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American Society of Hematology 2015 Analyst & Investor Event

Saturday, December 5, 2015

Agenda

Welcome and Introductions	**Dr. John Scarlett** President & CEO, Geron Corporation
Data Presentations:	
Dynamics of Mutations in Patients with ET Treated with Imetelstat (ASH Abstract #57)	**Dr. Elisabeth Oppliger Leibundgut** Department of Hematology and Clinical Research, University Hospital and University of Bern, Switzerland
Telomerase Inhibitor Imetelstat Therapy in Refractory Anemia with Ring Sideroblasts with or without Thrombocytosis (ASH Abstract #55)	**Dr. Bart Burington** VP Biometrics, Geron Corporation
Overview of IMbark™ and IMerge™ Studies under Collaboration Agreement with Janssen	**Dr. John Scarlett** President & CEO, Geron Corporation
Q&A	

Forward-Looking Statements

Except for the historical information contained herein, this presentation contains forward-looking statements made pursuant to the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Investors are cautioned that statements in this presentation regarding: (i) timing and management of planned and potential clinical trials of imetelstat to be conducted under the collaboration agreement with Janssen, including the current Phase 2 clinical trial in MF and the planned Phase 2/3 clinical trial in MDS, and other potential activities under the collaboration agreement with Janssen; (ii) the safety and efficacy of imetelstat; (iii) the current designs of the Phase 2 clinical trial in MF and planned Phase 2/3 clinical trial in MDS, including planned reviews or analyses of clinical data; and (vi) other statements that are not historical facts, constitute forward-looking statements. These statements involve risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. These risks and uncertainties, include, without limitation, risks and uncertainties related to: (i) the uncertain, time-consuming and expensive product development and regulatory process, including whether Geron and Janssen will succeed in overcoming all of the clinical safety and efficacy, technical, scientific, manufacturing and regulatory challenges in the development and commercialization of imetelstat; (ii) regulatory authorities permitting the clinical trials to begin or continue to proceed; (iii) Janssen's ability to enroll patients in any of the planned or potential clinical trials of imetelstat; (iv) the fact that Janssen may terminate the collaboration agreement for any reason; (v) whether imetelstat is safe and efficacious, and whether any future efficacy or safety results may cause the benefit-risk profile of imetelstat to become unacceptable; (vi) the ability of Geron and Janssen to protect and maintain intellectual property rights for imetelstat; (viii) Geron's dependence on Janssen, including the risks that if Janssen were to breach or terminate the collaboration agreement or otherwise fail to successfully develop and commercialize imetelstat and in a timely manner, Geron would not obtain the anticipated financial and other benefits of the collaboration agreement and the clinical development or commercialization of imetelstat could be delayed or terminated; and (ix) whether imetelstat can be applied to any or to multiple hematologic malignancies. Additional information on the above risks and uncertainties and other factors that could cause actual results to differ materially from those in the forward-looking statements are contained in Geron's periodic reports filed with the Securities and Exchange Commission under the heading "Risk Factors," including Geron's quarterly report on Form 10-Q for the quarter ended September 30, 2015. Undue reliance should not be placed on forward-looking statements, which speak only as of the date they are made, and the facts and assumptions underlying the forward-looking statements may change. Except as required by law, Geron disclaims any obligation to update these forward-looking statements to reflect future information, events or circumstances.

2015 Annual Meeting of the American Society of Hematology

Dynamics of Mutations in Patients with ET Treated with Imetelstat

Elisabeth Oppliger Leibundgut, PharmD[1], Monika Haubitz, PhD[1*], Bart Burington, PhD[2*], Oliver G. Ottmann, MD[3*], Gary Spitzer, MD[4], Olatoyosi Odenike, MD[5], Michael A McDevitt, MD, PhD[6], Alexander Roeth, MD[7], David S. Snyder, MD[8] and Gabriela M. Baerlocher, MD[1]

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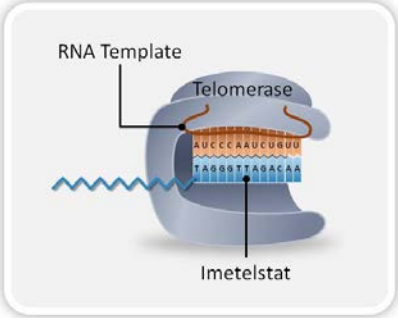
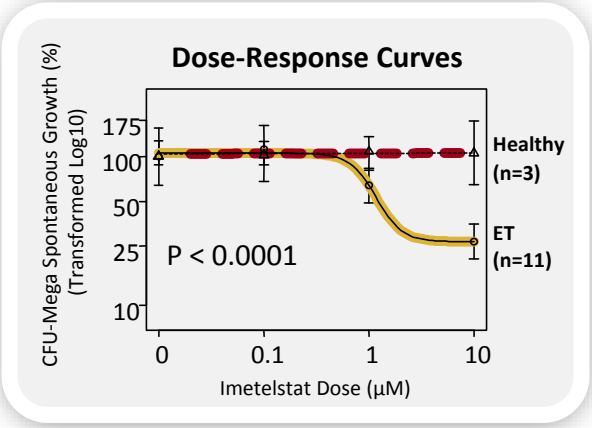
** Designates author as not being an ASH member*

Imetelstat: First-in-class Telomerase Inhibitor

- First telomerase inhibitor in clinical development
- 13-mer oligonucleotide with palmitoyl lipid tail
- Competitively binds to RNA template of telomerase
- Potent inhibitor of telomerase enzyme activity



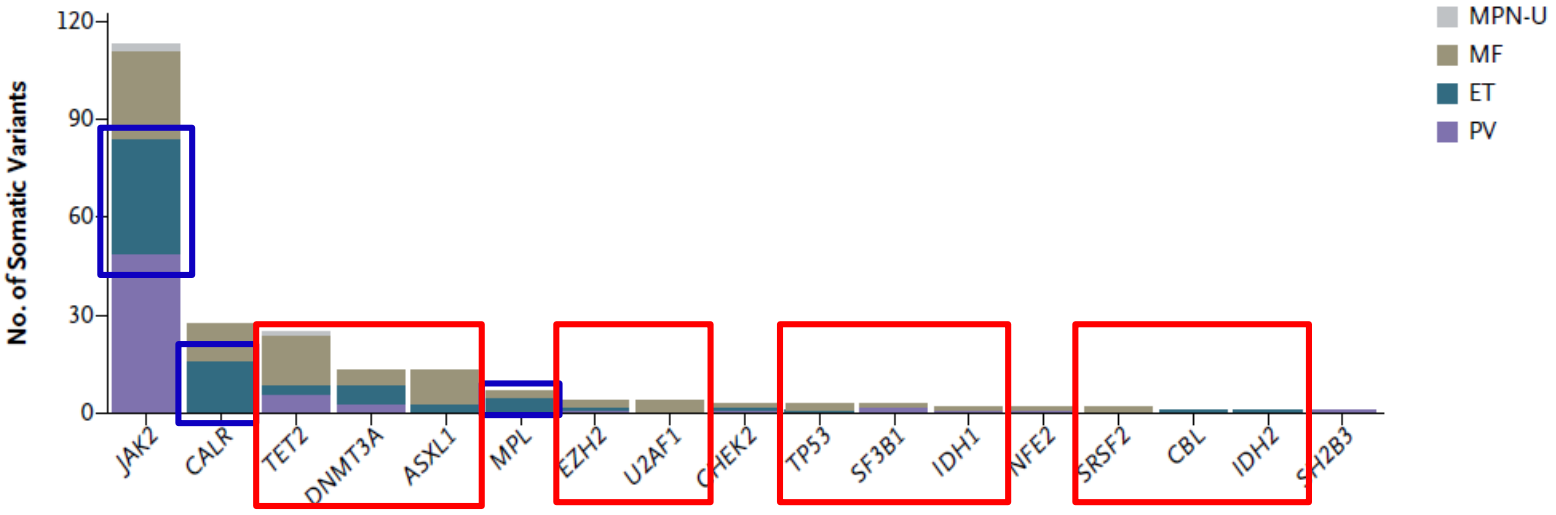
Imetelstat Reduces Neoplastic Progenitor Proliferation *in vitro*:



- Imetelstat inhibits neoplastic megakaryocyte growth from patients with ET but not from healthy individuals

Presented at the 2011 ASH Annual Meeting (Gabriela Baerlocher)

Background: Mutations in ET and Other MPNs



Nangalia J, et al., N Engl J Med. 2013

- Response to imetelstat in MF patients was negatively influenced by ASXL1 mutations and favorably impacted by SF3B1 and U2AF1 mutations

  Tefferi et al., ASH 2014

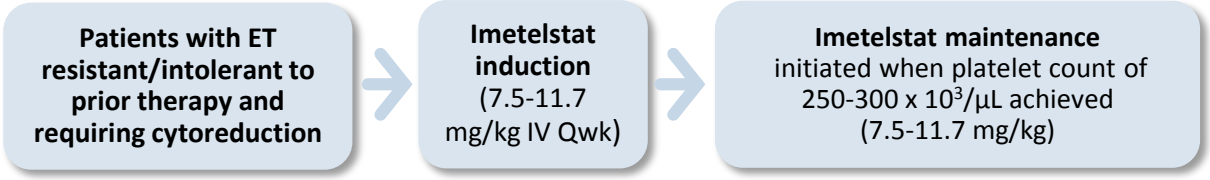
- Lower response to INFa therapy in CALR-mutated ET patients with >1 mutation

  Kiladjan et al., Blood 2015

- Resistance to INFa of TET2 mutant clones in JAK2-mutated PV

  Kiladjan et al., Leukemia 2010

Phase II Study Design



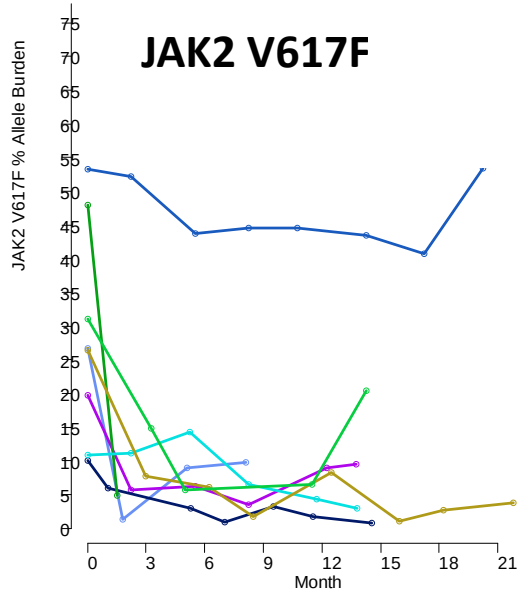
Endpoint	
Primary	• Best Overall Hematologic RR (CR + PR) within 1st yr of treatment
Secondary	• Duration of hematologic response
	• Molecular Response (JAK2 V617F /MPL W515^{mt} patients)
	• Safety and tolerability

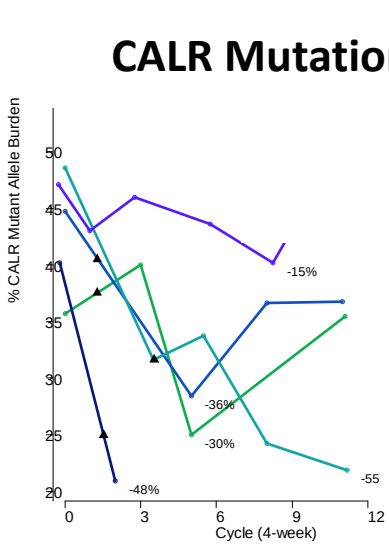
- 18 patients were enrolled in the study
- 4 patients were resistant to prior therapies, 9 were intolerant, and 5 were both
- Median time since diagnosis was 7.2 years (range 0.3-24.9)

Baerlocher GM, Oppliger Leibundgut E, et al. N Engl J Med. 2015

Previously Reported: Hematologic and Molecular Response

- All 18 patients had a hematologic response, with complete responses in 16
- Molecular responses were seen in 7/8 patients with JAK2 V617F
- CALR and MPL allele burdens were also reduced





Mutation types:

- 3 type 1
- 1 type 2
- 1 novel (c.1092_1124del)

Presented at the 2014 ASH Annual Meeting (Gabriela Baerlocher)

Aims

- To assess the dynamics of additional mutations besides *JAK2* V617F, *CALR* and *MPL* mutations as an additional exploratory endpoint
- To investigate their association with clinical, hematologic and molecular response

Methods

- Mutational screening was performed by targeted sequencing using AmpliSeq technology on the Ion Torrent PGM instrument.
- The custom-designed gene panel covered the coding and adjacent intronic sequences of 15 genes, and a pre-designed gene panel was used for TP53.
- The mean coverage was 1474x. Additional annotations were performed using COSMIC version 37, ClinVar, PolyPhen-2, SIFT and IARC TP53.

Gene panel

ASXL1, CBL, DNMT3A, EZH2, IDH1, IDH2, JAK2, MPL, SF3B1, SRSF2, SOCS1, TET2, TP53, U2AF1 and ZRSR2

Additional Mutations at Baseline by Driver Mutation

	Driver Mutation				
Additional Mutation (Baseline)	**CALR (N=5)**	**JAK2 V617F (N=9)**	**MPL (N=2)**	**Triple-neg (N=2)**	**Total (N=18)**
ASXL1	-	1 (11%)	-	-	1 (6%)
DNMT3A	1 (20%)	2 (22%)	1 (50%)	-	4 (22%)
TET2	2 (40%)	1 (11%)	-	-	3 (17%)
CBL	-	1 (11%)	-	-	1 (6%)
EZH2	1 (20%)	-	-	-	1 (6%)
TP53	2 (40%)	4 (44%)		-	6 (33%)
Spliceosome (SF3B1, U2AF1, ZRSR2)	1 (20%)	1 (11%)	1 (50%)	1 (50%)	4 (22%)
# of Patients with Any Additional Mutation	2 (40%)	6 (67%)	1 (50%)	1 (50%)	10 (56%)

Individual patients may have mutations in more than one gene

Additional mutations were observed at baseline in all driver mutation subgroups

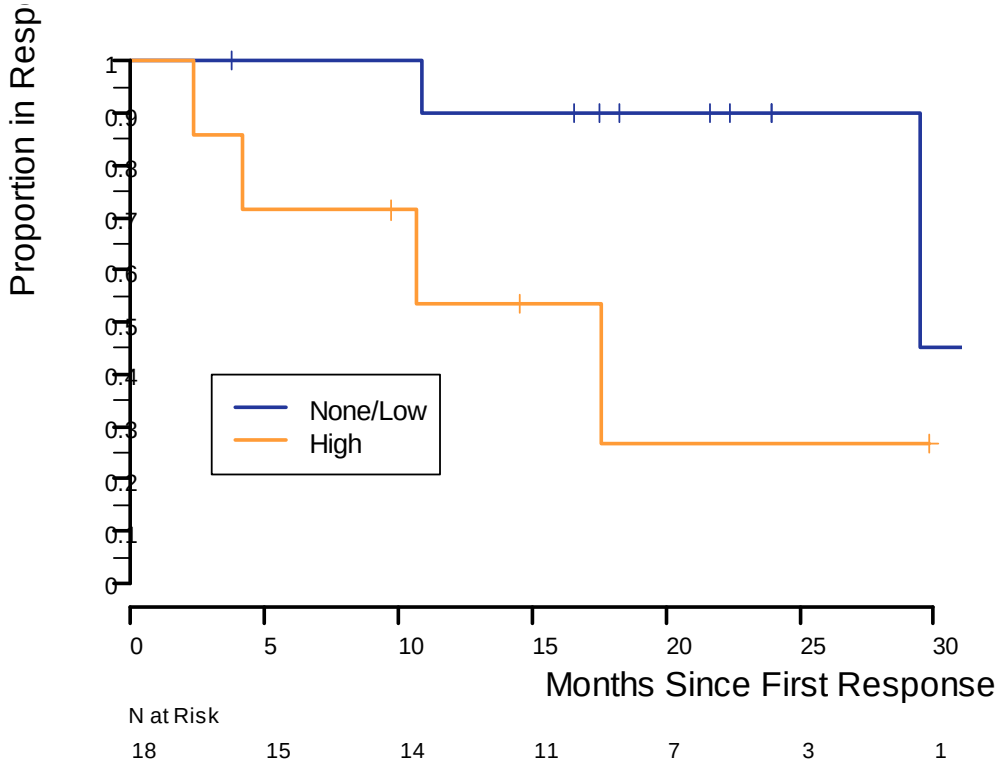
Clinical Features by Level of Additional Mutations at Baseline

	None / Low Level (N=11)	High Level [a] (N=7)
Age, median	56	61
Years Since Diagnosis, mean	8.6	9.3
# Prior Therapies, median	2	3
Doses per Cycle, Cycles 4-6, mean	1.5	1.7
Hematologic CR	10 (91%)	6 (86%)
Best Driver Mutation Allele Burden Reduction, mean[b]	-65%	-57%
Thromboembolic Event	1 (9%)	2 (29%)
Loss of Platelet Response to Therapy	1 (9%)	2 (29%)
Transformation to MF	1 (9%)	2 (29%)

a. High Level is defined as total additional mutant allele burden at baseline > 20%
b. N=16 for this analysis; Triple-negatives are excluded.

7 / 18 of patients (39%) had High Level additional mutant allele burden at baseline

Duration of Response by Allele Burden of Additional Mutations at Baseline

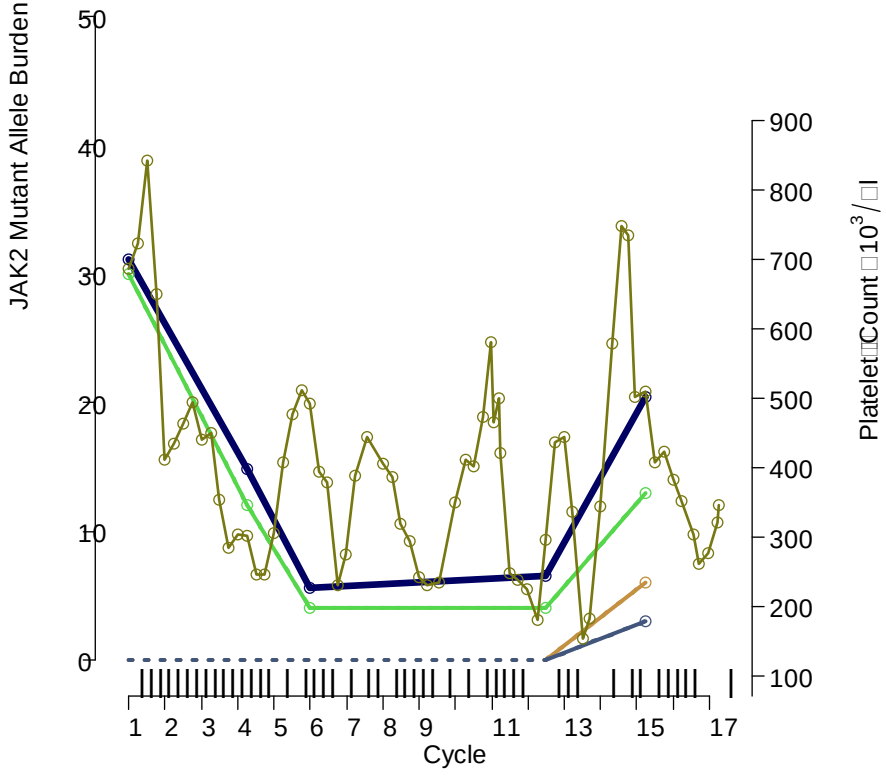


	None / Low N=11	High N=7
# of Events[a]	2	4
Hazard Ratio (95% CI)	1.5 (0.8, 26.1)	
P-value	0.053	

a. Loss of response due to thromboembolic event, resistance to treatment or progression to MF.

Patients with a high total additional mutant allele burden at baseline had a shorter duration of response (18 months vs 30 months).

Patient with an ASXL1 Mutation and Advanced Disease

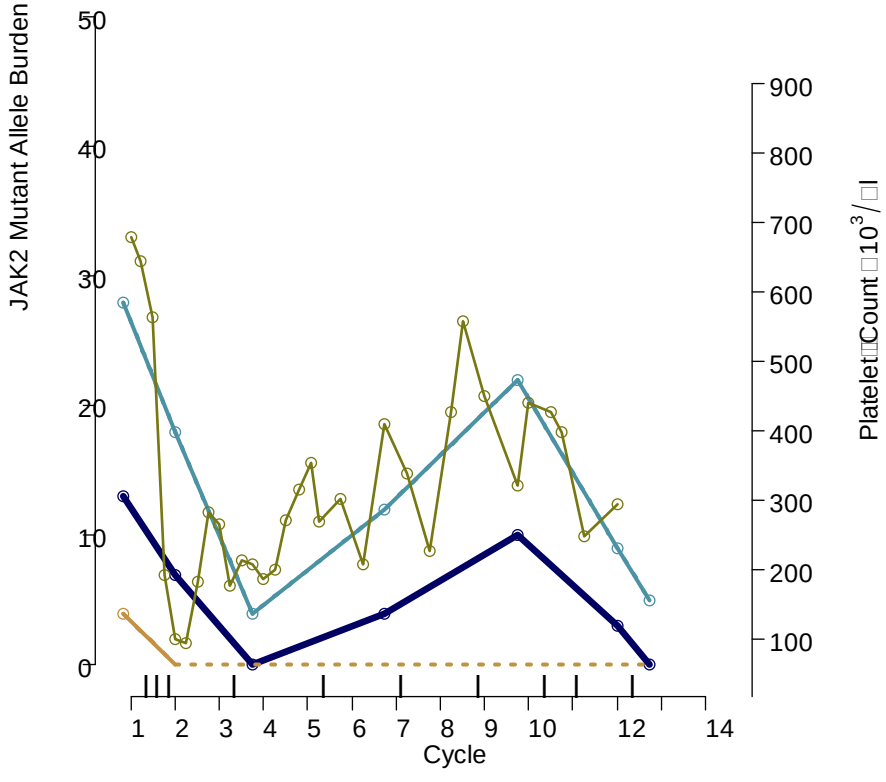


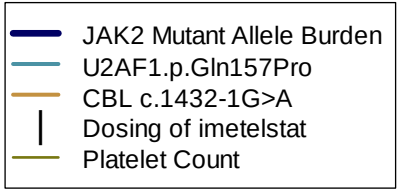
- Good initial molecular response
- Frequent dosing required to maintain response for 11 months
- Late-emerging TET2 and TP53 mutation were observed
- 7 months after imetelstat termination the patient transformed to MF

Patient 17	
Sex/Age	F/61
Years Since Diagnosis	11
# Prior Therapies	3
Doses per Cycle, Cycles 4-6 (percentile)	2.7 (83rd)
Hematologic Response	CR
DoR (months)	10.7
Thromboembolic Event	Yes[a]
Transformation to MF	Yes
Loss of Platelet Response to Therapy	No

a. Grade 2 retinal ischaemia

Patient with a U2AF1 Mutation

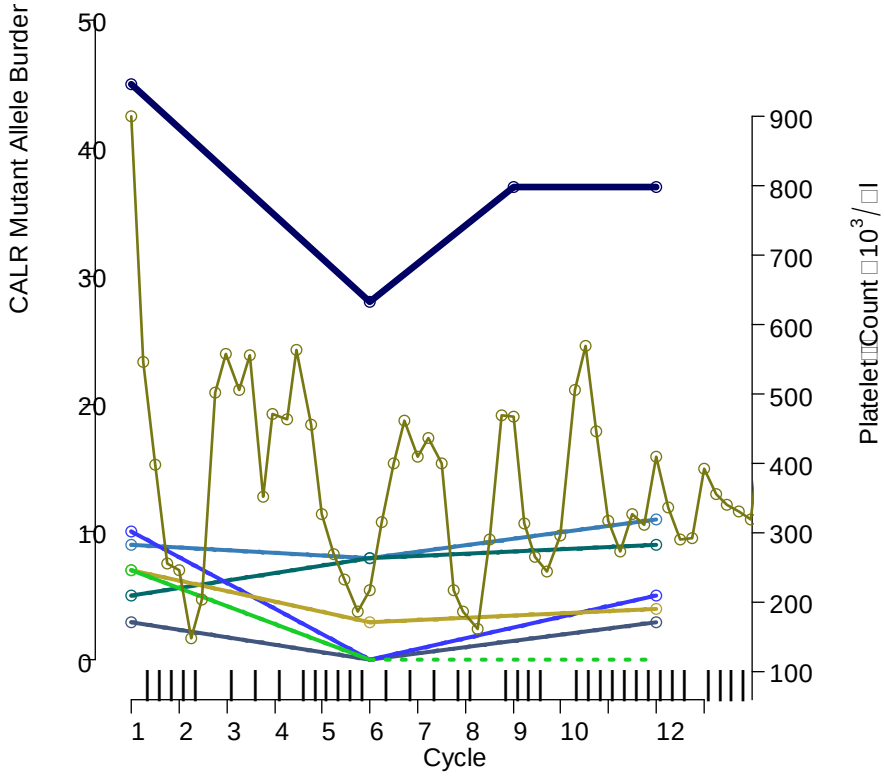




- Rapid molecular response
- Only infrequent dosing required to maintain platelet levels
- Mutant allele levels fluctuated with dosing

Patient 9	
Sex/Age	M/48
Years Since Diagnosis	1.3
# Prior Therapies	1
Doses per Cycle, Cycles 4-6 (percentile)	.67 (33rd)
Hematologic Response	CR
DoR (months)	9.7+
Thromboembolic Event	No
Transformation to MF	No
Loss of Platelet Response to Therapy	No

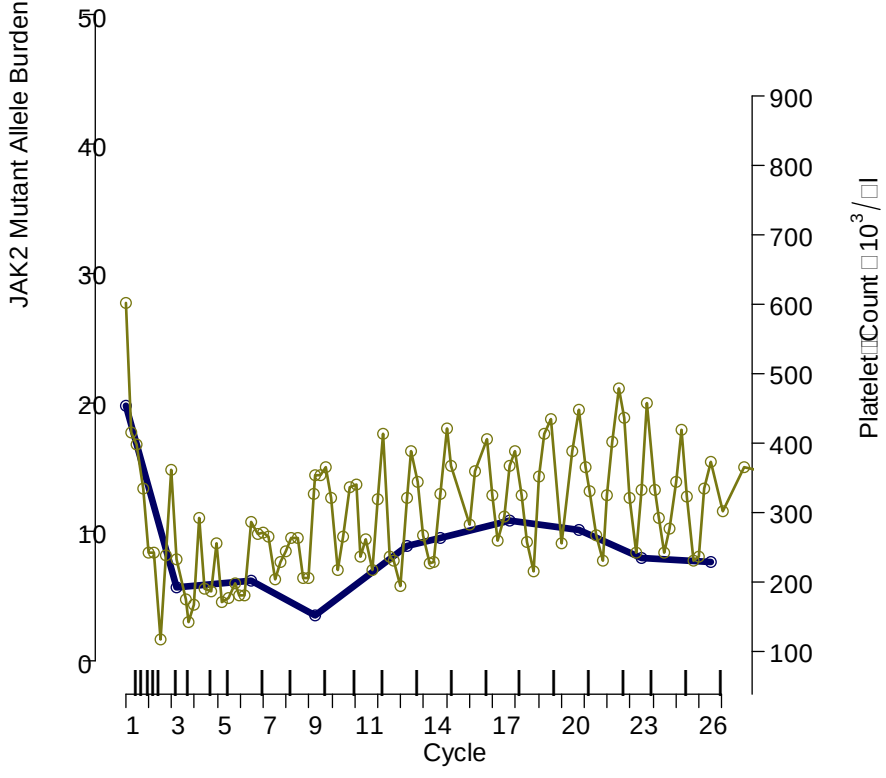
Patient with Multiple Mutations



- Disease was genetically complex after 20 years
- Initial CALR mutant reduction was not sustained
- Patient required frequent dosing and became resistant

Patient 4	
Sex/Age	F/67
Years Since Diagnosis	20
# Prior Therapies	3
Doses per Cycle, Cycles 4-6 (percentile)	3 (89^{th})
Hematologic Response	CR
DoR (months)	17.6
Thromboembolic Event	No
Transformation to MF	Yes
Loss of Platelet Response to Therapy	Yes

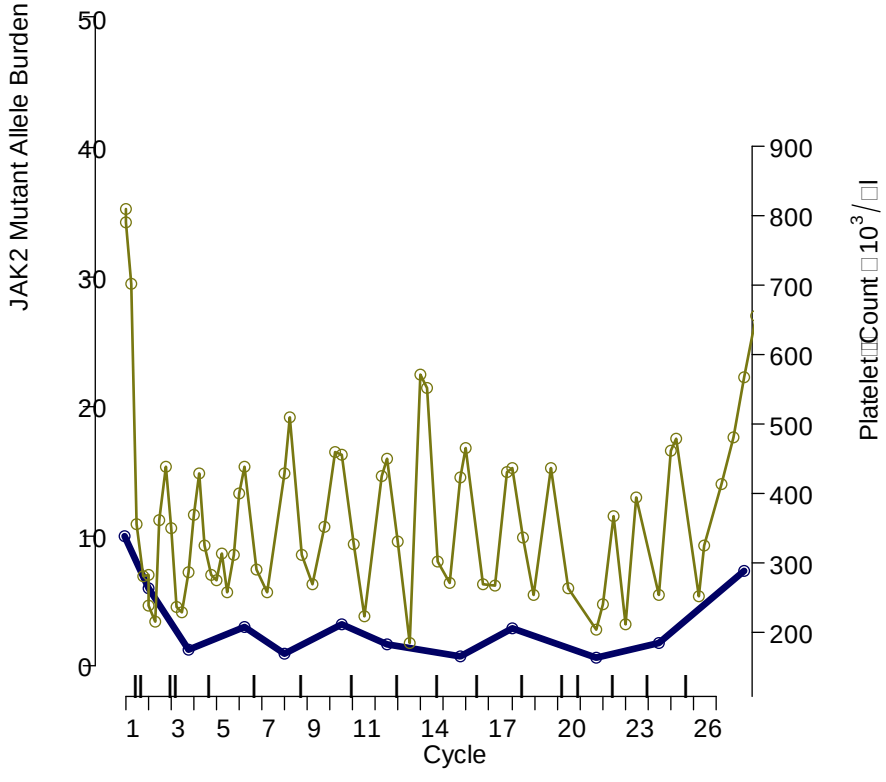
JAK2 V617F Mutated Male Patient with No Additional Mutation



- Patient with rapid and durable molecular response and good clinical outcome

Patient 3	
Sex/Age	M/60
Years Since Diagnosis	3.3
# Prior Therapies	3
Doses per Cycle, Cycles 4-6 (percentile)	1 (44th)
Hematologic Response	CR
DoR (months)	24+
Thromboembolic Event	No
Transformation to MF	No
Loss of Platelet Response to Therapy	No

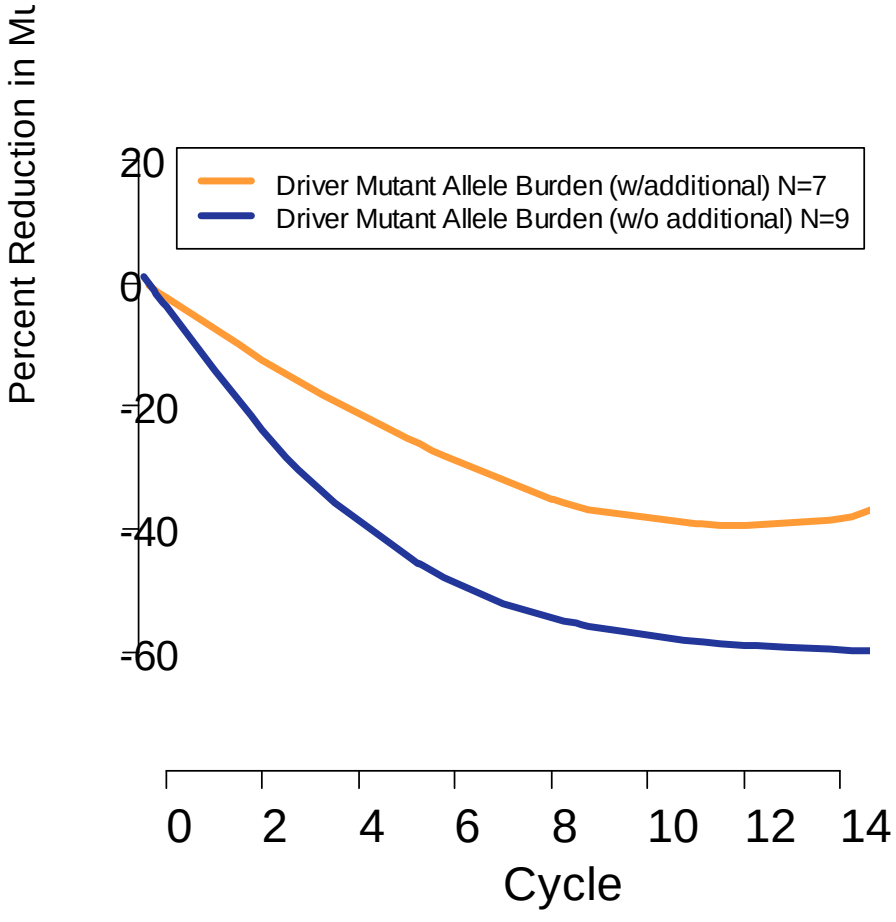
JAK2 V617F Mutated Female Patient with No Additional Mutation



- Patient with rapid and durable molecular response and good clinical outcome

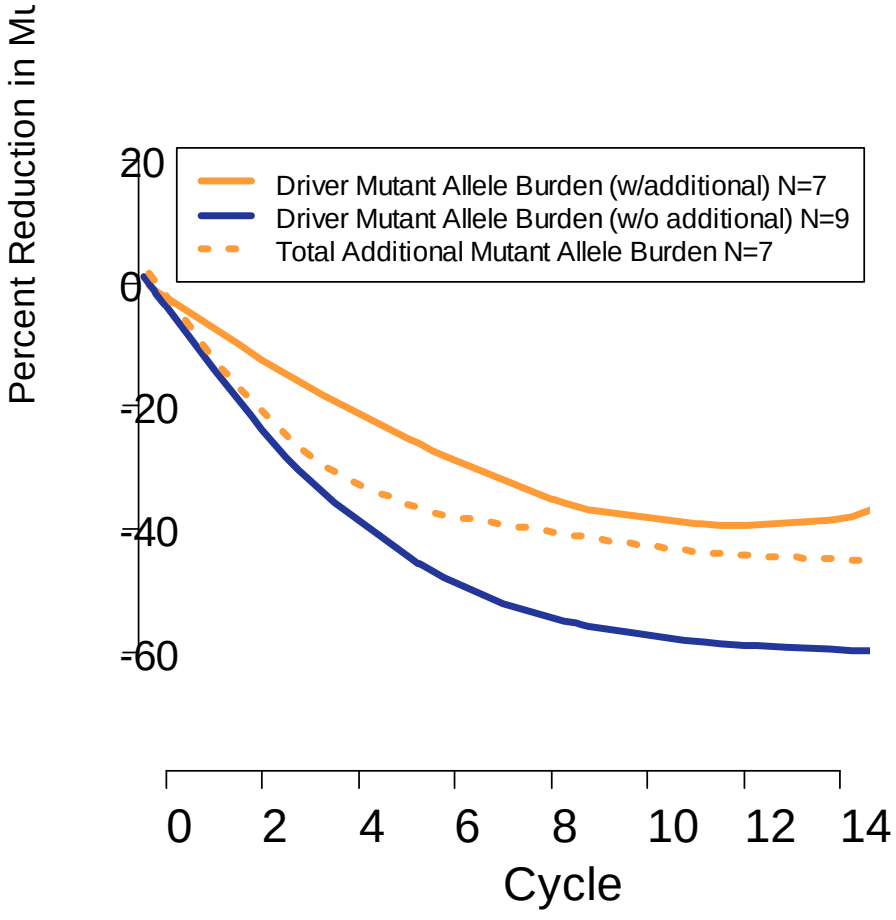
Patient 5	
Sex/Age	F/55
Years Since Diagnosis	0.3
# Prior Therapies	1
Doses per Cycle, Cycles 4-6 (percentile)	0.67 (33rd)
Hematologic Response	CR
DoR (months)	25+
Thromboembolic Event	No
Transformation to MF	No
Loss of Platelet Response to Therapy	No

Average Driver and Additional Mutation Allele Burden Over Time



- Driver mutation response appears deeper and more prolonged in patients with additional mutant allele burden lower than 5%

Average Driver and Additional Mutation Allele Burden Over Time



- Driver mutation response appears deeper and more prolonged in patients with additional mutant allele burden lower than 5%
- Additional mutant allele burden declines with driver mutant allele burden

Conclusions

Imetelstat treatment reduces allele burdens of non-driver mutations

- 50% of these highly pretreated patients carried 1-6 mutations in addition to the driver mutation, suggesting genetic instability
- The majority of mutated clones were suppressed by imetelstat treatment and tracked with the driver mutation
- High-level additional mutations at baseline correlated with shorter duration of response ($p= 0.053$)
- Overall, most patients in this study reached rapid and sustained hematologic and molecular responses within 3-6 cycles of treatment

These data confirm imetelstat's potential to inhibit concomitant neoplastic clones in patients with ET

Acknowledgements

All of the patients, caregivers and staff who have participated in this study

and

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Telomerase Inhibitor Imetelstat Therapy in Refractory Anemia with Ring Sideroblasts with or without Thrombocytosis

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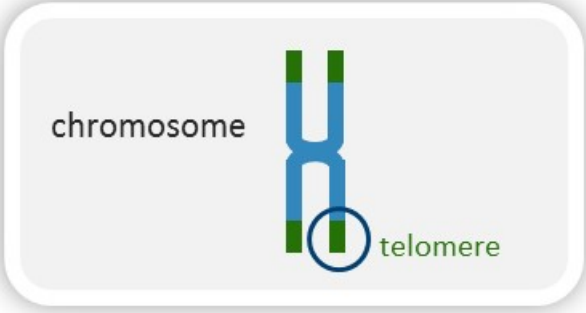
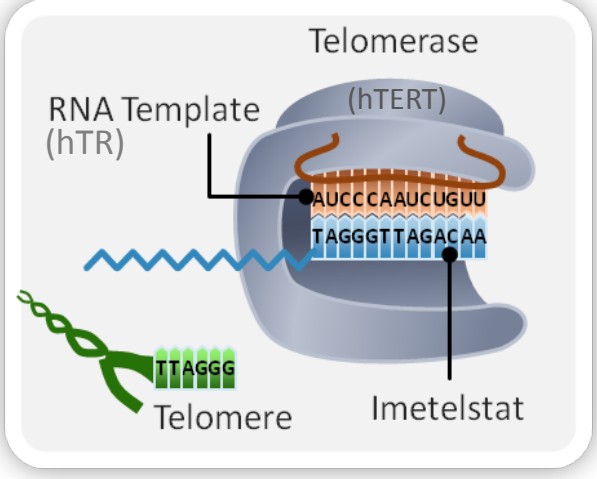
Imetelstat: A Telomerase Inhibitor



Imetelstat binds to RNA template preventing maintenance of telomeres



Telomerase enzyme:

- Reverse transcriptase comprised of an RNA component (hTR) and a reverse transcriptase catalytic protein subunit (hTERT)
- Binds to the 3' strand of DNA and adds TTAGGG nucleotide repeats to offset the loss of telomeric DNA occurring with each replication cycle
- Not active in somatic cells; **transiently upregulated in normal hematopoietic progenitor cells to support controlled proliferation**
- **Highly upregulated in malignant progenitor cells, enabling continued and uncontrolled proliferation**

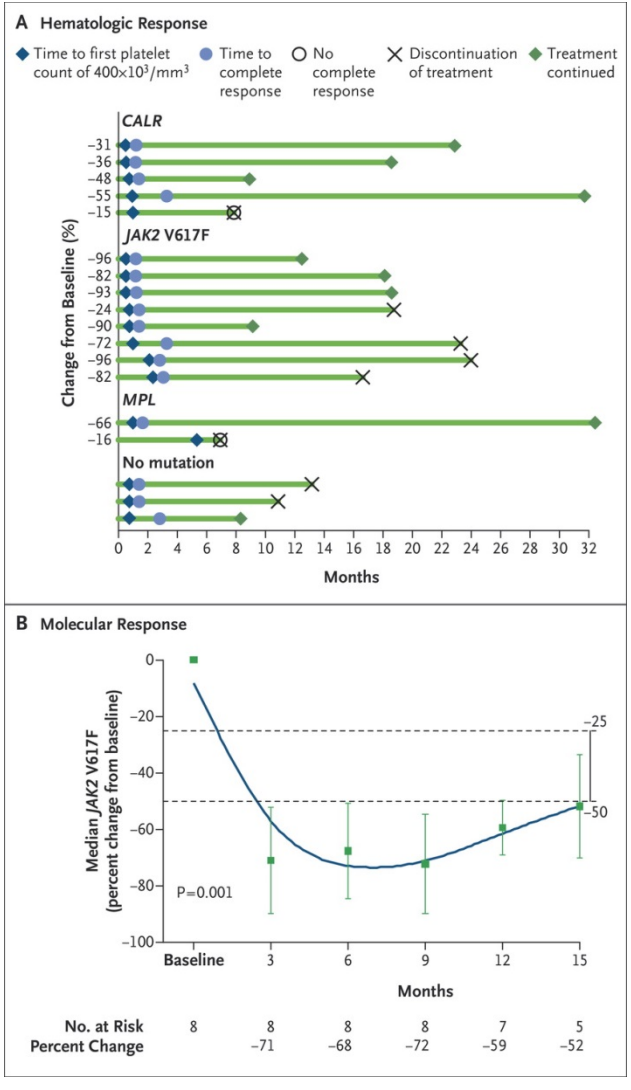
Imetelstat:

- **Proprietary:** 13-mer thio-phosphoramidate oligonucleotide complementary to hTR, with covalently-bound lipid tail to increase cell permeability/tissue distribution
- **Long half-life** in bone marrow, spleen, liver (estimated human t½ = 41 hr with doses 7.5 – 11.7 mg/kg);
- **Potent competitive inhibitor of telomerase**: IC_{50} = 0.5-10 nM (cell-free)
- **Target:** malignant progenitor cell proliferation

1. Dikmen ZG et al. *Cancer Res* 2005;65(17):7866-73; 2. Hochreiter AE et al. *Clin Cancer Res* 2006;12(10):3184-92; 3. Joseph I et al. *Cancer Res* 2010;70(22):9494-504)

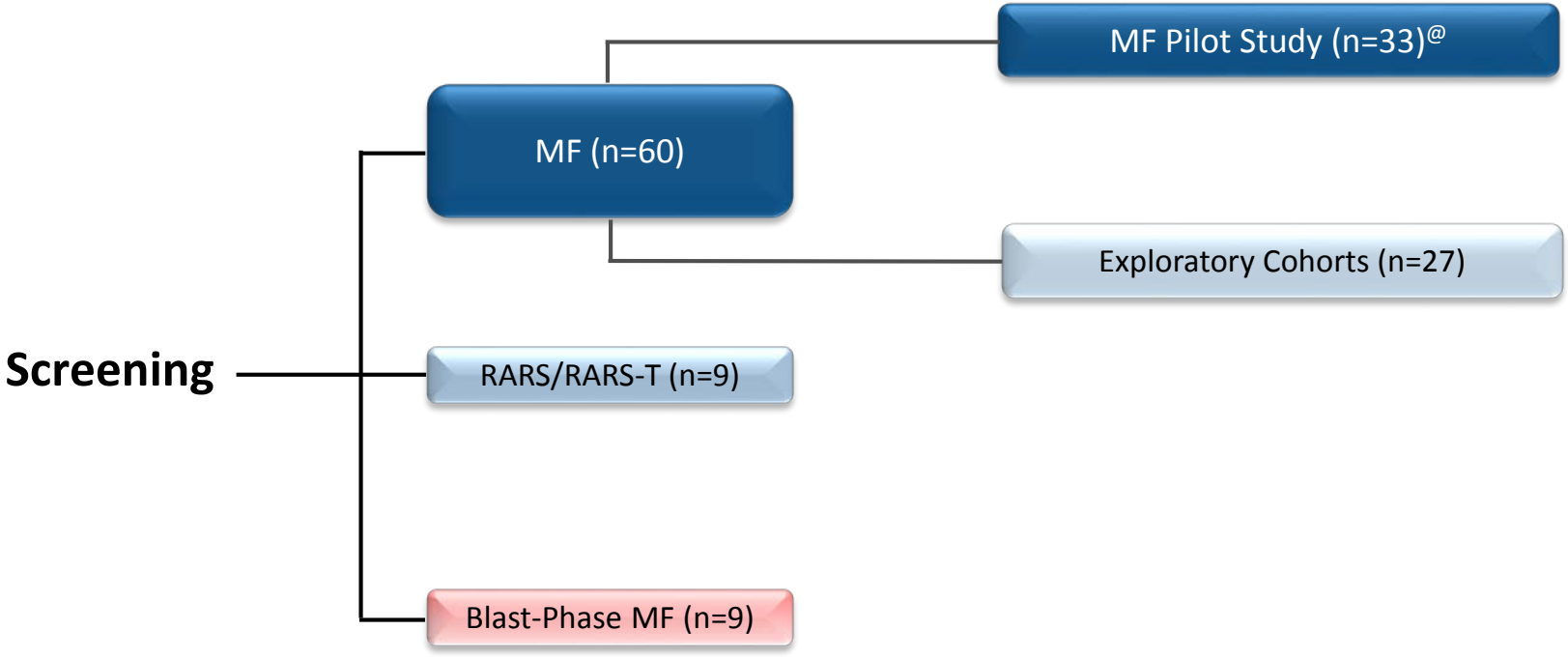
Hematologic and Molecular Responses in ET Patients who Received Imetelstat

- CR in 16 (89%) of 18 patients
- PR in the remaining 2 (11%)
- Median time to CR 1.4 months
- Partial molecular response in 7 of 8 *JAK2* mutated cases
- Molecular responses also seen with *CALR* and *MPL* mutated cases



Baerlocher GM et al. *N Engl J Med* 2015;373:920-928.

Study Overview



@Dose: Imetelstat, 2-hour intravenous infusion of 9.4 mg/kg every 3 weeks for Arm A and 9.4 mg/kg every week x 4 and then every 3 weeks for Arm B.

Rationale for the Current Study: Imetelstat Activity in Myelofibrosis

	Total (N = 33)
Best Response by IWG-MRT	N (%)
Overall Response (CR+PR+CI)	12 (36.4%)
Complete Remission (CR)	4 (12.1%)
Partial Remission (PR)	3 (9.1%)
Clinical Improvement (CI) by Anemia	1 (3.0%)
Clinical Improvement (CI) by Spleen	4 (12.1%)
Stable Disease (SD)	21 (63.6%)

CR/PR: 21.2%

- All 4 CR patients achieved reversal of BM fibrosis and 3 achieved complete molecular response
- 3 CR/PR patients who were transfusion dependent at baseline became transfusion independent
- 4 CR/PR patients with splenomegaly at baseline achieved splenic response

Tefferi A et al. *N Engl J Med* 2015;373(10):908-19

Key Molecular Profile of Myelofibrosis Patients Treated with Imetelstat and Achieved Complete (CR) or Partial (PR) Remission

CR/PR	*JAK2* Mutation	*ASXL1* Mutation	*CALR* Mutation	Spliceosome Mutation	IDH Mutation
CR	Y	N	N	*U2AF1*	N
CR	Y	N	N	*U2AF1*	N
CR	Y	N	N	N	N
CR	Y	N	N	*SF3B1*	N
PR	Y	N	N	*SRSF2*	N
PR	Y	N	N	N	N
PR	Y	N	N	N	N

Tefferi A et al. *N Engl J Med* 2015;373(10):908-19

Association Between Response and Molecular Markers in Myelofibrosis Patients Treated with Imetelstat

CR/PR by Mutation Status

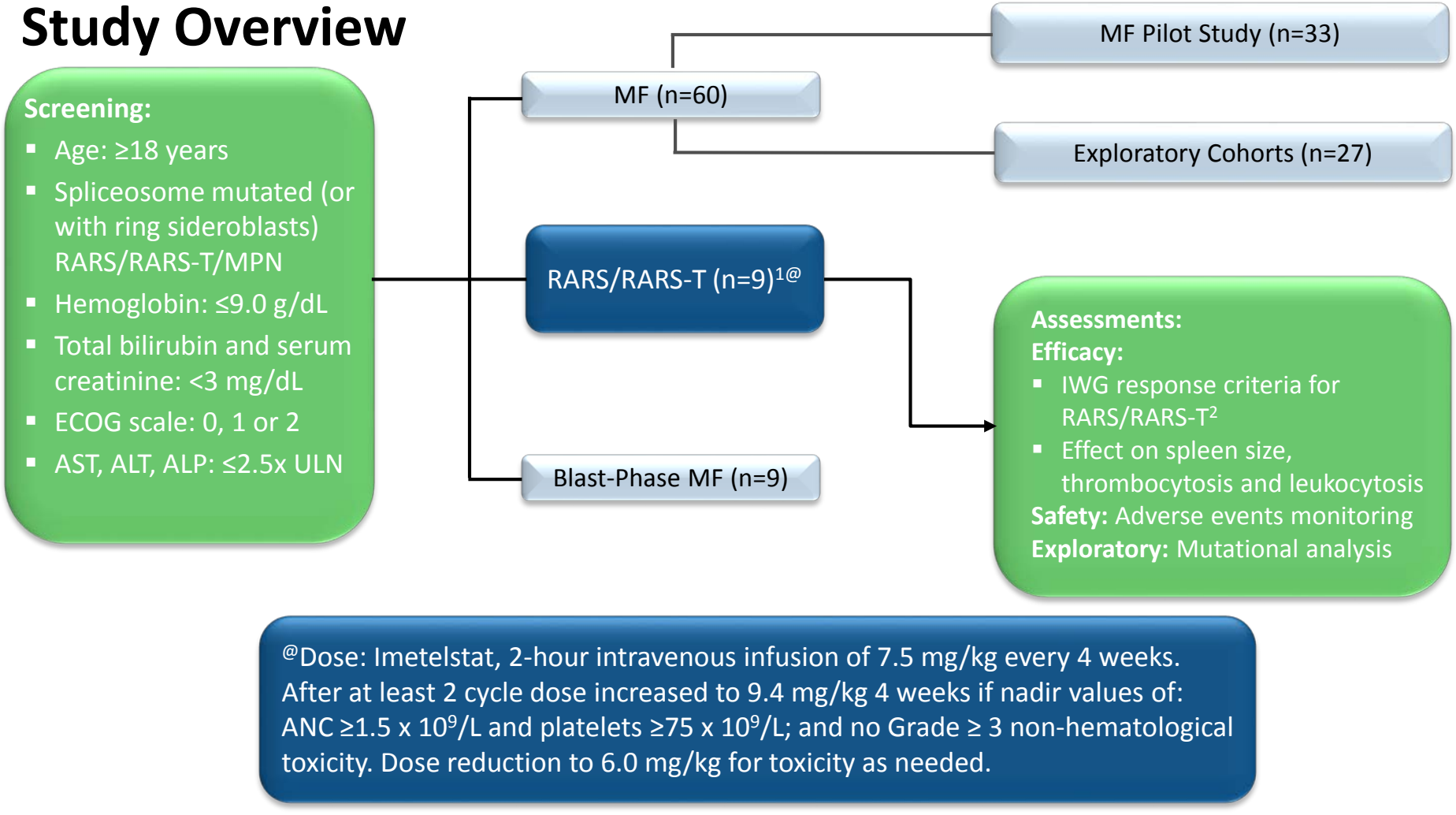
Mutation Type	Mutant	WT	P-value¥
Spliceosome	4/11 (36.4%)	3/22 (13.6%)	0.186
SF3B1/U2AF1	3/8 (37.5%)	4/25 (16.0%)	0.32
JAK2V617F	7/26 (26.9%)	0/7 (0%)	0.299
ASXL1	0/11 (0%)	7/22 (31.8%)	0.067
CALR	0/6 (0%)	7/27 (25.9%)	0.301

CR by Mutation Status

Mutation Type	Mutant	WT	P-value¥
Spliceosome	3/11 (27.3%)	1/22 (4.5%)	0.097
SF3B1/U2AF1	3/8 (37.5%)	1/25 (4.0%)	0.036
U2AF1	2/5 (40.0%)	2/28 (7.1%)	0.099
JAK2V617F	4/26 (15.4%)	0/7 (0%)	0.555
ASXL1	0/11 (0%)	4/22 (18.2%)	0.276

Tefferi A et al. *N Engl J Med* 2015;373(10):908-19

Study Overview



@Dose: Imetelstat, 2-hour intravenous infusion of 7.5 mg/kg every 4 weeks. After at least 2 cycle dose increased to 9.4 mg/kg 4 weeks if nadir values of: ANC ≥1.5 x 10^9/L and platelets ≥75 x 10^9/L; and no Grade ≥ 3 non-hematological toxicity. Dose reduction to 6.0 mg/kg for toxicity as needed.

1. Vardiman JW et al. *Blood* 2009;114(5):937-51; 2. Cheson BD et al. *Blood* 2006; 108(2):419-25.

Results: Demographics and Baseline Characteristics

Parameter	RARS/RARS-T Patients (N = 9)
Median Age (Range; Years)	70 (54-93)
Men, n (%)	7 (78)
RARS/RARS-T Subtype, n (%)	
RARS	3 (33)
RARS-T	5 (56)
RARS/RARS-T/MPN Overlap	1 (11)
Median Hemoglobin (Range; g/dL)	8.4 (6.7-9.8)
IPSS Risk Category, n (%)	
Intermediate-1	7 (78)
Intermediate-2	2 (22)
Previously Treated, n (%)	7 (78)
Prior Treatments, Median (Range)	3 (1-4)
Prior ESA, n (%)	6 (67)
Prior Lenalidomide, n (%)	3 (33)
Abnormal Karyotype, n (%)	2 (22)
Transfusion Dependent, n (%)	8 (89)
Marked Splenomegaly, n (%)	1 (11)
Leukocytosis, n (%)	3 (33)
Thrombocytosis, n (%)	3 (33)

ESA, erythropoiesis-stimulating agents; IPSS, International prognostic scoring system; MF, myelofibrosis; MPN, myeloproliferative neoplasms; RARS, refractory anemia with ring sideroblasts; RARS-T, refractory anemia with ring sideroblasts with thrombocytosis

Grade ≥3 Non-Hematologic AEs[@]

Event	RARS/RARS-T Patients, (N=9) n (%)
Aspiration	1 (11)
Fatigue	1 (11)
Lipase increased	1 (11)
Heart failure[#]	1 (11)
Hypotension[#]	1 (11)
Hypocalcaemia[#]	1 (11)
Hyperglycemia[#]	1 (11)
Duodenal ulcer[#]	1 (11)
Hypoalbuminemia[#]	1 (11)
Cardiac arrest[#$]	1 (11)

[@] Excluded liver function test abnormalities

[#]All events occurred in a single patient

[$]Grade 5 event, with pre-existing cardiovascular disease history and unrelated to imetelstat

Liver Function Tests: Worsening from Baseline

		Worst Post-Baseline CTC Grade (N=9)	
	Any Worsening n (%)	1 n (%)	2 n (%)
ALP	6 (67)	5 (56)	1 (11)
AST	6 (67)	5 (56)	1 (11)
ALT	3 (33)	3 (33)	0
Total Bilirubin	1 (11)	0	1 (11)

Worsened defined as CTC grade elevated after baseline

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTC, common terminology criteria

- No discontinuations due to liver function test abnormalities
- These abnormalities were mostly reversibly, especially after treatment termination

Grade 3-4 Hematologic Toxicities

	Worst Grade	RARS/RARS-T Patients, (N = 9) n (%)
Anemia	3	6 (67)
	4	–
Neutropenia	3	4 (44)
	4	2 (22)
Thrombocytopenia	3	2 (22)
	4	1 (11)

- Mild/Moderate cytopenias present at baseline
  - Anemia: Grade 2 = 6 patients and Grade 3 = 3 patients
- No prolonged (≥4 Weeks) Grade ≥3 hematological toxicities observed

Treatment Discontinuations

Patient Status and Reason for Treatment Discontinuation	RARS/RARS-T Patients (N=9) n (%)
On Treatment	4 (44)
Discontinued Treatment	5 (56)
Insufficient Response or Alternative Therapy	2 (22)
Disease Progression/Relapse	1 (11)
Death*	1 (11)
Adverse Event/Side Effects/Complications**	1 (11)

*Cardiac arrest in patient with pre-existing cardiovascular disease history and unrelated to imetelstat

**Discovery of second malignancy

RARS, refractory anemia with ring sideroblasts; RARS-T, refractory anemia with ring sideroblasts with thrombocytosis.

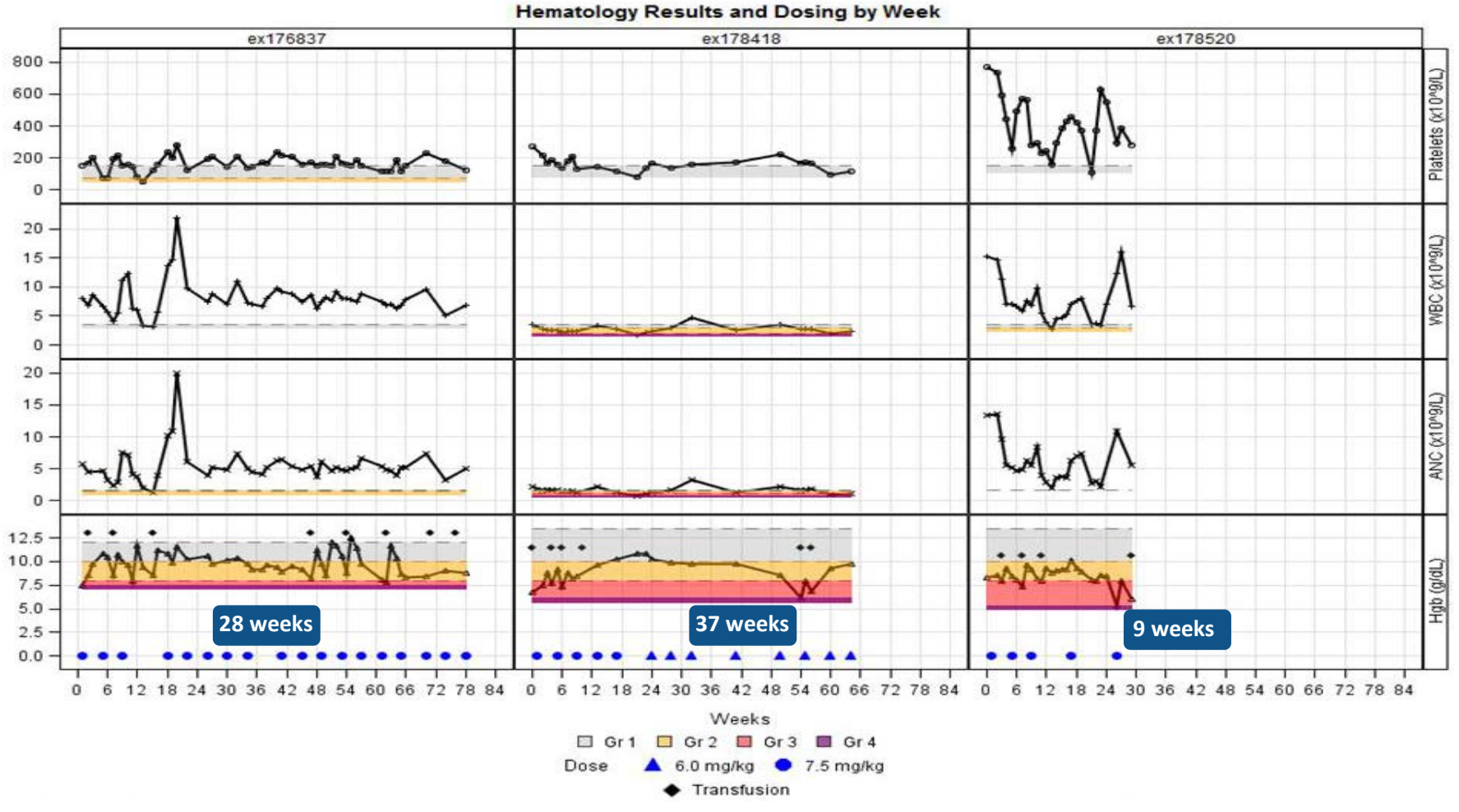
Transfusion Independence in Imetelstat Treated Patients

- **Total RARS/RARS-T patients: N=9; 8 of 9 were TD**
  - TD definition prior study entry: 4 units/8 weeks
- **RBC-TI: 3 out of 8 patients (37.5%)**
  - TI definition: transfusion free for rolling 8-week period
  - Median TI duration = 28 weeks (9-37 weeks)

	Time to TI (weeks)	TI Duration (weeks)
RARS/RARS-T Patient 1	9	28
RARS/RARS-T Patient 2	14	37
RARS/RARS-T Patient 3	11	9

TD, transfusion-dependence; TI, transfusion-independence; RARS, refractory anemia with ring sideroblasts; RARS-T, refractory anemia with ring sideroblasts with thrombocytosis.

Transfusion Independence Duration of Responders on the Study



Additional Clinical Benefits

	Clinical Benefit
RARS/RARS-T Patient 4	>50% decrease in palpable spleen size (16 cm at baseline)
	Decrease in transfusion rate: 6 units prior to treatment to 2 units on treatment
RARS/RARS-T Patient 5	Neutrophil and platelet count normalization
RARS/RARS-T Patient 6	Neutrophil and platelet count normalization
RARS/RARS-T Patient 7	Erythroid hematologic improvement (hemoglobin increased by 1.5 mg/dL)

Note: 1 of 3 transfusion independent patients had resolution of leukocytosis and thrombocytosis.

Mutation Status

- *JAK2* mutation: *n* =3
- *SF3B1* mutation: *n* = 7 (K700E = 4; H662Q = 2; K666N = 1)
- Post-treatment analysis showed no effect on mutations

CONCLUSION

Imetelstat has clinically meaningful activity in some patients with RARS or RARST and the safety profile is acceptable enough to warrant further studies in these and related MDS.

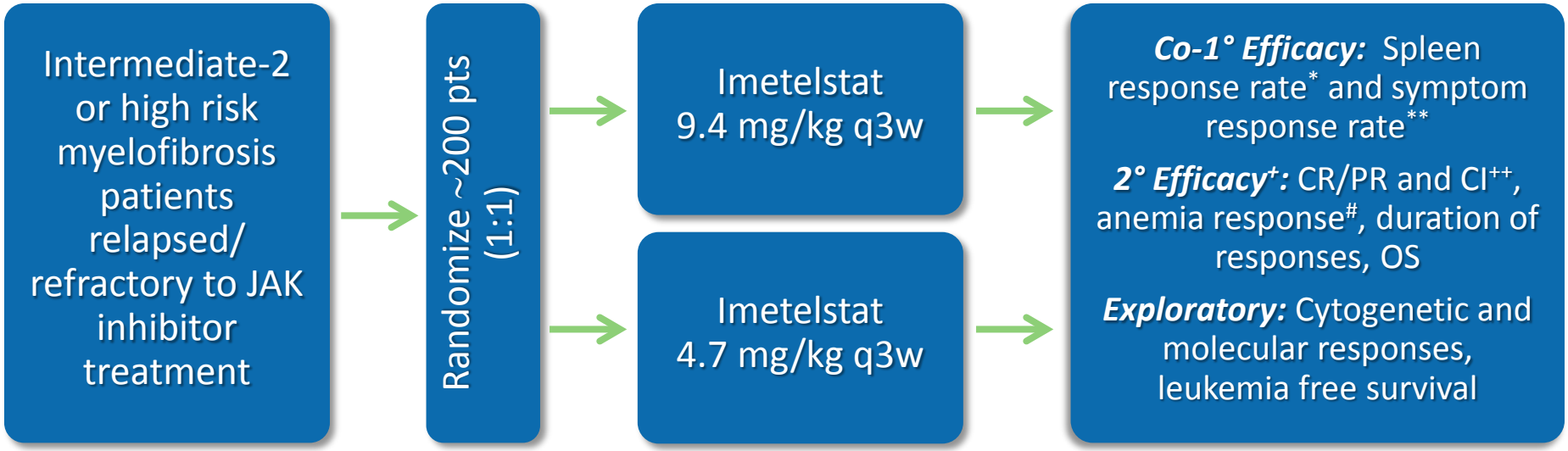
- **Possible explanations for the less than expected rate and depth of response to imetelstat, in RARS/RARST, compared to that seen in *SF3B1/U2AF1* mutated patients with myelofibrosis**
  - Use of a lower dose regimen in RARS/RARS-T (7.5 mg/kg every 4 weeks) vs MF (9.4 mg/kg every 3 weeks)
  - Differences in mutation content, clone size or hierarchy of clonal acquisition
  - Other differences in disease biology

Overview of IMbark™ and IMerge™ Studies under Collaboration Agreement with Janssen

Phase 2 Trial in Myelofibrosis (IMbark™)

An open label, single-blind study being conducted by Janssen Biotech, Inc.

- Multi-center across North America, Europe, and Asia
- Objectives: Define proper dosing and confirm efficacy using current validated regulatory endpoints
- Opened for enrollment in July 2015; first patient dosed in September 2015



* Spleen response rate defined as the percentage of participants who achieve a ≥35% reduction in spleen volume at Week 24 from baseline measured by imaging scans.

** Symptom response rate defined as the percentage of participants who achieve ≥50% reduction in Total Symptom Score (TSS) at Week 24 from baseline as measured by the modified Myelofibrosis Symptom Assessment Form (MFSAF) version 2.0 diary.

+ Complete list of secondary endpoints can be found on clincialtrials.gov.

++ Complete remission (CR) or partial remission (PR), and clinical improvement (CI) per modified 2013 IWG-MRT criteria.

Anemia response per 2013 IWG-MRT criteria.

q3w = every 3 weeks; OS = overall survival

IMbark™
Rationale for Study Design

Patient Population

Targets significant unmet medical need population

- No approved alternative therapies beyond Jakafi
- Median survival reported to be approximately 6 months
- 3-year discontinuation rate for Jakafi ~86%
  - Major reasons: loss of therapeutic effect and lack of response

Endpoints

Co-primary endpoints reflect current validated regulatory pathway

- Spleen response and symptom response were basis for approval of Jakafi

Secondary endpoints capture depth of responses

- To enable differentiation of imetelstat efficacy compared to JAK inhibitors
- To support imetelstat as a highly innovative and potentially transformative treatment

Dosing Arms

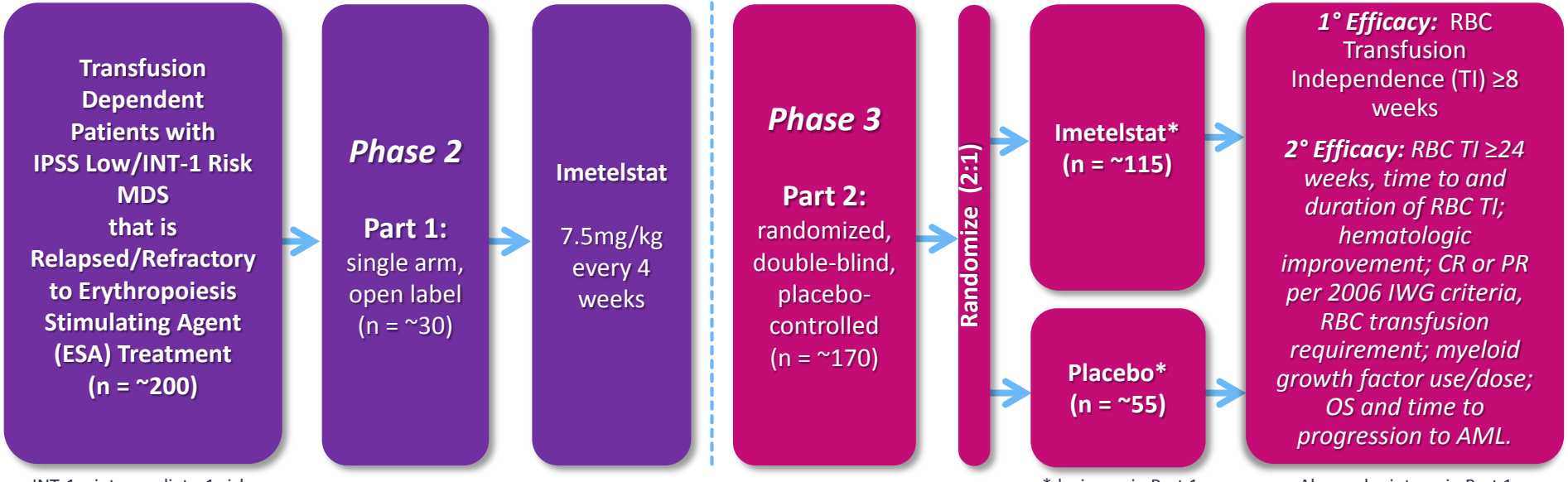
Covers potential therapeutic range of the drug

- 9.4 mg/kg q3w: appropriate max dosing regimen used in the MF pilot study
- 4.7 mg/kg q3w: lowest dose in which target engagement (telomerase inhibition) is predicted

Phase 2/3 Trial in MDS (IMerge™)

A two part, global, multi-center study to be conducted by Janssen Biotech, Inc.

- Objectives: Part 1 to evaluate safety and efficacy of imetelstat to advance to Part 2; Part 2 to compare imetelstat to placebo using a regulatory validated endpoint
- Part 2 enabled based on Janssen's assessment of a satisfactory benefit-risk profile
- **Opened for enrollment in December 2015**



INT-1 = intermediate-1 risk

*dosing as in Part 1

Also endpoints as in Part 1

Supportive care permitted in both arms: RBC transfusions, myeloid growth factors per investigator discretion as clinically needed and local guidelines

More information on ClinicalTrials.gov

IMerge™ Rationale for Study Design

Patient Population

Targets significant unmet medical need population

- Chronic anemia remains clinical problem in lower risk MDS
- No approved alternative therapies upon resistance or relapse to ESAs*

Endpoints

Primary endpoint reflects current validated regulatory pathway

- Transfusion independence can reduce potential for iron overload

Secondary endpoints capture depth of responses

- For potential differentiation of imetelstat efficacy compared to current therapies

Dosing Regimen

Same regimen as used in Mayo Clinic Pilot Study MDS-RARS cohort

- Dosing adjustments allowed in the study

*Except lenalidomide in the del 5q patients with transfusion-dependent anemia

Q&A