ONCONOVA THERAPEUTICS

Corporate Presentation

February 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 financing on favorable terms, the success of our clinical trials and our ability to obtain regulatory approvals and other risk factors outlined in our annual and quarterly reports filed 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.

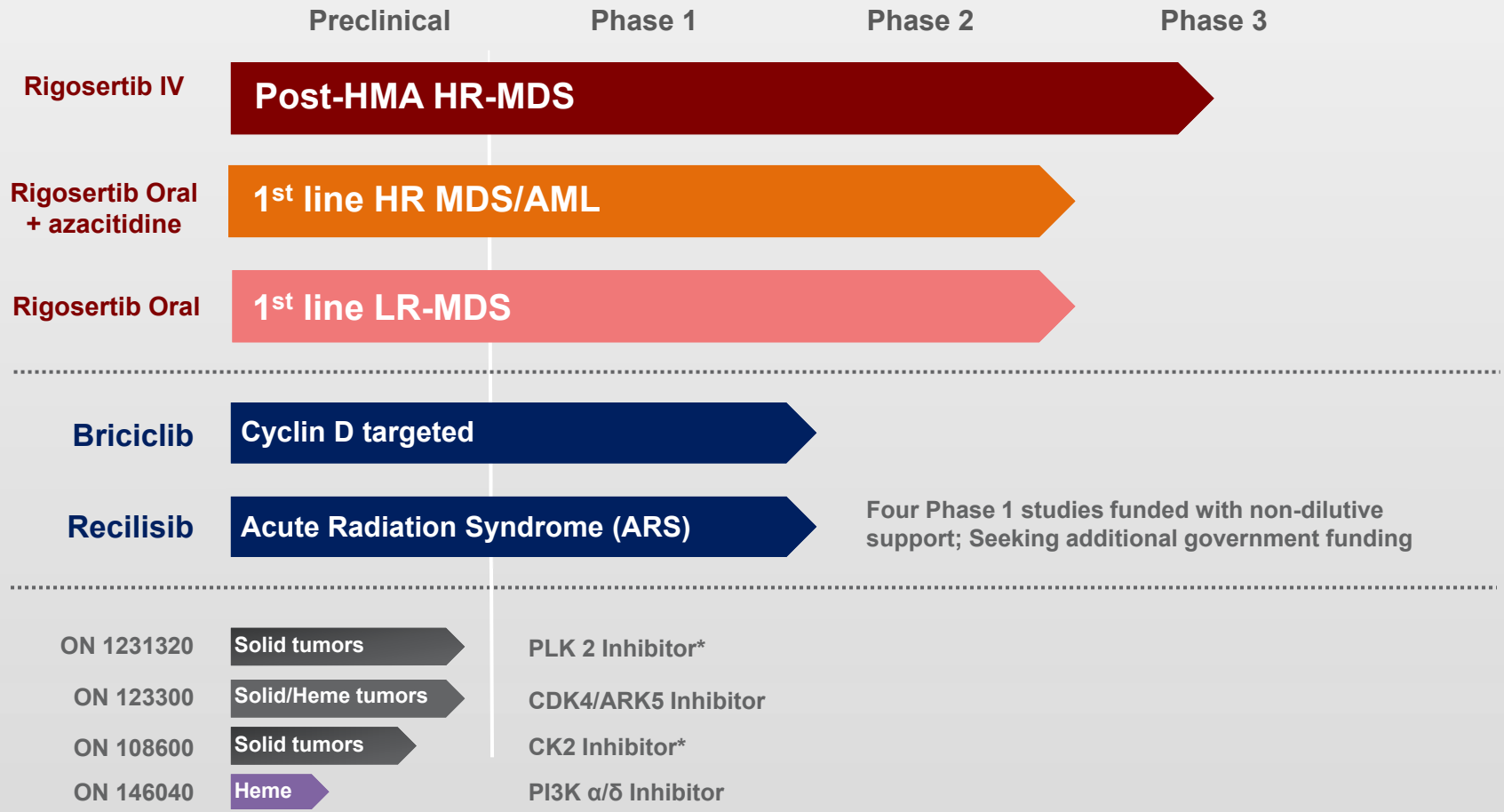
Onconova at a Glance

- NASDAQ Ticker Symbol: ONTX
- Cash: ~$57M at 9/30/14 (unaudited)
- Market Cap (2/6/2015): ~$55M
- Headquarters: Newtown, PA
- History: founded in 1998; novel cancer therapeutics

Investment Highlights

- Lead compound rigosertib a Phase 3 stage NCE
  - Multiple clinical indications in MDS
  - Intravenous and oral formulations
  - Orphan designation in US, EU and Japan
  - Composition of matter patent until 2026
- Sizable market opportunity with significant unmet medical need
- Onconova retains US and other commercial rights
  - Partnered with Baxter for Europe
  - Partnered with SymBio for Japan/Korea
- Deep early-stage pipeline

Three Clinical Programs and Deep Non-clinical Pipeline



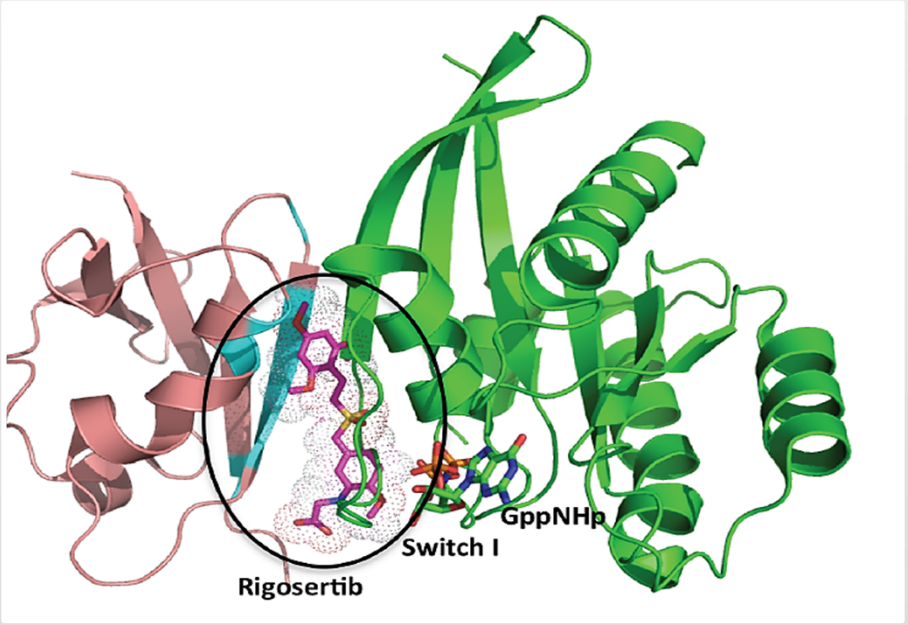
All product candidates are NCEs originating from proprietary chemical library

*Collaboration with GVK Biosciences to develop to proof of concept

Rigosertib: Mechanism of Action

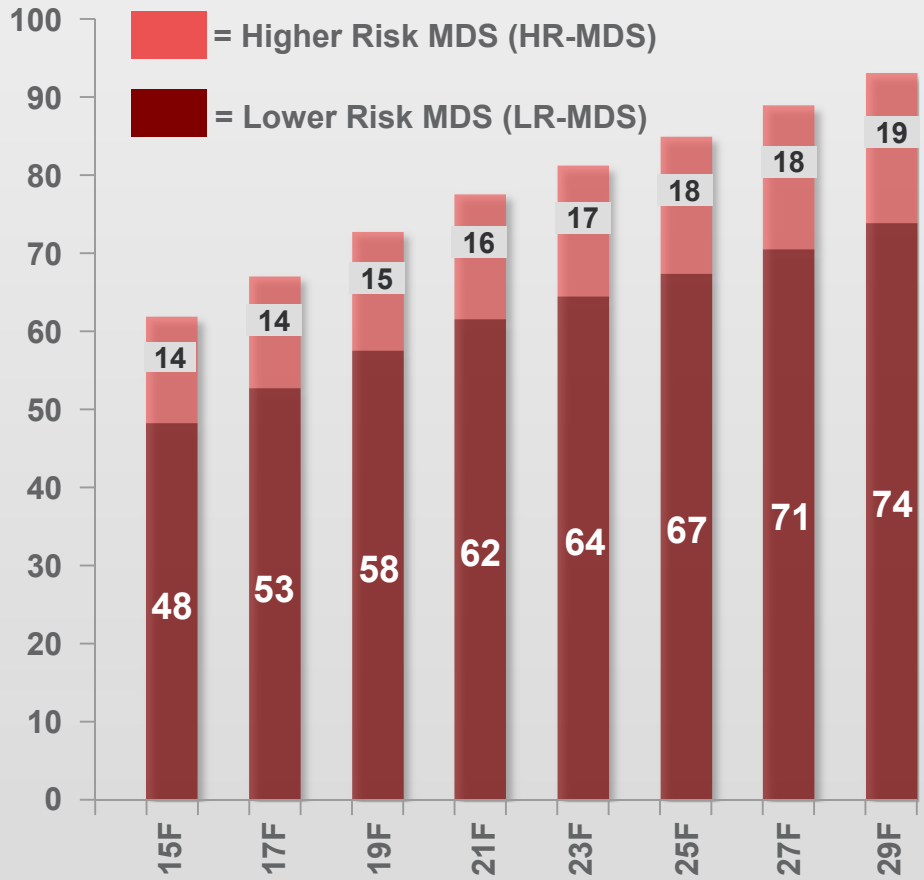
- Targets Ras Binding Domain (RBD)
  - RBD is found in multiple signaling pathways (Ras, Raf, PI3K etc.)
- Effects through PI3K + PLK pathways
  - PI3K pathway inhibition blocks tumor survival signals leading to apoptosis
  - PLK pathway inhibition results in mitotic arrest leading to apoptosis
  - Biomarkers available for each pathway

Binding of Rigosertib to RBD



MDS: Sizable Market Opportunity with Significant Unmet Needs

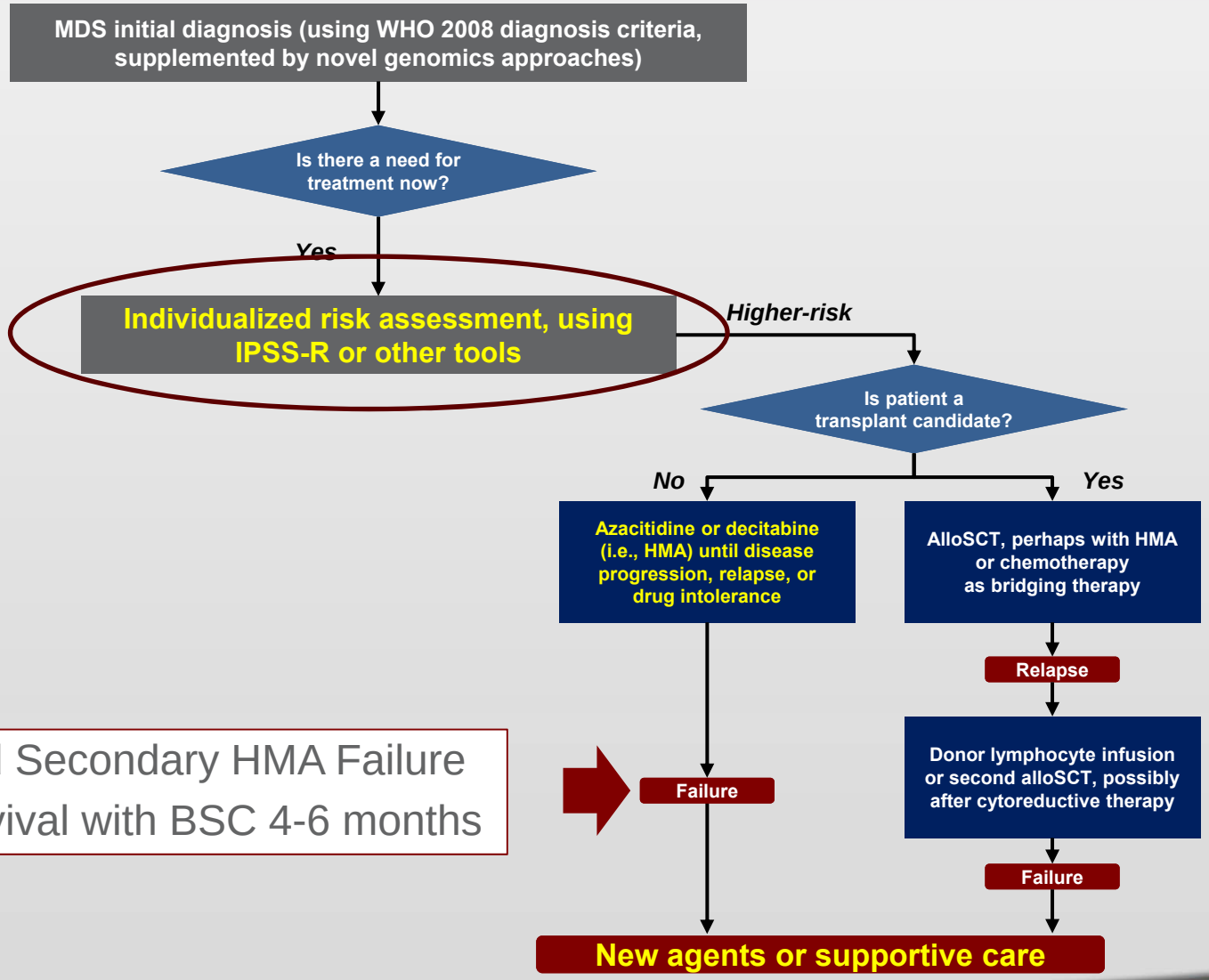
Diagnosed Prevalence (in thousands) of MDS in US (2015-29F)



Sources: Janney Montgomery Scott, Cleveland Clinic Journal of Medicine, Journal of Clinical Oncology, American Journal of Medicine, Leukemia and Lymphoma Society, SEER, US Census data, and L.E.K. analysis

- Est. 2014 prevalence of MDS ~59K, incidence ~17.8K
- HR-MDS patients are treated with hypomethylating agents (HMA)
- For post-HMA MDS patients, no approved therapies available
- LR-MDS patients have good survival but suffer consequences of cytopenias and transfusions
- Need for well-tolerated combination therapies for all patients

MDS Higher Risk Treatment



- Primary and Secondary HMA Failure
- Median survival with BSC 4-6 months

*Bejar & Steensma, 2014.

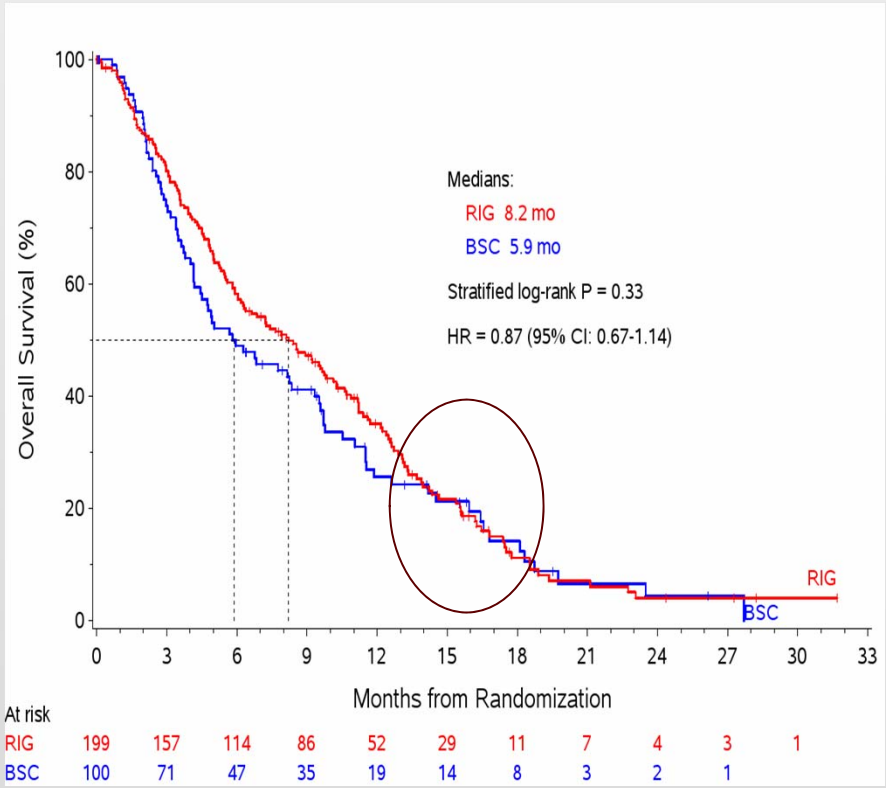
Rigosertib: Potential to Transform the Treatment of Patients with HR-MDS

Phase 3 Stage	*Phase 2 Trial Underway*
Post-HMA HR-MDS	**1st Line MDS/AML**
Single-agent activity in *Primary HMA Failures* and *IPSS-R VHR*	Activity in first and second-line patients reported in Phase 1 trial
Intravenous	***Oral***

ONTIME Trial Primary Efficacy Results: ITT Patient Population

- Continuous infusion using a portable pump; 1800 mg daily dose
- 299 post-HMA HR-MDS patients enrolled in trial
- 2:1 randomization, rigosertib vs. BSC

Parameter	Rigosertib N=199	BSC N=100
Number (%) of deaths	161 (81%)	81 (81%)
Median follow-up (months)	17.6	19.5
Median survival (months)	**8.2**	**5.9**
Stratified HR (rigosertib/BSC)	0.87	
95% CI	0.67 - 1.14	
Stratified log-rank p-value*	0.33	



ONTIME: Patients Classified by Primary or Secondary HMA Failure

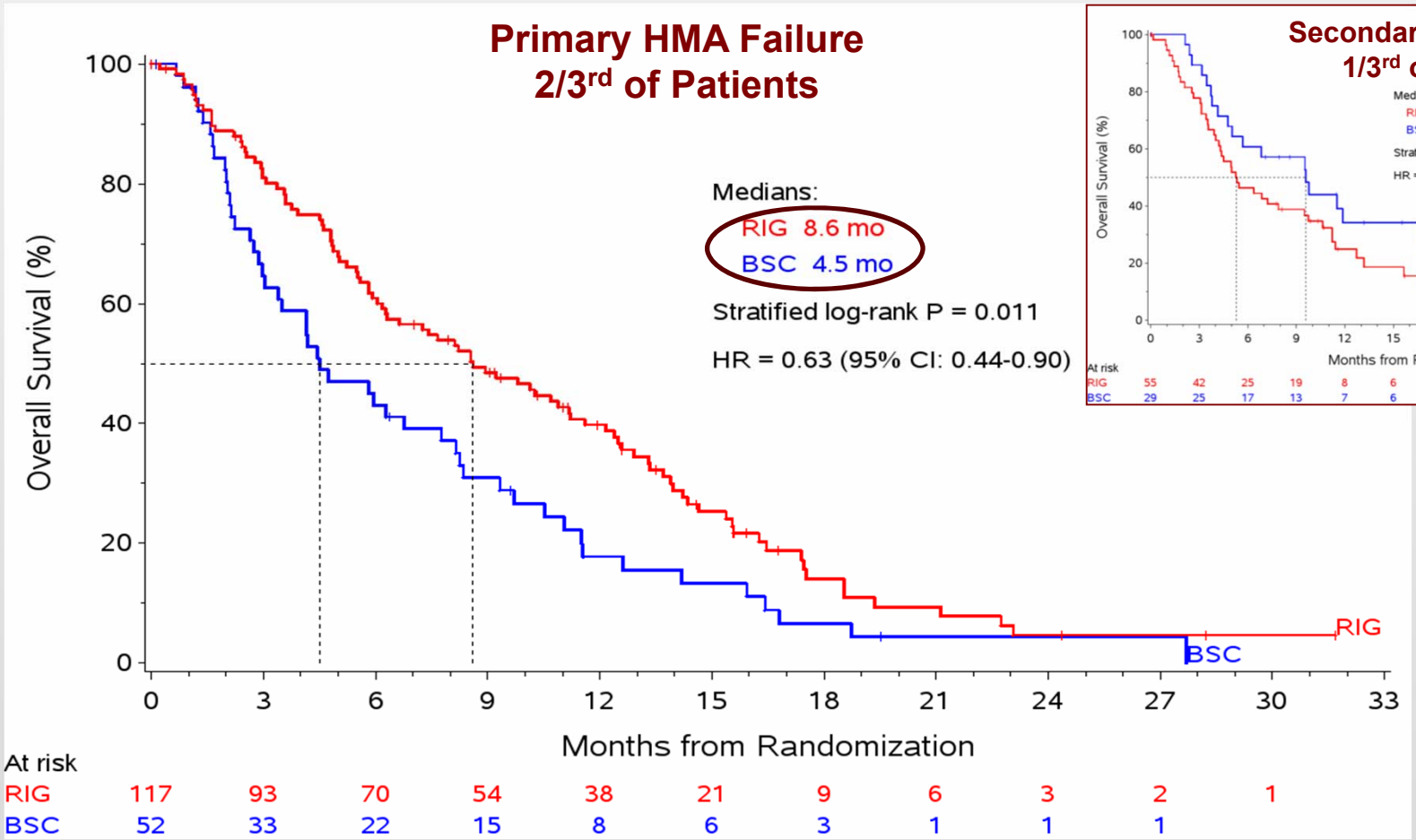
- "Primary HMA failure" was defined as no response to or progression during HMA therapy (median OS=4.6 months)
  - 55% of population in Prebet paper (+9% intolerant)
  - 64% of population in ONTIME (no intolerant)

- "Secondary HMA failure" was defined as relapse after HMA therapy (median OS=7.4 months)
  - 36% of population in Prebet paper
  - 36% in ONTIME

- An independent, centralized, blinded, retrospective evaluation of response provided support of investigator assessments

Prebet et al, *J Clin Oncol* 2011;29:3322-7; Jabbour et al, *Cancer* 2010;116:3830-4.

ONTIME: Survival for Patients Defined by Type of HMA Failure

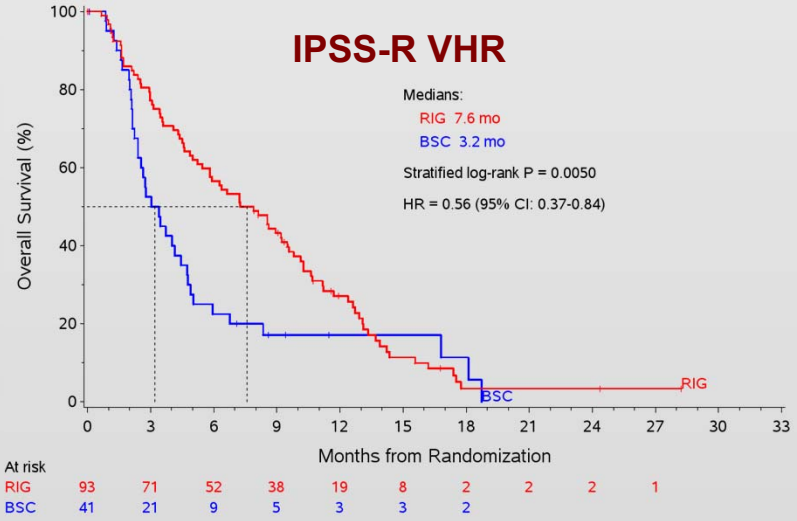


Based on blinded, centralized assessment ;
Per Prebet 2011, "Primary HMA Failure" was defined as either no response to or progression during HMA therapy

ONTIME Trial Subgroups With Better Overall Survival

- Rigosertib treatment-related improvement in OS was noted in the following well-balanced subgroups:
  - Primary HMA failure (64% of pts: HR = 0.63; p = 0.011); 4.1 months
  - IPSS-R Very High Risk (45% of pts: HR = 0.56; p = 0.005); 4.4 months

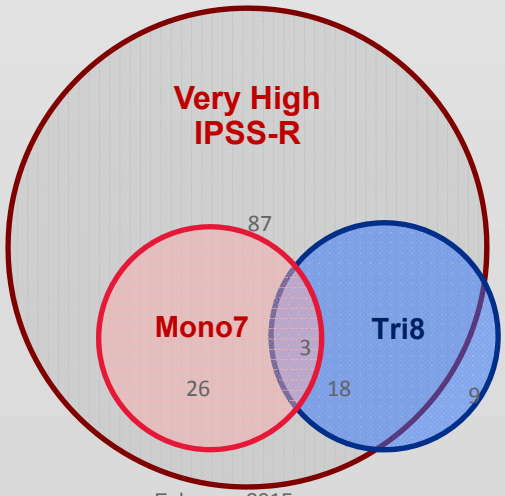
Subgroup	Rigosertib N	Rigosertib mOS	BSC N	BSC mOS	HR (95% CI)	p-value
Primary HMA Failure	127	8.6	57	4.5	0.63 (0.44-0.90)	0.011
IPSS-R Very High Risk	93	7.6	41	3.2	0.56 (0.37-0.84)	0.005



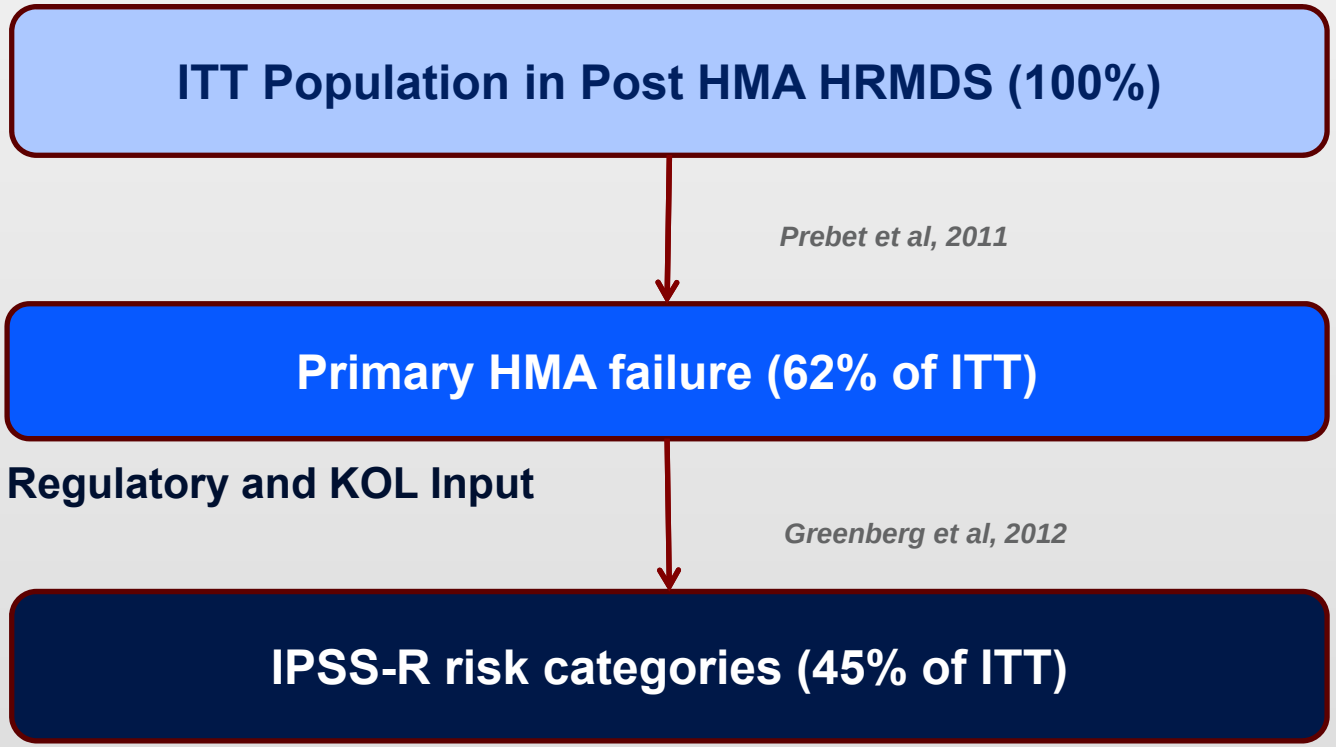
ONTIME: Survival of Patients in Cytogenetic Subgroups and IPSS-R

Patients of certain karyotype or IPSS-R Very High score have shorter median survival in the BSC group.

Subgroup	Rigosertib		BSC		HR (95% CI)	p-value
	N	Median (mos)	N	Median (mos)		
Monosomy 7 (10%)	16	5.6	13	**2.8**	0.24 (0.09-0.66)	0.003
Trisomy 8 (10%)	22	9.5	8	**4.5**	0.34 (0.12-0.95)	0.035
IPSS-R VHR (43%)	**93**	**7.6**	**41**	**3.2**	**0.56 (0.37-0.84)**	**0.005**



Evolution of Proposed Indication

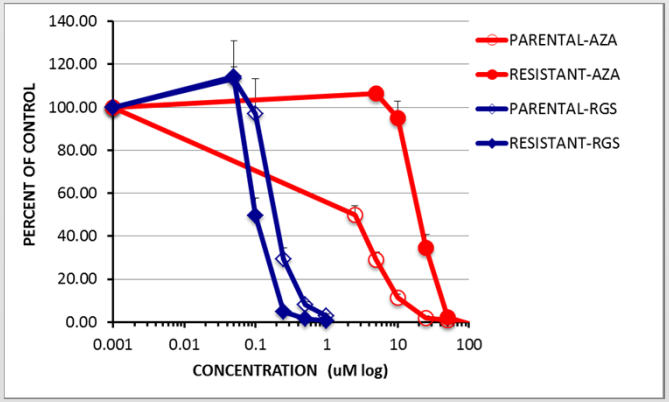


- Of the approximately 18,000 prevalent US MDS patients, 25% have HR-MDS
- IPSS-R scoring is routine for all patients
- **Depends on multiple factors with most weight for karyotype**
- Strongly correlated with Overall Survival and Medical Need

Rigosertib is Synergistic with Azacitidine in Preclinical Studies

- Rigosertib and Azacitidine in combination have synergistic activity
- Sequential exposure achieved maximum synergy
- Rigosertib is active in azacitidine resistant cells

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



Combination Studies conducted by Dr. Silverman (MSSM); *US Patents: 8106033B2; 20100305059
Resistant cells developed in Japan; studies conducted at Mount Sinai Hospital

Combination Trial Design in MDS/AML

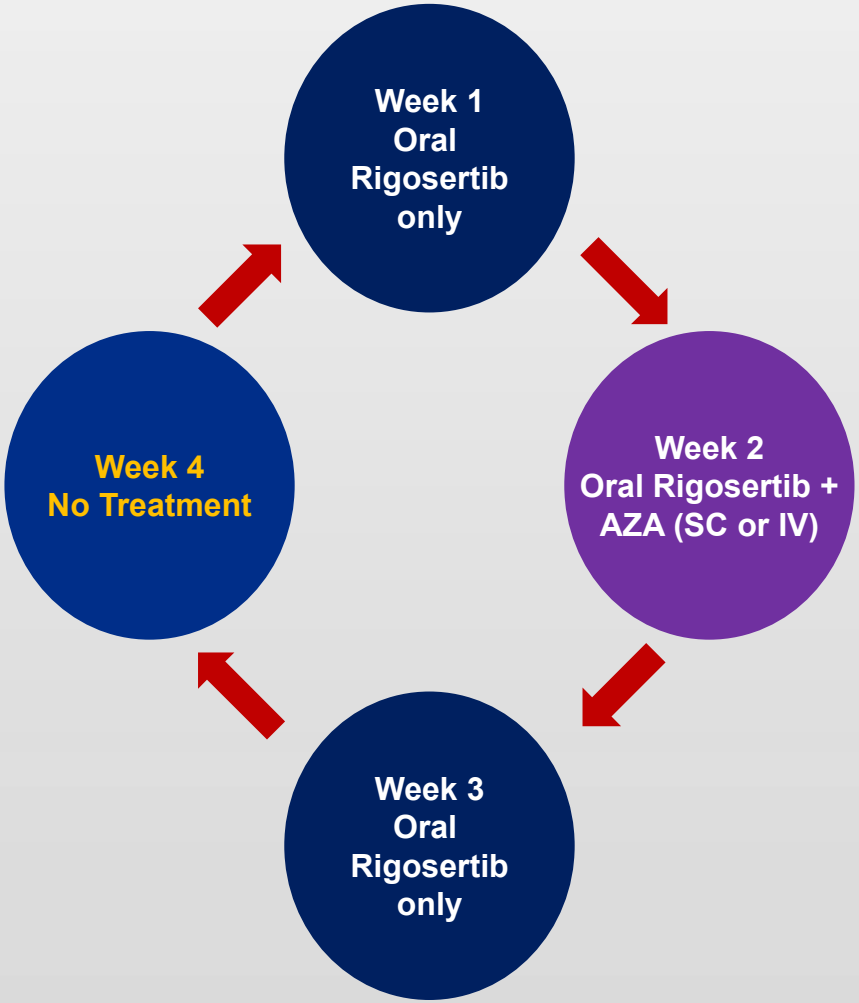
- Trial design integrates preclinical findings regarding sequence and synergy
- Treatment regimen:

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

Week 2: Oral rigosertib + AZA (75 mg/m^2)

Week 3: Oral rigosertib BID

Week 4: No treatment



Combination Trial Design in MDS/AML

- Phase 2 ongoing in US/EU
  - Simon Minimax two-stage design
  - Can be expanded based on data
  - Investigators: Lewis Silverman, Guillermo Garcia-Manero, Pierre Fenaux
- Currently enrolling patients with:
  - MDS (Both HMA naïve and HMA failure)
  - CMML
  - RAEB-t/non-proliferative AML treated with ≤ 1 prior salvage therapy
- Efficacy endpoint:
  - Number of patients achieving complete remission (CR), partial remission (PR), or bone marrow CR (mCR) according to 2006 IWG criteria

Response to Combination Treatment

Pt	Diag	Prior HMA	% BM base-line	% BM after tx	Response	
					BM	HI
1	MDS	No	2	1	**CRi**	PLT
2	AML	No	40	0	**mCR**	
3	AML	No	22	N/A	NE	
4	MDS	AZA	0	0	SD	
5	AML	No	59	N/A	NE	
6	AML	No	21	<5	**CRi**	PLT
7	MDS	No	2	1	**mCR**	
8	MDS	No	2.5	2	NE	
9	AML	DEC	25	N/A	NE	
10*	**MDS**	**DEC**	**12**	**1**	**CRi**	**Eryth, Neut**
11	CMML	AZA	2	3	SD	
12*	**MDS**	**AZA**	**4**	**1**	**CRi**	**PLT, Eryth, Neut**

Pt	Diag	Prior HMA	% BM base-line	% BM after tx	Response	
					BM	HI
13	AML	DEC	47	40	NE	
14	MDS	DEC	7	24	PD	
15	MDS	No	9	<5	**mCR**	
16	AML	AZA	25	4	**mCR**	
17	MDS	AZA	15	5	**mCR**	
18	AML	AZA	64	45	NE	

AZA = azacitidine; DEC = decitabine; mCR = marrow complete remission; Cri = complete remission with incomplete blood count recovery; NE = not evaluable; SD = stable disease; PD = progression of disease; PLT = platelet; eryth = erythroid; neut = neutrophil

*Response after progression on a hypomethylating agent (HMA)

HI = hematological improvement

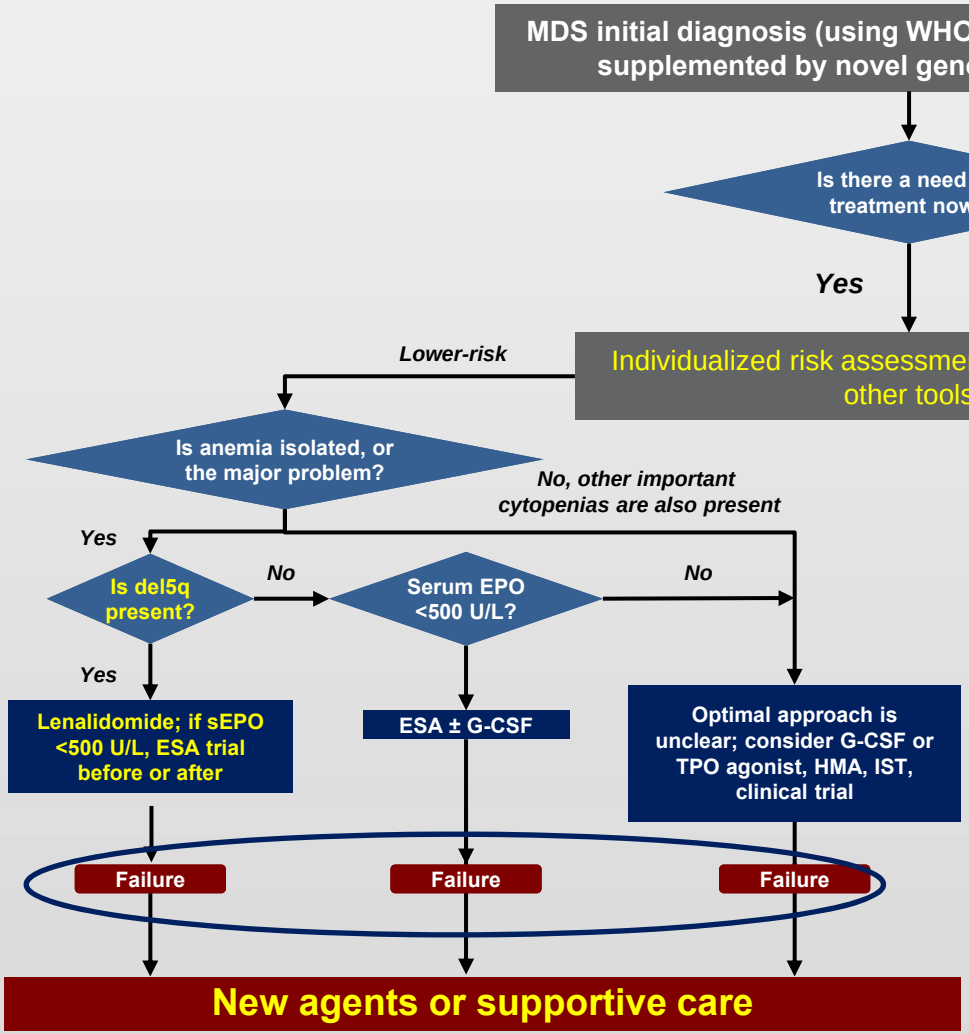
Data presented at ASH 2014

Rigosertib: Potential to Transform the Treatment of Patients with LR-MDS

Phase 2 Trials Enrolled

1st Line LR-MDS
Phase 2 efficacy data being reconciled with *genomic marker* and dose optimization ***Oral***

MDS Lower Risk Patients Have Few Treatment Options



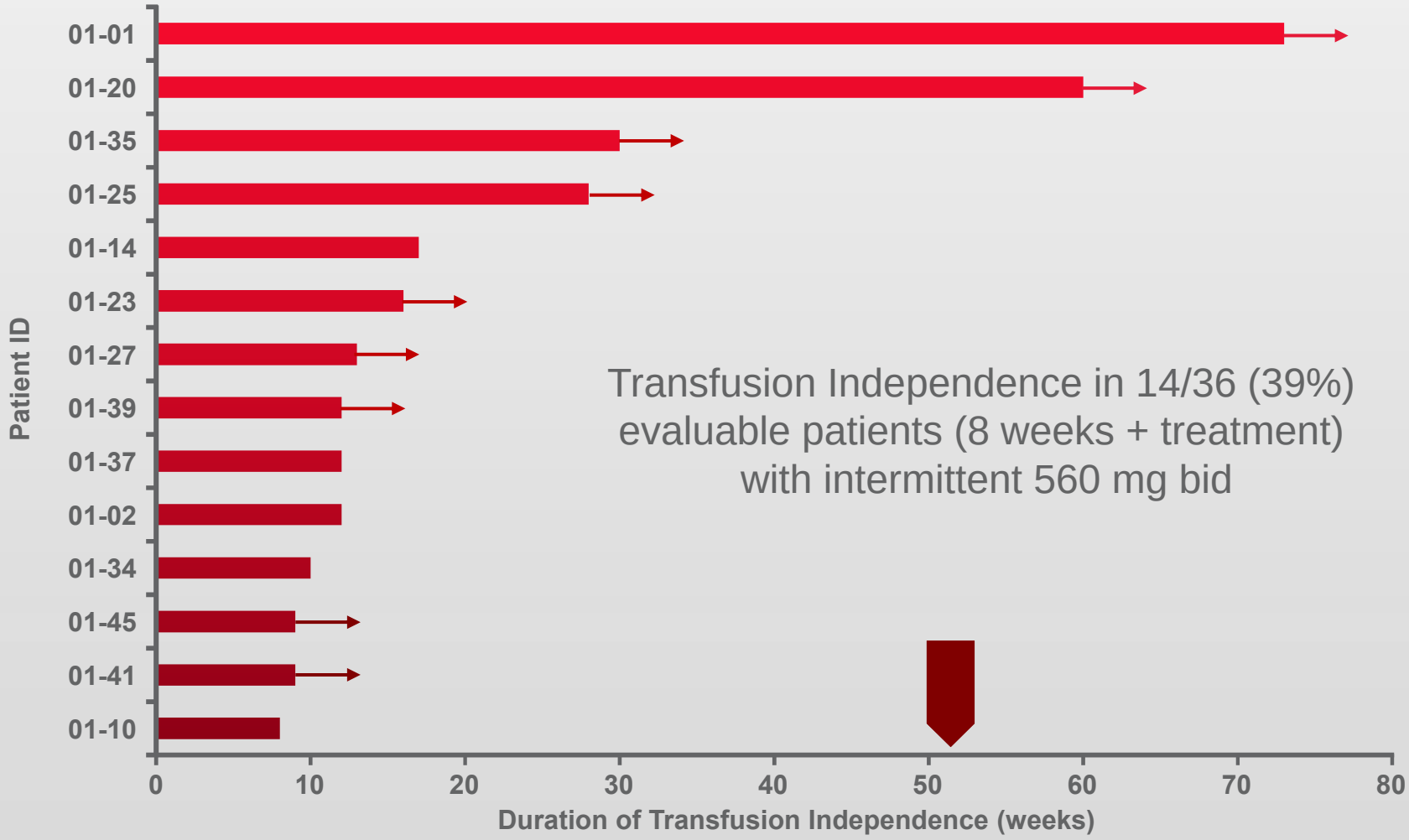
Bejar & Steensma, 2014

- EPO is not a durable solution
- Transfusions are wrought with risks
- No new therapy for non-del5q patients

Durable Transfusion Independence in LR-MDS Patients Treated with Rigosertib

Phase 2 data presented at ASH 2013

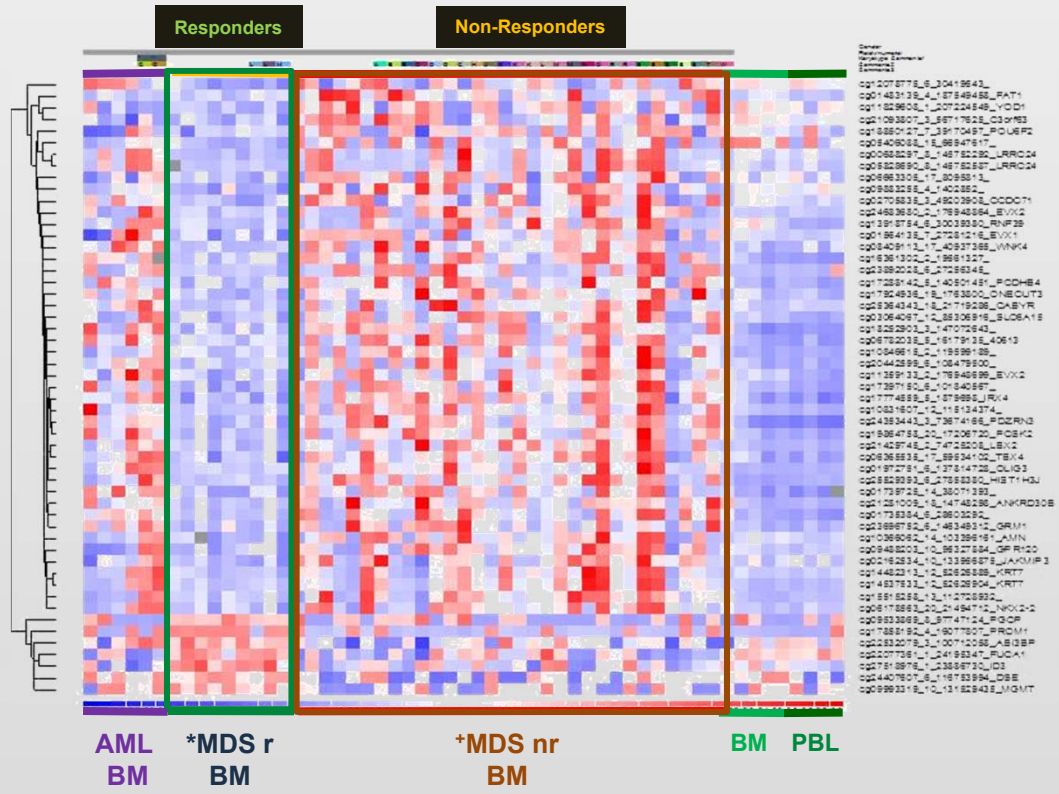
Patient Stratification Tool?



Transfusion Independence in 14/36 (39%) evaluable patients (8 weeks + treatment) with intermittent 560 mg bid

DNA Methylation Analysis Distinguishes Rigosertib Responder LR-MDS Patients

Genomic Methylation Signature Associated with Response in LR-MDS



- Methylation analysis of
  - Marrow from AML patients
  - Marrow from rigosertib-treated LR-MDS patients
  - Marrow from healthy volunteers (BM)
  - Peripheral blood from healthy volunteers (PBL)
- **Baseline methylation pattern can help distinguish responding patients from non-responders**

*MDS r BM = bone marrow from LR-MDS patients known to respond to treatment with rigosertib
+MDS nr BM = bone marrow from LR-MDS patients known to not respond to treatment with rigosertib

Development Pathway for Rigosertib in 1st Line LR-MDS

- Ongoing activities
  - Dose/schedule optimization for optimal activity without urinary tolerability issues
  - Development of a genomic prognostic test
- Regulatory guidance from FDA and European countries obtained

Rigosertib: Potential to Transform the Treatment of Patients with MDS

Phase 3 Stage	*Phase 2 Underway*	*Phase 2 Trials Enrolled*
Post-HMA HR-MDS	**1st Line MDS/AML**	**1st Line LR-MDS**
Single-agent activity in *Primary HMA Failures* and *IPSS-R VHR*	Activity of *combination* with azacitidine supported by Phase 1 results	Phase 2 efficacy data being reconciled with *genomic marker* and dose optimization
Pivotal trial design	**Presentation of Phase 2 efficacy data in Q2-2015**	**Genomic marker validation**
Intravenous	***Oral***	***Oral***

ONCONOVA THERAPEUTICS

Milestones and Financials

2015 Milestones

- Rigosertib IV as 2nd-line HR-MDS
  - Finalize Phase 3 protocol
- Rigosertib Combination with azacitidine in MDS/ AML
  - Additional data presentation in Q2
  - Phase 2 enrollment complete in Q2
- Rigosertib Oral in Lower Risk MDS
  - Update on genomic validation marker and dose optimization in Q2/Q3

Submitted abstracts for presentations at AACR (April), MDS Foundation (May) and ASCO (June)

Financials

- Cash: ~$57M at 9/30/14 (unaudited)
- Manage cash runway through 2015
  - Start of Phase 3 trial subject to appropriate financing
- Focused development plan