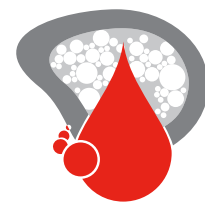



AAMDSIF

MDS Research Summary *from the*
2016 AMERICAN SOCIETY OF HEMATOLOGY ANNUAL MEETING

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



AA·MDS
INTERNATIONAL FOUNDATION



The Aplastic Anemia and MDS International Foundation (AAMDSIF) 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 58th Annual Meeting of the American Society of Hematology (ASH) in December 2016. 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.

Aplastic Anemia and MDS International Foundation
4330 East West Highway, Suite 230
Bethesda, MD 20814
(301) 279-7202 or (800) 747-2820
info@aamds.org
www.aamds.org



Copyright © 2017, Aplastic Anemia and MDS International Foundation

This publication is made possible through an unrestricted education grant from Celgene Corporation.

INTRODUCTION

Dear Patient or Caregiver,

The purpose of this guide is to provide you with the most up-to-date information about the latest new research into the biology and treatment of myelodysplastic syndromes (MDS), as presented at the 58th Annual Meeting of the American Society of Hematology (ASH) Annual Meeting in December 2016.

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 AAMDSIF 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,
AAMDSIF 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/2016/webprogram>**. 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.*

50

Using Genetic Information for Prognosis in Treated Patients with MDS

Karam Al-Issa, M.D.; Ahmad Zarzour, M.D.; Tomas Radivoyevitch, Ph.D.; Matt Kalaycio, M.D.; Betty K. Hamilton, M.D.; Aaron T. Gerds, M.D., M.S.; Sudipto Mukherjee, M.D., Ph.D., M.P.H.; Vera Adema, Ph.D.; Michael J. Clemente, M.S.; Bhumika Patel, M.D.; Cassandra M. Hirsch; Anjali S. Advani, M.D.; Bartlomiej P Przychodzen, M.Sc.; Hetty E. Carraway, M.D., M.B.A.; Jaroslaw P Maciejewski, M.D., Ph.D.; Mikkael A. Sekeres, M.D., M.S.; Aziz Nazha, M.D.

Researchers have developed several different systems to determine the prognosis of patients with MDS. These systems include the International Prognostic Scoring System (IPSS), revised IPSS (IPSS-R), World Health Organization Classification-Based Prognostic Scoring System (WPSS), and MD Anderson Prognostic Scoring System (MDPSS). Experts created all of these systems, except for the MDPSS, based on data from patients with MDS that had not yet been treated.

This study compared the ability of each system, alone or in combination with genetic information, to correctly predict outcomes in patients whose MDS had been treated. The study used data on 610 patients who had received, on average, two different types of treatment.

Key findings:

- Mutations in the *EZH2*, *TP53*, *RUNX1*, and *NPM1* genes had a negative impact on overall survival.
- Mutations in the *SF3B1* gene had a positive impact on survival.
- Adding information on these genes to the prognostic scoring systems improved each system's ability to accurately predict patient outcomes.
- Adding the genetic data to the IPSS changed 37% of patients in the lower-risk category to a higher-risk category and 5% of those in the intermediate-1 category to the low-risk category.
- In the WPSS, the genetic data changed 21% of patients from lower risk to higher risk and 24% from higher risk to lower risk.
- In the MDPSS, the genetic data changed 19% of patients from lower risk to higher risk category and 22% from intermediate-1 to low risk.
- In the IPSS-R, the genetic data changed 59% of patients from intermediate risk to higher risk.

Conclusions:

- Adding genetic data to MDS prognostic models can improve their predictive power, even in treated MDS patients.
- Adding genetic information can change patients' risk categories.

51

Do Numbers of Driver Mutations Predict Response to Treatment in Patients with MDS?

Guillermo Montalban-Bravo, M.D.; Ana Alfonso Pierola, M.D., Ph.D.; Feng Wang, Ph.D.; Song Xingzhi; Elias J. Jabbour, M.D.; Tapan M. Kadia, M.D.; Farhad Ravandi, M.D.; Jorge E. Cortes, M.D.; Courtney D. DiNardo, M.D.; Naval Daver, M.D.; Gautam Borthakur, M.D.; Naveen Pemmaraju, M.D.; Marina Konopleva, M.D., Ph.D.; Graciela M. Nogueras-Gonzalez; Xuelin Huang, Ph.D.; Carlos E Bueso-Ramos, M.D., Ph.D.; Keyur Patel, M.D.; Andrew Futreal, Ph.D.; Hagop M. Kantarjian, M.D.; Koichi Takahashi, M.D.; Guillermo Garcia-Manero, M.D.

Hypomethylating agents (HMAs), such as azacitidine (Vidaza®) and decitabine (Dacogen®), are the standard treatment for MDS. About 40–60% of patients respond to these drugs, typically for about 12–14 months. Outcomes are poor for those who stop responding to HMAs.

The purpose of this study was to identify biological markers of response to HMAs. The researchers evaluated data on mutations in 28 genes from 180 patients with newly diagnosed MDS (median age 67 years) or chronic myelomonocytic leukemia (CMML) before treatment with an HMA. Of the 180 patients, 66 (37%) had a complete response to HMA treatment, meaning that no cancerous cells could be detected in their bone marrow.

Key findings:

- A total of 123 patients (68%) had at least one detectable mutation.
- The most frequently detected mutations were in *TET2* (23% of patients), *TP53* (16%), and *RUNX1* (12%).
- Patients with an *ASXL1* mutation had a lower likelihood of a complete response to HMAs.
- Patients with a complete response to HMA treatment tended to survive longer if they had higher-risk MDS, but the same was not true for patients with lower-risk MDS.

Conclusions:

- The number of mutations that drive cancer progression could be a marker of response to HMAs in patients with MDS and CMML.
- Using genetic data at diagnosis might help predict the patient's response to treatment and outcomes.

297

Monitoring Genetic Mutations Over Time in Patients with MDS

Sangmin Lee, M.D.; John Barnard, Ph.D.; Amy E. DeZern, M.D., M.H.S.; Jaroslaw P. Maciejewski, M.D., Ph.D.; Najla Alali, M.S.; David P. Steensma, M.D.; Ellen K. Ritchie, M.D.; Pinkal Desai, M.D.; Guillermo Garcia-Manero, M.D.; Fatima Ali; Nicole Rizzo; Duane C. Hassane, Ph.D.; Rami S. Komrokji, M.D.; Mikkael A. Sekeres, M.D., M.S.; Gail J. Roboz, M.D.

Certain gene mutations are common in patients with MDS. Profiling each patient's genetics is becoming a standard part of the diagnostic evaluation. But the value of monitoring genes in patients with MDS at several different times is not known.

This study assessed the impact of monitoring 94 patients with MDS at least twice during the course of their disease. The investigators compared the mutations at the first time point with those at subsequent time points. On average, patients' genes were assessed twice, 3 months apart.

Key findings:

- Overall, 32 patients (34%) acquired at least one more mutation at a subsequent test.
- Regardless of the patient's age or IPSS score, patients with more mutations at the first evaluation in the core gene set (*ASXL1, EZH2, ETV6, RUNX1, TP53*) did not survive as long.
- Patients who acquired one or more new mutations after the first test did not survive as long, regardless of age, IPSS score, or number of mutations at the first test point.
- The rate of progression of acute myelogenous leukemia (AML) was higher, 62%, in patients who acquired at least one additional mutation than in those who did not (37%).
- More patients (36%) whose disease progressed to AML acquired new mutations than those who didn't develop AML (17%).
- 33% of patients lost a mutation after the first test, but this had no effect on survival.

Conclusions:

- Acquiring new mutations in subsequent testing is associated with poor overall survival in patients with MDS, regardless of age, sex, or IPSS score.

298

Genetic Mutation Analysis to Diagnose Unexplained Blood Cell Shortages

Luca Malcovati, M.D.; Anna Gallì; Erica Travaglino; Ilaria Ambaglio, M.D.; Ettore Rizzo; Elisabetta Molteni; Chiara Elena, M.D.; Silvia Catricalà; Elisa Bono, M.D.; Antonio Bianchessi, M.D.; Gabriele Todisco, M.D.; Elisa Rumi, M.D.; Virginia Valeria Ferretti; Elli Papaemmanuil, Ph.D.; Seishi Ogawa, M.D., Ph.D.; Mario Cazzola, M.D.

Figuring out whether unexplained cytopenia (blood cell shortage) is due to MDS, acute myelogenous leukemia, or another bone marrow failure disease is challenging. In the last several years, scientists have found associations between several gene mutations and bone marrow failure diseases. But their usefulness for diagnosing unexplained cytopenia is still not clear.

This study assessed the usefulness of 42 gene mutations for predicting outcomes in patients with unexplained cytopenia. The study included 873 patients. After a median of 22 months, 447 patients developed a bone marrow failure disease.

Key findings:

- Mutations were most common in *TET2* (25% of patients), *ASXL1* (15%), *SRSF2* (14%), *SF3B1* (11%), *DNMT3A* (10%), and *RUNX1* (9%).
- Patients with none of the tested mutations had an 83% chance of not having a bone marrow failure disease.
- Patients with two or more mutations had a 94% chance of having a bone marrow failure disease.
- Patients with an *SF3B1* mutation had a 99% chance of having MDS.

Conclusions:

- Certain mutated genes and combinations of mutations could identify patients with a high likelihood of having MDS or other bone marrow failure disease.
- Analyzing genes in blood cells could improve approaches to diagnosing unexplained cytopenia.

223

Lenalidomide and Epoetin Alfa (EA) for Lower-Risk MDS: Results of the E2905 Intergroup Study

Alan F. List, M.D.; Zhuoxin Sun, Ph.D.; Amit Verma, M.D.; John M. Bennett, M.D.; Kathy L. McGraw, Ph.D.; Lisa Ann Nardelli; Jaroslaw P Maciejewski, M.D., Ph.D.; Jessica K. Altman, M.D.; Puneet Cheema, M.D.; David F. Claxton, M.D.; Rami S. Komrokji, M.D.; Selina Luger, M.D.; Ryan Mattison, M.D.; Tim Wassenaar, M.D.; Andrew Artz, M.D.; Charles A Schiffer, M.D.; Martin S. Tallman, M.D.

Recombinant human erythropoietin (rHuEPO) is an effective treatment for anemia in some patients with lower-risk MDS. But options for those who don't respond are limited. Lenalidomide (Revlimid®) can improve the bone marrow's ability to form healthy red blood cells. This treatment can allow patients with lower-risk MDS who have anemia to avoid blood transfusions for up to 10 months.

The purpose of this phase III clinical trial was to find out whether lenalidomide could overcome resistance to rHuEPO. The investigators compared treatment with lenalidomide alone to lenalidomide and epoetin alfa, an rHuEPO, in 195 patients (median age 74 years) with lower-risk or intermediate-1-risk MDS. All patients had anemia that did not respond to rHuEPO or they could not be treated with rHuEPO for other reasons. On average, patients needed transfusions with two red blood cell units a month.

Key findings:

- Red blood cell counts improved in a higher proportion of patients treated with a combination of lenalidomide and epoetin-alfa (26%) than in those treated with lenalidomide alone (10%).
- Among 116 patients evaluated at week 16, 33.3% of those in the combination therapy group had higher red blood cell counts, compared to 14.3% of those in the lenalidomide-only group.
- The response to combination therapy lasted a median of 25 months in the combination treatment group.
- Side effects were similar in the two treatment groups.

Conclusions:

- Lenalidomide restores sensitivity to rHuEPO in patients with lower-risk MDS who do not respond to rHuEPO alone without increasing side effects.

114

Combination of a New Drug, E7727, with Oral Decitabine in Patients with MDS: Final Results of Phase I Clinical Trial

Guillermo Garcia-Manero, M.D.; Olatoyosi Odenike, M.D.; Philip C. Amrein, M.D.; David P. Steensma, M.D.; Amy E. DeZern, M.D., M.H.S.; Laura C. Michaelis, M.D.; Stefan Faderl, M.D.; Hagop M. Kantarjian, M.D.; James N. Lowder, M.D.; Pietro Taverna, Ph.D.; Aram Oganessian, Ph.D.; Xiaoping Zhang, Ph.D.; Mohammad Azab, M.D.; Michael R. Savona, M.D.

Treatment with the hypomethylating agents (HMAs) azacitidine (Vidaza®) and decitabine (Dacogen®) is effective in patients with intermediate-1, intermediate-2, and high-risk MDS. But these drugs have to be injected several times a month as long as the drugs are working. An HMA that patients could take by mouth at home would be more convenient. This type of drug might also increase the chance that the patient will get the full prescribed treatment, especially if they respond to these drugs for a long time.

It's hard to make oral forms of azacitidine and decitabine, however, Cytidine deaminase (CDA), an enzyme, in the gut and liver rapidly clears these drugs from the bloodstream.

This phase I clinical trial assessed different doses of a combination of oral decitabine with a new drug, E7727, which inhibits CDA. The study included 43 adults with intermediate-risk or high-risk MDS or chronic myelomonocytic leukemia (CMML). Their median age was 72 years.

Key findings:

- The most common serious effects were low blood cell counts as well as low white blood cell count with fever.
- Patients had no side effects involving the digestive system that were related to the drug.
- As of the writing of this abstract, 32% of patients had responded to the combination treatment.
- Of 23 patients who needed regular red blood cell transfusions before the study, 6 stopped needing transfusions.
- Of 6 patients who needed regular platelet transfusions, 2 stopped needing these transfusions.

Conclusions:

- The combination of E7727 and oral dacogen had similar effects and a similar safety profile to injected decitabine.
- Rates of responses and transfusion independence were similar to those for injected decitabine, even among patients who had been treated with injected decitabine in the past.

343

MDS Treatment with Enasidenib (AG-221), an Inhibitor of the IDH2 Gene

Eytan M. Stein, M.D.; Amir T. Fathi, M.D.; Courtney D. DiNardo, M.D.; Daniel A. Pollyea, M.D.; Ronan T. Swords, M.D., Ph.D.; Gail J. Roboz, M.D.; Robert Collins; Mikkael A. Sekeres, M.D.; Richard M. Stone, M.D.; Eyal C Attar; Alessandra Tosolini; Qiang Xu, Ph.D.; Michael Amatangelo, Ph.D.; Ira Gupta, M.D.; Robert D. Knight, M.D.; Stéphane De Botton, M.D., Ph.D.; Martin S. Tallman, M.D.; Hagop M. Kantarjian, M.D.

About 5% of patients with MDS and 15% of those with acute myelogenous leukemia (AML) have a mutation in the *IDH2* gene. In previous studies, patients with AML who had the *IDH2* mutation responded to enasidenib (also known as AG-221/CC-90007).

This phase I clinical trial was the first to evaluate the safety and efficacy of different doses of enasidenib in 16 adults (median age 67 years) with MDS and the *IDH2* mutation. At the start of the study, 3 patients had had a relapse after stem cell transplantation and 11 had not responded to previous treatment with azacitidine (Vidaza®) or decitabine (Dacogen®).

Key findings:

- Twelve patients stopped the treatment before the final analysis for a range of reasons, including disease progression, patient death, and stem cell transplantation.
- Thirteen patients had serious side effects, most often high bilirubin in blood (5 patients), pneumonia (4 patients), low platelet counts (3 patients), and low potassium (3 patients).
- Among the 15 patients whose results could be evaluated, 8 (53%) responded, including 1 patient who had a complete response (no detectable cancer cells).
- Of 10 patients treated previously with azacitidine or decitabine, 5 (50%) responded to enasidenib, including the patient with a complete response.
- Of the 4 patients with no prior MDS treatment, 2 responded.

Conclusions:

- Patients tolerated daily enasidenib treatment by mouth well.
- More than half of these patients with MDS who had an *IDH2* mutation responded to treatment.
- Assessment of *IDH2* mutations can identify MDS patients who might benefit from enasidenib.

966

H3B-8800, an Experimental Treatment for Bone Marrow Failure Diseases with Spliceosome Mutations

Silvia Buonamici, Ph.D.; Akihide Yoshimi, M.D., Ph.D.; Michael Thomas; Michael Seiler, Ph.D.; Betty Chan, Ph.D.; Benjamin Caleb; Rachel Darman, Ph.D.; Peter Fekkes, Ph.D.; Craig Karr, Ph.D.; Gregg F. Keaney, Ph.D.; Virginia M. Klimek, M.D.; Kaiko Kunii; Linda Lee; Stanley Chun-Wei Lee, Ph.D.; Xiang Liu, Ph.D.; Carol Meeske; Yoshiharu Mizui, Ph.D.; Eric Padron, M.D.; Eunice Park, Ph.D.; Ermira Pazolli, Ph.D.; Sudeep Prajapati, Ph.D.; Justin Taylor, M.D.; John Wang, Ph.D.; Markus Warmuth, M.D.; Lihua Yu, Ph.D.; Ping Zhu, M.D.; Omar Abdel-Wahab, M.D.; Peter G Smith, Ph.D.

RNA molecules and proteins splice together certain sequences in RNA to form messenger RNA molecules that can produce proteins that work properly. Spliceosomes are groups of proteins that help splice messenger RNA.

Spliceosome mutations are common in patients with MDS, chronic myelomonocytic leukemia (CMML), and acute myelogenous leukemia (AML). Recent data suggest that cells with spliceosome mutations are sensitive to drugs that affect splicing, but cells without these mutations do not have this sensitivity.

The investigators describe H3B-8800, which is effective for bone marrow failure diseases in experimental mice.

Key findings:

- In several experiments in cells, H3B-8800 had a similar effect on splicing regardless of which spliceosome genes had mutations.
- The effects of H3B-800 were strongest in AML cells with *SF3B1* or *SRSF2* mutations.
- In experimental mice with *SF3B1* and *SRSF2* mutations, H3B-8800 treatment affected RNA splicing and inhibited the growth of cancerous cells.
- The effects were stronger with higher doses.
- In experimental mice with CMML, H3B-8800 substantially reduced leukemia cells in animals with spliceosome mutations but not in mice without these mutations.

Conclusions:

- H3B-8000 is a novel treatment that kills bone marrow cells that have a spliceosome mutation but has much less effect on healthy cells.
- Studies of H3B-8800 are underway in patients with MDS, AML, and CMML.

TREATMENTS AFTER HYPO METHYLATING AGENT FAILURE

345

Pembrolizumab for MDS after Failure of Hypomethylating Agent Treatment

Guillermo Garcia-Manero, M.D.; Martin S. Tallman, M.D.; Giovanni Martinelli, M.D.; Vincent Ribrag, M.D.; Hui Yang, M.D., Ph.D.; Arun Balakumaran, M.D., Ph.D., SM; Sabine Chlosta, M.D.; Yayan Zhang, Ph.D.; B. Douglas Smith, M.D.

Pembrolizumab (Keytruda®) blocks the PD-1 protein on the surface of T cells, which are type of immune cell. The PD-1 blockage triggers the T cells to find cancer cells and kill them.

This abstract summarizes the results for 28 adults with intermediate-risk or high-risk MDS (median age 73 years) who participated in a Phase Ib clinical trial of pembrolizumab for various blood cancers. Patients had not responded to at least four cycles of treatment with a hypomethylating agent, such as azacitidine (Vidaza®) and decitabine (Dacogen®).

Key findings:

- 10 patients (36%) had treatment-related side effects. The most common were low thyroid activity in 4 patients (14%) and fatigue in 3 patients (11%).
- Two patients stopped their pembrolizumab treatment because of treatment-related side effects.
- None of the 27 patients evaluated had a complete remission, but 1 patient had a partial remission, for an overall response rate of 4%.
- Of the 26 patients who did not have a complete remission, 3 (11%) had a complete response in bone marrow, 14 (52%) had stable disease, and 3 (11%) had improved blood cell counts.
- 89% of patients with intermediate-1 MDS were still alive at 1 year and 57% were still alive at 2 years.

Conclusions:

- Most pembrolizumab side effects were manageable.
- Pembrolizumab is potentially beneficial in patients with MDS who did not respond to initial HMA treatment.

TREATMENTS AFTER HYPOMETHYLATING AGENT FAILURE

348

Chemotherapy in Higher-Risk MDS and Acute Myelogenous Leukemia after Treatment Failure

Brian Ball, M.D.; Rami S. Komrokji, M.D.; Lionel Ades, M.D., Ph.D.; Mikkael A. Sekeres, M.D., M.S.; Amy E. DeZern, M.D., M.H.S.; Lisa Pleyer, M.D., Df; Norbert Vey, M.D., Ph.D.; Antonio Almeida, M.D., Ph.D.; Ulrich Germing; Thomas Cluzeau; Uwe Platzbecker, M.D.; Steven Gore; Pierre Fenaux, M.D., Ph.D.; Thomas Prebet, M.D., Ph.D.

Hypomethylating agents (HMAs), such as azacitidine (Vidaza®) and decitabine (Dacogen®), are standard treatment for higher-risk MDS. It's also standard treatment for acute myelogenous leukemia (AML) in patients who can't be treated with chemotherapy. But only about 40% of these patients respond to HMAs, and all eventually have a relapse.

This study compared responses, relapse rates, and overall survival for different chemotherapy regimens in patients with higher-risk MDS or AML that did not respond to HMAs or whose disease progressed after HMA treatment. The researchers analyzed data on 366 adults treated with intensive chemotherapy between 2005 and 2015 after ending their HMA treatment.

Key findings:

- About 40% of patients responded to the chemotherapy.
- On average, patients survived 10 months after treatment.
- At 1 year, half the patients had had a relapse. The relapse rate at 2 years was 71%.
- The relapse rate was higher for patients who had been treated with chemotherapy before HMAs and those whose cancer progressed when they did not respond to HMAs.
- Patients who had stem cell transplantation after chemotherapy survived longer than those who didn't have transplantation.

Conclusions:

- Chemotherapy in patients who haven't responded to HMAs or whose cancer progressed in spite of HMA treatment is a valid treatment option.
- The response rates and transplant rates in patients treated with chemotherapy after HMA failure are better than with other treatments.

53

Using Genetic Mutations to Help Make Decisions about Stem Cell Transplantation for Patients with MDS

Marianna Rossi, M.D.; Matteo Giovanni Della Porta; Andrea Bacigalupo, M.D.; Massimo Bernardi, M.D.; Bernardino Allione, M.D.; Maria Teresa van Lint; Pietro Enrico Pioltelli, M.D.; Paola Marengo, M.D.; Alberto Bosi, M.D.; Maria Teresa Voso, M.D.; Simona Sica, Maria Cuzzola; Emanuele Angelucci, M.D.; Anna Galli; Silvia Zibellini; Ettore Rizzo; Chiara Milanese; Benedetto Bruno, M.D., Ph.D.; Fabio Ciceri, M.D.; Francesca Bonifazi, M.D.; Armando Santoro; Emilio Paolo Alessandrino, M.D.; Alessandro Rambaldi, M.D.; Mario Cazzola, M.D.

The only cure for MDS is hematopoietic stem cell transplantation (HSCT). This procedure involves the infusion of healthy blood-forming (hematopoietic) stem cells from a healthy donor with the same immune system markers as the patient. The donor's stem cells enter the bone marrow, where they form healthy blood cells.

This study's purpose was to try to develop a system to predict outcomes after HSCT in patients with MDS or acute myelogenous leukemia (AML) that had evolved from MDS. The investigators analyzed mutations in 34 genes that are common in patients with bone marrow cancers. The data came from 401 patients who had HSCT between 1997 and 2013.

Key findings:

- Based on the data from the 401 patients, the investigators developed a system that assigns a score for the risk of relapse after transplantation in MDS or AML that had evolved from MDS.
- They assigned 1 point to each of the following:
 - More than 10% abnormal blasts (immature white blood cells) in bone marrow
 - Poor or very poor risk according to the Revised International Prognostic Scoring System
 - Failure to respond to initial chemotherapy
 - Mutations in *ASLX1*, *RUNX1*, or *TP53* genes
- The system grouped patients into four risk groups based on their total score: low (0 points), intermediate (1 or 2 points), high (3 points), or very high (4 points).
- The researchers then calculated the probability of surviving for at least 5 years.

Conclusions:

- Taking genetic mutations into account improves the ability to predict outcomes in patients with MDS or AML that evolved from MDS after HSCT.
- This model could help improve treatment decisions.

69

Changes in Genes Predict Outcomes in Patients with MDS Undergoing Stem Cell Transplantation

R. Coleman Lindsley, M.D., Ph.D.; Wael Saber, M.D., M.S.; Brenton G. Mar, M.D., Ph.D.; Robert A Redd, M.S.; Michael D Haagenson, M.S.; Peter V Grauman; Stephen R. Spellman, M.B.S.; Stephanie J. Lee, M.D.; Tao Wang, Ph.D.; Michael R. Verneris, M.D.; Katharine C. Hsu, M.D., Ph.D.; Katharina Fleischhauer, M.D.; Corey S. Cutler, M.D., M.P.H.; Joseph H. Antin, M.D.; Donna S. Neuberg, Sc.D.; Benjamin L. Ebert, M.D., Ph.D.

The only cure for MDS is hematopoietic stem cell transplantation (HSCT). This procedure involves the infusion of healthy blood-forming (hematopoietic) stem cells from a healthy donor with the same HLA (immune system) markers as the patient. The donor's stem cells enter the bone marrow, where they form healthy blood cells.

The purpose of this study was to use data on genetic changes after HSCT for MDS between 2005 and 2014 in 1,514 patients.

Key findings:

- Outcomes in patients with the *TP53* mutation were poor, regardless of age and other patient characteristics.
- In patients 40 and older without *TP53* mutations, outcomes were poorest in:
 - Those with RAS pathway mutations (median survival of 11 months and high risk of relapse)
 - Those with *JAK2* mutations (median survival of 6 months and high risk of transplant-related death)
- Among patients younger than 40 without a *TP53* mutation:
 - The survival rate was 49% for those with MDS that developed after previous cancer treatment, a low platelet count at HSCT, or at least 15% of blasts (abnormal immature white blood cells) in bone marrow.
 - The survival rate was 81% for patients who had none of these high-risk features.

Conclusions:

- *TP53* mutations are the most important predictor of prognosis in patients with MDS who undergo HSCT, regardless of other patient characters or genetic mutations.

1500 Stem Cell Transplantation for Patients with *GATA2* Deficiency

*Dennis D. Hickstein, M.D.; Nirali N Shah, M.D.;
Alexandra Freeman, M.D.; Christa Zerbe, M.D.; Steven
M. Holland, M.D.*

GATA2 deficiency is a genetic disease that can cause severe infectious, breathing problems, and inherited MDS/acute myelogenous leukemia (AML). The only effective treatment is hematopoietic stem cell transplant (HSCT).

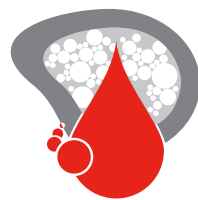
The investigators assessed the outcomes of HSCT in 24 patients (average age 25 years) with *GATA2* mutations. Patients received different treatments before the procedure to reduce the number of cancerous cells as well as different treatments after HSCT to prevent graft-versus-host disease (GVHD).

Key findings:

- Twenty-two of the 24 patients were alive and disease free after an average of 13 months.
- Two patient who received a transplant from an unmatched related donor died of AML or GVHD.
- Four of 13 patients who received stem cells from a related donor developed serious GVHD.
- Abnormalities in chromosomes disappeared in 13 patients with MDS.
- In 23 patients, white blood cell counts were in the normal range.

Conclusions:

- HSCT reverses the signs and symptoms of *GATA2* deficiency with few serious side effects, even in patients with other serious medical concerns.



AA·MDS
INTERNATIONAL FOUNDATION

4330 East West Highway, Suite 230
Bethesda, MD 20814
(800) 747-2820 | (301) 279-7202
www.aamds.org

