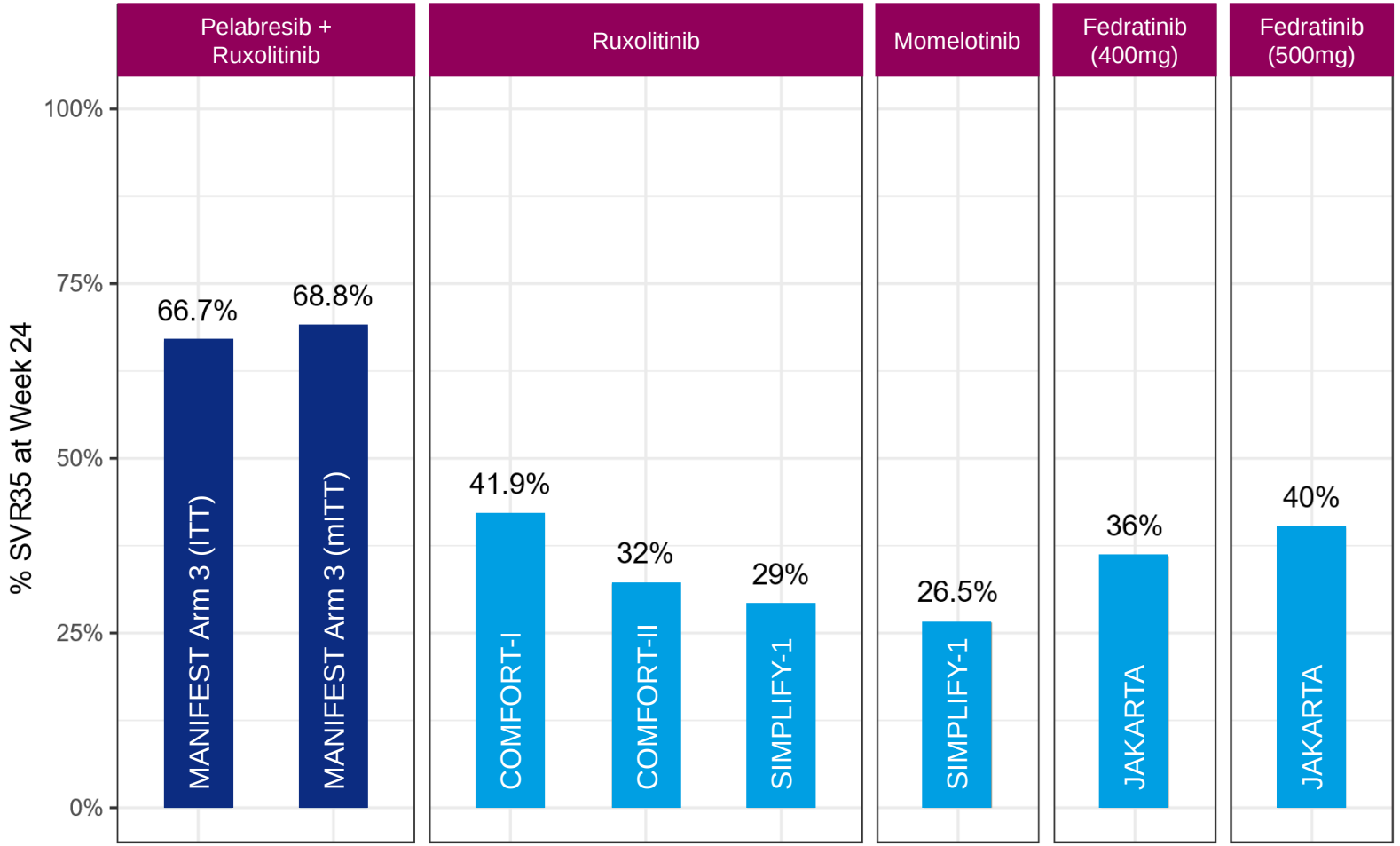
# Arm 3: Not Associated With Added or Limiting Toxicity

| TEAEs of all grades that occurred in ≥20% of patients | | All Grade N=84* n (%) | Grade 3 N=84* n (%) | Grade 4 N=84* n (%) |
|---|---|---|---|---|
| **Hematologic Events** | Anemia | 36 (43%) | 29 (35%) | 1 (1%) |
| | Thrombocytopenia† | 46 (55%) | 14 (17%) | 3 (4%) |
| **Nonhematologic Events** | **Gastrointestinal events** | | | |
| | Diarrhea | 36 (43%) | 2 (2%) | 0 |
| | Constipation | 25 (30%) | 0 | 0 |
| | Nausea | 24 (29%) | 0 | 0 |
| | Abdominal pain‡ | 22 (26%) | 0 | 0 |
| | **Other nonhematologic events** | | | |
| | Respiratory tract infection§ | 34 (41%) | 8 (10%) | 2 (2%) |
| | Asthenic conditions¶ | 32 (38%) | 1 (1%) | 1 (1%) |
| | Musculoskeletal pain** | 27 (32%) | 0 | 0 |
| | Dizziness†† | 23 (27%) | 0 | 0 |
| | Cough | 20 (24%) | 0 | 0 |
| | Dysgeusia | 20 (24%) | 0 | 0 |
| | Dyspnea | 19 (23%) | 4 (5%) | 0 |
| | Headache | 18 (21%) | 0 | 0 |
| | Muscle spasms | 17 (20%) | 0 | 0 |

- Serious adverse events reported in ≥2 pts were anemia, pyrexia and COVID-19 (3 pts each), gastrointestinal hemorrhage, multiple organ dysfunction syndrome, pneumonia, respiratory tract infection, urinary tract infection, fall and respiratory failure (2 pts each)
- Twelve pts (14%) reported TEAEs that led to pelabresib discontinuation; 6 (7%) of them were due to hematological TEAEs
- Eight Grade 5 TEAEs were reported in 7 pts
  - Acute respiratory distress syndrome due to ruxolitinib withdrawal (2 pts each), MOF due to COVID (reported as two separate TEAEs in the same pt), MOF due to sepsis secondary to pneumonia, respiratory failure due to COVID-19, bacterial endocarditis and urinary tract infection
  - All were assessed by the PI as not related to pelabresib, except MOF due to sepsis secondary to pneumonia

*Safety-evaluable population: received at least one dose of study drug at the time of the data cut; †Includes TEAE platelet count decrease; ‡Includes TEAE abdominal pain upper; §Includes TEAEs of upper respiratory tract infection, viral upper respiratory tract infection, bronchitis, sinusitis, rhinitis, nasopharyngitis, pneumonia, COVID-19, COVID-19 pneumonia and influenza; ¶Include TEAEs of asthenia, fatigue, lethargy and malaise; **Includes TEAEs of arthralgia and myalgia; ††Includes TEAEs of balance disorder and vertigo. MOF, multiorgan failure.

# MAIC of Pelabresib + Ruxolitinib Compared with Ruxolitinib, Fedratinib and Momelotinib




- High degree of balance accounting for 8 prognostic variables
- Superiority on SVR and TSS with combination pelabresib and ruxolitinib in JAKi naïve patients
- Similar results in ITT and mITT

Gupta V, et al. EHA 2022. Abstract P1029 | **Pelabresib (CPI-0610) is an investigational new drug and has not been approved by any regulatory authority**

# Arm 1: Pelabresib Monotherapy in Myelofibrosis

## MANIFEST Arm 1: Refractory /resistant, intolerant or ineligible for JAKi treatment

### Study Population

- No longer on ruxolitinib
- DIPSS Int-2 or higher[1]
- Platelet count ≥ 75 x 109/L
- TD cohort: ≥2 units of RBC transfusions/mo for 12 wks
- Non-TD cohort must have baseline spleen size of >450 $cm^3$

### Arm/Cohort

**Transfusion Dependent (TD) (Cohort 1A)**
N=36/60, **Ongoing**

**Non-transfusion Dependent (Non-TD) (Cohort 1B)**
N=50, **Completed**

### Endpoints

| TD cohort (1A) | |
|---|---|
| **Primary Endpoint** | **Key Secondary** |
| TD to TI | SVR35, TSS50 |

| Non-TD cohort (1B) | |
|---|---|
| **Primary Endpoint** | **Key Secondary** |
| SVR35 | TSS50 |

- DIPSS: Dynamic International Prognostic Scoring System
- [1]Patients with DIPSS Int-1 were allowed to enroll prior to the protocol amendment
- SVR35: Spleen volume response defined as ≥35% reduction from baseline (MRI or CT) after 24wk
- TSS50: Total symptom score response defined as ≥50% total symptom score reduction from baseline after 24-wk
- TD to TI: Conversion from Transfusion Dependent (TD) to Transfusion Independent (TI), defined as absence of RBC transfusions over any consecutive 12-wk period

# Arm 1: Pelabresib Monotherapy Anemia Improvement[1,2]

## Arm 1A TD cohort: TD to TI conversion

| | |
|---|---|
| TD to TI conversion | 16% (4/25) |
| Median TI duration | 41 wks (range 31, 53) |
| Median time to TI conversion | 32 wks |

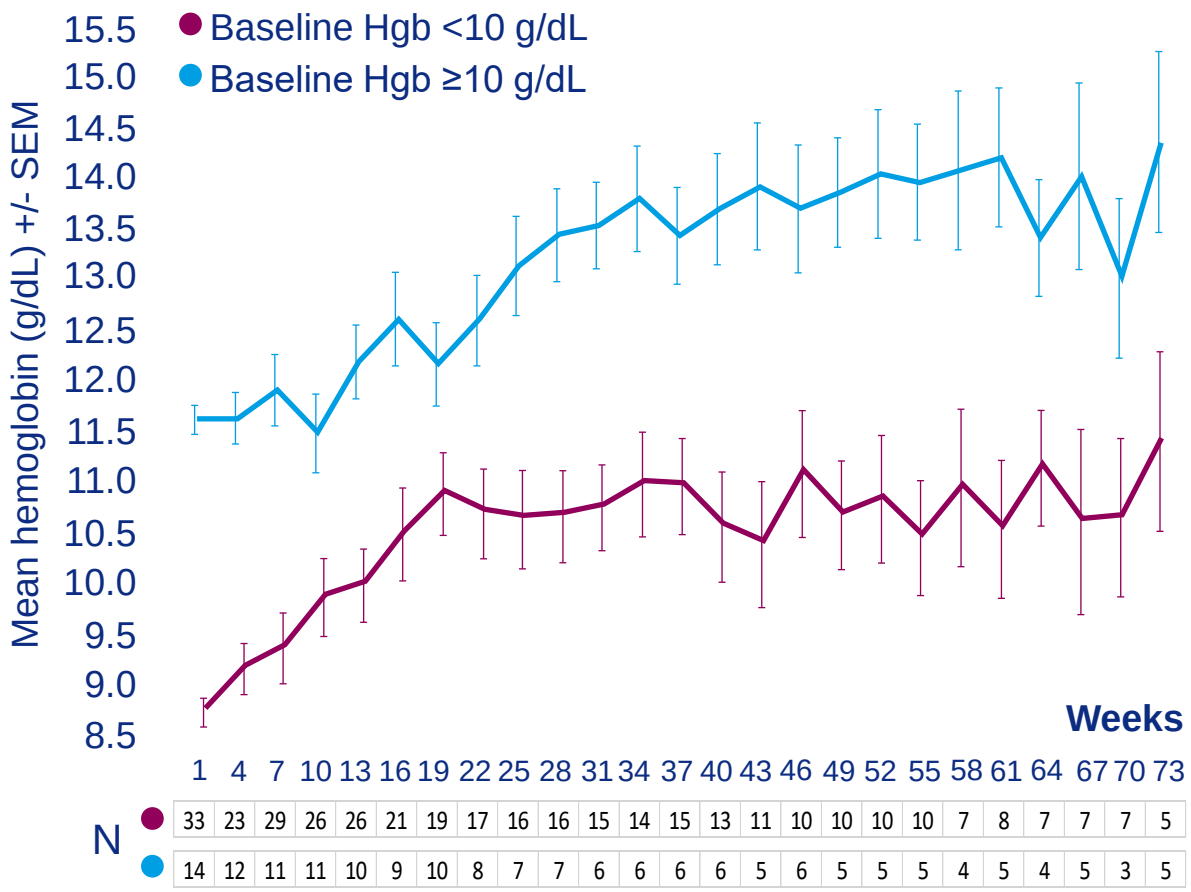
[1]The TD to TI conversion (primary endpoint for TD cohort) defined as absence of RBC transfusions over any 12-week period. Cohort enrolment ongoing. Patients evaluable if non-missing baseline, ongoing and received 12 wks of treatment or discontinued at any time point. TI duration: Longest duration between transfusions for TI pts; Time to TI conversion: Time to last transfusion prior to conversion for TI pts

## Arm 1B Non-TD cohort: Hemoglobin response

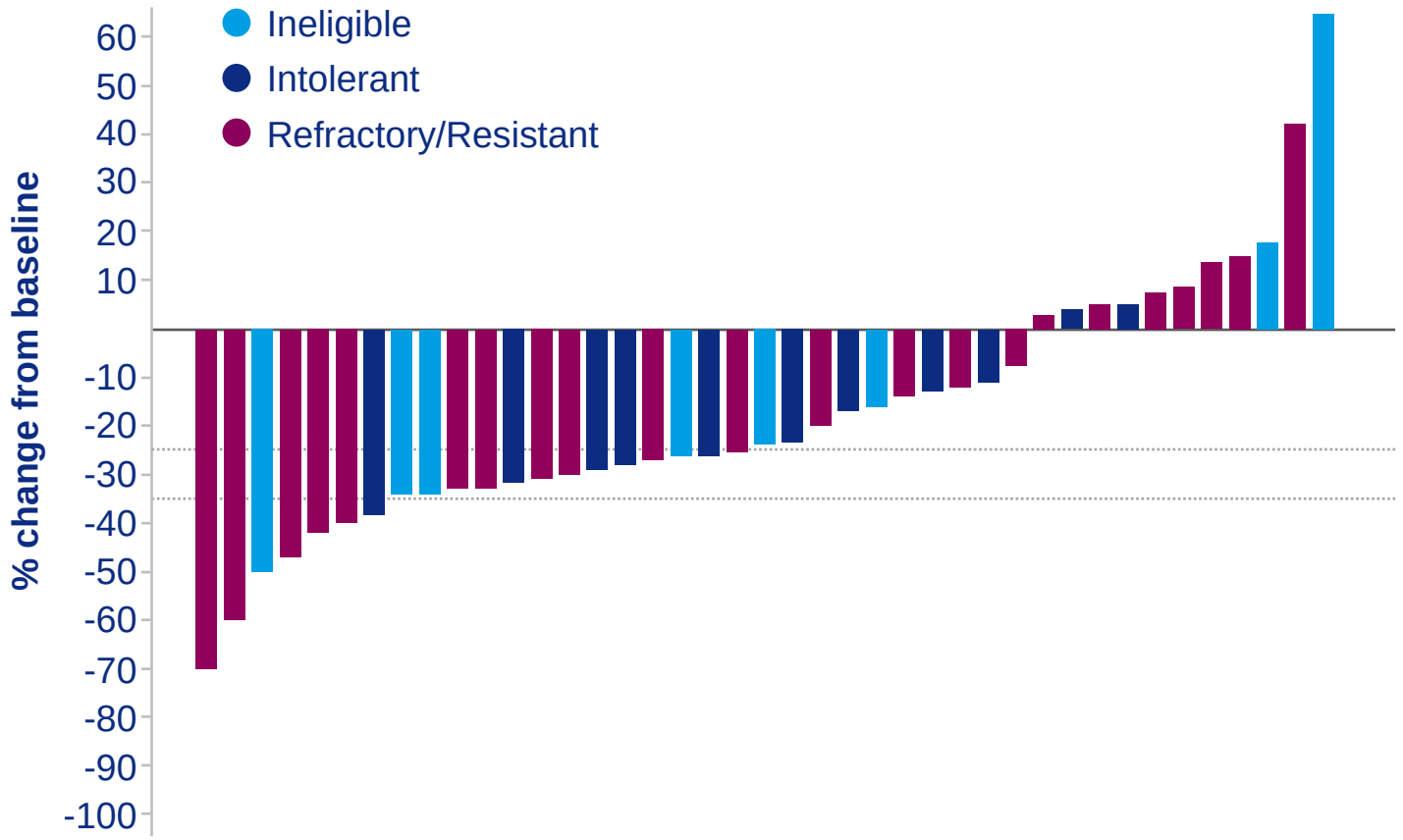
| | JAKi R/R | JAKi IE | JAKi IN | Overall |
|---|---|---|---|---|
| **Hemoglobin response**[1] | 34% (11/32) | 66% (2/3) | 41% (5/12) | 38.3% (18*/47) |

- R/R: Refractory resistant; IE: Ineligible; IN: Intolerant
- [2]Hemoglobin response (secondary endpoint): Post-baseline mean Hgb increase of at least 1.5g/dL is required for any 12 wks RBC transfusion free period.
- *Median time between prior JAKi therapy and study entry is 17 months; 3 patients (2 JAKi R/R, 1 JAKi IN) received ruxolitinib within 3 months of study entry.
- [3]Mean Hgb over time: Hgb values within 12 wks after transfusion are excluded; 3 patients non-evaluable due to missing baseline

## Arm 1B Non-TD cohort: Mean hemoglobin over time[3]



# Arm 1: Spleen Volume Percent Change at Week 24




**Arm 1B Non-TD cohort primary endpoint:**

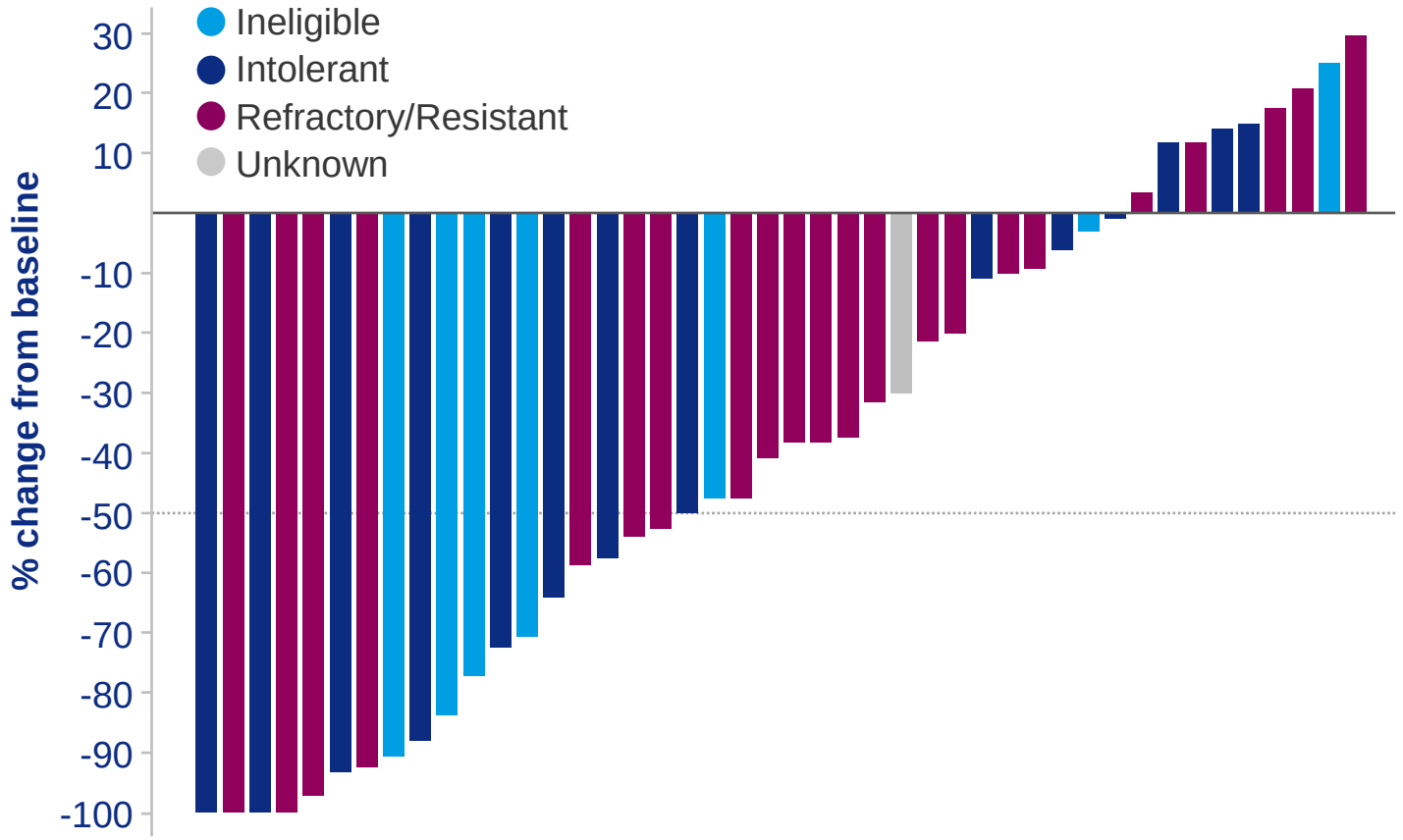
SVR35 at week 24

18% (7/38)

| | Arm 1 (TD and Non-TD) N=64 |
|---|---|
| **SVR35** | 11% (7/64) |
| **SVR25** | 31% (20/64) |
| Median spleen volume % change | -24% |
| Mean spleen volume % change | -17% |

- SVR: Spleen volume reduction per local radiology review; SVR25: ≥25% reduction in spleen volume from baseline; SVR35: ≥35% reduction in spleen volume from baseline
- Patients evaluable if non-missing baseline and week 24 spleen assessment or discontinued at any time without wk 24 spleen assessment
- 22 patients non-evaluable: 4 pts due to missing baseline and 18 ongoing pts without wk 24 assessment. 23 pts discontinued without having wk 24 assessment included as non-responders
- Patients evaluable for SVR at wk 24: JAKi ineligible (n=10); JAKi intolerant (n=15); JAKi refractory/resistant (n=38); 1 patient with unknown subgroup

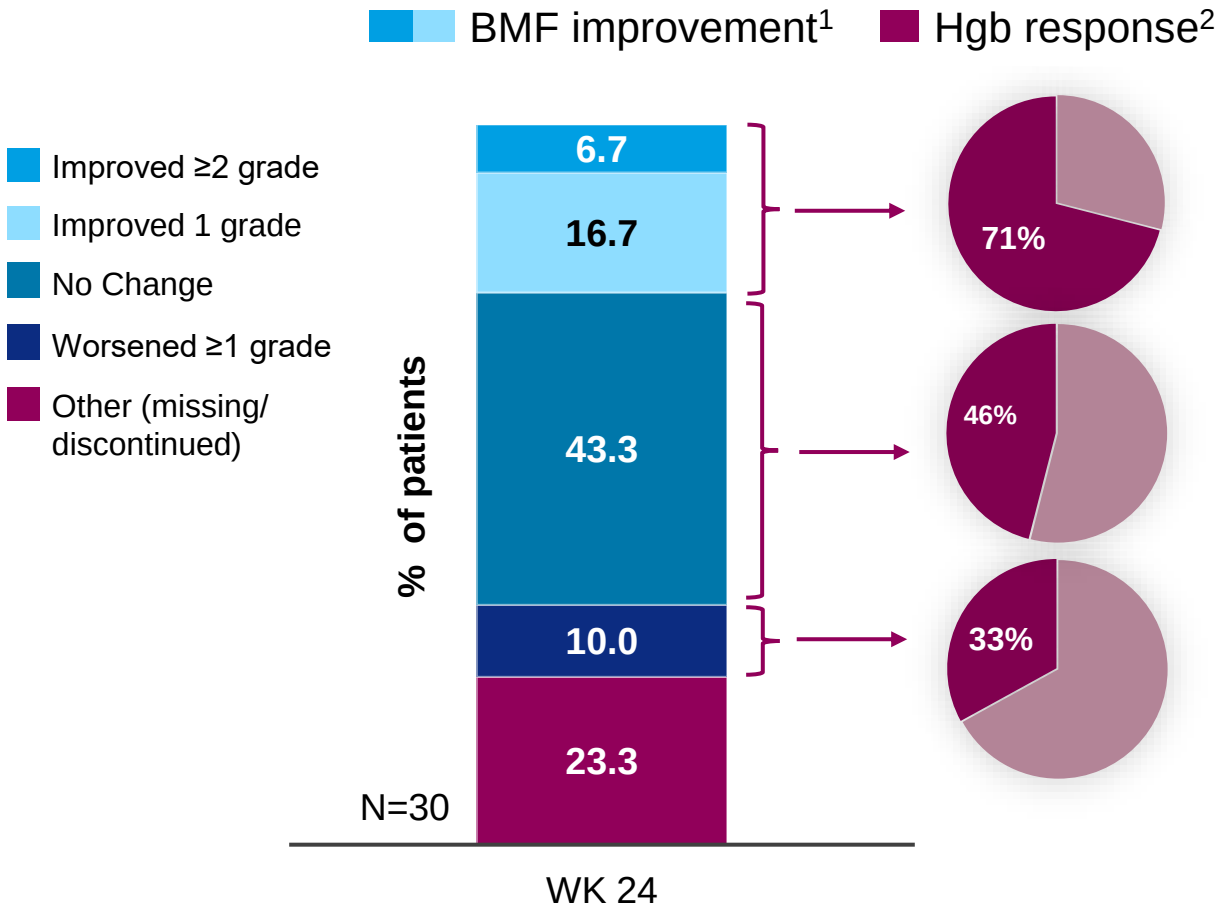
# Arm 1: TSS Percent Change at Week 24




| | Arm 1 (TD and Non-TD) N=64 |
|---|---|
| **TSS50** | 28% (18/64) |
| Median TSS % change | -40% |
| Mean TSS % change | -40% |

- TSS: Total Symptom Score; TSS50: ≥50% reduction in total symptom score from baseline
- Patients evaluable if non-missing baseline and week 24 TSS assessment or discontinued at any time without wk 24 TSS assessment
- 22 patients non-evaluable: 7 pts due to missing baseline and 15 ongoing pts did not reach wk 24 as of data cut-off. 20 patients discontinued without wk 24 assessment are included as non-responders
- Patients evaluable for TSS at wk 24: JAKi ineligible (n=8); JAKi intolerant (n=18); JAKi refractory/resistant (n=37); UNK: 1 patient with unknown subgroup

# Arm 1: Bone Marrow Fibrosis Improvement[1] Per Central Read and Hemoglobin Response[2]

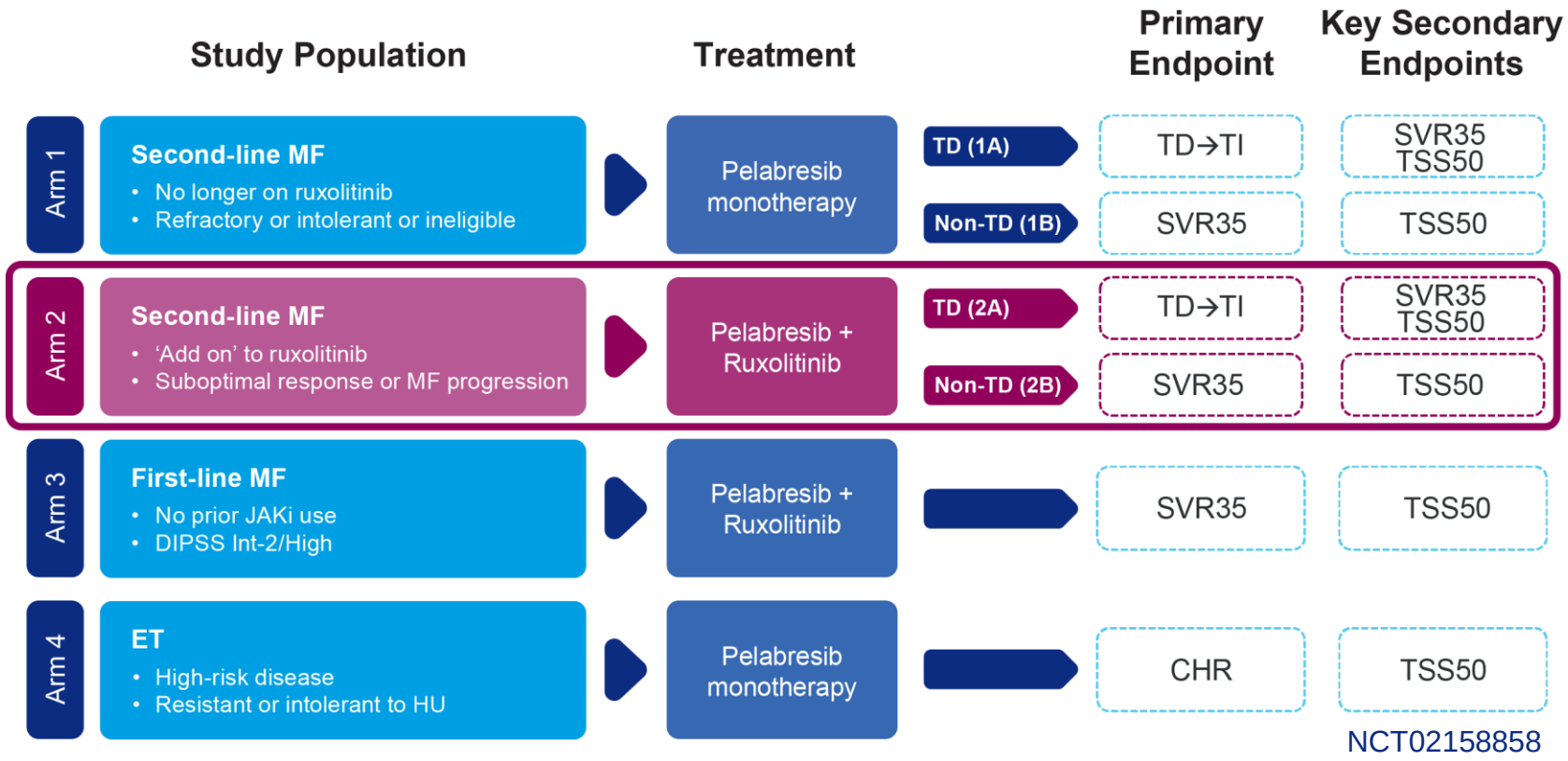



- 71% (5/7) of the patients with BMF improvement were also hemoglobin responders[2]
- 47% (14/30) of patients had grade 3 BMF at baseline, 3/16 (19%) patients with grade 1/2 BMF at baseline had BMF worsening

- [1]Exploratory endpoint: Patients evaluable if non-missing baseline bone marrow assessment
- [2]Secondary endpoint: Post-baseline mean Hgb increase of at least 1.5g/dL for any 12 wks RBC transfusion free period
- BMF: bone marrow fibrosis grade by central pathology review; maturing data with central review ongoing

# Arm 2: Suboptimal Responders to Ruxolitinib

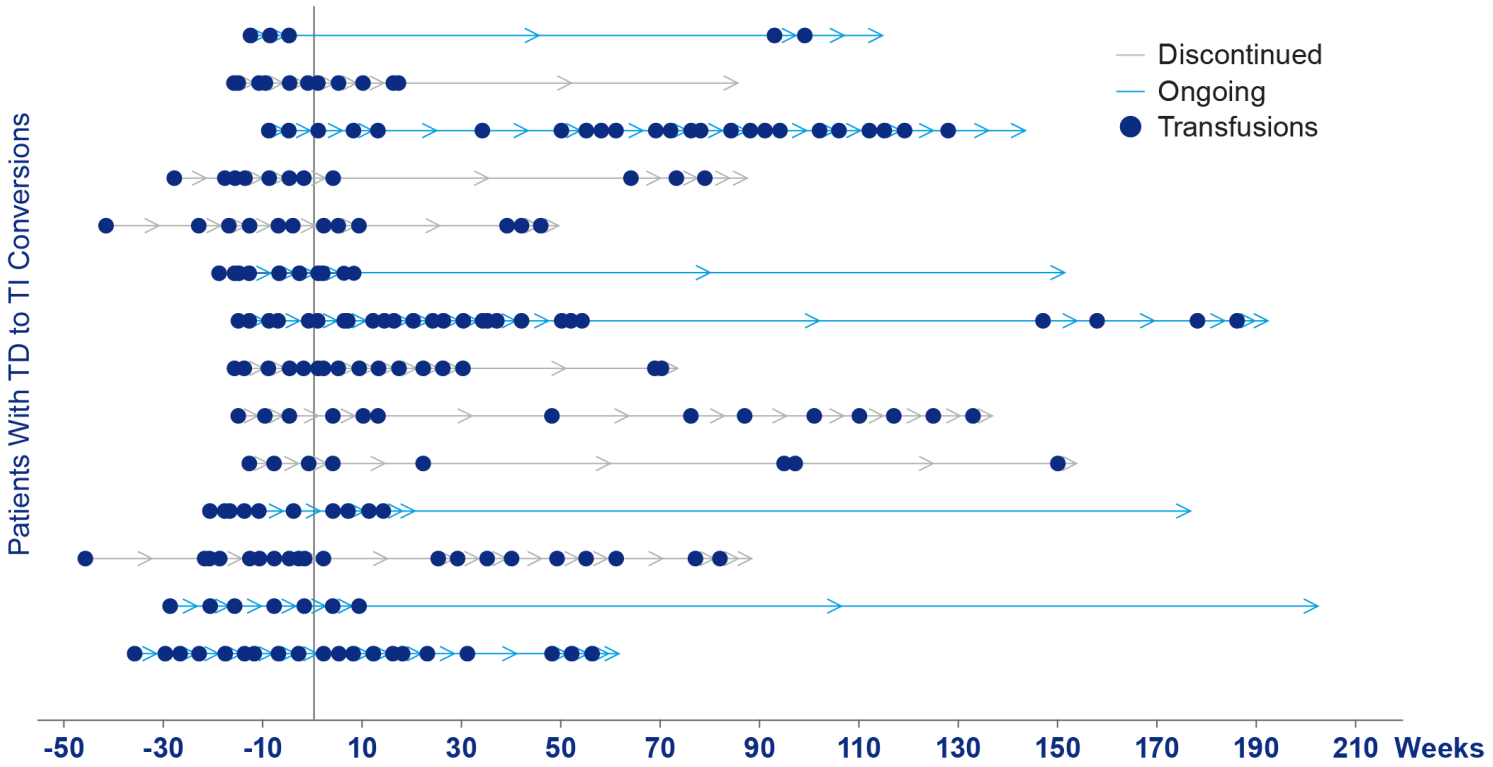
MANIFEST: Ongoing, global, open-label Phase 2 study investigating pelabresib in myelofibrosis and essential thrombocythemia




CHR, complete hematologic response; DIPSS, Dynamic International Prognostic Scoring System; ET, essential thrombocythemia; HU, hydroxyurea; Int-2, intermediate-2; JAKi, Janus kinase inhibitor; MF, myelofibrosis; SVR35, ≥35% reduction in spleen volume at Week 24; TD, transfusion dependent; TI, transfusion independent; TSS50, ≥50% reduction in total symptom score at Week 24.
Clinicaltrials.gov. NCT02158858. Available at: https://clinicaltrials.gov/ct2/show/NCT02158858. Accessed April 26, 2023.

# Arm 2: Anemia Responses with Add-on Strategy

## TD to TI conversion

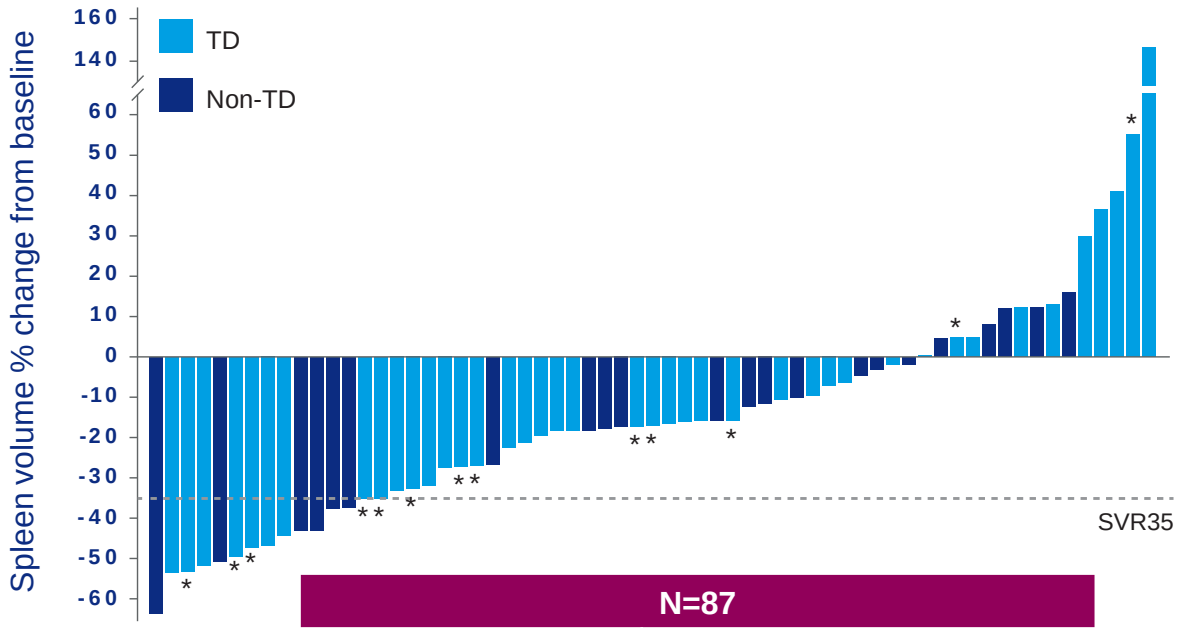



| TD to TI conversion | |
|---|---|
| **TD to TI conversion** | 36.8% (14/38) |
| **Median TI duration** | 37 weeks (range 15–192) |
| **Median time to TI conversion** | 66 weeks |

The TD to TI conversion (primary endpoint for TD cohort) is defined as the absence of red blood cell transfusions over any 12-week period. Patients evaluable if nonmissing baseline, ongoing and received 12 weeks of treatment or discontinued at any time point. TI duration: Longest duration between transfusions for TI patients; Time to TI conversion: Time to last transfusion prior to conversion for TI pts.
TD, transfusion dependent; TI, transfusion independent.

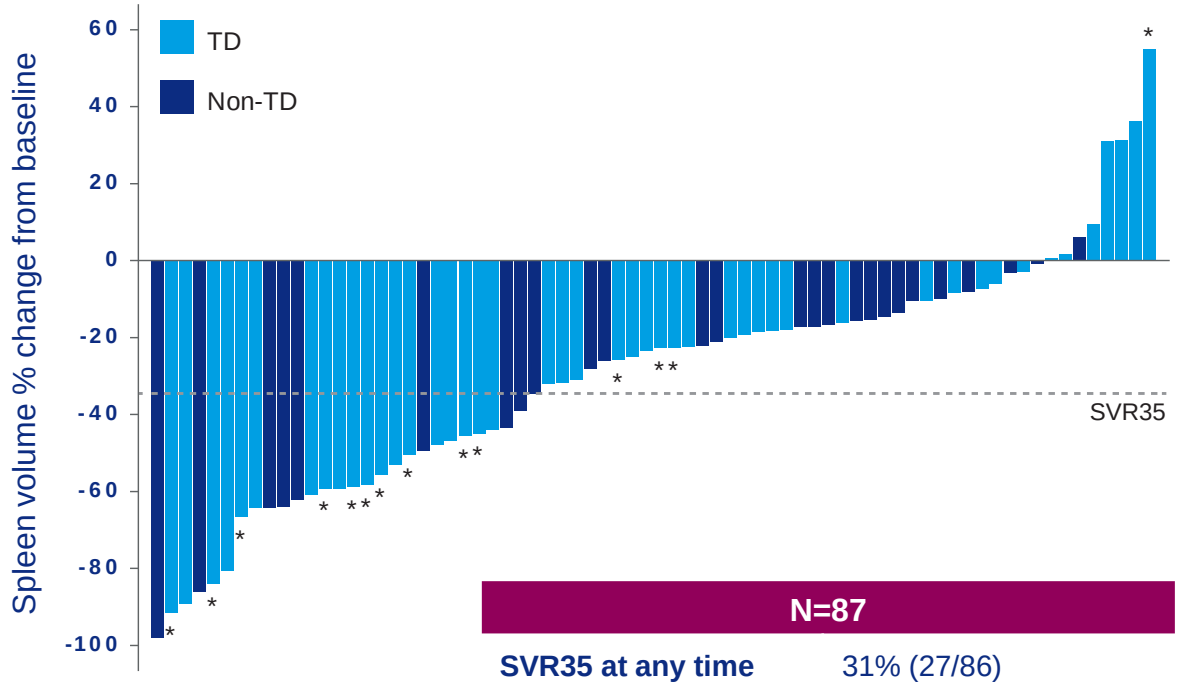
# Arm 2: Spleen Responses with Add-on Strategy

## Spleen Volume Reduction at Week 24, by Local Review




| N=87 | |
|---|---|
| **SVR35 at Wk 24** | All: 17% (15/86)<br>TD: 16% (9/57)<br>Non-TD: 21% (6/29) |
| **SVR25 at Wk 24** | 26% (22/86) |
| **Median % SVR** | –17% |

## Best Reduction in Spleen Volume at Any Time, by Local Review

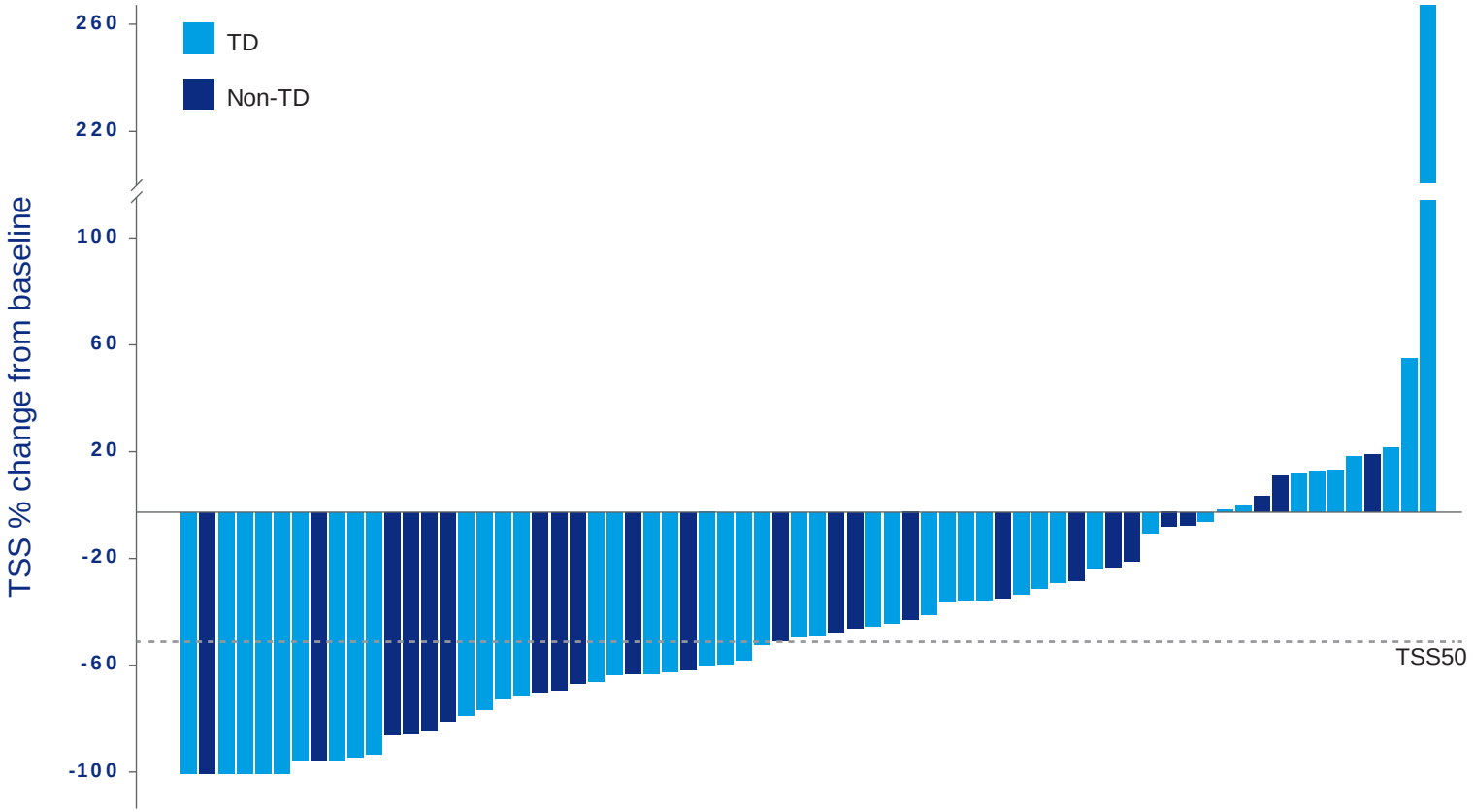



| N=87 | |
|---|---|
| **SVR35 at any time** | 31% (27/86) |

*Patient converted from TD (transfusion dependent) to TI (transfusion independent) for ≥12 weeks.
Patients are evaluable for SVR35 at Wk 24 if they have had a Wk 24 assessment by the data cutoff date or discontinued without a Wk 24 assessment at any time.
One patient was nonevaluable for SVR35 due to missing baseline. The SVR35 response rate decreased from the previously reported rate at ASH 2021 due to a change in the source data of one patient.
SVR, spleen volume reduction; SVR25, ≥25% reduction in spleen volume from baseline; SVR35, ≥35% reduction in spleen volume from baseline; Wk, week

# Arm 2: Symptom Improvement with Add-on Strategy

## Total symptom score at Week 24

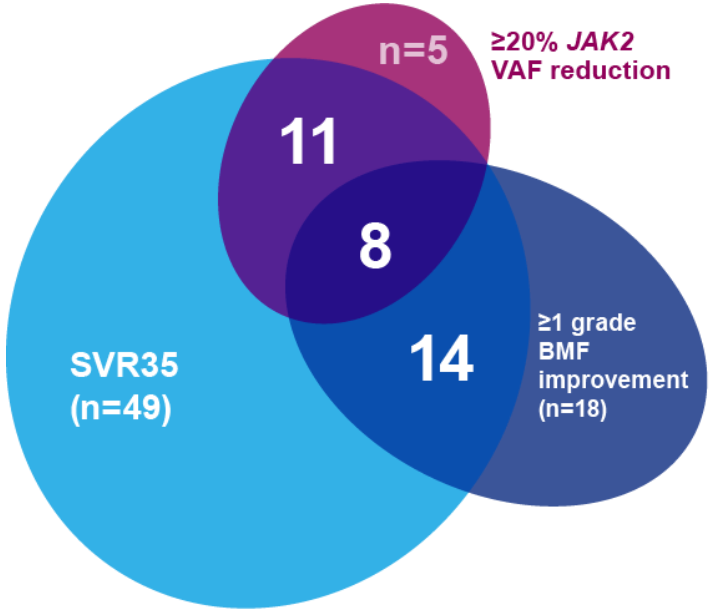



| N=87 | |
|---|---|
| **TSS50 at Wk 24** | All: 38% (32/85)<br>TD: 37% (21/57)<br>Non-TD: 39% (11/28) |
| **Median TSS % change** | –48% |

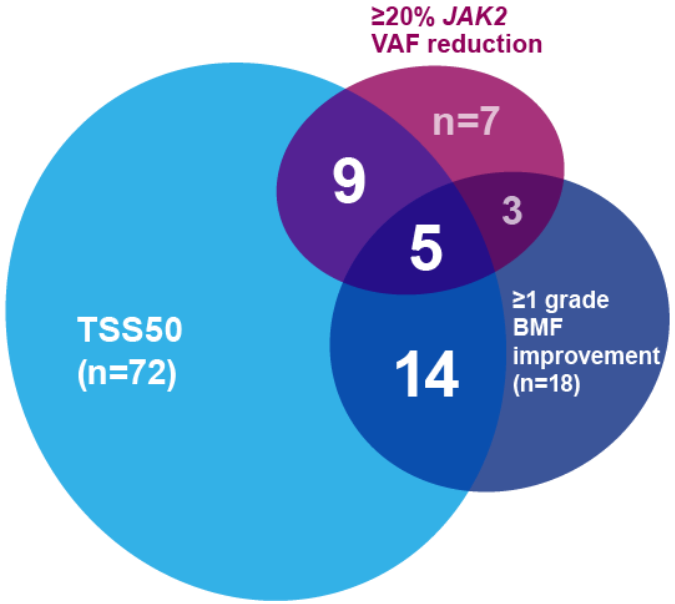
Percentage change in total symptom score between baseline and Wk 24, as measured by MFSAF v4.0. Patients are evaluable for TSS50 at Wk 24 if they have had a Wk 24 assessment by the data cutoff date or discontinued without a Wk 24 assessment at any time.
MFSAF, Myelofibrosis Symptom Assessment Form; TSS, total symptom score; TSS50, ≥50% total symptom score reduction from baseline; TD, transfusion depedndent;

# MANIFEST Arms 1–3: Clinical Responses Associated with *JAK2 V617F* VAF Reduction and ≥1 Grade Improvement in BMF at Week 24

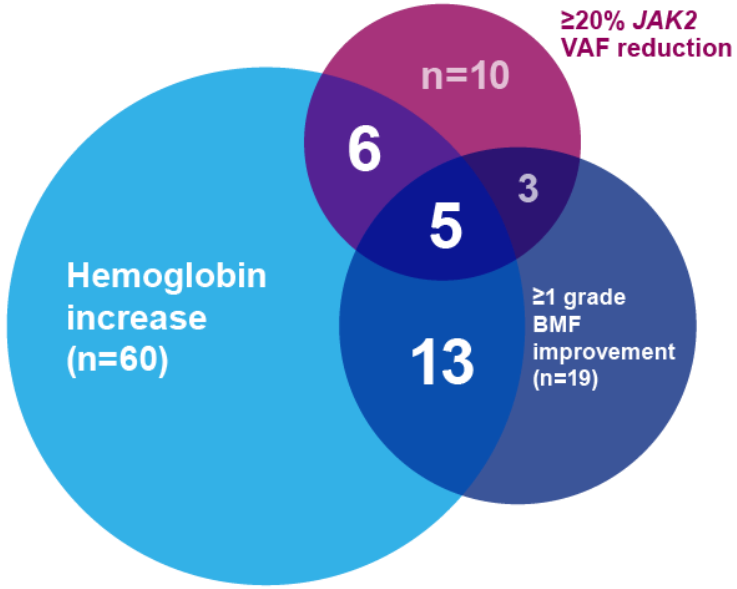
## All patients who had clinical responses, *JAK2 V617F* VAF reduction and BMF improvement at Week 24 were JAKi treatment naïve (Arm 3)




33/82 (40%) of SVR35 responders had *JAK2 V617F* VAF reduction and/or BMF improvement




28/100 (28%) of TSS50 responders had *JAK2 V617F* VAF reduction and/or BMF improvement

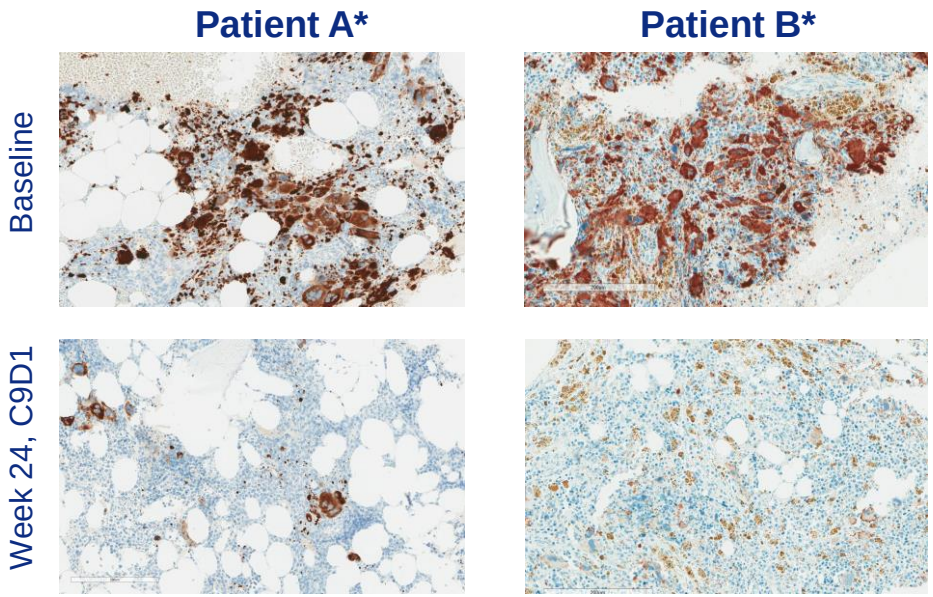



24/84 (29%) patients with hemoglobin improvement had *JAK2 V617F* VAF reduction and/or BMF improvement

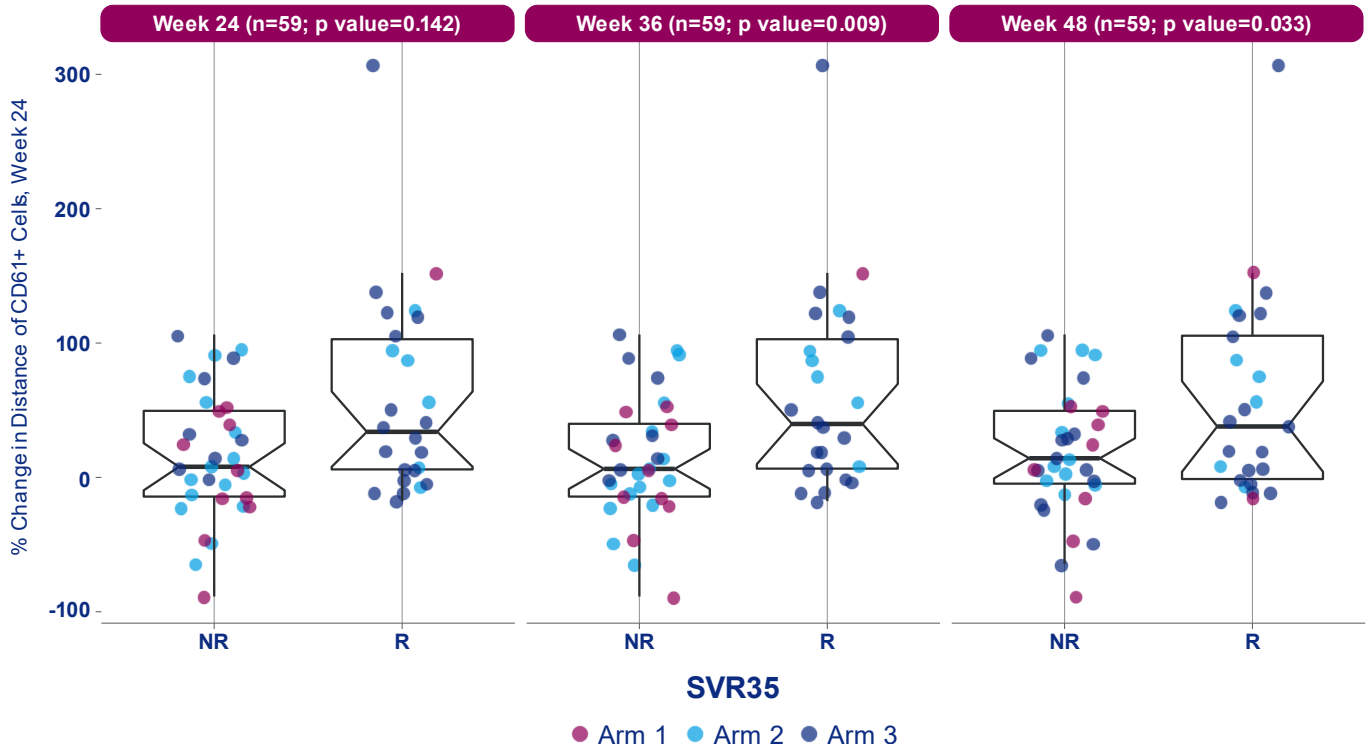
Hemoglobin increase: Hgb assessment within 2 weeks after RBC transfusion were excluded from the analysis; any level of increase from baseline (ranges of increase: Arm 1, 0.1–4.2 g/dL; Arm 2, 0.1–2.5 g/dL; Arm 3, 0.1–3.8 g/dL).

# Correlation Between Megakaryocyte 'Declustering' in Bone Marrow and SVR35 Response

## SVR35 responders

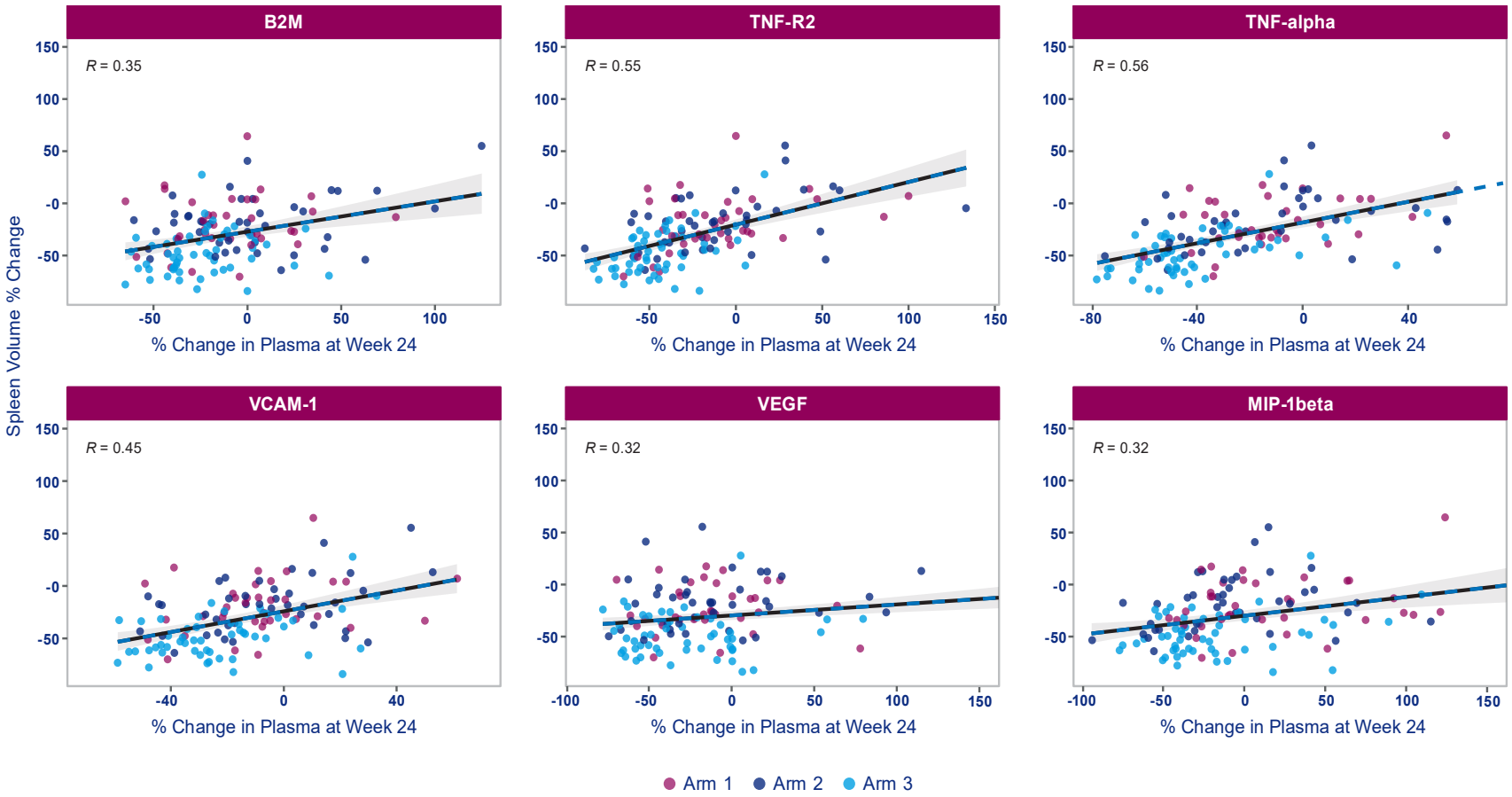



Slide pairs were stained centrally for CD61; scanned and digital images were evaluated for CD61 distance.
CD61 distance: mean distance between nuclei in a field with variable number of nuclei and up to 10 fields per image; QC review of each slide: each 400 $mm^2$ field must pass QC criteria.




*Images and examination results used with patient consent. Data previously presented at EHA 2022 Annual Meeting, June 9–12, 2022; Vienna, Austria.
P values were computed by logistic regression with age and gender adjustment.
CD61, platelet glycoprotein IIIa; NR, nonresponders; R, responders.

# Correlation of Plasma Cytokine Changes with Spleen Volume Changes at Week 24




## Overview of Cytokines

| Cytokine | NF-kB signaling | MF elevated |
|---|---|---|
| B2M | √ | |
| TNF-R2 | √ | √ |
| TNF-alpha | √ | √ |
| VCAM-1 | √ | √ |
| VEGFa | √ | √ |
| MIP-1beta | √ | √ |

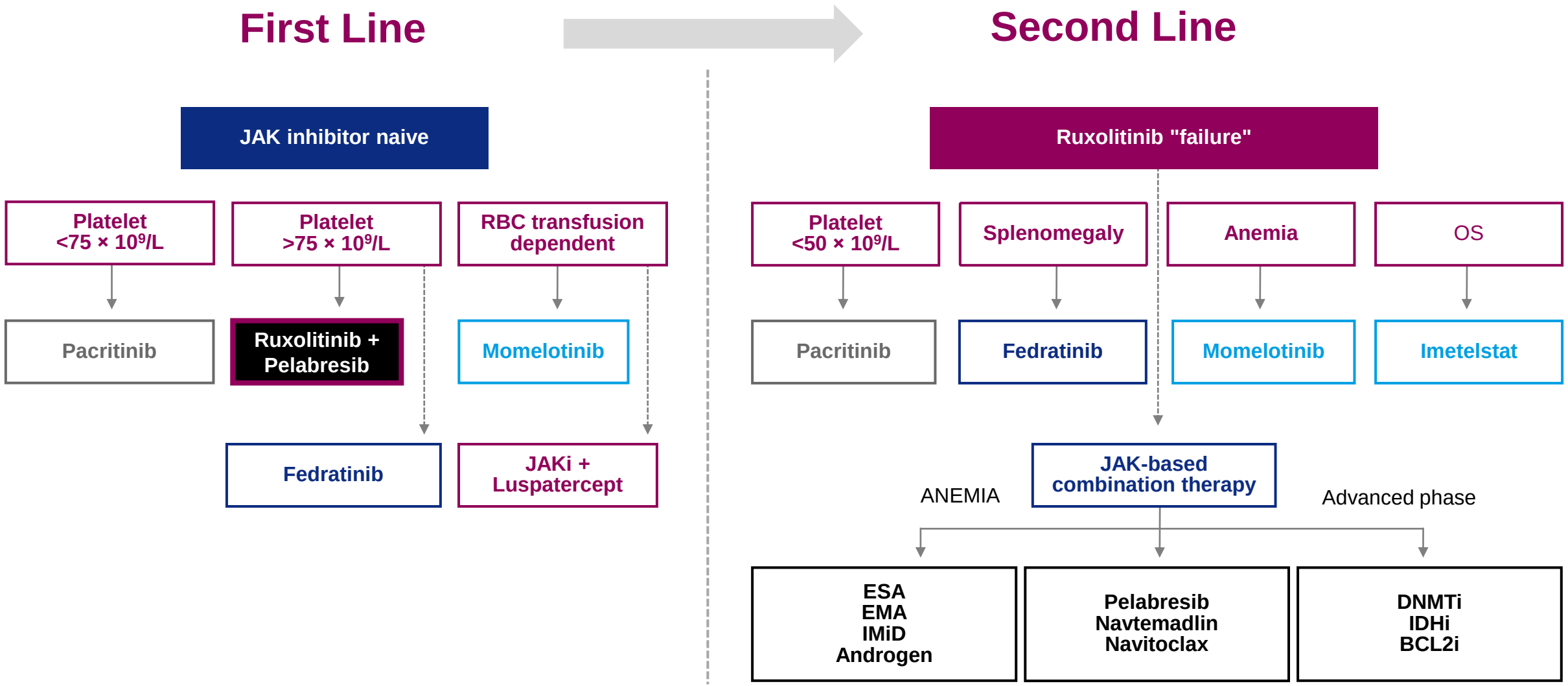
- Reduction in plasma levels of cytokines was associated with spleen volume reduction at Week 24

NF-κB, nuclear factor kappa B.

# Summary

- BET inhibition is **rational** and supported by pre-clinical data
- The combination of pelabresib and ruxolitinib is **clinically active**
  - + Deep and durable spleen and symptom data in the JAK inhibitor naïve setting (ARM 3)
  - + Evidence of salvage in spleen and symptom in the add-on (ARM 2)
  - + Single agent spleen, symptom and anemia activity in the relapsed/refractory setting (ARM 1)
- **Well-tolerated** therapy
  - + Easy to manage low grade GI toxicity
  - + Reversible cytopenias rarely lead to discontinuation
- Correlative evidence of **biologic disease modification**
  - + BMF reduction in a 1/3 of treated patients
  - + Reduction in JAK2V617F VAF ≥20% in 38% of treated patients
  - + Megakaryocyte declustering and association with spleen response
- **PARADIGM SHIFT**: MANIFEST-2, a Phase 3 randomized double-blind trial of pelabresib + ruxolitinib vs placebo + ruxolitinib in JAKi treatment-naïve patients with myelofibrosis is ongoing (NCT04603495)

# 3 Year Outlook for Myelofibrosis



# 05

# Pelabresib Clinical Development Roadmap

**TIM DEMUTH, M.D., Ph.D.**
Chief Research & Development Officer, MorphoSys

# Phase 3 MANIFEST-2 Study Investigating Pelabresib Plus Ruxolitinib as a First-Line Myelofibrosis Treatment

**431** JAK-inhibitor-naïve patients were randomized in the MANIFEST-2 study

| STUDY POPULATION | DESIGN/SIZE | TREATMENT ARM/COHORT | ENDPOINTS |
|---|---|---|---|
| JAK-inhibitor-naïve myelofibrosis patients | Double-Blind Randomization | Pelabresib + Ruxolitinib<br>Placebo + Ruxolitinib | **Primary:** SVR35 at 24 weeks<br>**Key Secondary:** TSS50 at 24 weeks (MF-SAF v4.0) |

MF-SAF, Myelofibrosis Symptom Assessment Form

MANIFEST-2 fully enrolled with topline data expected by the end of 2023

# New Phase 2 Data Underscore Potential Clinical Benefit of Pelabresib in Myeloid Diseases

*MANIFEST Phase 2 study arm 4 presented at ASCO and EHA 2023 Annual Meetings*

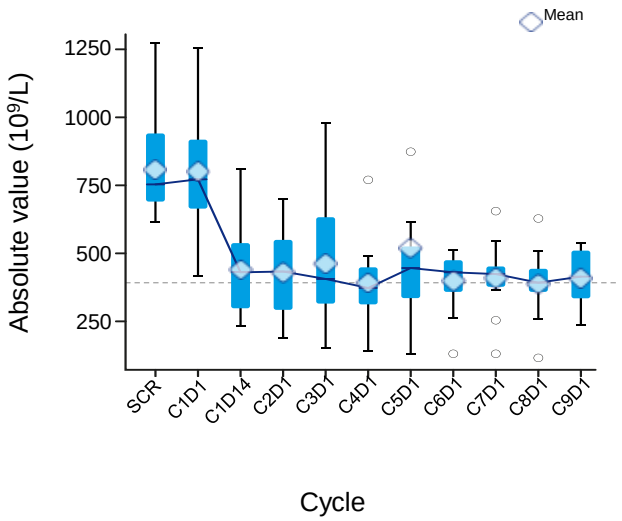
| STUDY POPULATION | DESIGN/SIZE | ENDPOINTS |
|---|---|---|
| High-risk essential thrombocythemia<br><br>Refractory or intolerant to hydroxyurea*<br><br>≥ two symptoms average score ≥3/ TSS ≥15<br><br>Platelets >600 × $10^9$/L | Pelabresib monotherapy<br>N=21 | **Primary:**<br>Complete hematologic response (confirmed – CHR)<br><br>**Secondary:**<br>Partial hematologic response (confirmed – PHR)<br><br>Symptom Improvement (MPN-SAF) |

Complete Hematologic Response (CHR): Normal platelet and white blood cell count with these labs confirmed after 3 weeks, and a normal spleen size
Partial Hematologic Response (PHR): Platelets 400 – 600 and normal white blood cell count with these labs confirmed after 3 weeks
Hematologic Response is confirmed, when conditions are met in two consecutive cycles; unconfirmed, when conditions are met in one cycle but not in the next cycle
MPN-SAF, Myeloproliferative Neoplasm Symptom Assessment Form
Passamonti F, et al. EHA 2023. S168
*Refractory or intolerant criteria, as per Barosi, et al. 2007.

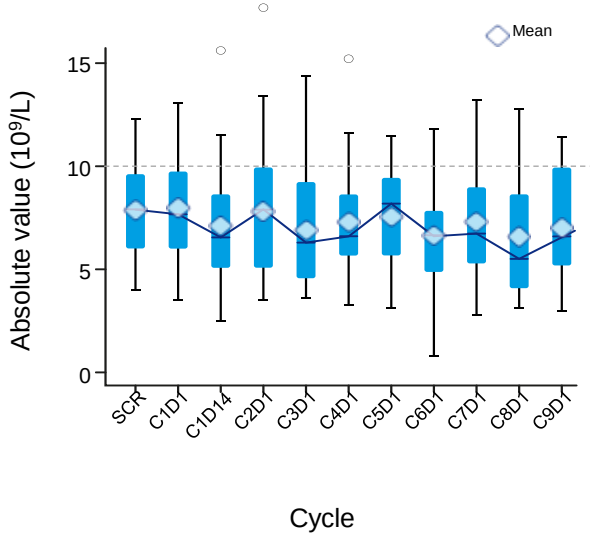
# 90% of Essential Thrombocythemia Patients Had Complete or Partial Hematologic Responses

*At data cut-off (July 29, 2022), results show that pelabresib monotherapy is normalizing platelets over time without causing anemia or thrombocytopenia*

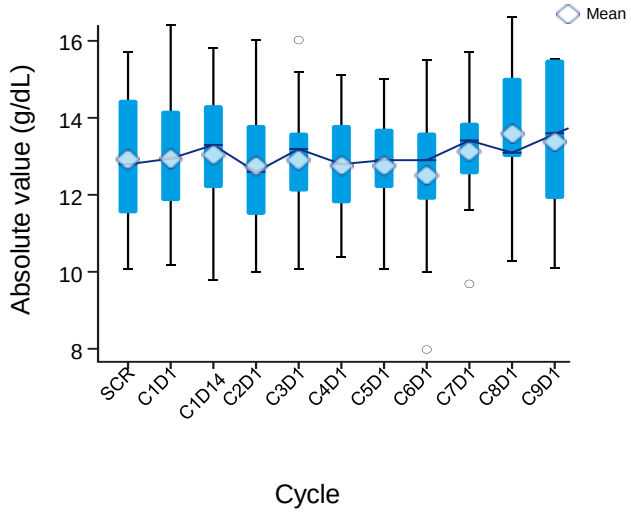
## PLATELETS OVER TIME




## WHITE BLOOD CELL OVER TIME




## HEMOGLOBIN OVER TIME




**CHR or PHR (Confirmed)**

**60%**

(12/20)

**CHR or PHR (Unconfirmed)**

**90%**

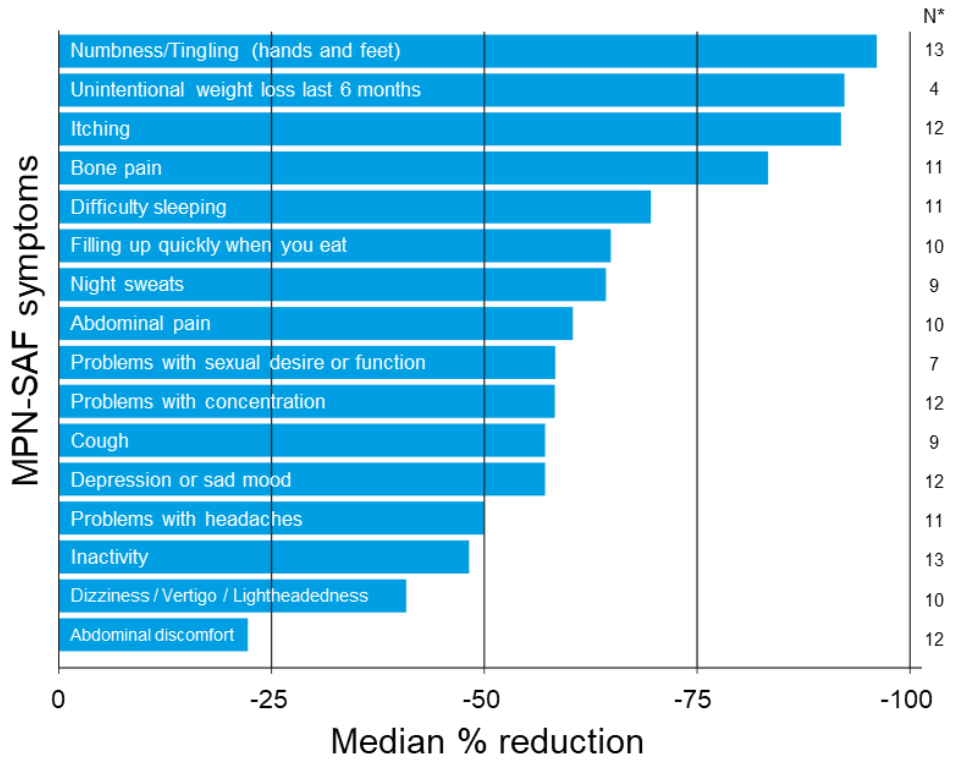
(18/20)

SCR, screening
Data cut-off July 29 2022
Passamonti F, et al. EHA 2023. S168

The most common nonhematologic adverse events were nausea, diarrhea and dysgeusia. Hemorrhagic or thromboembolic events were reported in 30% of patients. No grade 4 events or higher were reported.

# Symptom Reduction was Observed Across All Domains of the Myeloproliferative Neoplasm Symptom Assessment Form

## BEST PERCENTAGE REDUCTION IN MPN-SAF SYMPTOMS




At data cut-off (July 29, 2022), one-half of patients had ≥50% reduction in total symptom score from baseline at any time

| N=14* | MPN-SAF SYMPTOMS |
|---|---|
| TSS50 at anytime | 50% (7/14) |
| Median % TSS reduction at Week 12 | -31% |

*Patients with non-missing and nonzero baseline symptom score.

TSS, total symptom score assessed based on MPN-SAF; TSS50, ≥50% reduction in total symptom score from baseline.
MPN-SAF, Myeloproliferative Neoplasm Symptom Assessment Form
Fever not depicted in the figure due to zero baseline.
Data cut-off July 29 2022
Passamonti F, et al. EHA 2023. S168

# Focused on First-Line Myelofibrosis in 2023, with Expansion into Other Myeloid Diseases in 2024 and Beyond

## MYELOPROLIFERATIVE NEOPLASMS AND ADJACENCIES

### PIVOTAL STAGE

**MYELOFIBROSIS**

- Deliver Phase 3 MANIFEST-2 data by end of 2023
- Prepare for U.S. and Europe regulatory filings

### CLINICAL PROOF OF CONCEPT STAGE

**LOWER-RISK MYELODYSPLASTIC SYNDROMES (MDS)**

- Initiate Phase 2 study in 2024

**ESSENTIAL THROMBOCYTHEMIA (ET)**

- Phase 2 proof-of-concept results

# Committed to Unlocking the Full Potential of Pelabresib in Myelofibrosis and Beyond

## FOUNDATIONAL TEATMENT POTENTIAL IN 1L MYELOFIBROSIS

- Synergistic effects between BET and JAK inhibition
- Prolonged improvement in SVR35 and TSS50 at 24, 40 and 60 weeks
- Changes in biomarkers suggest disease-modifying effect

## BLOCKBUSTER POTENTIAL IN 1L MYELOFIBROSIS

- ~18,000 patients in the U.S., ~3,200 patients diagnosed each year
- At diagnosis, ~90% of patients have intermediate- or high-risk disease

## DEVELOPMENT IN OTHER MYELOID DISEASES

- Phase 2 study in lower-risk MDS to be initiated in 2024
- Proof-of concept data in ET

Kleppe M, et al. Cancer Cell 2018;33:29–43.e7
Mascarenhas J, et al. ASH 2022. Abstract 238.

# 06

# Q&A

**JEAN-PAUL KRESS, M.D.**

**TIM DEMUTH, M.D., Ph.D.**

**JOHN MASCARENHAS, M.D.**

**GABRIELA HOBBS, M.D.**

# Thank you!

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