HIGHLIGHTS FROM THE

2010 American Society of Hematology Annual Meeting

A Summary of Abstracts for Patients with Myelodysplastic Syndromes (MDS) and their Caregivers

Aplastic Anemia & MDS INTERNATIONAL FOUNDATION
The Aplastic Anemia & MDS International Foundation, Inc. (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 abstracts presented at the 52nd Annual Meeting of the American Society of Hematology (ASH) in December 2010. 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.
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 52nd Annual Meeting of the American Society of Hematology (ASH) Annual Meeting in December 2010.

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”—i.e., 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. By reviewing the information presented in the booklet, we hope you will:

◆ Learn how ongoing research on MDS may affect the diagnosis, treatment and prognosis of patients in the near term as well as the more distant future
◆ Understand how researchers are approaching the most promising areas of MDS therapy
◆ Learn about the importance of clinical trials in identifying novel therapies for MDS
◆ Know the most important issues about MDS which you may want or need to understand and to ask your health care providers about as part of your ongoing treatment

Please note that the research results discussed at the ASH Annual Meeting often involve experimental drugs that are not approved for general use by the Food and Drug Administration (FDA) 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 healthcare related to MDS.

If you are interested in participating in research studies such as those discussed in this booklet, we encourage you to speak to 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.

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The abstracts summarized in this booklet may be viewed on the American Society of Hematology Web site at http://ash.confex.com/ash/2010/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.
Research Update on MDS Diagnosis and Treatment
Now Available on the Online Learning Center (OLC):
www.AAMDS.org/Learn

In January, 2011, AA&MDSIF produced two webinars on the latest MDS diagnosis and treatment research as reported at the 52nd Annual Meeting of the American Society of Hematology (ASH). These webinar programs are now posted on the Online Learning Center and are available for viewing. In addition to the audio presentation and accompanying slides, a synchronized transcript of each presentation is also available. These special education programs cover the following:

- New Strategies for Diagnosing and Classifying MDS: Can This Change Treatment Outcomes?
- Emerging Treatments and New Protocols for MDS Therapy

To view these and other archived webinars, visit our Online Learning Center and choose Archived Webinars.

The Online Learning Center (OLC) is your comprehensive information source on all aspects of bone marrow failure diseases. Created expressly for patients and their families, caregivers and advocates, all OLC content is free and available to anyone with access to a computer and a high-speed Internet connection. In addition to archived webinars, here is what else you will find on the OLC:

- Live webinars conducted by the nation’s leading experts
- Innovative interactive learning modules
- Interviews with experts on aplastic anemia, MDS and PNH
- Webcasts of pre-recorded presentations

More than 30 programs are now available, and more being added all the time. Here are just a few:

- Beating Fatigue
- Bone Marrow Transplantation for MDS
- Complementary and Alternative Therapies: Myths, Realities and Opportunities
- Fundamentals of Hematology and Bone Marrow Failure Diseases
- Growth Factors: Examining the Risks and Benefits
- Iron Overload: Prevention, Diagnosis and Treatment
- MDS: Current Thinking on the Disease, Diagnosis and Treatment

AA&MDSIF Online Learning Center: www.AAMDS.org/Learn

Don’t have Internet access? Go to your public library or local community center, or ask a friend or family member to help you with next time you visit.
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Prognostic Models

About one third of the time, myelodysplastic syndrome (MDS) progresses to acute myelogenous leukemia (AML). AML is a blood cell cancer. Studies have identified some of the genes that seem to play a role in the development of MDS and its progression to AML.

Researchers have developed several prognostic scoring systems. These systems are based on information on the genetics of patients with MDS, their blood cell counts, bone marrow blasts (abnormal, immature cells), and other data. Doctors use these scoring systems to decide what type of MDS the patient has. They also use the scores to predict the likelihood that the disease will progress to AML and choose the best treatments.

Many studies are ongoing of genes and other information that might help predict the course of a patient’s MDS. Experts hope that the results of these studies will increase understanding of MDS. The study results could also lead to the development of new treatments and help doctors choose the right treatments for each patient.

440 Prognostic Impact of JAK2V617F Mutation in MDS: a Matched Case Control Study


A small percentage of patients with MDS have a mutation, or change, in the JAK2V617F gene. The French Intergroup of Myeloproliferative Disorders collected data on 161 patients from 19 medical centers in France. These patients had MDS and the JAK2V617F gene mutation. Researchers compared these patients to patients who had MDS who did not have the mutation. Patients with the JAK2V617F gene mutation tended to have higher white blood cell (WBC), absolute neutrophil (a type of white blood cell), and platelet counts. They also had a smaller proportion of marrow blasts (abnormal, immature cells). Their MDS was less likely to progress to AML and they tended to live longer than patients without the mutation.

The next step in this research is to confirm the results in a prospective study.

444 Validation of the Newly Proposed MD Anderson Prognostic Risk Model for Patients with Myelodysplastic Syndromes

Maria Corrales-Yepez, Jeffrey E. Lancet, M.D., Alan F. List, M.D., Mohamed A. Kharfan-Dabaja, M.D., Teresa Field, M.D., Ph.D., Eric Padron, M.D., and Rami S. Komrokji, M.D.

The International Prognostic Scoring System (IPSS) is a tool that doctors use to evaluate the likelihood that a patient’s MDS will progress to AML. They also use this information to choose the right treatment for the patient. The IPSS has several limitations. For example, it does not take into account the patient’s age, overall health, or level of cytopenia (shortage of blood cells).

In this study, researchers at the H. Lee Moffitt Cancer Center in Tampa, Florida, evaluated the M.D. Anderson Scoring System (MDAS). This tool does not have many of the IPSS’s limitations. The researchers collected data on 844 patients with MDS from the Moffitt Cancer Center data and patient charts. They calculated the MDAS score for each patient and used this information to classify the patients’ disease into four categories.

Median survival times were longest for patients with low-risk MDS and shortest for those with high-risk MDS. MDS progressed to AML in many fewer cases of low-risk MDS than high-risk MDS.
The authors concluded that the MDAS risk model predicted overall survival in patients with MDS and their risk of progressing to AML. The MDAS is a useful addition to the IPSS. However, a prospective study should further assess the MDAS’s usefulness for making treatment decisions.

**605 Comorbidities and Overall Survival in Myelodysplastic Syndromes (MDS): Development of a Prognostic Model Incorporating IPSS and Age with ACE-27 Comorbidity Index**

Kiran Naqvi, M.D., Maria E Suarez-Almazor, M.D., Ph.D., Sagar Sardesai, M.D., Jeong Oh, M.D., M.P.H., Carlos Vigil, M.D., Sherry Pierce, R.N., B.S., Xiudong Lei, Ph.D., Jianqin Shan, Ph.D., Hagop M. Kantarjian, M.D., and Guillermo Garcia-Manero, M.D.

People with MDS often have comorbidities, or diseases or conditions in addition to their MDS. The M.D. Anderson Cancer Center leukemia group in Houston, Texas, studied the effects of comorbidities on the survival of patients with MDS. They used the results to develop a prognostic model, or tool to predict the course of these patients’ MDS.

Risk scores in this model were based on patient age and score on the IPSS and Adult Comorbidity Evaluation-27 (ACE-27). Doctors use the IPSS to assess the likelihood that a patient’s MDS will progress to leukemia. The ACE-27 is a tool to measure a patient’s comorbidities. Researchers grouped the risk scores from the new model into three categories: low, intermediate, and high risk.

Patients with lower-risk MDS according to the new model tended to survive much longer than those in the high-risk group. The results show that having more severe comorbidities affects survival in patients with MDS. This new tool could help predict survival in patients with MDS based on their comorbidities.

**606 Comorbidities Indexes in Patients Treated with 5-Azacitidine Are a Useful and Easily Applicable Tool to Refine Prognostic Evaluation**

Alessandro Sanna, M.D., Laura Cannella, M.D., Antonella Gozzini, M.D., Massimo Breccia, M.D., Francesca Sassolini, M.D., Alberto Bosi, M.D., Giuliana Alimena, M.D., and Valeria Santini, M.D.

People with MDS tend to be older and many of these patients have comorbidities, or diseases or conditions in addition to MDS. An Italian group studied the effect of comorbidities and the number of comorbidities on elderly patients’ responses to Vidaza® (azacitidine), an MDS treatment.

The researchers analyzed data on 59 elderly patients (average age 69) with MDS who had been treated with azacitidine. The results showed that having comorbidities does not increase the risk that an older patient with MDS will have serious side effects due to azacitidine. However, patients with more or more serious comorbidities tended to survive for less time than those without comorbidities and those with less serious comorbidities.

The authors recommend that doctors evaluate comorbidities in their patients with MDS. This will give doctors a better sense of how these patients are likely to do.

**1 Impaired Hydroxylation of 5-Methylcytosine in TET2 Mutated Patients with Myeloid Malignancies**


Mutations, or changes, in the TET2 gene are common in many bone marrow cancers. The researchers showed that the TET2 gene mutation plays a role in the inherited changes to the genes of people with bone marrow cancer.
Gene Discoveries

Researchers have identified some of the genes that seem to play a role in the development of MDS and its progression to AML. Different genetic mutations or lesions (injuries to genes) might also explain why people with MDS have such different symptoms and survival times. Experts hope that the results of these studies will increase understanding of MDS, lead to the development of new treatments, and help doctors choose the right treatments for each patient.

295 Whole Exome Analysis of Myelodysplastic Syndromes Using Next-Generation Resequencing Technology

Kenichi Yoshida, M.D., Masashi Sanada, M.D., Yasunobu Nagata, M.D., Ryoichiro Kawahata, Ph.D., Motohiro Kato, M.D., Ph.D., Aiko Matsubara, Ph.D., Jyuniko Takita, M.D., Ph.D., Hiroya Morii, M.D., Ph.D., Ken Ishiyama, M.D., Ph.D., Takayuki Ishikawa, M.D., Ph.D., Shuichi Miyawaki, M.D., Naoshi Obara, M.D., Ph.D., Shigeru Chiba, M.D., Ph.D., and Seishi Ogawa, M.D., Ph.D.

A Japanese group of researchers used a new technology (called target-capture resequencing technology) to study the genes of 10 patients with MDS. Their goal was to identify all of the lesions, or injuries, that occur in the genes of patients with MDS.

The researchers compared the genetic lesions in patients with MDS to the results from healthy patients without MDS.

The results suggest that the new technology is a powerful method for identifying new genetic mutations, or changes, that play a role in the development of MDS.

299 Detection of Novel Mutations In MDS/AML by Whole Genome Sequencing


Researchers from Washington University in St. Louis, Missouri, sequenced the whole genome from normal skin and bone marrow tumor samples from a patient whose MDS had progressed to AML. Whole-genome sequencing is a laboratory process that maps out the person’s entire DNA sequence.

The researchers identified 10 genetic mutations, or changes, that were present in both the MDS and AML samples. They also found 12 mutations only in the AML samples. The 12 mutations that the researchers found only in the AML samples might play an important role in the progression of MDS to AML.

300 Point Mutations in Myelodysplastic Syndromes Are Associated with Clinical Features and Are Independent Predictors of Overall Survival

Rafael Bejar, M.D., Ph.D., Kristen Stevenson, Omar Abdel-Wahab, M.D., McConkey Marie, Ph.D., Katherine Lin, James Randall McAuley, Kevin Cheung, M.D., Naomi Galili, Ph.D., Guillermo Garcia-Manero, M.D., Hagop M. Kantarjian, M.D., Azra Raza, M.D., Ross Levine, M.D., Donna Neuberg, Sc.D., and Benjamin L. Ebert, M.D., D.Phil.

The researchers examined samples from 438 patients with MDS to identify mutations, or changes, in genes that are associated with cancer development.
They identified mutations in more than 15 genes in at least half of the samples. The researchers also identified mutations in certain genes that were associated with certain MDS symptoms. These symptoms included thrombocytopenia, or a shortage of platelets in the bloodstream, and high blast (abnormal, immature cells) counts. In addition, the researchers found mutations in three genes (RUNX1, TP53, and ASXL1) in more than one-quarter of samples that appear to be associated with shorter survival.

607 Identification of Oncogenic EZH2 Mutations In Myelodysplastic Syndromes and Related Myeloid Malignancies

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The researchers identified mutations, or alterations, in a group of genes known as the polycomb family. This new class of genetic lesions might play a role in the development of leukemia.

608 Recurrent DNMT3A Mutations in Patients with Myelodysplastic Syndrome

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Researchers at Washington University in St. Louis, Missouri, have previously identified mutations, or changes, in the DNMT3A gene in 62 of 281 patients with AML. Patients with these mutations tended to survive less long than patients without the mutations.

In the study described in this abstract, the researchers found DNMT3A gene mutations in 12 of 150 samples from patients MDS. These 12 patients had similar symptoms to the 138 patients who did not have the mutations. But patients with the mutations had a significantly worse survival times than patients without the mutation. Patients with the mutations also tended to have shorter event-free survival (or survival time without relapse) than patients without the mutations.

Researchers will need to examine samples from more patients to better understand the effect of DNMT3A mutations on MDS outcomes.

851 High-Throughput Mutational Profiling In AML: Mutational Analysis of the ECOG E1900 Trial

Jay P. Patel, Omar Abdel-Wahab, Mithat Gonen, Maria E. Figueroa, M.D., Hugo F. Fernandes, M.D., Zhuoxin Sun, Ph.D., Janis Racevskis, Pieter Van Vlierberge, Igor Dolgalev, Janice Cheng, Agnes Viale, Nicholas Socci, Adriana Heguy, Rhett Ketterling, Robert E. Gallagher, M.D., Mark R. Litzow, M.D., Jacob M. Rowe, Adolfo Ferrando, M.D., Ph.D., Elisabeth Paiset, Ph.D., Martin S. Tallman, M.D., Ari M. Melnick, and Ross Levine, M.D.

The authors describe several genetic mutations that were present in 398 patients who had AML and had not yet undergone leukemia treatment. Patients with some of these mutations were less likely to respond to chemotherapy, and other mutations were associated with shorter or longer survival.

These findings provide insight into the development of AML. Eventually, doctors will be able to test patients for mutations like the ones these authors studied. They will be able to use the findings to predict how their patients’ disease is likely to do in the future and choose the best treatment for each patient.
Molecular Predictors of Azacitidine Response

The current standard treatment for high-risk MDS (MDS that is likely to progress to AML) is Vidaza® (azacitidine). Azacitidine treatment is also an option for patients with low-risk MDS. This treatment can increase survival in some patients. Experts believe that azacitidine works by helping bone marrow cells grow and reproduce normally.

Researchers are currently studying how azacitidine works and trying to identify the patients who are most likely to benefit from this drug.

439 Presence of TET2 Mutation Predicts a Higher Response Rate to Azacitidine in MDS and AML Post-MDS

Raphael Itzykson, Olivier Kosmider, Thomas Cluzeau, Veronique De Mas, Francois Dreyfus, Bruno Quesnel, M.D., Ph.D., Odile Beyne-Rauzy, Norbert Vey, M.D., Veronique Gelsi-Boyer, Sophie Raynaud, Claude Preudhomme, Lionel Ades, M.D., Pierre Fenaux, M.D., Ph.D., and Michaela Fontenay

French researchers studied the genes of 103 patients whose MDS had progressed to AML. All of these patients had been treated with azacitidine. The study’s goal was to find mutations, or alterations, in genes that doctors could use to predict whether a patient’s disease would respond to azacitidine treatment.

The researchers found mutations in the TET2 gene in 17 patients. Patients with TET2 mutations were more likely to respond to azacitidine. However, survival times were no different in patients with and without the TET2 mutations.

The researchers concluded that testing for the TET2 mutations, in addition to other routine tests, might help doctors predict how long patients with MDS are likely to survive. In addition, TET2 mutations might play a role in how sensitive a patient’s MDS is to azacitidine.

125 Polycomb Complex Group Gene Mutations and Their Prognostic Relevance in 5-Azacitidine Treated Myelodysplastic Syndrome Patients


The goal of this study was to understand the role of mutations, or changes, in the ASXL1 and EZH2 genes in MDS. The study included 63 patients with MDS who had received Vidaza® (azacitidine) treatment.

Researchers from Kings College Hospital in London, United Kingdom, found mutations in the ASXL1 gene in patients with more normal cytogenetics (the study of chromosomes, or the part of the cell containing genetic information) but not in patients with abnormal cytogenetics. Several patients with normal cytogenetics and several patients with abnormal cytogenetics had a mutation in the EZH2 gene. Almost all patients with the EZH2 mutation responded to azacitidine.

The authors concluded that mutations in the ASXL1 and EZH2 genes are common in patients with MDS who have better cytogenetics. Patients with these mutations tend to survive longer and have longer progression-free survival after azacitidine therapy.
Familial MDS

**LBA-3 GATA2 is a New Predisposition Gene for Familial Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML)**

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In some families, several members have mutations, or changes, in the **RUNX1** and **CEBPA** genes that make them more susceptible to developing MDS and AML.

An international group of researchers identified mutations in another gene, known as **GATA2**, in some families that are associated with an increased risk of MDS and AML. In these families, people with MDS or AML have the **GATA2** mutation and people without the disease do not have the mutation. Family members with the **GATA2** mutation also do not have the conditions that patients often have before developing MDS or leukemia. These conditions include thrombocytopenia (a shortage of platelets in the bloodstream) and eosinophilia (large numbers of white blood cells that play a role in allergic reactions). In most patients in these families, the disease develops quickly, often “out of the blue.”

These findings could have implications for genetic testing and the development of treatments. The results show that patients who have the **GATA2** mutations need aggressive treatment because their MDS is likely to progress quickly. This discovery could also provide new tools for understanding the role of **GATA2** in the development of leukemia.

**Diagnosis Changing at Specialized Centers**

**1870 Discrepancy in Diagnosis of Myelodysplastic Syndrome (MDS) Between Referral and Tertiary Care Centers: Experience at MD Anderson Cancer Center (MDACC)**

Kiran Naqvi, M.D., Guillermo Garcia-Manero, M.D., Carlos E. Bueso-Ramos, Sherry Pierce, R.N., B.S., Tapan Kadia, M.D., Gautam Borthakur, M.D., Zeev Estrov, M.D., Farhad Ravandi, M.D., Stefan Faderl, M.D., Hagop M. Kantarjian, M.D., and Elias Jabbour, M.D.

The M.D. Anderson Cancer Center leukemia group in Houston, Texas, studied differences in the final diagnosis of patients at a specialized care center and the center that initially referred the patient to the specialized center. The study included 915 patients who came to the M.D. Anderson Cancer Center between September 2005 and December 2009. These patients had received a diagnosis of MDS from their original medical center. The authors reviewed each patient’s medical record, including the results of testing on the patient’s bone marrow.

The authors found differences in diagnoses from the original medical center and the M.D. Anderson Cancer Center in 150 patients. For example, 40% of these patients had a diagnosis of refractory anemia (RA), refractory anemia with ringed sideroblasts (RARS), or refractory cytopenia with multilineage dysplasia (RCMD) from their original center. However, the M.D. Anderson experts gave 77% of these patients a diagnosis of refractory anemia with excess blasts (RAEB).
PART A: New Strategies for Diagnosing and Classifying MDS

Many patients who received different diagnoses from the two centers had RAEB with transformation. They also had a higher-risk status according to the IPSS (a scoring system that identifies how quickly a patient’s MDS is progressing) than patients who received the same diagnosis at both centers.

The authors found no survival differences between patients who did and did not receive different diagnoses. However, receiving a different diagnosis at M.D. Anderson did have an effect on treatment recommendations, clinical trial eligibility, and disease predictions for some patients.

The results show how difficult MDS is to diagnose. In addition, a patient’s MDS type has only a limited effect on how quickly the disease will progress.

Platelet Count and Survival

Platelets are a type of blood cell that plays a key role in blood clotting. People with MDS often have low platelet counts, a condition known as thrombocytopenia. Researchers are currently studying the impact of platelets and thrombocytopenia on survival in patients with MDS.

2905 Associations between Platelet Count and Survival and Disease Progression in Thrombocytopenic Patients with Myelodysplastic Syndromes

Mellissa Yong, Ph.D., M.P.H., Carrie Kuehn, M.A., M.P.H., Michael Kelsh, Ph.D., M.P.H., M.A., Meghan Wagner, M.P.H., Allen Yang, M.D., Ph.D., and Janet Franklin, M.D., M.P.H.

The authors evaluated the effects of platelet counts on survival in patients with MDS and the progression of MDS to AML. The study included 303 patients with MDS and thrombocytopenia.

Survival time was lowest among patients with lower platelet counts and highest among patients with higher platelet counts. Patients with lower platelet counts were more likely to die than patients with higher platelet counts. However, the time that MDS took to progress to AML did not differ by platelet count.

The authors concluded that platelet counts in patients with MDS and thrombocytopenia might be relevant to their chances of survival. However, platelet count does not seem to have any effect on the risk that the patient’s MDS will progress to AML.

4021 Thrombocytopenia Predicts for Poor Survival in Patients with Lower Risk Myelodysplastic Syndromes (MDS)

Raymond Cruz, M.D., Naomi Galili, Ph.D., Ghulam Sajjad Khan, M.D., and Azra Raza, M.D.

The goal of this study was to learn whether thrombocytopenia (a shortage of platelets in the bloodstream) in patients with lower-risk MDS affects survival. The study included 1,402 patients who had received an MDS diagnosis between 1987 and 2010.

More patients with high-risk MDS, according to the IPSS (a scoring system that identifies how quickly a patient’s MDS will progress), had thrombocytopenia than patients with intermediate-1 or low-risk MDS. Patients with lower-risk MDS and without thrombocytopenia tended to survive longer than patients with thrombocytopenia. As platelet counts dropped, survival time tended to decline. Patients with low-risk MDS and very low platelet counts had similar survival rates to patients with higher-risk MDS.

The authors concluded that thrombocytopenia increases the risk of poor survival in patients with lower-risk MDS. This information could help physicians choose the best treatment for patients with low-risk MDS.
Low Albumin and Survival

4001 Hypoalbuminemia Is an Independent Prognostic Factor in Myelodysplastic Syndromes

Maria Corrales-Yepez, M.D., Mohamed A. Kharfan-Dabaja, M.D., Jeffrey Lancet, M.D., Alan F. List, M.D., Eric Padron, M.D., Dana Rollison, Ph.D., P.K. Epling-Burnette, Pharm.D., Ph.D., Ling Zhang, M.D., Teresa Field, M.D., Javier Pinilla-Ibarz, M.D., and Rami S. Komrokji, M.D.

Albumin is a type of protein, or major component of cells in the body. The authors studied the possible usefulness of studying albumin levels in the blood for predicting the course of MDS. They analyzed information from the charts of 844 patients with MDS who visited the Moffitt Cancer Center in Tampa, Florida, between January 2001 and December 2009.

The median survival time was highest in patients with higher albumin levels. MDS progressed to AML most often in patients with lower albumin levels than in patients with higher albumin levels. In patients with a given risk level of disease according to the IPSS (a scoring system that identifies how quickly a patient’s MDS will progress), overall survival was longest in those with higher albumin levels.

The authors concluded that serum albumin levels can be used to predict how quickly patients’ MDS will progress to AML and how long they are likely to survive. Albumin levels might also provide clues about patients’ general health, other diseases and conditions, and ability to carry out daily activities.

Cardiac Iron Overload

2906 Highly Transfused MDS Patients Often Have Cardiac Iron Overload, as Shown by MRI Assessment

Laurent Pascal, Odile Beyne Rauzy, Sabine Brechignac, Dominique Vassilieff, Olivier Ernst, Céline Berthon, Emmanuel Gyan, Francois Dreyfus, Pierre Fenaux, M.D., Ph.D., and Christian Rose

The goal of this study was to evaluate the impact of iron overload on cardiac disease in patients with MDS who received regular blood transfusions. The study included 73 French patients, including 54 on iron chelation therapy to remove extra iron from their bodies.

The study showed moderate iron overload in the hearts of 19% of patients who had received regular blood transfusions and severe iron overload in 4%. Patients who had received more red blood cells in their transfusions had higher iron overload.

In conclusion, iron overload seems to be only one of several factors that cause heart disease in patients with MDS.
Combination Azacitidine and Histone Deacetylase (HDAC) Inhibitor Therapy

The current standard treatment for high-risk MDS is Vidaza® (azacitidine). This treatment can increase survival. However, up to half of all patients with MDS do not benefit from azacitidine therapy. Furthermore, response to treatment typically lasts less than 2 years.

These abstracts describe the results from two Phase II clinical trials that compared the effects of azacitidine alone to the effects of a combination of azacitidine and a histone deacetylase (HDAC) inhibitor. HDAC inhibitors interfere with the genetic changes that play a role in MDS.

In the US Leukemia Intergroup’s E1905 study, researchers randomly assigned 150 patients with MDS, AML, or chronic myelomonocytic leukemia (CMML) to treatment with 10 days in each cycle of azacitidine alone or 10 days of azacitidine plus entinostat, an HDAC inhibitor. The second Phase II clinical trial compared azacitidine alone with a combination of azacitidine and the HDAC inhibitor vorinostat.

601 Prolonged Administration of Azacitidine with or without Entinostat Increases Rate of Hematologic Normalization for Myelodysplastic Syndrome and Acute Myeloid Leukemia with Myelodysplasia-Related Changes: Results of the US Leukemia Intergroup Trial E1905

Thomas Prebet, M.D., Ph.D., Steven D. Gore, M.D., Zhuoxin Sun, Ph.D., Mark Juckett, M.D., Lisa Malick, Mitchell R Smith, M.D., Ph.D., Elisabeth Paietta, Ph.D., Magdalena Czader, M.D., Janice Gabrilove, M.D., Harry P Erba, DM, Ph.D., Martin S. Tallman, M.D., and Steven D. Gore, M.D.

The researchers analyzed data from the US Leukemia Intergroup’s E1905 study. The analysis found no significant difference in the proportions of patients who developed normal blood cell counts in response to azacitidine and those who received azacitidine and entinostat. More patients who received combination therapy had thrombocytopenia (a shortage of platelets in the bloodstream) and fatigue.

The authors concluded that adding entinostat to azacitidine did not improve patients’ responses to azacitidine significantly.

4013 A 10 Day Schedule of Azacitidine Induces More Complete Cytogenetic Remissions than the Standard Schedule in Myelodysplasia and Acute Myeloid Leukemia with Myelodysplasia-Related Changes: Results of the E1905 US Leukemia Intergroup Study

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The authors analyzed data from the US Leukemia Intergroup’s E1905 study. Their goal was to measure the effects of the different treatments on abnormal chromosomes. Chromosomes are the part of the cell that contains genetic information.

The researchers found usable information on 65 patients from the study. Of these 65 patients, 9 experienced complete cytogenetic response, meaning that doctors could not detect any abnormal chromosomes after treatment.

The results showed no difference in response rates between patients on azacitidine alone and those on azacitidine and HDAC inhibitors.
604 Phase II Study of 5-Azacitidine and Vorinostat in Patients (pts) with Newly Diagnosed Myelodysplastic Syndrome (MDS) or Acute Myelogenous Leukemia (AML) not Eligible for Clinical Trials Because Poor Performance or Presence of Other comorbidities

Guillermo Garcia-Manero, M.D., Elihu H. Estey, M.D., Elias Jabbour, M.D., Tapan Kadia, M.D., Zeev Estrov, M.D., Jorge Cortes, M.D., Patricia Ann Boone, and Hagop M. Kantarjian, M.D.

Most MDS and AML clinical trials exclude patients with poor kidney or liver function or who have other diseases, including other types of cancer or HIV infection. Without treatment, these patients often survive less than 60 days.

This Phase II clinical trial tested Vidaza® (azacitidine) in combination with ZOLINZA® (vorinostat), an HDAC inhibitor. The study included patients with MDS or AML who had poor kidney or liver function, HIV, another type of cancer, or other diseases.

The authors’ analysis included 18 patients. Most patients tolerated the treatment well, although one patient developed severe nausea and vomiting. At the time of this analysis, 11 patients had survived for 60 days and 8 had survived even longer. Three patients had achieved a complete response, or the disappearance of all signs of cancer. Another four had a complete marrow response (meaning that their bone marrow had less than 5% abnormal blasts, or abnormal, immature cells).

The authors concluded that the combination of azacitidine and vorinostat seems as safe and effective in patients with MDS or AML and other diseases and conditions as in the patients that clinical trials usually include. Patients with MDS and other diseases and conditions should receive treatment. The results raise questions about the eligibility criteria for Phase I and II clinical trials.

Oral Azacitidine

603 Evaluation of Oral Azacitidine Using Extended Treatment Schedules: A Phase I Study

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The Food and Drug Administration (FDA) has approved the parenteral administration (through the vein or by injection) of Vidaza® (azacitidine) for 7 consecutive days every 28 days for patients with MDS. But giving azacitidine every day might make the drug more effective. In addition, an oral version (that patients could take by mouth) of the drug would be convenient and make it possible to administer lower doses over more days.

In this Phase I clinical trial, the authors administered oral azacitidine once or twice every day to patients with MDS, AML, or CMML for 14 or 21 days. At the time they wrote this abstract, the authors had evaluated data on 25 patients.

Two patients in the 14-day treatment group experienced a side effect (nausea and vomiting) that required physicians to reduce their dose of the drug. No patients in the 21-day treatment group experienced a side effect that required a change in dose. More patients in the 21-day group experienced neutropenia, or a shortage of neutrophils—a type of white blood cell—with fever than in the 14-day group. In both the 14- and 21-day treatment groups, some patients experienced complete remission (no evidence of cancer), marrow complete remission (almost no abnormal cells in the bone marrow), or higher blood cell counts.
The authors concluded that patients generally tolerate 14- and 21-day oral dosing of azacitidine well and the responses of their disease to the therapy were promising. The authors were still assessing the results of the twice-daily dosing.

Azacitidine Dosing

Vidaza® (azacitidine) was the first FDA-approved drug for treating all types of MDS. The drug can increase blood cell counts, reduce the need for red blood cell transfusions, and reduce the number of blasts (abnormal cells) in the bone marrow. The recommended starting dose of Vidaza is 75 mg/m² for 7 days. This treatment cycle should be repeated every 4 weeks. However, the dose can be increased to 100 mg/m² after two cycles if the disease does not respond to treatment.

Researchers have compared the effectiveness of different doses or dosing schedules of azacitidine.

1853 Effectiveness of Various Dosage Regimens of Azacitidine in Patients with Myelodysplastic Syndromes: Safety and Efficacy Final Data from the Spanish Azacitidine Compassionate Use Registry

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The Spanish government’s regulatory agency approved azacitidine for MDS treatment in Spain in 2009. Before 2009, the drug was available for clinical trials or compassionate use. The term “compassionate use” refers to a treatment’s use outside of a clinical trial before the treatment has received approval from a country’s regulatory agency.

A Spanish research group analyzed data on the compassionate use of azacitidine in 181 patients with MDS in Spain before the drug received marketing approval. These patients had received azacitidine on days 1–5, days 1–5 and 8–9, or days 1–7 of a 28-day cycle.

Most patients responded to the drug after treatment on days 1–5 and 8–9. About half of all patients treated on days 1–7 responded, compared to slightly more than one third of those treated on days 1–5. More patients in the groups treated on days 1–5 and days 1–5 and 8–9 experienced neutropenia (a shortage of neutrophils, a type of white blood cell, in the bloodstream) or thrombocytopenia (a shortage of platelets in the bloodstream).

The authors concluded that in routine clinical practice, azacitidine has different effectiveness and tolerance depending on the dosing schedule used. Effectiveness and tolerance were best in patients who waited fewer days for the next cycle.

4029 Azacitidine Low-Dose Schedule in Low-Risk Myelodysplastic Syndromes. Preliminary Results of a Multicenter Phase II Study

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Studies have shown that azacitidine lengthens survival in patients with high-risk MDS. But few studies had examined azacitidine’s safety and efficacy in patients with lower-risk MDS.
The aim of this Italian Phase II clinical trial was to study azacitidine in 34 patients with earlier phases of MDS.

At the time of this analysis, data on 30 patients with low- or intermediate 1-risk MDS were available. The patients had been treated with 75mg/m^2 of azacitidine each day for 5 days every 4 weeks. Almost two-thirds of patients responded to the treatment, and some had a complete remission (doctors could detect no cancer cells). In patients whose MDS responded to the drug, the response lasted at least 11–14 months after they stopped azacitidine treatment. In general, patients tolerated the drug well.

The authors concluded that a low-dose schedule of azacitidine might be a reasonable and effective treatment for low-risk MDS and might produce long-lasting responses. However, the authors urged doctors to be cautious about using azacitidine in patients with low-risk MDS who have other diseases, severe neutropenia (a shortage of neutrophils, or a type of white blood cell, in the bloodstream), or thrombocytopenia (a shortage of platelets in the bloodstream).

Azacitidine or Decitabine in CMML

CMML is a cancer that begins in the bone marrow cells that form blood cells and then spreads throughout the bloodstream. Patients with CMML have high levels of monocytes, a type of white blood cell that destroys bacteria.

Some experts classify CMML as a type of MDS because patients with the disease have abnormal cells in their bone marrow. However, CMML is different from other types of MDS in that patients have too many blood cells, not too few. The World Health Organization therefore created a new category—mixed myelodysplastic/myeloproliferative cancers—for CMML.

The FDA has approved Vidaza® (azacitidine) and Dacogen® (decitabine) for treating CMML.

**4017 Efficacy of Azacitidine In the Treatment of Chronic Myelomonocytic Leukemia**

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The authors reviewed data on 35 patients with CMML who had received azacitidine treatment at the Moffitt Cancer Center in Tampa, Florida, between July 2004 and December 2009.

Overall, almost half (48.6%) of these patients experienced some level of response to azacitidine. Median overall survival was 25 months.

The authors concluded that responses to azacitidine in patients with CMML were similar to responses in patients with other forms of MDS in azacitidine studies.

**4023 Treatment of Advanced CMML by Azacitidine (AZA) in a Compassionate Program. The GFM Experience in 38 Patients**

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To date, no drug has shown a clear benefit in treating CMML. Although a few small studies have examined the use of Dacogen® (decitabine) for MDS, these studies included patients with very different characteristics and used different doses of the drug. The authors examined data on 38 patients with CMML in France who had completed at least one cycle of azacitidine.

Twenty patients experienced a response to azacitidine. Of these patients, 9 experienced a
complete response to treatment (no evidence of cancer cells). Of the 20 patients whose disease responded, one died (but did not have a relapse), about half experienced a relapse, and the rest continued to respond after a median of 26 months. Median overall survival was 24 months in patients with CMML compared with 7 months in those whose CMML had progressed to AML.

In conclusion, azacitidine was clearly effective in CMML, especially in patients whose CMML had not progressed to AML.

4032 Decitabine is Effective and Safe In Patients with Chronic Myelomonocytic Leukemia

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Researchers from the M.D. Anderson Cancer Center in Houston, Texas, analyzed data on 17 adults with CMML, a type of MDS. These patients had received Dacogen® (decitabine) treatment in 3-day or 5-day cycles. Most of these patients had intermediate-1 disease (meaning that about half will survive for 3.5 years and 25% will develop AML within 3.3 years).

Most patients had no evidence of CMML, less than 5% blasts in their bone marrow, higher blood cell counts, or stable disease after treatment.

The authors concluded that CMML in these patients responded to decitabine treatment and its safety profile was acceptable.

Azacitidine Outcomes

Azacitidine (azacitidine) was the first FDA-approved drug for treating all types of MDS. The drug can increase blood cell counts, reduce the need for red blood cell transfusions, and reduce the number of blasts (abnormal cells) in the bone marrow.

2931 Therapeutic Response to Azacitidine (AZA) In Patients with Secondary Myelodysplastic Syndromes (sMDS) Enrolled In the AVIDA Registry

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Experts do not know the impact of azacitidine treatment on patients with secondary MDS. Secondary MDS results from treatment (such as radiation or chemotherapy) for another disease. The authors analyzed data on 37 patients with secondary MDS and 280 patients with primary MDS (which did not result from a prior treatment). All patients underwent azacitidine treatment.

At least half the patients with secondary MDS had higher red blood cell or platelet counts after azacitidine treatment. Similar proportions of patients with secondary MDS and primary MDS had higher blood counts as a result of azacitidine treatment. In general, rates of side effects were similar in patients with primary and secondary MDS. However, patients with secondary MDS were more likely to have thrombocytopenia (shortage of platelets) or infections.

In conclusion, patients with secondary MDS were as likely to respond to azacitidine treatment as patients with primary MDS. Patients with both types of MDS tolerated the treatment well.

Another 226 had responded at first but their disease came back later. Patients tended to survive longer if they were female, younger, had fewer blasts (abnormal, immature cells in the bone marrow), and had received at least six cycles of azacitidine. Patients who received a stem cell transplant or an experimental drug tended to survive longer than others.

Rabbit Antithymocyte Globulin (ATG)

ATG is a drug that weakens the immune system, preventing it from attacking the bone marrow. This allows the bone marrow to make healthy bone cells. Manufacturers create ATG from the blood of rabbits or horses.

602 Phase 2 Multicenter Trial of Rabbit Antithymocyte Serotherapy in Myelodysplastic Syndrome: Rate of Hematological Improvement Associated with Pre-Treatment Disease Duration

Researchers from the H. Lee Moffitt Cancer Center in Tampa, Florida, examined the response and safety of rabbit ATG for MDS treatment.

The authors analyzed data on 21 patients from this Phase II, non-randomized clinical trial. MDS responded to the rabbit ATG in 9 patients within 3 months of treatment. Patients whose MDS responded to ATG had received their MDS diagnosis much more recently than those who did not respond.
The study showed that rabbit ATG is safe in patients with MDS and MDS sometimes responds to this treatment. The results also suggest that rabbit ATG might be most effective if patients receive it when their MDS is at an early stage.

**LBA-4 A Randomized Trial of Horse versus Rabbit Antithymocyte Globulin in Severe Acquired Aplastic Anemia**

*Phillip Scheinberg, M.D., Colin O Wu, Ph.D., Priscila Scheinberg, M.S., Barbara Weinstein, R.N., Olga Nunez, R.N., Elaine M Sloand, M.D., and Neal S. Young, M.D.*

Horse ATG is standard treatment in patients with severe aplastic anemia who are not good candidates for stem cell transplantation. Rabbit ATG is more powerful than horse ATG and has different effects on the immune system.

In this study, researchers from the National Heart, Lung, and Blood Institute of the National Institutes of Health randomly assigned 120 patients with severe aplastic anemia to treatment with horse ATG or rabbit ATG. Most patients in the horse ATG group responded to treatment, compared to about one third in the rabbit ATG group.

The authors concluded that horse ATG is a much better first treatment than rabbit ATG for severe aplastic anemia.

**Lenalidomide**

Revlimid® (lenalidomide) is a drug that slows down the growth of the blood vessels that feed abnormal cells. The drug also kills abnormal cells in the bone marrow. Lenalidomide is especially effective for treating anemia in patients with lower-risk MDS who have an abnormality in chromosome 5q. However, many patients become dependent on blood transfusions after lenalidomide treatment.

**976 Risk of AML Evolution in Lower Risk MDS with Del 5q Treated with or without Lenalidomide. A Report by the Groupe Francophone des Myelodysplasies (GFM)**

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In 2007, the French health agency established a compassionate use program for lenalidomide in patients with low- or intermediate 1-risk MDS who had the 5q chromosome abnormality. This program allowed doctors to give lenalidomide to patients who were not part of a lenalidomide study, even though the French regulatory agency had not yet approved the drug’s marketing.

The Groupe Francophone des Myelodysplasies in Bobigny, France, analyzed data on 95 patients with lower-risk MDS and the chromosome 5q abnormality. All patients had received their diagnosis between 1988 and 2007. These patients had received lenalidomide treatment. Within 30 to 67 weeks after they started lenalidomide treatment, MDS had progressed to AML in 6 patients.

The authors compared the 95 patients treated with lenalidomide to patients whose MDS had similar features but who had not received lenalidomide. MDS progressed to AML in slightly fewer patients who received lenalidomide. Survival was longer in patients in the lenalidomide group than in patients who did not receive lenalidomide. However, the difference was not statistically significant (meaning that the difference could have happened by chance).
In conclusion, progression rates to AML in patients with low-risk MDS and the chromosome 5q abnormality treated with lenalidomide are not greater than in patients not treated with lenalidomide. In addition, the data showed no significant differences in survival.

**2923 Lenalidomide Reexposure After Short Interruption in Del(5q) MDS Patients at Relapse of Transfusion Dependence**

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Researchers from Duisburg and Hannover, Germany, reported on their experience with trying to help patients stop needing blood transfusions after lenalidomide treatment. The study included five patients with low- or intermediate-1 risk MDS who had the 5q chromosome abnormality. All of the patients had received lenalidomide treatment in a clinical trial and their MDS had responded to the treatment. They had stopped needing blood transfusions for a while but started needing transfusions again. The authors treated the patients with lenalidomide a second time.

Three of the five patients stopped needing transfusions and continued not to need transfusions. The other two patients continued to need transfusions and the authors stopped their lenalidomide treatment after 3 or 4 months. In both these patients, MDS progressed to a more advanced stage or to AML.

Current guidelines recommend stopping lenalidomide in patients who start needing blood transfusions. But this study suggests that lenalidomide can help some of these patients avoid blood transfusions. However, the authors could not predict which patients would respond to lenalidomide after becoming dependent on blood transfusions.

**4002 Lenalidomide (LEN) in Lower-Risk Myelodysplastic Syndromes (MDS) with Karyotypes other than Deletion 5q and Refractory to Erythropoiesis-Stimulating Agents (ESAs)**

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Erythropoiesis-stimulating agents (ESAs) encourage the body to make more red blood cells. ESAs can often cure anemia in patients with lower-risk MDS. However, patients often need blood transfusions again within 2 years. Also, not all patients respond to ESAs.

This study from the French Groupe Francophone des Myelodysplasies included 31 patients with lower-risk MDS and the 5q chromosome abnormality. These patients had received ESA treatment. Their anemia had not responded to treatment or their response to treatment did not last. These patients then received lenalidomide treatment.

Lenalidomide effectively treated anemia in 13 patients within the first 3 months. Anemia reappeared in four patients within 4 to 16 months, but the other patients had no anemia after as long as 2 years. Some patients developed neutropenia (or a shortage of neutrophils—a type of white blood cell) or thrombocytopenia (a shortage of platelets in the bloodstream).

The study showed that lenalidomide can help patients with low-risk MDS and the 5q chromosome abnormality avoid transfusions. Furthermore, these patients tolerate lenalidomide well.
Eziatiostat

2910 Phase 2 Randomized Multicenter Study of Extended Dosing Schedules of Oral Ezatiostat HCl (Telintra), a Glutathione Analog Prodrug GSTP1-1 Inhibitor, in Low to Intermediate-1 Risk Myelodysplastic Syndrome (MDS)

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TELINTRA® (ezatiostat) stimulates the bone marrow to produce blood cells and kill blasts (abnormal, immature cells).

This Phase II clinical trial evaluated the efficacy and safety of different ezatiostat dosing schedules in patients with MDS. The researchers randomly assigned 73 patients with low- or intermediate 1-risk MDS to 3 grams of ezatiostat every day for 2 weeks or 2 grams every day for 3 weeks. A 1-week rest period followed the treatment period in both groups.

The two dosing schedules had similar effects on blood count improvements. About one third of patients who had required red blood cell transfusions stopped needing transfusions or needed fewer transfusions after treatment. Most patients tolerated the ezatiostat treatment well.

The authors concluded that ezatiostat reduces the need for red blood cell transfusions in patients with MDS. The drug can even stop some patients from needing transfusions and can improve red blood cell, white blood cell, and platelet counts. The drug can be effective in patients who have received lenalidomide treatment in the past and those who have never been on lenalidomide.

Erlotinib

1854 Erlotinib for Treatment of Myelodysplastic Syndromes: A Phase II Clinical Study

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Tyrosine kinases are enzymes (proteins that carry out important functions in cells) that play a role in communications between cells. Erlotinib is a drug that inhibits tyrosine kinases. Researchers from the H. Lee Moffitt Cancer Center in Tampa, Florida, analyzed data from an ongoing Phase II clinical trial of erlotinib treatment for MDS.

The 23 patients enrolled in the study take erlotinib by mouth every day for 16 weeks. All of these patients had undergone treatment with Vidaza* (azacitidine) or Dacogen* (decitabine) in the past. Patients whose disease responded to treatment after 16 weeks kept taking erlotinib until their disease returned or showed signs of progressing. Four of the 23 patients responded to erlotinib. The most common side effects were diarrhea, low platelet counts, and rashes.

In conclusion, erlotinib is safe in patients with MDS. The drug can prevent high-risk MDS from progressing to leukemia in patients whose disease did not respond to azacitidine or decitabine.

Sapacitabine

1857 A Randomized Phase 2 Study of Sapacitabine, an Oral Nucleoside Analogue, in Older Patients with MDS Refractory to Hypomethylating Agents

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Sapacitabine is a drug that kills dividing cells, slowing down the growth of cancer cells. The authors reported some preliminary results from a Phase II clinical trial of three different doses of sapacitabine in older patients. These patients’ MDS has not responded to hypomethylating agents (which kill unhealthy cells in bone marrow), such as Vidaza® (azacitidine) and Dacogen® (decitabine), in the past.

As of July 2010, 61 patients had been treated with sapacitabine for an average of 230 days. Fourteen of these patients had responded to sapacitabine. Response rates were higher in patients taking 300 mg of sapacitabine twice a day for 1 week than in patients taking 200 mg twice a day for 1 week or 400 mg 3 days a week for 2 weeks. Some patients experienced mild to moderate side effects, including fatigue, nausea, diarrhea, and constipation.

The authors concluded that all three tested doses of sapacitabine appear to be safe. Response rates were highest in patients on one of the two 7-day dosing schedules.

**Oral Clofarabine**

1869 Preliminary Results of Fixed-Dose Oral Clofarabine (CLO) in Patients Who Have Failed Hypomethylating Agents for the Treatment of Myelodysplastic Syndromes (MDS)

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Experts do not agree on the appropriate treatment for MDS that does not respond to one of the three FDA-approved drugs for MDS.

This is the first study of oral clofarabine in patients with higher-risk MDS or MDS that has progressed to AML and who have not responded to a hypomethylating agent (agents that kill unhealthy cells in bone marrow), such as Vidaza® (azacitidine) and Dacogen® (decitabine). Clofarabine interferes with the growth of cancer cells, which eventually die.

The authors reported results from 22 patients in an ongoing Phase II clinical trial of oral clofarabine. Patients had undergone treatment with decitabine, azacitidine, or both in the past. These patients had experienced a reappearance of their MDS and 13 had not responded to hypomethylating agent treatment.

Serious side effects of clofarabine included anemia, thrombocytopenia, and pneumonia. All patients who received 25 mg survived but some patients on the 35 mg and 55 mg doses died. Almost one third of study participants responded to treatment, including one patient who had no evidence of MDS.

These preliminary results suggested that 25 mg of oral clofarabine per day for 5 days in patients who have undergone hypomethylating treatment for MDS has an acceptable response rate and safety profile.

**Estybon**

Only about half of all patients with intermediate- or high-risk MDS respond to azacitidine, a hypomethylating agent. Hypomethylating agents kill unhealthy cells in bone marrow. Few treatment options are available for patients whose MDS does not respond to hypomethylating agent treatment.

Patients with MDS need new treatment options. One option that experts are studying is Estybon (ON 01919.Na). This drug blocks some proteins that cells need to grow and kills cancer cells. ON 01919.Na has shown promising results in Phase I/II clinical trials in patients with MDS.
2944 Evaluation of ON01910.Na in Patients with a Myelodysplastic Syndrome (MDS) or Acute Myeloid Leukemia (AML) Relapsed or Refractory to Hypomethylating Agents: A Phase I Study
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A clinical trial of ON 01910.Na is taking place in patients with blood cancers, including MDS. In the Phase I component of this study, patients are receiving a wide range of intravenous (IV) doses of ON 10910.Na for 72 to 144 hours every 2 weeks for four cycles. Next, they receive treatment every 3 to 4 weeks.

The authors reported results from 10 patients with MDS or AML that had not responded to a hypomethylating agent or had returned after hypomethylating agent treatment. Half of the patients had shown a response to the treatment in their bone marrow. Patients had survived from 7 to 16 months. Four of five patients who responded to treatment had MDS (rather than AML) before starting treatment and all five patients who did not respond had AML. The most common side effects were fatigue, anorexia, and nausea.

In conclusion, ON 01910.Na seems to be safe in patients with MDS or AML that has not responded to hypomethylating agent treatment or that relapsed after treatment. The drug reduces blasts (immature, abnormal cells in the bone marrow), destroys MDS clones (copies of blood-forming cells in the bone marrow), and improves blood counts in some patients. Patients who respond to treatment survive longer. Future research needs to identify how ON 01910.Na works and which patients will benefit from the drug.

4010 Treatment of Higher Risk Myelodysplastic Syndrome Patients Unresponsive to Hypomethylating Agents with ON 01910.Na
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The authors reported results from an ongoing Phase II clinical trial on 10 patients with intermediate- or high-risk MDS that had not responded to azacitidine, decitabine, or both. These patients underwent IV ON 01910.NA treatment.

At the time of this report, half the patients had experienced some response to the drug. Some patients had side effects related to the drug. Two patients stopped the drug because of side effects or because their disease had progressed to AML. Biological tests showed that the drug apparently changed the signaling of cancer cells.

The authors concluded that the drug’s effects and patients’ ability to tolerate the drug appear to be promising.

Panobinostat

4015 Preliminary Results of a Phase II Trial of Panobinostat (LBH589) in Refractory Myelodysplastic Syndromes (MDS) Patients
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Panobinostat blocks the activities of histone deacetylases. These proteins help turn genes on and off in cells. The authors designed this Phase II clinical trial to evaluate the responses to panobinostat in patients whose MDS had not responded to hypomethylating agent treatment or that relapsed after treatment. Hypomethylating agents kill unhealthy cells in bone marrow.
At the time the authors wrote this abstract, they had analyzed data on 10 patients. After two 28-day cycles, 7 of 10 patients had stable disease and MDS had progressed in 2 patients. Three patients experienced serious side effects. After an average of 69 weeks, nine patients were still alive.

The study findings suggest that patients with MDS that has not responded to hypomethylating agents tolerate panobinostat well. Future studies should assess the drug’s safety and efficacy in combination with other MDS treatments.

**Hematopoietic Growth Factors**

Patients with MDS have low counts of red blood cells, white blood cells, platelets, or two or three of these types of cells. Hematopoietic growth factors help the bone marrow make more healthy blood cells.

**442 Long-Term Outcome of Anemic Non Del 5q Lower-Risk MDS Refractory to or Relapsing After Erythropoiesis Stimulating Agents (ESAs)**


ESAs encourage the body to make more red blood cells. ESAs are often the first treatment for anemia in patients with lower-risk MDS. However, some patients do not respond to ESAs and their average response only lasts about 2 years.

Until now, research has not found out what happens to patients whose MDS does not respond to ESAs or whose disease comes back after they respond to the treatment.

The French Groupe Francophone des Myelodysplasies analyzed data from 94 patients whose lower-risk MDS had not responded to MDS and 83 patients whose disease had relapsed after responding at first.

On average, patients whose disease never responded to ESAs survived for 43 months and 18% developed AML. Patients who were younger than 75 tended to survive longer than older patients. The only factor that seemed to affect length of survival was cytogenetics, or abnormalities in chromosomes.

In patients whose MDS returned after responding to ESAs at first, average survival was 53 months and almost 10% developed AML. Age and cytogenetics apparently did not affect outcomes in these patients.

The results show that most patients whose lower-risk MDS does not respond to ESAs or comes back after responding and patients whose MDS does respond to ESAs have similar survival times and a similar risk of progression to AML.

**1885 Update from an Open-Label Extension Study Evaluating the Long-Term Safety and Efficacy of Romiplostim In Thrombocytopenic Patients (Pts) with Myelodysplastic Syndromes (MDS)**

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The goal of this study was to evaluate the safety and efficacy of long-term use of Nplate® (romiplostim). This drug helps the bone marrow make more platelets. The researchers analyzed data from 40 patients with MDS who had participated in a romiplostim study and then joined a romiplostim extension study. On average, patients had undergone romiplostim treatment for almost a year.
Most patients had mild to moderate side effects. The most common side effects were nosebleeds, fatigue, and coughing. No patients died during the study. In three patients, the MDS progressed to AML. Patients were less likely to experience serious bleeding the longer they stayed on romiplostim. Fewer patients received a platelet transfusion over time, and platelet counts increased in 34 patients.

Iron Chelation and Blood Counts

Most patients have anemia, or low red blood cell counts, when they first receive an MDS diagnosis. These patients often need red blood cell transfusions. Red blood cells carry iron. Patients with MDS who have had many red blood cell transfusions often develop high levels of iron, known as iron overload. Iron overload can damage the body’s tissues and organs. Iron chelation drugs can remove the extra iron from the body.

Some studies have shown that iron chelation therapy can improve blood cell counts or reduce the need for red blood cell transfusions in patients with MDS.


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The studies showing the benefits of iron chelation therapy in patients with MDS were based on individual patients or small studies. This international group of authors reported the results of their analyses of data on 341 patients from the European Prospective Investigation into Cancer and Nutrition (EPIC). All of these patients had MDS and iron overload. Study personnel treated these patients with EXJADE® (deferasirox), an iron chelator.

During deferasirox treatment, about one third of patients experienced an improvement in their red blood cell counts or needed fewer blood transfusions.

The reasons why iron chelation treatment had these effects are not clear. A larger study needs to confirm the results of this study and provide more information on the effects of deferasirox in patients with MDS.

2928 Iron Chelation Therapy with Deferasirox in Transfusion Dependent Myelodysplastic Syndrome Patients. Preliminary Report from the Prospective MDS0306 GIMEMA Trial

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This Italian Phase III clinical trial tested the safety and efficacy of EXJADE® (deferasirox), an iron chelation treatment, in 159 patients with MDS. All of the patients had needed regular red blood cell transfusions for an average of 20 months and their iron levels were high.

This analysis included data from 62 patients who stayed on deferasirox for a year. The other patients dropped out of the study because, for example, their MDS got worse or they could not stand the side effects. Very few patients who stayed in the study for the full year had a serious side effect. Average iron levels decreased significantly in those who took the drug for a year. One patient stopped needing blood transfusions after deferasirox treatment.

The data show that deferasirox can lower iron levels in patients with MDS who can keep taking the drug for a year.
More Ways to Get Help

The Aplastic Anemia & MDS International Foundation (AA&MDSIF) is here to help. We provide the following services:

- Personalized support from patient educators
- Free educational materials on many topics related to MDS
- Online Learning Center
- Patient and family conferences
- Peer Support Network
- Print and electronic newsletters with important information and updates
- Clinical trials information

Contact us today. Here’s how:

📞 Call us:
(301) 279-7202 or (800) 747-2820

✉️ Email us:
info@aamds.org

🌐 Go to our Web site:
www.AAMDS.org

Remember – you are not alone. We are standing by to support you in any way we can.