Disclosures

- Palandri, F. – Nothing to disclose

- Bomedemstat is an investigational drug has not yet been approved by the US Food and Drug Administration and is only available through clinical trial participation

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Phase 2 Study of the LSD1 Inhibitor IMG-7289 (Bomedemstat) for the Treatment of Essential Thrombocythemia (ET)

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LSD1 is a key regulator of hematopoietic differentiation

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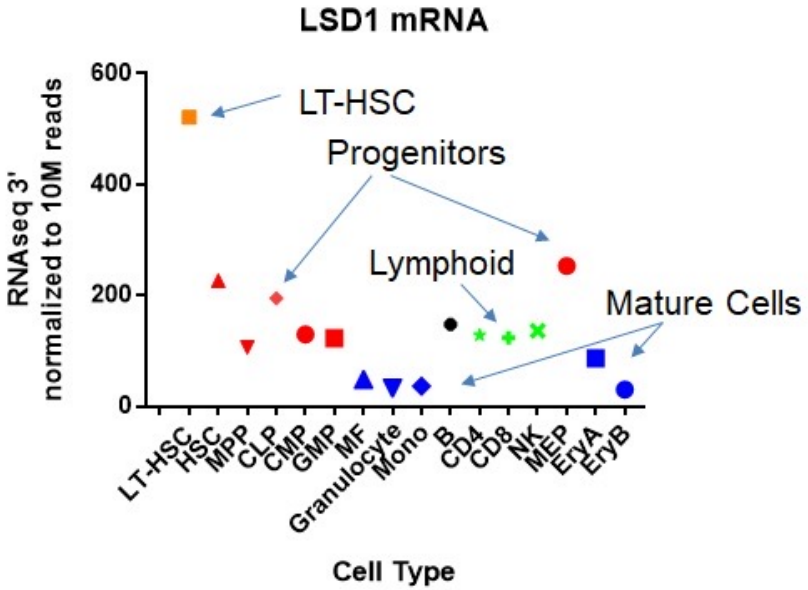
- LSD1 (Lysine-specific demethylase 1) demethylates H3K4 and other chromatin-associated proteins, *e.g.*, p53
- Loss of LSD1 activity is associated with loss of self-renewal in malignant HSCs[1]
- LSD1 is required for the differentiation of megakaryocyte-erythroid progenitors to mature megakaryocytes[2]
- Overexpressed in MPNs[3]



[1]Harris et al 2012; [2]Sprussel et al. 2012; [3]Neibel et al. 2014; [4]Lara-Astiaso et al. 2014

Introduction to Bomedemstat

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- Bomedemstat is an irreversible inhibitor of LSD1
- Discovered and developed by Imago
- PK and dose-response data support once-daily dosing
- No apparent penetration across the blood-brain barrier
- Bomedemstat has been evaluated in 170+ patients with advanced myeloid malignancies*
- Updated results from the Phase 2 study evaluating bomedemstat in essential thrombocythemia who have failed at least one standard therapy are presented here

*IMG-7289-CTP-101, IMG-7289-CTP-102 and IMG-7289-CTP-201

Study Design

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IMG-7289-CTP-201 is an ***ongoing*** Phase 2 global study to assess the safety, efficacy and pharmacodynamics of IMG-7289 (bomedemstat) in patients with ET.

Primary Endpoints

- Safety and tolerability
- Platelet count reduction (≤400 x 10^9/L) in the absence of thromboembolic events

Secondary Endpoints

- Symptom reduction (MPN-SAF TSS)
- Durability of platelet and WBC count reduction
- Changes in mutant allele frequencies (MAF)

Key Eligibility Criteria

- Dx of ET
- Failed at least one standard therapy
- Platelet count >450 x 10^9/L
- Hemoglobin ≥10 g/dL
- Peripheral blasts <1%
- Fibrosis Score <2 per protocol criteria (modified from Arber *et al*., 2016)

Bomedemstat Treatment Plan

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- IMG-7289 (bomedemstat) PO once daily (QD)
- Each patient dose-titrated to platelet count *per* dosing rules
- Starting dose is 0.6 mg/kg QD
- Up-titrations may occur every 4 weeks to target platelet range of 200-400 x 10^9/L

Platelet Count (x 10^9/L)	Hb (g/dL)	Dose Titration (mg/kg/d)
>400	≥10	Increase by 0.2
≥200 and ≤400	≥10	Maintain Dose
50-199	≥10	Decrease by 0.1
Any	≥8.5 and <10	Decrease by 0.15
<50	<8.5	Hold dose

Enrollment and Treatment Status

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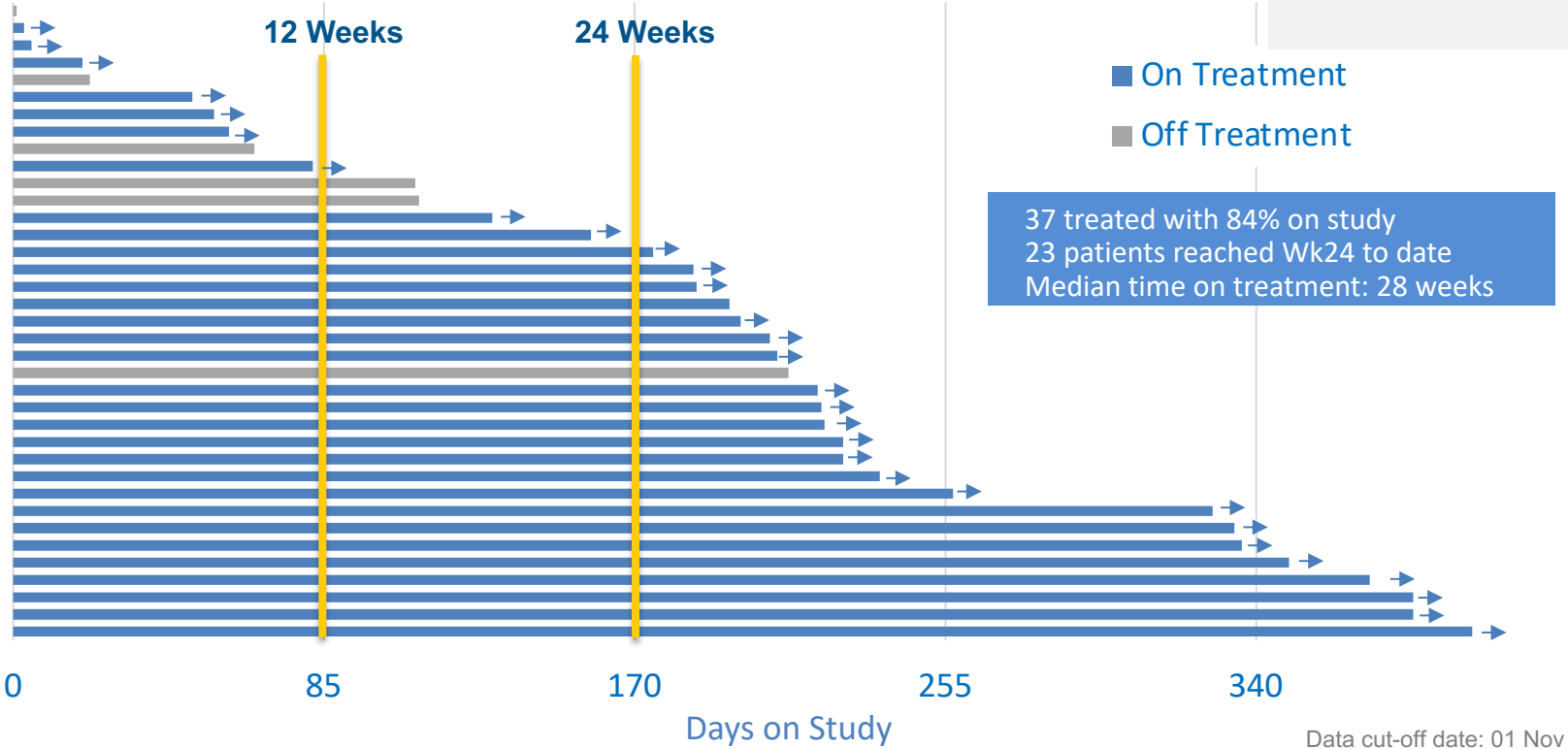

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Baseline Characteristics

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Characteristic	N = 36
Median age (range)	68 (42 – 85)
Male	15 (42%)
Mean blood counts (range)[#]	
WBC	9.4 x 10^9/L (4.4 – 30.6)
Hemoglobin	13.1 x g/dL (9.4* – 16.5)
Platelet Count	863 x 10^9/L (457 – 2220)
[#]1 value missing	
Mutations (%)	
JAK2	36%
CALR	39%
Triple Negative	6%
≥ 1 myeloid disease-associated mutation	19%
Unavailable	19%
Median (MPN-10 TSS) Symptom score (range) (N=21 with TSS ≥ 10)	30 (11 – 74)

Prior Therapies	N = 36
Most Recent Prior Therapy	
Hydroxyurea	27 (75%)
Met ELN resistance/intolerance criteria	24 (89%)
Failure Reasons:	
1. Unacceptable HU-related non-hematologic toxicities[1]	21
2. Platelet count >600 ×10^9/L[2]	3
3. Platelet count >400 × 10^9/L and WBC <2.5 ×10^9/L at any HU dose	1
4. Platelet count >400 × 10^9/L and Hb <10 g/dL at any HU dose	0
Anagrelide	4 (11%)
Interferon	3 (8%)
Ruxolitinib	1 (3%)
Busulfan	1 (3%)
Earlier Prior Therapies	5 x HU, 2 x Anagrelide, 1 x aspirin, 1 x Rux, 1 x IFN, 1 x Busulfan

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*Protocol deviation [1]Toxicities including fever, mucocutaneous manifestations or leg ulcers; [2]Following a daily dose of ≥3g for at least 3 mo

Safety and Tolerability

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Preferred Term (N=37)	Any Grade AEs	Grade 3/4 AEs
Dysgeusia	18 (49%)	0
Constipation	12 (32%)	1 (3%)
Arthralgia	9 (24%)	0
Fatigue	9 (24%)	0
Diarrhoea	6 (16%)	0
Headache	6 (16%)	1 (3%)
Thrombocytopenia	6 (16%)	1 (3%)
Pain in extremity	5 (14%)	0
ALT increased	4 (11%)	0
Alopecia	4 (11%)	0
Anaemia	4 (11%)	1 (3%)
Contusion	4 (11%)	0
Dizziness	4 (11%)	0
Oedema peripheral	4 (11%)	1 (3%)

- **Bomedemstat is generally well-tolerated with few Grade 3/4 AEs (3.6%; 12/335)**
- Most common AE was dysgeusia – all events were Grade 1/2 with 2/18 leading to treatment discontinuation
- **Eight SAEs, two of which were related and both led to dose interruption** (thrombocytopenia and mouth haemorrhage)
- One unrelated thrombotic event – pulmonary embolism

Any grade of AE occurring at a frequency of >10% of patients included regardless of relatedness; total number of events = 335

Primary Objective: Reduction in Platelet Count

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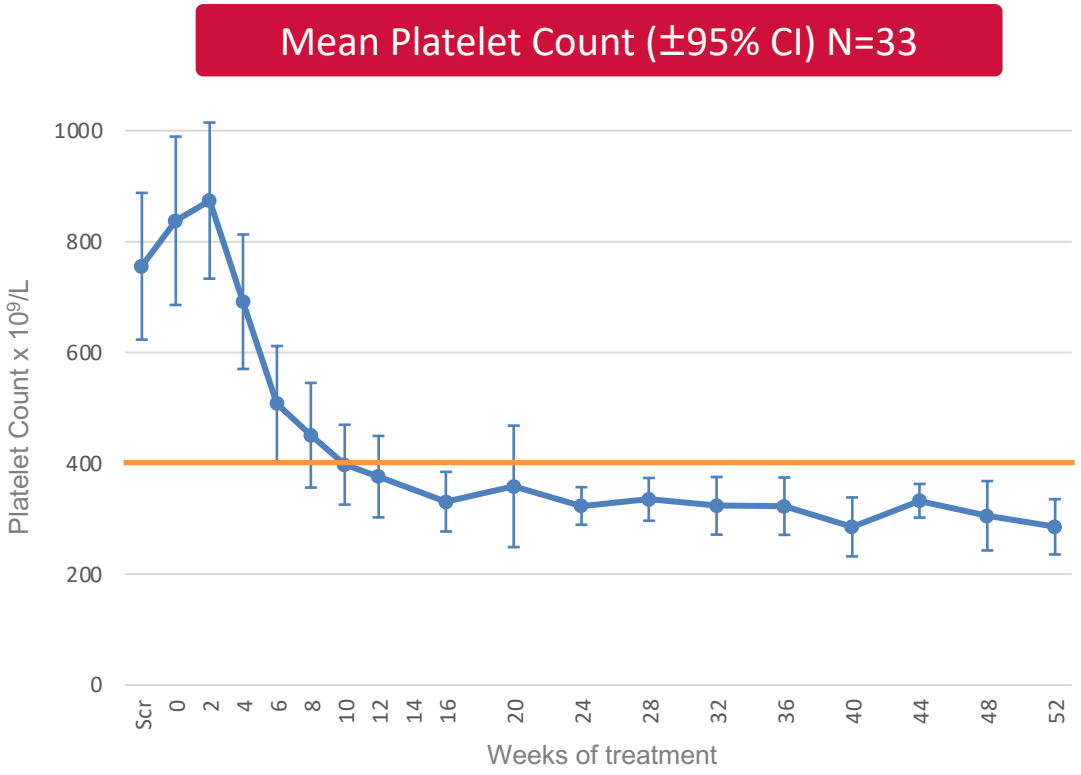

In the 29 patients treated for >6 weeks:

- 100% patients experienced a reduction in platelets
- 93% of patients achieved a platelet count of ≤400 x 10^9/L
- Response Rate*: 90% (26/29)

*Platelet count ≤400 x 10^9/L without thromboembolic events

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Primary Objective: Reduction in Platelet Count

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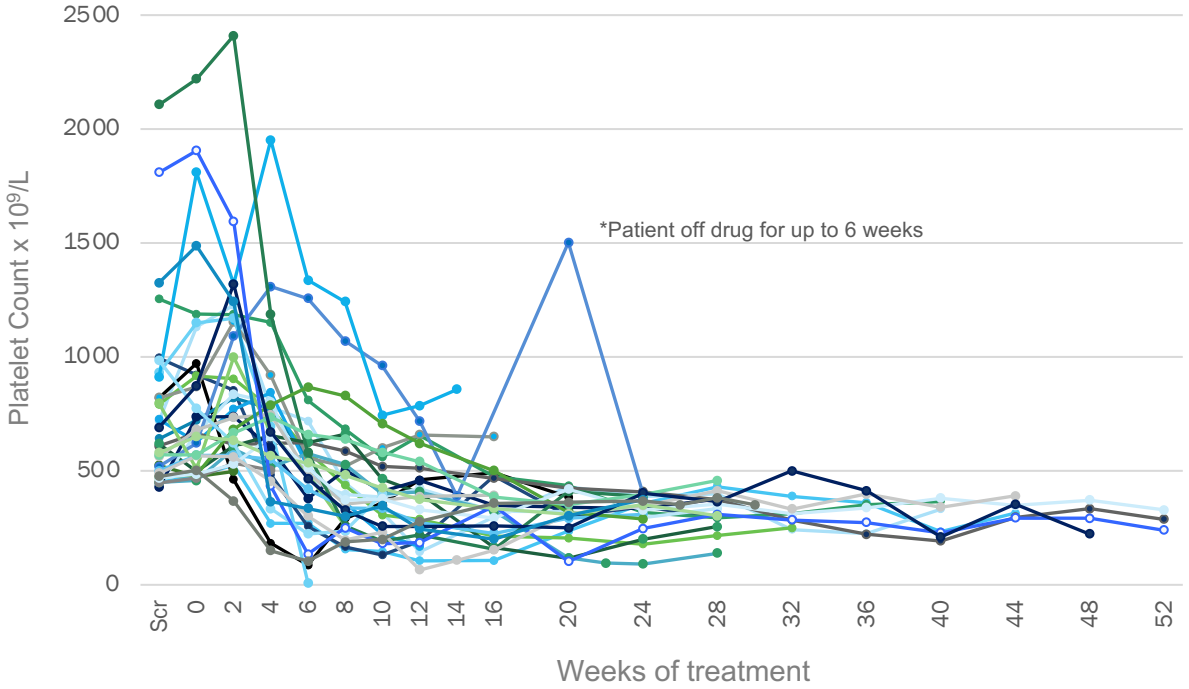
Individual Platelet Counts (N=33)



In the 27 patients treated for at least 12 weeks:

- Mean reduction of 496 x 10^9/L at Week 12 (N=27)
- Durability of response: to date 52% of patients achieved 12 consecutive weeks ≤400 x 10^9/L

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Platelet Count Response Across Mutation Status

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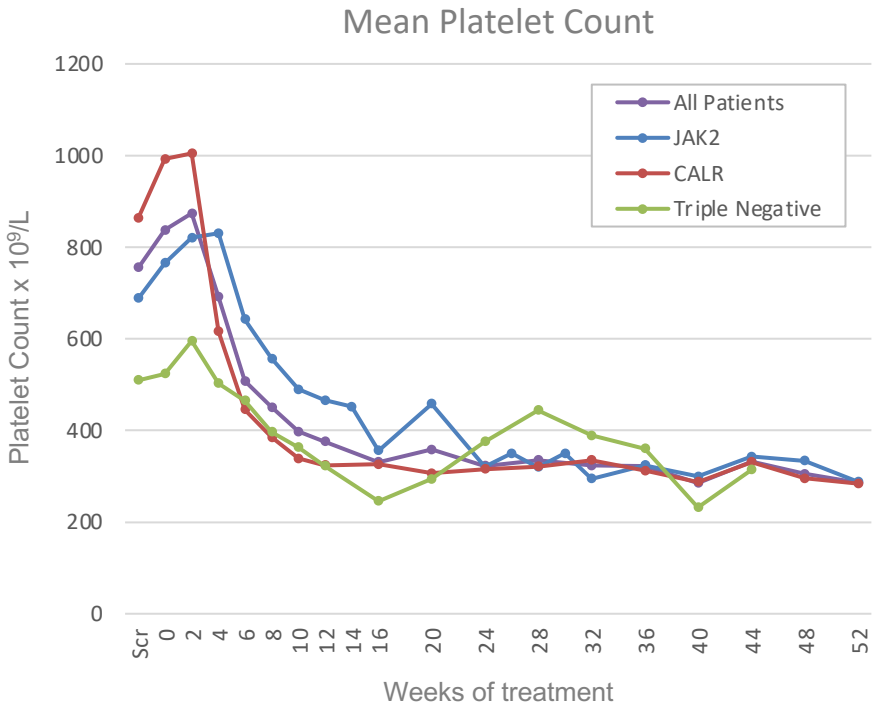
Mutation	No. of Patients*	Mean Baseline Platelet Count (x10^9/L)	Platelet Count Response (%)
All Pts	**30**	**838**	**93%**
CALR	13	993	100%
JAK2^{V617F}	13	765	83%
Triple Negative	2	524	100%

*Patients with mutation status and platelet counts available

Patients with *CALR* mutations have a similar platelet count response to *JAK2* mutated patients



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Lowers WBC and Maintains Hemoglobin Levels

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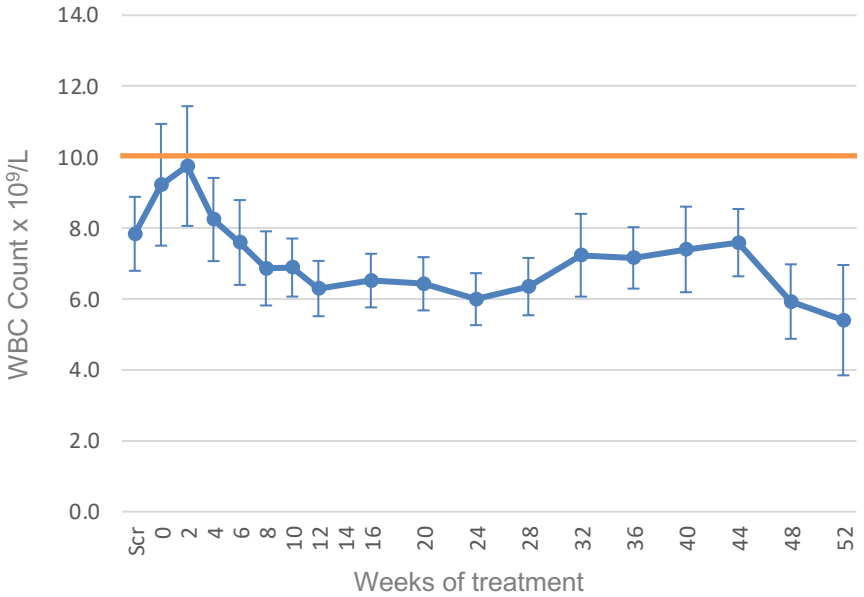
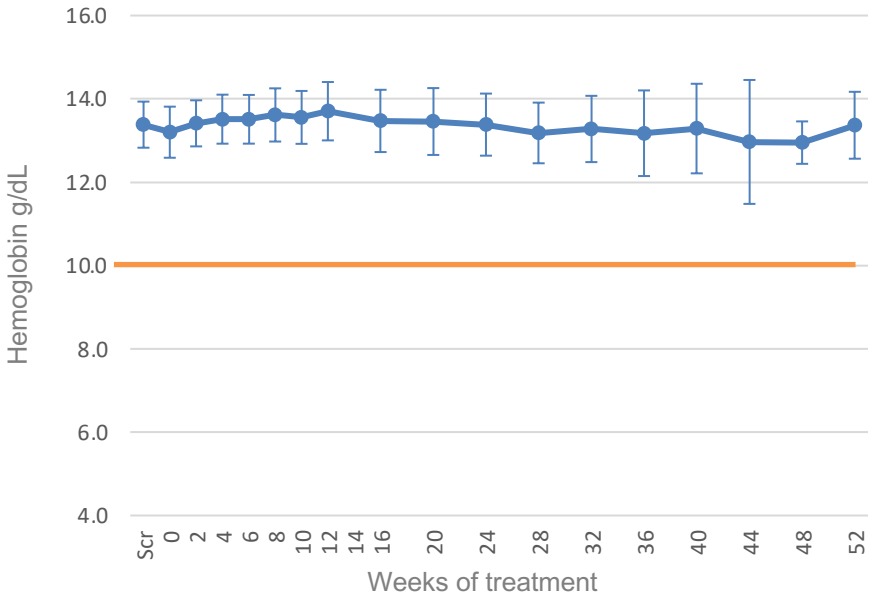
Mean WBC (±95% CI) N=33



Mean Hemoglobin (±95% CI) N=32



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Reduction in Total Symptom Score

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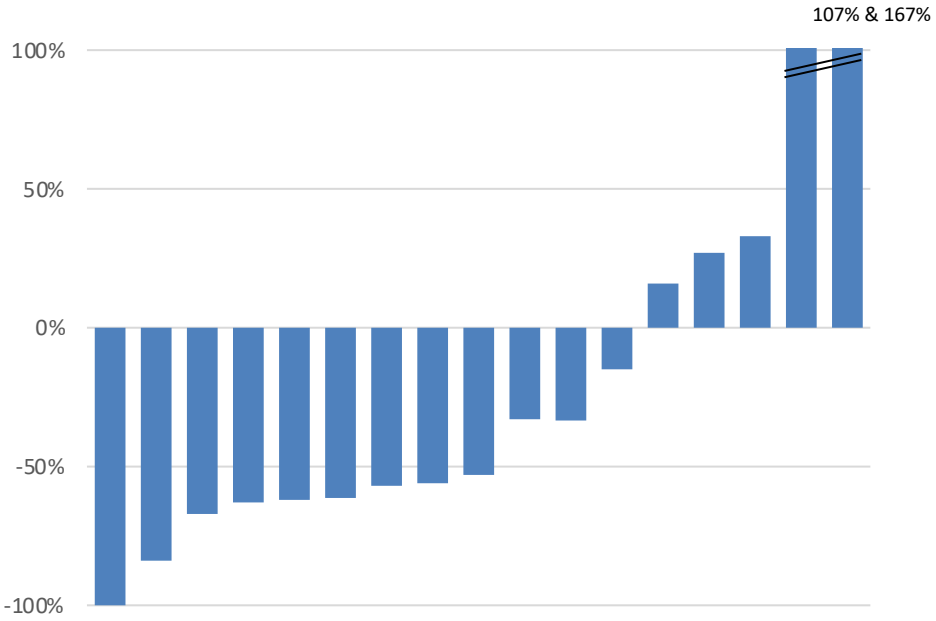
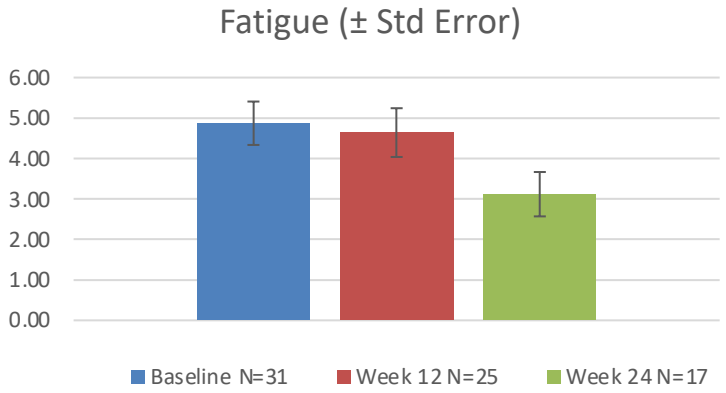
TSS % Change at 24 weeks
(Patients with >0 at Day 1, N=17)



N at Day 1 with Score >0 = 31 NB 1 excluded (012-202)

- **71%** had a decrease in TSS
- **53%** had a decrease of >50%
- **47%** had a decrease of ≥10 points



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Conclusions

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- Bomedemstat (IMG-7289) is generally well tolerated in ET patients
  - Majority of AEs were low-grade
- Bomedemstat as monotherapy demonstrates significant clinical activity:
  - Normalization of platelet and WBC counts while maintaining hemoglobin
  - Symptomatic improvement for some patients with significant MPN symptoms
  - All genotypes respond to bomedemstat
- Development Plans
  - The ET study remains open for enrollment (NCT04254978*)*
  - Planning for Phase 3 study in ET is underway
  - Bomedemstat in PV is currently enrolling (NCT04262141)

Thank you to Investigators and Study Participants!

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