From the Guest Editor's Desk

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WHAT CAUSES MDS?

Introduction

Amongst the most frequent questions asked by patients soon after the diagnosis of MDS are:

“Why me?”

“What causes MDS?”

“Could I have done anything different to avoid getting MDS?” and “Can my children get it?”

The simple answer to these questions is that for the vast majority of patients, we have few clues as to the cause of their MDS.

The study of the causes of these diseases is proving difficult for the following reasons:

1. MDS is more than one disease
2. Few comprehensive patient registries exist to accurately determine who gets the different subtypes of MDS (e.g. age/sex distribution)
3. Determining the length of time to develop MDS is difficult

More Than One Disease

The diagnostic process involves categorising an individual’s disease into one of five French-American-British (FAB) groups or one of six World Health Organisation (WHO) subgroups (the latter excluding sub-types CMMML and the old RAEB-t). These classification systems recognise the differences in the bone marrow appearance and the chromosome abnormalities within the different subgroups of MDS.

It does not therefore require a large leap of faith to expect that diseases that look different down a microscope (albeit with certain overlapping similarities), might have different causes.

Attempts to study the cause of MDS (“epidemiology”) have focussed mainly on case-control studies, consisting of questionnaires requesting information about the work and recreational background of MDS patients, compared with a “control” group of individuals who do not have MDS. Whilst these efforts are commendable, and the best that can be achieved, there are many limitations to such studies. These include “recall bias”, relying on the patient’s memory for accuracy, and size of the patient group studied, which in turn determines the “power” of the study, and hence the confidence that the results are truly accurate and not simply statistical chance. For the purposes of most of these studies, MDS has been considered as one disease, given that the numbers in each subgroup will be small.

Who Gets MDS?

MDS is a rare disease, whose incidence is 4 per 100,000. The disease becomes more common with increasing age, such that the incidence rises to >30 per 100,000 for people over 70 years of age. Males are more commonly affected than females, although there is some evidence that this is not so for Refractory Anemia with Ring Sideroblasts (RARS) (Dr. U. Germing, personal communication).
MDS in children is more infrequent still, and has different characteristics to the adult form. Examples of these differences include the spectrum of FAB/WHO types (RARS and 5q- syndrome are almost never seen in childhood), and of chromosome abnormalities (a higher proportion of children have abnormalities of chromosome 7).

MDS may also evolve from related disorders such as Aplastic Anemia (following immunosuppression treatment) or Paroxysmal Nocturnal Haemoglobinuria (PNH).

**How Long Does it Take to Develop MDS?**

For patients with de novo MDS, the latency time to disease development is unknown. From a biological angle, there will be at least two phases of disease development, namely 1) the time from the first damage in the bone marrow to the appearance of a change in the blood count, then 2) the time from the first blood count abnormality to the presentation with clinically relevant disease (usually symptoms of anaemia) (Figure 1). Both are impossible to study systematically at present.

For cases of MDS developing after exposure to an agent known or presumed to cause MDS, the latency period varies. This may be from 1–41 years for different radiation exposures,1 1–10 years for alkylator cytotoxic drugs,2,3 and more difficult to assess (but up to 30 years?) for benzene.4

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**Normal Bone Marrow Cell (+/- genetic predisposition)**

**EVENT(S) A**

**Initiation of MDS**

**EVENT(S) B**

**Latency period**

**EVENT(S) C**

**Symptoms of MDS develop**

**Transformation to AML in some patients**

![Figure 1. Biological steps in the development of MDS](image)

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**Established Causative Factors for MDS**

**Cytotoxic drugs**

Therapy-related MDS and AML (t-MDS/AML) are well-recognised though rare complications following cytotoxic drug therapy for malignant and some non-malignant (mainly autoimmune) diseases. The risk of developing t-MDS/AML following therapeutic radiotherapy remains less clear.5 Several classes of cytotoxic drugs are implicated, but alkylators most frequently cause an MDS phase. One of the major challenges in the treatment of highly curable diseases such as Hodgkin’s lymphoma is now to reduce the risk of late complications, and newer therapies should prove less likely to produce t-MDS/AML.

t-MDS/AML constitute <10% all cases of adult MDS however, and the study of t-MDS/AML as a model for the causes of de novo MDS is problematic. Many cases of t-MDS cannot be easily classified due to bone marrow fibrosis (scarring). RARS and CMML are relatively under-represented, and the chromosome abnormalities in t-MDS/AML differ from those of the de novo diseases.3 Survival of patients with t-MDS is also poorer than for de novo MDS.

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**Possible Causative Factors for MDS**

**Radiation**

MDS cases are reported in cohorts of people exposed to radiation, for treatment of diseases such as ankylosing spondylitis, or following exposure to the A-bomb in Hiroshima and Nagasaki. Some of these cases occurred up to 40 years after exposure and thus the precise association between the development of MDS and exposure to radiation is not possible to quantify. Similarly, weak associations between radiation exposure and MDS are identified in some (but not all) case-control epidemiology studies.

**Benzene**

Legislation now ensures that exposure to high concentrations of benzene in the workplace or the environment should not occur. Thus, the main
sources of exposure to low concentrations of benzene in daily life are tobacco smoke and petrol (cartoon). Tobacco smoking is a weak but consistent risk factor (less than two-fold) for MDS in several case-control studies, but also contains many other carcinogens in addition to benzene.

In contrast, exposure to high concentrations of benzene clearly causes bone marrow toxicity, usually aplasia, some of which will progress to MDS and/or AML.

Miscellaneous

Whilst each individual published case-control study has identified a number of occupations and substances, which may be risk factors for MDS, there is little consistency between these studies. An exhaustive list of these possible risk factors is therefore not helpful, as many will represent statistical chance or very weak relative risks.

The incidence of MDS increases with increasing age. This has been interpreted in two ways; the disease must result from a progressive accumulation of a lifetime’s exposure to a toxic agent or, the aged bone marrow “stem” cell is easier to damage than its younger counterpart. The process of “ageing” is not well defined, though much blame is heaped upon “free radicals”, defence against which deteriorates with age. It remains unclear in what way this may be relevant to diseases of older age such as MDS.

Is There an Inherited Tendency to Develop MDS?

The vast majority of MDS patients presenting in adulthood have no relatives with the disease, and no obvious inherited disease with a tendency to MDS. 30% children with MDS have other associated abnormalities, and some of these are part of well-recognised syndromes including Fanconi Anaemia, and Blooms Syndrome.

Families with several cases of MDS are described, but are exceptionally rare. Although still very rare, familial MDS may be more likely in the family of a child with monosomy 7. In the absence of other family members with MDS, it is safe to confirm that the disease is vanishingly unlikely to run down the generations.

How Can We Study the Cause in the Future?

A whole new avenue of research into the contribution of genetics to the cause of diseases, involves the study of natural variations in our DNA from person to person. These variations can often lead to changes in the function of cells, and may therefore affect the natural functions of a cell, such as neutralising toxic chemicals that enter the body. To date, no definite natural variation in a gene has been associated with increasing the risk of developing MDS, but this field is only in its infancy. Large numbers of patient samples are needed for such studies, particularly in MDS, where these large numbers are required for each of the FAB/WHO groups.

This initiative requires the development of large Biobanks, married to high-quality registries of clinical and laboratory information cataloguing the characteristics of each patient’s disease.

CONCLUSION

Despite more than a decade of dedicated effort from epidemiologists, clinicians and scientists, the cause of MDS remains largely unknown. It is inevitable that the different subtypes of MDS will have different causes. We must use the little high-quality demographic data (Who gets MDS?) to develop hypotheses, and test these in a combination of clinical and molecular epidemiology studies, which by definition will need to involve very large patient numbers. National and international collaborative efforts are underway to attempt to achieve this.

REFERENCES

August 2004 Starts the MDS Awareness Year

In order to promote awareness and educational initiatives for the public and healthcare professionals, we are designating August as the inaugural month for a year dedicated to MDS Awareness. As part of our outreach, we are planning a year-long awareness and educational campaign. This year the Foundation has expanded its outreach and participated in many new events:

**ASPH/O:** April 29–30, 2004
**BIO 2004:** June 6–9, 2004
**EHA:** June 10–13, 2004
**NYC Patient Forum:** August, 2004 (Date TBD)
**Inaugural Charity Golf Tournament:** August 9, 2004
**ASH:** December 4–7, 2004

Glossary

**Epidemiology:** The study of frequency and cause of disease.

**Incidence:** The number of new cases presenting per year in a given population.

**Power (of a study):** A calculation used in preparing a study to determine whether the study is capable of answering the question asked. The power is determined by the number of patients in the study and the size of the effect that the researchers expect to see and would consider to be medically important.

**Case-control study:** A widely used epidemiology method for studying cause of disease. A group of patients (“cases”) are compared with a matched group of individuals lacking the disease (usually healthy), “controls”.

**Relative risk:** The numerical chances of developing a disease in a given set of circumstances. In this context the chance of developing MDS if you are exposed to chemical x, or have genetic tendency y. Relative risk of 2 = two-fold, 4 = four-fold etc.

**Latency:** In this context, the “lag” time from the first event that might start the disease process to the time the disease presents to a doctor.

**De novo:** Disease presenting with no obvious factors known to cause the disease.


Celgene has provided the MDS Foundation with unrestricted educational grants to support the Foundation’s work.

April 04: The MDS Foundation’s Susan Hogan and Nancy Mrzljak promoted MDS Awareness at The American Society of Pediatric Hematology/Oncology Meeting in San Francisco, CA.

June 04: Kathy Heptinstall and Nancy Mrzljak provided attendees at EHA, Geneva, Switzerland, with up-to-date information from the Foundation.
FDA Approves Pharmion’s Vidaza™ for the Treatment of MDS

First Drug Approved for the Treatment of MDS

May 19, 2004: Pharmion Corporation today announced that it has received full approval from the U.S. Food and Drug Administration (FDA) to market Vidaza for the treatment of Myelodysplastic Syndromes (MDS). The FDA approved Vidaza for treatment of all five MDS subtypes. These subtypes include: refractory anemia (RA) or refractory anemia with ringed sideroblasts (RARS) (if accompanied by neutropenia or thrombo-cytopenia or requiring transfusions), refractory anemia with excess blasts (RAEB), refractory anemia with excess blasts in transformation (RAEB-T), and chronic myelomonocytic leukemia (CMMoL). Pharmion intends to make Vidaza commercially available within several weeks.

“The approval of Vidaza represents a significant milestone for Pharmion and, more importantly, represents an important new option for patients being treated for Myelodysplastic Syndromes,” said Patrick J. Mahaffy, president and chief executive officer of Pharmion. “Until today, there have been no approved therapies for the treatment of MDS. We are proud to have advanced the work of the National Cancer Institute, the Cancer and Leukemia Group B (CALGB) and other academic institutions and clinicians to the point that this drug can now be commercially available to treat this very serious and life-threatening disease.”

Vidaza is believed to exert its anticancer effects by causing demethylation, or hypomethylation, of DNA in abnormal blood-forming (hematopoietic) cells in the bone marrow as well as through its direct cytotoxic effect. Demethylation may restore normal function to tumor-suppressor genes which are responsible for regulating cell differentiation and growth. The cytotoxic effects of azacitidine cause the death of rapidly-dividing cells, including cancer cells that are no longer responsive to normal growth control mechanisms. Non-proliferating cells are relatively insensitive to Vidaza.

For more information or complete prescribing information about Vidaza, please call 1-866-PHARMION, or view full prescribing information online at www.pharmion.com.

Share Your Stories With The MDS Community

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!!!

PBS Presents

A new series on PBS, Healthy Body, Healthy Mind, offers a segment devoted to MDS and the MDS Foundation. Please check your local listing for this special segment of this new series.

The Foundation offers its special thanks for Celgene’s support of a new health and wellness TV series, Healthy Body, Healthy Mind.

For a VHS copy of a 30-minute documentary style program of “MDS” call 1-800-MDS-0839.
Response to TRISENOX® Therapy in MDS Patients

Responses Seen in High-Risk and Low-Risk Patients

In Europe

Preliminary data from a phase II clinical trial of TRISENOX® (arsenic trioxide) injection in patients with myelodysplastic syndromes (MDS) were presented at the 9th Congress of the European Hematology Association (EHA), held in Geneva, Switzerland. The multicenter European study, led by Norbert Vey, MD, of Institut Paoli-Calmettes, Marseille, France, was conducted in high-risk and low-risk MDS patients; the study findings showed that arsenic trioxide, administered as a single-agent, produced a hematologic response in 27% of study participants.

“These results establish the clinical activity of arsenic trioxide in MDS. Most notable was the high number of patients achieving transfusion independence. Given this positive activity in both low- and high-risk MDS patients and the good safety profile, TRISENOX® is a prime candidate to investigate in combination therapy,” stated Vey.

The objectives of the study were to determine the safety and efficacy of arsenic trioxide as a single agent in patients with low-risk and high-risk disease. (Low-risk patients were defined as those with low or intermediate-1 MDS according to the International Prognostic Scoring System, or IPSS, disease risk classification; high-risk patients were defined as those with intermediate-2 or high MDS according to IPSS.) Arsenic trioxide was administered at a dose of 0.3 mg/kg per dose for 5 days during the first week (loading dose), followed by 0.25 mg/kg per day twice weekly (maintenance dose).

Treatment responses were observed across all hematologic lineages in high-risk patients and included one complete response. In low-risk patients, responses were seen in two lineages: no neutrophil responses were observed. Of the 39 patients with low-risk MDS, 9 achieved responses (23%), including 5 patients with major responses (13%). Of the 62 high-risk MDS patients, 18 achieved responses (29%), and 16 of those were major responses (26%). The duration of response was approximately 4 months (median); however, the true duration of response is not yet known because 20 of 27 patients were still in the response phase at the time of the last assessment.

Of the 83 patients who were dependent on red blood cell transfusions at the start of the study, 16 (19%) became transfusion independent or had a 50% or greater decrease in transfusion requirements. Similarly, 5 of 38 patients (13%) who were dependent on platelet transfusions became transfusion independent or had a 50% or greater decrease in transfusion requirements.

Arsenic trioxide was generally well tolerated in this study, with most treatment-related adverse events mild to moderate in intensity and manageable. Only 3 patients experienced serious (grade 4) thrombocytopenia, neutropenia, or pulmonary edema.

Dr. Vey’s team concluded that the outpatient arsenic trioxide regimen evaluated in their study is safe, tolerable, and biologically active in MDS patients.

About TRISENOX® (Arsenic Trioxide)

TRISENOX®, the brand name of the injectable solution of arsenic trioxide, was approved in 2000 by the U.S. Food and Drug Administration (FDA) for the treatment of relapsed or refractory acute promyelocytic leukemia (APL), a rare, life-threatening hematologic malignancy. APL is one of eight subtypes of acute myeloid leukemia (AML), and represents 10 to 15% of the more than 20,000 patients diagnosed with AML each year. TRISENOX® was granted marketing authorization from the European Commission in March 2002.

TRISENOX® may exert its antitumor effects via the induction of programmed cell death (apoptosis) and/or the inhibition of new blood vessel growth to neoplastic tissue (angiogenesis). Although currently indicated for relapsed and refractory APL, TRISENOX® has also demonstrated favorable clinical results as an effective treatment for MDS as a single-agent therapy and in combination with thalidomide. TRISENOX® has been granted Orphan Drug Designation by the FDA for the treatment of MDS. TRISENOX® is also listed in the 2004 USP DI Volume III Approved Drug Products and Legal Requirements for MDS. TRISENOX® is currently being studied in more than 40 clinical trials in a variety of cancers and hematologic conditions.
In the United States

A phase II clinical trial conducted at several sites in the U.S. also examined arsenic trioxide as a single-agent therapy in low-risk and high-risk MDS patients. Alan List, MD, of the H. Lee Moffitt Cancer Center and Research Institute in Tampa, Florida, and colleagues reported the study’s findings at the 40th annual meeting of the American Society of Clinical Oncology in New Orleans, Louisiana in June. Of the 62 evaluable patients who received arsenic trioxide for approximately 4 months, 12 (19%) had responses, and 10 of these (16%) were major responses. When the responses were examined by disease risk, major responses were seen in high- and low-risk patients. Of the 29 low-risk patients, 8 (28%) achieved responses, 6 of which were major responses (21%). Of the 33 high-risk patients, 4 (12%) achieved responses, and all of these were major responses. The median duration of response was 4.2 months for erythroid responses, 5.9 months for neutrophil responses, and 4.0 months for platelet responses.

Treatment consisted of arsenic trioxide, given as an intravenous infusion at a dose of 0.25 mg/kg over 1 to 2 hours per day on days 1 to 5 and on days 8 to 12 every 28 days. (See Figure 1 for European vs. U.S. treatment regimens. Note that currently the European regimen is the most widely regimen used in clinical studies.)

As in the European study, the effect of arsenic trioxide treatment on transfusion dependence was encouraging. Of the 32 patients who were dependent on red blood cell transfusions at the start of the study, 5 (16%) achieved transfusion independence, and 1 of 7 (14%) patients who were dependent on platelet transfusions became transfusion independent.

One of the study authors, Dan Douer, MD, of the University of California/Norris Cancer Center in Los Angeles, commented on the impact of arsenic trioxide treatment: “TRISENOX® has been shown to increase the number of red cells as well as the two other blood cell types in MDS patients. The fact that several responding patients no longer required transfusions is very significant. Responses were seen not only in low-risk but also in the sicker, high-risk patients who often need more transfusions and are more difficult to treat.”

### Reference


### Arsenic Trioxide in Combination with Thalidomide

In addition to studies of its use as a single-agent therapy, arsenic trioxide has demonstrated clinical efficacy in MDS when combined with other chemotherapeutic agents. A recently published pilot study in 28 MDS patients (25 patients with primary MDS, 3 patients with secondary MDS) evaluated arsenic trioxide and low-dose thalidomide as a combination therapy regimen. The study hypothesis was that this “2-pronged” approach would provide additional benefits compared with single-agent arsenic trioxide therapy because of the distinct mechanisms of action of each component of the combination regimen. Indeed, 25% of the study participants had a multi-lineage response following treatment with arsenic trioxide and thalidomide.

Seven patients achieved responses, including 1 complete remission (hematologic and cytogenetic response); see Table 1. The duration of the

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**Table 1.** Dosing Regimens of Arsenic Trioxide in MDS Patients

<table>
<thead>
<tr>
<th>US Regimen</th>
<th>EU Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRISENOX® (arsenic trioxide) 0.25 mg/kg (10 doses/2 wk), 5 days/wk for 2 wk followed by no dosing for 2 wk</td>
<td>TRISENOX® 0.30 mg/kg for 5 days and 0.25 mg/kg twice weekly for an additional 15 weeks</td>
</tr>
</tbody>
</table>

**Figure 1.** Dosing Regimens of Arsenic Trioxide in MDS Patients

responses, observed in high-risk and low-risk patients, ranged from 2 to 9 months. Two tri-lineage responses were seen in patients with inv(3)(q21q26.2), a chromosome abnormality that is associated with overexpression of the EVI1 gene. Patients with MDS or AML who have high levels of EVI1 gene expression have been found to have a poor prognosis. Interestingly, in vitro studies have shown EVI1-expressing cells to be particularly sensitive to arsenic trioxide. This clinical study demonstrates that patients who express high EVI1 may preferentially respond to this combination therapy. Although 5 of the 28 patients expressed high EVI1 levels at study entry, the finding that 2 of these patients achieved a tri-lineage response with the combination therapy was surprising and encouraging. Furthermore, 1 of the 5 patients with high EVI1 levels had a minor erythroid response. It should be noted that patients who do not express high levels of EVI1 also responded to arsenic trioxide/thalidomide combination therapy.

**Table 1. Overall Response of Arsenic Trioxide and Thalidomide Combination Therapy in MDS Patients**

<table>
<thead>
<tr>
<th>FAB</th>
<th>Cytogenetics</th>
<th>Response</th>
<th>Duration, d</th>
</tr>
</thead>
<tbody>
<tr>
<td>RARS</td>
<td>46XX</td>
<td>HI-E minor (50% PRBC)</td>
<td>136</td>
</tr>
<tr>
<td>RAEB</td>
<td>46XY inv(3)(q21q26.2)</td>
<td>Trilineage</td>
<td>200</td>
</tr>
<tr>
<td>RAEB</td>
<td>46XY del(5)(q15q33)</td>
<td>HI-E major (100% PRBC/Hgb)</td>
<td>280</td>
</tr>
<tr>
<td>RAEB</td>
<td>46XY</td>
<td>HI-E major (100% PRBC/Hgb)</td>
<td>84</td>
</tr>
<tr>
<td>RAEB-t</td>
<td>45XY inv(3)(q21q26.2)</td>
<td>Trilineage CR</td>
<td>293</td>
</tr>
<tr>
<td>RAEB-t</td>
<td>47XY, +8</td>
<td>HI-ANC, RAEB</td>
<td>63</td>
</tr>
<tr>
<td>Unclassified</td>
<td>46XY</td>
<td>HI-E minor (50% PRBC)</td>
<td>107</td>
</tr>
</tbody>
</table>

FAB: French-American-British Classification of MDS Subtypes

The combination therapy regimen was generally well tolerated, and combining the two chemotherapeutic agents did not exacerbate toxicities. Fluid retention and myelosuppression were the major toxicities. All side effects were reversible upon treatment discontinuation.

“Results of this combination study appear to be different than the experience with thalidomide alone as the responses from the combination regimen are more commonly multi-lineage and more high-risk patients appear to be responding,” stated the lead investigator, Azra Raza, MD, of Rush-Presbyterian-St. Luke’s Medical Center in Chicago.

**Rationale for Use of Arsenic Trioxide in MDS**

The pleiotropic effects of arsenic trioxide on three distinct cellular pathways involved in the development of MDS—apoptosis, tumor cell differentiation, and angiogenesis—make it an attractive therapy for this disease. Arsenic trioxide affects upstream and downstream components of the apoptotic response, inducing cell death by the abrogation of cytokines necessary for the viability of dysplastic cells and increasing the permeability of the mitochondrial membrane, thus rendering the cells sensitive to apoptosis. Arsenic trioxide can also promote cell differentiation through G1 cell cycle arrest, via p21 and p27 activation. Finally, arsenic trioxide possesses anti-angiogenesis properties through the suppression of vascular endothelial growth factor (VEGF) in activated neovascularure present in the bone marrow. Collectively, the diverse and significant in vitro activity of arsenic trioxide has driven the study of its use as a possible therapeutic agent for MDS in the clinical setting.

**REFERENCE**


**Safety Profile of Arsenic Trioxide**

Patient data from phase I and II studies, as well as from compassionate use programs and postmarketing safety surveillance, have been used to compile a safety and toxicity profile of arsenic trioxide. As of May 2004, arsenic trioxide has been administered to 804 patients in clinical trials (188 MDS patients), and as of February 2004, an estimated 3135 patients in the U.S. and Europe (1277 MDS patients) have received arsenic trioxide in compassionate use programs or have been included in postmarketing safety surveillance.

The postmarketing experience of arsenic trioxide has shown that the drug-related side effects are generally similar to those observed in clinical trials. Importantly, postmarketing surveillance confirms that the adverse
events associated with arsenic trioxide are manageable and reversible when patient care is provided in accordance with TRISENOX® complete prescribing information.

Adverse events associated with arsenic trioxide, administered alone or in combination with other chemotherapeutic agents, are listed in Table 2. Most of the common adverse events reported in patients treated with arsenic trioxide are of mild or moderate intensity (grade 1 or 2). A generalized rash occurs in approximately 35 to 50% of patients, and topical antihistamines or corticosteroids can be used to treat associated symptoms such as pruritus. The rash is a nonspecific drug reaction and not a true hypersensitivity or allergic drug reaction. Nausea may be related to the infusion rate of arsenic trioxide, and antiemetics such as promethazine or prochlorperazine are effective in treating drug-related nausea. It should be noted that severe nausea and vomiting requiring prophylactic antiemetics are uncommon. As is the case with many chemotherapeutic drugs, adverse events decrease in incidence and severity with continued arsenic trioxide use and rarely require interruption of therapy.

Arsenic Trioxide in MDS: An Overview of Clinical Studies

Preliminary findings from clinical trials utilizing arsenic trioxide alone, or in combination with thalidomide, have yielded encouraging data for patients with MDS. Major and minor hematologic responses as well as effects on transfusion dependence can be viewed as significant achievements in improving the health and quality of life of MDS patients (see Tables 3 and 4).

### Table 2. Arsenic Trioxide Safety and Toxicity Profile

<table>
<thead>
<tr>
<th>Dose-limiting Toxicities</th>
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<tbody>
<tr>
<td>- Fluid retention, weight gain</td>
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<tr>
<td>- Neuropathy</td>
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<tr>
<td>- Myelosuppression (neutropenia)</td>
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</table>

<table>
<thead>
<tr>
<th>Common Side Effects Associated with Arsenic Trioxide</th>
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<tbody>
<tr>
<td>- Pain</td>
</tr>
<tr>
<td>- Fever</td>
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<tr>
<td>- Cytopenia</td>
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<tr>
<td>- Rash</td>
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<tr>
<td>- Nausea</td>
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<tr>
<td>- Dyspnea</td>
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<tr>
<td>- Diarrhea</td>
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<tr>
<td>- QT prolongation</td>
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<tr>
<td>- Edema</td>
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<td>- APL differentiation syndrome</td>
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<td>- Fatigue</td>
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</table>

**REFERENCE**


### Table 3. Summary of MDS Studies

<table>
<thead>
<tr>
<th>Study Principal Investigator</th>
<th>Treatment</th>
<th>No. Pts. (Evaluable)</th>
<th>RAEB/CMML (High-risk MDS)</th>
<th>RA/RARS (Low-risk MDS)</th>
<th>Total MDS</th>
<th>Transfusion Independence or Reduction of Transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I/II MDS (US) List et al. (2004)</td>
<td>Trisenox 0.25 mg/kg IV</td>
<td>67 (62)</td>
<td>4*133 (12%)</td>
<td>8/29 (28%)</td>
<td>12/62 (19%)</td>
<td>8/55 (15%)</td>
</tr>
<tr>
<td></td>
<td>Fluid retention, weight gain</td>
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<td></td>
<td>Neuropathy</td>
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<tr>
<td></td>
<td>Thalidomide 100 mg (po qd)</td>
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<td></td>
<td>Vitamin C 500 mg (po qd)</td>
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<tr>
<td></td>
<td>Thalidomide duration</td>
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<td></td>
<td>Study duration</td>
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<td></td>
<td>Evaluable—completed at least 3 cycles of Tx &amp; end-of-study bone marrow</td>
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</table>

*CMML=CR; †RAB=CR; ‡One responder was unclassified
Single-agent and combination arsenic trioxide studies provide a basis for potential alternative treatments for patients with MDS. Ongoing and future clinical trials utilizing arsenic trioxide in combination with 5-azacytidine or candidate therapies for MDS, such as GM-CSF and vitamin C, have been proposed. The results of these studies will allow evaluation of the therapeutic potential of arsenic trioxide for the treatment of MDS.

**Table 4. Summary of MDS Responses**

<table>
<thead>
<tr>
<th>Study</th>
<th>Response</th>
<th>Response Type</th>
<th>High Risk</th>
<th>Low Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase I/II MDS (US) List et al. (62 evaluable patients) (2004)</td>
<td>Erythroid Response</td>
<td>Major</td>
<td>2 (1 CR)</td>
<td>3</td>
</tr>
<tr>
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<td>Phase I/II MDS (EU) Vey et al. (101 evaluable patients) (2004)</td>
<td>Erythroid Response</td>
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<td>Phase I/II MDS (US) Raza et al. (2004)</td>
<td>Erythroid Response</td>
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International Working Group (IWG) Criteria
International Prognostic Scoring System (IPSS) Risk Classification

**REFERENCES**


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 healthcare 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.

The MDS Foundation is grateful for community support. Our work as a non-profit organization depends on public funding.

If you would like to contribute in this way, please write to us at:

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

or call us at 1-800-MDS-0839.

A Living Endowment donation has been made in honor of:

Dr. Norman Zwiebel

This donation has been submitted by:
The Silverman Family, Del Ray Beach, FL

A Living Endowment donation has been made in honor of:

Paul Hedding

This donation has been submitted by:
Wendell and Chris Wagner, Gregory, MI
Randy and Heidi Drake, Adrian, MI
Susan Mullinix, Adrian, MI
Barbara Fike, Dexter, MI
Lee and Mardelle Drake, Adrian, MI
Paul Drake, Kalamazoo, MI

Membership Information

The MDS Foundation would like to have you as a member. Membership is US$35 a year for physicians and other professionals. Patients, their families, and others interested in MDS may join at the reduced rate of $20.

Membership benefits include quarterly issues of the MDS News, a special subscription rate of $109 for Leukemia Research (a substantial discount from the current subscription rate of $1,193), 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: 1-800-MDS-0839
Fax: 609-298-0590
Outside the US only:
609-298-1035

Blood & Marrow Transplant Newsletter

Blood & Marrow Transplant Newsletter is published four times annually by BMT InfoNet.

To subscribe, contact:

BMT InfoNet
2900 Skokie Valley Road
Suite B
Highland Park, IL 60035

Toll free: 888-597-7674
Tel: 847-433-3313
Fax: 847-433-4599
E-Mail: help@bmtinfonet.org
Web: www.bmtinfonet.org

Patients: Your Help is Needed!

We would like to invite you to participate in selected study groups and share your experience living with MDS and the quality-of-life issues that you face. The information we develop will be used to educate healthcare professionals about MDS patients’ needs in dealing with these diseases. The number of groups and their location will depend upon the responses we receive. Please join us in this most important endeavor. Further developments will be posted on our website or for more information contact Audrey Hassan our Patient Liaison at 1-800-MDS-0839.
The Eighth International Symposium on MDS will be held in Nagasaki, Japan, from May 12–15, 2005. Professor Masao Tomonaga is President of the symposium's Organizing Committee.


A call for papers will be sent out shortly. The deadline for submission of abstracts is January 15, 2005.

The second announcement will be distributed within the next few weeks and will provide details on the scientific program, social events, and accommodations. You may obtain a copy by mail, phone, or fax. The Scientific Secretariat may be contacted as follows:

Symposium Secretariat
8th MDS Symposium
Nagasaki Brick Hall
Phone: (81)-95-849-7111
Fax: (81)-95-849-7113
Email: mds8th@convention.co.jp

We are looking forward to welcoming you to the 8th International Symposium on MDS next year!

Nagasaki City is located on the west side of Kyushu island. Rich in culture, Nagasaki was the Window to the World during the 17th–19th centuries (Shogun era), and provided Japan with its first contact with Western medicine via the Dutch traders that frequented this all important port. Since the atomic bomb was detonated in 1945, Nagasaki has become a symbolic city of peace in Japan. There you will find a small and beautiful city influenced by both European and Asian cultures.
MDS Patient Registry

The patient registry form has been revised and a patient authorization form has been developed to meet the new HIPAA guidelines. The Patient Registry will help further research into the etiology, diagnosis and treatment of MDS. Currently, the MDS Patient Registry is only accepting patients through our designated Centers of Excellence. A two page data sheet will be forwarded to investigators who wish to contribute patient's names to the Registry. The Registry is located at the MDS Foundation’s Statistical Center at the University of Rochester Cancer Center. The Foundation looks forward to building the Patient Registry with our Centers of Excellence. If you would like to become a Center of Excellence, please contact The Foundation at the address below.

The MDS Foundation
36 Front Street
PO Box 353
Crosswicks, NJ 08515
Phone: 1-800-MDS-0839 within the US
Outside the US only: 1-609-298-6746
Fax: 1-609-298-0590

About the Foundation

The Myelodysplastic Syndromes Foundation was established by an international group of physicians and researchers to provide an ongoing exchange of information relating to MDS.

Until the Foundation was set up, no formal working group had been devoted to MDS. During the past decade we have conducted seven international symposia—in Austria, England, the United States, Spain, Czech Republic, Sweden, and France. The Eighth International Symposium is being held May 12–15, 2005 in Nagasaki, Japan.

A major Foundation effort is our international information network. This network provides patients with referrals to Centers of Excellence, contact names for available clinical trials, sharing of new research and treatment options between physicians, and extension of educational support to both physicians and patients.

In response to the needs expressed by patients, families, and physicians, we have established patient advocacy groups, research funding, and physician education.

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

Our Website

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

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

We welcome your suggestions.

Please visit us at http://www.mds-foundation.org
The following centers have qualified as MDS Centers of Excellence:

### UNITED STATES

- **Barbara Ann Karmanos Cancer Institute**
  - Wayne State University
  - Detroit, Michigan

- **The Cancer Center of Hackensack**
  - University Medical Center Hackensack, New Jersey

- **Cedars-Sinai Medical Center**
  - UCLA School of Medicine
  - Los Angeles, California

- **City of Hope National Medical Center**
  - Duarte, California

- **Cleveland Clinic Foundation**
  - Taussig Cancer Center
  - Cleveland, Ohio

- **Dana-Farber Cancer Institute**
  - Boston, Massachusetts

- **Duke University**
  - Duke University Medical Center
  - Durham, North Carolina

- **Indiana University**
  - Indiana University Medical Center
  - Indianapolis, Indiana

- **Johns Hopkins Oncology Center**
  - Johns Hopkins Institutions
  - Baltimore, Maryland

- **Mayo Clinic**
  - Phoenix, Arizona

- **Medical College of Wisconsin**
  - Bone Marrow Transplant Program
  - Milwaukee, Wisconsin

- **Memorial Sloan-Kettering Cancer Center**
  - New York, New York

- **National Heart, Lung, and Blood Institute**
  - Bethesda, Maryland

- **New York Medical College**
  - Westchester Medical Center

- **Zalezn A. Arlin Cancer Center**
  - Vahalla, New York

- **New York Presbyterian Hospital**
  - Columbia College of Physicians and Surgeons
  - New York, New York

- **New York University School of Medicine**
  - North Shore University Hospital
  - Manhasset, New York

- **Oregon Cancer Center at Oregon Health & Science University**
  - Portland, Oregon

- **Roswell Park Cancer Center**
  - Buffalo, New York

### OUTSIDE THE UNITED STATES

- **A.C. Camargo Hospital–Cancer Center**
  - São Paulo, Brazil

- **Academic Hospital, Free University Amsterdam**
  - Amsterdam, The Netherlands

- **Athens University, Evangelismos Hospital**
  - Athens, Greece

- **B.S. retrofit” of the Swedish Hospital**
  - S. Giovanni Rotondo, Italy

- **Chiquita Economou**
  - Athens, Greece

- **Casa Sollievo Della Sofferenza Hospital**
  - Naples, Italy

- **Emanuel C. Besa**
  - Rochester, Minnesota

- **Memorial Sloan Kettering Cancer Center**
  - New York, New York

- **Bone Marrow Transplant Program**
  - Boston, Massachusetts

- **University of Alabama at Birmingham**
  - Birmingham, Alabama

- **University of Arizona**
  - Arizona Cancer Center

- **University of Chicago**
  - University of Chicago Medical Center

- **University of Nebraska**
  - University of Nebraska Medical Center

- **University of New Mexico**
  - Health Sciences Center

- **University of Pennsylvania**
  - University of Pennsylvania Cancer Center

- **University of Rochester**
  - University of Rochester Cancer Center

- **University of South Florida**
  - H. Lee Moffitt Cancer Center

- **University of Texas**
  - MD Anderson Cancer Center

- **University of Virginia**
  - Charlottesville, Virginia

- **Washington University School of Medicine**
  - St. Louis, Missouri

- **Washington University School of Medicine**
  - Barnes Jewish Cancer Center

- **The University of Texas**
  - The University of Southern Denmark

- **University of Vienna**
  - Vienna, Austria

### 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.
MDS Educational Resources for Clinicians

The Myelodysplastic Syndromes Pathobiology and Clinical Management
(Basic and Clinical Oncology Series/27)

Edited by:
John M. Bennett
James P. Wilmot Cancer Center
of the University of Rochester,
Rochester, New York, U.S.A.

May 2002/528 pp., illus., ISBN: 0-8247-0782-6/$165.00
CRC Press. 800-272-7737
When ordering, use code PAO50203

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.

A NEW CME PROGRAM AVAILABLE IN CD-ROM FORMAT


You may request this program by contacting the Foundation at 800-MDS-0839 or by logging on to our website: www.mds-foundation.org.

PATIENT INFORMATION AND EDUCATIONAL MATERIALS AVAILABLE FROM THE MDS FOUNDATION

A. Understanding Myelodysplastic Syndromes: A Patient Handbook
Peter A. Kouides, MD; John M. Bennett, MD

B. Transfusion-Dependent Iron Overload and MDS: A Handbook for Patients
Published by The Myelodysplastic Syndromes Foundation

C. Patient Diary
Published by The Myelodysplastic Syndromes Foundation

D. Your Journal: Learning About Myelodysplastic Syndromes (MDS)
Supported by a grant from Celgene Corporation.

All of these materials are available free of charge from the Foundation.

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.

Please contact us at:
1-800-MDS-0839 (phone)
or 609-298-0590 (fax).
Outside the US please call:
609-298-1035.

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

SuperGen has provided the MDS Foundation with unrestricted educational grants to support the Foundation’s work.
International Clinical Trials

The following trials are current as of the date of this newsletter. We will update the list in The MDS News each quarter. If you are a treating physician who would benefit from any such study, you may want to contact the appropriate institution. 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.

- **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.

U.S. Trials

**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.nci.nih.gov. This information includes basic study information, study lead organizations, study sites, and contact information. To access the information:

- Log on to www.nci.nih.gov
- Click on “Finding Clinical Trials”
- on the next screen look for “Ways to Find Clinical Trials” and
- 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. You can also contact 1-800-4-CANCER for more information.

**ADVANCED CANCERS: A NEW TRANSPLANT METHOD**

Researchers at the National Institutes of Health (NIH/DHHS) are investigating a new method of improving transplant results in individuals with advanced cancers. If you or someone you know are between the ages of 10 to 50 years old and have one of the following cancers: Myelodysplastic Syndrome, Leukemia, or Myeloproliferative Disorder, you may be able to participate in this clinical trial.

To find out if you qualify, please call 1-800-411-1222 or visit www.cc.nih.gov.

**Pharmion.** AZA PH GL 2003 CL 001. A Survival Study in Patients with High Risk Myelodysplastic Syndromes Comparing Azacitidine versus Conventional Care. The purpose of this study is to determine whether patients with high-risk myelodysplastic syndromes (MDS) treated with azacitidine have improved survival compared to conventional care treatments. The study will also assess the effect of treatments on response, duration of response, and transformation to acute myeloid leukemia (AML).

**Telik, Inc.** Phase I-IIa trial to evaluate the safety and efficacy of TLK199 in patients with myelodysplastic syndrome (MDS). Eligible patients must have a diagnosis of MDS, be at least 18 years old and ineligible or refusing bone marrow transplant.

**Novartis.** Phase I, open-label, dose escalating study to evaluate the safety, biologic activity and pharmacokinetic profile of LAQ824 in patients with relapsed or refractory AML, CLL, or CML in blast crisis, or advanced MDS. The
primary objective of this study is to determine the Maximum Tolerated Dose (MTD) and Dose Limiting Toxicity (DLT) of LAQ824 as a single agent when administered by intravenous infusion as outlined in the protocol.

An Open-label Phase II Trial of PKC412 Monotherapy in Patients with Acute Myeloid Leukemia and Patients with Myelodysplastic Syndrome PKC4122104. Patients who agree to participate in this trial will be screened for the FLT3 mutation. If positive, they will have a physical exam, blood test, EKG, chest x-ray, bone marrow aspirate and a pregnancy test.

For more information, please go to www.clinicaltrials.gov.

Other U.S. Trials

Barbara Ann Karmanos Cancer Institute, Detroit, MI. D-696. Allogeneic and syngeneic marrow transplantation in patients with acute non-lymphocytic leukemia. Contact: Jared Klein, MD. Phone: 313-963-2533.

Barbara Ann Karmanos Cancer Institute, Detroit, MI. POG A2971: Treatment Of Children with Down Syndrome and Acute Myeloid Leukemia, Myelodysplastic Syndrome, or Transient Myeloproliferative Disorder. Contact: Jeffrey Taub, MD. Phone: 313-963-2533.


Case Western Reserve University, Cleveland, OH. AZA PH GL 2003 CL 001. Multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Donna Kane, RN. Phone: 216-844-8609.

Case Western Reserve University, Cleveland, OH. CWRU-5Y97. Phase II trial using umbilical cord blood to evaluate the efficacy of transplantation to treat aplastic anemia and myelodysplastic syndromes patients. Eligible patients must have disease not responsive to medical therapy. Contact: Mary J. Laughlin. Phone: 216-844-8609.

Cedars-Sinai Medical Center, Los Angeles, CA. 02287. Phase II Trial of Paricalcitol in Myelodysplastic Syndromes to determine if an oral, relatively non-toxic, novel vitamin D3 compound, paricalcitol, (Zemplar) can improve red, white and platelet counts as well as decrease the risk of development of leukemia, without causing undue toxicity in patients with myelodysplastic syndromes (MDS). Patients will receive oral administration of paricalcitol in increasing doses. Contact: H. Phillip Koeffler, MD. Phone: 310-423-4609.

Children’s Hospital of New York Presbyterian, New York, NY. 01-504. Phase II trial using fludarabine, busulfan, and anti-thymocyte globulin (ATG) to evaluate the efficacy of reduced intensity allogeneic stem cell transplantation to treat MDS. Eligible patients must have 1) MDS and <5% bone marrow myeloblasts at diagnosis; 2) minimum of >10% CD33 positivity; 3) adequate organ function (renal, hepatic, cardiac and pulmonary); 4) age <65 years; 5) matched family donor (5/6 or 6/6), unrelated donor (5/6 or 6/6), or cord blood donor (3/6, 4/6, 5/6, 6/6). Contact: Mitchel S. Cairo, MD. Phone: 212-305-8316.


Cleveland Clinic Foundation, Cleveland, OH. Phase II trial of combination therapy with arsenic trioxide (Trisenox) and gemtuzumab ozogamicin (Mylotarg) for the treatment of adult patients with advanced myelodysplastic syndromes. Contact: Liz Kuczkowski. Phone: 216-445-3795.


Dana-Farber Cancer Institute, Boston, MA. Phase I Study of Vaccination with Lethally Irradiated, Autologous Acute Myeloblastic Leukemia Cells Engineered by Adeonviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor in Patients with Advanced Myelodysplasia or acute Myelogenous Leukemia. This is a study to determine the feasibility of preparing lethally irradiated autologous myeloblastic leukemia cells engineered by adenoviral mediated gene transfer to secrete GM-CSF in patients with myelodysplasia or acute myelogenous leukemia. The study will also investigate the safety and biologic activity of vaccination with lethally irradiated, autologous myeloblastic leukemia cells engineered by adenoviral mediated gene transfer to secrete GM-CSF in patients with advanced myelodysplasia or acute myelogenous leukemia. Contact: Ilene Galinsky. Phone: 617-632-3902.

Duke University Medical Center, Durham, NC. Phase II trial to assess the value of non-myeloablative allogeneic therapy (mini bone marrow transplant) for patients with aplastic anemia or myelodysplastic syndrome. Patients must have severe disease to be eligible and may have either a matched sibling, mismatched family member, or large cord blood unit found for use on our trial. Contact: David A. Rizzieri, MD at Rizzi003@nc.duke.edu.

Fred Hutchinson Cancer Research Center, Seattle, WA. FHCRC #1297. Radiolabeled BC8 (anti-CD-45) Antibody Combined with Cyclophosphamide and Total Body Irradiation Followed by HLA-Matched Related or Unrelated Stem Cell Transplantation as Treatment for Advanced Acute Myeloid Leukemia and Myelodysplastic Syndrome. Phase II trial to determine the efficacy (as measured by survival and disease-free survival) and toxicity of a regimen of cyclophosphamide, TBI, plus the maximum tolerated dose of I labeled BC8 (anti-CD45) antibody in patients with AML beyond first remission receiving HLA matched related hematopoietic stem cell transplants. Contact: J. Pagel, MD. Phone: 206-288-1024.

Fred Hutchinson Cancer Research Center, Seattle, WA. FHCRC #1591. Phase I trial to determine whether stable allogeneic engraftment from related and unrelated HLA-mismatched stem cell donors can be safely established using a non-myeloablative conditioning regimen plus escalating doses of the anti-CD52mAb Campath® in patients with hematologic malignancies. Contact: B. Sandmaier, MD. Phone: 206-288-1024.

Fred Hutchinson Cancer Research Center, Seattle, WA. FHCRC #1732. Phase II trial to evaluate the efficacy of non-myeloablative allogeneic HCT from related and unrelated donors for the treatment of patients with MDS and MPD, who are not candidates for conventional allogeneic HCTG due to advanced age or serious comorbid conditions. Contact: B. Sandmaier, MD. Phone: 206-288-1024.

Fred Hutchinson Cancer Research Center, Seattle, WA. FHCRC #1813. Phase III trial to compare the non-relapse mortality at 1-year after conditioning with TBI alone vs. fludarabine/TBI in heavily pretreated patients with hematologic malignancies at low/moderate risk for graft rejection who have HLA-matched related donors. Contact: B. Sandmaier, MD. Phone: 206-288-1024.

Fred Hutchinson Cancer Research Center, Seattle, WA. FHCRC #1536. Transplantation of peripheral blood stem cells from related or unrelated volunteer donors in patients with “less advanced” MDS. Conditioning therapy includes busulfan (targeted to a pre-determined plasma level) and cytoxan (targeted BUCY); patients up to 65 years of age. Contact: H.J. Deeg, MD. Phone: 206-288-1024.

Fred Hutchinson Cancer Research Center, Seattle, WA. FHCRC #1596. Transplantation from related donors for high-risk patients with MDS. Conditioning includes a “non-myeloablative” regimen of fludarabine and 200 cGy of total body irradiation. Patients are evaluated individually for eligibility. Contact: David Maloney, MD, PhD. Phone: 206-288-1024.


Fred Hutchinson Cancer Research Center, Seattle, WA. FHCRC #117. Transplantation of patients with aplastic anemia from related donors following conditioning with antithymocyte globulin (ATG) and cytoxan (CY). Patients up to 55 years of age. Contact: R. Storb, MD. Phone: 206-288-1024.

Fred Hutchinson Cancer Research Center, Seattle, WA. FHCRC #800. Transplantation from unrelated donors for patients with aplastic anemia who have failed immuno-suppressive therapy. Conditioning involves ATG, CY and 200 cGy of total body irradiation. Patients up to 55 years of age. Contact: H.J. Deeg, MD. Phone: 206-288-1024.

Fred Hutchinson Cancer Research Center, Seattle, WA. FHCRC #1641. Transplantation from unrelated donors for high-risk patients with MDS. Conditioning will be with a “non-myeloablative” approach using 200 cGy of TBI and fludarabine. No age restriction (other exclusion criteria exist). Contact: M. Maris, MD. Phone: 206-288-1024.

Fred Hutchinson Cancer Research Center, Seattle, WA. FHCRC #1723. Transplantation from related or unreleased donors for patients with advanced MDS or myeloproliferative disorders. Conditioning includes busulfan (targeted to a predetermined plasma level) and Cytoxan (targeted BUCY) with the addition of thymoglobulin; patients up to 65 years of age. Contact: H.J. Deeg, MD. Phone: 206-288-1024.


Froedtert Memorial Lutheran Hospital, Milwaukee, WI. AZA PH GL 2003 CL 001. Multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional

Georgetown University, Washington, DC. Clinical and biologic effects of arsenic trioxide in MDS. Contact: B. Mavromatis, MD. Phone: 202-784-0124.

H. Lee Moffitt Cancer Center, Tampa, FL. Contact: Razelle Kurzrock, MD.

H. Lee Moffitt Cancer Center, Tampa, FL. MCC# 13935. Phase I/II Trial of Subcutaneous Deacitabine (5-Aza-2′-deoxycytidine) Optimizing Genomic Methylation in Patients with Myelodysplastic Syndrome (MDS). Inclusion criteria: Histologically confirmed diagnosis of MDS or nonproliferative chronic myelomonocytic leukemia (CMML) according to FAB criteria, with IPSS category of Intermediate-2 or High. If cytogenetics are not available, patients with >10% and <30% marrow blasts are eligible. Soon to Open. Contact: Pamela Humble, RN. Phone: 813-632-8391.

H. Lee Moffitt Cancer Center, Tampa, FL. MCC# 13937. A Pharmacokinetic and Pharmacodynamic Study of Oral CC-5013 (LENALIDOMIDE; REVLIMID) In Subjects with Low- or Intermediate-1-Risk Myelodysplastic Syndromes. Inclusion criteria: Documented diagnosis of MDS that meets International. Prognostic Scoring System (IPSS) criteria for Low- to Intermediate-1-risk disease. Red blood cell (RBC) transfusion-dependent anemia defined as having received >4 transfusions of RBCs within 56 days of randomization of symptomatic anemia (Hgb <9.0 g/dl). Soon to Open. Contact: Pamela Humble, RN. Phone: 813-632-8391.

H. Lee Moffitt Cancer Center, Tampa, FL. MCC# 13927. A Phase I/II, two-arm, multicenter, dose-escalation study of LBH589 administered intravenously on two dose schedules in adult patients with advanced hematologic malignancies. Inclusion criteria: Patients with a cytopathologically confirmed diagnosis of AML, MDS, (RAEB, RAEHT), ALL, CLL, CML, multiple myeloma, NHL including CTCL who are either relapsed after or refractory to standard therapy, and are considered inappropriate candidates for standard therapy. Patients with a cytopathologically confirmed diagnosis of AML, MDS, (RAEB, RAEHT) who are previously untreated but due to age, poor prognosis, or concurrent medical conditions are considered inappropriate candidates for standard induction therapy, or those who refuse standard induction therapy. Contact: Pamela Humble, RN. Phone: 813-632-8391.

Indiana University Medical Center, Indianapolis, IN. AZA PH GL 2003 CL 001. Multicenter randomized open-label parallel group phase III trial of subcutaneous azacitadine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Larry Cripe, MD. Phone: 317-274-0901.


Johns Hopkins Oncology Center, Baltimore, MD. J9950. Phase I dose de-escalation to minimal effective pharmacologic dose trial of sodium phenylbutyrate in combination with 5-azacytidine in patients with myelodysplastic syndromes. Contact: Tianna Dauses. Phone: 410-502-7110.


Johns Hopkins Oncology Center, Baltimore, MD. J0252. Phase II study of the farnesyl transferase inhibitor Zarnestra in complete remission following induction and/or consolidation chemotherapy in adults with poor-risk acute myelogenous leukemia (AML) and high-risk myelodysplasias. Contact: Jackie Greer. Phone: 410-614-1329.


Los Angeles Hematology and Oncology Assoc., Los Angeles, CA. Phase I/II study of arsenic trioxide in combination with cytosine arabinoside in patients with MDS. Contact: C. Gota, MD. Phone: 818-409-0105.

MD Anderson Cancer Center, Houston, TX. Phase I/IIa Study of TLK199 HCl Liposomes for injection in Myelodysplastic Syndromes. Contact: Stefan Faderl, MD. Phone: 713-563-1688.

MD Anderson Cancer Center, Houston, TX. Open-Label, Phase II Study to Evaluate The Efficiency and Safety of the Farnesyl-transferase Inhibitor Zarnestra (R115777) in Subjects with High-Risk Myelodysplastic Syndrome (MDS). Contact: Razelle Kurzrock, MD.
MD Anderson Cancer Center, Houston, TX. ID02-266. Therapy of inversion (16) and T (8;21) AML/MDS with fludarabine and Ara-C. Contact Elihu H. Estey, MD. Phone: 713-792-7544.

MD Anderson Cancer Center, Houston, TX. Phase I/II Study of PR1 (NSC698102) Human Leukemia Peptide Vaccine with Incomplete Freund’s Adjuvant (NSC 675756). Contact: Jeffrey Molldrem, MD. Phone: 713-745-4820.

MD Anderson Cancer Center, Houston, TX. Phase II Open-Label Study of the Intravenous Administration of Homoharringtonine (CGX-635) in the Treatment of Myelodysplastic Syndrome (MDS). Contact: Jorge Cortes, MD. Phone: 713-794-5783.

MD Anderson Cancer Center, Houston, TX. Phase II Study Of Arsenic Trioxide In The Treatment Of Myelodysplastic Syndromes. Contact: Miloslav Beran, MD. Phone: 713-792-2248.

MD Anderson Cancer Center, Houston, TX. Phase II, Multicenter, Open-Label Study of the Safety and Efficacy of High-Dose Pulse Administration DN-101 (Calcitriol) in Patients with Myelodysplastic Syndrome. Contact: Guillermo Garcia-Manero, MD. Phone: 713-745-3428.

MD Anderson Cancer Center, Houston, TX. Randomized, Open-Label, Phase III Trial Of Decitabine (5-AZA-2’Deoxycytidine) Versus Supportive Care In Adults With Advanced-Stage Myelodysplastic Syndrome. Contact: Jean-Pierre Issa, MD. Phone: 713-745-2260.

MD Anderson Cancer Center, Houston, TX. Safety And Efficacy Trial Of Bevacizumab: Anti-VEGF Humanized Monoclonal Antibody (NSD 704865) Therapy For Myelodys-plastic Syndrome (MDS). Contact: Jorge Cortes, MD. Phone: 713-794-5783.

MD Anderson Cancer Center, Houston, TX. Phase II Study Of Neumega (Oprelvekin)(Interleukin-11) In Patients with Myelodysplastic Syndrome. Contact: Razelle Kurzrock, MD. Phone: 713-794-1226.

MD Anderson Cancer Center, Houston, TX. Multicenter Phase I/II Study Of Continuous Oral Administration Of SCH 66336 In Patients With Advanced Myelodysplastic Syndrome, Acute Myelogenous Leukemia, Chronic Myelogenous Leukemia In Blast Crisis, Acute Lymphoblastic Leukemia. Contact: Jorge Cortes MD. Phone: 713-794-5783.

MD Anderson Cancer Center, Houston, TX. Phase II Study of Intravenous Homoharringtonine in Chronic Myelogenous Leukemia (CML). Contact: Jorge Cortes, MD. Phone: 713-794-5783.

MD Anderson Cancer Center, Houston, TX. Therapy of Hypereosinophilic Syndrome, Polycythemia Vera, Atypical CML or CMML with PDGF-R Fusion Genes, or Mastocytosis with Gleevec (STI571). Contact: Jorge Cortes, MD. Phone: 713-794-5783.

MD Anderson Cancer Center, Houston, TX. DCTER Chemotherapy In Patients Ages 1 Through 49 With Untreated AML or High-Risk Myelodysplasia. Contact: Elihu Estey, MD. Phone: 713-792-7544.

MD Anderson Cancer Center, Houston, TX. Phase II study of clofarabine in combination with cytarabine (Ara-C) in pts ≥50 yrs with newly diagnosed and previously untreated acute myeloid leukemia (AML) and high-risk myelodysplastic syndrome (MDS) (≥10% bone marrow blasts). Contact: Stefan Faderl, MD. Phone: 713-745-4613.

MD Anderson Cancer Center, Houston, TX. DM02-203. Phase Ia, Open-Label, 3-Arm, Dose Escalation Study of PTK787/ZK 222584. Contact: Francis Giles, MD. Phone: 713-792-8217.

MD Anderson Cancer Center, Houston, TX. ID03-0044. Phase I Clinical Trial of Oral Suberoylanilide Hydroxamic Acid (SAHA) in Patients with Advanced Leukemias. Contact: Guillermo Garcia-Manero, MD. Phone: 713-745-3428.

MD Anderson Cancer Center, Houston, TX. DM01-646. Phase I Study of ABT-751 in Patients With Refractory Hematologic Malignancies. Contact: Francis Giles, MD. Phone: 713-792-8217.

MD Anderson Cancer Center, Houston, TX. ID99-059. Phase II trial using ATG and Fludarabine or Cyclosporine to evaluate the efficacy of immunosuppression to treat aplastic anemia and myelodysplastic syndromes patients. Eligible patients must have RA or RARS and low blood counts. Contact: Jeffrey Molldrem, MD. Phone: 713-745-4820.

MD Anderson Cancer Center, Houston, TX. ID99-059. Phase II trial using ATG/CSA; ATG/Fludarabine. Eligible patients must have MDS of subtype RA, blasts <5% in bone marrow that require >unit of PRBC/month for >2 months, platelet count <50,000/m3, or neutrophil count <500/m3, IPSS score >2. Contact: Jeffery Molldrem, MD. Phone: 713-745-4820.


Memorial Sloan-Kettering Cancer Center, New York, NY. 00-116. Pilot study of FR901228 or Depsipeptide (NSC#630176) for adult patients with advanced hematologic disorders. Contact: Virginia Klimek, MD. Phone: 212-639-6519.

Memorial Sloan-Kettering Cancer Center, New York, NY. 02-063. Tolerability and PK/PD of multiple oral doses of CT53518 in patients with acute myelogenous leukemia. Contact: Mark Heaney, MD, PhD. Phone: 212-639-2275.
If you are 10–50 years of age and have been diagnosed with advanced myelodysplastic syndrome, you may be eligible for a clinical trial of a transplant procedure that evaluates using peripheral blood stem cells from an HLA-mismatched family donor. Eligible patients are not asked to pay for their medical treatment and hospital costs. Contact: Laura Wisch. Phone: 301-402-0797.

New York Presbyterian Hospital, New York, NY. Phase I/II trial of Trisenox in combination with low dose Ara-C for the treatment of high-risk MDS and poor prognosis AML in patients >60 years. Contact: Gail Roboz, MD. Phone: 212-746-3126.

Measurable Disease Phase I and II Study of Imatinib Mesylate for Patients with Advanced Myelodysplastic Syndrome (MDS). Contact: Lewis Silverman, MD. Phone: 212-241-5520.


Phase I/II Pilot Study of Divalproex Sodium and All-Trans-Retinoic Acid (ATRA) in Relapsed or Refractory Acute Myeloid Leukemia (except M3, FAB Classification). Contact: Lewis Silverman, MD. Phone: 212-241-5520.


National Heart, Lung, and Blood Institute, Bethesda, MD. 04-H-0026. Randomized Trial of Daclizumab versus ATG for Myelodysplastic Syndrome. Clinical trial comparing the effectiveness of treatment with either a new immuno-suppressive drug (Daclizumab) or antithymocyte globulin (ATG) for patients with myelodysplastic syndrome. The study may help increase blood counts, reduce anemia symptoms, and/or reduce dependence on immuno-suppressive medications and transfusions. If you are determined to be eligible to participate and you agree to join, it will be determined by chance whether you receive either daclizumab or ATG. If the treatment you are assigned does not work, you may subsequently receive the other treatment. Contact: Laura Wisch. Phone: 301-402-0797.

National Heart, Lung, and Blood Institute, Bethesda, MD. 01-H-0162. Stem Cell Transplantation for Older Patients with Myelodysplastic Syndrome. If you are 55 to 75 years of age and have been diagnosed with MDS, you may be eligible for a transplant procedure designed to decrease a major transplant complication, graft-versus-host disease (GVHD). Under evaluation is a novel method of treating your donor's cells prior to transplant. You must have an HLA-matched brother or sister to participate. We will do the blood testing free of charge to see if your sibling is a match upon request. Contact: Laura Wisch. Phone: 301-402-0797.

National Heart, Lung, and Blood Institute, Bethesda, MD. 04-H-0112. Stem Cell Transplantation and T-Cell Add Back to Treat Myelodysplastic Syndromes. Clinical trial designed to decrease graft versus host disease, promote engraftment, and improve immune system recovery following a bone marrow stem cell transplant. You must have an HLA matched brother or sister donor to participate in this trial. Contact: Laura Wisch. Phone: 301-402-0797.

National Heart, Lung, and Blood Institute, Bethesda, MD. 03-H-0209. Stem Cell Transplant for MDS from a partially HLA-matched family member. Many patients are not considered for a stem cell transplant because an HLA-matched sibling or unrelated donor is unavailable. For such patients, the only curative option is a transplant from a partially HLA-matched family member. If you are 10–50 years of age and have been diagnosed with advanced myelodysplastic syndrome, you may be eligible for a clinical trial of a transplant procedure that evaluates using peripheral blood stem cells from an HLA-mismatched family donor. Eligible patients are not asked to pay for their medical treatment and hospital costs. Contact: Laura Wisch. Phone: 301-402-0797.


Oregon Health & Science University, Portland, OR. 7002. Tolerability and PK/PD of Multiple Oral Doses of CT53518 in Patients with Acute Myelogenous Leukemia. Contact: Peter Curtin, MD. Phone: 503-494-5064.


Oregon Health & Science University, Portland, OR. 7377. Randomized, Multi-Center, Double-Blind, Placebo-Controlled Trial Assessing the Safety and Efficacy of High-dose Pulse Administration DN-101 (Calcitriol) in Patients with Myelodysplastic Syndrome. Contact: Peter Curtin, MD. Phone: 503-494-5064.

Oregon Health & Science University, Portland, OR. 746-3126. Low-Dose TBI and Fludarabine Followed by Placental Blood Hematopoietic Stem Cells for the Treatment of Hematological Malignancies. Contact: Peter Curtin, MD. Phone: 503-494-5064.


Oregon Health & Science University, Portland, OR. 4252. Transplantation of Unrelated Donor Marrow or Placental Blood Hematopoietic Stem Cells for the Treatment of Hematological Malignancies. Contact: Peter Curtin, MD. Phone: 503-494-5064.

**Oregon Health & Science University, Portland, OR.** 6684. Nonmyeloablative PBSC Allografting from HLA Matched Related Donors Using Fludarabine and Low Dose TBI with Disease-Risk Based Immunosuppression. FHCRC Protocol #1596.00. Contact: Peter Curtin, MD. Phone: 503-494-5064.

**Oregon Health & Science University, Portland, OR.** 6370. Low Dose Total Body Irradiation and Fludarabine Followed by HLA Matched Allogeneic Stem Cell Transplantation for Hematologic Malignancies—A Multi-Center Study. Contact: Peter Curtin, MD. Phone: 503-494-5064.


**Roswell Park Cancer Institute, Buffalo, NY.** PTK787. Phase II study of an oral VEGF agent in myelodysplastic syndromes. Contact: Maria Baer, MD. Phone: 716-845-8840.

**Roswell Park Cancer Institute, Buffalo, NY.** RPC-02-03. Treatment of anemia in patients with low-and intermediate-risk MDS with darbepoeitin alfa. Multicenter, phase II trial also open at the University of Alabama (Birmingham), Loyola University Medical Center (Chicago), and Rochester General Hospital (Rochester, NY). Contact: Maria Baer, MD. Phone: 716-845-8840.

**Rush-Presbyterian-St. Luke’s Medical Center, Chicago, IL.** MDS 99-14. Pilot study of Thalidomide (Thalidomid) combined with Pentoxyfilline, Ciprofloxacin and Dexamethasone (PCD) in patients with myelodysplastic syndromes. This is a phase II trial using anticytokine and antiangiogenic therapy to evaluate the efficacy of Thalidomide (Thalomid) to treat MDS. Eligible patients must have MDS (RA, RARS or RAEB). Addendum: Reduced dose of Pentoxyfilline (400 mg po TID), No Cipro, No Decadron. Contact: Laurie A. Lisak, MMS. Phone: 312-563-2535.

**Rush-Presbyterian-St. Luke’s Medical Center, Chicago, IL.** MDS 2000-08. Pilot Study to Test The Efficacy of Gleevec (STI 571) in Patients with Myelodysplastic Syndromes. Given the clinical and molecular similarities between CML and CMMoL, especially those related to the activation of tyrosine kinase induced downstream events suggest that suppression of the same kinase in CMMoL by using an agent like Glivec may produce clinical benefit in these individuals. We propose to test this hypothesis by treating one cohort of 15 CMMoL patients with Gleevec or STI571 at 400 mg po daily. The second cohort of 15 patients [having translocation (5;12)] will likewise receive Gleevec or STI571 at 400 mg po daily. Response assessment will be made every 8 weeks and in case of disease progression, the patient will be removed from the study. Responding patients or those with stable disease will be treated for one year at least with the drug provided by Novartis. After the one-year period, further therapy will depend upon the discretion of the physician. Disease progression is defined as occurrence of acute leukemia, increase in BM blasts by 50% over pre-therapy values if the blast count was >5% to begin with, and worsening cytopenia. Contact: Laurie A. Lisak, MMS. Phone: 312-563-2535.

**Rush-Presbyterian-St. Luke’s Medical Center, Chicago, IL.** MDS 2002-02. Phase II trial to evaluate the efficacy of Trisenox in patients with MDS, followed by thalidomide in non-responders. Eligible patients must belong to IPSS int 1 or higher, have adequate hepatic and renal function as defined by specific laboratory parameters, and have an ECOG PS of 0–2. Patients will receive Trisenox alone for six months. Patients who do not respond will have thalidomide added to the regimen at 6 months. Contact: Laurie A. Lisak, MMS. Phone: 312-563-2535.

**Rush-Presbyterian-St. Luke’s Medical Center, Chicago, IL.** MDS 2000-04. Phase IIb study using Thymoglobulin in transfusion dependent patients with myelodysplastic syndrome. Open to FAB types RA, RARS, RAEB. Contact: Laurie A. Lisak, MMS. Phone: 312-563-2535.

**Rush-Presbyterian-St. Luke’s Medical Center, Chicago, IL.** MDS 2000-11. Pilot study to test the efficacy of infliximab (Remicade) in patients with low-risk myelodysplastic syndromes. Eligible patients must be transfusion dependent or hemoglobin <9 grams, and an IPSS score <1.5, and cannot have a history of clinically significant cardiac disease or CHF. Contact: Laurie A. Lisak, MMS. Phone: 312-563-2535.

**Rush-Presbyterian-St. Luke’s Medical Center, Chicago, IL.** MDS 2001-12. Pilot study to determine the clinical effects of the proteasome inhibitor PS-341 in patients with myelodysplastic syndromes. All FAB types are eligible. Contact: Laurie A. Lisak, MMS. Phone: 312-563-2535.


**Rush-Presbyterian-St. Luke’s Medical Center, Chicago, IL.** MDS 2002-02. Phase II trial to evaluate the efficacy of Trisenox in patients with MDS, followed by thalidomide in non-responders. Eligible patients must belong to IPSS int 1 or higher, have adequate hepatic and renal function as defined by specific laboratory parameters, and have an ECOG PS of 0–2. Patients will receive Trisenox alone for six months. Patients who do not respond will have thalidomide added to the regimen at 6 months. Contact: Laurie A. Lisak, MMS. Phone: 312-563-2535.

**Rush-Presbyterian-St. Luke’s Medical Center, Chicago, IL.** MDS 2000-08. Pilot Study to Test The Efficacy of Gleevec (STI 571) in Patients with Myelodysplastic Syndromes. Given the clinical and molecular similarities between CML and CMMoL, especially those related to the activation of tyrosine kinase induced downstream events suggest that suppression of the same kinase in CMMoL by using an agent like Glivec may produce clinical benefit in these individuals. We propose to test this hypothesis by treating one cohort of 15 CMMoL patients with Gleevec or STI571 at 400 mg po daily. The second cohort of 15 patients [having translocation (5;12)] will likewise receive Gleevec or STI571 at 400 mg po daily. Response assessment will be made every 8 weeks and in case of disease progression, the patient will be removed from the study. Responding patients or those with stable disease will be treated for one year at least with the drug provided by Novartis. After the one-year period, further therapy will depend upon the discretion of the physician. Disease progression is defined as occurrence of acute leukemia, increase in BM blasts by 50% over pre-therapy values if the blast count was >5% to begin with, and worsening cytopenia. Contact: Laurie A. Lisak, MMS. Phone: 312-563-2535.
Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL. MDS2003-01. Pilot Study to Determine the Clinical Efficacy of Coenzyme Q10 in Patients with Myelodysplastic Syndromes. We propose to treat 40 patients belonging to RA and or RARS or low risk and Int-1 categories of MDS patients with CoQ10 at a starting dose of 300 mg escalating as tolerated to 1200 mg po qday. Patients will begin taking 300 mg po BID with meals for Days 1–3. On Days 4–6, patients will take 300 mg po TID with meals. On Day 7 and onward, patients will take 300 mg po QID with meals. Patients will be treated for up to a year unless intolerable side effects and/or disease progression are noted. Responses will be continuously evaluated by weekly CBCs and bone marrows repeated every 16 weeks. Contact: Laurie A. Lisak, MMS. Phone: 312-563-2535.

Stanford University Medical Center, Stanford, CA. CTEP #2771. Safety and efficacy of bevacizumab: humanized monoclonal anti-VEGF antibody therapy for myelodysplastic syndrome. Contact: Peter Greenberg, MD or Kathy Dugan, RN. Phone: 650-723-8594.

Stanford University, Stanford, CA. Study of DARBEPOETIN ALFA in Patients with MDS. Primary objectives are 1) to assess erythroid response to DARBEPOETIN ALFA, as determined by changes in hemoglobin and/or red blood cell (RBC) transfusion-dependence. 2) to describe the safety profile of DARBEPOETIN ALFA in patients with MDS. Contact: Sylvia Quesada, R.N. Phone: 650-725-4041.

Stanford University, Stanford, CA. Bevacizumab in Treating Patients With Myelodysplastic Syndrome. Multicenter trial with participating centers in Arizona, California, Texas. Contact: Sylvia Quesada, RN Phone: 650-725-4041.

St. Jude Children's Research Hospital, Memphis, TN. DSAML. Treatment of children with down syndrome (DS) and acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), and transient myeloproliferative disorder (TMD). Contact: Nobuko Hijiya, MD. Phone: 901-495-3300.

St. Jude Children's Research Hospital, Memphis, TN. AML02. Collaborative trial for the treatment of patients with newly diagnosed acute myeloid leukemia or myelodysplasia. Contact: Jeffrey Rubnitz, MD, PhD. Phone: 901-495-3300.

St. Jude Children's Research Hospital, Memphis, TN. HAPSCT. Phase III randomized trial to evaluate haplo-identical stem cell transplantation utilizing purified CD34+ hematopoietic cells for patients with hematologic malignancies: a randomized study comparing positive and negative selection methodologies. Contact: Gregory Hale, MD. Phone: 901-495-3300.

St. Jude Children's Research Hospital, Memphis, TN. MUDSCT. Phase III controlled trial to evaluate hematopoietic stem cell transplantation for patients with hematologic malignancies: a comparison of T-cell depleted bone marrow with unmanipulated bone marrow. Contact: Edwin Horwitz, MD, PhD. Phone: 901-495-3300.

St. Jude Children's Research Hospital, Memphis, TN. REFSCST. Pilot study to evaluate haploidentical stem cell transplantation utilizing T-Cell depletion as therapy for patients with refractory hematological malignancies. Contact: Ely Benaim, MD. Phone: 901-495-3300.

Texas Oncology Medical City Dallas Hospital, Dallas, TX. D-0007. Randomized, open-label, Phase III trial of decitabine (5-aza-2’-deoxycytidine) versus supportive care in adults with advanced-stage myelodysplastic syndrome. This Phase III trial evaluates the efficacy of decitabine to treat MDS. Eligible patients may have de novo or secondary MDS. Growth factors (G-CSF, erythropoietin), steroids, hormones or chemotherapy for treatment of MDS are not allowed for 2 weeks prior to enrollment. Contact: Craig Rosenfeld, MD. Phone: 972-566-7790.

Texas Oncology Medical City Dallas Hospital, Dallas, TX. SMC-101-1020. Open-label, prospective, stratified, randomized, controlled, multicenter, phase IIb study of the impact of Thymoglobulin therapy on transfusion needs of patients with early myelodysplastic syndrome. This protocol evaluates Thymoglobin therapy for 4 days. Eligibility includes low risk MDS (RA, RAEB <10%), IPSS <1.0, transfusion dependence. No prior chemotherapy allowed. Contact: Craig Rosenfeld, MD. Phone: 972-566-7790.

Texas Oncology Medical City Dallas Hospital, Dallas, TX. T-MDS-001. Multicenter, randomized, double-blind, placebo-controlled trial comparing best supportive care and thalidomide for the treatment of anemia in patients with myelodysplastic syndrome followed by an open-label treatment with thalidomide. Recently, treatment with thalidomide has been reported to improve the anemia in some patients with MDS. The purpose of this study is to further evaluate the effect of thalidomide or placebo pills (50:50 chance) for 24 weeks. Thereafter, all subjects can receive thalidomide for an additional 24 weeks. The effect of treatment on transfusions and quality of life will be evaluated. Contact: Craig Rosenfeld, MD. Phone: 972-566-7790.

University of Alabama at Birmingham Comprehensive Cancer Center, Birmingham, AL. Phase I/IIa Study of TLK199 HCl Liposomes for injection in Myelodysplastic Syndromes. Contact: Peter Emanuel, MD. Phone: 205-975-2944.
University of Arizona Cancer Center, Tucson, AZ. HSC #02-11. Safety and efficacy trial of bevacizumab: anti-vegfa humanized monoclonal antibody therapy for MDS. Contact: Daruka Mahedevan, MD. Phone: 520-626-2340.

University of California at Los Angeles (UCLA) Medical Center, Los Angeles, CA. Randomized, multicenter, double-blind, placebo controlled trial assessing the safety and efficacy of thalidomide (Thalidomid) for the treatment of anemia in patients with myelodysplastic syndromes. Recently, treatment with thalidomide has been reported to improve the anemia in some patients with MDS. The purpose of this study is to further evaluate the effect of thalidomide or placebo pills (50:50 chance) for 24 weeks. Thereafter, all subjects can receive thalidomide for an additional 24 weeks. The effect of treatment on transfusions and quality of life will be evaluated. The most common side effects of thalidomide include severe birth defects, drowsiness, weakness, rash, shortness of breath, fluid retention, constipation, low blood pressure, decreased white blood counts, slow heart beats and nerve damage. Contact: Ron Paquette, MD. Phone: 310- 825-5608.

University of Louisville, Louisville, KY. #541.02. Pilot study of arsenic trioxide and amifostine for the treatment of myelodysplastic syndromes. Eligible patients must have a confirmed diagnosis of MDS. For patients with lower-risk only: documented red blood cell dependence, defined as the inability to maintain a hematocrit of >25% without transfusion support and patients with serum erythropoietin less than 200 IU/mL at screening should have failed to respond to a trial of recombinant erythropoietin (EPO) administered in accordance with institutional guidelines. Patients must have an ECOG PS 0-2 and adequate hepatic and renal function as evidenced by specific laboratory criteria. Contact: R. Herzig, MD. Phone: 800-234-2689.

University of Michigan Comprehensive Cancer Center, Ann Arbor, MI. Phase II trial of combination therapy with arsenic trioxide (Trisenox) and gemtuzumab ozogamicin (Mylotarg) for the treatment of adult patients with advanced myelodysplastic syndrome. Contact: Harry P. Erba, MD, PhD.


University of Texas Health Science Center at San Antonio, San Antonio, TX. Phase I/IIa Study of TLK199 HCl Liposomes for injection in Myelodysplastic Syndromes. Contact: Natalie Callander, MD. Phone: 210-617-5300 Ext. 4720.

University of Texas Health Science Center at San Antonio, San Antonio, TX. Randomized, double-blind, phase II study of the matrix metalloproteases inhibitor Prinomastat in patients having myelodysplastic syndromes. Eligible patients must be over 18 years of age and have a diagnosis of MDS of at least 8 weeks duration, hemoglobin <9.0 g/dL (or be transfusion dependent) with adequate renal/hepatic function of serum creatinine less than or equal to 1.5 mg/dL and serum total bilirubin less than or equal to 2.0 mg/dL. Contact: Natalie Callander, MD. Phone: 210-567-4848.

University of Washington, Seattle, WA. UW-26-245-B. Phase I trial using subcutaneous, outpatient injection to evaluate the efficacy of Interleukin-2 to treat MDS. Eligible patients must have either refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, or chronic myelomonocytic leukemia; more than 30 days since any prior treatment for MDS; Karnofsky performance status >70; serum creatinine <2.0 mg/dL; bilirubin <1.6 mg/dL or SGOT <150. Contact: John A. Thompson, MD. Phone: 206-288-2015.

University of Wisconsin, Department of Medicine, Madison, WI. HO 02402. Phase I/II trial to evaluate the efficacy of Ontak (Denileukin Diftotox) for treating MDS. Participants must have no prior treatment with Ontak or ATG and must be at least 18 years old. Contact: Mark Jucket, MD. Phone: 608-263-1836.

University of Wisconsin, Department of Medicine, Madison, WI. HO 02403. Phase II trial using Doxercalciferol (Vitamin D) for treating MDS. Participants must have no prior exposure to doxercalciferol and must be at least 18 years old. Contact: Mark Jucket, MD. Phone: 608-263-1836.

Vanderbilt University Medical Center, Nashville, TN. Phase II study of arsenic trioxide in myelodysplasia. Contact: Shubhada M. Jagasia, MD. Phone: 615-322-4752.

Wake Forest University School of Medicine, Winston-Salem, NC. CCCWFU-29203. Orthomolecular Vitamin D in Low-Risk Myelodysplastic Syndrome: Phase II trial using cholecalciferol (Vitamin D3) to evaluate the efficacy of 2000 IU Vitamin D3 daily for 6 months to treat MDS. Eligible patients must have MDS; IPSS score 0–1.0; life expectancy >1 year; no other concurrent therapy for MDS; no history of hypercalcemia. Contact: Istvan Molnar, MD. Phone: 336-716-5847.

Washington University School of Medicine, St. Louis, MO. Multicenter, randomized, open-label, parallel-group, Phase 3 trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Alisa Ruddell. Phone: 314-454-4095.

Washington University School of Medicine, St. Louis, MO. This study seeks individuals with bone marrow failure. Participants are asked to submit a sample of blood for gene and telomere analysis. Researchers are
investigating the hTR gene found on chromosome 3. Participants are also asked to submit their medical and family history information. This information is used to make correlations among the participants’ clinical features and the gene and telomere analysis. Contact: Jennifer Ivanovich, MS. Phone: 314-454-5076.


**European Trials**

**AUSTRALIA**

**The Newcastle Mater Misericordiae Hospital, New South Wales.** A multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Arno Enno. Phone: +61 2 4921 1215.

**Princess Alexandra Hospital, Queensland.** A multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Anthony Mills. Phone: +61 7 3240 2086.

**Royal Adelaide Hospital, South Australia.** A multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Noemi Horvath. Phone: +61 8 8222 3550.

**The Alfred Hospital, Victoria.** A multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Andrew Spencer. Phone: +61 3 9276 3392.

**The Royal Perth Hospital, Western Australia.** A multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Richard Herrman, MD. Phone: +61 8 9224 2405.

**ENGLAND**

**Kings College Hospital/Guys-Kings-Thomas School of Medicine.** Multi-center study of the role of 5-Azacytidine in high risk MDS. Contact: Professor Ghulam J. Mufti. Phone: 44 (0) 207-346-3080.

**Kings College Hospital/Guys-Kings-Thomas School of Medicine.** Randomized study of GCSF+Epo versus supportive care in low risk MDS. Contact: Professor Ghulam J. Mufti. Phone: 44 (0) 207-346-3080.

**The Royal Bournemouth Hospital.** Multi-centre study of the role of 5-Azacytidine in high risk MDS (beginning Spring 2004). Contact: Sally Killick, MD. Phone: 44 (0) 11202 704783.

**The Royal Bournemouth Hospital.** Multi-centre trial of CEP-701 in older patients with AML. Contact: Sally Killick, MD. Phone: 44 (0) 11202 704783.

**The Royal Bournemouth Hospital.** Low dose antithymocyte globulin in elderly patients with MDS and aplastic anaemia. Contact: Sally Killick, MD. Phone: 44 (0) 11202 704783.

**FRANCE**

**Institute Paoli Calmettes, Marseilles.** Phase I/II multi-center study of arsenic trioxide in patients with MDS. Contact: Norbert Vey, MD. Phone: +33 4 91223695.

**Institute Paoli Calmettes, Marseilles.** A multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Norbert Vey, MD. Phone: +33 4 91223695.

**Hopital Beaujon, Clichy.** A multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Pierre Fenaux, MD. Phone: +33 1 40874522.

**Chu Purpan, Toulouse.** A multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Guy Laurent, MD. Phone: +33 5 61772078.

**Chu De Nantes, Nantes.** A multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Beatrice Mahe, MD. Phone: +33 2 40083252.

**Che De Lille, Lille.** A multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Bruno Quesnel, MD. Phone: +33 3 20446640.

**Hopital Cochin, Paris.** A multicenter randomized open-label parallel group phase III trial of subcutaneous azacitidine plus best supportive care versus conventional care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Pierre Fenaux, MD. Phone: +33 1 40874522.
care regimens plus best supportive care for the treatment of Myelodysplastic Syndromes (MDS). Contact: Francois Dreyfus, MD. Phone: +33 1 58412120.

GERMANY


University Hospital Frankfurt/Main. Antithymocyte Globulin (ATG) and Cyclosporine (CSA) to Treat Patients with Myelodysplastic Syndromes. A randomized trial comparing ATG+CSA with best supportive care Amended Protocol SAKK 33/99. Contact: Wolf-K. Hofmann, MD. Phone: +49-69-6301-4802.

University Hospital Frankfurt/Main. Phase II Study with Thalidomide in patients with myelodysplastic syndromes. Contact: Wolf-K. Hofmann, MD. Phone: +49-69-6301-4802.

University Hospital Frankfurt/Main. LAQ824 (inhibitor of histone-deacetylase) in patients with relapsed/refractory AML, advanced CLL, CML in blast crisis or advanced MDS. Contact: Wolf-K. Hofmann, MD. Phone: +49-69-6301-4802.

University Hospital Freiburg. Phase II study of low-dose intravenous decitabine in patients aged >60 years with acute myeloid leukemia who are not eligible for standard induction chemotherapy. Contact: Michael Lübbert, MD, PhD. Phone: +49-761-270-3279.

University Hospital Freiburg. Intravenous low-dose decitabine versus supportive care in elderly patients with primary Myelodysplastic Syndrome (MDS) (>10% blasts or high-risk cytogenetics), secondary MDS or Chronic Myelomonocytic Leukemia (CMML) who are not eligible for intensive therapy: an EORTC-German MDS Study Group randomized Phase III study. Contact: Michael Lübbert, MD, PhD. Phone: +49-761-270-3279.

University Hospital Hamburg. Allogeneic stem cell transplantation after toxicity-reduced conditioning regimen with treosulfan and fludarabine for patients with MDS or sAML, who were not eligible for a standard conditioning regimen: a phase II study. Contact: Nicolaus Kröger, MD. Phone: +49-40-42803-4851.

University Hospital Hamburg. Dose-reduced versus standard conditioning followed by allogeneic stem cell transplantation in patients with MDS or sAML. A randomized phase III study (May 2004). Contact: Nicolaus Kröger, MD. Phone: +49-40-42803-4851.

HUNGARY

Semmelweis University School of Medicine, Budapest. Investigation of the multifactorial cause of iron overload by testing HFE gene mutations: C282Y and H63D, determination of copper and coeruleoplasmin level, analysis of transferring receptor mutation and also TNF-alpha promoter gene polymorphism in MDS patients. Contact: Judit Varkonyi, MD, PhD. Phone/Fax: 361-355-8251.

ITALY

Unit of Hematology and Stem Cell Transplantation, IRCCS “Casa Sollievo della Sofferenza” Hospital. A Phase III clinical trial comparing a single, weekly dose of recombinant erythropoietin alpha (40.000 units) alone versus the combination of this treatment plus low-dose thalidomide for anemic, low-risk MDS. Contact: Dr. Pellegrino Musto. Phone: 39 (0) 882-410295-539.

Unit of Hematology and Stem Cell Transplantation, IRCCS “Casa Sollievo della Sofferenza” Hospital. A Phase I/II clinical evaluating the effect of long-acting erythropoietin darboepoietin-alpha in low-risk, anemic MDS. Contact: Dr. Pellegrino Musto. Phone: 39 (0) 882-410295-539.

Unit of Hematology and Stem Cell Transplantation, IRCCS “Casa Sollievo della Sofferenza” Hospital. A Phase I/II clinical study on allogenic “conventional” and “mini” (non-myelosuppressive) peripheral blood stem cell transplantation in patients with high risk MDS. Contact: Dr. Pellegrino Musto. Phone: 39 (0) 882-410295-539.

POLAND

Jagiellonian University, Cracow. A randomized trial comparing Antithymocyte Globulin (ATG) and Cyclosporine (CSA) with best supportive care in patients with MDS. Contact: Pawel Sledziowski, MD. Phone: +48-12-421-3693.

Jagiellonian University, Cracow. Phase I/II study of Thalidomide in low-risk MDS. Contact: Paweł Sledziowski, MD. Phone: +48-12-424-7600.

Jagiellonian University, Cracow. Phase I/II study of Arsenic Trioxide in high-risk MDS. Contact: Marcin Sobocinski, MD. Phone: +48-12-424-7600.

THE NORDIC COUNTRIES

Nordic MDS Group. Maintenance treatment with 5-azacytidine in patients with advanced MDS and MDS-AML, who have obtained CR with intensive chemotherapy. An open perspective Phase II study NMDSG02B. Contact:
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.

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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.isbmr.org
- National Marrow Donor Program®: www.marrow.org
- Blood & Marrow Transplant Information Network: www.bmtinfonet.org

Inaugural MDS Foundation Charity Golf Tournament is a Huge Success

The MDS Foundation hosted its Inaugural Charity Golf Tournament on Monday, August 9th at Olde York Country Club in Chesterfield, NJ. Thank you to everyone who participated in this worthwhile event, the proceeds of which will benefit support and education in the myelodysplastic syndromes for physicians and patients. For more details, look for our upcoming Fall Edition of The MDS News and don’t forget to save the date for next year: Monday, August 1, 2005!
In Memorium

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AirLifeLine is a non-profit 501 (c) (3) organization that relies 100% on the generosity of volunteer pilots, as well as individual, corporate, and foundation contributions. AirLifeLine is the oldest and largest national volunteer pilot organization in the United States. For more information about AirLifeLine, visit www.AirLifeLine.org or call toll-free (877) AIR LIFE (877-247-5433).

RESOURCE DATABASE INFORMATION:
Agency Name: AirLifeLine
National Office
5775 Wayzata Blvd., Suite 700
Minneapolis, MN 55416
Phone: (952) 582-2980
Toll-free: (877) 727-7728
Fax: (952) 546-5885
Call here for: Outreach, development and administrative inquiries.

Operations Center
50 Fullerton Ct.
Suite 200
Sacramento, CA 95825
Phone: (916) 641-7800
Toll-free: (877) AIR LIFE (247-5433)
Fax: (916) 641-0600
Call here for: Passenger/pilot inquiries
TTY: Not available, but we can use a relay operator.
Website: www.AirLifeLine.org
E-mail: Info@AirLifeLine.org
Administrator: Randy Quast,
President & Volunteer Pilot

Contact Person for Agency Information:
Ginger Buxa
Director of Outreach
Ginger@AirLifeLine.org
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AirLifeLine is a national non-profit 501(c)(3), charitable organization funded entirely by tax deductible donations from individuals, foundations and corporations and the generosity of our volunteer pilots who donate the direct costs of every flight. Over 94% of all support and contributions donated to AirLifeLine goes directly to program services.

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If you need more information for your resource database or website listing, please contact:
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