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mds news

newsletter of the myelodysplastic syndromes foundation

MDS NEWS HIGHLIGHTS

FROM THE GUEST EDITOR'S DESK

- **The Clinical Impact of Abnormal Gene Expression in MDS**

  Presented by: Andrea Pellagatti, PhD and Jacqueline Boultwood, PhD

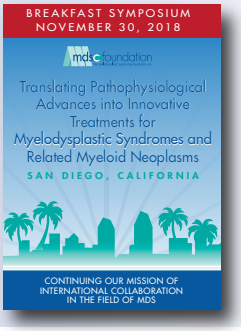
PLAN TO ATTEND OUR UPCOMING SYMPOSIA

2018 ASH BREAKFAST MDS FOUNDATION SYMPOSIUM

November 30, 2018 • San Diego, CA

15TH INTERNATIONAL SYMPOSIUM ON MYELODYSPLASTIC SYNDROMES

May 8–11, 2019
Copenhagen, Denmark



IN THIS ISSUE

GUEST EDITORIAL

Guest Editorial – The Clinical Impact of Abnormal Gene Expression in MDS

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The myelodysplastic syndromes (MDS) are a group of clonal hematopoietic stem cell (HSC) malignancies characterized by ineffective hematopoiesis leading to peripheral blood cytopenias, and patients show an increasing number of blasts in the bone marrow as the disease progresses.[1-2] The disease course and prognosis of MDS patients are highly variable, and approximately 30–40% of MDS cases progress to acute myeloid leukemia (AML).[2-3] It is important to determine the prognosis of MDS patients, since the treatment options range from supportive care to bone marrow transplantation.

Several prognostic scoring systems and risk models have been proposed for MDS[4], including the International Prognostic Scoring System (IPSS)[5] and the WHO classification–based prognostic scoring system (WPSS),[6] that are able to classify patients into risk groups with different survival rates. More recently, a revised IPSS (IPSS-R) was developed that has multiple refinements beyond the IPSS and showed an improved prognostic ability for MDS patient survival and evolution to AML.[7] Some of the criteria that form the basis of these scoring systems rely on the morphologic examination of bone marrow aspirates and are therefore subjective and prone to operator-dependent variation, although it should be noted that high concordance rates among experts have been reported.[8-10] The use of molecular markers, such as gene mutations and/or aberrantly expressed genes, offers great potential to help refine and improve the prediction of survival and disease progression in patients with MDS.

The value of aberrant gene expression for prognostication in MDS has been reported for a number of individual genes, including for example CDKN1C, PRAME, WT1 and RPS14.[11-14] The prognostic value of a scoring system based upon the combined expression of multiple genes — MN1, ERG, BAALC and EVI1 (MEBE) — has also been reported in MDS: a high MEBE score, defined as high expression of at least two of the four genes, predicted a significantly shorter overall survival and time to AML progression.[15]

The advent of microarray technology two decades ago enabled the interrogation of the expression levels of thousands of genes simultaneously. One of the first studies using microarray-based gene expression profiling (GEP) in MDS reported a set of 11 genes that could discriminate between IPSS-defined low-risk MDS patients, high-risk MDS patients and healthy controls with high accuracy.[16] A number of subsequent GEP-based studies identified gene signatures with prognostic value in MDS. Sridhar et al[17] described a 6-gene "poor risk" signature associated with the risk of transformation to AML, which provided additive prognostic information for IPSS-defined Intermediate-1 MDS patients[17]. In a GEP study by Mills et al[18], a prognostic classification model was generated that accurately discriminated patients with a rapid (within 18 months) transformation to AML from those with more indolent disease.[18] Our group investigated the relationship between gene expression levels and prognosis using GEP data on bone marrow CD34+ cells from a large group of MDS patients.[19] The expression levels of several genes, including LEF1, CDH1, WT1 and MN1, were found to be significantly associated with MDS patient survival. The association between dysregulated expression (or methylation) of these genes and MDS patient survival has been previously reported,[11,15,19,20] and our data confirmed these findings. In this study, we showed that LEF1 expression levels were lower in MDS patients with poor survival, and interestingly high LEF1 expression has been shown to be a favorable prognostic factor in AML.[21-22] In our study, we identified a 20-gene signature that outperformed other predictors including one which additionally used clinical information (determined using age, sex, and IPSS as clinical parameters). This prognostic gene signature based on CD34+ cells could significantly separate MDS patients with a good or poor prognosis in an independent GEP dataset obtained from the analysis of bone marrow mononuclear cells, enhancing the potential clinical applicability of the gene signature in routine practice.[19]

In parallel to GEP-based studies, huge strides were being made in the delineation of the mutational landscape of MDS with the application of next-generation sequencing (NGS) technology. Recurrent somatic mutations in several new genes, such as splicing factor genes,[23-25] were identified in a high proportion of MDS patients and implicated in the development

and/or progression of this disorder.[26-28] A number of these mutated genes were shown to provide important prognostic information: a landmark paper by Bejar et al[29] reported that mutations in ASXL1, TP53, EZH2, ETV6 and RUNX1 are independent predictors of poor survival in MDS.[29] In the light of these new findings, it becomes clear that one limitation of the above-mentioned GEP-based prognostication studies is that the likely effects of the underlying gene mutations on the expression profiles have not been investigated.

Given some of the advantages of the evaluation of gene mutations over gene expression, namely DNA being more stable and easier to handle than RNA and the qualitative assessment of the presence/absence of a gene mutation being easier to determine than the quantitative measurement of gene expression levels, an obvious question is whether there is scope for the use of gene expression for prognostic purposes in MDS. This important point was addressed by a comprehensive analysis in the study by Gerstung et al[30] which investigated the interconnections between mutations, gene expression profiles, clinical variables and patient outcome in MDS.[30] This study showed that the mutational status shapes the gene expression landscape, and identified many dysregulated genes associated with the most common gene mutations in MDS. A model investigating the influence of mutations and gene expression changes on clinical variables as well as patient survival showed that the transcriptome was the most powerful predictor of outcome, strongly suggesting that the incorporation of gene expression data into MDS prognostic scores may increase accuracy in outcome prediction.[30]

Several recent studies have harnessed the power of NGS, specifically RNA sequencing (RNA-seq), for the investigation of the MDS transcriptome in order to identify abnormal gene expression changes associated with disease biology and also gene signatures that provide prognostic information. Qiu et al[31] used RNA-mediated oligonucleotide annealing, selection, and ligation coupled with next-generation sequencing (RASL-seq) to interrogate over 5000 annotated alternative splicing events and explore how specific sets of splicing events might serve as biomarkers for MDS diagnosis and prognosis.[31] A risk score based on the weighted expression of 11 differential splicing events was shown to be independently associated with MDS prognosis and AML transformation, suggesting potential clinical relevance of altered splicing patterns in MDS.[31] In another study by Im et al.[32] RNA-seq was used to evaluate the transcriptome of bone marrow CD34+ cells of MDS patients and healthy controls.[32] Significant differential gene expression profiles between MDS and controls were identified, including 41 disease classifier genes. Moreover, two main GEP clusters could distinguish MDS patients based on their major clinical features, notably between patients whose disease remained stable and patients with rapid (within 12 months) transformation to AML.[32] A comprehensive transcriptomic analysis of bone marrow CD34+ cells from 100 MDS patients was performed by Shiozawa and colleagues.[33] Unsupervised clustering of gene expression data identified two subgroups, one of which was associated with a significantly shorter survival in both univariate and multivariate analysis and also included all patients who later progressed to leukemia. Importantly, the prognostic significance of this classification could be validated in an independent GEP data set, using a regression model that predicts the subgroups based on expression levels of 68 genes.[33] Several of these 68 genes, including MN1 and CXADR, overlap with those identified by our group as associated with MDS patient survival in a previous study using supervised principal components analysis.[34] Most recently, our group determined the aberrantly spliced genes and dysregulated pathways in CD34+ cells of 84 MDS patients, approximately half of which harbored splicing factor gene mutations.[35] We investigated the correlations between aberrant splicing events and clinical variables, and we identified 15 events significantly correlated with the percentage of bone marrow blasts, platelet count or absolute neutrophil count values in SF3B1 mutant MDS. Moreover, we identified 14 genes with isoforms which independently predict survival in MDS in multivariate models, with a striking enrichment in genes involved in the formation of extracellular exosomes and focal cellular adhesion. Some of these genes expressed isoforms which were significantly predictive of survival also in the AML cohort from the Cancer Genome Atlas (TCGA), thus implicating dysregulation of focal adhesion and extracellular exosomes as drivers of poor survival in MDS and AML.[35]

Several studies have thus demonstrated the potential utility of aberrant gene expression in the prediction of MDS patient survival and transformation to AML. Whilst some dysregulated genes are common between studies, the overlap of the identified gene signatures is limited. This most probably reflects differences in the cell type analyzed and in the data analysis pipelines used, as well as the study of relatively small cohorts of patients with different underlying mutation profiles. Clearly, sample size is an important factor and gene expression studies in larger patient cohorts are warranted. Such studies might be possible through international collaborative efforts including the ongoing International Working Group for the Prognosis of MDS (IWG-PM), which aims to integrate molecular and clinical data from thousands of MDS patients in order to further refine MDS prognostic scoring systems. It is hoped that the modeling of interconnected streams of data, including gene mutation and gene expression data, will provide optimal predictive performance and improve prognostication in MDS.

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JOIN US FOR A BREAKFAST SYMPOSIUM

Translating Pathophysiological Advances into Innovative Treatments for Myelodysplastic Syndromes and Related Myeloid Neoplasms

NOVEMBER 30, 2018

7:00 – 11:00 am

San Diego Convention Center, Room 6A

Breakfast will be served from 7:00 to 7:30 am.

PROGRAM OVERVIEW

This symposium will describe recent advances in our understanding of the pathophysiology of myelodysplastic syndromes and related myeloid neoplasms, and how these advances are being translated into more effective treatments for these patients.

LEARNING OBJECTIVES

- Describe how to use molecular genetics in diagnostic and prognostic evaluation of MDS.
- Discuss important factors when comparing High-risk MDS and AML.
- Recite the pathophysiology of myeloid neoplasms associated with spliceosome mutations.
- Explain the future of epigenetic therapy.
- Discuss recent advances in allogeneic transplantation and prospects for cellular therapy.

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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.

ACCREDITATION

CME/CE provided by AKH Inc., Advancing Knowledge in Healthcare.

Physicians: This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of AKH Inc., Advancing Knowledge in Healthcare and the Myelodysplastic Syndromes Foundation, Inc. (MDSF). AKH Inc., Advancing Knowledge in Healthcare is accredited by the ACCME to provide continuing medical education for physicians. AKH Inc., Advancing Knowledge in Healthcare designates this live activity for a maximum of 3.5 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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DON'T FORGET TO VISIT OUR MDS FOUNDATION BOOTH #1 IN THE NON-PROFIT EXHIBIT HALL

Welcome to MDS 2019

On behalf of the Scientific and Local Organizing Committees and the MDS Foundation, it is our pleasure to invite you to the 15th International Symposium on Myelodysplastic Syndromes taking place at the Tivoli Hotel & Congress Center in Copenhagen, Denmark from May 8-11, 2019. As in previous years, the Symposium will cover the most recent discoveries in MDS basic and translational research as well as all relevant clinical aspects of MDS diagnosis, prognosis, and management. The main lectures will be delivered by recognized international leaders in the field, and we look forward to including high-level research presentations, selected from the abstracts submitted by colleagues.

Furthermore, we are very happy to offer you the opportunity to visit wonderful Copenhagen in the spring – and it does not get better than that! Copenhagen is the lively capital of Denmark which features some of the happiest people in the world, the world's oldest monarchy and some of the world's best chefs. Enjoy everything from historic buildings, modern architecture and beautiful art to Tivoli gardens, harbor swims and alternative lifestyles in Christiania.

Join us for a vivid conference - and experience our special Danish way of life.

We look forward to seeing you all in Copenhagen!

Lars Kjeldsen, Jakob Werner Hansen and Kirsten Grønbæk
Symposium Chairs

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IMPACT WITH YOUR RESEARCH

Submit your abstracts and findings for the opportunity to present your MDS basic and translational research on MDS diagnosis, prognosis, and management, in Copenhagen.

Abstract topics include:

- Cytomorphology
- Epidemiology
- Normal, MDS, and leukemic stem cells
- Immune deregulation
- Predictive factors of response to treatment
- MDS in childhood
- Clinical trials
- And more

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The MDS/MPN International Working Group

Michael R. Savona MD
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The 2018 MDS/MPN IWG Biennial Meeting in Charlotte, NC, was a great opportunity to meet with IWG members and discuss plans for the group. The first day of the meeting was dedicated to a series of excellent talks on the state of the science in MDS/MPN. Special guests "Ken" Figueroa, Jason Gotlib, Amy Dezern, Courtney DiNardo and Virginia Klimek joined the working group, speaking on epigenetic signatures in CMML, and novel approaches in the treatment of MDS/MPN and CNL. Several members discussed mutational burden and clonal evolution in MDS/MPN, as well as ongoing approaches to tackle classification conundrums, response criteria, and risk stratification in MDS/MPN. The second day was completely dedicated to our group's clinical trial ambitions and plans to study novel therapies simultaneously in the US and Europe, and potentially, ultimately, globally. ***ABNL MARRO*** (A Basket study of Novel therapy for untreated MDS/MPN and Relapsed/Refractory Overlap Syndromes) is the infrastructure for our first studies in MDS/MPN. ABNL MARRO 001 (AM001) is the first fully funded study to be conducted by the IWG, and was reviewed at the meeting. AM001 will include 6 sites in the US, as well as sites in France, Spain, Italy and Germany. Subsequent concepts for AM002, AM003, and so forth, will be discussed by the IWG, and interested sites that may not have participated in AM001 will have priority options to participate in later trials.

The MDS/MPN IWG continues to attract interest and recently discussed plans for the upcoming start of ABNL MARRO-001 at the CMML Standards and Standardization Conference in Vienna, Austria, in August, 2018. The ABNLMARRO-001 study is an all-oral therapy for MDS/MPN patients and is due to start in Europe and the US in Spring 2019. ABNL-MARRO (A Basket study of Novel therapy for untreated MDS/MPN and Relapsed/Refractory Overlap Syndromes) is an international European-American cooperation providing the framework for collaborative studies to advance treatment of myelodysplastic/myeloproliferative neoplasms (MDS/MPN) and explore clinic-pathologic markers of disease severity, prognosis and treatment response. ABNL-MARRO leverages the expertise of the MDS/MPN International Working Group (IWG) research consortium to investigate novel treatment approaches in MDS/MPN. Centralized pathology and biospecimen management system allow for correlative studies to be conducted under the umbrella of the ABNL-MARRO.

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. Evaluation of mutational samples from 359 MDS patients with complex karyotypes demonstrated their strong associations with adverse clinical and cytogenetic abnormalities that are already incorporated into existing prognostic scoring systems, TP53 mutations, present in over half of these patients, also carry significant independent prognostic value for decreased survival for patients with MDS. This work, initially preliminarily presented at the 2017 14th International MDS Foundation Symposium held in Valencia, Spain, has recently been reported.[2]

Molecular-Clinical Correlative Results

Molecular and clinical data on 3392 MDS patients gathered by members of the IWG-PM-Molecular Committee were combined and analyzed and the abstract describing these findings was selected for an oral presentation at the ASH 2015 Annual Meeting in Orlando.[3] Survival data were available for 3200 patients. 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. Also presented at the meeting was the data aggregation update with integration of the data into cBioPortal. This is a mechanism for use of the data by all members of the group for their analyses for investigator-initiated projects.

Current Project Status, Plans for Analysis of Recent Samples

In addition to the above assessment of previous samples, the IWG-PM Molecular project has sequenced additional large numbers of MDS cases to further develop clinical-mutational correlations. To date,

work in Elli Papaemmanuil's laboratory have sequenced ~3400 samples from marrow or blood of treatment-naive MDS patients plus ~1300 samples from those having had disease-modifying therapy. Committee members of the IWG-PM will aid evaluation of clinical-mutational correlations available for most of these patients and the results of these will serve as the template with which to build an integrated molecular risk model for MDS. Preliminary discussion of these data will be presented at the 2018 ASH meeting's MDS Foundation MDS Symposium.[4]

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4. Bernard E, Update of Mutational Impact on Diagnostic and Prognostic Evaluation of MDS. Translating pathophysiological advances into innovative treatments for myelodysplastic syndromes and related myeloid neoplasms. MDS Foundation Symposium, ASH 2018.

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.

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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:

1. Miyazaki Y et al. Differing clinical features between Japanese and Caucasian patients with myelodysplastic syndromes: analysis from the international working group for prognosis of MDS. *Leuk Res*. 2018;Sept 6 [Epub ahead of print]. (https:// www.ncbi.nlm.nih.gov/pubmed/30219650)

   An analysis of the IWGP database with 300 patients of Japanese versus 5838 patients with Caucasian decent showed that the former tended to be younger with severe cytopenias and unique cytogenetics with less frequent del (5q). Although time to AML did not differ between groups, overall survival was significantly better in Japanese patients. Of note, the IPSS-R when applied within individual groups underlined survival risks as anticipated by the model thus providing an independent validation.

2. Wang Y et al. The consensus on the monitoring, treatment and prevention of leukemia relapse after allogeneic hematopoietic stem cell transplantation in China. *Cancer Lett*. 2018;438:63–75. (https://www.ncbi.nlm.nih.gov/pubmed/30217562)

   A panel of 23 Chinese allogeneic HSCT experts on behalf of the Chinese society of hematology HSCT workgroup evaluated available Chinese data in the light of global practice guidelines to build consensus on MRD monitoring, risk-stratification directed post-HSCT relapse management, and on the use of prophylactic modified donor lymphocyte infusion. The consensus is expected to harmonize and refine patient care across different provinces in China.

3. Itzykson R et al. Early platelet count kinetics has prognostic value in lower-risk myelodysplastic syndromes. *Blood Adv*. 2018;2(16):2079–2089. (https:// www.ncbi.nlm.nih.gov/pubmed/30126931)

   This study by the European MDS Registry members assessed whether a landmark deterioration in peripheral cytopenias be of prognostic value in lower risk MDS. The European LeukemiaNet Registry patients who had clinic visit at 6±1 mo from their first inclusion were assessed for drop in platelets or neutrophils. Among 807 eligible patients, a relative drop of >25% in platelets at landmark (6 mo) predicted a shorter 5-yr survival rate of 21.9%, p<0.0001 vs those with ≤25% drop (48.6%), which was regardless of baseline IPSS-R status or absolute platelet counts. No such effect was seen with neutrophil counts. Also, the landmark platelet drop >25%, showed compounding effect when combined with RBC transfusion dependence. This was also validated in an independent group of 335 lower risk MDS patients.

4. Ali AM et al. Severely impaired terminal erythroid differentiation as an independent prognostic marker in myelodysplastic syndromes. *Blood Adv*. 2018;2(12):1393–1402. (https://www.ncbi.nlm.nih.gov pubmed/29903708)

   Cell surface expression of glycophorin A, band 3 and integrin α-4 were assayed as markers of terminal erythroid differentiation (TED) in freshly obtained bone marrows of MDS patients (n=205 specimens from 113 patients) and normal subjects (n=16). A lack of quantifiable TED markers in terminal erythroblasts was noted in 27% MDS specimens which was associated with significantly poorer survival (56 mo vs 103 mo, p=0.0001). This observation retained significance even in a multivariate analysis across all IPSS-R categories. Additionally, SRSF2 mutations appeared to be frequent in patients with a lack of TED markers.

5. Moreno-Berggren D et al. Prognostic scoring systems for myelodysplastic syndromes (MDS) in a population-based setting: a report from the Swedish MDS register. *Br J Haematol*. 2018;181(5):614–627. (https://www.ncbi.nlm.nih.gov/pubmed/29707769)

   A large population based real world evaluation of 1329 MDS patients in Swedish nationwide register was conducted for prognostic validation of IPSS, IPSS-R and WPSS. The study estimated MDS incidence in Sweden at 2.9 per 100,000 inhabitants and concluded that IPSS-R had the best predictive power (p<0.001).

6. Ousseine YM et al. Association between health literacy, communication and psychological distress among myelodysplastic syndromes patients. *Leuk Res*. 2018;73:44–50. (https://www.ncbi.nlm.nih.gov/pubmed/30216938)

   Using a self-administered questionnaire 280 French and Australian MDS patients were surveyed via patients' national MDS organizations to understand MDS related distress and factors associated with it. Almost 60% patients reported inadequate health literacy. The impact of event scores (IES) for MDS related distress and difficulty in asking physician questions were both significantly higher among French as compared to the Australian patients. A multivariate analysis confirmed the inverse association of these two factors with a level of health literacy.

7. Oster HS et al. Is bone marrow examination always necessary to establish the diagnosis of myelodysplastic syndromes? A proposed non-invasive diagnostic model. *Leuk Lymphoma*. 2018;59(9):2227–2232. (https://www.ncbi.nlm.nih.gov/pubmed/29295649)

Using multivariate logistic regression with variables like gender, age, Hb, MCV, platelets and WBC in 48 MDS and 63 non-MDS patients, a model was constructed which could establish MDS diagnosis in half the patients avoiding invasive bone marrow examination.

8. Bell JA et al. Transfusion-free interval is associated with improved survival in patients with higher-risk myelodysplastic syndromes engaged in routine care. *Leuk Lymphoma*. 2018; Jun 22 [Epub ahead of print]. (https://www.ncbi.nlm.nih.gov/ pubmed/29932781)

   Higher risk MDS patients (n=229), who attained transfusion free interval of ≥60 days after 1st line therapy, demonstrated prolonged PFS and OS as compared to patients who did not (PFS: 16.9 mo vs 6.1 mo, p<0.01 and OS: 26.1 mo vs 11.8 mo, p<0.01).

TREATMENT:

Patient-Reported Outcomes:

1. Stauder R et al. Health-related quality of life in lower-risk MDS patients compared with age- and sex-matched reference populations: A LeukemiaNet study. *Leukemia*. 2018;32:1380–1392. (https://www.ncbi.nlm.nih.gov/pubmed/29572506)

   Using EQ-5D questionnaire at diagnosis in 1690 lower-risk MDS patients within European LeukemiaNet registry, health-related quality of life (HRQOL) was assessed. As compared to the age- and sex-matched controls, a significantly higher proportion of MDS patients exhibited anxiety/depression and difficulties in usual daily activity (p<0.001).

ESAs and Growth Factors

1. Gatterman N et al. Effect of deferasirox +erythropoietin vs erythropoietin on erythroid response in low/int-1 risk MDS patients: results of the phase 2 KALLISTO trial. *Eur J Haematol*. 2018; May 19 [Epub ahead of print]. (https://www.ncbi.nlm.nih.gov/pubmed/29777631)

   KALLISTO, an open-label randomized multicenter study compared a combination of deferasirox with erythropoietin (n=11) vs erythropoietin alone (n=12). The study did not show improvement in erythroid response rates with combination over erythropoietin alone at 12 weeks (primary endpoint) (HI-E- 27.3% vs 41.7% respectively), nor with a longer treatment at 24 weeks (27.3% vs 50% respectively). The tolerability of the combination however was acceptable.

Hypomethylating Agents:

1. Papageorgiou SG et al. The outcome of patients with high-risk MDS achieving stable disease after treatment with 5-azacitidine: a retrospective analysis of the Hellenic (Greek) MDS study group. *Hematol Oncol*. 2018; Aug 20 [Epub ahead of print]. (https://www.ncbi.nlm.nih.gov/pubmed/30129144)

   This study evaluated the merit of continuing 5-azacitidine treatment in patients achieving stable disease (SD) as the best response. Both median AML-free survival and overall survival were superior with continued therapy after SD as compared to the patients who discontinued therapy after SD (AML free survival- 38 mo vs 15 mo, p<0.001; OS- 20 mo vs 11 mo, p<0.001). Moreover, when compared to the patients who continued therapy after partial or complete response, the outcomes were comparable in patients with stable disease who continued therapy.

2. Mozessohn L et al. Azacitidine in the 'real-world': an evaluation of 1101 higher-risk myelodysplastic syndrome/ low blast count acute myeloid leukemia patients in Ontario, Canada. *Br J Haematol*. 2018;181(6):803–815. (https://www.ncbi.nlm.nih.gov/pubmed/29767427)

   This large real-world study with int-2/high risk MDS or low blast count AML (21–30% blasts) in Ontario, Canada included treatment with azacitidine in three schedules –7 consecutive days or 6 consecutive days or 5-2-2 day schedule. No survival difference was noted between schedules (p=0.87), however patients receiving at least 4 cycles, consistent with prior literature, demonstrated a superior survival (18 mo in patients with ≥4 cycles treatment vs 11.6 mo in all patients).

IMiDs:

1. Brunner AM et al. Impact of lenalidomide use among non-transfusion dependent patients with myelodysplastic syndromes. *Am J Hematol*. 2018; Jul 22 [Epub ahead of print]. (https://www.ncbi.nlm.nih.gov/pubmed/30033577)

   A USA medicare claims study of 676 patients receiving lenalidomide (≥65 yrs) were identified from SEER database. Transfusion dependence was noted in approx. 41% patients. Of the remaining non-transfusion dependent patients, approx. 30% did not have any claim for RBC transfusions. Among transfusion dependent patients transfusion independence (TI) was achieved in 31% by median time to TI of 4 weeks thus confirming the established activity of lenalidomide. The non-transfusion dependent patients demonstrated increased incidence of thromboembolic events compared to transfusion dependent patients (approx. 11% vs 6%, p=0.04). Also, compared to risk matched controls, lenalidomide did not seem to improve survival of the non-transfusion dependent patients.

Immunosuppressive Therapy:

1. Stahl M et al. The use of immunosuppressive therapy in MDS: clinical outcomes and their predictors in a large international patient cohort. *Blood Adv*. 2018;2(14):1765–1777.(https://www.ncbi.nlm.nih.gov/pubmed/30037803)

   The data from 15 centers in USA and Europe, showed 207 patients who received immunosuppressive therapy, the most common being ATG (anti-thymocyte globulin) + prednisone in

43% patients. Overall response rate was 48.8% including 11.2% CR and 30% RBC transfusion independence (RBC-TI). Higher rates of RBC-TI were seen in patients with hypocellular marrow. The median OS was 47.4 mo. Horse ATG + cyclosporin was more effective than rabbit ATG.

Allogeneic Bone Marrow Transplant:

1. Robin M et al. HLA mismatched donors in patients with myelodysplastic syndrome: an EBMT registry analysis. *Biol Blood Marrow Transplant.* 2018; Aug 30 [Epub ahead of print]. (https://www.ncbi.nlm.nih.gov/pubmed/30172776)

   The analysis of 833 MDS patients within EBMT registry, showed that patients receiving HSCT transplant from haplo-identical donors had superior long-term outcomes compared to unrelated cord blood transplants (PFS-p=0.003 and OS-p=0.002), while they were not significantly different when compared to HLA mismatched unrelated donor transplants (PFS-p=0.056 and OS-p=0.082). Also, the haplo-identical transplant showed lower risk of acute-GVHD than mismatched unrelated donor transplants (p=0.010).

2. Sengsayadeth S et al. Conditioning intensity in secondary AML with prior myelodysplastic syndrome/myeloproliferative disorders: an EBMT ALWP study. *Blood Adv*. 2018;2(16):2127–2135. (https://www.ncbi.nlm.nih.gov/pubmed/30143527)

   The acute leukemia working group (ALWG) of EBMT assessed the impact of myeloablative conditioning versus reduced intensity conditioning on outcomes of allogeneic hematopoietic cell transplant in patients with sAML post MDS/MPN. Both univariate and multivariate analyses demonstrated a favorable effect of myeloablative conditioning on cumulative relapse rate, leukemia free survival and on overall survival, while the conditioning regimens did not influence the non-relapse mortality rate.

3. Wermke M et al. Enhanced labile plasma iron and outcome in acute myeloid leukemia and myelodysplastic syndromes after allogeneic haemopoietic cell transplantation (ALLIVE): A prospective multicenter observation trial. *Lancet Haematol.* 2018;5(5): e201–e210. (https://www.ncbi.nlm.nih.gov/pubmed/?term=Wermke+and+labile+iron)

   The prospective observational study enrolled AML and MDS patients undergoing allogeneic hematopoietic cell transplant followed for 1 year. The study demonstrated that pretransplant liver iron content ≥ 125 µmol/g or those who had elevated enhanced labile plasma iron demonstrated significantly increased incidence of non-relapse mortality (p=0.039 and p=0.00034 respectively).

Novel Therapies:

1. Cortes JE et al. Glasdegib in combination with cytarabine and daunorubicin in patients with AML or high risk MDS: phase 2 study results. *Am J Hematol*. 2018; Aug 3 [Epub ahead of print]. (https://www.ncbi.nlm.nih.gov/pubmed/30074259)

   Glasdegib (hedgehog pathway inhibitor) was tested at 100 mg PO QD in a 28-day cycle as maintenance therapy (max 6 cycles) in patients achieving remission on Cytarabine+Daunarubicin (7+3) induction therapy and consolidation with 2–4 cycles of cytarabine 1g/m^2 BID on D1,3,5 of each cycle. The investigator assessed complete response (CR) was seen in 46.4% patients (40% in patients aged ≥55 yrs). Among all evaluable patients (n=69) the median OS was 14.9 mo with a 1-yr survival probability of 66.6%. The most common side effects included diarrhea and nausea. Phase 3 study is planned with this combination.

2. Zeidan AM et al. A multi-center phase I trial of ipilimumab in patients with myelodysplastic syndromes following hypomethylating agent failure. *Clin Cancer Res*. 2018;24(15):3519–3527. (https://www.ncbi.nlm.nih.gov/pubmed/29716921)

   This dose finding study evaluated ipilimumab monotherapy in higher risk MDS patients after hypomethylating agent failure at two dose levels; 3 mg/kg and 10 mg/kg. Due to increased risk of immune related adverse events at 10 mg/kg dose, expansion cohort was treated at 3 mg/kg. A prolonged stable disease ≥46 weeks was demonstrated as the best response in 29% patients treated with 3 mg/kg dose (n=24), while marrow CR was seen in one patient. Median survival for the group was 294 days.

PATHOBIOLOGY:

1. Idossa D et al. Mutations and karyotype predict treatment response in myelodysplastic syndromes. *Am J Hematol*. 2018; Aug 28 [Epub ahead of print]. (https://www.ncbi.nlm.nih.gov/pubmed/30152885)

   Cytogenetics and mutations detected by next generation sequencing in 357 patients showed that ASXL1 mutations (21% patients) were associated with poor response to both hypomethylating agents and lenalidomide but did not have an impact on outcomes with erythropoiesis stimulating agents. Furthermore, U2AF1 mutations (15% patients) too predicted inferior outcome with lenalidomide as did by high risk cytogenetics. In contrast, patients with SF3B1 mutations (32%) were more likely to respond to lenalidomide.

2. Padron E et al. Germ line tissues for optimal detection of somatic variants in myelodysplastic syndromes. *Blood*. 2018;131(21):2402–2405 (http://www.bloodjournal.org/content/bloodjournal/131/21/2402.full.pdf)

   Four candidate germ-line tissues, skin, hair follicles, T-cells and buccal mucosa were assessed for impact of quantity,

quality and hematopoietic contamination on detection of somatic mutations by using whole exome sequencing. Owing to ease of obtaining samples, adequacy of DNA yield and possibility of contamination from neoplastic variants, the study concluded that of the four tissues tested, T cells and/or buccal swabs would be the preferred germ line tissue samples for future analysis.

3. Basiorka AA et al. Assessment of ASC specks as a putative biomarker of pyroptosis in myelodysplastic syndromes: an observational cohort study. *Lancet Haematol*. 2018;5(9):393–402. (https://www.ncbi.nlm.nih.gov/pubmed/?term=ASC+specs+and+myelodysplastic)

   The apoptosis-associated speck-like protein containing a CARD (PYCARD, commonly known as ASC) adaptor protein polymerizes into large, filamentous clusters termed ASC specks that are released upon cytolysis. This single center study first showed increased levels of plasma-derived ASC specks in 177 MDS patients compared to 29 matched healthy controls ($p=0.034$) or patients with other hematologic malignancies ($p<0.05$) except myelofibrosis. These observations were subsequently validated in an independent cohort of MDS and healthy subjects.

4. Im H et al. Distinct transcriptomic and exomic abnormalities within myelodysplastic syndrome marrow cells. *Leuk Lymphoma*. 2018; Apr 4 [Epub ahead of print]. (https://www.ncbi.nlm.nih.gov/pubmed/29616851)

   With high throughput RNA sequencing 41 MDS specific disease classifier genes were determined. Two clusters of gene expression profiles distinctly related to stable disease vs transformation to AML within a year. When superimposed with exomic data, mutation subgroups emerged with distinct biological functional anomalies.

REVIEWS, PERSPECTIVES & GUIDELINES

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

1. Steensma DP How I use molecular genetic tests to evaluate patients who have or may have myelodysplastic syndromes. *Blood*. 2018; Sept 5, [Epub ahead of print]. (https://www.ncbi.nlm.nih.gov/pubmed/30185432)
2. MDS Guidelines for Brazil Parts 1–5. *Hematol Transfus Cell Ther*. 2018; 40(3): 255–282.(https://www.sciencedirect.com/journal/hematology-transfusion-and-cell-therapy/vol/40/issue/3)
3. Talati C, Sallman D and List A. SOHO state of the art and next questions: management of myelodysplastic syndromes with deletion 5q. *Clin Lymphoma Myeloma Leuk*. 2018; Jul 30, [Epub ahead of print]. (https://www.ncbi.nlm.nih.gov/pubmed/30097406)
4. Santini V. Society of hematologic oncology (SOHO) state of the art updates and next questions: myelodysplastic syndromes: *Clin Lymphoma Myeloma Leuk.* 2018;18(8):495–500. (https://www.ncbi.nlm.nih.gov/pubmed/29907542)
5. Hasserjian RP. Myelodysplastic syndrome update. *Pathobiology*. 2018; Jul 24 [Epub ahead of print]. (https://www.ncbi.nlm.nih.gov/pubmed/ 30041243)
6. Basood M, Oster HS and Mittelman M. Thrombocytopenia in patients with myelodysplastic syndromes: still an unsolved problem. *Mediterr J Hematol Infect Dis.* 2018;10(1):e2018046. (https://www.ncbi.nlm.nih.gov/pubmed/30002802)
7. Bennett JM. Morphologic dysplasia in myelodysplastic syndromes: how accurate are morphologists? *Leuk Res*. 2018;101(4):502–507.(https://www.ncbi.nlm. nih.gov/pubmed/29957243)
8. Mittelman M. Good news for patients with myelodysplastic syndromes and thrombocytopenia. *Lancet Haematol.* 2018;5(3):e100–e101.(https://www.ncbi.nlm.nih. gov/pubmed/29295649)
9. Greenbaum U et al. Can bone marrow cellularity help in predicting prognosis in myelodysplastic syndromes? *Eur J Haematol.* 2018;17(10):613–620. (https://www.ncbi.nlm.nih.gov/pubmed/29956845)
10. Mufti G et al. Diagnostic algorithm for lower-risk myelodysplastic syndromes. *Leukemia*. 2018:32(8):1679–1696. (https://www.ncbi.nlm.nih.gov/pubmed/29946191)
11. Shallis RM, Ahmad R and Zeidan AM. The genetic and molecular pathogenesis of myelodysplastic syndromes. *Eur J Haematol.* 2018;101(3):260–271. (https://www.ncbi.nlm.nih.gov/pubmed/29742289)
12. Bejar R and Greenberg PL. The impact of somatic and germline mutations in MDS and related disorders. *J Nat Compr Cancer Netw.* 2017;15:137–141. (https://www.ncbi.nlm.nih.gov/pubmed/28040723)

A special thanks to Suneel and Rhea Mundle for their great efforts in monitoring these important MDS peer-review publications.

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Our MDS Centers of Excellence are institutions that meet the highest standards for diagnosis, treatment and patient care. Your Center helps patients seeking first or second opinions and/or additional treatment options from experts in MDS. We currently have 71 Centers in the United States and 111 Centers in countries around the world. Our MDS Centers can be viewed here:
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- The work of your institution can be shared with our patient and professional contacts via our website and/or our social media channels. We can spread the word of your clinical trials, research projects, etc.

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
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- Available cytogenetics and/or molecular genetics
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MDS FUNDRAISING EVENTS

WORKING TOGETHER FOR MDS

MDS MONSTER DASH

Steve Perry selected and signed up for the Monster Dash Half Marathon on Oct. 27 in St. Paul, MN. He chose this race to run in memory of his dear friend, Greg Savage, because it will be in his spirit of fun – Halloween. He has yet to determine his costume but has already set up an online page for donors to make donations directly to the MDS Foundation. The Monster Dash donation page can be found here: **https://app.mobilecause.com/form/tXrJ7g**

He is also asking his friends and community to use the "text to donate" feature on their smart phones – Text MDSMonsterDash to 41444.

MODELING FOR MDS

THANK YOU to Laura Geltch and the models and photographers from BCC Models for donating the proceeds from your event held on July 7th at the Burlington Country Club, Westampton, New Jersey.

TOM "SHU" SHUEY MEMORIAL GOLF TOURNAMENT

Since 2014, the annual Tom "Shu" Shuey Memorial Golf Tournament has gathered members of the community to celebrate the life of this grandfather, father, and husband, who passed away in 2014 after battling MDS. Tom's son, Timothy Shuey, and his family held their fourth annual charity golf tournament on August 3rd. Shu was an avid golfer and one of Tim's biggest regrets was missing his last opportunity to golf with him. This inspired Tim and his family to organize an annual golf tourney in his memory. For years to come, they plan to keep Shu's memory in their hearts and minds, and continue to support the MDS Foundation.

BILL SPRINGER MEMORIAL GOLF OUTING

In memory of Bill Springer, Paul Howlett and his family held a charity golf tournament to help support the MDS Foundation on June 15th at the Williams Golf & Country Club in Weirton, WV. Jennifer Springer, Bill's widow, is grateful for the opportunity to host this event and she is hoping to make it an annual outing. She hopes the donation from the tournament can help others. That was her husband, Bill, always helping others.

MDS AWARENESS WALK

The MDS Foundation hosted its first-ever MDS Awareness Walk to raise awareness of myelodysplastic syndromes (MDS), an often unrecognized and under-diagnosed, rare group of bone marrow failure disorders that affects an estimated 12,000–20,000 people each year in the United States. Today, there are an estimated 60,000–170,000 diagnosed MDS patients in the United States, with this number expected to grow.

Although great strides have been made, more work needs to be done in MDS and to better understand the needs of patients. Inspired by those impacted by MDS, our hope with the first-ever MDS Awareness Walk is to start a movement with helping to further spread awareness and bring attention to this disease among the physician community as well as the general public.

MDS FOUNDATION, INC.
MDS AWARENESS WALK
BOSTON, MA • JULY 20, 2018

OUR MISSION WAS TO:

- Elevate the conversation around the unmet needs of those living with MDS.
- Bring together the MDS and rare disease community and create new connections.
- Reinforce our commitment, along with our partner organizations, to help improve the lives of MDS patients and those who care for them.
- Establish the need and momentum for future MDS walks across the country.

WE THANK OUR **WALK TO SPREAD MDS AWARENESS** SPONSORS

ACCELERON · agios · astex pharmaceuticals · Celgene
Daiichi-Sankyo cancerenterprise · janssen Oncology PHARMACEUTICAL COMPANIES OF Johnson & Johnson · NOVARTIS
ONCONOVA TARGETING CANCER | PROTECTING HEALTHY CELLS · samyang life's ingredients · Syros PHARMACEUTICALS · Takeda ONCOLOGY

THANK YOU to all of the volunteers who worked tirelessly for this event!

If you would like to start planning a community event for 2019, reach out to Tracey Iraca at tiraca@mds-foundation.org or call 609-298-1600.

THANK YOU for making the inaugural MDS Awareness Walk such an important part of our foundation's history and future.

FACT #1

12-20K

new cases of MDS are reported every year in the U.S., with an average of **33-55** people diagnosed in the U.S. every day.[3,4,5]

FACT #2

60-170K people

are estimated to live with MDS in the U.S. with an estimated **87,000** new cases each year worldwide.[6,7]

FACT #3

75% of MDS patients are **60+** years of age, and the disease also can affect **children** and **young adults**.[8,9]

FACT #4

1 OUT OF 3

MDS patients (or 30%) progress to acute myeloid leukemia (AML).[1]

FACT #5

UP TO 6 YEARS

is the average survival rate for lower risk patients (who do not receive a bone marrow transplant) and approximately **5 months** for high-risk patients.[10,11]

MDS FOUNDATION MEMBERSHIP

BENEFITS OF MEMBERSHIP

- You are part of the solution to change MDS outcomes. Your membership fee helps support global physician and patient educational initiatives, and helps to empower patients with courage and hope.
- Updates on the status of our Global Centers of Excellence and their live patient and family forum events that allow for more rapid dissemination of new research and treatment developments.
- Information on the latest clinical trials to potentially share or participate in.
- Access to MDS awareness materials to share with family and friends.
- Opportunities to participate in or host support group events with your friends and community.
- Receive two printed issues of *The MDS News*, which includes the latest on MDS research as well as inspiring patient and caregiver stories.

YOUR MEMBERSHIP MAKES A DIFFERENCE

$35 ***Community*** Membership *(includes benefits listed above)*

$70 ***Sharing Hope*** Membership *(includes benefits listed above as well as a membership scholarship for a patient or caregiver in need)*

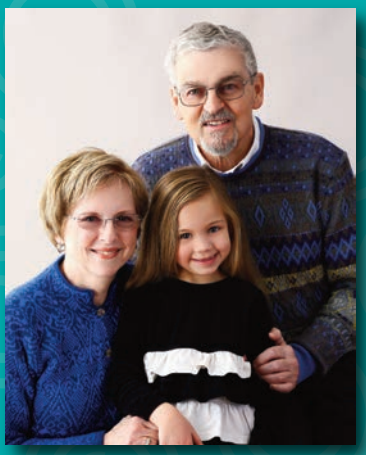
$250 ***Changing the Future of MDS***
Membership (includes benefits listed above as well as additional support for the MDS Foundation as we work together to change the future of MDS). Member names are listed on the MDSF website.

"She asked if I would like for her to make an appointment. We had an appointment WITHIN A WEEK and were treated royally. That is some seriously appreciated clout. Now anyone out there experiencing MDS in your family or with friends I tell from experience there is ONLY ONE KIND of doctor you should be seeing: A DOCTOR RECOMMENDED BY THE MDS FOUNDATION"

The Fournier Family

Tim Fournier, MDS Patient, 79 years old, 3 children, 8 grandchildren

TO BECOME A MEMBER VISIT:
https://www.mds-foundation.org/membership



"It took a long time to wrap our heads around a disease without a cure when my husband felt just fine – The MDS Foundation gave me the information I so badly needed to be a good caregiver. The MDS Foundation was there when we needed it desperately."

The Cook Family

Janice Cook, MDS Caregiver, 70 years old, 2 children, 1 grandchild ("Grandpa's best medicine")

"When I was diagnosed with MDS in 2008, the MDS Foundation became my primary source of accurate, comprehensive and understandable information about this complex and challenging bone marrow disease.

I donate to the MDS Foundation because it's an unparalleled resource for patients, caregivers, treatment providers and researchers. Additionally, I donate because of the wonderful, caring professional staff."

MDS patient, 68 years old

Thinking of joining the MDS Foundation as a Professional Member?

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.

CURRENT PROFESSIONAL MEMBERS:

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Thinking of joining the MDS Foundation as a Changing the Future of MDS Member?

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

BENEFITS OF MEMBERSHIP

- You are part of the solution to change MDS outcomes. Your membership fee helps support global physician and patient educational initiatives, and helps to empower patients with courage and hope.
- Updates on the status of our Global Centers of Excellence and their live patient and family forum events that allow for more rapid dissemination of new research and treatment developments.
- Information on the latest clinical trials to potentially share or participate in.
- Access to MDS awareness materials to share with family and friends.
- Opportunities to participate in or host support group events with your friends & community.
- Receive two printed issues of The MDS News, which includes the latest on MDS research as well as inspiring patient and caregiver stories.

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Clinical Studies – Research – Education

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Please join today!

www.mds-foundation.org/membership

Together, we are community resource of Hope for those living with MDS.

2019 PATIENT FORUMS

SPREADING THE NEWS WORLDWIDE

MARK YOUR CALENDAR FOR THE LOCATION NEAREST YOU!

FEBRUARY 2
Los Angeles, CA

MARCH 9
Phoenix, AZ

MARCH 30
Jacksonville, FL

APRIL 27
Pittsburgh, PA

MAY 11
Copenhagen, Denmark

JUNE 22
Baltimore, MD

JULY 20
Iowa City, IA

AUGUST 10
Seattle, WA

SEPTEMBER 14
Nashville, TN

OCTOBER 12
Westwood, KS

NOVEMBER 9
Dallas, TX

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, 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.

JUNE 13, 2018

Stockholm, Sweden

THANK YOU to Prof. Dr. Eva Hellström Lindberg and her team at Karolinska Institutet for the invaluable contribution you made at our Stockholm Patient Forum. A special shout out to Christian Pederson and Bo Karlsson from Blodcancerförbundet for assisting the MDS Foundation in organizing this event and for translating our resource booklet into Swedish. From the feedback we've received, the program was a great success. We appreciate the time that you took out of your busy schedules to join us and thank you for sharing your insights and expertise with our attendees. Your willingness to volunteer your time, energy, and support on behalf of patients and caregivers living with MDS is greatly appreciated!

For our Swedish speaking friends, the presentation slides and audio taping of this event can be found here:
http://www.mds-foundation.org/patient-and-family-forums/#2018-forums.

You and MDS

An Animated Patient's Guide to Myelodysplastic Syndromes

We are excited to announce the MDS Foundation's new online patient education resource, titled "You and MDS: An Animated Patient's Guide to Myelodysplastic Syndromes".

This resource is intended for patients with MDS, as well as family members and caregivers. You will find expert advice about MDS to help you discuss key issues with your health care provider and make important decisions related to management and treatment. Easy-to-understand animations with audio narration, expert video explanations, patient interviews, illustrated slide shows, and educational downloads are available to you. You are invited to provide feedback to help direct future content as this site becomes part of your personal information resource on MDS. We welcome you to this online community resource to improve your quality of life and health outcomes.

Learn more at www.YouAndMDS.com.

FIND THE TRUSTED RESOURCES YOU NEED...

You or someone you know has been diagnosed with MDS

Hearing the words Myelodysplastic Syndromes or MDS can be frightening. The diagnosis of MDS is often unexpected and filled with both immediate and long-term challenges. You probably have many questions. Have you accessed your complete set of tools to prepare, participate, and LIVE with MDS?

Dealing with MDS can be very difficult, but it helps to have helpful resources that are reliable and that you can trust.

To order your FREE copy of our resources available in multiple languages, please visit our website:
https://www.mds-foundation.org/material-order-form-4/

PRESS RELEASES

Celgene and Acceleron Announce Luspatercept Achieved Primary and Key Secondary Endpoints in PhaseIII 'Medalist' Study in Patients With Low-to-intermediate Risk Myelodysplastic Syndromes

- *Results showed significant improvement in red blood cell transfusion independence compared to placebo*
- *Safety profile generally consistent with previously published data*
- *Regulatory submissions planned in the US and Europe in the first half of 2019*

SUMMIT, N.J. and CAMBRIDGE, Mass. (June 28, 2018) – Celgene Corporation (NASDAQ: CELG) and Acceleron Pharma Inc. (NASDAQ: XLRN) today announced results from a phase III, randomized, double-blind, multi-center clinical study (MEDALIST). Luspatercept achieved a highly statistically significant improvement in the primary endpoint of red blood cell (RBC) transfusion independence of at least 8 consecutive weeks during the first 24 weeks compared to placebo.

MEDALIST evaluated the efficacy and safety of luspatercept versus placebo in patients with IPSS-R very low, low or intermediate risk myelodysplastic syndromes (MDS) with chronic anemia and refractory to, intolerant of, or ineligible for treatment with an erythropoietin-stimulating agent (ESA), ring sideroblast-positive and require frequent RBC transfusions.

In addition to achieving the primary endpoint of the study, luspatercept also met the key secondary endpoint of demonstrating a highly statistically significant improvement in RBC transfusion independence of at least 12 consecutive weeks during the first 24 weeks. Modified hematologic improvement-erythroid (IWG mHI-E), a meaningful secondary endpoint, was also achieved.

Adverse events observed in the study were generally consistent with previously published data.

"This result from the phase III MEDALIST trial demonstrates the potential clinical benefit of luspatercept as an erythroid maturation agent for the treatment of chronic anemia in patients with low-to-intermediate risk MDS," said Jay Backstrom, M.D., Chief Medical Officer for Celgene. "Based on these results, we look forward to preparing the dossier for global regulatory submissions and also investigating the clinical potential of luspatercept in ESA-naïve, low-to-intermediate risk MDS patients through the initiation of our phase III COMMANDS study."

"We are truly encouraged by the top-line results of MEDALIST and the potential to benefit the tens of thousands of patients suffering from low-to-intermediate risk MDS worldwide. We would like to thank the patients and investigators involved in the trial," said Habib Dable, President and Chief Executive Officer of Acceleron. "With other ongoing research in beta-thalassemia and myelofibrosis, we remain committed to exploring the potential of luspatercept to address a range of anemia-related diseases."

Data from MEDALIST will be submitted to a future medical meeting in 2018. The companies plan to submit regulatory applications in the United States and Europe in the first half of 2019.

Onconova Therapeutics Announces Plan For Expanding Rigosertib Clinical Trials For Patients With Myelodysplastic Syndromes (MDS) To South America With Pint Pharma

- *Pint Pharma to facilitate expansion of Phase 3 INSPIRE trial to Argentina, Chile, and Brazil in preparation for future studies of oral rigosertib*

NEWTOWN, PA, Aug. 21, 2018 (GLOBE NEWSWIRE) – Onconova Therapeutics, Inc. (NASDAQ:ONTX), a Phase 3-stage biopharmaceutical company focused on discovering and developing novel products to treat cancer, with a primary focus on myelodysplastic syndromes (MDS), today announced that its commercial partner, Pint Pharma GmbH, will assist in expanding access to clinical trials studying rigosertib, a novel and targeted anti-cancer compound currently in a Phase 3 study for the treatment of MDS, to several selected sites across South America. Pint Pharma is a European-based pharmaceutical company focused on the development, registration and commercialization of specialty-based treatments for the Latin American market and has successfully participated in clinical trials for hematological cancers.

"This assistance will help make rigosertib available to cancer patients on a fifth continent, following our ongoing clinical trials in North America, Europe, Asia and Australia. We are delighted to partner with Pint Pharma, which has a wide footprint in South and Central America, with first-hand experience in running clinical trials for malignant hematological disorders," said Dr. Ramesh Kumar, CEO of Onconova Therapeutics, Inc.

"We are excited to start helping Onconova open new clinical sites in Latin America. We are hopeful that Onconova will be able to start recruiting patients as soon as possible to continue the development of IV and Oral Rigosertib," said David Munoz, Chief Executive Officer of Pint Pharma. He added, "Rigosertib is highly complementary to our comprehensive hematology oncology portfolio, and will further strengthen our mission to enable the Latin American population with life-threatening conditions to live better lives by providing early and efficient access to innovative technologies."

Dr. Steven Fruchtman, President and Chief Medical Officer of Onconova, is working closely with Dr. Valnei Canutti, General Manager, Brazil, and Chief Medical Officer of Pint. Dr. Fruchtman commented, "Completion of the INSPIRE Trial and expanding the potential utility of rigosertib for cancer patients are our core objectives and we are delighted that our commercial partner will assist us in recruiting patients in the INSPIRE trial. There is a great medical need and interest to conduct studies in patients with higher risk MDS in this geographical region."

Dr. Canutti added, "We are looking forward to working with Dr. Fruchtman on this important initiative. My prior experience in MDS and our connections with Key Opinion Leaders across this continent will be greatly helpful as we collaborate with Onconova."

A Phase 1 open-label, non-randomized immuno-therapy trial to assess the safety of an adoptive T cell therapy for patients with higher risk myelodysplastic syndrome (MDS)

PersImmune, Inc., a San Diego based company founded in 2010, is developing a personalized adoptive cell therapy for myelodysplastic syndrome (MDS) using its proprietary PACTN (Personalized Adoptive immunotherapy by Cytotoxic T lympho-cytes targeted to patient-specific neoplastic cell Neoantigens) technology. PACTN consists of an infusion of T cells that specifically recognize and destroy the patient's neoplastic cells while sparing normal tissue. The therapy is intended for patients with intermediate, high, or very high risk MDS who have an inadequate response to or who decline standard therapy.

PersImmune has initiated enrollment of MDS patients in an open-label, non-randomized phase I clinical trial that will assess the safety of PACTN infusion for eligible patients. This approach uses patient's own T-cells (collected when the patient is diagnosed with MDS) to target mutations uniquely expressed by the malignant cells but not by normal ones (MDS-specific). The primary endpoints of this trial are to assess the safety, tolerability and maximum tolerated dose of the T cell therapeutic product. The observational secondary endpoints include assessment of disease response and measurement of survival of the infused T cells.

The study will enroll 9 to 15 participants and is still recruiting new patients.

Eligibility criteria:

- 18 years of age or older with MDS, preferably higher risk and a candidate for hypomethylating therapy.
- IMPORTANT: Patients must first be enrolled in PersImmune's blood collection protocol, at or shortly after initial diagnosis, in order for PersImmune to identify immunogenic MDS mutations and generate the PACTN T-cell product.
- Patients must be unresponsive to or decline standard MDS therapy (i.e., hypomethylating agents) and are not eligible for hematopoietic stem cell transplantation

Additional information for physicians and health care providers interested in referring a patient with MDS is available at www.clinicaltrials.gov (NCT03258359)

This study is currently being conducted at only at the University of California, San Diego, Medical Center, but additional sites in southern California are being recruited to participate.

Aprea Therapeutics Presents Results From Phase Ib/II Clinical Study of APR-246 and Azacitidine (AZA) in Patients with TP53 Mutant Myelodysplastic Syndromes (MDS) at the 2018 American Association of Cancer Research (AACR) Annual Meeting in Chicago

- *ORR (by IWG) of 100% in all evaluable patients: 6 CR (75%) and 2 mCR (25%)*
- *All CR patients achieved complete cytogenetic response*
- *No responding patients have experienced relapse*
- *No treatment-related serious adverse events or dose-limiting toxicities to date*

BOSTON, MA and STOCKHOLM, SWEDEN (April 16, 2018) – *Aprea Therapeutics Presents Results From Phase Ib/II Clinical Study of APR-246 and Azacitidine (AZA) in Patients with TP53 Mutant Myelodysplastic Syndromes (MDS) at the 2018 American Association of Cancer Research (AACR) Annual Meeting in Chicago*

Aprea Therapeutics today presented results at the 2018 AACR Annual Meeting from its ongoing Phase Ib/II clinical study in MDS. The ongoing study, sponsored by the Moffitt Cancer Center with financial support from the Evans MDS Clinical Research Consortium and the MDS foundation, evaluates the safety and efficacy of APR-246 in combination with azacitidine for the treatment of TP53 mutated MDS.

The overall response rate in 8 evaluable patients was 100%, with 6 patients achieving a complete response (CR) and 2 patients achieving a marrow CR (mCR). Median progression free survival (PFS) and overall survival (OS) have not been reached, and no responding patients have experienced relapse. At data cutoff, 4 CR patients had complete cytogenetic response, with results of additional CR patients pending analysis. One CR patient achieved mCR and partial cytogenetic response after receiving four days of APR-246 monotherapy. Relative to baseline, p53 immunohistochemistry scores and mutant TP53 variant allele frequency (VAF) were significantly decreased at time of disease assessment. Adverse events (AEs) during the APR-246 monotherapy lead-in phase were all grade 1. No dose-limiting toxicities have been experienced to date and no potentiation of the expected hypomethylating agent (HMA)-related safety profile has been observed.

David Sallman, MD, lead principal investigator of the clinical study from the Moffitt Cancer Center, said, "Responses have been achieved in all patients, including a 75% complete response rate, and accompanied by deep molecular remissions. The emerging clinical data from this study are very encouraging, particularly given the dearth of current therapeutic options for TP53 mutated MDS patients. Furthermore, the combination of APR-246 and azacitidine is well-tolerated, the maximum tolerated dose has not been reached and dose escalation in the study is ongoing."

Journal of Clinical Oncology publishes pivotal Phase 3 data for Jazz Pharmaceuticals' Vyxeos® (daunorubicin and cytarabine) Liposome for Injection

DUBLIN, JULY 19, 2018 – Jazz Pharmaceuticals plc (Nasdaq: JAZZ) announced today that data from the pivotal Phase 3 study of Vyxeos® (daunorubicin and cytarabine) liposome for injection compared to standard of care cytarabine and daunorubicin (7+3) were published online in the *Journal of Clinical Oncology*. The study evaluated the efficacy and safety of Vyxeos compared to 7+3 in 309 patients who were between 60 to 75 years of age with newly diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC), a rapidly progressing and life-threatening blood cancer.

The study met its primary endpoint as Vyxeos demonstrated a superior improvement in overall survival compared to the 7+3 treatment regimen. The median overall survival for the Vyxeos treatment group was 9.6 months compared with 5.9 months for the 7+3 treatment group (2-sided *p* value =0.005; HR [95% confidence interval]=0.69 [0.52, 0.90]). Vyxeos was also associated with a significantly higher remission rate than 7+3 with a complete response rate of 38% versus 26%; p=0.036. In addition, the overall rate of hematopoietic stem cell transplant (HSCT) was 34% in the Vyxeos arm and 25% in the 7+3 arm. The reported adverse reactions with Vyxeos were generally consistent with the known safety profile of cytarabine and daunorubicin therapy.

Vyxeos was approved by the U.S. Food and Drug Administration (FDA) in August 2017, and is the first FDA-approved treatment specifically indicated for adults with newly-diagnosed t-AML or AML-MRC. Data from the study formed the basis of the FDA application and the Marketing Authorization Application (MAA) to the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP).

"We are encouraged by the positive response to Vyxeos from U.S. health care professionals who had been waiting for an advancement in the treatment of these two types of patients with AML," said Allen Yang, MD, PhD, vice president and acting chief medical officer of Jazz Pharmaceuticals. "At Jazz we are keenly aware that every clinical trial result advances the science to help patients and we are committed to helping as many people as possible with Vyxeos."

Designed with Jazz's CombiPlex® proprietary technology, Vyxeos is a unique liposomal formulation that delivers a fixed-ratio of daunorubicin and cytarabine to the bone marrow that has been shown to have synergistic effects at killing leukemia cells in vitro and in animal models.

"Vyxeos is the first agent to significantly improve survival in older, fit AML patients with secondary AML," said Jeffrey E. Lancet, MD, Chair of the Department of Malignant Hematology at Moffitt Cancer Center and lead author of the publication. "Collectively, the Phase 3 clinical data support the adoption of Vyxeos for the treatment of adults with newly-diagnosed t-AML or AML-MRC."

Vyxeos has different dosage recommendations from other medications that contain daunorubicin and/or cytarabine. Do not substitute Vyxeos for other daunorubicin- and/or cytarabine-containing products.

In the Phase 3 study, patients in the Vyxeos arm received 44 mg/100 mg per m^2 (daunorubicin and cytarabine) liposome intravenously via a 90 minute infusion on days 1, 3 and 5 of induction (days 1 and 3 if a second induction was needed) and 29 mg/v65 mg per m^2 (daunorubicin and cytarabine) liposome on days 1 and 3 for consolidation. Patients in the 7+3 arm received induction with cytarabine 100 mg/m^2/day on days 1–7 by continuous infusion and daunorubicin 60 mg/m^2/day on days 1–3. For consolidation, cytarabine was dosed on days 1–5 and daunorubicin on days 1–2. Patients could receive up to 2 cycles of induction and 2 cycles of consolidation in each arm. Subsequent induction was recommended for patients who did not achieve a response and was mandatory for patients achieving >50% reduction in percent blasts.

For the primary endpoint of overall survival, Vyxeos demonstrated an improvement that was superior to the 7+3 treatment regimen. The median overall survival for the Vyxeos treatment group was 9.6 months compared with 5.9 months for the 7+3 treatment group (2-sided *p* value = 0.005; HR [95% confidence interval] = 0.69 [0.52, 0.90]). Vyxeos also was associated with a significantly higher remission rate than 7+3 with a complete response rate of 38% versus 26%; *p* = 0.036. In addition, the overall rate of hematopoietic stem cell transplant (HSCT) was 34% in the Vyxeos arm and 25% in the 7+3 arm. The overall, all-cause 30-day mortality was 6% in the Vyxeos arm and 11% in the 7+3 arm. During the first 60 days of the study, 14% (21/153) of patients died in the Vyxeos arm vs. 21% (32/151) of patients in the 7+3 treatment group.

The incidences of nonhematologic adverse events were comparable between arms, despite a longer treatment phase and prolonged time to neutrophil and platelet count recovery with Vyxeos. Fatal treatment-emergent CNS hemorrhage not in the setting of progressive disease occurred in 2% of patients in the Vyxeos arm and 0.7% of patients in the control arm. Six percent of patients in both the Vyxeos and control arm had a fatal adverse reaction on treatment or within 30 days of therapy that was not in the setting of progressive disease. The most common adverse reactions (incidence ≥25%) were bleeding events, fever, rash, swelling, nausea, sores in the mouth or throat,

diarrhea, constipation, muscle pain, tiredness, stomach pain, difficulty breathing, headache, cough, decreased appetite, irregular heartbeat, pneumonia, blood infection, chills, sleep disorders and vomiting.

CMS Grants New Technology Add-On Payment to Vyxeos® (daunorubicin and cytarabine) Liposome for Injection

DUBLIN, AUGUST 03, 2018 – Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the United States Centers for Medicare and Medicaid Services (CMS) granted approval for a New Technology Add-on Payment (NTAP) for Vyxeos® (daunorubicin and cytarabine) liposome for injection for the treatment of adults with newly diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC), a rapidly progressing and life-threatening blood cancer.

The Vyxeos NTAP will support Medicare beneficiaries' access to Vyxeos when they are treated in certain inpatient hospital settings. The NTAP payment is in addition to the diagnosis-related group (MS-DRG)-based reimbursement that hospitals receive under the Medicare Hospital Inpatient Prospective Payment System (IPPS). The NTAP designation is expected to remain in effect for a period of two to three years until the cost of Vyxeos is included in CMS's recalibration of the DRG payment rate.

The NTAP program is only available to new technologies meeting the definition of newness of the technology, exceeding cost criterion thresholds and demonstrating substantial clinical improvement over existing therapies.

"We value the decision by CMS to grant NTAP designation for Vyxeos as it underscores our belief that Vyxeos is an important treatment option for patients with newly-diagnosed t-AML or AML-MRC," said Mike Miller, executive vice president and U.S. commercial lead at Jazz Pharmaceuticals. "AML is a blood cancer most often seen in older adults and the NTAP payment will help improve Medicare beneficiaries' access to Vyxeos, the first FDA-approved treatment specifically for these patients."

Vyxeos was approved by the U.S. Food and Drug Administration in August 2017 and is the second product from Jazz Pharmaceuticals to receive a NTAP.

Vyxeos has different dosage recommendations from other medications that contain daunorubicin and/or cytarabine. Do not substitute Vyxeos for other daunorubicin- and/or cytarabine-containing products.

In the final rule concerning Hospital IPPS and Fiscal Year 2019, (scheduled for publication in the Federal Register on August 17, 2018), CMS states that: "After consideration of the public comments we received, we believe that based on the statistically significant increase in median survival rate from the Phase III Study 301, Vyxeos is a treatment option which offers a substantial clinical improvement over standard therapy for patients who have been diagnosed with AML. Therefore, we believe that Vyxeos meets the substantial clinical improvement criterion. Based on evaluation of the new technology add-on payment application and consideration of the public comments we received, we have determined that Vyxeos meets all of the criteria for approval for new technology add-on payments. Therefore, we are approving new technology add-on payments for Vyxeos for FY 2019."

Effective October 1, 2018, CMS has established the maximum NTAP amount of $36,425.00, which will provide incremental reimbursement of up to 50 percent of the Vyxeos Wholesale Acquisition Cost (WAC) of an average maximum of 9.4 vials when used in the IPPS hospital setting. Additional information on the CMS final rule and its discussion of NTAP and Vyxeos can be found on pages 551–575 of the pre-publication Federal Register: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/FY2019-IPPS-Final-Rule-Home-Page-Items/FY2019-IPPS-Final-Rule-Regulations.html?DLPage=1&DLEntries=10&DLSort=0&DLSortDir=ascending

Introduced in 2001, NTAP was created by Congress to help facilitate access to new, innovative technologies used to treat Medicare beneficiaries in the hospital inpatient setting.

Vyxeos® Receives Marketing Authorization in the European Union for Treatment of Certain Types of High-Risk Acute Myeloid Leukaemia

DUBLIN (August 27, 2018) – Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced that the European Commission approved Vyxeos® 44 mg/100 mg powder for concentrate for solution for infusion for the treatment of adults with newly diagnosed, therapy-related acute myeloid leukaemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC). Vyxeos is an advanced liposomal formulation that delivers a synergistic molar ratio of daunorubicin and cytarabine.

"Vyxeos is the first chemotherapy to demonstrate an overall survival advantage versus the standard of care in a Phase 3 study of older adult patients with newly diagnosed therapy-related AML or AML with myelodysplasia-related changes," said Daniel Swisher, president and chief operating officer at Jazz Pharmaceuticals. "Jazz is committed to making Vyxeos available to patients in the EU and we will now pursue rolling launches of Vyxeos across the European Union on a country-by-country basis as pricing and reimbursement decisions are made."

The European Commission approval extends to all European Union Member States, as well as Iceland, Norway and Liechtenstein.

"AML is a rare cancer in Europe and patients with therapy-related AML or AML with myelodysplasia-related changes have a particularly poor prognosis compared to

people with other forms of leukaemia," said Professor Charles Craddock CBE, Academic Director, Centre for Clinical Haematology at University Hospitals Birmingham NHS Foundation Trust. "Vyxeos is a new and clinically meaningful treatment option that provides a welcome advance for patients and health care professionals across the European Union."

The Marketing Authorisation Application (MAA) for Vyxeos included clinical data from five studies, including the pivotal Phase 3 study. Data from the Phase 3 study was published in the Journal of Clinical Oncology in July 2018. The study evaluated the efficacy and safety of Vyxeos compared to 7+3 chemotherapy in 309 patients 60 to 75 years of age with newly diagnosed t-AML or AML-MRC, a rapidly progressing and life-threatening blood cancer.

The study met its primary endpoint as Vyxeos demonstrated a superior improvement in overall survival compared to the 7+3 treatment regimen. The median overall survival for the Vyxeos treatment group was 9.6 months compared with 5.9 months for the 7+3 treatment group (2-sided *p*-value= 0.005; HR [95% confidence interval]=0.69 [0.52, 0.90]). Vyxeos was also associated with a significantly higher remission rate than 7+3 with a complete response rate of 37% versus 26%; *p*=0.036. In addition, the overall rate of hematopoietic stem cell transplant (HSCT) was 34% in the Vyxeos arm and 25% in the 7+3 arm. The reported adverse reactions with Vyxeos were generally consistent with the known safety profile of cytarabine and daunorubicin therapy.

The incidences of non-haematologic adverse events were comparable between arms, despite a longer treatment phase and prolonged time to neutrophil and platelet count recovery with Vyxeos. Fatal treatment-emergent CNS hemorrhage not in the setting of progressive disease occurred in 2% of patients in the Vyxeos arm and 0.7% of patients in the control arm. Six percent of patients in both the Vyxeos and control arm had a fatal adverse reaction on treatment or within 30 days of therapy that was not in the setting of progressive disease. The most common adverse reactions (incidence ≥25%) were bleeding events, fever, rash, swelling, nausea, sores in the mouth or throat, diarrhea, constipation, muscle pain, tiredness, stomach pain, difficulty breathing, headache, cough, decreased appetite, irregular heartbeat, pneumonia, blood infection, chills, sleep disorders and vomiting.

FDA Grants Approval of TIBSOVO®, the First Oral, Targeted Therapy for Adult Patients with Relapsed/ Refractory Acute Myeloid Leukemia and an IDH1 Mutation

Approval of TIBSOVO® was Based on Phase 1 Study Results, Including Rate and Duration of Complete Remission (CR) and CR with Partial Hematologic Recovery (CRh) and Rate of

- *Conversion to Transfusion Independence With Second IDHm Inhibitor Approved in Less Than A Year, Treatments Discovered and Developed by Agios Now Available for Relapsed/Refractory AML with an IDH1 or IDH2 Mutation*
- *AML Patients with IDH1 and IDH2 Mutations Represent ~20% of All Patients with AML2*

CAMBRIDGE, Massachusetts (July 20, 2018) – Agios Pharmaceuticals, Inc. (NASDAQ:AGIO), a leader in the field of cellular metabolism to treat cancer and rare genetic diseases, today announced that TIBSOVO® (ivosidenib) was granted approval from the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (R/R AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA approved test. TIBSOVO®, an oral, targeted inhibitor of the IDH1 enzyme, is the first and only FDA-approved therapy for patients with R/R AML and an IDH1 mutation.

"The FDA approval of TIBSOVO® – our first wholly owned drug and the second approved medicine from our research platform in less than a year – is an incredibly exciting milestone for our company and, importantly, for the approximately 6–10% of AML patients with an IDH1 mutation who have been waiting for new treatment options that work radically different than conventional chemotherapy," said David Schenkein, MD, chief executive officer at Agios. "I want to thank the patients and their caregivers, nurses and physicians who participated in our clinical trials. With their support and the dedication of Agios' employees, we are well on our way to becoming a sustainable multi-product biopharmaceutical company delivering medicines that have the potential to change how serious diseases are treated."

AML is a cancer of the blood and bone marrow marked by rapid disease progression and is the most common acute leukemia affecting adults with approximately 20,000 new cases estimated in the US each year. The majority of patients with AML eventually relapse. Relapsed or refractory AML has a poor prognosis. The five-year survival rate is approximately 27%. For 6 to 10 percent of AML patients, the mutated IDH1 enzyme blocks normal blood stem cell differentiation, contributing to the genesis of acute leukemia.

"AML patients who relapse or are refractory to available therapies have few, if any, treatment options," said Hagop M. Kantarjian, MD, professor and chair of the Department of Leukemia at The University of Texas MD Anderson Cancer Center. "The clinical study demonstrated that TIBSOVO® has the potential to deliver strong, durable responses as a single agent and can help patients achieve and maintain transfusion independence. IDH inhibitors represent a new class of noncytotoxic, targeted therapies for AML patients with IDH mutations."

FDA Grants Breakthrough Therapy Designation to Daiichi Sankyo's FLT3 Inhibitor Quizartinib for Relapsed/Refractory *FLT3*-ITD AML

- *Quizartinib has received FDA Breakthrough Therapy designation in patients with relapsed/refractory* FLT3-*ITD AML, a very aggressive form of the disease associated with poor prognosis*
- *Significant unmet medical need exists in relapsed/refractory AML, as available treatment options are limited and there are no approved targeted therapies for patients with relapsed/refractory* FLT3-*ITD AML*
- *Third Breakthrough Therapy designation granted by FDA for a compound in the oncology pipeline of Daiichi Sankyo, reinforcing the company's commitment to transforming science into value for patients with cancer*

TOKYO, MUNICH and BASKING RIDGE, NJ (August 1, 2018) – Daiichi Sankyo Company, Limited (hereafter, Daiichi Sankyo) announced that the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation to quizartinib, an investigational FLT3 inhibitor, for the treatment of adult patients with relapsed/refractory *FLT3*-ITD acute myeloid leukemia (AML).

"There have been limited advances over the past several decades for the treatment of relapsed/refractory *FLT3*-ITD AML, a very aggressive form of the disease associated with poor prognosis. Quizartinib is the first FLT3 inhibitor to significantly improve overall survival as an oral, single agent compared to chemotherapy in patients with relapsed/refractory AML with *FLT3*-ITD, an underlying driver of this subtype of AML," said Arnaud Lesegretain, Vice President, Oncology Research and Development and Head, AML Franchise, Daiichi Sankyo. "We are excited that quizartinib has received Breakthrough Therapy designation and we look forward to working closely with the FDA to bring this potential new treatment option to patients as quickly as possible."

Breakthrough Therapy designation is designed to expedite the development and regulatory review of medicines that may demonstrate substantial benefit over currently approved treatments, in order to more quickly bring new treatment options to patients with serious diseases. Significant unmet medical need exists in relapsed/refractory AML, as available treatment options are limited and there are no approved targeted therapies for patients with relapsed/refractory *FLT3*-ITD AML.

The designation was granted based on the results of the pivotal phase 3 QuANTUM-R study of quizartinib, which were presented during the plenary program at the 23rd Congress of the European Hematology Association in June 2018. QuANTUM-R is the first randomized phase 3 study to show that a FLT3 inhibitor, quizartinib, prolongs overall survival as an oral, single agent compared to chemotherapy in patients with relapsed/refractory *FLT3*-ITD AML.

The safety profile observed in QuANTUM-R appears consistent with that observed at similar doses in the quizartinib clinical development program. Incidence of treatment-emergent adverse events was comparable between patients who received single agent quizartinib (n=241) and those who received salvage chemotherapy (n=94). The most common adverse events (>30 percent, any Grade) in patients treated with quizartinib included nausea, thrombocytopenia, fatigue, musculoskeletal pain, pyrexia, anemia, neutropenia, febrile neutropenia, vomiting and hypokalemia.

AILERON THERAPEUTICS

Study Description: A Phase 1/1b study for patients with MDS or AML that have been treated with at least one prior therapy and have a wild-type TP53 gene. MDS patients must have high-risk disease and have failed or relapsed after treatment with azacitidine or decitabine. Patients are being treated with the investigational drug ALRN-6924, either alone (MDS and AML patients) or in combination with a low dose of cytarabine (only MDS patients and some AML patients who recently transformed from MDS). Doses and schedules available may vary over time.

Study Title: A Phase 1/1b Open-Label Study to Determine the Safety and Tolerability of ALRN-6924 alone and in combination with cytarabine (Ara-C) in Patients with Relapsed/Refractory Acute Myeloid Leukemia or Advanced Myelodysplastic Syndrome with Wild-Type TP53

Key Inclusion Criteria:

- AML or high-risk MDS that is no longer amenable to standard therapies
- Confirmed or anticipated wild-type TP53
- ECOG (Eastern Cooperative Oncology Group) performance status 0-2
- Adequate liver and kidney function

Key Exclusion Criteria:

- Myelodysplastic/myeloproliferative neoplasms
- The required use of any concomitant medications that are predominantly cleared by hepatobiliary transporters, organic anion transporter polypeptide [OATP] members OATP1B1 and OATP1B3, on the day of or within 48 hours after an ALRN-6924 infusion
- Prior allogeneic stem cell transplantation
- Leukemic blast count >25,000/µl
- Deletion of chromosome 17, or del(17p), unless one WT TP53 allele has been maintained
- Acute promyelocytic leukemia or AML with del(5q)
- Current central nervous system leukemic involvement

For more information on this study and a full list of eligibility requirements please visit www.clinicaltrials.gov, identifier NCT 02909972.

This study is currently being conducted at: Institute for Translational Oncology Research, Greenville, SC; Moffitt Cancer Center, Tampa, FL; Montefiore Einstein Cancer Center Bronx, NY; Oregon Health and Science University, Portland, OR; Sarah Cannon Research Institution, Denver, CO; Sarah Cannon Research Institution, Nashville, TN.

ALRN-6924 is an investigational agent and is not approved by the FDA or other regulatory agencies worldwide as a treatment for any indication.

Daiichi Sankyo Cancer Enterprise

The mission of Daiichi Sankyo Cancer Enterprise is to leverage our world-class, innovative science and push beyond traditional thinking to create meaningful treatments for patients with cancer. We are dedicated to transforming science into value for patients, and this sense of obligation informs everything we do. Anchored by three pillars we aim to deliver seven distinct new molecular entities over eight years during 2018 to 2025:

- Antibody Drug Conjugate Franchise
- Acute Myeloid Leukemia Franchise
- Breakthrough Science

Our powerful research engines include:

- Two laboratories for biologic/immuno-oncology and small molecules in Japan
- Plexxikon Inc., our small molecule structure-guided R&D center in Berkeley,CA

For more information, please visit: www.DSCancerEnterprise.com.

The Acute Myeloid Leukemia (AML) Franchise of the Daiichi Sankyo Cancer Enterprise

The AML Franchise is pushing the boundaries of science aiming to define a new standard of care for patients with AML, a fast-growing form of leukemia that has the lowest five-year survival rate of all leukemias. Advancements in the understanding of the molecular biology of AML are creating opportunities for our researchers to discover and develop therapies that target the underlying drivers of the disease.

For more than 30 years, the standard of care for the treatment of AML went unchanged in part due to the complex biology of AML. While a few new treatments have been approved recently, there is still significant unmet need and much work to be done to continue to expand the treatment options available for patients with AML. Our investigational AML Franchise is evaluating a portfolio of therapies that leverage three distinct strategies for the treatment of AML. Our investigational AML Franchise will evaluate combination regimens including these and other compounds for their potential to change the standard of care for patients with AML.

Daiichi Sankyo's Obligation & Commitment

We are dedicated to transforming science into value for patients, and this sense of obligation informs everything we do. As an anchor in the Daiichi Sankyo Cancer Enterprise, significant investment and resources have been committed to the investigational AML Franchise. The formation of the investigational AML Franchise underscores our commitment to understanding AML tumor biology and developing therapies that improve the depth and quality of responses by targeting AML on multiple fronts. Combination regimens, which may address the heterogeneity and polyclonality of the disease, may be key to changing the standard of care for AML. With a portfolio of compounds that target different AML drivers, our investigational AML Franchise is an ideal platform in which to study various combination therapies.

Daiichi Sankyo's Partnerships & Collaborations

Daiichi Sankyo Cancer Enterprise is actively pursuing partnerships and collaborations with experts and academic centers worldwide to help advance the science of AML. A collaboration with MD Anderson Cancer Center, one of the largest integrated leukemia centers worldwide, is focused on accelerating the development of novel therapies for AML. Multiple phase 1 and 2 clinical trials, led by MD Anderson, will be launched to evaluate our investi-gational compounds and multiple agents in combination regimens.

Incorporation of translational work, including exploration of novel biomarkers, as well as preclinical studies of new agents, is aimed at improving our understanding of mechanisms of resistance to existing and emerging treatments.

Daiichi Sankyo's Relentless Focus on Transforming Science

Molecular subtyping (classifying tumors into distinct categories based on molecular features) is creating new scientific opportunities to better understand the science behind AML and improve on current treatment options. Our investi-gational AML Franchise is currently developing a portfolio of therapies that leverage three distinct strategies. Pursuing multiple pathways and studying these investigational compounds in combination with other therapies may potentially enable us to deliver more effective treatment options and expedite development to reach patients sooner.

Our investigational AML Franchise is currently developing a portfolio of therapies that leverage three distinct strategies:

- Growth Factor Receptor Inhibition (FLT3 inhibitor)
- Tumor Suppressor p53 Reactivation (MDM2 inhibitor)
- Targeting Epigenetic Regulation (dual EZH1/EZH2 inhibitor, BRD4 inhibitor and IDH1 inhibitor)

Connect® MDS|AML Disease Registry

An MDS/AML Prospective Observational Study

Connect® MDS and AML: The Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML) Disease Registry

Celgene is researching the following objectives in patients with MDS, Idiopathic Cytopenias of Undetermined Significance (ICUS) and AML:

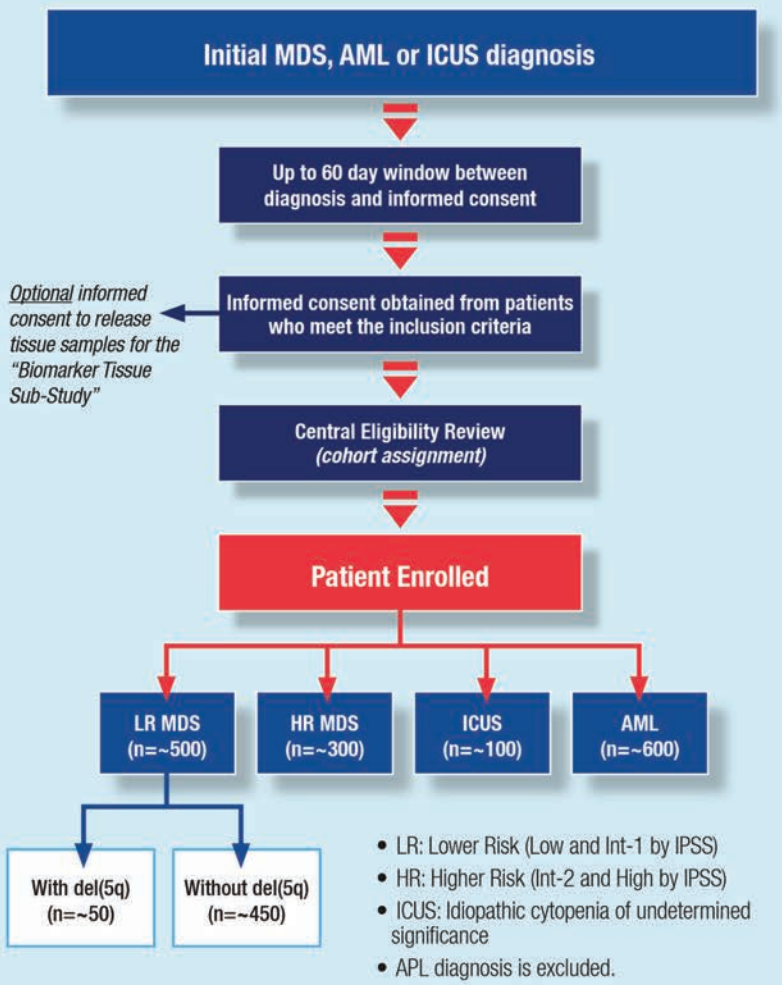
- Current and evolving patterns for diagnosing, treating, and monitoring patients
- Outcome measures
- How routine practice compares to national treatment guidelines
- Treatment patterns and outcomes in patients with del(5q), with or without additional cytogenetic abnormalities
- Association of patient characteristics, treatment regimens and clinical outcomes with patient-reported 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:

- Newly diagnosed,* primary or secondary MDS, ICUS or AML
- MDS/ICUS 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; and therefore proficient in either English or Spanish

*To be considered "newly diagnosed," the diagnosis must have been confirmed no more than 60 days prior to the date the patient signs the informed consent (ICF) documents.

Note: Concomitant patient enrollment in other studies is permitted.



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

Celgene

UBC2013-1018

Highlights of My MDS Story

Deb Erlanson
Austin, Texas

I'd like you to go see a hematologist because your blood counts have dropped for your last two visits" said the neurologist who had been treating me for multiple sclerosis (MS) the past 8 years. That's when I learned a hematologist deals with blood disorders — and that hematology often goes along with oncology, and I thought 'isn't that usually related to cancer?'

Between January and March 2009, I saw a hematologist locally and went through blood testing and a bone marrow biopsy (3 friends sat with me in the pre-op room and we laughed ourselves silly, which helped make the procedure a decent experience, as I was joking with the medical staff during the procedure!). Results appeared to be a cancer of the blood.

I went to MD Anderson Cancer Center in Houston for a second opinion, which required a second bone marrow biopsy and giving up over 20 vials of my blood for testing—I joked with the technician saying I thought I needed that blood more than she did! Results came in as Myelodysplastic Syndromes (MDS). MS medication stopped immediately, and treatments began for MDS. I was 51 years old.

My decision was to go to MD Anderson once a year and that doctor would call the shots on treatment and we would keep in touch as needed through secure emails. I went weekly to a local Texas Oncology office for lab work, treatment, and doctor visits. If anything unusual arose, the two doctors would talk. This allowed me to work full time in my busy office manager job and keep a somewhat normal routine going.

Beginning of April when I was getting a Procrit shot after labs were drawn, I told the nurse that I would be flying the next day to meet up with my family for a vacation. The nurse asked me to wait right there a moment; the doctor came from the other end of the office to tell me directly that I could not fly the next day because my red blood cell count was far too low and I would need to go to the hospital for a blood transfusion. What?!!!

Deb with her sons Jake & Jesse

Quickly I had to think of questions to ask, get the answers, and while they were setting me up to run to the hospital for a type and cross (another WHAT?!! moment for me), I called my parents to let them know I couldn't fly Saturday but was told I could fly on Sunday once I had new blood in me! What a whirlwind of new mental & bodily experiences for me those couple of days! Talk about stress — I had to learn all sorts of new lingo instantly, run to other appointments, and get poked and prodded a lot!

Deb receiving low-dose chemo in 2014.

And that began this past 9.5 year journey of me living with MDS.

I did weekly lab work for over 4.5 years in the oncology lab. I needed at least 1 blood transfusion every month at a local hospital, except for two times in all those years when my counts remained stable for 3 months — those months gave a bit of hope that my bone marrow had started working correctly once again, though that wasn't the case. With every blood transfusion came a type and cross beforehand, done at the hospital where I would receive the transfusion. This was all a lot of juggling of appointments around my normal work!

Following a transfusion of two pints of blood, my counts would drop week after week until the next transfusion pumped me back up. While the counts dropped, the area over my heart would ache; unintentionally rubbing on that area was a sign for others to know I was running on low, as was breathing harder and feeling very tired!

I finally had a port put in after 4.5 years of all those needle sticks! This changed things, as now I went to the infusion room to have labs drawn through the port, which also counted as a port flush. The nurses at the oncology office and the hospital were delighted when the port went in! I found out I was delighted, too. Finding working veins that weren't scarred, and that gave a good blood flow, had become a bit like doing a "Where's Waldo?" search. The port saved the day.... Guess I hadn't gotten a port the previous years, because I had hoped all along that the MDS would heal and I would not need to do bloodwork anymore — high hopes! After all, I'm a positive-outlook kind of person!

Procrit alone didn't work, so we shifted to a combination of Procrit and Plaquenil. Then on to Revlimid, which was a very controlled pill-related chemotherapy. I had to do survey and questionnaire-type work before getting the prescription in hand. We were then going to try Atgam, so I had to be admitted to the hospital and have them test

it on me first; but my body reacted poorly to that, so we didn't go that route. Then I did a year of low-dose chemotherapy with the Dacogen drip, which did not change anything (well, except for dropping 3 clothes sizes in that year!). The shift was made to try Cyclosporine.

During the 5.5 years of trying these various treatments, I kept up the weekly lab work and had monthly 2-pint blood transfusions with type and cross work beforehand. Twice in these years I went for a 2-to-3 month stretch without needing a transfusion, which created lots of excitement and hope, but apparently wasn't meant to be long term.

Back in February 2009, at the beginning of my MDS journey, I met Oscar at a church retreat and we hit it off, keeping in touch from February to April by email and phone. Eventually following each Saturday treatment of getting new blood, I would make the drive from Austin to San Antonio to visit with him when he finished work!

Despite the MDS (and underlying MS) within me, Oscar proposed, moved to be with me, and we married in January 2010!

Between years 4 and 5 of transfusions, the iron level in my body had risen, so chelation therapy using Desferal began following each transfusion from then on.

April 2016, Oscar and I attended the first-ever-in-Austin *MDS Foundation Patient and Family Forum*. Dr. Stuart Goldberg, from Hackensack University Medical Center NJ, spoke about iron overload, so we asked questions and he kindly allowed me to email him any further questions. Because of his help with information, I was able to talk with my doctors to make sure I did not need to get on a slow-removal iron medication. The Forum was where I finally met 2 other MDS patients for the first time since my diagnosis.

My first transfusion was April 2009; my final one was September 2014. In between I was juggling full time work with massive medical appointments, and aiming to stay positive and informed in the midst of chaos. I confided in my boss and several co-workers, who were very supportive; it took me up to 2 years to share with more of the managers so the word would start trickling as to why I was wearing medical bands on my arms, or why I had an IV attached to me. I typically did Thursday type and crosses for Saturday blood transfusions, to create the least amount of disruption in my work life.

The last treatment we tried — Cyclosporine — did something to help get my bone marrow back into normal production mode. September 2018 was my 4-year anniversary since the last blood transfusion! Once-weekly lab work shifted to every other week, then monthly, and now every 2 months so that we do a port flush with the lab work. Seeing the local doctor shifted from monthly, to every 2 month,s and is now every 4 months. I have continued to visit the MD Anderson doctor once a year. My medication has been tapered down considerably and I'm holding steady. I am presently considering having the port removed. We will see...

With everyone's body being different, it's great there are so many different medications to try. What works wonders for one person will not work at all for another. This story is significantly abbreviated, believe it or not! There are many funny and not so funny real-life events I omitted.

Things that happened from the MDS and/or from medications: Eyes yellowed; I bruised quickly; legs swelled; I ached over the heart; constipation; fatigue; metallic taste in the mouth; taste buds changed; hair thinning out; nausea; fever; weight loss; and raised iron level.

Things that helped with symptoms: Diuretic needed to reduce swelling; potassium needed while taking the diuretic; stool softener/right foods to help with constipation; ibuprofen to reduce inflammation at injection site; Valtrex to help heal from viral outbreaks; lidocaine to numb the port before heparin needle insertion; Desferal drip immediately following transfusions to push iron out of the body; Reiki & reading positive affirmations for overall wellbeing.

Deb and her husband Oscar, and parents, Marge and Bob

Things that helped me and the doctors: I kept notes in my phone every visit so I would know which medication went into which arm so the arm could be switched next visit! As I felt symptoms, I added notes in my phone to share with the doctor during my visits so he would know what was going on with me between visits. For the first few doctor visits and all the key ones thereafter, someone accompanied me so there would be another set of ears to listen and help to think of questions to ask. The doctors allowed us to record our visits so we could listen to the information and/or send on to family.

Things that I will always cherish: Blood donors; untiring support and love from my husband, all of my family and friends, my church family and the prayer chains, my boss/top managers/workmates, Facebook "family" cheerleaders; my mom's constant research on the internet to offer information to read and consider; developing a respectful and humor-filled relationship with my local oncology team, the MD Anderson doctor's team, and the hospital admitting/lab/oncology floor teams — for the 5.5 various medical treatment years, they all felt like a tight-knit family to me; the positive attitude and humor I held onto through it all; making sure to enjoy life and fit in some fun travel

Deb with her brother Tom, spouses, kids, nieces, and nephew.

outings (first time to Orlando for theme parks; camping in the country; train rides — all trips were done between transfusions so my energy and oxygen levels would be up!); and being able to be an active church volunteer. I lived through the worst of it and was delighted beyond belief to turn 60 and have my Air Force (Reserve) retirement funds start flowing — I waited 16 years from the time I retired for that date to arrive! I'm close to achieving a second retirement; and finally, the experiences I went through and the knowledge I gained — if they help me to help someone else, then bonus!

It's been a challenging and stormy journey, admittedly, but I'm delighted to be in the calm of the storm right now!

From ALL to AML – with MDS In Between

Valerie Fons
Washington Island, WI

Audrey Hassan, Patient Liaison at the MDS Foundation, answers phone messages promptly. Every time we talk, she offers a list of action items in response to my questions, accessing a network of resources partnered with a willingness to problem solve. She fields my questions and advocates for MDS Patient Forums as the place to gain more information about the disease. Following her advice, I read past Forum transcripts in the MDS online archives. In May 2017, the closest upcoming Forum to my Washington Island, Wisconsin, home was at the University of Chicago. I attended and heard a doctor say; "If a patient doesn't ask questions and make me feel uncomfortable during an appointment, I know the patient is not engaged or advocating." What a contrast with the medical provider who referred me to a psychiatrist for "disease adjustment disorder and OD," because I presented intense questions.

The MDS Foundation affirms information hunger as necessary and normal. From my experience, the Foundation models "information is power," and encourages being proactive. "Seek another opinion," Audrey tells me, "I have patients who have sought fourth and fifth opinions." Audrey identifies MDS Centers of Excellence and urges me to make an appointment. She mentions doctors at each center whom she knows and respects.

In addition to providing phone advice, Audrey follows up. She emailed me the star MDS Centers of Excellence list and reiterated her advice on the importance of seeking a second opinion. Her upbeat encouragement to "take another step" was different from the story I heard from the gowned oncology nurse who told me (between administering subcutaneous injections into my thigh) that her "patients stayed on Azacitidine (brand name Vidaza) then chose comfort care when they do not want to do this anymore." At the MDS Foundation, hope is strategy.

My journey of disease discovery and healing began in 2009, when fatigue became overwhelming. I would lay on the couch for an hour, thinking about getting a drink of water before I could walk to the sink and turn on the faucet. Flu season had begun when I reported my symptoms to the local clinic. After examining me, the medical provider concluded "It's viral. Gut it out." Never tell an endurance athlete to "gut it out." We know how. I returned to the local clinic five times and heard the same diagnosis before my husband carried me to the closest hospital emergency room, fifty miles from our home when I could no longer walk. The attending ER doctor ordered a CBC and found my blood counts whacked out. With no time nor energy to return home, pack a bag, or say goodbye, I was ambulanced from the Sturgeon Bay ER to a Green Bay hospital, one hundred miles from home. An oncologist/hematologist ordered a bone marrow aspiration that evening. The results showed Acute Lymphoblastic Leukemia. "Within forty-eight hours you would have been dead," the oncologist said as he stood at my hospital bedside, explaining the aggressive Larsen protocol that he had ordered to begin that very day. While I remained in the hospital for months, my husband stayed at our home to take care of our six children, ages six to fourteen.

Valerie with unrelated donor stem cells

Our six adopted children (L-R) Steven, Micala, Shammond, Joshua, Kayla, and Korrina, Ervin (Joe Ervin and Valerie Fons pictured in the photo)

By the time my ALL was beat into first remission, my feet had been sacrificed to drug-induced neuropathy. The doctor gave no guarantees but one recommendation — bone marrow transplant. In April 2010, I relocated to Seattle, where bone marrow transplants were pioneered at the Fred Hutch Cancer Research Center with Dr. Donnell Thomas who received a Nobel Prize in medicine for his work. Making a five-month commitment with Seattle Cancer Care Alliance and the University of Washington Medical Center, we teamed for my chance to live. My sister, Lynette, offered her perfectly matched marrow. My transplant was accomplished in May. I was home by August.

For seven years following transplant, I carried on with work and our busy family. Cancer was becoming a distant memory until December 2016, when my primary doctor ordered a CBC and blood test to check my thyroid. The results showed low blood counts to the extent that the oncologist at the regional hospital cleared a space on his calendar that very day. "Let's take a look," he said, inviting me to lay on the procedure table and submit to a bone marrow aspirate. When the results of the aspirate were known, I was given a diagnosis of MDS. "Therapy-induced," doctors called it. "Complicated," said

another member of the medical staff. "High risk," was the conclusion. I had never heard of MDS, did not want to hear about it, but the MDS Foundation is present and prepared to welcome all comers if we are ready or not. The rural Wisconsin hospital oncology library consists of two shelves with less than ten feet of educational material space. From the MDS Foundation, I received fat packets of literature from including research studies, personal stories, educational opportunities, and evidence of a robust, international network dedicated to understanding and treating my disease.

Because of my positive transplant experience with the Seattle Cancer Care Team in 2010, and continued communication with SCCA long term follow-up post-transplant, I returned to Seattle for MDS consultation and treatment. My sister met me in Seattle, willing to contribute her cells toward my recovery. I received two Donor Lymphocyte Infusions (DLI) with lymphocytes from my marrow donor. Though we achieved 100% donor cells documented in chimerism results, my MDS was not eradicated.

As my blood counts continued to decrease, I called Audrey Hassan again. "Get another opinion," she advised, and named other MDS star Centers of Excellence. I made an appointment at the MDS Star Center of Excellence in Madison. Following Dr. Mark Juckett's recommendation, concurring with SCCA, and my regional oncologist, I began seven-day courses of Vidaza each month beginning in April 2017. By July, the blasts in my marrow were 0.3. In early November, after five courses of Vidaza, I returned to SCCA and received a third DLI infusion of 33 million lymphocytes. By Thanksgiving, my blood counts began to plummet without recovery. By December, I was transfusion dependent. The IV RN told me not to worry. "I have patients who have been on transfusions for years," she explained. But, my dropping blood counts were not a symptom to merely manage and maintain with transfusions. Cancer was overtaking healthy blood cell production. By January 2018, another bone marrow aspirate and biopsy showed my MDS had morphed into AML with 40% blasts detectable in the marrow.

I received my AML diagnosis by phone on a Thursday night, with the recommendation to report Monday morning to the hospital in Green Bay to begin what the regional doctor termed "salvage induction." When I received his recommendation, Washington Island was encased in ice. Our ice breaker ferry was full on the morning run. I walked onto the boat because there was no room for my car. When we landed, the ferry captain jump started my 1990 Volvo station wagon, that sat in a snow bank, parked on the mainland. I drove 100 miles to St. Mary's Hospital in Green Bay by myself where a blood test registered my platelets at zero. I received two bags of platelets before a friend rendezvoused with me for the drive to the Milwaukee airport. I canceled my Green Bay Hospital option and returned to Seattle Cancer Care Alliance, arriving with HCT at 17. I met with a Leukemia team on January 30, and was admitted to University of Washington Medical Center enrolled in a GClam clinical trial on February 1.

After thirty-eight days, which included chemo and treatment for back-to-back infections, I was released from the hospital. Following extensive tests, ALL, MDS, and AML were not detectable. I was cleared for transplant number two and enrolled in a clinical trial using a radioactive isotope to reduce the amount of full-body radiation preparing my body for a stem cell transplant with an unrelated donor on May 2. I felt brutalized by the immune suppressing drugs but the donor cells were engrafted and my blood counts are better than I've had in a decade.

Following is a sample of what I am learning on my journey:

- Stay connected with the MDS Foundation. The information, leadership, and networking is invaluable.
- Remain vigilant when straddling care and connecting the dots between a local oncologist, regional center, and MDS Center of Excellence. Invite doctor to doctor conversations. Follow-up on blood and marrow samples sent to labs across country. I kept noticing time lags, and communication breakdowns. Eventually, I relocated to a Center of Excellence location for what I consider to be my best opportunity for medical intervention and the opportunity to thrive.
- Keep asking questions, advocating and engaging for self-care.
- Find ways to nurture yourself, tap into your sense of well-being, set goals and claim your narrative. When I received my MDS diagnosis, I was told I was dying and needed to settle my affairs. Near Easter time, my oncologist told me "you will just have to drink the cup." The prognosis was clear; "You will bleed to death from low platelets, or die from infection while neutropenic." When I got fed-up with dying, I wrote my own words to popular show tunes and started singing. Following is one song I sing which never fails to boost my spirit. I stand while I sing and use body motions to emphasis my message sung to the tune of "Singing in the Rain."

  My marrow is good.
  My marrow is good.
  I'm eating and exercising
  ... Doing what I should
  ... I'm sleeping at night
  I'm embracing life
  My marrow, my marrow is good.
- Grow deeper in loving relationships with a spirit of adventure and gratitude. Before and during my MDS, I was primary caregiver for my husband, Joe, who is in hospice care at home. I diaper and feed him. When the Hospice chaplain, social worker, or RN came to visit, they were faced with me, the spouse — sicker (seeking treatment) than the Hospice patient (seeking comfort care) lying in the hospital bed. Though my counts were low, I remained functional even when enduring a seven-

hour nosebleed in the middle of the night, mid-winter on our remote island, surrounded by Lake Michigan ice with the ice breaker ferry not running until dawn.

- Cry. Refuse to identify tears as breaking down. Welcome tears for the opportunity of breaking open to feelings and being a whole person rather than patient, lab rat, and scientific data point for a research project.
- Explore the workings of a higher power and incarnate power deep within. When I traveled to the MDS Patient Forum at the University of Chicago, I spent the night with a dear friend in Wilmette, Illinois. Across from the bed in her spare bedroom was an extraordinary print of a schooner at sea in a violent storm. In the picture, stricken men stood on deck while a turmoil of waves overtook the ship. "This is my life," I told my friend, as I pointed to the picture. "This is me in the storm of MDS, being overtaken in the crashing sea." "The picture is called "Rising Wind," she explained. "This picture is yours," she told me as she wrapped it up and placed it in my car. As I thanked her, I told her that I would hang the picture in the old water house at our farm and make the water house a Prayer Chapel. When I got home from the MDS Patient Forum, I went to work with help from friends and family, renovating the old water house into a Chapel. "Rising Wind," became the centerpiece of the building. Daily, I went into the Chapel and prayed. I found Psalm 93 which reads:

  The seas have lifted up, Lord, the seas have lifted up their voice; the seas have lifted up their pounding waves. Mightier than the thunder of the great waters, mightier than the breakers of the sea – the Lord on high is mighty.

  Every time I went to the hospital for my Vidaza injections, I took my bible with me and read Psalm 93 aloud as the drug was injected into my body. Returning home from the injections again and again, and praying in the Chapel with the

Prayer Chapel at Tipping Bucket Farm & Retreat Center

picture of "Rising Wind" before me, the storm of MDS began to look less severe. I began to believe and live the truth of God mightier than the MDS storm.

- Continue to change the world and make contributions every day. At Seattle Cancer Care Alliance, twenty days following my stem cell transplant, I was lying on a procedure table with my pants tucked down from my bottom, face toward the wall in position, waiting for the bone marrow aspirate procedure to begin. When the technician entered the room to receive the marrow samples, I asked him to come around the side of the bed so that I could look him in the eye. He introduced himself as "Reuben. Like the sandwich." Whenever I have a bone marrow aspirate and/or biopsy, I carry a symbol of faith with me to hold rather than staring at the sheets and my fear. On this day, I had a set of Compass Cards. The top card on the deck asked "How are you encountering God in new ways?" I started laughing. I've had more bone marrow aspirates than I can count. Through the procedure, I hang on with intensity in my happy place until it is over. When freed at the conclusion of the procedure, I oftentimes cry, shake, and pray aloud. When this aspirate was done, I felt emboldened and spoke out to Reuben. "What do you think?" I asked him. "Your mother is holding you for the first time after giving birth. Your father is standing by the hospital bedside looking into your precious newborn face, and one of them says "We shall name him Reuben. Like the sandwich." "No," I thundered. You are not like the sandwich. You are a child of God." When I paused, Reuben began to recount, as if he had almost forgotten, the origin of his name. In Hebrew, the name Reuben means "behold a son." The procedure room is a sacred space before any words are spoken, but, following my exchange with Reuben, we were more aware of the Holy with us.
- Report, report, report. Reporting is a way of contributing to research and the body of knowledge regarding the disease. Keep track of symptoms and side effects. In addition to reporting to my team, I called Celgene, the drug company making Vidaza when I noticed the drug injection sites on my body were inflamed. The RN at Celgene asked me to participate in making an Adverse

The Rising Wind by Montague Dawson

Reaction Report. She told me how extremely important it is for information to be gathered and documented about a drug. I had the pleasure of helping to change the world when I learned from Celgene that a pharmacist, withdrawing the drug from the vial is meant to discard and change the needle that has entered the manufactured vial before injection into the patient. I spoke with the local pharmacist, who said he was not aware of this practice and would immediately send an email to his team instructing the appropriate protocol in preparing the drug for injection. By reaching out and trying to connect the dots of what was happening with me, I helped myself and others.

- Access every supportive care person available — social work, therapy, chaplain, palliative care, integrative care teams, art and music therapy programs. These resource persons are the best way I know to gain traction processing, articulating what is happening, and access to being a whole, healthy person in the midst of disease.
- Never give up.

  Do all the good you can, By all the means you can, In all the ways you can In all the places you can, To all the people you can, As long as ever you can.

  John Wesley, English Evangelist
  1703 – 1791

Start doing what is necessary, then what is possible. Suddenly, you are doing the impossible.

– Saint Francis of Assisi

Valerie Fons is mom to six children ages 15 –23. The family share personal care for her husband (their dad) Joe, enrolled in Hospice at home. Valerie paddled a canoe 30,000 miles before becoming a United Methodist pastor and spiritual director. She leads teen vocational training at Bread & Water, LLC; L.A.U.N.C.H. Inc., and Tipping Bucket Farm and Retreat Center, extension ministry on Washington Island, Wisconsin, where she lives with her family and a dog named H.O.P.E.

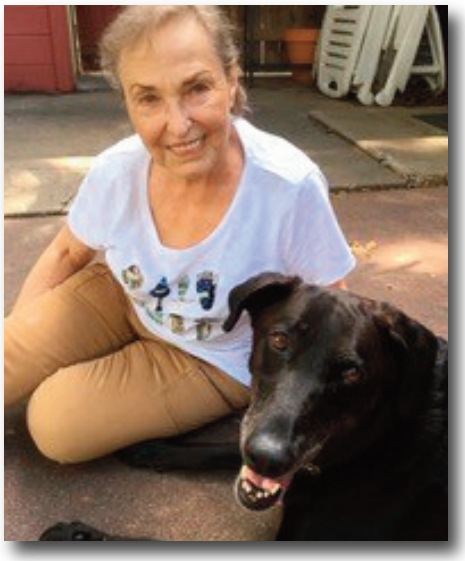
My MDS Journey

Beth Stanaland

Houston, Texas

In May of 2016, I went to my doctor for a routine physical expecting my usual "everything is fine" results. I had been feeling pretty tired, but I just attributed it to getting older. I was 76 and perhaps it was time for me to slow down a bit. There were other symptoms as well, shortness of breath, a change in complexion, and weight loss, but, again, I just thought it was due to normal ageing; it never occurred to me that I could be sick. So you can imagine my shock when the blood work came back and the doctor referred me to an endocrinologist, a hepatologist, and a hematologist. I was fine 15 months earlier at my last exam so something went terribly awry during those 15 months.

My first appointment was with the endocrinologist who tested me and confirmed Graves' disease. That accounted for the weight loss and it was an easy fix. I took a radio-iodine pill to destroy my thyroid and was put on thyroid replacement medicine. Next appointment was with the hepatologist who was concerned about my ferritin levels. An MRI showed no evidence



of liver disease, so, for now, he just continues to monitor my condition.

When I made an appointment with the hematologist I was surprised to see he was also an oncologist and his office was in a cancer center. What?!? I didn't have cancer (or so I thought), I was just anemic; surely, it was nothing serious. My blood work showed normal white cells and normal platelets but hemoglobin was 8.8. A bone marrow biopsy confirmed MDS. My subtype is refractory anemia with ringed sideroblasts (RARS) with a SF3B1 mutation and I was told that I was low-risk which means that I have a low risk of transforming to the deadly acute myeloid leukemia (AML) and I have an excellent prognosis. That was good news for me! My treatment plan was a blood draw every three weeks and an Aranesp injection if my hemoglobin (Hg) was below 11, and it was almost always below 11 so I got a shot every three weeks which kept my Hg in the tens. I learned that my Hg would never again be at normal (12 to 16 for women) but in the tens I felt functional albeit tired.

Prior to my diagnosis I had never heard of MDS and when I was diagnosed I was confused and in denial. I did not use the word cancer. In fact, when I asked my oncologist if I had cancer he said "No". My friends and family had never heard of MDS either, so I explained that it was a bone marrow failure but I never used the word cancer. At some point I learned that it is, indeed, cancer and has been recognized as such since 2008 so my doctor was either not up to date on MDS classification or was not being honest with me. Either way was not acceptable. Additionally, he was very non-communicative, using mostly one word answers to my questions, "Yes" "No" "Irrelevant" and it was a struggle to get information from him. I wanted a second

opinion and since I live in Houston I went to MD Anderson which is recognized by the MDS Foundation as a Center of Excellence. I saw Dr. Garcia-Manero who specializes in MDS and is a widely recognized leader in his field and I switched my care to him. My diagnosis, prognosis, and treatment plan remained almost the same. The only difference is that Dr. Garcia-Manero only authorizes an Aranesp injection if Hg is below 10, as opposed to below 11 as it was with my prior doctor. It has stayed in the nines so I still get a shot every three weeks. I definitely feel more fatigued with Hg levels in the nines instead of in the tens but I know that Aranesp carries the risk of heart attack or stroke and different doctors have different comfort levels with the target for Hg. and even though I am more fatigued now than I was when I was getting a shot when my Hg was below 11, I am still glad I switched my care. MDS is a terrible disease and I want to be under the care of an MDS specialist.

Overall, I feel pretty good and I am grateful for that. My only symptom is fatigue. I do not have pain and I do not feel sick, just extremely tired on some days so I have learned to make adjustments and accept new normals for my life. I had to give up my beloved hobby of wildlife rehabilitation because I could no longer make the commitment of time and energy required and that was a heartbreaking decision. I no longer leap out of bed in the morning; it takes me awhile to get going. I don't sleep well and I have less stamina so I take naps during the day when needed and I have reduced my social life. I haven't been to the gym in months. I mourn the person that I used to be and will never be again – that very fit, high energy, always happy, always busy, and highly productive person. But I refuse to let MDS define me! I have learned not to beat myself up on my slow days and not to think that I should do more; be more. I have learned that even on my bad days I know that I will be OK; just not that day. I still work part time, volunteer at the SPCA, spend time with friends, and I plan to get back to the gym but maybe for some of the senior classes instead of the body pump classes that I was attending. I also keep a 'grateful journal' and strive for a positive attitude.

The MDS Foundation has been a wonderful source of information and I have attended two of their forums. I highly recommend the forums for patients and caretakers if you are able to attend. I learned so much from the speakers and other MDS patients and it was great to spend some time getting to know them. While at one of the forums I learned of MDS Facebook closed groups and I subsequently joined two of them: Fight Myelodysplastic Syndrome and Fight Myelodysplastic Syndrome (MDS) Low Risk. Sometimes, patients need other patients.

Although I try to live in the present and enjoy life and live it as fully as I can, I can't help having some concerns about what may change in the future and how it may affect me. I know that Aranesp doesn't work indefinitely so eventually there may be different treatments and possibly difficult side effects. Will I need transfusions? Chelating drugs to treat iron overload? Chemo? Will I develop additional mutations or transition to another category which will alter prognosis and treatment? Will I need help if any of those scenarios occur? Who will be able to help? I live alone and my family lives out of town. I don't dwell on these fears but they are there, in the back of my mind, even though I know there is no sense worrying until there is something to worry about. For now, I am doing well and maybe I will always do well even with this dreaded, incurable disease. That is my hope.

Beth with her daughter and granddaughter.

The only cure for MDS is a bone marrow transplant for which I am not a candidate because of my age. That knowledge is sometimes overwhelming leading to a sense of despair but I try to keep my focus on "low risk" and "excellent prognosis" and the good things in my life. I am grateful for God, my family, my friends, and my MD Anderson team. Those are the big things but I also find other things almost every day that elicit feelings of gratitude. Humor is wonderful and I am grateful that I am smiling or laughing at something several times almost every day. I know that compared to many, I am the lucky one.

I highly recommend the forums for patients and caretakers if you are able to attend.

My Journey Since 2014

David Hintzke
Miramar, Florida

My journey with MDS started in February of 2014. I was having symptoms of fatigue, leg weakness, and shortness of breath. It was an effort to finish work each day. I knew something was not right because I just didn't feel good all the time.

At first, the doctors thought my symptoms were related to my existing heart issues. I was born with a bicuspid aortic valve and was having problems with atrial fibrillation which made me feel weak, tired and short of breath. I had an ablation and pacemaker inserted that took care of the ongoing heart problems.

In February 2014, I had labs completed during my annual exam, and my white blood count, red blood count, and platelets were low. My wife took charge and spoke with a hematologist who worked on her floor at Cleveland Clinic Florida, and a consult was scheduled. At first, the hematologist said "let's take a wait and see approach and repeat labs in one month." Labs were repeated and counts were still low so my hematologist moved forward with my first bone marrow biopsy in April 2014. The biopsy was inconclusive and did not show signs of MDS. My family and I were relieved and excited that we could go on a family cruise we planned for that summer.

In June of 2014, I went on the cruise and I continued to have no energy, felt weak all the time, and just did not feel good. Upon my return home, my hematologist repeated labs and we continued to wait and watch.

By September of 2014, my symptoms were worse and my counts continued to drop, so my hematologist scheduled bone marrow biopsy #2 which was a suboptimal sample. At that time, I also needed to have my first blood transfusion due to my blood counts being so low. In October of 2014, my hematologist decided we needed to do another bone marrow biopsy (#3), and that time the hematologist actually completed

Family picture post-transplant that was sent to David's donor.

the biopsy herself. Boy did she work hard to get a good sample! All my symptoms made her suspicious for MDS, and she needed to get an answer from the best sample possible.

In November of 2014, my 66th birthday, I had an appointment with my hematologist to get the results of biopsy #3. My wife and daughters went to that appointment. That was when I was told I had MDS with questionable fibrosis. My hematologist advised me that I needed a stem cell transplant within six months. My hematologist knew I needed more blood, and started me on Vidaza injections immediately. My family and I were in total shock. I knew I was sick but had never heard of MDS, and did not think I only had a few months to live without a transplant.

My Hematologist at Cleveland Clinic Florida, Dr. Fu, was wonderful. She guided us throughout my entire MDS journey. She made sure I, the patient, understood every step. She referred us to MDS Centers of Excellence for opinions. Our first consult was with Dr. Krishna V. Komanduri, M.D. at Sylvester Cancer Center at the University of Miami. Dr. Komanduri felt I was a very high-risk patient, but was willing to have me worked up to determine if I was a candidate for a transplant. Depending on the results of all pre-transplant tests, Dr. Komanduri would then decide, along with his team, if I was a transplant candidate. Dr. Komanduri also said he would look for a young male with a 10 out of 10 match to give me the best chance at a successful transplant. I asked Dr. Komanduri, "If I was your father what would you do?" He said "You have no choice, in order to live you must have a transplant."

We scheduled all the pre-transplant testing at the University of Miami and also traveled to Cleveland, Ohio for a second opinion. The transplant doctor at Cleveland Clinic Ohio felt I was too high of a risk for a transplant, due to MDS with possible fibrosis, and my other health issues. Cleveland Clinic Ohio recommended I look into clinical trials. The Cleveland Ohio Dr. said I was dealt a bad hand of cards in life. Once again, we all were devastated with the news. We left feeling hopeless, but my daughter said, "Dad, that was only one strike — let's go get two other opinions". We went back to our hotel and had a good cry. Once we got over crying, I said "Let's go get some Italian food and eat" since food has always been my comfort.

The day after we flew back home, we set up an appointment with my hematologist at Cleveland Clinic Florida. Dr. Fu has been my lifeline throughout this entire process. She has guided us in the most calming and educated fashion. When I went back to Dr. Fu, I told her what the two opinions said from UM and Cleveland Ohio, and I had decided not to go through with a transplant. She said if we get two no's we should still move forward and get a third opinion. Dr. Fu felt with my continued positive attitude and the will to live, I should move forward with the transplant.

My family continued to do research on MDS and attended the MDS Foundation's Family Forums, while I continued to do the work ups at Sylvester Cancer Center to get all the necessary medical clearances. In January of 2015, my children, wife and I

had a two hour visit with the transplant team at the University of Miami, and all of the risks of a transplant were explained to us in great detail. Again, I asked Dr. Komanduri, "What would you do if I was your father" and again he said "You do not have a choice, you only have six months to live without a transplant."

At this time, Dr. Komanduri and his team started the process of looking for a donor. My sister was tested, but she was not a suitable candidate. My sister was only 1/2 a match. We were told it could take a few months to find a match, and were hoping for a 10 out of 10 match with a young male. By January of 2015, I was requiring weekly blood transfusions, along with Vidaza injections. At this point I was getting worse. I had a few hospital admissions due to ilium bowel, pneumonia, and pulmonary embolism, which was a cause for concern. Due to the infections, my blasts had increased and we really were concerned that I would no longer be a candidate for transplant. Luckily, I recovered, and was cleared by the cardiology and pulmonary doctors at Sylvester Cancer Center and the transplant team. I did continue blood transfusions, and required Neupogen injections while I was waiting for a donor. I was also started on Exjade for iron overload due to so many blood transfusions. My hematologist at Cleveland Clinic Florida worked very diligently to keep me stable while we waited for a donor. As it turns out we had two donors identified, but for unknown reasons as it got closer to being admitted for transplant, the donors were not cleared.

In March of 2015, I had bone marrow biopsy #4 to make sure I was still a candidate for transplant. At this point my hematologist would continue to check labs and give me blood transfusion as needed. She was very concerned that if a donor was not found soon we would need to look into other medical options. I met with the transplant team again in April of 2015, and went through the steps for transplant and signed the consent for transplant. My transplant doctor spent 2.5 hours with me and my family, and went into great detail and discussed the pros and cons of chemotherapy, medications, and transplant once again. At that time, I needed to repeat an echocardiogram and pulmonary function test — all of which came out good for transplant.

Finally, the day came on June 11, 2015. We were notified that a donor was located and was a 10 out of 10 match! The plan was that I would have the triple lumen IV line placed on June 29, 2015, and admitted into the hospital for transplant on June 30, 2015. Chemo started on July 1, 2015 with a planned transplant date scheduled for July 7, 2015.

I can never express my sincere gratitude for the care my family, friends, nurses, and transplant team gave to me. They were all there throughout my transplant journey.

On transplant day, the cells arrived at 6:30 pm, however they had to be analyzed by the lab before the transplant process could begin. My family was able to be at my bedside along with a transplant doctor and a nurse. The donor cells were infused into me starting around 11:30 pm, and completed around 3:30 am. I slept through the entire process due to the Benadryl they gave me to keep me relaxed. I do remember waking up at one point and sticking my tongue out at my granddaughter who was staring at me with great concern.

After the transplant, I continued with blood transfusions for one month and I made sure to follow every instruction given to me by the transplant team. At one point I was on 19 different medications. My wife understood every medicine and guided me each day to ensure I was doing all I could to survive the transplant.

The transplant team had a treatment for whatever side effect I was having. I did have nausea, diarrhea, and sores in my mouth. For two weeks, I did not have an appetite, however I would drink Ensure which replaced eating because I was told I had to. This helped me keep whatever strength I did have. I always made sure to do whatever my health team told me to do. I felt that if the transplant was going to fail it wasn't going to be my fault.

When I was really struggling, I knew I needed to find a hobby to help my mind recover as well. I was not a reader but I have always liked music. I started to teach myself how to play the guitar. I went on a website and it taught me how to play certain songs. Word actually got out on the transplant floor that I was playing the guitar and the music therapists would come in and play with me. I was having problems with the strings hurting my fingers so the

Music Therapist and David

music therapist recommended I use a guitar with nylon guitar strings. My daughter heard about this and went to the guitar store and bought me a guitar with nylon stings so I could continue to play. This was a very special time for me because it kept my mind busy so I would not think about all the negatives of feeling sick, being isolated, hooked up to an IV pole and in the hospital. I also listened to music when I would feel sad, which also helped me a lot. The music therapist and I played a song that my wife recorded, and the therapist wanted to use it for an example for other patients to show how music therapy can help a patient going through a difficult medical illness.

My discharge date was 21 days post-transplant however, I had to go back to the transplant clinic daily to be checked. I had no problem with that since I just wanted to go back home. The night before my discharge, the midnight nurses asked if I would play my guitar for them. At 5 am that morning, the nurses came into my room while the head nurse and supervisor stood in the hallway to make sure all other patients where ok and they sat next to me on the couch and listened as I played for them. This was a special moment for me because I knew I was not only making a difference on how music made me feel but it also showed me they truly cared for me and enjoyed me playing.

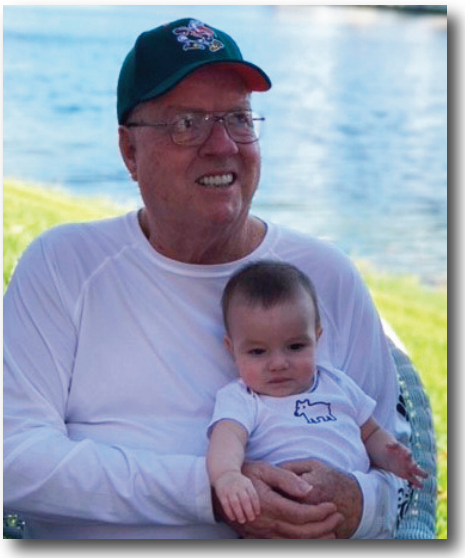
I had a few setbacks and had to be readmitted twice due to infections. The first sign of anything going wrong you must tell your transplant team. My wife knew immediately when I was not feeling well and that something was different. The transplant team always reacted quickly and they made sure to find the correct treatment immediately.

Thereafter, I finally made it to my 100th day and this was a day of celebration. In the following months I continued to make progress. I had issues with my kidneys due to Prograf medication but was seen by a nephrologist and she felt it would pass once I was off the Prograf. I was always followed and monitored closely. The day before Thanksgiving I had the triple lumen removed since I no longer required blood transfusions and fluids.

Two years post-transplant, I had a bone marrow biopsy. My last biopsy was in July 2017 which showed no signs of MDS and that I had 100% of the donor cells in me. My labs continue to improve and in July 2018 I will be three years post-transplant. I still have good days and bad days but I know I must keep moving and I am still recovering. I believe a body in motion stays in motion. I continue to improve in playing the guitar and I am now a mentor for the MDS Foundation, Be The Match and Fourth Angels. So many people helped me get through my transplant journey that I now feel it is time to give back and help others. When I was first diagnosed, I did not want to know what was ahead of me or even understand what MDS was, I just wanted to get through the transplant. My wife and daughter did all the research and found the teams that was best for me. I would say to the doctors just tell me what I need to do and I will do it. A positive attitude helped me through this tremendously.

I have a new normal since transplant. I still have fatigue and must listen to my body and rest when my body tells me to rest. My main issue is weakness in my legs, but I continue to walk and try to go to the gym three times a week to hopefully get my legs stronger. I am off all post-transplant medications, except for taking iron chelation therapy due to iron overload from over 100 blood transfusions before, and after, transplant.

I would like to say to all donors and potential donors out there "thank you for giving us another chance at life!" Without donors we would not be here today!



David and his grandson, Mason.

During my last visit with my hematologist and transplant doctor, I said I had something to say… "Thank you for giving me life so I can continue to watch my family grow". Actually, my family has grown within the last year, and I now have a new grandson named Mason. He is the son of my only son David, which means the Hintzke name will continue on.

I did get the information about my donor after two years post-transplant. He was 19 years old at the time of transplant, and from Germany. We did reach out to him twice by sending a picture of our family along with a t-shirt from UM and a special card signed by everyone in our family. Hopefully he knows how appreciative I am to him. I owe my life to him and all he did in order for me to have the transplant.

I would like to say to all donors and potential donors out there "thank you for giving us another chance at life!" Without donors, me and many others would not be here today! I would also like to thank all the medical professionals, caregivers, family, friends, and organizations that helped me and continue to help all of us patients. We could not do this without all of you!

The Roles of Caregiver For A Patient With MDS

Janice Cook
Columbus, Ohio

My narrative will chronicle the path from distracted wife, to medical secretary, to student, to note-keeper, to scheduler, to meal-planner, to researcher, to nurse, to pharmacist, to borderline pushy caregiver, and always best friend... with times of anxiety, frustration, fear, doubt, anger at the medical system, exhaustion, and feeling overwhelmed. As I write this, I am still a CAREGIVER in capital letters and it is still hard. It is my hope that some of the details below will help others in their journey.

DIAGNOSIS AND TREATMENT

In 2003, my husband Ron was told, at a routine yearly check-up, that he seemed to have "some sort of anemia going on." A B-12 deficiency ran in his family, and he began taking supplements every day. I did not pay much attention. Each year, his blood levels — red cells, white cells and platelets — would slip a little, but the family doctor said he would "keep an eye on them." In 2011, when Ron was 66 years old, that doctor retired and the new doctor said, "I would feel better if a hematologist told you everything is OK."

Caia and grandparents

Thus began my husband's journey with MDS and my journey as his Caregiver.

The hematologist looked at the CBC (complete blood count) at that first appointment and said the numbers did not raise any big flags. But then he looked at a chart I had prepared, tracking blood levels from routine check-ups from 2003 until mid-2011. (There were ten of them, since the doctor started running CBCs every six months in 2010.) When that hematologist looked at my chart and saw the gradual decline in white cells, red cells, and platelets, he immediately suspected Myelodysplastic Syndrome (MDS) and ordered a bone marrow biopsy. When he said there was a treatment, but no cure, we were in disbelief — mainly because Ron felt great and had NO symptoms anything was wrong — only those darned numbers on a piece of paper. We had never heard of MDS.

The first bone marrow biopsy confirmed the diagnosis, but we wanted a second opinion. And Ron wondered if his previous treatment for prostate cancer had triggered the MDS, as breast cancer treatments did for Robin Roberts of Good Morning America. (That was ruled out.) We finally ended up at The Cleveland Clinic in December of 2011 and a second bone marrow biopsy confirmed the diagnosis. The Cleveland Clinic hematologist then gave us a basic tutorial on how bone marrow makes white cells, red cells, and platelets and told us of the problems associated with low levels of each. He recommended that Vidaza treatments begin as soon as possible. The doctor, like the one back home in Columbus, looked at me earnestly, straight in the eyes, and said that Ron's neutrophil level of 0.6 was dangerously low. He straightforwardly told me that, if Ron developed a fever of 101.4, or above, I would need to get him to a medical facility within 30 minutes.

My heart was in my throat and it was at that time I strapped on my seat belt and took on the role of a soldier, a CAREGIVER. As I write this, seven years later, I am still a Caregiver, but the seat belt is not on quite as tight. I have learned a lot, and we have had a very bumpy road. Ron has been the REAL soldier, and his often difficult road continues into year #8.

I hope to share some tips for other caregivers.

From making that blood count chart, and from that quick tutorial from the hematologist, I decided I better get busy and learn as much as I could about MDS, about blood, about bone marrow, about treatment options, and about that one hope for a cure: the stem cell transplant. Our Columbus hematologist referred to the transplant early on, but said, "I hope Ron will never get to the point that he needs it."

Where does one learn about MDS? And where can one talk with other people dealing with blood cancers? (It took a while to even call this a blood cancer. I mean, how bad can something called a "syndrome" be?) One of my first sources was LLS — The Leukemia and Lymphoma Society. A group met monthly at a local hospital, so I went half a dozen times. There was a lunch and then a speaker, so I met other people in the battle and also learned new things. But most of those patients and caregivers were dealing with leukemia or lymphoma or myeloma. Only one other person had MDS.

About this time, I found the MDS Foundation on the internet. I read as much

as I could there. I wanted to be able to "talk the talk" with the doctors and nurses, so I had to learn words like "neutropenia." My little granddaughter had just learned the days of the week to the tune of "O My Darling Clementine" in pre-school. I borrowed the same tune and drilled the white cells into my head "O — basophils, eosinophils, neutrophils, and monocytes. And then there are the leukocytes, B and T and Killer Cells."

In the meantime, Ron had started Vidaza in early January, 2012 — seven treatments over nine days, with a new cycle starting every 28 days. That schedule changed our lives. We planned everything around those 28 day cycles. I went for the first few treatments — they usually took about 75 minutes from start to finish. But then Ron said he was fine and could spend the time reading so I could get on with things.

For the next four and a half years, I always went the first day of the cycle, when blood was drawn, and results were examined by the hematologist. He gave the "go-ahead" for the next nine days and then figured out when the next cycle would start. While Ron headed on to the infusion room, I took on the job of scheduling the next month. It often took me 20–45 minutes to sign in, wait, and then meet with a scheduler, in the hopes of arranging the blood draw, doctor appointment, and seven treatment times for one month from then.

I learned to be an advocate to get the early morning times that would allow my mostly-retired husband to "have a life." Sometimes it meant pushing back when I was told that the doctor would not be on the first day until 1:00, p.m. so the infusion would not start until 2:00 p.m. I knew the doctor had just told me he was available at 8:00 a.m., before doing rounds, and I knew that Ron was having a lot of trouble with nausea. I learned the names of the schedulers, always thanked them for their work, and they started to see me each month as a friendly presence in their often stressful job. It was tricky business to work around holidays, so I would do my homework, study the calendar, and have a plan in mind to assist the physician. If I had not taken on the role of "Scheduler," Ron would have had to do that job himself after he was done with the infusion, and that would have been hard.

Helping Ron deal with side-effects of the Vidaza treatments was a major role. It took more than a year for the doctor to figure out the most effective regimen of anti-nausea medication so that Ron did not feel badly all afternoon. He also suffered from constipation because of all the meds. During that first year, a MAJOR frustration was feeding us dinner. He did not feel good until suppertime and then was almost nauseous from hunger. But he did not know what he wanted to eat, and many things I would suggest sounded repulsive. I did not know what to do. Sometimes I would try to have three meals in mind and hope that one would work for him. Many nights, once he felt well enough, we would go out because that way he would have many choices in a restaurant. It was exhausting and frustrating for me, and I can only imagine what it was like for him.

Ron had pancytopenia — low red cells, low white cells, and low platelets. But only the white cells were terrible problematic, with the dangerous neutrophil level. If he had contracted pneumonia, he would not have been able to fend it off without heavy-duty antibiotics. I carried a thermometer with me at all times, the names of the medications he was on, and a print-out of the latest blood counts. I got a prophylactic supply of Cipro and had the doctor's phone number in my phone in the event we were somewhere, and Ron developed a fever. I learned to say. "My husband has pancytopenia and febrile neutropenia" so no time would be lost if he was in danger. We made the decision to go ahead with our plans to spend New Year's Eve in a beautiful secluded inn in a rural area, so I even charted the distance to the nearest hospital. I programmed it into my GPS and called the ER ahead of time to make sure someone would be on duty on New Year's Eve, and that they would have the drugs available for our situation, if need be. I kept all that to myself.

One of the biggest lessons for a Caregiver: TAKE CARE OF YOURSELF. Like they say on an airplane, put your oxygen mask on first, so you can then help the other person. Having a doctor look you straight in the eyes and tell you that you must have your feverish husband to a medical facility within 30 minutes does not lend itself to blissful sleep. I took care to see my doctor regularly and made sure I was able to sleep reasonably well. (I take Trazodone.) Inadequate sleep will not help you be a good Caregiver, so have your doctor help you if you have troubles sleeping.

Two years into the Vidaza treatments, Ron's numbers were quite decent, and I could relax. But I found I was still on high alert. I just could not relax. When combined with the extreme "meal" frustration, I decided I needed some mental health counseling. I needed to talk with someone and did not want to burden either of my grown children. And I really wanted to talk with someone who did not know my husband. I went to see a counselor twice and got it out of my system. In thinking through what I might tell this person, I figured out a number of things on my own. I made sure I was getting some exercise, eating well, and staying in touch with

friends. Teaching my piano students three days a week brought me great joy. ***Advice: You must take time for yourself and do things which bring you joy.*** And seek help if anxiety and/or depression are issues.

Ron's response to Vidaza treatments was quite remarkable. Since many people do not respond at all, and since lucky ones usually get benefit from it for maybe 14-18 months, we were always waiting "for the other shoe to drop." Each monthly blood draw was preceded by a nervous weekend. Our children, Ron's siblings, and some very close friends always wanted to know "what happened." So, I put together an e-mail address list of "Ron's Close Family and Close Friends," (18 people including nurse & doctor friends.) I emailed these people every 28 days to give an overview of the numbers and the plan going forward. This saved me time and protected my emotional state, since I could efficiently communicate with those closest to us. I could restrict the amount of time on the phone to just our two grown children when desired.

After the shock and adjustment of the first year on Vidaza, I turned my attention to learning about bone marrow transplantation, because we knew the clock was ticking. Again, I returned to the MDS Foundation website and others, like the Bone Marrow Infonet. I learned the difference between a bone marrow transplant and a stem cell transplant. I learned the difference between, and how to pronounce, "allogeneic" and "autologous." I joined the Graft-versus Host Disease Facebook Page and started reading human stories every day about GvHD. It was heart-wrenching to read about the post-transplant struggles. I knew FULL WELL that the people on this page had GvHD and that many transplant survivors do NOT have trouble with GvHD. But I am the kind of person who wants to consider all the angles.

I started many document files on various types of GvHD. I have one for skin, upper GI, gut, lungs, mouth, eyes, fascia. I learned about post-transplant fatigue. I learned that some people were so beaten

Teaching my piano students three days a week brought me great joy.

down by GvHD complications that they wished they had never had the transplant. And I learned how those reading such comments jumped into the arena, cheering each other on, and providing perspective — that life is certainly not the same as it was before the transplant, but the transplant had extended life … to see grandchildren born, to see kids get married, to celebrate more anniversaries, etc. I saw the best in people as they shared their innermost pain and thoughts, while others in the same boat shared love and compassion.

One of the documents I started was "Help for Caregivers." I studied lists of things to do to avoid caregiver burn-out. I collected a few inspirational quotes or articles to return to when I was feeling low. Sometimes late at night, after Ron was asleep, I would listen to audio or video talks on Caregivers that I found on the MDS page or the BMT INfonet page. I would sometimes cry as I listened to people describing exactly what I was going through, and I copied the links for future reference.

It was during this time I realized that transplantation is a huge undertaking and may not be the best choice for everyone. I came to the conclusion that this was not something my husband HAD to do. I am a proponent of "death with dignity" and I support organizations like Compassion and Choices, dealing with end of life choices. I did NOT share most of what I learned on the GvHD Facebook page, or from other sources with Ron — he did not want to think about being sick except when he absolutely needed to. Every now and then I would matter-of-factly mention that a stem cell transplant was an option, and when the time came, he would have to make a decision as to whether or not he wanted to go down that road.

About this time, I heard that the MDS Foundation would hold a Patient and Family Forum right in my own back yard, Columbus. Ron did not want to go. He was playing tennis that day and was still content to not know things he did not need to know. But I was there with bells on and felt energized to be a room with 19 people dealing with MDS — about nine MDS patients, their caregiver(s) and me. I sat next to a man who had just had his first Vidaza treatment and was nervously waiting to see if it would help him. I was able to tall him that hubby was on treatment #14, with good results. Many patients in that room were rather newly diagnosed and just trying to wrap their head around MDS: "What IS this?" It was great to meet Audrey Hassan and others from the MDS Foundation who had travelled from New Jersey. I met nurse Jean Ridgeway, who gave a great talk, and I heard an MDS specialist/physician from The Ohio State University Hospital. I got a copy of "Building Blocks of Hope" and "100 Questions and Answers about MDS."

It was then that I decided the MDS Foundation was a life-line to those of us dealing with this rare type of blood cancer. I read and re-read their publications. I stayed in touch. Ron and I started making yearly contributions to the MDS Foundation. I told many others about this organization, especially newly diagnosed patients who were feeling overwhelmed – like those in the waiting room at the blood clinic. I told our doctor about the MDS Foundation.

After two years of Vidaza treatments, in early 2014, our hematologist had sent us to the James Cancer Center in Columbus for a stem cell transplant consultation. We met with a transplant doctor and Ron had a bone marrow biopsy. Six weeks later, we had a follow-up appointment, at which time we were told that several potential

donors had been found after a search of the international registry. So, transplantation was a possibility and the question was: when should a transplant take place? Ron indicated that he was ready right then and there. The doctor said "Not so fast. Let's not go down that road until it is really necessary. As long as you are getting a good response and are in remission from Vidaza, let's leave well enough alone." And then he went on to tell Ron a little bit about the transplantation process, the amount of time in the hospital, and the potential consequences, from death to GvHD.

A year later, in August of 2015, Ron and I drove up to the Cleveland Clinic when a similar MDS Forum was held there. This time, Ron was ready to join me. He enjoyed meeting other people "in the same boat," and it was a blessing to me to once again interact with other MDS patients and their wonderful Caregivers. We heard presentations by Jean Ridgeway and an impressive doctor from The Cleveland Clinic. I loved the way he said that, in a person with MDS, young cells were like pre-schoolers. Some would get to second grade, some to fourth grade, but then never graduate from high school, and never become productive members of society. They just did not mature." I was able to use this simple description of blasts to help some people understand what MDS is. I got more help with one of the most frustrating things: how to understand a bone marrow biopsy report and what it all means. The doctors do not spend much time on this, in our experience, and Jean even said we could call her on the phone and she would help interpret!

In April of 2015, the numbers on the monthly blood tests started wavering and dropping. By February of 2016, Ron's neutrophil count sank and stayed below 1.0. He needed cataract surgeries in both eyes in late 2015, but they had to be carefully scheduled around the Vidaza treatment schedule. He had to have platelet transfusions before each one. I think there were 19 doctor appointments, in total, to get his cataracts fixed.

And then in February of 2016, Ron developed bad hip pain and found that he needed a hip replacement. It was now a race against the clock to get this surgery done while he could. The surgery took place in May, with a platelet transfusion late the night before. The platelet transfusions had to be CMV negative, which added an extra layer of time/effort. By this time, I had learned about Cytomegalovirus and had made a note which I carried in my wallet, in the event he needed an unexpected platelet transfusion. I had to explain to nurses that Ron was a stem cell transplant candidate and could not have platelets from a person who carried this virus. In one instance, that detail had NOT been included on the order, so everything stopped and was delayed two hours in order to obtain CMV negative platelets. This was one of many instances where I realized I had to have the knowledge to be member of the "medical team" and the confidence to raise questions right on the spot.

Our hematologist was involved in the scheduling of the hip transplant, to make sure this trauma to the system occurred at the time in the cycle when his body was best able to handle it. Vidaza treatments had to be suspended during the immediate recovery. Once they resumed and the summer proceeded, the handwriting was on the wall that Vidaza was no longer effective in controlling Ron's MDS. The last cycle took place in September. In total: 59 treatment cycles and 414 infusions.

We continued the work we had done for several years to "get our affairs in order." Now there was a sense of urgency to make sure I could cope in the event he did not survive. We had already written a new will, and we had Health Care Powers of Attorney and Living Wills. I finished up a "Family Love Letter," at the suggestion of our broker. This was a highly organized book where all our financial information including insurance policies, bank accounts, passport numbers, computer passwords, safe deposit box key locations, and other documentation was in one place. I showed my kids where this information could be found. ***Advice: Do not save these things for "later." Prepare for the worst and hope for the best.***

As we reflected on the five years we had just traveled, from diagnosis to end of treatment, we thought back on two men of about Ron's age, who had been taking Vidaza treatments together with him at the clinic. Due to HIPPA regulations, the nurses in the infusion room were not permitted to introduce these guys to each other. But perhaps it was not just coincidence that Ron found himself sitting next to two other men whose bags of meds looked an awful lot like his own. Over time, they struck up conversations and discovered that they were all attorneys and they all had MDS. And over time, the first dropped away because he was not healthy enough for a stem cell transplant. Then the second one, Mike, dropped away because a donor could not be found. He had eight children, but none were a match. Both of those lovely men are now deceased. Three days before Mike died, he asked his wife to send flowers to the hospital the day after Ron's hip replacement, cheering him on in his battle against MDS. Ron was "the lucky one," who had a chance for a cure.

THE STEM CELL TRANSPLANT AND THE HOPE FOR A CURE

We met with the transplant doctor in September, 2016, after it had been confirmed again that there was indeed at least one perfectly matched donor. The doctor somewhat assumed that Ron would want the transplant, and reminded him of the risks and the odds that he would survive and have a good quality of life. He put that at "35–40%." Ron made the decision to go for the cure. I put aside my reservations and embraced the decision with my whole heart.

If I thought caregiving was challenging before, it rose to a whole new level when the stem cell transplant was scheduled. Even though I had had a LONG time to learn about this procedure, there were still many questions and many unknowns. Unfortunately, many MDS patients and

their caregivers have little time or warning before the spectre of a transplant is large on the horizon.

Once the decision is made to have the stem cell transplant, there are many, many pieces that have to be set in motion. The patient must have yet another bone marrow biopsy, to see where the disease stands. If there are too many blasts (immature cells) in the bone marrow, in other words, more than 5% at most transplant centers, then the transplant will be postponed. Once the results come back, there is a window during which the patient goes through a battery of tests — on the lungs, the heart, and general health to make sure he/she is a good candidate for this grueling procedure. And then, the donor has to prepare. We were told our donor would be a 28-year-old German man.

During the eight weeks or so between the time the decision was made to stop Vidaza and the transplant, we tried hard to concentrate on the present and not the future. We went to Colonial Willliamsburg. We visited our kids and granddaughter. Part of my job was to schedule enjoyable "distractions" like movies, meeting friends for dinner, playing music together. I took over driving to all the appointments for testing, so Ron could sit back and chill as much as possible. Sometimes we had to go straight from one facility to the next, so I checked routes, parking, and took care of paperwork. As the testing came to a close, there was that one more crucial bone marrow biopsy, within a week of the admittance to the hospital. All eyes were on the number of blasts, and that number came back just barely in the "good enough" zone.

By one month before the transplant, I was starting to get pretty emotional. I knew full well that a percentage of transplant patients do not survive the first month and more do not survive the first 100 days. I found myself close to tears often, and that was not characteristic of me. I went in to see my family physician. The office had a new form I needed to fill out before my appointment. One question was, "Do you have a caregiver?" I looked at that twice, thought, "ME? have a caregiver?" And then I burst into tears. As I gathered myself up, the next question was, "Who is your emergency contact?" I again burst into tears because, for the first time, I could not list my husband.

I started a mild dosage of lexipro that afternoon. The doctor told me it would take three or four weeks to become fully effective. So, the timing was accidentally very good. By the time of the hospitalization, I was on a much more even keel. ***Advice: Caregiver — take care of yourself!***

During this time of anxiety, I had a great desire to talk with some other women whose husbands had MDS in their 60s or 70s and were successful transplant survivors. I reached out to a woman whose posts I had admired on the GvHD Facebook page. We exchanged email addresses and phone numbers and I called her in New York on a fall morning and we talked for an hour. Carol was a nurse, so her advice and counsel was especially informed and helpful. They were only six months out from transplant, so details were very fresh in her mind. I heard her husband in the background call out: "Tell her that it was not that big a deal — her husband should go for it!" She told me that the time in the hospital was easier than expected, and she told me that handling medications would be one of the hardest jobs once hospitalization was over. I REALLY paid attention, since this advice was coming from an experienced nurse.

I also reached out to the Bone Marrow Transplant Infonet and their "Caring Connection" program. I described what I needed, and they facilitated an online "introduction" to Bonnie in St. Louis. She told me of her husband, now almost four years out from the transplant. None of his eleven siblings were a match, and the donor was found right there in St. Louis! She told me how she restricted visitors to the hospital. She told me that things got very rocky after discharge and he had to be readmitted two weeks later. She kept family, especially children, away and had "Christmas in July" to keep him safe. She told me that prednisone makes a patient mean and the caregiver sometimes feels like a punching bag. She told me that she eventually held an event that signed more than 100 people into the bone marrow registry and which raised $10,000 for Be The Match!! I was inspired by this woman.

And the "National Bone Marrow Transplant Link" at www.nbmtlink.org put me in touch with a couple in California. We arranged a call, and at the appointed hour, it was the husband/patient who wanted to talk with me first. He was an internal medicine doctor and he called stem cell transplantation "medicine at its finest, cutting edge." He was able to give me lots of detailed medical information and I was heartened that he was four years post-transplant and almost able to go back to work. As a doctor, he had to make sure he was not jeopardizing himself by being around sick people. After a great and encouraging talk, he put his wife on the phone. She was a high school science teacher and a wonderful caregiver. She was very knowledgeable and gave me advice and encouragement. ***Advice: I highly recommend talking to others who know EXACTLY what you are going through and what the road ahead will bring.***

I made a second email list: "Family and Friends of Ron." This one was larger, over 90 people who wanted to be "in the loop." I learned early on that many people forwarded my messages to others, so I took

time and care to craft the messages the way I wanted them. I learned later that people REALLY wanted to understand the transplant process and appreciated the detail I provided. For almost one year, sending out these messages was my way of communicated with people. Everyone was really good about not calling me so that I could focus on my husband. ***Advice: Figure out a way to communicate and educate those in your circle of family and friends.***

At this time, I also put together a short list of about six of my closest friends who also lived close by. These were the kinds of friends I felt I could reach out to when I really needed help. My own studying of caregiving often mentioned the importance of letting others help you, instead of trying to do everything yourself. One day, three weeks into the hospitalization, I needed about five things and did not know when I would have the time, opportunity, or energy to do them. I sent out the list to this group and asked if anyone could take on one of these, and then "copy all" on their response. The next time I had a chance to check email, 90 minutes later, all five requests had been taken care of. Some of the items I needed were even on my front step when I got home from the hospital at the end of the day. ***Advice: Do not be reluctant to ask for help.***

THE HOSPITAL STAY

It is a little surreal to pack the bag and know your husband will be in the hospital for a month. We had a class or two to help us understand what would happen and what to bring. We knew he would need three pairs of pajamas or sets of clothing. (Jeans or regular pants might not work well in bed and with stomach upsets, so we opted for nice –looking pajama bottoms where the waist could be adjusted.) We knew he would have a central line in his chest, so would need a button-down shirt or pajama top so the line would be easily accessible. I figured, correctly, that the room might be cool and a bathrobe would feel good. The protocol at The James Cancer Center was that clothing could be worn only one day and would then need to be laundered. One set of clothes was "extra" in the event he needed to change in the middle of a day. Every evening when I left, I took a laundry bag of clothes with me. When I got home, I threw them into the washing machine and then had them ready to take back the next day.

I asked the transplant doctor if I should plan on staying in the room each night. (Unlike a lot of caregivers, I lived only a 15-minute drive from the hospital.) He advised me not to, saying that it was important that I be well-rested and ready to be the 24–7 support system once he gone home from the hospital. So, I followed that advice. I usually spent 9:30 am–1:30 pm with him and then went back from 6–9 pm. I met other caregivers who lived a long way away and had no choice but to live in the hospital or a nearby hotel. Our hospital had showers on the floor for caregivers.

I kept supplies for myself on a shelf – the 3-ring binder the hospital gave us with important information about the transplant and the medications he would be receiving; a notepad for my questions and observations; chapstick; a water bottle; a sweater; a bathrobe and PJs in the case of emergency (that happened once — the night of the first day after the transplant, when he spiked a fever and I was not comfortable leaving). I carried a small supply of my blood pressure medication in my purse, in case I was not able to be home. For him, we took the laptop computer, a CD player, a couple books and a Great Courses Audio Book.

It was important to get to know the team of nurses — RNs, LPNs and NPs — a little confusing at first — and assistants. The eraseboard in the room always listed the nurses and then we had an iPad which showed the team for the day and on which we ordered food.

The first day, which they called –7, was a busy one, because the central line was inserted, and other tests were run. The next six days of "conditioning" chemo were relatively uneventful, and Ron was able to walk the halls, watch TV, read, work on the computer, etc. Most people tolerate the regimen well and the days can be a little boring. Ron received "low dose" chemo because of his age. The conditioning essentially eliminates the old bone marrow, setting the stage for the transplanted cells. The next day is a day of recovery and then the day of the transplant arrives.

On the morning of November 10, 2016, in Germany, our donor finished the donation of his stem cells and the bag was put in a cooler and transported from that medical facility, across the ocean, to our hospital lab. It apparently arrived about 8:00 pm and was delivered to our room, after being checked out in the lab, at about 10:30 pm. At about 10:55 pm, I watched as the nurse hooked the bag into an IV line and the red liquid started up the tube and then entered his chest. Could it really be that this was the start of a new life — that the MDS could be cured? Only time would tell.

It was honestly a relief to have Ron in the hospital with a large medical team looking after his every need. After five years of caregiving and dealing with blood counts and medications, it was almost like a vacation to not have to worry about these things. The hospital month was busy going back and forth, taking care of the house, yard, plants, laundry, and sometimes taking food into him. I continued to teach my piano students (with Ron's encouragement) although they knew to check email in case I needed to cancel. That two or three hours/three days a week — of immersing myself into helping a child or an adult student make some beautiful music — was time for me and for my soul. I felt refreshed and renewed afterward. The one thing I would do differently would be to pay better attention to the drugs Ron was being given, so I would have had things better organized in my mind after he was released.

The first few days in the hospital, Ron was in isolation while last-minute tests were being run. Everyone coming into the room had to wear a mask, a gown and gloves. That's not hard for the medical personnel, when they are in and out in five

or ten minutes. But for me, that meant discomfort breathing, talking, drinking water, eating, etc. I wear glasses and it took a while to figure out how NOT to steam them up. The fourth day, the gown and gloves went away and I had to wear "only" the mask. There were many times when I neglected to drink enough water. It is important for the Caregiver to stay hydrated, as drinking water and eating food is far down on the list of priorities during the hospital stay. ***Advice: They are tracking his liquid intake. Do the same for yourself!***

There was a strict protocol of bathing. The whole process of taking a shower and then using special body wipes took almost an hour and a half! Ron was much more comfortable having me assist than a nurse, so I needed to be available in the morning to get the process started. (For one thing, hot water had to run for ten minutes before the shower could begin.)

I began to pay attention to how the nurses cared for the central line and how the lines had to be flushed. Carol had told me not to wait until the last minute to learn about meds, so I started studying about them. I asked the head nurse if I could practice flushing lines a week before he was discharged. Being a piano teacher means knowing that repetition is the best way to learn. So instead of the dummy being brought to me the day of discharge, I was able to practice on it several days, so I would be confident and competent at home. The last day, I did the actual flushing in the hospital while the nurse watched. ***Advice: be prepared, just like the scout motto.***

Ron wondered and worried about his hair falling out. He got a "buzz cut" the week before the hospitalization and he shaved off his beard but left the moustache. The hair started to fall out at about day 18 (I had been told that a patient reaches his "lowest point" at around the 17-day mark) and a male nursing assistant came in and shaved his head. The eyebrows and moustache thinned but never fell out. The hair came back in at about the 5th month. It came in really curly, courser and darker than it was before. Now, at 21 months, the hair and moustache are darker instead of gray, making him look younger. ***Advice: Hair, and what you look like, can be an emotional thing.*** Talk about it ahead of time and plan ahead. For one thing, we needed to tell the little granddaughter that Grandpa would be looking like Daddy Warbucks in Annie.

Ron was in the hospital all of November. This also happened to be National Caregivers Month. Volunteers came from room to room and tended to the caregivers, which was wonderful. One woman offered a neck and back massage, which I gladly accepted. She also did a breathing exercise with me. As a life-long singer, I have helped others do breathing exercises. But, as she helped me feel much better after some deep breathing, I realized I had not utilized this skill because I was so overwhelmed. It was good to be reminded of the power of deep breathing to help with stress, and I recommend learning some of the technics if you do not know them.

(The day before the transplant, I received a call that my recent mammogram showed a problem. I remember almost chuckling, like "Is this a test? Really?" After two months and several procedures, the lump was deemed to be a benign cyst. The timing of all this was pretty bad, but the outcome was welcome.)

Concerning visitors in the hospital: There were times he was bored and welcomed a visit by a friend or family member (children under the age of 12 are not allowed). Other days he felt punk and did not want to see anyone. It was good to "keep it loose" and have someone check before they made the trip. Visitors must wash hands and wear masks. At The James, patients are usually allowed to go outside the unit to visit with children or groups of people. When that happens, it is the patient who must wear a mask — and a heavy-duty one, not the light-weight one I wore in the room. Visitors outside the unit do not need to mask up. The patient is also allowed to go outside into one of the garden balconies, or visit other areas of the hospital, if they feel like it and wear the mask. They are, of course, hooked up to various IVs, so they have to take a pole with them. We went down once to see the Christmas tree in the lobby.

BACK HOME "2017 — A YEAR OF RECOVERY"

Things proceeded rather normally during the three weeks after transplant, while in the hospital. There were no fevers except that one (scary) one on night +1, and he had little nausea, no diarrhea, and ate well enough. He was up and around and was walking the halls well. His counts were monitored carefully and, as soon as his white count was high enough, he was discharged. He got home to his own bed, I was armed with many instructions, and we had a LOT of medications. The showering, the care of the central line, the flushing of the lines, the administration and organization of medications, the diet, keeping the surroundings as clean as possible — all were important in making sure he did not get sick while his fledgling immune system was so fragile.

Carol from New York had told me to have a packed bag ready to go by the door that had the current list of medications, the medications themselves, and a spare set of clothes, etc., in case there had to be a quick trip back to the hospital. That was on my mind the first full day back home. That afternoon, while I was teaching a brother/sister, a nurse called Ron to ask how he was doing his first day home. She asked if he had any pain and he replied that he had a little pain in one calf. She calmly told him to hang up and get in the car and come in. He relayed this information to me, and we were out the door in five minutes. Everyone was surprised that this guy who had been walking the halls the day before had developed a blood clot. So we spent the first "free" afternoon back at the hospital past closing time, getting evaluated and treated, and then going to the pharmacy to get a supply of Lovenox (blood thinner) injections. ***Advice: prepare the emergency bag before you go to bed on the very first night of discharge.***

Ron's sister who is an RN, arrived a day later, and stayed a week, which was very helpful in the adjustment to home. The nursing/caregiving was now almost a full-time job. And now we had to inject Lovenox into his abdomen twice a day. I think that was harder on us than it was on him, although he would debate that. During the time his sister was here, it was easy for one person to be with him while the other goes to the pharmacy or the grocery, or take care of errands. Once she left, I had to do those things myself or turn to my short list of dependable friends – and I did that. I had made notes when people said things like, "Let me know how I can help," or "I'd be happy to come sit with him when you need to go out." I took those remarks seriously and I followed up and asked those people for specific help. It was wonderful for me, and they truly appreciated being asked. So many people want to help and sometimes we don't allow them to because we feel overwhelmed. ***Advice: let people help you.*** Get organized enough to show them what you need.

By two weeks after being home, Ron was not eating or drinking well. I tried all kinds of nutritional drinks, but he just could not/would not drink. I worried about dehydration. He was struggling. We argued about it and it was not a happy time. Since the discharge, we were back the The James two or three times a week for blood checks. It was grueling, and it was problematic as the Christmas holidays were approaching and people were on vacation. (Because of rounds rotation and vacation time, we never saw Ron's transplant doctor until about eight weeks after the transplant!)

At the December 19th appointment, Ron was readmitted to the hospital with dehydration and an endoscopy was done to see if he had upper GI GVHD. He was pumped full of IV fluids, which was exactly what he needed. I always wondered how in the world a person could be so dehydrated that they had to be hospitalized, but I saw it with my own eyes. I was not upset by the fact that a routine check-up turned into a hospital stay, since I had read that many patients get readmitted in the first month back home. (I had the bag with pajamas and meds with me…) Ron was released two days later, doing a lot better. The tests had shown irritation in his stomach, which was relieved by medication. GVHD could not be ruled out. They made it clear to him that eating would be his "job" for a while and that drinking was even more important than eating.

Advice: You, the caregiver, must take charge early in this process. Even if the patient argues with you, you MUST follow the instructions of the team and report problems when they come up. I figured it was better to end up with a divorce than have him die in front of me from something I did not report. There will be MANY arguments with a stubborn patient, or one that does not understand all the issues, or one that is too sick to think straight. You have to keep your cool, understand that this not really who your spouse is, and use your own common sense and logic. It becomes very hard over time, to "walk the fine line" between being over-protective and "hyper," or being complacent and laid back. Being a Caregiver is a stressful and often thankless job. You just do the best you can.

As soon as we started post-transplant doctor visits, I took a special bag each time, which had his main medications and a small note pad for myself. I am still using this notebook 20 months later. I would always put down the date, the personnel we saw, the issues at the time, and the advice we were given, including changes of medication. It is, essentially, a diary of what happened and when. I am able to refer to it — to see, for instance, when the skin rash first appeared, etc. ***Advice: keep notes and have a list of issues to be addressed at each visit.*** If there have been symptoms, have a list of them and when they occurred.

And so, the recovery period proceeded. The doctor had schooled us by saying, "This will be a marathon, not a sprint. The year 2017 will be a year of recovery, in the hope that you will live to see the year 2027." Another doctor said over and over, "Good days and bad days. Good days and bad days."

During the first year, I never got sick, but I thought about it a lot. I thought how difficult it would be if I could not tend to him because I was sick and could make him sick. I thought about how I would need to ask someone to move in with us — and how I would have to isolate myself. We restricted how much we went out and where we went. We avoided sick people, even moving away from someone who sneezed or coughed. We washed hands all the time. Sometimes we would wear masks. He was only allowed to drink bottled water. I told students to stay away if they had even a tickle in their throats. ***Advice: Take care of yourself, because it is not a good thing when the Caregiver is sick.***

MEDICATION MANAGER

As I have mentioned before, keeping track of medications is one of the Caregiver's major jobs. I decided that working two weeks ahead was smart. I was given a nice 7-day box to take home by the hospital. I bought another, smaller one that was easier to put in a suitcase. Each box had at least two compartments per day. I made a list of prescription medications and supplements and put them in alphabetical order. I highlighted those that went in the pills containers I organized. (The pills he took on his own — like B-12, stool softener, sleep medication — those were there, but not highlighted.) Beside the name of the med, I put the purpose of it, the dosage, and when he started on it.

I titled this document with his name, birthday, and then this: "Allogeneic Stem-Cell Transplant (for MDS) November 10, 2016." Next was the doctor's name, phone number of The James, and the current date. Then I printed three out – one for my kitchen cabinet, and smaller versions for my wallet and for his wallet. I never had to

worry that, in the event of a car accident or a sudden illness, I would be without important information. ***Advice: Protect your patient by having life-saving information with you/him at all times.***

Then I would sit down in the evening, eliminate all distractions (early on, I even put in ear plugs) and organize all the highlighted pills in alphabetical order. It was hard to keep straight "two pills once a day" and "one pill twice a day." Bactrim was a "Monday and Friday only" medication. It was complicated, especially early on, when there were easily 28 pills a day to insert into these containers. Most were either "morning" or "evening" and not in between. By doing two weeks at one time, I was able to tell when the supply of each would run out. I would put a note on my calendar of when to call for a refill or request a new script. When there are no refills left, I usually go through the physician instead of the drug store. I am careful to get 30-day supply and NOT put it on automatic refill if this may not be a long-term medication. (I have a whole box-full of meds that were stopped. Some of them could have been 30-day supplies instead of 90.)

Once finished with the pills, and having double-checked everything, I would write "do pills" on my calendar for two weeks from that day, and "have pills?" three days before that. I forgot to do that once recently and relied on the drug store to do an automatic refill. Guess what happened? They dropped the ball, neglected to order it, and I had only three days left of a very important prostate medication, unrelated to the transplant. I was not content to express my frustration to the pharmacy tech who answered the phone. The next morning, I asked for the pharmacy manager and told her that, as a Caregiver, I did not need EXTRA STRESS like this. I told her that kind of error could NEVER happen again. She heard me clearly and now they order the next month's supply of this long-term and expensive medication the day I come in to pick up the current supply.

Advice: Find a way to be super-organized and focused about the medications. Work ahead so you don't have a crisis. And when you make a mistake, don't be too hard on yourself. It really helps when the patient knows what each pill is, and what it looks like. Ron has, fortunately, caught a few mistakes I have made in the past 21 months. Today is Day 640, so I have probably handled over 15,000 pills. (Somewhere along the line, I learned there is a day calculator online.)

THE SHOWER

Taking a shower will be a tiring event for the patient for several months. Keeping the central line dry will be a big responsibility. If it gets wet, it must be changed. Some caregivers have to change the dressing themselves once a week. Ron's was changed at the hospital once a week, so I did not have to worry about it – unless it got WET! I was taught how to change it, but I did not want to, if I could avoid it! The hospital gave me some protector shields to place over the area, but, as I witnessed at the hospital, they did not always seal the water out. I was given two sizes but learned that the smaller one was usually a better choice. I then bought several different kinds of water-proof tape, and I used it liberally to keep any water from seeping into the area.

It is awkward for the patent to shower with a central line. Ron made good use of the hand-held nozzle, directing the water away from his chest area as much as possible. With low blood levels, he was extremely cold following a shower, so getting him bundled up fast was important. There was usually a long rest period following the shower routine. The exhaustion/fatigue cannot be under-estimated. The central line came out at about day 80. ***Advice: The patient may need a lot of help showering, and the proper care of the central line is of extreme importance.*** A person can die from a central line infection.

PATIENT ADVOCATE

Dealing with Doctors and Asking Questions

Sometime around the third month, I asked the doctor a medication question at a routine visit and he replied in a curt manner. Later, he apologized and said he must have misunderstood what his assistant had told him before he entered the room. I was very guarded around him after that and was not unhappy when we found out he was moving out of state. In my opinion, it is the JOB of the caregiver to ask questions when they arise, in order to understand and do things properly. Caregivers must never be afraid or reluctant to question something when it does not seem right. There were several times when Ron might have received the wrong treatment if I had not asked questions. Medical personnel sometimes make mistakes, despite their best intentions.

Ron was taken off the antiviral Acyclovir at the one year mark. But I had read on the GvHD Facebook page that it was protocol in some transplant centers to leave patients on this drug for two or even five years in order to prevent shingles. I did not want Ron getting shingles! So, using the patient portal, I asked the team to discuss this and to report back if there was merit in leaving him on the drug. They came back and said it was fine to go back on it because it did prevent shingles. I believe they have now changed their protocol and leave patients on it for two years.

Advice: A Caregiver is really an advocate for the patient. If you have educated yourself, and if you make a suggestion or comment or ask a question in a respectful manner, there is no reason anyone should be offended by that. You are just doing your job. The Caregiver needs to

be treated like a member of the team, because the Caregiver is keeping the person alive at home.

We thought we might be able to do a three day get-away to Savannah in March, but that was wishful thinking. Ron had planned to go to a 2-day conference in mid-May, but that was also cancelled because of extreme fatigue. He was now 35 pounds lighter than before the transplant, and eating and drinking was still a challenge. His sense of taste began changing while Ron was in the hospital and continued for several months. The only thing that tasted the same was an orange, and he had one every day for a year. He even wrote a poem about it, called The Year of the Orange." It was again hard for me to provide nutrition because even things he used to like did not always taste right. ***Advice: It is good to have things to look forward to, like a trip.*** But be realistic and be smart: buy travel insurance because you may need to cancel at the last minute. Know that the altered sense of taste does not last forever.

Another blood clot happened within the first six months — in the other leg, and it involved four veins. The leg had considerable swelling for a over a year, and the decision was made to have Ron on blood thinners for the rest of his life. This time, we did not get medical treatment as quickly, since Ron thought it could wait until the next check-up in a week. In retrospect, I could have pushed harder to get the swelling checked out, but the dynamic between caregiver and patient changes over time and the patient needs to feel in control of his own destiny. Caregivers have to walk a fine line, and it is often hard to do.

By the middle of the 6th month post-transplant, I was frequently informing the team that he was really struggling. Then one day the doctor called and said it was time to consider the steroid Prednisone. Now, I knew that Prednisone was a double-edged sword, from reading posts on the Graft Vs Host Disease Facebook page for five years. I had a large file on all the problems associated with long-term use of Prednisone. But quality of life was a big issue at that point, so we decided to give it a try. We saw the doctor on a Monday and then again at the end of the same week. Ron was on 80 mg for just three days, then 60 for three or four days, and then weaned down at regular intervals. He was off Prednisone by early September. I must say that the effect was miraculous. Within 12 hours of the first pill, he "woke up" and started looking for food everywhere. He perked up, starting doing things again, and started gaining weight. He was happier, more engaged and we travelled! We took trips to Mackinaw and Washington DC. And we visited the granddaughter in New Jersey. He even played doubles tennis with his long-time buddies. But in October, he came down with his first post-transplant illness, "Parainfluenza #1."

The illness laid him low and he developed a cough that lingered for nine months. But after a couple weeks, he was doing better and was able to resume some activities. We began to understand that the time on Prednisone was an artificial boost. It was nice while it lasted. But, in real life, he was just plain exhausted a good part of the time.

By November of 2017, as Ron celebrated his first "Re-Birthday," we had received a letter from our German donor, in response to two I sent, one shortly after the transplant and one at the six-month mark. Although everything had to be anonymous and handled through channels, it was wonderful to thank this person for the gift of life and to learn a little about him. I told him that I had learned a LOT about what he had to go through on HIS end, and he replied that it was "nothing" and he would willingly donate again if my husband ever needed more of his cells.

Once the flu was under control, Ron completed his "baby shots." At periodic intervals, he was immunized against polio, hepatitis, diphtheria, pertussis, tetanus, etc. Friends and family were fascinated by this aspect. Many really "got it" at this point, understanding that Ron's immune system had had a complete makeover, leaving him defenseless. (We have recently learned that recipients sometimes inherit allergies from their donor.)

We had a new transplant physician and her protocol was to get a bone marrow biopsy at the one-year mark. That was a nervous time, but the results came back that his bone marrow was 100% donor cells, and there were no signs of MDS!! If I understand correctly two genetic mutations found in MDS had disappeared. Hallelujah! While it was too soon to think Ron was "cured," all signs were indicating that he had a good chance to be cured.

2018: ANOTHER YEAR OF RECOVERY

As I write this, we are two-thirds of the way through 2018, and Ron is 21months post SCT. The recovery has proven to be slow, with ups and downs. There is no tennis. There is fatigue. There has been some travel, including a trip to Europe! but there is too much fatigue now and we watch travel shows on television. There have been music performances — very tiring — but invigorating. But now there are hand cramps. There have been wonderful dinners out, and the celebration of our 50th wedding anniversary. We actually made it to 50! But there has been weight loss and FATIGUE. There have been fewer check-ups but more specialty visits – like dermatology and pulmonology. The family physician is taking over general health issues while the transplant team monitors the immune system. The blood counts are fabulous — the best in the past ten years, in some instances. There are still irregularities in some of the white cells, which is not uncommon at this stage. His immune system is still only at the fledgling stage. But he is not the person he was and only time will tell if this is "the new normal" or whether things will improve over time. That is certainly the hope and has happened for many people.

A month ago, I found my old cheerleading necklace from junior high

school. I polished it up and wear it a lot now. It is a reminder to me that the most important role for me now is to be a cheerleader.

In order for me to have a life beyond Caregiving, I have continued to have therapeutic massages once a month, and have continued to teach piano and mentor younger colleagues. I have made time for friends. I have seen my doctor regularly. But I did need to cut back on many other activities and ask friends to help me from time to time. I could have done better at lots of things — like walking daily, doing stretching exercises everyday, and like going to bed earlier. (Sometimes the quiet late in the evening, after he was off to bed, seemed so precious that I would stay up and get the things done that I really wanted to do.)

It takes enormous energy to be a Caregiver and enormous patience. It helps to have effective organization skills, and to be able to compartmentalize. You will go through many emotions and you must find healthy ways to deal with them. Be the Match does an outstanding job of sending literature throughout the transplant process, with lots of good advice for caregivers.

As I mentioned earlier, Caregiving is mostly a thankless task, but we do it for the person we love. I did, however get a real boost at about the one-year mark. Ron went to the hematology clinic to meet with the doctor who took care of him for the five years from diagnosis up to transplant. They talked about how things had unfolded and how hard it was for the doctor to know when to pull the plug on Vidaza treatments and send Ron off to a transplant. Ron relayed to me that the doctor told him he was alive and doing well for two reasons: the first was the fact that he was in very good health going into the transplant, active in music, work and tennis; the second was that he had me as his Caregiver. Of course, I cried when I heard that.

We just do the best we can, and then we hope for the best. We try to focus on the positive and find happy times in each day.

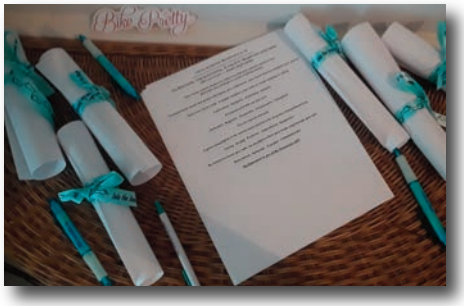
We just do the best we can, and then we hope for the best. We try to focus on the positive and find happy times in each day.

We feel tremendous gratitude for our donor and for all the medical people who have helped along the way, including the nurses in the infusion room for those 414 treatments; the receptionist who greeted Ron with a smile every day for 414 days; the researchers who invented Vidaza; the courier who hand-delivered the precious cells from Germany to Columbus; the nurse extraordinaire who calmly never missed a beat when Ron spiked the fever the night of Day 1 — who had six vials of blood drawn in the blink of an eye and arranged to have them raced down to the lab; to the nameless and faceless people in the lab; to the custodians who kept the hospital room so clean you could have eaten off the floor; to the people that have to do the bone marrow biopsies; to the doctors and personnel who worked on Christmas and New Years, when we were there; to the nurses who answered the phone in the middle of the night when you needed to ask a question; to the pharmacists at my local CVS who have helped me every step of the way... The list goes on and on. A sense of gratitude can be very healing.

It takes a team to help a person with MDS. I am happy to play a major part on that team.

Janice Cook is a nationally certified piano teacher living in Columbus, Ohio. She got her feet wet as a Caregiver when both of her children needed surgery in 9th grade. Her skills got stronger when her father had a rare form of terminal cancer and then when her husband developed an aggressive form of prostate cancer at age 55. And then came the MDS.

Coping and Caring Summer Dinner, Margate, NJ, July 28, 2018



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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).

LIVING ENDOWMENTS

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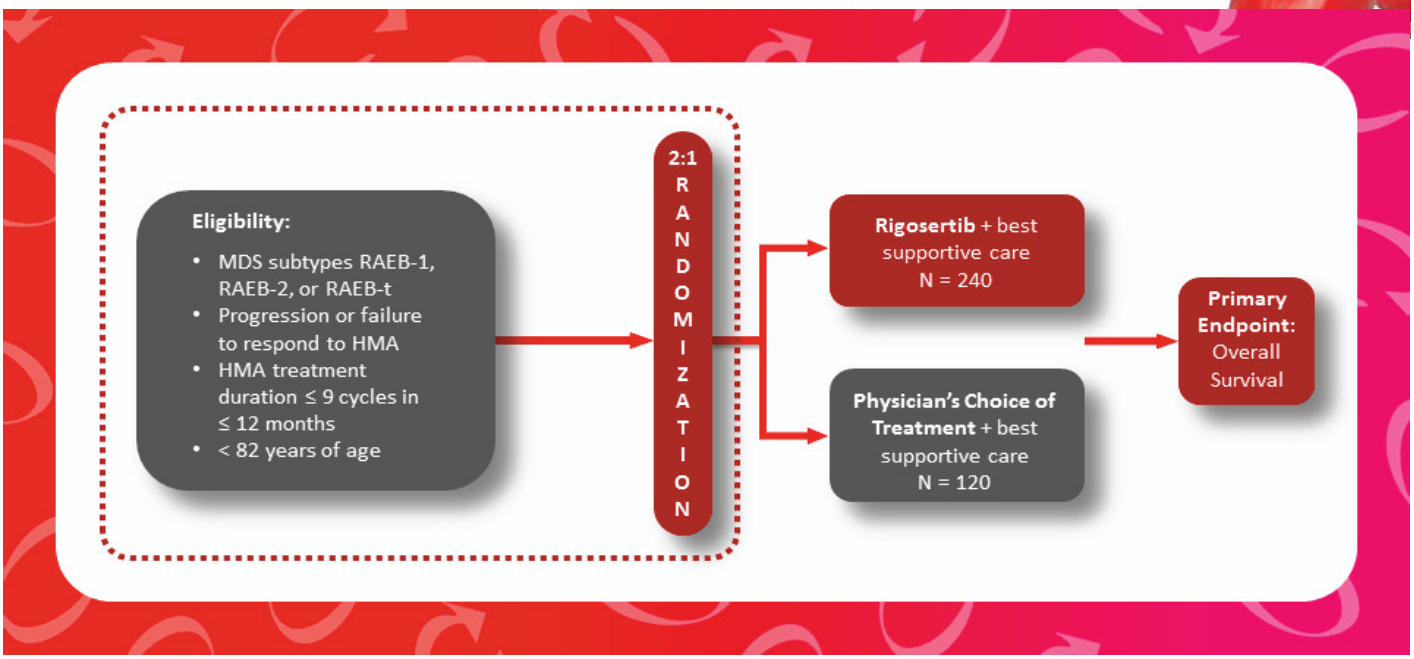
The Pivotal MDS Trial INSPIRE is Now Recruiting Patients

INternational Study of Phase III Intravenous RigosErtib

STUDY DESCRIPTION

A Phase 3, international, randomized, controlled study of Rigosertib + best supportive care versus physician's choice of treatment + best supportive care in patients with myelodysplastic syndrome (MDS) after failure of a hypomethylating agent (HMA).



PRIMARY ENDPOINTS

Overall survival in the intention-to-treat population and in patients with very high risk per the Revised International Prognostic Scoring System (Greenberg et al, *Blood* 2012).

INTERNATIONAL TRIAL

More than 170 trial sites

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

Rigosertib is an investigational agent and is not approved by the FDA or other regulatory agencies worldwide as a treatment for any indication.

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PEVONEDISTAT-3001

TAKEDA'S PANTHER: A NEW CLINICAL STUDY

A Phase 3, Randomized, Controlled, Open-label, Clinical Study of Pevonedistat Plus Azacitidine Versus Single-Agent Azacitidine as First-Line Treatment for Patients with Higher-Risk Myelodysplastic Syndromes, Chronic Myelomonocytic Leukemia, or Low-Blast Acute Myelogenous Leukemia.

Takeda Pharmaceuticals International Inc. is initiating a Phase 3 clinical study with the study drug Pevonedistat. The purpose of this study is to evaluate the efficacy and safety of pevonedistat plus azacitidine versus single agent azacitidine in participants with higher-risk myelodysplastic syndromes, chronic myelomonocytic leukemia and low blast acute myelogeneous leukemia. This study will look at the overall response, event free survival, and overall survival in people who take pevonedistat and azacitidine when compared to people who take single agent azacitidine.

The study will enroll approximately 450 participants. Once enrolled, participants will be randomly assigned (by chance, like flipping a coin) to one of the two treatment groups in a 28 day treatment cycles:

- Pevonedistat 20 mg/m2 and azacitidne 75 mg/m2 combination.
- Single agent azacitidine 75 mg/m2.

All participants will receive azacitidine via the intravenous or subcutaneous route. Participants randomized to the combination arm also will receive pevonedistat intravenous infusion).

This multi-center trial will be conducted worldwide. Patients may qualify for this study if:

- 18 years of age or older.
- Patients have intermediate, high, or very high risk MDS or CMML, based on the Revised International Prognostic Scoring System (IPSS-R), a standard prognostic tool.
- Patients have low-blast AML defined as 20% to 30% myeloblasts in the bone marrow (Low-Blast AML) and ≤30% myeloblasts in the peripheral blood and considered appropriate for azacitidine based therapy.

In order to refer a patient with MDS, CMML, or low blast AML for enrollment to this study and review eligibility criteria, physicians/health care providers should visit: www.clinicaltrials.gov (NCT03268954)

Contact: Takeda Study Registration Call Center +1-877-825-3327; medicalinformation@tpna.com

Takeda ONCOLOGY

PANTHER

Phase 3 Clinical Trials NOW ENROLLING

ASTRAL-2
Relapsed/Refractory AML

Guadecitabine (SGI-110) in AML

404-Patient Multicenter, Randomized, Open-Label, Study in Acute Myeloid Leukemia (AML) Patients Who Failed or Relapsed Following Prior Intensive Chemotherapy

For more information: www.clinicaltrials.gov
identifier: NCT02920008 or
email: ASTRAL-2@astx.com

ASTRAL-3
Relapsed/Refractory MDS or CMML

Guadecitabine (SGI-110) in MDS or CMML

408-Patient Multicenter, Randomized, Open-Label Study in Myelodysplastic Syndromes (MDS) or Chronic Myelomonocytic Leukemia (CMML) After Failure of Prior Azacitidine, Decitabine, or both

For more information: www.clinicaltrials.gov
identifier: NCT02907359 or
email: ASTRAL-3@astx.com

Ascertain
MDS and CMML

Oral ASTX727 in MDS & CMML (US & Canada)

A Phase 3, Randomized, Open-Label, Crossover Study of ASTX727 (Cedazuridine and Decitabine Fixed-Dose Combination) versus IV Decitabine in Subjects with Myelodysplastic Syndromes (MDS) and Chronic Myelomonocytic Leukemia (CMML)

For more information: www.clinicaltrials.gov
identifier: NCT03306264 or
email: Ascertain-1@astx.com

Otsuka

astex
A member of the Otsuka group

For a full list of eligibility requirements go to clinicaltrials.gov

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MYELODYSPLASTIC SYNDROMES

COPENHAGEN, DENMARK

8-11 MAY 2019

SAVE THE DATE

MDS 2019 Symposium Secretariat:
c/o Kenes International
Email: mds@kenes.com

For MDS Foundation Contact:
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