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

Novità dal Meeting della Società Americana di Ematologia

Torino
Centro Congressi Lingotto
19-21 febbraio 2026

Policitemia Vera e Trombocitemia Essenziale

Paola Guglielmelli
CRIMM- Center of Research and Innovation of MPN
Hematology Department, University of Florence & Azienda Ospedaliera Universitaria Careggi

DICHIARAZIONE NOME COGNOME

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Novartis					x	x	
GSK					x	x	
AOP					x	x	
Incyte						x	
Takeda						x	
Thermofisher						x	

Agenda

Polycythemia Vera

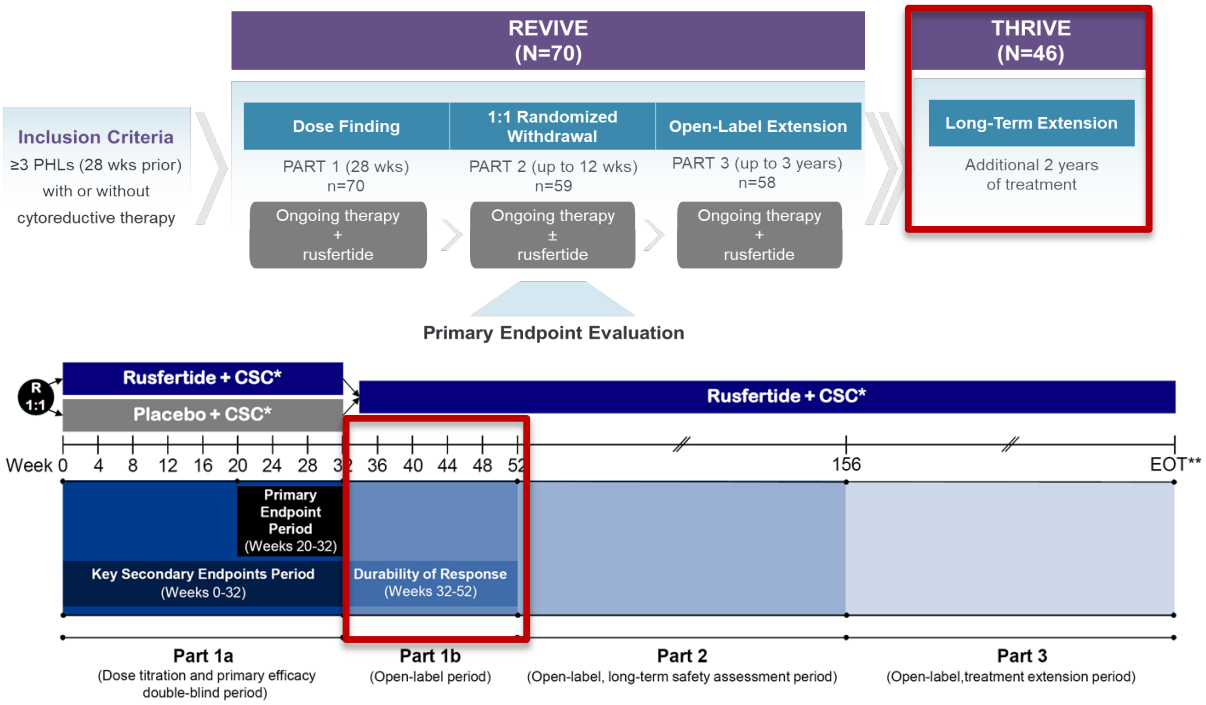
- Up-date on:
  - **Rusfertide** (Verify study and Thrive studies)
  - **Sapablursen** (IMPRESSION Study)
  - **Bomedestat** (Shorespan-004 Study)

Essential Thrombocythemia

- Up-date on:
  - **Ropeg-IFN** (ROP-ET Study)
  - **INCA033989** (INCA033989-101 and INCA033989-102 studies)
  - **Bomedestat** (Shorespan-017 study)

POLYCYTHEMIA VERA

Rusfertide



THRIVE Study

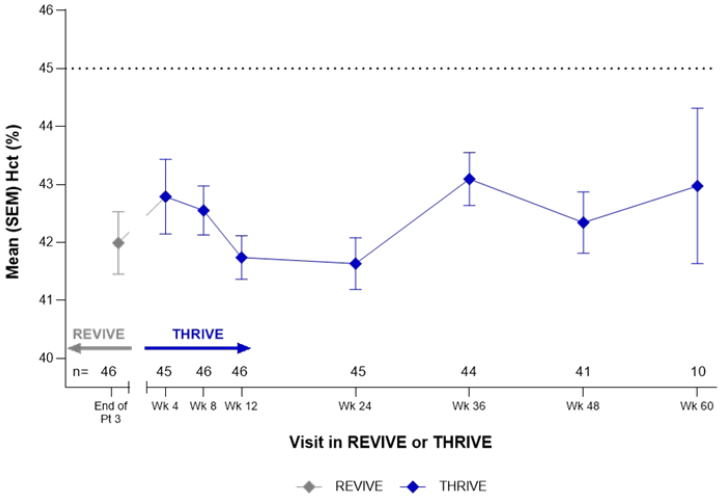
An open-label long-term extension study evaluating PV patients who participated in Phase 2 - REVIVE

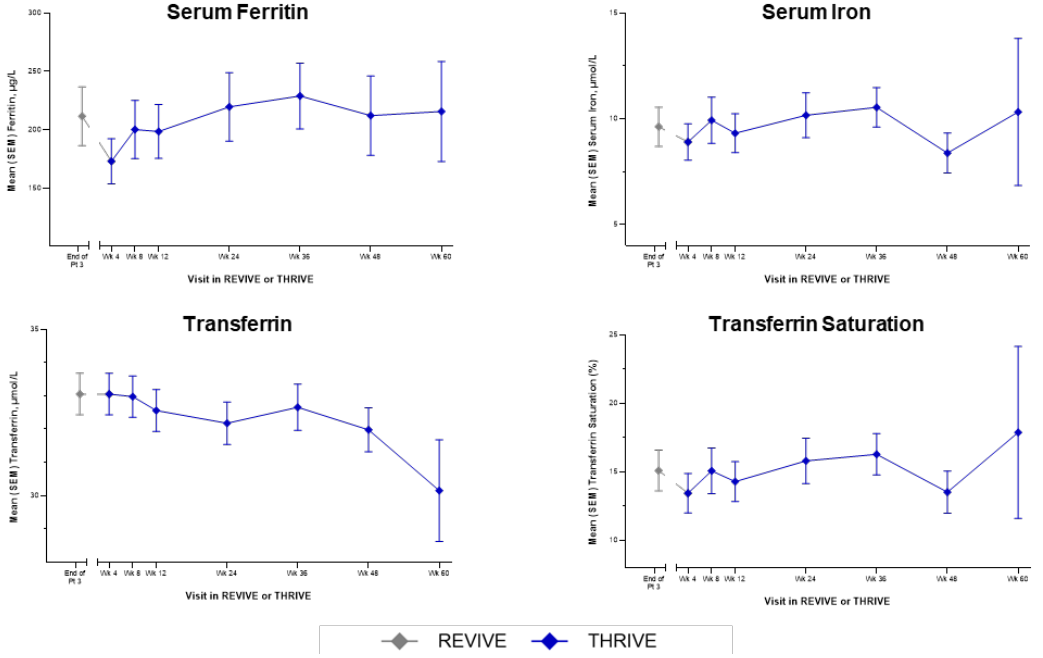
VERIFY Study

A phase 3, double-blind, placebo -controlled study of rusfertide for treatment of PV

Kuykendall AT et al. Blood (2025) 146 (Supplement 1): 81.; Pemmaraju N et al. Blood (2025) 146 (Supplement 1): 3810.

THRIVE Study: Long-Term Use of Rusfertide Led to Sustained Hct <45% and Improved Markers of Iron Deficiency

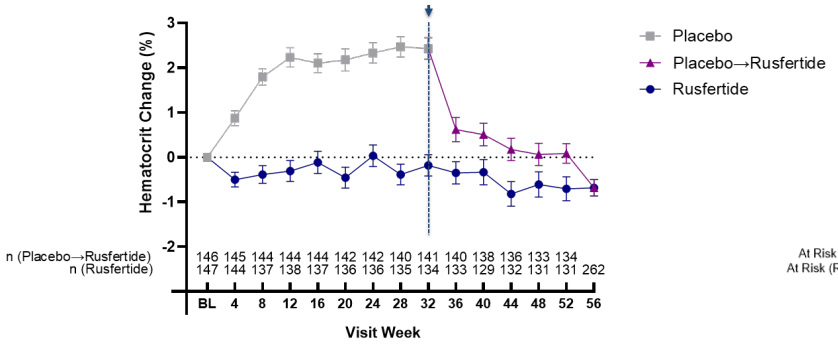


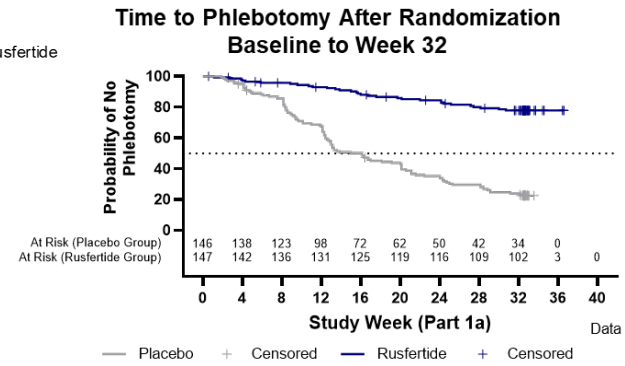


Pemmaraju N et al. Blood (2025) 146 (Supplement 1): 3810

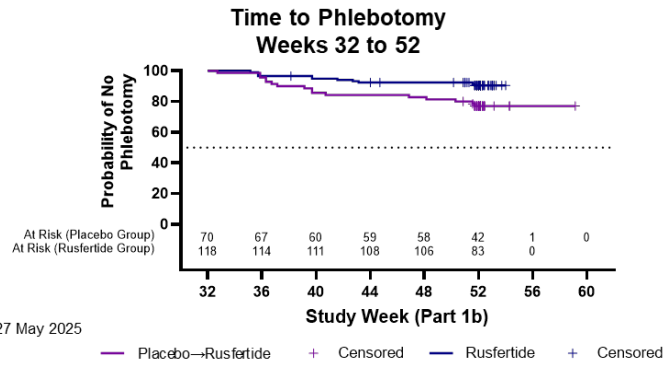
VERIFY Study: Rusfertide Provided Durable Control of Hct and Rapid Responses in Patients Who Switched From Placebo to Rusfertide

- In Rusfertide arm: Response rate increased with rusfertide from 77% at Weeks 20-32 to 84% at Weeks 40-52
- In Placebo Arm → Rusfertide : Response rate increased from 33% (Weeks 20–32) to 78% (Weeks 40–52)



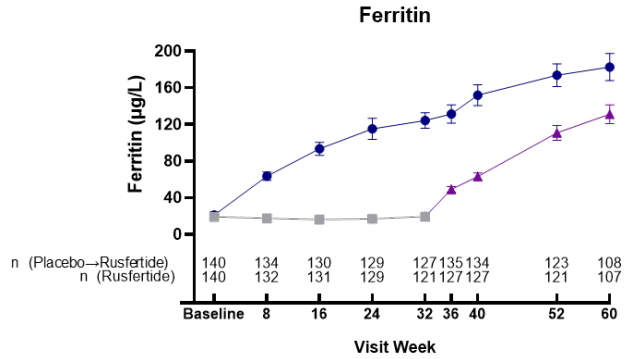


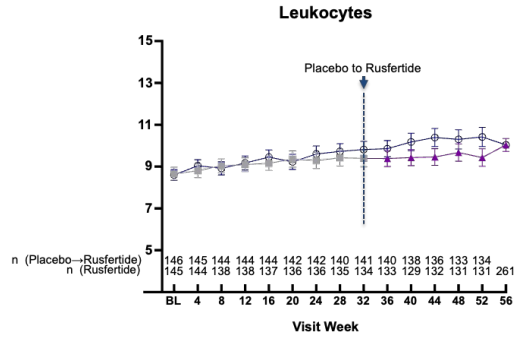
Data cutoff: 27 May 2025

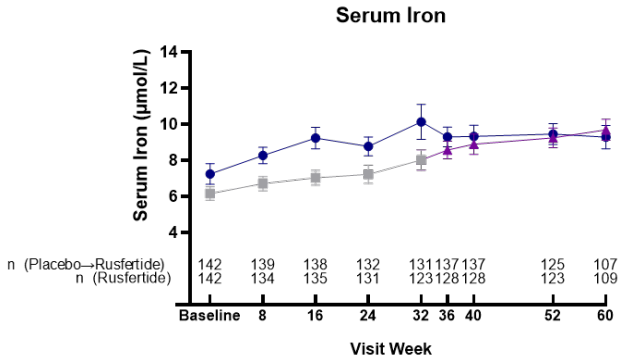


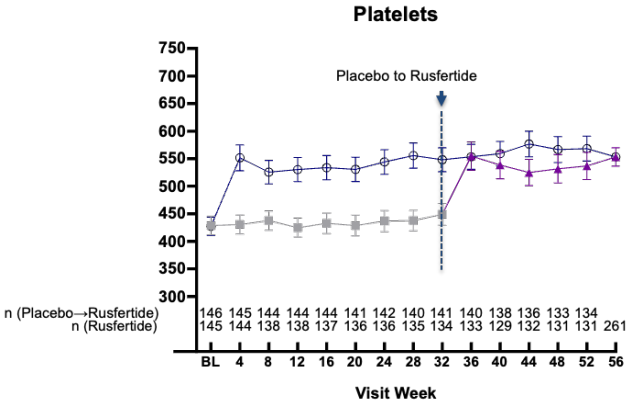
Kuykendall AT et al. Blood (2025) 146 (Supplement 1): 81.

VERIFY Study: Placebo-to-Rusfertide Switch Rapidly Normalized Iron Parameters with Modest Increases of WBC and PLT





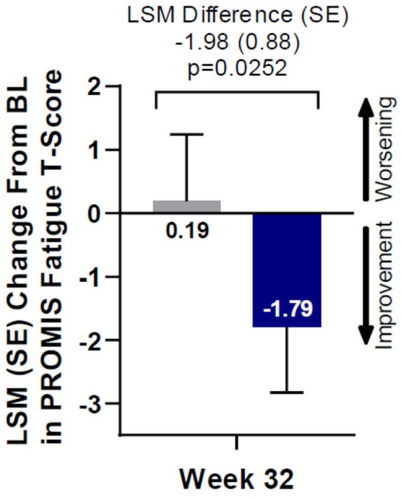


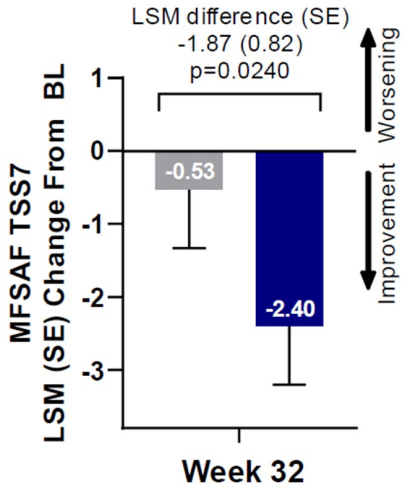


Kuykendall AT et al. Blood (2025) 146 (Supplement 1): 81.

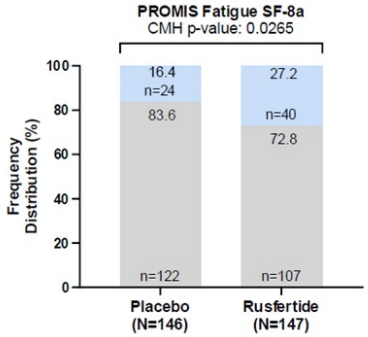
VERIFY Study: Rusfertide Significantly Reduced Fatigue and Overall Symptom Burden vs Placebo

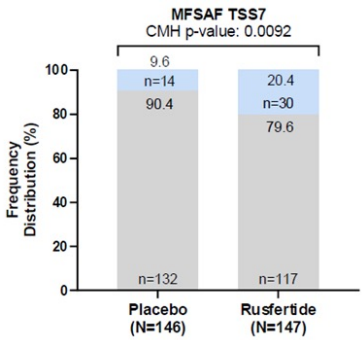
LSM level change from baseline

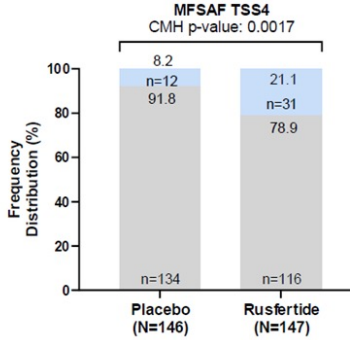




Proportions of patients reporting a meaningful within-person change Fatigue







Bankar A et al. Blood (2025) 146 (Supplement 1): 5588.

Rusfertide Continues to Demonstrate a Favorable Safety Profile

- Low rates of treatment discontinuation: 2.6% in Part 1b of VERIFY study and 2.2% in THRIVE study.
- Serious AEs occurred in 2.6% (VERIFY Part 1b study) and 17.4% (THRIVE study)

	Part 1a Baseline to Week 32		Part 1b Weeks 32-52	
Most Frequent TEAEs (≥10% in either group), n (%)	**PBO Group (n=146)**	**RUS Group (n=145)**	**PBO to RUS (n=140)**	**RUS to RUS (n=134)**
Patients with at least 1 TEAE	126 (86.3)	131 (90.3)	107 (76.4)	101 (75.4)
Injection site reactions[a]	48 (32.9)	81 (55.9)	46 (32.9)	13 (9.7)
Fatigue	23 (15.8)	23 (15.9)	13 (9.3)	12 (9.0)
Anemia	6 (4.1)	22 (15.2)	14 (10.0)	15 (11.2)
Headache	18 (12.3)	16 (11.0)	4 (2.9)	5 (3.7)
COVID-19	16 (11.0)	14 (9.7)	3 (2.1)	4 (3.0)
Pruritus	15 (10.3)	15 (10.3)	3 (2.1)	5 (3.7)
Patients with ≥1 cancer event, n (%)	8 (5.5)	3 (2.1)	2 (1.4)	4 (3.0)

Low incidence of TEs during rusfertide treatment:
- 1 patient each in Parts 1a and 1b in VERIFY study
- no new-onset TEs during THRIVE study

During THRIVE, 6 patients (13%) had a new-onset cancer event
5 (83%) had a prior history of non-PV cancer

Kuykendall AT et al. Blood (2025) 146 (Supplement 1): 81.; Pemmaraju N et al. Blood (2025) 146 (Supplement 1): 3810.

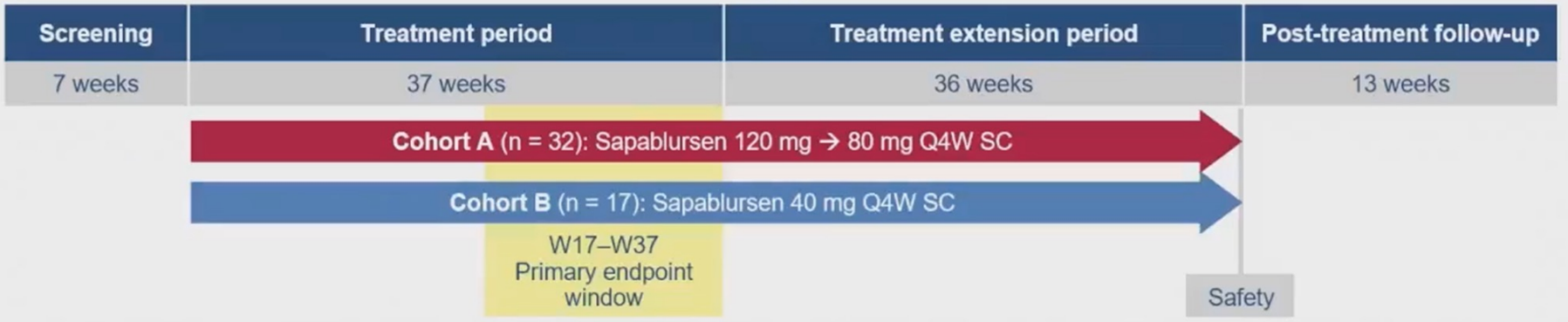
IMPRESSION Study: Phase IIa Randomized, Open-Label Trial of Sapablursen in Patients with Phlebotomy-Dependent PV

Key inclusion criteria[1]

- Clinical diagnosis of PV consistent with the WHO 2016 diagnostic criteria (*JAK2* mutation required)[2]
- Phlebotomy dependent (≥3 in the prior 6 months and 1 in the last 12 weeks prior to randomization)
- No eligibility restrictions based on hematocrit level
- Current or previous cytoreductive therapy not needed; if current, stable dose for ≥3 months

Key endpoints

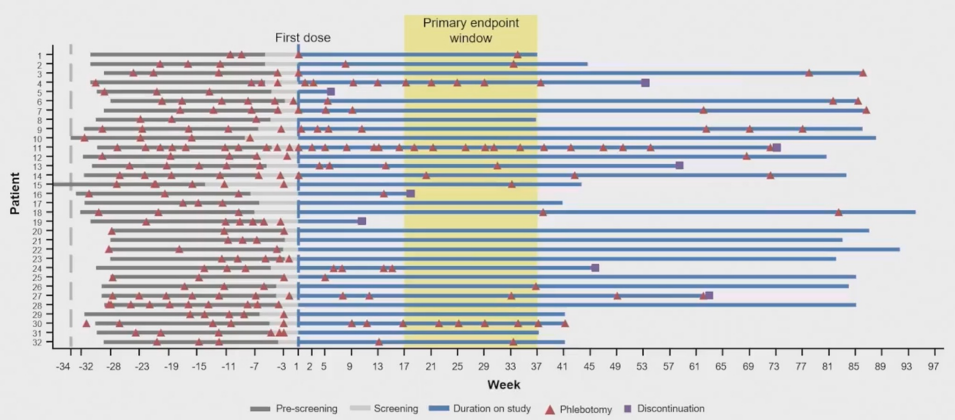
- Primary: Reduction in the weekly rate of phlebotomies
- Secondary: Change in mean MPN-SAF-TSS score
- Exploratory: Serum hepcidin and hematocrit control (<45%) without receiving phlebotomy (confirmation of hematocrit ≥45% was not required)
- Safety: Adverse events, vital signs, ECG, and clinical laboratory tests

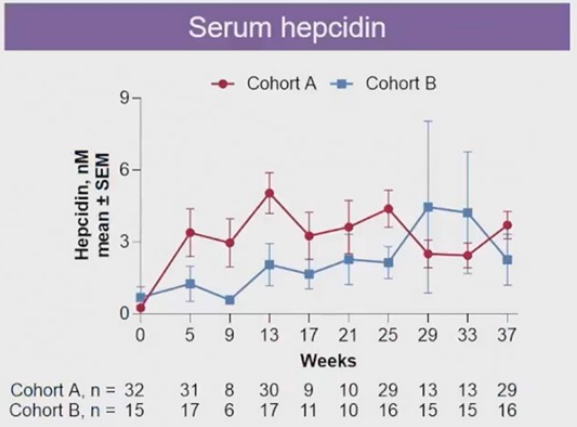


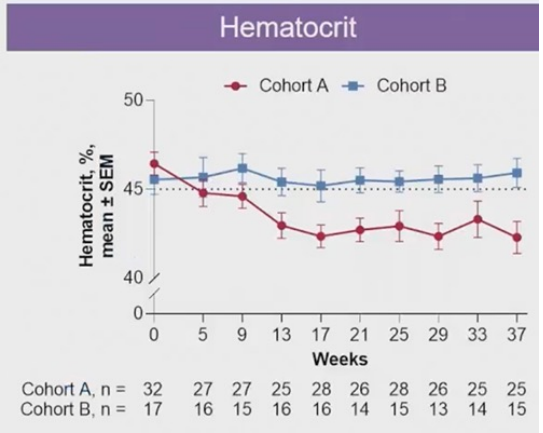
Palmer J. et al. Blood (2025) 146 (Supplement 1): 82.

Sapablursen Reduced the Phlebotomy Rate, Controlled Hematocrit and Reduced Serum Hepcidin level

- Enrolled N=49 (Cohort A n=32; Cohort B n=17); 40% low-risk;
- The median number of phlebotomies in the 6 months prior to the study was 5







- Sapablursen displayed a modest effect on WBC and PLT counts

Palmwer J. et al. Blood (2025) 146 (Supplement 1): 82.

Sapablursen Was Safe and Well Tolerated

n (%)	Cohort A (n = 32)	Cohort B (n = 17)	All Patients (N = 49)
TEAE	31 (97)	14 (82)	45 (92)
TEAE related to study drug	23 (72)	9 (53)	32 (65)
Serious TEAE	6 (19)	3 (18)	9 (18)
TEAEs leading to study drug discontinuation	2 (6)	2 (12)	4 (8)
TEAEs leading to death	1 (3)	0	1 (2)
TEAEs occurring in >10% of all patients			
Anemia	13 (41)	5 (29)	18 (37)
Fatigue	13 (41)	3 (18)	16 (33)
Diarrhea	7 (22)	3 (18)	10 (20)
Pruritus	7 (22)	3 (18)	10 (20)
Headache	9 (28)	1 (6)	10 (20)
Nausea	7 (22)	2 (12)	9 (18)
Dizziness	7 (22)	0	7 (14)
Arthralgia	5 (16)	2 (12)	7 (14)
Dyspnea	7 (22)	0	7 (14)
Constipation	4 (13)	3 (18)	7 (14)
Muscle spasms	4 (13)	2 (12)	6 (12)
COVID-19	4 (13)	1 (6)	5 (10)
AST increased	3 (9)	2 (12)	5 (10)
ALT increased	3 (9)	2 (12)	5 (10)

- The median dose of the Cohort A was reduced from 120 mg to 80 mg due to anemia
- 1 death due to AML transformation, which was deemed not related to Sapablursen

Palmwer J. et al. Blood (2025) 146 (Supplement 1): 82.

Safety and Efficacy of Bomedestat in PV Patients Resistant or Intolerant to Cytoreductive Therapy : Shorespan-004 Phase 2 Study

Starting dose 40mg/QD PO tritated to a Hct Target of <42%

52 weeks

After 52 weeks, eligible to an extensions study

20 Patients enrolled and treated with Bomedemstat

5 completed treatment
7 transitioned to extension study
8 discontinued :
- 4 Withdrawal by pts
- 2 Physisician decision
- 1 AE
- 1 Disease Progression

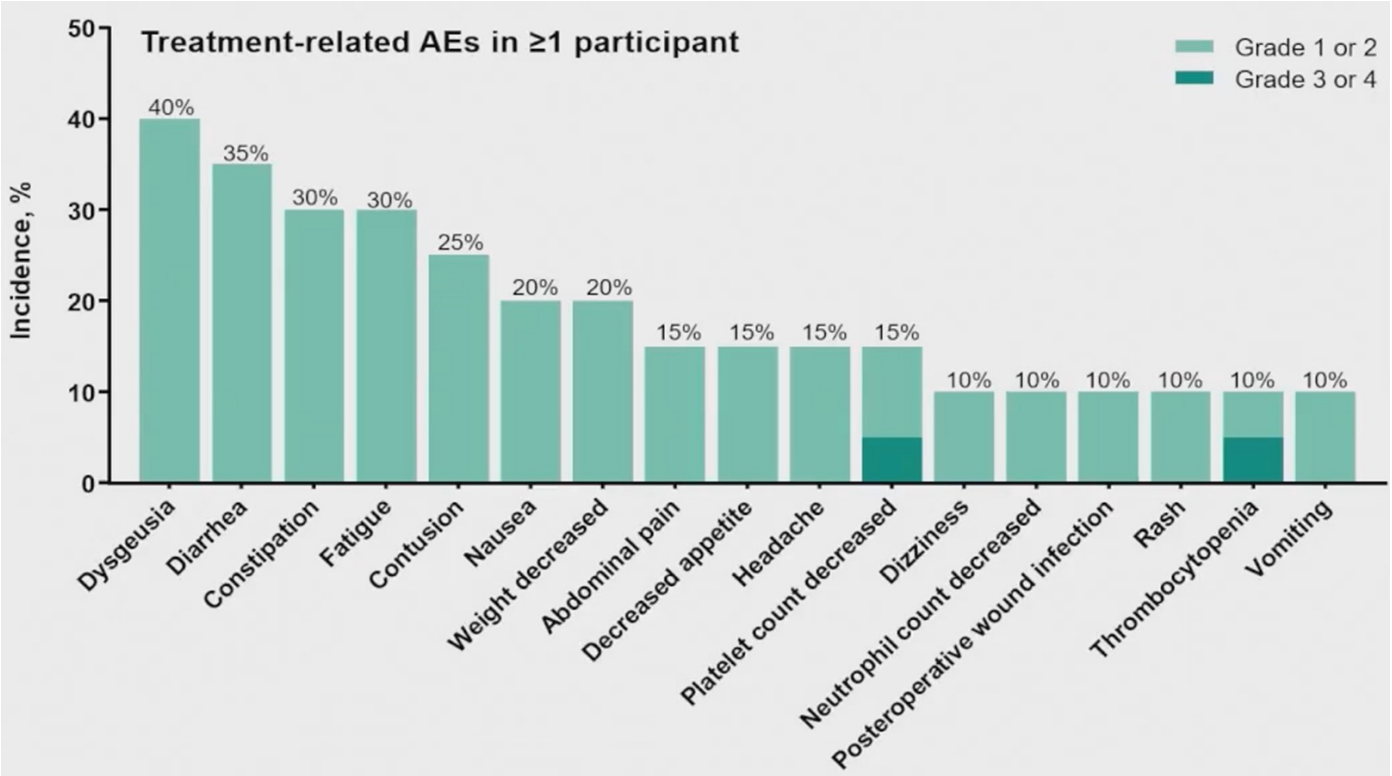
Primary End Points:
- Safety and tollerability up to week 52
- Hct reduction <45% by week 36 (≥12weeks without plhebotomy)

Secondary End Points:
- Durability of Hct reducion<45% w/o plebotomy
- Incience and durability of Hematological resposne
- Incidence of Thrombotic or hemorragic events
- Incidence of SVR
- Progression (PPV-MF, MDS, AML)

Exploratory:
- Symptoms burden (MSAF , PGIC)
- Change in Inflammatory cytokines and growth factors

Rein L. et al. Blood (2025) 146 (Supplement 1): 83.

Bomedemstat Had an Acceptable Tolerability Profile in PV

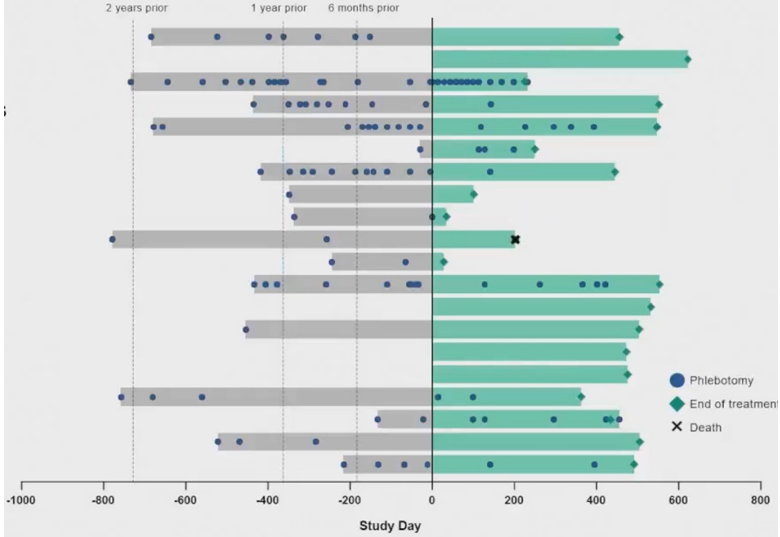


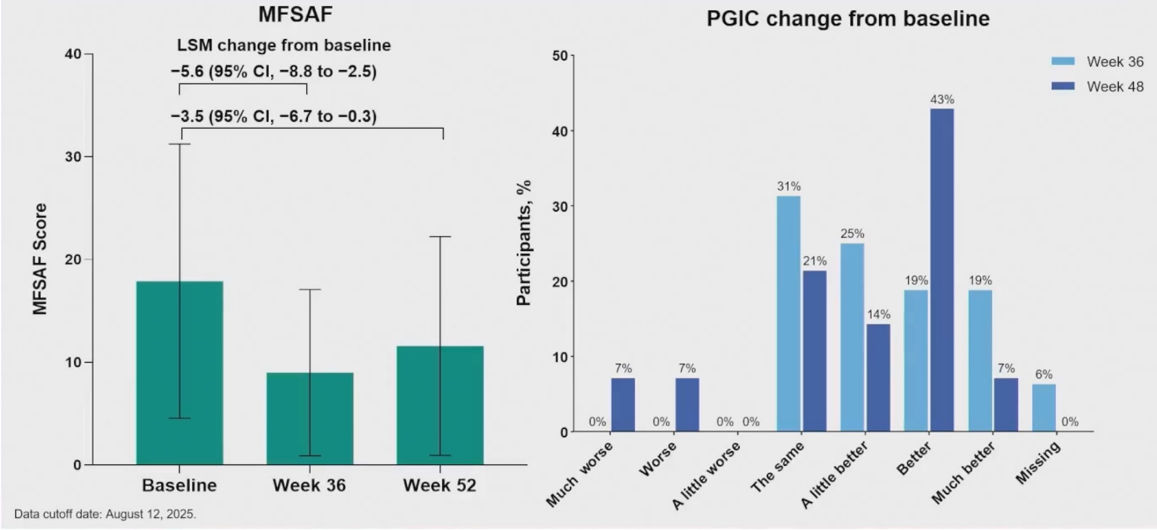
Rein L. et al. Blood (2025) 146 (Supplement 1): 83.

Bomedemstat Reduced Phlebotomy Rate, Improved Blood Cell Counts and Controls Symptoms

At W52, 50% reached Hct <45%, maintained >12 weeks without phlebotomy

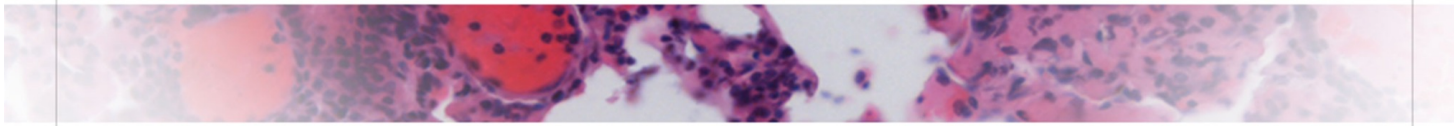
- 90% had hct reduction to <45% any time
- 90% had PLT response and 95% WBC response any time





Rein L. et al. Blood (2025) 146 (Supplement 1): 83.

ESSENTIAL TROMBOCYTHEMIA



Ropeginterferon alfa-2b in essential thrombocythemia of all risk levels ineligible for standard cytoreduction: 12-month primary endpoint analysis from the ROP-ET phase 3 study

Jean-Jacques Kiladjian, Haifa Kathrin Al-Ali, Jiri Mayer, Ciprian Tomuleasa, Francesca Palandri, Eloise Beggiato, Valentín García Gutiérrez, Andreas Reiter, Florian Heidel, Joanna Gora Tybor, Mihaela Lazaroiu, Alberto Alvarez-Larran, Konstanze Döhner, Massimo Breccia, Arpád Illés, Sebastian Grosicki, Chloe James, Francisca Ferrer Marin, Evangelos Terpos, Ana Crisan, Veronika Buxhofer-Ausch, Stefan Schmidt, Albert Woelfler, Zsolt Nagy, Steffen Koschmieder, Olga Cerna, Vassiliki Pappa, Tomasz Sacha, Stefanie Schlager, Victoria Empson, Martin Unger, Kurt Krejcy, Christoph Klade

Abstract number: abs25-2199
634A. Myeloproliferative Syndromes: Clinical and Epidemiological

Primary Endpoint:

Durable (≥3 months) hematologic and clinical response after 12 months based on modified ELN criteria:

- Peripheral blood count remission (platelets ≤400×109/L and leukocytes <10×109/L)
- Absence of thrombotic/hemorrhagic events and disease progression,
- Absence or non-progression in disease-related signs (splenomegaly)
- Symptom improvement measured by the MPN-Symptom Assessment Form Total Symptom Score

Kiladjian JJ. et al. Blood (2025) 146 (Supplement 1): 485.

Patient Characteristics and Risk Category

- 132 patients, the median age was 56.5 years and 58.3% were female, after a median time to diagnosis of 3.3 years
- Median PLT count was 579x10^9/L, 28% presenting with asymptomatic splenomegaly, and a median MPN-SAF TSS of 8.0
- 59.8% were *JAK2* mutated , 27.3% *CALR* mut, 11.4% *MPL* mut and 1.5% Triple neg

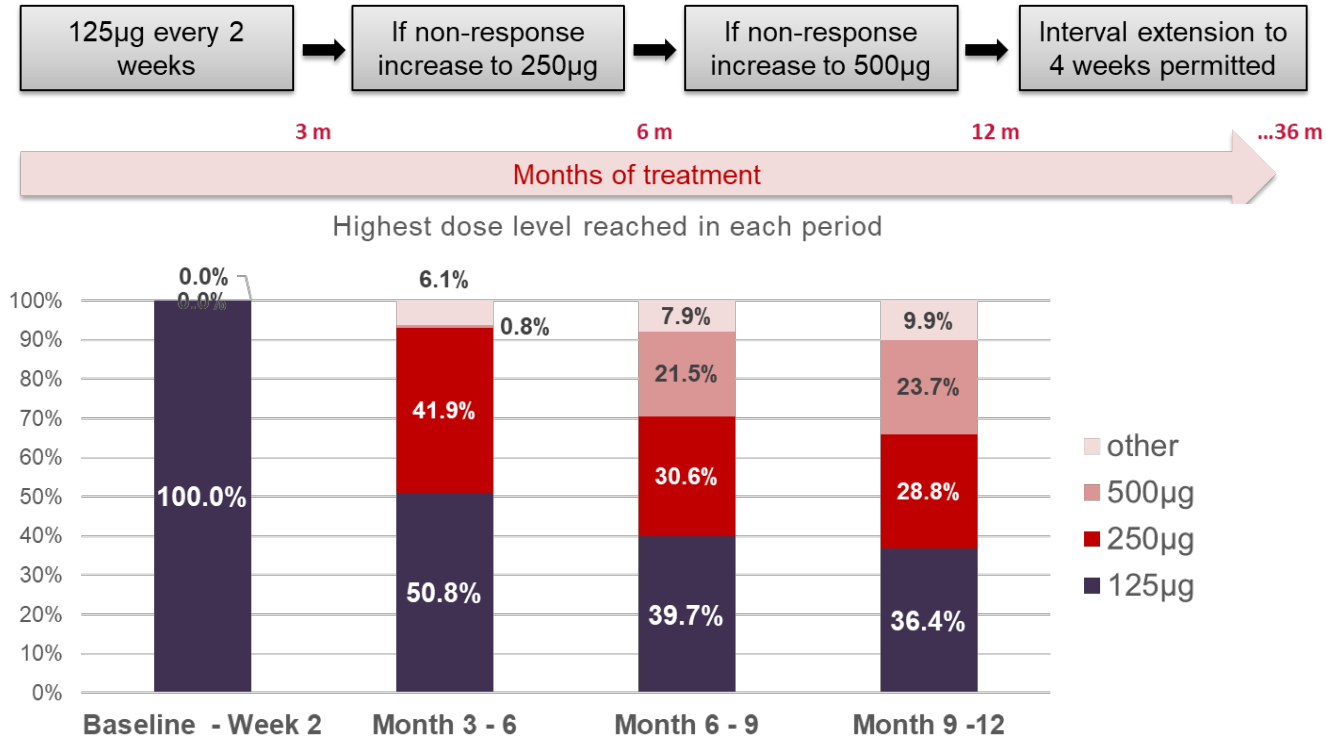
Characteristics	N=132
ET risk stratification at screening[1]	
Very low risk	26 (**20.0%**)[2]
Low risk	29 (**22.3%**)[2]
Intermediate risk	18 (**13.8%**)[2]
High risk	57 (**43.8%**)[2]
History of thrombosis or hemorrhage	37 (**28.0%**)
Thrombosis	28 (**21.2%**)[3]
Hemorrhage	10 (**7.6%**)[3]
History of progressive/symptomatic splenomegaly	4 (**3.0%**)
History of progressive disease-related symptoms	13 (**9.8%**)
Vasomotor/microvascular disturbances not responsive to aspirin	8 (**6.1%**)

Characteristics	N=132
Prior cytoreductive therapy	
No (treatment-naïve)	22 (**16.7%**)
Yes	110 (**83.3%**)
HU+ANA	49 (37.1%)
HU only	42 (31.8%)
ANA only	18 (13.6%)
HU+PB	1 (0.8%)
Any cytoreductive therapy resistance and/or intolerance	107 **(81.1%)**
Any cytoreductive therapy resistance*	33 (25.0%)
Any cytoreductive therapy intolerance*	95 (72.0%)

- Discontinuation rate : 10.6% (3 patients discontinued due to treatment-related adverse events)

Kiladjian JJ. et al. Blood (2025) 146 (Supplement 1): 485.

Ropeginterferon alfa-2b dose escalation



Kiladjian JJ. et al. Blood (2025) 146 (Supplement 1): 485.

ROP-ET Met Primary Endpoint

- At 12 months, 48.0% (95% CI: 39.1-57.1) patients showed a durable disease response

Individual parameters	Response Rate n/N(%)
Durable peripheral blood count remission response	77/118 (**65.3%**)
Absence of hemorrhagic or thrombotic events	127/132 (**96.2%**)
Absence of disease progression	132/132 (**100%**)
Absence or non-progression in disease-related signs (splenomegaly)	130/132 (**98.5%**)
Durable improvement or non-prog. in disease-related symptoms (TSS score)	96/114 (**84.2%**)

- Response was achieved at a low mean 2-weekly dose (193.8 µg ± SD 89.28 µg)
- Response rate improved with longer treatment duration: 33% (6 mo)> 50% (9 mo)> 60% (12 mo).
- At 12mo, 62.3% of patients showed improvement of symptoms compared to baseline
- No differences were observed according to driver mutation status.
- WBC and platelet counts decreased over time, while hemoglobin levels remained stable.

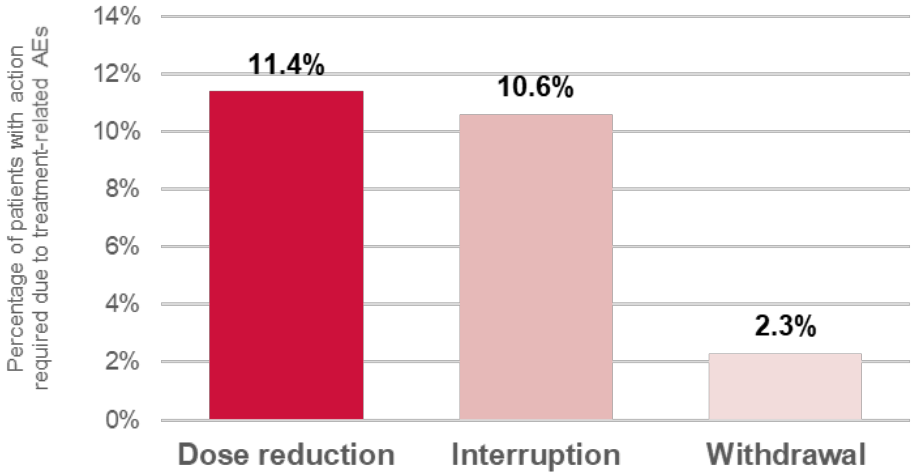
- Major thrombotic events occurred in 2 patients (1.5%).

Kiladjian JJ. et al. Blood (2025) 146 (Supplement 1): 485.

Ropeg-IFN -related Adverse Events

- Treatment-related AEs were reported in 73.5% of patients (5.3% Grade ≥3)

Adverse drug reactions ≥5%	Patients n(%)
Alanine aminotransferase increased	20 (**15.2%**)
Headache	20 (**15.2%**)
Gamma-glutamyltransferase increased	14 (**10.6%**)
Neutropenia	14 (**10.6%**)
Pruritus	14 (**10.6%**)
Aspartate aminotransferase increased	12 (**9.1%**)
Influenza like illness	12 (**9.1%**)
Asthenia	11 (**8.3%**)
Hepatic enzyme increased	11 (**8.3%**)
Bone pain	10 (**7.6%**)
Pyrexia	10 (**7.6%**)
Alopecia	9 (**6.8%**)
Anemia	9 (**6.8%**)
Diarrhea	7 (**5.3%**)



Kiladjian JJ. et al. Blood (2025) 146 (Supplement 1): 485.

Safety and Efficacy of INCA033989, a Novel First in Class Mutant Calreticulin–Specific Monoclonal Antibody, in Patients With Essential Thrombocythemia

Vikas Gupta,[1] John Mascarenhas,[2] Haris Ali,[3] David M. Ross,[4] Abdulraheem Yacoub,[5] Tania Jain,[6] Lynette Chee,[7] Aaron Gerds,[8] Jean-Jacques Kiladjian,[9] Ruben Mesa,[10] William Shomali,[11] Makoto Yoshimitsu,[12] Rosa Ayala Diaz,[13] Joan How,[14] Steffen Koschmieder,[15] Caroline McNamara,[16] Yosuke Nakaya,[17] Francesca Palandri,[18] Francesco Passamonti,[19] Andrew Perkins,[20] Bethan Psaila,[21] Raajit Rampal,[22] Natasha Szuber,[23] Frank Stegelmann,[24] Alessandro Maria Vannucchi,[25] Hiroki Yamaguchi,[26] Jason Gotlib,[11] Jyoti Nangalia,[27] Chenwei Tian,[28] Betty Lamothe,[28] Erin Crowgey,[28] Tatiana Zinger,[28] Evan Braunstein,[28] Claire Harrison[29]

[1]Princess Margaret Cancer Centre, Toronto, ON, Canada; [2]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [3]City of Hope Medical Center, Duarte, CA, USA; [4]Royal Adelaide Hospital, Adelaide, SA, Australia; [5]The University of Kansas Cancer Center, Kansas City, KS, USA; [6]Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore, MD, USA; [7]Peter MacCallum Cancer Centre and The Royal Melbourne Hospital, Melbourne, VIC, Australia; [8]Cleveland Clinic, Cleveland, OH, USA; [9]Saint-Louis Hospital, Paris Cité University, INSERM, Paris, France; [10]Wake Forest University Baptist Medical Center, Winston-Salem, NC, USA; [11]Stanford Cancer Institute/Stanford University School of Medicine, Stanford, CA, USA; [12]Kagoshima University Hospital, Kagoshima, Japan; [13]12 de Octubre University Hospital, Madrid, Spain; [14]Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, MA, USA; [15]RWTH Aachen University, Faculty of Medicine, and Center for Integrated Oncology (CIO-ABCD), Aachen, Germany; [16]Royal Brisbane and Women's Hospital, Brisbane, QLD, Australia; [17]Department of Hematology, Osaka Metropolitan University Graduate School of Medicine, Osaka, Japan; [18]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy; [19]Fondazione IRCCS Ca Ganda Ospedale Maggiore, Milan, Italy; [20]The Alfred Hospital, Melbourne, VIC, Australia; [21]University of Oxford, Oxford, UK; [22]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [23]Hôpital Maisonneuve-Rosemont, Montreal, QC, Canada; [24]Universitätsklinikum Ulm, Ulm, Germany; [25]Azienda Ospedaliero-Universitaria Careggi, Florence, Italy; [26]Nippon Medical School Hospital, Tokyo, Japan; [27]The Sanger Institute, Cambridge, UK; [28]Incyte Corporation, Wilmington, DE, USA; [29]Guy's and St Thomas' NHS Foundation Trust, London, UK

- **INCA033989-101** (NCT05936359; outside the US) and **INCA033989-102** (NCT06034002; US only) are phase 1, first-in-human, multicenter, open-label studies evaluating INCA033989 in patients harboring a *CALR* exon-9 mutation with high-risk ET or MF (as monotherapy or in combination with ruxolitinib)
- INCA033989 was administered intravenously every 2 weeks (range 24-2500 mg)

ET

- Diagnosis of ET (2022 WHO criteria)
- Presence of mut*CALR* exon 9
- High risk, defined as: ≥60 years of age *or* history of thrombosis *or* history of major bleeding *or* extreme thrombocytosis
- Documented resistance/intolerance to ≥1 line of prior cytoreductive therapy
- Platelet count >450 × 10^9/L
- Concomitant therapy with anagrelide or hydroxyurea permitted

Primary Endpoints

- Dose-limiting toxicities
- Treatment-emergent adverse events

Secondary Endpoints

- Response using ELN response criteria[1]
- Symptom improvement (MPN-SAF TSS)
- Changes in allele burden of mut*CALR*
- Pharmacokinetic parameters

Gupta V et al. Blood (2025) 146 (Supplement 1): 1024.

INCA033989 Monotherapy is Well Tolerated

55 *CALR* mut ET HR pts with resistance/intolerance to ≥1 line of prior cytoreductive therapy
Concomitant therapy with anagrelide or hydroxyurea were permitted

Most common TEAEs (≥14.5% of patients)

TEAE, n (%)	Total (N=55)
Fatigue	17 (30.9)
Headache	15 (27.3)
URTI	15 (27.3)
Anemia	11 (20.0)
Diarrhea	10 (18.2)
Pruritus	10 (18.2)
Arthralgia	9 (16.4)
Dizziness	9 (16.4)
Lipase increase	9 (16.4)
Nausea	9 (16.4)
Amylase increase	8 (14.5)

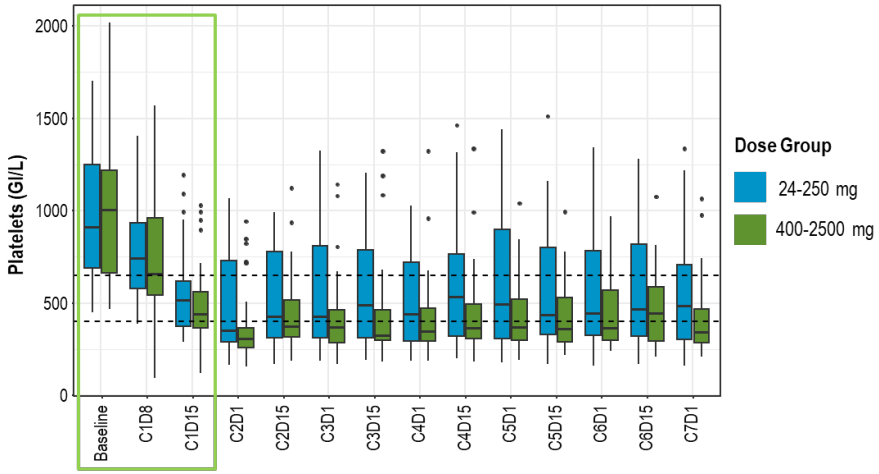
- 65.6% experienced Treatment-related TEAEs
- Most common Grade≥3 TEAEs:
  - Neutopenia (7.3%) ,
  - Anemia (3.6%)
  - amylase and lipase increased (3.6%)

Gupta V et al. Blood (2025) 146 (Supplement 1): 1024.

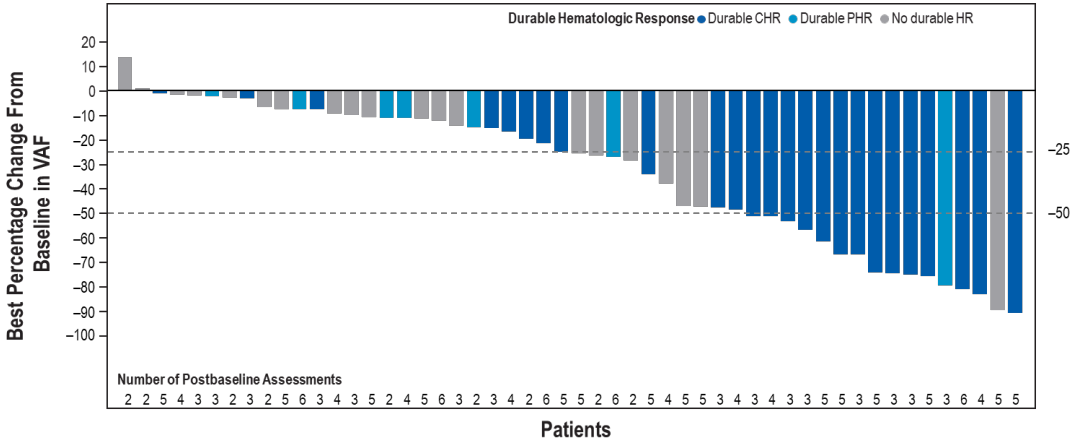
Hematologic and Molecular Response with INCA033989

- 71% of pts discontinued concomitant cytoreduction therapy after a median time to discontinuation of 23.0 (1.0-322.0) days
- Higher doses (400-2500 mg) were associated with higher rapid and durable hematologic responses (CHR 83.3%)
- 96.2% of pts reduced mut*CALR* VAF (PMR=31%)

Durable PLT coun Reduction



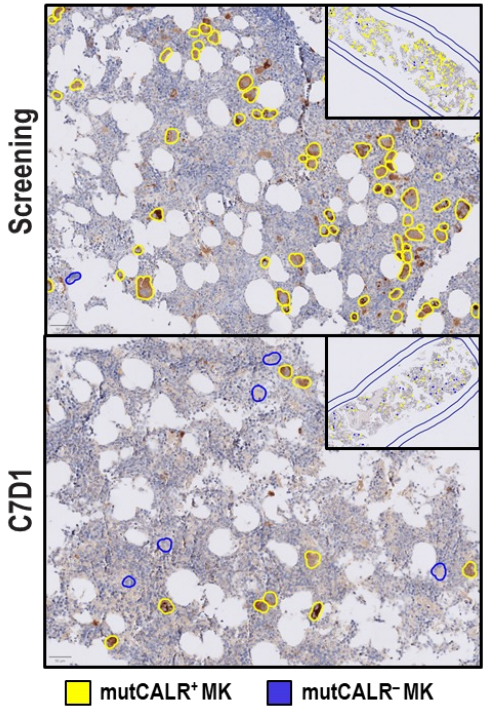
Reduction in mutCALR VAF from baseline



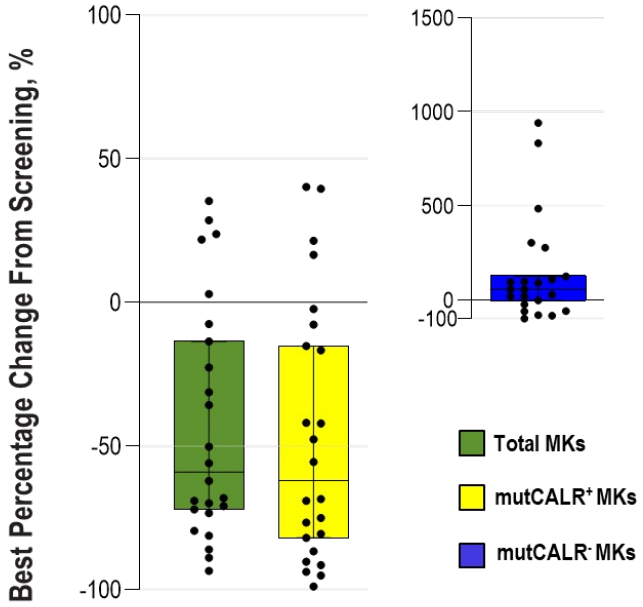
Gupta V et al. Blood (2025) 146 (Supplement 1): 1024.
Psaila B et al. Blood (2025) 146 (Supplement 1): 71.

INCA033989 Improves Bone Marrow Hematopoiesis

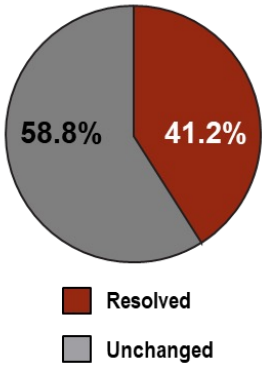
MK Staining by mutCALR IHC



Changes in Bone Marrow MK (n=24)*



MK Clustering† (n=34)

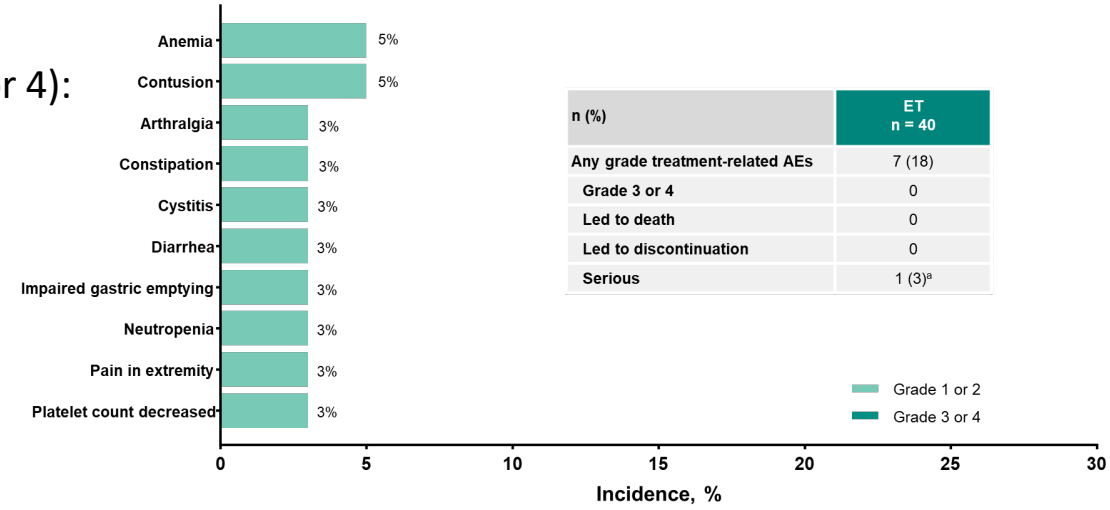


Gupta V et al. Blood (2025) 146 (Supplement 1): 1024.
Psaila B et al. Blood (2025) 146 (Supplement 1): 71.

Bomedemstat Has a Manageable Safety Profile in ET
Shorespan-017 Study

- 40 ET pts treated with a median of 8.1 months
- SAE occured in 18% of pts: Emergence of dysgeusia was not observed
- 88% of pts reported any-cause AEs (20% Grade 3 or 4):
  - 23% Diarrhea
  - 13% Contusion
  - 10% Abdominal pain
  - 10% Upper respiratory tract infection
- 23% had dose modification for AEs
- 1 (2.5%) discontinued treatment due to AEs

Treatment-Related AEs



n (%)	ET n = 40
Any grade treatment-related AEs	7 (18)
Grade 3 or 4	0
Led to death	0
Led to discontinuation	0
Serious	1 (3)[a]

Ross D et al. Blood (2025) 146 (Supplement 1): 2033.

Conclusions – Polycythemia Vera

- Iron/hepcidin pathway is an attractive tool to control erythocytosis in PV, with a reassuring safety profile and the potential to improve symptom burden (Rusfertide, Sapablursen)

- Targeting alternative pathways to JAK/STAT (Bomedestat) opens the way to personalized therapies in PV

Conclusions – Essential Thrombocythemia

- Ropeginterferon alfa-2b was well tolerated and was associated with significant blood count normalization, symptom improvement, and no progression at 12 months.
- A novel, first-in-class, fully human monoclonal antibody anti-mutCALR (INCA033989) holds significant promise as a targeted therapy for patients with ET
- Bomedemstat has a manageable long-term safety profile in ET