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): **December 5, 2016**

Onconova Therapeutics, Inc.

(Exact name of Registrant as specified in its charter)

Delaware	**001-36020**	**22-3627252**
(State or Other Jurisdiction of Incorporation or Organization)	(Commission File Number)	(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:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 8.01. Other Events

On December 5, 2016, Onconova Therapeutics, Inc. (the "Company") issued a press release regarding information presented by way of a poster and abstract at the American Society of Hematology (ASH) Annual Meeting. Copies of the press release, poster and abstract are attached hereto as Exhibits 99.1, 99.2 and 99.3, respectively, and are incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits.

99.1	Press release issued by the Company dated December 5, 2016.
99.2	Poster titled: Combination of Oral Rigosertib and Injectable Azacitidine in Patients with Myelodysplastic Syndromes (MDS): Results from a Phase II Study
99.3	Abstract titled: 3167 Combination of Oral Rigosertib and Injectable Azacitidine in Patients with Myelodysplastic Syndromes (MDS): Results from a Phase II Study

SIGNATURE

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: December 5, 2016

Onconova Therapeutics, Inc.

By: /s/ Mark Guerin
Name: Mark Guerin
Title: Chief Financial Officer

EXHIBIT INDEX

Exhibit No.	Description
99.1	Press release issued by the Company dated December 5, 2016.
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ONCONOVA
TARGETING CANCER | PROTECTING HEALTHY CELLS

Onconova Presents Phase 2 Data from Oral Rigosertib and Azacitidine Combination Trial in Higher-Risk Myelodysplastic Syndromes (HR-MDS) at 2016 ASH Annual Meeting

—35% Complete Remission (CR) Rate for Combination in 1st-line Higher-risk MDS Patients—

—Updated Median Duration of Complete Response of 8 Months in All Responding Patients—

NEWTOWN, PA, December 5, 2016 — Onconova Therapeutics, Inc. (NASDAQ: ONTX), a clinical-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer, today announced the presentation of data from a Phase 2 clinical trial of oral rigosertib and azacitidine in higher-risk myelodysplastic syndromes (HR-MDS) at the 58th American Society of Hematology (ASH) Annual Meeting in San Diego, California.

"The complete remission rate amongst HMA-naïve HR-MDS patients is higher and responses occur more rapidly and durably with the oral rigosertib combination compared to historic single-agent azacitidine," commented Lewis R. Silverman, M.D., lead investigator in the trial and Associate Professor of Medicine, Hematology and Medical Oncology, at the Icahn School of Medicine at Mount Sinai. "Furthermore, the addition of oral rigosertib to azacitidine does not substantially change the adverse event profile of single-agent azacitidine, and thus may overcome the limitations identified in other HMA-based combinations."

The current standard of care for higher-risk MDS patients is one of two approved hypomethylating agents (azacitidine and decitabine, approved by the FDA in 2004 and 2006). Although these drugs are currently the standard of care in HR-MDS therapy, their overall response rate and duration of benefit is limited to a subset of eligible patients and all responding patients ultimately progress. Thus, there is an urgent need for improving therapeutic options for newly diagnosed HR-MDS patients. The 09-08 trial tested oral rigosertib in combination with injectable azacitidine in a dose ranging study (Phase 1), followed by an expansion cohort (Phase 2) to evaluate the efficacy and safety of the combination. Both 1st-line and 2nd-line HR-MDS patients were included in the study.

Summary of Presented Data from the 09-08 Combination Therapy Trial

Patient Demographics:

- Thirty-three of 40 MDS patients enrolled were evaluable for response at the time of this analysis.
- The median age was 66, with 73% of male patients. ECOG performance status was 0 or 1 in 95% of the patients. IPSS-R distribution was: 7.5% Low, 12.5% Intermediate, 37.5% High, 32.5% Very High and 10% unknown.

Safety/Tolerability of the Combination:

- Oral rigosertib (560 mg qAM, 280 mg qPM) was administered on Day 1-21 of a 28-day cycle. Azacitidine 75 mg/m^2/day SC or IV was administered for 7 days starting on Day 8.

- The combination of oral rigosertib and azacitidine was well tolerated.
- Adverse events of Grade $\geq$3 experienced across all cycles with the combination included thrombocytopenia (33%), neutropenia (30%), haematuria (13%), dysuria (8%), diarrhoea (3%) and arthralgia (3%).
- Notably, the side effects were similar to those previously reported for azacitidine administered alone.

Efficacy of the Combination:

- Thirty-three (20 HMA naïve; 13 HMA resistant) MDS patients were evaluable for efficacy analysis per IWG 2006 criteria (Cheson et al., *Blood* 2006).
- 25 of 33 (76%) patients responded per IWG — 85% of HMA naïve patients experienced a response and 62% of HMA resistant patients experienced a response.
- 7 of 20 (35%) HMA naïve and 1 of 13 (8%) HMA-resistant patients achieved a complete remission (CR). The median duration of CR was 8.0 months, which compares very favorably to the historic duration of CR and PR with single-agent azacitidine of 3.2 months(1).
- Hematologic improvement (HI) was observed in 11 of 33 patients (33%) and the median duration of response was 7.4 months for erythroid response, 8 months for platelet response, and 6.2 months for neutrophil response. Marrow CR was observed in 16 of 33 (48%) patients and the median duration of response was 12.3 months. Marrow CR combined with HI was observed in 10 of 33 (30%) patients.

The poster entitled, "Combination of Oral Rigosertib and Injectable Azacitidine in Patients with Myelodysplastic Syndromes (MDS): Results from a Phase II Study," was presented by Dr. Shyamala Navada of Mount Sinai School of Medicine at the Myelodysplastic Syndromes Session on Sunday, December 4, 2016 at the ASH Annual Meeting in San Diego, California. A copy of the poster is available by visiting the Scientific Presentations section under the Investors & Media tab of Onconova's website.

"We are pleased by the positive efficacy signal observed over extended periods of treatment, and the acceptable tolerability of oral rigosertib and azacitidine in 1st-line HR-MDS," stated Ramesh Kumar, Ph.D., President and CEO of Onconova. "We presented Phase 2 data to the FDA as part of our End-of-Phase 2

meeting in September 2016, and based on these discussions, we are designing a randomized, placebo controlled Phase 3 clinical trial comparing the combination of oral rigosertib plus azacitidine to azacitidine plus placebo in 1st-line HR-MDS patients with the primary composite endpoint of CR and PR rate per 2006 IWG criteria. Based on our discussions with the FDA the primary efficacy endpoint of this trial will be composite response and not survival, permitting accelerated evaluation of outcomes."

Comprehensive Safety Assessment of Rigosertib in MDS Patients

In a second poster at the conference a safety review of 557 MDS/AML patients treated with rigosertib in clinical studies, including the randomized Phase 3 ONTIME trial was presented. The poster entitled, "Comprehensive Analysis of Safety: Rigosertib in 557 Patients with Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML)," can be accessed by visiting the Scientific Presentations section under the Investors & Media tab of Onconova's website.

About Onconova Therapeutics, Inc.

Onconova Therapeutics is a Phase 3 clinical-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer. Onconova's clinical and pre-clinical stage drug development candidates are derived from its extensive chemical library and are designed to work against specific cellular pathways that are important in cancer cells, while causing minimal damage to normal cells. The Company's most advanced product candidate, rigosertib, is a small molecule inhibitor of cellular signaling and acts as a RAS mimetic. These effects of rigosertib appear to be mediated by direct binding of the compound to the RAS-binding domain (RBD) found in many RAS effector proteins, including the Raf and PI3 kinases. Rigosertib is protected by issued patents (earliest expiry in 2026) and has been awarded Orphan Designation for MDS in the United States, Europe and Japan. In addition to rigosertib, two other candidates are in the clinical stage, and several candidates are in pre-clinical stages. For more information, please visit http://www.onconova.com.

About Oral Rigosertib

The oral form of rigosertib provides a more convenient dosing for use where the duration of treatment may extend to multiple years. To date, more than 350 patients have been treated with the oral formulation of rigosertib, either as a single agent or in combination with other drugs. Phase 1 studies with oral rigosertib were conducted in hematological malignancies, lower-risk MDS and solid tumors. Combination therapy of oral rigosertib with azacitidine and chemoradiotherapy has also been explored.

About IV Rigosertib

The intravenous form of rigosertib has been employed in Phase 1, 2, and 3 clinical trial involving more than 800 patients, and is currently being evaluated in the randomized Phase 3 global INSPIRE trial as 2nd-line treatment for patients with higher-risk MDS, after failure of hypomethylating agent, or HMA, therapy. This formulation is suited for patients with advanced disease and provides long duration of exposure and ensures adequate dosing under a controlled setting.

References

(1)Fenaux et al for the international Vidaza High risk MDS survival study group, Lancet Oncology 2009, 10:223-232.

Forward Looking Statements

Some of the statements in this release are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, which involve risks and uncertainties. These statements relate to future events or Onconova Therapeutics, Inc.'s future operations, clinical development of Onconova's product candidates and presentation of data with respect thereto, regulatory approvals, expectations regarding the sufficiency of Onconova's cash and other resources to fund operating expenses and capital expenditures, Onconova's anticipated milestones and future expectations and plans and prospects. Although Onconova believes that the expectations reflected in such forward-looking statements are reasonable as of the date made, expectations may prove to have been materially different from the results expressed or implied by such forward-looking statements. Onconova has

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attempted to identify forward-looking statements by terminology including "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "should," "approximately" or other words that convey uncertainty of future events or outcomes. These statements are only predictions and involve known and unknown risks, uncertainties, and other factors, including Onconova's need for additional financing and current plans and future needs to scale back operations if adequate financing is not obtained, the success and timing of Onconova's clinical trials and regulatory approval of protocols, and those discussed under the heading "Risk Factors" in Onconova's most recent Annual Report on Form 10-K and quarterly reports on Form 10-Q.

Any forward-looking statements contained in this release speak only as of its date. Onconova undertakes no obligation to update any forward-looking statements contained in this release to reflect events or circumstances occurring after its date or to reflect the occurrence of unanticipated events.

CONTACT: Onconova Therapeutics

Benjamin Hoffman, 267-759-3036

bhoffman@onconova.us

Combination of Oral Rigosertib and Injectable Azacitidine in Patients with Myelodysplastic Syndromes (MDS): Results from a Phase II Study

Shyamala C. Navada,MD[1], Guillermo Garcia-Manero, MD[2], Katherine P. Hearn, BSN[2], Rosalie Odchimar-Reissig, RN[1], Erin P. Demakos, RN, CCRN[1], Yesid Alvarado, MD[2], Naval Daver, MD[2], Courtney DiNardo, MD[2], Marina Konopleva MD, PhD[2], Gautam Borthakur, MD[2], Pierre Fenaux, MD, PhD[3], Michael E. Petrone, MD, MPH[4], Patrick S. Zbyszewski, MBA[4], Steven M. Fruchtman, MD[4], Lewis R. Silverman, MD[1]

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

BACKGROUND

- Azacitidine (AZA) is first-line therapy for patients (pts) with higher-risk MDS.
- Rigosertib interferes with the RAS-binding domains of RAF kinases and inhibits the RAS-RAF-MEK and the PI3Ks pathways.
- In vitro, the combination of rigosertib with AZA synergistically inhibits growth and induces apoptosis of leukemic cells in a sequence–dependent manner (rigosertib administered prior to AZA) (Skidan, AACR 2006).
- Phase I results of this study in pts with MDS or AML showed the combination of oral rigosertib and standard-dose AZA to be well-tolerated with evidence of efficacy (Navada, Blood 2014).

OBJECTIVES

- To investigate the safety and toxicity of the combination of oral rigosertib and AZA in pts with MDS
- To evaluate the activity of the combination of oral rigosertib and AZA with respect to IWG response and hematologic improvement

METHODS

- Oral rigosertib was administered twice daily on Day 1-21 of a 28-day cycle.
- Dose was escalated to the recommended Phase II dose (RPTD: 560 mg qAM, 280 mg qPM).
- Azacitidine 75 mg/m^2/day SC or IV was administered for 7 days starting on Day 8.
- A CBC was performed weekly and a bone marrow aspirate and/or biopsy was done at baseline, on Day 29, and every 8 weeks thereafter.

RESULTS

Demographics

- The combination of oral rigosertib and AZA has been administered to 40 pts with MDS.
- Pts were classified into the following MDS risk categories per the IPSS (Greenberg et al, Blood 1997): intermediate-1 (12 pts), intermediate-2 (15 pts), high-risk (13 pts).
- Median age was 66 years; 73% of pts were male; and ECOG performance status was 0 or 1 in 95% of pts.
- Prior HMA treatment consisted of azacitidine (12 pts), decitabine (4 pts), and both (1 pt).

Efficacy

- The 33 MDS pts who were evaluable for response have received 1-37+ cycles of study treatment (median, 6 cycles).
- Overall responses according to IWG criteria (Cheson, Blood 2006) were observed in 25 (76%) of the 33 evaluable pts with MDS (Table 1).
- When overall response is defined as CR plus PR plus HI, defined here as Clinical Benefit Response, 58% of all evaluable pts and 70% of the evaluable HMA-treatment-naïve pts demonstrated responses.
- Median duration of response was 7.4 months for erythroid response, 8 months for platelet response, and 6.2 months for neutrophil response
- Median duration of remission (CR, PR) was 8 months for the combination compared to the 3.2 months reported for AZA alone (Fenaux et al for the international Vidaza High risk MDS survival study group, Lancet Oncology 2009, 10:223-232)

Safety

- The most common treatment-emergent adverse events were constipation, diarrhea, nausea, haematuria, dysuria, and fatigue (Table 3); the most common serious AEs were febrile neutropenia (10%), urinary tract infection (10%), pneumonia (8%), pneumonia fungal (8%), and acute renal failure (8%).

Table 3: Most Common Treatment-emergent AEs Among Pts with MDS, All Grades (N = 40)

MedDRA Preferred Term	Number (%) of Patients	
	All Grades	Grade ≥3
Any TEAE	40 (100)	38 (95)
Constipation	18 (45)	-
Diarrhoea	17 (43)	1 (3)
Nausea	17 (43)	-
Haematuria	16 (40)	5 (13)
Dysuria	16 (40)	3 (8)
Fatigue	16 (40)	-
Decreased appetite	15 (38)	-
Thrombocytopenia	13 (33)	13 (33)
Pyrexia	13 (33)	-
Neutropenia	12 (30)	12 (30)
Arthralgia	11 (28)	1 (3)

MedDRA = Medical Dictionary of Regulatory Activities

Hematology Trends for Patient 101-006

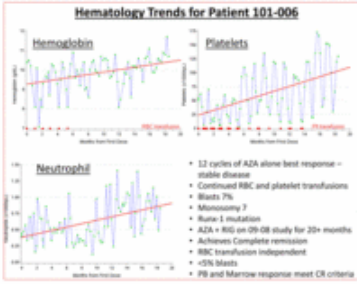


Table 1: Response per IWG 2006

	Overall evaluable (N=33)	No prior HMA (N=20)	HMA resistant (N=13)
Complete Remission	8 (24%)	7 (35%)	1 (8%)
Partial Remission	0	0	0
Marrow CR + Hematologic Improvement (HI)	10 (30%)	6 (30%)	4 (31%)
Marrow CR alone	6 (18%)	3 (15%)	3 (23%)
Hematologic Improvement alone	1 (3%)	1 (5%)	0
Stable Disease	8 (24%)	3 (15%)	5 (38%)
Overall IWG Response	25 (76%)	17 (85%)	8 (62%)
Clinical Benefit Response	19 (58%)	14 (70%)	5 (38%)

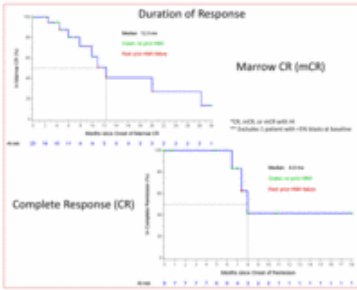
HMA resistant = Primary refractory or relapsed after treatment with hypomethylating agents

Table 2: Response per IWG 2006 Criteria by IPSS-R* Subgroup

	Low N=3	Intermediate N=5	High N=15	Very High N=13	Unknown N=4
Response per IWG 2006					
CR	1 (33)	2 (40)	2(13)	3(23)	0
mCR	1 (33)	1(20)	6 (40)	6 (46)	2(50)
SD	1 (33)	1 (20)	4 (27)	1 (8)	1(25)
PD	0	0	0	0	0
NE	0	0	3(20)	3 (23)	1(25)
Hematologic Improvement					
Erythroid Response	0	2(40)	5(33)	6(46)	0
Platelet Response	1(33)	2(40)	5(33)	6(46)	1(25)
Neutrophil Response	1(33)	3(60)	5(33)	4(31)	0
Overall Response	2(66)	4(80)	8(53)	9(69)	2(50)

*International Prognostics Scoring System-Revised (Greenberg, Blood 2012)

Duration of Response



CONCLUSIONS

- Oral rigosertib in combination with AZA demonstrates an overall response rate of 76% in pts with MDS, including an 85% response rate among pts who had not previously been treated with an HMA, and a 62% response rate among pts with prior HMA failure.
- The combination was well-tolerated in pts with MDS. Repetitive cycles of the combination can be safely administered without evidence of cumulative toxicity. Addition of rigosertib does not substantially change the adverse event profile of single agent azacitidine and thus may overcome the limitations identified in other HMA based combination studies.
- The CR rate in HMA naïve patients is higher and responses occur more rapidly with the combination than with single agent AZA
- Further exploration of this combination is warranted in a randomized trial in defined MDS populations.

REFERENCES

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.

Greenberg P, Cox C, LeBeau MM, et al. International scoring system for evaluating prognosis in myelodysplastic syndromes. Blood 1997; 89:2079-88.

Greenberg PL, Tuechler H, Schanz J, et al. Revised International Prognostic Scoring System for Myelodysplastic Syndromes. Blood 2012;120(12): 2454-65.

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

Skidan I, Zinzar S, Holland J, Reddy R, Reddy EP, Silverman L. Toxicology of a novel small molecule ON 01910Na on human bone marrow and leukemic cells in vitro. AACR Meeting Abstracts, Apr 2006;309-Abstract 1310.

ASH | 58th Annual Meeting & Exposition
San Diego, CA · December 3-6, 2016

3167 Combination of Oral Rigosertib and Injectable Azacitidine in Patients with Myelodysplastic Syndromes (MDS): Results from a Phase II Study

Myelodysplastic Syndromes—Clinical Studies
Program: Oral and Poster Abstracts
Session: 637. Myelodysplastic Syndromes—Clinical Studies: Poster II
Sunday, December 4, 2016, 6:00 PM-8:00 PM
Hall GH (San Diego Convention Center)

Shyamala C. Navada, MD*(1), Guillermo Garcia-Manero, MD(2), Katherine P. Hearn, BSN, RN(2)*, Rosalie Odchimar-Reissig, RN(1)*, Erin P. Demakos, RN, CCRN(1)*, Yesid Alvarado, MD(2), Naval Daver, MD(2), Courtney D. DiNardo, MD, MSCE(2), Marina Konopleva, MD, PhD(2), Gautam Borthakur, MD(2), Pierre Fenaux, MD, PhD(3), Michael E. Petrone, MD, MPH(4), Patrick Simon Zbyszewski, MBA(4)*, Steven M. Fruchtman, MD(4) and Lewis R. Silverman, MD(1)*

(1)Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai, New York, NY
(2)Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX
(3)Saint-Louis Hospital, University Paris 7, Paris, France
(4)Onconova Therapeutics, Inc., Newtown, PA

Background:

Based on a model suggesting leukemia can be driven by combined effect of mutations in an epigenetic gene (DNMT3) and Ras, the combination of a hypomethylating agent (HMA) such as azacitidine (AZA) and a Ras mimetic such as rigosertib (RIG) may have enhanced activity in both MDS and AML. The mechanism of action for RIG (Athuluri-Divakar et al, Cell 2016) documents its interference with the RAS-binding domains of RAF kinases and inhibition of the RAS-RAF-MEK and the PI3Ks pathways. In vitro, the combination of RIG with AZA was found to act synergistically to inhibit growth and to induce apoptosis of leukemic cells in a sequence-dependent manner (exposure to RIG first, followed by AZA) (Skidan et al, AACR 2006). Rigosertib's low bone marrow toxicity in pre-clinical assays, effective inhibition of human hematopoietic tumor cell lines, and its synergy with AZA suggests the potential value of combination treatment for patients (pts) with MDS.

Phase I results of the current clinical study in pts with MDS or AML showed the combination of oral RIG and standard-dose AZA to be well-tolerated with evidence of efficacy (Navada et al, Blood 2014). The phase II portion of the study was initiated to further evaluate the combination in pts with MDS.

Methods:

Phase II results are presented for HMA-treatment-naïve MDS pts and for those with MDS failing to respond to or progressed on a prior HMA. Oral RIG was administered twice daily on Day 1-21 of a 28-day cycle at the recommended Phase II dose (RPTD: 560 mg qAM and 280 mg qPM). AZA 75 mg/m^2/d SC or IV was administered for 7 days starting on Day 8. A CBC was performed weekly and a bone marrow aspirate and/or biopsy were performed at baseline, D29, and then every 8 weeks thereafter.

Results:

The combination of oral RIG and injectable AZA has been administered to a total of 54 pts, of whom 40 were pts with MDS including HMA-treatment-naïve (N=23) and previously HMA treated pts (N=17). Median age was 66 years (range 25-85); 73% of pts were male; and ECOG performance status was 0, 1, and 2 in 23%, 73%, and 5%, respectively. 17 pts received prior HMA therapy: 12 AZA, 4 decitabine, and 1 both. Patients have received 1-36+ cycles of treatment (median, 6 cycles), with a median duration of treatment of 25 weeks (range 4 to 145+ weeks). 8 (20%) and 2 (5%) of pts have been treated for more than 1 and 2 years, respectively.

Table 1 shows the response per IWG 2006 criteria (Cheson, Blood 2006) among 33 evaluable patients. The response per IWG 2006 was complete remission (CR) in 8 (24%), concurrent marrow CR and hematologic improvement (HI) in 9 (27%), marrow CR alone in 7 (21%), and HI alone in 1 (3%). When overall response is defined as CR plus PR plus HI - responses with improvement in marrow function and thus either normalization of the peripheral blood count or lineage improvement — defined here as Clinical Benefit Response - 55% of all evaluable pts and 70% of the evaluable HMA-treatment-naïve patients showed responses meeting these criteria.

Table 1: Response per IWG 2006

	Overall evaluable (N=33)	No prior HMA (N=20)	Prior HMA (N=13)
Complete Remission	8 (24%)	7 (35%)	1 (8%)
Partial Remission	0	0	0
Marrow CR + hematologic improvement	9 (27%)	6 (30%)	3 (23%)
Marrow CR alone	7 (21%)	3 (15%)	4 (31%)
Hematologic improvement alone	1 (3%)	1 (5%)	0
Stable disease	8 (24%)	3 (15%)	5 (38%)
Overall IWG Response	25 (76%)	17 (85%)	8 (62%)

Clinical Benefit Response	18 (55%)	14 (70%)	4 (31%)

Median time to initial response was 2 cycles (2.2 months), and median time to best response was 3 cycles (3.3 months). Median duration of response was 8 months for CR, 14.3 months for marrow

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CR, 7.4 months for erythroid response, 8 months for platelet response, and 6.2 months for neutrophil response.

Clinical response is classified by IPSS-R risk categories below.

Table 2: Response per IWG 2006 Criteria by IPSS-R Risk

	Low	Intermediate	High	Very high	Unknown
N	**3**	**5**	**15**	**13**	**4**
Response per IWG 2006					
CR	1	2	2	3	0
mCR	1	1	6	6	2
SD	1	1	4	1	1
NE	0	0	3	3	1
Hematologic Improvement					
Erythroid response	0	2	3	6	0
Platelet response	1	2	4	6	1
Neutrophil response	0	1	4	4	0
Overall response	3	3	4	6	1

IPSS-R = International Prognostic Scoring System – Revised (Greenberg et al, Blood 2012)

The most frequently reported adverse events are nausea (41%), fatigue (39%), diarrhoea (37%), constipation (37%), dysuria (28%), decreased appetite (28%), haematuria (24%, 8% Grade 3), pyrexia (24%), dizziness (22%), thrombocytopenia (20%), back pain (20%), dyspnoea (20%), and cough (20%).

Eight deaths were reported on study with most common causes including infection and progression of disease.

Conclusions:

The combination of oral RIG and standard-dose AZA was well tolerated in repetitive cycles in pts with MDS. Response per IWG 2006 criteria was observed both in HMA-treatment-naïve patients (85%) and in patients after failure of prior HMA therapy (62%); employing Clinical Benefit Response as the criteria, these groups had 70% and 31% response, respectively. These clinical results confirm the preclinical synergistic interaction with the combination of RIG and AZA reported by Skidan et al, and suggest that the combination can overcome clinical resistance to HMAs. Based on these results, a Phase III study of the combination of oral RIG and AZA in patients with MDS is planned.

Disclosures: Navada: *Onconova Therapeutics, Inc.:* Research Funding. **Daver:** *Karyopharm:* Honoraria, Research Funding; *Pfizer:* Consultancy, Research Funding; *Sunesis:* Consultancy, Research Funding;

Ariad: Research Funding; *Otsuka:* Consultancy, Honoraria; *Kiromic:* Research Funding; *BMS:* Research Funding. **DiNardo:** *Novartis:* Other: advisory board, Research Funding; *Abbvie:* Research Funding; *Daiichi Sankyo:* Other: advisory board, Research Funding; *Agios:* Other: advisory board, Research Funding; *Celgene:* Research Funding. **Konopleva:** *Reata Pharmaceuticals:* Equity Ownership; *Abbvie:* Consultancy, Research Funding; *Genentech:* Consultancy, Research Funding; *Stemline:* Consultancy, Research Funding; *Eli Lilly:* Research Funding; *Cellectis:* Research Funding; *Calithera:* Research Funding. **Fenaux:** *Celgene, Janssen,Novartis, Astex, Teva:* Honoraria, Research Funding. **Petrone:** *Onconova Therapeutics, Inc.:* Employment. **Zbyszewski:** *Onconova Therapeutics, Inc.:* Employment. **Fruchtman:** *Onconova:* Employment. **Silverman:** *Onconova Therapeutics, Inc.:* Patents & Royalties: Co-Patent holder for the combination of azacitidine and rigosertib, Research Funding.

**signifies non-member of ASH*

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2021 L Street NW, Suite 900, Washington, DC 20036
Phone 202-776-0544 | Fax 202-776-0545