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# ASH 2014 Analyst & Investor Event

## December 8, 2014

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**President & CEO, Geron Corporation**

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**Queensland Institute of Medical Research**

# 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) the anticipated effectiveness of the Collaboration Agreement; (ii) Geron's receipt of an initial payment and potential receipt of development, regulatory and sales milestones, as well as royalties on potential future sales of imetelstat commercialized under the Collaboration Agreement; (iii) planned and potential clinical trials of imetelstat to be conducted under the Collaboration Agreement, including the Initial Phase 2 MF Study and the Initial Phase 2 MDS Study, and other potential activities under the Collaboration Agreement; (iv) the safety and efficacy of imetelstat; (v) Geron's desire to diversify its products; (vi) financial projections and expectations; and (vii) 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 ability of the parties to satisfy all of the conditions for the effectiveness of the Collaboration Agreement, including the expiration or termination of waiting periods under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended; (ii) the uncertain and time consuming product development and regulatory process, including whether the parties will succeed in overcoming all of the clinical safety and efficacy, technical, scientific, manufacturing and regulatory challenges in the development and commercialization of imetelstat; (iii) the fact that Geron may not receive any initial, milestone, royalty or other payments from Janssen because Janssen may terminate the Collaboration Agreement for any reason; (iv) the ability of Geron and Janssen to protect and maintain intellectual property rights for imetelstat; (v) 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; (vi) whether imetelstat is safe and efficacious; (vii) whether Geron will obtain additional products or engage in any strategic transaction; (viii) whether Geron spends more during the fourth quarter of 2014 than expected; and (ix) other risks described in Geron's Securities and Exchange Commission (SEC) filings, including under the heading "Risk Factors". Additional information and 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 SEC under the heading "Risk Factors," including Exhibit 99.1 of Geron's current report on Form 8-K filed on November 13, 2014. 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.

# Telomerase Inhibition and Imetelstat in Hematologic Malignancies

Background Information



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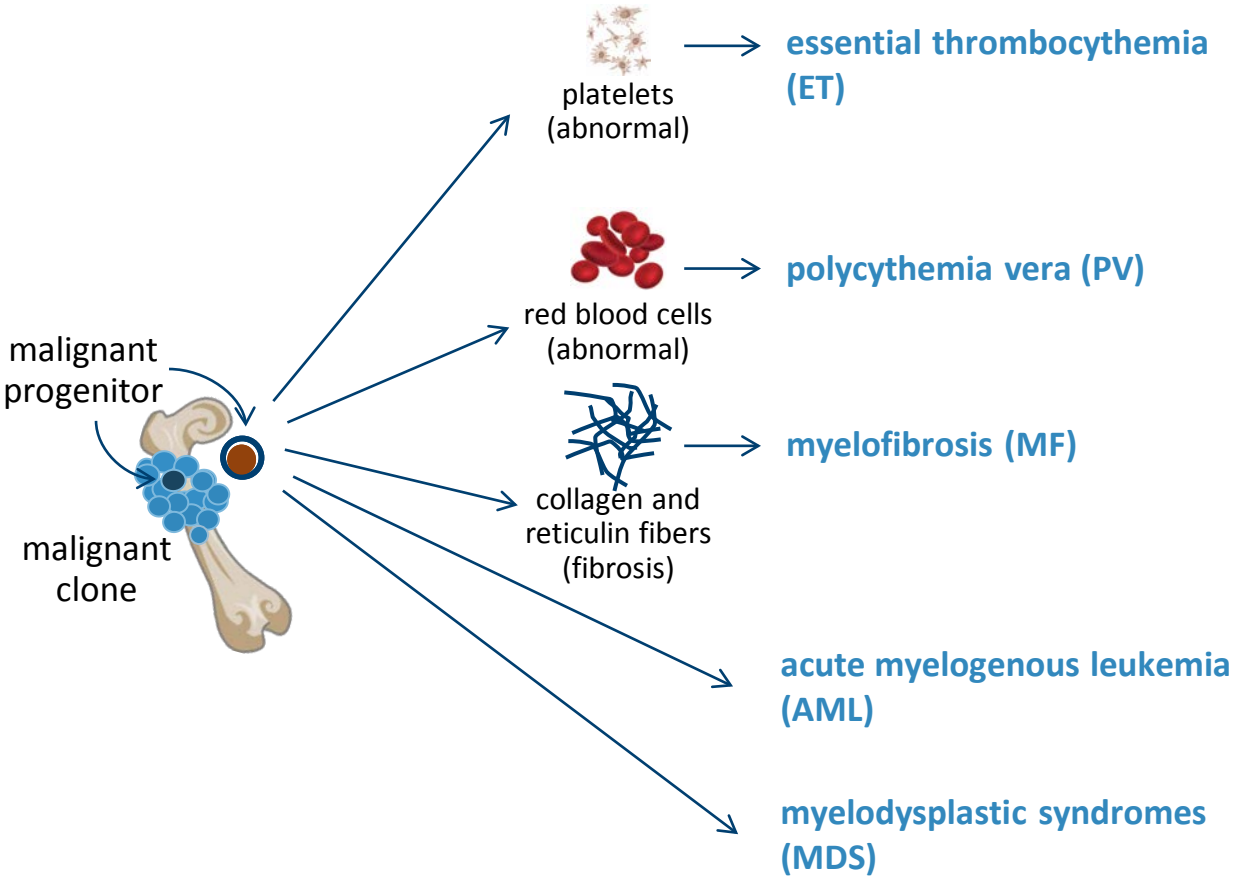
# Hematologic Malignancies Arise from Malignant Progenitor Cell Clones in the Bone Marrow



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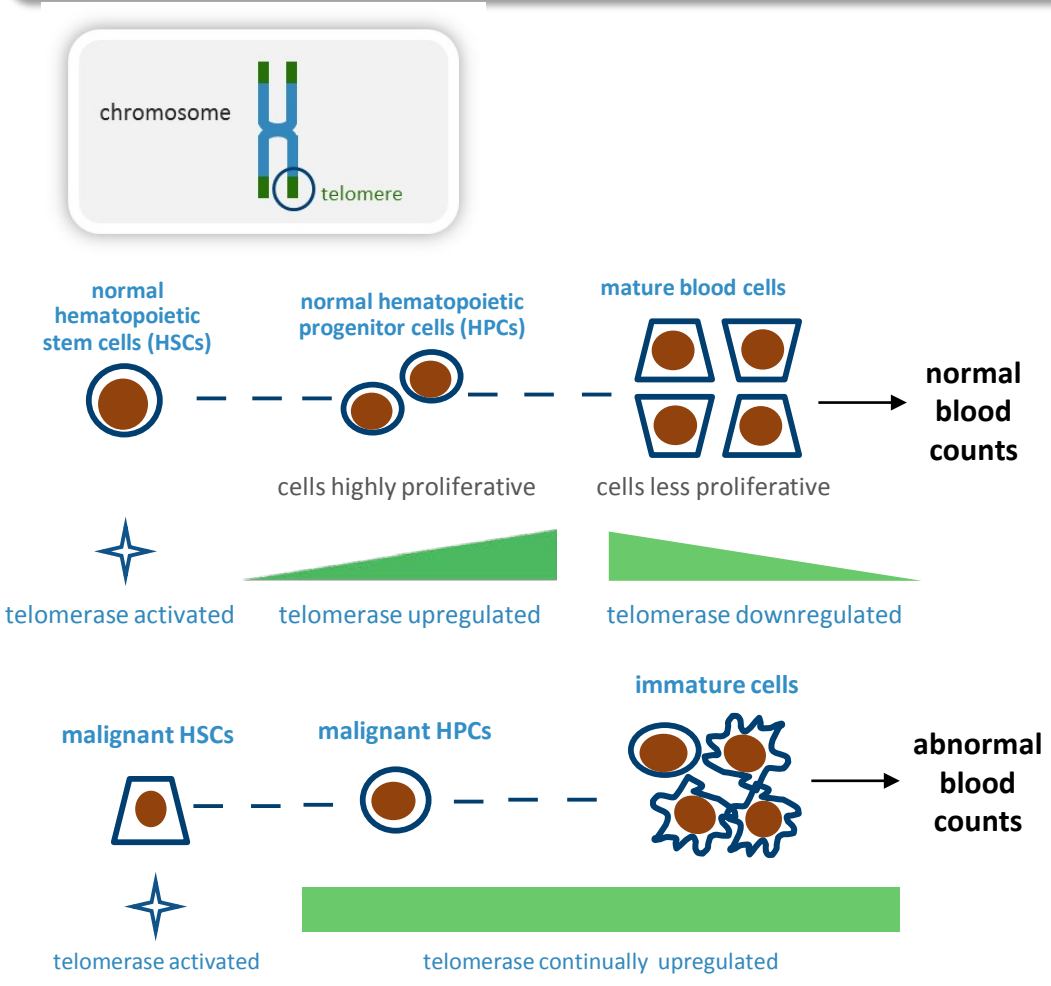
# Telomerase: A Novel Hematologic Malignancy Target




## 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**



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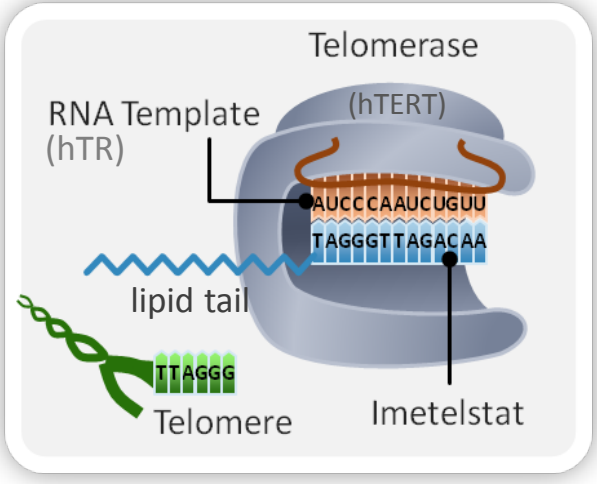
# Imetelstat: A Telomerase Inhibitor

**imetelstat binds to RNA template preventing maintenance of telomeres**




- **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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# *In Vitro* Proof-of-Concept: Imetelstat Selectively Inhibits Malignant Hematopoiesis in Spleens from Patients with Myelofibrosis (ASH 2014)*


**Effect of imetelstat on hematopoiesis in *in vitro* cultures**

- **Minimal effects on hematopoiesis from normal cord blood**
- **Selective inhibition of the proliferation of hematopoietic stem cells and myeloid progenitor cells in cultures derived from myelofibrosis spleens**
- **Preferential depletion of malignant hematopoietic progenitor cells**

*Abstract# 1879: Effects of Imetelstat on CD34+ Cells of Patients with Myelofibrosis, Wang X, Hoffman R, *et al.*



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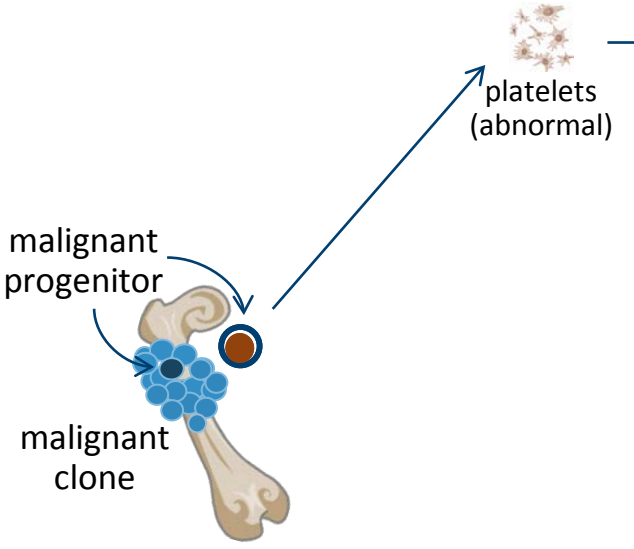
# Essential Thrombocythemia: First Clinical Proof-of-Concept




## essential thrombocythemia (ET)

- **100% hematologic response rate (18/18)**
  - **durable:** median time on therapy is 14 months (range 3 months - 2.5 years)
- **88% JAK2V617F molecular response rate (7/8)**
  - **deep**: JAK2V617F allele burden reduced by between 72% to 96%
  - **durable:** maintained in 86% (6/7) patients
- **100% CALR molecular response rate (5/5)***
  - **CALR** allele burden reduced by between 15% to 55%*

*Abstract# 408: Monitoring of CALR Allele Burden in Patients with Essential Thrombocythemia Treated with Imetelstat, a Telomerase Inhibitor, Reveals Rapid and Substantial Molecular Responses, Baerlocher G, *et al.*



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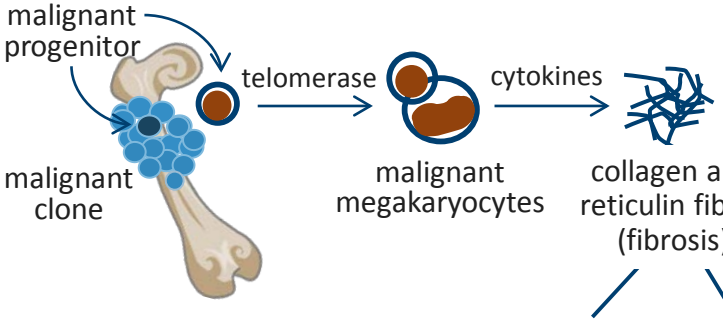
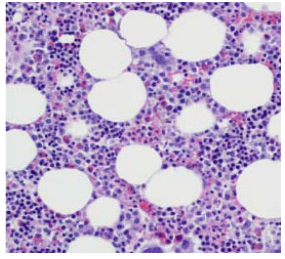
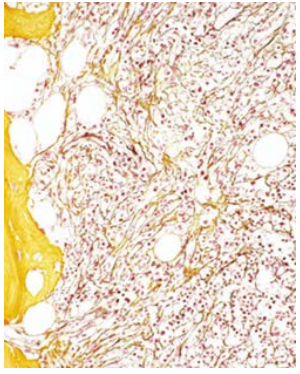
# Myelofibrosis (MF): Disease Process and Characteristics

- **Megakaryocytic hyperplasia**
  - **Fibrosis** thought to be induced by cytokines produced by **megakaryocytes** originating from the malignant progenitor cell clone[1]
  - **Constitutional symptoms** (e.g., fever, weight loss, night sweats, pruritus) present in approximately 35%[2] of patients also thought to be due to cytokines produced by malignant **megakaryocytes**
- Impaired bone marrow hematopoiesis shifts blood production to spleen and liver (palpable **splenomegaly** in approximately 80%[3] of patients)
- **Serious and life-threatening** illness
  - Leukemic transformation to AML (blast-phase MF)
  - Thrombohemorrhagic complications associated with dysfunctional hematopoiesis



**normal bone marrow**



**advanced fibro-osteosclerosis**

[1] J Clin Oncol 2005; 23:8520-8530 – [2] Mayo Clin Proc 2012; 87:25 – [3] J Clin Oncol 2011; 29:392-397



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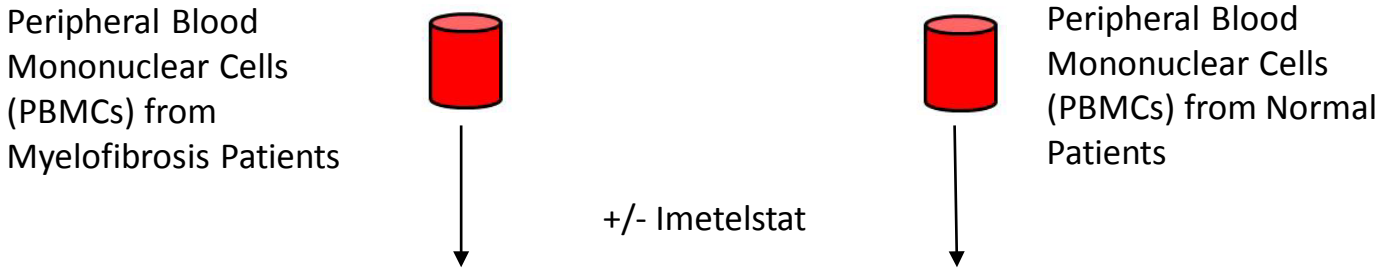
# *In Vitro* Proof-of-Concept: Imetelstat Selectively Inhibits Malignant Megakaryopoiesis (ASH 2014)*




**Effect of imetelstat on megakaryopoiesis in *in vitro* cultures**

- **Selective inhibition of the proliferation of malignant megakaryocytic progenitor cells in cultures derived from myelofibrosis PBMCs**
- **Reduction in number of malignant megakaryocytes in cultures derived from myelofibrosis PBMCs**
- **Inhibition of late-stage megakaryocytic maturation in cultures derived from both myelofibrosis and normal PBMCs**

*Abstract# 4592: Imetelstat (GRN163L), a Telomerase Inhibitor Selectively Affects Malignant Megakaryopoiesis in Myeloproliferative Neoplasms (MPN), Iancu-Rubin C, Hoffman R, *et al.*

# Preliminary Results from Myelofibrosis Pilot Study

## Results of the first 33 MF patients enrolled in the study

## Data as of September 10, 2014



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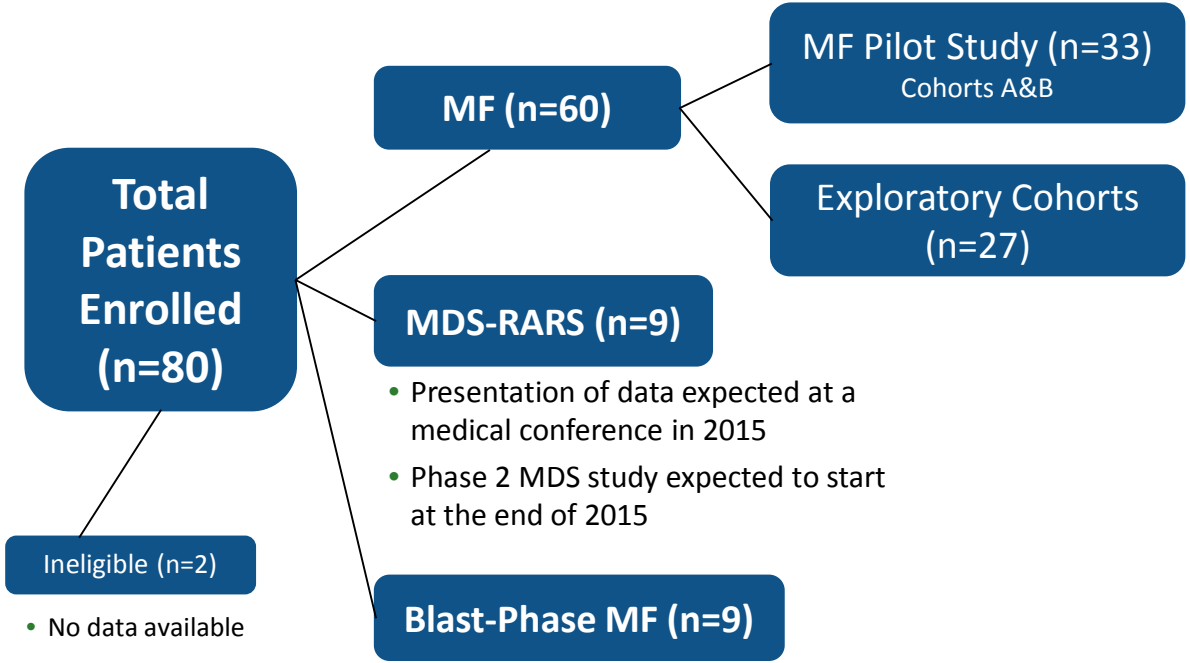
# Top-Line Observations from MF Pilot Study (n=33)

- **Data continues to suggest that imetelstat has disease-modifying activity in MF**
  - Continue to observe unprecedented and durable remissions (CR+PR)
  - Recent exome analyses have strengthened the evidence that imetelstat's principal mechanism of action in MF is inhibition of the malignant progenitor cell clone
- **No new safety signals have been observed**
  - Myelosuppression continues to be the principal dose-limiting toxicity

# Study Overview




- Presented at ASH 2014 earlier today
- Publication expected

- Exploratory dosing regimens in which the initial dose and/or treatment intervals were altered and combinations of candidate biomarkers used to assign patients to these altered dosing regimens

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- No new safety signals observed
- Neither the dosing regimens nor the combinations of biomarkers used for prospective treatment assignments led to improved treatment outcomes
- Results not expected to alter the immediate development path forward for imetelstat
- No current presentation plans

- Presentation of data expected at a medical conference in 2015
- Phase 2 MDS study expected to start at the end of 2015

- Anti-leukemic activity observed
- Combination regimens likely needed
- AML is currently in the Janssen/Geron clinical development plan

- No data available



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# Myelofibrosis Pilot Study Schema (n=33)

Principal Investigator:
**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=19):**
9.4 mg/kg
q3 weeks*

**Cohort B (n=14):**
9.4 mg/kg weekly
FOR FIRST CYCLE ONLY
then q3 weeks*

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

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



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# Patient Demographics and Baseline Disease Characteristics

| | Total (n=33) |
|---|---|
| Median Age (range; years) | 67.0 (53.0-79.0) |
| Male | 22 (66.7%) |
| Myelofibrosis Subtype | |
| Primary | 18 (54.5%) |
| Post-ET | 5 (15.2%) |
| Post-PV | 10 (30.3%) |
| DIPSS-plus Risk Status | |
| Intermediate-2 risk | 16 (48.5%) |
| High Risk | 17 (51.5%) |
| Previously Treated | 26 (78.8%) |
| Median # of Prior Treatments (range) | 2 (1–6) |
| Prior JAK inhibitors | 19 (57.6%) |
| Abnormal Karyotype | 16 (48.5%) |
| Unfavorable Karyotype per DIPSS-plus | 6 (18.2%) |
| Transfusion Dependent | 13 (39.4%) |
| Constitutional Symptoms[±] | 21 (63.6%) |
| Palpable Splenomegaly | 23 |
| Median (range; cm) | 15.0 (5.0-33.0) |

ET = Essential Thrombocythemia; PV = Polycythemia Vera; [±] 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.



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

| | 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/CI: 36.4%**

**CR/PR: 21.2%**

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

*CR (3 Arm A, 1 Arm B); PR (1 Arm A, 2 Arm B)

# Manifestations of Disease Addressed in Remission

**all manifestations of disease must be addressed in patients to achieve a remission**

| Patient number | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| **Best response per IWG criteria** | **CR** | **CR** | **CR** | **PR** | **PR** | **CR** | **PR** |
| Normal cellularity and reversal of bone marrow fibrosis | ✓ | ✓ | ✓ | ✓ | x | ✓ | x |
| Normal peripheral blood counts and smears | ✓ | ✓ | ✓ | x | ✓ | ✓ | ✓ |
| Anemia response or transfusion independence | ✓ | ✓ | — | ✓ | — | — | ✓ |
| Complete resolution of splenomegaly (by palpation) | ✓ | ✓ | ✓ | — | ✓ | ✓ | ✓ |
| Complete resolution of symptoms | — | ✓ | ✓ | — | ✓ | ✓ | ✓ |

remission

clinical improvement

— = disease manifestation not present at baseline



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# Duration of Treatment and Treatment Discontinuations

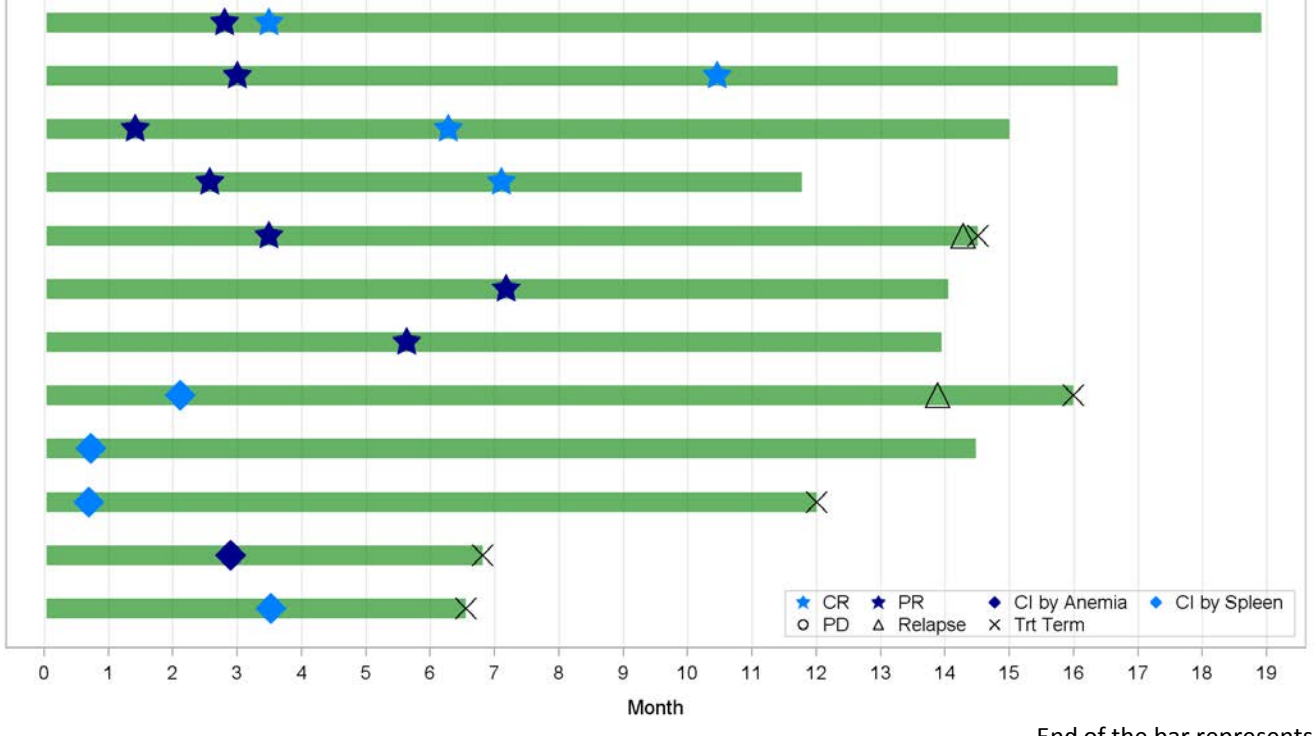
- Median duration of treatment: 11 cycles (range 2-21)
- Median time on treatment:
  - CR/PR/CI: 14.3 months (range 6.5-18.9)
  - Others: 6.9 months (range 1.4-16.4)
- 24 patients (72.7%) have discontinued treatment, mainly because of insufficient response (n=15) despite stable disease or due to disease progression (n=4)

| Patient Status and Reason for Treatment Discontinuation | Total (n=33) |
|---|---|
| On Treatment | 9 (27.3%) |
| Discontinued Treatment: | 24 (72.7%) |
| SD but "Insufficient Response/Alternative Therapy" | 15 (45.5%) |
| Disease Progression/Relapse | 4 (12.1%) |
| Death[@] | 2 (6.1%) |
| Adverse Event/Side Effects/Complications[¥] | 2 (6.1%) |
| Other Complicating Disease[#] | 1 (3.0%) |

[@]One death due to upper GI hemorrhage (unrelated to imetelstat per investigator assessment), the other due to intracranial hemorrhage with febrile neutropenia after prolonged myelosuppression (possibly related to imetelstat)
[¥]One case of thrombocytopenia and the other persistent thrombocytopenia
[#]Pre-existing problems with atrial fibrillation

# Onset and Durability of Response for CR/PR/CI Patients

- **Complete or partial remission in 7 of 33 (21.2%) patients (4 CR; 3 PR)**
  - Median onset of remission at 5 cycles (range 1-9)
  - 6 CR/PR remain in remission with median duration of 11.1 months (range 6.9-16.2)
- **Overall response CR/PR/CI (clinical improvement) in 12 of 33 (36.4%) patients**




End of the bar represents last cycle

# Efficacy Results: Spleen Response and Transfusion Independence

| | Total |
|---|---|
| **Spleen Response (by palpation lasting ≥ 12 weeks)*** | 8/23 (34.8%) |
| **Transfusion dependent becoming transfusion independent** | 4/13 (30.8%) |

**Spleen response (by palpation)**: Response must last at least 12 weeks; baseline splenomegaly that is palpable at 5-10 cm, below the LCM, becomes not palpable, OR a baseline splenomegaly that is palpable at >10 cm, below the LCM, decreases by ≥50%

*Median spleen size at baseline 15 cm below the LCM (range 5-33 cm)

*12/23 (52.2%) patients with palpable spleen at baseline achieved at least 50% reduction in palpable spleen size

**Transfusion independence**: Requires absence of any packed red blood cells (PRBC) transfusions during any consecutive 12-week interval with a hemoglobin level of ≥8.5 g/dL

# Efficacy Results: Exploratory Endpoints

- **Broad spectrum of benefit not just limited to the patients achieving CR, PR or CI, but is observed in the majority of patients treated with imetelstat**

| | N | Complete or Partial Resolution | Complete Resolution | Partial Resolution[#] |
|---|---|---|---|---|
| **Circulating Blasts** (≥1% at baseline) | 21 | 17 (81.0%) | 14 (66.7%) | 3 (14.3%) |
| **Leukoerythroblastosis**[&](≥2% at baseline) | 27 | 22 (81.5%) | 13 (48.1%) | 9 (33.3%) |
| **Marked Leukocytosis** (>25 x$10^9$/L at baseline) | 10 | 8 (80.0%) | 3 (30.0%) | 5 (50.0%) |
| **Thrombocytosis** (> 450 x$10^9$/L at baseline) | 11 | 11 (100.0%) | 10 (90.9%) | 1 (9.1%) |

[#] Partial resolution:>50% reduction from baseline
[&] ≥5% in splenectomized patients



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# Safety Results: Grade ≥3 Non-Hematologic Adverse Events[@]

| | All (n=33) | Related (n=33) |
|---|---|---|
| Fatigue | 3 (9.1%) | |
| APTT | 2 (6.1%) | |
| Atrial fibrillation | 2 (6.1%) | |
| Heart failure | 2 (6.1%) | |
| Hyperkalemia | 2 (6.1%) | |
| Ejection fraction decreased | 1 (3.0%) | |
| Intracranial hemorrhage [#] | 1 (3.0%) | 1 (3.0%) [¥] |
| Febrile neutropenia | 1 (3.0%) | 1 (3.0%) [¥] |
| Upper GI hemorrhage [#] | 1 (3.0%) | |
| Hyponatremia | 1 (3.0%) | |
| Lipase increased | 1 (3.0%) | |
| Lung infection | 1 (3.0%) | |
| Pain | 1 (3.0%) | |
| Pyoderma gangrenosum [Σ] | 1 (3.0%) | |
| Small intestinal obstruction | 1 (3.0%) | |

[@] Excluded myelosuppression which is presented in separate table

[#] Grade 5 event; [¥] same patient ; [Σ] the pyoderma gangrenosum is associated with a post-op (splenectomy) complication

# Safety Results: All Grade ≥3 Hematologic Toxicities

- Cytopenias are the main dose limiting toxicity which appear to be manageable with dose modification and retreatment guidelines

| | Worst CTC Grade | Arm A (n=19) | Arm B (n=14) | Total (n=33) |
|---|---|---|---|---|
| Thrombocytopenia | 3 | 8 (42.1%) | 1 (7.1%) | 9 (27.3%) |
| | 4 | 2 (10.5%) | 5 (35.7%) | 7 (21.2%) |
| Neutropenia | 3 | 4 (21.1%) | 2 (14.3%) | 6 (18.2%) |
| | 4 | 2 (10.5%) | 4 (28.6%) | 6 (18.2%) |
| Anemia | 3 | 7 (36.8%) | 9 (64.3%) | 16 (48.5%) |
| | 4 | – | – | – |
| Leukopenia | 3 | 3 (15.8%) | 6 (42.9%) | 9 (27.3%) |
| | 4 | 2 (10.5%) | 1 (7.1%) | 3 (9.1%) |

Hematologic toxicity is defined as worsening in CTC grade after baseline

# Safety Results: Prolonged Myelosuppression

- Prolonged myelosuppression (Grade 4 cytopenias lasting ≥4 weeks) observed in a small number of patients who received weekly dosing

| | | Arm A (n=19) | Arm B (n=14) | Total (n=33) |
|---|---|---|---|---|
| G3/4 Lab Lasted≥4 Weeks | Thrombocytopenia | 5 (26.3%) | 3 (21.4%) | 8 (24.2%) |
| | Neutropenia | 1 (5.3%) | 2 (14.3%) | 3 (9.1%) |
| | Either | 5 (26.3%) | 5 (35.7%) | 10 (30.3%) |
| G4 Lab Lasted ≥ 4 Weeks | Thrombocytopenia | 0 | 1 (7.1%) | 1 (3.0%) |
| | Neutropenia | 1 (5.3%) | 1 (7.1%) | 2 (6.1%) |
| | Either | 1 (5.3%) | 2 (14.3%) | 3 (9.1%) |

# Myelofibrosis Pilot Study
# Exome Analysis

Data as of December 5, 2014



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# Patient 1 - CR

Baseline
(12/17/12)

→

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

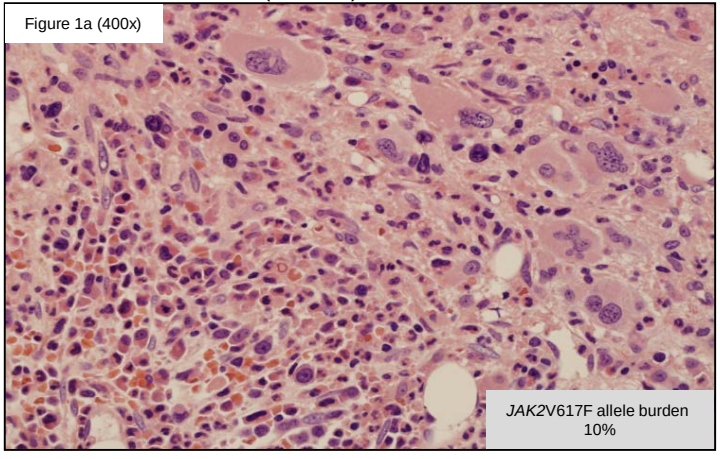

Figure 1a (400x)

*JAK2*V617F allele burden 10%

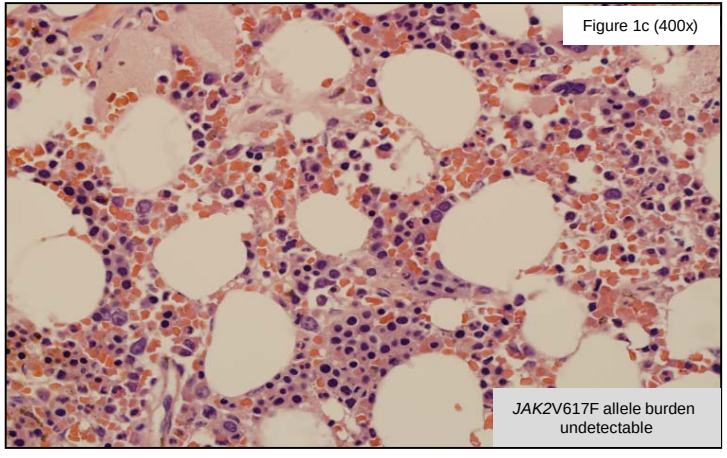

Figure 1c (400x)

*JAK2*V617F allele burden undetectable

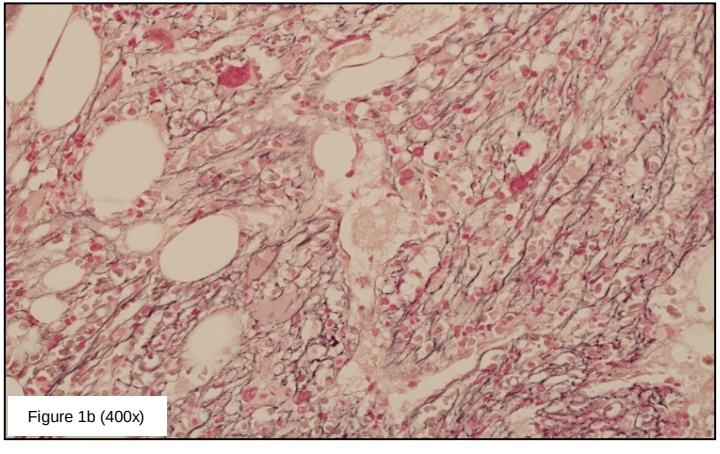

Figure 1b (400x)

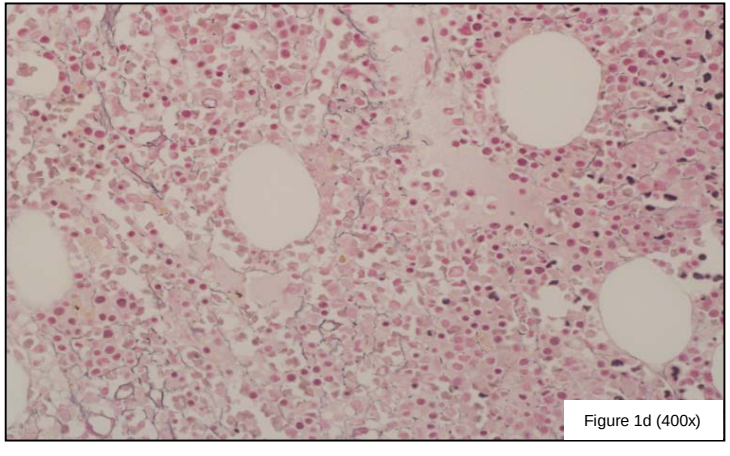

Figure 1d (400x)



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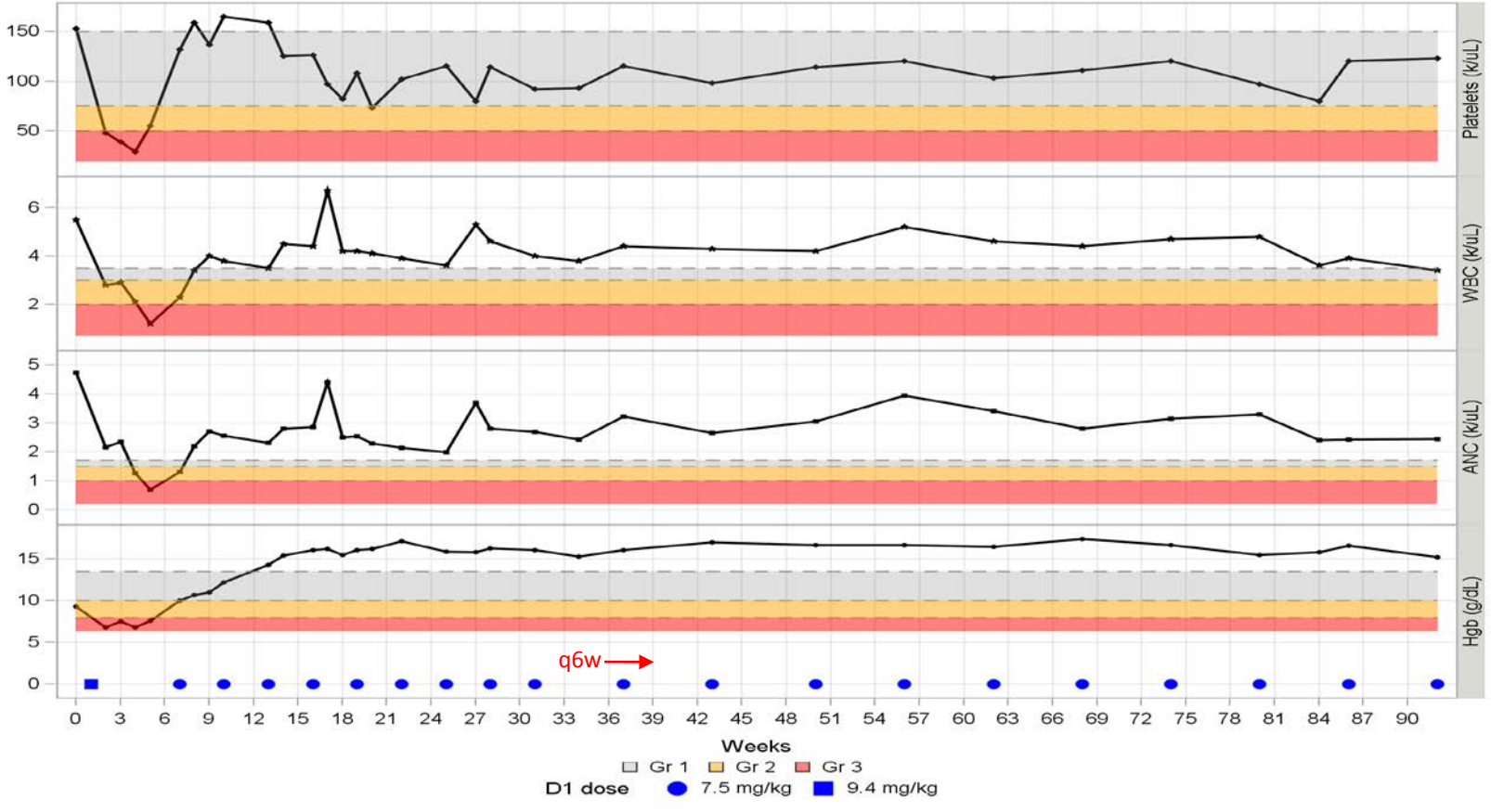
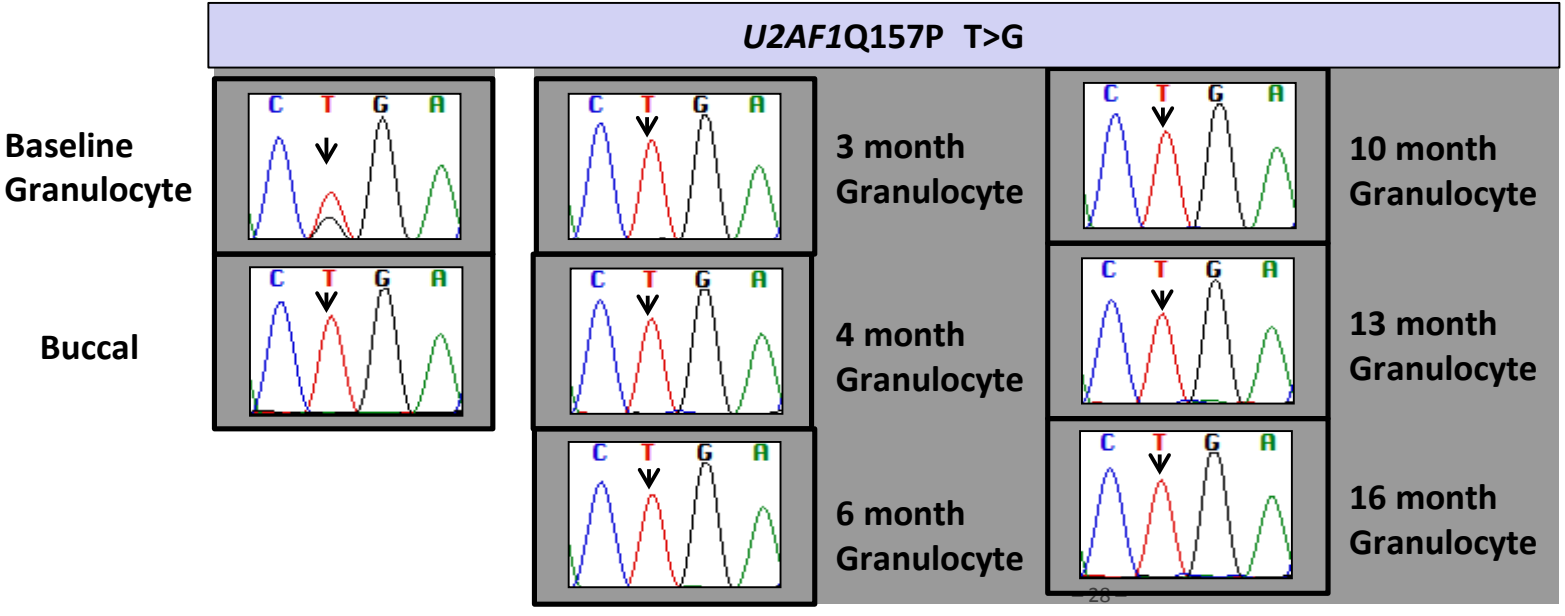
# Patient 1 - CR

**Patient 1: 73 y/o male,**
**JAKi-naïve, PMF, DIPSS+ intermediate-2 risk, 4 prior treatments/failed pomalidomide**

**Partial remission at 2 cycles;**
**Complete remissions at 4 cycles; Remain in remission at q6w treatment interval**



# Patient 1 - CR

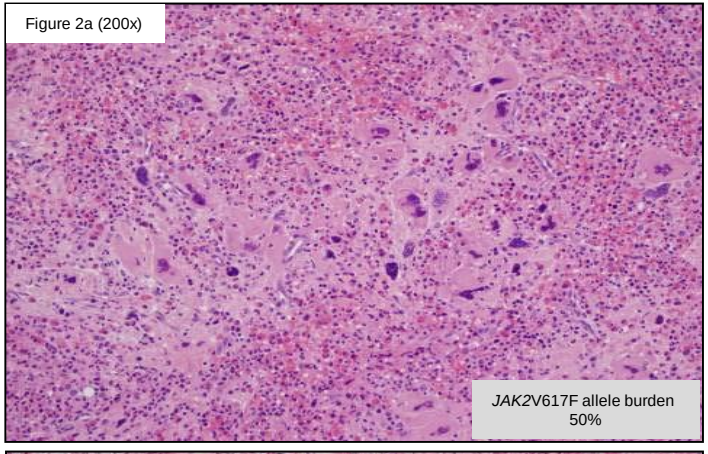

U2AF1Q157P T>G
Baseline Granulocyte
Buccal
3 month Granulocyte
4 month Granulocyte
6 month Granulocyte
10 month Granulocyte
13 month Granulocyte
16 month Granulocyte
C T G A

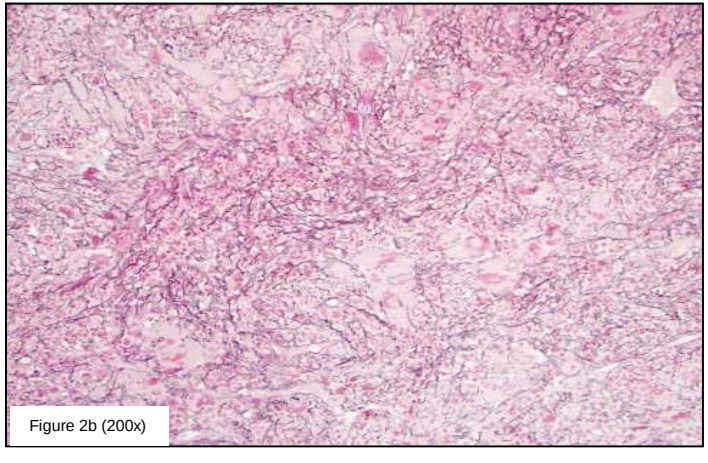
# Patient 2* - CR

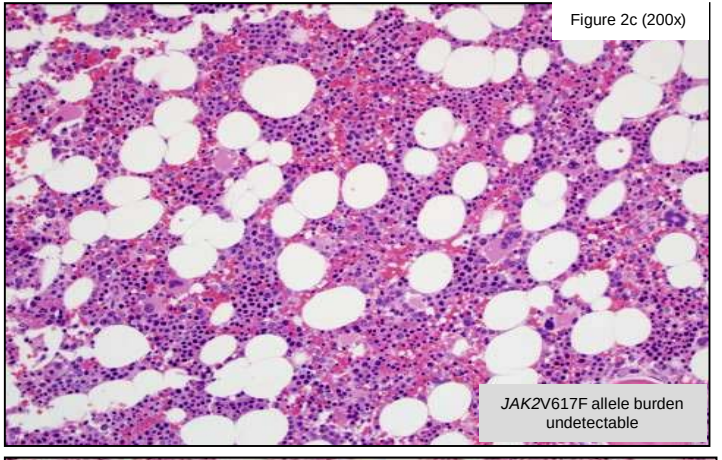
Baseline
(4/29/13)

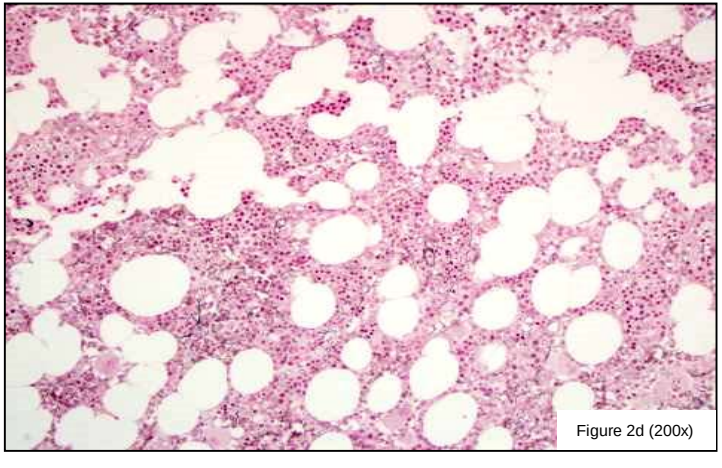
→

3-months post-imetelstat therapy
(7/24/13)




* Presented at ASH 2013 as Patient 3-CR



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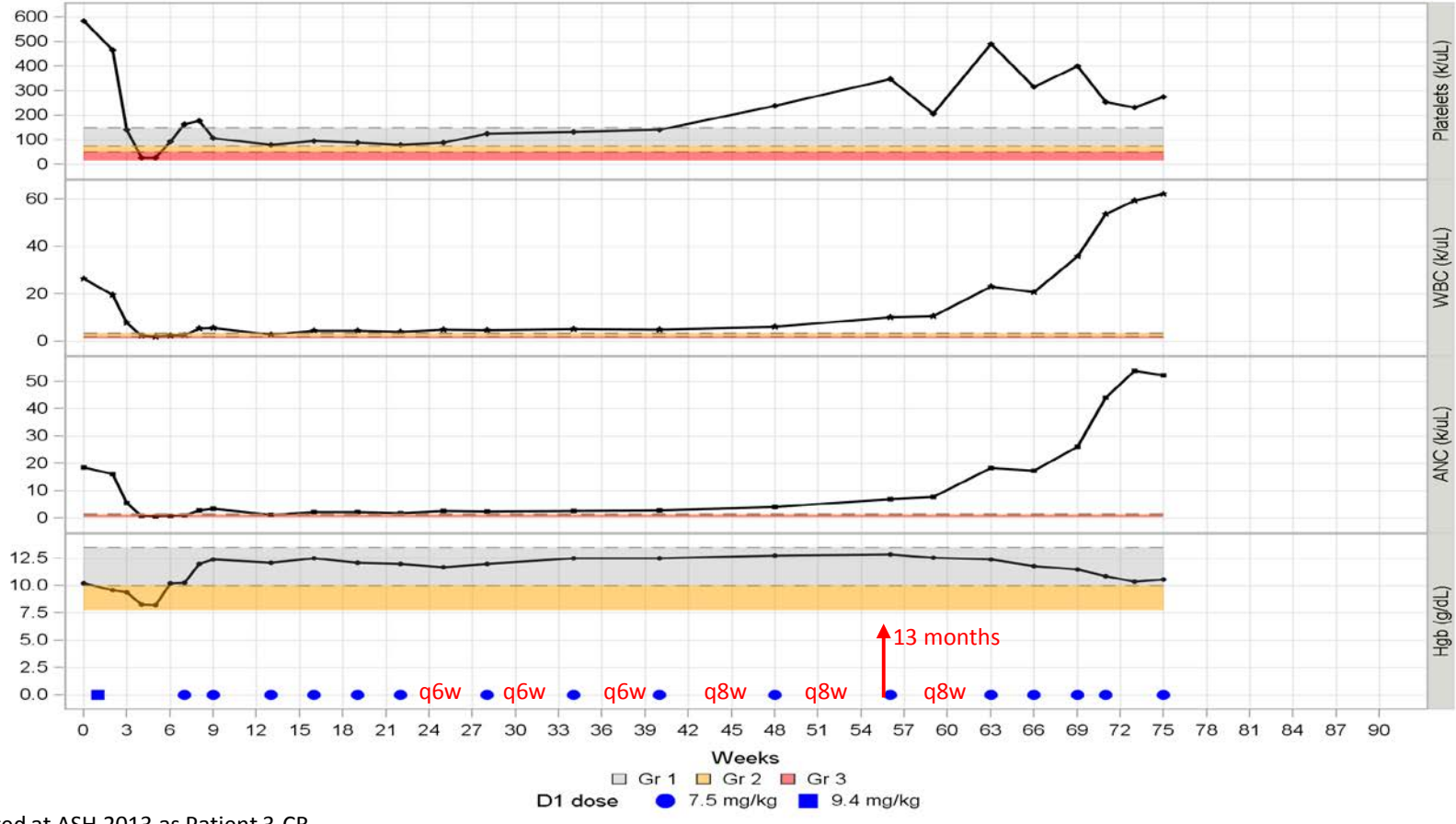
# Patient 2* - CR

**Patient 2: 79 y/o male,**
**JAKi-naïve post-ET MF, DIPSS+ high risk, 2 prior treatments, constitutional symptoms, splenomegaly**

**Partial remission at 1 cycles;**
**Complete remissions at 7 cycles;**
***Relapsed after dosing interval lengthened to q8w***




* Presented at ASH 2013 as Patient 3-CR



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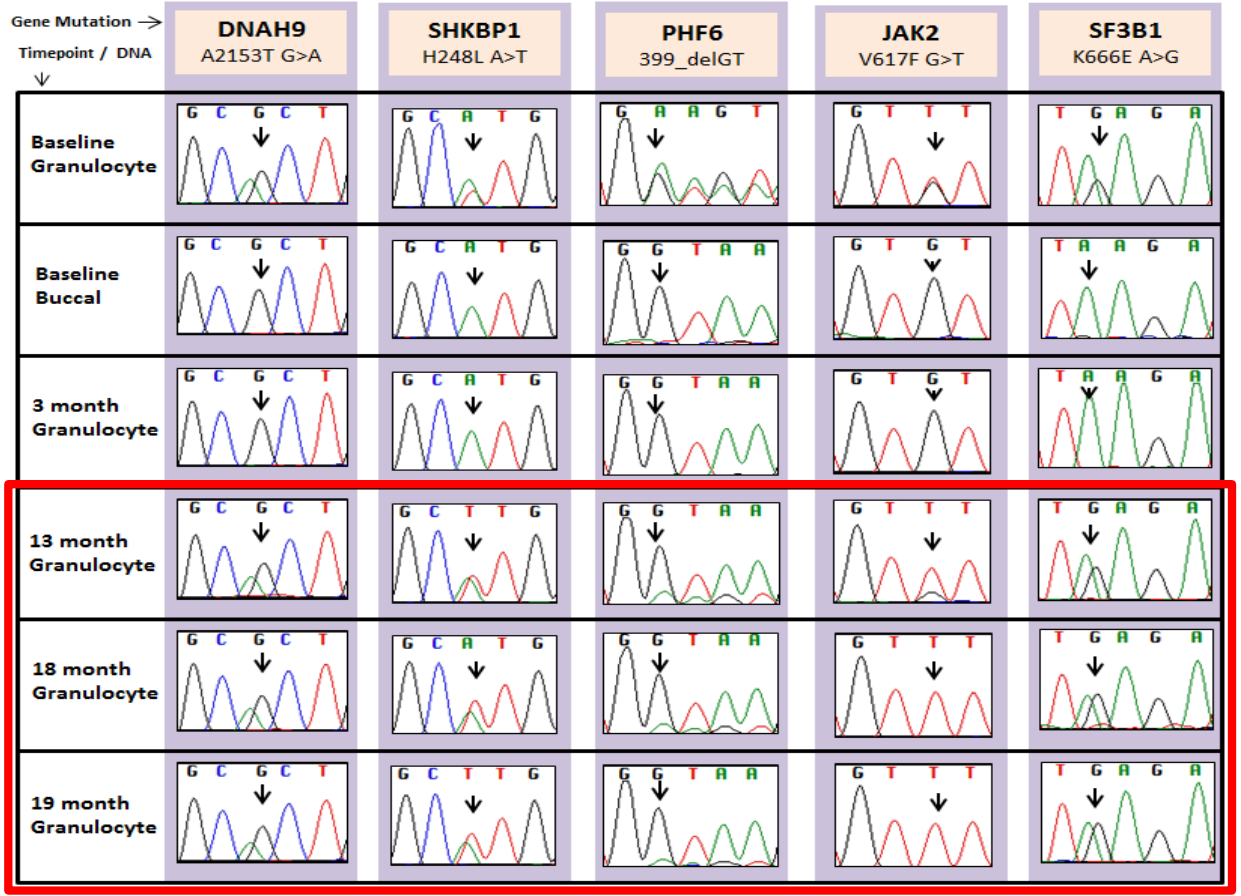
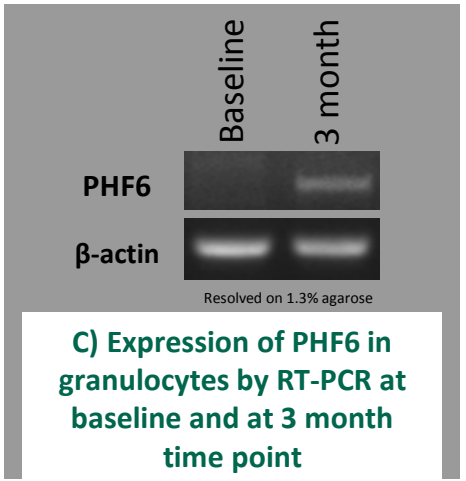
# Patient 2* - CR

## A) Exome sequencing of matched PBMC/PMN from baseline and 3 month PMN

| Type of Mutation | Gene ID | Chr | Pos (hg19) | Ref | Alt | Protein Change | % PBMC | % Baseline PMN | % 3 month PMN | Cosmic |
|---|---|---|---|---|---|---|---|---|---|---|
| INSERTION | *PHF6* | X | 133511785 | GGT | GGT/G | | 93.0% | 53.0% | 0.0% | 0 |
| SNV | *JAK2* | 9 | 5073770 | G | T | V617F | 93.0% | 57.0% | 2.0% | 29906 |
| SNV | *SF3B1* | 2 | 198267361 | A | G | K666E | 46.0% | 32.0% | 2.0% | 6 |
| SNV | *SHKBP1* | 19 | 41086741 | A | T | H248L | 40.0% | 42.0% | 0.0% | 0 |
| SNV | *DNAH9* | 17 | 11650930 | G | A | A2153T | 48.0% | 31.0% | 0.0% | 0 |

## B) Validation of relevant mutations by sanger sequencing at baseline vs. follow-up




**C) Expression of PHF6 in granulocytes by RT-PCR at baseline and at 3 month time point**

* Presented at ASH 2013 as Patient 3-CR

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# Myelofibrosis Pilot Study: Key Conclusions

- **Data continues to suggest that imetelstat has disease-modifying activity in MF**
  - Unprecedented remissions (CR+PR) by IWG-MRT criteria observed
    - 21.2 % (7/33) remission rate (4 CR and 3 PR)
    - All 4 CR patients experienced reversal of bone marrow fibrosis including 3 with complete molecular response
  - Remissions are durable (median 11.1 mos; range 6.9-16.2 as of Sept 10, 2014)
  - Overall response (CR+PR+CI) rate of 36.4% (12/33)
- **Myelosuppression is the principal dose-limiting toxicity**
  - Believed to be an on-target effect on progenitor cells
  - Clinically manageable through dose hold rules and dose modifications
- **No new safety signals have been observed**
- **The potential association between patient response and specific mutations warrant further exploration in future studies**
- **Next step: Phase 2 study in MF expected to start in mid-2015**

# Preclinical Proof-of-Concept in Acute Myelogenous Leukemia (AML)

Role of telomerase in AML
Activity of imetelstat in AML

**Steven Lane, M.D., Ph.D.**
**Queensland Institute of Medical Research**




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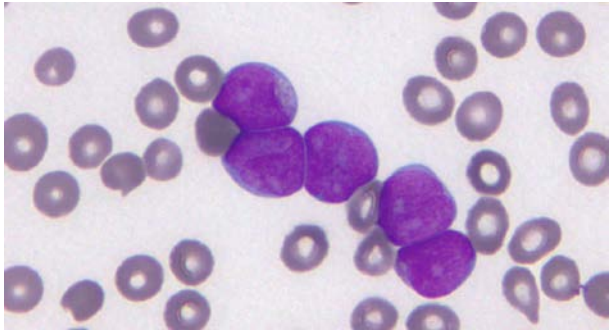
# Acute Myelogenous Leukemia (AML)

- Incidence ~ 19000/yr in USA*
- Mortality ~ 10,500/yr in USA#
  - Infections
  - Bleeding
  - Infiltration of organs with cancer cells
  - Complications of treatment
- Current treatment comprises chemotherapy (an anthracycline with cytarabine) which is largely unchanged for 40 yrs
- Patients >60 yrs old, most patients die of AML (survival ~10%)
- Despite initial response to chemotherapy, most patients will relapse$
  - Relapsed disease is incurable (with standard therapy)
- AML oncogenes bind and activate telomerase
- In this mouse study, we have shown that telomerase is essential for AML maintenance and recurrence/relapse after treatment@



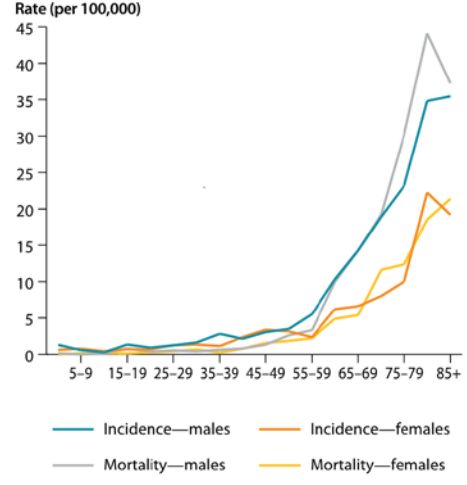



**Figure B.2b: Acute myeloid leukaemia incidence and mortality rates[d] by age at diagnosis, 2007**

*seer.cancer.gov; cancer.org/cancer #AIHW Cancer statistics;
$Leukemia; 2010:1751-9; @Bruedigam *et al.*, 2014 Cell Stem Cell, *In Press*



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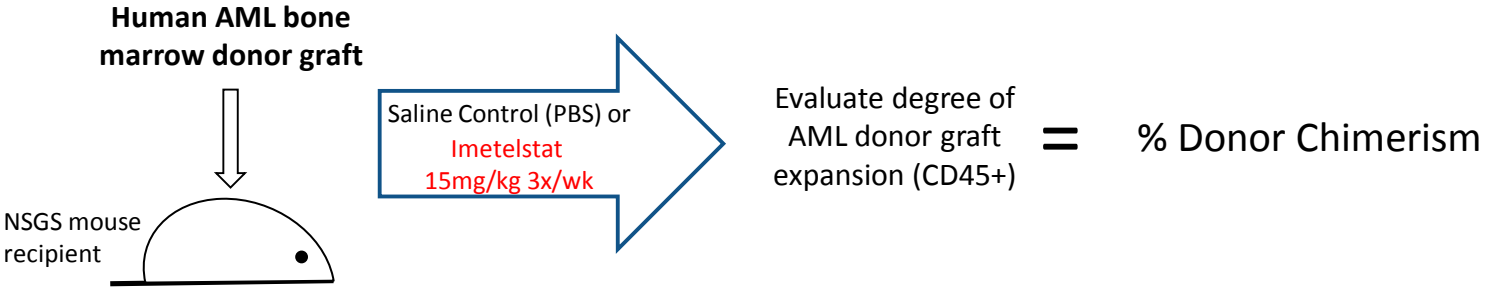
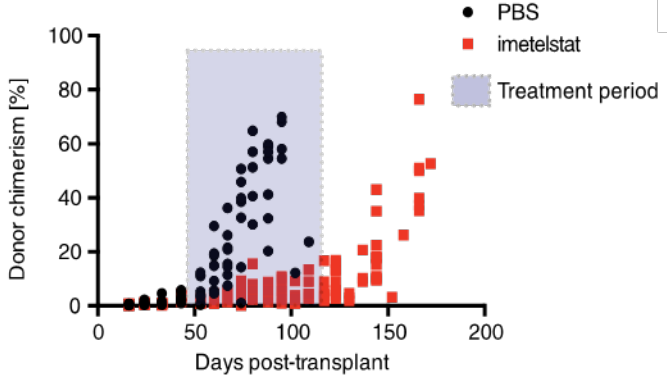
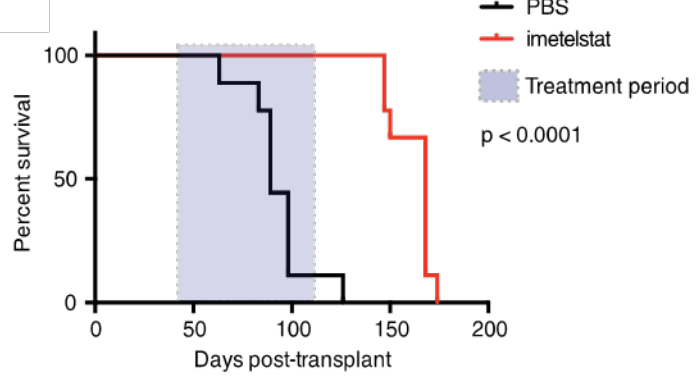
# Imetelstat Impairs Human AML Leukemic Stem Cell (LSC) Function and Prolongs Survival in Human Primary AML Xenografts




Imetelstat inhibits expansion of AML leukemic cells




Inhibition of AML leukemic expansion confers a survival advantage

Bruedigam C., et al. **Cell Stem Cell** 2014, *In Press*



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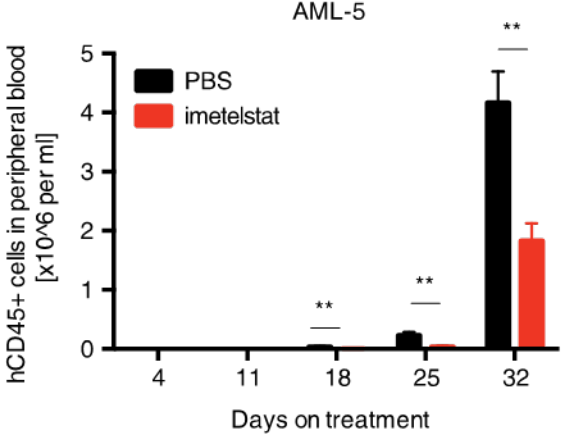
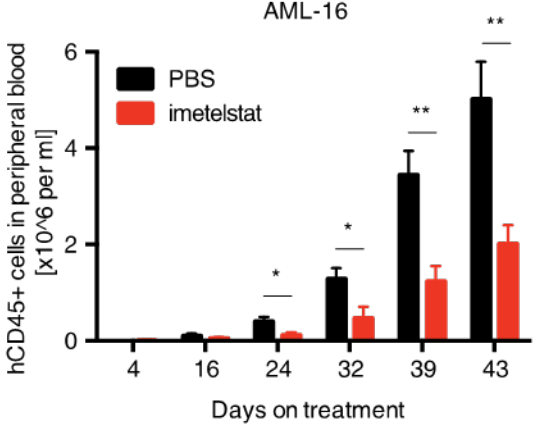
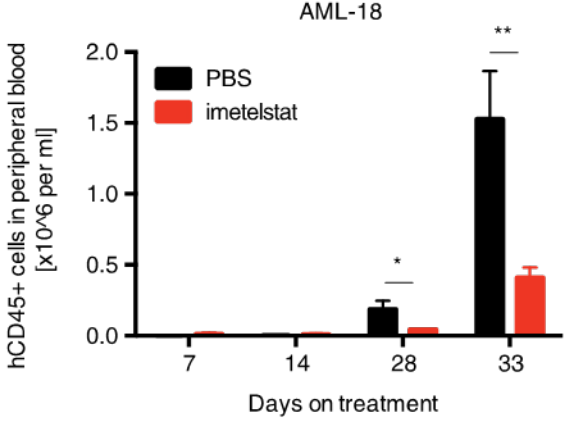
# Imetelstat Inhibits Leukemic Expansion From Multiple Subtypes of AML Donor Grafts

| Xenograft | FAB subtype | Cytogenetics | Known mutations and other notes |
|---|---|---|---|
| AML-5 | M2 | Monosomy 7 | WT1 (SNP A->G at R16754) |
| AML-16 | M4 | Normal | FLT3-ITD+;<br>NPM1+* (SNP G->T at W288C);<br>IDH2* (SNP G->A at R140);<br>WT1* (SNP A->G at R16754) |
| AML-18 | M1 | t(9;11), MLL translocation | KRAS (SNP G->C at G12D/V/A or G13D/A);<br>WT1 (SNP A->G at R16754) |




Bruedigam C., et al. **Cell Stem Cell** 2014, *In Press*



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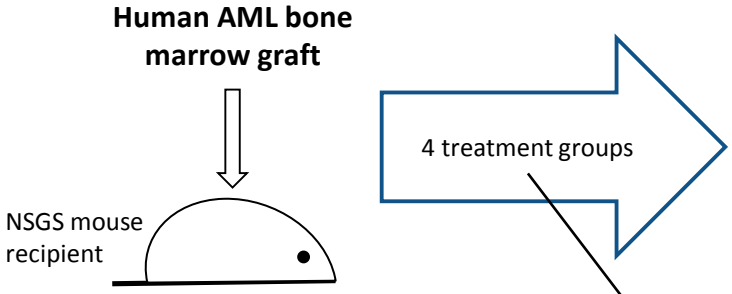
# Effect of Adding Imetelstat to Doxorubicin Chemotherapy




Evaluate degree of AML donor graft expansion (CD45+) = % Donor Chimerism

## Assigned Treatment Groups

| Group | Doxorubicin | Imetelstat 3x/wk |
|---|---|---|
| PBS/Saline | - | - |
| Imetelstat | - | + |
| Doxorubicin | + | - |
| Imetelstat + Doxorubicin | + | + |

Bruedigam C., et al. **Cell Stem Cell** 2014, *In Press*



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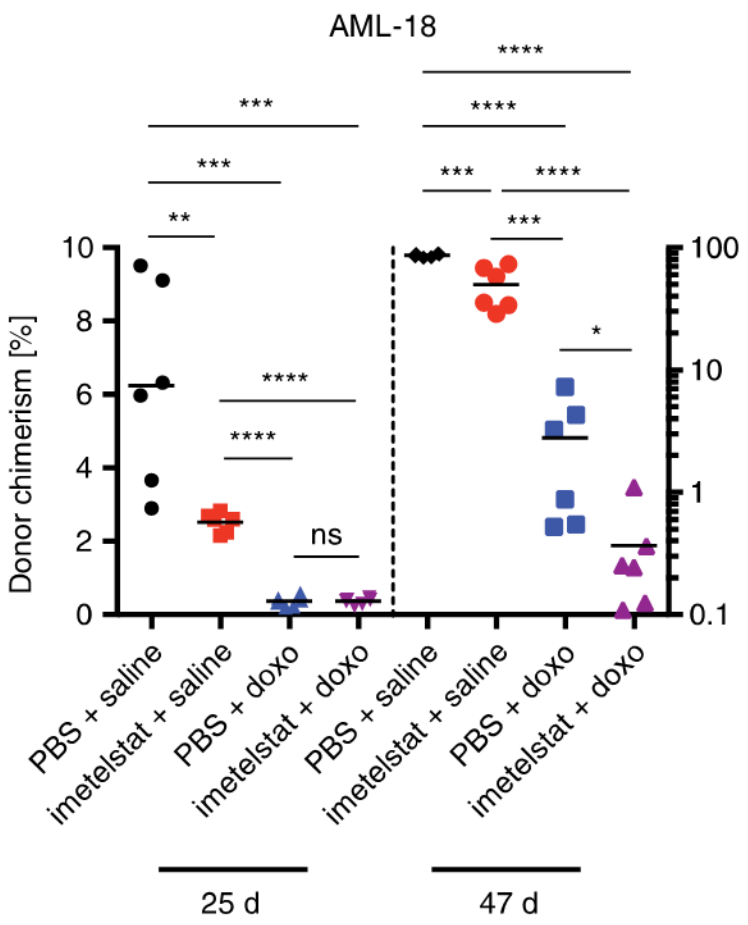
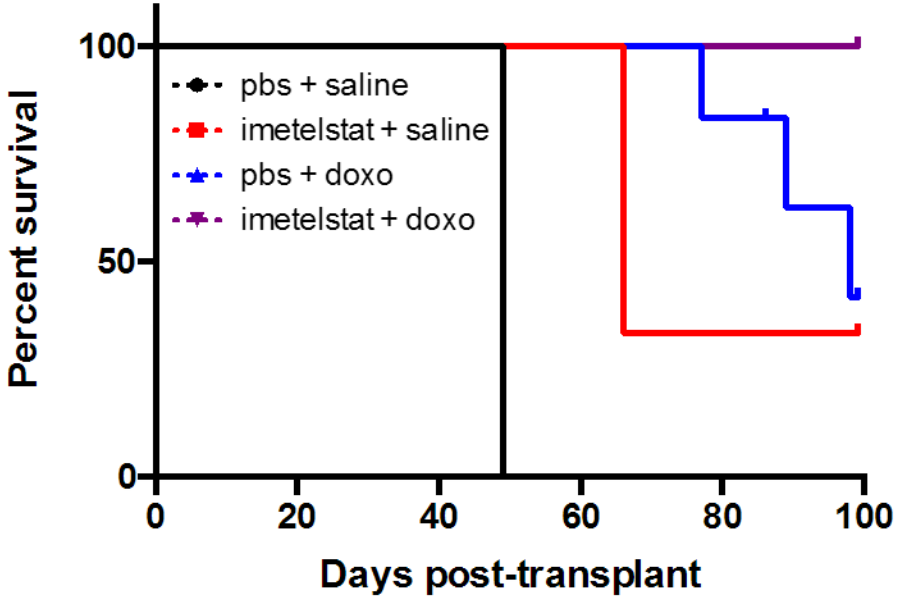
# Imetelstat + Doxorubicin Prolongs Survival in Human AML Xenografts




Bruedigam C., et al. **Cell Stem Cell** 2014, *In Press*



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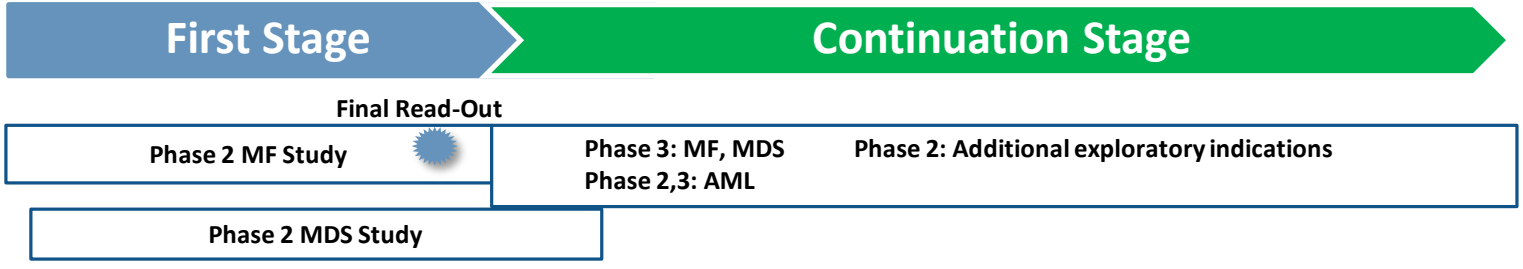
# *In Vivo* Preclinical Study in AML: Key Conclusions

- **Telomerase is a key mediator of LSC survival and function**
- **Imetelstat can be used to target telomerase and deplete LSCs**
- **Combining imetelstat with doxorubicin chemotherapy may be an effective strategy for preventing AML relapse**
- **Overall conclusion: strong rationale for testing imetelstat in AML patients**

# Future Clinical Development of Imetelstat

# Collaboration with Janssen for Exclusive Global Development of Imetelstat




- Janssen to execute Phase 2 MF and Phase 2 MDS studies
- Janssen to provide Continuation Decision upon final read-out of Phase 2 MF study

- Geron has Opt-In right to share further US development and promotion costs
- Under Opt-In, Geron may co-promote by providing 20% of US sales force in lieu of paying 20% promotion costs

| First Stage Economics | |
|---|---|
| **Cost Share** | 50% Geron<br>50% Janssen |
| **Upfront** | $35M |

| Continuation Stage Economics | | |
|---|---|---|
| | **Opt-In** | **Opt-Out** |
| **Cost Share** | 20% Geron<br>80% Janssen | 100% Janssen |
| **Continuation/US Rights Fee** | $65M | $135M |
| **Dev/Reg Milestones** | up to $470M | up to $415M |
| **Sales Milestones** | up to $350M | up to $350M |
| **Royalty % Tier *** | Mid teens to low twenties | Double digit to mid-teens |

* Calculated on worldwide net sales in any countries where regulatory exclusivity exists or there are valid claims under patent rights exclusively licensed to Janssen

# Upcoming Events

- **MDS-RARS data from Mayo Clinic (presentation expected at 2015 medical conference)**
- **Initiation of Phase 2 MF study (expected start mid-2015)**
- **Initiation of Phase 2 MDS study (expected start end 2015)**

# Q&A