**FALL 2015** 



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# **MDS** NEWS HIGHLIGHTS

# FROM THE GUEST EDITOR'S DESK

**13th International MDS Symposium: An Overview** Presented by Symposium Chair: Steven D. Gore, MD Yale University School of Medicine



# PLAN TO ATTEND OUR UPCOMING SYMPOSIA

**ASH 2015 MDS FOUNDATION BREAKFAST SYMPOSIUM** 

**December 4, 2015 Orlando**, Florida

**14TH INTERNATIONAL SYMPOSIUM ON MYELODYSPLASTIC SYNDROMES** May 3-6, 2017 Valencia, Spain



MDS FUNDRAISING EVENTS

CAREGIVERS: COPING AND CARING



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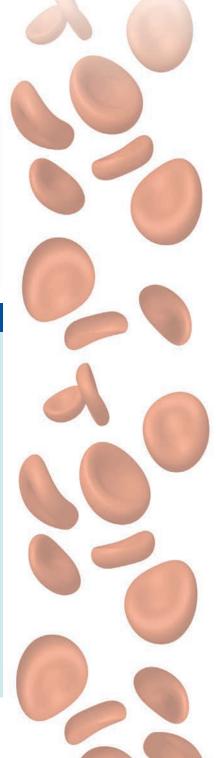
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## www.mds-foundation.org

# FROM THE GUEST EDITOR'S DESK

#### **GUEST EDITORIAL**

# 13th International MDS Symposium: An Overview



Steven D. Gore, MD Director of Hematologic Malignancies Yale University School of Medicine New Haven, Connecticut, USA

#### **A Capital Symposium**

From April 29 – May 2, 2015, the MDS Foundation and I, along with the Scientific Subcommittee, welcomed 1,030 delegates to Washington, DC, for the 13th bi-annual MDS Symposium. Participants came from 58 countries. This was the first Symposium in the Americas since the 1994 Chicago meeting, and only the second in the Western Hemisphere. As always, the Symposium affords MDS investigators, clinicians, patients, and advocates the opportunity to share and celebrate scientific progress, recognize how far we need to go, and importantly network to form collaborations which will lead to cures for these diseases. To this end, we opened with both celebration and reflection—a classic United States Revolutionary War fife and bugle corps opened the symposium, followed by a beautiful rendition of "America the Beautiful" performed by Janna Pelle, whose father Anthony Pelle died of myelodysplastic syndromes.

The 13th Symposium took a new approach to forma, by offering two parallel tracks: Next Gen MDS offered plenary talks followed by state-of-the-science presentations selected from the abstracts. Topics covered included: MDS Genomics and Epigenomics, Epigenetics and Splicing Factors, Preclinical and Mouse Models, Microenvironment, Innate Immunity and Bone Marrow Failure States, The Aging Stem Cell, Epidemiology and Outcomes Research, MDS Predisposition, Biology of As always, the International Symposium affords MDS investigators, clinicians, patients, and advocates the opportunity to share and celebrate scientific progress

MDS progression, and the Best of Clinical Trial Abstracts. The advances in MDS biology since we met in Berlin, particularly in genomics, epigenomics, stem cell biology, and the brand new field of splicing factors were breathtaking. Ben Ebert led off the symposium with thoughts on "Making the next Quantum Leap in MDS;" the presentations which followed over the next several days strongly supported the contention that quantum leaps will be forthcoming.

No less exciting was the MDS Clinical State-of-the-Art track. This set of wellattended talks continued the previous tradition of clinical "plenary" sessions, which included education for clinicians as well as summaries of the latest in clinical data. Topics included: Molecular Diagnostics, Prognostication, Supportive Care including Chelation, Overlap Syndromes including Chronic Myelomonocytic Leukemias, Management of lower risk MDS and Management of higher risk MDS including stem cell transplant. Particularly provocative were a point-counterpoint debate on whether allogeneic stem cell transplantation cures MDS (in which transplanters took the NO position), and a roundtable on designing the one clinical trial which could have the greatest impact on MDS. Several outstanding clinicians discussed difficult diagnostic and therapeutic cases, and as always, the morphology workshop led by Drs. Bennett and Goasguen, the nursing education forum, and the patient forum were well attended and extremely well received.

Special Lectures from Dr. Jimmie Holland and from Sally Ann Roberts, the sister of the US television news broadcaster Robin Roberts, who has undergone allogeneic stem cell transplant for therapyinduced myeloid neoplasm, reminded us why we are in this business: taking care of patients in a compassionate, humanistic manner, and helping patients and families through their difficult struggles to survive with the best quality of life.

Success was further celebrated at our Gala Networking Event held in the spectacular National Building Museum, the site of many presidential inaugural balls. Raggs and the All Stars Band set the right tone for forgetting about science and "shaking your blues away." We learned that two German MDS investigators are particularly adept at demonstrating European Club moves.

My goals in chairing the 2015 symposium were to increase the number and focus on primary scientific presentations-making the meeting a more robust scientific symposium-and to highlight the "Young Turks" of the field. I am extremely proud that we accomplished both goals extremely well. To this end I am indebted to my Scientific Subcommittee for their hard work in planning the program and reviewing abstracts: Gregory Abel, Corey Cutler, Joachim Deeg, Ben Ebert, Elihu Estey, Tim Graubert, Moshe Mittelman, Mikkael Sekeres, and Matt Walter. Sue Hogan and the Foundation Staff as usual were amazing and incredibly hard working resources, and Kenes provided the organizational glue to make the meeting happen.

Five months later, I can only speculate as to how much more progress has already been made. I am grateful that my friend and colleague Guillermo Sanz is already hard at work to ensure that the 2017 symposium in Valencia, Spain, will continue the growth of this Symposium which is so critical to our mission.









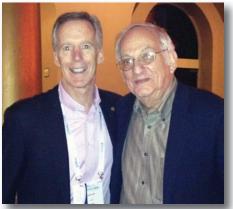


HIGHLIGHTS FROM 13TH INTERNATIONAL SYMPOSIUM ON MYELODYSPLASTIC SYNDROMES April 29–May 2, 2015 WASHINGTON, D.C., USA















## Missed out on MDS 2015?

Well, not to worry - view the free webcasts of the 9 plenary sessions along with presentation highlights that took place during the symposium: http://www.onclive.com/conference-videos/mds-2015.

### PLENARY SESSIONS



PLENARY 1 Making the Quantum Leap in MDS Treatment Benjamin L. Ebert



PLENARY 4 Mouse Models of microRNA Deficiency in MDS Aly Karsan, MD



PLENARY 7 MDS Stem Cells (and Aging) Christopher Y. Park, MD, PhD



PLENARY 2 Insights from Epigenomic Studies is MDS; Biological and Clinical Implications Maria E. Figueroa, MD



PLENARY 5 Myelodysplastic Syndromes (MDS) Microenvironment Wolf-Karsten Hofmann, MD



PLENARY 8 Epidemiology and Outcomes in MDS



PLENARY 3 Modeling Splicing Factor Mutations in MDS Matthew J. Walter, MD



PLENARY 6 Chronic Innate Immune Signaling in MDS Daniel Starczynowski, PhD

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**INTERVIEWS** 



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PLENARY 9 Inherited Predisposition to Myeloid Malignancies Lucy A. Godley, MD, PhD



Guillermo Garcia-Manero, MD Deferasirox in Iron Chelation Therapy for MDS

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Gail J. Roboz, MD Molecular Mutations in MDS

Amer Zeidan, MBBS, MHS Subsequent MDS in Prostate Cancer Patients After Radiotherapy

Amer Zeidan, MBBS, MHS

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**MDSF 2015** 



Sara M. Tinsley, MS, PhD, ARNP, AOCN Quality of Life in Patients with High-Risk MDS



Rami S. Komrokji, MD Risk Stratification of Therapy-Related MDS

Bart L. Scott, MD Connect MDS and AML: A Disease Registry



Guillermo Garcia-Manero, MD Rigosertib in Patients with High-Risk MDS After Failure of Hypomethylating Agents

### MDS 2015 SYMPOSIUM SPECIAL LECTURES

# MDS 2015 Was Proud to Present Two Special Lectures Held During The Symposium



## "AGING AND ILLNESS: COPING WITH THE DOUBLE WHAMMY" Dr. Jimmie Holland

Dr. Jimmie Holland – founder of the subspecialty psycho-oncology. Thanks to the work of Dr. Holland, and other proponents of psycho-oncology, cancer diagnosis and therapy are now better understood and more sensitively treated. Dr. Holland has devoted her career to helping patients, their families, and medical staff as they cope with the psychological burden of cancer and its treatment. *Copies of Dr. Holland's presentation are available upon request.* 



## "SISTERS STRONG"

### Ms. Sally-Ann Roberts

Sally-Ann Roberts is an anchorwoman for WWL-TV in New Orleans, Louisiana. She has been a member of the news team since 1977 and co-anchors the Eyewitness Morning News with Eric Paulsen. She is the sister and bone marrow donor of Robin Roberts, a co-anchor of ABC-TV's 'Good Morning America.' Ms. Sally-Ann Roberts has reported thousands of stories over the years but most enjoys reporting good news. Each week she profiles a volunteer in the community who is helping others under her 'Quiet Hero' report every Tuesday during the 5 p.m. newscast. She is also the author of three books, *Going Live...An Anchorwoman Reports Good News*, the novel *Angelvision*, and the very inspirational *Your Power is On. View Ms. Sally-Ann Roberts's presentation at http://www.mds-foundation.org/special-lecture-sisters-strong/.* 

### **13TH INTERNATIONAL ABSTRACTS**

# If you missed MDS 2015, not to worry...

All the abstracts have been compiled into one digital journal for you to learn and gain from the incredible work submitted. Was your abstract showcased at the symposium?

To view the MDS 2015 abstracts published in Elsevier's digital journal *Leukemia Research*, please access the link below.

*Leukemia Research* – Volume 39 – Supplement 1 – April 2015 can be viewed digitally at:

## http://lr-39-s1.elsevier.cc/files/assets/ basic-html/page-1.html



# POSTER PRESENTATIONS

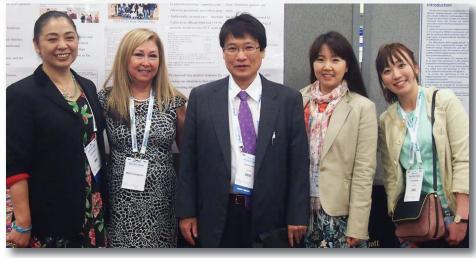
# Take a look at the posters that were displayed at MDS 2015











# RESEARCH

13TH INTERNATIONAL SYMPOSIUM ON MYELODYSPLASTIC SYNDROMES

# Congratulations TO OUR 2015 YOUNG INVESTIGATOR GRANT WINNERS



**Rose Ann Keam Young Investigator Award Winner** 

# Dechen Lin, PhD

Funded by: Dr. Jennifer Keam & Family

#### Grant Year: 2015-2017

Research Center: Cedars-Sinai Medical Center, UCLA School of Medicine, Los Angeles, CA USA

#### **Research Title:**

### Investigation of Aberrant mRNA Splicing Induced by ZRSR2 Mutation in the Pathogenesis of Myelodysplastic Syndromes Summary:

Myelodysplastic syndromes (MDS) are a heterogeneous group of clonal diseases marked by ineffective hematopoiesis with bone marrow (BM) hyperplasia and blood cytopenia. Molecular pathogenesis of MDS remains incompletely understood with limited therapeutic options. Our recent genomic investigations of MDS found that the ZRSR2 gene is mutated in 3-10% of MDS samples which impairs its normal function. Our experiments demonstrate that the ZRSR2 protein is required for RNA processing in the cells, and that ZRSR2 is important for hematopoietic differentiation. Our objective, using ZRSR2 as a focus, is to discover how aberrant RNA processing plays a role in the pathogenesis of MDS and to provide a mechanistic foundation for the development of therapies targeting the spliceosome machinery in MDS.



**MDS Foundation Young Investigator Award Winner** Petter Woll, PhD

Funded by: The MDS Foundation, Inc.

#### Grant Year: 2015-2017

Research Center: Karolinska Institute, Stockholm, Sweden

**Research Title:** 

### Unraveling the Role of Alternative Splicing in Normal and MDS Hematopoietic Stem and Progenitor Cells Summary:

Because of their short half-life, millions of mature blood cells are continuously replenished from a rare population of hematopoietic stem cells. Understanding the precise mechanisms involved in this process is of considerable relevance for human health and disease, as these regulatory stages frequently are hijacked in hematologic malignancies. More than 90% of human genes undergo alternative splicing, which can generate multiple isoforms with different functions from individual genes, adding further complexity to the regulation of gene function. Recent identification of recurrent mutations in genes involved in mRNA splicing in patients with hematopoietic malignancies, in particular in myelodysplastic syndromes, implicates alternative splicing as an important regulator of normal blood development and leukemic transformation. The proposed research program is focused on first characterizing the extent of alternative isoform usage during the earliest stages of normal blood differentiation, and how this impacts on the ability of rare hematopoietic stem cells to generate mature blood cells in both mouse and man. Secondly, the impact of mRNA splicing on blood development will be investigated by knocking out components of the mRNA splicing machinery. And finally, we will investigate the impact of recurrent mutations in the splicing machinery during distinct stages of blood development in order to understand how these mutations contribute to establish and propagate MDS disease. Importantly, this has translational importance, considering the high frequency of mutations targeted to the splicing machinery in hematologic malignancies, as well as in relationship to the need to develop more targeted therapies aimed at eliminating the propagating leukemic stem cells.

### 2015 TITO BASTIANELLO YOUNG INVESTIGATOR AWARDS



# Ashley Basiorka

Funded by: Tito Bastianello Young Investigator Award Grant Year: 2015 Research Center: Moffitt Cancer Center, Tampa, FL USA

#### **Research Title:**

Activation of Redox-Sensitive Inflammasomes Underlies the Biological Phenotype of Myelodysplastic Syndromes

**Statement:** To date, ineffective hematopoiesis in MDS has been attributed to high fractions of proliferating bone marrow progenitors with an increased propensity to undergo apoptotic cell death. Nevertheless, this non-inflammatory form of cell death cannot account for the inflammatory nature of these disorders. Our findings indicate that despite remarkable genetic heterogeneity, this and other key biological features of MDS are explained by the activation of the NLRP3 pattern recognition receptor by danger-associated molecular pattern (DAMP) signals such as S100A9, and ROS generated by NADPH oxidase in response to DAMP receptor activation and somatic gene mutations. NLRP3 activation culminates in the execution of the pyroptotic cell death cascade with elaboration of inflammatory cytokines such as interleukein-1 $\beta$  (IL-1 $\beta$ ) and IL-18, cation influx accompanied by cell swelling and activation of  $\beta$ -catenin supporting propogation of the MDS clone. Inhibition of NLRP3 inflammasome activation or S100A9 neutralization suppressed ROS generation, pyroptosis,  $\beta$ -cetenin activation and restored effective hematopoiesis. Our data illustrate that activation of the redox-sensitive NLRP3 inflammasome is a hallmark of lower-risk MDS, irrespective of molecular genotype. These findings have the capacity to transform our understanding of the pathobiology underlying MDS, and more importantly indicate that strategies that neutralize S100A9 or inhibit pyroptotic signaling offer therapeutic potential in these disorders.



# Dr. Eirini Papapetrou

**Funded by:** Tito Bastianello Young Investigator Award Grant Year: 2015 Research Center: Icahn School of Medicine at Mount Sinai, New York, NY USA

#### **Research Title:** Functional Dissection of Del(7q)-MDS with Patient-Derived Induced Pluripotent Stem Cells

**Statement:** Loss of the long arm of chromosome 7 (del7q) is a frequent karyotypic abnormality in MDS that is associated with poor prognosis and increased risk of progression to leukemia. Although this abnormality has been recognized since decades, we still do not understand the mechanism and the specific genes implicated. Large-scale chromosomal deletions are much harder to study than point mutations because a large number of genes are included in the deletion and modeling in the mouse is hampered by incomplete syntemy. To overcome these obstacles, we took advantage of cutting-edge stem cell and genome editing technologies to capture and reproduce chr7q deletions in human pluripotent stem cells. Specifically, we derived induced pluripotent stem cells (iPSCs) with del(7q) from bone marrow cells of MDS patients. In parallel, we engineered chr7q deletions of various lengths in normal iPSCs through chromosome engineering technologies. Thus we were able to show that the culprit is reduced gene dosage (haploinsufficiency) and to pinpoint candidate genes on chr7q. This study opened a new research avenue to understand the pathogenesis of del(7q)-MDS and provided a new platform for the study of MDS more generally. The technologies developed can be more broadly applied to the study of other disease-associated chromosomal deletions.

#### Broader Significance of the MDS-iPSC Model:

This study functionally dissected the genetic mechanism of MDS with chromosome 7q deletion (del7q) and pinpointed genes that may be critical to its pathogenesis. The first induced pluripotent stem cell (iPSC) lines from patients with MDS were derived and a new model for the study of MDS was established. This model can be used for basic research into the pathogenesis of MDS, as well as for translational studies to guide clinical decision-making. By connecting MDS genotypes with phenotypes, we can begin to understand the disease mechanisms and identify recurrently dysregulated pathways. This can in turn lead to predictions regarding drug responses, to new hypotheses for clinical translation and to identification of new therapeutic targets for drug development. These iPSC lines can also find use in drug screens to discover new compounds or repurpose existing ones, as well as in personalized medicine approaches.

### 2015 TITO BASTIANELLO YOUNG INVESTIGATOR AWARDS (continued)



# Dr. Rebekka Schneider-Kramann

Funded by: Tito Bastianello Young Investigator Award **Grant Year: 2015** 

Research Center: Brigham and Women's Hospital, Chestnut Hill, MA USA

#### Research Title: Terminal Erythroid Differentiation Defect and Activation of the Innate Immune System in Mice with Ribosomal **Protein S14 Haploinsufficiency**

Statement: We generated a novel mouse model with conditional knockout of Rps14, a gene linked to the characteristic anemia of del(5q) MDS. We found that Rps14 haploinsufficiency causes a p53-dependent erythroid differentiation defect resulting in progressive anemia and megakaryocyte dysplasia. We performed quantitative proteomics in purified erythroblasts in order to identify proteins affected by ribosomal haploinsufficiency. We identified significantly increased expression of proteins involved in innate immune signaling, in particular the S100A8/A9 protein complex. Recombinant S100A8 was sufficient to induce an erythroid differentiation defect in wild-type cells. We rescued the erythroid differentiation defect in Rps14 haploinsufficient HSCs by genetic inactivation of S100a8 expression using CRISPR/Cas9. Our data indicate an unexpected link between haploinsufficiency for a ribosomal gene, Rps14, activation of the innate immune system and inhibition of erythropoiesis. Inhibition of this process, potentially through pharmacologic targeting of \$100A8, could improve red blood cell production in del(5q) MDS. These findings underscore a molecular link between the genetic abnormalities in MDS patients, activation of the innate immune system, and ineffective hematopoiesis that characterizes the disease.



# Dr. Marcin Wlodarski

Funded by: **Grant Year: 2015** Tito Bastianello Young Investigator Award **Research Center:** University of Freiburg, Freiburg, Germany

#### Research Title: GATA2-Related Myelodysplastic Syndromes (MDS): Prevalence, Clinical Characteristics and Prognosis

**Statement:** The project deals with the identification of inherited causes of MDS. We identified GATA2-deficiency as the most common germline driver of primary MDS in childhood. It accounts for 15% of all of the cases with advanced disease, and shows very high prevalence in children with monosomy 7. Strikingly, >70% of all adolescents with monosomy 7 carry germline GATA2 mutations as a predisposing condition. The majority of GATA2 mutations in pediatric cohorts occur de novo, and generally this disease shows very high penetrance for hematologic and immunologic symptoms in children and young adults. From the clinical standpoint, the overall survival and outcome of stem cell transplantation is not negatively influenced by GATA2 mutations in pediatric MDS.



# Dr. Amer Zeidan

Funded by:

**Grant Year: 2015** Tito Bastianello Young Investigator Award Research Center; Yale Cancer Center, New Haven, CT USA

Research Title: Disease-Specific Costs of Care And Survival Among Medicare-Enrolled Patients With Myelodysplastic Syndromes (MDS) Statement: With the advent of effective but very expensive therapies, the costs of care for patients with cancer continue to rise and contribute significantly to the rapidly increasing costs of health care in the United States (USA). Additionally, substantial geographic variations in healthcare spending, including spending on cancer care, have been documented in the USA. Yet, little is known about regional variation in the cost of treating patients with myelodysplastic syndromes (MDS) and whether the costs of care for these patients correlate with survival. We therefore sought to evaluate the relationship between MDS-specific costs of care and survival outcomes among elderly Medicare-enrolled beneficiaries with MDS in the USA. A total of 8,564 patients diagnosed with MDS between 1/1/2005 and 12/31/2011 were identified from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Medicare database and were followed through death or end of study (12/31/2012). The two-year overall survival (OS) rate was 48.7%. The two-year MDS-specific costs per patient ranged between \$43,950 and \$83,961 across 12 states. In the multivariate models, two-year state-level MDS-specific costs were

2013-2015

#### 13TH INTERNATIONAL SYMPOSIUM ON MYELODYSPLASTIC SYNDROMES

### 2015 TITO BASTIANELLO YOUNG INVESTIGATOR AWARDS (continued)

not associated with survival (Reference: lowest tertile; hazards ratio [HR] for middle tertile, 1.02, 95% confidence interval [CI]: 0.93–1.12, *p*-value=0.74; and HR for highest tertile, 0.99, 95% CI: 0.92–1.06, *p*-value=0.73). These results indicate that Medicare expenditure on elderly MDS patients varied substantially across 12 states in the USA during the two years post-diagnosis. Notably, higher expenditures on MDS treatment did not translate into better survival even after adjustment for relevant variables. The lack of association between costs of care and survival warrants additional research as it may represent potential opportunities for cost-saving interventions without compromising patient outcomes.

#### AWARD RECIPIENTS: A FOLLOW-UP



# Chantana Polprasert, MD

Funded by: The MDS Foundation, Inc. Grant Year: 2013-2015 Research Center: The Cleveland Clinic Foundation, Cleveland, OH USA

#### **Research Title:** Splicing Defects Due to Loss of RNA Helicase Function: Novel Molecular Therapeutic Targets

**Summary:** We have identified a familial AML syndrome characterized by long latency and germline mutations in the gene coding for the DEAD-Box helicase DDX41 located on chr. 5q35. Recurrent somatic DDX41 mutations were identified in myeloid neoplasms; around 50% of cases in patients with germline mutations harbored somatic point mutations in the other allele. In addition to mutations, DDX41 locus was deleted in 26% of MDS cases with del(5q) and resulted in haploinsufficient expression. DDX41 defects led to loss of tumor suppressor function due to altered pre-mRNA splicing and RNA processing. Somatic mutations were also found in other RNA helicase genes, suggesting that they constitute a family of tumor suppressor genes in myeloid neoplasms.

**Program's Results to Date:** We performed Next generation sequencing and followed by deep targeted sequencing in 1,043 patients with myeloid neoplasms in our cohort. We identified 13 cases with novel, not previously described, recurrent somatic mutations in DEAD-Box helicase gene, DDX41. Subsequent analysis also revealed 17 cases with recurrent GL DDX41 mutation, which is frameshift insertion at position 140. Deletions of the long arm of chr.5 involving DDX41 locus, which is 5q35.3, were present in approximately 6% of all cases and resulted in decreased DDX41 mRNA levels.

Because of the discovery of the canonical GL mutation, we found some of them showing family history of leukemia, we identified 7 families characterized by germline (GL) mutations of DDX41. We also found DDX41 somatic mutations coinciding with GL mutations in biallelic fashion.

Median age at presentation for patients with DDX41 mutations is 68 year-old. We found that 50% of GL DDX41 mutationt AML harbors somatic DDX41 mutation and also 50% of somatic mutation harbors GL mutations. DDX41 mutations and deletions occurred more frequently in patients with advanced MDS and in AML. Overall, patients with either DDX41 mutations or deletions had inferior overall survival (OS). Interestingly, patients with DDX41 defects showed lenalidomide responsiveness.

DDX41 appears to be an essential gene, as the inactivating GL frameshift insertion mutation was not found among patients with del5q with DDX41 locus and no offspring of DDX41 knockout mice have been observed to date. To validate the results of in vitro studies, we performed xenograft experiments with cell lines in which DDX41 was knocked down and demonstrated accelerated tumor growth compared to control.

Involvement of RNA helicases in RNA splicing has been previously described. We performed proteomic study to further elucidate a role for DDX41 in the spliceosome. Among proteins which were co-precipitated with DDX41, spliceosomal protein is the top functional group associated with DDX41. Many of the spliceosomal protein complexes, including U1, U5, A complex interact with DDX41 strongly indicating that DDX41 is involved in spliceosomal function. Furthermore, we compared deep whole RNA sequencing in deletions, mutants and low expression of DDX41 versus WT cases. DDX41 defects were associated with more exon skipping and more exon retention in 61 and 95 genes, respectively. These results suggested that DDX41 interacts with spliceosomal protein complexes and results in missplicing pattern of specific downstream genes.

In summary, we discovered DDX41 as a novel TSG in myeloid malignancy. We found somatic missense mutations and deletions in DDX41 occur in myeloid neoplasms and are exemplary of other RNA helicases affected by mutations in leukemia. GL DDX41 mutations are associated with the development of hereditary MDS and AML with long disease latency. Germline DDX41 mutations can predispose to AML and promote acquisition of somatic DDX41 mutations in biallelic fashion. DDX41 expression is haploinsufficient in del(5q) involving DDX41 locus and additional 6% of diploid cases. DDX41 is a spliceosomal gene and the defects in this gene result in specific missplicing pattern.

# FROM THE FOUNDATION

#### MDS FOUNDATION INTERNATIONAL WORKING GROUP FOR PROGNOSIS IN MDS

## LATEST NEWS REGARDING THE MOLECULAR MUTATION PROJECT OF THE IWG-PM

#### Mutations Predict Prognosis Independent of the IPSS-R: Overview

The International Prognostic Scoring System (IPSS) and IPSS-R were developed by the International Working Group for Prognosis in MDS (IWG-PM) under the aegis of the MDS Foundation and have become the dominant clinical tools for predicting prognosis in patients with myelodysplastic syndromes (MDS).1 A prognostic scoring system that integrates gene mutations into the known critical clinical features would have great additive utility for improved determination of prognosis in patients with MDS and has the potential for widespread clinical use. The ongoing project of the IWG-PM Molecular Committee (IWG-PM-M) has shown, with the IPSS-R and other scoring systems, using larger molecularly characterized datasets, that mutations are independent predictors of patients' overall survival. This finding justifies a prognostic scoring system that will integrate clinical and genetic features.

#### Prognostic Impact of TP53 Mutations

A central aim of the IWG-PM Molecular project is to develop a large database of MDS patients with deep clinical annotation and genetic sequencing data for clinical, biologic and possibly therapeutic purposes. In addition to the analysis of previous samples, sequencing additional MDS cases will be performed to further develop the database.

As a first project for the IWG-PM molecular database, the impact of TP53 mutations in MDS demonstrated that this status divides MDS patients with complex karyotypes into distinct prognostic risk groups, with those carrying the mutation having poorer prognoses. Despite their strong associations with adverse clinical and cytogenetic abnormalities that are already incorporated into existing prognostic scoring systems, TP53 mutations carry significant independent prognostic value for decreased survival for



patients with MDS. This work was presented at the 2014 American Society of Hematology Meeting<sup>2</sup> with updating at the 2015 13th International MDS Foundation Symposium held in Washington, D.C.

#### **Recent Molecular Results**

Recently, molecular and clinical data on 3392 MDS patients gathered by members of the IWG-PM-Molecular Committee were combined and analysed and the abstract describing these findings was selected for an oral presentation at the upcoming ASH Annual Meeting in Orlando.<sup>3</sup> Survival data were available for 3200 patients. The 27 genes sequenced in at least half of the cohort and mutated in >1.5% of samples were included for analysis. Mutations in 12 genes were strongly associated with shorter overall survival in univariate analyses. The large size of the cohort allowed for more precise estimates of survival in the less frequently mutated genes. IPSS-R risk groups could be determined for 2173 patients and were strongly associated with survival. Adjusting the hazard ratio of death for IPSS-R risk groups identified several mutated genes with independent prognostic significance. Patients without mutations in any of the major adverse genes represented over half of the fully sequenced cohort and had a longer median survival than patients with adverse mutations even after correction for IPSS-R risk groups. A mutation score based on survival risk will be proposed and internally validated. The impact of somatic mutations in patients traditionally considered lower risk will also be explored.

# Current Project Status, Plans for Sequencing of New Samples

In addition to the above assessment of previous samples, the project will sequence additional large numbers of MDS cases to further develop our database and mutational evaluations. An automated sample manage-



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ment system was recently implemented that links sample reception to library preparation and sequencing submission. The results of these analyses will serve as the template with which to build an integrated molecular risk model for MDS.

- Greenberg PL, Tuechler H, Schanz J, et al. Revised international prognostic scoring system for myelodysplastic syndromes. *Blood*. 2012;120: 2454-2465.
- 2.Bejar R, Papaemmanuil E, Haferlach T, Garcia-Manero G, Maciejewski JP, Sekeres MA, Walter MJ, Graubert TA, Cazzola M, Malcovati L, Campbell PJ, Ogawa S, Boultwood J, Bowen D, Tauro S, Groves M, Fontenay M, Shih L-Y, Tuechler H, Stevenson D, Neuberg D, Greenberg PL, Ebert BL. TP53 Mutation Status Divides MDS Patients with Complex Karyotypes into Distinct Prognosic Risk Groups: Analysis of Combined Datasets from the IWG-PM-Molecular Prognosis Committee. Proc Am Soc Hematology, San Francisco, December, 2014, abstract. *Blood.* 2014; 124 (21):#532.
- 3.Bejar R, Papaemmanuil E, Haferlach T, Garcia-Manero G, Maciejewski JP, Sekeres MA, Walter MJ, Graubert TA, Cazzola M, Malcovati L, Campbell PJ, Ogawa S, Fenaux P, Hellstrom-Lindberg, Kern W, Boultwood J, Pellagatti A, Bowen D, Tauro S, Groves M, Vyas P, Quek L, Nazha A, Thol F, Heuser M, Shih L-Y, Padron E, Sallman D, Komrojki R, List A, Santini V, Fontenay M, Campbell P, Tuechler H, Stevenson D, Neuberg D, Greenberg P, Ebert BL. Somatic Mutations in MDS Patients Are Associated with Clinical Features and Predict Prognosis Independent of the IPSS-R: Analysis of Combined Datasets from the IWG-PM-Molecular Committee, ASH 2015 abstract, Orlando, December 2015.

This global project is being coordinated by Ben Ebert and Peter Greenberg (co-Chairs), Rafael Bejar and Ellie Papaemmanuil, with statistical support by Donna Neuberg, Kristin Stevenson and Heinz Tuechler.

#### THE AMERICAN SOCIETY OF HEMATOLOGY 57TH ANNUAL MEETING & EXPOSITION • DECEMBER 2015

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On behalf of the MDS Foundation and our Board of Directors, please join us for our upcoming Satellite Symposium:

#### BREAKFAST SYMPOSIUM

# New Insights into the Pathogenesis and Treatment of MDS

### Friday, December 4, 2015 7:00-11:00 am

#### Hyatt Regency Orlando Orlando, Florida

*This is a Friday Satellite Symposium preceding the 57th ASH Annual Meeting.* 

### **TARGET AUDIENCE**

This activity is intended for physicians, oncology nurses, nurse practitioners, physician assistants, pharmacists and other health care professionals interested in the treatment and management of patients with Myelodysplastic Syndromes.

#### LEARNING OBJECTIVES

Upon completion of this course, the participant will be better able to:

- Describe molecular and biologic features which are useful for classifying MDS and aiding in therapeutic decisionmaking
- Describe some newer condition regimens available and their selections for MDS patients
- Describe alternative treatment approaches for patients whose disease has failed to respond to first line therapy
- Describe the differences in molecular findings and treatment options for CMML

VISIT THE MDS FOUNDATION BOOTH: #**1921** 

### FACULTY

#### Theo J.M. de Witte, MD, PhD

Professor of Hematology Radboud University Medical Center Radboud Institute of Molecular Life Sciences Nijmegen, The Netherlands

#### Pierre Fenaux, MD, PhD

Professor of Hematology Hôpital Saint Louis Paris VII University Paris, France

#### Guillermo Garcia-Manero, MD

Professor of Medicine Chief, Section of Myelodysplastic Syndromes Department of Leukemia, Division of Cancer Medicine The University of Texas MD Anderson Cancer Center Houston, Texas

Elli Papaemmanuil, PhD Assistant Member Epidemiology and Biostatistics Center of Molecular Oncology Memorial Sloan Kettering New York City, New York

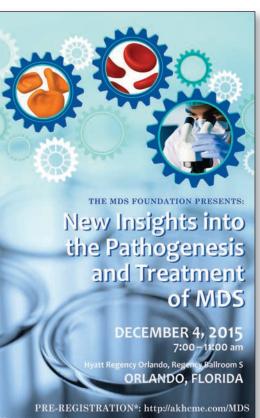
Irving L. Weissman, MD Stanford University School of Medicine Director, Institute for Stem Cell Biology and Regenerative Medicine Director, Stanford Ludwig Center for Cancer Stem Cell Research and Medicine

Professor of Pathology and Developmental Biology Stanford, California

#### **AGENDA**

7:30 am – 7:40 am **Program Overview and Objectives** *Stephen Nimer, MD* 

7:40 am – 8:15 am Molecular Landscape of MDS and Its Clinical Implications Elli Papaemmanuil, PhD



\*Pre-registration does not guarantee admission—please arrive early.

This is a Friday Satellite Symposium preceding the 57th ASH Annual Meeting.

8:15 am – 8:50 am Pathogenetic Features of Hematopoiesis in MDS: Focus on Aging Irving Weissman, MD

8:50 am – 9:25 am **CMML: From Biology to Treatment** *Pierre Fenaux, MD, PhD* 

9:25 am – 10:00 am **Therapeutic Options After First Line Treatment Failure** *Guillermo Garcia-Manero, MD* 

10:00 am – 10:35 am Allogeneic Hematopoietic Stem Cell Transplantation in MDS: ELN/US Recommendations Theo J.M. de Witte, MD, PhD

10:35 am - 11:00 am Questions/Answers/Discussion

#### MDS FOUNDATION DEVELOPMENT COMMITTEE

# Announcing the MDSF Development Committee



### Meet... John Bennett, MD

Founding Member and First Chairman of the MDS Foundation. Current Board Member. Dr. Bennett assists by guiding the work of the Development Committee and acts as a liaison between the Committee and the MDS Foundation Board of Directors.



### *Meet...* Jennifer Keam, MD

Jennifer is a physician (radiation oncologist). Jennifer and her husband have committed to funding a grant in support of Young Investigators researching the disease in honor of her mother, Rose Ann Keam, who passed of MDS (see page 7).



*Meet...* Rudy Luna

Rudy wrote the story and directed the film, "My First Miracle" to be aired in January of 2016. Rudy's father passed of MDS. A portion of the film's proceeds will be donated to MDSF (see page 52).



### *Meet...* Sandra Madden

Author and widow of David Madden, actor (*The Partridge Family* cast), who passed of MDS. Sandra has recently completed a new book entitled, REUBEN KINCAID *Remembered...* which will include a

### **MISSION STATEMENT:**

The newly formed Development Committee provides the Foundation with guidance, counsel, and assistance in the implementation of financial development and disease awareness strategies.

chapter on MDS and mention the Foundation. Proceeds to go to MDSF (see page 24).



### *Meet...* Julia McGuire

Julia has a personal connection with the MDS disease and is an Executive Vice President with Campbell & Company, a fundraising and communications organization based in Chicago. Julia has 25 years of fundraising/development experience with not-for-profit organizations, 15 of those in consulting. She has been involved in campaigns ranging from \$1 million to \$300 million dollars. Julia has offered to share her insight and guidance with the Development Committee.



### Meet... Nancy Nussbaum

Published "Annie's Sweet

Tooth" a cookbook in honor of her sister who passed of MDS – all proceeds donated to MDSF. A second cookbook will be coming in 2016 (see page 24).



### Meet... Rochelle Ostroff-Weinberg

Widow of former MDS Foundation Board member, Bob Weinberg, who passed from MDS. Coordinates MDS Family Coping and Caring Luncheons three times per year (see page 25).



# *Meet...* Paul Wenzel

Has held 8 annual Karen A. Wenzel Memorial Golf Tournaments in honor of his mother who passed from MDS – all proceeds donated to MDSF (see page 22).

#### MDSF INTERNATIONAL BOARD OF DIRECTORS

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# **IN YOUR OWN WORDS**

"My grandfather just got diagnosed with MDS. Your website was a godsend and I will be donating to the foundation." *Misty K.* 

# "Thank you ever so much for all the information.

My sister said she had a wonderful conversation over the phone; am happy to have made a connection as we want to be proactive in our approach. I would appreciate all the information sent to me, also be sent to my sister as I am finding this to be very informative. Thank you!"

Sue R.

#### TESTIMONIALS

"You all have been SO helpful with my new role here! I can't thank you enough...perhaps we can get these MDS patients some peace with all of the information and treatment they go through. Again, thank you." *Ella-Mae S.* 

### "So impressed with the online version of the 'Building Blocks of Hope' that I would like a hard copy.

I need to study this material in detail. THANK YOU very much." *Marion R.* 

"Thanks so much for allowing me to read about my condition...I was diagnosed in August 2012...please send me all of the books." Sandy S. "Thank you for such an excellent resource that has helped our family." *Carl N.* 

"Very good website, just diagnosed with MDS." John R.

"I really am thankful for your foundation. I really want to learn as much as I can about MDS to better help my best friend through this time." *Emily A.* 



# **\*\*NEW\*\* TRANSLATED PATIENT RESOURCES ARE HERE!**

The MDS Foundation is excited to be able to offer our patient and caregiver resources in several languages!!! Please use the links below to access these translations.



### WHAT DOES MY BONE MARROW DO?

This booklet gives patients and caregivers general information on bone marrow function and how it is affected by MDS.

### http://www.mds-foundation.org/bone-marrow-handbook

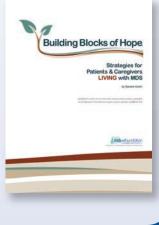
\*Available in Chinese, Danish, Dutch, German, Italian, Portuguese, Russian, Spanish and Turkish. Translations in Armenian and French coming soon!

### **BUILDING BLOCKS OF HOPE**

This comprehensive resource contains information on MDS, available treatments and iron overload. It also gives MDS patients and their caregivers tools to take an active part in their MDS journey. Access this link to view an online version of the handbook, download a complete PDF of the handbook; and to view additional international versions of the handbook.

### http://www.mds-foundation.org/bboh/#International-Handbooks

\*Available in Canadian English, Canadian French, Chinese, French, German, and Turkish. Current translations in process: Armenian, Australian, Danish, Dutch, Japanese, and Spanish.



# **MDS** RESOURCES

## Highlights of Latest Literature in MDS

#### Suneel D. Mundle, PhD Rhea Mundle

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

#### EPIDEMIOLOGY, DIAGNOSIS AND PROGNOSIS:

 Cogle CR. Incidence and burden of the myelodysplastic syndromes. *Curr Hematol Malig Rep.* 2015;10(3):272–281 (http://www.ncbi.nlm. nih.gov/pubmed/26134527)

The review compared the US population based registry estimates of MDS incidence vs. those seen with the searches conducted on electronic pathology reports or other novel case capture methods and demonstrated that the population based registries may underestimate the incidence. The medicare billing claims data review estimated MDS prevalence at 60,000–170,000 in the USA with a projection to grow in future. A cost burden of MDS related transfusions estimated as a 3-year mean was at \$88,824 for those who needed transfusion vs. \$29,519 for the non-transfused MDS cases.

 Loghavi S et al. TP53 overexpression is an independent adverse prognostic factor in de novo myelodysplastic syndromes with fibrosis. *Br J Hematol.* 2015;171(1):91–99 (http://www.ncbi. nlm.nih.gov/pubmed/26123119)

Sixty-seven cases of de novo MDS with moderate to severe reticulin fibrosis (MDS-F) were the subject of this investigation. TP53 overexpression was assessed by dual color CD34/TP53 immuno-histochemistry. TP53 mutations assayed with next generation- or Sanger- sequencing methods showed mutations in approximately 47% cases. TP53 overexpression correlated with TP53 mutations, blast count, abnormal cytogenetics and high/very-high IPSS-R groups. In a multivariate analysis, TP53 expression independently predicted shorter survival ( $p \le 0.001$ ) and particularly in CD34+ cells, was associated with shorter overall and leukemia-free survival.

- 3. Belli CB et al. Myelodysplastic syndromes in South America: A multinational study of 1080 patients. Am J Hematol. 2015;90(10):851-858 (http://www.ncbi. nlm. nih.gov/pubmed/26104573) A first epidemiological study from South America retrospectively compared MDS patients, primarily from three countries, Argentina (n=635), Brazil (n=345) and Chile (n=100). Chilean cohort showed higher preponderance of younger patients with higher F/M ratio, while Brazilian group had higher incidence of RARS category. As compared to Argentinian series, both Brazilian and Chilean patients had significantly lower Hb levels. The overall survival was significantly lower in Chilean patients (35 mo, p=0.03), as compared to Argentinian (56 mo) or Brazilian (55 mo) patients.
- Fega KR et al. Non-hematologic predictors of mortality improve the prognostic value of the international prognostic scoring system for MDS in older adults. J Geriatr Oncol. 2015;6(4):288–298 (http://www.ncbi. nlm. nih.gov/pubmed/26073533)

A single institution retrospective study of 114 consecutive MDS patients with  $\geq$ 65 years of age between 2006–2011 who had quality of life assessment at baseline showed an 'ease of taking long walks' as one of the significant predictors of mortality (HR=0.44) in a multivariate analysis among the other clinical predictors including serum albumin, therapy related MDS and IPSS score.

- 5. Efficace F. Prognostic value of self-reported fatigue on overall survival in patients with myelodysplastic syndromes: a multicentre, prospective, observational, cohort study. Lancet Oncol. 2015 Set 21 [Epub ahead of print] (http://www.ncbi.nlm.nih.gov/pubmed/26404501) This study aimed to assess if self-reported fatigue severity can help predict survival for MDS. Adult patients from 37 centers in Europe, USA and East Asia with intermediate-2/high-risk MDS were asked to complete a quality of life assessment, indicating their fatigue score using EORTC questionnaire-core 30. Between Nov 10, 2008 and Aug 13, 2012, 280 patients (median age 71 yrs) had median overall survival from diagnosis of 17 months. In analysis, overall survival was associated with higher self-reported fatigue score among the other predictors like increasing age, transfusion dependency,  $\geq 2$  ECOG performance status, increased WBC count, high-risk IPSS score.
- 6. de Swart et al. Validation of the revised International Prognostic Scoring System (IPSS-R) in patients with lower-risk myelodysplastic syndromes: a report from the prospective European LeukemiaNet MDS (EUMDS) registry. Br J Haematol. 2015;170(3):372–783 (http:// www.ncbi.nlm.nih.gov/pubmed/25907546)

This report described baseline characteristics, disease management and outcome of 1000 EUMDS registry based lower-risk MDS patients. The assessment identified low/very low (n=247) or high/very high (n=32) risk patients within intermediate-1 category. The revised IPSS scoring (IPSS-R) was superior to IPSS in both predicting disease progression and survival. The distribution of supportive care (transfusion/growth factors/ iron) vs. monitoring within 2 years of diagnosis was 70:30.

7. Koenecke C et al. Impact of the revised International Prognostic Scoring System, cytogenetics and monosomal karyotype on outcome after allogeneic stem cell transplantation for myelodysplastic syndromes and secondary acute myeloid leukemia evolving from myelodysplastic syndromes: A retrospective multi-center study of the European Society of Blood and Marrow Transplantation. Hematologica. 2015; 100(3):400-408 (http://www.ncbi.nlm.nih.gov/pubmed/25552702) Among the total of 903 patients classified in 5 risk groups of IPSS-cytogenetic classification, poor and very poor categories had an independent impact on shorter relapse free and overall survival compared to very good, good and intermediate categories. The study thus provided an important validation for the revised five-group classification.

#### **TREATMENT:**

#### **Demethylating Agents:**

1. Narayan R et al. Sequential azacitidine plus lenalidomide in previously treated elderly patients with acute myeloid leukemia and higher risk myelodysplastic syndromes. *Leuk Lymphoma*. 2015 Sept 16 [Epub ahead of print] (http://www.ncbi. nlm.nih.gov/pubmed/26374199) A phase II study with elderly AML/MDS patients who had previous exposure to a hypomethylating agent and/or immunomodulatory agent, assessed treatment with azacitidine at 75 mg/m2 SQ/IV daily for day 1–7 and with lenalidomide at 50 mg PO daily on day 8–28 for a median of 2 cycles. In 32 evaluable patients overall response rate was 25% with overall survival of 9.8 months in responders vs. 4 months in non-responders (p=0.016). Neutropenic fever was the major adverse event.

 Papageorgiou SG et al. Treatment with 5azacytidine improves clinical outcome in high-risk MDS patients in the real-life setting: A single center observational study. *Hematology*. 2015 Jul 28 [Epub ahead of print] (http://www.ncbi. nlm.nih.gov/pubmed/26218077)

A retrospective study evaluated 56 high-risk MDS patients who received 5-AZA between 2005–2013 in an outpatient clinic at 75 mg/m2 sc, 7 total doses (5 week days on, 2 weekend days off, 2 week days on). The results showed overall response rate of 50% with CR in 21.2%, PR 3.8%, HI 25% and stable disease in 34.6%. The estimated event free and overall survival were at 11 mo and 17 mo respectively. Survival was especially improved in responding patients.

 Ye XN et al. Epigenetic priming with decitabine followed by low-dose idarubicin/cytarabine has an increased anti-leukemic effect compared to traditional chemotherapy in high-risk myeloid neoplasms. *Leuk Lymphoma*. 2015 Sept 15. [Epub ahead of print] (http://www.ncbi.nlm.nih.gov/ pubmed/26372888)

A sequential combination of decitabine 20 mg/ $m^2/day$  on day 1–3 followed by Idarubicin 3 mg/ $m^2/day$  on day 5–7, with cytarabine 30 mg/ $m^2/day$  on day 7–14, was administered to 30 patients with high-risk MDS or AML evolved from MDS, or relapsed/refractory AML. The significantly high complete remission rate of approximately 67% was postulated to be indicative of a priming effect of decitabine on conventional chemotherapy.

#### IMiDs:

 Zeidan AM et al. Lenalidomide treatment for lower risk nondeletion 5q myelodysplastic syndromes patients yields higher response rates when used before azacitidine. *Clin Lymphoma Myeloma Leuk*. 2015 Sept 2 [Epub ahead of print] (http://www. ncbi.nlm.nih.gov/pubmed/26440749)

In a study of 63 low-risk MDS patients without 5q deletion, subsequent to ESA failure, a significantly higher Hematopoietic Improvement in Erythroid lineage (HI-E) was found when lenalidomide was administered before vs. after azacytidine (38% vs. 12%, p=0.04). No additional benefit in terms of leukemic transformation or overall survival was noted with a specific sequence of the two agents.

2. Beier F et al. Telomere dynamics in patients with del (5q) MDS before and under treatment with lenalidomide. Leuk Res. 2015 Sept 21 [Epub ahead of print] (http://www.ncbi.nlm.nih.gov/pubmed/26427727) Telomere length (TL) dynamics were assessed in 5q del MDS patients enrolled in the LEMON-5 study. Compared to age-matched healthy controls, the peripheral blood and/or bone marrow hematopoietic cells from patients showed significant loss of TL, which correlated with the duration of disease from diagnosis and extent of cytopenias. With respect to a corresponding baseline TL, following 6 months of lenalidomide treatment and attaining cytogenetic response, a significant recovery of TL was noted indicative of a shift toward normalization of hematopoiesis.

- 3. Weiss L et al. Real-world analysis of the Celgene Global Drug Safety database: Early discontinuation of lenalidomide in patients with myelodysplastic syndromes due to non-serious rash. Ther Clin Risk Manag. 2015;11:1355-1360 (http://www.ncbi.nlm.nih.gov/pubmed/26379438) The study examined rash in MDS patients treated with lenalidomide in real-world as documented in the Celgene Global Drug Safety database in comparison with MDS-003/004 clinical trials. Most rash adverse events were non-serious (CGDSD, 91%) or grade 1/2 (MDS-003/004, 87%-93%). Rash occurring at a median of 9 days after treatment initiation was the leading cause of permanent discontinuation of lenalidomide within 2 two cycles in 72% patients in the real world. In contrast, only 2-3% rash adverse events led to treatment discontinuation in MDS-003/004 trials.
- Tinsley SM, Kurtin SE and Ridgeway JA. Practical management of lenalidomide-related rash. *Clin Lymphoma Myeloma, Leuk.* 2015 June 15 Suppl: S64–S69 (http://www.ncbi.nlm.nih.gov/pubmed/ 26297281)

The registration clinical trial toxicity profile of lenalidomide across all indications noted most common adverse events of hematologic nature with grade 3 or more events as a reason for drug discontinuation. However, in the postmarketing setting an analysis of the Celgene Global Drug Safety database brought to light a non-serious rash as the leading cause of permanent drug discontinuation. The rarity of  $\geq$ grade 3 rash in registration trial may highlight differences in the management of rash in the real world. The rash observed was mild to moderate presenting as patchy, raised, macular skin lesions or sometimes as localized urticaria, which might be associated with pruritus.

#### Hematopoietic Stem Cell Transplantation:

 Sandhu KS et al. Umbilical cord blood transplantation outcomes in acute myelogenous leukemia/ myelodysplastic syndromes patients ≥70 years old. *Biol Blood Marrow Transplant*. 2015 Sept. 25 [Epub ahead of print] (http://www.ncbi. nlm.nih.gov/pubmed/26415559)

In a four year period within single institute, of the 70 total transplant patients with  $\geq$ 70 years of age, 10 patients received umbilical cord blood (UCB) transplant. In these UCB patients, at 2 years, non-relapse mortality (20%), relapse (30%), disease free survival (50%) and overall survival (60%), were similar to those in another series of 60–69 years old patients indicating the feasibility of UCB transplant in  $\geq$ 70 years old.

 Guièze R et al. Management of myelodysplastic syndromes relapsing after allogeneic hematopoietic stem cell transplantation: A study by the French Society of Bone Marrow Transplantation and Cell Therapies. *Biol Blood Marrow Transplant*. 2015 Aug 6. [Epub ahead of print] (http://www.ncbi. nlm.nih.gov/pubmed/26256942)

One hundred forty seven consecutive patients relapsing after allogeneic HSCT for MDS were studied. The post-transplant treatments included immunotherapy (2nd transplant or donor lymphocyte infusion, n=62) or cytoreductive treatment (n=39) or palliative/supportive care (n=46) with 2 year survival rates of 32%, 6% and 2% respectively in these three groups (p<0.001 for immunotherapy).

 Robin M et al. Comparison of unrelated cord blood and peripheral blood stem cell transplantation in adults with myelodysplastic syndromes after reduced-intensity conditioning regimen: a collaborative study from Eurocord (Cord blood Committee of Cellular Therapy & Immunobiology Working Party of EBMT) and Chronic Malignancies Working Party. *Biol Blood Marrow Transplant*. 2015;21(3):489–495 (http://www.ncbi. nlm.nih.gov/pubmed/25529382)

In a large series of high-risk MDS patients (n=631), post reduced-intensity conditioning, mobilized peripheral blood stem cells (n=502) from unrelated donor as compared to umbilical cord blood transplant (n=129) showed superior neutrophil engraftment (98% vs. 78%, p<0.001), lower 2 year non-relapse mortality (31% vs. 42%, p=0.03), better overall survival (49% vs. 30%, p<0.001) and Disease free survival (44% vs. 28%, p<0.001). The report suggested 10/10 HLA matched unrelated donor as an alternative when matched sibling is unavailable.

#### Biosimilars

- 1. Danylesko I et al. Biosimilar filgrastim (Tevagrastim, XMO2) for allogeneic hematopoietic stem cell mobilization and transplantation in patients with acute myelogenous leukemia/ myelodysplastic syndromes. Biol Blood Marrow Transplant. Sept 4. [Epub ahead of print] (http://www.ncbi.nlm.nih.gov/pubmed/26343949) A prospective study with HLA-matched healthy sibling donors of 24 AML/MDS patients evaluated a biosimilar human GCSF, Tevagrastim, in comparison with a historical control of sibling donors treated with filgrastim (Neupogen). Mobilization of CD34+ hematopoietic stem cells in peripheral blood was assessed with a 10  $\mu$ g/kg sc dose for 4 days. The yield of CD34+ stem cell mobilization in healthy donors and engraftment in corresponding patients included in tevagrastim group were comparable to the filgrastim historical controls. No new safety signal was noted with tevagrastim.
- 2. Giordano G et al. Biosimilar epoetin  $\alpha$  is as effective as originator epoetin  $\alpha$  plus liposomal iron (Sideral®), vitamin B<sub>12</sub> and folates in patients with refractory anemia: A retrospective real-life approach. Mol Clin Oncol. 2015;3(4):781-784. In a retrospective study, 92 MDS patients were treated between 2008–2012, with 40,000 IU weekly sc of a biosimilar epoetin a currently approved in Europe, HX575 (n=46) or established original epoetin a.(n=46). Adequate iron, vitamin B12 and folate support was provided. The study showed comparable results between the biosimilar and original epoetin groups with respect to time for 1g/dL increase in serum hemoglobin (4 vs 5 weeks), time to attain 12 g/dL serum hemoglobin (10.5 vs 12 weeks), transfusions required (7 vs 5 patients) and median cost of therapy (1354 vs 1536 Euros/mo).

#### Novel Agents:

 Jilg S et al. Blockade of BCL-2 proteins efficiently induces apoptosis in progenitor cells of high-risk myelodysplastic syndromes patients. *Leukemia*. 2015 Jul 8 [Epub ahead of print] (http://www. ncbi.nlm.nih.gov/pubmed/26153654)

Bone marrow mononuclear cells from primary samples of 124 MDS or secondary AML patients and 57 age-matched healthy volunteers were subjected to a treatment with anti-BCL2 agents ABT-737 or ABT-199. The drug sensitivity read as reduction in CD34+ cell number or colony forming capacity, could be demonstrated in high-risk/sAML samples, whereas the low-risk MDS or healthy donor samples remained unaffected.

#### **PATHOBIOLOGY:**

 Ganster C et al. New data shed light on Y-lossrelated pathogenesis in myelodysplastic syndromes. *Genes Chromosomes Cancer*. 2015 Sept 23 [Epub ahead of print](http://www.ncbi.nlm.nih.gov/pubmed/26394808)

The significance of Loss of Y-chromosome (LOY) in MDS was tested by determining the percentage of LOY in clonal CD34+ peripheral blood cells in comparison to normal CD3+ T-cells of 27 MDS patients using FISH analysis. The results were compared to those of 32 elderly men without hematologic diseases and 25 young blood donors. LOY was found in CD3+ cells of 5.8% of elderly MDS patients and 2.5% elderly men without hematologic diseases. In contrast LOY was significantly higher in CD34+ cells of the MDS patients versus the elderly men without hematologic disease (43.3% vs. 13.2%, p=0.005) indicating that LOY has age related basis but is also associated with MDS.

 Malcovati L et al. SF3B1 mutation identifies a distinct subset of myelodysplastic syndromes with ringsideroblasts. *Blood*. 2015;126(2):233–241 (http://www. ncbi.nlm.nih.gov/pubmed/25957392)

A mutation analysis in relation to disease characteristics and patient outcome was performed on 293 patients with myeloid neoplasm with  $\geq 1\%$  ring sideroblasts. Particularly, SF3B1 mutation was evident in 81% of RARS/RCMD-RS. A multivariate analysis showed lower cumulative incidence of disease progression (p=0.018) and better overall survival (p=0.003). A co-existing mutation in DNA methylation gene was correlated to multilineage dysplasia in SB3F1 mutated patients without any further impact on patient outcome.

#### **REVIEWS, PERSPECTIVES & GUIDELINES**

The following articles provide significant review of literature and/or innovative perspective on the state-ofthe-art in MDS or discuss therapeutic management guidelines and identify need for additional prospective studies.

- Mughal TI et al. An international MDS/MPN working group's perspective and recommendations on molecular pathogenesis, diagnosis and clinical characterization of myelodysplastic/myeloproliferative neoplasms. *Haematologica*. 2015;100(9):1117–1130 (http://www.ncbi.nlm.nih.gov/pubmed/ 26341525)
- Komrokji RS. Treatment of higher-risk myelodysplastic syndromes after failure of hypomethylating agents. *Clin Lymphoma Myeloma Leuk*. 2015 June 15 Suppl: S56–S59 (http://www. ncbi.nlm.nih.gov/pubmed/26297279)
- Greenberg PL. Synergistic interactions of molecular and clinical advances for characterizing the myelodysplastic syndromes. *J Natl Compr Netw.* 2015;13(7):829–832 (http://www.ncbi.nlm. nih.gov/pubmed/26150576)
- Steensma DP. Myelodysplastic Syndromes: Diagnosis and Treatment. Mayo Clin Proc. 2015; 90(7):969–983 (http://www.ncbi.nlm.nih.gov/ pubmed/26141335)
- Deeg J. Treatment ethics, quality of life and health economics in the management of hematopoietic malignancies in older patients. *Bone Marrow Transplant.* 2015;50(9):1145–1149 (http://www. ncbi.nlm.nih.gov/pubmed/26052908)
- 6. Jonas BA and Greenberg PL. MDS Prognostic Scoring Systems – Past, Present and Future. In *Best Practice & Research*, Clinical Haematology, Editorin-Chief: M. Tallman, Virginia Klimek, Elsevier, Inc: Myelodysplastic syndrome. Vol 28(1):3–13, 2015 (http://www.ncbi.nlm.nih.gov/pubmed/25659725)

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

# **INTERNATIONAL MDS FOUNDATION NURSE LEADERSHIP BOARD**



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# Meet the MDS Health Experts



INTRODUCING...

Natalie Singer, MSc, BSc, SPQ-Cancer Care

Natalie Singer



West of Scotland Cancer Centre Glasgow, Scotland

Medical Specialty: SPQ-Cancer Care, Macmillan Hematology CNS

What led you to the nursing field? When I was a little girl nursing was always my dream job. Initially, I wished to be a ward sister but with the emergence of the Clinical Nurse Specialist role that took my interest instead.

What interested you in hematology/myelodysplastic syndromes in general? The field of Hematology Nursing is one that offers variety and many challenges. In particular, myelodysplastic syndromes bridge a large age range and recently with the emergence of new and exciting treatments it is no longer 'the silent disease'. What is the most gratifying part of your job? Meeting patients and establishing a relationship at a time in their lives when they can be most vulnerable and the ability to make the 'journey easier'



## INTRODUCING...

#### Barbara A. Rodgers, RN, BSN, OCN

Barbara Rodgers

Excellence: Spattle Capper Care Alliance, Spattle WA

MDS Center of Excellence: Seattle Cancer Care Alliance, Seattle, WA

Medical Specialty: Nursing Hematology

Medical School: AA degree at Olympic College and BSN at Chamberlain School of Nursing

**What led you to the nursing field?** I'm a caregiver at heart – I spent 20 years caring for my family and managing a home day care. The nursing field was a natural progression of those nurturing roles.

What interested you in hematology/myelodysplastic syndromes in general? I enjoyed the challenge of caring for patients with a hematology disease and learning new treatment options.

What is the most gratifying part of your job? I enjoy meeting new patients and their families and developing those long-term relationships. In addition, I enjoy learning from Drs. Joachim Deeg and Bart Scott.



#### Catherine Vassili, RN, MN (Nurse Practitioner), INTRODUCING... Grad Cert (Cancer Nursing)

Catherine Vassili



MDS Center of Excellence: Peter MacCallum Cancer Centre, Melbourne, Australia

Nursing Specialty: Haematology/Oncology

Nursing School: Australia Catholic University, Melbourne University, La Trobe University

Nursing Specialty: Leukaemia/MDS/MPN and Nurse Practitioner Candidate at the Peter MacCallum Cancer Centre

Board Certification: Registered Nurse

What led you to the nursing field? I have always had a keen interest in health sciences and I enjoy caring for people. There are also many different career opportunities within the nursing field so it was an ideal career path for me.

What interested you in hematology/myelodysplastic syndromes in general? Haematology is such a fascinating, diverse and dynamic area of health care. Our understanding of these malignancies and management options are continually evolving which makes it an exciting field to be a part of.

What is the most gratifying part of your job? The therapeutic relationships I have had the privilege of developing with our patients and their loved ones. Working within a team that strives to optimise patient care.

(Continued)

# Sexuality Among Older Adults With MDS

Corien Eeltink, RN, MA, ANP Clinical Nurse Specialist VU University Medical Center Amsterdam, The Netherlands MDS Nurse Leadership Board

#### Introduction

Sexuality and the desire for intimacy are essential and important Quality of Life issues from birth until death. Sexuality has its own meaning to each individual, also to older adults. Sexuality may include touching, caressing, fantasy, masturbation, physical closeness, and the warmth created by emotionality.

Sexual difficulties are quite common. About 40–45% of adult women and 20–30% of adult men have at least one sexual dysfunction. The most frequent problems among women are low sexual desire, vaginal dryness, and inability to climax. Among men, erectile difficulties are most common.

Decreases in general health status seems to be a risk factor for developing a sexual dysfunction. Other common risk factors are the presence of chronic diseases like diabetes mellitus or cardiovascular disease, psychiatric or psychological disorders, and having no sexual partner. Sexual problems are very common during and after cancer treatment. Aging seems to be an important risk factor for developing a sexual dysfunction, mainly because there is an increasing risk of chronic diseases or use of medications as one gets older.

Medical doctors and nurses find sexuality difficult to talk about. Meanwhile, also older patients struggle with assumptions preventing communicating sexual issues. As a result, patients probably receive little or no assistance in dealing with the effects of cancer and its treatment on sexuality, leading to sexual problems not being recognized and addressed.

#### How Can This Be Improved?

Perceiving sexual difficulties does not mean that a sexual relationship becomes impossible or even necessarily difficult. There are various therapeutic options available to patients to achieve maximum sexual capacity, even in old age. The American Cancer Society has provided written information about sexuality and cancer, specific for male and female patients: http://www.cancer.org/treatment/ treatmentsandsideeffects/physicalsideeffec ts/sexualsideeffectsinmen/sexualityforthe man/sexuality-for-the-man-with-cancertoc, and http://www.cancer.org/treatment/ treatmentsandsideeffects/physicalsideeffec ts/sexualsideeffectsinwomen/sexualityfort hewoman/sexuality-for-the-woman-withcancer-toc.

If you think you need help for a sexual problem, try to discuss this with your doctor. If you think your cancer specialist can't help you, think of your family doctor or another member of the health care team, or ask to be referred for help. There are many different programs and specialists who can help you find the answers you need.

### Future Plans Regarding Sexuality Among Patients With Myelodysplastic Syndromes

At the 13th International Symposium on Myelodysplastic Syndromes in Washington DC, April 30, 2015, the Nurse Leadership Board discussed sexuality among older adults with MDS. Changes in sexuality have not been studied in patients with MDS. Furthermore, sexuality is not frequently discussed with our patients. We have agreed that we would start with providing written information and inviting the patient to discuss sexual concerns with us, and that we would ask our patients whether the disease or treatment have caused problems in patients' sexuality and potential relationships. Only by addressing the topic we can find out if our patient perceives a problem. We also had to conclude that patient preferences have not been studied yet and that future research needs to focus on changes in sexuality, information needs regarding sexuality, and effect of discussing sexual issues on sexuality of MDS patients.

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# LATEST NEWS

#### **CELGENE CORPORATION**

Celgene Corporation Enters into Strategic Immuno-Oncology Collaboration with AstraZeneca to Develop PD-L1 Inhibitor Program for Patients with Serious Blood Cancers

# APRIL 24, 2015 – BOUDRY, Switzerland (BUSINESS WIRE)

Celgene International II Sàrl, a wholly owned subsidiary of Celgene Corporation (NASDAQ:CELG) today announced that it has entered into a strategic collaboration with MedImmune Limited, a wholly owned subsidiary of AstraZeneca PLC, to develop and commercialize an anti-PD-L1 inhibitor, MEDI4736, for hematologic malignancies. Approximately 1.75 million patients globally suffer from blood cancer and many are in need of new treatment options.

MEDI4736 is a human monoclonal antibody directed against programmed cell death ligand 1 (PD-L1), which helps tumors avoid detection by the immune system. Tumor cells use PD-L1 to turn off the immune system just as it begins to mount a response against them. MEDI4736 helps turn the immune system back on, allowing it to continue its attack on cancer.

"The potential of rationally combining immunotherapies such as MEDI4736 with existing and novel hematology compounds creates new opportunities for patients with blood cancers to live longer, better lives," said Jacqualyn A. Fouse, Ph.D., President, Global Hematology and Oncology for Celgene. "This strategic collaboration leverages the deep expertise of AstraZeneca/MedImmune in immunooncology along with the experience of Celgene in the study and treatment of blood cancers. This collaboration advances Celgene's already deep, diverse scientific platform to include checkpoint inhibitors, an area of significant promise in hematology."

Dr. Bahija Jallal, Executive Vice President at MedImmune, said: "We are excited about

#### PRESS RELEASES

our strategic collaboration with Celgene, a globally recognized leader in treatments for hematological cancers. This agreement is a great example of how we are accelerating the development of medical innovation in our portfolio in collaboration with other experts, in order to bring life-enhancing new medicines to patients faster. Together with Celgene, we are designing a programme for our anti-PD-L1 that will explore its full clinical potential as a game-changing treatment that could activate the patients' immune system to fight and change the course of blood cancers in this area of high unmet need."

Under the terms of the agreement, Celgene will collaborate with AstraZeneca to develop the anti-PD-L1 antibody MEDI4736 in hematology and make an upfront payment of \$450 million. Celgene will lead clinical development across all new clinical trials within the collaboration and be responsible for all costs associated with these trials until December 31, 2016, after which it is responsible for 75% of these costs. Celgene will also be responsible for the global commercialization of approved MEDI4736 indications in hematology, and will receive royalty rates starting at 70 percent of worldwide sales from all uses in hematology.

Royalty rates will decrease gradually to 50 percent over a period of four years after the first date of commercial sales. This collaboration agreement will become effective upon the expiration or termination of the applicable waiting periods under all applicable antitrust laws.

This strategic collaboration will initially focus on the development of MEDI4736 as combination therapy with Celgene's pipeline of products and other novel agents for hematologic disorders. Over time, the collaboration could expand to include other assets.

MEDI4736 is not approved in any country for any indication.

#### About MEDI4736

MEDI4736 is a human monoclonal antibody directed against programmed cell death ligand 1 (PD-L1), which helps tumors avoid detection by the immune system. MEDI4736 is currently being evaluated in several disease states, including lung, melanoma and head and neck cancer.

TO VIEW THE COMPLETE PRESS RELEASE GO TO: http://ir.celgene.com/releasedetail. cfm?ReleaseID=908439

### SUPPORTING THE MDS FOUNDATION

Shop on AmazonSmile and Choose The MDS Foundation as Your Charity

# Amazonsmile You shop. Amazon gives.

When you purchase items through the Amazon Smile program, Amazon.com will contribute funds to support the MDS Foundation. As one MDSF donor puts it: "I purchase a lot of things for personal and business use on Amazon.com. If you go to www.smile.amazon.com and choose the MDS Foundation a 0.5% of the purchase will be donated to the Foundation. It's small, I know, but if a lot of people did it, it would certainly add up."

# PATIENTS & CAREGIVERS LIVING WITH MDS FORUMS

SPREADING THE NEWS WORLDWIDE

# MARK YOUR CALENDAR FOR THE LOCATION NEAREST YOU!

★ February 27, 2016 in honor of Rare Disease Day

> Tampa, FL Los Angeles, CA

**April 2, 2016** Austin, TX

**May 7, 2016** Lebanon, NH

★ June 25, 2016 Boston, MA Birmingham, AL

September 10, 2016 Baltimore, MD Dallas, TX

Cottober 29, 2016
 in honor of
 MDS World Awareness Day
 Denver, CO
 New York, NY

Register Today FOR OUR FREE EVENTS

## LEARN MORE AT: www.mds-foundation.org/patient-and-family-forums/

Many patients and caregivers have never met another person diagnosed with MDS until they connected with them at one of our forums. If you've never attended one before, you won't want to miss this opportunity to meet others and to learn more about MDS, current treatments, and emerging therapies from leading experts. Not only will you find answers, support and hope for MDS but you will learn tips and strategies for patients and caregivers **LIVING** with MDS.

# **INTERNATIONAL** HIGHLIGHTS

#### MAKING CONNECTIONS AROUND THE WORLD

### VIENNA, AUSTRIA JUNE 2015

# Photos from our Austrian MDS Patient Forum held 12 June 2015.

**THANK YOU** to Prof. Drs. Pfeilstöcker, Wimazal, Germing, Sperr, and Valent for the invaluable contribution you all made at our Vienna Patient Forum. From the feedback we've received, the program was a great success. One patient told us that now he has hope! For our German speaking friends, the audio/visual taping of this event can be viewed here on our website:

#### http://www.mds-foundation.org/mds-patientforum-vienna-austria/







### **MDS AWARENESS POSTCARDS**



The idea behind the picture is that one cannot identify who has MDS. Three people in this picture have been diagnosed with MDS. Patients are sometimes hurt by comments along the lines of "but you don't look sick."

dk	Husk
2. patientstøttegruppe	Frimæri
5 DK Patientstattegruppen – en frivillig inisation for MDS patienter og pårørende. I fokus på at fremme oplysning om MDS, tage patientinteresser og skabe patient- ærk. d tig ind og læs mere på: dkpg.mdS-and-you.info	

SO PROUD OF THE DANISH

See their new MDS awareness postcards, which they intend to distribute through the hematological clinics in Denmark.

MDS SUPPORT GROUP!!!

### **CONGRATULATIONS!**



Our very dear friend, **Bill Pearson**, accepting a well-deserved award from the *Leukemia Lymphoma Society Canada* as recognition for his fundraising efforts and his peer-to-peer telephone support for patients LIVING with MDS.

# **MDS** FUNDRAISING EVENTS

#### WORKING TOGETHER FOR MDS

#### TOM "SHU" SHUEY MEMORIAL GOLF TOURNAMENT



Tom Shuey passed away last year after battling MDS. He was an avid golfer and his son, Timothy Shuey's biggest regret was missing his last opportunity to golf with him. This inspired Tim and his family to organize a golf tournament in his memory. Their tournament on August 21 was a huge success with beautiful weather to boot. They had 144 golfers, 25 volunteers, and dinner for 170 people afterwards. It is Tim's hope that this

Tom "Shu" Shuey

event will be the first of many and will be a day to get family and friends together to remember his father, and to help raise money and awareness for MDS. \$5,500.00 was raised.



THANK YOU Shuey Family!!!



### KAREN A. WENZEL MEMORIAL GOLF TOURNAMENT

On Saturday, August 22, Paul Wenzel held his

*his mom, Karen* annual charity golf tournament named in memory of his mother, Karen, who passed away from MDS in 2006. Eight years of tourneys have raised over \$30,000. For years to come, Paul will keep his mother's memory in our hearts and minds, and continue to support the MDS Foundation.



Wenzel Family

#### BITTER END BENEFIT CONCERT



July 1, 2015 marked the 1 year anniversary of Anthony Pelle's passing and although we never met him we feel we know him through his daughter Janna. Janna is an MDS Advocate in the truest sense. In honor of her Dad, both while he was alive and even in the wake of his passing, she continues to be involved with the MDSF, sharing her story in our newsletter, creating her music album The Show Must Go On, and performing at our 13th Int'l Symposium. On August 10th she organized

an MDS Awareness & Benefit Concert at the Bitter End in New York City with 20 performing artists. Thank you to all who came out and to all the incredible musicians who donated their time and their talent! To date, Janna has donated over \$3,500.00 to the MDSF.

Janna Pelle's album Pre-order new #KEYCHANGE through @PledgeMusic now! 10% proceeds go to @MDSFoundation, RELEASE ON #THANKSGIVING2015. It's her first concept album on the evolution of the keyboard instrument through the means of pop music. Each track on the album is performed by a different keyboard instrument from harpsichord to synthesizer. Inspired by David Byrne's book, "How Music Works," Janna focuses on how music composition has changed throughout history due to the spaces it was performed in and decided to take this idea and focus specifically on the piano.





It was a wonderful event that not only raised money but also signed up 26 new potential lifesaving bone marrow donors!



LET'S SEE YOUR SWAB FACE!

#### WORKING TOGETHER FOR MDS



ATV 'TRASH THE DRESS FOR MDS" BENEFIT IN MEMORY OF TAYLOR MOEN Shelly Helm Guzek

organized an ATV wheeler ride and mud run on September 15th in memory of her son, Taylor Moen

Taylor and his Mom

who passed away on October 26, 2014. There was a 6 hour 4-wheeler ride with a mud pit to "Trash the dress for MDS" with \$1,776.00 of the proceeds being donated to the MDSF. Her son asked her shortly before he passed to try to find a cure or get the word out regarding MDS as he suffered with it for years. Shelly wants to continue this event as an annual tradition adding some humor and making this a unique ride to give Taylor some good laughs up in heaven and for any of those who have lost a loved one to MDS.

#### SUTTLE WEDDING -



In lieu of gifts, Michelle Lamberton and her fiancé John asked that donations be made to the MDS Foundation in honor of their wedding on April 18, 2015 and in memory of her mother, Ms. Kathleen Edwards.

Michelle's Mom, Ms. Kathleen Edwards. Kathleen Edwards They hope the donations will help find a cure for MDS.



Michelle and John's wedding



Shelly with her granddaughter Brynn

#### **RUNNING FOR AWARENESS**

Dylan Seth, fifth grader at New Canaan Country School, runs to raise awareness about MDS and the MDS Foundation. Her mother, who is battling MDS, is hoping to find a bone marrow donor.







Muddiest Rider Winner



We are very grateful to families and friends of MDS patients who make generous donations in memory of their loved ones. We applaud all for your valiant efforts. THANK YOU SO MUCH! Our work as a non-profit organization depends on public funding. If you would like to contribute in this way, or if you have a unique idea of your own, please contact us.

#### PLEASE HELP SUPPORT THE WORK OF THE MDS FOUNDATION



# YANKEE CANDLE FUNDRAISING

The MDS Foundation Yankee Candle Fundraiser has begun and will continue through January 2016! Shop online, at your convenience, for fabulous holiday candles and gifts. Treat yourself, too!

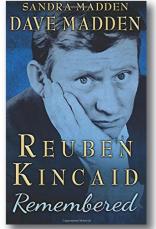
# https://www.yankeecandlefundraising.com/home.htm CUSTOMER NUMBER – 990087182

**IMPORTANT:** Please be sure that the customer number above appears on your order form or MDSF will not receive credit. Using this customer number, Yankee Candle will generously donate **40%** profit to MDSF.

A big thank you to Nancy Nussbaum! Nancy will be publishing a second volume of her *Annie's Sweet Tooth (and other savory delights!)* cookbook in honor of her sister, Ann Cosenza Hallberg, who passed away from MDS in

November of 2009. This Yankee Candle fundraiser is to support Nancy's publishing costs (approximately \$2,000). Please help us make this fundraiser a success!





# **REUBEN KINCAID** Remembered

Dave Madden, the comedian and actor perhaps best known as Reuben Kincaid in The Partridge Family, passed away in January of 2014 after a five-year struggle with MDS.

An accomplished magician and musician, Dave enjoyed almost fourteen years of retirement before developing MDS. In this revised, edited, and updated edition of *Reuben on Wry*, Dave's wife, writer Sandra Madden (**http://sandramadden.com/**), included a final chapter devoted to Dave's MDS journey. Thank you, Sandra!

Each purchase of *Reuben Kincaid Remembered* will support the work of the MDS Foundation.

Available through Amazon at:

http://www.amazon.com/Reuben-Kincaid-Remembered-Memoir-Madden/dp/1517676223.

# **COPING** AND CARING

#### **OUR CAREGIVER STORIES**

# The MDS Family: Coping and Caring Luncheons

The Annual April and July MDS Family: Coping and Caring events. In loving memory of Bob Weinberg, MDS Foundation's Board member and friend.

### Coping and Caring Luncheon, Philadelphia, PA



Hillary Sachs, Oncology Dietician, offering guidance on eating to maintain strength and energy. (See Hillary's article on page 26)







Dr. Lee Jones, Exercise Scientist, sharing how exercise may aid cancer treatment.



#### **COPING AND CARING**

# Nutritional Considerations in MDS

#### Hillary Sachs, MS, RD, CSO, CDN Board Certified Oncology Dietician

Myelodysplastic syndromes is a complex disorder that affects the bone marrow from making new blood cells normally. Signs and symptoms can vary from person to person. In general however, proper and adequate nutrition can aid the body's ability to regenerate new and healthy cells as best as possible.

### Managing Symptoms Anemia

According to the Mayo Clinic, "anemia is a condition in which you don't have adequate healthy red blood cells to carry adequate oxygen to your tissues." In turn, this may make you feel tired or weak. Choosing nutrient dense foods rich in iron,  $B_{12}$  and folate can ensure that the body has all of the building blocks it needs for when it is able to produce new red blood cells.

These foods include (note: wash all produce well; if neutropenic, discuss with medical team):

- Beets and beet greens
- Dark green leafy vegetables like kale, spinach, broccoli, swiss chard
- Dark colored fruits like berries, cherries, figs and grapes
- Nuts like almonds, walnuts and brazil nuts
- Grass fed beef
- Black rice and quinoa
- Bone broths

For people who need to absorb extra iron, here are a few tips:

- 1) Pair a source of iron with a source of vitamin C for extra absorption
  - a. Peanut butter and strawberries on sprouted bread
  - b. Brown rice, black beans and peppers
  - c. Shrimp with lemon and lime
  - d. Hamburger with tomato
- 2) Use a cast iron skillet

### HERE'S WHAT ATTENDEES ARE SAYING ABOUT THEIR COPING AND CARING LUNCHEON EXPERIENCE

"It was very nice to meet you on Saturday at the White Dog Cafe. What a nice place. My wife and I really appreciate what you do for The MDS Foundation. I wish we had more time to talk. Looking forward to July. It's very powerful to hear and learn what other people go through." *Phil V.* 

"We were at your event on Saturday at the White Dog Cafe. I just wanted to thank you for your kindness, and allowing us to express our feelings. We are so glad we attended, and finally met other people going through this complex disease. It was such a wonderful event, and so informative for both of us. You do such great work for people with this disease, and for that alone we are so grateful. When I found the MDS Foundation on the internet, I decided to call.... And they sent us all these informative booklets which really helped us understand better. He was just diagnosed last June, so this is still new to us. The MDS Building Blocks of Hope were there when we needed help understanding. Thank you Rochelle, for giving me some relief, knowing you and the MDS Foundation are there to reach out to is a gift to us."

Maureen V.

"It was good to connect with other MDS families and hear what Lee had to say about his exercise research. Of course, the food was delicious, too – as usual! Take care, all you lovely people!"

Amy L.

"Thank you for hosting the coping and caring event. It was wonderful to meet you and all the others. Robert was so happy that we came and it was the first time he opened up to a group. Thank you again."

Carol M.

"How great to see these pictures of this wonderful group. Thanks so very much for including me (and of course, Joyce). Both of us valued our time with you a year ago, and look forward to re-joining the group when you meet in the fall and/or winter. All good wishes, and much gratitude for all the incredible ways you are helping so many. I know your incredible husband would be very proud of you — I know I am!"

Ann W.

For people who are looking to minimize iron absorption due to iron overload after a transfusion, here are a few tips:

- Drink coffee with your meal
- Drink tea with your meal
- Eat a source of calcium with your meal

#### Neutropenia

According to the Mayo Clinic, neutropenia "is an abnormally low count of neutrophils, a type of white blood cell that helps fight off infections, particularly those caused by bacteria and fungi."

#### Since our white blood cells help to fight infection, it is important to follow the USDA's food safety precautions for people with cancer if your white blood cells are low: http://www.fda.gov/downloads/Food/ FoodborneIllnessContaminants/UCM3127 61.pdf.

#### In addition, there are certain foods/ supplements that may help to support our natural immunity

#### Foods

- Foods high in vitamin D: mushrooms, fish, sundried tomatoes, dairy/dairy alternatives
- Foods high in zinc: mushrooms, cooked oysters, wheat germ, pumpkin seeds
- Foods high in vitamin C: tomatoes, broccoli, peppers, cherries, strawberries, citrus
- Foods high in selenium: brazil nuts, tuna (chunk light has least amount of mercury), mushrooms, chicken, turkey

#### **Supplements**

(Note: always speak with your medical team before taking supplements!)

- Ginger can thin blood, may decrease bioavailability of cyclosporine
- Elderberry caution with drugs metabolized via CYP34A
- Astragalus caution with lithium, may thin blood
- Reishi mushrooms may thin blood; caution with autoimmune conditions
- Goldsenseal may interfere with INR tests; may increase bilirubin; inhibits CYP34A and CYP2D6
- \*According to MSKCC About Herbs and Botanicals

#### Thrombocytopenia

According to the Mayo clinic thrombocytopenia "is a condition in which you have a low platelet count. Platelets are colorless blood cells that help blood clot." In order to help keep platelet counts up as high as possible, it is important to consider the following nutritional factors:

• Eat adequate amounts of protein-while protein needs can fluctuate with age,

medical condition and activity, on average someone with MDS needs about 1.1–1.3 grams per kilogram of body weight of protein which is an increase from the standard 0.8-1.0 grams per kilogram of body weight, which the average person needs. 1.1–1.3 grams per kilogram amounts to about 50-60 grams for a 100 pound person, 75–89 grams for a 150 pound person and 100–118 grams for a 200 person. Protein rich foods include animal products like dairy, chicken, fish, eggs, beef, lamb, etc. It also includes vegetarian options like tofu, beans, nuts and certain grains/seeds like quinoa and hemp.

**COPING AND CARING** 

- Consume adequate amounts of calcium and dark green vegetables as they may help provide baseline clotting factors.
- Consume sesame oil and pineapple (not necessarily eaten together). This tip is purely anecdotal claimed by many naturopaths. Unfortunately more research needs to be done to understand if this is true and if so what the mechanisms are. However, there are not really any downsides to consuming these foods.

# Minimizing Risks From a Nutrition Perspective

While the cause of MDS is mainly unknown, the American Cancer Society put out a statement with regards to benzenes and blood cancers. They state: "Benzene is known to cause cancer, based on evidence from studies in both people and lab animals. The link between benzene and cancer has largely focused on leukemia and cancers of other blood cells." While benzene exposure is mainly related to cigarette smoke, there are other environmental exposures like petroleum. From a nutrition perspective, in 2005 the FDA conducted an investigation on sodas and diet sodas and found some brands had higher than acceptable amounts of benzenes in their beverages. Follow up investigations were conducted shortly thereafter to ensure companies complied with standards.

Proper and adequate nutrition can aid the body's ability to regenerate new and healthy cells as best as possible... A healthy diet is a key component to keeping well as you transition into cancer survivorship.

#### **Components to Longevity**

A healthy diet is a key component to keeping well as you transition into cancer survivorship. The American Institute of Cancer Research has ten specific recommendations for cancer prevention. Highlights include being as lean as possible without being underweight, being physically active and consuming a wide variety of fruits and vegetables. Find a Certified Specialist in Oncology (CSO) in to discuss individual vour area recommendations. Here's to your health! http://www.aicr.org/reduce-your-cancerrisk/recommendations-for-cancer-prevention/ https://ams.eatright.org/eweb/DynamicPag e.aspx?Site=CDRNEW&WebKey=8EAD AFE4-F1E1-4309-B21C-66D3CC2AA112.

Hillary Sachs, MS RD CSO CDN is a Board Certified Oncology Dietician with a private practice focused on health, wellness and oncology nutrition. She is passionate about the relationship that proper nutrition has on general health and quality of life. She was privileged to attend the MDS Coping and Caring Group held in Philadelphia in April and looks forward to future collaborations.

She can be contacted at: hillarysachsnutrition@gmail.com or www.hillarysachsnutrition.com

#### **OUR CAREGIVER STORIES**

# I Miss Her Everyday...

#### Susan Weeda Lee's Summit, MO

Mary Lou Haefele... for me, she is "Mom". My mom had 6 children, and I am the youngest. She grew up with a younger brother and very loving parents and spent as much time as possible in her youth riding and caring for her beloved horses. She was very much on the straight and narrow so I found it so hilarious when she said she and her brother used to ride their horses up to lover's lane and kick the car doors of the couples making out. It's so out of character for the mother that I've always known. She also told me that she never really liked kids that much growing up and was surprised she had 6 of them, but we were without a doubt, her pride and joy. She never missed an opportunity to give a hug or say, "I love you". All family gatherings were loud and full of laughter and when the grandchildren started arriving, things just got louder and funnier.

She and my dad ran a greenhouse business, and she was fortunate enough to retire in 1983 at the age of 55. In 1988, my mom was diagnosed with a totally enclosed malignant lung tumor. After having 2/3 of one lung removed, she recovered and went on about her life. There was no chemotherapy or radiation required, and we all felt fortunate that we still had our mom. Prior to the surgery, she walked 5 miles every day, 5-6 days a week, but after the surgery she said she could never get back to 5 miles. She could walk 3 miles, but not 5. In 1998, my parents moved to a retirement community and soon after, with his health failing, we put my dad into a nursing home. My mom just couldn't care for him 24 hours a day at that point, and that's what he required. He passed away in 2002.

My mom was always social. She was the salesperson in our parent's business so putting her among a lot of people her age was a dream come true. She had so many friends in her new neighborhood. She enjoyed playing games – dominos, cards,



rummycube, etc, but she enjoyed nothing in life more than playing bingo. She knew every local place that held bingo games. My niece used to stay with her during the summer, and said "sometimes Grandma played bingo on Monday, Tuesday, Wednesday, and Thursday". It was so funny. In 2000, Mom began to struggle breathing, and I mean literally walking across the room caused her to be out of breath. Around 2002, she had her first knee replacement, and in 2003 or 2004 she had her second one. This was the first time that I realized there was a blood issue. You know how it is before surgery, they take blood and verify counts. I don't even know what the counts were, but I know she got a transfusion. She went to a rehab place after the surgery and I went to see her. She was walking all over with the walker and not out of breath - not at all. She mentioned the transfusion, and I knew then the breathing issue was blood related.



I went with her to her very first appointment with the blood doctor. I remember him saying that she was losing red blood cells but they didn't know why, and we would just let things go and see what happens. He just called it anemia. Looking back on it, I think the doctor knew exactly what was wrong, but with no real treatment they didn't do any testing to verify it. Eventually, of course, the benefits of the transfusion wore off and her breathing was back to being totally lousy. She forgot about breathing so well after the transfusion and thought her breathing issues were related to her lung surgery. She also had asthma, and she attributed it to that as well. In reading other stories, I know we were lucky if there is such a thing with MDS. She just kept going... there weren't hospital stays or any other procedures. But her breathing was so bad. She told all of her friends she was anemic, but never believed the breathing was related to the anemia.

In 2011, I went to Las Vegas with her. I got on her about her breathing and told her that I knew it was blood related. Instead of making an appointment with the blood doctor when she got home, she made an appointment with her pulmonary doctor. She got inhalers and other medication and thought she was better. She wasn't, but she thought she was so I didn't say any more. She was, in general, very happy and there wasn't a good reason to push her for additional testing.

In June of 2014, my mom got a really bad cold. In July, my daughter Lisa's boyfriend proposed, and we planned a get together after the proposal. My mom could not come... she still had this cold and she had it for the entire summer.

MDS was a part of my mom's life for what I would estimate to be 15 years, but we didn't get an official diagnosis until a traumatic fall. Yearly in Kansas City, they hold the American Royal horse show. She and I used to go to the show routinely, but hadn't done so for a long time. So on November 15, 2014, we went with my husband, Rick, and my younger daughter,

#### **OUR CAREGIVER STORIES**

Jamie. We walked around the stable prior to the horseshow and petted some of the horses and then made our way to the show. She knew a lot about horses and showed us how they would lead with one leg or the other, and seemed to know the winners. We even laughed when we figured out one of the riders was William Shatner. She had driven to my house prior to the show and then we drove from there. For the first time ever, my mom parked in the street and not in the driveway like she usually did. When we got home, she hugged me, hugged Jamie and took two steps before I could hold onto her and walk her to her car. The second step was devastating. She hit the edge of the driveway and the yard. Her foot turned, her legs and arms gave out, and she lay lifeless at the end of my driveway. She didn't answer for what seemed like forever, but she finally did. We called 911 and she was transported to the hospital. Diagnosis: broken neck - C1 and C2. For me, totally devastating. Surgery was not an option due to age but we were told she would be able to manage with this break. About 2 weeks after the fall, she started having serious headaches. With no exact reason and wanting to explore all options, a bone marrow test was run. Diagnosis: Myelodysplastic Syndrome, Phase RAEB-1. We got this diagnosis on December 21, 2014. Honestly, at the time, this didn't faze me at all as I knew she had an issue for years and thought she would live for years longer. However, I'm an internet reader and looked up RAEB-1. Life expectancy was two years or less. I was devastated and vowed to not read any more about it. My daughter's wedding was 61/2 months away, and I desperately wanted her there. The long lingering cold now made sense to me. She just didn't have the blood required to fight it off.

I do not know whether it was the MDS or the fall or the combination of the two, but after her fall, she pretty much quit eating. Every time she went to the doctor, she was losing weight. She would put food in her mouth, chew and chew, and eventually spit it into a napkin. This went



on for approximately four months until they decided to give her medical marijuana to stimulate her appetite. I don't know what would've happened without the fall, but I had never seen anyone just not eat. Obviously, this affected her strength, and she was in and out of rehab facilities and hospitals from November through the end of March. In April, we moved her to an assisted living facility.

In March, I received a phone call from my youngest brother. He and my sister had been to the blood doctor with my mom. The doctor told them, without my mom present, that eventually the transfusions would not be effective, and a decision would have to be made about stopping them. My sister asked him how long she would have after she needed a transfusion and didn't get one. She asked him if my mom would have weeks. He said no, only days. Yet again, I was devastated. The wedding was July 11th. This was March. Could we possibly get her somewhat healthy for the next four months? Now when she received a transfusion, I would start my internal clock so I would know how long she would go before getting another transfusion. But the time kept getting shorter. I don't believe she ever went more than three weeks from March on. I remember being on the phone with two of my brothers and them telling me that she may be trying hard to hold on for the

wedding, and that I may need to give her permission to go. I wasn't ready for that. I wanted my mom here, not just for the wedding but also beyond that. But she had already changed. No longer did I get phone calls from her routinely. When I called her, she didn't answer anymore and she didn't see that I had called and then called me back. In some way, I feel like I was getting trained for her not being here. She always called - and now she wasn't. This disease was taking its toll, and I hated every minute of it. I always imagined her being on the Today show for her 100th birthday. By now, I knew she wasn't going to make it to 87, let alone 100.

My mom loved playing games. Bingo was her favorite game but we played Rummycube. It was hard watching her not be able to play this game anymore. She didn't even know she was putting down incorrect colors or numbers. Even as late as January, I could play this game with her and she knew all the rules - you didn't dare make a move that wasn't within the rules. By April, she was mixing incorrect colors and numbers. It was hard to watch. Her red cells, platelets and white cells were dropping and it was affecting every aspect of her life. During the last few months of her life, her platelets were never above 11,000 and at one point were 3,000.

I went to see my mom one evening in May and happened to be the only one there. She was very emotional and as per her

#### **OUR CAREGIVER STORIES**

usual, asked if everything was done for the wedding. She asked about the wedding every time I saw her. I asked her if she wanted to see Lisa in her dress and she said yes. Lisa came over that night and I have pictures of my mom with her. It was the best we could do. I know that I held on longer than my siblings that my mom would be able to make the wedding, but by this time I knew it wouldn't happen. The transfusions were closer and closer together, just as we were told would happen.

On May 25, the six of us gathered with my mom to discuss stopping the transfusions. At her last doctor appointment, and prior to what proved to be her last transfusion, her hemoglobin was 6.8 – the lowest it had ever been prior to a transfusion. She was so tired. The doctor didn't want to do another one, but I requested it. I then met with him, and he explained that she had leukemia. That was the first time we had heard that word. I knew it could progress to leukemia, but wasn't expecting to hear that word. She had a final transfusion on May 13, 2015. She said she didn't think there was any need to do any more transfusions. I knew then, that at best, I would have my mom for 2 weeks or less. I called the blood doctor to have them stop the blood draws. The orders were put in but for some unknown reason the blood draw was taken anyway on May 28th. That afternoon we got the results -Hemoglobin was 5.7.

Her will to live was so strong. Her friend came to see her on May 29. She hadn't seen her for awhile and when she did, she immediately got out of her chair to hug her. I couldn't believe she could function at all with hemoglobin so low. We figured by then her hemoglobin was around 5. Her headaches were getting very severe. We assumed the lack of oxygen was hurting her brain and decided to call in hospice. That was on May 29, 2015. We could not control pain at that time. My sister and I and my 2 daughters were down the hall meeting with the hospice rep. We left my mom dozing in her chair, but when we got back, she had



gotten up and walked by herself to the bathroom – no walker, no cane, no assistance whatsoever. Looking back on it, it was amazing she could do that.

My mom was moved to hospice on May 29, 2015 at approximately 7 pm. By the next day, she was still somewhat communicating with us. She would come in and out of responsiveness. At one point, she asked me if I was OK. I honestly don't remember how I answered that, but I knew I wasn't OK. But there was one other very painful moment for me. I reached over her and she put her arm around my neck. We were cheek to cheek and she said to me "please help me live." I couldn't help her live, and I still cry when I think about that.



She loved the 6 of us and we were the joy of her life. She just didn't want to leave us and all of our crazy family get togethers. I will never forget her saying this to me, and I will never forget that complete and total helplessness. I couldn't just give her a pill and make it all better.

On May 31, 2015 at 4:12 am, surrounded by all six of her children and one of her grandchildren, my mom took her final breath. I miss her every day, and I hate the disease that took her from us. I am heartbroken that she missed my daughter's wedding, and as a family we decided to designate any memorials for her toward research for a cure for this disease. I hope that others will do the same.



# **PATIENT** STORIES

## **15 Years Post-Diagnosis**

#### Pam Wishart Victoria, British Columbia

Sitting at the computer preparing to write about my version of MDS I realize I never expected to be alive to do this 15 years post-diagnosis. I haven't had a transplant. I don't have transfusions because of an antibody which makes it almost impossible to find compatible blood. I'm also someone who functions reasonably with hemoglobin in the high 60s. I know this won't go on forever but, at 72, I find it much easier to deal with a chronic, probably fatal, disease than I did at 56.

My current life is very good. We moved from Montreal, Quebec, to Victoria, BC, in 2008 and it's a beautiful part of the world with walks along the ocean and through the woods with my husband and our whippet (now only one). Don't get me wrong, I do have bad days, but at the moment the good far outnumber them. And, on a bad day, I have the luxury of being able to do very little.

I am on the Board of the Aplastic Anemia & Myelodysplasia Association of Canada (AAMAC) where I have many opportunities to interact with other patients and provide help and hope where I can. I also volunteer with the Leukemia & Lymphoma Society of Canada (LLS) as part of their First Connection Program. Do I realize how lucky I am to be able to do this? You bet I do!

Looking back, my diagnosis of MDS could have been made in 1997 when a routine complete blood count (CBC) showed I was anemic, hemoglobin: 105 g/L. My folate and B12 were normal but I was told to take iron which I did for a while. At the time, my health concern was the increasing lack of mobility in my hips and nothing else was done.

In the summer of 1999, I took a scuba course and after a "wreck" dive to 60 ft. I was breathless and couldn't get out of the water without help! Later that year, I was amazed at how breathless I became while hiking up a mountain. Still, neither of these



Sitting at the computer preparing to write about my version of MDS, I realize I never expected to be alive to do this 15 years post-diagnosis.

got me to make a doctor's appointment. What did was how hard my heart was beating after climbing 10 stairs to the bedroom and the strange pains in my abdomen. My physician ordered a CBC and other tests, the result, hemoglobin of 81 g/L, my red cells too big and too few and too many platelets. I was immediately referred to a hematologist whom I saw early in 2000. You all know what was next, a bone marrow biopsy (BMB).

During the first visit with the haematologist, I didn't ask a lot of questions. However, I did ask if it was okay to exercise. He asked what exercise, and I mentioned spinning and step classes and tennis. He gave me a look and replied, "No, no exercise. Nothing." This was a huge relief. I no longer had to push myself to go to the gym or even to play tennis, something I really enjoyed but was finding increasingly difficult.

It is really hard to remember how scared I was when I heard this. I knew enough about medicine to know that it could be, and probably was, very serious. Waiting the 8 days for the biopsy, and then the result, was a nightmare. I was only 56 years old, could this really be it? One thing I've never done is ask why me; I realise worse happens to a lot of other people, adults and children, so why not me but that didn't help much!

I have a BSc in Biochemistry and an interest in medicine, a combination which gave me the vocabulary to read, and understand what I read, in the Harrison's Textbook of Medicine we had at work. It lived in my office while I was awaiting the results and I read and reread everything about anemia. There was no mention of MDS but there was mention of incurable anemias, and those were the ones I focused on.

The results of the BMB showed I most likely had one of three or four diseases, one of which was leukemia, although my hematologist felt that was unlikely. I remember being told that all three diseases were serious — well, hearing the term 'leukemia' told me this too. Most of us might not recognize the terms MDS and myelofibrosis, but I think we all dread hearing 'leukemia.'

My hematologist was an excellent choice for me. Dr. Laryea always answered questions, took the time to educate me and never appeared rushed. He started me on epoetin alfa (Eprex® here in Canada) which I took for 7 years after which it stopped working, and an iron supplement until my ferritin level increased. He also suggested a second opinion and referred me to a teaching hospital. By June 2000, I had a definite diagnosis, MDS-RA with normal chromosomes. The megakaryocytes (platelet precursors) in my bone marrow also showed abnormalities.

Armed with this new information, I calculated my International Prognostic Scoring System (IPSS) rating and figured my prognosis was 2 to 8 years. The eight years didn't sound too bad, still a long way

away but the two had me totally freaked out, irritable and on the verge of tears a lot of the time. While I had no problem understanding the number, I know I was never able to believe it. At the time there was a figure of 9+ years in the upper, righthand corner of the IPSS table and I so badly wanted to be in it.

By this time the Eprex® and/or the iron were helping my body make red cells and my hemoglobin was in the high 90s. The highest my hemoglobin has been since diagnosis is 102 g/L and that was that summer. By the next year it was decreasing but slowly and I still felt reasonably well. I was back to playing tennis and even the gym for a while. The nervousness and irritability I'd felt for years continued. I probably wasn't easy to be around. I remember being resentful about having to spend what I felt were my last years working, up at 5:20, out by 5:50, all in order to beat the traffic.

As an only child, one of the hardest things I had to do was tell my 83-year old mother. In the end, I told her I had a serious form of anemia which was why I was so often feeling tired and irritable. And that was what I told my two adult sons who, despite being supportive, to this day probably can't tell you the name of what I have!

Life went on much as before until March 2002 when my husband was diagnosed with rectal cancer and needed surgery, chemotherapy, and radiation. When diagnosed with a terminal disease, we focus on ourselves and tend to forget that other people still get sick too but now, rather than worrying about me, we started to worry about him. His prognosis was a 40 to 60% chance of 5 year survival. He's now 13 years post-diagnosis! We both learnt a lot during this time including that we want different levels of information, he wants the minimum necessary to make informed decisions and I want as much as I can get. We both learnt to accept the other's approach.

By the end of 2002, my hemoglobin values were back in the low 80s and I was able to go on long term disability in early



Snorkelling is probably most indicative of who I am...

2003. I was elated, no more getting up before dawn, no more fighting the traffic and no deadlines to be met. Despite the difficulties of low hemoglobin my life was much improved, there was definitely a good side to this disease.

My husband liked it too. No longer was I as irritable as before, and with me at home, he was able to adopt one of his daughter's dogs, Diesel, a four-year old whippet. Diesel taught me to like dogs and was with us until May of this year. She also made sure I got out at least once a day summer and winter.

In 2003, I attended a patient education seminar in San Francisco. It was marvellous to walk into a hotel conference room filled with people like oneself, all with a connection to MDS... In 2003, I attended a patient education seminar in San Francisco. It was marvelous to walk into a hotel conference room filled with people like myself. There I also met a board member from AAMAC, who very much impressed me with her knowledge of MDS. She's the reason I'm on the Board.

And then things changed, January 2004, hemoglobin 73 g/L, February 75 g/L and Dr. Laryea told me it was time for a transfusion. I wasn't particularly worried about the transfusion, just the idea that I was about to become transfusion-dependent. Not only did that mean my disease was worsening but I'd need chelation in the not too distant future, something I dreaded.

Still, the transfusion process itself didn't worry me. I read up on possible problems and learnt about the risks associated with transfusions but they didn't much concern me. Little did I know that I would soon become well-acquainted with one: hemolysis. My body, so bad at producing red cells would prove to be excellent at producing an antibody to II blood. II is a marker on the red cell but isn't quite the same as the usual red cell antigens. We're all born ii and become II at around 18 months of age. Adults who are ii are extremely rare and I still don't know how they are found!

The result, I had hemolytic reactions to the first two attempts to transfuse me despite the blood being correctly typed and the cross-matches being fine.

Tests were done to determine the reason for the reaction in the weeks following the first one but no antibodies that could cause hemolysis were found. After the second reaction more testing was done and it was determined that I needed ii blood. The first bags came from the U.S. and I was transfused successfully but then developed another antibody. Blood was found for me in France. It had been donated and several bags cryogenically frozen. I used up the supply.

My hemoglobin was usually in the 70s, then 60s through the next several years, levels at which I discovered I can function without

too many problems, but then in early 2009 it dropped to 50 g/L. I probably had a cold which always causes it to drop 10 to 20 g/L. We had moved from Montreal to Victoria in 2008 and this was the first transfusion I'd needed since then. Héma-Québec still had two bags of the cryogenically frozen packed red blood cells and they were flown to BC. For a number of reasons, preparing cryogenically frozen blood for transfusion is not always successful and, unfortunately, this was one of those times.

More testing of my blood was done and no evidence was found to support my need for ii blood. Again blood was typed and cross-matched and, again, I had a hemolytic reaction. More testing, more blood and another hemolytic reaction followed. Even more testing, HLA- matched blood found, and this time a febrile reaction. Finally some ii blood was found and I was successfully transfused. Over the next three years I had a few successful transfusions, all with ii blood. I have not had a transfusion since early 2012 mainly because of the difficulty in obtaining blood quickly, if at all.

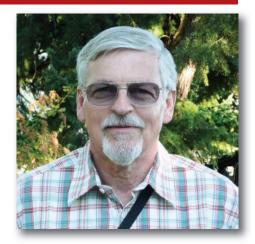
I've been told I don't have an ii marker on my red cells so why the hemolysis? My theory, the MDS caused a mutation in the II marker and my body now recognizes "normal" II as foreign while ii is accepted in much the same way as Rh- can be given to Rh+ people. I'd love to know the answer.

Other things were happening in these years. Because of the problems in transfusing me I took thalidomide for 6 months in 2004, first at 50 mgs/day then 100 mgs/day. I hated it but persevered. If anything, it lowered my hemoglobin but, and this was something I had read sometimes happened, my hemoglobin went up to 91 g/L after I stopped the drug and it stayed high for several months.

I was also hospitalised for 10 days that year with deep vein thromboses and pulmonary emboli and I had to take an anticoagulant for several months. Not something I was comfortable doing given my low hemoglobin. Again I was lucky that Dr. Laryea prescribed prednisone in 2005, a drug I am still taking. It's not the drug of choice for MDS and has many undesirable sideeffects. Given my situation, there weren't really any other options. At first 50 mgs/day every other week, then 100 mgs/day for 5 days with 16 off as I asked if I really had to take it every other week, later still 25 mgs/day for 5 days with 9 days off, and since April 2014, every day, starting at 15 mgs/day then reducing slowly to the 7.5 mgs/day I'm now taking. I also take a drug to protect my GI tract.

My hemoglobin fluctuated while on the cycles but, since starting the daily dose, it has remained fairly stable, usually in the high 60s, sometimes low 70s. For years I wasn't sure it worked then, on vacation in Europe in 2012, I contracted what I suspect was a norovirus. The vomiting meant I lost the prednisone and I hadn't thought to pack extra to restart the cycle. It was 10 days before we returned home and I was exhausted. My hemoglobin was 51 g/L. I knew finding blood, if even possible, took several weeks. I started my prednisone and three days later could feel the change and within three weeks my hemoglobin was 70 g/L. Up to then I had never been sure the prednisone actually had an effect, now I'm a believer! For me, it works. Yes, I have a number of side effects including decreasing bone density but so do many of my friends.

Now, in 2015 there is so much more information about MDS than there was in 2000. The Internet makes it easy for us to find such marvelous resources as the MDS Foundation, AAMAC and all the other organisations throughout the world who supply us with information, support and fund research. Although there has not been much new in the way of treatment recently more and more is being discovered at the gene level, giving us hope that treatments will improve and perhaps even be individually tailored.



### My MDS Journey Samuel Ronald Cook, Jr. Columbus, Ohio

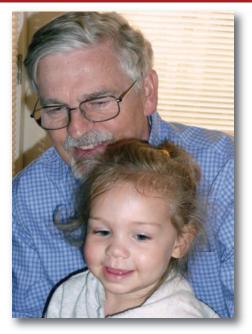
I am a lawyer, largely retired, who lives in Columbus, Ohio. I am 70 years of age and have enjoyed unusually good health my entire life. The sole exception has been a fifteen-year battle with prostate cancer, which has proven quite successful to this point notwithstanding an initial surgical failure. I have been treated with antiandrogens for the past nine years, and, after many years experiencing a rising PSA, there has been for three years no medically-detectable evidence of the disease in my body. My prostate cancer is unrelated to my MDS, but, as I will explain later in this article, the treatments of the two diseases might have some connection.

Given my good medical history, I was stunned when I was first diagnosed with MDS in mid-2011 following a bone marrow biopsy at Columbus Oncology and Hematology Associates. My family physician had begun to notice a decline in the readings for many of my blood lines in 2006. I had suffered none of the symptoms that typically accompany declining levels in these blood lines-no fatigue, bleeding, bruising, frequent illnesses, or swelling. My initial MDS diagnosis was confirmed by a second opinion from the MDS group at the Cleveland Clinic. The initial risk assessment placed me in what is now designated as the low-risk category.

My hematologist recommended that I be treated with infusions of Vidaza. The burden that the monthly nine-day treatment cycle (seven treatment days interrupted by a weekend with no treatments) would place on my life was quite troubling, but there seemed no options except one at the Cleveland Clinic that would have been even more burdensome in terms of time and travel commitments. Meanwhile, I continued to experience no symptoms other than the low blood count readings.

The Cleveland Clinic staff concurred with my Columbus doctor's recommended course of treatment. I began Vidaza infusions in early January of 2012, and my blood count readings after a few months returned to levels that were above any serious danger zone. I had to learn how to cope with the side effects of the treatments and of the drugs I took to deal with some of those side effects. The various side effects included sores in the mouth and soreness of the tongue; dehydration; constipation; and anxiety. The last of these side effects was unexpected, and I initially assumed that the anxiety I experienced resulted from some family history of this problem. I later learned that anxiety is sometimes a side effect of Vidaza treatments. Whatever the cause in my case, the condition proved to be almost completely eliminated by a mild form of medication.

The only side effect that was really problematic when I began treatments was the moderate nausea I would experience from about an hour after each treatment ended until about four hours after that. My first Vidaza treatments had been preceded by an infusion of Zofran in order to alleviate nausea. This was successful for that purpose, but I did not like the heaviness I would feel in my legs for the rest of each day on which I received a treatment. This was particularly problematic on the three days each week, including two treatment days, when I was continuing to play tennis.



I tried other medications taken orally to combat nausea, but they did not prevent or reduce the nausea. Then, after about fifteen months, my doctor and I found an antinausea regimen that worked perfectly. The first step was to counter my tendency to have an acid stomach by taking a Pepsid AC tablet twice each day. The second step was to take a Compazine tablet on each treatment day one hour before the treatment. (Compazine alone had previously proved to be ineffective.) The final step was to take a Zofran tablet immediately after each treatment. This regimen totally eliminated any nausea and did not seem to have any additional side effects.

After a few treatment cycles, it was clear that my wife and I would have to organize our lives around the 9-day treatment period, followed by 19 days of freedom from treatments.

During my journey of diagnosis and treatment, I have had the benefit of an exceptional caregiver: my wife, Janice. Among her contributions from the onset of my problematic blood tests were the keeping of meticulous records as to (1) the progress of my blood readings and (2) the probable future scheduling of my treatments (typically looking twelve months ahead). The first of these was helpful to my hematologist as I began my treatments, and the second became important as we sought to continue living active and productive lives within the time and travel restrictions imposed by my treatment regimen. My wife also attended to keeping my many prescriptions up to date and to monitoring our relationships with our health insurers.

After a few treatment cycles, it was clear that my wife and I would have to organize our lives around the nine-day treatment period, followed by nineteen days of freedom from treatments. Once we had solved the nausea problem, the disruption of my activities on each treatment day was less serious than I had expected. The infusion facility was near to my home, and I was typically away from my house for less than two hours on each treatment day. Although I sometimes experienced drowsiness during the hours following a treatment, I was able to make good use of the balance of each treatment day.

Allowing for the limitations and scheduling issues created by my overall treatment schedule, I continued with all my regular activities. I continued to direct and perform with the medieval and Renaissance ensemble of which my wife was also a member, The Early Interval. I also continued to give solo recitals of medieval storytelling combined with performance on the medieval harp. I continued to walk regularly and to play tennis three times each week, and I began playing tennis competitively at a higher level than I had previously been playing.

My wife and I were forced by my absolute neutrophil count to cancel a

long-planned trip to Maui during the first months of my treatments, but we thereafter continued to travel in the nineteen-day periods during which I had no treatments. We both continued to play with an ukulele ensemble that I formed in 2009. I continued to garden and to tend to my collection of two dozen bonsai plants. I continued throughout my treatments to write articles on early music, as well as to write poetry, and I selfpublished both a book of poetry and an instructional book on playing the 12th- and 13th-century harp. I also continued to practice nonprofit law on a part-time basis and to serve on several nonprofit boards.

I used the periods of inactivity caused by nausea in the first year and a quarter of treatments to digitize my collection of over five thousand family slides. The soreness in my mouth would sometimes influence my choice of foods, and one concession I have had to make due to the dehydration issues caused by the medication was to give up enjoying single-malt Scotch and bourbon. However, I have continued to enjoy a beer or a glass of wine several times each week.

My hematologist initially told me he hoped Vidaza would be successful for me and continue to be effective for at least six months. While reliable statistics are hard to find, the best information I have been able to discover shows that Vidaza treatments are most typically effective for about twenty-four months. As I write this account of my MDS journey, treatments have been effective for me for over forty-three months. I am obviously grateful that I have experienced such a result. I am also very grateful for all the care I have received from the infusion room nurses at Columbus Oncology and Hematology Associates and all the valuable information that has been provided by the MDS Foundation. I remain hopeful for the future of my treatments, particularly since I recently learned of one patient in another state for whom Vidaza treatments have been effective at this point for five years.

As to why these treatments have worked for so long in my case, the most logical conclusion is that my body is unusually responsive to Vidaza. My exercise regimen may also play a part in fighting the disease, as may the fact that I began treatments when I was younger than many MDS patients. It may be worth noting, however, that, in an effort to enhance the effect of antiandrogens taken in connection with treatment for residual prostate cancer, I have for almost five years been taking a daily dose of 1000 mgs of pomegranate extract. I had begun daily doses of this supplement at half this strength five years earlier.

I remain hopeful for the future of my treatments... I recently learned of one patient for whom Vidaza treatments have been effective for five years.

Although I have never had much confidence in herbal remedies, I had discovered that at least two studies had found pomegranate to be helpful in fighting prostate cancer. Although this may be entirely coincidental, for the past three years I have had no medically detectable PSA in my blood. I have recently become aware of studies suggesting that pomegranate extract may also be helpful in treating several other cancers, including some leukemias. The unanswerable question is whether the pomegranate could be enhancing the effect of the Vidaza.

The exact benefits of the Vidaza treatments have been somewhat difficult for me to interpret over time. The levels in my various blood lines have never fully returned to normal. However, after the initial several months of treatments, they have remained out of any real danger zone. The absolute neutrophils, although constantly varying, have generally remained



in a range of 1.2 to 2.2. That count had dipped to 0.6 two months before I began treatments and dipped as low as 0.4 after two months of treatments. My platelets have remained in a range of 108 to 148, and my hemoglobin readings have remained in a range of 12.0 to 13.1. That being said, my monthly blood tests show a slightly different picture every month, and the various numbers do bounce around from month to month.

When the Vidaza treatments had proved to be effective for about two years, my hematologist suggested that we should consider my eligibility for a stem cell transplant. My understanding is that such a transplant holds out some hope that it can effect a cure. Following his advice, I was evaluated for a transplant at the James Cancer Hospital. I was found to be a suitable candidate for a transplant, and a search of the national donor database produced one perfect match. However, the transplant doctor recommended that, in view of the unexpected ongoing effectiveness of my Vidaza treatments, I not proceed with a transplant until the treatments are no longer effective. Given the various risks associated with the transplant procedure and the fact that the prospect of a cure is far from certain, I have happily followed his recommendation, and my journey continues.

# **AML** CORNER

#### AML CORNER: PRESS RELEASES & ANNOUNCEMENTS

Sunesis Pharmaceuticals Presents New Data from VALOR Evaluating Vosaroxin in Older Patients with Acute Myeloid Leukemia at the 20th Congress of the European Hematology Association

JUNE 12, 2015 – San Francisco, California Sunesis Pharmaceuticals, Inc. (Nasdaq: SNSS) announced today additional results of the VALOR trial, a Phase 3 study of vosaroxin and cytarabine in adult patients with relapsed or refractory acute myeloid leukemia (AML). The results are being presented today, Friday, June 12th from 5:15 p.m. to 6:45 p.m. Central European Time at the acute myeloid leukemia (AML) poster session of the 20th Congress of the European Hematology Association (EHA) taking place in Vienna, Austria.

VALOR is a randomized, double-blind, placebo-controlled Phase 3 trial which enrolled 711 adult patients with first relapsed or refractory AML at 124 leading sites in 15 countries. Patients were stratified for age, geographic region and disease status and randomized one to one to receive either vosaroxin and cytarabine or placebo and cytarabine. Detailed results of the VALOR trial were presented in the "Late Breaking Abstracts" session of the American Society of Hematology (ASH) Annual Meeting in December 2014. Data from the post-hoc analysis of VALOR patients age 60 years and older who received allogeneic transplant after treatment with vosaroxin or placebo plus cytarabine were presented at the American Society of Clinical Oncology Annual Meeting in May 2015 and now at the EHA Congress.

Among the new data presented today are detailed results from the subgroups of patients age 60 years and older (451 out of 711 enrolled in VALOR) with late relapse (n=87) and refractory and early relapse disease (combined n=364).

Among patients with late relapse disease, overall survival (OS) and leukemia-free survival (LFS) were comparable between treatment arms. The complete remission (CR) rate was 57% and 28% (p=0.0064) and event-free survival (EFS) was 5.5 months versus 2.3 months (HR=0.65, p=0.0852) for vosaroxin/cytarabine and placebo/cytarabine, respectively. Thirty- and 60-day all-cause mortality among these patients was 11% and 18% versus 2% and 14% for vosaroxin/ cytarabine and placebo/cytarabine, respectively.

Among patients with refractory and early relapse disease (combined n=364), a population known to have poorer outcomes, OS was 6.5 months versus 3.9 months for vosaroxin/cytarabine and placebo/cytarabine, respectively (HR=0.69, p=0.0008). CR rates in this population were 26% and 10% (p=0.0001) for vosaroxin/cytarabine and placebo/cytarabine, respectively. Among

### AN IMPORTANT NEW FEATURE

New data recently presented at the 20th Congress of the European Hematology Association (EHA) on its lead drug candidate for acute myeloid leukemia (AML), vosaroxin. Sunesis recently completed a global Phase 3 trial with more than 700 AML patients with relapsed or refractory disease where vosaroxin was evaluated in combination with cytarabine. This combination demonstrated a potential benefit in patients with the poorest expected outcomes — those over 60 years old, and in particular those over 60 with refractory or early relapse disease.

Roughly 30% of the patients diagnosed with MDS will progress to AML, one of the most deadliest of cancers for older adults. While there have been improvements in supportive care and transplantation, it has been nearly 40 years since there has been a new treatment available for these patients. This is why investigational compounds like vosaroxin — an anticancer quinolone derivative (AQD), a class of compounds that has not been used previously for the treatment of cancer — are particularly important.

these patients, LFS was 9.7 months versus 5.5 months (HR=0.50, p=0.0424) and EFS was 1.7 months versus 1.3 months (HR= 0.59, p<0.0001) for vosaroxin/cytarabine and placebo/cytarabine, respectively. Thirty- and 60-day all-cause mortality among these patients was comparable, at 10% and 21% versus 11% and 25% for vosaroxin/ cytarabine and placebo/cytarabine, respectively.

In all patients age 60 years and older, Grade 3 or higher non-hematologic adverse events that were more common in the vosaroxin combination arm were gastrointestinal and myelosuppressionrelated toxicities, consistent with those observed in previous company trials. The rate of serious adverse events related to treatment was 74% and 60% for vosaroxin/cytarabine and placebo/ cytarabine, respectively.

"AML is a disease that primarily affects older patients, and clinical outcomes among these patients is abysmal," said Farhad Ravandi, M.D., Professor of Medicine, Department of Leukemia, University of Texas MD Anderson Cancer Center, and a principal investigator of the VALOR study. "These patients have had few options outside of clinical trial enrollment. Results from the analyses presented today show compelling survival and durable responses with comparable early mortality for the vosaroxin and cytarabine treatment arm in the older refractory and early relapse patients. Given these results, I believe vosaroxin represents an important new treatment option."

"In over four decades of research, there has been far too little progress in the treatment of AML," said Patricia J. Goldsmith, CEO of CancerCare®. "This need is particularly pronounced in those patients age 60 and older with the fewest options. Progress for these patients cannot wait."

The two poster presentations (Abstracts #4192 and #4693, Hall C), titled "Improved survival in patients  $\geq$ 60 with first relapsed/refractory acute myeloid leukemia treated with vosaroxin plus cytarabine vs placebo plus cytarabine: results from the Phase 3 VALOR study" and "Allogeneic transplant in patients  $\geq$ 60 years of age with first relapsed or refractory acute myeloid leukemia after treatment with vosaroxin or placebo plus cytarabine: results from VALOR," will be available on the Sunesis website at www.sunesis.com.

#### About QINPREZO<sup>™</sup> (vosaroxin)

QINPREZO<sup>™</sup> (vosaroxin) is an anti-cancer quinolone derivative (AQD), a class of compounds that has not been used previously for the treatment of cancer. Preclinical data demonstrate that vosaroxin both intercalates DNA and inhibits topoisomerase II, resulting in replicationdependent, site-selective DNA damage, G2 arrest and apoptosis. Both the U.S. Food and Drug Administration (FDA) and European Commission have granted orphan drug designation to vosaroxin for the treatment of AML. Additionally, vosaroxin has been granted fast track designation by the FDA for the potential treatment of relapsed or refractory AML in combination with cytarabine. Vosaroxin is an investigational drug that has not been approved for use in any jurisdiction.

The trademark name QINPREZO is conditionally accepted by the FDA and the EMA as the proprietary name for the vosaroxin drug product candidate.

#### About AML

AML is a rapidly progressing cancer of the blood characterized by the uncontrolled proliferation of immature blast cells in the bone marrow. The American Cancer Society estimates that there will be approximately 20,830 new cases of AML and approximately 10,460 deaths from AML in the U.S. in 2015. Additionally, it is estimated that the prevalence of AML across major global markets (U.S., France, Germany, Italy, Spain, United Kingdom and Japan) is over 75,000. AML is generally a disease of older adults, and the median age of a patient diagnosed with AML

#### AML CORNER: PRESS RELEASES & ANNOUNCEMENTS

is about 67 years. AML patients with relapsed or refractory disease and newly diagnosed AML patients over 60 years of age with poor prognostic risk factors typically die within one year, resulting in an acute need for new treatment options for these patients.

To view the complete press release go to: http://ir.sunesis.com/phoenix.zhtml?c=194116&p =irol-newsArticle print&ID=2058835

#### Celgene's Vidaza® (Azacitidine For Injection) Approved By The European Commission As New Treatment For Elderly Patients With Acute Myeloid Leukaemia

Expanded indication brings medicine to greater number of elderly AML patients who are not eligible for haematopoietic stem cell transplantation and have >30% myeloblasts in their bone marrow.

#### **OCTOBER 30, 2015** – Boudry, Switzerland

Celgene International Sàrl, a wholly owned subsidiary of Celgene Corporation (NASDAQ: CELG) today announced that the European Commission (EC) has approved VIDAZA® (azacitidine for injection) for the treatment of adult patients aged 65 years or older with acute myeloid leukaemia (AML) who are not eligible for haematopoietic stem cell transplantation (HSCT). The VIDAZA Marketing Authorisation has been updated to include this new indication in AML, covering patients who have >30% myeloblasts according to the WHO classification; previously, the indication covered AML patients with <30% blasts. Myeloblasts are white cells in the bone marrow; in AML, their functioning is disrupted and results in numerous non-functioning white cells, which can potentially interfere with the body's ability to control infections and can lead to anaemia and haemorrhages.

For many patients, AML is typically associated with a poor prognosis particularly for those patients who cannot tolerate potentially curative therapies like stem cell transplantation. In Europe, more than 14,000 people suffer from AML, and most of these patients will die within less than one year. As an acute leukaemia, AML progresses rapidly and is typically fatal within months if stem cell transplantation is not an option. In elderly patients ( >65 years), overall survival with AML has not improved in more than 40 years, and there is a clear need for treatments that can support this patient population.

"Today's announcement brings hope to patients with AML, particularly the elderly and more frail patients who cannot undergo intensive therapies such as stem cell transplantation," said Hervé Dombret, M.D., Chief, Blood Disease Department (Leukaemia Unit), University Hospital Saint-Louis, AP-HP, Paris, France. "Azacitidine has demonstrated a median overall survival of 10.4 months in these patients, which is a clinically relevant benefit and gives us a new treatment option in a previously underserved group of patients."

Adds Tuomo Pätsi, President of Celgene in Europe, Middle East and Africa (EMEA): "Celgene is committed to bringing innovative medicines to patients with haematological diseases including AML. The approval of VIDAZA in this segment of AML patients now gives us a new opportunity to help these patients and underscores our commitment to delivering medicines that can have a significant impact on patients with severe and debilitating diseases. Our next step will be to work with each of the member countries to provide access to VIDAZA in this indication, ensuring that patients who can benefit from its use have the opportunity to do so."

The EC decision is based on data from AML-001, a global, multi-centre, randomized, openlabel pivotal study of patients at least 65 years old with newly diagnosed or secondary AML with >30% bone marrow blasts. VIDAZA plus best supportive care (n=241) was compared with conventional care regimens (n=247). Median overall survival (OS), the primary endpoint of the study, was 10.4 months (95% CI 8.0-12.7 months) for patients receiving azacitidine compared with 6.5 months (95% CI: 5.0-8.6) for patients receiving conventional treatment regimens (HR=0.85 [95% CI 0.69, 1.03], stratified log-rank p=0.1009). One-year survival rates with azacitidine and conventional treatment regimens were 46.5% and 34.2%, respectively (difference 12.3% [95% CI: 3.5%-21%]).

In the study, grade 3–4 anaemia, neutropenia, febrile neutropenia, and thrombocytopenia rates, respectively, were 16%, 26%, 28%, and 24% with azacitidine; 5%, 5%, 28%, 5% with best supportive care; 23%, 25%, 30%, 28% with low-dose Ara-Cytarabine; and 14%, 33%, 31%, 21% with intensive chemotherapy.

The EC decision for the use of VIDAZA in adult patients with AML who are not eligible for HSCT follows the positive opinion issued by the Committee for Medicinal Products for Human Use (CHMP) in September 2015. Additionally, because this new therapeutic indication brings significant clinical benefit in comparison with existing therapies as determined through the Regulatory Review process, VIDAZA will receive extended market protection in all its indications for an additional year throughout the European Economic Area.

Today's approval marks the fourth new product or extension of the indication approved by the EC in the EU for Celgene in 2015.

In the United States, VIDAZA is not indicated for treatment of patients with AML. VIDAZA is indicated for treatment of patients with the following French-American-British (FAB) myelodysplastic syndromes subtypes: refractory anaemia (RA) or refractory anaemia with ringed sideroblasts (RARS) (if accompanied by neutropenia or thrombocytopenia or requiring transfusions), refractory anaemia with excess blasts (RAEB), refractory anaemia with excess blasts in transformation (RAEB-T), and chronic myelomonocytic leukemia (CMMoL).

To view the complete press release go to: http://ir.celgene.com/releasedetail.cfm?ReleaseID =939462

#### **NEW CLINICAL STUDY ANNOUNCEMENT**

Azacitidine with/without Glasdegib (PF-04449913) in first line intermediate to high-risk MDS, AML and CMML Patients

#### Now Enrolling: NCT02367456

Pfizer is conducting a clinical study to determine the safety, efficacy, PK and PD of Glasdegib (PF-04449913) or placebo when combined with azacitidine in patients with previously untreated Intermediate-2 or High-Risk Myelodysplastic Syndromes (MDS), Acute Myeloid Leukemia (AML) with 20–30% blasts and multi-lineage dysplasia, or Chronic Myelomonocytic Leukemia (CMML). This study is being conducted at multiple hospitals and institutions around the world and includes two components: (a) a Phase 1b open -label safety lead in component and (b) a Phase 2 randomized double-blind component. In the Phase 1b component, approximately 10 patients will be enrolled and will receive Glasdegib (PF-04449913) and azacitidine and in the Phase 2 component, 160 patients will be randomized to receive to receive either Glasdegib (PF-04449913) (Arm A) or placebo (Arm B) in combination with azacitidine.

If you are a physician or health care provider and would like to refer a patient for enrollment into this clinical trial OR if you are an MDS, AML, or CMML patient please see additional information and contact details at the following websites:

https://clinicaltrials.gov/ct2/show/NCT02367456

https://trialinfoemail.pfizer.com/pages/landing.aspx?StudyID=B1371012&StudyName=A%20STUDY %200F%20PF%2004449913%20IN%20COMBINATION%20WITH%20AZACITIDINE%20IN%20 PATIENTS%20WITH%20PREVIOUSLY%20UNTREATED%20INTERMEDIATE%202%20OR%20 HIGH%20RISK%20MYELODYSPLASTIC



An MDS/AML Prospective Observational Study

# Connect<sup>®</sup> MDS and AML: The Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML) Disease Registry

Celgene is researching the following objectives in MDS and AML patient populations:

- Current and evolving patterns for diagnosing, treating, and monitoring patients
- Outcome measures
- How routine practice compares to national treatment guidelines
- Treatment patterns and outcomes in patients with del(5q), with or without additional cytogenetic abnormalities
- Association of patient characteristics, treatment regimens and clinical outcomes with patientreported Health Related Quality of Life (HRQoL) and economic outcomes
- Clinical outcomes based on treatment in patients with or without mutations
- Correlation between mutation detection/allele burden in bone marrow and peripheral blood samples
- Molecular and/or cellular marker's relation to prognostic classification, drug mechanism of action and clinical and treatment outcomes

#### Select eligibility criteria:

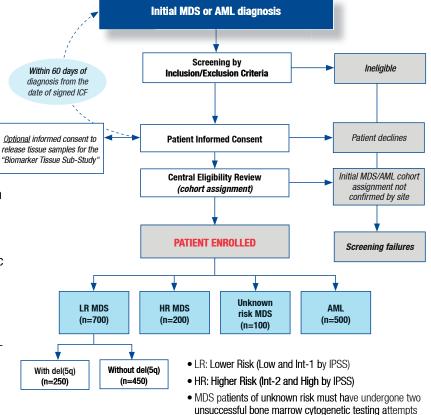
- Will diagnosed,\* primary or secondary MDS or AML
- MDS patients must be at least 18 years
- AML patients must be at least 55 years of age
- Patients must be willing and able to complete enrollment and follow-up HRQoL instruments, for which patients must be proficient in either English or Spanish

\*To be considered "newly diagnosed," a patient's confirmed diagnosis must be made up to 60 days prior to the date of ICF signature.

Note: Concomitant patient enrollment in other studies is permitted.

#### Physicians - you could be an Investigator if:

- When the supports clinical trials
- Your site sees at least 2 suspected MDS or AML patients per quarter



APL diagnosis is excluded.

To learn more about this MDS/AML Disease Registry Study, contact: connectmdsaml-registry@celgene.com (ClinicalTrials.gov Identifier: NCT01688011)



#### **AML CORNER: PATIENT STORIES**

# MDS: 18 Years Later...

### Andrea Lacey United Kingdom

In 2004, I wrote an article for this newsletter to provide an outline of my story and to say how I was doing 10 years on from my diagnosis of MDS with RAEB-t. I thought you might be interested in reading my story a further 11 years on!

Firstly, I'll provide a brief summary of my MDS story which began in January 1994 following a routine medical when my doctor identified I had anaemia. Following numerous blood tests which culminated in several bone marrow tests, my diagnosis was made and I began treatment as soon as it was confirmed my brother, Rob, was a suitable donor. My only option was a bone marrow transplant, and I was so fortunate Rob's bone marrow was compatible.

Following the transplant in October 1994, we duly waited the 100 days, only to find out it hadn't been successful and this is when things started to become really messy. My consultant was absolutely amazing and we reached an agreement that whilst I continued to breath, he would continue to treat me! In reality though, we both knew the options weren't great. Fairly quickly my MDS returned and we spent 1995 trying different treatments to keep me going. By the end of the year, the MDS had moved into acute myeloid leukaemia. I'd started my journey with a 40% chance of the treatment working and this had dipped to an estimated 5%. Short of doing nothing, or just having more chemo, my consultant suggested a completely new treatment called donor lymphocyte infusion. To the best of my knowledge this treatment had been tried once previously, and without a positive outcome. It didn't work for me the first time either, but after another two large doses of chemotherapy, it finally did the trick. By now it was February 1997, and I was well and truly ready to get on with my life again!

In the early years following treatment I had to take care to protect myself from



Photo taken in Yorkshire shortly after Andrea's diagnosis, April 1994

bugs and colds while I gave my body the chance to build up my immune system. I was warned to avoid chicken pox, but managed to pick it up within the first year. I was very lucky because it didn't cause me too many problems. There were a few other side effects, but nothing that couldn't and hasn't been managed.

Since my last article, I have kept fairly well and there have been no relapses of MDS or AML. When my consultant told me to get on with my life and only to return and see him if I felt unwell, I took him at his word! I returned just once for a bone marrow test because I felt unwell. Fortunately the results came back clear. Overall, I'm active, continue to work at the university and have just gotten on with enjoying life. More recently though, a few things have happened and these are what have prompted me to revisit MDS and leukaemia again.

Over the years, I rarely looked back on those times. It wasn't that I was blasé about it; I just found it all too painful. This changed a couple of years ago however, when an old school friend was diagnosed with leukaemia. I hadn't seen him for years, but when I heard he was ill I contacted him through Facebook. It was then that I managed to open my 'Pandora's box' of keepsakes from my MDS/AML experience. To see if there was anything in there that might be of use to him, and to remind myself of what it had really been like so that I could be of better support to him and his wife.

At this point, I had no idea that within a matter of months, I would be diagnosed with breast cancer! I had my first operation in April 2014, and started chemo at the end of May. Well, if I wished to be reminded of the experience of chemo, I no longer needed 'Pandora's box'! The memories soon came flooding back. My consultant was very mindful of my previous treatments and consulted a professor specialist before tailoring my chemo. I was also able to have more radiotherapy, and was something of a (vintage!) curio in the radiotherapy department because of all the total body irradiation I had received all those years ago.

I think my point for mentioning this is that even if you have already had heavy doses of chemotherapy and radiotherapy, it is possible to have more. I won't pretend it was a bed of roses, but now that it is over, I am very much hoping this will be my last liaison with cancer. I am now back at work, continuing to enjoy life and am looking forward to my next era – I'm 50 now!

My friend has since found out that his bone marrow transplant was unsuccessful, but he remains very upbeat and positive about his future.



Andrea ringing the bell after her final chemotherapy in June 2015.

#### **AML CORNER: PATIENT STORIES**

# Making A Difference...

### Susan Tonry *Windsor, New Jersey*

When I was asked to write an article for this newsletter, my immediate reaction was yes, of course! This reaction was primarily based on a good friend who came into my life at a very difficult time for both of us. She had MDS. I had Acute Myeloid Leukemia. We were both headed for bone marrow transplants as a last resort for a cure. We became each other's support and shared information on the different protocols our chosen hospitals were planning for transplant. Marian was just one of the special patient friends I got to know in the three years of treatment that followed for us. Although we had different diseases we shared many of the same experiences in and out of the hospital. Here is my story ...

It was January 27, 2009 when I received news that would forever change my life. I was a 39 year old full-time working mother of three. I'd spent the past 18 years blazing a successful career path in the world of finance and accounting while raising my three children, and I was TIRED. More than tired, I was completely exhausted and could barely get up and dressed without extreme effort and shortness of breath. I remember wiping down the bathroom counter and having to lie down in bed for fear of passing out. This was highly unusual, as all my life I was very active and lived a healthy lifestyle. I thought perhaps I had Mono or Lyme's disease; things that would typically be related to extreme fatigue. Still I gave it my all and went to work every day because as all working moms can relate; you save your days for when your kids need you. Then that fateful morning I dragged myself into work, contemplating on the way if I should turn around and go home or head to an emergency room. I decided to go to work since it was closest at that moment.

When I arrived, there was a phone call from a doctor I'd never met who held my



blood tests done the day prior by my local family physician. He told me straight up that he believed I had leukemia and I needed to get transported to the hospital immediately. It was urgent and I was not to drive, as I was severely anemic and needed a blood transfusion and a bone marrow biopsy upon arrival. A bed was reserved for me before I even received a call and he told me to pack a bag for three days and he would know for sure by then. Three days turned into 32 days, and chemotherapy began that night.

For the next three years I battled AML; starting with the idea that since I was young and healthy that five months of chemotherapy combined with blood and platelet transfusions may just kick it. I would come to find out that these things weren't enough, and a relapse several months later brought me the news of requiring a bone marrow transplant.

I enjoyed those months in between though, believing I was cured. I took up a craft I always wanted to learn during those recovery months before I planned to go back to work. I'd spent the better part of 20 years in the financial markets, first in Mutual Funds then in Public Finance for healthcare facilities. I only took time off work if the kids needed me; I believed in putting my all into my career and then doubling back home and putting my all into being the best mother and wife as well leaving absolutely no time for myself anywhere in the picture. I took two quilting classes and I was hooked. I declared a goal of creating 40 quilts to celebrate turning 40 to give to my fellow patients suffering as I had in the hospital with long inpatient hospital stays away from family and friends. I wanted to give them hope and comfort in the only way I could and through my new therapy, quilting. I accomplished this goal, and then some, and delivered 60 quilts to the patients that December. (Marian was one of the first recipients.) The same day I received the news that my leukemia was back. It was devastating to hear the news, and that I would require a marrow donor match to survive. They would start looking. Fortunately, a donor match was found quickly and preparation began for a transplant two months later. Again, I thought I dodged a bullet



#### AML CORNER: PATIENT STORIES

recovering nicely over the next several months until relapse after relapse sent me home in 2011 with the expectation of death in a week. Obviously I did not pass or I wouldn't be writing this article today. The doctors couldn't explain my recovery with science and believe my faith was a driving factor. It was a long and hard recovery. I was completely disabled, unable to move my body or swallow, but I hung on and prayed for the future of my children.

Once I began to turn around, I didn't know how long it was going to last given my track record of relapses so I decided 'forget going back to work;' I have to spend the rest of my time here on earth with my children and doing for others. This is what is important and what I am supposed to be doing with my life. Otherwise, why did I survive once again? I have to spend the rest of my time here on earth with my children and doing for others. This is what is important and what I am supposed to be doing with my life.

This propelled me to learn everything I could about building a non-profit charity that could benefit other blood cancer patients and their families by providing hope and comfort in the long inpatient treatments and cold sterile conditions required for the safety of immune-compromised patients.



### www.quiltsforcomfort.org



#### AML CORNER: A PEDIATRIC STORY

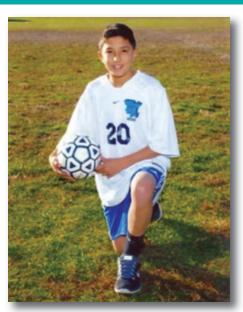
# A Mother's World with a Teen Diagnosed with Pediatric MDS

Jennifer Vargas Hopewell Junction, New York

#### 13 and Unaware of MDS

Ramiro was an active 13 year old playing soccer, basketball and lacrosse. During the spring of 2013, I noticed increased bruising after practices and games. As a concerned mother, I worried it could be "leukemia" but was told the bruising was related to the sports. Only unexplained bruising was a concern.

In August 2013, I took Ramiro for his annual physical. I expected to hear I had a healthy young boy, as I did every year. But this year I would receive a phone call that Ramiro's blood counts were abnormal. Our pediatrician told me that it might be a lab error and not to worry. Ramiro seemed healthy to me so I didn't worry, and thought it probably was a lab error. Ramiro returned the next day for repeat lab work.



Unfortunately, the blood counts were still not in a normal range and actually decreased. The pediatrician explained to me what was going on with Ramiro's blood. To be honest, I didn't hear anything he said. All I heard was "wah-wah" like in Charlie Brown. I just wanted to know, "Does Ramiro have leukemia?" When I asked the pediatrician he answered, "This is not my specialty, and I will need to refer you to a hematologist/oncologist". I did not know what to think. I didn't want to think the worst but couldn't help it. Deep down my husband and I were hoping whatever was wrong could be corrected with medication or even a vitamin.

## Frequent Visits to the Hematologist/Oncologist – The Beginning of Our "New Normal"

During our 1st visit with the hematologist/ oncologist, the doctor told us that Ramiro's blood report did not match his physical appearance. He continued to say Ramiro was a picture perfect healthy looking boy. We agreed, so why the abnormal blood count? He asked us a series of questions such as; any unexplained fevers? Joint pain? Bloody noses? Bruising? We answered "yes" to bruising and told him we noticed an increase during sports last spring. Ramiro was playing on 2 soccer teams at this time so he had some bruises to show the doctor. But the doctor didn't seem too alarmed because the bruises were

#### AML CORNER: A PEDIATRIC STORY

explainable. "Unexplained bruising" he said was a concern. He decided to monitor Ramiro's blood for a few weeks to see if there were any changes.

Every Monday morning before school, I took Ramiro for a blood draw. Every Tuesday, I received a call that his counts had dropped again and I was asked a series of questions about Ramiro's condition. I would answer "no" to every question. What could be going on that his counts were dropping but yet he had no other symptoms?

In late October the hematologist/ oncologist called to tell me that Ramiro needed to have a bone marrow biopsy. He explained that his blood counts were not recovering and he needed to see if his bone marrow was healthy. I wasn't surprised by this next step but I don't think I really understood the seriousness of what it meant. Ramiro appeared to be an active healthy 13 year old.

The Tuesday before Thanksgiving, I received a call from the hematologist/ oncologist that he had the results of the biopsy but these results could not be shared over the phone, they had to be shared in person. I wanted to ask him to just tell me but I knew he wouldn't. I had peace but tried not to think about it too much until after Thanksgiving.

On December 3, we arrived at the doctor's office and I was so nervous. Ramiro said he was "okay and wasn't worried." Being that we had to meet face to face I knew the news wasn't going to be good, but wasn't sure how bad. I had peace and knew whatever it was we would get through it. The doctor called me and my husband into his office first. In summary, he told us that our 13 year old son had tested positive for Monosomy 7 and had the beginning signs of leukemia. He needed to do another biopsy to determine an accurate diagnosis to get Ramiro the treatments he needed. The next biopsy wouldn't be until early January. In the meantime Ramiro needed to continue with weekly blood draws.

We were told that MDS was very uncommon in children and he would need treatment immediately. He was considered high-risk for developing acute myeloid leukemia (AML) because of the Monosomy 7.

#### **Affected by Pediatric Cancer**

On January 22, 2014, we learned Ramiro had Pediatric MDS and Monosomy 7. We were told that MDS was very uncommon in children and he would need treatment immediately. He was considered high-risk for developing acute myeloid leukemia (AML) because of the Monosomy 7. It wasn't a question of "will he get AML" it was a question of "when". We were also told that the AML that he would develop would be very aggressive and difficult to treat. The only treatment option available to Ramiro was aggressive chemotherapy and a bone marrow transplant. He explained that this was a harsh treatment, and there was the possibility that it may not be successful. My daughter Elena (then 11 years old) was suggested by the doctor as a possible donor. However, he explained to us that there was only a 25% chance she would be a match for her brother, and we would probably have to go to the registry bank.

The thought of a bone marrow transplant was extremely overwhelming. Ramiro would have to stop attending school, stop participating on his various sports teams, stop playing drums on the worship team at his youth group, and live in and out of the hospital for an entire year. Why would my husband and I want to put our child through such an aggressive treatment that may or may not work? Was it really necessary? As soon as we came home from that appointment we knew we needed a second opinion. We wanted to get Ramiro whatever treatment he needed, but we wanted to be sure it was necessary and would make him better and not worse.

#### **Prayers for a Miracle**

I spent many hours in prayer and reading my Bible. I knew God knew everything and would lead us through this process. At the same time, I knew He had the power to heal my son so I desperately prayed for complete healing. As I was seeking God for direction, I spent a lot of time googling Pediatric MDS and Monosomy 7. To my disappointment, I found no information on Pediatric MDS. I desperately wanted to hear a success story of another child who overcame Pediatric MDS or find another mother/caregiver of a child I could relate with. The information I did find about MDS found in adults and Monosomy 7 confirmed what the doctor told us. Without the transplant, Ramiro's bone marrow would fail and he would develop AML. More and more I realized he needed a bone marrow transplant. But I needed to know for sure his diagnosis was correct and he would receive the best care with his diagnosis.



#### AML CORNER: A PEDIATRIC STORY

### God Leads Us to a Center of Excellence for a Second Opinion

God led us to Dana Farber Cancer Institute/Boston Children's Hospital for a second opinion. The initial draw was that they had high success rates for bone marrow transplants in pediatric patients. We also learned they are an MDS Center of Excellence and specialize in pediatric MDS. We were so thankful this door was opened for us. We met with Dr. Inga Hofmann and she thoroughly explained pediatric MDS and Monosomy 7. She performed Ramiro's third bone marrow biopsy to confirm his diagnosis and no existence of leukemia cells. During the biopsy I took Elena for a blood draw to see if she was a match for her brother. Hours later his diagnosis of MDS and Monosomy 7 was confirmed and no leukemia was found. A few days later Dr. Hofmann called to tell me that Elena was not only a match, but a 100% perfect match for her older brother. We knew without a doubt Ramiro was to receive treatment and his bone marrow transplant with Dana Farber Cancer Institute at Boston Children's Hospital (BCH).

#### 6 Weeks in the Hospital

My husband and I both took leaves from our teaching positions and our family of four moved to Boston for Ramiro's care. Ramiro was admitted into BCH on April 13, 2014 to have a central line inserted and to begin aggressive rounds of chemotherapy. I lived at the hospital with Ramiro 24/7. It was important for him to know that I would be his voice when necessary and to





After his transplant, Ramiro's energy level increased substantially... He was full of faith and determined to be healed and fully recovered from this life threatening diagnosis.

make sure he was comfortable. Although Ramiro needed these treatments, he made it very clear to me that he did not want to be held back with school and sports. The child specialist at the hospital arranged for Ramiro to be tutored while in Boston. Every day I would wake Ramiro for his tutoring session so he could complete the 8th grade on time. I would feel bad waking him up at 11 am for tutoring because in the midst of everything, school was not the priority. But Ramiro would remind me that he wanted to finish the 8th grade so he could start high school with his class. To keep Ramiro physically active, we began walking the halls of the Stem Cell Transplant Unit. After a week of walking during chemo, Ramiro began to track our walks learning he was walking a mile a day. As long as he felt good we kept our afternoon walks part of our daily routine. In between rounds, treatments and our

walks in the unit, I would tutor Elena at the hospital so she would finish the 6th grade on time with her class.

To keep Ramiro's spirits high while in the hospital, I made many of the routine things we did at home a part of our hospital ritual. We would eat dinner together around the small hospital table in his room. The evening would be full of laughs as we would play a board game, Heads Up or Wheel of Fortune together. On the weekends, we would gather around Ramiro's bed and watch a family movie together.

On April 24, 2014, Ramiro received his 100% perfect matched bone marrow from his younger sister Elena. He went through chemo and transplant with minimal side effects and no complications. After his transplant, Ramiro's energy level increased substantially. He increased his daily walk to 3 miles sometimes and began walking in the evenings for a total of 32+ miles while inpatient. He was full of faith and determined to be fully recovered from this life threatening diagnosis.

On May 25, 2014, Ramiro engrafted and was discharged as an outpatient. We stayed at the Ronald McDonald House in Boston for an additional 4 weeks before we were able to return home in New York.



#### AML CORNER: A PEDIATRIC STORY

#### **Our New Normal at Home**

After transplant, Ramiro basically had no immune system. We were told if he was to become sick he would need to be admitted back into the hospital. Our family had to prepare to live in isolation for an estimated 9 months until all restrictions were lifted. No family and friends were permitted to visit with us inside our home nor were we able to visit them in their homes. Ramiro could not go to the movies, mall, church, friend's house, school or any other public place during this time. Ramiro was able to visit with healthy friends and family outside during the summer and most of the fall.

I woke up early every morning and disinfected everything within our home. Regularly I went to our local grocer to purchase local fruits and vegetables. Ramiro was on a restricted diet and had to have his food specifically prepared fresh for him. As a family we followed every instruction given to us to the best of our ability. On August 2, 2014, Ramiro reached transplant day +100 with no side effects, complications or being readmitted back into the hospital.

#### **Need for Pediatric MDS Support**

It was so nice to have our comforts of home again but I began to feel lonely. I missed being around other mothers and families that understood what we were going through. Living at the Ronald McDonald House was tight for our family of 4 but I did like that when we were outside we ran into other families we could relate to.

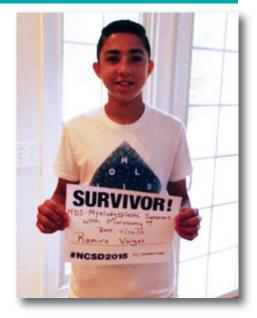
I researched the internet for support available to Pediatric MDS families but had no success. While everyone around us returned to their normal routines of work and school, our family lived a life of isolation for several more months. I had to continue my leave from my job to care for Ramiro. He needed home tutoring as he was unable to attend school due to his compromised immune system and needed numerous medications throughout the day. Ramiro and I kept ourselves busy journaling this miracle we were living, baking and taking many walks. On January 1, 2015, all of Ramiro's restrictions were lifted and slowly he was able to resume all his activities before diagnosis.

With each passing month, Ramiro and I discussed how important it was for us to support and help other families in the same situation. As a first step in providing support, I have started a Facebook page for Families of Pediatric MDS.



With each passing month, Ramiro and I discussed how important it was for us to support and help other families in the same situation. As a first step in providing support, I have started a Facebook page for Families of Pediatric MDS.

https://www.facebook.com/ Familiesofpediatricmds



#### Healed of MDS and Monosomy 7

On May 29, 2015, we learned Ramiro was officially cleared of MDS and Monosomy 7.

His blood will be checked in 6 months and a thorough screening would be done again in 1 year. Ramiro is now 15 years old and is looking forward to starting his sophomore year of high school with his class in September. He has returned to soccer and is currently training to rebuild his strength to join the high school soccer team. We are so thankful to God for protecting and healing Ramiro. We are thankful to Dr. Inga Hofmann for her dedication to Pediatric MDS research and the awesome care Ramiro received from every doctor, nurse and child life specialist at Dana Farber Cancer Institute/Boston Children's Hospital. A special thank you to the MDS Foundation for providing grants for research and helping raise awareness of MDS.



# **MDS** CENTERS OF EXCELLENCE



Would you like your treatment center to become part of the referral system for MDS patients and be designated as a Center of Excellence?

To be recognized as a Center of Excellence, an institution must have the following:

- An established university (or equivalent) program
- Recognized morphologic expertise in MDS
- Available cytogenetics and/or molecular genetics
- Ongoing research, including Institutional Review

Please contact the Foundation for further information and an application form for your center. The following centers have qualified as MDS Centers of Excellence:

Svlvester Comprehensive Cancer Center,

University of Florida Shands Hospital

**Emory Winship Cancer Institute** 

Emory University School of Medicine

The Blood and Marrow Transplant

Cardinal Bernardin Cancer Center

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Center of Northwestern University

**Rush University Medical Center** 

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Our Professional Members are recognized on our MDS Foundation website as well as in our printed newsletters. Professional members also enjoy discounted registration rates at our biennial International Symposia, as well as a discounted subscription rate to Leukemia Research. In addition, membership fees help to support educational programs, events, research and advocacy efforts.

To join the MDS Foundation and help us fulfill our mission of moving closer to a cure for MDS, please visit our website at http://www.mds-foundation.org/professional-annual-membership-application.

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# Support the MDSF!



Please make a tax-deductible donation today. Kindly use the enclosed donation envelope or go to **www.mds-foundation.org** to make your donation.



Please think of the MDS Foundation in your holiday giving this year and help people LIVING with MDS.

THANK YOU FOR YOUR CONTINUED SUPPORT!

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Honor or memorialize your loved one at: www.mds.foundation.org/donate or contact us at 800-MDS-0839 (within US), 609-298-1035 (Outside US).

# SPECIAL ANNOUNCEMENT



MY FIRST CHRISTMAS THE MOVIE RAISING MDS AWARENESS IS NOW MY FIRST MIRACLE!!

LOOK FOR MORE NEWS AS WE GET CLOSER TO THE MOVIE'S RELEASE DATE NOW SLATED FOR JANUARY 2016.



At 17 years old, Angelica suffers from Myelodysplastic Syndromes (MDS) and receives regular chemotherapy as treatment. With her parents struggling with cancelled health insurance and her health declining, Angelica's life depends on a bone marrow transplant. The search for such a donor is exceedingly difficult, however she needs a multiracial donor, making the search nearly impossible. Despite her severe condition, she finds friendship and love in 17 year old homeless runaway Sean. Together they witness a miracle proving that God works in mysterious ways. In this heartwarming Christmas film, Angelica will ultimately experience a love deeper than she could have ever expected.

# A CHRISTMAS MOVIE ABOUT LOVE, FAITH, FAMILY, AND DEALING WITH MDS















Quinton Aaron

Sean Patrick Flanery

erie Cruz Matthew Rauch

Jeremy London

Juan Castano

We are thrilled to be in partnership with the MDS Foundation, to whom we are donating 5% of this campaign's donations, and 5% of the film's proceeds! http://www.yaleproductions.com/my-first-miracle.html

Get YOUR digital download or Pre-Release DVD today!



Vist us on Facebook: MyFirstMiracle



# **INSPIRE** (INternational Study of Phase III Intravenous RigosErtib)

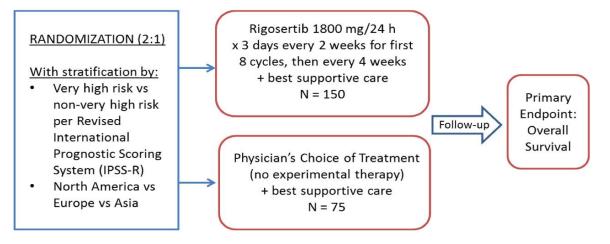
Currently recruiting patients with myelodysplastic syndromes (MDS) progressing during, failing to respond to, relapsing after, or intolerant to Vidaza<sup>®</sup> (azacitidine) or Dacogen<sup>®</sup> (decitabine).

# **STUDY DESCRIPTION**

Phase III, randomized, controlled study of rigosertib (ON 01910.Na) vs physician's choice of treatment in patients with myelodysplastic syndromes (MDS) after failure of azacitidine or decitabine. Patients in both arms will be monitored closely throughout the trial and hospital stays are not required.

ENDPOINTS	KEY INCLUSION CRITERIA	KEY EXCLUSION CRITERIA
<ul> <li>Primary</li> <li>Overall survival (OS) in the ITT population</li> </ul>	<ul> <li>MDS classified as RAEB-1, RAEB-2, or RAEB-t</li> <li>Progression, failure to respond to,</li> </ul>	<ul> <li>Eligible for induction chemotherapy or allogeneic stem cell transplantation</li> <li>Treatment with any investigational therapy, cytarabine at any dose, lenalidomide, or any other therapy targeted to the treatment of MDS (other than growth factors and other supportive care measures) within 4 weeks of planned randomization</li> </ul>
<ul> <li>OS among pts with very high risk per the Revised International Prognostic</li> </ul>	intolerance to, or relapse following azacitidine (AZA) or decitabine (DEC)	
Scoring System (IPSS-R) Secondary	<ul> <li>At least one cytopenia</li> <li>Duration of prior HMA therapy</li> <li>≤ 9 months</li> </ul>	
<ul> <li>OS among pts with monosomy 7 or trisomy 8 chromosomal abnormalities</li> <li>Objective response per IWG</li> </ul>	<ul> <li>Last dose of AZA or DEC within</li> <li>6 months of randomization</li> </ul>	
<ul><li>Bone marrow blast response</li><li>Hematologic improvement</li></ul>	<ul><li>&lt; 80 years of age</li><li>ECOG performance status of 0-2</li></ul>	
Pharmacokinetics		<ul> <li>Other active malignancy</li> </ul>

# **STUDY SCHEMA**



For additional information on this study, please call the INSPIRE help line at 1-267-759-3676 or visit www.clinicaltrials.gov, identifier: NCT02562443



www.onconova.com

# **NOW ENROLLING**



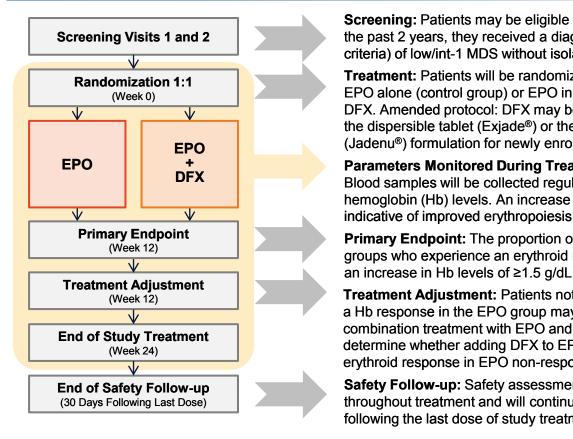
### Overview

KALLISTO is an open-label, Phase II, pilot study of deferasirox (DFX) and erythropoietin (EPO) versus EPO alone in patients with lower-risk myelodysplastic syndromes (MDS).

EPO is a hormone that stimulates red blood cell production (erythropoiesis) in the bone marrow. Treatment with EPO can increase healthy blood cell counts in patients with MDS. DFX - an orally-administered iron chelator may act synergistically with EPO to increase the production of healthy red blood cells.

The objective of KALLISTO is to test whether this potential synergy of DFX and EPO (versus EPO alone) improves erythropoiesis in patients with lower-risk MDS (low/int-1 per International Prognostic Scoring System [IPSS] criteria).

# Study Schedule



Screening: Patients may be eligible for inclusion if, within the past 2 years, they received a diagnosis (per IPSS criteria) of low/int-1 MDS without isolated del(5g)

Treatment: Patients will be randomized to receive either EPO alone (control group) or EPO in combination with DFX. Amended protocol: DFX may be dosed using either the dispersible tablet (Exjade®) or the film-coated tablet (Jadenu®) formulation for newly enrolled patients

**Parameters Monitored During Treatment:** Blood samples will be collected regularly to assess hemoglobin (Hb) levels. An increase in Hb levels is

**Primary Endpoint:** The proportion of patients in both groups who experience an erythroid response (defined as an increase in Hb levels of  $\geq 1.5$  g/dL)

Treatment Adjustment: Patients not demonstrating a Hb response in the EPO group may switch to combination treatment with EPO and DFX. This will help determine whether adding DFX to EPO improves the erythroid response in EPO non-responders

Safety Follow-up: Safety assessments will occur throughout treatment and will continue for 30 days following the last dose of study treatment

To learn more about KALLISTO, call Novartis Pharmaceuticals (1-888-669-6682) or contact your local Novartis Medical Science Liaison (ClinicalTrials.gov Identifier: NCT01868477)



Novartis Pharmaceuticals Corporation East Hanover, New Jersey 07936-1080

# HAVE YOU OR SOMEONE YOU KNOW BEEN DIAGNOSED WITH MYELODYSPLASTIC SYNDROMES (MDS)?

# **ANNOUNCING A CLINICAL RESEARCH TRIAL**

# Pharmacokinetic Guided Dose Escalation and Dose Confirmation With Oral Decitabine and Oral CDAi in Patients With MDS

# **ABOUT THE STUDY**

ASTX727 is an oral dose combination investigational drug, of oral decitabine + E7727, an inhibitor of the metabolism of decitabine. Intravenous decitabine is one of the approved drugs by the FDA for this use. The trial is designed to define the doses of both drugs so that the blood levels of decitabine after oral administration look like what is seen with IV decitabine.

# **ELIGIBILITY**

- Ages Eligible for Study: 18 Years and older
- Genders Eligible for Study: Both
- Accepts Healthy Volunteers: No

# **CRITERIA**

### Inclusion Criteria:

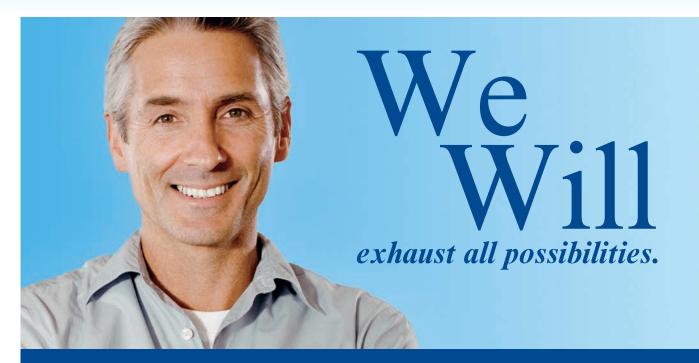
- IPSS low, intermediate -1, intermediate-2, or high-risk MDS (including CMML) in Dose Escalation and Dose Confirmation-Randomization; only intermediate-2, or high-risk MDS in Dose Confirmation-Open Label
- ECOG 0 to 2
- No major surgery within 2 weeks of starting study treatment
- No cytotoxic chemotherapy within 2 weeks of starting study treatment
- Able to swallow pills

### Exclusion Criteria:

- Previous treatment with 2 or more courses of decitabine (all stages) or azacitidine (Dose Confirmation stage only)
- Treatment with investigational therapy within 2 weeks of study treatment
- Uncontrolled medical disease(s) or active, uncontrolled infection
- Diagnosed with AML
- Active uncontrolled gastric or duodenal ulcer
- Known history of HIV or hepatitis C or B

### For more information on this study, visit www.clinicaltrials.gov

### Identifier: ASTX727-01



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Fax: 1-800-822-2496



# Do you have myelodysplastic syndromes (MDS)? You may be eligible for this clinical study

### Announcing the QUAZAR Lower-Risk MDS Study

QUAZAR Lower-Risk MDS is a study for people with MDS who need blood transfusions due to low red blood cell counts (called anemia) and low platelet counts (called thrombocytopenia).

## The QUAZAR MDS Study

#### Treatment

Participants will be randomly assigned by a computer into 2 groups.

One group will be treated with CC-486 (oral azacitidine) plus best supportive care and the other will be treated with placebo (sugar pill) plus best supportive care. The CC-486 Group This group will be given CC-486 along with best supportive care, if needed.

The Placebo Group This group will be treated with placebo and best supportive care, if needed.

#### Disease Status Evaluation

After about 6 months of treatment, your doctor will perform a checkup to see if you are able to continue in the study. If you can continue, your doctor will give you checkups after every 28 days to see how you are doing on treatment.

#### Follow-up

If you stop treatment for any reason, your doctor will follow-up with you to see how you are doing every month for the first year and every 3 months afterward.

### You may qualify for this study if you\*

- · Are age 18 years or older
- · Have been diagnosed with MDS
- · Have low red blood cell counts and are dependent on blood transfusions
- · Have low blood platelet counts

### You may not be eligible for this study if you\*

- · Have had previous stem cell transplants
- Have been treated with VIDAZA<sup>®</sup> (azacitidine for injection) or DACOGEN<sup>®</sup> (decitabine for injection)

\* Additional criteria apply. DACOGEN is a registered trademark of Eisai Inc. and Janssen Pharmaceuticals, Inc. VIDAZA is a registered trademark of Celgene Corporation.

#### For more information about this study

- Call 646-307-8079 or toll-free at 866-743-9791
- E-mail QuazarMDSstudy@emergingmed.com
- Scan the QR code





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# www.mdsdiagnosis.com – a quick overview

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- 7 lessons
- 6 courses
- 8 patient profiles

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- News in the field of MDS
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# INTRODUCTION NEWSLETTER FOR CHINA AND INDIA

# YOU HAVE THE OPPORTUNITY TO GIVE US FEEDBACK

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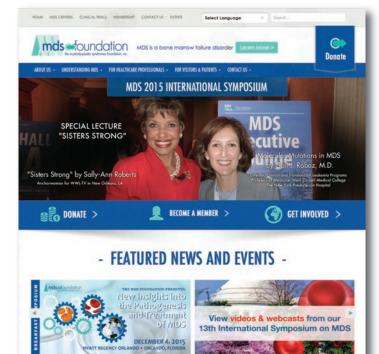
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### **MDS FOUNDATION**

# **CONNECT WITH US!**



# **GET ANSWERS & SUPPORT**

# MDS PATIENT MESSAGE BOARD

Whether you are a patient, spouse, caregiver, family member or friend; newly diagnosed or have lived with myelodysplastic syndromes for years, thanks to the internet we have something for you. The *MDS Message Board* is a discussion site where you



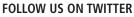
can ask questions, get answers, or give answers.

We hope that you will find this to be a very valuable resource in your journey LIVING with MDS. We have recently revised the format of our forum to be much more user friendly. We are encouraging everyone to go online at http://www.mds-foundation.org/forums/forum/patient-message-board to sign up, browse and join in the discussion!

# www.mds-foundation.org/forums/ forum/patient-message-board



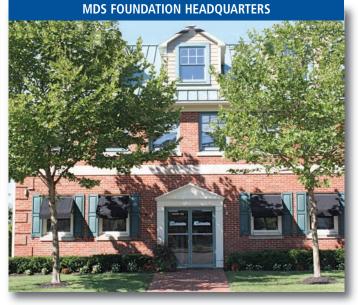
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