ONCONOVA THERAPEUTICS

Myelodysplastic Syndromes (MDS) Key Opinion Leader Breakfast Meeting

December 16, 2015

Safe Harbor Summary

This presentation contains forward-looking statements about Onconova Therapeutics, Inc. based on management's current expectations which are subject to known and unknown uncertainties and risks. Onconova has attempted to identify forward-looking statements by terminology including "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately" or other words that convey uncertainty of future events or outcomes. Our actual results could differ materially from those discussed due to a number of factors, including, but not limited to, our ability to raise additional equity and debt financing on favorable terms, the success of our Phase 2 and Phase 3 trials of rigosertib, our ability to obtain regulatory approval of rigosertib and other risk factors outlined in our filings with the Securities and Exchange Commission. We are providing this information as of the date of this presentation and do not undertake any obligation to update any forward-looking statements, whether written or oral, that may be made from time to time, as a result of new information, future events or otherwise.

Introduction

Ramesh Kumar, Ph.D.
President and Chief Executive Officer

Today's Speakers

- **Guillermo Garcia-Manero, M.D**. – Chief of the Section of Myelodysplastic Syndromes, Deputy Chair of Translational Research, Co-Director of the DNA Methylation Core, and Professor in the Department of Leukemia at The University of Texas MD Anderson Cancer Center

- **Lewis R. Silverman, M.D**. – Associate Professor of Medicine in Hematology and Medical Oncology and Assistant Professor of Oncological Sciences at the Icahn School of Medicine at Mount Sinai

- **Steven Fruchtman, M.D.** – Chief Medical Officer, Onconova

Agenda

- **Rigosertib in combination with azacitidine for MDS and AML**

  Lewis R. Silverman, M.D.

- **Next steps for rigosertib + azacitidine combination**

  Steven Fruchtman, M.D.

- **Overview of HR-MDS and INSPIRE Phase 3 trial**

  Guillermo Garcia-Manero, M.D.

- **Q&A**

A Phase II Study of the Combination of Oral Rigosertib and Azacitidine in Patients with Myelodysplastic Syndromes (MDS)

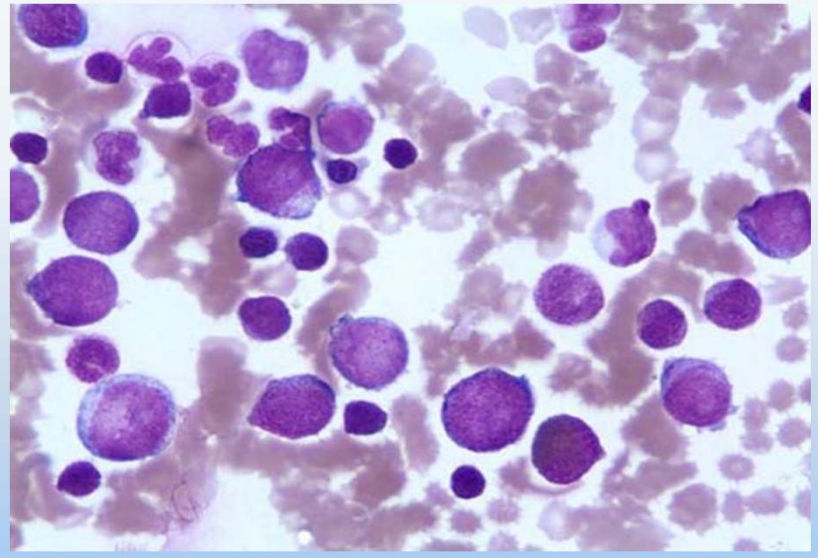
American Society of Hematology, 2015
Orlando, FL

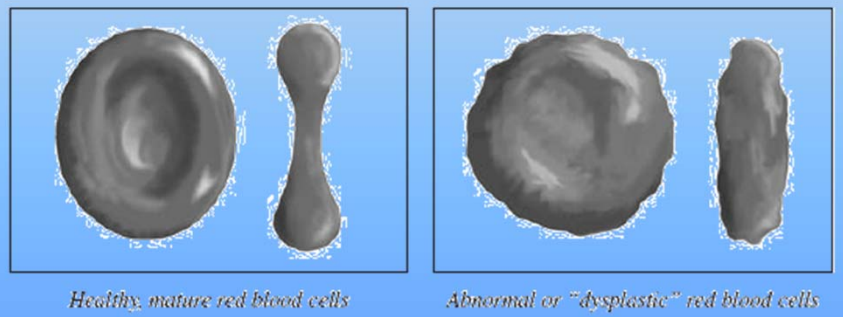
Shyamala C. Navada, MD[1], Lewis R. Silverman, MD[1], Katherine Hearn, RN[2], Rosalie Odchimar-Reissig, RN[1], Erin Demakos, RN[1], Yesid Alvarado, MD[2], Naval Daver, MD[2], Courtney DiNardo, MD[2], Marina Konopleva, MD[2], Gautam Borthakur, MD[2], Pierre Fenaux, MD[3], Steven Fruchtman, MD[4], Nozar Azarnia, PhD[4], Guillermo Garcia-Manero, MD[2]

[1]Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY; [2]MD Anderson Cancer Center, Houston, TX; [3]Hôpital St Louis/Université Paris; [4]Onconova Therapeutics, Inc., Newtown, PA

What is MDS?

Microscopic View of MDS Bone Marrow





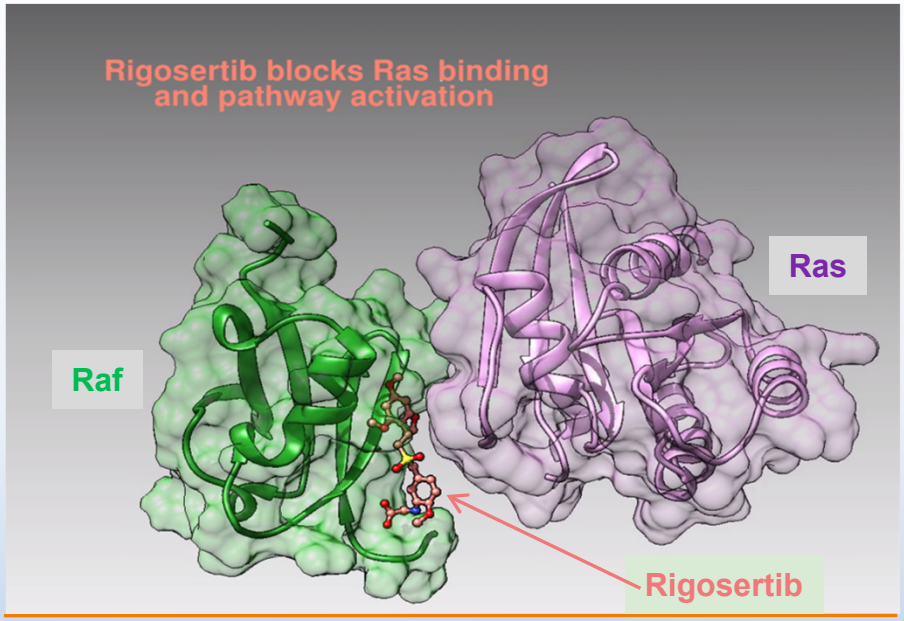
Healthy, mature red blood cells

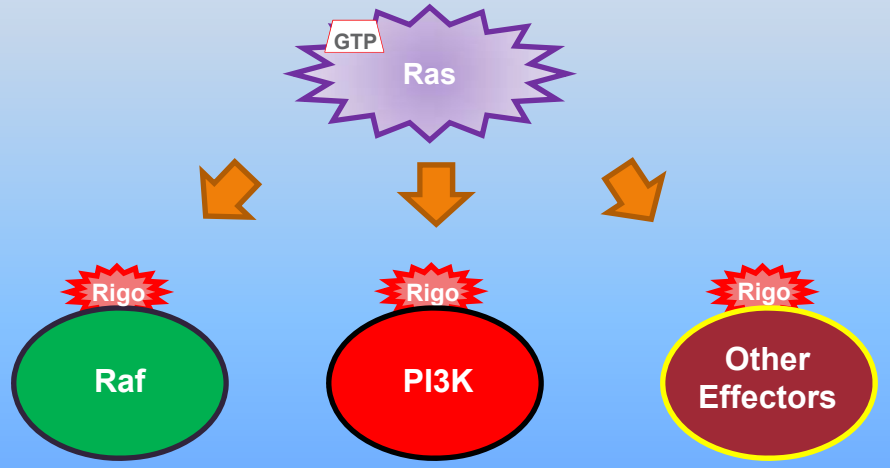
Abnormal or "dysplastic" red blood cells

- **Definition**: Evidence of bone marrow failure and abnormal development of one or more of the types of circulating cells, with 5%-30% immature blast (leukemic type) cells in the bone marrow
- **Major Problems:** Bleeding, infections, iron overload from multiple red blood cell transfusions
- **Cause**: Unknown, with possible causes including chemicals and radiation, or chemotherapy treatment

Background: Rigosertib

- Inhibits cellular signaling as a Ras mimetic by targeting the Ras-binding domain (RBD)
- Novel MOA blocks multiple cancer targets and downstream pathways PI3K/AKT and Raf/PLK
- Mechanism may impact aberrant signaling in MDS
- Initial studies indicate clinical activity in patients with MDS and AML
- Both oral and IV rigosertib are available – this study used the oral formulation





Divakar et al, AACR Annual Meeting 2014; abstract LB-108; Olnes et al, Leuk Res 2012;36:964-5; Chapman et al, Clin Cancer Res 2012;18:1979-91.

Background: Treatment of Higher-risk MDS

- Azacitidine is standard of care (SOC) for higher-risk MDS patients
- Clinical responses in MDS 45-50%[a]
  - CR rate 7-17%
  - Trilineage response rate of 24%
- All patients ultimately relapse or fail to respond; these patients have a poor prognosis, with a median overall survival (OS) of only 4-6 months[b]
- Currently, there are no accepted standard therapies after HMA failure

a Silverman LR, McKenzie DR, Peterson BL, et al. Further analysis of trials with azacitidine in patients with myelodysplastic syndrome: studies 8421, 8921, and 9221 by the Cancer and Leukemia Group B. J Clin Oncol 2006;24(24): 3895-3903.

b Prebet T, Gore SD, Estemi B, et al. Outcome of high-risk myelodysplastic syndrome after azacitidine treatment failure. J Clin Oncol 2011;29(24):3322-7.

Rigosertib is Synergistic with Azacitidine in Preclinical Studies

- Sequential exposure with rigosertib followed by azacitidine achieved maximum synergy

Combination Drug	CI	Ratio	Description
Rigosertib* (125 nM) + 5AzaC (2 uM)	0.44	1:62.5	Synergism
Rigosertib (125 nM) + 5AzaC (4 uM)	**0.30**	**1:31.25**	**Strong synergism**
Rigosertib (250 nM) + 5AzaC (2 uM)	0.68	1:125	Synergism
Rigosertib (250 nM) + 5AzaC (4 uM)	0.57	1:62.5	Synergism
Rigosertib (500 nM) + 5 AzaC (2 uM)	0.63	1:250	Synergism
Rigosertib (500 nM) + 5AzaC (4 uM)	0.75	1:125	Moderate synergism

- Rigosertib is active in azacitidine-resistant cell line

Skiddan I, Zinzar S, Holland JF, et al. Toxicology of a novel small molecule ON1910Na on human bone marrow and leukemic cells in vitro. AACR Abstract 1310, April 2006; 47:309.

Background

- Phase 1 combination was well tolerated with evidence of efficacy in patients with MDS*

- The adverse event profile of combining azacitidine with oral rigosertib was similar to single-agent azacitidine

** Navada S, Garcia-Manero G, Wilhelm F, et al. A phase I/II study of the combination of oral rigosertib and azacitidine in patients with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). ASH 2014; Abstract 3252.*

Eligibility Criteria for Phase 2

Diagnosis

- MDS, CMML
- IPSS Int-1, Int-2, or High risk

Prior Treatment

- Prior HMAs permitted
- No prior rigosertib

Demographics

ECOG PS ≤ 2

Age ≥ 18 years

Organ Function

- Creatinine ≤ 2.0 mg/dL
- Total bilirubin ≤ 2.0 mg/dL
- ALT/AST ≤ 2.5 x ULN

Study Endpoints
Response Criteria per IWG 2006*

- Complete response, partial response or bone marrow response
- Hematologic improvement in neutrophil, platelet, and erythroid response
- Safety and tolerability of combination

** Cheson BD, Greenberg PL, Bennett JM, et al. Clinical application and proposal for modification of the International Working Group (IWG) response criteria in myelodysplasia. Blood 2006;108: 419-25.*

Combination Trial Design
Sequence Suggested by Preclinical Findings

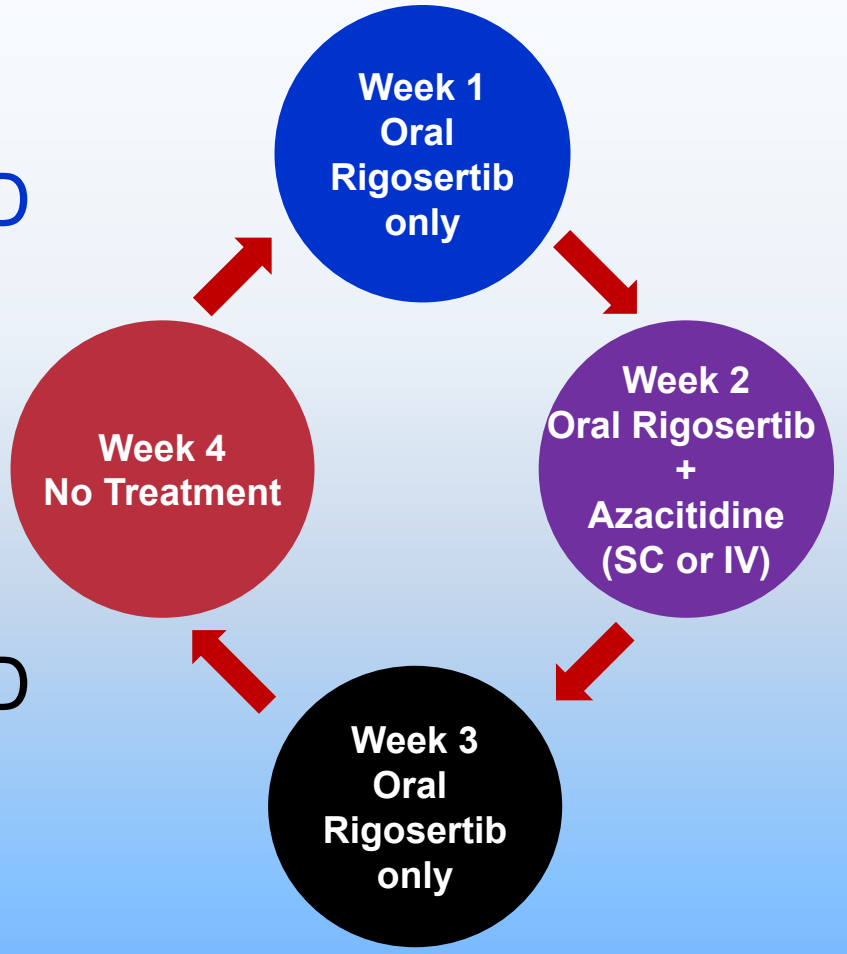
Treatment regimen:

Week 1: Oral rigosertib BID (560 mg AM/280 mg PM)

Week 2: Oral rigosertib + azacitidine (75 mg/m^2/day SC or IV)

Week 3: Oral rigosertib BID

Week 4: No treatment



Navada S, Garcia-Manero G, Wilhelm F, et al. A phase I/II study of the combination of oral rigosertib and azacitidine in patients with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). ASH 2014; Abstract 3252.

Methods

- **Phase 1** - Escalating-dose cohorts of oral rigosertib with standard-dose azacitidine in a classic 3+3 design in patients with MDS, CMML, or AML
- Recommended rigosertib Phase 2 Dose - 560 mg in AM and 280 mg in PM
- **Phase 2** - Patients with MDS and CMML, previously untreated, or had failed or progressed on a prior HMA
- Bone marrow aspirate/biopsy at Baseline, Week 4, and every 8 weeks after
- This analysis includes only the MDS patients from phase 1 and phase 2

Patient Characteristics

Number of MDS patients treated		37
Age	Median Range	64 25-85
Sex	Male Female	27 (73%) 10 (27%)
ECOG performance status	0 1 2	9 (24%) 27 (73%) 1 (3%)
IPSS classification	Intermediate-1 Intermediate-2 High	10 (27%) 15 (41%) 12 (32%)
IPSS cytogenetic risk	Good Intermediate Poor Unknown	8 (22%) 14 (38%) 9 (24%) 6 (16%)
Prior HMA therapy	Azacitidine Decitabine Both	10 (27%) 3 (8%) 1 (3%)

Efficacy Results

Number of MDS patients treated		37
Evaluable for response (8 Ph1, 22 Ph2)		30
Overall response		23 (77%)
Hematologic response*	Complete remission	6 (20%)
	Partial remission	0
	Marrow CR	16 (53%)
	Stable disease	6 (20%)
	Progressive disease	1 (3%)
Hematologic improvement*		1 (3%)
Not evaluable		3 (10%)
Too early to evaluate		4 (13%)
Median duration of treatment (months)		4 (1-27+)

* Per IWG 2006

Lineage Response per IWG 2006

Marrow CR (N=16)	Evaluable HI P/E/N HI P/E HI – none HI – TETE	12 3 (25%) 3 (25%) 6 (50%) 4
Hematologic improvement* (N=26)	Any lineage Erythroid (E) Platelet (P) Neutrophil (N)	13 (50%)* 11 12 7

*Includes patients with CR, HI and mCR lineage responses among evaluable patients

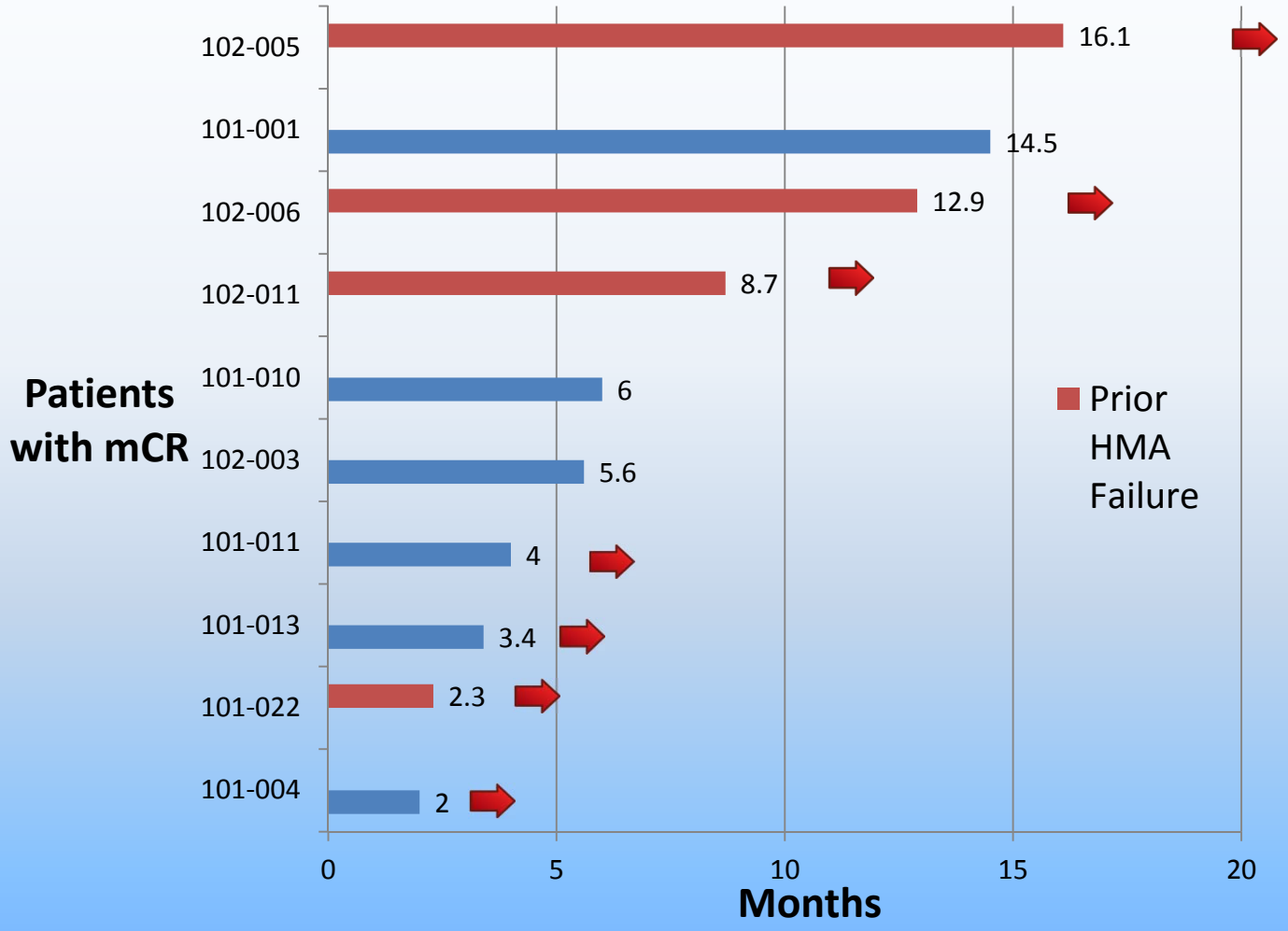
TETE = too early to evaluate

Overall Response per IPSS Subgroup

IPSS	# Pts	CR	PR	mCR	HI	SD	PD	NE	RR
Int-1	10	3	0	2	1	2	0	2	75%
Int-2	15	2	0	6	3*	4	1	2	62%
High	12	1	0	8	3*	0	0	3	100%

* Concurrent marrow CR and hematologic improvement

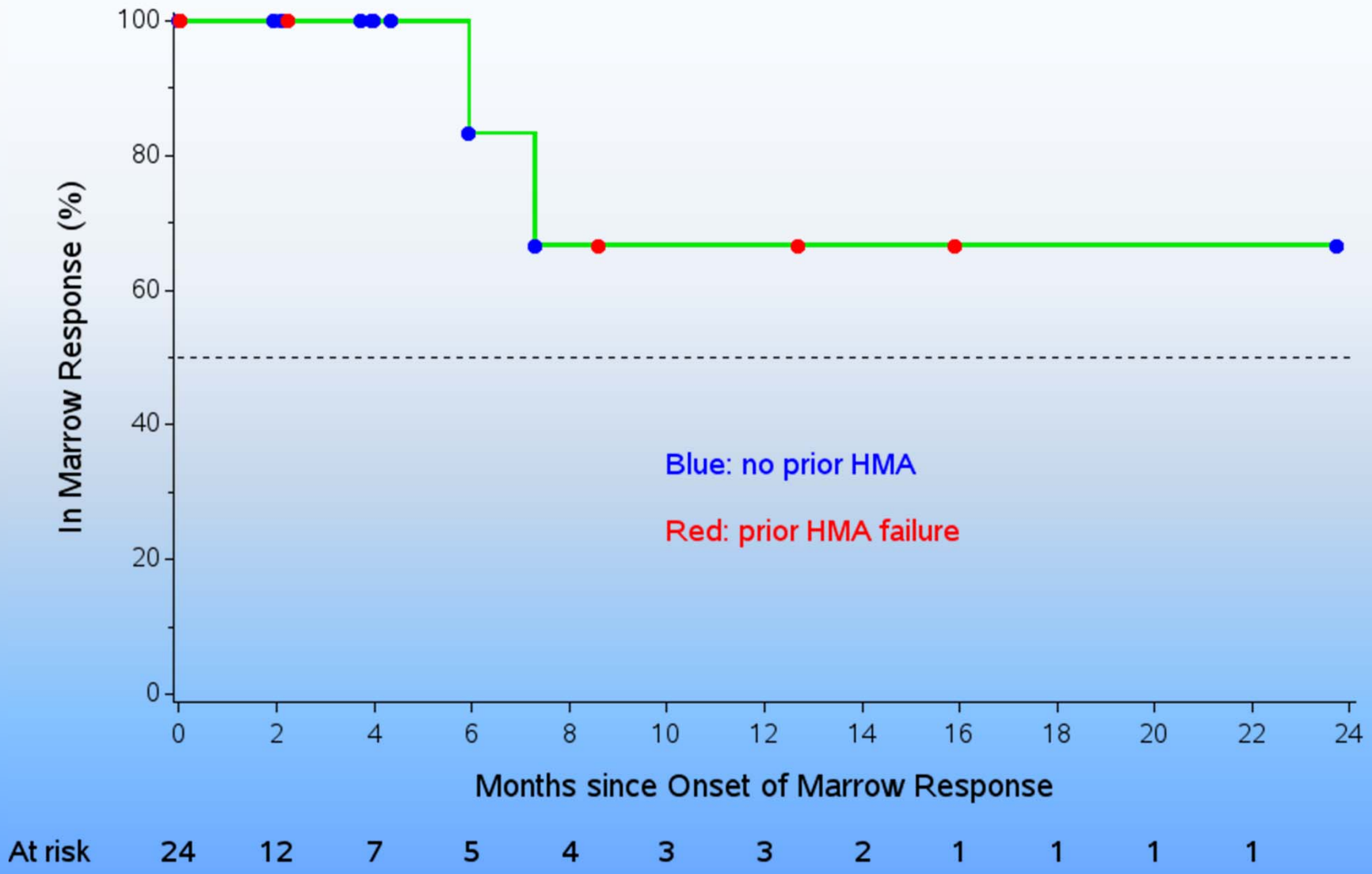
Duration of Marrow CR



Marrow response was ongoing at the time of the last assessment

Not shown are 12 patients who are pending marrow assessment after achieving mCR

Duration of Marrow Response



Efficacy: MDS Patients with Prior HMA Failure

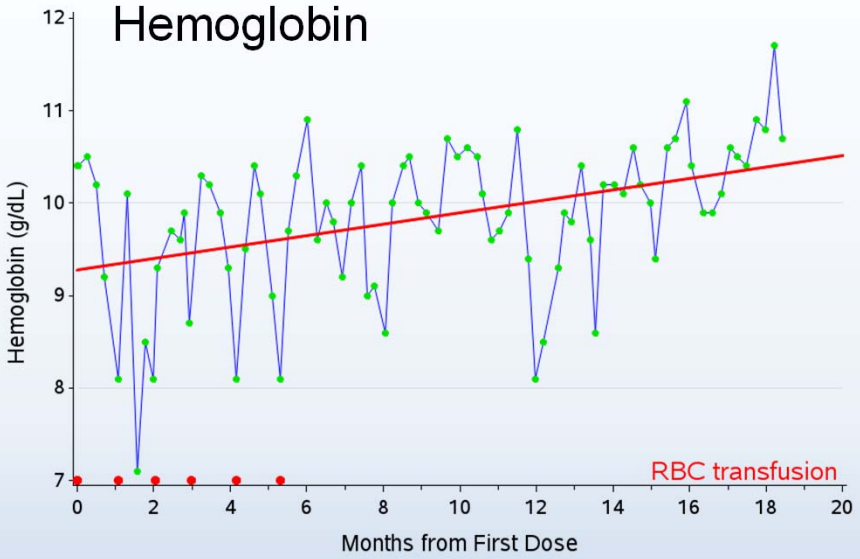
Number of patients evaluable for response (3 Ph1, 8 Ph2)	11 (8 AZA, 2 DAC, 1 both)
Number of prior HMA cycles	4-20
Hematologic response per IWG 2006	7 (64%)
CR	1
PR	0
mCR	4
mCR with concurrent HI	2
Stable disease	3
Progressive disease	1
Hematologic improvement (trilineage)	3
HMA-naïve patients (N=19) response per IWG	16 (84%)

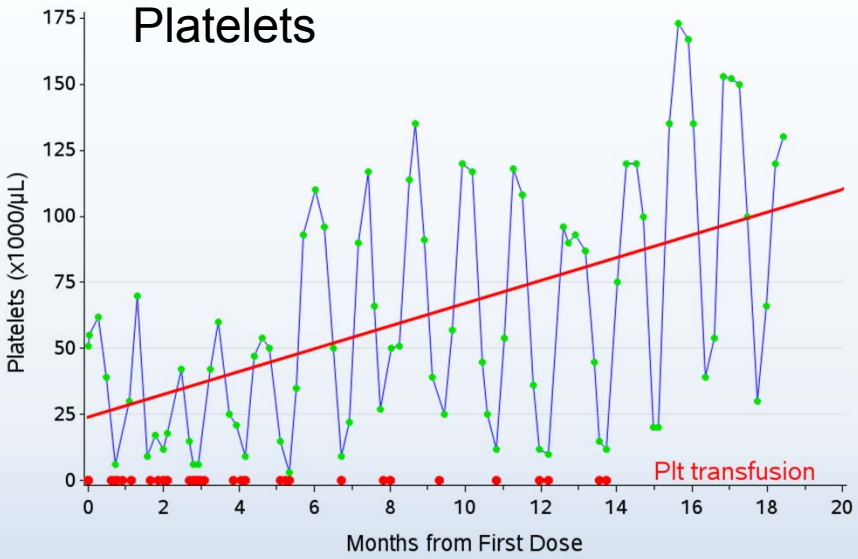
Response per IPSS Subgroup with Prior HMA Failure

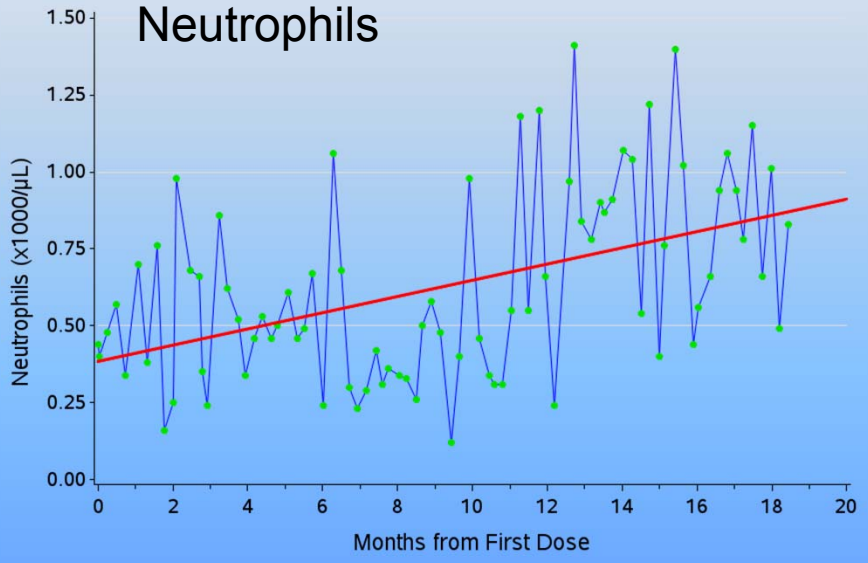
IPSS	# Pts	CR	PR	mCR	HI	SD	PD	NE	RR
Int-1	3	0	0	2	0	1	0	0	67%
Int-2	7	0	0	2	1*	2	1	2	40%
High	4	1	0	2	1*	0	0	1	75%

* Concurrent marrow CR and hematologic improvement

Hematology Trends for Patient 101-006







- 12 cycles of AZA – stable disease
- RBC and platelet transfusions
- Blasts 7%
- Monosomy 7
- Runx-1
- AZA + RIG in 09-08 for 20+ months
- Complete remission
- RBC transfusion independent
- <5% blasts
- PB CR criteria

Fatal Serious Adverse Events

Number of MDS pts treated	37
Number (%) of deaths*	3 (8%)
Multi-organ failure	1
Worsening of AML	1
Sepsis	1

*** No death was considered to be treatment-related**

Most Common (≥ 10%) Treatment-emergent Adverse Events (N = 37)

MedDRA Preferred Term	Cycle 1		Cycles ≥2	
	All Grades	Grade ≥3	All Grades	Grade ≥3
Constipation	7 (19%)	-	8 (22%)	-
Cough	6 (16%)	-	5 (14%)	-
Decreased appetite	6 (16%)	-	6 (16%)	-
Diarrhoea	7 (19%)	-	7 (19%)	1 (3%)
Dizziness	5 (14%)	-	4 (11%)	-
Dysuria	6 (16%)	-	7 (19%)	-
Fatigue	10 (27%)	-	7 (19%)	-
Haematuria	5 (14%)	1 (3%)	5 (14%)	2 (5%)
Hypokalaemia	5 (14%)	1 (3%)	3 (8%)	1 (3%)
Injection site pain	4 (11%)	-	1 (3%)	-
Nausea	10 (27%)	-	6 (16%)	-
Neutropenia	4 (11%)	4 (11%)	8 (22%)	8 (22%)
Pyrexia	9 (24%)	-	3 (8%)	-
Tachycardia	4 (11%)	-	2 (5%)	-
Thrombocytopenia	9 (24%)	9 (24%)	5 (14%)	5 (14%)

Conclusions

- Oral rigosertib and azacitidine demonstrated an overall response rate of 77% in patients with MDS.
- 64% of patients who had previously received an HMA and either did not respond or relapsed, responded to the combination; this represents a novel and important observation.
- The combination is well tolerated in patients with MDS and has a safety profile similar to single-agent azacitidine.
- Repetitive cycles of the combination can be safely administered without evidence of cumulative toxicity.
- Further exploration of this combination is warranted in defined MDS populations.

2006 IWG Response Criteria for MDS*

Category	Hematologic Response Criteria (responses must last at least 4 weeks)[a]

Complete remission (CR)	• Bone marrow: ≤ 5% myeloblasts with normal maturation of all cell lines.
	• Persistent dysplasia will be noted (dysplastic changes should consider the normal range of dysplastic changes)
	• Peripheral blood:
	  • Hemoglobin (Hgb) ≥ 11 g/dL (untransfused, patient not on erythropoietin)
	  • Neutrophils ≥ 1.0 x 10^9/L (not on myeloid growth factor)
	  • Platelets ≥ 100 x 10^9/L (not on a thrombopoietic agent)
	  • Blasts 0%

Partial remission (PR)	• All CR criteria (if abnormal prior to treatment), except: • Bone marrow blasts decreased by ≥ 50% compared with pretreatment but still > 5% • Cellularity and morphology not relevant
Marrow CR	• Bone marrow: ≤ 5% myeloblasts and decrease by ≥ 50% over pretreatment • Peripheral blood: if hematologic improvement (HI) responses, they will be noted in addition to the marrow CR
Stable disease (SD)	Failure to achieve at least PR, but no evidence of progression for > 8 weeks

a For a designated response (CR, PR), relevant response criteria must be noted on at least 2 successive determinations at least 1 week apart after an appropriate period following therapy (eg, 1 month or longer).

** Cheson BD, Greenberg PL, Bennett JM, et al. Clinical application and proposal for modification of the International Working Group (IWG) response criteria in myelodysplasia. Blood 2006;108:419-25.*

2006 IWG Response Criteria for MDS*

Hematologic Improvement[a]	Response Criteria (responses must last at least 8 weeks)[b]
Erythroid response (pretreatment, < 11 g/dL)	• Hgb increase by ≥ 1.5 g/dL • Relevant reduction of units of red blood cell (RBC) transfusions by an absolute number of at least 4 RBC transfusions/8 wk compared with the pretreatment transfusion number in the previous 8 wk. Only RBC transfusions given for a Hgb of ≤ 9.0 g/dL pretreatment will count in the RBC transfusion response evaluation.
Platelet response (pretreatment, < 100 x 10^9/L)	• Absolute increase of ≥ 30 x 10^9/L for patients starting with >20 x 10^9/L • Increase from < 20 x 10^9/L to >20 x 10^9/L and by at least 100%
Neutrophil response (pretreatment, < 1.0 x 10^9/L)	At least 100% increase and an absolute increase > 0.5 x 10^9/L
Progression or relapse after HI	At least 1 of the following: • At least 50% decrement from maximum response levels in granulocytes or platelets • Reduction in Hgb by ≥ 1.5 g/dL • Transfusion dependence

a Pretreatment counts averages of at least 2 measurements (not influenced by transfusions) ≥ 1 week apart (modification)

b For a designated response (CR, PR), relevant response criteria must be noted on at least 2 successive determinations at least 1 week apart after an appropriate period following therapy (eg, 1 month or longer).

** Cheson BD, Greenberg PL, Bennett JM, et al. Clinical application and proposal for modification of the International Working Group (IWG) response criteria in myelodysplasia. Blood 2006; 108:419-25.*

ONCONOVA THERAPEUTICS

Next steps for development of rigosertib + azacitidine combination

December 16, 2015

Steven Fruchtman, M.D.

Key Activity Data from Rigosertib Combination Trial (Study 09-08)

- Evaluable HMA-naïve patients per IWG 2006 criteria
  - **ORR (84%)** compares favorably to IMiD and HDACi combinations with azacitidine
  - CR in 5/19
  - Marrow response:
    - mCR in 10/19
    - mCR with concurrent HI in 5/19

- Evaluable HMA-failure patients per IWG 2006 criteria
  - **ORR (64%):**
    - Signal clearly demonstrates effect of rigosertib in the combination
    - Supports rigosertib activity in 2nd-line patients – focus of INSPIRE Phase 3 trial

Key Safety Data from Rigosertib Combination Trial (Study 09-08)

Azacitidine[1]

Adverse Event	Grade ≥3
Haematuria	2.3%
Anemia	13.7%
Neutropenia	61.1%
Thrombocytopenia	58.3%

Rigosertib + Azacitidine

Adverse Event	Grade ≥3
Haematuria	5.4%
Anemia	NR
Neutropenia	21.6%
Thrombocytopenia	27.0%

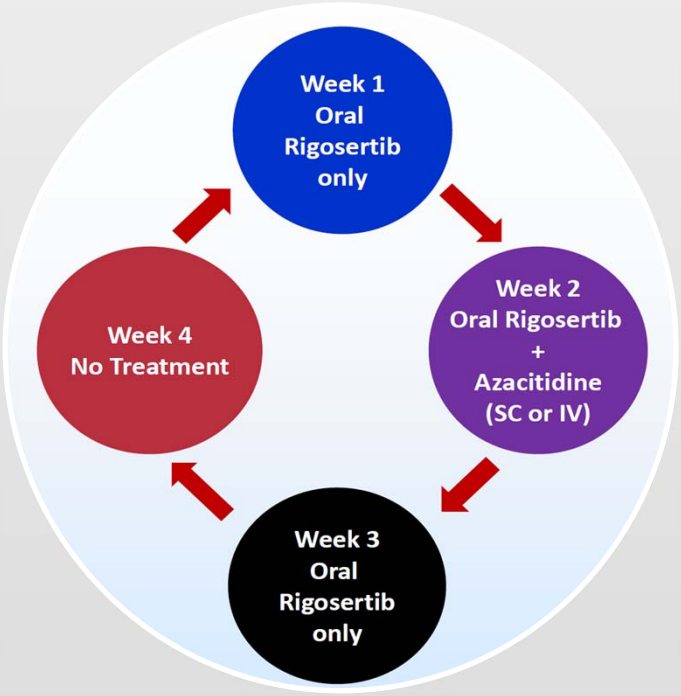
- Rigosertib + azacitidine generally well tolerated
- 4/37 MDS patients withdrew due to AE
- 2/37 MDS patients had dose reduction
- AE profile with combination did not differ from reported toxicities of azacitidine alone[1]

[1] http://www.vidaza.com/pi.pdf

Opportunities for Combination Rigosertib + Azacitidine

HMA-Naïve HR-MDS

- Expands MDS indication
- Oral dosing and minimal toxicity valuable differentiators vs. other HMA combos
- Randomized Phase 2 anticipated to confirm signal

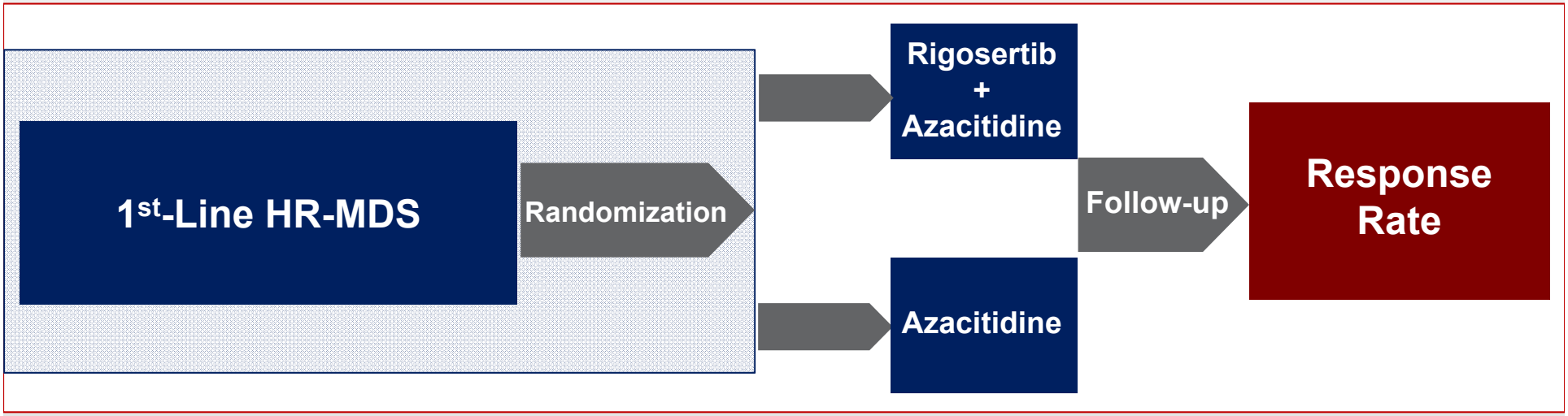


AML >30% Blasts

- Expansion into second myeloid malignancy
- EMA approval of azacitidine in elderly AML provides regulatory path
- Phase 2 trial in elderly AML not eligible for 7+3

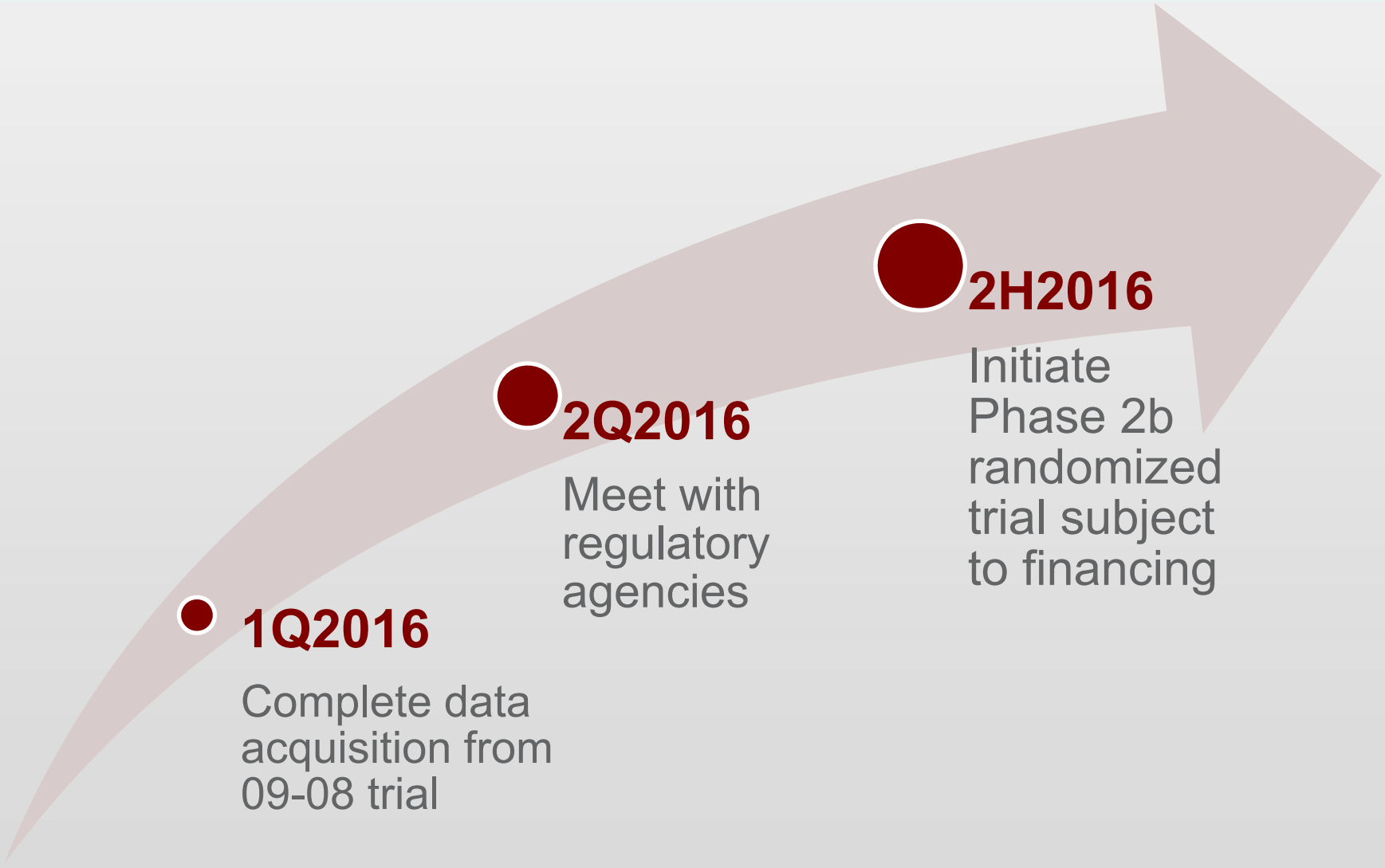
MDS AML

Proposed Design of Phase 2b Combination Trial in HR-MDS



- HMA-naïve HR-MDS
- Primary Endpoint: Response Rate per IWG criteria

Timeline to Initiation of Phase 2b Randomized Trial



Opportunities Beyond MDS

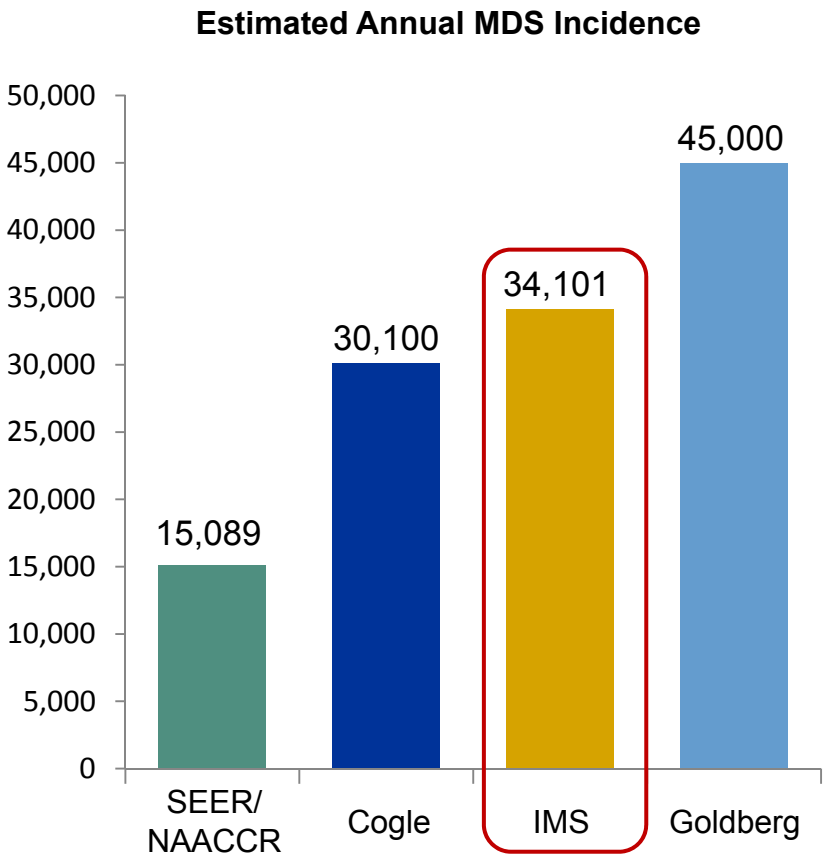
- HMAs are an important part of AML treatment landscape
  - Activity in elderly AML patients not considered fit for chemotherapy
  - Azacitidine approval by EMA in elderly AML in 2015 provides regulatory path for combination studies in AML
- AML patients in Phase 1 portion of rigosertib + azacitidine combination trial achieved mCR and CRi responses
- Responses and tolerability profile present opportunity in AML for further development of combination

Guillermo Garcia-Manero, M.D.
Professor of Medicine
Department of Leukemia
Chief; MDS Section
University of Texas MD Anderson Cancer Center

Rigosertib Trials in HR-MDS
ONTIME to INSPIRE

MDS Epidemiology

Incidence Likely Higher than Cancer Registries Suggest

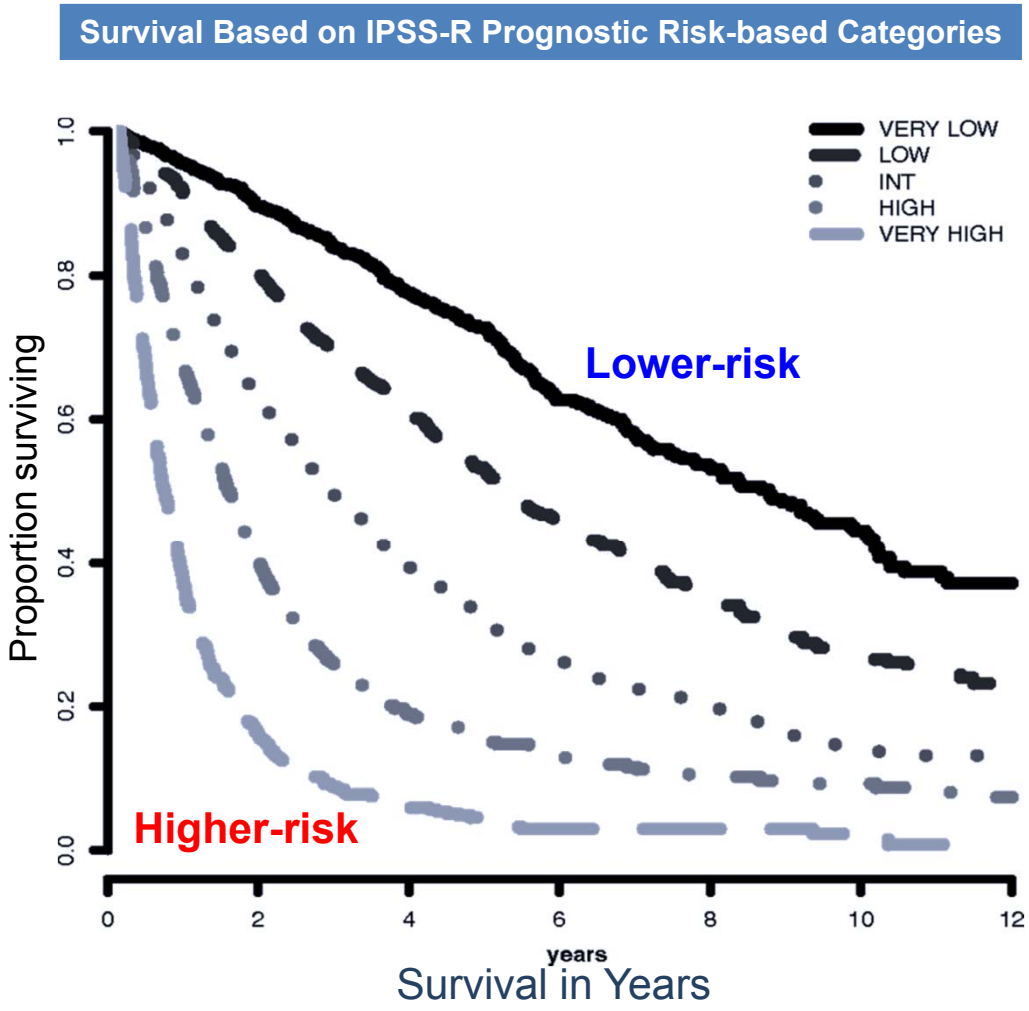


- IMS analysis reviewed claims data for MDS population based on MDS diagnosis (238.7x)[1]
- Identified **34,101 newly diagnosed patients** in the U.S. (MAT June 2012)
  - ~47% of the MDS diagnosed patients are classified as Watch and Wait or not treated
- Incidence of MDS identified and treated patients are growing ~6%
  - Treatment penetration [HMAs, Revlimid] is ~14%

1. 238.7, 238.72 - .76

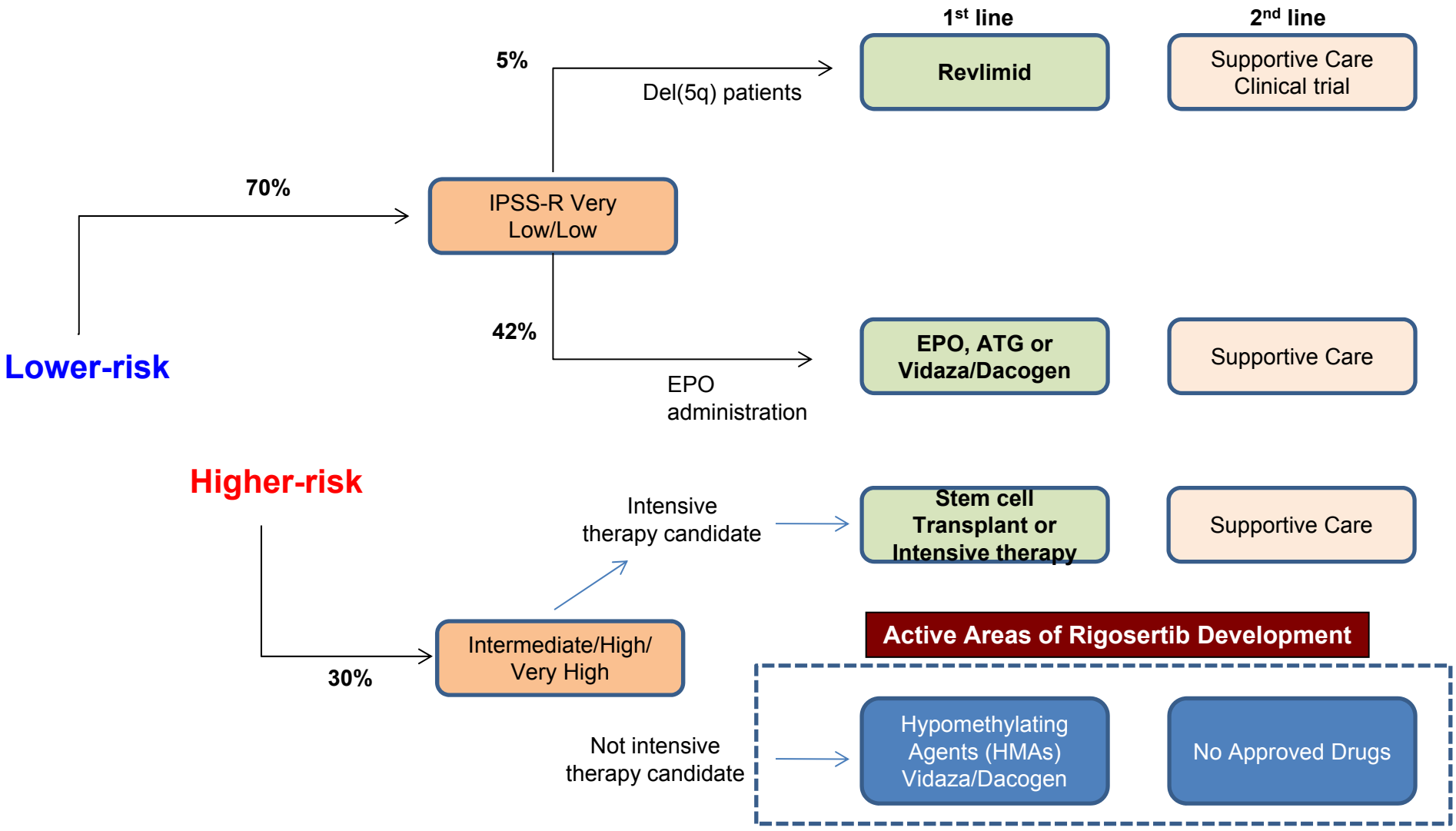
Sources: Goldberg SL, Chen E, Corral M, Buo A, Mody-Patel N, Pecora AL, Incidence and Clinical Complications of Myelodysplastic Syndromes Among US Medicare Beneficiaries; *J Clin Oncol* 2010 (28):2847-52, IMS Patient Diagnoses Study 2012

Prognostic Scoring System for MDS



- A (1-10 scale) scoring system called IPSS-R
- Patients wih higher IPSS-R scores have shorter expected survival
- IPSS-R score is used to determine most appropriate course of treatment

Treatment Flow for MDS



MDS Treatment Options

Rigosertib positioned for patients who do not benefit from currently available agents

Initial Therapy

Products	Comments	Pros	Cons
Vidaza (azacitidine) Celgene	• First to market • Oral formulation trial pending	• Effective • Positive survival labeling	• Non-desirable side effect profile • Not curative
Dacogen (decitabine) Daichi-Sankyo	• Not as widely used • Second to market	• Effective • Perceived higher potency	• No survival data • Launched with poor dosing schedule, changed to MDACC schedule • Not curative
Revlimid (lenalidomide) Celgene	• Largest use MM • Branded; no generics	• SoC in 5q (del) MDS • Oral formulation more convenient for lower risk patients	• Frequent neuropathy • Less effective than HMA's • Not curative

- Dacogen is approved for AML in Europe; Vidaza approval for elderly AML in EU
- Both Vidaza and Dacogen are now available as generic drugs

Standard of Care

	5-azacytidine (Silverman, JCO 2001 et 2006)	Decitabine (Kantarjian Cancer 2006)
Study	Randomized vs BSC	Randomized vs BSC
patients	99	89
Response rate		
- CR + PR	11%	22 (25%)
- HI	36%	NA
Response duration	15 months	9 months
Time to AML transf.	21 months	11 months
Survival	20 months	NA

Phase 3 Program

IV Rigosertib for HR-MDS after HMA Failure

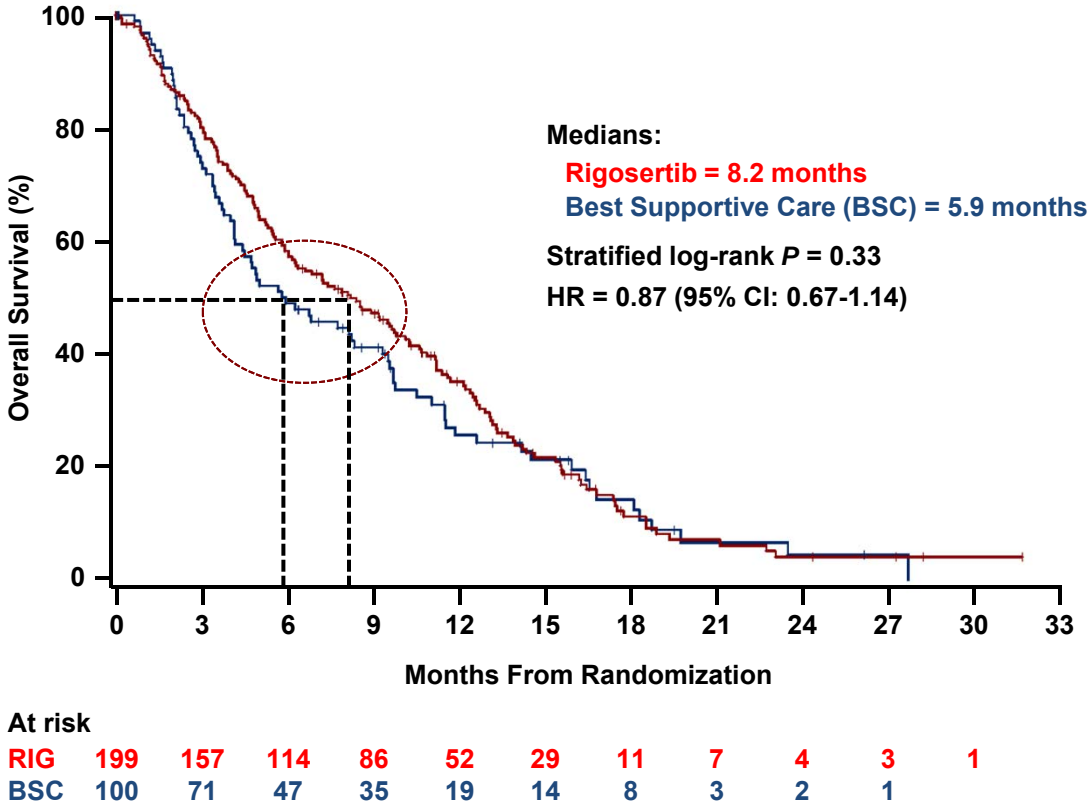
ONTIME Study Design

Phase III, randomized, controlled, safety & efficacy study comparing rigosertib + BSC* vs BSC* alone (2:1)

- Adult pts who had ***relapsed after, failed to respond to, or progressed during HMA therapy***
- 299 pts enrolled at 87 sites in US and Europe
- Rigosertib administered as 1800 mg/24 hr for 72 hrs as a continuous IV ambulatory infusion
- Pts stratified by bone marrow blast count (5-19% vs 20-30%)
- Primary endpoint = overall survival
- Top-line analysis based on 242 events (deaths; ≥ 80% maturity)
- Secondary analysis in pre-defined and post-hoc subgroups
- Median follow-up of >18 months

*BSC=Best supportive care: RBC & platelets; growth factors; hydroxyurea to manage blastic crises when pts transition to leukemia; pts on the BSC arm also allowed low-dose cytarabine, as medically justified.

Phase 3 (ONTIME) Trial Results

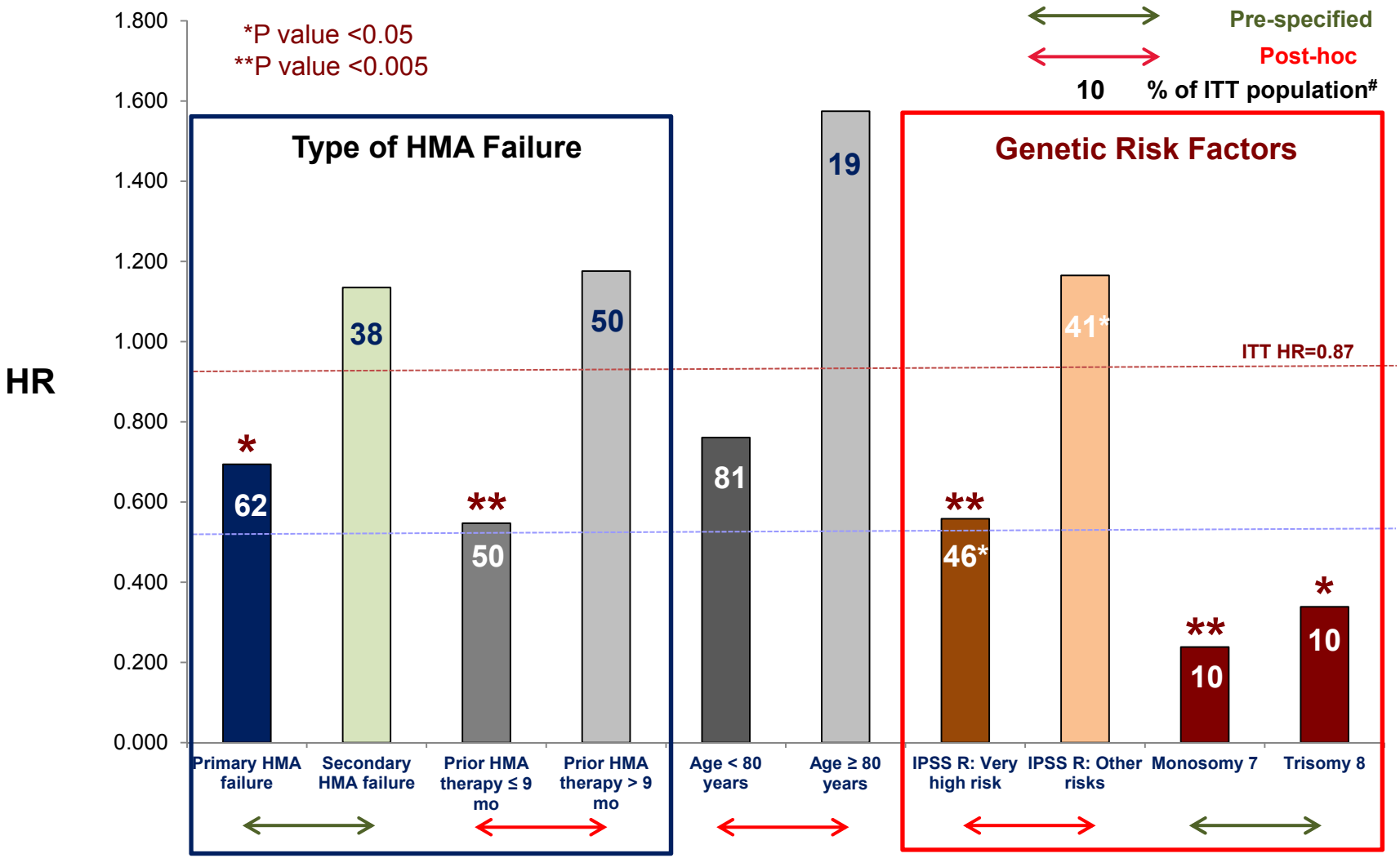


- First ever randomized Phase 3 trial in 2nd-line HR-MDS
- Followed single-arm studies conducted in front-line and HMA-failed HR-MDS patients
- ONTIME did not meet primary efficacy endpoint of overall survival
- Results explained by the heterogeneity of HR-MDS patients
- Analysis identified homogeneous population likely to benefit from IV rigosertib

Safety and Tolerability in Phase 3

- **Median dose intensity = 92%**
  - **Dose reductions in 5% of pts**
- **No significant compliance or operational issues related to ambulatory continuous infusion**
- **AEs ≥ Grade 3: 79% rigosertib, 68% BSC**
- **Low incidence of myelotoxicity (anemia 23%, thrombocytopenia 21%, leukopenia 7%)**
  - **No cardiac signal**

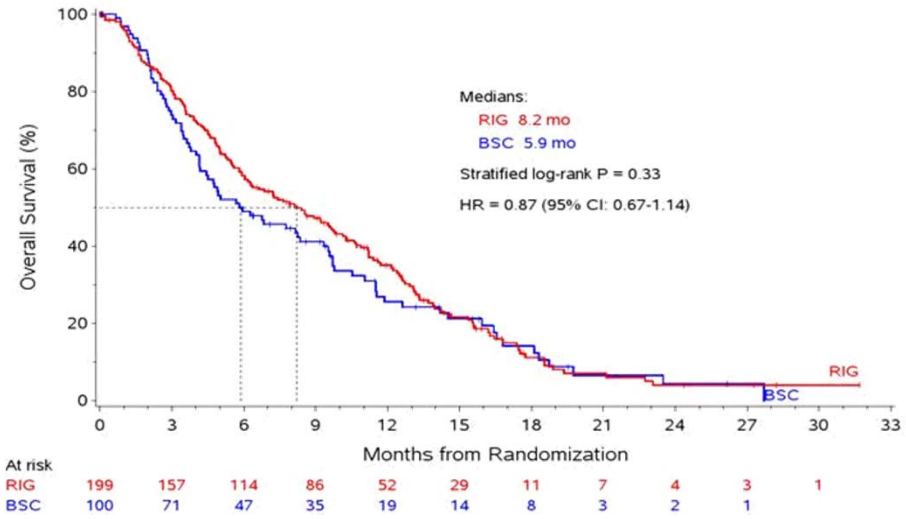
Survival Benefit in Subgroups



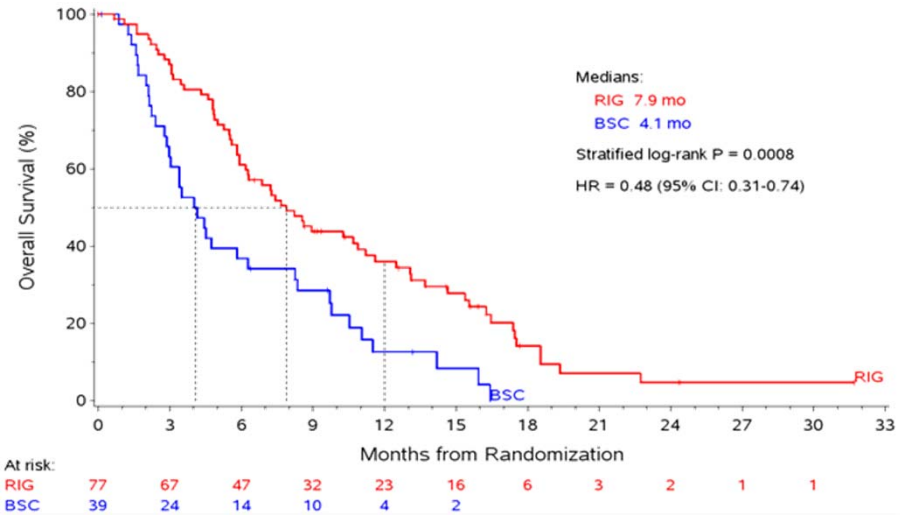
#does not add to 100 due to patients with unknown IPSS-R scores

Focused Patient Population for New Phase 3 INSPIRE Trial

ITT for ONTIME Trial



Simulated ITT (<9 months; < 80years) for INSPIRE Trial

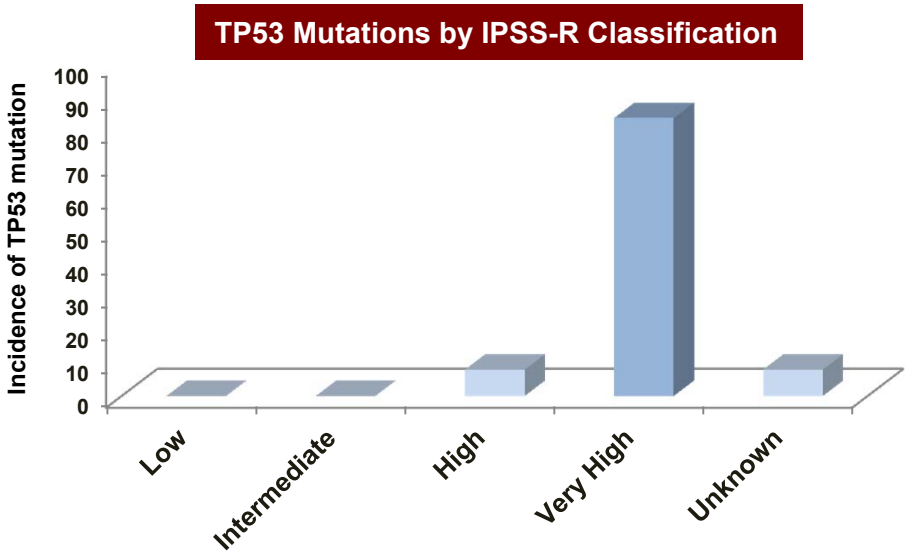


ONTIME Mutations

- Mutations in TET2 and EZH associated with favorable prognosis to HMA and mutations in TP53 associated with poor response to HMAs (Santini, 2014)
- Mutations in TP53, ASXL, RUNX1, EZH2 and ETV6 are associated with poor-prognosis

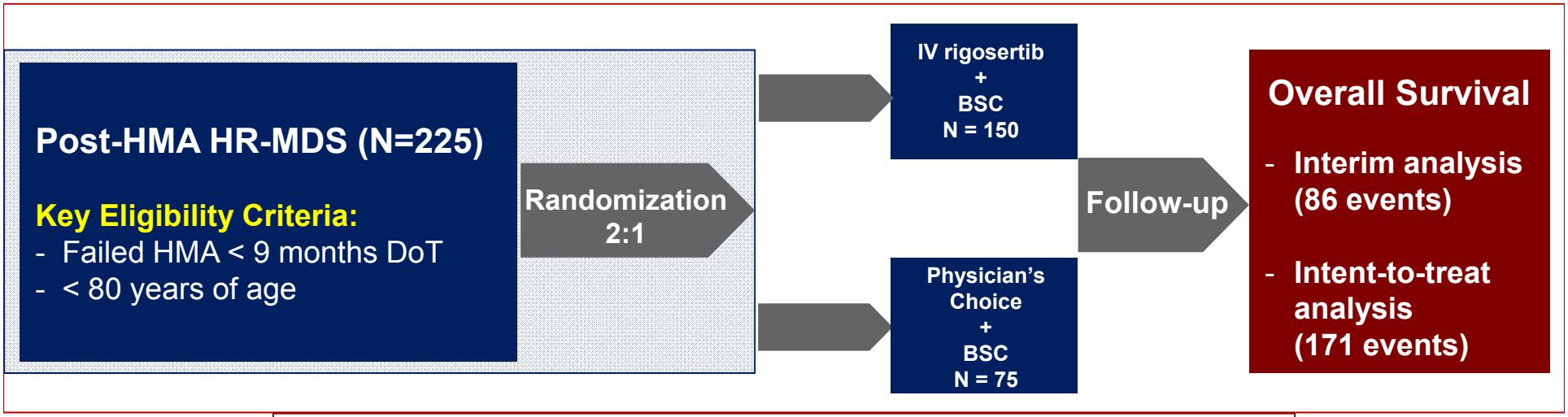
Mutation in	(%)	Rank
	N=111	
ASXL1 gene	19	3
CBL gene	2	
DNMT3A gene	10	8
ETV6 gene	3	
EZH2 gene	4	
IDH1 gene	3	
IDH2 gene	6	
KRAS/NRAS gene	4	
NPM1 gene	1	
RUNX1 gene	11	7
SF3B1 gene	14	4
SRSF2 gene	28	1
STAG2 gene	1	
TET2 gene	14	4
TP53 gene	22	2
U2AF1 gene	12	6

Highlighted: >10%



- 100% of Monosomy 7 and Trisomy 8 patients tested carried one or more myeloid mutations
- Older patients (>80 years) had fewer TP53 mutations
- Complex karyotype patients had more mutations
- IPSS-R VHR had the most TP53 mutations

Design of New Phase 3 INSPIRE Trial



- Stratification at randomization
  - Very High Risk vs. other IPSS-R
  - U.S. vs. Europe vs. Asia
- Statistical analysis
  - α for ITT = 0.0397; α for IPSS-R VHR = 0.01
  - Trial can succeed in two ways

INSPIRE TRIAL CORRELATIVE SCIENCE

1. **Sequential analysis of cytogenetics**

2. **Sequential genomic analysis (Next Generation Sequencing)**

3. **Correlation between bone marrow and peripheral cytogenetic abnormalities**

ONCONOVA THERAPEUTICS

Q&A