
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, DC 20549

FORM 8-K

**CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934**

Date of Report (Date of earliest event reported): **March 5, 2014**

Onconova Therapeutics, Inc.

(Exact name of Registrant as specified in its charter)

Delaware
(State or Other Jurisdiction
of Incorporation or Organization)

001-36020
(Commission
File Number)

22-3627252
(I.R.S. Employer
Identification No.)

**375 Pheasant Run
Newtown, PA 18940
(267) 759-3680**

(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

Not Applicable

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
 - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17CFR 240.14a-12)
 - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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Item 8.01 Other Events

On March 5, 2014, Onconova Therapeutics, Inc. presented information at the Annual Cowen Healthcare Conference, a copy of which is attached hereto as Exhibit 99.1 and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits.

99.1 Slides presented by Onconova Therapeutics, Inc. on March 5, 2014.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: March 7, 2014

Onconova Therapeutics, Inc.

By: /s/ Ajay Bansal

Name: Ajay Bansal

Title: Chief Financial Officer

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EXHIBIT INDEX

Exhibit No.	Description
99.1	Slides presented by Onconova Therapeutics, Inc. on March 5, 2014.

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**34th Annual
Cowen Healthcare Conference**

March 5, 2014

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 Final Prospectus 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.

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Investment Highlights



- **Rigosertib** – PI3K/PLK targeted drug for a range of cancers
 - Phase 3 top-line data in higher risk MDS patients released
 - Next step is discussions with regulators in 2Q 2014
 - Phase 3 trial of Oral rigosertib in lower risk MDS in 2H 2014
 - Partnered in Europe (Baxter) and Japan (SymBio)
 - Onconova retains US and other rights
- **Deep pipeline** of earlier stage cancer programs
- Year-end 2013 cash balance ~\$100m
 - Cash burn for 2013 ~\$61m

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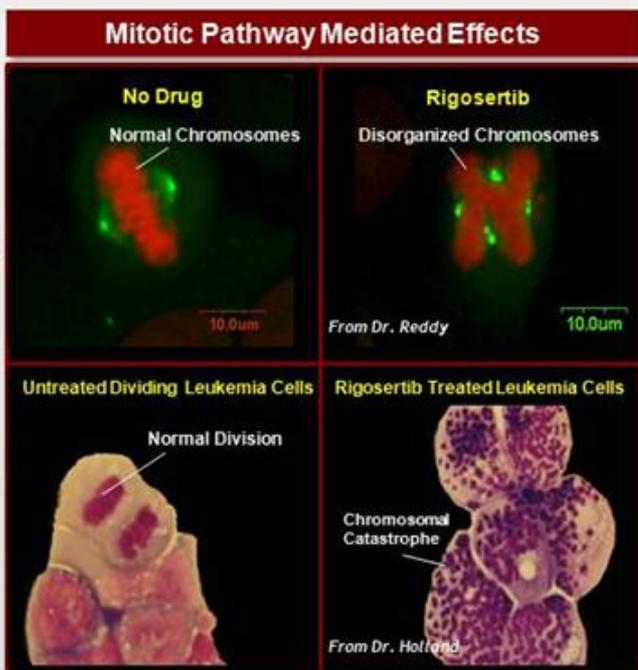
Rigosertib

Mechanism of Action and Safety Profile

Rigosertib: Dual Pathway Inhibitor



- Targets PI3K + PLK pathways
 - Kinomesan: PIK3CA and RIOK1
 - Right panel shows “polo” effect 
- Interacts with Ras Binding Domain
 - Multiple signaling pathways affected
- Composition of matter valid until 2026
- Orphan designation for MDS



Overview of Safety Findings



- Favorable risk-benefit profile overall to date (>1,000 patients)
- Lack of significant myelosuppression, cardiotoxicity, or neurotoxicity
- Generally, no need for premedication during the studies
- Potential safety signals are being monitored on an ongoing basis
- Risk-benefit analysis by DSMC for pivotal study, 3 meetings
 - Recommended continuation of trial without modifications

Lack of Suppression of Normal Bone Marrow



Bone Marrow Cellularity Over Time in Rigosertib Treated MDS Patients (from early stage trials)

Stage	Number of Patients	Bone Marrow Cellularity
Pre-Treatment	37	61%
Follow-Up 1	37	68%
Follow-Up 2	16	69%
Follow-Up 3	11	64%

- Cellularity is a measure of normalcy of bone marrow
- Rigosertib preserves bone marrow cellularity
- Bone marrow preservation is beneficial in MDS patients

No change from pre-treatment in BM cellularity over time

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Rigosertib in Higher Risk MDS

Treating Higher-risk MDS

M. Sekeres, *Blood*, 2014;829-836; published online on December 20, 2013



- Higher-risk myelodysplastic syndromes (MDS) are defined by patients who fall into higher-risk group categories in the original or revised International Prognostic Scoring System.
- Survival for these patients is dismal, and treatment should be initiated rapidly.
- Standard therapies include the **hypomethylating agents** azacitidine and decitabine, which should be administered for a minimum of 6 cycles, and continued for as long as a patient is responding.
- Once a drug fails in one of these patients, further treatment options are limited, median survival is <6 months, and consideration should be given to clinical trials.

The Bleak Outlook for Patients With MDS After Hypomethylating Agents Fail

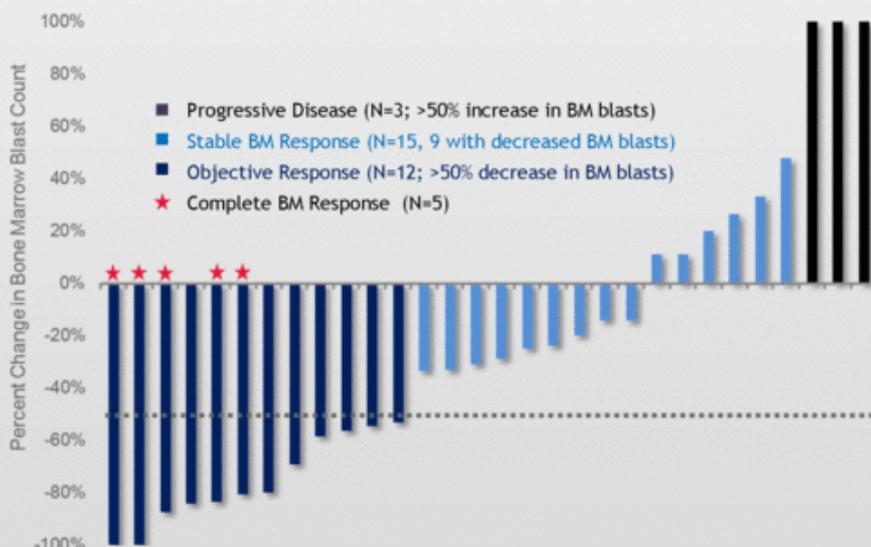
Prébet T, Gore SD, Esterni B, et al. Outcome of high-risk myelodysplastic syndrome after azacitidine treatment failure. *J Clin Oncol*. 2011;29:3322-3327.

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Marrow Blast Response in 2nd-Line Higher Risk MDS Patients



Earlier Stage Trials: Best Bone Marrow Responses After Rigosertib IV Treatment in 30 RAEB-1, -2, -t MDS Patients Previously Treated With Hypomethylating Agents



Bone marrow biopsy from 30/39 rigosertib treated higher risk MDS patients who failed Vidaza/Dacogen

- Change in bone marrow blast after receiving rigosertib IV
- These patients similar to patients enrolled in pivotal Phase 3 MDS trial

Hematological Improvement (HI) 5/30

N 01-01: Platelets, ANC
 04-05-02: Platelets
 04-15-04: ANC
 04-17-11: RBC, ANC
 04-17-12: Platelets

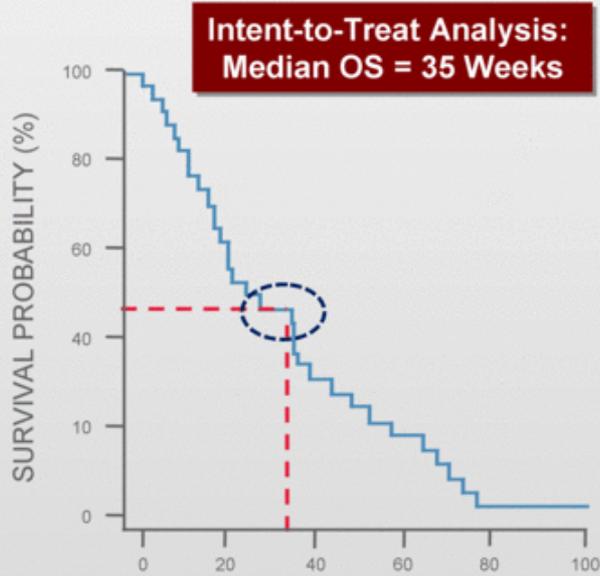
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Overall Survival Data in Post-HMA MDS Patients



From 4 earlier stage trials

- Overall survival for patients after hypomethylating agents failure is 17-22 weeks (4 publications)
- Median OS of 35 weeks for patients on rigosertib in an ITT analysis of 39 patients



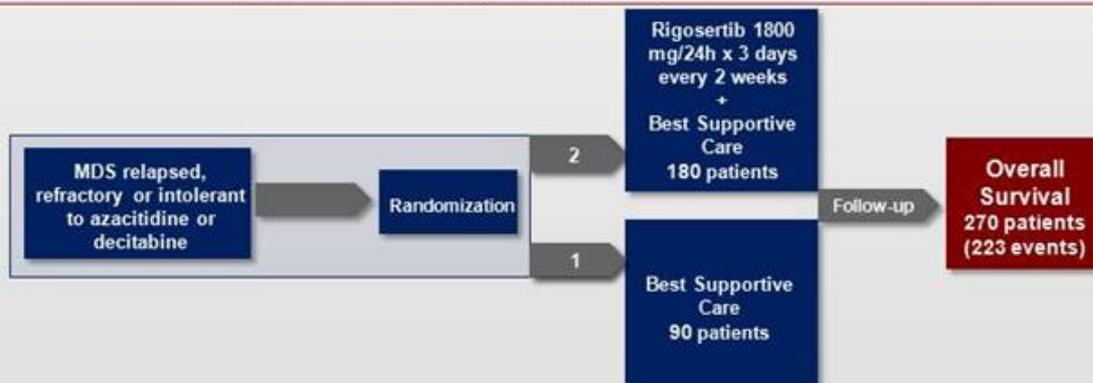
**These data are derived from trials done at 4 sites involving 79 total patients*;
39 of these were MDS patients after hypomethylating agents failure**

*Rigosertib IV studies 04-05, 04-15, 04-17 and 07-H-0225

Design of US/Europe Pivotal Phase 3 HR-MDS Trial Under SPA



- Rigosertib IV as a single agent in patients with MDS after failed prior azacitidine or decitabine therapy
- Continuous infusion using a portable pump; 1800 mg daily dose



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Post-HMA MDS Subgroups

Per 04-21 protocol



- **Progression** (according to 2006 IWG criteria) at any time after initiation of azacitidine or decitabine treatment during the past 2 years;

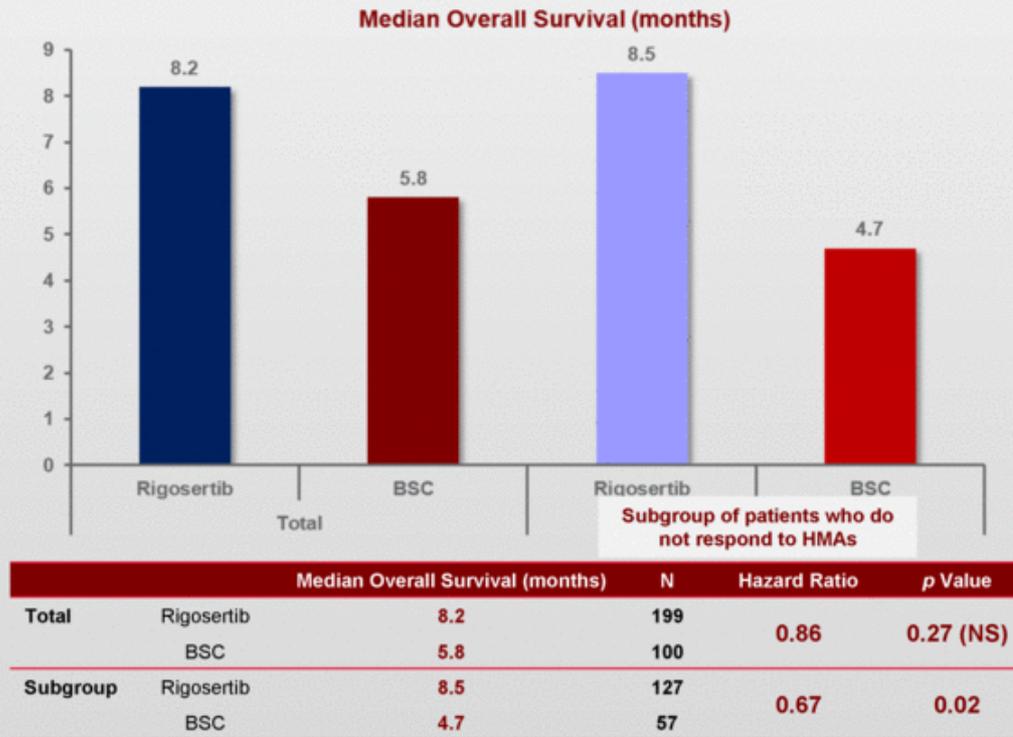
- 62% • **Failure to achieve** complete or partial response or hematological improvement (according to 2006 IWG) after at least six 4-week cycles of azacitidine or either four 4-week or four 6-week cycles of decitabine administered during the past 2 years;

- 38% • **Relapse** after initial complete or partial response or hematological improvement (according to 2006 IWG criteria) observed after at least six 4-week cycles of azacitidine or either four 4-week or four 6-week cycles of decitabine administered during the past 2 years;

- **Intolerance** to azacitidine or decitabine defined by drug-related \geq Grade 3 liver or renal toxicity leading to treatment discontinuation during the past 2 years;

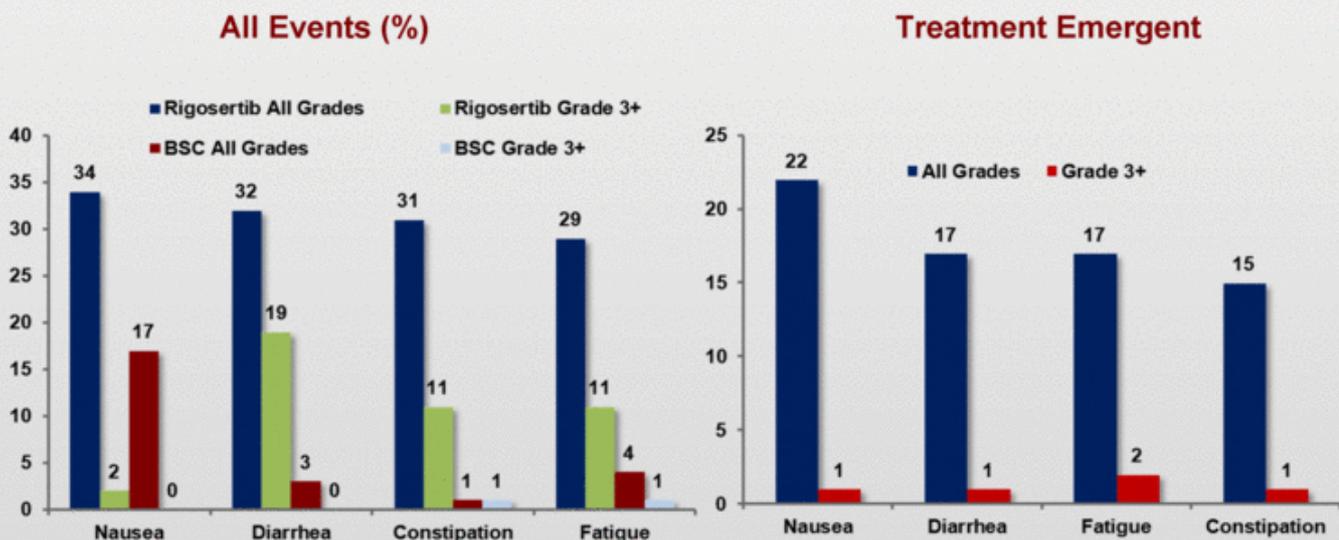
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Overall Survival Estimation From Top-line Analysis



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Preliminary Safety Analysis of ONTIME Trial at Top-line Analysis



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Completed and Ongoing Trials



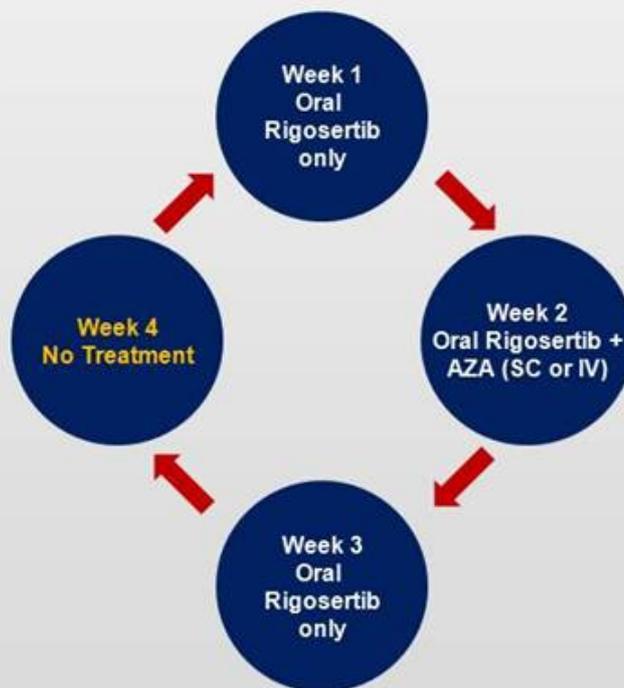
- Phase 3 ONTIME trial
 - 299 patients
 - 199 + 100
 - 89 sites in 6 countries
 - Low drop-out rate
 - Drug well tolerated
 - Median treatment 10 weeks
 - Most treated at full dose
 - SPA in the US
 - Enrolled post-HMA
 - Patients who did not respond to HMAs
 - Patients who responded and then relapsed
- Phase 3b 04-24 trial
 - 90 patients
 - 19 enrolled
 - Post-HMA patients
 - Progressed on HMAs
 - No control arm
- Phase 1/2 Trial 09-08
 - Combination with Vidaza
 - Phase 1 Portion
 - 140, 280, 560 rigosertib dose
 - Indicated dose of SC/IV Vidaza
 - Phase 2 Portion
 - 40 patients including Phase 1

Phase 1/2 First-line Combination Study in MDS



*Studies conducted by Dr. Silverman of Mount Sinai showed strong synergism between rigosertib and azacitidine**

- Up to 40 patient multi-site study
 - oral rigosertib + azacitidine combination
- Phase 1 stage:
 - ascending dose 3/6 cohorts
- Phase 2 stage:
 - Simon Minimax two-stage design
 - 15 patients followed by 13 patients
- Objectives:
 - Determine safety and PK
 - Assess efficacy (IWG 2006 criteria)
 - Select phase 2 dose



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*US Patents: 8106033B2; 20100305059



Rigosertib in Lower Risk MDS

Treating Lower-risk MDS

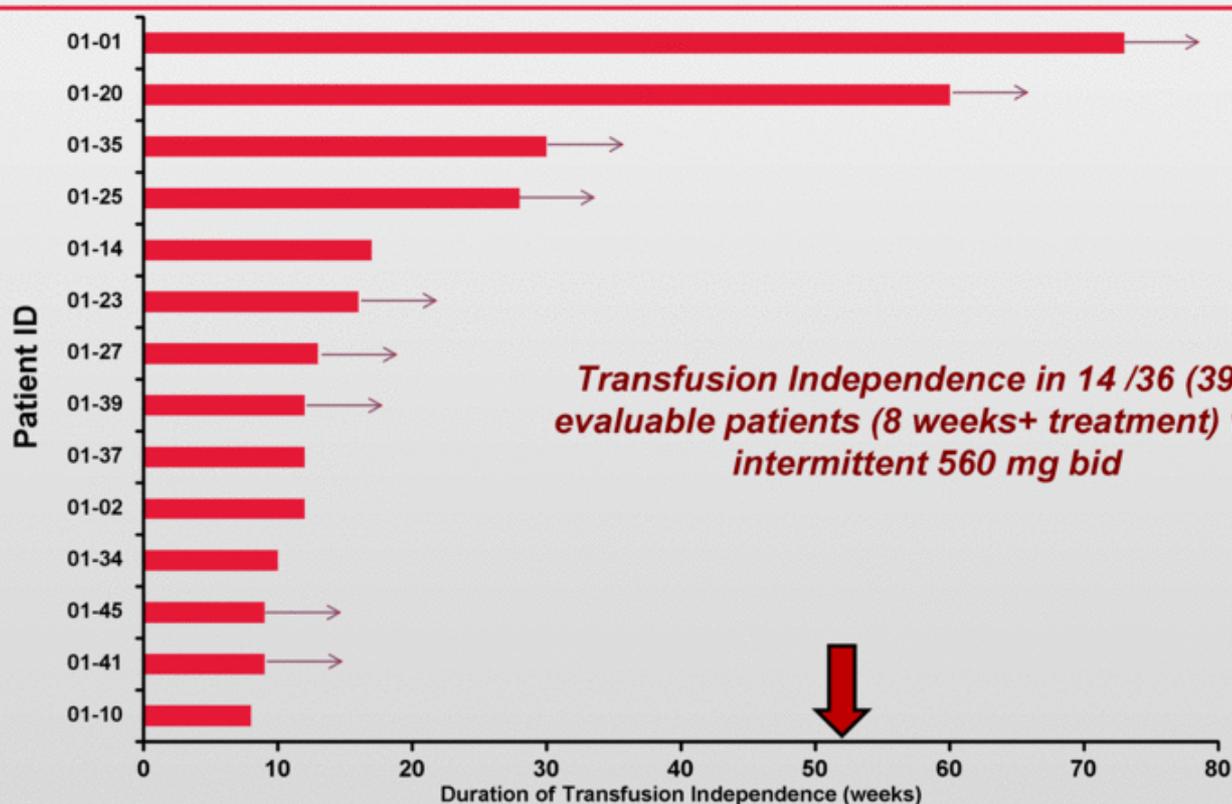
P. Fenaux, Blood, 121(21):4280-6; Epub 2013 Apr 10



- Lower-risk myelodysplastic syndromes (MDSs) are defined as having low or intermediate 1 risk by the International Prognostic Scoring System and are characterized mainly by anemia in most cases.
- **Supportive care--primarily red blood cell transfusions** remains an important component of their treatment, but exposes patients to insufficient correction of anemia, alloimmunization, and organ iron overload (for which the role of iron chelation remains debated).
- Treatment aimed at preventing anemia recurrence should therefore be used whenever possible.
- **Erythropoiesis stimulating agents** remain the first-line treatment of anemia in most lower-risk MDS without del(5q),
- Whereas anemia of low-risk MDS with del 5q responds to **lenalidomide** in two-thirds of the cases, but this drug should be used cautiously because profound cytopenias may occur initially.
- **Treatment after failure of those first-line therapies are disappointing overall, with many patients eventually requiring long-term transfusions**

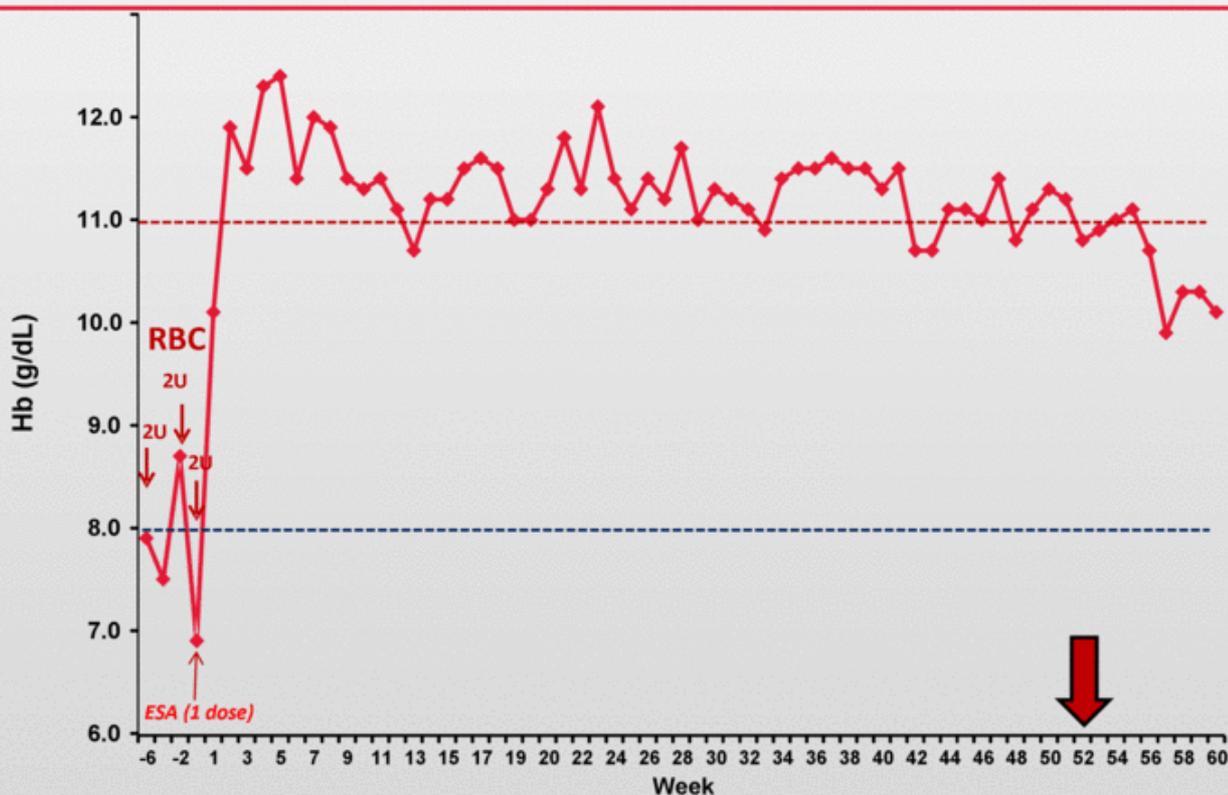
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Durable Transfusion Independence in LR-MDS Patients Treated With Oral Rigosertib



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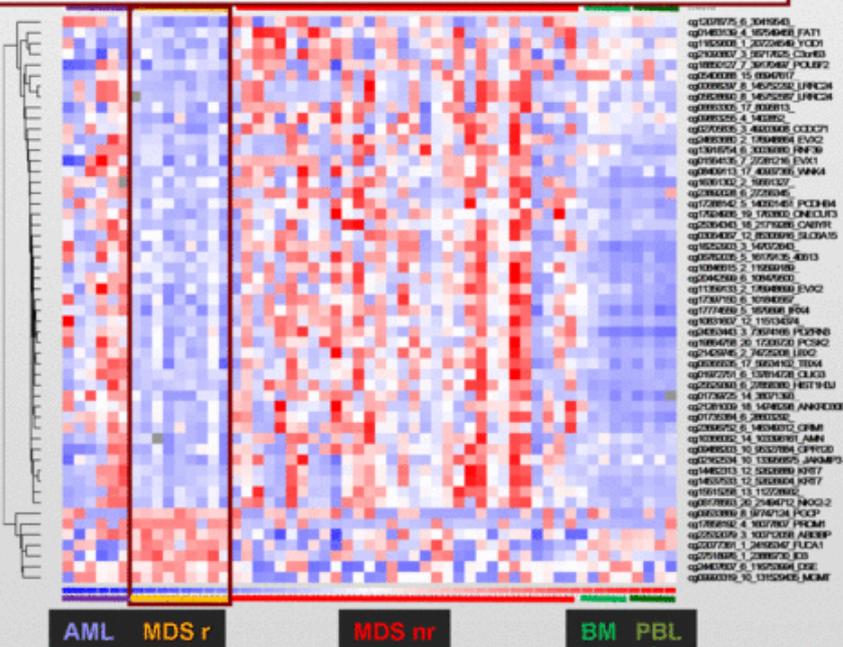
Transfusion Independence in LR-MDS Patient Previously Treated With ESA and Lenalidomide



DNA Methylation Analysis Identifies Hypomethylated Loci in Rigosertib Responder LR-MDS Patients



Genomic DNA from bone marrow (BM) of AML patients, BM of rigosertib treated MDS patients, and normal BM or peripheral blood cells of control normal subjects tested for methylation status



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- Functional annotation of hypo- and hypermethylated genes which best distinguished responders from non-responders
- The genes most affected by methylation were related to regulation of transcription followed by genes involved in cell-cell adhesion, inflammatory response, apoptosis and proliferation
- Ongoing work to select small gene panel of best markers to predict response

Phase 3 Trial for LR-MDS



- Discussions with FDA
 - May seek an SPA
- Design
 - Placebo controlled
 - ESA refractory patients
 - Oral 560/280 dosing; 2/3 weeks schedule
- Response based
 - Transfusion Independence lasting at least 8 weeks
- Plan to start in H2-2014
- EU consultation following protocol completion

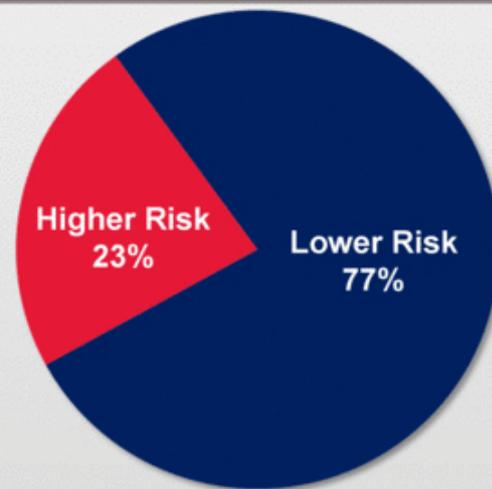
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Unmet Needs in Higher and Lower Risk MDS Market



- Est. 2011 US incidence ~15,600*
- Est. 2011 US prevalence ~52,000*
- Vidaza and Dacogen 2012 sales
 - US sales of Vidaza + North American sales of Dacogen reported > \$550** million
 - Last FDA approval in 2006 (Dacogen)
- No approved second-line treatment available for patients failing Vidaza/Dacogen
- Only a minority of lower risk patients have an approved therapy (Revlimid)

Breakdown of MDS by Risk Category



Higher Risk includes High and Intermediate-2 IPSS categories; Lower Risk includes Low and Intermediate-1 IPSS categories

*Decision Resources
**As reported by Celgene and Astex

Rigosertib MDS Trials and Milestones



IV and Oral Formulations

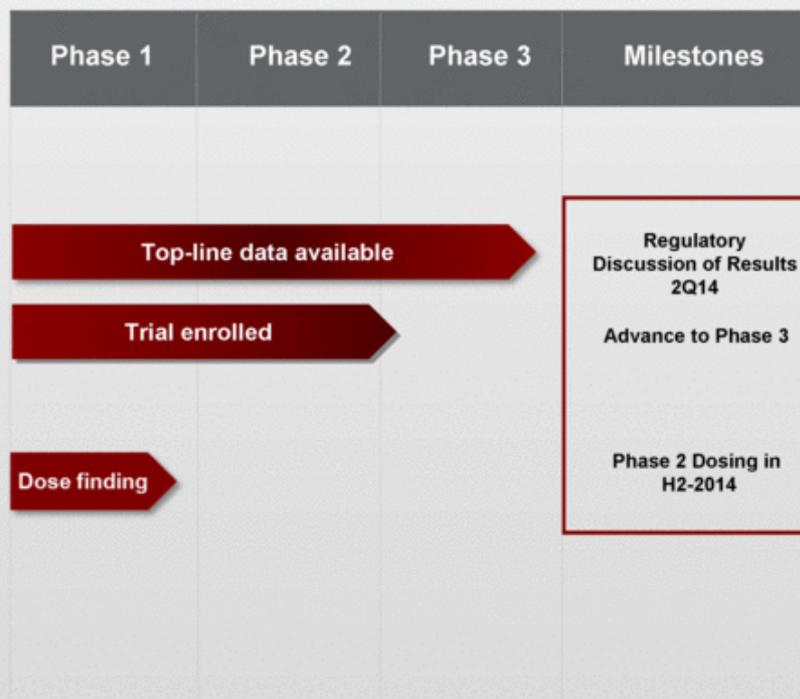
Rigosertib Single-agent

2nd-line in Higher Risk MDS (IV)

1st-line in Lower Risk MDS (Oral)

Rigosertib in Combination

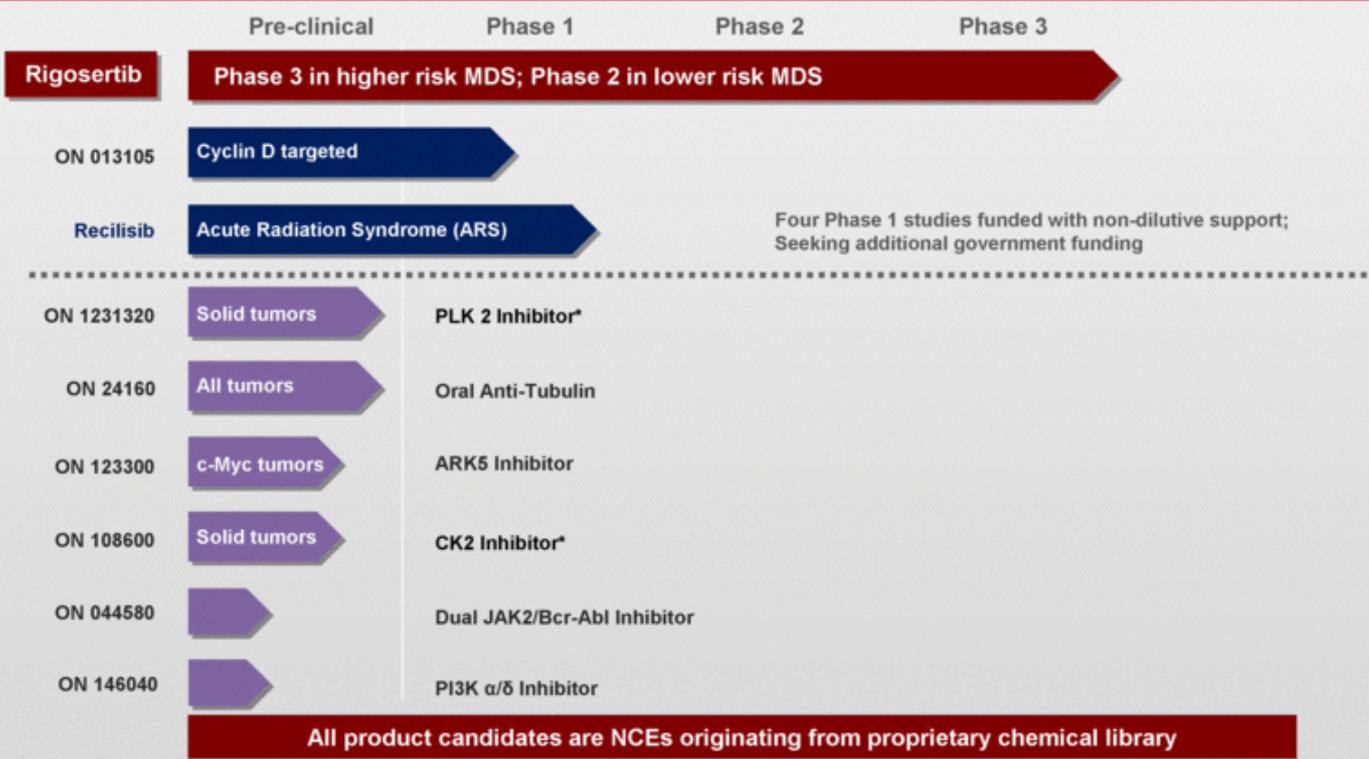
1st-line MDS (Oral)
Azacitidine Combination





Appendix

Three Clinical Programs and Deep Non-clinical Pipeline



*Collaboration with GVK Biosciences to develop to proof of concept