Disclosures

- Gill H – Nothing to disclose

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

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A Phase 2 Study of IMG-7289 (Bomedemstat) in Patients with Advanced Myelofibrosis

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LSD1 is a key regulator of hematopoietic differentiation

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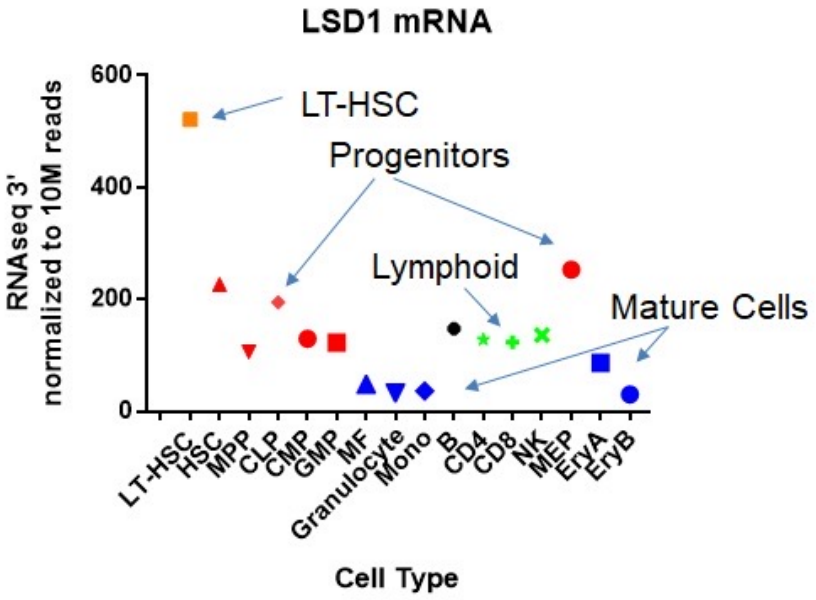
- LSD1 (Lysine-specific demethylase 1) demethylates H3K4 and other chromatin-associated proteins, *e.g.*, p53
- Loss of LSD1 activity is associated with loss of self-renewal in malignant HSCs[1]
- LSD1 is required for the differentiation of megakaryocyte-erythroid progenitors to mature megakaryocytes[2]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



[1]Harris et al 2012; [2]Sprussel et al. 2012; 3Neibel 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 suggest 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 advanced myelofibrosis are presented here

Study Design

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IMG-7289-CTP-102 is an ***ongoing*** Phase 1/2 global study of IMG-7289 (bomedemstat) in patients with MF

Primary Endpoints

- Safety and tolerability
- Pharmacokinetics in first 15 patients
- Spleen volume reduction

Secondary Endpoints

- Symptom reduction (MPN-SAF TSS)
- Changes in cytokine profiles
- Changes in mutant allele frequencies (MAF)
- Changes in bone marrow (BM) fibrosis

Key Eligibility Criteria

- Dx of PMF, PET-MF, or PPV-MF
- Refractory or resistant to, intolerant of, inadequate control by, or ineligible for, available approved therapies
- IPSS Intermediate-1, -2 or High-risk disease
- **Platelets ≥100 x10^9/L**
- Peripheral blasts ≤10%
- Spleen of ***any size***
- ECOG PS ≤2

Bomedemstat Treatment Plan

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- IMG-7289 (bomedemstat) PO once daily (QD)
- Each patient dose-titrated to a target platelet count of 50-75 x 10^9/L
- Phase 1/2a Starting Dose was 0.25 mg/kg (QD) (N=18)
- Phase 2b Starting Dose was 0.5 mg/g (N = 25) and, later, 0.6 mg/kg (N = 46) QD

Enrollment Status and Patient Disposition

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Phase 1/2a (N=18)	Completed 12 Weeks	Reason Off Treatment Pre- Wk 12 (N=3)
Week 12	15 (83%)	Adverse Event = 2 Limited Clinical Benefit = 1
Median Duration of Treatment: 165 days (range 27-562)		

Phase 2b (N=71*)	Completed 24 Weeks	Reason Off Treatment Pre-Wk 24 (N=28)
Week 24	42 (58%)	Adverse Events (not related) = 7 Adverse Events (related) = 8 PI decision = 3 Other = 6 Disease Progression = 3 Limited Clinical Benefit = 1
1 patient remains on treatment pre-Week 24; 34 patients ongoing post Week 24		
Median Duration of Treatment: 177 days (range 13-825)		

- Enrollment completed in May 2021 with a total of 89* patients
- 39% of all patients remain on study
- Anticipate study completion in 2022

*Note Pt 020-102 re-entered as 020-103 and is not counted as a new patient except for Adverse Events

Data cut-off date: 31Oct 2021

Baseline Characteristics:

Most are high risk and heavily pre-treated

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Characteristic	N = 89
Median age (range)	68 (35– 88)
Male	46 (52%)
Disease subtype	
PMF	41 (46%)
Post-ET MF	30 (34%)
Post-PV MF	18 (20%)
IPSS Risk Classification	
Intermediate-1	6 (7%)
Intermediate-2	35 (39%)
High	47 (53%)
Missing	1 (1%)
Mean blood counts (range)	
WBC	20.8 x 10^9/L (1.2 – 111.6)
Hemoglobin	10.1 g/dL (5.2 – 15.8)
Platelet Count	394 x 10^9/L (100 - 2188)

Characteristic N=89	
Median spleen length (N=72 with palpable spleen)	12 cm BLCM (1-32)
Median spleen volume	1351 cm^3 (99-6819)*
Median Symptom score (MPN-10 TSS) (N=55 with TSS ≥20)	25 (range: 0-82)†
Mutations (%)	
JAK2	64%
CALR	22%
MPL	7%
Triple Negative	3%
High-Molecular Risk#	38%
No sample	3%
Median No. Prior Therapies^	2 (0-6)
Ruxolitinib	74
Anagrelide	9
Fedratinib	2
Hydroxyurea	38

*4 values missing; †4 values missing or incomplete; ^2 values missing; #HMR = *U2AF1, IDH1, IDH2, ASXL1, EZH2*

Safety and Tolerability

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Preferred Term (N=90)	Any Grade AEs	Grade 3/4 AEs
Thrombocytopenia	42 (47%)	35 (39%)
Dysgeusia	29 (32%)	0
Anaemia	29 (32%)	20 (22%)
Diarrhoea	27 (30%)	0
Nausea	25 (28%)	2 (2%)
Fatigue	22 (24%)	4 (4%)
Constipation	21 (23%)	1 (1%)
Oedema peripheral	18 (20%)	1 (1%)
Arthralgia	16 (18%)	0
Abdominal pain	15 (17%)	1 (1%)
Decreased appetite	14 (16%)	2 (2%)
Pruritus	14 (16%)	2 (2%)

- Bomedemstat is generally well tolerated
- Most common hematologic AE, thrombocytopenia, is anticipated because dose titration rules target Grade 2 (50-75 x 10^9/L)
- The most common non-hematologic AE **related** to bomedemstat was dysgeusia (n=27, 30% of patients) with 1 patient who discontinued

Any grade of AE occurring at a frequency of >15% included regardless of relatedness; total number of events = 1443

Total Symptom Score (TSS) at 24 weeks

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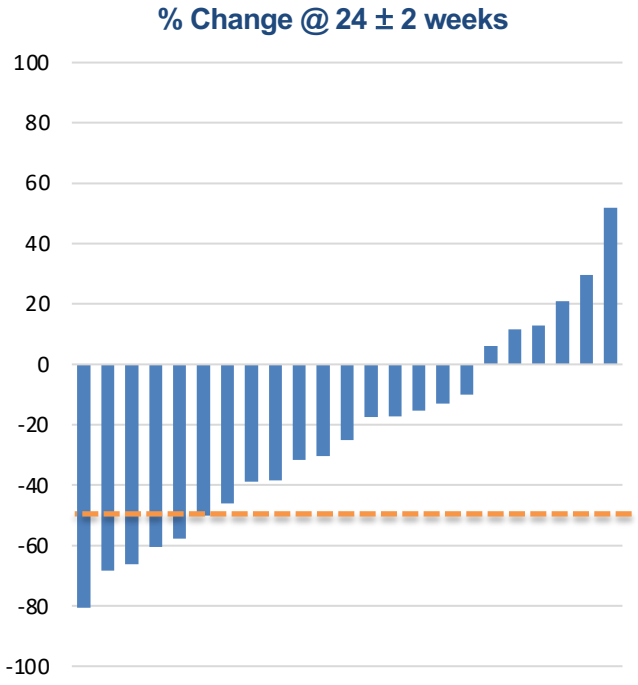
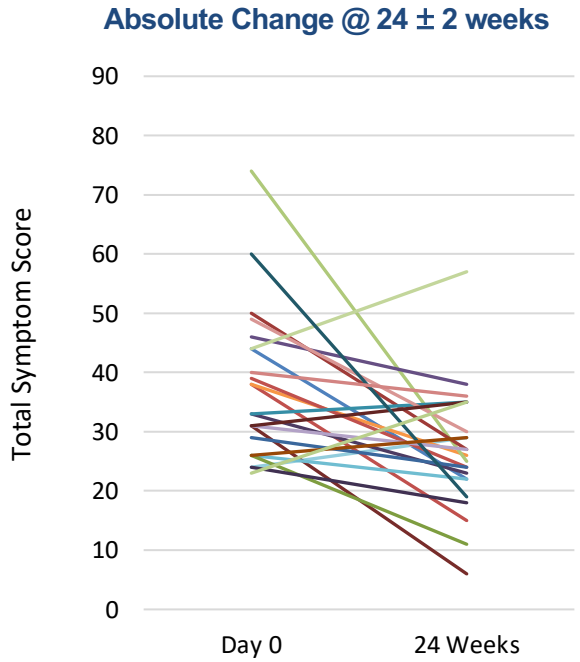
Changes in MPN-SAF TSS – Patients with significant symptom burden (≥20)





- 17/23 **(74%)** had a decrease in TSS
- 6/23 **(26%)** had a decrease of ≥50%

Data cut-off date: 31Oct 2021

Spleen Volume Reduction at 24 Weeks

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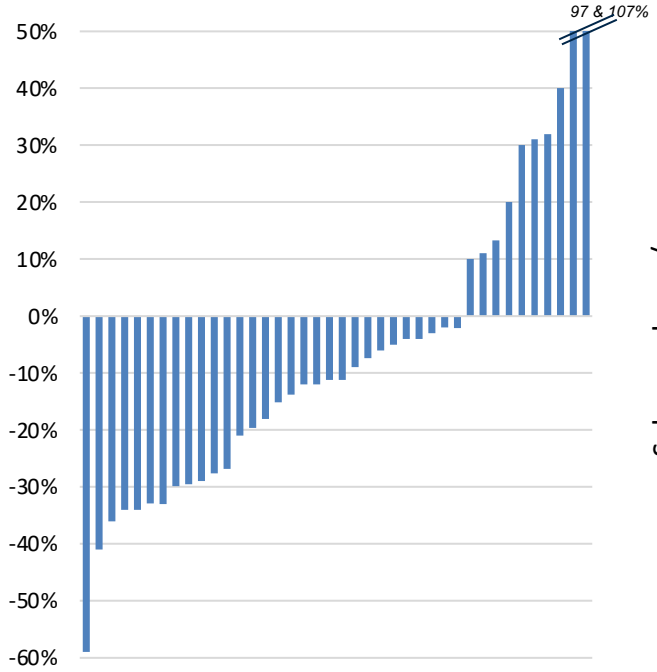
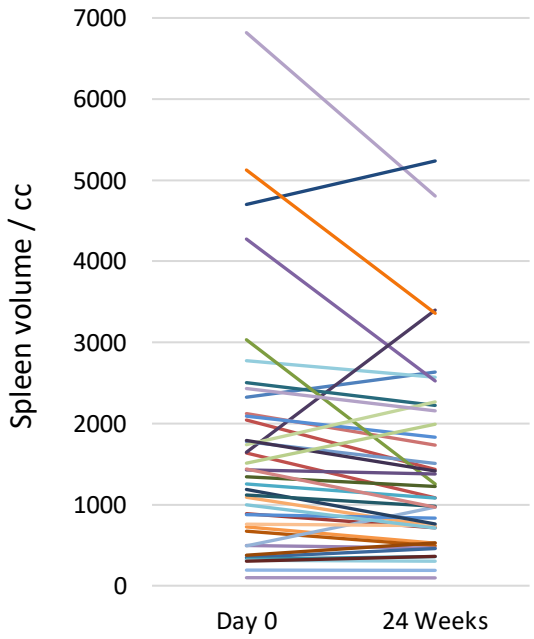
Change in Spleen Volume

% Change @ 24 ± 2 weeks



Absolute Change @ 24 ± 2 weeks



All spleen sizes allowed at study entry

- 30/40 **(75%)** had any decrease
- 14/40 **(35%)** had ≥20% decrease
- 3/40 **(8%)** had ≥35% decrease

Data cut-off date: 31Oct 2021

Changes in Hemoglobin

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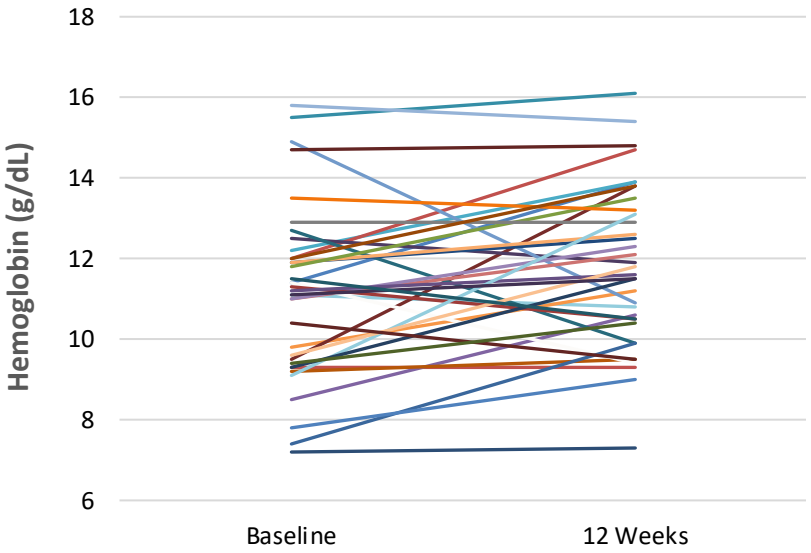
Changes in Hb in Tx-Independent Patients



In patients (N=36*) who were **transfusion-independent** at baseline, at 12 weeks:

- 89% (32/36) had stable or improved Hb
  - 44% (16/36) had an increase ≥1.0 g/dL
  - 44% (16/36) had stable Hb Δ <±1.0 g/dL

In patients (N=17*) who were **transfusion-dependent** at baseline, to last time on study:

- 59% (10/17) had stable or reduced transfusion burden
- 1 patient became transfusion-independent

Data cut-off date: 31Oct 2021

* Exclusions due to: ET prior to Wk12

Impact on Mutant Alleles

261 genes serially sequenced by NGS to an average depth of 1015 bp

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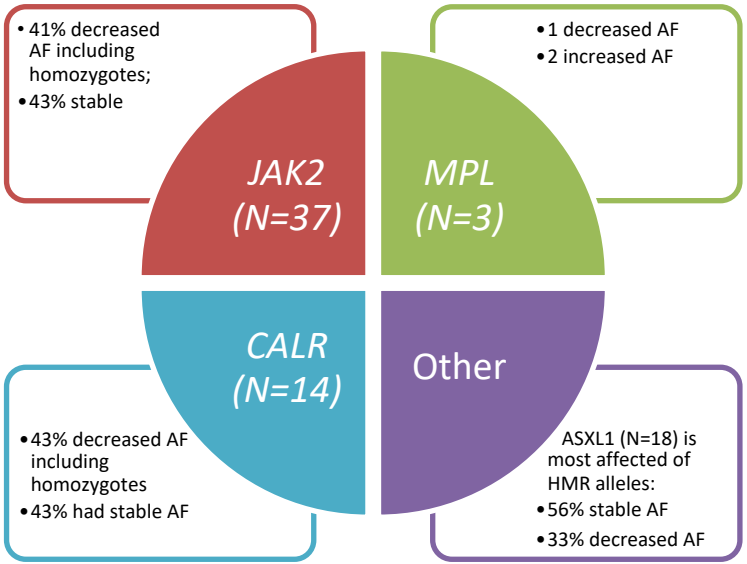
Changes in Specific Mutant Alleles



AF = Allele frequency

Overall Changes in Allele Frequency

- 45% showed stable AFs (N=127)
- 36% showed a reduction in AF
- 19% showed an increase in AF

- There were 4 complete molecular responses (AF → 0)

- No new mutations or transformation to AML in treatment for up to >600 days

Standard deviation in this study at a read depth of 1000 is ~5%

Change defined as ≥5% for heterozygotes, ≥10% for increase/ ≥2.5% decrease for homozygous clones for up to >600 days

Change from pre-dose to last timepoint *on drug* ± 2days

Conclusions

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- Bomedemstat (IMG-7289) as monotherapy for patients with advanced myelofibrosis offers a distinct clinical benefit profile:
  - Generally safe and well tolerated to date
  - Shows improvements in symptom scores, spleen volumes, and anemia
  - 81% of allele frequencies are stable or decreased including driver and HMR mutations such as *ASXL1*
  - No new mutations or transformation to AML in patients with a high-risk of progression

- A study of the combination of bomedemstat and ruxolitinib is planned
- Studies of bomedemstat for the treatment of ET (NCT04254978) and PV (NCT04262141) are currently enrolling

Thank you to Investigators and Study Participants!

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Investigators - APAC

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- Ruben Mesa – M.D. Anderson, San Antonio

Imago BioSciences

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- Philippa Quy
- Amber Jones
- Jennifer Dias
- Ria Kleppe
- Georges Natsoulis
- Willis Navarro
- Wan-Jen Hong
- Hugh Rienhoff

Special thanks to our top recruiting sites in each region!

Back-Up Slides

Bomedemstat Treatment Plan – Back-Up Slide

- IMG-7289 (bomedemstat) PO once daily
- Each patient dose-titrated to a target platelet count of 50-75 x 10^9/L
- Starting dose was initially 0.25 mg/kg once daily for the Phase 1/2a (N=18), and then 0.5 mg/g (N = 25) and 0.6 mg/kg once daily in the Phase 2b (N= 46)

Platelet Count (x10^9/L)	%Platelet Reduction (from previous visit)	Dose Titration
≥200	<75% decrease OR increase	Increase 0.15 mg/kg/d
100-199	<75% decrease OR increase	Increase 0.1 mg/kg/d
100-199	≥75% decrease	Maintain
40-99	<50% decrease OR increase	Maintain
40-99	≥50% decrease	Down-titrate 0.1 mg/kg/d
25-39	N/A	Decrease dose 25%
<25	N/A	Hold Dose

Changes in Transfusion Frequency

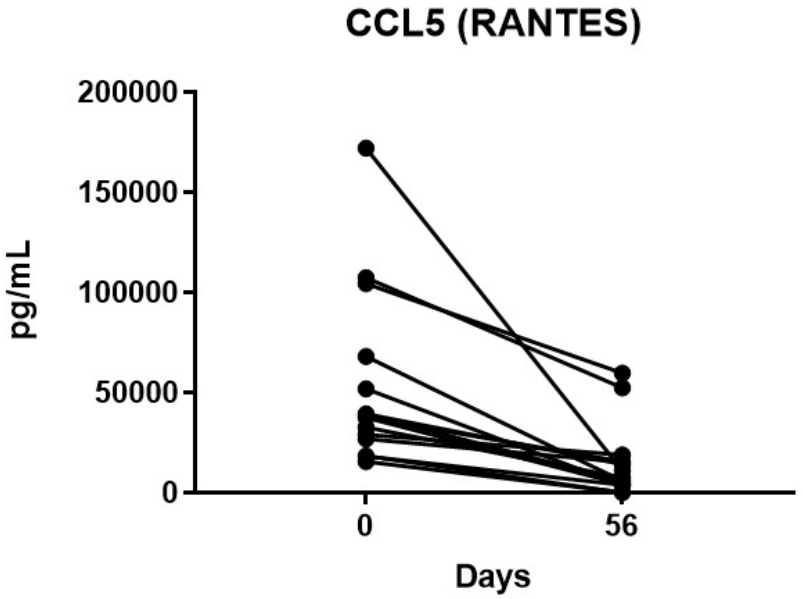
Change in Transfusion Burden in Transfusion-Dependent Patients (N=17**)	
Transfusion Independent	1 (6%)
Improved (≥1 unit/mo decrease)	2 (12%)
Stable (Δ<1 unit/mo)	7 (41%)
Worsening (≥1 unit/mo increase)	7 (41%)

**Exclusions due to: ET prior to Wk 12, <6 units recorded and/or insufficient pre-dose Tx data

In patients (N=17*) who were transfusion-dependent at baseline, to last time on study:

- 59% (10/17) had stable or reduced transfusion burden
- 1 patient transfusion independent

Reduction in Inflammatory Chemokines



CCL5 (RANTES) is chemokine secreted in bone marrow by activated T cells.