POST-ORLANDO 2025
Novità dal Meeting della Società Americana di Ematologia

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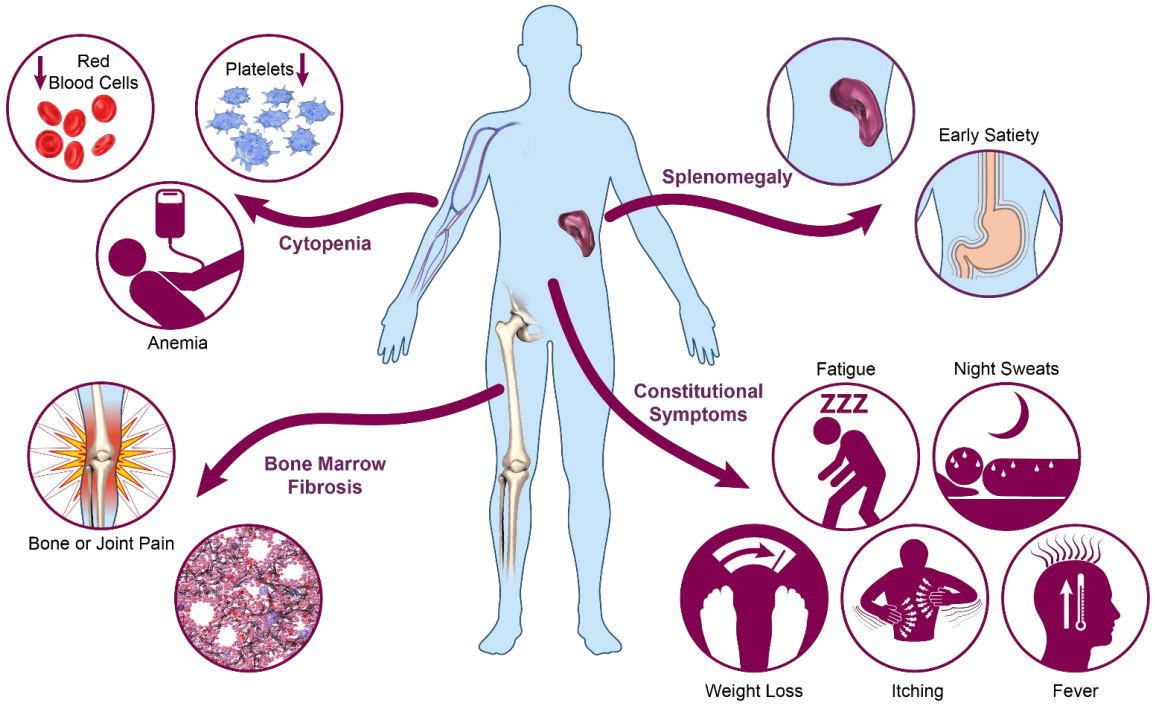
Sobi			X				X
AOP			X				X

Myelofibrosis: A Rare, Progressive, Debilitating Disease with Significant Burden

Clinical Manifestations of Myelofibrosis[1]



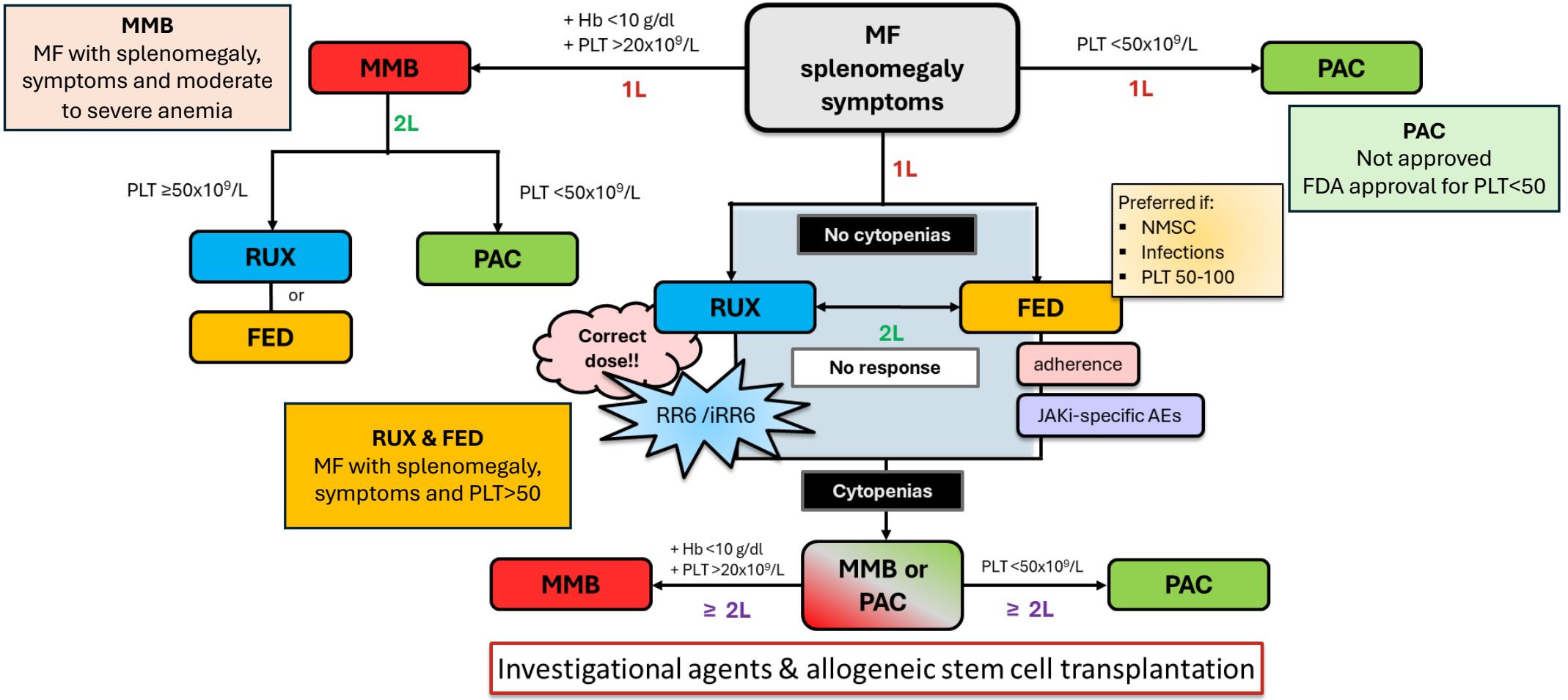
Significant impact on quality of life

- Estimated Incidence: 0.47-1.98 per 100,000[2]
- Estimated Prevalence: 1.76-4.05 per 100,000[2]
- Median age of diagnosis: ~ 65 y[3]
- At diagnosis, ~90% of patients have intermediate- or high-risk disease → worse prognosis and higher likelihood of disease-associated symptoms[3]
- Heterogeneous symptoms can lead to delays in diagnosis[1-3]

RBC, red blood cell.

[1] Tefferi A. *Am J Hematol.* 2018;93(12):1551-1560. [2] Garmezy B, et al. *Blood Rev.* 2021;45:100691. [3] National Organization for Rare Disorders (NORD). Primary Myelofibrosis. Published 2020. Available at: https://rarediseases.org/rare-diseases/primary-myelofibrosis/#affected. Accessed May 15, 2023.

JAK Inhibitor Treatment Algorithm in Myelofibrosis



Speaker's personal opinion

Adapted from Masarova L, Chifotides HT. Blood. 2025 Apr 17;145(16):1724-1737

WHAT ARE THE LIMITATIONS OF JAK2 inhibitors IN MF?

1

Inadequate management of Cytopenia

Reversal of anemia improves QoL and may increase survival

Increasing PLT count may enable medical therapy

2

Suboptimal response in many patients

Complete resolution of splenomegaly and symptoms in a minority of patients

3

High rate of therapy discontinuations

50-70% rate of JAK2 inhibitors discontinuation at 3-5 yrs

4

Disease persistence

There is no clear evidence of a disease-modifying activity or cure
One-third of evaluable JAK2V617F-positive patients had a >20% reduction in allele burden or regression of BM fibrosis

5

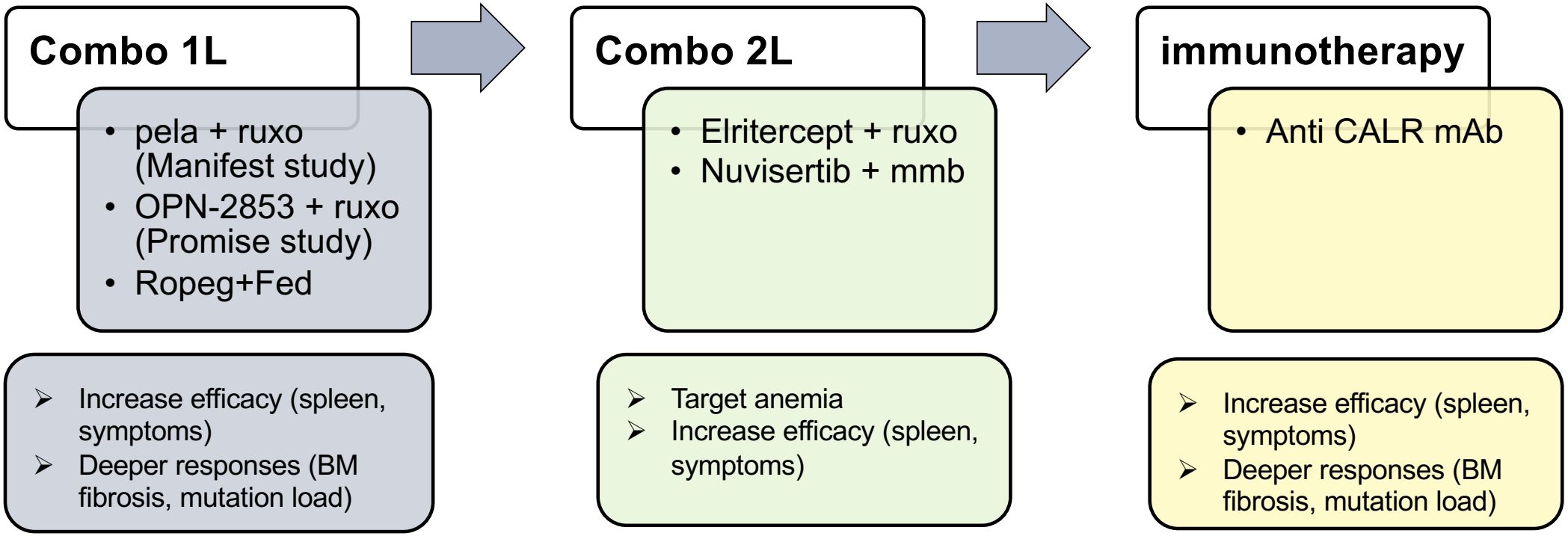
Progression to accelerated/blast phase

The rate of disease progression is not improved by JAK2 inhibitors
Therapy of advanced phase remains unsatisfactory

FED, fedratinib; JAK2, Janus kinase 2; MF, myelofibrosis, NMSC, non-melanoma skin cancer; PLT, platelet; QoL, quality of life; RUX, ruxolitinib.

1. Harrison C, et al. N Engl J Med. 2012;366:787-798: 2. Mesa R, et al. J Clin Oncol. 2017;35:3844-3850; 3. Verstovsek S, et al. N Engl J Med. 2012;366;799-807; 4. Pardanani A, et al. JAMA Oncol. 2015;1:643–651; 5. Food and Drug Administration. JAKAFI Package Insert. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/202192lbl.pdf; 6. Food and Drug Administration. INREBIC Package Insert. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212327s000lbl.pdf; 7. Food and Drug Administration. VONJO Package Insert. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208712s000lbl.pdf; 8. Tremblay D, et al. Cells. 2021;10(5):1034; 9. Palandri F, et al. Cancer. 2023;129(11):1704-1713; 10. Barbui T, et al. Leukemia. 2019;33:1996-2005; 11. Polverelli N, et al. Br J Haematol. 2021;193:356-368; 12. Polverelli N, et al. Am J Hematol. 2017;92(1)37-41; 13. Polverelli N, et al. Hematol Oncol. 2018;36(3):561-569; 14. Elli EM, et al. Front Oncol. 2019;9:1186; 15. Palandri F, et al. Cancer 2022;128(13):2449-2454; 16. Palandri F, et al. Cancer. 2022;128(13):2449-2454; 17. Tremblay D, Mesa R. Future Oncol. 2022;18(20):2559-2571.

ASH 2025 in Myelofibrosis
Addressing the Limitations of JAK2 Inhibitors



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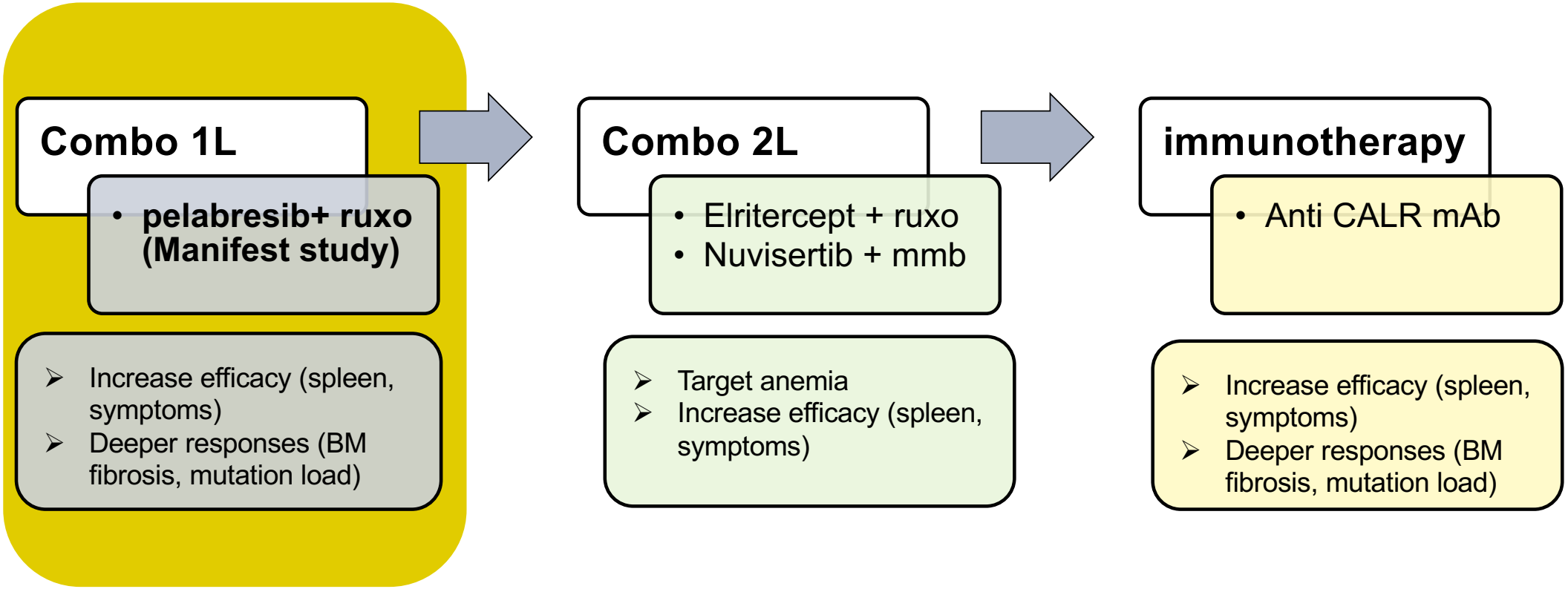
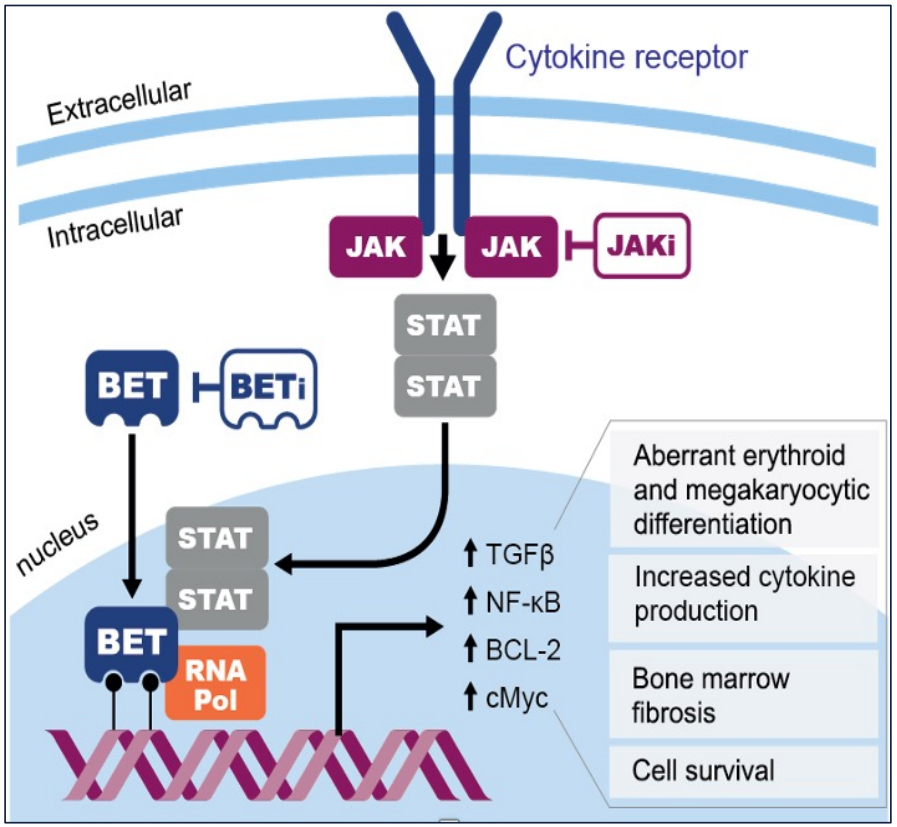


96w of MANIFEST-2 study
Pelabresib+RUX vs. Placebo+RUX (JAKi naïve)



Pelabresib (CPI-0610) is a selective inhibitor of BET proteins (BRD2, BRD3, BRD4, BRDT), key epigenetic regulators that bind acetylated histones and activate transcription of genes involved in proliferation, inflammation, and aberrant megakaryopoiesis.

By blocking BET activity, pelabresib decreases expression of genes driving: -NF-κB activation; Pro-inflammatory cytokine production (e.g., TNF-α, IL-6); Abnormal megakaryopoiesis,

Manifest-2 study
N=430
PLT ≥100 x 10^9/L 100%

Median age 66 yrs
33% Hb ≤10 g/dl,
59% int-1 DIPSS,
~40% HMR mutated

48% of pts on study at W96

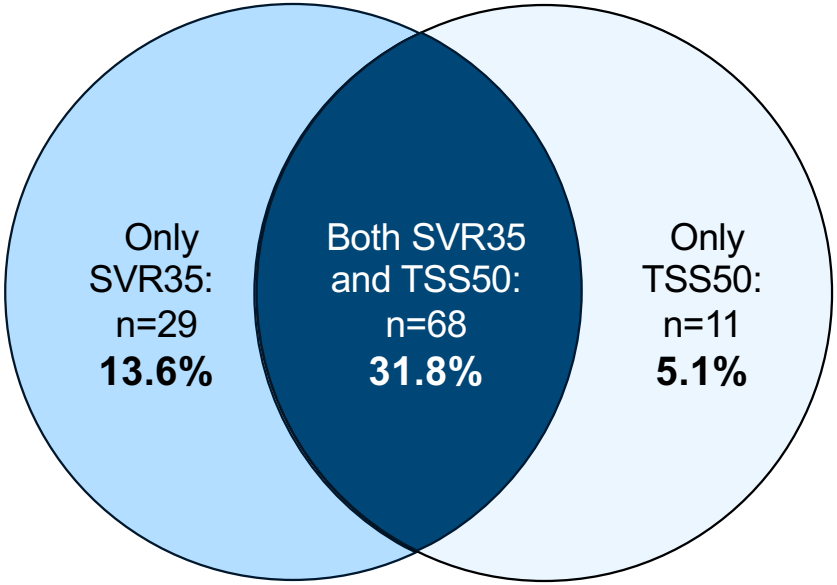
Rampal et al, oral ASH 2025

Twice as many patients achieved both SVR35 and TSS50 responses with PELA+RUX vs PBO+RUX at Week 96

PELA+RUX (N=214)

SVR35 response:
97 patients (**45.3%**)

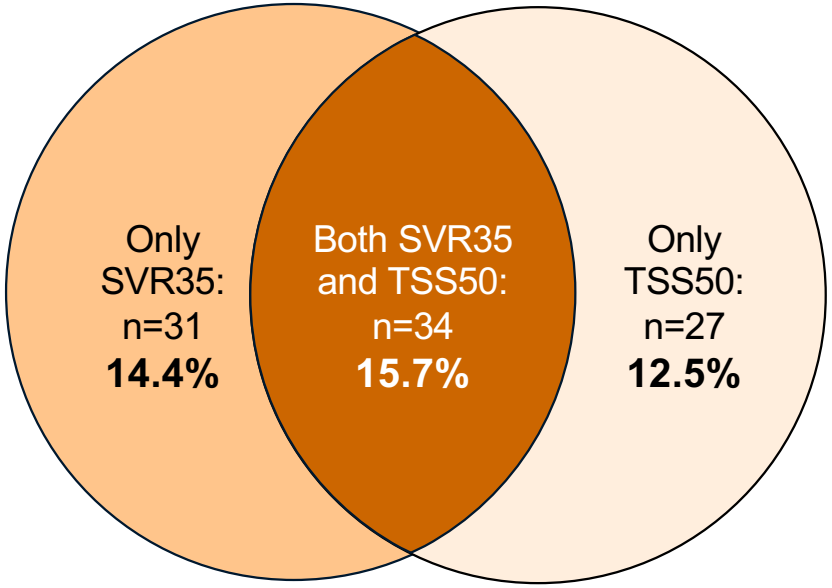
TSS50 response:
79 patients (**36.9%**)



PBO+RUX (N=216)

SVR35 response:
65 patients (**30.1%**)

TSS50 response:
61 patients (**28.2%**)



The dual SVR35 and TSS50 response observed with PELA+RUX was maintained from Week 24 (40.2% vs 18.5%[1]) to Week 96

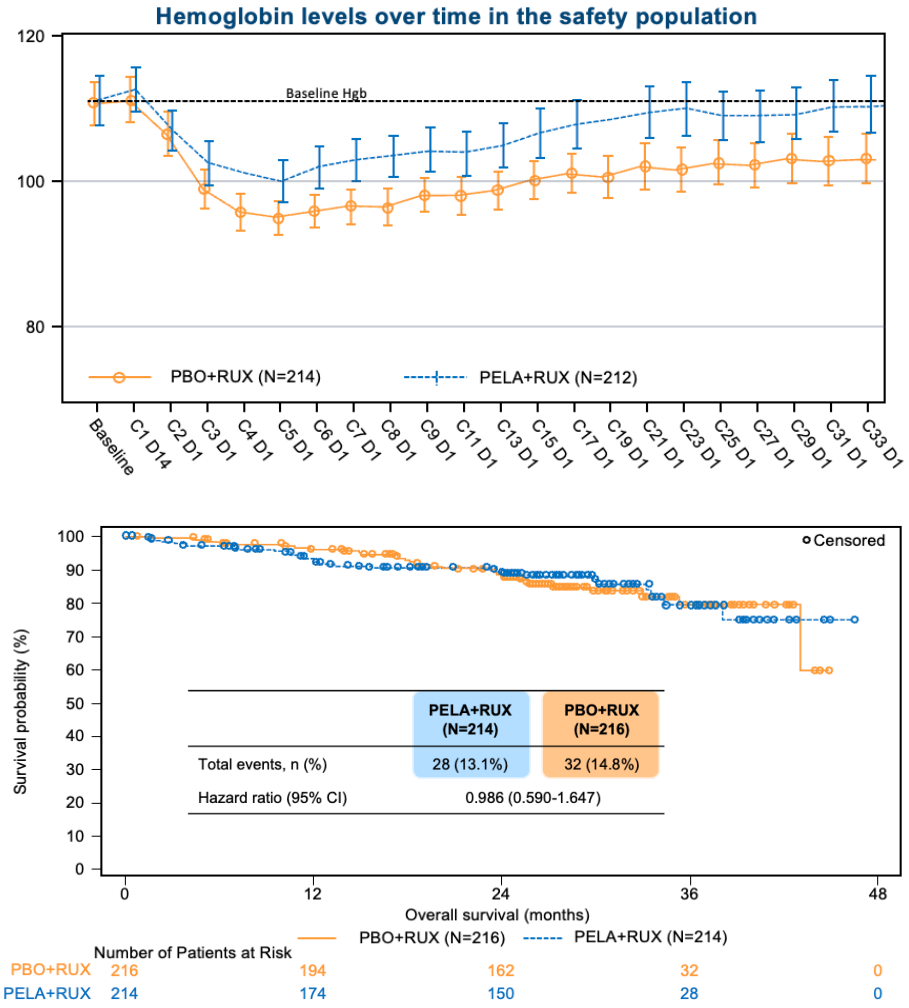
TSS50 reduced but without statistical significance

Data cutoff date: March 2, 2025.
Analysis is not pre-specified in the study protocol and has been performed post-hoc.
PBO, placebo; PELA, pelabresib; RUX, ruxolitinib; SVR35, ≥35% reduction in spleen volume from baseline; TSS50, ≥50% reduction in total symptom score from baseline.

1. Rampal R, *et al. Nat Med* 2025;31:1531-1538.

Oral 910 presented at: American Society of Hematology (ASH) Annual Meeting; December 6 - 9, 2025; Orlando, Florida

96w of MANIFEST-2 study
Pelabresib+RUX vs. Placebo+RUX (JAKi naïve)



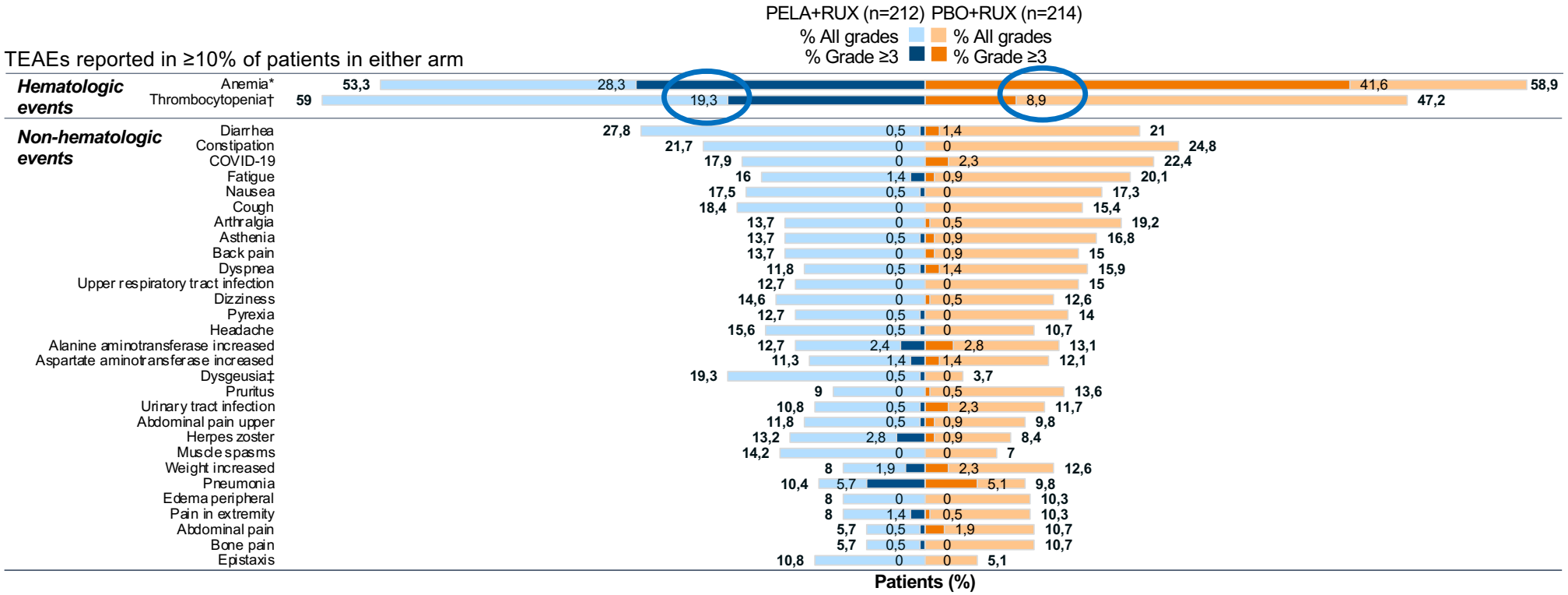
Bone Marrow Fibrosis Grade	PELA+RUX (N=80*)	PBO+RUX (N=80*)
Improved by ≥1 grade	52.5%	27.5%
Worsened by ≥1 grade	13.8%	32.5%

Pela+RUX: greater reductions in megakaryocyte and reticulin fiber densities, and larger increases in CD71+ erythrocyte progenitor cells compared with PBO+RUX

	PELA+RUX†	PBO+RUX
Accelerated phase, % (n/N)	2.3 (5/216)	1.9 (4/214)
Blast phase, % (n/N)	5.1 (11/216)	3.7 (8/214)

Rampal et al, oral ASH 2025

Treatment-emergent adverse events were similar between treatment arms at the Week 96 data cutoff

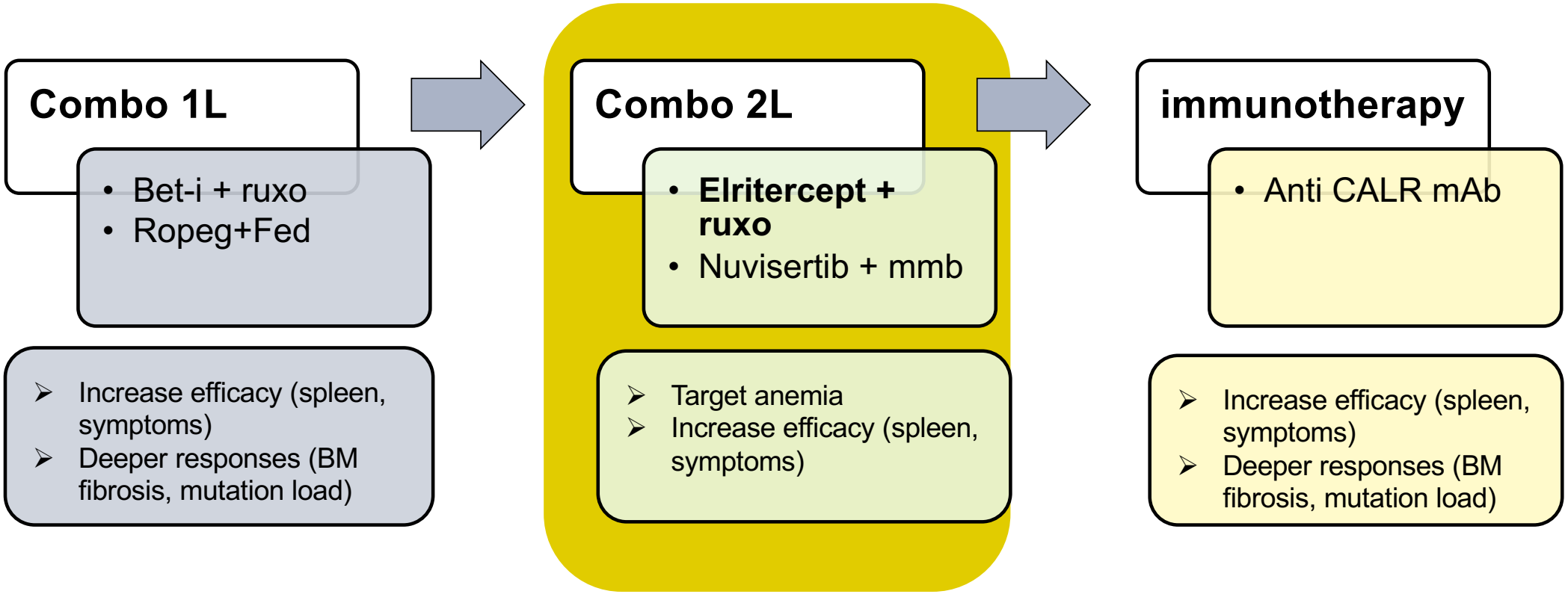


The majority of TEAEs in both treatment arms were low grade (Grade ≤2)

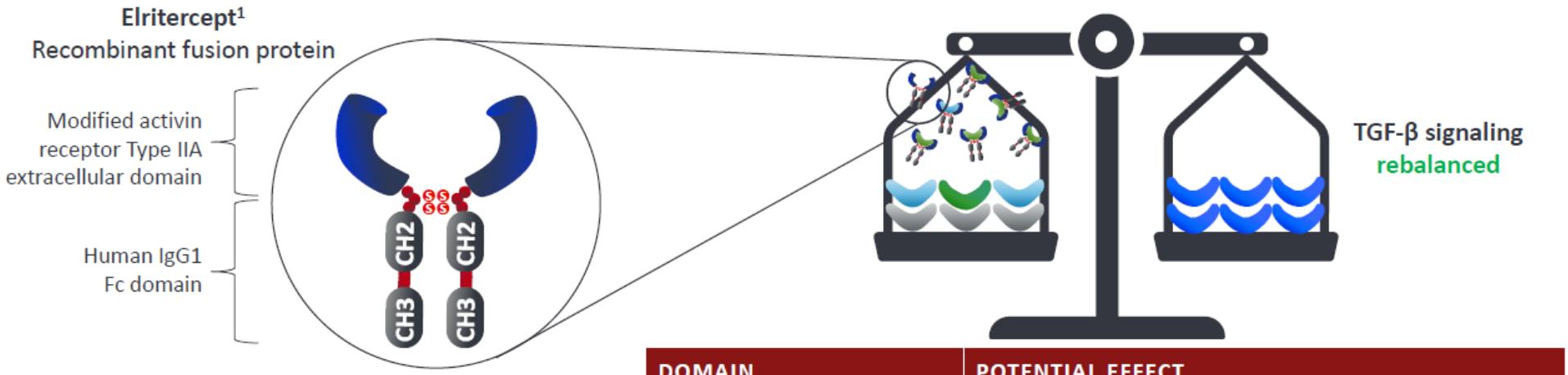
Data cutoff date: March 2, 2025.
AEs are coded using the MedDRA dictionary Version 26.0. A TEAE for the double-blinded treatment period is defined as an AE that has a start date on or after the first dose of PELA/PBO and before 30 days after the last dose of PELA/PBO or before the start of alternative (off-study) treatment for MF, whichever occurs first. * 'Anemia' includes preferred terms of anemia and hemoglobin decrease; † 'Thrombocytopenia' includes preferred terms of thrombocytopenia and platelet count decrease; ‡ Dysgeusia was successfully managed in most patients by dose modifications of PELA.
AE, adverse event; COVID-19, coronavirus disease 2019; MedDRA, Medical Dictionary for Regulatory Activities; MF, myelofibrosis; PBO, placebo; PELA, pelabresib; RUX, ruxolitinib; TEAE, treatment-emergent adverse event.

Oral 910 presented at: American Society of Hematology (ASH) Annual Meeting; December 6 - 9, 2025; Orlando, Florida

ASH 2025 in Myelofibrosis
Addressing the Limitations of JAK2 Inhibitors



Elritercept (KER050)



Elritercept is an investigational modified activin receptor type IIA ligand trap designed to neutralize specific ligands of the TGF-β superfamily that suppress hematopoiesis

SC injections, once every 3 weeks

DOMAIN		POTENTIAL EFFECT
	Erythropoiesis	Enhanced differentiation and maturation at all stages
	Thrombopoiesis	Enhanced differentiation and maturation at all stages
	Bone	Increased bone formation; potential to improve the osteohematopoietic niche
Fe	Iron metabolism	Improved iron homeostasis
	Cardiovascular	Ameliorated cardiac strain

Elritercept is an investigational therapy. The MOA is based on preclinical data. Clinical safety and efficacy have not been determined. Preclinical data may not indicate clinical efficacy. Clinical efficacy can only be established through clinical studies.
CH, constant heavy chain; GDF, growth differentiation factor; Fc, fragment crystallizable; IgG, immunoglobulin G; MOA, mechanism of action; TGF, transforming growth factor

1. Lachey J, et al. Blood Adv 2025;9:193-200; 2. Verma A, et al. J Clin Invest 2020;130:582-9

Restore Phase 2 Study

Primary MF, Post-ET or Post-PV MF with Anemia

Part 1: Dose Escalation 0.75 mg/kg to 4.5 mg/kg Q4W	Part 2: Dose Expansion RP2D (3.75 mg/kg Q4W)
Monotherapy: JAK inhibitor relapsed, refractory, intolerant or ineligible	**Monotherapy:** JAK inhibitor relapsed, refractory, intolerant or ineligible
Elritercept + ruxolitinib*	**Elritercept + ruxolitinib***

We present results from the elritercept + ruxolitinib arm of part 2 (n=38)

Population

- Baseline Hgb <10 g/dL, with or without transfusions and platelet count ≥25 x 10^9/L
- On ruxolitinib for ≥8 weeks, stable dose for ≥4 weeks
- Transfusion dependent (TD): ≥3 RBC units/12 weeks
- Non-transfusion dependent (NTD): 0–2 RBC units/12 weeks

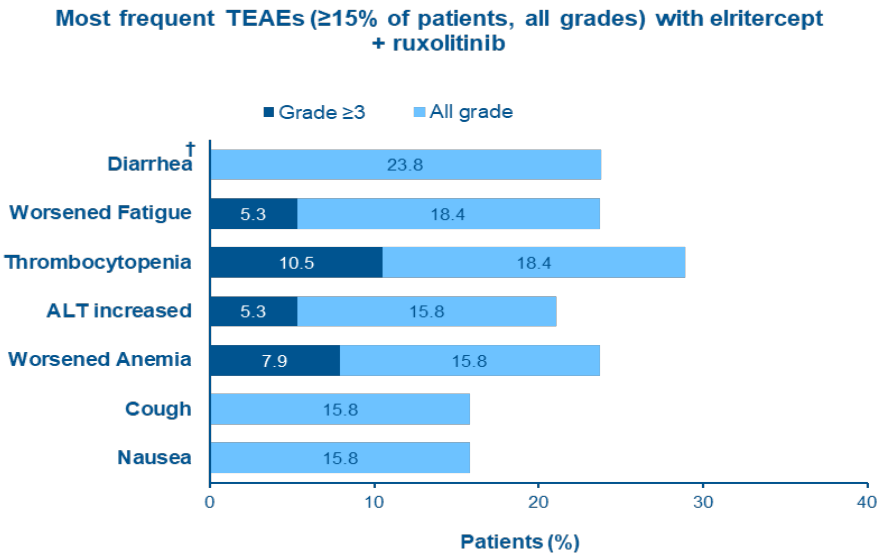
- Median age 71 yrs
- Median prior ruxo: 44 wks
- Median Hb: 8.3 g/dl, TD: 60.5%
- Notable spleen despite RUX: Median Spleen Volume 950 cc

At the time of data cut-off:
- 28 of 38 patients (73.7%) ongoing
- Median duration 47.4 weeks

*Patients continued to take their pre-study dose of ruxolitinib; dose increases were not permitted during the first 12 weeks after C1D1.
ET, essential thrombocytosis; Hgb, hemoglobin; MPN-SAF TSS, Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score; PROMIS SF, Patient-Reported Outcomes Measurement Information System short form; PV, polycythemia vera; Q4W, every 4 weeks; RBC, red blood cell; RP2D, recommended phase 2 dose; VAF, variant allele frequency.

Safety overview

n (%)	Elritercept + ruxolitinib (N=38)
Elritercept exposure in months, median (range)	10.9 (1.2–20.6)
Doses of elritercept received, median (range)	11.0 (1.0–22.0)
Patients with elritercept up-titration, n (%)	21 (55.3)
Any TEAEs, n (%)	38 (100)
Grade ≥3	23 (60.5)
TESAEs, n (%)	13 (34.2)
TEAEs leading to, n (%)	
Elritercept dose reduction	1 (2.6)
Elritercept dose interruption	7 (18.4)
Elritercept discontinuation	2 (5.3)
Ruxolitinib dose reduction	7 (18.4)
Ruxolitinib dose interruption	1 (2.6)
Ruxolitinib discontinuation	1 (2.6)
On-study death,* n (%)	1 (2.6)



Elritercept was well-tolerated when given with ruxolitinib, with no grade ≥3 diarrhea and low rates of grade ≥3 TEAEs

Speaker's personal summary

Efficacy overview

Global Phase 3 study planned in 2026

Key baseline characteristics: Patients had severe anemia; ≥60% were TD; notable splenomegaly

Median treatment duration was 47.4 weeks. Study treatment was ongoing in 28 of 38 patients (73.7%)

At the 36 weeks assessment:

- 43.5% of patients achieved RBC-TI ≥12 weeks
- 39.1% of patients achieved long responses with RBC-TI ≥16 weeks
- 65.2% of patients achieved at least a 50% reduction in RBC transfusion

Among TD and NTD patients:

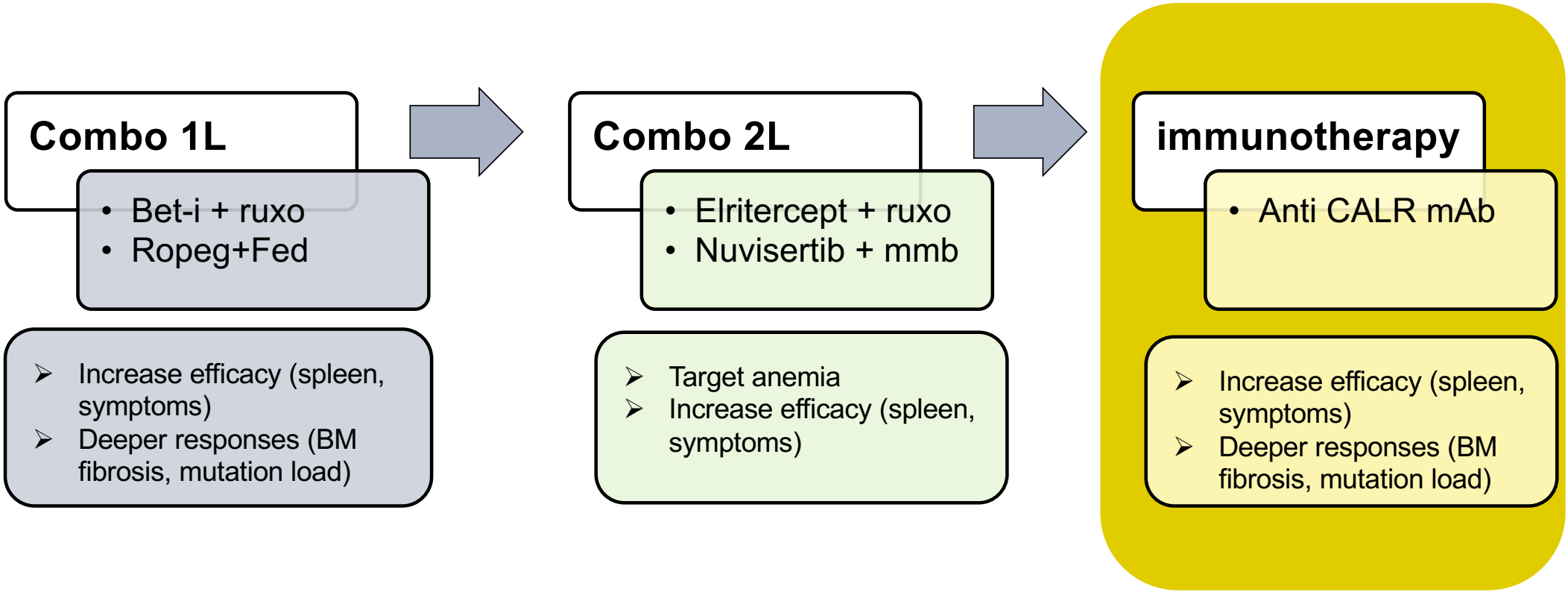
- 70.4% (19/27 evaluable) achieved a reduction in TSS by Week 24, including 18.5% who achieved ≥50% reduction
- 18.8% of pts (6/32 evaluable) experienced ≥5-points improvement in PROMIS Fatigue T score by Week 24

Throughout the study, 5 in 24 patients (20.8%) achieved a maximum SVR of ≥25%; 2 in 24 (8.3%) had a SVR ≥35%.

These findings support elritercept as a differentiated therapy in the treatment of patients with anemia and MF, whether it due to underlying disease, treatment with JAK inhibitors, or both, and warrant further clinical development

Speaker's personal summary

ASH 2025 in Myelofibrosis
Addressing the Limitations of JAK2 Inhibitors



Safety and Efficacy of the Mutant Calreticulin–Specific Monoclonal Antibody INCA033989 as Monotherapy or in Combination With Ruxolitinib in Patients With Myelofibrosis: Preliminary Results From Dose Escalation of Two Global Phase 1 Studies

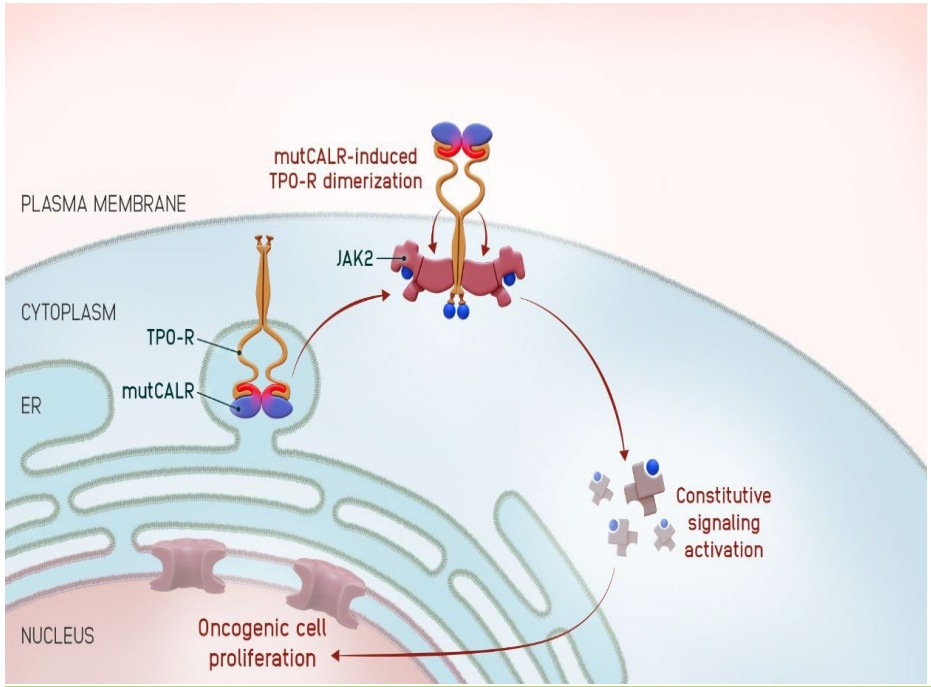
John Mascarenhas,[1] Haifa Kathrin Al-Ali,[2] Vikas Gupta,[3] Haris Ali,[4] Francesca Palandri,[5] Francesco Passamonti,[6] Raajit Rampal,[7] Aaron Gerds,[8] Tania Jain,[9] Sanjay Mohan,[10] Steffen Koschmieder,[11] Caroline McNamara,[12] Andrew Perkins,[13] Bethan Psaila,[14] Vincent Ribrag,[15] William Shomali,[16] Rosa Ayala Diaz,[17] Mikkel Helleberg Dorff,[18] Claire Harrison,[19] Stephen Oh,[20] Frank Stegelmann,[21] Alessandro Maria Vannucchi,[22] Abdulraheem Yacoub,[23] Jason Gotlib,[16] Jyoti Nangalia,[24] Chenwei Tian,[25] Betty Lamothe,[25] Erin Crowgey,[25] Tatiana Zinger,[25] Evan Braunstein,[25] David M. Ross[26]

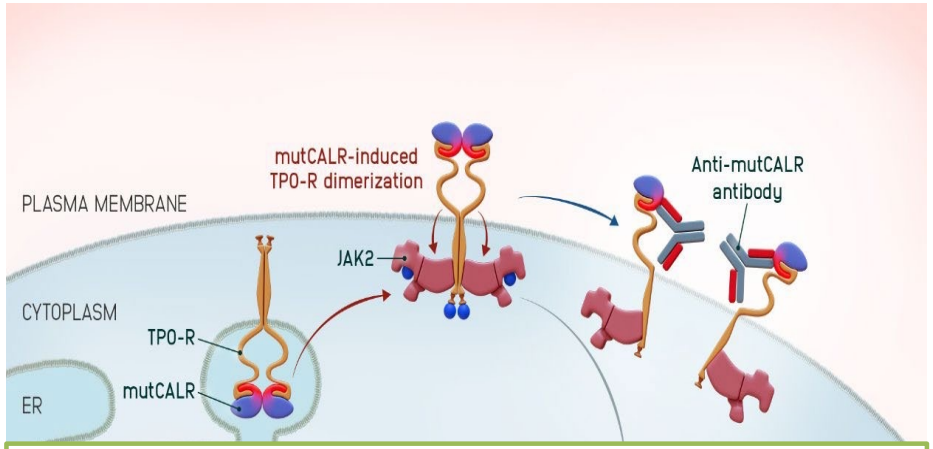
[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]University Medicine Halle, Saale, Germany; [3]Princess Margaret Cancer Centre, Toronto, ON, Canada; [4]City of Hope Medical Center, Duarte, CA, USA; [5]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [6]Fondazione IRCCS Ca Ganda Ospedale Maggiore, Milan, Italy; [7]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [8]Cleveland Clinic, Cleveland, OH, USA; [9]Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD, USA; [10]Vanderbilt University Medical Center, Nashville, TN, USA; [11]Faculty of Medicine, RWTH Aachen University, and Center for Integrated Oncology (CIO-ABCD), Aachen, Germany; [12]Royal Brisbane and Women's Hospital, Brisbane, Australia; [13]The Alfred Hospital, Melbourne, Australia; [14]University of Oxford, Oxford, UK; [15]Institut Gustave Roussy, Villejuif, France; [16]Stanford Cancer Institute/Stanford University School of Medicine, Stanford, CA, USA; [17]12 de Octubre University Hospital, Madrid, Spain; [18]University of Copenhagen, Copenhagen, Denmark; [19]Guy's and St Thomas' NHS Foundation Trust, London, UK; [20]Washington University School of Medicine, St. Louis, MO, USA; [21]Universitätsklinikum Ulm, Ulm, Germany; [22]Azienda Ospedaliero-Universitaria Careggi, Florence, Italy; [23]The University of Kansas Cancer Center, Kansas City, KS, USA; [24]The Sanger Institute, Cambridge, UK; [25]Incyte Corporation, Wilmington, DE, USA; [26]Royal Adelaide Hospital, Adelaide, Australia

Presented at the 67th ASH Annual Meeting & Exposition • Orlando, FL, USA • December 6-9, 2025

INCA033989 Is a mutCALR-Targeted Therapy for Patients With MF and Essential Thrombocythemia (ET)

- INCA033989 has a unique mechanism of action compared with other available therapies
  - INCA033989 is a novel, fully human, high-affinity, Fc-silenced, immunoglobulin G1 monoclonal antibody that selectively targets mutCALR in complex with thrombopoietin receptor to inhibit oncogenic signaling and proliferation of cells[1]





1. Spleen volume ≥450 mL or palpable spleen ≥5 cm
2. Monotherapy (n.52)
- Intolerant, resistant, or ineligible for JAKi treatment
3. Combination therapy (n. 20)
- Prior RUX for ≥12 weeks & suboptimal response

INCA033989 was administered intravenously every 2 weeks (24-2500 mg)

1. Reis, et al. *Blood.* 2024;22:2336-2348.

ER, endoplasmic reticulum; JAK2, Janus kinase 2; MF, myelofibrosis; mutCALR, mutations of calreticulin; TPO-R, thrombopoietin receptor (myeloproliferative leukemia protein).

INCA033989 in MF Safety Overview

MONOTHERAPY (n. 52)

- No dose-limiting toxicities were observed; the maximum tolerated dose was not reached (dose range 24-2500 mg)
- Twelve patients experienced **increased AST and/or ALT**: 9 (75.0%) grade 1 and 2 (16.7%) grade 2; Increased AST and/or ALT resolved in 10/12 patients

	N=52			
TEAE, n (%)	Any Grade	Grade 1	Grade 2	Grade ≥3§
Anemia	16 (30.8)	7 (13.5)	5 (9.6)	4 (7.7)
Fatigue	14 (26.9)	9 (17.3)	5 (9.6)	0
Thrombocytopenia	13 (25.0)	7 (13.5)	2 (3.8)	4 (7.7)¶
Arthralgia	11 (21.2)	6 (11.5)	5 (9.6)	0
AST increased	11 (21.2)	8 (15.4)	2 (3.8)	1 (1.9)
Cough	11 (21.2)	9 (17.3)	2 (3.8)	0
Diarrhea	11 (21.2)	10 (19.2)	1 (1.9)	0
Headache	11 (21.2)	7 (13.5)	4 (7.7)	0
Leukopenia	11 (21.2)	1 (1.9)	6 (11.5)	4 (7.7)¶
Nausea	11 (21.2)	9 (17.3)	2 (3.8)	0
Pruritus	11 (21.2)	10 (19.2)	1 (1.9)	0
Hyperglycemia	10 (19.2)	6 (11.5)	3 (5.8)	1 (1.9)
Neutropenia	10 (19.2)	0	5 (9.6)	5 (9.6)¶
Nasal congestion	8 (15.4)	6 (11.5)	2 (3.8)	0
Pain in extremity	8 (15.4)	7 (13.5)	1 (1.9)	0

COMBO THERAPY (n.20)

- No dose-limiting toxicities were observed; the maximum tolerated dose was not reached (dose range 70-2500 mg)
- Four patients experienced **increased AST and/or ALT**; all events were grade 1/2, and they were resolved in 2 pts
- Grade ≥3 TEAEs include anemia (30.0%), neutropenia (10.0%), thrombocytopenia (10.0%), abscess limb (5.0%), AMI (5.0%), DLBCL (5.0%), OSAS (5.0%), and stomatitis (5.0%)

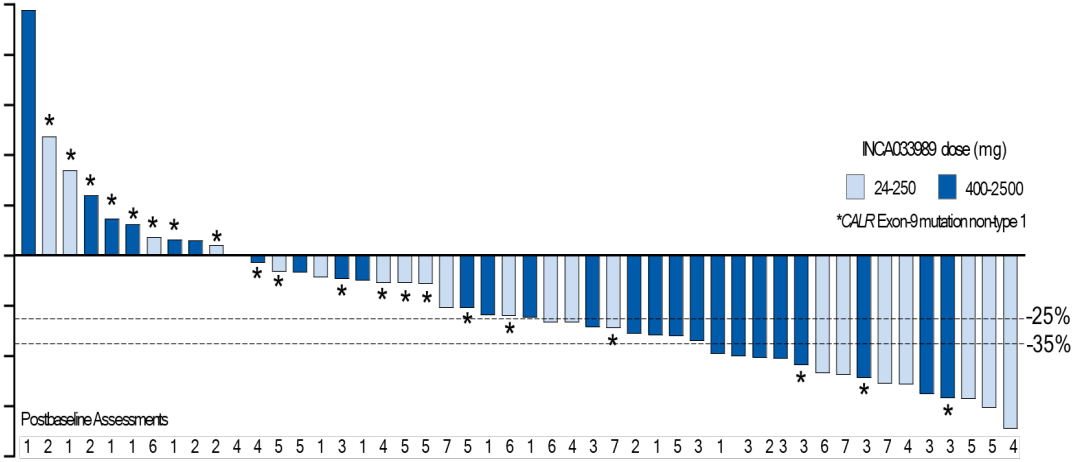
Speaker's personal summary

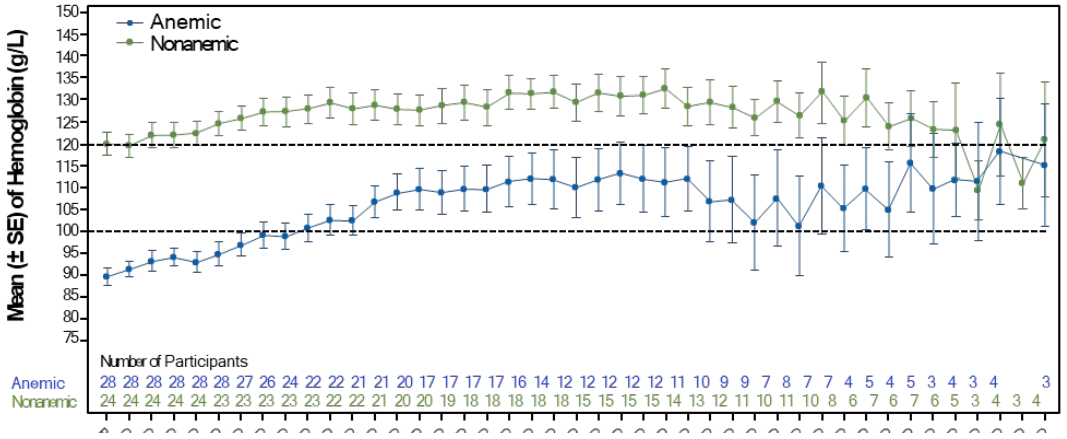
INCA033989 Monotherapy Efficacy overview

- Median (range) duration of exposure was 46.2 (4.6, 104.6) weeks
- As best SVR, **23 (47.9%) patients had SVR25**, and 15 (31.3%) patients achieved SVR35
- Type 1 CALR mutations more likely to respond on spleen

- 42/45 (93.3%) patients experienced improved symptoms, with **27 (60.0%) achieving TSS50**

- At baseline, median (range) hemoglobin among patients with anemia was 92 (70, 108) g/L
- **Anemia response occurred in 14/25 (56%)** of evaluable‡ anemic patients; most patients achieved a major response





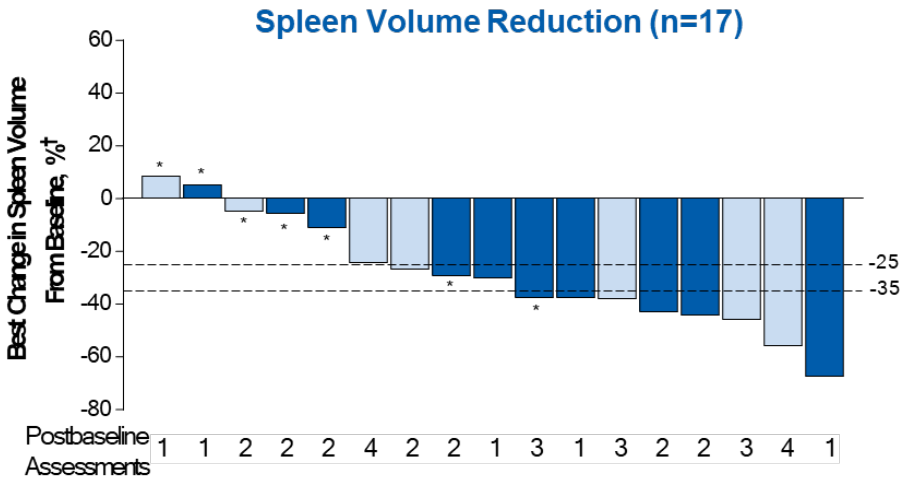
Speaker's personal summary

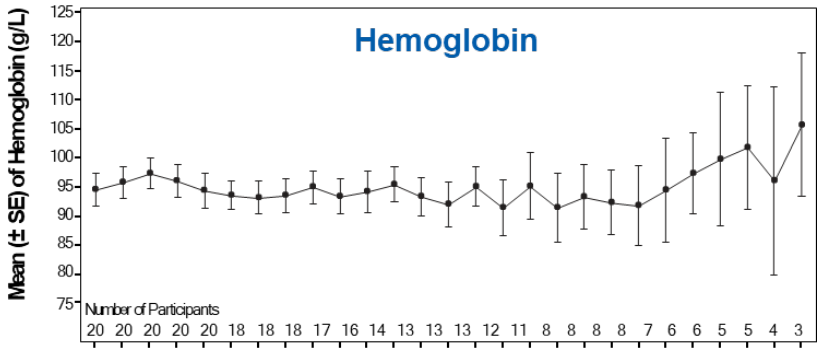
INCA033989 Combo-therapy Efficacy overview

- As best SVR, 11/20 patients achieved SVR25, and 8 patients achieved SVR35
- Among evaluable patients at week 24 (n=12), 6 (50%) had SVR25 and 3 (25%) had SVR35

- 13/16 (81.3%) patients experienced symptom improvements; 2/8 (25%) patients achieved TSS50 at week 24

- Among 14 evaluable patients, 86% had stable anemia during the study (TDA, n=1; non-TDA, n=11); 1 patient (non-TDA) had a major anemia response

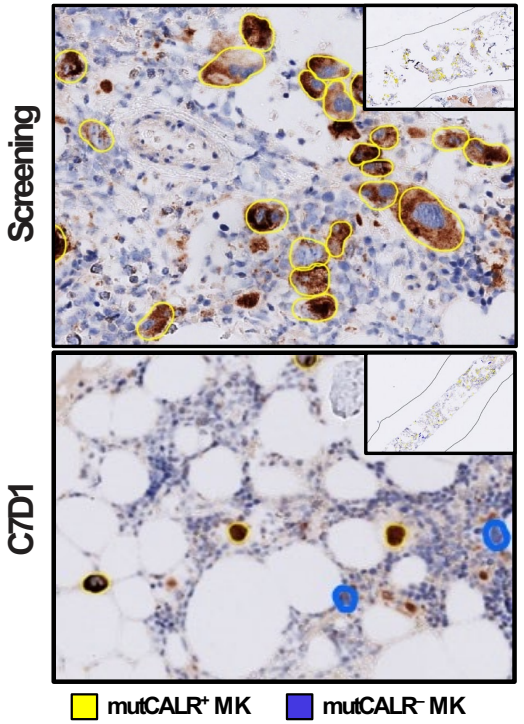




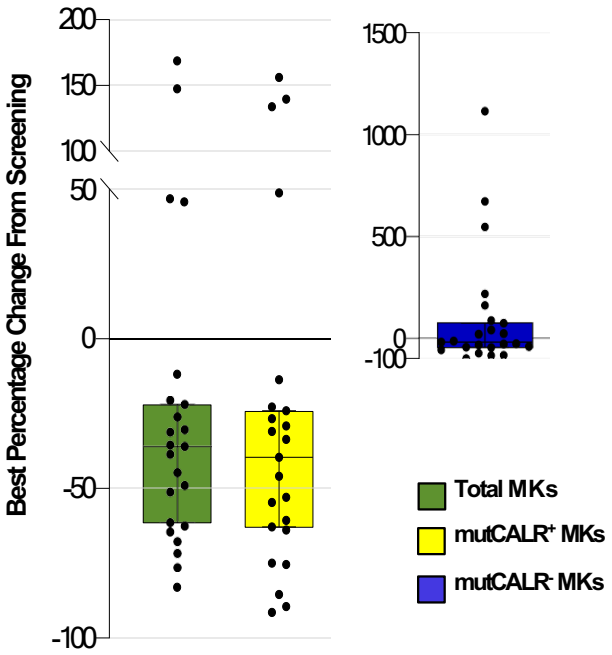
Speaker's personal summary

Improvement in Bone Marrow Pathology With INCA033989

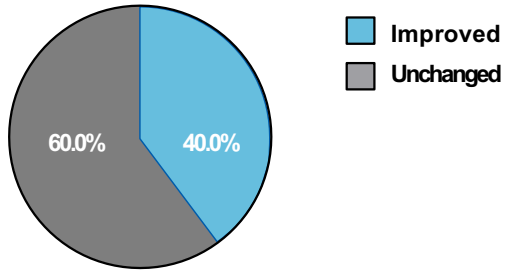
mutCALR IHC



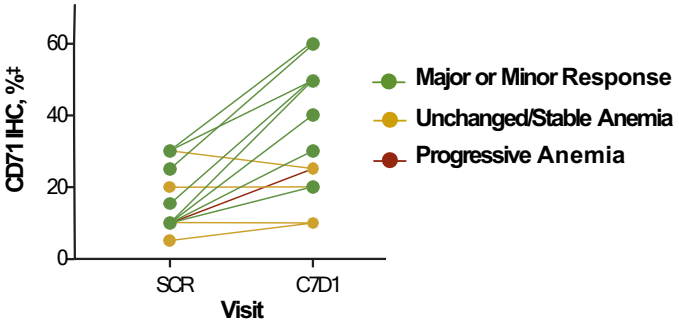
Patients With MF (n=23)*



Fibrosis Grade† (n=30)



Erythroid Progenitors (Anemic Patients, n=14)



- Reduction of mutCALR⁺ MK and increase of wild-type (mutCALR⁻)
- Reduction of BMF
- Increase in progenitor cells

WHAT ARE THE LIMITATIONS OF JAK2 inhibitors IN MF?

1

Cytopenias

Reversal of anemia improves QoL and may increase survival
Increasing PLT count may enable medical therapy

2

Suboptimal response in many patients

Complete resolution of splenomegaly and symptoms in a minority of patients

3

High rate of therapy discontinuations

50-70% rate of JAK2 inhibitors discontinuation at 3-5 yrs

4

Disease persistence

There is no clear evidence of a disease-modifying activity or cure
One-third of evaluable JAK2V617F-positive patients had a >20% reduction in allele burden or regression of BM fibrosis

5

Progression to accelerated/blast phase

The rate of disease progression is not improved by JAK2 inhibitrs
Therapy of advanced phase remains unsatisfactory

FED, fedratinib; JAK2, Janus kinase 2; MF, myelofibrosis, NMSC, non-melanoma skin cancer; PLT, platelet; QoL, quality of life; RUX, ruxolitinib.

1. Harrison C, et al. N Engl J Med. 2012;366:787-798: 2. Mesa R, et al. J Clin Oncol. 2017;35:3844-3850; 3. Verstovsek S, et al. N Engl J Med. 2012;366;799-807; 4. Pardanani A, et al. JAMA Oncol. 2015;1:643–651; 5. Food and Drug Administration. JAKAFI Package Insert. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/202192lbl.pdf; 6. Food and Drug Administration. INREBIC Package Insert. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212327s000lbl.pdf; 7. Food and Drug Administration. VONJO Package Insert. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208712s000lbl.pdf; 8. Tremblay D, et al. Cells. 2021;10(5):1034; 9. Palandri F, et al. Cancer. 2023;129(11):1704-1713; 10. Barbui T, et al. Leukemia. 2019;33:1996-2005; 11. Polverelli N, et al. Br J Haematol. 2021;193:356-368; 12. Polverelli N, et al. Am J Hematol. 2017;92(1)37-41; 13. Polverelli N, et al. Hematol Oncol. 2018;36(3):561-569; 14. Elli EM, et al. Front Oncol. 2019;9:1186; 15. Palandri F, et al. Cancer 2022;128(13):2449-2454; 16. Palandri F, et al. Cancer. 2022;128(13):2449-2454; 17. Tremblay D, Mesa R. Future Oncol. 2022;18(20):2559-2571.

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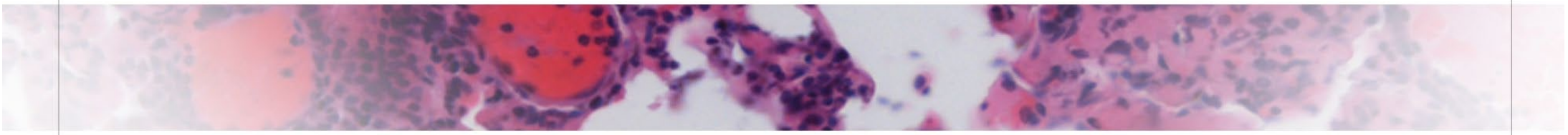


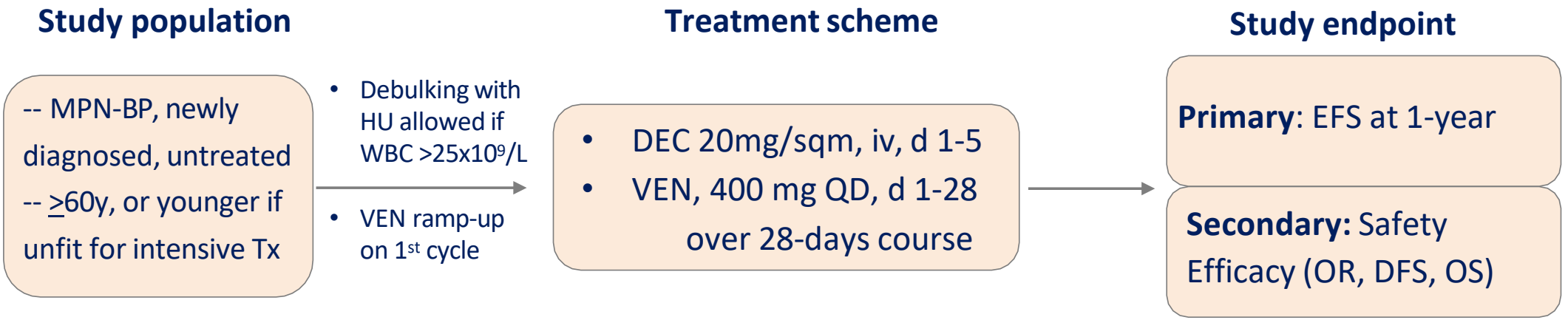
Venetoclax and Decitabine in Myeloproliferative Neoplasm Blast Phase (MPN-BP): Results of ENABLE, a *GIMEMA* and *AIRC-MYNERVA* Multicenter, Phase 2 trial

Alessandro M. Vannucchi, F Mannelli, F Crupi, J Caroprese, M Lomi, A Enderti, S Soddu , A Piciocchi , A Rambaldi, G Caocci , M Bocchia, E Audisio, A Curti, F Pane, E Borlenghi , M Breccia, N Bartalucci, M Frigeni, O Mulas, C Zuanelli Brambilla, C Frairia, C Papayannidis , F Grimaldi, L Masina, M Rondi , M Sanna, P Musto, P Salutari, P Chiusolo, E Coviello, M Luppi, D Cilloni, L Signori, L Malcovati, MP Martelli, MG Della Porta, R Manfredini, MT Voso, P Fazi, M Vignetti, P Guglielmelli

for the ENABLE trialists

ENABLE is an Academic, Multicenter, Phase II Study

- ENABLE investigated the safety and efficacy of venetoclax (VEN) + decitabine (DEC) therapy in patients with MPN-BP who are unfit for intensive chemotherapy



- **Hypothesis and sample size:** to show improvement of EFS at 1-year from 15% in historical controls to 25% with VEN-DEC, a total of 101 pts are required
- **EFS=** time between treatment start and either primary refractory disease (no OR after 2 courses of VEN-DEC), first relapse after achieving CR or death (whichever the cause)

EFS, Event free survival. OR, overall response (CR,CRi,MLFS). DFS, disease free survival. OS, overall survival. HU, hydroxyurea.

ENABLE Efficacy Overview

- A total of 101 patients, 72 patients (66%) were categorized as HMR
- **Overall Response: 46% C1 (CR 21%), 44% in C2 (CR 21%)**
- EFS and OS rate of 32% and 48% were recorded at 12 months
- ***The study met the primary endpoint of improving EFS at 1-year from 15% in historical controls to 25% in patients treated with VEN-DEC in ENABLE study***
- Longer EFS and OS after VEN/DEC were predicted by early achievement of response at cycle 1 and **absence of *SRSF2, U2AF1* and *TP53* mutations**
- ***There was no unexpected safety signal***. Hematologic AEs were frequent and manageable with dose intensity reduction.

VEN/DEC may represent a first-choice treatment of MPN-BP, with results comparable to those reported in the elderly/unfit patients with de-novo AML

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Thanks for your attention!

Prof. Pier Luigi Zinzani