HIGHLIGHTS FROM THE

2011 American Society of Hematology Annual Meeting

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

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

This booklet offers summaries of abstracts presented at the 53rd Annual Meeting of the American Society of Hematology (ASH) in December 2011. 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 53nd Annual Meeting of the American Society of Hematology (ASH) in December 2011.

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 people living with 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 sometimes involve experimental drugs that are not approved for general use by the Food and Drug Administration (FDA) or investigation 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/2011/webprogram/keywordindexm.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 early 2012, AA&MDSIF produced webinars on the latest diagnosis and treatment research as reported at the 53rd 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

Many programs are available to help you learn about your disease. 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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Doctors use scoring systems to decide what type of MDS a person has, what the expected course of the disease may be and help them to choose the best treatments. Researchers have developed several prognostic scoring systems based on MDS patients’ test results such as: blood cell counts, bone marrow blasts (abnormal, immature cells), and genetic testing.

**Prognostic Scoring Systems**

**1720 Validating the Lower-Risk MD Anderson Prognostic Scoring System (LR-PSS) and the Revised International Prognostic Scoring System (IPSS-R) for Patients with Myelodysplastic Syndromes**

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Many doctors use the International Prognostic Scoring System (IPSS) to evaluate each patient’s test results and recommend appropriate therapy. But some patients with a low IPSS score, which indicates a low risk of progressing to AML, have a poorer prognosis than the IPSS indicates.

This study evaluated two new scoring systems for patients with MDS with a low IPSS score:

- The lower-risk prognostic scoring system (LR-PSS), which was designed to identify patients with low-risk MDS and a poor prognosis.
- The Revised IPSS (IPSS-R), which measures more patient factors than the original IPSS.

The study included 664 patients with lower-risk MDS who were treated at either the Cleveland Clinic or M.D. Anderson Cancer Center between 1991 and 2010. Median patient age was 70 years at the Cleveland Clinic and 67 years at the M.D. Anderson Cancer Center.

Key Findings:

- According to the LR-PSS, 156 patients (25%) with low or intermediate-1 risk based on the IPSS had a poor prognosis. Another 47 patients (12%) with intermediate-1 disease had a good prognosis.
- According to the IPSS-R, 164 patients (27%) with a low or intermediate-1 score based on the IPSS had intermediate-, high-, or very high-risk disease. Another 5 patients (1%) with intermediate-1 disease had a very good prognosis.
- The IPSS, LR-PSS, and IPSS-R all predicted overall survival well. But the LR-PSS was better for predicting overall survival than the IPSS-R.

Conclusion: The LR-PSS and IPSS-R are useful tools for predicting survival for patients with low-risk disease.

**1729 Prognostic Impact of Comorbidities in a Cohort of 788 MDS Patients Based on a CIRS-G Derived Score. A MDS Piedmont Registry Prospective Study**

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Individuals with MDS may have other health concerns (comorbidities) as well. These comorbidities can have a major impact on the best treatment for that patient. For this reason, doctors need to evaluate each patient’s comorbidities when choosing the best treatment for that patient.

The goal of this study was to evaluate the usefulness of the Cumulative Illness Rating Scale of Geriatrics (CIRS-G), a comorbidities scoring system for older patients, for evaluating comorbidities in patients with MDS. A group...
of Italian researchers analyzed data on 788 patients with MDS who had enrolled in an Italian patient registry between 1999 and 2010. Of these patients, 78% had lower-risk MDS and the rest had intermediate-2 or high-risk MDS. Of these patients, 67% were 70 years old or older. Doctors had used the CIRS-G to evaluate these patients at diagnosis.

Key Findings:
• Most patients in the study had only mild comorbidities.
• The most common causes of severe impairment were high blood pressure, heart conditions, and hormone-related conditions.
• Comorbidities had no impact on a patient’s risk of progressing to AML.
• Having severe comorbidities based on the CIRS-G increased the risk of death.
• Severity of comorbidities according to the CIRS-G, age, and IPSS classification affected patients’ overall survival.

Conclusions:
The CIRS-G is a useful tool for evaluating patients with MDS at diagnosis and during disease management. Comorbidity severity based on the CIRS-G and age used with IPSS can provide an accurate estimate of survival.

Gene Discoveries

3 Somatic Mutation of SF3B1, a Gene Encoding a Core Component of RNA Splicing Machinery, in Myelodysplasia with Ring Sideroblasts

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P. Andrew Futreal, Michael R Stratton, Peter J. Campbell, and Mario Cazzola
Refractory anemia with ring sideroblasts (RARS) is a type of MDS in which more than 15% of red blood cells in the bone marrow contain ring-shaped iron deposits known as ring sideroblasts. These individuals have a low red blood cell count that can't be treated with iron or vitamins. Experts have recently identified mutations, or changes, in certain genes that are associated with RARS.

The purpose of this study was to use information about changes in the genes of 8 patients with RARS to better understand how MDS develops in the body. Six patients had a mutation in the SF3B1 gene, so the authors decided to study this mutation more carefully in patients with MDS or AML that had developed from MDS.

Key Findings:
• An SF3B1 mutation was present in 150 of 533 (28%) patients with MDS.
• Ninety-seven percent of patients with a mutation in the SF3B1 gene had ring sideroblasts in their bone marrow.
• Patients with an SF3B1 mutation were likely to survive longer and had a lower risk of progression to AML than patients without the mutation.

Conclusions:
SF3B1 is the first gene to be strongly associated with a specific cell structure, ring sideroblasts, in MDS. Detecting SF3B1 mutations could improve the assessment of survival and risk of progression to AML.
Impact of Molecular Mutations on Treatment Response to Hypomethylating Agents in MDS

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Hypomethylating agents like azacitidine (Vidaza®) and decitabine (Dacogen®) are valuable for treating MDS. However, not all patients respond to these therapies. Researchers have discovered some genetic changes that explain how MDS develops and might be useful for predicting which patients will respond to certain types of treatment.

To evaluate the usefulness of certain genetic changes for predicting response to hypomethylating agent treatment, the authors studied 88 patients with MDS who had been treated with azacitidine, decitabine, or both. Median patient age was 69 years and patients had been followed for a median of 18 months. Forty patients (45%) had a mutation in the DNMT3A, TET2, IDH1/2, EZH2, ASXL1, UTX, KRAS, TP53, or SF3B1 genes.

Key Findings:
- Patients with a change in the DNT3A, ASXL1, or TET2 gene were more likely to respond to a hypomethylating agent than patients without the mutation.
- Patients with changes in a combination of DNMT3A, TET2, IDH1, and/or IDH2 genes also had better responses to hypomethylating agent treatment than patients without these combinations.
- Survival without disease progression was better in patients with the TET2 mutation.

Conclusions:
Genetic testing for biological markers can help physicians determine how well an individual will respond to treatment. Mutations in a combination of DNMT3A, TET2, IDH1, and/or IDH2 genes might influence patient response to hypomethylating agents, especially azacitidine. This combination of genetic mutations might be a useful biological marker to predict the course of MDS and choose the right treatment for each patient.

NEW STRATEGIES FOR CLASSIFYING MDS
Treatment for MDS often includes the use of medication such as hypomethylating agents that kill abnormal cells in bone marrow. Azacitidine (Vidaza®), a hypomethylating agent, is the current standard treatment for other types of MDS. Azacitidine treatment is also an option for patients with low-risk MDS. Azacitidine works by helping bone marrow cells grow and reproduce normally. Decitabine, (Dacogen®) is another hypomethylating agent that is used to treat MDS.

Lenalidomide, (Revlimid®) slows down the growth of the blood vessels that feed abnormal cells. This medication also kills abnormal cells in the bone marrow. Lenalidomide is especially effective for treating lower-risk MDS with deletion of chromosome del5q.

### Azacitidine and Erythropoietin

**3798 Evaluation of Azacitidine in Transfusion-Dependent, Epo-Refractory Patients with Lower-Risk Myelodysplastic Syndrome**

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Erythropoietin (EPO) and granulocyte colony-stimulating factor (G-CSF) are treatments that encourage the body to make more blood cells in the bone marrow. When used alone or in combination, EPO and G-CSF help about 30% of patients with low- or intermediate-1-risk MDS stop needing regular blood transfusions. Azacitidine, (Vidaza®) is another treatment option that can help patients with lower-risk MDS need fewer blood transfusions.

This study looked at whether azacitidine leads to transfusion independence in patients with lower-risk MDS who don’t respond to EPO or G-CSF, as well as the benefits of combining azacitidine and EPO. The authors reported on 21 patients. 15 had been treated with azacitidine alone and 6 patients who had been treated with a combination of azacitidine and EPO. All patients had low-risk or intermediate-1-risk MDS and needed transfusions of at least four red blood cell units every 4 weeks. Median patient age was 69 years and patients had had MDS for a median of 2 years. Eighteen of the patients were male. All of the patients had not responded to EPO and G-CSF for at least 8 weeks. Patients were treated with six cycles of azacitidine, followed by three more azacitidine cycles and EPO in those who still needed regular red blood cell transfusions.

**Key Findings:**
- Adding EPO to azacitidine did not lead to transfusion independence.
- Twelve patients had at least one serious side effect. The most common effects were febrile neutropenia (shortage of neutrophils, a type of white blood cell, with fever), infection, and diarrhea.
- Three patients had to stop the study treatment because of long-lasting neutropenia or because their MDS progressed to AML.

**Conclusions:**
The response rate to azacitidine was lower in this study than in previous studies that had less strict enrollment criteria. More studies are needed to look at the benefits of combining azacitidine and EPO.
Azacitidine and Lenalidomide

3799 Safety and Efficacy of a Combination of 5-Azacitidine Followed by Lenalidomide in High-Risk MDS or AML Patients with Del (5q) Cytogenetic Abnormalities – Results of the “AZALE” Trial

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Up to half of patients with high-risk MDS or AML respond to azacitidine (Vidaza®). Azacitidine has fewer side effects than chemotherapy. Patients with a del5q chromosome deletion (del 5q) do not respond as well to azacitidine as those with other forms of MDS. However, lenalidomide (Revlimid®) is an effective treatment in some patients with del del5q MDS.

This Phase I clinical trial tested a combination of lenalidomide and azacitidine in 20 patients with high-risk MDS, AML that had relapsed or had not responded to other treatments, or newly diagnosed AML. All of the patients had del 5q and none was eligible for conventional chemotherapy. Median age was 69 years and the median time since diagnosis was 8 months. Seven of 15 patients, in the study, showed a p53 gene mutation.

Patients received azacitidine treatment at one dose for the first 5 days, followed by rising doses of lenalidomide for the next 14 days. Patients, who had a complete remission, or the disappearance of all signs of MDS or AML, were treated with a combination of azacitidine and lenalidomide every 8 weeks until their disease progressed.

Key Findings:
- Four patients (20%) had to stop treatment because of infections, thrombosis (blood clot), or low blood cell counts.
- 13 (65%) showed improvement in their blood or bone marrow with stable disease after treatment.
- Five of 7 (71%) patients with a mutation in the p53 gene responded to the combination treatment.

Conclusions:
Azacitidine and lenalidomide can be effective when used in combination to treat MDS. The combination seems to be especially effective in patients with high risk MDS, del 5q and p53.

607 Final Results from the Phase 2 Continuation Study of the Lenalidomide and Azacitidine Combination in Patients with Higher-Risk Myelodysplastic Syndromes (MDS)

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This Phase II clinical trial was designed to evaluate the safety and efficacy of a combination of lenalidomide (Revlimid®) and azacitidine (Vidaza®) treatment for higher-risk MDS. The study included 36 patients with a median age of 68 years. Thirteen patients (36%) were female, and median time from diagnosis was 8 weeks. All patients had intermediate-1, intermediate-2, or high-risk MDS. The patients were treated with 75 mg/m2 of azacitidine each day for 5 days and 10 mg of lenalidomide each day for 21 days of a 28-day cycle. All patients had at least five cycles of treatments during the study.
Key Findings:
- The most common complications were neutropenia (shortage of neutrophils, a type of white blood cell) with fever, heart or lung problems, and infections.
- 71% of the 35 patients responded to the treatment.
- Median time to response was 3 months.
- Patients who achieved a complete response survived for a median of 27 months at the last study assessment.

Conclusions:
The combination of lenalidomide and azacitidine is well tolerated and effective for treating higher-risk MDS.

Azacitidine and Panobinostat

459 Determination of a Phase II Dose of Panobinostat in Combination with 5-Azacitidine in Patients with Myelodysplastic Syndromes, Chronic Myelomonocytic Leukemia, or Acute Myeloid Leukemia

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Panobinostat is an drug that changes gene activity in MDS. The main goal of this Phase I clinical trial was to find the maximum dose that patients could tolerate of panobinostat combined with Vidaza® (azacitidine). The researchers also measured the combination’s safety, side effects, and effectiveness against acute myeloid leukemia (AML).

The study included 31 patients (median age 70 years) with MDS, chronic myelomonocytic leukemia (CMML), or AML. The patients were given 20 mg of oral panobinostat on days 3, 5, 8, 10, 12, and 15 of a 28-day cycle. All of the patients were also treated with azacitidine on the first 7 days of each cycle. If the patients didn’t have serious side effects, their doctor increased their panobinostat dose by 10 mg during the next 28-day cycle.

Key Findings:
- One patient had to stop taking panobinostat at 20 mg due to neutropenia (shortage of neutrophils, a type of white blood cell) with fever. Three patients stopped taking panobinostat at 30 mg because of dehydration and fatigue, colitis (inflammation in the colon), or irregular heartbeats. Two patients stopped panobinostat at 40 mg as a result of high bilirubin levels in the blood (a sign of liver problems) or nausea and vomiting.
- The most common side effects were digestive problems, fatigue, and low blood cell counts.
- Four of 16 patients with AML or CMLL (2 at 30 mg and 2 at 40 mg) achieved a complete response, and 6 patients (4 at 30 mg and 2 at 40 mg) had stable disease after a median of two treatment cycles (2 months).

Conclusions:
Panobinostat at 30 mg/day was effective in combination with azacitidine in patients with intermediate-2 or high-risk MDS, CMML, or AML. More studies are needed to be certain of its safety and effectiveness in larger numbers of patients.
Azacitidine and Vorinostat

608 Final Report of a Phase II Study of 5-Azacitidine and Vorinostat in Patients with Newly Diagnosed Myelodysplastic Syndrome (MDS) or Acute Myelogenous Leukemia (AML) not Eligible for Clinical Trials because Poor Performance and Presence of Other Comorbidities

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Clinical trials of treatments for MDS or AML often exclude patients with other health problems (comorbidities) or limited ability to perform routine activities (poor performance status), those with HIV or another form of cancer. These patients, without the benefit of treatment, survive less than 60 days. The authors conducted a Phase II clinical trial of azacitidine (Vidaza®) and vorinostat (Zolinza®) in patients who were not eligible for other clinical trials.

The maximum of 30 people were able to participate. Median patient age was 74 years. Patients were treated with 75 mg/m2 of azacitidine every day for 5 days every 3 to 6 weeks and 200 mg of vorinostat three times a day on days 1–5 of each azacitidine cycle.

Key Findings:
• Patients tolerated the combination treatment well, except that one patient developed severe nausea and vomiting.
• 80% of patients survived for at least 60 days with a median of 7 months.
• 30% had complete remission. Of the 16 patients whose disease did not respond to the azacitidine and vorinostat, 8 had stable disease for more than 8 weeks.

Conclusions:
A combination of azacitidine and vorinostat has similar safety and effectiveness in patients with comorbidities. The results call into question the customary eligibility criteria for Phase I and II clinical trials.

Decitabine

3812 Randomized Open-Label Phase II Study of Decitabine in Patients with Low- or Intermediate-1 Risk Myelodysplastic Syndromes


The goal of this Phase II clinical trial was to find out whether low-dose subcutaneous (under the skin) doses of decitabine (Dacogen®) might be effective and safe in patients with lower-risk MDS. Two groups of patients with low- or intermediate-1 risk MDS underwent subcutaneous administration of decitabine on 3 consecutive days every 28 days (Arm A) or every 7 days for 21 days (Arm B).
The average of these 65 patients age was 68 years with 69% being men. The average time between diagnosis and decitabine treatment was 3.6 months. About a third (29%) of the patients had low-risk MDS.

Key Findings:
• The trial ended early because overall improvement was superior.
• 40% of patients stopped needing transfusions.

Conclusions:
Subcutaneously administered decitabine is effective and well tolerated in patients with lower-risk MDS. The results of this trial exceeded their positive expectations and was able to stop earlier than expected.

**Erythropoiesis-Stimulating Agents**

**2799 Treatment with Erythropoietic Stimulating Agents in IPSS Lower Risk MDS: Outcome Comparison between 5q- and Non 5q- MDS Cases**

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Patients with MDS have low counts of red blood cells, white blood cells, and/or platelets. By encouraging the body to make more red blood cells, erythropoiesis-stimulating agents (ESAs) can cure anemia in many patients with lower-risk MDS. But not all patients respond to ESAs, such as patients with 5q chromosome deletion abnormality (del 5q). Also, patients who are treated with ESAs often need blood transfusions again within 2 years.

This study’s goal was to compare the safety and effectiveness of ESAs in patients with lower-risk MDS with and without del 5q.

The researchers studied the medical records of 239 patients with low-risk and intermediate-1-risk disease who had been treated with ESAs. Eighty-two patients had del 5q and 75% of these patients were female. Only 37% of patients without del 5q were female.

Key Findings:
• Levels of natural EPO, a protein that causes the bone marrow to make more RBCs, were higher at diagnosis in patients with del 5q.
• Patients with lower EPO levels in the blood at diagnosis had a better response to ESAs.
• Response rates to ESAs were 18% in patients with del 5q and 57% in patients without del 5q. In addition, responses to ESAs didn’t last as long in patients with del 5q as in patients without it.

Conclusions:
Patients with del 5q are less likely to respond to ESAs. Their natural EPO levels tend to be higher at diagnosis and stay higher than in patients without del 5q. ESAs might be useful as first-line treatment for patients with lower-risk MDS.
Stem Cell Transplant and Hypomethylating Agents

1707 Allogeneic Hematopoietic Stem Cell Transplantation (AHSCT) Versus Hypomethylating Agents (HMA) in Patients with Myelodysplastic Syndrome (MDS): A Case-Control Study

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Hematopoietic stem cell transplant (HSCT) is the only cure for MDS. This procedure involves the infusion of healthy blood-forming (hemapoietic) stem cells from a donor. The donor’s stem cells (known as a graft) enter the bone marrow, where they form cells. The transplant is allogeneic when the cells come from a donor who is not the patient.

Only a small proportion of patients with MDS are eligible for the procedure. Patients who do undergo HSCT have a risk of complications. The authors compared data on 53 patients who had undergone an allogeneic HSCT with data on a control group of 40 patients treated with a hypomethylating agent, such as azacitidine (Vidaza®) or decitabine (Dacogen®), between January 1988 and April 2008 at the M.D. Anderson Cancer Center. None of the patients had been treated for MDS before their HSCT or the hypomethylating agent treatment. Median patient age was 51 in the HSCT group and 54 in the control group.

Key Findings:
• 61% responded to hypomethylating treatment
• 52%) achieved a complete response with the hypomethylating treatment.
• Median survival was 25 months in the hypomethylating agent group.
• 23% of patients treated with a hypomethylating agent survived for at least 8 years.
• Median survival was 26 months in the HSCT group.
• 24% of patients who underwent HSCT survived for at least 8 years

Conclusions:
Hypomethylating treatment produces similar survival rates at 2 and 8 years to stem cell transplants in MDS.
**IMPACT OF TREATMENT ON QUALITY OF LIFE**

2796 Association of Changes in Transfusion Status with Changes in Health-Related Quality of Life of Real-World Patients with MDS across Six Months of Treatment with Azacitidine

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Patients with MDS who need regular blood transfusion report poorer quality of life than those who are transfusion independent. The purpose of this study was to learn more about relationship between transfusion dependence or independence and quality of life in patients with MDS during azacitidine (Vidaza®) treatment by reviewing information from 156 patients with MDS who had been treated with azacitidine for at least 56 days.

Key Findings:
- At the start of the study, 85 patients needed regular blood transfusions but only 44 still needed transfusions at 6 months.
- Health improved in patients who stopped needing transfusions but got worse in those who still depended on transfusions.
- Patients’ physical functioning improved over time, but emotional, mental, and social functioning did not.
- Transfusion-independent patients reported less fatigue than patients who needed regular transfusions.

Conclusions: Quality of life improves for MDS patients taking azacitidine when they no longer need regular transfusions. Improvement was seen in physical and role function as well as reduced fatigue.

3151 An Evaluation of Health Care Utilization, Risk of Infection and Bleeding Among MDS Patients during Periods of Transfusion Dependence or Independence with or without Lenalidomide Therapy

B. Douglas Smith, M.D., Dalia Mahmoud, Henry J. Henk, Ph.D., and Zeba M. Khan, Ph.D.

One of the goals of lenalidomide (Revlimid®) treatment is reducing the need for regular blood transfusions. Lenalidomide might also prevent some of the other challenges with MDS such as bleeding problems and infections.

The authors studied information from a national U.S. health plan on 3,574 patients who had been treated for MDS between 2007 and 2009. The patients were 66 years old, on average, and 51% were male.

Key Findings:
- Infections and bleeding were most common in patients who needed transfusions and who were not on lenalidomide.
- Hospitalizations and emergency room visits were more common in patients who needed transfusions, regardless of whether the patients were being treated with lenalidomide at the time.

Conclusions: Lenalidomide may be having an effect on the underlying biology of MDS due to the decrease in infections and bleeding. Patients on active lenalidomide treatment do not have higher rates of hospitalization or emergency room visits.
Patients with MDS often have infections due to neutropenia (low counts of neutrophils, a type of white blood cell) and bleeding due to thrombocytopenia (low platelet counts). These complications can lead to emergency room visits, hospitalizations, and disease-related death.

The study included 3,886 patients who had enrolled in a national U.S. health plan and were treated for MDS between 2007 and 2009. The average patient age was 67 years. The authors examined the frequency of infections and major bleeding in patients with MDS. The authors compared periods when patients received blood transfusions or active treatment with azacitidine (Vidaza®), decitabine (Dacogen®), or lenalidomide (Revlimid®) to when they were not.

Key Findings:
• Patients on active treatment had more infections and bleeding than those not on active treatment.
• Infections and major bleeding were less common during periods of transfusion independence.
• Rates of infections and bleeding events were similar in all transfusion-dependent patients.

Conclusions:
Active MDS therapy reduces patients’ risk of infection and serious bleeding, use of health care resources, and frequency of MDS-related symptoms. The authors suggest that active treatment be considered in all transfusion-dependent MDS patients.
NEW STRATEGIES FOR PREDICTING TREATMENT RESPONSE AND COMPLICATIONS

Predictors of Hypomethylating Agent Response

3811 Predictive Parameters for Infections during Azacitidine Therapy in High Risk MDS Patients

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Neutropenic fever caused by a shortage of neutrophils (a type of white blood cell) is a known side effect of azacitidine (Vidaza®). Patients with this complication run a high risk of infection. Antibiotics and granulocyte colony-stimulating factor (G-CSF) can sometimes prevent febrile neutropenia. But predicting which patients will develop this complication and therefore need antibiotics or G-CSF is challenging.

A group of Israeli researchers developed a predictive model of infection during each azacitidine cycle. They based their model on information from 82 patients with high-risk MDS and 16 patients with AML who had undergone azacitidine treatment. Of these 98 patients, 57 (58%) were male and 65 (67%) did not need regular blood transfusions. Their median age was 71 years and the median time between diagnosis and start of azacitidine treatment was 187 days.

Key Findings:
• The most significant risk factors for infections during azacitidine therapy were dependence on blood transfusions before starting azacitidine treatment and a low platelet count before each cycle.
• Although neutropenia and age are risk factors for infections in general, they did not have a significant effect on patients’ risk of infection in this study.

Conclusions:
Each patient’s platelet count and whether or not that patient depends on blood transfusions are important considerations before each azacitidine cycle. This information can be useful to predict the patient’s infection risk and decide whether to give the patient antibiotics, G-CSF, or adjust the treatment plan.

3841 Platelet Doubling after the First Azacitidine Cycle is a Promising Predictor for Response in MDS, CMML and AML Patients in the Dutch Azacitidine Compassionate Patient Named Program

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Several studies have shown that azacitidine (Vidaza®) is an effective treatment for high risk MDS, AML, and CMML. This study was designed to evaluate azacitidine’s efficacy for low and intermediate risk MDS, AML, and CMML in the real-world conditions of daily practice.

The study included 90 patients with MDS, CMML, or AML who had been treated in a Dutch program. The Dutch authorities had given the investigators temporary permission to use azacitidine even though these patients weren’t part of a clinical trial. The patients underwent five cycles, on average, of azacitidine treatment.
NEW STRATEGIES FOR PREDICTING TREATMENT RESPONSE AND COMPLICATIONS

Key Findings:
• After the first azacitidine cycle, 14 of the 90 patients had improved their platelet count to levels at least twice as high as before treatment and were seen in all risk groups.
• Patients with a higher platelet count after one treatment cycle tended to survive longer than patients whose platelet count didn't rise as quickly.
• Azacitidine was equally effective in low and intermediate risk MDS.

Conclusions:
Azacitidine was shown to be effective for patients with different risk levels of MDS, CMML, and AML.

Predictors of HSCT Response

4126 Early Hematopoietic Stem Cell Transplant Is Associated with Improved Outcomes in Children with MDS
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Hematopoietic stem cell transplant (HSCT) is the preferred treatment for childhood MDS. A group of researchers analyzed data from 37 children, adolescents, and young adults who had HSCT at the University of Minnesota Amplatz Children’s Hospital between 1990 and 2010. The patients’ ages ranged from 1 to 21 years. Of these patients, 20 had primary MDS and the remaining 17 had secondary MDS, which is a result of a prior treatment or disease.

Key Findings:
• 89% of achieved engraftment.
• Overall survival was 70% at one year and 53% at 3 years.
• 19% of patients had chronic graft-versus-host disease (GVHD) at one year.

Conclusions:
Referral for HSCT soon after diagnosis is recommended for children with MDS.

Predictors of Treatment Complications

3014 Prognostic Pre-Transplant Factors in Myelodysplastic Syndromes Primarily Treated by Allogeneic Hematopoietic Stem Cell Transplantation: A Retrospective Study on Behalf of the MDS Subcommittee of the Chronic Leukaemia Working Party of the EBMT
Eline Cremers, Anja van Biezen, StatAnalyst, Liesbeth C. de Wreede, Ph.D., Marijke Scholten, Antonin Vitek, Jürgen Finke, Uwe Platzbecker, M.D., Dietrich Beelen, Rainer Schwerdtfeger, Liisa Volin, Nikolaos Harhalakis, Anton Schattenberg, Arnon Nagler, Theo de Witte, M.D., Ph.D., and Nicolaus Kröger

Patients who undergo an allogeneic HSCT sometimes have excess iron in the blood (iron overload). Over time, iron overload can damage organs and tissues.

To study the effects of iron overload on relapse and survival after HSCT, the authors looked at information about 201 adults who had received allogeneic HSCT for MDS. Median patient age was 49 years, 59% of patients were male, and median time between diagnosis and transplant was 8 months. All of the patients received pre-transplant conditioning with chemotherapy or radiation.
NEW STRATEGIES FOR PREDICTING TREATMENT RESPONSE AND COMPLICATIONS

Key Findings:
• Overall survival was affected by iron levels in the blood, MDS subtype based on the World Health Organization’s classification system, and number of red blood cell units transfused before transplant.
• Success was also affected by patient age, blood counts, relationship of the donor, gender of the donor, time between diagnosis and HSCT, and whether the patient had comorbidities (diseases or conditions in addition to their MDS).

Conclusions:
• Iron overload and comorbidities do not have a significant impact on HSCT outcomes.
• The number of transfusions before HSCT increases the risk of relapse and reduces overall survival.
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.