ASH 2013 Analyst & Investor Event

December 9, 2013

John A. Scarlett, MD
President & CEO

Forward-Looking Statements

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Agenda

- **Background: myelofibrosis and imetelstat**
- **Preliminary results from Mayo Clinic investigator-sponsored trial (IST) of imetelstat in myelofibrosis presented at ASH Annual Meeting (abstract #662)**
  - Geron's independent efficacy analysis of the first 22 MF patients enrolled in the study
  - Investigator's findings related to safety of the first 33 MF patients enrolled
- **Q&A**

Imetelstat for Treating Myelofibrosis – Top Line Observations

- **Geron's independent review of the data from the first 22 patients in the Mayo Clinic IST suggests that imetelstat has disease-modifying activity in MF**
  - Unprecedented remissions (CR+PR) by IWG-MRT criteria observed in 5/22 patients
  - Clinical improvement (CI) by IWG-MRT criteria observed in another 4/22 of patients
  - Overall response (CR+PR+CI) rate of 40.9% (9/22 patients)
- **Myelosuppression is the principal dose-limiting toxicity**
  - Believed to be an on-target toxicity due to effects on progenitor cells
  - Manageable through dose hold rules and dose modifications

Myelofibrosis and Imetelstat

Disease Characteristics and Unmet Medical Need

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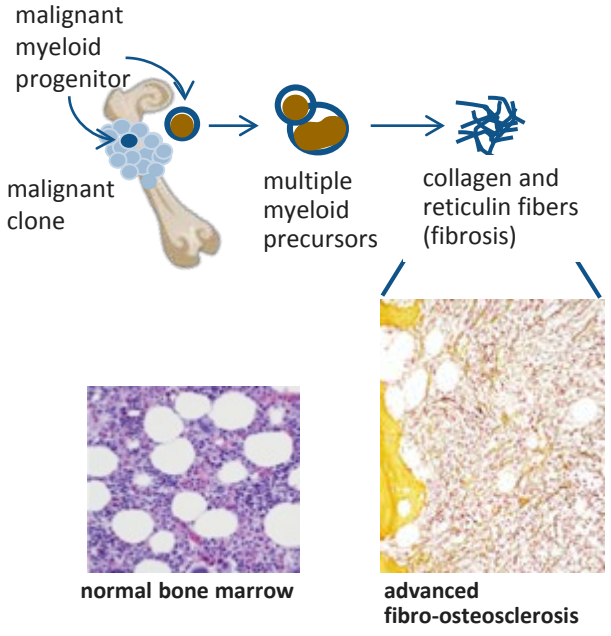
Myelofibrosis: A Disease Originating in the Bone Marrow

- Malignant clonal myeloproliferation and atypical megakaryocytic hyperplasia leads to bone marrow fibrosis and impaired hematopoiesis
- Fibrosis thought to be induced by cytokines produced by the malignant progenitor cell clone[1]
- Impaired bone marrow hematopoiesis shifts blood production to spleen and liver (palpable splenomegaly in up to 80%[2] of patients)
- Constitutional symptoms (e.g., fever, weight loss, night sweats, pruritis) present in approx. 35-50%[3] of patients are thought to be due to abnormal cytokine expression
- Serious and life-threatening illness
  - Leukemic transformation to AML
  - Thrombohemorrhagic complications associated with dysfunctional hematopoiesis

1. Blood 2008, 112(6):2190-8
2. J Clin Oncol 2011; 29:392-397
3. Mayo Clin Proc 2012; 87:25



DIPSS+ Risk Group	Score	Median Survival
Low risk	0	15.4 years
Intermediate-1 risk	1	6.5 years
Intermediate-2 risk	**2-3**	**2.9 years**
High risk	**4-6**	**1.3 years**

J Clin Oncol. 2011, 29(4):392-7

The Unmet Medical Need: Achieving Remissions

- **Allo-HCT (allogeneic hematopoietic cell transplantation) only current treatment that can result in complete remission of disease**
  - Generally limited to <10% patients due to lack of suitable donors, older age and co-morbidities
  - Though improved regimens available, still associated with significant morbidity, mortality and risk of relapse
- **Only rare, anecdotal reports of remissions with drug therapy**
  - Recent report of first case of BM fibrosis remission after 3 years of ruxolitinib treatment reflects the rarity of such events[1]
  - Interpretation of some literature reports confounded by inclusion of low risk and intermediate-1 patients with intermediate-2 and high risk

1. Haematologica Epub ahead of print 20; Sep 2013

Rapid Remission of Bone Marrow Fibrosis is Possible with Effective Therapies

- **MF: Sequential analysis in Allo-HCT patients with grade 2 or grade 3 fibrosis at baseline showed near or complete resolution (to grade 1 or 0)[1]:**
  - 69% at day 100; 93% at day 365
- **CML: Bone marrow fibrosis occurs in 20-40% of patients[2] and is associated with significantly greater morbidity and mortality[3]**
  - Treatment with imatinib has been reported to result in rapid resolution of fibrosis
  - 2-5 months in chronic-phase CML,[4,5] as well as accelerated and blast phase CML[5]

1. Blood 2009; 114: 5264-70
2. Balliers Clin Haematol 1998; 11:721-749
3. Leukemia 2003; 17:2444-2453
4. Blood 2002; 100: 435-441
5. Blood 2002; 99: 381-383

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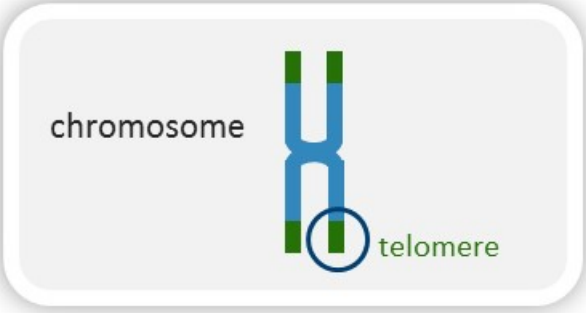
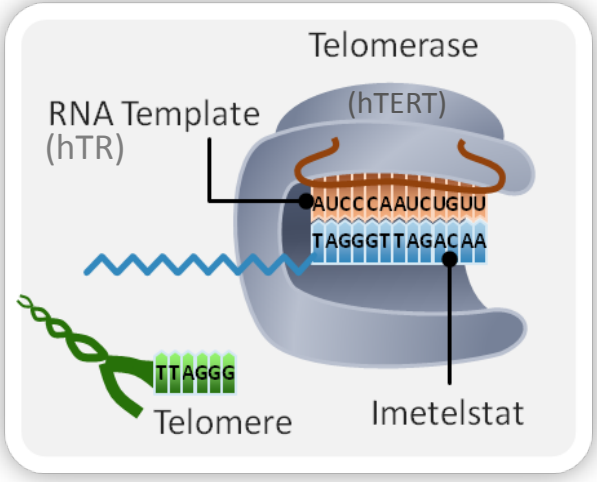
Imetelstat: A Telomerase Inhibitor



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:** IC50 = 0.5-10 nM (cell-free)
- **Target:** malignant progenitor cell proliferation

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Preliminary efficacy results from Mayo Clinic investigator-sponsored trial of imetelstat in myelofibrosis

Geron's independent efficacy analysis of the first 22 MF patients enrolled in the study

Investigator-Sponsored Single Center Study in Myelofibrosis

Principal Investigator & Study Sponsor:
Ayalew Tefferi, MD – Mayo Clinic, Rochester

High risk or intermediate-2 (DIPSS Plus)

Primary or secondary (post-PV or post-ET) myelofibrosis

→

Single Agent Imetelstat
2hr i.v. infusion

Cohort A (n=11):
9.4 mg/kg
q3 weeks#

Cohort B (n=11):
9.4 mg/kg
weekly cycle 1,
then q3 weeks#

→

***1° Endpoint*:**
- Overall response rate (CR, PR or CI) per IWG-MRT criteria

***2° Endpoints*:**
- Spleen response
- Anemia response
- Safety/tolerability

Dose reductions and dose holds allowed for toxicity

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Analysis Performed by Geron

- **Obtained and reviewed updated data available as of October from Mayo Clinic, including summary tables, patient listings, and pathology reports**
  - Patients: first 22 (11 in Arm A and 11 in Arm B)
  - Data cutoff: 18 October 2013
- **Onsite review of the patient charts and clinical database**
- **Consistent with the analysis performed and presented earlier today by investigator**

Revised IWG & ELN Primary Outcome Criteria for Response in Myelofibrosis[1]

CR: complete remission	• normal cellularity and reversal of bone marrow fibrosis ***and*** • normal peripheral blood counts and smears ***and*** • complete resolution of symptoms and splenomegaly
PR: partial remission	• as CR with bone marrow response but without full recovery of peripheral blood counts ***or*** • as CR without bone marrow response
CI: clinical improvement	• anemia, spleen ***or*** symptoms response ***and*** • no progressive disease or increase in severity of anemia, thrombocytopenia or neutropenia
spleen response / **anemia response** / **symptoms response**	• improvements in splenomegaly, anemia ***or*** symptoms • stabilization of the other criteria ***not*** required

Duration ≥12 weeks to qualify as a response under any category

[1]Tefferi, A et al. Revised response criteria for myelofibrosis: International Working Group-Myeloproliferative neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) consensus report. Blood 122: 1395-1398, 2013

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Patient Demographics

	Arm A (n = 11)	Arm B (n = 11)	Total (n = 22)
Median Age (range; years)	68.0 (54.0–76.0)	69.0 (53.0–79.0)	68.0 (53.0–79.0)
Male	7 (63.6%)	9 (81.8%)	16 (72.7%)
Previously Treated	8 (72.7%)	10 (90.9%)	18 (81.8%)
Myelofibrosis Subtype			
Primary Myelofibrosis	4 (36.4%)	5 (45.5%)	9 (40.9%)
Post–ET Myelofibrosis	1 (9.1%)	5 (45.5%)	6 (27.3%)
Post–PV Myelofibrosis	6 (54.6%)	1 (9.1%)	7 (31.8%)
DIPSS-Plus Risk Status			
Intermediate-2 Risk	7 (63.6%)	1 (9.1%)	8 (36.4%)
High Risk	4 (36.4%)	10 (90.9%)	14 (63.6%)

ET = Essential Thrombocythemia; PV = Polycythemia Vera

Clinical Disease Characteristics at Baseline: Organomegaly & Symptoms

	Arm A (n = 11)	Arm B (n = 11)	Total (n = 22)
Palpable Splenomegaly			
5 to < 10 cm	0 (0.0%)	1 (9.1%)	1 (4.5%)
≥ 10cm	7 (63.6%)	5 (45.5%)	12 (54.5%)
Median (Range in cm)	19.0 (13.0–25.0)	11.0 (8.0–23.0)	16.0 (8.0–25.0)
Palpable Hepatomegaly			
5 to < 10 cm	1 (9.1%)	1 (9.1%)	2 (9.1%)
≥ 10 cm	0 (0.0%)	1 (9.1%)	1 (4.5%)
Constitutional Symptoms±	8 (72.7%)	7 (63.6%)	15 (68.2%)

± DIPPS+ assessment of symptoms at baseline: Includes unexplained persistent fever > 38.3°C (or > 101°F) during past six months, unexplained non-menopausal night sweats during past six months, unexplained weight loss > 10% body weight in the previous six months and unexplained, non-articular bone pain during past six months.

Previous Treatment for Myeloproliferative Neoplasms

Prior Regimen	Arm A (n = 11)	Arm B (n = 11)	Total (n = 22)
Any Prior Treatment	8 (72.7%)	10 (90.9%)	18 (81.8%)
Median # of Treatments (range)	2 (1–4)	2 (1–4)	2 (1–4)
Hydroxyurea	4 (36.4%)	6 (54.5%)	10 (45.5%)
JAK2 Inhibitor	5 (45.5%)	4 (36.4%)	9 (40.9%)
Anagrelide	0	3 (27.3%)	3 (13.6%)
Pomalidomide	2 (18.2%)	1 (9.1%)	3 (13.6%)
Splenectomy	2 (18.2%)	0	2 (9.1%)

Note: Other therapies with n=1 of each: busulfan, cladribine, decitabine, epoetin alpha, erythropoietin, lenalidomide, prednisone, radiotherapy-spleen/liver, thalidomide, rituximab, anti-thymocyte globulin clinical trial, ruxolitinib clinical trial, pomalidomide trial.

Efficacy Assessment

- **Original protocol (October 2012) used the 2006 IWG-MRT criteria[1]**
- **2013 IWG-MRT criteria[2] were adopted after their publication in June**
- **Enrollment of all 22 patients was complete by May 2013, therefore some procedures were not in place at baseline and precluded full adoption of the updated criteria, specifically:**
  - Imaging studies were not performed for assessment of the spleen response endpoint; spleen and liver assessments were by palpation only
  - No patient-reported instrument was used to assess symptoms response; symptom data captured on adverse event form for symptoms response analysis (not CR/PR)
  - Mayo Clinic standard procedures were used for investigator assessment of baseline symptoms and resolution of symptoms for CR and PR

1. Tefferi et al. 2006 Blood 108: 1497-1503
2. Tefferi et al. 2013 Blood 122: 1395-1398

Duration of Follow-Up & Discontinuations

- **As of October 2013, the median duration of follow-up*:**
  - Arm A: 7.6 months (range 1.3–10.4)
  - Arm B: 4.8 months (range 1.6–5.6)
  - Overall: 5.3 months (range 1.3–10.4)

* Defined as time between date of first dose and date of last contact in the clinical database as of the data cutoff date.

Patient Status and Reason for Treatment Discontinuation	Arm A (n = 11)	Arm B (n = 11)	Total (n = 22)
On Treatment	8 (73%)	9 (82%)	17 (77%)
Discontinued Treatment:			
Disease Progression		1 (9%) [a]	1 (5%)
Died on Study	1 (9%) [b]	1 (9%) [c]	2 (9%)
Other	2 (18%) [d,e]		2 (9%)

a Non-responder; spleen became palpable.

b Death due to GI variceal bleed which is considered unrelated to imetelstat by investigator.

c Death due to intracranial hemorrhage with febrile neutropenia after prolonged myelosuppression which is considered possibly related to imetelstat by investigator.

d Transformation to CMML and off-study death from AML; both events were considered unrelated to imetelstat by the investigator.

e Discontinued due to lack of response.

Efficacy Results: Primary Endpoint (Overall Response by IWG-MRT)

	Arm A (n = 11)	Arm B (n = 11)	Total (n = 22)
Best Response by 2013 IWG-MRT	N (%)	N (%)	N (%)
Overall Response (CR+PR+CI)	3 (27.3%)	6 (54.5%)	9 (40.9%)
Remission (CR+PR)	2 (18.2%)	3 (27.3%)	5 (22.7%)
Complete Remission (CR)	2 (18.2%)[1]	1 (9.1%)	3 (13.6%)
Partial Remission (PR)		2 (18.2%)	2 (9.1%)
Clinical Improvement (CI)	1 (9.1%)	3 (27.3%)[2]	4 (18.2%)

Pending 12-week durability assessment:

[1]One patient who met the PR criteria on 4/30/2013 and converted to CR on 10/9/2013 (Arm A)

[2]One patient who met CI-by Liver Response on 10/14/2013 (Arm B)

Response Parameters for Patients Who Achieved CR or PR (IWG-MRT)

- **Median onset time to CR or PR of 2.8 months (range 1.4 – 3.0)**

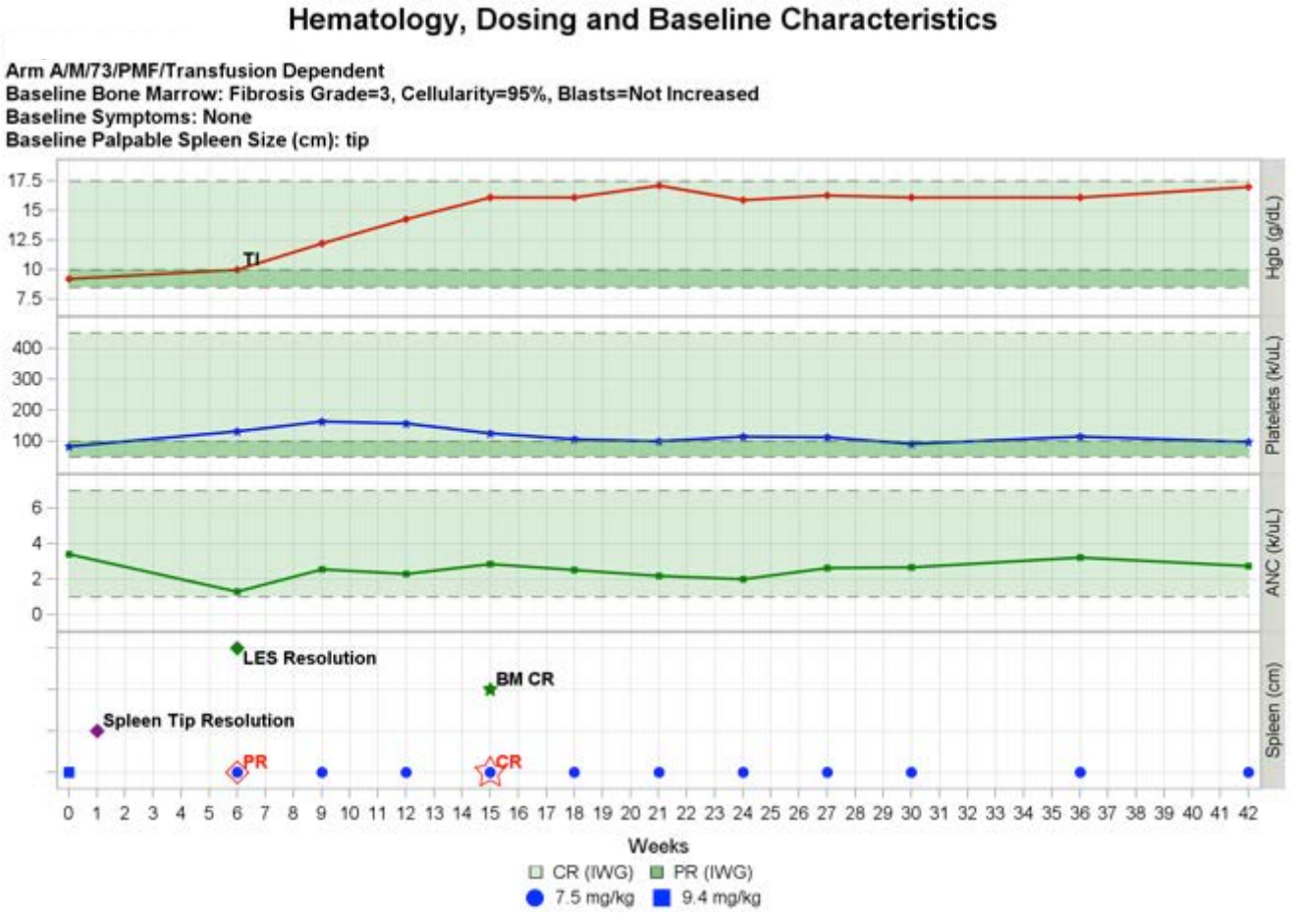
Patient	Arm	Bone Marrow	Anemia or Transfusion Requirement	Leukocytosis	Thrombo-cytosis	Leukoerythro-blastosis	Organomegaly by Palpation	Symptoms	Best IWG-MRT Response
1	A	CR	Response: transfusion independence	n/a	n/a	CR	Spleen tip: resolved	n/a	**CR**
2	A	CR	Response: transfusion independence	n/a	n/a	CR	Spleen tip: resolved	Weight loss: resolved	**CR****
3	B	CR	n/a	Complete Response*	Complete Response	CR	Spleen 10cm: resolved	Night sweats: resolved	**CR**
4	B	CR	Hemoglobin increased to ≥ 10 g/dL	Complete Response	Complete Response	CR	n/a	n/a	**PR**
5	B	No CR	n/a	Complete Response*	Complete Response	CR	Spleen 8cm: resolved	Night sweats, Weight loss: resolved	**PR**

CR = complete remission; PR = partial remission; Complete response = resolution or normalization of blood counts; LCM = below left costal margin; n/a = not applicable (not present at baseline)

* Marked leukocytosis or white blood cells (WBC) ≥ 25 x 10^9/L at baseline.

** Pending 12-week duration: met PR criteria on 4/30/2013 and converted to CR on 10/9/2013.

Patient 1 - CR

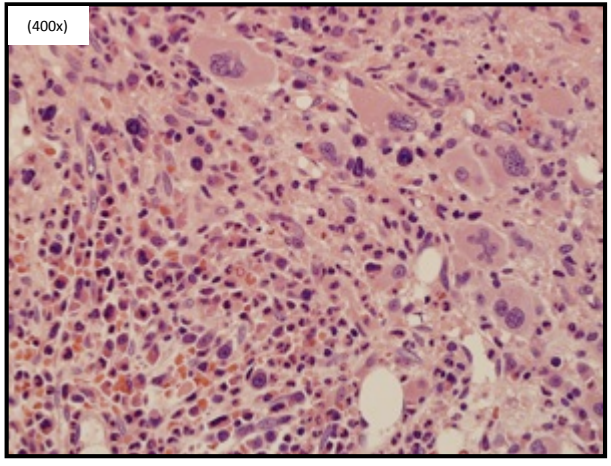


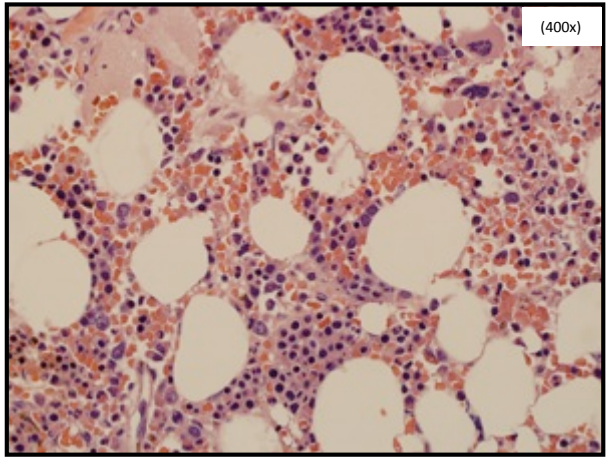
Only Baseline and Day 1 lab results of each cycle are presented; Only initial onset of responses noted

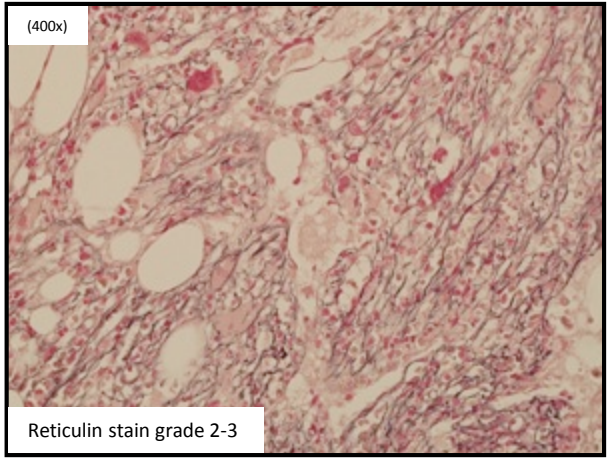
Patient 1 - CR

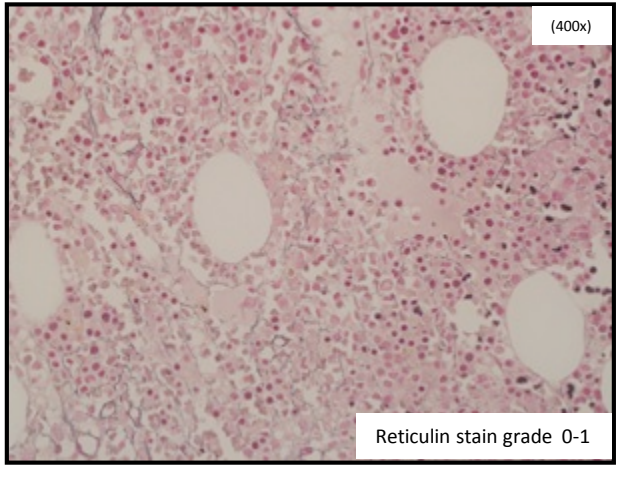
Baseline
(12/17/12)

7-months post-imetelstat therapy
(7/15/13)









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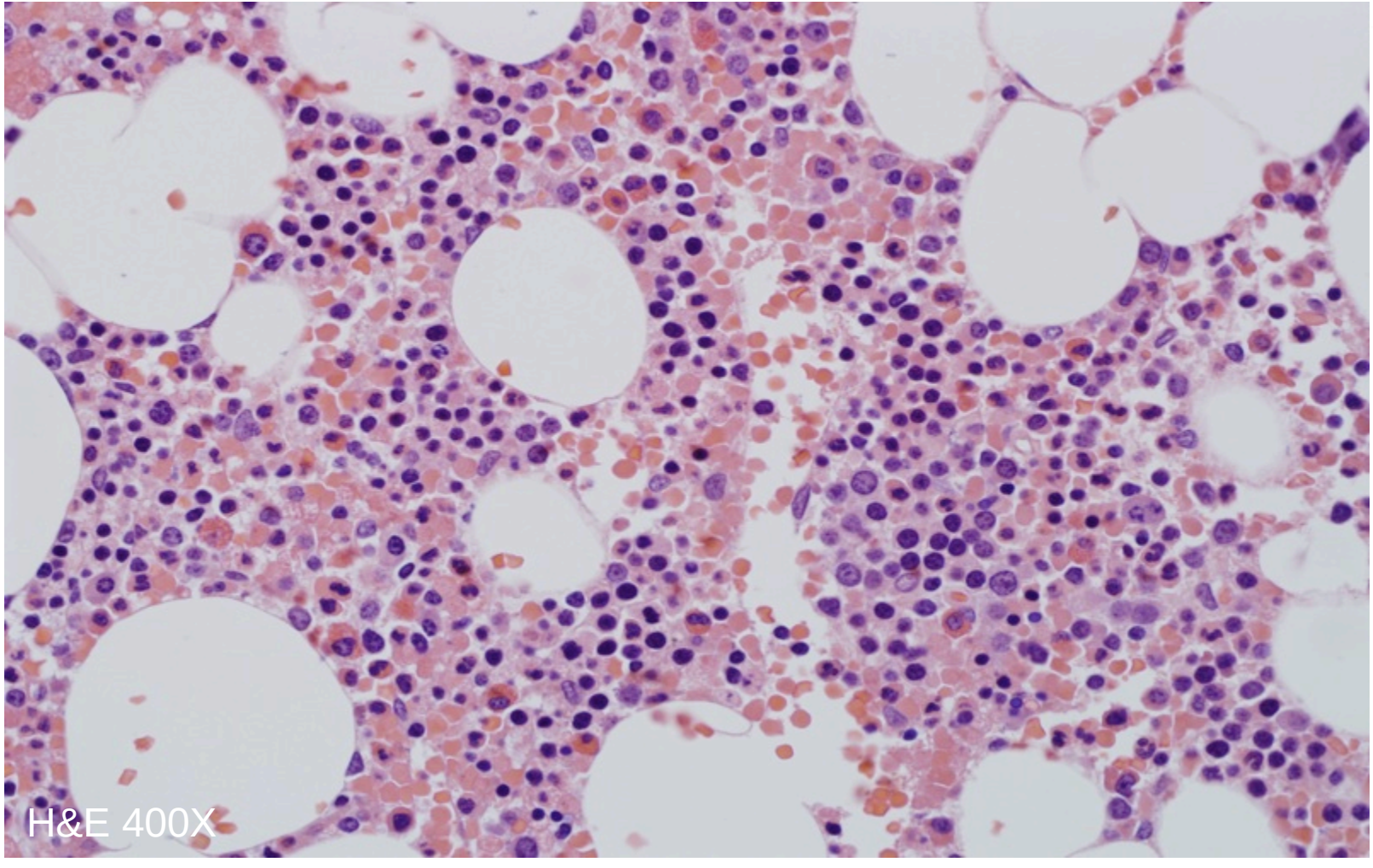
Patient 1 - CR: seven-months post-imetelstat therapy, megakaryocytes quantitatively and morphologically became unremarkable with only rare abnormalities



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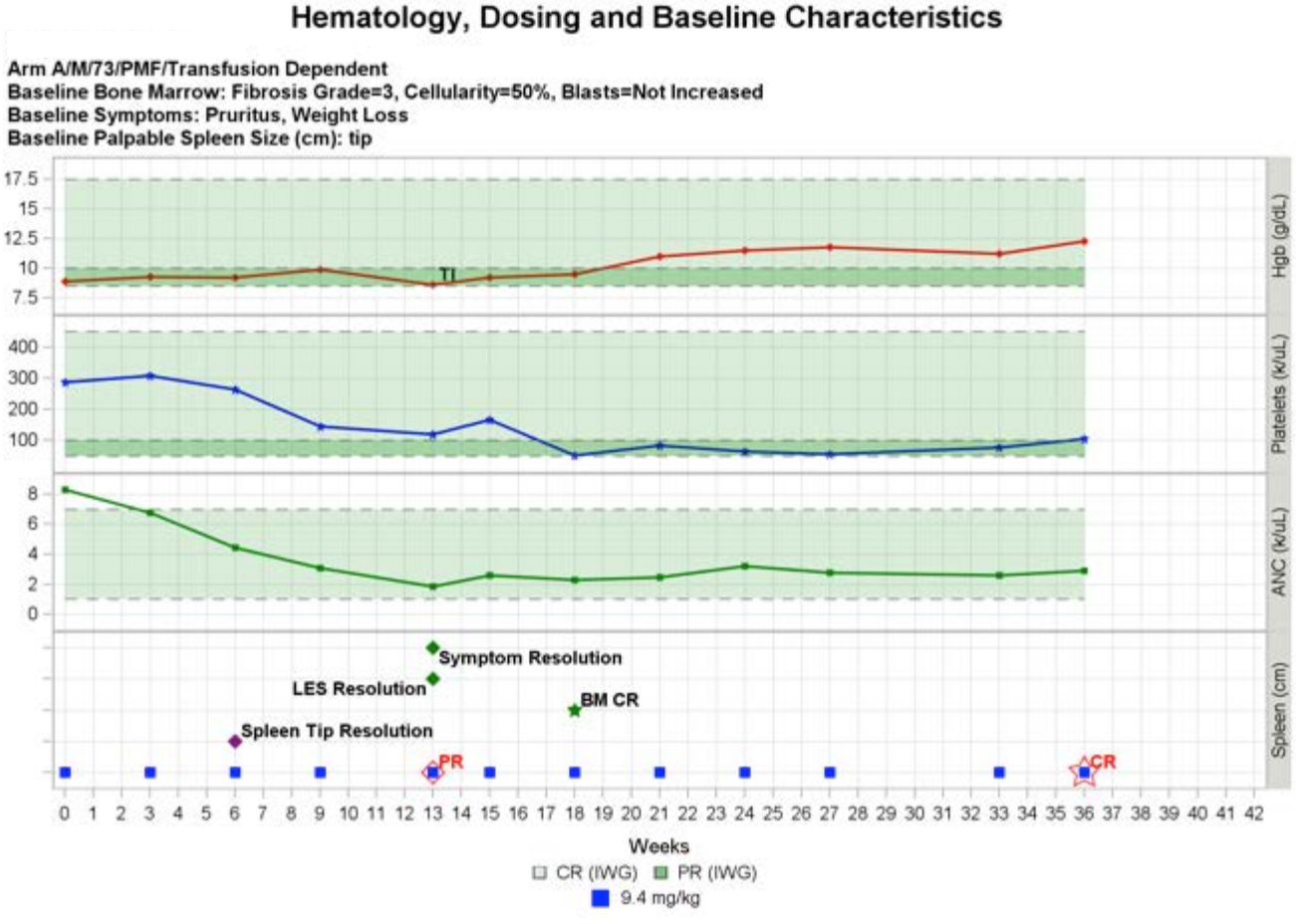
Patient 2 - CR



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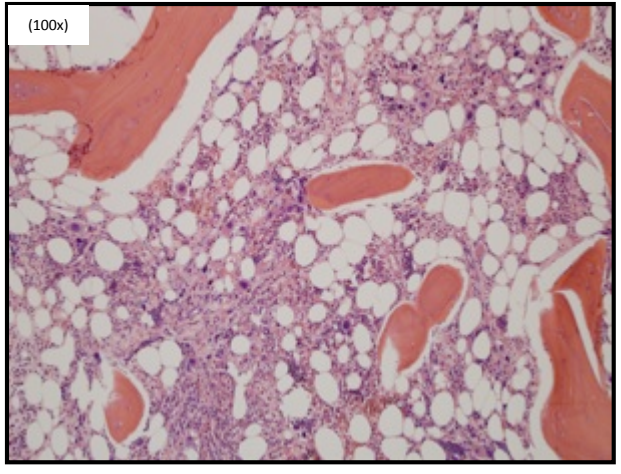
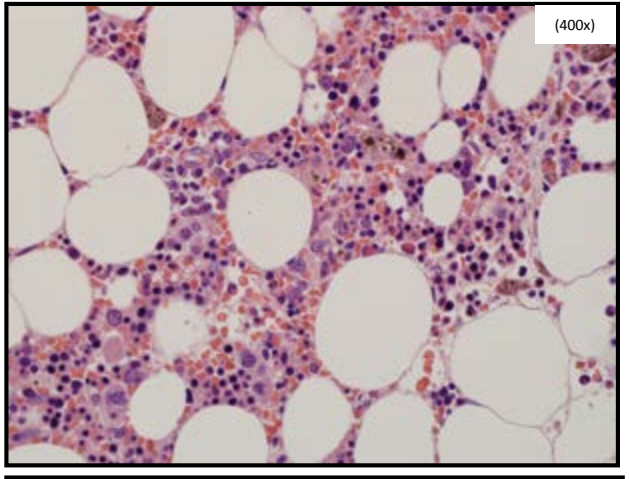
Patient 2 - CR

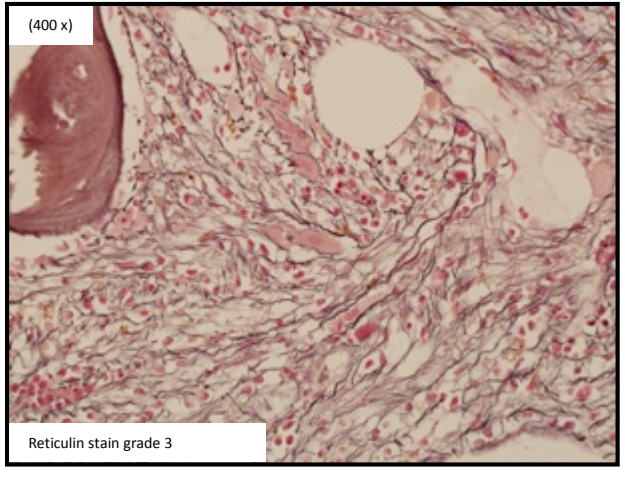
Baseline
(1/28/13)

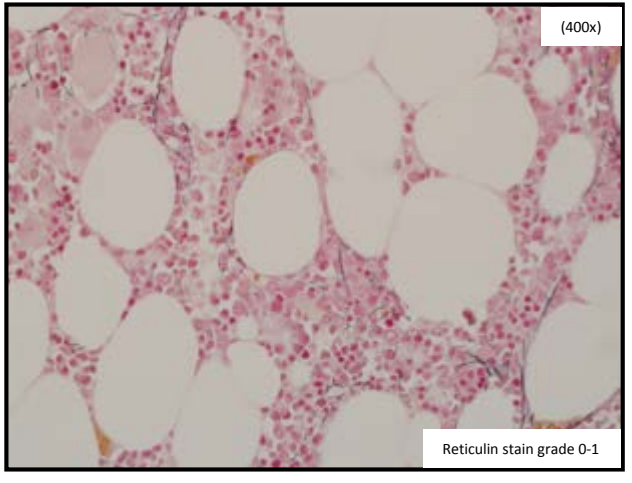
→

5.5-months post-imetelstat therapy
(7/18/13)









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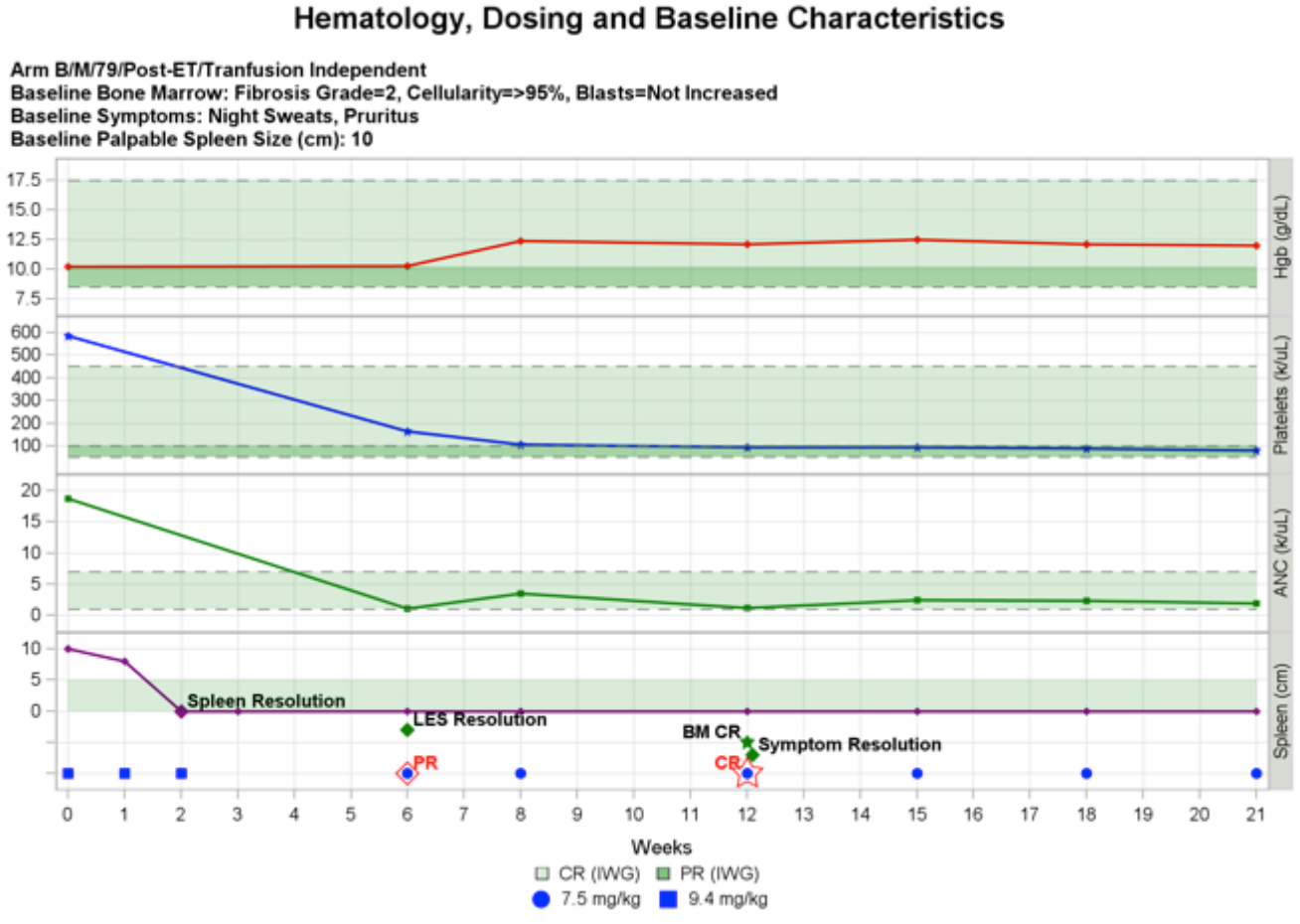
Patient 3 - CR



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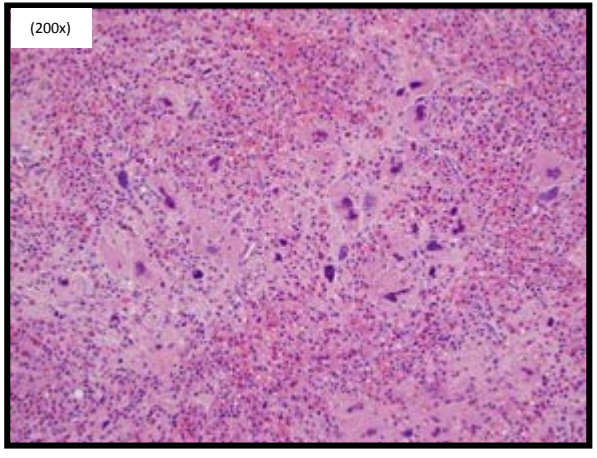
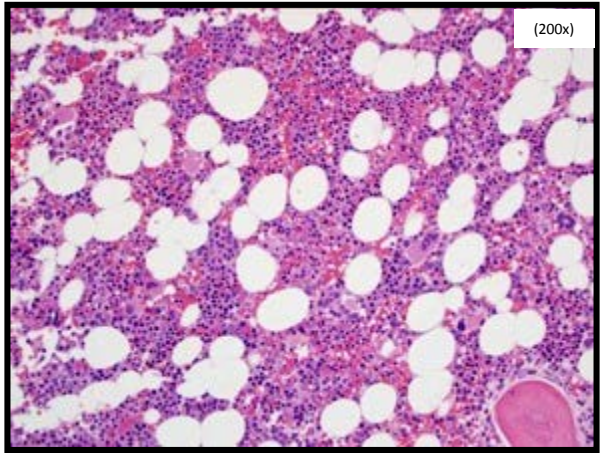
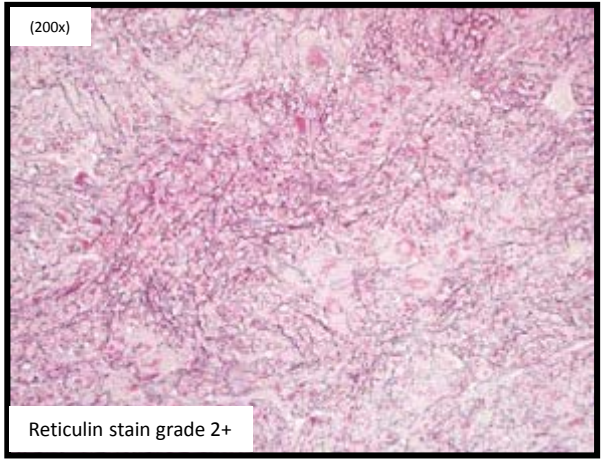
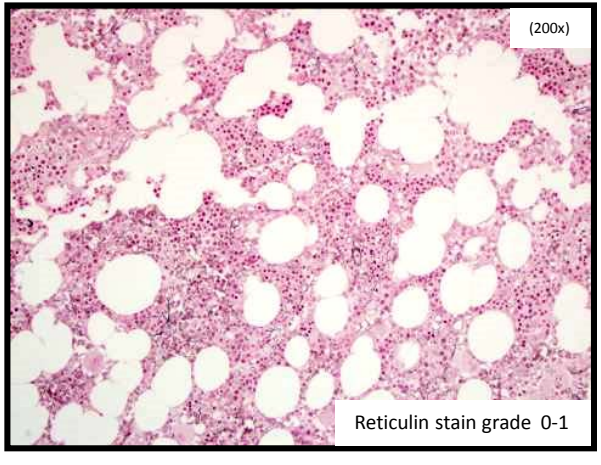
Patient 3 - CR

Baseline → 3-months post-imetelstat therapy









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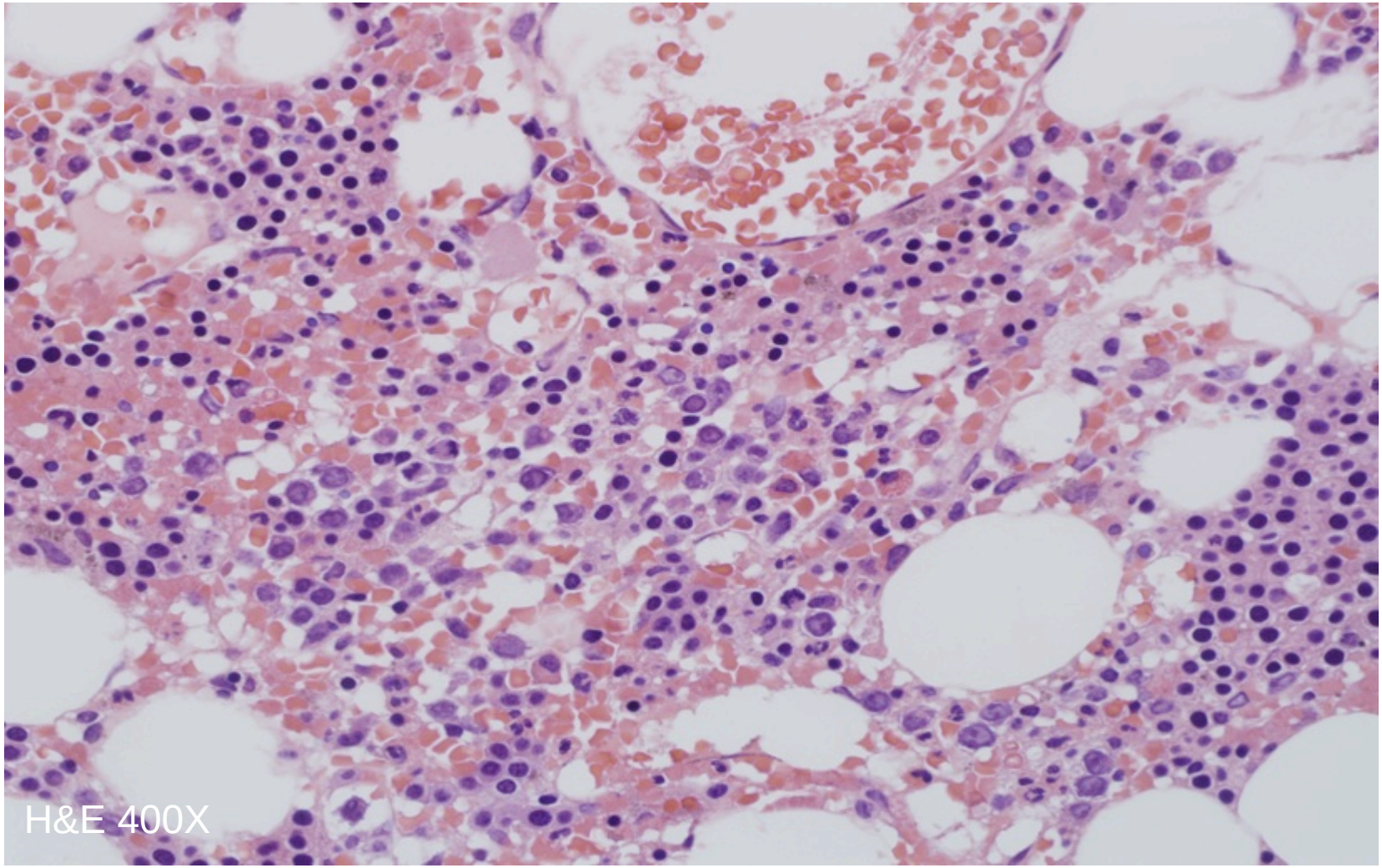
Patient 3 - CR: six-months post-imetelstat therapy:
"*Normocellular bone marrow with normal trilineage hematopoiesis. No bone marrow fibrosis*"



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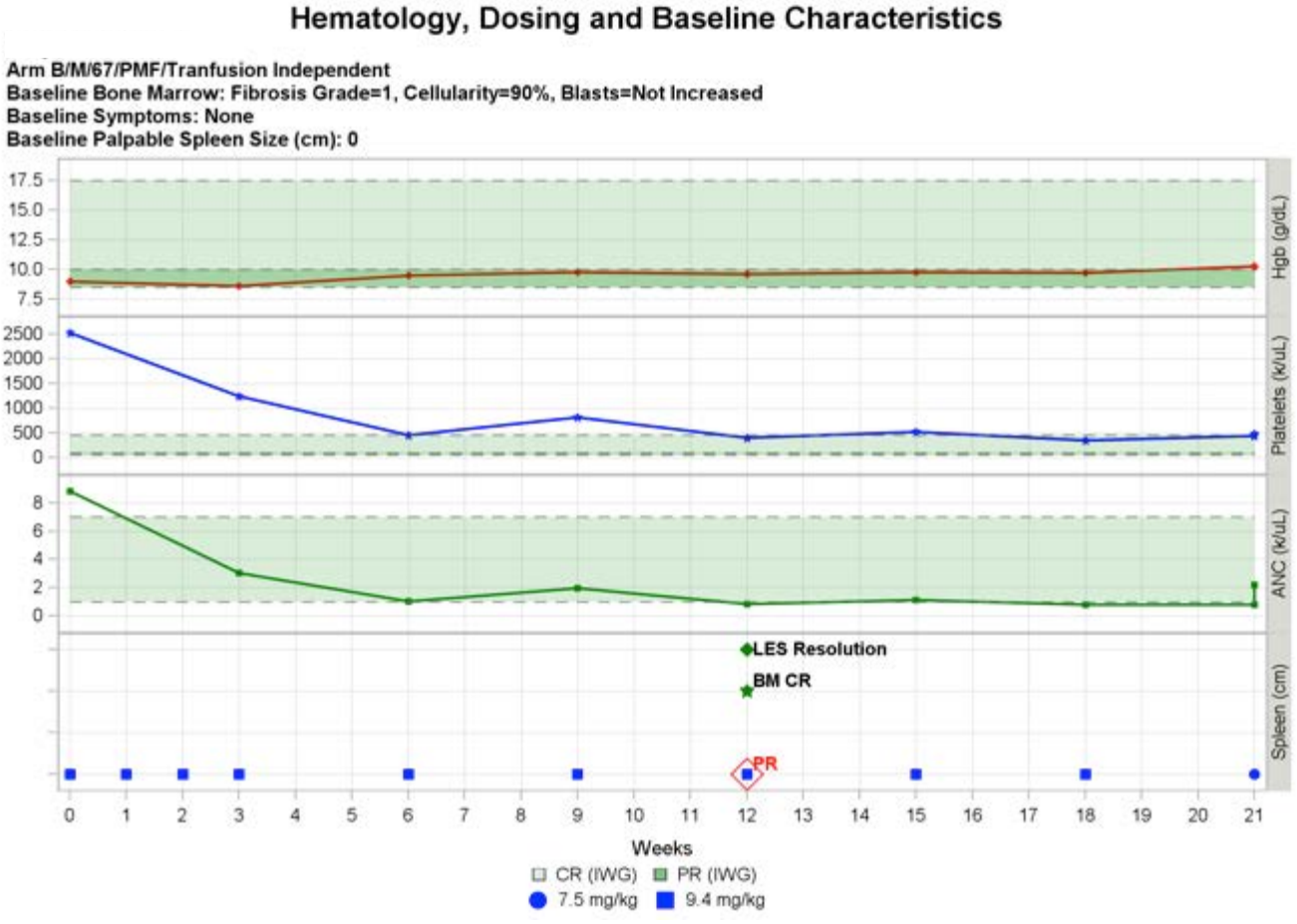
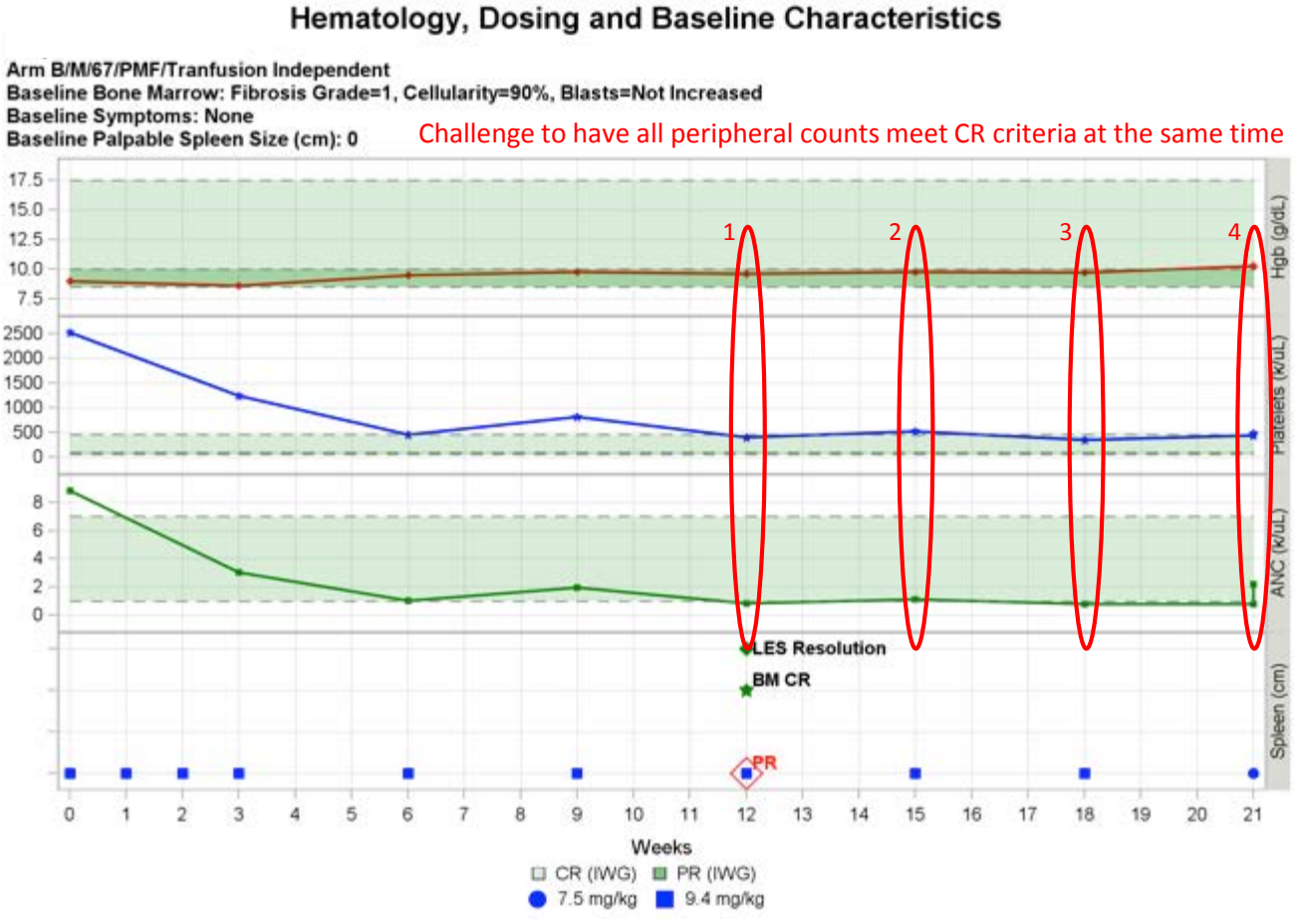
Patient 4 – PR (with Bone Marrow CR)



Only Baseline and Day 1 lab results of each cycle are presented; Only initial onset of responses noted

Patient 4 - PR (Bone Marrow CR)



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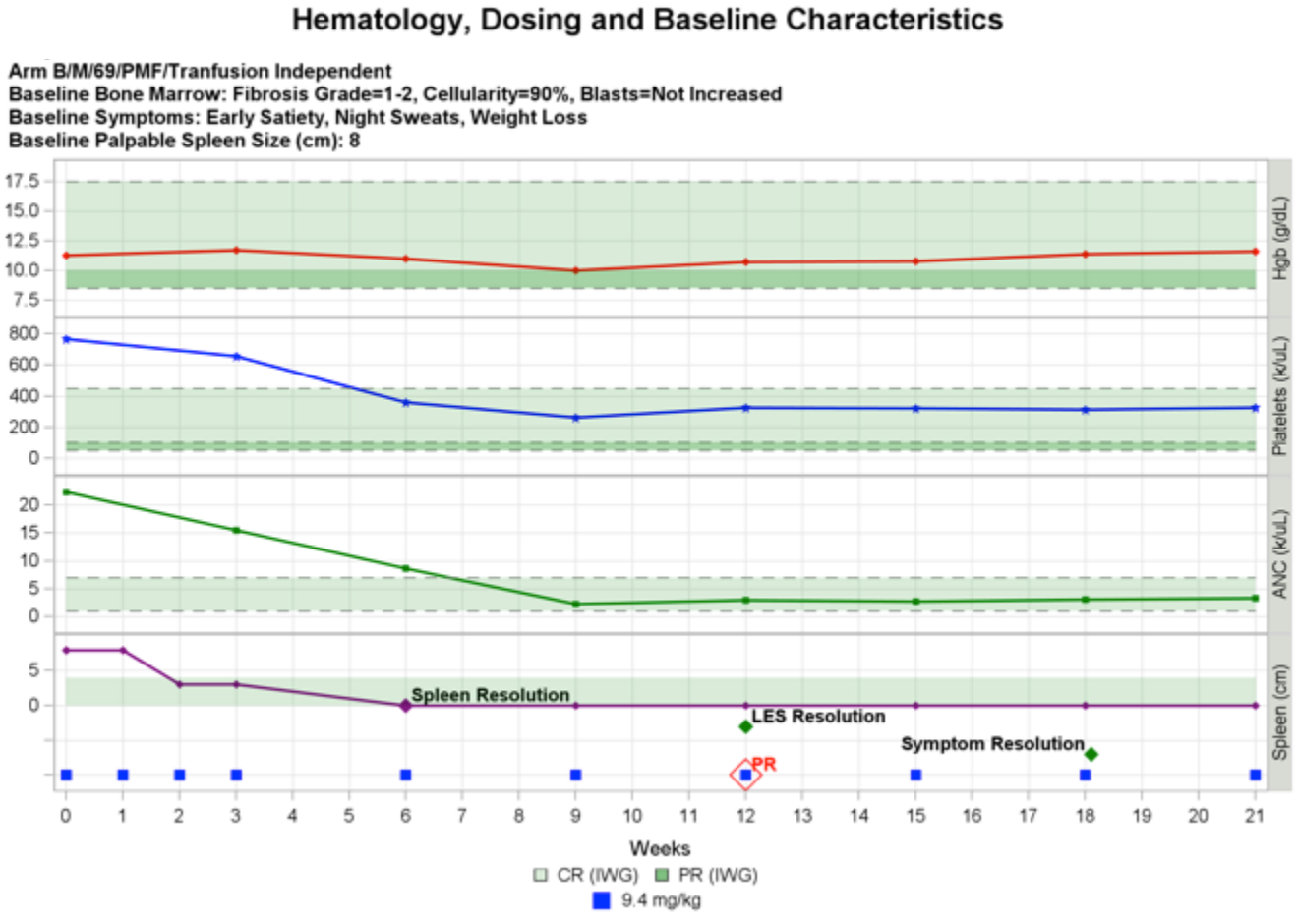
Patient 5 - PR



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Efficacy Results: Spleen, Anemia and Symptoms Responses

Secondary Endpoints	Arm A	Arm B	Total
Spleen Response (by palpation)	2/7 (28.6%)	3/6 (50%)	5/13 (38.5%)
Anemia Response	3/5 (60%)	1/7 (14.3%)	4/12 (33.3%)

- **Symptoms response was observed in 10/13 (77%) of patients**

Spleen response: defined as *either* ≥ 50% decrease if baseline ≥ 10 cm *or* becoming non-palpable if baseline 5 to < 10 cm. Spleen size measured by physical examination (palpable distance from the left costal margin).

Anemia response: defined as *either* becoming transfusion independent if dependent at baseline *or* gaining ≥ 2 g/dL in hemoglobin level if transfusion-independent but with a hemoglobin level < 10 g/dL at baseline.

Symptoms response: defined as 50% reduction from baseline in grade.

Exploratory Endpoints: Impact on Blasts, Leukocytosis & Thrombocytosis

- **Benefit not just limited to the patients achieving CR, PR or CI**

	Arm A	Arm B
Circulating Blasts (≥1% at baseline)	n = 6	n = 8
Complete Resolution	6 (100 %)	5 (62.5%)
Partial Resolution**	0	1 (12.5%)
Leukocytosis (counts >ULN at baseline)	n = 7	n = 8
Complete Resolution	3 (42.9%)	4 (50%)
Partial Resolution	3 (42.9%)	1 (12.5%)
Marked Leukocytosis (> 25 x 10^9/L)	n = 3	n = 6
Complete Resolution	0	3 (50.0%)
Partial Resolution**	3 (100%)	1 (16.7%)
Thrombocytosis (counts >ULN at baseline)	n = 3	n = 6
Complete Resolution	2 (66.7%)	5 (83.3%)
Partial Resolution**	0	0

* Normalization of counts ≤ ULN
** > 50% reduction from baseline
ULN = upper limit of normal range (per Mayo Clinic laboratory reference ranges)

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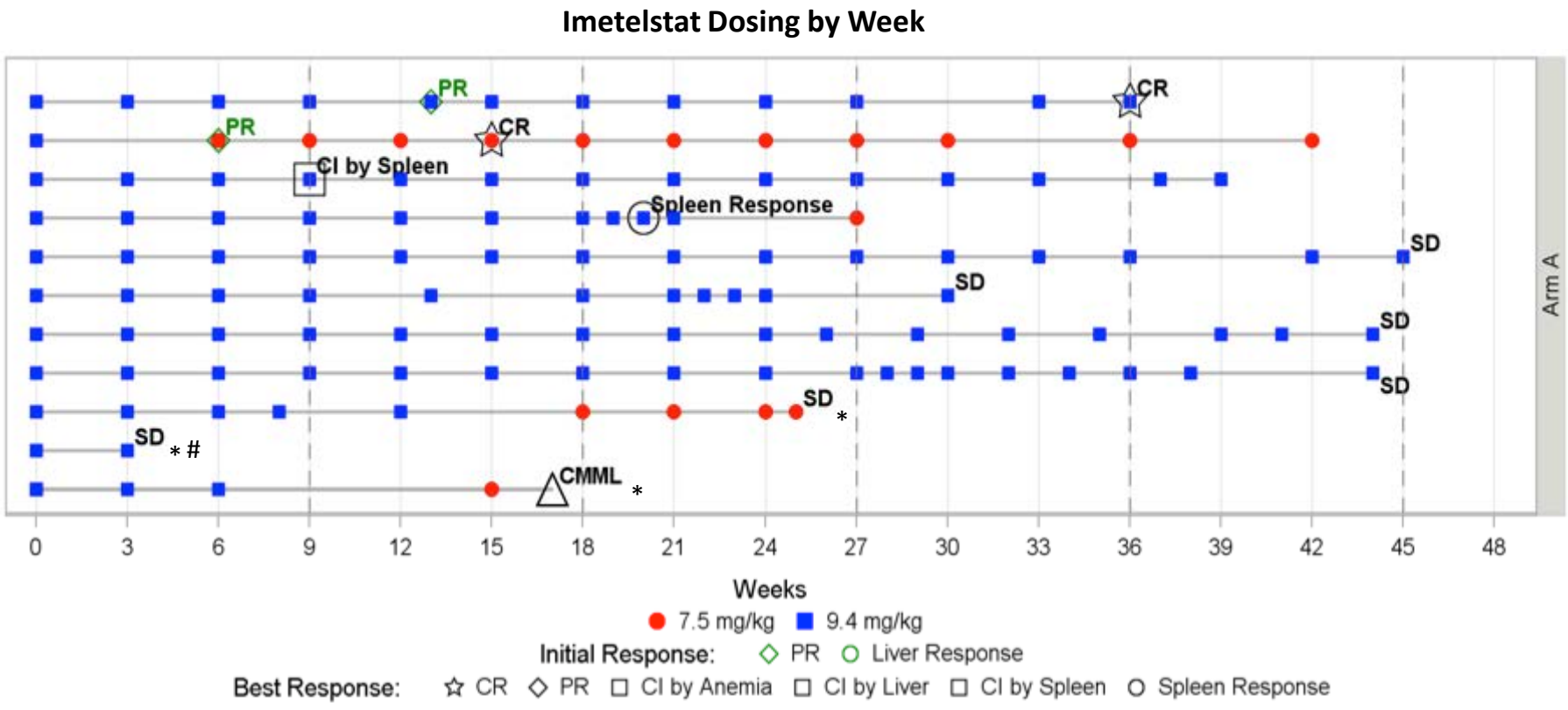
Patient Response Status & Dosing: Arm A



*Indicates patient had discontinued treatment.
Died on study (GI bleed unrelated to imetelstat per investigator assessment).
Only initial onset of responses noted.

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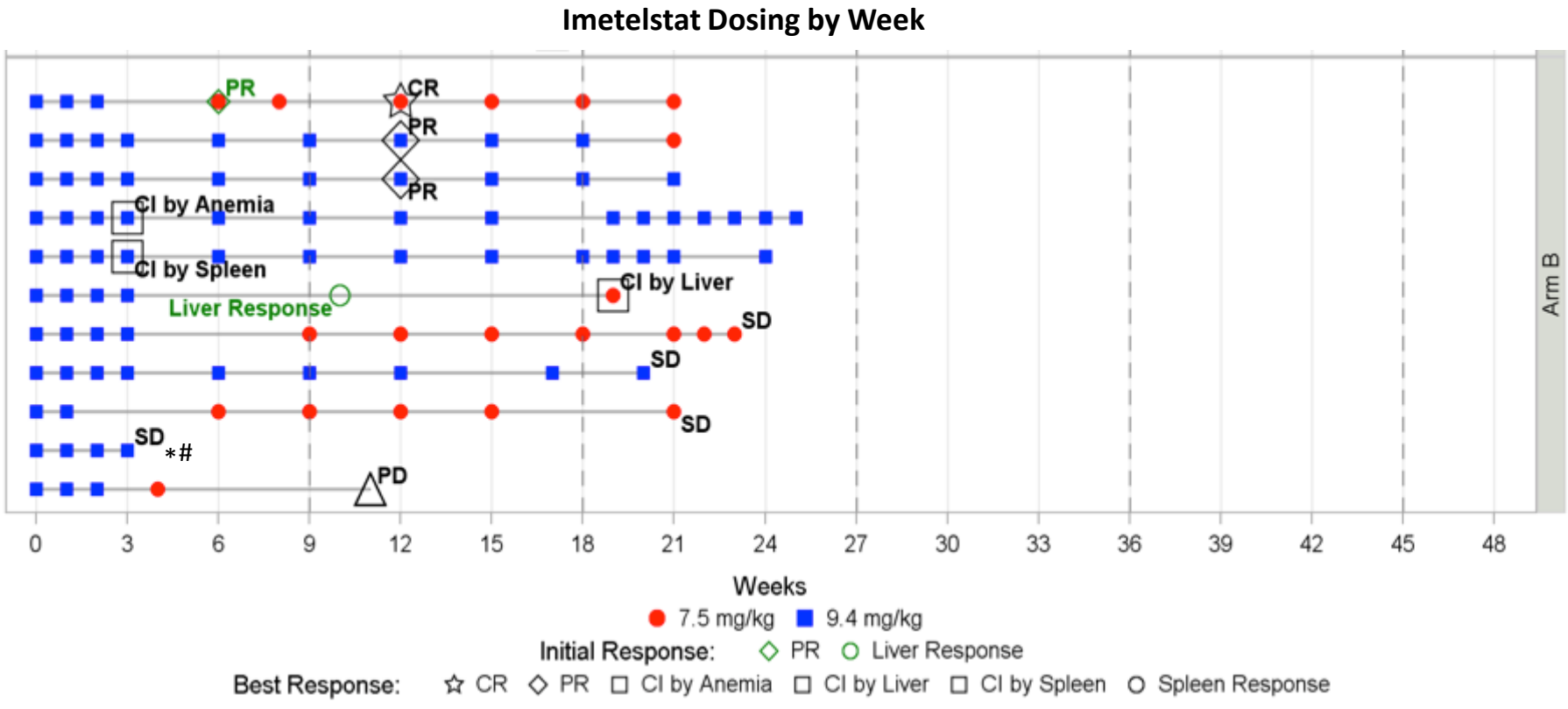
Patient Response Status & Dosing: Arm B



*Indicates patient had discontinued treatment.
Died on study (intracranial bleed related to imetelstat per investigator assessment).
Only initial onset of responses noted.

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Efficacy Conclusions

- **Geron's independent review of the data from the first 22 patients in the Mayo Clinic IST suggests that imetelstat has disease-modifying activity in MF**
  - Unprecedented remissions (CR+PR) by IWG-MRT criteria observed in 5/22 patients
    - Bone marrow reversal in 4/5 CR+PR patients
    - Resolution of splenomegaly in all 4 CR+PR patients with splenomegaly prior to treatment
    - Resolution of symptoms in all 3 CR+PR patients with symptoms prior to treatment
  - Clinical improvement (CI) by IWG-MRT criteria observed in another 4/22 of patients
  - Overall response (CR+PR+CI) rate of 40.9% (9/22 patients)
  - No patients with CR, PR, or CI have lost their response to date
  - Some clinical benefit was seen in the majority of patients, including resolution of circulating blasts, leukocytosis and thrombocytosis

Preliminary safety results from Mayo Clinic investigator-sponsored trial of imetelstat in myelofibrosis

Mayo Clinic analysis of the first 33 MF patients enrolled in the study

Original Plan

Principal Investigator & Study Sponsor:
Ayalew Tefferi, MD – Mayo Clinic, Rochester

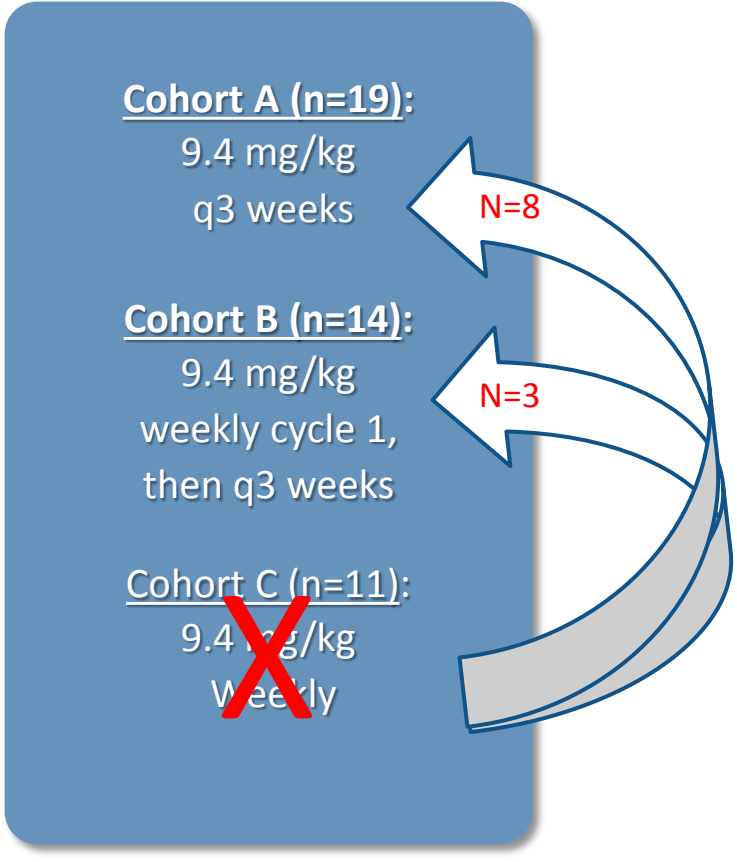
Cohort A (n=11):
9.4 mg/kg
q3 weeks

Cohort B (n=11):
9.4 mg/kg
weekly cycle 1,
then q3 weeks

Cohort C (n=11):
9.4 mg/kg
Weekly

Additional 11 Patients Distributed to Arm A & B (n=33)

Principal Investigator & Study Sponsor:
Ayalew Tefferi, MD – Mayo Clinic, Rochester



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Patient Disposition (n=33)

Current disposition

	All patients (*n*=33)
Follow-up in months; median (range)	7.0 (4.3-13.0)
Currently still on treatment	24 (73%)
Treatment discontinuation	9 (27%)
Dose-reduced	12 (36%)

Reasons for treatment discontinuation	n
Lack of response	6
Transformation into CMML	1
Death: unrelated	1
Death: related	1

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Safety Results (n=33)

All grade 3/4 extramedullary adverse events not related to myelosuppression

(Includes all events regardless of attribution)

	All patients (*n*=33)	Arm A (*n*=19)	Arm B (*n*=14)
Fatigue	3 (9%)	1 (5%)	2 (14%)
A-fib	2 (6%)	2 (11%)	
ALP	2 (6%)	1 (5%)	1 (7%)
Heart failure	1 (3%)	1 (5%)	
Hyponatremia	1 (3%)	1 (5%)	
GI bleed	1 (3%)	1 (5%)	
Hyperkalemia	1 (3%)		1 (7%)
Pruritus	1 (3%)		1 (7%)
Intestinal obstruction	1 (3%)		1 (7%)

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Safety Results (n=33)

Treatment-related toxicity of imetelstat among 33 patients with high/int-2 risk myelofibrosis

Extramedullary not related to myelosuppression	All patients N=33	Arm A N=19	Arm B N=14
Grade-1 nausea	5 (15%)		
Grade-1 vomiting	1 (3%)		
Grade-1/2 fatigue	4 (12%)		
Grade-2 hyperbilirubinemia	2 (6%)		
Grade-2 APTT increase	1 (3%)		
Myelosuppression			
Grade-3/4 neutropenia	7 (21%)	2 (11%)	5 (36%)
Grade-3/4 thrombocytopenia	10 (30%)	5 (26%)	5 (36%)
Grade-3/4 anemia	4 (12%)	1 (5%)	3 (21%)
Grade-4 neutropenia	4 (12%)	1 (5%)	3 (21%)
Grade-4 thrombocytopenia	4 (15%)	0	4 (29%)
Grade-5 CNS bleed and febrile neutropenia	1 (3%)	0	1 (7%)

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Safety Observations

- **Myelosuppression is the principal dose-limiting toxicity**
  - Believed to be an on-target toxicity due to effects on progenitor cells
  - Manageable through dose hold rules and dose modifications
  - To mitigate against risk of severe, persistent cytopenias, Mayo Clinic protocol amended to raise hematologic threshold for retreatment, include more stringent monitoring and dose adjustment criteria
- **Non-hematological adverse events generally mild to moderate and not dose-limiting**

Imetelstat for Treating Myelofibrosis – Key Conclusions

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Q&A