**What is MDS?** (MDS Foundation, 2011)

- MDS is a group of bone marrow disorders. The bone marrow is the factory for the production of blood cells including red blood cells, white blood cells, and platelets. In MDS, the bone marrow is abnormal because of a variety of malignant changes. The result is ineffective production of normal mature blood cells, resulting in low blood counts (cytopenias). Various subtypes of the disease exist with variable prognoses, treatment options, and risk of developing leukemia.

**Is MDS cancer?** (Bejar et al., 2011)

- The diagnosis of MDS requires a bone marrow biopsy and aspirate. The specimen is analyzed by pathologists specializing in blood disorders. The diagnosis of MDS requires specific malignant features such as dysplasia or cytogenetic abnormalities. Research has identified molecular abnormalities thought to play a role in the development of MDS. Given the underlying malignant features of the disease, MDS is considered a form of blood cancer.

**What causes MDS?** (Greenberg et al., 2011; Sekeres, 2011; Sekeres et al., 2011)

- The cause of MDS is unknown in more than 80% of diagnosed patients. It is more common in men (male to female ratio is 4.5:2 per 100,000). As with many types of cancer, older age is a predisposing factor. The majority (86%) of patients with MDS are older than age 60. Exposure to chemicals such as benzene and other solvents and tobacco smoke are known to increase the risk of developing MDS. Patients who receive certain types of chemotherapy or radiation treatment for other cancers may be at increased risk of developing treatment-related MDS.

**Is MDS inheritable?** (Sekeres, 2011)

- Inherited genetic predisposition for developing MDS and congenital abnormalities is rare.
- Before 1973, only 143 cases of MDS were reported. Today, based on data analysis techniques, the estimated incidence varies from 15,000–162,000 cases per year. The wide variation in these data highlights the challenging diagnostic features of MDS. As diagnostic features of MDS become more familiar to clinicians, MDS is detected more often in patients presenting with cytopenias (low blood counts). The development of therapeutic options may increase the number of patients considered for diagnostic evaluation. Increasing numbers of patients are being treated with cytotoxic therapies, raising the potential for secondary malignancies, including MDS (Cogle et al., 2011; Ma et al., 2007; Sekeres, 2011).

**What are the symptoms of MDS?** (Kurtin, 2011)

- Many patients are asymptomatic and are diagnosed on routine screening. Others present with vague symptoms associated with one or more cytopenias (low blood counts).
  - Fatigue, shortness of breath, palpitations (common anemia symptoms)
  - Fever, recurrent or prolonged infections (common neutropenia symptoms)
  - Bruising, petechiae, or bleeding (common thrombocytopenia symptoms)

**How is MDS diagnosed?** (Kurtin, 2011; National Comprehensive Cancer Network, 2011)

- The initial patient evaluation most often includes a complete blood count (CBC), which reveals normocytic or macrocytic anemia, normal to decreased numbers of neutrophils, and variable platelet counts. Anemia is observed in 90% of patients with MDS, either at initial presentation or during the course of their disease. A careful history and additional laboratory analysis should be pursued to exclude other causes of cytopenias.

**What are my treatment options?** (Greenberg et al., 2011)

- Treatment selection for MDS is individualized based on recognized disease characteristics and risk analysis. Treatment options vary by region based on approval mechanisms. The goals of therapy for MDS are based on individualized disease characteristics, patient characteristics, and risk category. In the United States, the International Prognostic Scoring System (IPSS) categorizes the MDS subtypes into two major groups: low- and intermediate-1–risk or intermediate-2– or high-risk. The goal of therapy for each category differs based on expected survival and risk of leukemic transformation. A revised IPSS is being developed to further refine these risk categories and guide treatment selection. The World Health Organization Prognostic Scoring System, with similar treatment guidelines, is commonly used in Europe.

**How likely am I to get better with the treatment?**

- The response to treatment for patients with MDS varies according to IPSS risk categories as well as other prognostic indices. Allogeneic bone marrow transplantation remains the only potential cure to date. However, patients may benefit from currently available therapies, and durable responses have been reported.

**How long will the treatment take to work?**

- A minimum of four to six months of treatment is required to evaluate initial response, and the best response may not be evident until after as many as nine months of therapy.

**How long can I expect to be treated?** (Kurtin, 2011)

- Because of the limited number of treatment options and the incurable nature of the disease, disease-modifying treatments for MDS are continued until disease progression or unacceptable toxicity.

**What are the common side effects of treatment, and what can be done to control them?** (Kurtin, 2011; Kurtin & Demakos, 2010)

- The most common side effect for all therapies for MDS is myelosuppression including anemia, neutropenia, and thrombocytopenia.
  - Weekly complete blood count, differential, and platelet counts are recommended for the first eight weeks of treatment.
  - Cytopenias are expected to get worse before they get better.
  - Supportive care strategies are encouraged, including growth factors and transfusions.
  - Drug-specific guidelines for dose modifications or holidays are provided by each drug manufacturer based on clinical trials.
- Nausea and vomiting: all agents
  - Administration of antinausea medication is an effective strategy to minimize nausea and vomiting.
- Constipation: all agents—also thought to be related to administration of $5HT_3$ antagonist antiemetics
  - A regular bowel regimen that includes a stool softener and laxatives, as needed, will reduce the severity of constipation associated with treatment.
- Renal and hepatic toxicities—more common in older adults
  - Baseline and ongoing laboratory analysis will allow early identification and prompt intervention for potential renal and hepatic toxicities associated with treatment.
- Drug-specific adverse events

*(Continued on the next page)*

## APPENDIX A. Most Frequently Asked Questions by Patients With Myelodysplastic Syndromes (MDS) and Their Caregivers Participating in the MDS Foundation Patient Advocacy Programs or Quality-of-Life Sessions

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*(Continued from the previous page)*

  - Azacitidine: injection-site reactions
  - Lenalidomide: rash, pruritus, diarrhea, safety program for lenalidomide
- Iron overload
  - Chelation therapy may be associated with cytopenias and renal and hepatic toxicities.

**What new treatments are on the horizon to treat patients with MDS?** (Garcia-Manero, 2011, Kurtin, 2011)

- Clinical trials continue to explore treatment options for MDS and are always recommended for diseases that have limited treatment options, such as MDS. These trials offer hope to patients who have had limited benefit from approved therapies or have high-risk disease thought to have limited potential for benefit from these therapies. Each country has approved mechanisms for clinical trial oversight and drug approval.

**Are blood transfusions dangerous?** (Kurtin, 2011; National Comprehensive Cancer Network, 2011)

- The normal body mechanism for control of iron stores is highly efficient. Each unit of transfused blood delivers iron in excess of the normal daily requirements. After repeated transfusions, excess iron storage exceeds the levels that can be controlled by normal iron homeostatic mechanisms, leading to the formation of toxic iron storage and subsequent cellular damage.
- A strong correlation exists between transfusion intensity (number of units received over time) and organ damage.
- Iron accumulation results in end-organ damage.
  - Heart: congestive heart failure
  - Liver: elevated liver function tests, hepatomegaly, pain
  - Endocrine glands: diabetes
  - Bone marrow: dysfunctional hematopoiesis
- Based on these data, transfusion dependence is considered an indication to initiate disease-modifying treatment for MDS

**How do I select a bone marrow transplantation center?** (National Marrow Donor Program, 2011)

- There are many factors to consider when choosing a transplantation center. Some patients look at a center's experience with certain diseases or ages of patients. Other patients choose a center close to their family and friends. Some things you and your referring doctor can find out about transplantation centers are the following.
  - What experience does this transplantation center have?
  - What do transplantation center survival statistics mean?
  - How does the number of transplantations conducted for your disease at this center compare with other centers?
  - What are the patient- and donor-matching levels required at this center?
  - What are some of the pretransplantation costs at this center?
  - Is this center covered under your insurance plan?

**What can I do to keep myself healthy?**

- The general principles of a healthy lifestyle remain important. A balanced diet, daily activity and exercise as tolerated, and participation in activities of enjoyment are important to maintain optimal health and well-being. Ongoing management of other health conditions is important to optimal health and continued eligibility for future treatment options.

## APPENDIX A. Most Frequently Asked Questions by Patients With Myelodysplastic Syndromes (MDS) and Their Caregivers Participating in the MDS Foundation Patient Advocacy Programs or Quality-of-Life Sessions *(Continued)*

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