AA&MDSIF

MDS Research Summary
From the 2013 American Society of Hematology Annual Meeting

A Summary of Selected Scientific Abstracts for Patients with Myelodysplastic Syndromes (MDS) and their Caregivers
The Aplastic Anemia & MDS International Foundation (AA&MDSIF) is an independent non-profit organization. Our mission is to support patients, families, and caregivers coping with:

- Aplastic anemia
- MDS (myelodysplastic syndromes)
- PNH (paroxysmal nocturnal hemoglobinuria)
- Related bone marrow failure diseases

This booklet offers summaries of selected abstracts presented at the 55th Annual Meeting of the American Society of Hematology (ASH) in December 2013. It provides some of the most up-to-date information about new research into the biology and treatment of myelodysplastic syndromes (MDS).

Although the information in this booklet has undergone a thorough, independent medical review to insure its accuracy, this information is not intended to be a substitute for the advice of your doctor. You should always seek medical advice from a qualified physician. For more information, call us at (800) 747-2820, or visit us online at www.AAMDS.org.

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Dear Patient or Caregiver,

The purpose of this booklet is to provide you with the most up-to-date information about new research into the biology and treatment of myelodysplastic syndromes (MDS), as presented at the 55th Annual Meeting of the American Society of Hematology (ASH) Annual Meeting in December 2013.

The ASH Annual Meeting is the world’s largest professional gathering of hematologists and hematological oncologists—i.e., doctors who care for patients with blood disorders or blood and bone marrow cancers. This conference is where many major findings in the field of blood and marrow disorders are first announced to attendees, the larger medical and scientific community, and the media.

New information that researchers hope is important enough to be presented at this meeting is submitted a few months ahead of the conference in the form of an “abstract”—a brief summary of the study and its results—and authors of the most interesting and noteworthy abstracts are asked by ASH to present their research in more detail, either in the format of a tacked-up printed poster or an oral (podium) presentation.

We selected the ASH abstracts in this summary because we feel they are the most relevant and important for patients who currently have MDS to know about. Please note that the research results discussed at the ASH Annual Meeting often involve experimental drugs that are not yet approved by the Food and Drug Administration (FDA) for general use or investigations of potential new uses of previously approved treatments. By providing summaries of the research presented, we do not intend to recommend or endorse any particular medication or treatment approach. Our goal is simply to inform you about current news and trends in research related to MDS.

If you are interested in participating in research studies such as those discussed in this booklet, we encourage you to speak with your doctor about clinical trials or to visit www.clinicaltrials.gov.

As always, please contact AA&MDSIF if you have questions about these summaries or any aspect of managing your disease.

Mikkael Sekeres, MD, MS

The Cleveland Clinic Taussig Cancer Institute
Member, AA&MDSIF Medical Advisory Board

The abstracts summarized in this booklet may be viewed on the American Society of Hematology Web site at https://ash.confex.com/ash/2013/webprogram/start/html. You may type in the abstract number or title in the search box. Any conflicts of interest or other relevant disclosures by the study authors are noted in each abstract.
The Role of Early TP53 Mutations on the Evolution of Therapy-Related AML

Terrence Neal Wong, M.D. Ph.D., Giridharan Ramsingh, M.D, Andrew Young, Dong Shen, Chris Miller, Ph.D., Tamara Lamprecht, B.S., Sharon Heath, Robert S. Fulton, Elaine R. Mardis, Ph.D., Li Ding, Peter Westervelt, M.D., Ph.D., John Welch, M.D., Ph.D., Matthew J. Walter, M.D., Timothy Graubert, M.D., John F. DiPersio, M.D., Ph.D., Timothy J. Ley, M.D., Todd E Draley, M.D., Ph.D., Richard K Wilson, Ph.D., and Daniel C. Link, M.D.

Chemotherapy and/or radiation treatment sometimes causes acute myeloid leukemia (AML) or myelodysplastic syndromes (MDS). Patients with therapy-related AML are more likely than those with primary AML (not related to previous chemotherapy or radiation therapy) to have mutations, or changes, in the TP53 gene and abnormalities in chromosomes 5 and 7. Patients with therapy-related AML or MDS are less likely than those with primary AML or MDS to respond to treatment or experience long-term remission.

A potential cause of therapy-related MDS and AML might be TP53 mutations in hematopoietic stem cells (HSCs), which develop into blood cells. HSCs with these mutations might be more successful at surviving than HSCs without the mutation in patients undergoing chemotherapy. To test this hypothesis, the authors developed a novel genomic sequencing technique that could identify very small numbers of HSCs with the TP53 mutation. They used blood or bone marrow samples from 7 patients that had been collected 3–10 years before they developed treatment-related AML or MDS. The authors also created a type of model known as a chimera, in which they transplanted HSCs from one organism to another. This model contained HSCs with normal and mutated TP53.

Key Findings:

- Two patients had a TP53 mutation. One of these patients had had the mutation 6 years before developing treatment-related AML. The other patient had developed the mutation 3 years before being diagnosed with treatment-related MDS.
- In the chimera, the HSCs with mutated TP53 did not survive longer than HSCs without the mutation.
- When HSCs with the TP53 mutation were treated with N-ethyl-N-nitrosourea, an agent that causes genetic mutations, they had a significant growth advantage.

Conclusions:

- HSCs that acquire TP53 mutations as a result of the normal aging process might have a survival advantage in patients undergoing therapy that is toxic to their cells. This survival advantage might explain why such a large proportion of patients with treatment-related AML or MDS have a TP53 mutation.
- The early development of a TP53 mutation in a single founder clone (or copy of an HSC) probably contributes to the frequent chromosomal abnormalities and poor response to chemotherapy in many patients with treatment-related AML or MDS.

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ASH 518 & ASH 521

The following two abstracts (518 and 521) are summarized together.

ASH 518

Clinical “MUTATOME” of Myelodysplastic Syndrome; Comparison to Primary Acute Myelogenous Leukemia

Hideki Makishima, M.D., Ph.D., Thomas LaFramboise, Ph.D., Bartlomiej P Przychodzen, Ph.D., Kenichi Yoshida, M.D., Matthew Ruffalo, B.S., Inés Gómez-
BIOLOGY AND GENETICS OF MDS AND AML

Seguí, M.D., Holleh D. Husseinzadeh, M.D., Yuichi Shiraishi, Ph.D., Masashi Sanada, M.D., Yasunobu Nagata, M.D., Yusuke Sato, M.D., Aiko Sato-Otsubo, Kenichi Chiba, Ph.D., Hiroko Tanaka, B.A., Tsuyoshi Nakamaki, M.D., Wolf-Karsten Hofmann, M.D., Shuichi Miyawaki, M.D., Lee-Yang Shih, M.D., Shigeru Chiba, M.D., Ph.D., Satoru Miyano, Ph.D., Naoko Hosono, M.D., Ph.D., Chantana Polprasert, M.D., Swapna Thota, M.D., Brittney Dienes, Kathryn M Guinta, Yogen Saunthararajah, M.D., Mikkael A. Sekeres, M.D., M.S., Seishi Ogawa, M.D., Ph.D., and Jaroslaw P. Maciejewski, M.D., Ph.D., FACP

ASH 521

Landscape of Genetic Lesions in 944 Patients with Myelodysplastic Syndromes

Yasunobu Nagata, M.D., Vera Grossmann, Ph.D., Yusuke Okano, Ulrike Bacher, M.D., Genta Nagae, M.D., Ph.D., Susanne Schnittger, Ph.D., Yusuke Shiozawa, M.D., Ayana Kon, M.D., Tamara Alpermann, Kenichi Yoshida, M.D., Masashi Sanada, M.D., Andreas Roller, Ph.D., Nirosan Nadarajah, M.Sc., Yuichi Shiraishi, Ph.D., H. Phillip Koeffler, M.D., Ph.D., Hans-Ulrich Klein, Ph.D., Martin Dugas, M.D., Kenichi Chiba, Ph.D., Hiroko Tanaka, B.A., Alexander Kohlmann, Ph.D., Satoru Miyano, Ph.D., Claudia Haferlach, M.D., Hiroyuki Aburatani, M.D., Ph.D., Wolfgang Kern, M.D., Seishi Ogawa, M.D., Ph.D., and Torsten Haferlach, M.D.

Some of the key factors in the development of myelodysplastic syndromes (MDS) are abnormal chromosomes and alterations (mutations) in genes that develop after conception. Next-generation sequencing makes it possible to identify the patterns in these changes.

Two groups of researchers used state-of-the-art technologies to study genetic mutations in people with MDS. One study included 706 patients with low-risk or high-risk MDS according to the International Prognostic Scoring System, myelodysplastic/myeloproliferative (MDS/MPN) neoplasms, or secondary acute myelogenous leukemia (sAML; AML that develops in patients who have had MDS or another bone marrow failure disease). The second team analyzed specimens from 944 patients with various subtypes of MDS.

Key Findings:
- Only 6 genes—TET2, SF3B1, ASXL1, SRSF2, DNMT3A, and RUNX1—were mutated in at least 10% of patients with MDS.
- SF3B1 mutations were associated with significantly longer survival, whereas mutations in 25 genes were associated with shorter survival.
- A combination of mutations in 14 genes along with age, gender, blood cell counts, and chromosomal abnormalities was used to group patients into four categories by overall survival rates: low risk (95% survival rate at 3 years), intermediate risk (69% survival rate), high risk (33% survival rate), and very high risk (5% survival rate).
- As MDS progressed, the average number of mutations per patient increased (from 2.2 in lower-risk MDS to 2.8 in higher-risk MDS and 3.4 in sAML).
- Mutations in TET2, DNMT3A, ASXL1, and U2AF1 apparently developed early in the development of MDS, while those of the IDH, RTK, and cohesin families seemed to happen later in the process.

Conclusions:
- Analyzing multiple target genes in MDS is feasible and provides an invaluable tool for improving the diagnosis of MDS, classifying patients, and, especially, predicting the course of the disease.
Distinct Pattern of Genomic Changes Associated with Smoking in Patients with Myelodysplastic Syndromes (MDS)

David J. Seastone, D.O., Ph.D., Sudipto Mukherjee, M.D., Ph.D., MPH, Zaher K. Otrock, M.D., Paul Elson, Sc.D., Michael K. Keng, M.D., Bartlomiej Przychodzen, Ph.D., Hideki Makishima, M.D., Ph.D., Brittney Dienes, Sean Hobson, Kristin Dodd, R.N., Tracy Cinalli, RN, Ramon V Tiu, M.D., Yogen Saunthararajah, M.D., Jaroslaw P. Maciejewski, M.D., Ph.D., FACP, and Mikkael A. Sekeres, M.D., M.S.

People who smoke have a higher risk of developing myelodysplastic syndromes (MDS), and smokers with MDS don’t tend to survive as long as nonsmokers with MDS. The goal of this study was to identify the mutations (changes) in genes that are associated with smoking in patients with MDS. The study included 151 patients who visited the Cleveland Clinic between 2000 and 2012. Of these patients, 42% were female, and their median age at diagnosis was 68. About three-quarters of the patients had de novo MDS, meaning that their MDS was not caused by a previous treatment or another disease. About half (81 patients, 54%) were former smokers and 11% were current smokers.

Key Findings:

• The most common mutations were in TET2 (19% of patients), SF3B1 (15%), ASXL1 (14%), DNMT3A (11), and U2AF1 (10%).
• Three-quarters of current smokers and former smokers had at least one of the common mutation, compared to 52% of nonsmokers.
• One quarter of current and former smokers had mutations in genes involved in modifying histone (a protein that helps control the activity of genes) compared to 11% of patients who had never smoked.

Conclusions:

• Smoking is associated with higher numbers of genetic mutations in people with MDS.
• Smoking in people with MDS seems to be associated with mutations in different genes than the mutations in people with MDS who have never smoked.

Differences in Perceptions of Disease and Treatment Effectiveness and Adherence Between Physicians and Patients with Myelodysplastic Syndromes (MDS)

David P. Steensma, M.D., Richard M. Stone, M.D., John Huber, M.S., Betsy Dennison, M.S., R.N., and Mikkael A. Sekeres, M.D., M.S.

Myelodysplastic syndromes (MDS) are complex conditions and are described using terms that can be quite confusing. The drugs used to treat MDS often have to be administered over several cycles to maximize their effectiveness. Patients need to understand the disease and how it’s treated to help ensure that they have the best possible outcomes.

To better understand how physicians and patients perceive MDS and treatment decisions, the authors surveyed 477 patients with MDS (52% male) and 61 physicians registered with AA&MDSIF. About half the physicians saw 5 to 19 new patients with MDS each year. The questionnaire for patients had 57 questions, and the one for physicians had 49 questions.
Key Findings:

- Only 29% of patients reported that MDS is “curable,” compared to 52% of physicians.
- Compared to patients, physicians tended to overestimate the benefits of treatment to quality of life.
- Physicians also underestimated the negative effects of MDS treatment on patients’ ability to do their regular activities.
- The most common reasons cited by both patients and physicians for stopping treatment early were making the patients feel too sick to continue, side effects interfering with the patient’s regular activities, and the burden of treatment outweighing the benefits to the patient.

Conclusions:

- Patients with MDS and physicians have different views of the benefits of MDS treatment.
- Better communications might improve patients’ and physicians’ understanding of MDS and the impact of MDS treatment, leading to better treatment compliance and responses to treatment.

What This Means For Patients

In this study, 477 patients and 120 health care professionals were surveyed about their perceptions of MDS and treatment patterns. Patients, physicians and non-physician health care professionals have differing perspectives on MDS and MDS therapy, with physicians viewing the treatment experience less favorably than patients but having a more favorable view of the potential benefits of specific therapies than patients. While most physicians were aware of what comprises an appropriate treatment course for the 3 FDA approved drugs for MDS, some were not. Additionally, patients with MDS often do not consider MDS a form of “cancer” even though MDS is classified as such by the World Health Organization, and most patients as well as most non-physician health care professionals are unaware that MDS can be cured in some cases through stem cell transplantation. This study highlights some specific education needs for both patients with MDS and health care professionals.

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ASH 1530
Effect of Comorbidities in Myelodysplastic Syndrome by Revised-IPSS and Age

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Doctors use the International Prognostic Scoring System (IPSS) to classify a patient’s myelodysplastic syndrome (MDS) based on the percentage of blasts, or immature cells, in the bone marrow; number and severity of chromosome changes in blasts; and whether the patient has low levels of certain blood cells. The revised IPSS (IPSS-R) is based on the same factors as the IPSS, but emphasizes chromosomal abnormalities more than high blast counts and includes more information than the IPSS.

Comorbidities, or health problems other than MDS, affect treatment outcomes and patient survival. The aim of this study was to find out the
Patient Factors and Impact on MDS

Effects of comorbidities in patients whose MDS has been classified according to the IPSS-R. The study included 600 patients (67% male, median age 66 years) who had been followed for 54 months, on average.

Key Findings:

- Median survival was 28 months in patients with no comorbidities, 16 months for those with mild comorbidities, 14 months for those with moderate comorbidities, and 9 months for those with severe comorbidities.
- Median survival by R-IPSS category was 47 months for patients with very low-risk MDS, 34 months for those with low-risk MDS, 21 months for those with intermediate-risk MDS, 16 months for those with high-risk MDS, and 6 months for those with very-high-risk MDS.
- The severity of comorbidities affected overall survival in patients with intermediate-, high-, or very-high-risk MDS according to the IPSS-R but had no effect on survival in those with low-risk or very-low-risk MDS.
- Severity of comorbidities affected median overall survival in patients aged 65 years or older but not in those younger than 65.

Conclusions:

- Comorbidities affect survival in patients with MDS, especially those with more advanced MDS and those who are younger than 65.
- Among patients in the intermediate-, high-, and very-high-risk MDS according to the R-IPSS, patients with more severe comorbidities have significantly shorter survival than those with no comorbidities.
- Assessing comorbidities in patients with MDS might be useful for figuring out their prognosis.

ASH 1566
Clinical and Molecular Features of Young Patients with Myelodisplastic Syndromes (MDS)

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Myelodysplastic syndromes (MDS) are rarely hereditary and are uncommon in children and young adults. In younger people, MDS might have different characteristics and be associated with mutations (changes) in different genes than MDS in older adults.

A group of researchers from the Cleveland Clinic’s Taussig Cancer Center compared initial diagnosis, family history of cancer and blood diseases, abnormalities in chromosomes, and genetic mutations in patients with MDS. The study included 1,030 patients (median age 71 years) with MDS, MDS/myeloproliferative neoplasm (MPN), and secondary acute myelogenous leukemia (sAML; which develops in patients who have had MDS or another bone marrow failure disease). The researchers divided the patients into two groups by age: those aged 14–49 years and those aged 50 years or older.

Key Findings:

- Patients who were younger had higher-risk disease than older patients.
- Family history of cancer or blood diseases was similar in the two age groups.
- Deletions in the long arm of chromosome 20 were more common in older than younger patients.
- The average number of somatic (non-inherited) mutations in genes was higher (2.4 per patient) in older patients than in younger ones (1.8 per patient).
PATIENT FACTORS AND IMPACT ON MDS

• RUNX1, PHF6, and TP53 were the most frequently mutated genes in MDS in the younger population. Mutations of these genes are associated with inherited syndromes that increase the risk of blood cancers.
• Non-inherited mutations in TET2 and ASXL1 were the most common in the older group.

Conclusions:
• MDS in younger patients tends to be diagnosed at a more advanced stage.
• MDS in younger patients is less commonly affected by deletions in the long arm of chromosome 20 or by mutations in TET2.

ASH 2761
The Revised IPSS (IPSS-R) Predicts Response to Erythropoietic Stimulating Agents (ESA) in Pts with Classical IPSS Low or Intermediate-1 (Int 1)- MDS: A Joint Retrospective Study of the GFM, Düsseldorf Registry and Fism

Valeria Santini, Jennifer Schemenau, M.D., Alessandro Levis, Enrico Balleiari, M.D., Rosa Sapena, Lionel Ades, Agnès Guerin, Odile Beyne-Rauzy, M.D., Ph.D., Marie Pierre Gourin, Stéphane Cheze, Aspasia Stamatoullas, M.D., Alessandro Sanna, M.D., Daniela Gioia, Giani Cametti, M.D., Dario Ferrero, M.D., Emmanuel Raffoux, Christian Rose, M.D., Poloni Antonella, M.D., Thomas Prebet, M.D., Ph.D., Shanti Ame, M.D., Laurence Legros, M.D., Ph.D., Pierre Fenaux, M.D., Ph.D., Ulrich Germing, M.D., François Dreyfus, M.D., and Sophie Park

Doctors use the International Prognostic Scoring System (IPSS) to classify myelodysplastic syndromes (MDS) as low, intermediate 1, intermediate 2, or high risk. The category is based on the percentage of blasts, or immature cells, in the bone marrow; number and severity of chromosome changes in blasts; and whether the patient has low levels of certain blood cells. A group of experts recently created a revised IPSS (IPSS-R). The IPSS-R is based on the same factors as the IPSS but emphasizes chromosomal abnormalities more than high blast counts and includes more information than the IPSS.

The authors evaluated the value of the IPSS-R for predicting responses to erythropoietin-stimulating agent (ESA) treatment in 456 patients (45% female, 94% older than 60 years) with low-risk or intermediate-risk-1 MDS. All of the patients were treated with ESAs for at least 12 weeks in France, Germany, or Italy.

Key Findings:
• Red blood cell counts increased in 85% of patients in the very-low-risk group according to the IPSS-R, 68% of those in the low-risk group, 48% of those in the intermediate-risk group, and 31% of those in the high-risk group.
• IPSS-R category, level of the hormone erythropoietin (which instructs bone marrow stem cells to make red blood cells) in the blood, and iron levels in the blood were associated with red blood cell counts.
• IPSS-R categories predicted overall survival accurately.

Conclusions:
• The IPSS-R—and, especially, a score based on IPSS-R category and levels of erythropoietin and iron in the blood—can be used to accurately predict which patients with MDS are likely to have shorter survival with ESAs and might need other treatments.
NeW tHERAPIES

ASH 386
A Phase II Trial of Epigenetic Modulators Vorinostat in Combination with Azacitidine (azaC) in Patients with the Myelodysplastic Syndrome (MDS): Initial Results of Study 6898 of the New York Cancer Consortium


Azacitidine (Vidaza®) is a hypomethylating drug that kills unhealthy cells in the bone marrow of people with myelodysplastic syndromes (MDS). It is the first drug shown to increase survival in patients with higher-risk MDS. About half of patients respond to azacitidine. Vorinostat (Zolina®) is a histone deacetylase (HDAC) inhibitor that interferes with the genetic changes involved in MDS. About 20% of patients respond to vorinostat used as a single agent.

The purpose of this Phase II clinical trial was to assess the responses of patients to a combination of azacitidine and vorinostat at doses that have been shown to be safe and effective in a Phase I clinical trial. Of the study’s 39 patients (18 female, mean age 67 years), 12 had high-risk, 12 had intermediate-2 risk, and 8 had intermediate-1 risk MDS according to the International Prognostic Scoring System. The MDS of 7 patients was not classified. Patients were divided into three cohorts that were treated with different doses of the two drugs:

- Cohort 1: 55 mg/m2 azacitidine every day on days 1–7 and 200 mg twice daily of vorinostat on days 3–16
- Cohort 2: 75 mg/m2 azacitidine every day on days 1–7 and 300 mg twice daily of vorinostat on days 3–9
- Cohort 3: 55 mg/m2 azacitidine every day on days 1–7 and 200 mg twice daily of vorinostat on days 3–9

Key Findings:

- Of 33 patients whose response could be evaluated, 23 responded to the treatment. Response rates were 70% in Cohort 1, 73% in Cohort 2, and 67% in Cohort 3.
- On average, the response lasted 16 months. The duration of response by cohort was 10 months in Cohort 1, 23 months in Cohort 2, and 27 months in Cohort 3.
- Median overall survival was 21 months. Survival by cohort was 10 months for Cohort 1, 37 months for Cohort 2, and 19 months for Cohort 3.
- The main side effects were fatigue during the first three cycles in 8–16% of each cohort and vomiting, diarrhea, and dehydration in 8% of each cohort.

Conclusions:

- The combination of azacitidine and vorinostat is safe in patients with MDS and is well tolerated over several cycles.
- The combination of azacitidine and vorinostat seems to be more effective than azacitidine alone.
- Administration of vorinostat over 7 days (as in Cohorts 2 and 3) seems to be associated with longer-lasting response and longer overall survival.

What This Means For Patients

The hypomethylating agent azacitidine reverses gene silencing and is the first agent demonstrated to improve survival in patients with higher-risk MDS. Exposure of cells in culture to vorinostat, a histone deacetylase inhibitor (HDACI), after azacitidine further reactivates
NEW THERAPIES

silenced genes. The purpose of this study was to determine the response rate of MDS patients treated with the combination of azacitidine and vorinostat at the doses established as safe and effective in a prior Phase I clinical trial. Among 33 patients evaluable for response, 23 (70%) responded after an average of two cycles, with responses lasting an average of 16 months. Treatment was well tolerated.

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ASH 387
Phase 1 Dose-Escalation/Expansion Study of ARRY-614 in Patients with IPSS Low/Int-1 Risk Myelodysplastic Syndromes

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Two proteins, the p38 mitogen-activated protein kinase (p38) and the Tie2 receptor tyrosine kinase, suppress the formation of blood cells in the bone marrow of patients with myelodysplastic syndromes (MDS). By stopping p38 and Tie2 from inhibiting blood cell formation, a new drug, ARRY-614, appears to restore normal bone marrow function.

The goal of this Phase I clinical trial was to find the best dose of ARRY-614 for a Phase II clinical trial and to evaluate the drug’s safety and effectiveness. Study participants took capsules of ARRY-614 once or twice daily over 28-day cycles. The study included 62 patients with low-risk (16 patients) or intermediate-1 risk (46 patients) MDS according to the International Prognostic Scoring System. Median patient age was 72 years, and patients had been treated with three types of therapies, on average, for MDS in the past. All patients had had a low count of at least one blood cell type. The doses used were 200 to 1,000 mg daily (50 patients) or 100 to 200 mg twice daily (12 patients) for a median of 13 weeks.

Key Findings:

• In the 54 patients whose responses could be evaluated, blood cell counts increased in 12 (22%). Of the 31 patients treated for at least 16 weeks, 9 (29%) had higher blood cell counts.

• At least some patients responded to each of the doses tested of ARRY-614.

• The highest dose that patients could tolerate was 800 mg once daily because 2 of 6 patients had atrial fibrillation at a daily dose of 1,000 mg.

• The most common side effects related to ARRY-614 (which at least 5% of patients had) were rash, nausea, atrial fibrillation, decreased appetite, fatigue, lack of energy, and vomiting.

Conclusions:

• ARRY-614 capsules were well tolerated.

• Doses of up to 800 mg twice daily of ARRY-614 seemed to suppress the activity of p38.

• ARRY-614 was associated with higher counts of different types of blood cells.

• ARRY-614 might be a treatment option for patients with lower-risk MDS who don’t respond to standard treatments.
ASH 1576
Azacitidine and Lenalidomide Combination in Higher-Risk Myelodysplastic Syndromes—Preliminary Results of the Vilen-01 Protocol
Moshe Mittelman, M.D., Kalman Filanovsky, M.D., Hanna Rosenbaum, M.D., Pia Raanani, M.D., Andrei Braester, M.D., Neta Goldschmidt, M.D., Ilana Hellman, Ph.D., Ilya Kirgner, M.D., Chava Perri, and Howard S Oster, M.D., Ph.D.

The hypomethylating agents azacitidine (Vidaza®) and decitabine (Dacogen®) kill unhealthy cells in the bone marrow of people with myelodysplastic syndromes (MDS). These drugs are standard therapy for higher-risk MDS. Lenalidomide (Revlimid®), which slows down the growth of blood vessels that feed abnormal cells, is used to treat both lower-risk and higher-risk MDS and acute leukemia.

A group of Israeli researchers is conducting a Phase II clinical trial, known as ViLen-01, to evaluate the safety and efficacy of a combination of azacitidine and lenalidomide. The trial has three phases:

1. Six monthly cycles of azacitidine (75 mg/day on days 1–5), followed by lenalidomide (10 mg/day on days 6–21), and then a break on days 22–28.
2. Six monthly cycles of azacitidine lasting 5 days each
3. Treatment with lenalidomide only for 12 months

Key Findings:
• As of July 2013, 7 medical centers had enrolled 18 patients with higher-risk MDS or lower-risk MDS who need regular red blood cell transplants, are resistant to treatment with erythropoietin, and have chromosomal abnormalities.
• Eight patients (44%) had a complete response, meaning that they had no signs of MDS, after finishing the first phase.
• Five other patients had improved red cell counts and stopped needing regular blood transfusions.
• One patient’s platelet counts increased.

Conclusions:
• These results need to be confirmed in randomized clinical trials.
• These preliminary data in a small group of patients with higher-risk MDS, who would normally have a poor prognosis, show that treatment with both azacitidine and lenalidomide appears to have a high response rate and be reasonably safe.

ASH 2752
A Randomized Phase II Study of Sapacitabine in MDS Refractory to Hypomethylating Agents
Guillermo Garcia-Manero, M.D., Selina M Luger, M.D., Stuart Goldberg, M.D., Jessica K. Altman, M.D., Martha Arellano, M.D., Meir Wetzler, M.D., Karen Seiter, M.D., Judy Chiao, M.D., and Hagop M Kantarjian, M.D.

Sapacitabine is an experimental drug that damages DNA in cancer cells, which stops them from growing and reproducing.

The purpose of this multicenter, randomized, Phase II clinical trial was to evaluate three dosing schedules of sapacitabine. The study included patients who were at least 60 years old with myelodysplastic syndromes (MDS) that did not respond to the hypomethylating agents azacitidine (Vidaza®) and decitabine (Dacogen®). All patients had intermediate-2 or higher-risk MDS according to the International Prognostic Scoring System. The main study endpoint was survival at 1 year.
NEW THERAPIES

The study’s 63 participants (median age 73 years) were randomly assigned to treatment with sapacitabine in one of the following groups:

1. 200 mg twice a day for 7 days every 4 weeks
2. 300 mg once a day for 7 days
3. 100 mg once a day for 5 days per week over 2 weeks

Patients stayed on the treatment until they developed unacceptable side effects or their MDS progressed.

Key Findings:

- As of the writing of this abstract, 9 patients had responded. Response rates were 19% in the 200 mg group, 10% in the 300 mg group, and 14% in the 100 mg group.
- At 1 year, 38% of patients in the 200 mg group, 24% of those in the 300 mg group, and 33% of those in the 100 mg group were still alive.
- MDS did not progress for more than 16 weeks in 21 patients.
- Common side effects included fatigue, nausea, diarrhea, and constipation. Most side effects were mild to moderate.

Conclusions:

- Sapacitabine appears to be safe and active at all three dosing schedules tested.
- The median survival rate in all three groups appears to be higher than the median survival rate of patients who have stopped responding to hypomethylating agents.
- The 200 mg dosing regimen had the best 1-year survival and response rates.
Aplastic Anemia, MDS, and PNH 2014 Regional Conferences
DIAGNOSIS, TREATMENT, AND MANAGING THE NEW NORMAL

Meeting You Where You Are
LOS ANGELES, CA | APRIL 5
PHILADELPHIA, PA | MAY 17
DETROIT, MI | JULY 26
LOUISVILLE, KY | SEPTEMBER 20
NEW ORLEANS, LA | OCTOBER 11
MIAMI, FL | NOVEMBER 8

Follow Your Disease Track

Agenda (See Website for More Detailed Agenda)

7:30 - 8:30 AM Check-in and Breakfast
8:30 - 8:50 AM Conference Welcome
9:00 - 10:30 AM Session A: Your Life Changing Phase of Diagnosis
10:30 - 10:45 AM Break
10:45 - 12:00 PM Session B: Your Life Changing Phase of Treatment
12:00 - 1:45 PM Lunch and AA&MDSIF Program
2:00 - 3:00 PM Session C: The Life Long Phase of Living with a Chronic Disease - Managing Your New Normal
3:00 - 3:15 PM Break
3:15 - 5:00 PM Session D: Finding Strength in Numbers - Peer Support Forums

Named Research Funds Help AA&MDSIF Provide Answers, Support, and Hope

The Aplastic Anemia & MDS International Foundation (AA&MDSIF) provides patients and their families with answers, support and hope. While each of our programs and services touch on all three, our research grants inspire the most hope. AA&MDSIF promotes international collaboration of medical researchers who are working together to find effective treatments and cures for aplastic anemia, myelodysplastic syndromes (MDS) and paroxysmal nocturnal hemoglobinuria (PNH), and related bone marrow failure diseases. For more than twenty years, the AA&MDSIF has provided financial support for research that leads to new insights into the causes of bone marrow failure disease and the development of new therapeutic approaches. To date, AA&MDSIF has awarded more than $3.5 million in research grants to 61 researchers to advance the study of bone marrow failure diseases.

Research programs include:

• Named Research Funds, which support scientific/medical research projects with two-year grants of $30,000 per year for either a new or established investigator to test new ideas and explore other research leads in aplastic anemia, MDS, PNH, and other bone marrow failure diseases. Named Research Funds can be created in tribute to a loved one.

• The Research is Hope Fund, which supports Aplastic Anemia, MDS, PNH, and other bone marrow failure disease research. Contributions from families and individuals are combined to fund two-year research grants of $30,000 per year.

Many options are available to you to create a Named Research Fund: pledged over two or three years, established with a gift of stock or appreciated securities, or created through a bequest or estate gift*. To learn more, please contact the AA&MDSIF Development Office at 301-279-7202 or www.aamds.org.

AA&MDSIF has earned the “exceptional” designation from Charity Navigator for achieving at least nine consecutive 4-star evaluations. AA&MDSIF is among only 1% of charities to receive this designation. As a tax-exempt 501(c)(3) charitable organization, gifts to AA&MDSIF are tax-deductible to the fullest extent of the law. Always rely on your attorney or other qualified advisors to guide you through your estate planning process.
IN PRINT

Fact Sheets
- AA&MDSIF Social Media
- Bone Marrow and Stem Cell Transplantation
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- Communities of Hope
- Financial Resources
- How to Evaluate Health Information on the Internet
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To order a patient packet, call (301) 279-7202 x116, or order online at www.AAMDS.org/Info.

* Available in Spanish  ** Available in Spanish and French

Patient Guides
- Your Guide to Understanding Aplastic Anemia**
- Your Guide to Understanding MDS**
- Your Guide to Understanding PNH
- Living Well With Bone Marrow Failure Disease*
- Standing Up for Your Health
- What to Expect From Treatment: A Guide to Understanding FDA-Approved Drug Therapies for Myelodysplastic Syndromes (MDS)

IN PERSON

Phone Support for Personal Attention
Please contact our Patient Educator at (800) 747-2820, option 1, or by email at info@aamds.org, for answers on a wide range of questions, including information on treatment options, clinical trials, financial resources, and more.

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The Support Connection is a national network of trained volunteers, including patients, caregivers, and family members who offer information, personal experience, coping strategies, problem solving skills, and informational resources to people just like themselves.

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To connect with a Support Connection volunteer, call (800) 747-2820, option 1 and speak with our Patient Educator, who will match you with one of our volunteers. You can also email info@aamds.org.

ONLINE

Aplastic Anemia & MDS International Foundation
Online Learning Center
www.AAMDS.org/Learn

The Online Learning Center has information for patients and families on treatment options and issues, and living well – topics including fatigue, nutrition, emotional coping, and caregiving. Learn at your own pace and in the style that suits you best!

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