



THE MDS NEWS

The Newsletter of The Myelodysplastic Syndromes Foundation

From the Guest Editor's Desk

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Molecular Pathways of Apoptosis in MDS

Introduction

Last decade witnessed significant advances in the understanding of the pathobiology of myelodysplastic syndromes (MDS). Several independent studies in different demographic populations have now confirmed the finding of excessive intramedullary apoptosis in bone marrow of MDS patients as the major biologic basis for clinical presentation of variable peripheral blood cytopenias in these disorders.^{1,2} The parallel advances in the fields of general molecular techniques and in the understanding of apoptotic cell death process per se since early 1990s were immediately

extrapolated to MDS, providing many novel insights into pathobiology and leading to development of various innovative therapeutic regimens for these disorders. A new concept of anti-apoptotic therapy thus emerged in the treatment of MDS.^{3,4} The prominent anti-apoptotic agents used so far such as Pentoxifyllin, Thalidomide, and Enbrel were directed at manipulating the action of apoptogenic cytokines and particularly, Tumor Necrosis Factor-alpha (TNF α). The clinical trials with these agents have chiefly yielded partial responses in encouraging percentage of MDS patients.⁵ It has been observed that Enbrel (a TNF α receptor-immunoglobulin fusion protein from Immunex, Inc.) primarily caused improvement in platelet and neutrophil counts, while Thalidomide related to an improvement in hemoglobin status. It is a subject to future investigation if diverse molecular pathways of apoptosis uncovered in MDS marrows so far are differentially affected by individual agents that in turn may correlate with the heterogeneous outcome of anti-apoptotic therapy with specific agents. Clearly, it's only through a comprehensive understanding of the cobweb of apoptotic pathways that we can hope in future to improve the efficacy of anti-apoptotic therapeutic strategy.

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Mediators of Apoptosis in MDS

As reviewed elegantly by many authors at several occasions in the past, apoptosis in MDS appears to be cytokine-mediated. Although, several cytokines have been found to be increased in concentration in the bone marrow, in all likelihood TNF α serves as the master switch of apoptosis in most cases of MDS with increased apoptosis.^{1,2,6} The levels of Interferon gamma (IFN γ) and interleukin 1beta (IL1 β) have also been found to be higher in MDS marrow, which actually would work in conjunction with TNF α to modulate the intracellular apoptotic signaling. Interestingly, a direct inhibition of these three cytokines has so far not been shown to suppress apoptosis of cells from MDS marrow. Abrogation of another ligand receptor interaction, viz. Fas/Fas-L however could directly lower apoptosis of MDS cells.^{7,8} Indeed, TNF α may bring about apoptosis via Fas system. While on the one hand TNF α and IFN γ have been shown to upregulate Fas and Fas-L expression, on the other hand TNF α

(continued on page 2)

simultaneously downregulates the negative regulator of Fas called Fas-associated phosphatase 1 (Fap-1).⁹ The downstream intracellular signaling of Fas though in general is very complex and involves several interlinked biochemical pathways.¹⁰ Three major Fas-related apoptotic pathways seen in many cell types; viz., ligand-mediated, mitochondrially mediated and E2F1-dependent, are described below.

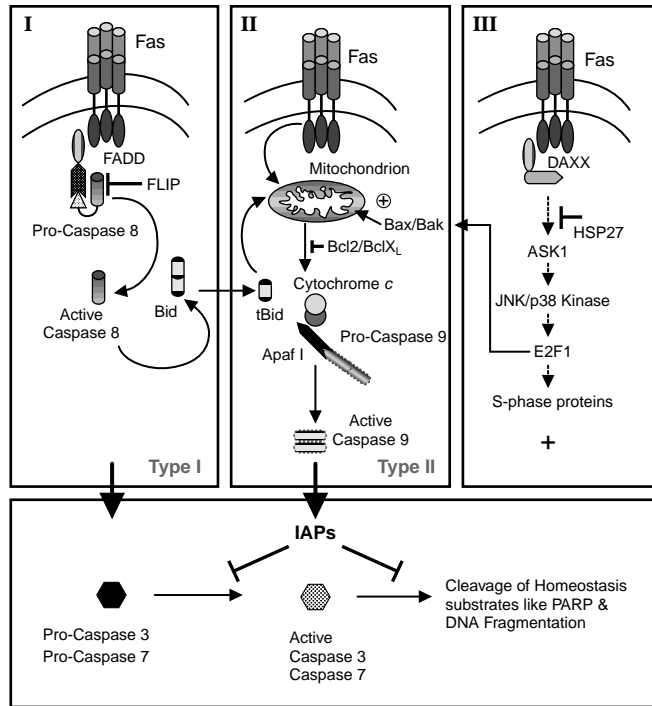


Figure 1. Multiple ramifications of Fas signaling— Three major pathways (I) Ligand-mediated, (II) Mitochondrially mediated, and (III) E2F1-dependent. Note the cross-talk among the three pathways. Evidence for the existence of all three pathways has been reported in MDS. Please see text for details.

Cellular Apoptotic Pathways

The pathways illustrated in Figure 1 have been most well investigated downstream of Fas/Fas-L interaction, which operate individually, as well as in concert in different cell types under unique circumstances. Interestingly, the principle signaling machinery in these pathways though seems to be shared by many different apoptotic stimuli. Noticeably, all these pathways involve an intricate interplay of cysteine proteases known as caspases.¹⁰ As depicted in Figure 1, Fas/Fas L interaction (pathway I) in most cells results in formation of the death inducing signaling complex (DISC), comprising an adapter protein called Fas associating death domain (FADD) and a proenzyme form of caspase 8, which upon recruitment to the DISC is proteolytically activated.

FADD-like interleukin 1 β -converting enzyme (FLICE)-inhibitory protein (FLIP) has been shown to inhibit caspase 8 activation in the DISC. Once activated, caspase 8 can directly trigger a cascade of proteolytic activation of other caspases eventually leading to apoptotic DNA fragmentation. Additionally, caspase 8 can cause the cleavage of a Bcl-2 family member, called Bid. The truncated Bid (tBid) then translocates to mitochondria, where by hitherto incompletely resolved mechanism, it perturbs the mitochondrial membrane potential and facilitates the formation of mitochondrial permeability transition pore (PTP), causing a release of cytochrome c (Cyto c). The pro-apoptotic members of Bcl-2 family; Bax and Bak are among those considered to be structurally involved in PTP, while the anti-apoptotic members like Bcl-2, and Bcl-XL antagonize this process. The Cyto c released in the cytoplasm complexes with apoptotic protease activating factor 1 (Apaf-1) and pro-caspase 9 leading to the activation of caspase 9. In cells (e.g. BJAB cell line) where sufficient levels of DISC are noted, primarily a direct activation of downstream effector caspases, 3,6,7 occurs following caspase 8 activation and the mitochondrially mediated branch of Fas-signaling pathway (pathway II, Figure 1) in these cells may serve only as a signal amplifying event. These are regarded as type I cells in the field of apoptosis biology. While, in some other cell types like Jurkat cell line, there are insufficient amounts of DISC and the death-mediating caspase activation follows only after perturbation of mitochondrial membrane potential. These cells are regarded as type II cells with mitochondria-dependent type II Fas signaling pathway. It may be noted that, many other non-ligand apoptogenic stimuli such as radiation, chemotherapeutic agents, hypoxia, oxidative stress, etc. have been shown to exclusively follow the mitochondrially mediated apoptotic pathway II. Similarly, depending on the nature of a stimulus, pathway III could also occur either in a ligand-dependent or -independent manner, and is mediated by E2F1 activity. Figure 1 shows ligand-dependent E2F1 pathway III. Fas/Fas-L interaction can activate E2F1 transcription factor subsequent to DD-associated protein (DAXX) and p38 mitogen activated protein kinase. Alternatively DNA damage due to physical agents could directly activate E2F1 in a ligand-independent pathway (not indicated in Figure 1).¹¹ Regardless, the downstream events following E2F1 activation appear to route the apoptotic death through mitochondrial involvement. E2F1 activation relates to upregulation of Bax that

alters mitochondrial potential, releases Cyto c, and finally activates caspase 3 in all likelihood via caspase 9.¹² Interestingly however, E2F1 activation may also bring about transcriptional activation of some S-phase proteins causing the phenomenon of signal antagonism.¹³

Status of Apoptotic Pathways in MDS

Initial investigations in MDS had highlighted the role of ligand-mediated pathway involving Fas/Fas-L, and a cascade of caspases 8, 1 and 3 with eventual Poly ADP Ribose Polymerase (PARP) cleavage and DNA fragmentation.^{8,14} Parallel observations made on the stoichiometric high ratio of pro- vs. anti-apoptotic Bcl2 family member proteins though remained lost from the main Fas-mediated apoptotic pathway I until the involvement of mitochondrially mediated pathway II surfaced in the recent studies that revealed a drop in mitochondrial membrane potential, upregulation of Bax, release of Cyto c and activation of caspases 9 and 3.^{2,8,15-18} Intriguingly, the mitochondrial apoptotic pathway has mainly been shown especially in erythroid progenitors in sideroblastic anemia.^{17,18} Contrastingly, in a mixed group of different FAB categories erythroid progenitor apoptosis was shown to be Fas-dependent.¹⁹ Initially in patients with refractory anemia with ringed sideroblasts (RARS)²⁰ and later in an extensive series of studies by our group^{21,22} in MDS patients in general, mitochondrial dysfunction has also been characterized by mitochondrial gene mutations (e.g. Cyto c oxidase I and II) affecting key respiratory chain enzymes and in turn heme synthesis as well as scavenging of free oxygen radicals. Finally, our group has recently shown elevated activity of E2F1 and increased levels of cyclin D1 correlating with signal antagonism in MDS marrows.¹³ It remains to be seen if E2F1 activation interlinks with mitochondrially mediated apoptotic pathway in MDS marrows as well as reported previously in other cell types.

Markers of Distinct Apoptotic Pathways

The anti-apoptotic therapy would yield better responses if the knowledge of the existence of specific apoptotic pathways guides the choice of a therapeutic agent. Although only a few studies have tried to find such correlates in MDS, the observations nonetheless have been very interesting. For instance the mitochondrially mediated apoptosis seems to correlate with detection of high numbers of ringed sideroblasts and its exclusivity from Fas ligand mediated apoptosis becomes apparent in an

anecdotal study with a detection of specific cytogenetics abnormality, del 4p.¹⁷ In contrast, MDS patients with +8 abnormality in different FAB categories have been shown to have Fas mediated apoptosis.²³ On the other hand, abnormalities of chromosome 7 and 20q- have been correlated with low apoptosis in general irrespective of FAB category.^{23,24} Further, a high incidence of apoptosis in S-phase cells (signal antagonism) would be indicative of E2F1 dependent pathway.¹³ Lastly, increased levels of anti-apoptotic Bcl2 family members in CD34+ blasts is indicative of resistance to apoptosis and proximity to leukemic transformation.²⁵ It may be noted that all these findings await confirmation and would have tremendous potential benefit in therapeutic decisions while employing anti-apoptotic therapy to MDS.

Concluding Remarks

The anti-apoptotic therapeutic approach has elicited encouraging partial responses. Different available and potential agents in this regimen need to be tested for their effectiveness on different apoptotic pathways discussed above. A factual selection of the agent based on the predominance of a distinct apoptotic pathway in an individual patient will indeed enhance the treatment outcome and bring the concept of personalized medicine closer to reality even in a complex field of MDS. Moreover, recognition and development of specific markers for distinct pathways would ease clinical utilization of the decade-old major biologic finding of excessive apoptosis in MDS. A significant future advancement will however only be realized after delineation of the causative agents underlying different pathways of apoptosis in MDS.

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Thank You to Our Pharmaceutical Partners

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



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

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- Recognized morphologic expertise in MDS
- Available cytogenetics and/or molecular genetics
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- Board-approved clinical trials
- Documentation of peer-reviewed publications in the field
- The ability and intention to register patients in the MDS International Registry database

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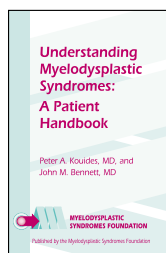
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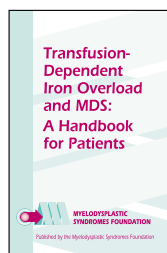
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Arsenic trioxide was viewed as a therapeutic agent as early as in ancient Greece and Rome, when Hippocrates administered arsenic as an ulcer remedy. From the eighteenth century until the 1930s, Fowler's Solution, a mixture containing potassium arsenite, was given to patients with chronic myeloid leukemia for control of leukocytosis. The compound was also used to treat rheumatism, epilepsy, heart palpitations and a whole host of other medical conditions. In 1910, Paul Ehrlich, the founder of modern day chemotherapy, experimented with arsenic and discovered the organic arsenical compound salvarsan, which was used to treat syphilis until the discovery of antibiotics.

Despite arsenic's long history as a medicinal agent, the public's perception has been negatively influenced by its use as a poison. Such poisonings are acute and extreme, and are triggered by ingestion of very high amounts of arsenic over a short period of time. The dose of arsenic in TRISENOX[®] is comparatively small and it is administered over time at a carefully measured rate. In addition, TRISENOX[®] is produced with the highest quality standards. When used appropriately, TRISENOX[®] can be a safe and an effective treatment for some malignancies.

Unlike conventional chemotherapy, TRISENOX[®] does not act like a traditional cytotoxic antineoplastic. Although its most important target of action in MDS is not known, TRISENOX[®] induces apoptosis and differentiation in malignant cells. TRISENOX[®] is currently approved for the treatment of relapsed or refractory acute promyelocytic leukemia (APL)¹ for which it is considered a standard of care. Accumulating evidence also now suggests that TRISENOX[®] may have a role in the treatment of patients with other hematological malignancies, including MDS.² TRISENOX[®] has received orphan drug designation from the FDA for the treatment of MDS.² As of June 2003, approximately 122 patients with MDS have been treated with TRISENOX[®] in clinical trials. An additional 694 patients with MDS have received the drug in general practice.³ The preliminary results of 3 clinical trials have recently been reported, providing insight into the therapeutic potential of this agent (Table 1).

Clinical Trials of TRISENOX[®] in MDS

Monotherapy Trials

A multicenter phase 2 trial conducted in the United States included patients with MDS of all French-American-British (FAB) subtypes with significant hematologic deficits or disease risk features. Patients were divided into those with lower-risk MDS (defined as International Prognostic Scoring System [IPSS] low and intermediate-1 risk categories) and those with higher-risk MDS (defined as IPSS intermediate-2 and high risk categories). TRISENOX[®] 0.25 mg/kg/dose was administered as a 1 to 2 hour infusion 5 days per week for 2 weeks followed by a 2 week treatment hiatus. Assessments were performed in the fourth week of every other 4-week cycle (ie, every 8 weeks). Evaluable patients received between 1 and 13 cycles of treatment.⁴ To date, 50 patients have been enrolled of which 30 are evaluable for efficacy and 35 are evaluable for safety. The median age was 69.5 years (range 35–93).⁴ Among the 30 evaluable patients, 10 (33%) had a International Working Group (IWG)-defined hematologic response, including 1 patient who achieved a complete remission. An additional 15 patients had stable disease while 5 experienced disease progression. There were 3 responses among patients with higher-risk MDS while 6 lower-risk MDS patients responded. Durations of response ranged from 115 days to 630+ days. Among patients with a hematologic response, 3 became transfusion independent while another 3 had reduced transfusion requirements.⁴ This regimen was generally well

tolerated with very few severe drug-related non-hematologic side effects. The most common adverse events were exacerbation of thrombocytopenia, neutropenia, leukopenia, and skin reactions.

Another multicenter trial conducted in France used an alternate maintenance dosage regimen for TRISENOX[®] while producing similar results.⁵ Using the same eligibility criteria as the American trial, the French study administered TRISENOX[®] as a 0.3 mg/kg/dose 1 to 2 hour intravenous infusion for 5 days in the first week (loading dose) followed by a maintenance dose of 0.25 mg/kg/dose twice weekly thereafter. Sixty-seven patients have been enrolled to date in this study of which 37 are evaluable for efficacy and 53 for safety. Evaluable patients received treatment between 1 and 6 months. The median age was 67 years (range 42–81).⁵ Nine patients (6 higher-risk, 3 lower-risk) achieved a hematologic response for an overall objective response rate of 24%. An additional 23 patients had stable disease while 5 had disease progression. The responses have been maintained for between 90 and 300+ days. Among responders, 6 became transfusion independent.⁵ Treatment was generally well tolerated with the most commonly reported adverse effects similar to those reported in the American trial (neutropenia, thrombocytopenia, leukopenia, diarrhea, and pruritus). The majority of adverse events were mild to moderate in intensity.⁵

Combination Therapy Trials

Since TRISENOX[®] and the immunomodulatory agent thalidomide have complementary mechanisms of action, combination regimens of these agents have the potential to produce additive clinical benefit. Such regimens may both promote the growth advantage of normal progenitors through alterations of the bone marrow microenvironment while also suppressing the abnormal clone.

The safety and efficacy of TRISENOX[®] in combination with thalidomide was evaluated in an open-label, single-center, phase 2 trial. The dosage of TRISENOX[®] was the same as that used in the American monotherapy trial (0.25 mg/kg 5 days per week for 2 weeks followed by 2 weeks off). The thalidomide dosage was 100 mg/day and was not escalated during the duration of the study (1 year).⁶ To date, 28 patients have been enrolled and 14 are evaluable. Twelve patients had lower-risk MDS while 16 had higher-risk disease.⁶ The median age was 65 years (range 51–84). There were 7 hematologic responses (4 with higher-risk and 3 with lower-risk

MDS) among the 14 evaluable patients for an overall response rate of 50%. Stable disease was seen in another 3 patients while 4 had progressive disease. The time to response (median 76 days) was variable with some patients requiring 6 months of therapy to achieve a response. Responding patients had a median response duration of 136+ days. Four of the responding patients became transfusion independent.⁶ One notable finding was that 2 of the 4 patients with the chromosome 3 (inv[3][q21q26.2]) abnormality had a trilineage response. This abnormality is typically associated with overexpression of the EVI-1 transcription factor and is characterized by a poor prognosis in both MDS and acute myeloid leukemia. Responses in patients with novel cytogenetic abnormality have not been observed in prior studies involving single-agent thalidomide. The 2 non-responding patients with the abnormal chromosome 3q were removed from study treatment prematurely, and were not evaluable for response. A follow-up study is underway evaluating sequential regimens of TRISENOX[®] with or without thalidomide to determine whether thalidomide contributes to the efficacy of this treatment.⁶

Future Directions

There are several ongoing trials investigating TRISENOX[®]-based regimens in the treatment of MDS (Table 2). These include both monotherapy trials exploring novel schedules and those evaluating combination therapy with chemotherapy agents or growth factors. The TRISENOX[®] dosage schedule applied in the French trial (loading followed by maintenance) is being incorporated into most of the ongoing clinical trials because of the schedule's convenience and comparable activity to the American study schedule (2 weeks on/2 weeks off).

Conclusions

TRISENOX[®] is a novel agent in the treatment of MDS with the potential of providing excellent therapeutic activity. Preliminary trials have demonstrated clinical activity with durable responses in both higher- and lower-risk patients. Additional trials will help to better define which patients are most likely to benefit. For example, TRISENOX[®] (± thalidomide) may be particularly useful for patients who harbor an abnormality of chromosome 3 (inv[3][q21q26.2]), an abnormality associated with a poor prognosis. The results of ongoing clinical trials are eagerly awaited and will help to define the role of this highly promising new agent.

Table 1. Clinical Trials Evaluating TRISENOX® in MDS

Study	No. Evaluable Patients	Response Rate (n [%])			Hematologic Response			Transfusion Independence or Reduction (n)
		CR	PR	SD	Monolineage	Bilineage	Trilineage	
List et al ⁴	30	1 (3%)	0	15 (50%)	8 (27%)	1 (3%)	0	6
Vey et al ⁵	37	0	0	23 (62%)	7 (19%)	2 (5%)	0	6
Raza et al ⁶	14	0	0	3 (21%)	5 (36%)	0	2 (14%)	4

CR=complete response; PR=partial response; SD=stable disease

Table 2. Ongoing Trials Investigating TRISENOX® Alone or in Combination With Other Agents in the Treatment of Myelodysplastic Syndromes

Protocol Title	Investigator (Institution)*	Treatment Regimen
TRISENOX® Monotherapy		
■ Phase II study of TRISENOX® in patients with MDS	M. Beran (MD Anderson Cancer Center)	TRISENOX® 0.25 mg/kg/d days 1–5, then twice weekly x 11 weeks
■ Pilot study of TRISENOX® in patients with MDS	S. Luger (U of Pennsylvania)	TRISENOX® 0.25 mg/kg/d days 1–5 and 8–12, then twice weekly x 10 weeks
TRISENOX® plus Cytosine Arabinoside		
■ Phase I/II study of TRISENOX® in combination with cytosine arabinoside in patients with MDS	C. Gota (LA Hem/Onc); R. Lemon (Cancer and Blood Institute of the Desert)	TRISENOX® 0.25 mg/kg/d days 1–5, then twice weekly x 7 weeks, then no therapy for 2 weeks If CR or PR, repeat TRISENOX® cycle above x 2 If no response, repeat TRISENOX® cycle above and add Ara-c 20 mg/m ² /d days 1–5 and 29–33
TRISENOX® plus Granulocyte-Macrophage Colony-Stimulating Factor		
■ Clinical and biologic effects of TRISENOX® in MDS	B. Mavromatis (Georgetown U)	TRISENOX® 0.25 mg/kg/d days 1–5, then twice weekly x 9 weeks followed by 2 weeks rest GM-CSF 5 mg/kg twice weekly on weeks 1–12
TRISENOX® plus Amifostine		
■ Pilot study of TRISENOX® and amifostine for the treatment of myelodysplastic syndrome and multiple myeloma	R. Herzig (U of Louisville)	Cycle 1: TRISENOX® 0.25 mg/kg/d days 1–5 x 1 week, then twice weekly for 3 weeks Amifostine 300 mg/m ² 3 days/week x 3 weeks with 1 week off. Subsequent cycles: TRISENOX® 0.25 mg/kg/d twice weekly for 4 weeks. Amifostine 300 mg/m ² 3 days/week x 3 weeks with 1 week off.

Ara-c=cytosine arabinoside; CR=complete response; GM-CSF=granulocyte-macrophage colony-stimulating factor; PR=partial response.

*For further information on TRISENOX® clinical trials, contact Dr. Robert Earhart, Vice President of Medical Affairs for Cell Therapeutics, Inc., at 206-272-4412.

References

1. Trisenox® (arsenic trioxide) injection prescribing information. 2001. Cell Therapeutics.
2. List AF. New approaches to the treatment of myelodysplasia. *Oncologist*. 2002;7:Suppl 1:39–49.
3. Garzon F, Ellison R, Kirkhart B, Singer J. Updated safety experience with Trisenox (Arsenic Trioxide) injection. Presented at the 8th Congress of the European hematology Association, 12–15 June, 2003, Lyon, France.
4. List AF, Schiller GJ, Mason J, Douer D, Ellison R. Trisenox® (arsenic trioxide) in patients with myelodysplastic syndromes (MDS): preliminary findings in a phase 2 clinical study. Presented as a poster at the 7th International Symposium on Myelodysplastic Syndromes, Paris, France, May 15–18, 2003.
5. Vey N, Dreyfus F, Guerci A, Fenoux P, Burnett A, Bosly A, et al. Trisenox® (arsenic trioxide) in patients (pts) with myelodysplastic syndromes (MDS): preliminary results of a phase 1/2 study. Presented as a poster at the 7th International Symposium on Myelodysplastic Syndromes, Paris, France, May 15–18, 2003.
6. Raza A, Buonamici S, Reddy P, Lisak L, Tahir S, Gezer S, et al. Myelodysplastic syndromes (MDS) patients with high evi-1 expression respond well to a combination of arsenic trioxide (Trisenox®) and thalidomide. Presented as a poster at the 7th International Symposium on Myelodysplastic Syndromes, Paris, France, May 15–18, 2003.

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

The Foundation Announces New Educational Programs

The MDS Foundation is pleased to announce the following educational initiatives:

CME Monograph:

"Controversies in Classification and An Optimistic Look at New Treatment Options"

Alan F. List, MD, Editor

This monograph discusses new data from ongoing clinical trials, controversies regarding the classification of MDS, and improvements in stem cell transplantation.

The program is approved for 2 hours of CME credit upon completion. There is no charge for this educational activity.

MDS Teleconference:

"The Changing Landscape in the Treatment of MDS"

This 15-minute teleconference provides the latest information on the Myelodysplastic Syndromes, including classification, prevalence, current research, and treatment guidelines. Information will also be provided about a new therapy for MDS: CC-5013, its initial clinical trial performance and the availability of two new trials for you and your patients.

For information on how to participate in either of these two programs, please contact the MDS Foundation at 1-800-MDS-0839 or visit our website at www.mds-foundation.org.



Making cancer more treatable™

Cell Therapeutics, Inc. has provided the MDS Foundation with unrestricted educational grants to support the Foundation's work.

Gifts to the Foundation

The MDS Foundation relies entirely on gifts and membership fees to further its work. We would like to acknowledge the generosity of the following individuals and organizations that have recently provided gifts to the Foundation:

**John and Carol Bennett
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New York, NY**

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Atherton, CA**

The MDS Foundation is very grateful for the heartfelt support of its donors. Our work as a non-profit organization depends on public funding. If you would like to contribute or if you have a unique idea of your own, please write to us at:

36 Front Street
PO Box 353
Crosswicks, NJ 08515

or call us at 1-800-MDS-0839

Patient Symposiums Are Being Established By The MDS Foundation

We are pleased to announce that we are currently developing patient symposiums nationwide to be centered around our MDS Centers of Excellence. Our upcoming special conferences will afford patients and their guests the opportunity to listen to guest speakers who are experts in MDS. They will also be given the opportunity to participate in a question and answer session with the medical presenters. These programs will begin 2004. Further developments will be posted on our website or for more information contact the Patient Liaison at 1-800-MDS-0839.

The 2nd International Congress of the Myeloproliferative Diseases and Myelodysplastic Syndromes was held on October 15th at the New York Hilton Hotel.

We were very pleased that our Chairman, Dr. John Bennett was one of the featured speakers on MDS, as was Alan F. List, a member of our Board. Our Centers of Excellence were well represented by Dr. Richard Silver from New York Presbyterian Hospital, Dr. Jerry Spivak from Johns Hopkins, Tiziano Barbui from Italy, Ayalew Tefferi from The Mayo Clinic, Dr. List from the University of South Florida, and Dr. Bennett from the University of Rochester.

Share Your Stories

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



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

International Clinical Trials: An Update

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.

MDS CLINICAL TRIALS ANNOUNCEMENT

Celgene Corporation initiated two new MDS Trials in June 2003 in cooperation with the MDS Foundation. If you would like more information please call the Foundation at 800-MDS-0839 or visit our web site and e-mail us.

CC-5013-MDS-002: "A Multicenter, Single-arm, Open-label Study of the Efficacy and Safety of CC-5013 Monotherapy in RBC Transfusion-dependent Subjects with Myelodysplastic Syndromes"

CC-5013-MDS-003: "A Multicenter, Single-arm, Open-label Study of the Efficacy and Safety of CC-5013 Monotherapy in Red Blood Cell Transfusion-dependent Subjects with Myelodysplastic Syndromes Associated with a Del (5Q) Cytogenetic Abnormality"

Novacea. DN101-003. This study is a research study for patients with a blood disorder called myelodysplastic syndromes (MDS) who are dependent on repeat blood transfusions. It involves treatment with DN-101 (a formulation of calcitriol designed specifically for oncology and hematology) that is being investigated to determine if it may improve symptoms of fatigue and reduce the need for repeat blood transfusions.

Results of previous laboratory and clinical studies have suggested that calcitriol may be useful in treating MDS. Up to 46 patients with low- and intermediate-1 risk MDS who are red blood cell transfusion dependent because of severe anemia will be enrolled in this study at 10 research centers in the United States.

For more information, please go to www.novacea.com.

Other U.S. Trials

Alta Bates Cancer Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: David Irwin, MD. Phone: 510-204-1591.

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

Cancer & Blood Disease Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Gustavo Fonseca, MD. Phone: 352-746-0707.

Cancer & Blood Disease Center. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Gustavo Fonseca, MD. Phone: 352-746-0707.

Cedars-Sinai Medical Center. Phase II study to determine if an oral, relatively non-toxic, novel vitamin D3 compound, paricalcitol, (Zemlar) 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.

Cleveland Clinic Foundation. IRB5777. A 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: Liz Kuczkowski. Phone: 216-445-3795.

Cleveland Clinic Foundation. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Liz Kuczkowski. Phone: 216-445-3795.

Cleveland Clinic Foundation. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Liz Kuczkowski. Phone: 216-445-3795.

Dana-Farber Cancer Institute. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Richard M. Stone, MD. Phone: 617-632-2214.

Dana-Farber Cancer Institute. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Richard M. Stone, MD. Phone: 617-632-2214.

Desert Hematology Oncology Medical Group, Inc. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Luke Dreisbach, MD. Phone: 760-568-3613.

Drexell University College of Medicine. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Emmanuel Besa, MD. Phone: 215-842-6980.

Drexell University College of Medicine. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Emmanuel Besa, MD. Phone: 215-842-6980.

Florida Cancer Specialists. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: James Reeves, MD. Phone: 239-274-9930.

Fred Hutchinson Cancer Research Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: H. Joachim Deeg, MD. Phone: 206-667-5985.

Fred Hutchinson Cancer Research Center. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: H. Joachim Deeg, MD. Phone: 206-667-5985.

Fred Hutchinson Cancer Research Center. FRCRC #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. #1596. Transplantation from related donors for high risk patients with MDS. Conditioning includes a "non-myeloblastic" 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. FHCRC #1478. Non-transplant therapy for "less advanced" MDS with ATG plus Enbrel. No age restrictions. Contact: H.J. Deeg, MD. Phone: 206-667-4324.

Fred Hutchinson Cancer Research Center. 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. FHCRC #800. Transplantation from unrelated donors for patients with aplastic anemia who have failed immunosuppressive 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. FHCRC #1641. Transplantation from unrelated donors for high risk patients with MDS. Conditioning will be with a "non-myeloablative" approach using 200 cGy of TB1 and fludarabine. No age restriction (other exclusion criteria exist). Contact: M. Maris, MD. Phone 206-288-1024.

Fred Hutchinson Cancer Research Center. FHCRC #1723. Transplantation from related or unrelated 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.

Fred Hutchinson Cancer Research Center. FHCRC #1781. Non-transplant therapy for "less advanced" transfusion-dependent MDS with DN-101 (Calcitriol). No age restrictions. Contact: H.J. Deeg, MD. Phone: 206-288-1024.

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

Indiana University Medical Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Larry Cripe, MD. Phone: 317-274-3545.

Johns Hopkins Oncology Center. J0136. Vaccination in peripheral stem cell transplant setting for acute myelogenous leukemia: The use of autologous tumor cells with an allogeneic GM-CSF producing bystander cell line. Contact: Julie Yerian. Phone: 410-614-1766.

Johns Hopkins Oncology Center. J0255. A Phase II study of the farnesyl transferase inhibitor Zarnestra in previously untreated poor-risk acute myeloid leukemia and myelodysplastic syndromes. Contact: Jackie Greer. Phone: 410-614-1329.

Johns Hopkins Oncology Center. J0051. Dose finding study of bryostatins-1 and GM-CSF for resistant myeloid malignancies. Contact: Julie Yerian. Phone: 410-614-1766.

Johns Hopkins Oncology Center. J9950. A 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 Dausers. Phone: 410-502-7110.

Johns Hopkins Oncology Center. J9879. A Phase I, dose-finding trial of sodium phenylbutyrate in combination with all trans-retinoic acid (ATRA) in patients with myelodysplastic syndromes and acute myeloid leukemia. Contact: Karen Friel. Phone: 410-502-7114.

Johns Hopkins Oncology Center. J0253. Phase I clinical-laboratory study of the histone deacetylase (HDA) Inhibitor MS-275 in adults with refractory and relapsed hematologic malignancies. Contact: Jackie Greer. Phone: 410-614-1329.

Johns Hopkins Oncology Center. J0252. A 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.

Johns Hopkins Oncology Center. J9852. Granulocyte macrophage-colony stimulating factor (GM-CSF) after T-lymphocyte-depleted allogeneic BMT for myelodysplastic syndromes. Contact: Tianna Dausen. Phone: 410-502-7110.

Kaiser Permanente Northwest Region Center for Health Research. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Negandra Tirumali, MD. Phone: 503-331-6500.

Kaiser Permanente Northwest Region Center for Health Research. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Negandra Tirumali, MD. Phone: 503-331-6500.

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

Mayo Clinic, Rochester, MN. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Ayalew Tefferi, MD. Phone: 507-284-2511.

Mayo Clinic, Rochester, MN. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Ayalew Tefferi, MD. Phone: 507-284-2511.

MD Anderson Cancer Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Deborah Thomas, MD. Phone: 713-745-4616.

MD Anderson Cancer Center. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Deborah Thomas, MD. Phone: 713-745-4616.

MD Anderson Cancer Center. An Open-Label, Phase II Study to Evaluate the Efficiency and Safety of the Farnesyltransferase Inhibitor Zarnestra (R115777) in Subjects with High-Risk Myelodysplastic Syndrome (MDS). Contact: Razelle Kurzrock, MD. Phone: 713-794-1226.

MD Anderson Cancer Center. 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. A Phase I/II Study of PR1 (NSC698102) Human Leukemia Peptide Vaccine with Incomplete Freund's Adjuvant (NSC 675756). Contact: Jeffrey Molldrem, MD. Phone: 713-563-3318.

MD Anderson Cancer Center. 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. Phase II Study of Arsenic Trioxide in the Treatment of Myelodysplastic Syndromes. Contact: Miloslav Beran, MD. Phone: 713-792-2248.

MD Anderson Cancer Center. Phase I/IIA Study of TLK199 HCL Liposomes for Injection in Myelodysplastic Syndrome. Contact: Stefan Faderl, MD. Phone: 745-4613.

MD Anderson Cancer Center. 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. A 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. Safety and Efficacy Trial of Bevacizumab: Anti-VEGF Humanized Monoclonal Antibody (NSD 704865) Therapy for Myelodysplastic Syndrome (MDS). Contact: Jorge Cortes, MD. Phone: 713-794-5783.

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

MD Anderson Cancer Center. 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. 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. 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) ($\geq 10\%$ bone marrow blasts). Contact: Stefan Faderl, MD. Phone: 713-745-4613.

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

Medical College of Georgia. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Oscar Ballester, MD. Phone: 706-721-2505.

Memorial Sloan-Kettering Cancer Center. 99-057. A Phase I study of salicylate for adult patients with advanced myelodysplastic disorders, acute myelogenous leukemia or chronic lymphocytic leukemia. Contact: Virginia Klimek, MD. Phone: 212-639-6519.

Memorial Sloan-Kettering Cancer Center. 00-116. A 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. 02-004. A randomized, multi-centered, double-blind, placebo-controlled trial assessing safety and efficacy of thalidomide for the treatment of anemia in red blood cell transfusion-dependent patients with MDS. Contact: Virginia Klimek, MD. Phone: 212-639-6519.

Memorial Sloan-Kettering Cancer Center. 01-021. Phase I clinical trial of oral suberoylanilide hydroxamic acid-SAHA (MSK 390) in patients with advanced solid tumors and hematologic malignancies. Contact Mark Heaney, MD, PhD. Phone: 212-639-2275.

Memorial Sloan-Kettering Cancer Center. 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.

Memorial Sloan-Kettering Cancer Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Stephen Nimer, MD. Phone: 212-639-7871.

Memorial Sloan-Kettering Cancer Center. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Stephen Nimer, MD. Phone: 212-639-7871.

Mt. Sinai Medical Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Lewis Silverman, MD. Phone: 212-241-5520.

Mt. Sinai Medical Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Lewis Silverman, MD. Phone: 212-241-5520.

New York Hospital-Cornell. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Richard T. Silver, MD. Phone: 212-746-2855.

New York Hospital-Cornell. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Richard T. Silver, MD. Phone: 212-746-2855.

Northwest Georgia Oncology Centers. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Robert Hermann, MD. Phone: 770-281-5105.

Oregon Health & Science University. 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. 7597. A Phase 2, Multicenter, Open Label Study of 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. 7377. A Randomized, Multi-Center, Double-Blind, Placebo-Controlled Trial Assessing the Safety and Efficacy of Thalidomide (Thalomid®) for the Treatment of Anemia in Red Blood Cell Transfusion-Dependent Patients with Myelodysplastic Syndromes. Contact: Peter Curtin, MD. Phone: 503-494-5064.

Oregon Health & Science University. 7039. A Randomized Controlled Trial of Posaconazole (SCH56592) vs. Standard Azole Therapy for the Prevention of Invasive Fungal Infections Among High-Risk Neutropenic Patients. Contact: Peter Curtin, MD. Phone: 503-494-5064.

Oregon Health & Science University. 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. 6756. Low-Dose TBI and Fludarabine Followed by Nonmyeloablative Unrelated Donor Peripheral Blood Stem Cell Transplantation Using Enhanced Postgrafting Immunosuppression for Patients with Hematologic Malignancies and Renal Cell Carcinoma—A Multi-Center Trial. Contact: Peter Curtin, MD. Phone: 503-494-5064.

Oregon Health & Science University. 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. 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.

Oregon Health & Science University. 6615. Non-Myeloablative Allogeneic Hematopoietic Cell Transplantation for the Treatment of Myelodysplastic Syndromes and Myeloproliferative Disorders (Except CML). Contact: Peter Curtin, MD. Phone: 503-494-5064.

Oregon Health & Science University. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Peter Curtin, MD. Phone: 503-494-5064.

Oregon Health & Science University. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Peter Curtin, MD. Phone: 503-494-5064.

Roswell Park Cancer Institute. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Maria Baer, MD. Phone: 716-845-5975.

Roswell Park Cancer Institute. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Maria Baer, MD. Phone: 716-845-5975.

Rush-Presbyterian-St. Luke's Medical Center. Phase II trial of Trisenox with or without Thalidomide in patients with MDS. Contact: Azra Raza, MD. Phone: 312-455-8474.

Rush-Presbyterian-St. Luke's Medical Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Azra Raza, MD. Phone: 312-455-8474.

Rush-Presbyterian-St. Luke's Medical Center. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Azra Raza, MD. Phone: 312-455-8474.

Stanford University Medical Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Peter Greenberg, MD. Phone: 650-725-8355.

Stanford University Medical Center. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Peter Greenberg, MD. Phone: 650-725-8355.

Stanford University Medical Center. 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.

St. Jude Children's Research Hospital. AML02. A 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. HAPSCT. A Phase III randomized trial to evaluate haploidentical 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. MUDSCT. A 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. REFSCT. A 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.

St. Luke's Oncology and Hematology Associates. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Ronnie Kirschling, MD. Phone: 218-249-3081.

St. Vincents Comprehensive Cancer Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Sanford Kempin, MD. Phone: 212-604-6010.

Swedish Cancer Institute. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Hank Kaplan, MD. Phone: 206-386-2828.

Swedish Cancer Institute. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Hank Kaplan, MD. Phone: 206-386-2828.

The Mayo Clinic, Jacksonville, FL. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Alvaro Aspitia-Moreno, MD. Phone: 904-953-7291.

The Mayo Clinic, Jacksonville, FL. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Alvaro Aspitia-Moreno, MD. Phone: 904-953-7291.

The Mayo Clinic, Scottsdale, AZ. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: John Camoriano, MD. Phone: 480-301-8335.

University of Arizona Cancer Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Alan List, MD. Phone: 520-626-2340.

University of Arizona Cancer Center. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Alan List, MD. Phone: 520-626-2340.

University of Arizona Cancer Center. Phase I/II study of continuous oral administration of SCH 66336 in patients with advanced myelodysplastic syndromes. Contact: Alan List, MD. Phone: 520-626-2340.

University of Arizona Cancer Center. Phase II multicenter study of arsenic trioxide in patients with myelodysplastic syndromes (CTI, HSC 01-196). Contact: Alan List, MD. Phone: 520-626-2340.

University of Arizona Cancer Center. A 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 (Schering Plough, HSC 01-132) Contact: Alan List, MD. Phone: 520-626-2340.

University of Arizona Cancer Center. A Phase 1A, open-label, 3-arm, dose-escalation study of PTK787/ZK 222584 administered orally on a twice-daily dosing schedule in patients with relapsed or refractory acute myelogenous leukemia (AML) (ARM 1), or patients with secondary and poor prognosis AML, advanced myelodysplastic syndrome (RAEB and RAEBT), and poor prognosis elderly patients with de novo AML (Arm 2), or patients with agnogenic myeloid metaplasia (Arm 3) (Novartis Pharmaceuticals HSC 02-27). Contact Alan List, MD. Phone: 520-626-2340.

University of Arizona Cancer Center. Safety and efficacy trial of bevacizumab: anti-vegf humanized monoclonal antibody therapy for MDS (HSC # 02-11) Contact: Alan List, MD. Phone: 520-626-2340.

University of Chicago Medical Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Richard A. Larson, MD. Phone: 773-702-6783.

University of Chicago Medical Center. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Richard A. Larson, MD. Phone: 773-702-6783.

University of Louisville. Pilot study of arsenic trioxide and amifostine for the treatment of myelodysplastic syndromes. Contact: R. Herzig, MD. Phone: 800-234-2689.

University of Miami Sylvester Comp Cancer Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Eric Lian, MD. Phone: 305-243-6611.

University of Miami Sylvester Comp Cancer Center. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Eric Lian, MD. Phone: 305-243-6611.

University of Pennsylvania Cancer Center. A pilot study of valproic acid in patients with MDS. Contact: Selina Luger, MD. Phone: 215-662-6348.

University of Pennsylvania Cancer Center. Pilot study of arsenic trioxide in patients with MDS. Contact: Selina Luger, MD. Phone: 215-662-6348.

University of Rochester James P. Wilmot Cancer Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: J.J. Iftikharuddin, MD. Phone: 585-275-1941.

University of Rochester James P. Wilmot Cancer Center. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: J.J. Iftikharuddin, MD. Phone: 585-275-1941.

University of Texas, MD Anderson Cancer Center. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Deborah Thomas, MD. Phone: 713-792-7026.

University of Texas, MD Anderson Cancer Center. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Deborah Thomas, MD. Phone: 713-792-7026.

Wake Forest University School of Medicine. Orthomolecular Vitamin D in Low-Risk Myelodysplastic Syndrome: An Open-Label Clinical Trial. A pilot trial where patients with low-risk MDS are treated with 2000 IU daily vitamin D3 for 6 months. Contact: Istvan Molnar, MD. Phone: 336-716-5847.

Wake Forest University School of Medicine. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Bayard Powell, MD. Phone: 336-716-7970.

Wake Forest University School of Medicine. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Bayard Powell, MD. Phone: 336-716-7970.

Washington University School of Medicine. A 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. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Alisa Ruddell. Phone: 314-454-4095.

Washington University School of Medicine. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Alisa Ruddell. Phone: 314-454-4095.

Western Pennsylvania Cancer Institute. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Charles Schiffer, MD. Phone: 313-745-8910.

Western Pennsylvania Cancer Institute. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Charles Schiffer, MD. Phone: 313-745-8910.

Winthrop University Hospital. CC-5013-MDS-002. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes. Contact: Alexander Hindenburg, MD. Phone: 516-663-9500.

Winthrop University Hospital. CC-5013-MDS-003. A multicenter, single-arm, open-label study of the efficacy and safety of CC-5013 monotherapy in RBC transfusion-dependent subjects with myelodysplastic syndromes associated with a del (5q) cytogenetic abnormality. Contact: Alexander Hindenburg, MD. Phone: 516-663-9500.

European Trials

ENGLAND

Kings College Hospital/Guys-Kings-Thomas School of Medicine. Multi-center study of the role of 5-Azacitidine 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-center study of the role of 5-Azacitidine in high risk MDS (beginning Spring 2004). Contact: Sally Killick, MD. Phone: 44 (0) 11202 704783.

The Royal Bournemouth Hospital. Multi-center 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

Marseilles, France. Phase I/II multi-center study of arsenic trioxide in patients with MDS. Contact: N. Vey, MD. Phone: 800-916-9280. Email: clinicaltrial@ctiseattle.com

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. Phone: +49-69-6301-4802.

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

University Hospital Frankfurt/Main. 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: Wolf-K. Hofmann. 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. 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 Luebbert, MD. 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 Luebbert, MD. Phone: +49-761-270-3279.

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 ceruloplasmin level, analysis of transferrin receptor mutation and also TNF α 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 darbepoietin-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 allogeneic "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: Prof. Aleksander B. Skotnicki, MD. Phone: +48-12-421-3693.

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

Jagiellonian University, Cracow. Phase III clinical trial of Amifostine/pentoxifylline/ciprofloxacin/dexamethasone for low-risk MDS. Contact: Janusz Krawczyk, 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

MAP Study. Diagnostic study on hypoplastic MDS, aplastic anemia and PHN. Contact: Torben Plesner, MD. Phone: 011-46-85-858-0000.

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 MNMDSG02B. Contact: Eva Hellström-Lindberg, MD, PhD. Phone: 011-46-85-858-0000.

Nordic MDS Group. Effects of anemia in MDS quality of life, cardiac function and health care costs. An open, non-randomized Phase II study NMDSG03A. Planned to start December 2003. Contact: Herman Nilsson-Ehle. Phone: 011-46-85-858-0000.

SCOTLAND

Ninewells Hospital University of Dundee. Cti 1061. Phase I/II study of arsenic trioxide in patients with myelodysplastic syndromes. Contact: David Bowen, MD. Phone: 011-44-1382-86011.

Ninewells Hospital University of Dundee. Double-blind, randomized, placebo-controlled study on low-dose melphalan for treatment of high-risk myelodysplastic syndromes (MDS) with normal or reduced bone marrow cellularity (PI Claudio Denslinger, Stuttgart, Germany). Contact: David Bowen, MD. Phone: 011-44-1382-86011.

Ninewells Hospital University of Dundee. Identification of markers for early response to the combination of epoietin and G-CSF in the anemia of MDS. Contact: David Bowen, MD. Phone: 011-44-1382-660111.

**To submit information on
your clinical trials for publication,
you can fax (609-298-0590)
us at the Foundation.**

**Please include a contact person,
a phone number, and if
applicable, the trial number.**

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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.



PHARMION

*Pharmion has provided the MDS Foundation
with unrestricted educational grants
to support the Foundation's work.*

Patient Services

AirLifeLine: For nearly 25 years, **AirLifeLine** has helped people overcome the obstacle of distance and access to healthcare. Through a nationwide network of 1,500 volunteer pilots, AirLifeLine coordinates *free* air transportation for people in need. AirLifeLine's generous and compassionate volunteer pilots—men and women from all 50 states with a wide variety of backgrounds—donate flights in their personal general aviation aircraft. Passengers fly *totally free*, as often as necessary and for as long as needed, to reach medical care or for numerous other humanitarian needs. Since 1978, and AirLifeLine volunteer pilots have flown over 30,000 missions. In 2002, AirLifeLine volunteer pilots provided free air transportation for nearly 9,500 passengers (men, women, and children), saving them over \$4 million in commercial travel expenses, helping them reach medical treatment that would otherwise be inaccessible.

Although the vast majority of its passengers fly for medical reasons, AirLifeLine pilots also offer free flights for other humanitarian reasons. Each summer, AirLifeLine's volunteer pilots distribute the children from Chernobyl to host homes across the U.S. for a two-month summer respite. They also transport hundreds of children to health-related summer camps each year. And, within 48 hours of the terrorist attacks on 9/11/01 and while most aircraft were still grounded, AirLifeLine volunteer pilots were in the air transporting emergency service personnel, disaster victims, blood and medical supplies in support of disaster relief efforts in New York City and Washington, D.C.

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 or (877) 727-7728

Program Description: Since 1978, AirLifeLine has helped to ensure equal access to healthcare and improve the quality of life for thousands of people throughout the United States by coordinating free air transportation for those in need.

Services Provided: AirLifeLine coordinates the following services:

1. Transporting people with medical and financial need to reach medical care far from home.
2. Transporting people with time-critical needs associated with a transplant procedure.
3. Transporting precious cargo such as organs, blood, tissue and medical supplies.
4. Providing free air support for disaster relief efforts in times of crisis.
5. Providing flights for numerous other humanitarian needs.

Funding Source: 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.

Volunteer Opportunities: AirLifeLine is currently seeking volunteer pilots in many areas of the country. For more information, visit www.AirLifeLine.org or call (877) AIR LIFE.

Passenger Eligibility: Our volunteer pilots fly passengers free of charge and as often as



necessary for diagnosis, treatment, and follow-up care, and for other humanitarian reasons.

1. AirLifeLine passengers must be ambulatory or need little or no assistance to board and exit the aircraft.
2. Passengers must be medically stable and able to fly in an unpressurized aircraft.
3. Passengers must demonstrate financial need.

Application Method:

To request a free flight, just call toll-free (877) AIR-LIFE (877-247-5433). In urgent situations, a coordinator can be paged after normal business hours. Just call (877) AIR LIFE and follow the paging instructions on the voice mail message.

You may also request a flight by visiting www.AirLifeLine.org.

Service Area:

All U.S. states, parts of Canada & Mexico

Cost/Fees: None, but donations accepted

Waiting List:

None, but 1-2 weeks advance notice is preferred

Target group: Anyone with financial need who needs air transportation

Age Range: All

Handicap Access: Somewhat, depending on type and size of aircraft

Languages: English and Spanish

If you need more information for your resource database or website listing, please contact: Ginger Buxa, Director of Outreach (877) 727-7728, E-Mail: Ginger@AirLifeLine.org

Be a Bone Marrow Donor

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

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

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, 2005 in Nagasaki, Japan.

One major role of the Foundation is our international information network. This network provides patients with referrals to Centers of Excellence, contact names for available programs, sharing of new research and treatment options, and extension of educational support to both physicians and patients. Ultimately, we hope to provide funding and oversight for international studies in MDS.

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

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>



Pfizer has provided the MDS Foundation with unrestricted educational grants to support the Foundation's work.

In Memorium

**A memorial fund has been established in the name of
Mr. Albert Appel**

Donations have been made in Mr. Appel's memory by:

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**A memorial fund has been established in the name of
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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

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In Memorium (continued from page 23)

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Phoenix, AZ

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Brian Rothstein
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Tricia Valentine and
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Donations have been made in Mr. Tanis' memory by:

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