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mds news
newsletter of the myelodysplastic syndromes foundation

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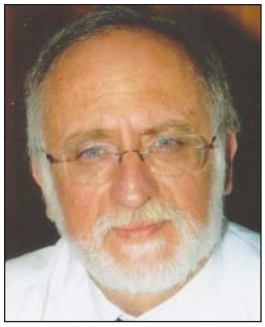
From the Guest Editor's Desk

10th Int'l Symposium on Myelodysplastic Syndromes



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Patras, Greece: May 6–9, 2009

The city of Patras, the third largest city in Greece and the Cultural and Convention Center of its university, had the honor of hosting the 10th International Symposium on Myelodysplastic Syndromes, May 6–9, 2009. In this symposium, all new information on the classification, pathogenesis, prognostic factors, and on the latest treatment approaches for MDS were discussed. The symposium was attended by approximately 1200 participants originating from 55 countries all over the world, a really satisfactory figure in view of the emerging news updates on the flu pandemic the first days of May. The symposium was chaired by Professor Nicholas Zoumbos, Head of the Department of Internal Medicine and Hematology at the University of Patras, and whose main interest and involvement is the area of bone marrow failure syndromes and MDS in particular.

During the two and a half active days of the symposium, 42 invited lectures were presented in 11 plenary sessions by distinguished expert speakers. Moreover, there were 36 selected oral communications, and by adding the six presentations of the young investigator's plenary session, a total number of 42 oral presentations were given, which is higher than the respective number of the previous symposia. There were 139 poster presentations, divided into two sessions, and 181 submitted abstracts for presentation. The symposium venue was nice, with continuous availability of coffee, refreshments, and snacks. The fine weather also permitted many participants the opportunity to visit the famous ancient ruins of Delphi and Olympia, which stand at a distance of about 100 kilometers from Patras.

The Opening Ceremony was bright and consisted of music and folk dancing, the *Suzanne Fleischman Memorial Lecture* and a lecture on Greek medical history. The musical part of the ceremony combined the traditional Greek music and the folk dancing by the employees and students of the University of Patras Dance Club, with the modern adaptation of Manos Hatzidakis' "Reflections," performed by the Greek Rock Band "Raining Pleasure." The *Suzanne Fleischman Memorial Lecture* was given by David Cella, Professor of Psychiatry and Behavioral Sciences at Northwestern University Feinberg School of Medicine, Evanston, Illinois, and was entitled "Symptom and treatment burden: Effect on the quality of life." Finally, the archeologist Professor Michael Petropoulos gave a very interesting lecture, presenting the Asclepius Temples of Peloponnese and analyzed their significance as medical, social, and spiritual centers of the ancient times. The opening ceremony ended with a reception in the foyer of the Convention Center.

There were also some important novelties presented at this symposium. First, the Young Investigator Plenary Session was introduced, in which the six better original research abstracts, presented by investigators younger or equal to 35 years old, were presented. Indeed, there were six very interesting presentations, all of which were equally awarded. Second, a "Challenge the Expert" session, chaired by Moshe Mittelman and Constantinos Tsatalas, was organized for the first time. In this session, four interesting case studies were presented, with unique clinical features and courses, which flared up lively discussion with the audience. Third, for both poster sessions there was a poster walk, chaired by a symposium committee, which encouraged discussion on the presented material and improved communication between presenters and other participants. The poster committees evaluated all posters and awarded the best poster of each area of interest of MDS. Finally, a Patient and Family Forum was organized for the first time. This was a three hour informative session, adapted for patients and non-health professionals in general, in which the natural course, clinical features, newer treatment modalities, follow-up recommendations and guidelines, as well as issues of psychological support and of quality-of-life were analyzed. This forum was attended by approximately 70 patients and their relatives and/or caregivers, and was particularly successful, in view of all the questions which were addressed. In fact some patients, unable to attend for various reasons, have asked to reorganize such an informative patient-addressed forum.

The "Tito Bastianello Award," which launched in Florence in 2007 to support MDS research in memory of the homonymous person who died of MDS, was given to all the presenters of the Young Investigator's Plenary Session.

Particularly interesting and once more very successful was the Morphology Workshop, chaired by John Bennett and Jean Goasguen and attended by about 150 participants. It became clear that even now, in the era of the very sophisticated diagnostic methods, morphology remains the cornerstone for diagnosis and prognosis of MDS.

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The Nursing Educational Program on MDS, which was initially introduced at the 9th International Symposium on MDS in Florence, was successfully organized for the second time by the MDS Foundation Nursing Advisory Board *(see page 12)*. The Nursing Program was arranged this time in parallel with the rest of the scientific program of the symposium and was held in two sessions, split into two consecutive afternoons. The Nursing Program was organized and directed by Kathy Heptinstall, and the availability of a concurrent translation into Greek gave the enthusiastic group of 30–35 nurses the opportunity to attend the event. It appears that the Nursing Program is going to be a standard part of the educational program of every MDS international symposium in the future.

Following is a review of some of the most important information which was presented during the 10th International Symposium on MDS.

Approaching Immune Pathogenesis and Other Pathogenetic Aspects of MDS

The role of the immune system in the pathogenesis of MDS is evolving. Substantial information on this issue was discussed during the 10th International Symposium of MDS. The first roundtable of invited speakers and many oral and poster presentations were dedicated to the immune pathogenesis of MDS. Dr. G. Mufti reviewed the existing experience, supporting that all types of MDS share a more or less prominent underlying immunopathogenetic component. Dr. S. Nakao focused his lecture on the role of the immune system in the pathogenesis of low-risk MDS. He reported that about 20% of the patients with RA and RCMD, particularly those with profound thrombocytopenia and low bone marrow megakaryocyte count, bear PNH+ cells. These patients should be distinguished and should not be treated with chemotherapy or with hypomethylating agents but with immunosuppression, using ATG+cyclosporine-A. In support of the above-mentioned data are the data from a Greek group from Athens (A. Efthimiou et al.), who found PNH+ cells in 11 out of 71 patients with MDS.

Dr. Epling-Burnette et al. investigated the relationship between treatment with ATG, peripheral blood lymphocyte subpopulations and homeostatic T-cell proliferation. They found that effector memory cells comprise the dominant T-cell population and CD8+ T-lymphocytes predominate, with a high rate of homeostatic turnover. These cells are directed by specific cytokines implicated in the pathogenesis of MDS and can be used in the monitoring of response to various immunomodulatory treatments.

Clonal expansion in MDS is at least in part influenced by the interaction of the effector cells of the immune system and the dysplastic hematopoietic cells. Dr. A. Kondo et al. from Tokyo presented data showing that B7-H1 co-stimulatory molecules, expressed on blast cells of patients with MDS, interact with their receptors (PD-1 molecules) on T-cells and induce T-cell apoptosis. Blocking the B7-H1#PD-1 co-inhibitory pathway in co-culture experiments of MDS cell lines and normal T-lymphocytes resulted in increased T-cell proliferation and decreased apoptosis. Therefore, the aberrant expression of B7-H1 molecules on MDS progenitors might represent a mechanism of escape of immune surveillance and of clonal expansion.

These effector T-cells are mainly or exclusively distributed in the bone marrow and may not be found in the peripheral blood. Dr. F. Alfinito et al. from Naples showed that in the bone marrow of patients with low/intermediate-1 risk MDS adaptive immune effector cells and CD4+CD25^{high} Foxp3+ cells (T-reg) are clustered and can be found in association with CD54+CD8+ T-lymphocytes. In this study, the proportion of marrow T-regs paralleled the IPSS score, and therefore this proportion could represent another prognostic factor for MDS.

Another group from Tokyo (H. Tamura et al.) investigated the significance of the expression of WT1 mRNA and of anti-WT1 antibodies in patients with MDS and AML evolved from MDS. They found that WT1 mRNA levels were positively correlated with disease aggressiveness, the IPSS score, and negatively with the overall survival of patients; whereas levels of IgM- and IgG anti-WT1 were positively correlated with platelet count and survival. Therefore, anti-WT1 immunotherapy might represent a form of targeted therapy for specific subgroups of patients with MDS.

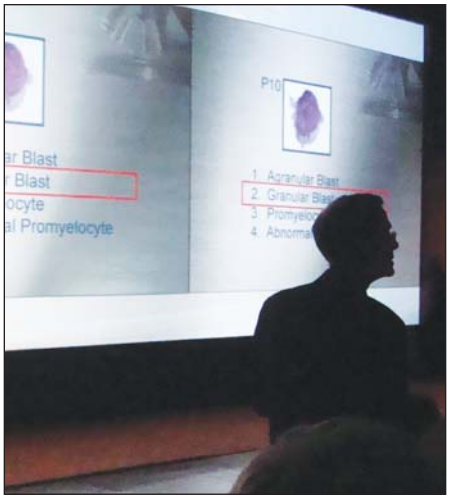
Finally, the group from Patras (E. Solomou, N. Zoumbos et al.) investigated the induction of expression Th17 and Th1/17 cells in peripheral blood mononuclear cells of patients with MDS, following PHA stimulation. Th17 as well as Th1/17 cells were found significantly increased in patients with MDS compared to controls. These CD4+ cell subpopulations are the IFN-α secreting cells, through the activation of the transcription factor T-bet, and may be implicated in the pathogenesis of MDS.

Regarding other pathogenetic aspects of this disease, at least four symposium presentations focused on the role of oxidative stress, expressed as levels of intracellular Reactive Oxygen Species (iROS), as a mechanism of inducing cellular senescence and genomic instability, and hence favoring the development of cytogenetic abnormalities and disease evolution. Since measurement of iROS by flow cytometry is used more and more in various research studies, L. Chan et al. from Toronto evaluated the reliability of this technique and found that, although the intraexperimental variation is very low, measuring the same person's iROS levels in consecutive days produces significant inter-experimental variation, probably due to instability of the reagent. In another presentation the same group found a very strong correlation between the iROS levels of peripheral blood lymphocytes with those of bone marrow lymphocytes and of CD34+ cells in normal subjects and in patients with low-risk MDS, but no correlation in patients with high-risk MDS and AML, apparently due to increased oxidative stress which occurs in the bone marrow of these patients. The Patras group (G. Voukelatou et al.) measured iROS levels in 23 patients with MDS and 12 matched controls, and correlated the results with the amount of modified proteins, estimated by OxyBlot and with the levels of the antioxidant enzymes catalase and Mn-superoxide dismutase. They found increased iROS levels in both low- and high-risk MDS patients and concurrently higher amounts of modified proteins from oxygen free radicals. Interestingly, the expression of the two antioxidant enzymes were found decreased in the CD34+ cell compartment of the patients, a finding implying antioxidant enzyme insufficiency as an additional mechanism of generation of oxidative stress in the progenitor cells of MDS patients. In another presentation from Patras (D. Watson et al.), the mean baseline DNA damage in peripheral blood cells detected with the comet assay was found increased in two out of four patients with MDS. Moreover, the incubation of the cells with H_2O_2 resulted in significant elevation of DNA damage indexes in MDS patients compared to controls.

Employees and students of the University of Patras Dance Club.

The issue of cellular senescence as possibly contributing to the pathophysiology of MDS was approached in the invited lecture of A. Kimura who mentioned a recent finding of his group that BMI-1 expression of CD34+ cells is correlated to IPSS and may represent a prognostic marker of disease progression. BMI-1 is a gene involved in the RAS downstream signal, and its expression is important for the intensive cellular proliferation and self-renewal of the cell. Mutations of the BMI-1 gene are associated with a phenotype of delayed or arrested proliferation without block of differentiation, which is a phenotype of cellular senescence. In a presentation of the Patras group (I. Constandinidou et al.), although they did not find differences in BMI-1 expression on CD34+ cells of patients with MDS, they did find higher levels of p16 and of phosphorylated p53 in low-risk MDS, suggesting that cellular senescence may contribute to the ineffective hematopoiesis of MDS.

In another presentation the C3ORF9 gene encoding X010 protein was studied on 131 patients with various MDS subgroups and was found over expressed in patients with RA, RAEB and RAEBt, downregulated in CMML, and normal in RARS. The significance of these findings is as yet uncertain. H. Karlic et al. from Vienna investigated the function of estrogen receptor (ER), osteocalcin (OCN) and fat metabolism genes in 23 patients with MDS, and three matched controls. They reported a significant inhibition of all studied gene expression, due to hypermethylation, in 15 of the patients with less aggressive MDS, but not in the seven patients with RAEB and in two with AML, also studied. The interpretation of these findings is that genes regulating lipid and bone metabolism, also affecting the apoptotic process, are altered in many patients with MDS, and this should be further investigated. A similar approach was presented by P. Matsouka et al., who investigated the serum profile of metabolism-related cytokines in 72 patients with MDS. Their results demonstrated significantly elevated serum levels of osteocalcin and adiponectin and significantly decreased levels of leptin, insulin and IGF-1, compared to serum levels of 41 normal controls, whereas levels of grelin and PTH did not differ significantly between the two groups. The low levels of IGF-1 and leptin in patients with MDS were considered to be in accordance with the high rate of apoptosis of their bone marrow cells, since these are strongly antiapoptotic metabolic regulators.



Dr. John Bennett, MDS Foundation Chairman


Kathy Heptinstall (far right), MDS Foundation Operating Director, with attending nurses.

It is evident that many aspects of the lipid- and other metabolic pathways have not yet been clarified or even investigated in MDS, and their study may help the clarification of some important clinical features of these syndromes.

New Possible Molecular Targets in MDS

The continuous progress in the understanding of the molecular mechanisms, which are implicated in the pathogenesis of MDS, may identify new molecular targets for the design of tailored therapies, addressed to those patients who might carry a specific molecular marker. One such target might be TET2 gene. Four presentations in the 10th International Symposium of MDS investigated the mutational status of TET2 in MDS. In one presentation by the Groupe Francophone des Myelodysplasies, 59 mutations of this gene were identified in 46 out of 206 tested patients, more commonly among RAEB-1 patients, and in accordance to that study a group from the Netherlands and Belgium found mutations of this gene in 26% of 102 patients tested. In another work from Cleveland, mutations of the TET2 gene were associated with proliferative features of the MDS, CMML, or AML evolved from MDS, but no prognostic impact was found. According to another French group, TET2 is a tumor-suppressor gene, and its mutations occur in a CD34+CD38- cell and favor various evolution-promoting events. Other presentations have investigated different aspects of disease initiation and progression.

The issue of telomere length and of telomerase activity and its possible pathogenetic role in disease evolution of MDS has been reviewed in a nice lecture by Neal Young and has been investigated by three groups, leading to an equal number of interesting presentations. Professor Young with his vast experience on aplastic anemia reported that although response to immunosuppressive treatment of patients with aplastic anemia is not influenced by telomerase activity and telomere length, relapse rate and clonal evolution are significantly more common among patients with shortened telomeres and impaired telomerase activity. A Greek group from Thessaloniki (E. Verrou et al.) investigated the expression of hTERT mRNA variant transcripts A and B in 40 patients with MDS and 17 with AML. They found alternatively spliced hTERT mRNA variants, especially the Adel isoform in patients with low-risk MDS, implying a reduction of telomerase activity and consequently increased genomic instability. A group from Ukraine (D. Bazyka et al.) reported significantly lower telomere length and increased rate of apoptosis in 23 patients with RA, compared to controls, whereas the Czech group (H. Cechova et al.)

reported that treatment with hypomethylating agents increased significantly telomere length and telomerase activity.

One feature of leukemic cells might be the modulation of some nuclear receptors. A group from Toronto (C. Ichim et al.) found that, by up-regulating the orphan nuclear receptor NR2F6 in a chimeric mouse model, the animals exhibited morphological features of myelodysplastic syndromes, and a significant proportion of them developed acute leukemia. Since the expression of this receptor has been found to be deregulated among patients with MDS and CMML, one could anticipate that blocking this nuclear receptor might result in the prevention of the delay of leukemic transformation in patients with MDS.

Another well-recognized feature of the leukemic cells is survival advantage and resistance to chemotherapy-induced apoptosis. This is accomplished among others and by the upregulation of HSP90, and at least in solid tumors by the overexpression of Focal Adhesion Kinase (FAK). By evaluating 170 patients with MDS at diagnosis, a French group (L. Campos et al.) presented data of increased expression of HSP90, FAK, phosphorylated FAK and Akt in mononuclear cells and CD34+ cells of patients with RAEB, as compared to patients with RA and CMML. Interestingly, the inhibition of HSP90 in vitro by 17-AAG was associated by activation of apoptosis of these cells.

In two other presentations the proteasome activity was found to be decreased in both CD34+ and CD34- cells of patients with MDS, as compared to controls. This might be attributed to mutations of the *c-Cbl*, an E3 ubiquitin ligase, and these mutations were associated with poor prognosis of the patients. The attenuation of the activity of proteasome was interpreted as a mechanism possibly contributing to disease progression in MDS, by preventing the elimination of abnormal, mutated or oxidized proteins and prolonging the activity of activated tyrosine kinases, thus enhancing leukemic transformation.

A cooperative Greek group (I. Dahabreh et al.) investigated the frequency of JAK2 V617 mutation among 265 patients with MDS and found that only nine patients (3.4%) carried the mutation. The frequency was higher among patients with del-5q (8%), and patients carrying this mutation had higher neutrophil and platelet count, but no other difference in any morphologic or prognostic feature was noted. Finally, a Swedish group, investigating mechanisms of disease progression in 32 patients with del-5q, found that seven out of nine patients, whose disease evolved either as AML or with the acquisition of additional chromosomal abnormalities, expressed p53 and aberrant cytoplasmic nucleophosmin at the time of initial diagnosis; therefore, they suggest the expression of any of these two markers in these patients is an adverse prognostic factor.

Understanding the Pathophysiology of del(5q) and the Mechanism of Action of Lenalidomide

The impressive results of treatment with lenalidomide in patients with low-risk MDS, and particularly in those carrying the del-5q chromosomal abnormality, has stimulated many investigators and research groups to clarify the underlying pathophysiology of this specific chromosomal abnormality and the mechanism of action of lenalidomide in these patients. During the 10th International Symposium on MDS, there were many informative presentations on this topic.

The group from Salamanca-Spain (C. Santamaria et al.), which recently reported the existence of cytogenetic aberrations in mesenchymal stem-cells (MSC) of patients with MDS, presented new data demonstrating that MSC of these patients contain increased mRNA levels of PDGFα, TNFα and IL-32. mRNA levels of the latter two cytokines, as well as of FGF4, were found particularly elevated among patients with del-5q, thus explaining the development of a proapoptotic and thrombopoietic microenvironment, which characterizes this chromosomal abnormality. The Czech group has analyzed morphologic and prognostic aspects of dysmegakaryopoiesis and dyserythropoiesis among patients carrying del-5q in their karyotype, whereas L. Napoleone et al. presented a familial occurrence of MDS and del-5q.

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Dr. Wobus et al. from Dresden reported that although the in vitro treatment of MSC with lenalidomide did not alter the immunophenotypic profile of these cells, it did increase the cobblestone areas of hematopoietic stem cells on MSC layers and increased the production of IL-6 and IL-8. These effects were observed in cell culture of normal controls.

In another presentation from Toronto (R. Shapiro et al.), cyclooxygenase-2 and CD31 expression, reflecting micro vessel density, were both found elevated in the bone marrow of patients with del-5q, in contrast to other WHO types of low-risk

MDS. This feature may represent an additional mechanism of success of lenalidomide treatment in this particular group of patients.

The group from Karolinska Institute of Stockholm studied the adhesion properties of CD34+ cells from patients with del-5q to a murine stromal cell line and compared them with those of normal CD34+ cells. The CD34+ cells of patients with del-5q exhibited increased adhesiveness to stromal cells and a consequent decrease rate of apoptosis, which were abrogated by the addition of lenalidomide or of recombinant SPARC. Therefore, it appears that decreased expression of SPARC leads to increased adhesion of del-5q CD34+ progenitors to their microenvironment and may explain their growth advantage over normal CD34+ cells. Lenalidomide was capable of reversing this growth advantage of the clonal cells at least in part by increasing SPARC expression.

There were five presentations analyzing various aspects of treatment with lenalidomide in patients, mainly with low-risk MDS. The preliminary results of the prospective single-arm phase II Japanese study (H. Harada et al.) designed for patients with del-5q showed that all 11 patients responded favorably, with complete cytogenetic response in seven out of ten patients. According to the Italian cooperative study (E. Oliva et al.) designed for patients with del-5q alone and focused on efficacy and quality of life among 13 evaluable patients, Hb response was achieved by six, of whom five became transfusion-independent. Since treatment schedule was the continuous daily administration of 10 mg of lenalidomide, 10 patients required drug discontinuation and dose reduction. The same group has planned to investigate the gene expression profile before and after lenalidomide treatment, but comparative results are not yet available. The Greek cooperative study (A. Symeonidis et al.-Hellenic MDS Study Group) is a retrospective analysis of the efficacy and safety of lenalidomide in a cohort of 73 patients with MDS, 49 with del-5q alone, 12 with additional abnormalities over del-5q, 6 with normal karyotype and 6 with other karyotypic abnormalities not including del-5q. After a median follow-up of 15 months, 48 of the 67 evaluable patients demonstrated a favorable response, which was CR in 39 patients. CR was obtained by 33 of 49 patients with del-5q alone and by 5 out of 12 patients exhibiting additional abnormalities over del-5q. Of interest, bone marrow lymphoid nodules, which were present in 33 patients before treatment, disappeared in 18 out of 21 favorably responded patients, suggesting that their presence might be associated with a pathogenetic role in these patients. The French study (M. Sebert et al.) is also a retrospective analysis of 75 patients with low- and intermediate-1 IPSS, belonging to all WHO subtypes, from del-5q to RAEB-1. A favorable response was achieved by 49 (65%). About 80% of the patients exhibited grade 3–4 cytopenias, leading to transient discontinuation of lenalidomide in almost half of them. Twelve patients discontinued the drug prematurely, and three patients (two with RAEB-1 and one with additional abnormalities over del-5q) evolved to AML. Finally, the German study (A. Giagounidis et al.) focused on the duration of response after lenalidomide discontinuation. Among eight patients who discontinued lenalidomide after achieving remission, four continue to remain in remission 7 to 54 months after drug withdrawal, while even those who stopped lenalidomide before the achievement of cytogenetic remission continued to be in hematological remission for more than 12 months.

Iron Chelation in MDS: More Than Just Removing the Excess of Iron From the Patient

Over the past few years it has become increasingly evident that reducing iron overload in regularly transfused patients with MDS represents a major issue of the supportive care of the patients. However, it appears that effective iron chelation treatment may offer the patients much more than merely removing the excess of iron from the tissues. The issue of iron chelation was abundantly discussed during the 10th International Symposium on MDS. There was a round table of invited speakers dedicated to current questions and answers on chelation therapy in MDS.

It appears that effective iron chelation treatment may offer the patients much more than merely removing the excess of iron from the tissues. The issue of iron chelation was abundantly discussed during the 10th International Symposium on MDS.

Dr. L. Chan from Toronto presented the consequences of chronic iron overload on normal hematopoiesis, using a mouse model in which the animals were injected increasing iron load for 21 consecutive days. Three months later mice exhibited macrocytosis and increased levels of intracellular Reactive Oxygen Species (ROS) in their lin-CD45+ bone marrow cells. The same group demonstrated that the intracellular ROS content of CD34+ bone marrow cells from 34 patients with MDS and heavy iron overload was strongly correlated with serum ferritin levels. The correlation was stronger in patients with RAEB, whereas no correlation was found in patients without iron overload. This work confirmed that simply evaluating serum ferritin levels is a sufficient tool to monitor more complicating parameters of iron status in the body and pretty nicely reflects the severity of iron toxicity at the cellular level.

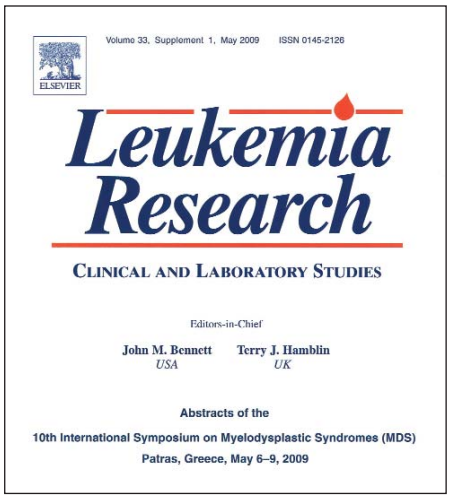
Dr. Ohyashiki et al. from Tokyo reported the effects of in vitro treatment with deferasirox on three human myeloid leukemia cell lines as well as on peripheral blood mononuclear cells from four patients with

AML. They found an enhanced expression of REDDI and its downstream protein Tuberin (TSC2), which down-regulates the mTOR pathway. As a result, the S6 ribosomal protein was found significantly repressed. These findings imply that iron chelation may inhibit leukemic cell growth.

The Turin group of Prof. G. Saglio has presented new data on NF-κB inhibition in mononuclear cells of patients with MDS and of two leukemic cell lines induced by deferasirox, but not by the other two iron chelators deferoxamine and deferiprone. The increased activity of NF-κB in mononuclear cells of patients with MDS was not correlated with the iron load status. Moreover, a group from Prague (J. Krijt et al.) presented data, demonstrating that iron overload opposes the erythropoietic stimulatory effects induced by rh-Epo through the inhibition of hepcidin down-regulation. Thus it appears that iron chelation treatment may indeed prevent, at least to some degree, disease progression towards a more aggressive form of MDS or AML.

The abstracts of the 10th International Symposium on MDS published by ***Leukemia Research*** *are now available upon request by contacting the MDS Foundation at 800-MDS-0839.* ***A DVD-ROM of selected presentations from this symposium will be available soon.***

Abstracts Now Available!



MDS IRON-OVERLOAD DETECTION: INSIGHT SURVEY

MIDIS Reveals Key Thoughts on Managing Iron Overload in MDS

We are pleased to share the results from MIDIS (MDS Iron-Overload Detection: Insight Survey)—the first European survey among haematologists on the subject of iron toxicity in myelodysplastic syndromes (MDS). 60–80% of patients with MDS will develop symptomatic anaemia during the course of their disease, and 80–90% of these will benefit from red blood cell transfusions to improve their haemoglobin levels. Despite the benefits that patients receive from regular transfusions, those who become dependent on transfusions will develop iron overload, known to cause progressive damage to the heart, liver and endocrine organs if not adequately treated with iron chelation therapy.

MIDIS is a joint initiative by the European School of Haematology, the MDS Foundation and Novartis Oncology, who would like to thank all the physicians who took part in the survey. It was initiated to gain helpful insights into what haematologists across Europe perceive to be the barriers to the optimal detection and management of iron toxicity in patients with MDS. MIDIS will lead to the development of a range of educational initiatives aimed at improving detection and treatment of iron-overloaded patients with MDS.

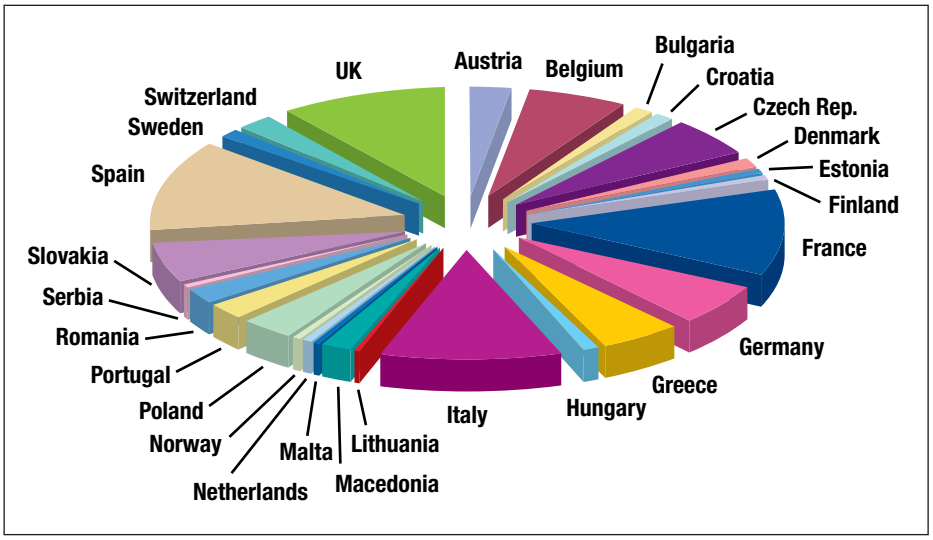


Figure 1. European Pie. *Countries of residence of the 338 physicians who participated in MIDIS.*

The 15-minute MIDIS survey, which comprised 33 structured and five open-ended questions, was translated into Dutch, French, German, Italian, Spanish and Swedish. It was initiated at the 2008 annual meeting of the American Society of Hematology, and was promoted through e-mails, letters and flyers distributed at conferences, as well as links via the MDS Foundation and European School of Haematology websites. The survey was completed by 338 physicians—mostly haematologists—from 27 European countries (Figure 1). Together, the respondents were a highly skilled group of physicians; 26% had more than 25 years' experience of treating patients.

The results showed that the majority of respondents thought that detecting iron overload in transfusion-dependent patients with MDS is important (46% replied that this was 'very important' and 27% thought it was 'important'). They indicated that one of the key barriers to detecting iron overload was levels of serum ferritin (a common test for iron overload) not being regularly monitored in transfusion-dependent patients.

Most physicians also felt that treating iron overload was 'very important' or 'important'. 90% of the physicians said they treated their iron-overloaded patients with MDS with iron chelation therapy, and a total of 38% of the transfusion-dependent patients they saw in their clinics were chelated. Dr Aristoteles Giagounidis, of St. Johannes Hospital, Duisburg, Germany, and advisor to the MDS Foundation, said "this figure of 38% is indicative of the proportion of patients who are candidates for iron chelation therapy, and reflects physicians' active iron chelation treatment strategy."

MIDIS demonstrated that the key barriers to treatment for the remaining patients were limited patient life expectancy (<1 year) and older patient age (especially ≥85 years). While limited life expectancy is in line with recommendations made by various European guidelines for the treatment of MDS, the guidelines do not recommend an age range for patients who are most likely to benefit from iron chelation therapy. The MIDIS results conveyed that patients aged 75 years or older are less likely to be chelated than younger patients (Figure 2).

The Düsseldorf MDS registry cites the median age of patients at diagnosis of MDS as 72 years (Figure 3). Experts agree that the prognosis and physiological condition of the patient should be assessed rather than the chronological age in terms of treatment selections.

The MIDIS study revealed that patients were selected to receive iron chelation therapy based on their serum ferritin level, the rate of increase of their serum ferritin level, or the number of red blood cell units or transfusions that the patients had received (Figure 4). Candidacy for allo-stem cell-transplantation was also a strong trigger for initiating iron chelation therapy. These markers are also in line with the MDS treatment guidelines that have been published by the MDS Foundation.

In May 2009, results from the MIDIS study were presented at the 10th International Symposium on Myelodysplastic Syndromes, which took place in Patras, Greece, where they were well received.

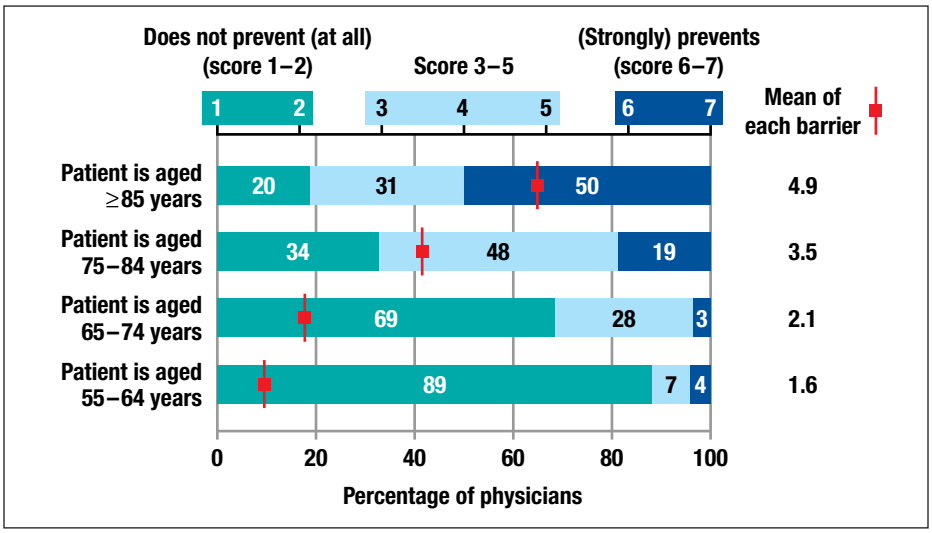


Figure 2. Age as a Barrier to Iron Chelation Therapy. *MIDIS showed that patient age ≥75 years prevented physicians from initiating iron chelation therapy.*

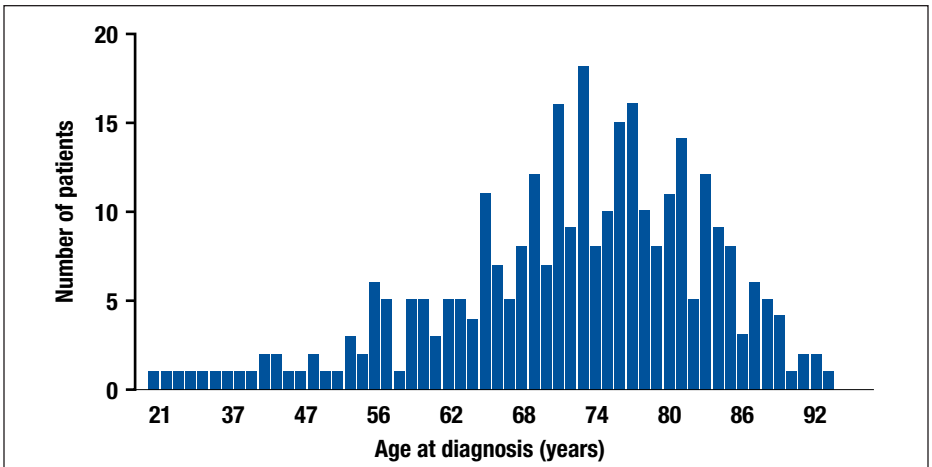


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Figure 3. Age at Diagnosis. *The age distribution of 308 patients with MDS from the Düsseldorf MDS Registry.*

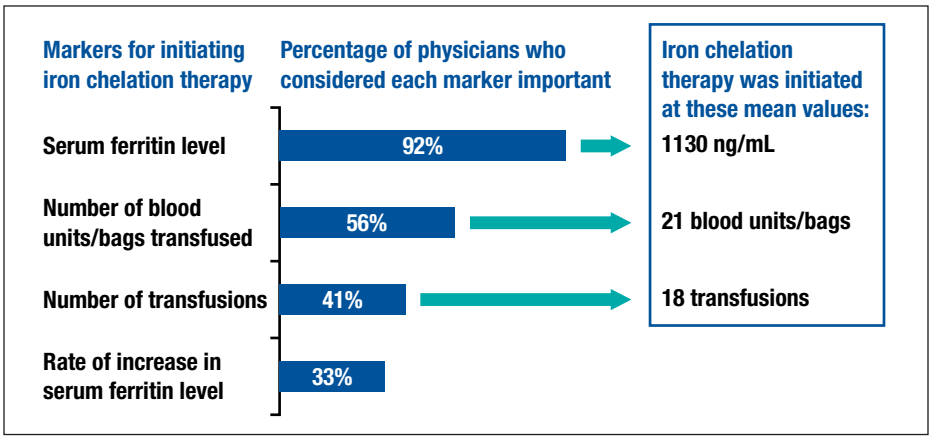


Figure 4. Triggers for Iron Chelation Therapy. *Each marker served as an indicator of when to initiate iron chelation therapy.*

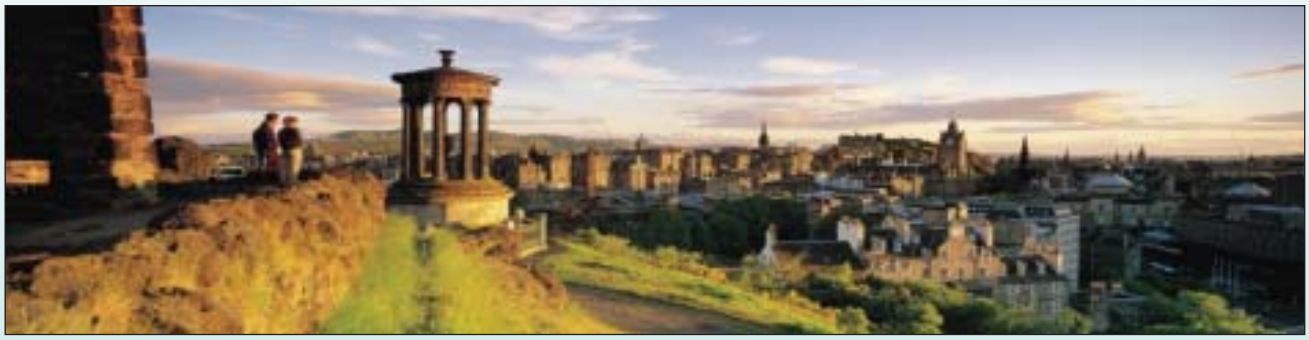
Foundation Plans International Symposia Through 2013

The MDS Foundation has approved applications for the next two International Symposia. These symposia are scheduled for 2011 in Edinburgh, Scotland, and 2013 in Berlin, Germany.

PLAN TO ATTEND

The 11th International Symposium on Myelodysplastic Syndromes

MAY 19–22, 2011 • EDINBURGH, SCOTLAND



Eleventh International Symposium: Spring 2011

Edinburgh, Scotland

Sponsor: David T. Bowen, MD

Twelfth International Symposium: Spring 2013

Berlin, Germany

Sponsor: Wolf-Karsten Hofmann, MD, PhD

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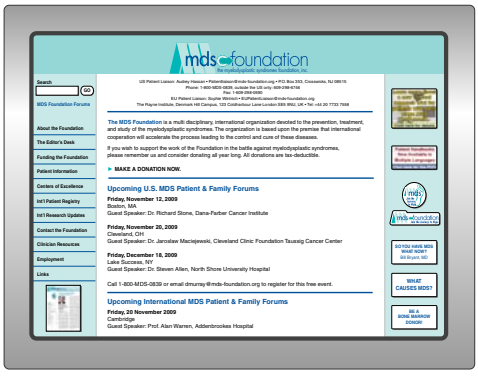
Now on **facebook** and **twitter!**

The MDS Foundation is now on Facebook and Twitter. Sign up to connect with us now! **Keep up to date on all the news, events and happenings with the Foundation.**

To find our page on Facebook, type "The MDS Foundation" in the search box located in the top right corner. Once you are there, become a fan to receive updates. Then in the top left corner click the "more" button then "suggest to friends" and send to all your friends.

When the Page is updated with current Foundation information, a notice is sent to all the fans newsfeeds. The Page also allows for Fans to leave comments for others to read or begin a topic in a Discussion Forum.

Twitter is a free service that lets you keep in touch with people through the exchange of quick, frequent answers to one simple question. Follow us on Twitter at http://twitter.com/MDSFoundation to start receiving the MDS Foundation's tweets.



We hope to see you on the web!

OUR SITE TO SEE!

www.mds-foundation.org

ANNOUNCEMENT FROM MDS FOUNDATION

The MDS Foundation Says National Comprehensive Cancer Network Recommends New Treatments For Acute Myeloid Leukemia

New Options Added For Patients Over 60 Years Old

Crosswicks, NJ (October 2009) –

The Myelodysplastic Syndromes (MDS) Foundation says updated guidelines from the National Comprehensive Cancer Network indicate new, low-intensity treatments are now recommended for older patients with acute myeloid leukemia (AML), an aggressive form of leukemia that in many cases progresses from MDS. The updated guidelines add VIDAZA® and DACOGEN® as low intensity treatment options for AML patients over 60 years old. Clolar® was also listed as a possible intermediate intensity treatment option for certain subsets of these patients. VIDAZA was previously listed as the first "preferred" treatment for high-risk patients with MDS.

"These are important new treatment options for AML where the majority of patients are elderly and cannot tolerate intense chemotherapy," said Kathy Heptinstall, Operating Director of the Myelodysplastic Syndromes Foundation. "These guidelines reflect the progress being made in treating both AML and MDS and on behalf of our patients we are encouraged to see these developments put into practice."

The National Comprehensive Cancer Network (NCCN) develops evidence-based treatment guidelines from experts in each field of cancer based on published studies. In addition to the drug therapies, guidelines for AML patients who are eligible for stem cell transplants now say umbilical cord blood can be used for patients who do not have an appropriate donor available.

Because these latest guidelines for AML are very specific as to subsets of patients including adverse features, chromosome abnormalities and co-morbidities, the MDS Foundation believes it is especially important for patients to seek care from knowledgeable specialists and for specialists to be conversant with the details of the NCCN recommendations.

MDS is a malignant condition of cells in the bone marrow. Patients require blood transfusions that can lead to iron overload, and the condition can progress to AML a serious form of leukemia. Nearly 13,000 AML patients are diagnosed each year in the United States. Median survival is less than one year.

More information about the guidelines can be found on the NCCN website or through the MDS Foundation.

MDS PRACTICE AND TREATMENT SURVEY

MDS Practice and Treatment Survey

The MDS Foundation recognizes that data on many aspects of MDS worldwide is sketchy or nonexistent. While individual investigators have developed databases to track MDS within their individual sites or working groups, that information is not located within one easily accessible database.

To assist in the development of useful information, the Foundation has recently initiated the first Patient Registry and data from the Foundation's Centers of Excellence are currently being entered.

COMPLETE THE SURVEY TODAY!
(BEGINS ON PAGE 57)

Since it will be some time before these data are mature and usable, the Foundation has attempted to design a survey that we hope will assist in describing some of the issues related to MDS worldwide as well as the treatments being utilized in this disease. A pilot of this survey has already been completed with some selected Centers of Excellence. While we know that this information is, in most instances, based on subjective criteria, it can assist in identifying educational and research opportunities in the near term and until more accurate data are available.

The results of this expanded survey will be shared with each of our Centers of Excellence and used by the Foundation to assess new educational and research opportunities. Please assist us by completing this brief survey online or in this issue of *The MDS News*. Go to www.mds-foundation.org and click on the *Physician* or *Nursing Practice & Treatment Survey*.

Surveys are available online in the following languages: Spanish, Italian, German, and Dutch.

Thank you in advance for your consideration in completing this form.

Young Investigator's Award

Raising The Next Generation of MDS Investigators

MDS is an enigmatic disease that is not yet well understood by scientists, physicians, and researchers. It is essential to develop the new generation of researchers so that the causes of these syndromes are identified as soon as possible. To ensure that this future generation of researchers flourishes, the MDS Foundation awarded two fellowships of $50,000 each in 2009 (see below).

The Foundation is dedicated to furthering the research into MDS and invited young investigators (under 40 years of age) from institutions that form our MDS Centers of Excellence to submit their proposals. Four years ago, the Foundation initiated this series of grants; two awards will be made this year, and subsequent awards will be granted annually.

On December 4, 2009, a formal awards ceremony will be held in conjunction with the American Society of Hematology's annual meeting in New Orleans, Louisiana.

mds foundation
the myelodysplastic syndromes foundation, inc.

THE YOUNG INVESTIGATOR GRANT PROGRAM FOR FELLOWS IN HEMATOLOGY

In December 2005 The Myelodysplastic Syndromes Foundation, Inc., initiated a series of grants "The Young Investigator's Grant Program for Fellows in Hematology." These awards are granted annually.

The Grant Review Committee selected Andrew Finch's grant submission entitled "The Role of p53 Pathway in the Pathogenesis of Shwachman Diamond Syndrome" and Ramon Tiu's submission entitled "TET2 Mutations as Marker of Epigenomic Instability in MDS: Therapeutic Implications" as recipients for the 2010 Young Investigator Grants.

Andrew John Finch, PhD
University of Cambridge
Cambridge, UK

Ramon Tiu, MD
Cleveland Clinic Foundation
Cleveland, Ohio USA

The Foundation is dedicated to furthering the research into MDS and invites Young Investigators (under the age of 40) to submit either basic or clinical research proposals into the causation, epidemiology, molecular biology, cytogenetics, morphology, prognosis, or management of the Myelodysplastic Syndromes.

THE YOUNG INVESTIGATOR GRANT PROGRAM
is supported by

Celgene · Eisai · NOVARTIS ONCOLOGY · gsk GlaxoSmithKline Oncology · AMGEN · MSD ONCOLOGY

Meeting Highlights and Announcements

On behalf of the MDS Foundation and our Board of Directors, thank you for joining us for our recent Satellite Symposia:

MDS MISSION FOR NURSING EDUCATION

THE 34TH ANNUAL CONGRESS OF THE ONCOLOGY NURSING SOCIETY (ONS)

Practical Therapeutic Options & Approaches: Keeping MDS Patients on Track (Case-Based)

San Antonio, Texas
April 30, 2009

The MDS Foundation was pleased to participate in the ONS annual meeting held this year in San Antonio, Texas, where we presented the Foundation's third annual symposium in conjunction with ONS. Our Satellite Breakfast Symposium—Practical Therapeutic Options & Approaches: Keeping MDS Patients on Track (Case-Based)—was held on April 30, 2009, at the Marriott San Antonio Riverwalk Hotel.

At least 195 nurses participated in our breakfast symposium. This program centered on case-based presentations and included cases for both low- and high-risk MDS, transplant patients, and provided key information on dealing with the issues patients face in psycho-social and adverse events, and quality of life. The need to track patients effectively formed an interactive component of the symposium.

Our distinguished faculty included:

Erin Demakos, RN, CCRC
Mount Sinai School of Medicine
New York, NY

Sandy Kurtin, RN, MS, AOCN, ANP-C
Arizona Cancer Center
Tucson, AZ

Jean Ridgeway, RN
University of Chicago Medical Center
Chicago, IL

Erik Aerts, RN
University Hospital Zürich, Switzerland

Topics included:

- Advances in MDS: Clinical and Research Update
- Treating Low-Risk Patients (Case Presentation)
- Utilizing Decitabine Effectively
- Utilizing Azacitidine Effectively
- Transplant as a Therapeutic Option in Young MDS Patients: Nursing Considerations

Photo courtesy of The Oncology Nurse and American Photography and Video.

Peggie Aaron, Carol Duryea, and Deborah Murray greet visitors at the MDS Foundation booth in San Antonio.

For a copy of the DVD-ROM, which contains all of the slide presentations from this session, please contact the MDS Foundation at 1-800-MDS-0839.

10TH INTERNATIONAL SYMPOSIUM ON MDS

MDS Nursing Education Sessions Held at the 10th Int'l Symposium on MDS

Patras, Greece
May 7–8, 2009

This two-day nursing education symposium held May 7–8, 2009, at the University of Patras provided a definitive overview of MDS as a disease, new information regarding quality-of-life in MDS patients, resources that are available to nurses and their patients, new definitions and research in morphology and cytogenetics that are important in the evolution of the prognostic scoring systems (IPSS and WPSS), treatment strategies, and drug therapy, as well as the first look at a unique tool for online tracking of MDS patients.

At the conclusion of this program, the participants were able to understand MDS as a disease, comprehend the issues surrounding the new treatments for MDS, discuss nursing strategies to help MDS patients understand treatments, increase compliance, and manage side effects of treatments; understand quality-of-life issues facing MDS patients and their caregivers/family; and understand the resources available to help MDS patients and provide that information to patients and families.

DINNER SYMPOSIUM

EFFECTIVE THERAPEUTIC DECISION MAKING IN MDS:

IMPROVING PATIENT OUTCOMES AND QUALITY OF LIFE

FRIDAY, DECEMBER 4, 2009

6 PM – 9:30 PM

Ernest N. Morial Convention Center
New Orleans, Louisiana

Dinner will be served from 6 to 6:30 pm
Rooms 270–282

Symposium: *Auditorium B/C*

Seating will be on a first-come, first-served basis.

VISIT THE MDS FOUNDATION BOOTH: #214

THIS SYMPOSIUM WILL BE AVAILABLE ON CD-ROM ON DECEMBER 6TH AT THE MDS FOUNDATION BOOTH.

AMERICAN SOCIETY OF HEMATOLOGY

PLEASE PLAN TO ATTEND!

AGENDA

6:00 – 6:30 pm
Dinner

6:30 – 6:45 pm *Alan F. List, MD, Chair*
Welcome and Introduction, Program Goals and Objectives

6:45 – 7:15 pm *John M. Bennett, MD*
Evolution in the Prognostic Systems in MDS: What Does that Mean in Terms of Diagnosis and Staging?

7:15 – 7:45 pm *Moshe Mittelman, MD*
Anemia – How Do You Treat It? The Low-risk Patient at Risk for Rapid Progression

7:45 – 8:15 pm *Lewis R. Silverman, MD*
High-risk MDS: Traditional Treatments and Advanced Therapeutic Options

8:15 – 8:45 pm *H. Joachim Deeg, MD*
Issues in Transplant: Early versus Late

8:45 – 9:30 pm
David Cella, PhD
What is the Patient's Reality? The View from the Other Side

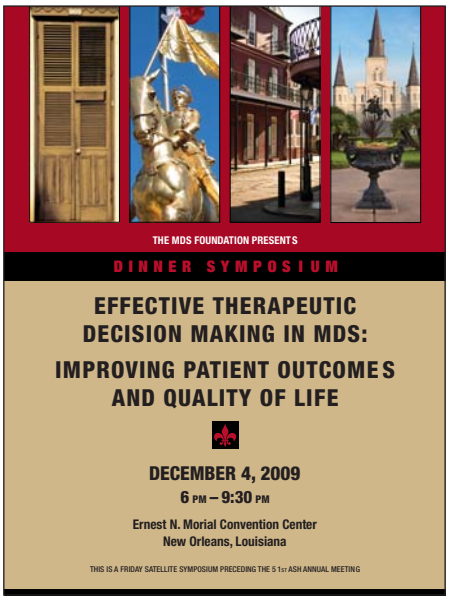
LEARNING OBJECTIVES

At the conclusion of this activity participants will be able to:

- Discuss the most current information on MDS therapy and tracking, diagnostic/prognostic system updates, and the state of disease knowledge
- Utilize updated WHO Classification and IPSS Prognostic systems to effectively classify and stratify patients
- Understand the potential for improved outcomes for MDS patients with effective therapeutic choices
- Utilize therapies approved for MDS more effectively
- Understand the need for effective tracking of clinical variables, transfusions, and therapy to monitor changes in MDS patients
- Discuss the potential for improved quality of life in MDS patients due to improved clinical knowledge

PROGRAM OVERVIEW

This program will provide participants with the opportunity not only to learn about the most recent changes to the scientific knowledge of MDS but to match their clinical knowledge of MDS with that of a panel of experts in MDS diagnosis, therapy, and quality of life. Accurate diagnosis, stratification of MDS patients, treatment choices, and assessment of therapeutic results (including quality of life issues) provides everyone involved in treating MDS, including this "Expert Panel", with continuous challenges to optimization of outcomes. The Expert Panel will present a series of "real life" cases to the attendees coupled with brief scientific updates that may affect the therapeutic choices of the participants. Verbal interaction and electronic decision making will allow for full participation



by the audience and provide them with the opportunity for challenging discussions with the experts and other participants regarding options in treatment and the potential effects on patient outcomes.

FACULTY

Alan F. List, MD, *Chair*
H. Lee Moffitt Cancer Center
and Research Institute, Tampa, Florida

John M. Bennett, MD
University of Rochester
Rochester, New York

David Cella, PhD
Northwestern University
Feinberg School of Medicine
Chicago, Illinois

H. Joachim Deeg, MD
Fred Hutchinson Cancer Research Center
University of Washington School of Medicine
Seattle, Washington

Moshe Mittelman, MD
Sackler School of Medicine
Tel-Aviv Sourasky Medical Center
Tel-Aviv, Israel

Lewis R. Silverman, MD
Myelodysplastic Syndrome Program
Myeloproliferative Disease
Clinical Research Consortium
Mount Sinai School of Medicine
New York, New York

EUROPEAN HEMATOLOGY ASSOCIATION

Therapeutic Decision Making in the Treatment of MDS: Challenging the Experts

Internationales Congress Centrum Berlin, Germany June 4–7, 2009

The Myelodysplastic Syndromes Foundation presented its fourth adjunct symposium at the 14th Congress of the European Hematology Association in Berlin. The symposium was greeted by standing room only, and 1000 copies (on DVD-ROM) were distributed on Friday and Saturday of the EHA meeting. The expert panel presented brief overviews of "real life" cases and only the most recent treatment advances. Verbal interaction and electronic decision making allowed for full participation by the audience and provided them with the opportunity for challenging face-to-face discussions with the experts and other participants.

The International Congress Center, Berlin, Germany served as the venue for EHA 2009.

This educational video will be available to audiences both via our educational website and on DVD for continued use. Translations of educational materials in Czech, Dutch, French, German, Greek, Hebrew, Hungarian, Italian, Japanese, Polish, Portuguese, Romanian, Spanish, Swedish, and Turkish were also provided free of charge at our booth.

Agenda

- **Introduction**
  David T. Bowen, MD, Chairman
- **Treating Low-risk MDS: Evidence-based Therapy**
  Moshe Mittelman, MD
- **RARS-t: Issues in Management and Treatment**
  Mario Cazzola, MD
- **Innovative Management of INT-1**
  David T. Bowen, MD
- **Effective Therapeutic Choice in High-risk MDS**
  Pierre Fenaux, MD
- **The Role of Induction Chemotherapy in High-risk MDS**
  Theo J.M. deWitte, MD, PhD
- **Reframing Treatment Schema**
  David T. Bowen, MD

For a copy of the DVD-ROM, which contains all of the slide presentations from this session, please contact the MDS Foundation at 1-800-MDS-0839.

5TH INTERNATIONAL CONGRESS ON MYELOPROLIFERATIVE DISEASES AND MYELODYSPLASTIC SYNDROMES

5th International Congress on Myeloproliferative Diseases and MDS

New York, NY November 5–7, 2009

The 5th International Congress on Myeloproliferative Diseases and Myelodysplastic Syndromes was held on November 5–7, 2009, just across the river from Manhattan at the New York Marriott at The Brooklyn Bridge in Brooklyn, NY. Since the inaugural Congress in 2001, this meeting has grown to nearly 600 attendees and has become one of the premier forums for discussion on the latest advances in myeloproliferative diseases and myelodysplastic syndromes.

Guided by the expertise of the leaders in the fields of molecular biology, pathology, immunology, and translational and clinical research, this Congress allowed attendees the forum to update their knowledge in the field, confirm their current practices and receive valuable take-home information on exciting new screening and staging modalities, management approaches, and emerging treatment options.

John M. Bennett, MD and Alan F. List, MD served as chairmen of the session on MDS. Dr. Bennett is the chairman of the MDS Foundation and Dr. List serves as a member of the Foundation's Board of Directors. The scientific symposium included the following topics:

Classification, morphology, and pathogenesis of myelodysplastic diseases by John M. Bennett, MD; *The interface of aplastic anemia and MDS: treatment measures* by Neal S. Young, MD; *Current treatment, including hypomethylating agents* by Alan F. List, MD; *New drugs in MDS – Treatment of iron overload* by Gail J. Roboz, MD; *Which transplant and when for patients with MDS?* by Richard E. Champlin, MD; Keynote Address: *Normal and neoplastic stem cells in health and disease* by Irving Weissman, MD.

Nancy Mrzljak and Audrey Hassan discussing the Foundation with a congress attendee.

Scientific Developments in the Management of Myelodysplastic Syndromes

Sandra E. Kurtin, RN, MS, AOCN, ANP
Arizona Cancer Center
University of Arizona, Tucson
Tucson, Arizona

Reprinted from The Oncology Nurse

Several key scientific events within the past decade have shaped the current strategy for management of myelodysplastic syndromes (MDS). The majority of these have occurred in the past 5 years. An improved understanding of this heterogeneous group of myeloid stem-cell malignancies, including insights into key elements of the malignant clone, the bone marrow microenvironment, and the variability in disease trajectory, have been key to clinical advances.

A revised World Health Organization (WHO) classification system has been recently published incorporating this new information.[1] Hematopathologists and clinicians must develop the ability to translate data obtained using older definitions into current clinical trials that will be based on the revised nomenclature. The rate of scientific discovery creates a number of challenges to clinical application of the findings, including transition of practice patterns, education of the clinician and the patient, safety, and financial or reimbursement obstacles.

Table 1. Novel Agents and Targeted Therapies for the Treatment of MDS

Mechanism of Action	Therapeutic Compound	Application
Immunosuppression	ATG, cyclosporine	Low-risk hypocellular disease
Immune modulation	Thalidomide, lenalidomide	Low to intermediate-1 risk, in particular del(5q) In combination with demethylating agents
Inhibitors of angiogenesis	Bevacizumab, lenalidomide, thalidomide, arsenic trioxide	Variable applications
DNA hypomethylation	Azacitidine, decitabine	All risk categories
Inhibition of histone deactylation	Valproic acid, depsipeptide, MS275	In combination with demethylating agents or purine analogs
Oncogene deactivation	Farnesyl transferase inhibitors: tipifarnib, lonafarnib	In combination with demethylating agents or purine analogs
Enzyme and kinase inhibition	TLK199, Src family kinase inhibitors, p38 MAPK inhibitor	In clinical trials for variable populations
Purine analogs	Clofarabine, cytarabine	Combinations for high-risk MDS in the elderly
Monoclonal antibodies	Gemtuzumab ozogamicin	High-risk disease in the elderly
Thrombopoiesis-stimulating hormone	Romiplostim	Treatment-associated thrombocytopenia in all risk categories

Core Therapies

The establishment of an epidemiological data reporting system specific to MDS in the United States has validated similar trends in incidence and age to those in the more established data from European sites.[2,3] These data provide a critical resource for analysis of therapies for MDS and confirm that the highest incidence is in individuals more than 70 years of age. There is an expected increase in incidence as the population ages.

To date, allogeneic stem-cell transplants are the only potentially curative therapy for MDS. This is not an option for the majority of MDS patients, however, based on age, comorbid conditions, and donor availability. Therefore, treatment strategies that are feasible in the older population will be the core of MDS therapy. Improved quality of life, limited toxicity, reduced need for hospitalization, and affordability will be critical to successful therapies. Oncology clinicians will need a basic understanding of treating the older adult with cancer.

The term myelodysplastic syndromes was first used in 1982 by John Bennett, MD, and colleagues, who differentiated MDS from acute myeloid leukemia.[4] The clinical application of scientific advances in the diagnosis, risk stratification, and treatment of MDS since the disease was recognized as a unique entity have been concentrated in the past 5 years. Three active agents—azacitidine, decitabine, and lenalidomide—are currently approved by the US Food and Drug Administration (FDA) in the United States as well as many other countries for the treatment of MDS. Direct clinical comparison of these agents is limited as each of these drugs has only recently been approved for use in the setting of monotherapy and broad inclusion criteria (all risk groups).

Based on key clinical trials and ongoing investigation, the first treatment guidelines for MDS were developed by the National Comprehensive Cancer Network in 2004. They have been revised a number of times each year since then, consistent with the relatively new understanding of key aspects of this disease and strategies for treatment. In addition, definitions of response, desired primary end points (survival vs response), and evolving recommendations for risk-

adapted treatment selection based on prognostics and individual patient profiles continue to evolve. A comparative trial using azacitidine and decitabine, which are both demethylating agents, is planned for 2009. Development of novel agents with unique therapeutic targets is ongoing (Table 1). Key clinical trials for FDA-approved therapies for MDS will be highlighted in this review with discussion of the implications for clinical practice and patient care.

Risk-Adapted Therapy for MDS

Harris and colleagues[1] in the revised WHO classification for MDS state that "classification is the language of medicine: disease must be described, defined, and named before it can be diagnosed, treated, and studied." Understanding the pathobiology of MDS has allowed identification of therapeutic targets and refinement of treatment strategies, including the concept of risk-adapted therapy. The heterogeneous nature of the disease entities described within the MDS nomenclature presents a challenge for hematopathologists and clinicians.

The integration of the International Prognostic Scoring System (IPSS) and, more recently, the World Health Prognostic Scoring System (WPSS) have guided the selection of therapy based on projected disease trajectory and the risk of leukemic transformation. The accepted classification for clinical manage-ment uses two primary categories: low to intermediate-1 risk or intermediate-2 to high-risk disease based on blasts percentage, cytogenetic profile, and number of cytopenias. Several studies have proposed additional adverse risk factors, including thrombocytopenia, transfusion burden, lactic dehydrogenase, and performance status.[5-9] Continued review is certain as an improved understanding of the pathobiology of this disease and resulting clinical implications are realized.

Lower risk MDS is accepted as a chronic myeloid malignancy with an emphasis on improved hematopoiesis, including transfusion independence, improved quality of life, and extended overall survival (OS). Treatment until disease progression or unacceptable toxicity is now an accepted paradigm, emphasizing the need to refine supportive care strategies.[10,11]

In addition, trials using the immunomodulatory agent lenalidomide for low-intermediate risk MDS have elucidated a difference in mechanism of action for selected patient subsets. Analysis of the data from the three lenalidomide trials in MDS suggests that lenalidomide has a different mechanism of action in patients with or without chromosome 5q deletion, a possible direct cytotoxic effect on the malignant clone with del(5q) and effect on the microenvironment in patients without the deletion of chromosome 5q.[12-14] Cytogenetic responses have been shown to correlate with improved survival in patients with chromosome 5q deletion. A follow-up evaluation of six patients participating in the MDS-001 trial indicated the response to lenalidomide to be durable with sustained transfusion independence up to 6.5 years and provided evidence of sustained cytogenetic remissions in some patients.[14]

Higher risk disease presents a particular challenge in the older population, in whom the focus of treatment is on survival, suppression of the leukemic clone, and management of disease and treatment toxicities. A fundamental principle of active therapy for any stage of MDS is that sustained treatment for a minimum of 3 to 4 months is necessary to effectively evaluate efficacy, and the depth of response may continue to improve up to 6 to 9 months after initiating therapy.[15] The challenge is in aggressively managing potential toxicities during the initial therapy to minimize gaps in treatment or unnecessary discontinuation of therapy.[16] Data supporting the potential to improve OS in this disease, even in patients with high-risk features, reinforce the need to refine clinical strategies for supportive care.

Chromosome 7 abnormalities are an unfavorable risk factor in MDS. An important study by Mufti and colleagues[17] indicated a survival benefit with standard-dose azacitidine in high-risk MDS, including chromosome 7 abnormalities (–7/del[7q]). For the 57 patients with –7/del(7q) alone or as part of a complex karyotype, the hazard ratio (HR) for risk of death was 0.33 (95% confidence interval, 0.16–0.68), indicating that azacitidine reduced the risk of death by 67% in these patients. OS was significantly longer in the azacitidine group than in the conventional care response group (13.1 months vs 4.6 months).

Fenaux and colleagues studied 358 patients with intermediate-2 or high-risk MDS.[18] The primary end point was OS in patients treated with azacitidine 75 mg/m^2 per day on days 1 through 7 for 28 days compared with conventional chemotherapy (cytarabine [ARA-C]/daunorubicin 7+3, or low-dose ARA-C). The patients treated with azacitidine had a significant improvement in OS compared with conventional care (P=.0001, HR=0.58). Median survival was improved, from approximately 15 months on conventional care to 24.4 months with azacitidine treatment. Approximately 52% of patients treated with azacitidine were alive at 2 years compared with 26% of patients who received conventional care. Considering the original survival data from the IPSS and WPSS with median survival of 1.2 years for intermediate-2 and 4 months for high-risk disease, this provides hope to patients with MDS. This is the first trial in MDS to document a survival advantage for active therapies.

Wijermans and colleagues reported results from a phase 3 trial using low-dose decitabine versus best supportive care for 223 patients with high-risk MDS.[19] Decitabine was administered at a dose of 15 mg/m^2 intravenously over 4 hours every 8 hours for 3 consecutive days (n=119) versus base supportive care (n=114). In a population of patients with intermediate-2 or high-risk MDS (93%), many of whom had poor cytogenetic risk profiles (46%), the median OS was not significantly longer with the decitabine group (10.1 months vs 8.5 months). It is important to note that patients who did achieve a complete response received a maximum of eight cycles, and the median number of cycles in this high-risk group was three. Given the recent shift toward treatment until progression and the expectation of a minimum of 4 to 6 months of therapy before achieving a response,

these disappointing data may be a reflection of clinical trial design. It underscores the challenge of integrating rapidly changing primary end points into a meaningful clinical trial and the importance of continued enrollment of patients in clinical trials.

Supportive Care

Supportive care strategies have also been refined and are recognized as essential components of the overall treatment strategy, including quality of life. The goals of therapy have shifted from supportive care alone to aggressive management of cytopenias, including achievement of transfusion independence, iron chelation therapy, and development of new cytokines for the treatment of thrombocytopenia. Myelosuppression is the most common dose-limiting toxicity associated with active therapies, and thus strategies to minimize cytopenias may allow patients to maintain active therapy.

Iron overload is associated with increased morbidity and mortality in patients with MDS, and iron chelation therapy has been shown to improve OS.[5,8] Sanz and colleagues studied 2994 patients with primary MDS. The majority of these patients (78) had low-intermediate-1 risk disease.[5] The study end points were OS and leukemia-free survival (LFS). Results of the study showed that red blood cell (RBC) transfusion-dependency (OS-HR=7.20, $P<.001$; LFS-HR=2.9, $P<.001$) and iron overload (OS-HR=2.11, $P<.001$; LFS-HR=1.57, $P<.001$) have prognostic value independent of the IPSS score. This study is thought to confirm the validity of adding RBC transfusion dependency to the revised WHO prognostic scoring system. It also supports transfusion dependence as a valid indicator for initiation of active therapies. Patients with MDS should be screened using a serum ferritin at the time of diagnosis with continued monitoring of these values. Ferritin levels >1000 have been shown to be associated with adverse outcomes.

Myelosuppression is the most common treatment-related toxicity in therapeutic regimens for MDS. Thrombocytopenia is a particular challenge because of the increased risk of bleeding in a primarily elderly population.

Romiplostim, a thrombomimetic agent, was used in combination with azacitidine and compared with azacitidine and placebo. In patients receiving romiplostim, the platelet count before each course of therapy and the platelet nadir were higher than the counts for patients in the placebo group. In addition, the group receiving the romiplostim required fewer platelet transfusions, and the incidence of grade 3 bleeding events was lower.[20] The addition of this type of agent to active therapies for MDS, which require several months for maximum response while inducing significant myelosuppression, can provide the supportive care necessary to maintain therapy long enough to achieve response.

Table 2. Key Concepts in the Treatment of MDS

- Myelodysplastic syndromes represent a myeloid stem-cell malignancy
- Clinical trial end points have shifted from efficacy and safety alone to include improved overall survival
- Complete eradication of the malignant clone is not necessary to prolong survival, but suppression is associated with transfusion independence, cytogenetic response, improved survival, and a reduced risk of leukemic transformation
- Clinical responses often require a minimum of 4 to 6 months of therapy, and prolonged therapy (treating until disease progression or unacceptable toxicity) is likely to become the standard approach
- Concurrent supportive care is essential to optimal therapeutic outcomes including iron chelation, transfusion management, cytokine support, and aggressive management of comorbidities; however, supportive care does not affect the underlying disease
- Treatment-related MDS is associated with a poor prognosis and will require specific approaches to treatment that are similar to those used for acute myeloid leukemia
- MDS is most common in individuals over the age of 70; therefore, treatment strategies that are feasible for the older adult will be the core of MDS therapy

Summary

The robust pace of scientific discoveries relative to understanding the pathobiology of MDS and the development and clinical application of therapies based on this understanding provides great hope for patients and clinicians. Several key concepts for effective treatment of MDS have been identified (Table 2). There are still many questions unanswered and a need to continue refinement of the diagnostic and risk stratification for this disease. New agents will be necessary to provide continued treatment options. This underscores the benefit of clinical trial participation in diseases with limited available treatment options and evolving scientific discoveries. MDS is one of many diagnoses with a rapidly changing treatment paradigm based on scientific advances and clinical management strategies. The goals of therapy in patients with MDS are to improve quality of life, minimize toxicity, improve hematopoiesis, reduce cytopenias, achieve transfusion independence, and prolong survival. These outcomes have now been realized in several of the studies discussed. Consideration of the unique needs of the elderly patient are critical to achieve optimal clinical management and quality of life; however, advanced age alone should not exclude older patients from active therapies.

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Air Transportation Options for Patients

Air transportation resources may be available for patients considering travel to one of the participating sites that are part of the NIH Rare Diseases Clinical Research Network (RDCRN).

Angel Flight's volunteer pilots provide flights in single-engine, four-six seat general aviation aircraft to patients at no charge. To be eligible, patients must be medically stable, ambulatory, and able to sit upright in an aircraft seat during flight. Angel Flights are for patients in financial need and who have their medical status certified by their doctors. An escort may accompany the patient, and children may be accompanied by both parents.

Flight distances are limited to 1,000 miles. Weight restrictions apply, and luggage is limited to 50 pounds. Safety is a primary concern. Pilots will not fly in poor weather. Patients need to be flexible, have a backup plan or be willing to reschedule their appointments.

If you are interested in finding out if Angel Flight meets your air transportation needs to participate in a clinical research study, contact Marita Eddy at 301-451-9646 or meddy@mail.nih.gov.

For patients who live farther than 1,000 miles, other resources may be available through Mercy Medical Airlift.

Mercy Medical Airlift (MMA), a non-profit organization celebrating 25 years of medical air transportation experience, manages programs and services available to patients with both common and rare diseases.

If you are flying to any of the RDCRN facilities or going to a study at the NIH Clinical Center in Bethesda, Maryland, contact Marita.

For patients who are looking for travel help to other locations, call the National Patient Travel Center at 800-296-1217 or check www.patienttravel.org.

UNITED AIRLINES CHARITY MILES

❒ I want to help **Mercy Medical Airlift** provide free air transportation to patients in financial need.

Please process a gift of _____ Dividend Miles from my United Airlines account.
(Please fill in number of miles – donations must be in 1,000 mile increments)

Name: _____
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Email Address: _____

United Mileage Plus Account Number: _____

United.Com Password: _____

Phone Number: _____

Address: _____

City: _____ State: _____ Zip Code: _____

Signature: _____ Date: _____

Remarks: _____

_____

_____

_____

_____

Please mail to:
Marita Eddy, Angel Flight-MMA
NIH Office of Rare Diseases Research
6100 Executive Blvd. MSC 7518
Bethesda, Maryland 20892

25,000
Frequent Flyer Miles equals 1 round-trip ticket

Patient Forums and Support Groups

Patient Support Group Initiative

The MDS Foundation has developed a strategy for setting up patient groups nationwide and assistance is now available to organize support groups for MDS patients. At this time, we would like to enlist the help of our patient members in facilitating these member-run groups.

Would you be interested in joining with a few other people to help start a needed support group for MDS? Monetary assistance is now available to help you develop a self-help group. The purpose of this group is to exchange information and resources, to provide comfort and support to patients and caregivers, and to explore the challenges of living with myelodysplastic syndromes.

Studies and other literature show that patients facing chronic or terminal illnesses, as well as their families and friends, benefit in numerous ways from participating in patient support groups. These groups not only provide a source for obtaining current information on the disease, treatment options and research, they also offer a supportive environment in which to express fears and concerns and share experiences with others coping with similar conditions. In fact, patients who participate regularly in support groups report reductions in stress, depression, and even pain.

Any member of the Foundation, patients, friends, family members, and caregivers are invited to join with us to move this project forward.

Boston Patient and Family Forum

Boston, MA • November 12, 2009

Dr. Richard Stone of Dana-Farber Cancer Institute addresses patients and their guests.

MDS Patient and Family Forum attendees in Boston, Massachusetts.

MDS Foundation Patient Liaisons

PLEASE CONTACT:

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P.O. Box 353
Crosswicks, NJ 08515
Tel: 1-800-MDS-0839
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Fax: 609-298-0590

EU Patient Liaison

Sophie Wintrich
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123 Coldharbour Lane
London SE5 9NU, UK
Tel: +44 20 7733 7558

Highlights From Around the World...

MDS Patient & Family Forum
Leeds, UK
April 14, 2009

Dr. David Bowen of St. James's Institute of Clinical Oncology presented current issues in MDS.

Group discussion with patients and caregivers.

David Hall, Chairman of the MDS UK Patient Support Group.

Toronto MDS Patient and Family Forum
Toronto, Canada • October 6, 2009

Dr. Karen Yee from Princess Margaret Hospital during her MDS presentation.

Toronto patients and caregivers learning about the latest treatment options in MDS.

MDS Patient and Family Forum – Pittsburgh, PA • October 21, 2009

Nurse Joan Latsko educating patients and their guests in Pittsburgh.

Dr. James Rossetti from the Western Pennsylvania Cancer Institute was the guest speaker.

Spreading the Word Worldwide – Quality-of-Life and Patient Education Forums

Ongoing meetings in the US and Europe addressing QoL issues for MDS patients. The Foundation serves as an effective educational conduit for information regarding the most updated treatment options, clinical studies, referrals to Centers of Excellence, and other information concerning the Myelodysplastic Syndromes. Patient forums have been held to date in:

UNITED STATES

- New York City, New York *(October 2004, December 2006)*
- Tampa, Florida *(November 2004)*
- Palo Alto, California *(December 2004)*
- Scottsdale, Arizona *(February 2005)*
- Chicago, Illinois *(March 2005)*
- Philadelphia, Pennsylvania *(December 2005, February 2006, April 2007)*
- Pittsburgh, Pennsylvania *(February 2006, October 2009)*
- Oak Brook, Illinois *(January 2007)*
- Dallas, Texas *(January 2007)*
- Seattle, Washington *(March 2007, August 2009)*
- Covina, California *(March 2007)*
- Rochester, Minnesota *(June 2007)*
- Baltimore, Maryland *(September 2007, June 2009)*
- Philadelphia, Pennsylvania *(February 2008, July 2009)*
- Rochester, New York *(April 2008)*
- Los Angeles, California *(May 2008, August 2009)*
- Scottsdale, Arizona *(May 2008)*
- San Antonio, Texas *(August 2008, September 2009)*
- Atlanta, Georgia *(November 2008)*
- Columbia, South Carolina *(March 2009)*
- Chicago, Illinois (*July 2009)*
- Bethesda, Maryland *(August 2009)*
- Birmingham, Alabama *(August 2009)*
- Hackensack, New Jersey *(September 2009)*
- Boston, Massachusetts *(November 2009)*
- Lake Success, New York *(December 2009)*

CANADA

- Toronto, Ontario *(October 2009)*

EUROPE

- Edinburgh, Scotland UK *(March 2005)*
- Paris, France *(January 2006)*
- Bournemouth, England UK *(February 2006, November 2009)*
- London, England UK *(February 2006, September 2008)*
- Hamburg, Germany *(April 2006)*
- Leeds, England UK *(May 2006, April 2009)*
- Marseille, France *(May 2006)*
- Vienna, Austria *(July 2006)*
- Prague, Czech Republic *(September 2006)*
- Stockholm, Sweden *(September 2006)*
- Freiburg, Germany *(February 2007)*
- London, United Kingdom *(May 2007)*
- Florence, Italy *(May 2007)*
- Dubrovnik, Croatia *(September 2007)*
- Sinaia, Romania *(October 2007)*
- Toulouse, France *(May 2008)*
- Copenhagen, Denmark *(June 2008)*
- Lund, Sweden *(September 2008)*
- Ontario, Canada *(September 2009)*
- Tel Aviv, Israel *(January 2009)*
- Frankfurt, Germany *(March 2009)*
- Stockholm, Sweden *(April 2009)*
- Patras, Greece *(May 2009)*
- Berlin, Germany *(June 2009)*
- Cambridge, England UK *(November 2009)*

SOUTH AMERICA

- Buenos Aires, Argentina *(November 2008)*

Established MDS Patient Support Groups

UNITED STATES

- Chicago, Illinois Support Group meets on the fourth Tuesday of the month from 1:30–3:00 pm at Northwest Community Hospital's Cancer Service department (lower level), 800 W. Central Road, Arlington Heights, Illinois. Contact Kim Jensen at kjensen@nch.org or call 847-618-6914.
- Puget Sound, Washington Support Group meets on the third Tuesday of the month at 6:30 pm at the Puget Sound Blood Center, 921 Terry Avenue, Seattle, Washington. Contact Steve Kessler at steve@Qamonline.com or call 800-877-0168.
- San Francisco Bay Area Support Group meets on the second Sunday of the month at 2 pm at the Park Blvd. Presbyterian Church, 4101 Park Blvd., Oakland, California. Contact 800-MDS-0839 for more information.

CANADA

- Toronto, Ontario Support Group. Contact William Pearson at william.pearson@sympatico.ca or call 905-561-699 for information on upcoming meetings.

EUROPE *(Countryside Groups)*

- France: Association Connaître et Combattre les Myélodysplasies
- United Kingdom: UK MDS Patient Forum
- Czech Republic: Czech Republic MDS Forum

Patient Advocacy

Remembering Suzanne Fleischman (1948–2000)

Professor Suzanne Fleischman died from complications of CMML in transformation on February 2, 2000. An internationally renowned authority in French and romance languages she was intrigued by the medical jargon that is pervasive in our patient interactions. As a spokesperson for the MDS patient community, she shared her hard-won knowledge of this disease with patients worldwide. She was our first patient advocate and delivered the most meaningful address at the 1999 MDS symposium of all the hundreds of talks presented. As she stated so eloquently in her talk at the 5th International MDS Symposium in Prague:

"From the moment of diagnosis MDS patients live under a mantle of chronic illness with scant hope of cure. Our diseases are rare and unfamiliar to the population at large… my agenda is to communicate to physicians those issues that are of concern to us."

Her last posting on January 19, 2000 to the MDS community of patients on the Internet was typical of Suzanne — *"know how much it means to me and how gratified I feel knowing that you all have benefited from whatever I could pass along and share with you to make your lives a little better."*

She will be missed.

As the recipient of a large bequest from her estate, the MDS Foundation has established the Suzanne Fleischman Memorial Lecture, which is a perpetual lectureship to honor Dr. Fleischman at all of our international MDS symposia. The lectures focus on the many concerns eloquently expressed by Suzanne during her lifetime as an advocate for patients with MDS.

The 2009 Suzanne Fleischman Memorial Lecturer was Dr. David Cella. His topic was *Symptom and Treatment Burden: Effect on Quality of Life*. In his presentation, Professor Cella discussed several of the quality-of-life issues and outcome measures that arise and should be a major component of our discussions with patients and their loved ones early in the overall management of MDS.

Dr. Cella is a graduate of Northwestern University and received his PhD in Clinical Psychology from Loyola University of Chicago. Currently, he is Professor of Psychiatry and Behavioral Sciences at Northwestern University Feinberg School of Medicine. He serves as Executive Director of the Center on Outcomes, Research and Education. He has built a clinical and research program with an emphasis on quality of life and outcome evaluation in cancer treatment research. Dr. Cella has several grants and contracts to study quality of life and outcome evaluation. In 2008, he received the International Society for Quality of Life President's Award. He has produced over 300 publications over the past 25 years.

Suzanne Fleischman Memorial Fund for Patient Advocacy

A fund has been established by the MDS Foundation in memory of Suzanne Fleischman. Contributions may be sent to the Foundation with a notation designating the *Suzanne Fleischman Memorial Fund for Patient Advocacy.*

New donations have been made by:

Edward Fleischman
Prescott, AZ

Fay J. Wanetick
Pittsburgh, PA

Roslyn Raney
Menlo Park, CA

Purchase MDS Awareness Pins

The MDS Foundation has enameled lapel pins for you to wear with pride and to increase public awareness about MDS. The pins are available in either a rectangular or circular design with a $3.99 donation to The MDS Foundation.

mds foundation
Join the Journey to Hope

To order your pins, call 1-800-MDS-0839.

The pins were created especially for the MDS Foundation to contribute to the effort to help people worldwide living with MDS. Your donation will help increase awareness of this little known disease, which is the most common of the hematologic malignancies. Please ask your family and friends to wear these pins in support of our mission!

mds
Join the Journey to Hope

Advocate Experience

Raymond W. Malles

I was fortunate to be asked to represent the MDS Foundation as a patient advocate after receiving a call from Novartis Oncology. Inasmuch as this task was "right up my alley," I readily accepted.

My first meeting with others, representing the full spectrum of cancer advocacy, was on March 11, 2009, in Morristown, NJ. There was a follow-up conference call during the summer and the second meeting this September in Cambridge, MD. Part of this recent gathering included a guided tour of the Novartis Research Laboratory. Never having been exposed to this environment, I was totally amazed. The research process in this facility is totally controlled by a vast computer system—including the introduction of robots. This company stores in excess of three million compounds they have developed and use to discover new oncology products. As a research scientist embarks on a path to deal with a targeted form of cancer, he or she orders specific combinations (from the stored compounds) for testing. The robotic system gathers precise amounts of the selected compounds, and stores the new combination in a controlled environment to observe the results. This tedious process involves untold amounts of time and effort. The staff indicated drug development typically takes fifteen to twenty years to develop and to reach the marketplace. In between, there are many dead ends and failed expectations. Complications are encountered in many ways as the company pursues its objective. Unexpected results along the way often force scientists to change their course. The seemingly endless chemical analysis, animal testing, clinical trials and FDA approvals shape the lives of everyone devoted to this noble cause. The obvious goal is to treat and hopefully cure disease in all of its forms.

Part of our meeting included a presentation on clinical trials. This area of the development process is not easily understood by the average citizen, hence my awakening! Controls and restrictions imposed by the Food and Drug Administration spell out every aspect of a trial. Specific goals are established, and measurements against these goals determine if a path will continue or be abandoned. Patient safety is the primary objective. There are several types of clinical trials, and none are utilized in every case. The task of obtaining patients willing to participate in a clinical trial is huge. I, for one, would willingly be a part of a trial should I reach a plateau where my treatment regimen is failing and I meet the criteria for inclusion. Anyone dissatisfied with their treatment and progress should explore the clinical trials that may help them. Continue to monitor the **MDS-Foundation.org** website where active trials are described.

My opening paragraph mentioned that being an advocate was "right up my alley." In keeping with that statement, I offer you a comprehensive video that addresses our disease from a patient's perspective. I have learned so much from personal investigation, involvement in MDS Patient Forums and experience that I applied my talents to create this educational video. The Foundation was kind enough to provide a link on their website. On the opening web page, simply click the "links" on the lower left side. On the next page, select the three parts found on the lower right side. The last part is an interview of another MDS patient. There are a few areas where background voices make listening difficult, but I felt its content was important regardless. It was someone other than me who can hopefully educate others. The video might serve to inform friends and family who don't quite understand the complexities of MDS. Please give them a try.

Considering what I have learned since being diagnosed with MDS, it is not difficult to see why medical treatment in this country is expensive. The long and involved development process, high salaries of the "best and the finest," numerous failed attempts, and costly clinical trials systematically add to the final product cost. I, for one, believe our healthcare system is the best in the world. Debating the areas needing change certainly does not signal a complete overhaul of our healthcare system. I believe fine tuning is all that is necessary.

GIVE A GIFT OF HOPE...

Journey to Hope Bracelet

Lovin' Kisses Beading
Promoting MDS Awareness

Sandy Madrigal, Designer/Creator
P.O. Box 2541
Davenport, Iowa 52809-2541

Visit www.lovinkissesbeading.com.

This handcrafted bracelet was created to draw attention to Myelodysplastic Syndromes. My design is dedicated to the loving memories of my mother, Betty, and my sister, Linda. They were diagnosed with MDS just eight weeks apart. Both fought the disease bravely and with great dignity.

Now I'm doing what I can to continue their fight. Each bracelet is only $20.00 (plus S&H). Visit my website for details. A portion of the proceeds from the sale of my bracelets will be donated to the MDS Foundation to help further their research and create awareness.

Women's Journey to Hope Bracelet

Men's Journey to Hope Bracelet

MDS Patients Share Their Stories...

The Foundation would like to invite patients and their families to share their stories with others in the MDS community. Living with MDS poses challenges, and many of you have stories that provide hope to others. Please contact the Foundation, if you would like us to publish your story.

SUBMITTED FROM OKLAHOMA, USA

My MDS Journey

Kirby Stone

INTRODUCTION

Before starting my MDS Journey I would like to offer some suggestions:

- Educate yourself on MDS
- Find a doctor you are comfortable with who has experience treating MDS patients
- Keep a positive attitude and never give up
- Take advantage of Patient Conferences

Until early 2004 I had been exceptionally healthy. I had never spent a night in a hospital. I was born at home in a small town in Oklahoma in 1941. In July 2002 I was diagnosed with Celiac disease, which is gluten intolerance and is an autoimmune disorder. Eliminating gluten from the diet cures the symptoms so it can be controlled.

In late 2003, I had a routine physical exam. While on vacation at Kitty Hawk, NC, for the celebration of the first century of flight, I received a phone call that suggested I should have my blood counts rechecked when I returned home to Cincinnati, OH.

DIAGNOSIS

In mid-January 2004, the blood test was repeated and it revealed low blood counts: platelets=86, WBC=2.2, Hgb=11.9. I felt fine but my doctor wanted me to see a hematologist/oncologist. On January 27, 2004, the hematologist performed a BMB in his office during my first visit with him. He indicated he was testing me for leukemia and myelodysplasia. He never indicated how serious a disease myelodysplasia was.

MDS Patient Kirby Stone and wife Nancy.

My wife and I knew leukemia was serious but had never heard of myelodysplasia. We even asked him to spell it for us before we left his office.

At home we quickly searched the Internet for myelodysplasia and were SHOCKED when we read of the seriousness of MDS. We felt it was the doctor's responsibility to explain how serious this might be. The MDS Foundation has been very helpful in providing information throughout the period of my illness.

My wife, Nancy, has been a wonderful caregiver throughout my journey with MDS and we are always together for every doctor's visit, bone marrow biopsy and other treatments. I will use the term "we" throughout this description of "our" fighting this disease, since we are always together. I could not survive without her loving assistance.

February 4, 2004 we returned to the hematologist's office where he reviewed the results of the BMB. He diagnosed my disease as MDS with the blasts at 6–7%. His suggested treatment was to have blood drawn every month to see what the progression was. He said that Thalidomide was the only drug available, but it had serious side effects and its effectiveness would eventually stop. We asked him to fill in the blanks on a form to rate the MDS; I had tri-lineage effects, and blasts over 5%, putting me at RAEB-1.

The prognosis for life expectancy was not good even at this initial diagnosis.

Our first impressions with the hematologist were not good; he in no way tried to explain the seriousness of the disease and, in our opinion, offered no "reasonable" treatment.

I was a retired research engineer and had also had a BS in Chemistry. I had been involved in research since the early 1960's and was not willing to just sit by and watch the MDS get worse. Our research on the Internet had educated us as to the seriousness of the disease, and that clinical trials might be available. Both AA/MDS International Foundation and MDS Foundation personnel were very helpful in providing names of doctors and institutions that might offer clinical trials for MDS.

We have friends who have a home in Tucson, AZ. I called the Arizona Cancer Center at Tucson — a center of excellence for MDS. We were planning to visit Tucson in mid-February and arranged a meeting with Dr. Mahadevan, the director of MDS research at ACC. On February 16, 2004 we met with Dr. Mahadevan and his research nurses. He was concerned that my MDS could "blast off" quickly since it was already in the excess blast stage. One of the complicating factors was the fact that as one of Jehovah's Witnesses, I do not take blood transfusions of any kind; therefore strong chemotherapy couldn't be tolerated. Dr. Mahadevan thought they could treat me and suggested we apply to enter a trial at ACC.

We returned home to Cincinnati and researched other options, calling several doctors, hospitals, etc., but found no other trials that were open. Revlimid was in clinical trials but no trials were open and "compassionate use" was not an option from Celgene.

Nancy and I decided to travel back to Tucson and try to enter the trial using Avastin. We arranged to stay in Tucson as long as needed.

On March 1, 2004 a BMB was performed at ACC. The results were back on March 4, 2004 with the blasts at 12.5%. The results were of concern to us but ACC did not seem too concerned. On March 19, 2004, we

were called by ACC and informed that I would not qualify for the trial. It seems the BMB slides had been sent to Stanford University and the analysis there was that the blasts were 18–19% and this was too close to AML for me to qualify for the trial. Since Stanford University controlled the trial we had no recourse but to return to Cincinnati. We were told that we should return to our home to be near our support systems, since in their opinion, I had three to four months to live. A wonderful nurse practitioner at ACC who had worked with us suggested we could try Thalidomide at 100 mg/day or low-dose Ara-C after returning to Ohio. She has been a real encouragement to us over all the years.

The return trip from Tucson, AZ to Cincinnati, OH was a sad and difficult journey. We had no real hope at that moment and the loss of a chance at the clinical trial left us devastated. We had not been able to find any trial or treatment anywhere else.

On a side note, Avastin did not prove to be effective on MDS patients, so my rejection from the trial at the University of Arizona actually proved to be a blessing, as will be noted on my further treatment successes.

THE FIRST LEG OF THE JOURNEY: TREATMENT WITH THALIDOMIDE

Returning to Cincinnati we searched for a hematologist/oncologist that would try to treat the MDS aggressively rather than just watching and waiting. My work in research and engineering would not let me take such a passive approach. I always felt a proactive approach was best in dealing with any situation.

We found a wonderful hematologist/oncologist who had helped a dear friend of ours with chronic leukemia a few years before. On April 14, 2004 we met Dr. B and discussed my situation. He did a BMB that day and said to give him a week to get the results and come up with a treatment plan. He said he "would help us and would treat my MDS." Nancy and I were very happy to have a doctor who would try to treat my MDS aggressively. I had been diagnosed with it on February 4, 2004 and it was now April 20, 2004. I had not received any treatment or medication for MDS as of that date.

On April 21, 2004, we found the blasts were now at 14–16% increasing from the 12.5% at the Arizona Cancer Center. Dr. B started me on Thalidomide at 100 mg/day on April 21, 2004. At that point in time there were no drugs specifically for MDS. Thalidomide had been successfully used for multiple myeloma patients and had been tried in an "off-label" use for MDS with some success.

Within three weeks my platelets and Hgb were increasing, and within five weeks all counts were increasing. My response to Thalidomide was exceptional. Procrit and Neupogen were used as needed initially but were later discontinued as all the blood counts returned to good values.

On September 22, 2004 a BMB revealed NO DYSPLASTIC CELLS and the blasts at <2%. We were thrilled at the results.

My treatment with Thalidomide continued positive for 32 months until late 2006. On December 6, 2006 a BMB revealed the blasts were at 4.5%, the platelets had dropped to 86, and the WBC to 3.6. We decided to change to Revlimid, now available "off-label" to patients who did not have the 5q chromosome deletion.

Over the 2.5+ years of my journey up to that point, I had eight BMBs to monitor my bone marrow conditions. Dr. B was keeping careful track of my MDS.

THE SECOND LEG OF THE JOURNEY: TREATMENT WITH REVLIMID

On December 24, 2006 I started treatment with Revlimid at 10 mg/day. The results were almost immediately good with the platelets increasing to the 170's in one month. The other counts also increased nicely.

Revlimid was much easier to take than Thalidomide, having much fewer side effects. I had sustained some neuropathy — numbness in my hands and feet — with the Thalidomide. This did not increase further with the Revlimid and seemed to be reduced somewhat over the next few months.

VOLUNTEER TO HELP OTHER PATIENTS: ANOTHER LEG OF MY MDS JOURNEY

Fairly early in my battle with MDS I found the internet web sites for MDS patients. These services allow patients to ask questions and receive answers regarding their disease and treatments. Over the years I met many wonderful people who helped me to cope with MDS. With some I developed a close relationship — contacting them directly via email or by phone.

I also volunteered to receive calls from other MDS patients — some recently diagnosed. These calls allowed me to give encouragement to new patients. Being able to discuss your disease with another patient can help you cope with MDS. Medical advice is not the purpose of these discussions; rather it is to listen and perhaps relate your experiences in dealing with MDS. Over the years I have talked with many other MDS patients, and it is a rewarding experience.

The patient conferences are a wonderful way to meet other patients and hear truly expert doctors speak on treatments for MDS. The group meetings with other MDS patients are always very encouraging and informative. I encourage any MDS patient and their caregivers to attend these conferences.

Being able to discuss your disease with another patient can help you cope with MDS. Medical advice is not the purpose of these discussions; rather it is to listen and perhaps relate your experiences in dealing with MDS. Over the years I have talked with many other MDS patients, and it is a rewarding experience.

ANOTHER LEG ON MY JOURNEY: SEEKING TO FIND ANOTHER TREATMENT

In mid-2008 my good response to Revlimid started to wane. My platelets and WBC started a slow decrease. This is often the case with Revlimid, and we tried reducing dosages over a period of a few months in an attempt to find a successful dose.

On October 8, 2008, a BMB revealed 6% blasts and a record low for my platelets. My doctor and I decided to stop Revlimid. By May of 2009 the blasts had increased to 16–17%.

Since mid-November we have tried four cycles of Vidaza and one Dacogen cycle. None of these new medications seemed to be controlling the MDS. We are seeing some success using Thalidomide for the second time, after being off of it for three years.

I've had a long success against MDS — over five years as an RAEB-2 patient. At diagnosis the numbers suggested I might live only a few months. This time has enabled me to spend more time with my grandchildren and to encourage other MDS patients.

We have learned that one should never give up, since newer treatments continue to be developed. I've still not spent a night in a hospital... and hope to keep it that way.

ALWAYS keep a positive attitude and learn as much as you can about MDS in your journey.

SUBMITTED FROM CANADA

My Story

William Pearson

I'm a 73 year-old retiree, although I still do some consulting — keeping my finger in the pie, so to speak.

In the fall of 2002, I was in Poland on a consulting assignment. A normal day would start by walking from our hotel to the office, about two kilometers. Most days we would travel by car to about five different steel companies. My role was to study the operation which required, in many cases, taking stairs to the operating deck and general walkabouts. About a week into my project it started when climbing the stairs at one of the steel companies — I had to rest a number of times. Instead of walking to and from the hotel I started taking a taxi.

On my return to Canada my first visit was to see my family doctor. She ordered blood tests which indicated my hemoglobin was a low 7.9.

The next step was a referral to a local hematologist, Dr. S. Gee. She did further blood work, again resulting in low hemoglobin and a white cell count of 2.5. My platelets were of normal value. Following a bone marrow test I was diagnosed as having MDS. My reaction was "what is MDS?" Dr. Gee went into details of the disease with my wife Janet and myself. Dr. Gee is still very supportive and accessible. Tests taken on January 27, 2003, showed my Hb. 8.1, WBC 2.4, and platelets 353. On the following visit, Dr. Gee said she wanted to try me on a drug called Danazol. The drug had a low percentage of success, less than 15%, but it had a positive effect on me. June 16 my Hb. reached 101. I had blood tests every month for two years (2004–2005) and during that time my Hb. averaged 11.1. In April 2006, I suffered a setback. My hemoglobin dropped to the low 80's. They put me through a number of diagnostic tests (colonoscopy/gastroscopy) to rule out an internal bleed. There was no bleed. I was then transfused four units of red cells and another bone

MDS Patient William Pearson and wife Janet.

marrow. My hemoglobin was still in the low 90's. This continued through to June 2007. Between June and September I was transfused another nine units of red cells. I had another bone marrow and received a call from Dr. Gee one evening advising me that the MDS had slightly worsened. NK cells were reactive, but no sign of leukemia. On a follow-up appointment with Dr. Gee in August 2007, she asked permission to refer me to Princess Margaret Hospital in Toronto to see if I would qualify for a study group or clinical trial.

September 5, 2007: I had my first appointment at Princess Margaret Hospital (which has the designation of Center of Excellence by the MDS Foundation). As one would surmise, I had but another bone marrow done by Dr. K. Yee. She also asked permission to take an additional sample of my bone marrow for research.

During the period of September 12, 2007 to January 10, 2008, I was transfused 16 more units of red cells. During that time I had CT scans and many tests involving my blood, which all proved negative. My ferritin level became a concern. On October 31, Dr. Yee indicated she wanted to try me on a drug called Cyclosporine — which would be covered by the provincial government upon approval. My type of MDS did not fall into any ongoing clinical trials of other drugs being used for MDS. At that point she was unsure what the outcome would be with this drug. On December 11, 2007, she called me at home to say she had approval for me to start Cyclosporine on January 1, 2008. On

January 18, 2008: I received approval from my medical carrier that they would support me if I was required to take Exjade because of iron overload. January 20th: She called and wanted me to start magnesium and watch my blood pressure (due to some of the side effects of Cyclosporine). January 23, 2008: I started a mild blood pressure medication. Cyclosporine appeared to be working. By the end of January my Hb. was 11.7. February 13: CT of liver was ordered as my ferritin was still very high. CT was done February 28. March 12: Hb. was 13.0; next meeting would determine Exjade start. April 9: Hb. was 13.8 and we had to increase magnesium. Dr. Yee and Janet together agreed to try a phlebotomy instead of Exjade, of course with my approval. I was to discuss therapeutic phlebotomy at my local hospital with Dr. Gee. May 7: Hb. 14.1. During the period from May 2008 to December 2008, I had four therapeutic phlebotomies, and my hemoglobin ranged from a high of 14.3 to a low of 11.8. Another MRI would be done in February 2009. On July 22, 2008, Dr. Yee started to reduce my dosage of Cyclosporine, decreased in increments of 25 mg, the last being in March of 2009. I was reduced to 50 mg twice daily. This started a downswing of my hemoglobin. In May 2009 my cyclosporine dosage increased to 175 mg twice daily. During the down-swing, my Hb. was between 10.1–11.4. On October 7, 2009 my Hb. was 12.7.

From the fall of 2002 to the present I have had 170 hospital visits.

MDS has changed my life, but I can still golf, take vacations, remain active in my consulting business, and spend time with my grandchildren. I am an ambassador and first connection volunteer for The Leukemia and Lymphoma Society. I also support the MDS Foundation where I can.

What makes this all happen:

- I have a most understanding soul mate, my wife Janet, who attends all my meetings, appointments and keeps me on track—she doesn't let me miss taking meds, etc.
- My family doctor, Dr. Liberatore, whose quick action got me a referral to Dr. Gee, and who has followed and monitored my progress through this period.
- Dr. Gee, who diagnosed me as being an MDS patient and started my early treatment, and was quick to move me forward to the next level which was to Princess Margaret Hospital and Dr. Yee.
- Dr. Yee — I really can't say enough about the care, follow up, etc. that I receive. Her sense of humor and her accessibility make the visits to PMH more comforting.
- The support I received from the MDS Foundation, and, locally, The Leukemia and Lymphoma Society.
- A patient forum in our local area, and volunteers from MacMaster University Hospital.

Princess Margaret Hospital is 1.5 hours away from where I live. Because of the continuous monitoring I receive, the blood tests between my visits to Princess Margaret are done at my local hospital, Joseph Brant Memorial, under the direction of Dr. Gee. During my out of Province vacation I was able to have my blood work done at the local hospital in Campbell River, British Columbia.

Learn More About MDS: Join the Journey to Hope for MDS

What is MDS?

- The myelodysplastic syndromes (MDS) are a family of similar diseases that share many common characteristics and affect tens of thousands of individuals worldwide. This number reflects only those patients who are properly diagnosed. These disorders are a primary disease of the bone marrow and share several characteristics of the acute leukemias; however, MDS far exceeds any of the leukemias in prevalence. We are seeing many more cases each year and that number will increase greatly over the next decade as the baby boomers age and diagnosis improves.
- The primary cause of these disorders is unknown; however, the chemotherapy regimens that are utilized to provide curative therapy to patients with certain malignancies (lymphomas, testicular cancer, and breast cancer) can lead to the development of secondary MDS.
- Until recently treatment consisted only of supportive care including blood transfusions (red blood cells or platelets), and treatment with growth factors like erythropoietin (EPO) with G-CSF or GM-CSF. There are now three drugs approved for the treatment of MDS: Vidaza® (azacitidine), Dacogen® (decitabine), and Revlimid® (lenalidomide). At present, there are two FDA-approved drugs for the treatment of transfusion-dependent iron overload: Exjade® (deferasirox) and Desferal® (deferoxamine). None of these are curative.

How to Help:

- Bone marrow transplantation is often the only chance of survival. Nearly 70% of the patients are without a match. The need is especially critical in racial and ethnic minority groups.
- As a not-for-profit organization, the MDS Foundation depends entirely on public funding in the form of individual gifts, donations from individual and corporate entities, and membership fees to further our work.
- To learn how to support the MDS Foundation, go to the Foundation's website at www.mds-foundation.org.

Patient Tributes

Wirral Walk in Memory of Ian Denton

Wirral Peninsula, UK
May 17, 2009

Ian was a very lively character with a very quick wit and wonderful sense of humour. This was evident in all aspects of his life, home and at work. He was very well known in the community. He had been the sub-postmaster in two busy post offices which we had run together for the last 8 years. He enjoyed playing golf, was a season ticket holder at his beloved Everton Football Club, along with our son Andrew, and he was also a keen fisherman. Ian was a very sociable man, always the life and soul of any gathering, and his loud, infectious laugh could always be heard above everyone else. But most of all he was a real family man, a fantastic Dad to Steph and Andy and we were just a very close, happy family.

We became concerned towards the end of 2007 as Ian was feeling tired all the time, and had lost a lot of weight. We were eventually able to talk him into going for a full medical assessment. The results showed that although he was healthy in every other way (he had never been ill in the 25 years I had known him), he was anaemic. After a further 6 months of tests, he was diagnosed in June 2008 with LGL leukaemia (a very rare but very treatable form of the disease). We were almost relieved that we now knew what the problem was, and we were told that a mild course of chemo in tablet form would probably sort him out. But shortly after this diagnosis we were told that they had found something else in the bone marrow biopsy — myelodysplasia. This again is not very common, especially in people under 60, but it is not only difficult to diagnose but also difficult to treat. It attacks the bone marrow, affecting blood cell production and it is one of those diseases that you can have in different degrees. Although there are various new treatments that can help some people to control some of the symptoms, the only cure is a successful bone marrow transplant. In Ian's case, he quickly became transfusion dependent and we were told he would need a bone marrow transplant as soon as possible. The biggest threat to him at this time though, was infection, as the disease had made his immune system practically nonexistent.

Alison Denton and her children, Stephanie and Andrew at the Wirral Walk in 2009. The family walked in memory of Ian Denton.

After being told on 13th of October that they had a perfect donor match for his bone marrow transplant, Ian was back in hospital on the 14th with another infection.

This time it was to prove too much for him and we lost him on October 22, 2008.

As a family we are still in shock, struggling to come to terms with our loss and not a day goes by when we don't miss him desperately. It has left a huge hole in our lives.

On Sunday, May 17, 2009, 42 of us took part in the Wirral Coastal Walk, which is a 15 mile walk around the Wirral Peninsula. We started at Seacombe Ferry Terminal (famous as a landing stage for the "Ferry across the Mersey" to Liverpool) and ended up at Thurstaton, which overlooks the River Dee. Although the morning started off bright, 90 minutes into the walk, we were treated to horizontal rain, closely followed by huge hailstones. 40 out of the 42 completed the walk despite the weather, and we managed to raise over £7500 (+$11,000) for the MDS foundation. Many of the walkers were friends of our two children, Stephanie and Andrew, who were in the middle of their GCSE and A level exams but took the time to support us in our efforts. We also received many donations from customers at the post office in Upton, where Ian was sub-postmaster until diagnosed with LGL leukaemia and myelodysplasia last June (and which I have now taken over the running). We have been touched by so many kind people who have given up their time and donated generously in memory of Ian, and we can't thank them enough for their support. We sincerely hope our efforts will help others to win their battles with MDS.

– Alison Denton

Group photo of Wirral walkers, Wirral Peninsula, UK

Wirral Walk – Ian Denton Memorial Fund

A fund has been established in memory of Ian Denton.

Donations have been made by:

Alison Denton, *Wirral, UK*
P. Denton, *Wirral, UK*
G.J. & A.C. Denton, *Wirral, UK*
P. Fardoe, *Wirral, UK*
Wirral Grammar School, *Wirral, UK*
HSBC Golf Society Liverpool *Liverpool, UK*
Ralph P.K. Carmichael, *Wirral, UK*
D.H. Carmichael, *Wirral, UK*
Sophie Carmichael, *Wirral, UK*
William Carmichael, *Wirral, UK*
E.C. Wyn Carmichael, *Wirral, UK*
C.W. & L. Jones, *Wirral, UK*
P. & E. Kinsella, *Wirral, UK*
Jennifer Harris, *Wirral, UK*
S.P. & P. O'Gorman, *Wirral, UK*
I. & J.R. Bolshaw, *Wirral, UK*
C. & D. Chamberlain, *Wirral, UK*
E. Lewis & N. Rodgers, *Wirral, UK*
W.R. Fisher, *Wirral, UK*
R.D. Raynor, *Wirral, UK*
Colin N. Woolley, *Wirral, UK*
S.J. Jones, *Wirral, UK*
D.B. & H. Bell-Jones, *Wirral, UK*
H. Betteley, *Wirral, UK*
DEVA Medical Electronics Ltd *Wirral, UK*
Susan Bloom, *Wirral, UK*
G.G. & M.V. Box, *Wirral, UK*
H. Burke, *Wirral, UK*
Mark P. & Andrea Carri, *Wirral, UK*
J.S.A. Cecil, *Wirral, UK*
Atlanta Healthcare Ltd, *Wirral, UK*
B.F. Mountain & R. Clarke, *Wirral, UK*
T.J. Cox, *Wirral, UK*
S.A. & K.M. Crabtree, *Wirral, UK*
L. & A. Creme, *Wirral, UK*
J. Drake, *Wirral, UK*
Julia Gibson Associates Ltd *Wirral, UK*
AMP Vehicle Finance Ltd, *Wirral, UK*
T. Fifield, *Wirral, UK*
S.J. & R.A. Goodwin, *Wirral, UK*
Gouldman Music Ltd, *Wirral, UK*
W. Hope & L. Kelly-Hope, *Wirral, UK*
K.E. & C.M. Jones, *Wirral, UK*
Andrew M. & Sally A. Kay, *Wirral, UK*
Charlie Landsborough Enterprises Ltd *Wirral, UK*
I. & A. Lees, *Wirral, UK*
L.M. Nottingham, *Wirral, UK*
The Port of Mostyn Ltd, *Wirral, UK*
E. & A.J. O'Neill, *Wirral, UK*
J.L. & D.J. Pattinson, *Wirral, UK*
J.E. Price, *Wirral, UK*
Neville Robinson–Krown Print *Wirral, UK*
N. & K.L. Roe-Ely, *Wirral, UK*
G.D. & B.E. Smith, *Wirral, UK*
Evan J. & Helena L. Taylor, *Wirral, UK*
N. & M.L. Topham, *Wirral, UK*
A.M. & J.E. Walsh, *Wirral, UK*
J.R.W. & H.A.W. Williams, *Wirral, UK*
Estelle Jordan Marketing and PR Ltd *Wirral, UK*
G.A. Roberts, *Wirral, UK*
L.B. Crombie, *Wirral, UK*
M.G. & N. Cornish, *Wirral, UK*
N.A. Stanley, *Wirral, UK*
M.P. Wilkinson, *Wirral, UK*
S. Saunders, *Wirral, UK*
Noel Guildford–Guildford Consulting *Wirral, UK*
M.T. Haywood, *Wirral, UK*

Ian Denton Memorial Fund: *Andrew Denton (Ian's son, far right) and school friends from the Wirral Grammar School for Boys participated in the Wirral Walk in May to benefit the MDS Foundation.*

University of Pennsylvania Health System

Penn Program for Stress Management

Stressed? Want to learn how to manage your symptoms of stress more effectively? The Penn Program for Stress Management is a mindfulness-based stress management program that uses powerful meditation-based techniques as the primary tool for long-term stress management. Mindfulness is taught as a scientific, systematic approach in which participants learn to rest attention in the moment-to-moment awareness of their experience of physical sensations, thoughts and feelings. Participants of the program thoroughly explore mindfulness and its uses in reducing the symptoms of stress that are experienced in the body and mind. 7 class locations in the Philadelphia region.

To learn more about this program go to www.pennhealth.com/stress or contact:

PENN Program for Stress Management
3930 Chestnut Street, 6th floor
Philadelphia, PA 19104

Phone: 215-615-2774
Fax: 215-615-2729
E-mail:
stress.management@uphs.upenn.edu
www.pennhealth.com/stress

Son Raises Funds for MDS Research

Walter Cahall
Portland, OR

My father, Clem Cahall, passed away on October 4, 2008, after his two-year battle with Myelodysplastic Syndrome, or MDS. I had often thought about running a marathon, and when I discovered the date of the Portland Marathon was this October 4th, 2009, I knew that I was meant to take on this challenge to honor his memory.

I also competed in the Portland Marathon to help support the MDS Foundation, a multi-disciplinary, international organization devoted to the prevention, treatment, and study of myelodysplastic syndromes. The foundation's staff was very helpful with getting my fundraising efforts organized.

I was very touched by the generosity of family, friends, and co-workers during this fundraising drive. Many people were like myself and had not heard of MDS before my father's diagnosis. I also made new connections with other people who have had family afflicted with this syndrome.

Even before the marathon's starting gun fired, I felt victorious: everyone's contributions totaled over $2000! This tremendous support inspired my drive all the way through the finish line. For those who helped to make this drive a success, I am extremely grateful. And for the love and memory of my Dad, I am eternally grateful.

Walter Cahall (left,) with Dad Clem

Walter Cahall and family at the Portland Marathon Finish Line, Oct 4, 2009.
Walter (left) with mother Eleonore Cahall, sister Darleen Cahall, sister Cheryl Costales. Walter is holding a photo of Dad Clem along with the MDS logo that he wore during the race. He also put his Dad's name on his racing bib.

Clem Cahall Memorial Fund

Donations have been made by:

David Biggs
Portland, OR

Eleonore L. Cahall
Lake Oswego, OR

Keith Barrow
Aurora, OR

Snyder & Foster, CPA LLC
Portland, OR

Lisa Preble
Gladstone, OR

Barry Raber
Portland, OR

John Lancaster
Tigard, OR

Heather Campbell
Gladstone, OR

Jack Rust
Fairfax, VA

Northwood Business Services
Portland, OR

Frederick Hirsch
Portland, OR

Carl W. Foster CPA LLC
Portland, OR

Catherine Speake
Seattle, WA

Jan Moran
Portland, OR

Tom Hendrie
Wilsonville, OR

Carollyn Farrar
Portland, OR

Deanna Ricci
Portland, OR

Sabrina Lindquist
Happy Valley, OR

Northwest Natural Gas Co.
Portland, OR

Anita White
Sherwood, OR

Amanda Briles
Portland, OR

Bruce A. Kaiser
Tigard, OR

Robert Bell
Tigard, OR

Peg Pfab
Aloha, OR

Paul Halvorson
Portland, OR

Carol Ann Sloan
Vancouver, WA

Ginna Raahauge
Gilroy, CA

Thomas & Claire Collier-Hoffmann
Portland, OR

Maria Mattis
West Linn, OR

51 Healthy Foods You Can Say "Yes" To

Reprinted from Tufts University Health & Nutrition Letter

Hardly a day goes by without the news media reporting some food that's been found to be bad for you. One day it's processed meats; the next, it's baked goods made with transfatty acids. Faced with this litany of "don'ts," you can start to wonder whether any food is OK to eat. Heart-healthy foods are particularly vexing.

In fact, scientists know of a whole cornucopia of healthy foods you can choose from. Not only are there plenty of food choices that are OK—many foods can actually give your body a boost. Your daily diet can supply everything from essential nutrients to compounds that have been positively associated with preventing diseases and minimizing the toll of aging. These are foods you can enthusiastically say "yes!" to as part of a well-rounded diet.

This list represents merely a sampling of the variety of foods you can choose in a nutritious diet. (We could pretty much list all fruits and vegetables, for instance, but that would make this list either long or boring or both.) This sampling is designed to give you ideas for meals and even snacks that point your eating plan in the right direction. Any one food on the list isn't necessarily "better" for you than other choices.

Enjoy with our compliments —
Dave Fryxell, Tufts University

1. ACORN SQUASH

A source of lycopene, folate and vitamins A and C, winter squash of all sorts also gives you dietary fiber. Plus acorn squash, for example, is rich in potassium — almost 900 milligrams per cup.

2. ALMONDS ♥

A good source of potassium, almonds, like other nuts, are low in saturated fat and high in unsaturated fats. But they're also high in calories, so substitute almonds for a snack that's high in trans- or saturated fat; otherwise the added calories offset any heart-healthy benefits. Recent research from the Antioxidants Research Laboratory at Tufts' Jean Mayer USDA Human Nutrition Research Center on Aging has demonstrated an antioxidant synergy between flavonoids and vitamin E in whole almonds. Almonds are also a source of riboflavin, magnesium and zinc.

3. APPLES

You know what they say about keeping the doctor away? An apple a day may not be quite that powerful, but apples are a good source of fiber, and a medium-sized apple has only 80 calories. Red apples are among the fruits highest in quercetin, which researchers are studying for possible antioxidant benefits. But the antioxidants are concentrated in the skin, so don't peel before eating.

4. APRICOTS

A good source of vitamins A and C, apricots also are a way to get lycopene, which has been associated with cancer prevention in men *(see tomatoes, below)*.

5. ASPARAGUS

With just 25 calories in eight medium-sized asparagus spears, you get 25 percent of your daily vitamin A and 15 percent of your vitamin C, plus essential folic acid.

6. BANANAS ♥

A good source of magnesium, which protects against bone loss and is associated with heart health, bananas are also packed with potassium. With 422 milligrams of potassium in one medium banana, you're getting almost 10 percent of the 4,700 milligrams the Institute of Medicine says you need. Potassium helps lower blood pressure and reduces the risk of kidney stones and bone loss.

7. BARLEY ♥

Looking for ways to get the whole-grain servings recommended in the new federal dietary guidelines? (Six to 13 servings of grains depending on your caloric intake, of which at least half should come from whole grains.) Try cooking up some barley—also a good source of iron and minerals—in place of white rice. But make sure you're buying whole-grain barley, not the "pearl" variety with the healthful outer husk removed. Whole grains have been associated with protection against heart disease and cancer, and may help control diabetes. Other good whole-grain choices of this type include bulgur, buckwheat groats (also known as kasha), millet and quinoa *(see below)*.

8. BEEF EYE OF ROUND

While studies continue to suggest it's smart to limit your red-meat consumption, when you've gotta have beef, eye of round is the leanest cut. A three-ounce serving has nearly half your daily protein and just 160 calories. Beef is a good source of zinc and vitamin B_6.

9. BLUEBERRIES ♥

Tufts researchers are studying blueberries for their antioxidant benefits, including the possibility that they may boost brain functions that weaken as we age. Other scientists have found in animal testing that blueberries may lower cholesterol levels. Blueberries are also a good source of vitamin K, which Tufts researchers suggest may play a role in preventing osteoporosis and hardening of the arteries. Berries of all sorts are good choices, too: Blackberries, for example, also deliver vitamin K, along with a quarter of your daily vitamin C in just a half-cup. If berries are out of season, try frozen berries blended into a smoothie.

10. BRAN FLAKES

Research shows that breakfast really is "the most important meal of the day," and bran flakes can get you off to a good start. You'll get lots of fiber and magnesium—plus many other nutrients if you pick a moderately fortified cereal. Remember to use skim or low-fat milk and to go easy on the sugar. Need a touch of sweetness? Top your bran flakes with some berries (see above) or other fruit.

11. BROCCOLI

You probably don't need any convincing that broccoli, the classic "good for you" vegetable, is a healthy choice. But one of the biggest changes in the government's new food pyramid is an increased emphasis on dark green vegetables — like broccoli and leafy greens such as spinach and kale. Most Americans need to double or triple their intake of dark green veggies.

12. BROWN RICE

Part of the push to replace processed foods with whole grains means eating more brown rice instead of the white stuff you probably grew up on. Whole grains like brown rice include the bran and germ of the natural grain that are lost in processing to make white rice, which contains only the inner endosperm. A lot of good stuff gets lost in the bargain: Brown rice has almost 10 times as much phosphorus and potassium as white rice, for instance.

13. BRUSSELS SPROUTS

Another no-surprise inclusion, brussels sprouts may do your body even more good than you'd guess. A half-cup of brussels sprouts — only about four sprouts — delivers 235 micrograms of vitamin K, which is almost double what the average American gets in a whole day.

14. CANOLA OIL ♥

Here's where substitution is really the key: Replacing butter, lard or other saturated fats with vegetable oils that contain monounsaturated and polyunsaturated fats can pay dividends for your heart. Canola oil is the very lowest in saturated fat, with other choices such as safflower and soybean oil close behind; the differences are small enough that you should pick whichever polyunsaturated oil you prefer. Olive oil has the highest proportion of monounsaturated fat and has earned heart-healthy labeling from the FDA, but it's not necessarily best. Let taste drive your choice: When you want flavor-free oil, go with polyunsaturated; when you want flavor, pick olive or peanut oils. Whichever you choose, remember that all fat contains 120 calories a tablespoon — so go easy, and don't add fat to your diet just to get more vegetable oil.

15. CANTALOUPE

That orange color inside should clue you in that cantaloupe is a great source of beta-carotene — 100 percent of your daily value in a single cup. Cantaloupe is no slouch in the vitamin C count, either, with 113 percent of daily needs per cup. Other melons such as honeydew are also good choices, though lower in both beta-carotene and vitamin C.

16. CARROTS

You knew carrots were good for you, but did you know how good? Carrots are a prime example of why it's important to eat a "rainbow" of different fruits and vegetables representing the whole spectrum of colors. This orange option delivers 150 percent of your daily vitamin A in just half a cup, plus lesser percentages of a variety of other vitamins and minerals.

17. CAULIFLOWER

Don't let the pasty white color fool you. Cauliflower is a cruciferous vegetable (meaning it's from the mustard family), just like broccoli and brussels sprouts. Compounds in cruciferous vegetables have been suggested as possible cancer protectors. In any case, cauliflower packs a nutritional punch, with 45 percent of your daily vitamin C in just half a cup.

18. CHICKEN BREASTS ♥

Boneless, skinless chicken breasts offer great convenience and a good way to get protein (half your daily value in a three-ounce serving) without a lot of fat (three grams total, including just one gram of saturated fat) or calories (140, only 18 percent of them from fat). Broil, bake or grill — don't fry — to keep chicken a smart choice.

19. COLLARD GREENS

Another option in the dark green vegetable category, collard greens are packed with vitamin A. You'll get 150 percent of your daily value of A in just a half-cup of cooked collard greens, plus 30 percent of your vitamin C and 15 percent of calcium.

20. CRANBERRY JUICE

Studies suggest cranberry juice can help ward off urinary-tract infections and might even prevent periodontitis and gingivitis by keeping bacteria from adhering to your teeth and gums. It's also loaded with vitamin C. Look for juice that's artificially sweetened to avoid added sugar. *(Note that cranberry juice can interact with the blood-thinning medication warfarin to cause bleeding.)*

21. KALE

Here's another vitamin-A powerhouse as well as a way to up your intake of dark green vegetables. Like most leafy greens, kale is a source of lutein. A mere half-cup of cooked kale also rewards you with almost seven times the recommended daily amount of vitamin K.

22. KIDNEY BEANS ♥

Rich in fiber, iron and protein, beans of all sorts can be a key ingredient in an occasional meatless meal. They're also a source of potassium and magnesium, as well as folate, which some researchers are studying for potential benefits to the brain. Beans of all types — besides kidney, for instance, black, pinto and navy — are good choices and nutritionally similar. Kidney beans give you marginally the most protein and fiber with the fewest calories, but pintos are tops in folate. Cook your own using dried beans, to avoid added salt in canned beans.

23. MACKEREL ♥

Less familiar than other cold-water fish, mackerel is worth adding to your seafood repertoire because it also contains heart-healthy omega-3 fatty acids. It's also a good dietary source of vitamin D, as well as of selenium, which has antioxidant benefits. (Small children and pregnant women should eat mackerel sparingly, however, because of the risk that some fish may have high levels of mercury.)

24. MILK (NON-OR LOW-FAT)

That ad campaign urging you to get milk is on-target — as long as you stick to skim or low-fat milk. Drinking milk makes it easy to meet the new dietary guidelines' recommendation to get the equivalent of three cups of dairy products daily. In addition to delivering calcium, fortified milk is among the best ways to get vitamin D, which your body needs in tandem with calcium to build bone strength to prevent osteoporosis.

25. OATMEAL ♥

Besides the benefits of starting your day with a healthful breakfast, and besides the fact that oatmeal helps you get whole grains, oatmeal has been shown to lower cholesterol. You can also lower blood cholesterol with oat bran and with cold cereal made from oatmeal or oat bran. *(Watch out for instant oatmeal packages, though, which typically contain lots of extra sugar.)*

26. OKRA

A food better known in southern states, okra is a good source of folate and also gives you 20 percent of your vitamin C needs in just half a cup. A recent study suggests that okra, along with eggplant and whole grains, among other foods, can be part of a cholesterol-lowering diet. (Breading and frying okra, southern-style, adds so many calories that it offsets any health benefits, however!)

27. ORANGES

Of course, you already know about the benefits of eating from the "sunshine tree" — notably, getting more than a day's dose of vitamin C in just one navel orange. Oranges also are a pretty good source of potassium.

28. PEACHES

Peaches and similar fruit such as nectarines deliver modest amounts of vitamins (especially A and C), niacin and minerals (particularly potassium), while satisfying your craving for something sweet — all at a tiny price in calories (only 40 in a medium-sized peach).

29. PEANUT BUTTER ♥

Most of the fat in peanut butter remains monounsaturated, making "PB" an option as a sandwich substitute for meats high in saturated fat. A two-tablespoon serving has eight grams of protein and 25 percent of your daily niacin. There's no nutritional difference between creamy and crunchy peanut butter — just texture.

30. POPCORN

Air-popped popcorn (easy on the salt and butter!) makes a filling whole-grain snack. A cup of plain air-popped popcorn has just 30 calories.

31. PORK LOIN ♥

This is the leanest cut of "the other white meat" (actually a red meat). A three-ounce serving delivers 32 percent of daily protein needs with just 2.5 grams of saturated fat and 120 calories. Because it's so lean, be careful to cook pork loin to the safe internal temperature of 160 degrees but not beyond. Use a meat thermometer, and remove from the heat 5–10 degrees before it's done, as the pork will keep cooking while "resting." Even if still pink in the center, pork is safe to eat at 160 degrees.

32. PRUNES

Prunes aren't just your mom's constipation cure. A half-cup of dried prunes does provide a quarter of your daily fiber, sure, but you're also getting potassium and vitamin A, plus vitamin B_6 and powerful antioxidants.

33. QUINOA

Another whole-grain option (see the listing for barley for more), quinoa is catching on as an alternative to refined grains and other mealtime "starch" choices. Remember to rinse it well before cooking.

34. ROMAINE LETTUCE

This salad staple counts toward your daily goal of eating more leafy greens, and delivers vitamin A and C along with a tasty crunch. Boston, Bibb and red or green leaf lettuces are other good salad choices (easy on the fatty dressings!), though not as vitamin-packed. Iceberg lettuce has only a fraction of the nutritional value of its greener, darker kin.

35. SALMON ♥

The classic example of fish with heart-healthy omega-3 fatty acids, salmon can be broiled, baked or grilled to make a main dish. Keep in mind, however, that even fat that's good for you comes with a caloric price tag — 160 in a three-ounce serving of farmed salmon, 120 for the same portion of wild Atlantic salmon. If you occasionally opt for canned salmon with the bones, you'll also get calcium in the bargain.

36. SARDINES ♥

Another fatty fish that's rich in omega-3s, sardines are also a good source of vitamin D and (eaten with the bones) calcium.

37. SHREDDED-WHEAT CEREAL

In addition to the benefits of a healthy breakfast, shredded wheat cereal gives you a good start on your daily goal of 400 milligrams of magnesium, which has been associated with reduced risk of diabetes. Just two regular-sized biscuits have 80 milligrams of magnesium.

38. SPINACH

Popeye was onto something here. Besides being the quintessential dark leafy green and rich in vitamins A and K (plus some folate), spinach is also packed with lutein. Researchers have found that lutein consumption is associated with a reduced risk of macular degeneration, the leading cause of vision loss and blindness in people age 65 and older.

39. STRAWBERRIES

Like most berries (see blueberries, above), grapes and prunes, strawberries contain anthocyanins, powerful antioxidants that improve circulation and may have other health benefits. Strawberries are also a good choice for folate and vitamin C.

40. SWEET POTATOES

Try sweet potatoes instead of regular potatoes. They have more beta-carotene (a whopping 25,000 IU in one baked sweet potato with skin), vitamin C, folate, calcium and manganese than white spuds.

41. TEA

What to drink with all this? Try a nice cup of freshly brewed tea instead of a sugary soft drink. Research has suggested many possible benefits from the phytonutrient antioxidants in tea, called catechins; the strongest scientific evidence is for reducing heart disease. There's not a significant difference in antioxidants between caffeinated and decaffeinated tea, but we're not talking about herbal teas here. Iced tea contains only low concentrations of catechins, however. Premixed iced-teas and ready-to-drink teas are likewise low in antioxidants — but laden with sugar.

42. TOFU

The range of benefits hoped for from tofu and other soy products has been called into question, but tofu can still be a smart substitute for meat in your meal planning. It's a good source of protein and calcium if it's been prepared with calcium carbonate.

43. TOMATOES

Men have been gobbling tomatoes ever since research suggested that the lycopene therein may be protective against prostate cancer; a recent study points to a similar effect for pancreatic cancer in men. Tomatoes are also a good choice for lutein, and a single medium tomato contains half your daily value of vitamin C.

44. TUNA ♥

Besides being a good choice for omega-3s, tuna is high in vitamins B_6 and B_{12} as well as protein. If you buy canned tuna, opt for waterpacked, not oil-, and resist the impulse to mix it with fatty mayo; try low-fat mayo or mayonnaise mixed with low-fat yogurt.

45. TURKEY BREAST ♥

Like its poultry cousin, chicken, skinless turkey breast delivers plenty of protein — 38 percent of daily needs in a three-ounce portion — without a lot of fat (five grams, including 1.5 grams of saturated fat). Turkey is also rich in B vitamins and selenium. Besides making a good main dish, sliced turkey breast can substitute for processed meats in your sandwiches.

46. WALNUTS ♥

Remember what we said about almonds? The same goes for walnuts: They're low in saturated fat, free of cholesterol and high in unsaturated fats, but only a good idea when replacing foods packed with saturated fat. Although a quarter-cup of walnuts contains four grams of protein, you're also consuming 160 calories. Walnuts are relatively high in essential minerals and in folate.

47. WATERMELON

A good source of lycopene, a cup of watermelon also gives you about 20 percent of your daily vitamin C and 15 percent of vitamin A, with only 45 calories.

48. WHITE FISH ♥

While fatty fish such as salmon have the added benefit of omega-3s, white fish such as flounder, cod and sole are also outstanding choices. A three-ounce serving of cod, for example, offers 30 percent of your daily protein with only 68 calories and less than one fat gram. Fish sticks and fish sandwiches don't count as healthy choices, however — go with baked, broiled or grilled fish.

49. WHOLE-GRAIN BREAD

The new federal dietary guidelines encourage Americans to consume the whole-grain equivalent of at least three one-ounce slices of bread daily. Switch to whole-grain bread to get started—but check the label to make sure the first ingredient is a whole grain. Don't be fooled by terms such as "multi-grain," "100 percent wheat," "cracked wheat" or "seven-grain."

50. WHOLE-GRAIN PASTA

If you've been put off by tough, grainy whole-wheat pasta in the past, it's time to give it another try. In the first quarter of 2005 alone, more than 28 new wholegrain pastas were introduced, taking advantage of new technology to make tastier products.

51. YOGURT (NON- OR LOW-FAT)

Here's a delicious way to get your daily dairy. Besides calcium, yogurt gives you protein, magnesium and a variety of vitamins including B_{12}. It's even been linked to better breath. (Yogurt doesn't have vitamin D, however, so it's no substitute for milk.) Instead of sugared varieties, control calories by adding your own fresh fruit to plain, low-fat yogurt.

www.tuftshealthletter.com

Be a Bone Marrow Donor

For those patients diagnosed with a fatal blood disorder, bone marrow transplantation (BMT) is often the only chance of survival. Related donors provide suitable matches only 33 percent of the time. This leaves nearly 70 percent of patients without a match. The need is especially critical in racial and ethnic minority groups.

Registering as a donor is simple. A blood sample is all you need to enter your tissue type into the National Marrow Donor Program (NMDP) computerized registry. If you are in good health and between the ages of 18 and 55, you can contact NMDP at 1-800-MARROW-2. They will send additional information, including the NMDP center nearest you.

Give the Gift of Life!

Other sites of interest:

ASBMT™ American Society for Blood and Marrow Transplantation:
www.asbmt.org

International Bone Marrow Transplant Registry:
www.isbmtr.org

National Marrow Donor Program®:
www.marrow.org

Blood & Marrow Transplant Information Network:
www.bmtinfonet.org

Blood & Marrow Transplant Resources:
www.BMTresources.org

Bone Marrow and Cord Blood Transplantation:
http://bloodcell.transplant.hrsa.gov

Over 140 Things You Need to Know about Your Autologous Bone Marrow or Stem Cell Transplant is available online at www.BMTresources.org or call 414-870-4850, ISBN# 0-9768060-0-2/Price: $11.95. Contains over 140 invaluable tips to help transplant patients sail through their procedures.

Thank You to Our Pharmaceutical Supporters

We would like to thank our pharmaceutical supporters for their commitment to the Foundation and its work. They have contributed in the form of educational grants, which maintains not only this newsletter but also the development of the MDS homepage on the World Wide Web, the Center of Excellence program, continuing medical education programs, the Patient Registry, and the dissemination of patient information.

Patient Referrals

Myelodysplastic syndromes can be difficult to diagnose and treat. It is important for both patients and their families to know that optimal treatment is available and that quality of life can be enhanced.

If you would like information about treatment options, research, or quality of life, we would be glad to help. The Foundation offers a variety of patient services, including preferential referrals to the Foundation's MDS Centers of Excellence. We can also help identify physicians and centers to support you if you are travelling and need assistance.

Please contact us at:
1-800-MDS-0839

Outside the US please call:
+44 20 7733 7558

You can visit our website at:
http://www.mds-foundation.org.

Sign Up for MDS Essentials E-News

The Foundation has created a new electronic E-Newsletter to provide healthcare professionals and patients from around the world with timely information in a cost-effective manner. The MDS Essentials E-Newsletter is the electronic version of our quarterly newsletter. Receive up-to-date information on clinical trials, research, and news by simply subscribing online at:

www.mds-foundation.org

mds centers of excellence

Would you like your treatment center to become part of the referral system for MDS patients and be designated as a Center of Excellence? To be recognized as a Center of Excellence, an institution must have the following:

- An established university (or equivalent) program
- Recognized morphologic expertise in MDS
- Available cytogenetics and/or molecular genetics
- Ongoing research, including Institutional Review
- Board–approved clinical trials
- Documentation of peer-reviewed publications in the field
- The ability and intention to register patients in the MDS International Registry database

Please contact the Foundation for further information and an application form for your center.

The following centers have qualified as MDS Centers of Excellence:

UNITED STATES

ALABAMA

University of Alabama at Birmingham Comprehensive Cancer Center
Birmingham, Alabama
James M. Foran, MD

ARIZONA

Mayo Clinic Hospital
Phoenix, Arizona
Ruben A. Mesa, MD/James L. Slack, MD

University of Arizona Arizona Cancer Center
Tucson, Arizona
Daruka Mahadevan, MD, PhD

CALIFORNIA

Cedars-Sinai Medical Center UCLA School of Medicine
Los Angeles, California
H. Phillip Koeffler, MD

City of Hope National Medical Center
Duarte, California
Stephen J. Forman, MD

Stanford University Medical Center
Stanford, California
Peter L. Greenberg, MD

UCLA Center for Health Science UCLA School of Medicine
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University of Southern California Keck School of Medicine
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St. Petersburg, Florida
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Mayo Clinic
Jacksonville, Florida
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Gainesville, Florida
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International Clinical Trials: An Update

NATIONAL CANCER INSTITUTE TRIALS

As we go to press the National Cancer Institute (NCI) has listed more than 100 clinical trials that focus on myelodysplastic syndromes. Full study information on these trials is available at www.cancer.gov. This information includes basic study information, study lead organizations, study sites, and contact information. To access the information:

- Log on to www.cancer.gov
- Click on "Search for Clinical Trials"
- Click on "Type of Cancer" and type in 'myelodysplastic syndromes'
- Hit search

This search will provide you with all the trials currently underway in MDS. You may also sort by trials that only focus on treatment or trials that only focus on supportive care.

To view listings of additional studies you can log onto www.clinicaltrials.gov. You can also contact 1-800-4-CANCER for more information.

If you are an MDS patient, you may wish to discuss a trial with your primary treating physician to see if you qualify as a candidate.

Clinical trials study new interventions (drugs or procedures) to evaluate their safety and effectiveness in humans. Trials follow a careful set of steps, allowing for the systematic gathering of information to answer questions and confirm hypotheses that were formed earlier, in either laboratory experiments or preliminary trials.

A clinical trial falls into one of four phases:

Phase I. This is the first time a drug is used in humans. The trial is designed to determine dosage, route of administration (oral, intravenous, or by injection), and schedule of administration (how many times a day or week). In this phase researchers also begin to determine the drug's safety. The phase I trial is normally conducted in healthy adults and enrolls only a small number of people.

New Research Protocol Listings

The MDS Foundation wants you to know about clinical trials of investigational treatment options for patients with MDS and has updated its International Clinical Trials list on our website and for distribution.

Please contact us for a detailed listing featuring new protocols:

Website: www.mds-foundation.org
Email:
uspatientliaison@mds-foundation.org

or call 800-MDS-0839 and the current clinical trials will be sent to you.

Clinical trials often have very specific eligibility requirements. Please talk with your doctor to help decide which, if any, trials might be right for you.

Please note that the information is provided strictly as a resource and is not an endorsement of any physician, institution, or treatment.

Phase II. Patients with the disease receive the drug at dose levels determined in the earlier phase. The phase II trial begins to determine the effectiveness of the drug and provides more information about its safety.

Phase III. The drug is tested alone or against an approved standard drug. The typical phase III trial enrolls a large number of patients. If it is a comparison trial, patients may be randomly assigned to receive either the new drug or the standard intervention.

Phase IV. In phase IV the drug, already approved by the FDA and available to the public, undergoes continued evaluation. The phase IV designation is rare.

Some trials—screening studies evaluating supportive care or prevention—are not conducted in phases. In these trials a group following a certain disease combating strategy, such as a detection method, is compared to a control group.

A CRITICAL NEW CLINICAL TRIAL

Myelodysplastic Syndromes (MDS) and Anemia: Potential New Treatments Through Clinical Research

The MDS Foundation is active in supporting MDS patients including maintenance of access to therapy with erythropoietin-stimulating agents (ESAs). Johnson & Johnson Pharmaceutical Research and Development (J&JPRD) has structured the EPOANE3018 protocol with input from the FDA to demonstrate the benefit and safety of epoetin alfa treatment in MDS patients.

Research to date suggests that epoetin alfa is effective in reducing the need for red blood cell transfusions in patients with early stages of MDS. The purpose of this study is to explore whether it will decrease the need for blood transfusions and increase the hemoglobin level in patients with early stage MDS and anemia. While the Centers for Medicare and Medicaid Services (CMS) did not make MDS a part of their original decision due to the 'definition' that MDS is not cancer, the Foundation strongly feels that this will not be the case in the long term.

Many MDS patients rely on ESAs for the management of their disease. This trial will play an important part in decisions that will determine the future treatments for MDS patients. The use of this supportive and comprehensive data can then serve to have a positive influence over future decisions by CMS or to possibly change the labeling for ESAs to include approval for use in bone marrow failure diseases by the FDA.

EPOANE3018 Study

Anemia (a drop in the body's red-blood-cell count) is the most common blood abnormality in the early stages of MDS. Treatments that can reduce or delay the need for blood transfusions may improve and extend better quality of life for persons with early stage MDS. More research is needed to evaluate such treatments and to obtain FDA approval for use in patients with early disease who are not yet transfusion dependent.

In the EPOANE3018 study, epoetin alfa will be evaluated in patients with early stage MDS, who are not yet treatment dependent, to see if it can delay the need for transfusion. Transfusion dependence is defined as the requirement of an average of two units of adult sized red blood cell units per month. Patients with early stage MDS who have no or low red blood cell transfusion requirements are included in this study because there currently are limited treatment options for MDS patients who have anemia but are not requiring red blood cell transfusions on a regular basis.

Research to date suggests that epoetin alfa is effective in reducing the need for transfusions in patients with early stages of MDS. Epoetin alfa is a manufactured form of the human hormone erythropoietin, which stimulates the production of red blood cells.

Epoetin alfa is distributed in the United States, the European Union, and other countries under several brand names including PROCRIT®, EPREX®, and ERYPO® for the treatment of other related disease conditions.

If you are a patient with early stage MDS and anemia who is not yet transfusion dependent or a health professional caring for a patient, and would like to receive more information about this study, please refer to the contact information at the end of this article.

What is the purpose of this study?

The purpose of the EPOANE3018 clinical research study is to explore the use of epoetin alfa, to see if it will decrease the need for blood transfusions and increase the hemoglobin level in patients with early stage MDS and anemia.

Who qualifies for this study?

To qualify for this study you must:

- Be at least 18 years of age
- Have been diagnosed with MDS
- Have an International Prognostic Scoring Systems (IPSS) score of Low- to Intermediate-1 Risk Disease
- Have anemia (a hemoglobin count of 10 g/dL or below)
- Not transfusion dependent (<4 red blood cell units during a consecutive 8-week period) in the past 6 months

What can you expect if you are eligible and enroll in this study?

- Before any study related procedures are performed, the study doctor will discuss the study in detail with you, including any potential risks or benefits.
- If you participate, you will be randomly assigned (by chance, like flipping a coin) to one of three investigational treatment schedules:
  - Epoetin alfa 40,000 IU (1 mL) given once a week by subcutaneous (under the skin) injection
  - Epoetin alfa 80,000 IU (2 mL) given once a week by subcutaneous injection
  - Placebo given once a week by subcutaneous injection. Half of this group will be assigned to 1 mL dosing and the other half will be assigned to 2 mL dosing.
- You will visit the study center each week during a 48-week Study Treatment Phase for blood tests, assessment of disease progression, to receive study drug and periodic measurement of iron stores.
- You may continue to receive the investigational study drug beyond the 48-weeks if you do not require transfusions and your doctor feels that you are benefiting from the treatments.

- All patients will receive current standard of care for anemia management.
- You will continue to have safety evaluations for 4 1/2 years following study participation. These visits for the most part should coincide with routine scheduled visits to your doctor for your condition.

For doctors caring for a patient(s) with early stage MDS who may be a candidate(s) for this study:

- Approximately 450 subjects will be randomly assigned to one of the study drug schedules
- The Study Phases include:
  - Pre-randomization (Screening) Phase: Day 1 to 14
  - Study Treatment Phase:

    Day 1/Week 1 to Week 48
  - Safety Assessment Phase, consisting of:
    - Short Term Safety (Week 52) or Early Withdrawal from treatment visit
    - Long Term Safety Assessments until progression to AML, death, or the clinical cutoff is reached, which-ever occurs first
- An Independent Data Monitoring Committee (IDMC) will periodically review overall safety data throughout the study.
- An Independent Central Pathology Reviewer will review bone marrow samples and peripheral blood counts for assessment of disease progression.

To learn more about participating in the EPOANE3018 study or to refer a patient to this study, please contact the MDS Foundation by E-mailing us at: CTC@mds-foundation.org or by calling our toll free EPOANE3018 study number: 1-888-813-1260 (within the US) or 609-298-7741 (outside of the US).

We look forward to talking with you and working together to find new and better treatments for patients with early stage MDS.

About the Foundation

Who Are We?

The Myelodysplastic Syndromes Foundation, Inc., was established in 1994 by an international group of physicians and researchers to provide education about MDS to physicians and patients, support for MDS research, patient support and advocacy.

During the past decade, we have independently solicited funding for ten international symposia that have been attended by over 7,000 individuals — physicians and patients. These symposia are held biannually and have greatly improved our knowledge of these disorders and continue to provide physicians worldwide with the most up-to-date information on research in MDS. The 10th International Symposium will be held in Patras, Greece May 6–9, 2009.

At the Third International MDS meeting, attended by epidemiologists, pediatricians (yes, this does occur in children), pathologists, hematologists, oncologists, and bone marrow transplantation experts, a survey indicated a very strong interest in, and a great need for, developing a permanent working group of scientists and patient advocates. Up until that time, no formal working group was devoted to these syndromes. The MDS Foundation was born.

What Does the Foundation Do?

The Foundation works to maintain an international information network to share new research and new treatment options as rapidly as possible, to provide information and educational support for both physicians and patients, and, ultimately, to provide funding and oversight for international studies of MDS. Currently the Foundation supplies patients, physicians, and other interested parties with information in the form of a quarterly newsletter, The MDS News and MDS Essentials our e-newsletter. The Foundation's website includes patient and physician information. Our web address is http:/www.mds-foundation.org.

The Centers of Excellence Program designates institutions that meet the highest standards for diagnosis, treatment, and patient care. These Centers form the referral base for patients seeking first or second opinions and/or additional treatment options from experts in MDS. The Foundation provides patients with a priority referral to any Center of Excellence.

Patient Advocacy groups are being formed worldwide and information is available that assists MDS patients and their loved ones to understand these diseases and the treatment options that are available.

How Can You Help?

Funding for the Foundation comes from pharmaceutical companies, Foundation memberships, memorials and donations from private individuals. While we have come a long way in the 15+ years since the Foundation was established we have a long way to go. Funding is the base for realizing the Foundation's research and education goals.

The MDS Foundation is a publicly supported not-for-profit organization, exempt from federal income tax under section 501(C)(3) of the IRS code.

How Can We Help You?

Please do not hesitate to contact the Foundation if you have any questions.

MDS International Headquarters:

US Patient Liaison
36 Front Street, PO Box 353
Crosswicks, NJ 08515

Within the US: 1-800-MDS-0839
Outside the US: 609-298-6746
Fax: 609-298-0590
uspatientliaison@mds-foundation.org

EU Office:

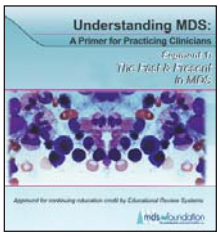
EU Patient Liaison
The Rayne Institute
123 Coldharbour Lane
Denmark Hill Campus
London SE5 9NU, UK

Tel/Fax: +44 20 7733 7558

Educational Resources

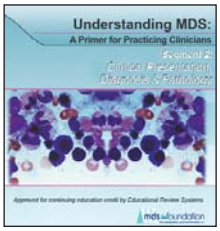
Understanding MDS: A Primer for Practicing Clinicians

Visit **www.mds-foundation.org** and click on The MDS Foundation Resource Center to take advantage of this comprehensive program, and other informative programs coming soon, designed to provide you with tools and information that will assist you in administering the best care to your patients.



Segment 1 – *The Past & Present in MDS*

Segment 1 provides insight into the history of MDS, development of the MDS classification and prognostic systems, and a glimpse into the future of MDS diagnosis, research and treatment.

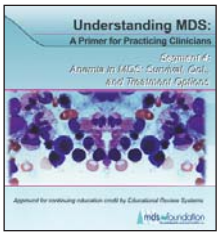


Segment 2 – *Clinical Presentation, Diagnosis & Pathology*

Segment 2 provides insight into the clinical picture of adult and pediatric MDS, primary and secondary MDS, FAB and WHO Classification system, and rationale for the proposed MDS pediatric classification system.

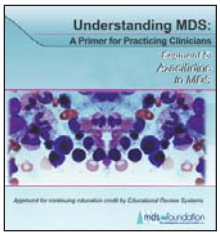
Segment 3 – *Ineffective Hematopoiesis: Considerations in Diagnosis & Treatment*

Segment 3 provides insight into the pathogenic mechanisms that contribute to the development of MDS, including the altered bone marrow microenvironment of MDS in terms of cells, cytokines, growth factors, receptors, and microvasculature; dyserythropoiesis in MDS, and therapeutic targets and approved drugs for the treatment of MDS.



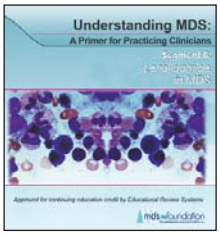
Segment 4 – *Anemia in MDS: Survival, QoL, & Treatment Options*

Segment 4 is an overview of supportive care with a focus on RBC transfusions and its effect on the morbidity and mortality of MDS patients. This segment also looks at the quality of life issues from the perspectives of the physical, functional, emotional, social and cost impacts on the patient with MDS.



Segment 5 – *Azacitidine in MDS*

Segment 5 looks at the mechanism of action of the MDS treatment, azacitidine and patient selection criteria for use. The labeled and licensed indications as well as associated risks of azacitidine are reviewed.



Segment 6 – *Lenalidomide in MDS*

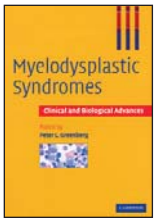
Segment 6 looks at the mechanism of action of the MDS treatment, lenalidomide and patient selection criteria for use. An overview of the labeled and licensed indications as well as associated risks is reviewed.

This multi-segment program will allow participants to choose the segments that interest them and to learn at their own pace. Segments may be completed via a written program, online in our technologically advanced MDS Foundation Educational Center, or via CD-ROM on their personal computer. **This multi-segment program is available in the following languages: *English, French, German, Italian, Japanese and Spanish.***

The program is approved for 1 hour of CME credit upon completion. There is no charge for this educational activity.

The Myelodysplastic Syndromes Foundation strives to serve as an effective conduit for information regarding the most updated treatment options, clinical studies, referrals to Centers of Excellence, and other information concerning MDS. Please bookmark our site, www.mds-foundation.org, and check back frequently for new, informative programs.

Help the Foundation and Buy Your MDS Textbooks From Us!



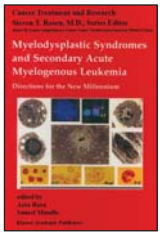
Myelodysplastic Syndromes: Clinical and Biological Advances

Peter L. Greenberg, MD
Stanford University Medical Center

Hardback, Nov. 2005/320 pp., illus.
ISBN: 0521496683/$125.00**
Cambridge University press

As the current major comprehensive reference on all aspects of the clinical classification underlying pathogenetic mechanisms and treatment of the myelodysplastic syndromes, *Myelodysplastic Syndromes* stands out as the definitive text on the genetics, pathophysiology, and clinical management of this wide range of syndromes. Authored by international experts, this book provides a state-of-the-art update of the current status and recent advances in the field. The chapters cover all aspects of the myelodysplastic syndromes, from an in-depth analysis of the multifactorial nature of this disease, including a careful assessment of stromal, immunological and stem cell abnormalities, to a review of recent molecular and cytogenetic discoveries and insights.

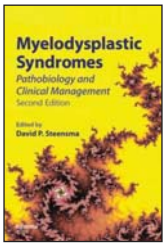
This book will be a valuable resource to clinicians and researchers who wish to learn more about myelodysplastic syndromes.



Myelodysplastic Syndromes & Secondary Acute Myelogenous Leukemia: Directions for the New Millennium (Cancer Treatment and Research)

Edited by:
Azra Raza, MD; Suneel D. Mundle, PhD
June 2001/278 pp., illus.
ISBN: 0792373660/$198.00**
Springer Science+Business Media, Inc.

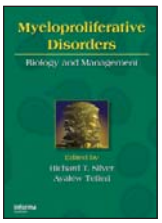
Myelodysplastic syndromes are to the bone marrow what pneumonia is to the lungs; the response of an organ to a variety of etiologic insults like aging, toxic exposure, infections and auto-immunity. Among infectious causes alone, pneumonia could be the result of a variety of possible pathogens including bacterial, viral, tuberculous or fungal agents. Similarly, MDS cannot be treated as a single disease. Attempts to harness the inherent complexity of MDS by devising "classifications" which group the various syndromes as one disease is as misguided as saying that a pneumonia is not infectious because it did not respond to antibiotics. Progress in the field will occur faster when we re-analyze this premise. Therefore, until a clearer picture of the disease emerges it is best to treat each of the MDS syndromes as a separate entity. Having no classification is better than a misleading one. This book is our attempt to define the most crucial questions related to MDS that need to be addressed immediately through logic, analysis and rigorous experimentation. If the emerging problems appear daunting, then instead of being overwhelmed by them, we should follow the advice of the great 20th century thinker Antonio Gramsci, "pessimism of the intellect must be faced with the optimism of will."



Myelodysplastic Syndromes, Second Edition: Pathobiology and Clinical Management (Basic and Clinical Oncology)

Edited by:
David P. Steensma, MD
November 2008/536 pp., illus.
ISBN: 978-01420074390/$225.42**
Informa HealthCare

This reference provides a comprehensive overview of the latest research detailing the etiology, epidemiology, treatment, and detection of myelodysplastic syndromes (MDS)—identifying effective therapeutic regimens, adverse environmental and genetic factors, and efficient modalities of supportive care that improve patient survival and enhance quality of life.



Myeloproliferative Disorders: Biology and Management

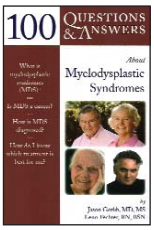
Edited by:
Richard T. Silver, MD; Ayalew Tefferi, MD

October 2007/240 pp., illus.
ISBN: 9781420061628/$161.96**
CRC Press: 800-272-7737

Myeloproliferative disorders, written by international renowned experts in the field, examines:

- New and developing diagnostic protocols and algorithms and supportive care regimens
- The evolution and classification of recent myeloproliferative disorders
- Advancements and the implications arising from clinical care and practice
- The activating JAK2V617F developed in a chapter by top experts
- The overlap between myeloproliferative disorders and myelodysplastic syndromes
- The importance of histopathology and cytogenetics on understanding these diseases

With the recent discovery of JAK2 mutations in myeloproliferative disorders, medical science has taken a revolutionary stride forward toward understanding the pathogenesis of these diseases. This new advancement translates not only to a more rapid and reliable diagnosis, but also allows groundbreaking research into the development of new therapeutics. Written in an easy-to-follow text myeloproliferative disorders gives the practicing clinician a single source answer to classification, diagnosis, management, and recent advances in this disorder.



100 Questions & Answers About Myelodysplastic Syndromes

By:
Jason Gotlib, MD, MS;
Lenn Fechter, RN, BSN

December 2007/172 pp., illus.
ISBN: 9780763753337/$19.95**

Jones and Bartlett Publishers:
800-832-0034; www.JBpub.com

Whether you're a newly diagnosed patient, a survivor, or loved one of someone suffering from MDS, this book offers help. The only text available to provide both the doctor's and patient's views, *100 Questions & Answers About Myelodysplastic Syndromes*, provides practical, authoritative answers to 100 of the most common questions asked. Written with commentary from actual patients, this is an invaluable resource for anyone struggling with the medical, physical, and emotional turmoil of this disease.

***All prices are in US dollars.*

To order, call
The MDS Foundation:
1-800-MDS-0839

TERMS OF THE OFFER:

All individual orders must be prepaid by check or money order or charged on Visa, Mastercard, or AmEx). Canadian residents, please add 7% GST. Residents of CA and NY, please add local sales tax.

Shipping and handling charges for North America are $6.00 for the first book and $1.75 for each additional book. Outside North America (only credit card orders accepted)—$9.00 for first book; $5.00 for each additional book.

Highlights of Latest Literature in MDS

Suneel D. Mundle, PhD

Listed below are citations of some new publications relevant to MDS (pathogenesis, clinical characterization, management, etc.). To access the complete article log on to www.pubmed.gov.

DIAGNOSIS AND PROGNOSIS:

1. Sperr WR et al. Comorbidity as prognostic variable in MDS: comparative evaluation of the HCT-CI and CCI in a core dataset of 419 patients of the Austrian MDS study group. *Ann Oncol*. 2009 July 15 *[Epub ahead of print]*.

   This retrospective study of 419 patients with de novo MDS in a multivariate analysis demonstrated comorbidity as an independent prognostic factor in low to intermediate-1 categories.

2. Neukirchen J et al. Platelet counts and haemorrhagic diathesis in patients with myelodysplastic syndromes. *Eur J Haematol*. 2009 Jun 22 *[Epub ahead of print]*.

   A Duesseldorf registry study demonstrates thrombocytopenia as a strong predictor of short survival, with or without hemorrhagic complications.

TREATMENT:

General:

1. Frytak JR et al. Estimation of economic costs associated with transfusion dependence in adults with MDS. *Curr Med Res Opin*. 2009;25(8):1941-1951.

   A study on MDS patients identified between May 2000 and September 2003 from US longitudinal retrospective claims database revealed association of transfusion dependence with an incremental cost of $31,255 per patient per year.

Growth Factor:

1. Greenberg P et al. Treatment of myelodysplastic syndromes patients with erythropoietin with or without granulocyte colony-stimulating factor: results of a prospective randomized phase III trial by the Eastern Cooperative Oncology Group (E1996). *Blood*. 2009;114:2393-2400.

   This phase III prospective randomized trial evaluated the efficacy and safety of EPO ± G-CSF with supportive care (n=53) vs. supportive care alone (n=57) for the treatment of low risk MDS. The response rates in the two groups were 36% vs. 9.6% respectively. With a median follow up of 5.8 years, no difference was seen in the rates of overall survival or leukemic transformation between the two study arms. On the EPO ± G-CSF treatment arm, increased survival was observed for erythroid responders vs. non-responders.

Demethylating Agents:

1. Martin M et al. A phase II study of 5-day intravenous azacitidine in patients with myelodysplastic syndromes. *Am J Hematol*. 2009 Jun 24 *[Epub ahead of print]*.

   Patients with MDS were treated with 75 mg/m^2/day azacitidine IV infusion for 5 days every 28 days. Twenty two evaluable patients showed median PFS-11.3 mo, OS-14.8 mo and a greater degree of gene demethylation in responders.

2. Steensma DP et al. Multicenter study of decitabine administered daily for 5 days every 4 weeks to adults with myelodysplastic syndromes: The alternative dosing for outpatient treatment (ADOPT) trial. *J Clin Oncol*. 2009 Jun 15 *[Epub ahead of print]*.

   US FDA approved dosing of decitabine is 15 mg/m^2 IV every 8 hours for 3 days. This study assessed a dose of 20 mg/m^2 IV daily for 5 days every 4 weeks in MDS patients. Ninety-nine patients were enrolled with ORR-32%, CR-17%. Among the patients showing improvement, 82% had a demonstrable response at the end of cycle 2.

Lenalidomide:

1. Dürr D et al. Lenalidomide in 5q minus myelodysplastic syndrome: how long is enough? *Ann Hematol*. 2009 Jun 24 *[Epub ahead of print]*.

   A case report shows hematologic and cytogenetic response to lenalidomide, a cytogenetic relapse within a year of cessation of lenalidomide, but no hematologic relapse even after 26 months from discontinuation of lenalidomide.

2. Kurtin SE and List AF. Durable long-term responses in patients with myelodysplastic syndromes treated with lenalidomide. *Clin Lymphoma Myeloma*. 2009;9(3):E10-13.

   A long term follow up on six responders to lenalidomide is reported. Transfusion independence was noted to sustain over 4.5 years with continued lenalidomide treatment even in 3 of the four del 5q patients who had persistence of the cytogenetic abnormality.

Other Agents:

1. Raza A et al. Phase 1-2a multicenter dose-escalation study of ezatiostat hydrochloride liposomes for injection (Telintra® TLK199), a novel glutathione analog prodrug in patients with myelodysplastic syndrome. *J Hematol Oncol*. 2009;2:20.

   Five dose levels between 50–600 mg/m^2 IV dose on days 1–5 every 14 days were assessed in fifty-four enrolled patients. The most common AE were grade 1 or 2 and primarily constitutional in nature. Trilineage responses were observed in 4/16 patients with trilineage cytopenia. Among the other 38, Hematologic Improvement was noted in nine patients.

2. Raza A et al. Phase 1 multicenter dose-escalation study of ezatiostat hydrochloride (TLK199 tablets), a novel glutathione analog prodrug in patients with myelodysplastic syndrome. *Blood*. 2009;113(26):6533-6540.

   Ten dose levels between 200–6000 mg of TLK199 tablets were given in divided doses on days 1–7 of 21 day cycle (max 8 cycles) in a total of 45 low, int-1, and int-2 MDS patients. No dose limiting toxicities were seen. The most common AEs were non-hematological and of grade 1 or 2 in nature. A total of 17 hematologic responses were observed with 11 being at doses 4000–6000 mg/day.

PATHOBIOLOGY:

1. Langemeijer SM et al. Acquired mutations in TET2 are common in myelodysplastic syndromes. *Nat Genet*. 2009;41(7): 838-842.

   SNP array-based genomic profiling and genomic sequencing of 102 MDS patients identified acquired deletions and, missense and nonsense mutations in TET2 gene in 26% of patients. The TET2 mutations were seen in all bone marrow lineages including in CD34+ cells suggesting its early onset in the disease evolution.

2. Delhommeau F et al. Mutation in TET2 in myeloid cancers. *N Engl J Med*. 2009; 360(22):2289-2301

   TET2 mutation was studied by gene sequencing in 320 patients. TET2 mutations were seen in 19% MDS, 12% MPD, 24% AML, and 22% CMML.

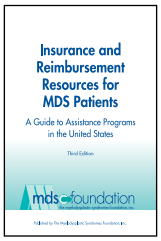
3. Sridhar K et al. Relationship of Differential Gene Expression Profiles (GEPs) in CD34+ Myelodysplastic Syndrome Marrow Cells to Disease Subtype and Progression. *Blood*. Oct 2, 2009 *[Prepublished online ahead of print]*.

   Microarray analysis demonstrated 1175 genes significantly differentially expressed by MDS vs normal CD34+ marrow cells, requiring a minimum of 39 genes to separately classify these patients. Major GEP differences were demonstrated between normal and MDS patients and between several MDS subgroups: (1) those whose disease remained stable (sMDS) vs those who subsequently transformed (tMDS) to acute myeloid leukemia (AML) within 14 months; (2) between del(5q) and other MDS patients. A 6-gene 'poor risk' signature was defined which was associated with AML transformation and provided additive prognostic information for IPSS Intermediate-1 patients. Over-expression of genes generating ribosomal proteins and for other signaling pathways (Myc, Wnt) was demonstrated in the tMDS patients. These data provided molecular criteria refining prognostic categorization and associated biologic processes in MDS.

We would like to thank Suneel Mundle, a member of the MDS Foundation, for his assistance in monitoring these important peer-review publications on MDS.

Insurance and Drug Reimbursement Resource Guide

We have assembled a listing of insurance and drug reimbursement resources for MDS patients. It is important to know that there is support for those who cannot afford medicine or other healthcare costs. We hope this new resource will be beneficial in helping you with your medical needs.



This guide to assistance programs in the United States is available for download from the Foundation's website or can be ordered in booklet form upon request.

MDS Foundation Publications

MDS Handbooks Now Available in Multiple Languages

■ Understanding Myelodysplastic Syndromes: A Patient Handbook

In addition to English, the Handbook is available in the following languages:

ARABIC · CZECH · DUTCH · FRENCH · GERMAN · GREEK · HEBREW · HUNGARIAN · ITALIAN
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Patient Information & Educational Materials Available from the MDS Foundation

- The MDS News
- MDS Essentials: Foundation's E-Newsletter
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Great Neck, NY

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Buffalo Grove, IL

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Commack, NY

Ruth Zipkin
Locust Valley, NY

Bob and Joan Altman
Katonah, NY

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Rivervale, NJ

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Great Neck, NY

A Living Endowment

Many families are affected by living with the reality of MDS. There is an extraordinary way to contribute to the MDS Foundation and support our mission of working as a resource for patients, families, and health-care professionals.

A commitment to donate to the Foundation on occasions of loss, birthdays, and anniversary remembrances can be made. Honor your friends or family members on these occasions with a donation, and the MDS Foundation will send an acknowledgment to the recipient, recognizing the occasion.

A Living Endowment donation has been made in honor of:

Sister of Mrs. Doris Schwartz

Father of Dr. Phil Coudrai

Mr. Alan Root (Graduation from Law School)

Jacob Gruber & Family (In Memory of Mother)

Marilyn Steinback (Birthday)

Robert Frutkin (Birthday)

Dr. & Mrs. Neil Schlackman (Birthday)

These donations were submitted by:
Geoff & Sandy Goldworm
Jupiter, FL

A Living Endowment donation has been made in honor of:

Ms. Sherri Koehntopp

This donation was submitted by:
Betty Lou Lindholm, *Shoreview, MN*

A Living Endowment donation has been made in honor of:

Joey Weinberg

This donation was submitted by:
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mds foundation
the myelodysplastic syndromes foundation, inc.

Membership Information

The MDS Foundation would like to have you as a member. Membership is US$40 a year for physicians and other professionals. Patients, their families, and others interested in MDS may join at the reduced rate of $25.

Membership benefits include quarterly issues of the MDS News, a special subscription rate of $119.00 for Leukemia Research (a substantial discount from the current institutional subscription rate of $2,373), and the worldwide Centers of Excellence patient referral service.

If you would like additional information, please contact us at:

The MDS Foundation
36 Front Street
P.O. Box 353
Crosswicks, NJ 08515

Phone: 800-MDS-0839
Fax: 609-298-0590

Outside the US only:
609-298-1035

Our Website

The MDS Foundation website is for healthcare professionals, patients, and other interested people. The Professional Forum and the Patient Forum are integral parts of our website.

The website is constantly being updated to better serve the needs of our patients, their families, and the physicians who treat them.

Please visit us at:
www.mds-foundation.org.

The MDS Foundation is a publicly supported organization, exempt from federal income tax under section 501 (c)(3) of the IRS code.

Myelodysplastic Syndromes Practice and Treatment Survey

Sponsored by the MDS Foundation, Inc.

THERE ARE 2 WAYS TO COMPLETE THIS SURVEY
(IT SHOULD TAKE NO MORE THAN 10 MINUTES OF YOUR TIME):

1. Simply complete this form, detach and return it to the MDS Foundation via mail or fax.
2. Complete the survey online by logging on to our website at **www.mds-foundation.org**.

Overview and Objectives: The MDS Foundation recognizes that data on many aspects of MDS worldwide is sketchy or nonexistent. While individual investigators have developed databases to track MDS within their individual sites or working groups, that information is not located within one easily accessible database.

The Foundation has attempted to design a survey that we hope will assist in describing some of the issues related to MDS worldwide as well as the treatments being utilized in this disease. While we know that this information is, in most instances, based on subjective criteria it can assist in identifying educational and research opportunities in the near term and until more accurate data is available.

The results of this expanded survey will be shared with each of our Centers of Excellence and used by the Foundation to assess new educational and research opportunities. Thank you in advance for your consideration in completing this form.

1. **Please indicate country in which you practice:** _____

   Is your practice based at: ❒ An academic hospital ❒ A community-based hospital ❒ Private practice

2. **How many MDS patients do you treat in your practice or institution each year?**

   ❒ None ❒ 1 to 10 ❒ 11 to 25 ❒ 26 to 50 ❒ 51 to 100 ❒ More than 100

3. **In the past five years did the number of patients you see for MDS increase, decrease, or remain the same? (Please check one.)**

   ❒ Increased ❒ Decreased ❒ Remained the same

4. **If the number of patients you see has <u>increased</u> please tell us why you feel this increase has occurred?**

   (Please specify by typing or writing your response below.)

5. **How often do you see each of your MDS patients?** ❒ Monthly ❒ Every 3–6 months ❒ Annually

   ❒ Only with clinical indication of disease progression ❒ Never, they are referred

6. **Do you tell your patients that MDS is a cancer?** ❒ Yes ❒ No

   Why or why not? *(Please specify by typing or writing your response below.)*

7. **When patients are referred to you how are they classified by the referring physician?** *(Please check all that apply.)*

   ❒ Not categorized ❒ International Prognostic Scoring System (IPSS) ❒ French-American-British (FAB)

   ❒ World Health Organization (WHO) ❒ Other *(If other, please specify by typing or writing your response below.)*

8. **How are patients classified in your practice or institution?** *(Please check all that apply.)*

❒ Not categorized ❒ IPSS ❒ FAB ❒ WHO

❒ Other *(If other, please specify by typing or writing your response below.)*

9. **If you do assign an IPSS or WPSS score, who at your institution assigns the cytogenetic score?**

❒ Cytogeneticist ❒ Hematologist ❒ Other

10. **Do you monitor your MDS patients with regular bone marrow standard cytogenetics?**

❒ Yes ❒ No ❒ Only with clinical indication of disease progression

11. **If your order cytogenetics and diagnostic BM cytogenetics produces no analyzable metaphase spreads, do you**

❒ Repeat the test immediately ❒ Repeat the test at the next scheduled BM ❒ Order FISH for del(5q) only

❒ Order FISH for all or some of the common chromosome aberrations observed in MDS, namely, del(5q), del(7q), +8, MLL(11q23), del(20q)

❒ Do nothing ❒ Not applicable, I do not usually order cytogenetics

12. **How often do you request BM standard cytogenetics for MDS patients?**

❒ Only at disease presentation only to confirm/rule out a suspected MDS ❒ Every 3 months ❒ Every 6 months

❒ Annually ❒ Only with clinical indication of disease progression ❒ Never

13. **How how often does the cytogenetics result impact on your management of patients with MDS?**

❒ Always ❒ Sometimes ❒ Seldom ❒ Never

14. **What would be a clinically reasonable turn-around-time for MDS cytogenetics?**

❒ 3 days ❒ 7 days ❒ 14 days ❒ 21 days

15. **What percentages of your MDS patients belong in the following IPSS risk categories?**
(Please enter the number before the %. Total should be 100%.)

_____% Low _____% Intermediate-1 _____% Intermediate-2 _____% High ❒ Unknown

16. **What percent of patients in <u>each</u> of these categories are transfusion-dependent?**
(Please enter the percentage in front of each category.)

_____% Low _____% Intermediate-1 _____% Intermediate-2 _____% High ❒ Unknown

17. **Do you monitor ferritin levels in your transfusion-dependent patients?** ❒ Yes ❒ No

18. **How do you determine when to begin chelation therapy in RBC transfusion-dependent patients?**

❒ Increased ferritin levels: ❒ >1,000 ❒ >2,000 ❒ Other amount

❒ Number of transfusions: How many on average?

❒ Other criteria *(Please specify by typing or writing your response below.)*

19. **What percentage of your transfusion-dependent patients are receiving chelation therapy?** _____%

20. **Has the availability of Deferasirox (Exjade®) increased the number of transfusion-dependent patients you place on chelation therapy?**

❒ Yes ❒ No

21. Will you begin chelation therapy earlier? ❒ Yes ❒ No

22. What percent of the low- to intermediate 1-risk MDS patients you see are being:

_____% Provided with supportive care only

_____% Watched (with no intervention)

_____% Actively treated

23. What percent of the intermediate 2- and high-risk MDS patients you see are being:

_____% Provided with supportive care only

_____% Watched (with no intervention)

_____% Actively treated

24. How important are cytogenetic findings in treatment decisions for your MDS patients?

❒ Very important ❒ Somewhat important ❒ Important ❒ Not Important

25. If you answered that cytogenetic findings are important, which of the currently identified abnormalities most influence your decisions?

26. What types of supportive care are used in your center? (Please check all that apply.)

❒ Transfusions only (RBC, platelet) ❒ Growth factors (G/GM-CSF)

❒ Vitamins ❒ Antibiotics

❒ Other *(If other, please specify type of supportive care by typing or writing below.)*

27. Do you use EPO? ❒ Frequently ❒ Sometimes ❒ Seldom ❒ Never *(skip to question 31)*

28. How do you identify patients who may benefit from therapy with EPO?

29. In which diagnosis do you most often use EPO? ❒ RA ❒ RARS ❒ RAEB ❒ CMML

30. How do you decide that a patient is non-responsive to EPO?

❒ No response after 6 weeks of therapy ❒ No response after 12 weeks of therapy

❒ Patient remains transfusion-dependent ❒ Other *(If other, please specify by typing or writing your response below.)*

31. Do you use ATG? ❒ Frequently ❒ Sometimes ❒ Seldom ❒ Never *(skip to question 34)*

32. In which diagnosis do you most often use ATG? ❒ RA ❒ RARS ❒ RAEB ❒ CMML

33. What type of ATG do you use?

❒ Thymoglobulin® (rabbit ATG) ❒ Lymphoglobulin, Atgam® (horse ATG)

❒ Fresenius ATG ❒ Other *(If other, please specify by typing or writing your response below.)*

34. Based on the information available to you, which of the following drugs do you feel will be most useful in treating MDS in each risk category? *(Please place a number on the line next to the treatment,* ***with 1 being the most useful and 8 being not useful at all****, and specify risk category.)*

	RISK CATEGORY			
	Low	**Intermediate 1**	**Intermediate 2**	**High**
____ Arsenic trioxide (Trisenox®)	❒	❒	❒	❒
____ Anti-thymocyte globulin (ATG)	❒	❒	❒	❒
____ Cyclosporin	❒	❒	❒	❒
____ Danazol	❒	❒	❒	❒
____ Deferiprone	❒	❒	❒	❒
____ Erythropoietin (Procrit®, Aranesp®, Epogen®)	❒	❒	❒	❒
____ Deferasirox (Exjade®)	❒	❒	❒	❒
____ Desferoxamine (Desferal®)	❒	❒	❒	❒
____ Azacytidine (Vidaza™)	❒	❒	❒	❒
____ Lenalidomide (Revlimid™)	❒	❒	❒	❒
____ Lonafarnib	❒	❒	❒	❒
____ Decitabine (Dacogen™)	❒	❒	❒	❒
____ Telintra™	❒	❒	❒	❒
____ Thalidomide (Thalidomid®)	❒	❒	❒	❒
____ Valproic acid	❒	❒	❒	❒
____ Zarnestra™	❒	❒	❒	❒

____ Other *(If other, please specify by typing or writing your response below.)*

35. In your opinion, what would be most helpful in increasing the referral of patients with possible or presumed MDS to a hematology practice?

❒ Education of primary care physicians, specialists in private practice or small hospitals, and medical students

❒ Patient awareness and education programs

❒ Improved dissemination of data from clinical trials

❒ More clinical trials

❒ More therapeutic options

❒ Other *(If other, please specify by typing or writing your response below.)*

36. Would you be interested in participating in new clinical studies? ❒ Yes ❒ No

37. Would you be interested in participating in a registry or additional surveys? ❒ Yes ❒ No

If you have answered yes to questions 36 or 37, please provide your contact information below:

Name: _____

Address: _____

_____

Phone: _____ Fax: _____

E-mail: _____