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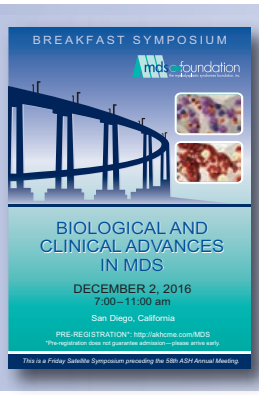
MDS NEWS HIGHLIGHTS

FROM THE GUEST EDITOR'S DESK

- **The Role of Peripheral Blood FISH Cytogenetics for the Diagnosis and Prognosis of MDS**

Presented by: ***Prof. Dr. med. Detlef Haase, Dr. med. Julie Schanz, Dr. med. Friederike Braulke, Dr. nat. techn. Christina Ganster***



PLAN TO ATTEND OUR UPCOMING SYMPOSIA

ASH 2016 MDS FOUNDATION BREAKFAST SYMPOSIUM

December 2, 2016 • San Diego, California

14TH INTERNATIONAL SYMPOSIUM ON MYELODYSPLASTIC SYNDROMES

May 3–6, 2017 • Valencia, Spain

IN THIS ISSUE

GUEST EDITORIAL

Guest Editorial: The Role of Peripheral Blood FISH Cytogenetics for the Diagnosis and Prognosis of MDS

Prof. Dr. med. Detlef Haase
Dr. med. Julie Schanz
Dr. med. Friederike Braulke
Dr. nat. techn. Christina Ganster
Department of
Hematology and Oncology
University of Göttingen
Göttingen, Germany

Abnormality	%	Localization	N (pts. examined)	Author
TET2-Deletion	**11.5**	4q24	44	*De Olivera (2013), Med. Oncol*[2]
EGR1-Deletion	**5.6** **2.7*** **1.9#** **4.6+**	5q31	1473	*Lai Y-Y (2015), Leuk Res*[4] *Mallo (2008), haematologica*[5]
-7/7q-	**3.9** **8.7**	7cen->7q34 "	433 1473	*Adema (2013), Leuk Res*[3] *Lai Y-Y (2015), Leuk Res*[4]
+8	**6.3**	8pter ->8qter	1473	*Lai Y-Y (2015), Leuk Res*[4]
TEL/ETV6-Deletion	**4.6**	12p13	367	*Braulke (2015), Genes Chromos. Cancer*[6]
20q-Deletion	**5.8**	20q11->20q13	1473	*Lai Y-Y (2015), Leuk Res*[4]
Y-loss	**4.1**	Yq11->Yqter	1473	*Lai Y-Y (2015, Leuk Res*[4]

*At least 20 metaphases analyzed; #10-19 metaphases; +1–9 metaphases

Table 1. FISH-abnormalities in MDS with normal karyotype by CBA, published data

Introduction

Chromosome banding analysis (CBA) is still the gold standard of cytogenetic diagnostics in MDS. The recent IPSS revision underscored the high impact of the karyotype to prognostication in relation to blast counts, hemoglobin value, platelets and neutrophil counts. The higher weight which was assigned to cytogenetic findings clearly improved the predictive power of IPSS-R in comparison to the old IPSS1. However, also CBA has its limitations. These mainly reside in the need for dividing cells from bone marrow aspirate, since only rarely appropriate metaphase analysis can be successfully performed on peripheral blood. CBA also can be hampered or even made impossible by bone marrow fibrosis which can occur in a substantial subset of patients with MDS. The same is true for intrinsic hypoplastic MDS forms. Long lasting therapy with demethylating agents also may lead to hypoplastic bone marrow (bm). Furthermore, certain aberrations such as small deletions can be missed by CBA. MDS are chronic and dynamic diseases with a high probability of genetic evolution over time possibly forcing the treating physicians to adapt their therapeutic strategies during the course of the disease. Given the advance of effective, partially targeted treatments such as Lenalidomide and Dimethyl-Transferase-inhibitors (DMTI) and upcoming treatments directly targeting genetic defects, it becomes more and more important to survey abnormal clones and their response to therapy by frequent monitoring. Repeated bone marrow punctions to achieve an adequate monitoring, however, mean an unacceptable burden for most of the often frail MDS patients. Thus alternatives for CBA of bone marrow cells are urgently needed. We believe that to this respect fluorescence in situ hybridization (FISH) -analyses of peripheral blood represents an attractive option.

Additional Value of FISH in MDS with a Normal Karyotype or Insufficient Metaphase Yield

Independent from the source of material examined, several groups have addressed the question whether interphase FISH can provide additional information in cases with a normal karyotype, insufficient metaphase yield or rather small cell clones. The most frequent abnormality not detected by CBA was deletion of TET2 (12%),[2] followed by partial or total monosomy 7 (up to 9%),[3,4] 20q-deletion[4] and 5q-deletion (in 2 to 6%),[5] 12p-deletion (5%)[6] and loss of Y-chromosome (4%)[4] (**Table 1**). For the proof of monosomy 7/del(7q) by FISH, a negative prognostic effect was demonstrated.[3]

For the TET2-deletion, it is quite obvious that, in most cases, the deletion is too small for detection by CBA. The same holds true for TEL/ETV6-deletions.[5] A 5q-deletion sometimes might be really kryptic as observed recently in our lab (**Figure 1**). However, in most instances, when it is missed by CBA this might be due to problems to get the cell clone into proliferation in vitro.

FISH-analysis of Peripheral Blood

To our knowledge, apart from our own studies, only two prospective trials based on a meaningful number of cases addressed the value of FISH from peripheral blood in comparison to bone marrow FISH-analysis.

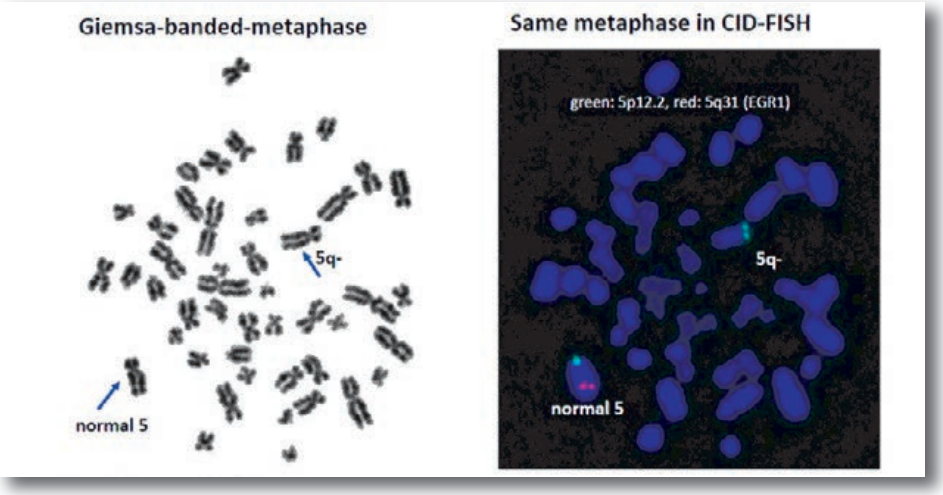


Figure 1. Proof of a kryptic EGR1-/5q-deletion by relocalization of the banded metaphase and FISH-analysis with the informative EGR1-FISH-probe at the identical metaphase (Haase, unpublished)

In 2009 with support by the MDS Foundation, an international multicentric diagnostic study with participation of 15 centers from 8 countries was launched aiming to answer the question whether "a peripheral blood (pb) sample will yield the same diagnostic and prognostic cytogenetic data as the concomitant bone marrow (bm) in myelodysplasia". In a pilot phase, the concordance among sites proved to be excellent. In the second phase of the study, a total of 100 MDS patients were prospectively accrued to the study. A FISH panel consisting of eight probe sets, designed to detect the most frequent chromosome abnormalities in MDS [-5/5q, -7/7q-/der(1;7), +8/8q-, -11/+11/11q-/add (11q), 12p-/+21/t(12;21), -13/13q-, 17p- and 20q-/i(20q)/i(20p)], was performed on both specimen types, pb and bm. CBA of pb was unsuccessful in 51% of cases examined. FISH was informative (concordant with bm/pb CBA) in 95% of cases, with 51% of pb FISH demonstrating an abnormal clone. FISH was discordant in 5% of bm and pb samples, while CBA and FISH of bm and pb were discordant in 12% and 9% of samples, respectively.

In 12 cases, abnormal CBA findings with normal FISH findings were explained by the failure of the FISH panel to trace the described clonal chromosomal abnorm alities (e.g. t(8;10), trisomy 19, -Y). When bm and pb FISH indicated an anomaly, typically the percentage of positive cells was lower in the pb than that observed in the bm, as can be expected. It was concluded that while CBA of bm remains the "gold standard" at diagnosis of MDS, evaluation of interphase nuclei by FISH from pb could be used for follow-up (non-diagnostic) on MDS patients. It may be equally informative, as well as less costly and stressful, than a bm sample. Combination of both techniques can increase sensitivity and number of informative cases.[7]

In a prospective study, Coleman and colleagues compared FISH results from bone marrow with peripheral blood in 48 cases with suspected MDS or AML. A FISH panel of four probes detecting -5/5q, -7/7q-, +8 and 20q- was applied. They found abnormal pb FISH results in 69% of 26 cases with abnormal bm FISH. On the other hand pb FISH was abnormal in 23% of 22 patients with normal bm FISH. In the entire cohort of 433 patients FISH in general was abnormal in 14% of cases with <20 normal metaphases and in 19% of cases with no metaphase yield. By CBA alone 26.3% had an abnormal karyotype. By combination with FISH karyotypic abnormalities were found in 31.4% of patients. 136 pts. had any cytogenetic change of which 16.2% were identified only by FISH.[8]

CD34+ FISH of Peripheral Blood

Background

In patients with Myelodysplastic Syndrome (MDS) chromosomal aberrations represent an important component in pathogenesis, diagnosis, prognosis and therapeutic decision making. The gold standard method for cytogenetic diagnostics in MDS is still the conventional chromosome banding analysis of bone marrow metaphases, providing an overview of the whole chromosome complement and the assessment of the karyotype according to the International System of Human Cytogenetic Nomenclature (ISCN).[9] For many chromosomal anomalies typical for MDS, corresponding probes are available for Fluorescence-in-Situ-Hybridization (FISH) analyses. Several studies have focused on the possible benefit of additional FISH-testing of bone marrow blood cells in MDS.[2-8,10-14] In 2001, Vehmeyer et al. described an increased number of myeloid CD34+ progenitor cells circulating in the peripheral blood of MDS patients.[15] They found a positive correlation between the amount of CD34+ circulating cells in pb and advanced MDS stages. Later, Haase et al. could show that in MDS and acute myeloid leukemia (AML) CD34+/CD38- bone marrow cells show the same clonal chromosomal aberrations as observed in routine metaphase analysis.[16,17] Based on these data, we chose CD34+ myeloid progenitor cells circulating in peripheral blood for further analyses.

Method

First, we tested a FISH-probe panel on unselected and enriched CD34+ bone morrow blood cells in addition to sufficient karyotyping on bm metaphases. CD34+ myeloid progenitor cells circulating in the peripheral blood were enriched using immunomagnetic activated cell separation (MACS®, Miltenyi Biotec GmbH, Bergisch Gladbach, Germany). Out of 20ml of pb, a number of 80 000 to 400 000 CD34+ cells could be enriched (0.2-1.5% of all peripheral nucleated cells).[18] After immunomagnetic cell sorting, CD34+ cells were analyzed by FISH techniques using comprehensive FISH-probes, detecting

most of the aberrations typical for MDS: LSI 1p36SO/1q25SG™, LSI EGR1(5q31)/D5S23,D5S721(5p15.2)™, LSI CSF1R (5q33-q34)/D5S23,D5S721 (5p15.2)™, LSI D7S522(7q31)/CEP7™, LSI CEP8 Spectrum Orange™, LSI MLL DualColor™, LSI TEL/AML1 ES™, LSI 13(RB1) 13q14™, LSI IGH/BCL2™, LSI TP53 (17p13.1)™, LSI D20S108(20q12)™, CEP X SpectrumOrange™/Y SpectrumGreen™ (Abbott GmbH & Company, KG, Wiesbaden, Germany) and XL TET2TM (MetaSystems GmbH, Altussheim, Germany).

CD34+FISH-trial

In a small pilot study, we performed the proof of principle of a new method to monitor MDS patients from peripheral blood.[18] We could show that analysing CD34+PB cells by FISH using comprehensive probe panels is feasible in low-risk as well as in high risk MDS patients. Furthermore, the results from peripheral blood correlated well with the results of conventional banding analyses as the gold standard method. In a second step we started a prospective German diagnostic study (CD34+FISH-Study, ClinicalTrials.gov: NCT01355913) to follow MDS patients by sequential FISH analyses from pb in a sense of a molecular-cytogenetic monitoring. In total, 360 MDS patients were monitored up to 3 years by sequential FISH analyses of immuno-magnetically enriched CD34+ peripheral blood cells using comprehensive FISH probe panels every 2–3 months with a total number of 19,516 FISH analyses.[19] In every case of bone marrow aspirates available, comparative additional FISH analyses of unselected and selected CD34+ bm were performed in parallel to conventional banding analyses. We could show that CD34+pb-FISH results correlate significantly with bm-banding analysis. Furthermore, we demonstrated that the enrichment step is necessary using pb because otherwise the clone sizes detected by FISH are too small and too close to the probes cut-off value for valid cytogenetic information during follow-up. Our data show that the enrichment step was not required in case of FISH analyses on bm cells, the clone sizes differed not significantly between enriched and unselected bm FISH analyses.[19]

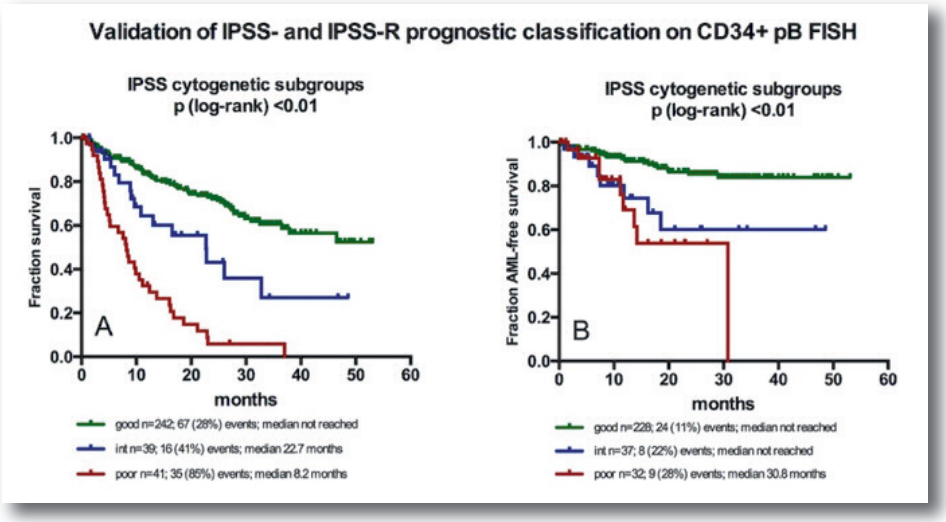


Figure 2. Cytogenetic prognostic classification as defined by IPSS/-R by using CD34+pb- FISH[22]

This method was chosen for cytogenetic monitoring in a prospective German phase-I clinical trial for heavily pretreated high-risk MDS patients who received a combination therapy of Azacitidine and Lenalidomide (AZALE, University of Dresden, Germany, ClinicalTrials.gov: NCT00923234).[20] We could show that CD34+pb-FISH was able to serve as a cytogenetic monitoring to detect response to therapy as well as treatment failure.

The method was also applied in another prospective German phase-II-clinical trial for low-risk MDS patients with isolated 5q-deletion to be treated with lenalidomide (LE-MON-5, University of Düsseldorf, Germany, EudraCT:2008-001866-10) and could prove its feasibility as a reliable non-invasive cytogenetic monitoring from pb.[21]

The results from peripheral blood correlated well with the results of conventional banding analyses as the gold standard method.

Evaluation of the Prognostic Impact of CD34+pb FISH

Since FISH analyses of CD34+ cells from the peripheral blood were established as a reliable method to perform cytogenetic analyses in MDS, there was some interest whether the results of this method can be used to evaluate the prognosis in MDS as valid as by chromosome banding analysis. So far, the evaluation of prognostic systems in MDS, most actually the IPSS-R,[1] was based on chromosome banding analyses (CBA) without considering results from FISH. However, in the daily clinical practice, a method to evaluate prognosis from a peripheral blood sample without the need to perform a bone marrow biopsy, would be of great value, especially in patients that are not eligible for or not willing to accept a BM biopsy. Thus, a retrospective analysis including a total number of 3,230 patients with MDS was conducted in order to investigate the comparability of the prognostic predictive power in CBA versus CD34 pB FISH.[22] Based on our results that analyzing circulating CD34+ cells by FISH is a reliable method to survey an aberrant clone in peripheral blood, that it is feasible in high-risk as well as in low-risk MDS and is representative for the clonal situation in the bone marrow,[18,19] it was of special interest whether: a) prognostic classification by IPSS and IPSS-R based on CD34+ pB FISH is reliable, b) severe limitations are

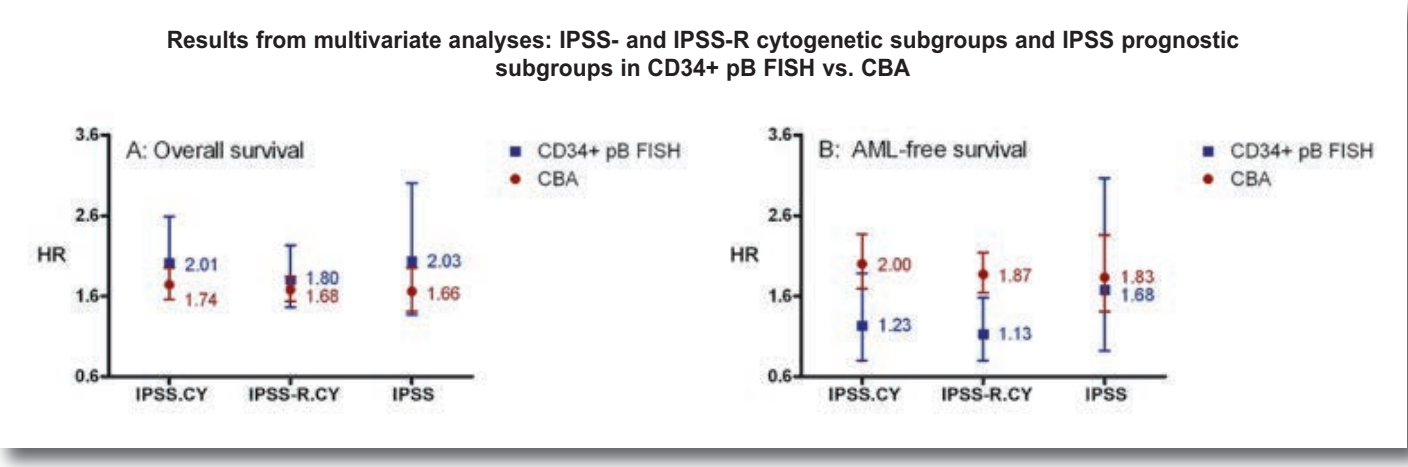


Figure 3. Cytogenetic prognostic classification comparing CD34+ pB FISH and CBA (Braulke at al. 2015)

observable and c) the method is able to replace the gold standard of cytogenetic prognostic classification, the CBA.

The study demonstrated that the cytogenetic classification as defined by IPSS (**Figure 2**) and IPSS-R is feasible and reliable.

In a second step, it was proven by a multivariate analyses adding a control group of 2,902 patients analyzed by CBA published before,[23] that the results from CD34+ FISH are not significantly different regarding their predictive power (**Figure 3**). However, the study also showed that there are some limitations that lead to the conclusion that CD34+pb-FISH is a method able to amend, but not to replace CBA. The main points are:

a) Abnormalities not detectable by the probe panel used in CD34+ pB FISH are overlooked
b) Different clones, possibly evolved from an evolutional process, cannot be separated by FISH. Unrelated clones are undetectable by this method.
c) The complexity of the clone and the number of abnormalities, which is of great prognostic importance, is sometimes underestimated by CD34+pb-FISH.

Thus, taken these results together, CBA remains the gold standard of prognostic classification of MDS. However, CD34+ pb-FISH can be of great value as an alternative method if CBA is not feasible.

Clonal Evolution

It is well known that clonal evolution is associated with an adverse prognosis in MDS patients.[24,25] Principally, evolution of the clone towards complex or more complex changes can occur via different pathways: a) a stepwise accumulation of karyotype abnormalities over the time of the disease and b) a catastrophic single event that results in a substantial chromosomal instability, finally resulting in a multitude of chromosomal abnormalities and rearrangements and cell to cell variations. In MDS, a clonal evolution that took place in the past can be often observed at the time of the first diagnosis when several different clones evolving from each other are seen in the first cytogenetic examination. When evolution occurs as a stepwise process or later in the disease its detection can be difficult because this is only possible by performing frequent sequential cytogenetic analyses during the course of the disease. However, the observation of the clone in vivo over a long time period is scientifically desirable, but ethically problematic because it is unacceptable for the patient to perform bone marrow punctations in short time intervals. Beyond its prognostic meaning, a "clonal surveillance" would be of great interest to understand the mechanisms of clonal evolution and their patterns in MDS and their link to the course of the disease. Performing CD34+ FISH on peripheral blood has the potential to overcome the problem of sequential cytogenetic analyses by offering a method that is indolent for the patient, valid and reliable. Thus, the method will be of great value to understand clonal evolution in MDS in the future. The German LeMon[5] trial was a first step in that direction. In this study, a large number of patients with del(5q) MDS were treated with lenalidomide and the cytogenetic course of these patients was observed using the CD34+ pb-FISH method in a frequently repeated design. First results from this study and the clonal course of these patients will be published in the near future.

Discussion

There is an increasing body of evidence provided by several independent groups and international collaborations that FISH analyses of peripheral blood in MDS adds significantly to an improvement of clinical management. FISH analyses of pb samples are feasible, reliable and can cover most relevant cytogenetic changes if an adequate comprehensive probe panel is used.[7,18,19]

Pb FISH is a good alternative if chromosome banding analysis of bm specimens is not possible. A further attractive option is to use pb FISH to frequently monitor the karyotype during the course of the disease and to follow abnormal clones and/or timely detect clonal evolution. It is also a good device to objectivate therapy response without the need for repeated bone marrow punctations. The use of nonenriched pb cells for FISH however, bears the risk to

miss a substantial portion of smaller clones. Also, the follow-up of unenriched pb might be problematic since the portion of cells not belonging to the MDS clone can fluctuate over time interfering with a reliable longitudinal survey of clones. To this respect pb FISH can be optimized by the use of immunomagnetically enriched CD34+ blood cells. This technique can overcome the above mentioned flaws with quite low additional expenditure and acceptable costs. Even a prognostication adapted to the IPSS/IPSS-R is possible. The individual course from our lab shown in **Figure 4** exemplifies the value and potential of the CD34-FISH-technique (unpublished data).

In this borderline case between RA and RAEB-1, we always had to struggle with low metaphase yield making cytogenetics unreliable. However, by applying CD34pb-FISH we were able to establish a reliable and informative cytogenetic monitoring nevertheless. We even could detect abnormalities not found in the metaphase fraction. It allowed us to detect clonal evolution and leukemic transformation very early before clinical deterioration and to react on this by rapid start of therapy escalation ending up in successful allogeneic stem cell transplantation and enduring complete remission.

There is an increasing body of evidence provided by several independent groups and international collaborations that FISH analyses of peripheral blood in MDS adds significantly to an improvement of clinical management.

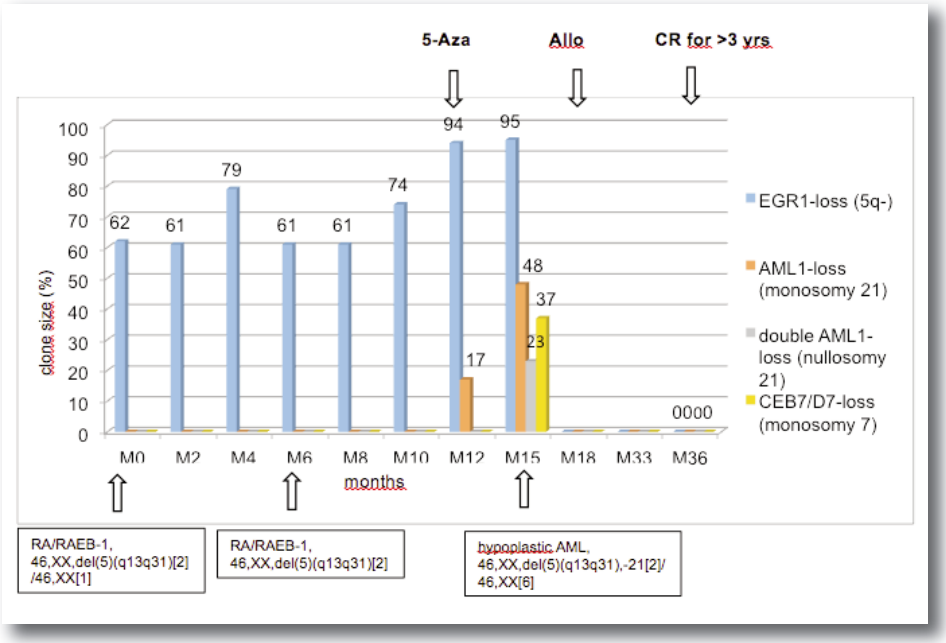


Figure 4. Course of FISH results in a patient with RAEB-1 and initially isolated del(5q).
The columns show the proportion of cells affected by cytogenetic aberrations (clone size) in CD34+ peripheral blood cells (PBC) the numbers above each show the percentage of the resp. abnormality. In addition to 5q-, the patient gained as a further subclonal aberration a loss of one AML1-signal 12 months after start of monitoring of CD34+ PBC without significant clinical signs of progression. Nevertheless 5-Aza was started. Before, bm examinations at months 0 and 6 had revealed a borderline morphology between RA and RAEB-1 and confirmed FISH results by metaphase analysis although showing a low metaphase yield. At month 15 further cytogenetic progression was observed (only by CD34+pb FISH) with an increase of cells with loss of one AML1-signal and the emergence of two new additional (subclonal) changes (cells with loss of the second AML1-signal and monosomy 7). Again no signs of clinical deterioration were evident. Worried about that, we performed a bone marrow examination showing the transformation into a hypoplastic AML. Therapeutic strategy was modified and an allogeneic stem cell transplantation was performed at month 18 with the patient now in continuous complete remission since over three years.

Comment on Guest Editorial in MDS News, Vol. 22, Issue 1

We were asked to comment on the Guest Editorial in the spring/summer newsletter of the Myelodysplastic Syndromes Foundation. Here, Tucker and Karsan discussed the superiority of DNA microarray analysis (DMA) over conventional cytogenetics and that a combination of DMAs and next generation panel sequencing (NGS) might make karyotype analysis redundant in the future.

Micorarrays can be performed on bone marrow as well as on peripheral blood[27,28] and could therefore, just as FISH, overcome the need for bone marrow and for metaphases. Unlike FISH, microarrays would detect aberrations genome-wide and were therefore thought to increase the number of informative cases.

However, both methods, DMAs and NGS, at least at the actual state, have their own specific limitations, especially concerning sensitivity, uncovering of clonal architecture and the uncertainty of prognostic relevance tested in a large patient cohorts not treated with disease modifying therapies. The authors argue that there are fewer abnormalities in the cytogenetic risk categories compared to the multitude of those observed. From a certain point of view, this is correct. However, the rarity of these changes by itself implies that only a small subgroup of patients (8.9%)[26] is affected by them, thus making this problem much smaller as claimed by Tucker and Karsan. At the moment, an international activity of the IWG-PM is under way collecting prognostic data of very rare isolated cytogenetic abnormalities

in MDS, and data will be published soon. We agree with the statement that DAM is very suitable to detect kryptic CNAs und copy number neutral LOH (CN-LOH) and thus can add important genetic information. However, this is a quite rare phenomenon in MDS too.

In our lab conventional cytogenetics, FISH-analysis, DMA as well as NGS are well-established and used for research purposes as well as in routine analyses, which allows us to judge about the pros and cons of each method in direct comparison. We evaluated 146 MDS/sAML cases with conventional karyotyping, FISH (56% of cases on circulating CD34+ cells) and DMA (40% of cases on circulating CD34+ cells). By conventional karyotyping, the frequency of informative abnormal cases was 60%, by FISH it was 58%. The frequency of informative cases increased to 71% if FISH and DMA were considered. In 11/146 (8%) cases DMA identified an abnormality when conventional karyotyping and FISH did not (6x due to CN-LOH, 5X due to rare abnormalities below the ~10 Mb resolution of standard karyotyping). Aberrations, only detected by DMA and not by FISH, were CN-LOHs in regions commonly affected in MDS with known prognostic significance; but also rare aberrations with unknown prognostic significance. In cases with normal conventional karyotyping and normal FISH, DMAs could probably add cytogenetic information. Microarray would be useful to prove clonality, but so far, cryptic aberrations are often of unknown prognostic significance and the effect of the amount of genetic material abnormal by DMA on prognosis is unclear. To this respect we have to keep in mind that the data set used for the establishment of the IPSS-R is unique, due to its size (7012 fully characterized pts.) and due to the fact that pts. were not treated with disease modifying therapies, thus more or less representing natural course of the disease. To be able to define prognosis of rare DMA-abnormalities would long for a data set of comparable size and features, which is very unlikely to be achievable ever again. Another problem is the low sensitivity of DMA which ranges between 20 and 30% clone size, while sensitivity of CBA is in the range of 10% and of interphase FISH around 5%. Another important point is that, at the moment, no other method than CBA can decipher a given clonal architecture directly. That means that without CBA you can do some statistical calculations but you rarely can be sure that the abnormalities you detect belong to one single clone, reside in completely independent clones or are distributed over several different subclones. While the prognostic relevance of different combinations of cytogenetic changes was clarified[26] this has not been comprehensively achieved for NGS, or combined results of DMAs and NGS.

We think that, at the moment, none of the discussed technologies can substitute another one. However, the combined use of them can be beneficial for individual patient´s management increasing the amount of genetic information substantially.

References

1. Peter L. Greenberg, Heinz Tuechler, Julie Schanz, Guillermo Sanz, Guillermo Garcia-Manero, Francesc Solé, John M. Bennett, David Bowen, Pierre Fenaux, Francois Dreyfus, Hagop Kantarjian, Andrea Kuendgen, Alessandro Levis, Luca Malcovati, Mario Cazzola, Jaroslav Cermak, Christa Fonatsch, Michelle M. Le Beau, Marilyn L. Slovak, Otto Krieger, Michael Luebbert, Jaroslaw Maciejewski, Silvia Magalhaes Yasushi Miyazaki, Michael Pfeilstoecker, Mikkael Sekeres, Wolfgang R. Sperr, Reinhard Stauder, Sudhir Tauro, Peter Valent, Teresa Vallespi, Arjan van de Loosdrecht, Ulrich Germing, and Detlef Haase. Revised International Prognostic Scoring System (IPSS-R) for Myelodysplastic Syndromes. *Blood*. 2012 Sep 20;120(12): 2454–65. Epub 2012 Jun 27
2. de Oliveira FM, Miguel CE, Lucena-Araujo AR, de Lima AS, Falcão RP, Rego EM. FISH analysis for TET2 deletion in a cohort of 362 Brazilian myeloid malignancies: correlation with karyotype abnormalities. *Med Oncol*. 2013 Mar;30(1):483. doi: 10.1007/s12032-013-0483-1. Epub 2013 Feb 7.
3. Ademà V, Hernández JM, Abáigar M, Lumbreras E, Such E, Calull A, Dominguez E, Arenillas L, Mallo M, Cervera J, Marugán I, Tormo M, García F, González T, Luño E, Sanzo C, Martín ML, Fernández M, Costa D, Blázquez B, Barreña B, Marco F, Batlle A, Buño I, Martínez-Laperche C, Noriega V, Collado R, Ivars D, Carbonell F, Vallcorba I, Melero J, Delgado E, Vargas MT, Grau J, Salido M, Espinet B, Melero C, Florensa L, Pedro C, Solé F. Application of FISH 7q in MDS patients without monosomy 7 or 7q deletion by conventional G-banding cytogenetics: does -7/7q- detection by FISH have prognostic value? *Leuk Res*. 2013 Apr;37(4): 416-21. doi: 10.1016/j.leukres.2012. 12.010. Epub 2013 Jan 18.
4. Lai YY, Huang XJ, Li J, Zou P, Xu ZF, Sun H, Shao ZH, Zhou DB, Chen FP, Liu ZG, Zhu HL, Wu DP, Wang C, Zhang Y, Li Y, Hou M, Du X, Wang X, Li W, Lai YR, Zhou J, Zhou YH, Fang MY, Qiu L, Wang XM, Zhang GS, Jiang M, Liang YM, Zhang LS, Chen XQ, Bai H, Lin JY. Standardized fluorescence in situ hybridization testing based on an appropriate panel of probes more effectively identifies common cytogenetic abnormalities in myelodysplastic syndromes than conventional cytogenetic analysis: a multicenter prospective study of 2302 patients in China. *Leuk Res*. 2015 May;39(5):530-5. doi:10.1016/j.leukres. 2015.02.005. Epub 2015 Feb 18.
5. Mallo M1, Arenillas L, Espinet B, Salido M, Hernández JM, Lumbreras E, del Rey M, Arranz E, Ramiro S, Font P, González O, Renedo M, Cervera J, Such E, Sanz GF, Luño E, Sanzo C, González M, Calasanz MJ, Mayans J, García-Ballesteros C, Amigo V, Collado R, Oliver I, Carbonell F, Bureo E, Insunza A, Yañez L, Muruzabal MJ, Gómez-Beltrán E, Andreu R, León P, Gómez V, Sanz A, Casasola N, Moreno E, Alegre A, Martín ML, Pedro C, Serrano S, Florensa L, Solé F. Fluorescence in situ hybridization improves the detection of 5q31 deletion in myelodysplastic syndromes without cytogenetic evidence of 5q-. *Haematologica*. 2008 Jul; 93(7):1001-8. doi: 10.3324/haematol.13012.
6. Braulke F, Müller-Thomas C, Götze K, Platzbecker U, Germing U, Hofmann WK, Giagounidis AA, Lübbert M, Greenberg PL, Bennett JM, Solé F, Slovak ML, Ohyashiki K, Le Beau MM, Tüchler H, Pfeilstöcker M, Hildebrandt B, Aul C, Stauder R, Valent P, Fonatsch C, Bacher U, Trümper L, Haase D, Schanz J. Frequency of del(12p) is commonly underestimated in myelodysplastic syndromes: Results from a German diagnostic study in comparison with an international control group. *Genes Chromosomes Cancer*. 2015 Dec;54(12):809-17. doi: 10.1002/gcc.22292. Epub 2015 Sep 10.
7. Athena M. Cherry, Marilyn L. Slovak, Lynda J. Campbell, Kathy Chun, Virginie Eclache, Detlef Haase, Claudia Haferlach, Barbara Hildebrandt, Anwar M. Iqbal, Suresh C. Jhanwar, Kazuma Ohyashiki, Francesc Sole, Peter Vandenberghe, Daniel L. VanDyke, Yanming Zhang, and Gordon W. Dewald (2012) Will a Peripheral Blood (PB) Sample Yield the Same Diagnostic and Prognostic Cytogenetic Data as the Concomitant Bone Marrow (BM) in Myelodysplasia? *Leuk Res*. Jul;36(7):832-40. Epub 2012 Apr 25.

8. Coleman JF1, Theil KS, Tubbs RR, Cook JR. Diagnostic yield of bone marrow and peripheral blood FISH panel testing in clinically suspected myelodysplastic syndromes and/or acute myeloid leukemia: a prospective analysis of 433 cases. *Am J Clin Pathol*. 2011 Jun;135(6):915-20. doi: 10.1309/AJCPW10YBRMWSWYE.
9. ISCN: an international system for human cytogenetic nomenclature (2016)/editors, Jean McGowan-Jordan, Annet Simons, Michael Schmid. Basel; New York: Karger [2016]
10. Costa D, Valera S, Carrió A, Arias A, Muñoz C, Rozman M, et al. Do we need to do fluorescence in situ hybridization analysis in myelodysplastic syndromes as often as we do? *Leuk Res*. 2010;34:1437-41.
11. Jiang H, Xue Y, Wand Q, Pan J, Wu Y, Zhang J, et al. The utility of fluorescence in situ hybridization analysis in diagnosing myelodysplastic syndromes is limited to cases with karyotype failure. *Leuk Res*. 2012;36:448-52.
12. Pitchford CW, Hettinga AC, Reichard KK. Fluorescence In Situ Hybridization testing for -5/5q-, -7/7q-, +8, and del(20q) in Primary Myelodysplastic Syndrome Correlates With Conventional Cytogenetics in the Setting of an Adequate Study. *Am J Clin Pathol*. 2010;133: 260-64.
13. Kwon WK, Lee JY, Mun YC, Seong CM, Chung WS, Huh J. Clinical utility of FISH analysis in adition to G-banded karyotype in hematologic malignancies and proposal of practical research. *Korean J Hematol*. 2010; 45:171-76.
14. Pinheiro RF and Chauffaille MLLF. Comparison of I-FISH and G-banding for the detection of chromosomal abnormalities during the evolution of myelodysplastic syndrome. *Braz J Med Biol Res*. 2009; 42:1110-1112.
15. Vehmeyer K, Haase D, Alves F. Increased peripheral stem cell pool in MDS: an indication of disease progression? *Leuk Res*. 2001; 25:955-59.
16. Haase D, Feuring-Buske M, Könemann S, Fonatsch C, Troff C, Verbeek W, Pekrun A, Hiddemann W, Wörmann B. Evidence for malignant transformation in acute myeloid leukemia at the level of early hematopoietic stem cells by cytogenetic analysis of CD34+ subpopulations. *Blood*. 1995;86(8):2906-2912.
17. Haase D, Feuring-Buske M, Schäfer C, Schoch C, Troff C, Gahn B, Hiddemann W, Wörmann B. Cytogenetic analysis of CD34+ subpopulations in AML and MDS characterized by the expression of CD38 and CD117. *Leukemia*. 1997;11(5):674-679.
18. Braulke F, Schanz J, Jung K, Shirneshan K, Schulte K, Schuetze C, et al. FISH Analysis of Circulating CD34+ Cells as a New Tool for Genetic Monitoring in MDS: Verification of the Method and Application to 27 MDS Patients. *Leuk Res*. 2010;34:1296-1301.
19. Braulke F, Jung K, Schanz J, Goetze K, Muller-Thomas C, Platzbecker U, et al. Molecular cytogenetic monitoring from CD34+ peripheral blood cells in myelodysplastic syndromes: first results from a prospective multicenter German diagnostic study. *Leuk Res*. 2013;37:900-906.
20. Platzbecker U, Braulke F, Kündgen A, Götze K, Bug G, Schönefeldt C, Shirneshan K, Röllig C, Bornhäuser M, Naumann R, Neesen J, Giagounidis A, Hofmann WK, Ehninger G, Germing U, Haase D, Wermke M.: Sequential combination of azacitidine and lenalidomide in del(5q) higher-risk myelodysplastic syndromes or acute myeloid leukemia: a phase I study. *Leukemia*. 2013 Jun;27(6):1403-7.
21. Schuler E, Giagounidis A, Haase D, Shirneshan K, Büsche G, Platzbecker U, et al. Results of a multicenter prospective phase II trial investigating the safety and efficacy of lenalidomide in patients with myelodysplastic syndromes with isolated del(5q) (LE-MON 5). *Leukemia*. 2015;30(7):1580-1582.
22. Braulke F, Platzbecker U, Müller-Thomas C, Götze K, Germing U, Brümmendorf TH, Nolte F, Hofmann WK, Giagounidis AA, Lübbert M, Greenberg PL, Bennett JM, Solé F, Mallo M, Slovak ML, Ohyashiki K, Le Beau MM, Tüchler H, Pfeilstöcker M, Nösslinger T, Hildebrandt B, Shirneshan K, Aul C, Stauder R, Sperr WR, Valent P, Fonatsch C, Trümper L, Haase D, Schanz J. Validation of cytogenetic risk groups according to International Prognostic Scoring Systems by peripheral blood CD34+FISH: results from a German diagnostic study in comparison with an international control group. *Haematologica*. 2015 Feb;100(2):205-13. doi: 10.3324/haematol. 2014.110452. Epub 2014 Oct 24.
23. J. Schanz, H. Tüchler, F. Solé, M. Mallo, E. Luño, J. Cervera, I. Granada, B. Hildebrandt, M.L. Slovak, K. Ohyashiki, C. Steidl1, C. Fonatsch, M. Pfeilstöcker, T. Nösslinger, P. Valent, A. Giagounidis, C. Aul, M. Lübbert, R. Stauder, O. Krieger, Guillermo Garcia-Manero, Stefan Faderl, Sherry Pierce, M.M. Le Beau, J.M. Bennett, P. Greenberg, U. Germing and D. Haase. A new, comprehensive cytogenetic scoring system for primary myelodysplastic syndromes and oligoblastic AML following MDS derived from an international database merge. *J Clin Oncol*. 2012 Mar 10;30(8):820-9. doi: 10.1200/JCO.2011.35.6394. Epub 2012 Feb 13
24. Bernasconi P, Klersy C, Boni M, Cavigliano PM, Giardini I, Rocca B, Zappatore R, Dambruoso I, Calvello C, Caresana M, Lazzarino M. Does cytogenetic evolution have any prognostic relevance in myelodysplastic syndromes? A study on 153 patients from a single institution. *Ann Hematol*. 2010 Jun; 89(6):545-51. doi: 10.1007/s00277-010-0927-z. Epub 2010 Mar 9.
25. Claudia Haferlach, Melanie Zenger, Tamara Alpermann, Susanne Schnittger, Wolfgang Kern, Torsten Haferlach. Cytogenetic Clonal Evolution in MDS Is Associated with Shifts towards Unfavorable Karyotypes According to IPSS and Shorter Overall Survival: A Study on 988 MDS Patients Studied Sequentially by Chromosome Banding Analysis. *Blood*. 2011 118:968, abstract
26. J. Schanz, H. Tüchler, F. Solé, M. Mallo, E. Luño, J. Cervera, I. Granada, B. Hildebrandt, M.L. Slovak, K. Ohyashiki, C. Steidl1, C. Fonatsch, M. Pfeilstöcker, T. Nösslinger, P. Valent, A. Giagounidis, C. Aul, M. Lübbert, R. Stauder, O. Krieger, Guillermo Garcia-Manero, Stefan Faderl, Sherry Pierce, M.M. Le Beau, J.M. Bennett, P. Greenberg, U. Germing and D. Haase. A new, comprehensive cytogenetic scoring system for primary myelodysplastic syndromes and oligoblastic AML following MDS derived from an international database merge. *J Clin Oncol*. 2012 Mar 10;30(8):820-9. doi: 10.1200/JCO.2011.35.6394. Epub 2012 Feb 13
27. Mohamedali AM, Gaken J, Ahmed M, Malik F, Smith AE, Best S, et al. High concordance of genomic and cytogenetic aberrations between peripheral blood and bone marrow in myelodysplastic syndrome (MDS). *Leukemia*. 2015 Sep; 29(9): 1928-1938.
28. Ganster C, Shirneshan K, Salinas-Riester G, Braulke F, Schanz J, Götze KS, et al. A Comprehensive Genetic Analysis of MDS Patients From Peripheral Blood Combining FISH- and SNP-Array-Analysis. ASH Annual Meeting Abstracts 2012 November 16, 2012; 120(21):4926.

THE AMERICAN SOCIETY OF HEMATOLOGY 58TH ANNUAL MEETING & EXPOSITION • DECEMBER 2016

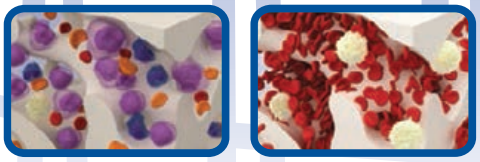
JOIN US FOR A BREAKFAST SYMPOSIUM

BIOLOGICAL AND CLINICAL ADVANCES IN MDS

DECEMBER 2, 2016

7:00 – 11:00 am

San Diego Convention Center, San Diego, California
West Building, Room 6A



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

TARGET AUDIENCE

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

LEARNING OBJECTIVES

- Describe the new WHO classification of MDS
- Describe molecular features which are useful for classifying MDS and aiding in diagnosis and therapeutic decision-making
- Describe differences in therapy-related MDS which need consideration for their treatment
- Describe immune-related mechanisms and treatment approaches for patients with MDS
- Describe novel biologic approaches for treating anemias associated with MDS

FUNDING

This activity is jointly-provided by The Myelodysplastic Syndromes Foundation, Inc. and AKH Inc., Advancing Knowledge in Healthcare, Inc. This activity is supported by an educational grant from Celgene Corporation and Onconova Therapeutics, Inc.

FACULTY

Stephen Nimer, MD
Sylvester Comprehensive Cancer Center
University of Miami

Rafael Bejar, MD, PhD
Assistant Professor
University of California,
San Diego Moores Cancer Center
La Jolla, California

Robert Hasserjian, MD
Associate Professor of Pathology
Massachusetts General Hospital
and Harvard Medical School
Boston, Massachusetts

Richard A. Larson, MD
Professor of Medicine
University of Chicago
Chicago, Illinois

Uwe Platzbecker, MD
Professor of Hematology
University Hospital
Carl Gustav Carus
Dresden, Germany

Daniel T. Starczynowski, PhD
Associate Professor
Cincinnati Children's Hospital
Medical Center
Cincinnati, Ohio

PROGRAM OVERVIEW

New clinical classification of MDS, as well as the evaluation of the implications of molecular mutations, have generated valuable advances for aiding management of patients with this disease. These recent findings will be discussed during this program. The unique nature of treatment-related MDS as a specific subset of MDS will also be reviewed. Given the understanding of immunologic abnormalities in MDS, therapeutic interventions using immune checkpoint inhibitors and T-cell based therapies will add to this discussion, as will a number of the novel treatments using biologic targeted approaches for anemias and higher risk patients.

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 (MDS) Foundation. 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 credit commensurate with the extent of their participation in the activity.

Physician Assistants: NCCPA accepts *AMA PRA Category 1 Credit*™ from organizations accredited by ACCME.

Pharmacists: AKH, Inc., Advancing Knowledge in Healthcare is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. AKH, Inc., Advancing Knowledge in Healthcare approves this knowledge-based activity for 3.5 contact hour(s) (0.35 CEUs). UAN 0077-9999-16-072-L04-P.

Nursing: AKH, Inc., Advancing Knowledge in Healthcare is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. This activity is awarded 3.5 Contact Hours.

DON'T FORGET TO VISIT OUR MDS FOUNDATION BOOTH #3027 IN THE EXHIBIT HALL

mds foundation
the myelodysplastic syndromes foundation, inc.

THE 14TH INTERNATIONAL SYMPOSIUM ON
MYELODYSPLASTIC SYNDROMES

2017
MAY 3 - 6
Valencia, Spain

ADVANCING RESEARCH & PATIENT CARE

Welcome to MDS 2017


Guillermo Sanz

On behalf of the Scientific and Local Organizing Committees and the MDS Foundation, it is our pleasure to invite you to the 14th International Symposium on Myelodysplastic Syndromes taking place in Valencia, Spain from May 3-6, 2017. As in previous years, the Symposium will cover all relevant clinical aspects of MDS diagnosis, prognosis, and management as well as the newest data in MDS basic and translational research. The main lectures will be delivered by recognized international leaders but we also expect to include high-level research talks selected from the abstracts submitted by attendees. Further, we are very happy to offer you the opportunity to visit Valencia, a city with a perfect combination of tradition and modernity. Located in the East of Spain, on the shores of the Mediterranean Sea, Valencia has a unique charm and is one of the cities in Europe that has experienced the most significant growth over recent years in terms of events and international recognition. This is due to the renovation of the historical city center and the creation of new cultural and environmental sites such as the City of Arts & Sciences and the Oceanographic Marine Park. Valencia has mild weather all year long with more than 300 days of sunshine per year, more than 20 km of beaches, a varied gastronomy and the home of the paella, and a Mediterranean way of life. The venue, the Valencia Conference Center, is a modern building designed by Norman Foster and is ideally located. It takes only 10 minutes to reach the historic city center (excellent links by metro, bus and tram), is only 5 km (10 minutes) from the international airport at Manises, and offers over 1,000 hotel rooms within walking distance.

We look forward to seeing you in Valencia!

Guillermo Sanz
Symposium Chair

MDS 2017 Symposium Secretariat:
c/o Kenes International
Email: mds@kenes.com
For MDS Foundation Contact:
US number: 1-800-MDS-0839
Outside the US: 1-609-298-1035

www.mds2017.kenes.com

Wednesday, May 3, 2017

Time	Exhibition Area	Auditorium 1	Auditorium 2	Auditorium 3	Off Site
12:00 - 14:00			Workshop I - Cytometry Alberto Orfao, Spain Ticket		
14:00 - 16:00				Workshop II Genetics Francesc Solé, Spain Ticket	
16:00 - 18:00			Workshop III Cytomorphology John Bennett, USA Jean Goasguen, France Ticket		
18:30 - 20:00		Opening Ceremony • Clonal diversity and clonal evolution in MDS progression Timothy Graubert, USA			
20:00 - 21:30	Welcome Reception				

Ticket - Pre-registration and payment required to attend

legend:
- Plenary Session
- Interactive Session
- Parallel Session
- Social Event
- Oral Session
- Best Abstracts
- Industry Sessions
- Patients Forum
- Guided Poster Session
- Meet the Expert

MDS 2017

Thursday, May 4, 2017

Time	Exhibition Area	Auditorium 1	Auditorium 2	Auditorium 3	Off Site
07:30 - 08:30		Meet the Expert	Meet the Expert	Meet the Expert	
08:30 - 10:00		**MDS biology and pathogenesis 1** 08:30 MDS: a stem cell disorder Stephen D. Nimer, USA 08:50 - Driver and late occurring somatic mutations Elli Papaemmanuil, USA 09:10 - Epigenetic deregulation Maria E Figueroa, USA 09:30 - Oral Presentation 09:45 - Oral Presentation			
10:00 - 10:30	Coffee Break, Exhibition & Poster Viewing				
10:30 - 12:00		**MDS biology and pathogenesis 2** 10:30 - Aging, CHIP, and MDS - David P. Steensma, USA 10:50 - The aberrant spliceosome machinery Seishi Ogawa, Japan 11:10 - Deregulation of the innate immune system Alan F. List, USA 11:30 Oral Presentation 11:45 Oral Presentation			
12:00 - 13:30		**Diagnosis and prognosis of MDS / New challenges & new approaches** 12:00 - 2016 WHO classification: main changes Ulrich Germing, Germany 12:20 - Cytogenetics: still alive? - Francesc Solé, Spain 12:40 - Somatic mutations: a role for improving diagnosis and risk assessment? Rafael Bejar, USA 13:00 - Oral Presentation 13:15 - Oral Presentation			
13:30 - 15:30	Lunch Break, Exhibition & Poster Viewing	13:45-15:15 Industry Supported session – Pipeline Session not included in the CME/CPD Program			
15:30 - 17:00		Oral session 1	Oral session 2		
17:00 - 17:30	Coffee Break, Exhibition & Poster Viewing				

Time	Exhibition Area	Auditorium 1	Auditorium 2	Auditorium 3	Off Site
17:30 - 19:00		**Biology and Management of CMML** 17:30 - Relevance of flow cytometry, cytogenetics, somatic mutations, and epigenetic alterations in CMML Eric Solary, France 17:50 Risk assessment in CMML – Luca Malcovati, Italy 18:10 - Current management and investigational approaches Eric Padron, USA 18:30 - Oral Presentation 18:45 - Oral Presentation		Nurse Session A	
19:00 - 20:00		Predicting response to therapy 19:00 - Prediction of ESAs and lenalidomide benefit Maria E. Díez Campelo, Spain 19:20 - Prediction of azacitidine benefit Raphael Itzykson, France 19:40 - Predicting transplantation outcomes Matteo G. Della Porta, Italy	**Health Economics and Outcome Research** 19:00 - Regulatory aspects and cost **effectiveness analysis of** drugs in Europe David Bowen, UK 19:20 - Cost of care of MDS patients in USA TBA 19:40 - Patient Reported Outcomes in MDS Fabio Efficace, Italy	Nurse Session B	
20:00 - 20:10					
20:10 - 21:10			Industry Supported session not included in the CME/ CPD Program	Industry Supported session not included in the CME/ CPD Program	

legend:
- Plenary Session
- Interactive Session
- Parallel Session
- Social Event
- Oral Session
- Best Abstracts
- Industry Sessions
- Patients Forum
- Guided Poster Session
- Meet the Expert

MDS2017

Friday, May 5, 2017

Time	Exhibition Area	Auditorium 1	Auditorium 2	Auditorium 3	Off Site
07:30 - 08:30		Meet the Expert	Meet the Expert	Meet the Expert	
08:30 - 10:00		**Singular subtypes of MDS** 08:30 - Insights into the mechanism of action of lenalidomide in patients with deletion 5q Benjamin Ebert, USA 08:50 - Clonal evolution in aplastic anemia and hypoplastic MDS Ghulam J. Mufti, UK 09:10 - New developments in childhood MDS Charlotte M. Niemeyer, Netherlands 09:30 - Oral Presentation 09:45 - Oral Presentation			
10:00 - 10:30	Coffee Break, Exhibition & Poster Viewing				
10:30 - 12:00		**Therapy-1 Current options** 10:30 - How I treat MDS patients? Pierre Fenaux, France 10:50 - Management of MDS with 5q- after lenalidomide failure Aristoteles Giagounidis, Germany 11:10 - Looking for the best partner for hypomethylating gents in higher-risk patients Mikkael Sekeres, USA 11:30 - Oral Presentation 11:45 - Oral Presentation			
12:00-13:30		**Therapy-2 New developments** 12:00 - Clinical trials in Europe Lionel Ades, France 12:20 - Clinical trials in USA Guillermo García-Manero, USA 12:40 - New agents for anemic patients: modified activin receptors Uwe Platzbecker, Germany 13:00 - Oral Presentation 13:15 - Oral Presentation			
13:30-15:00	Lunch Break, Exhibition & Poster Viewing	13:45-14:45 Industry Supported session – Pipeline Session not included in the CME/CPD Program			

Time	Exhibition Area	Auditorium 1	Auditorium 2	Auditorium 3	Off Site
15:00 - 16:30		**Therapy-3 Allogeneic hematopoietic cell transplantation** 15:00 - Candidates and timing Theo de Witte, The Netherlands 15:20 - Pre- and post-transplant strategies to reduce relapse Charles Craddock, UK 15:40 - New stem cell donor sources and regimens for transplantation David Valcarcel, Spain 16:00 - Oral Presentation 16:15 - Oral Presentation			
16:30 - 17:00	Coffee Break, Exhibition & Poster Viewing				
17:00 - 18:00		**Caring for the patient with MDS** 17:00 - Iron overload in MDS. Is there something new? Norbert Gattermann, Germany 17:20 - Thrombocytopenia in MDS Valeria Santini, Italy 17:40 - Comorbidity index and comprehensive geriatric assessment in treatment decision Fernando Ramos, Spain	**Controversial issues in MDS** 17:00 - How do I diagnose MDS using currently available tools? Torsten Haferlach, Germany 17:20 - Choosing the appropriate denominator for counting BM blasts Leonor Arenillas, Spain 17:40 - Do all MDS subtypes reduce life expectancy? Arturo Pereira, Spain		
18:00 – 19:15	Guided Poster Session				
20:00 - 22:30					Networking Event

Saturday, May 6, 2017

Time	Exhibition Area	Auditorium 1	Auditorium 2	Auditorium 3	Palacio de Congresos de Valencia (Room TBA)
08:30 - 10:00		Oral session 3	Oral session 4		Patients Forum
10:00 - 10:30	Coffee Break				
10:30 - 12:00		Best Abstracts Session			
12:00 - 12:30		Closing remarks and farewell			

Registration

	Early bird fee until and including March 6, 2017	Regular fee From March 7 until April 26, 2017	Late/Onsite fee From April 27, 2017
MDSF member	€ 550.00	€ 650.00	€ 750.00
Non member	€ 650.00	€ 700.00	€ 800.00
Nurse**	€ 200.00	€ 250.00	€ 300.00
Student**	€ 150.00	€ 200.00	€ 225.00
Morphology Workshop	€ 25.00	€ 25.00	€ 40.00
Flow cytometry Workshop	€ 25.00	€ 25.00	€ 40.00
Genetics Workshop	€ 25.00	€ 25.00	€ 40.00
Networking Dinner	€ 100.00	€ 100.00	€ 100.00

FEES FOR ALL MEETING PARTICIPANTS INCLUDE

- Participation in scientific sessions
- Entrance to the exhibition
- Opening ceremony and welcome reception
- The printed material of the Symposium
- A certificate of attendance
- Coffee and Lunch breaks - as indicated in the program

MDS2017

Accommodation

MDS 2017 Symposium participants enjoy special rates on hotels.

Choose from a wide selection of beautiful and comfortable rooms, close to the venue and city center, catering to all budgets.
Booking a hotel with the MDS 2017 Symposium offers you a one-stop shop, with comprehensive service and personal touch, ensuring that your stay in Valencia, Spain is flawless.

Visit: https://hotel.kenes.com/en/congress/mds17 for more details.

MDS Patient and Family Forum

Valencia, Spain
Saturday, May 6th, 2017

This FREE event will be held at the Palacio de Congresos de Valencia
Avda. Cortes Valencianas, nº 60
46015 Valencia (España)
Beginning at 08:30 A.M.

Networking Events

The Networking dinner, meet the speakers and faculty event will take place at the Oceanographic Valencia on Friday, May 5 at 20:00.

MDS FOUNDATION INTERNATIONAL WORKING GROUP FOR PROGNOSIS IN MDS

Latest News Regarding the Molecular Mutation Project of the IWG-PM

Mutations Predict Prognosis Independent of the IPSS-R: Overview

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

Prognostic Impact of TP53 Mutations

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

As a first project for the IWG-PM molecular database, the impact of TP53 mutations in MDS demonstrated that this

Dr. Peter Greenberg speaking at the IWG-PM meeting during the 2015 ASH Congress.

status divides MDS patients with complex karyotypes into distinct prognostic risk groups, with those carrying the mutation having poorer prognoses. Despite their strong associations with adverse clinical and cytogenetic abnormalities that are already incorporated into existing prognostic scoring systems, TP53 mutations carry significant independent prognostic value for decreased survival for patients with MDS. This work was presented by Dr. Rafael Bejar at the 2014 American Society of Hematology Meeting[2] with updating at the 2015 13th International MDS Foundation Symposium held in Washington, D.C.

Recent Molecular Results

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

Current Project Status, Plans for sequencing of new samples

In addition to the above assessment of previous samples, led by Dr Elli Papaemmanuil, the project is sequencing additional large numbers of MDS cases to further develop our database and mutational evaluations. An automated sample management system was recently implemented that links sample reception to library preparation and sequencing submission. The results of these analyses will serve as the template with which to build an integrated molecular risk model for MDS.

References

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

Shih L-Y, Padron E, Sallman D, Komrojki R, List A, Santini V, Fontenay M, Campbell P, Tuechler H, Stevenson D, Neuberg D, Greenberg P, Ebert BL. Somatic Mutations in MDS Patients Are Associated with Clinical Features and Predict Prognosis Independent of the IPSS-R: Analysis of Combined Datasets from the IWG-PM-Molecular Committee, ASH 2015 abstract, Orlando, December 2015. *Blood*. 2015;126 (23), #907.

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

The MDS/MPN International Working Group

Myelodysplastic syndromes represent a heterogeneous group of disease entities with diverse clinical features, genetic composition, natural history, and response to therapy. Mounting evidence has suggested that several MDS 'subtypes' are distinct enough that they should be considered unique disease entities. To this end, in 2008 the World Health Organization designated four clinical entities to be recognized as bona fide diseases with overlapping dysplastic and proliferative features. These include Chronic Myelomonocytic Leukemia (CMML), atypical CML (aCML), Juvenile Myelomonocytic Leukemia (JMML), and Myelodysplastic/Myeloproliferative Neoplasms Unclassifiable (MDS/MPN-U). Since this reclassification, many investigations have confirmed the unique molecular underpinnings and clinical trajectories of each of these diseases. However, this stratification has resulted in rare diseases that require collaborative efforts to make transformative changes in patient care.

The MDS/MPN International Working Group (MDS/MPN IWG) was originally developed in 2012. The work of this initial group resulted in the first two peer-reviewed publications. By the end of 2013, membership was expanded to include a CMML multi center project, and the group enlisted the support of the MDS Foundation. The overarching goal of this group is to identify key knowledge gaps in the area of MDS/MPNs and facilitate international, collaborative, translational science geared to rapidly improve our understanding of these fatal neoplasms. The current membership includes 32 investigators, from 20 centers, across 7 countries.

Work from collaborations within this group has resulted in several peer-reviewed publications:

- A consensus recommendation for response criteria that sets the foundation for a common endpoint across many MDS/MPN clinical trials.[2]
- A consensus review on the biology and clinical presentation of MDS/MPNs.[2]
- The development of an international CMML dataset that includes clinical and molecular data.[3]

Ongoing collaborations underway include:

- Expansion and prospective molecular sequencing of the international CMML data set.
- Exploring the consequence of an MDS/MPN diagnosis on quality of life.

MDS/MPN INTERNATIONAL WORKING GROUP

- Identify/Generating a consensus CMML prognostic model.
- Exploring the role of transplant in molecularly defined CMML subtypes.
- Implementing international clinical trials on both sides of the Atlantic.

References:

1. Savona MR, et al. An international consortium proposal of uniform response criteria for myelodysplastic/myeloproliferative neoplasms (MDS/MPN) in adults. *Blood*. 2105;125:1857-1865, doi:10.1182/blood-2014-10-607341.
2. Mughal TI, et al. An International MDS/MPN Working Group's perspective and recommendations on molecular pathogenesis, diagnosis and clinical characterization of myelodysplastic/myeloproliferative neoplasms. *Haematologica*. 2105;100:1117–1130, doi:10.3324/haematol.2014.114660.
3. Padron E. et al. An international data set for CMML validates prognostic scoring systems and demonstrates a need for novel prognostication strategies. *Blood Cancer*. 2015;5, e333, doi:10.1038/bcj.2015.53.

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. Steensma DP et al. Connect MDS/AML: Design of the myelodysplastic syndromes and acute myeloid leukemia disease registry, a prospective observational cohort study. *BMC Cancer*. 2016;16:652 (https://www.ncbi.nlm.nih.gov/pubmed/27538433)

   The present report provides design of the first prospective non-interventional observational registry for MDS/AML that will enroll approximately 1500 US patients from 150 community and academic centers. The disease diagnosis will be based on a central pathological review and the study will include 4 patient cohorts- lower risk MDS (low/int-1), higher risk MDS (int-2/high), AML and ICUS (idiopathic cytopenia of undetermined significance),

2. Arber DA et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. 2016;127(20):2391–2405. (https://www.ncbi.nlm.nih.gov/pubmed/27069254)

   Gene expression arrays and next-generation sequencing have brought to light several new molecular biomarkers for myeloid neoplasms especially in acute leukemias. In light of this knowledge the 2008 WHO classification is revised to reflect the consensus opinions of hemato-pathologists, hematologists, oncologists and geneticists. The present article details major changes and specific rationale behind them.

3. Greenberg PL et al. Cytopenia levels for aiding establishment of the diagnosis of myelodysplastic syndromes. *Blood*. 2016 Aug 17 [Epub ahead of print] (https://www.ncbi.nlm.nih.gov/pubmed/27535995)

   This letter to editor provides clarification on recently revised WHO criteria regarding the thresholds to be used for determining milder cytopenia when definitive morphologic and/or cytogenetic features of MDS are present. The authors recommend the use of standard hematologic values rather than the IPSS prognostic cutoff values to define such cytopenias for the diagnosis of MDS.

4. Yao CY et al. Distinct mutation profile and prognostic relevance in patients with hypoplastic myelodysplastic syndromes (h-MDS). *Oncotarget*. 2016 Aug 4 [Epub ahead of print] (https://www.ncbi.nlm.nih.gov/pubmed/27527853)

   In a series of 369 MDS patients classified per WHO 2008 criteria, 100 patients (approx. 27%) were diagnosed as hypocellular subtype. As compared to normo-/hyper-cellular MDS cases, these hypocellular patients tended to be lower risk with lower bone marrow and peripheral blood blast counts, had significantly lower incidence of RUNX1, ASKL1, DNMT3, EZH2 and TP53 mutations and demonstrated relatively longer overall survival.

5. Pfeilstöcker M et al. Time-dependent changes in mortality and transformation risk in MDS. *Blood*. 2016;128(7):902–910 (https://www.ncbi.nlm.nih.gov/pubmed/27335276)

   A retrospective study of 7212 primary untreated MDS cases from the IWG database for prognosis in MDS, showed that mortality and leukemic transformation rates diminished over time in higher risk patients, while remained stable in lower risk patients with hazards in different prognostic categories becoming similar after approximately 3.5 years essentially reaching equivalence after 5 years.

6. Bennett JM et al. Dysplastic erythroid precursors in the myelodysplastic syndromes and the acute myeloid leukemias: is there biologic significance (How should blasts be counted?). *Leuk Res*. 2016;47:63–69. (https://www.ncbi.nlm.nih.gov/pubmed/27258735)

   A study of % erythroid precursors (EP) within bone marrow aspirate blast count from >1400 MDS patients enrolled in Dusseldorf, Germany Adult MDS registry, showed no impact of % EP (including the FAB group's recommendation of "50% rule") on overall survival or leukemic transformation rates.

TREATMENT:

Hypomethylating Agents:

1. Thépot S et al. A randomized phase II trial of azacitidine +/- epoetin-β in lower-risk myelodysplastic syndromes resistant to erythropoietic stimulating agents. *Haematologica*. 2016;101(8):918–925. (https://www.ncbi.nlm.nih.gov/pubmed/27229713)

   The study prospectively compared outcomes of lower risk MDS relapsing after or refractory to ESA, if they were randomly treated with azacitidine or azacitidine + epoietin-β. Among the 98 patients randomized 1:1, transfusion independence was achieved after 6 cycles in comparable number of patients in both groups (approx. 16% with azacitidine alone or 14% with combination). So was the overall erythroid response similar in the two cohorts studied.

2. Zhang Z et al. increased PD-1/STAT1 ratio may account for the survival benefit in decitabine therapy for lower risk myelodysplastic syndrome. *Leuk Lymphoma*. 2016 Aug 11 [Epub ahead of print] (https://www.ncbi.nlm.nih.gov/pubmed/27686004)

   Among the 44 lower risk MDS patients treated with decitabine, 59.1% achieved overall response, and 53.8% achieved reduction in PRBC/Platelet transfusion burden with a median overall survival of 19 mo for the group. An increase in type1 CD8+ population was noted and amplification of PD-1/STAT1 ratio of 2–4 was associated with longer survival.

3. Zeidan A et al. Comparative clinical effectiveness of azacitidine versus decitabine in older patients with myelodysplastic syndromes. *Br J Haematol*. 2016 Sept 21 [Epub ahead of print] (https://www.ncbi.nlm.nih.gov/pubmed/27650975)

The study identified patients diagnosed with MDS between 2004-2011 in the US based SEER registry, who received ≥10 doses of either azacitidine or decitabine. With a median survival estimate of 15 mo (RAEB subset –12 mo), the study did not find significant difference with respect to the hypomethylating agent used (HR= 1.06, p= 0.37). A significantly shorter survival was noted in the present study with azacitidine treated RAEB patients as compared to previously reported survival for the same MDS subset in AZA-001 clinical study (11 mo vs. 24.5 mo, respectively).

4. Mittleman M et al. Azacitidine-lenalidomide (ViLen) combination yields a high response rate in higher risk myelodysplastic syndrome (MDS)-ViLen-01 protocol. *Ann Hematol*. 2016; 95(11): 1811–1818 (https://www.ncbi. nlm.nih.gov/pubmed/27546027)

   ViLen-01, a phase IIa study included treatment of high risk MDS with 6 month induction regimen of Azacitidine +lenalidomide followed by consolidation using azacitidine and maintenance with lenalidomide. A total of 25 subjects with significant co-morbidities in 88% were treated on the study (13 completing induction, 7 entered consolidation and 2 went into maintenance). Using IWG criteria, the authors reported 72% (18/25) ORR, 24% (6/25) CR, 12% (3/25) marrow CR, 36% (9/25) HI, PFS and OS both 12 mo. The safety profile was acceptable without any new signal for the combination over the expected AEs for individual agents.

IMiDs:

1. Santini V et al. Randomized phase III study of lenalidomide versus placebo in RBC transfusion-dependent patients with lower-risk non-del(5q) myelodysplastic syndromes and ineligible for or refractory to erythropoiesis-stimulating agents. *J Clin Oncol*. 2016;34(25):2988–2996 (https://www.ncbi.nlm.nih.gov/pubmed/27354480)

   A phase III randomized placebo controlled double blind study with 239 ESA refractory or ineligible lower risk patients assessed efficacy and safety of lenalidomide in non-del(5q) MDS. The primary end point of ≥8 wk transfusion independence was achieved with lenalidomide treatment in 26.9% patients vs. 2.5% on the placebo arm (p< 0.001). The median duration of TI with lenalidomide was 30.9 wks. Additionally ≥4 units reduction in PRBC transfusion at 112 days assessment time point was seen in 22% with lenalidomide, compared to none on the placebo arm. Neutropenia and thrombocytopenia were the most common adverse events.

Novel Therapies:

1. Schuler MK et al. Effects of a home-based exercise program on physical capacity and fatigue in patients with low to intermediate risk myelodysplastic syndrome- pilot study. *Leuk Res*. 2016; 47:128–135 (https://www.ncbi.nlm.nih.gov/pubmed/27326698)

   A prospective non-randomized feasibility study assessed evaluating safety and efficacy of home-based exercise intervention to overcome fatigue and build physical capacity was a subject of the present report. In a strength and endurance building training, of 21 total MDS patients, 15 (71%) continued on study till week 12 with 11 completing the program. Significant improvement in 6 min-walking distance exercise was seen. However no improvement was noted in fatigue scores.

PATHOBIOLOGY:

1. Li B et al. Colony-forming unit cell (CFU-C) assays at diagnosis: CFU-GM cluster predicts survival in myelodysplastic syndrome patients independently of IPSS-R. *Oncotarget*. 2016 Sept 18 [Epub ahead of print] (https://www.ncbi.nlm.nih.gov/pubmed/27655727)

   CFU-C assays of bone marrow samples from 365 consecutive newly diagnosed MDS patients with a median survival follow up of 22 mo, in multivariate analyses demonstrated that a cluster to CFU-G/M ratio of >0.6 was an independent risk factor for overall survival after adjusting for IPSS-R (HR-3.3, p= 0.005). Additionally the study also showed significantly lower BFU-E, CFU-E and CFU-G/M in MDS than normal bone marrows.

2. Obeng EA et al. Physiologic expression of SF3B1 (K700E) causes impaired erythropoiesis, aberrant splicing and sensitivity to therapeutic spliceosome modulation. *Cancer Cell*. 2016;30(3): 404–417 (https://www.ncbi.nlm.nih.gov/pubmed/27622333)

   SF3B1 mutations are frequent in MDS especially in RARS patients. The present study showed that introduction of a specific high frequency mutation SF3B1 (K700E) using a knockin mouse technique, caused erythroid dysplasia and macrocytic anemia. The spliceosome modulator, E7017 selectively killed the cells expressing SF3B1 (K700E), which may have therapeutic implications.

3. Hilgendorf S et al. Loss of ASXL1 triggers an apoptotic response in human hematopoietic stem and progenitor cells. *Exp Hematol*. 2016, Sept 8 [Epub ahead of print] (https://www.ncbi.nlm.nih.gov/pubmed/27616637)

   ASXL1 is frequently mutated in MDS. Using a specific small interfering RNA transduced in human cord blood CD34+ cells, ASXL1 expression was knocked down. This resulted in a significant reduction in myeloid stem cell number as well as their expansion potential and in particular caused apoptosis of erythroid progenitors at all stages of differentiation.

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. Bigenwald C et al. Are myelodysplastic syndromes and acute myeloid leukemia occurring during the course of lymphoma always therapy related? *Br J Haematol*. 2016 Sept 23 [Epub ahead of print] (https://www.ncbi.nlm.nih.gov/pubmed/27662562)

2. Bhatt VR and Steensma DP. Hematopoietic cell transplantation for myelodysplastic syndromes. *J Oncol Pract*. 2016;12(9):786–792. (https://www.ncbi.nlm.nih.gov/pubmed/27621329)
3. Zeidan AM, Stahl M and Komrokji R. Emerging biologic therapies for the treatment of myelodysplastic syndromes. *Expert Opin Emerg Drugs*. 2016;21(3): 283–300 (https://www.ncbi.nlm.nih.gov/pubmed/27486848)
4. Platzbecker U and Fenaux P. Recent frustration and innovation in myelodysplastic syndrome. *Haematologica*. 2016;101(8):891–893 (https://www.ncbi.nlm.nih.gov/pubmed/27478197)
5. Navada SC and Silverman LR. The safety and efficacy of rigosertib in the treatment of myelodysplastic syndromes. *Expert Rev Anticancer Ther*. 2016;16(8): 805–810 (https://www.ncbi.nlm.nih.gov/pubmed/27400247)
6. Malcovati L and Cazzola M. Recent advances in the understanding of myelodysplastic syndromes with ring sideroblasts. *Br J Haematol*. 2016;174(6): 847–858 (https://www.ncbi.nlm.nih.gov/pubmed/27391606)

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

ABOUT THE MDS FOUNDATION

Who Are We?

The Myelodysplastic Syndromes (MDS) Foundation, Inc. is an international organization devoted to the support and education of patients and healthcare providers in the fields of MDS and related myeloid neoplasms in order to accelerate progress leading to the control and cure of these diseases. By building an international community of physicians, researchers, and patients, we will make potentially curative therapies available for all patients with MDS.

What is MDS?

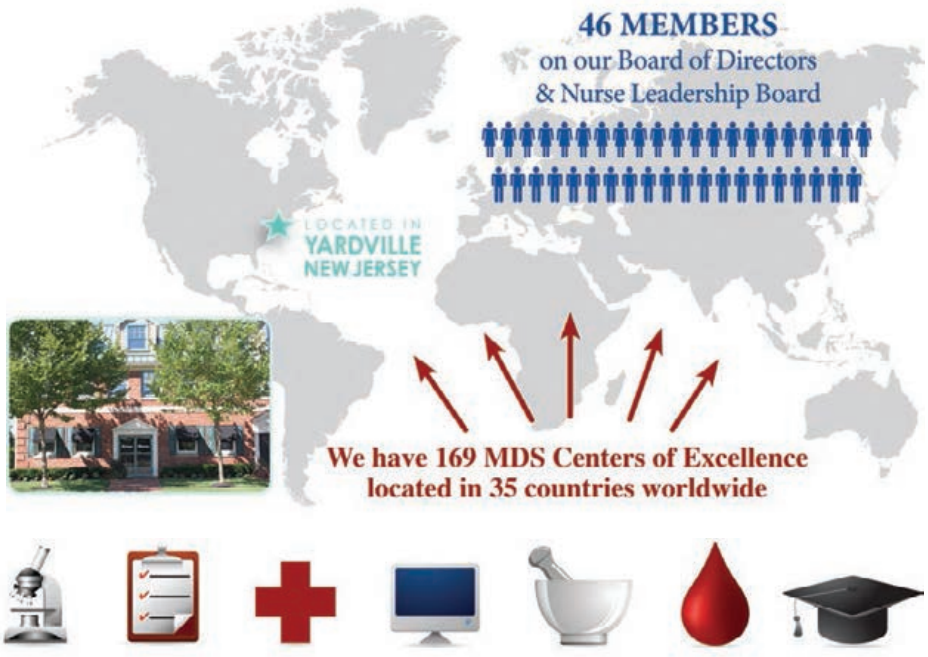
The myelodysplastic syndromes are a group of bone marrow disorders resulting in the ineffective production of normal mature blood cells. Many patients experience anemia from the lack of effective red blood cells, thereby requiring frequent blood transfusions. A shortage of white blood cells may cause malfunctioning of the immune system resulting in infections. Insufficient platelets can result in excessive bleeding. In about one-third of MDS patients, the disease transforms into acute myelogenous leukemia (also known as AML).

What We Do

The MDS Foundation provides research grants for scientific investigators, sponsors international working groups of scientists and physicians to further diagnostic, prognostic and treatment techniques, and disseminates information on state-of-the-art research, clinical trials and treatments among the professional and patient communities. The Foundation also refers patients to its collection of "MDS Centers of Excellence," maintains an electronic forum on its website for interaction and support among patients, and provides educational programs for both healthcare professionals and patients and their families.

Where We Are

The Foundation is located in Yardville, New Jersey and is active in more than 35 countries around the world. Our Board of Directors consists of physicians and nurses actively engaged in searching for a cure of the disease. Our Nurse Leadership Board is comprised of specialized nurses sharing information and teaching others how to care for MDS patients. Together, the Board of Directors and the Nurse Leadership Board consists of 46 members representing 16 countries. Please see our website www.mds-foundation.org for a complete list of our board members and other vital information about the disease and the Foundation.



Our Fundraising Efforts

As a tax exempt non-profit, section 501(c)3 organization, donations to the MDS Foundation qualify for a U.S. tax deduction (it is essential to consult with your tax advisor to confirm your own tax situation).

The MDS Foundation actively seeks financial support for our mission and programs to continue providing services such as the following:

- International Working Group for Prognosis in MDS (IWG-PM)
- Young Investigator Research Grants
- Hot-line for patients and caregivers to speak with our Patient Liaison at 800-MDS-0839
- Numerous Face to Face Patient Forums in multiple cities with presentations by local physicians
- Online Patient Forum monitored by experts
- Designation of Centers of Excellence (COE) meeting the highest standards for diagnosis, treatment, and patient care
- Patient Referrals to COEs
- *Building Blocks of Hope*© handbook (in print or online) with complete written and video information on the care and treatment of MDS
- The MDS News Email Alerts
- Biennial International MDS Symposia for professionals & continuing medical and nursing education programs

Donations can be made on our website by credit card or by check made payable and addressed to:

The MDS Foundation, Inc.
4573 South Broad St.
Suite 150
Yardville, New Jersey 08620

www.mds-foundation.org

MDS Manager: An mHealth Application for Patient and Caregivers LIVING with MDS

Sandra Kurtin, RN, MS, AOCN, ANP-C
Nurse Practitioner
The University of Arizona Cancer Center
Assistant Professor of Clinical Medicine
Adjunct Clinical Asst Prof of Nursing
PhD Candidate
The University of Arizona, Tucson, Arizona

Assisting patients and their caregivers to live with the highest quality of life possible despite the diagnosis of MDS is the primary mission of The Myelodysplastic Syndromes Foundation. Among the most recent educational initiatives is the *Building Blocks of Hope*®, a print and online interactive resource aimed at empowering patients and caregivers living with MDS.[1] Book 5 of the *Building Blocks of Hope*® is focused on staying well and taking an active part in the management of MDS (**Figure 1**). This is the inspiration for creating a digital tool, *MDS Manager*, aimed at expanding resources for patients and caregivers *LIVING* with MDS (**Figure 2**). Living with a cancer, including MDS, requires life-long learning to effectively mitigate adverse events and improve quality of life. Active involvement of the patient and their caregivers in managing their health may result in extended survival.[2] Engagement of the patient and their caregivers in expressing their wishes, and taking a part in the management of their health, including engaging in health technology as a tool for health self-management is essential. Health technology, including mHealth applications, offer expanding capabilities for engaging health consumers in health self-management.[3] However, despite the robust pace of mHealth development, empirical data specific to mHealth use in cancer survivors, particularly older adults, are limited.[4] Therefore, cancer in the older adult, including MDS, will remain a predominant health care concern and strategies for health self-management in this population, including mHealth technology, require disciplined and systematic review to guide ongoing research.[5]

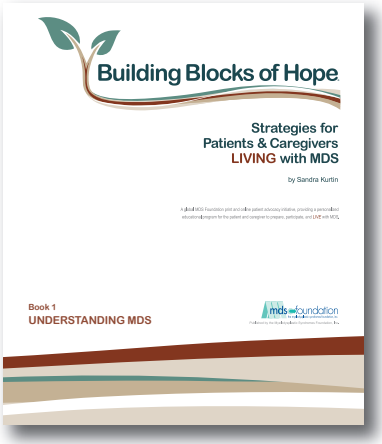


Figure 1. Building Blocks of Hope: Strategies for Patients & Caregivers LIVING with MDS

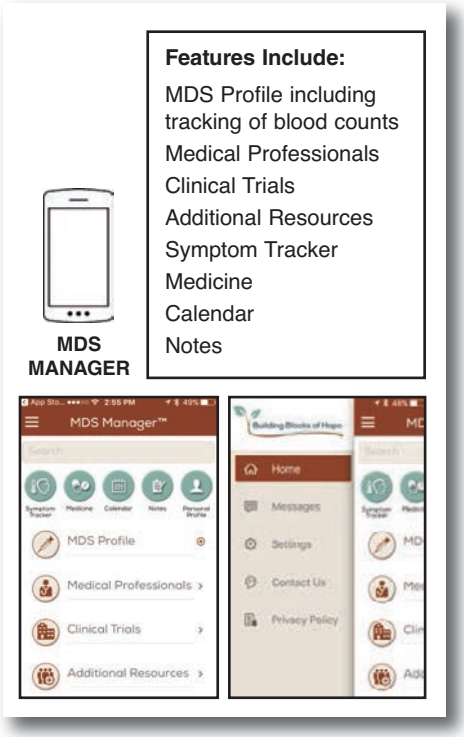


Figure 2.

Mobile health applications provide the capability for interactive, dynamic and untethered technology to support health self-management, however, their content and interventional elements need to be grounded in human computer interface design and health behavior and communication theory and practice.[4,6-8] Being an informed consumer of health information is the expected norm. The

average age of the MDS patient at diagnosis to be 73 years, and the estimated average life expectancy for individuals 75 years of age to be more than 10 years (10.94 males; 12.76 females).[9] User involvement in design, particularly in the older adult population, is a critical step in increasing the probability of continued use, necessary for behavioral change. *MDS Manager* (**Figure 2**) represents the synthesis of the success of the *Building Blocks of Hope*®, experiential knowledge, and systematic review of the literature relative to mHealth applications, health self-management and communicative health literacy.[1,5,10,11] User input, with inclusion of MDS survivors and their caregivers in pilot testing of *MDS Manager* has recently been completed and will be critical to refinement of the application prior to launching the application to the general MDS population.[12] Findings from this study will be presented at the 14th International Symposia on Myelodysplastic Syndromes to be held in Valencia, Spain. The refined *MDS Manager* will be introduced at the 58th American Society of Hematology Meeting and Exposition to be held in San Diego, California. *MDS Manager* will be launched in early 2017, including a research study testing bidirectional communication tailored to the individual MDS patient aimed at improving health-self management, technology engagement, communicative health literacy and clinical trials participation. *MDS Manager* will be available on both Android and IOS smartphones and tablets.

The majority of care for the MDS patient is provided in the outpatient setting, is episodic, and relies heavily on the ability of the patient and their caregivers to manage their care, report symptoms, and seek information to assist them in performing these tasks.[13] Therefore, it is imperative that we empower patients and caregivers to make informed choices about their care, track and report symptoms, and develop the skills and knowledge to take an active part in their care. *MDS Manager* provides an innovative tool that will assist patients and caregivers LIVING with MDS with the ability to keep track of blood counts, treatments, symptoms, provider and caregiver information, link to resources and clinical trials information, and is proposed to provide a tangible and meaningful strategy for improving health self-management.

References

1. Kurtin S. *Building Blocks of Hope: Strategies for Patients and Caregivers LIVING with MDS*. New Jersey: The Myelodysplastic Syndromes Foundation; 2012.
2. Jenerette CM, Mayer DK. Patient-Provider Communication: the Rise of Patient Engagement. *Seminars in oncology nursing*. 32(2): 134–143.
3. Jawed SI, Myskowski PL, Horwitz S, Moskowitz A, Querfeld C. Primary cutaneous T-cell lymphoma (mycosis fungoides and Sezary syndrome): part II. Prognosis, management, and future directions. *Journal of the American Academy of Dermatology*. 2014;70(2):223 e221–217; quiz 240–222.
4. Bender MS, Choi J, Arai S, Paul SM, Gonzalez P, Fukuoka Y. Digital technology ownership, usage, and factors predicting downloading health apps among caucasian, filipino, korean, and latino americans: the digital link to health survey. *JMIR Mhealth Uhealth*. 2014;2(4):e43.
5. Kurtin S. mHealth as a Means to Foster Health Self-Management in Older Adult Cancer Survivors. Unpublished work: The University of Arizona College of Nursing; 2016.
6. Nasi G, Cucciniello M, Guerrazzi C. The role of mobile technologies in health care processes: the case of cancer supportive care. *J Med Internet Res*. 2015;17(2):e26.
7. Vollmer Dahlke D, Fair K, Hong YA, Beaudoin CE, Pulczinski J, Ory MG. Apps seeking theories: results of a study on the use of health behavior change theories in cancer survivorship mobile apps. *JMIR Mhealth Uhealth*. 2015;3(1):e31.
8. Kurtin S. Specific Aims: Feasibility and usability of MDS Manager. Unpublished work: The University of Arizona College of Nursing; 2016.
9. Cogle CR. Incidence and Burden of the Myelodysplastic Syndromes. *Current hematologic malignancy reports*. 2015;10(3):272-281.
10. Kurtin S. Testing and Design of a Mobile Health Application aimed at Self-Management. The University of Arizona College of Nursing; 2015.
11. Kurtin S. Evaluation of a Mobile Health Application Aimed at Self-Management. The University of Arizona College of Nursing; 2015.
12. Kurtin S. Usability pilot testing of a health and life management mobile health application (mHealth App) for caregivers and patients living with Myelodysplastic Syndromes: The University of Arizona; 2016.
13. Kurtin S, Paterson P, Wintrich S, et al. Patient and family resources for living with myelodysplastic syndromes. *Clinical journal of oncology nursing*. 2012;16 Suppl:58–64.

Emily A. Knight, RN, BSN, OCN
Scottsdale, Arizona
United States

Sandra E. Kurtin
RN, MS, AOCN, ANP-C
Tucson, Arizona
United States

Petra Lindroos Kolqvist, RN
Goteborg, Sweden

Arno Mank, RN, PhD
Amsterdam, The Netherlands

R. Denise McAllister
MS, ARNP, AOCNP
Clearwater, Florida
United States

Cindy Murray, RN, MN, NP-adult
Toronto, Ontario
Canada

Geke Ong, RN
London, United Kingdom

Phyllis Paterson
RN, RSCN, Dip Onc
Cambridge, United Kingdom

Jean A. Ridgeway
MSN, APN, NP-C, AOCN
Chicago, Illinois
United States

Barbara A. Rodgers, RN, BSN, OCN
Seattle, Washington
United States

Jayshree Shah
APN-C, AOCNP, RN,
MSN, BSN, BS, CCRP
Hackensack, New Jersey
United States

Natalie Singer, MSc,
RN, BSc(Hons)
Glasgow, Scotland
United Kingdom

Samantha Soggee, RN, MN
Heidelberg, Victoria, Australia

Mary L. Thomas, RN, MS, AOCN
Palo Alto, California
United States

Sara M. Tinsley, PhD, ARNP, AOCN
Tampa, Florida
United States

Catherine Vassili, RN
Victoria, Australia

NEWS FROM AROUND THE WORLD

Cancer Epigenetics

Dr. I.M. Bennani-Baiti
President, Cancer Epigenetics Society
Vienna, Austria

For many cancer patients, time is of the essence. Despite its promises, the field of cancer epigenetics has been slow in translating its findings into tangible clinical applications. For example, 5-azacytidine, an epigenetic drug shown to more than double survival of mice with leukemia in 1964, and which showed a remarkable activity in cancer patients in clinical trials in 1975, was only in 2004 FDA-approved for the treatment of MDS, a cancer that until then had no other treatment, 40 years after its discovery! The Cancer Epigenetics Society is the official society for cancer epigenetics research whose goal is to speed up cancer epigenetics discovery and the translation of basic research into clinical practice. To do so, the Cancer Epigenetics Society is developing several tools and

Dr. Bennani-Baiti leads the efforts of the Cancer Epigenetics Society.

resources, including several open-access medical and scientific databases, thus allowing researchers and clinical oncologists access to cancer and epigenetics data at an unprecedented depth and speed. Our databases and other resources also help scientists generate soft lines of thinking by looking at the broader picture of cancer-related processes that can otherwise not readily be inferred from single articles. In addition, we have developed a publishing model that dramatically speeds up the time from research article submission to publication, while at the same time significantly increasing reproducibility, visibility, and impact. These measures should further help position the field of cancer epigenetics as a leader in cancer innovation and discovery. The Cancer Epigenetics Society (https://ces.b2sg.org) offers free membership to physicians, scientists, and students, and is currently funded only through charitable donations from individuals.

Dr. Bennani-Baiti is hoping to draw the attention of MDS researchers to CES to spark new research ideas and new lines of inquiries into MDS. He is the President of CES, but he also has a personal connection to MDS – his father is an MDS patient.

TESTIMONIALS

"I simply wanted to say, after reading your main page, that it was extremely well written and informative" It was direct without being alarmist, seemed quite fair in not exploiting data or attempting to use incomplete or partial research to further your cause (therefore making what you DO SAY much more trustworthy), and explained in very accessible terms everything one might want to know on a first investigation. Well done to whoever put this together! – *Bill P.*

"Thank you so much for all of your kind words of encouragement and all of the helpful information you have sent." This journey has a bright light for me and with people like you I know it will be alright. **–** *Rachel M.*

"Thank you for all you do for this orphan disease." – *Bob M.*

"Just diagnosed and find your website excellent" – *Edgar K.*

"The MDS Foundation was very good keeping us up to date with information on MDS." My husband had it for many years and all of the possible treatments were done. Sadden to say I lost my husband after 53 1/2 years of marriage. It happened this Feb. 2016. He was at home with me. I was the caregiver for many years. It was heart wrenching many times, sometimes happy good news times. ALL memories ones worth keeping and to always cherish forever. Thank you again MDS for helping me to comprehend a bit better the health issue. – *Kathryn H.*

"My daughter was excited to find your webpage and show it to me." My sister (she is 84) and I (I'm 77 and have MDS) watched the 3 minute *Building Blocks of Hope* video. I would very much like to receive one of the hard copy binders mentioned. I am currently undergoing chemo and receiving blood transfusions and feel like we have more questions than answers. I need all the hope I can get. Plus, it is difficult to get my sister and other family members to understand the symptoms (fatigue, anemia, etc.), seriousness of my condition (neutropenia, need for regular transfusions). Thank you for your website and for sending me a copy of your handbook. – *Donald G.*

"The German version of *Building Blocks of Hope* brochure arrived today – many, many thanks. It is an amazing collection of useful information"
– *Andy A.*

"My father-in-law was just diagnosed with MDS. I came across your website and am living with the wealth of information I have gathered already."
I believe these books will be a wonderful source of guidance. Thank you!!!
– *Celena O.*

Building Blocks of Hope

This program is designed to give patients and caregivers the in depth information that they are looking for and to allow them to take an active part in their MDS journey. The BBoH is available in several languages.

GLAM

LATIN-AMERICAN GROUP FOR MYELODYSPLASTIC SYNDROMES

- The Latin-American Group for Myelodysplastic Syndromes (GLAM) is a multi-disciplinary group integrated by health professionals with a common aim: study MDS from pathogenesis through clinical and therapeutic approaches.
- GLAM is evaluating the state-of-the-art of Myelodysplastic Syndromes (MDS) in the region to recognize strengths and drawbacks in order to improve and encourage local actions.
- This group was created in close relationship with different Latin-American Societies of Hematology in consideration of their own regulations and interests.

Objectives

- Contribute to progress in hematology, specifically in the field of MDS.
- Encourage scientific networking with other societies.
- Promote scientific and clinical research.
- Collaborate with national and regional health authorities.
- Develop local diagnostic and therapeutic guidelines and protocols.
- Organize continuous medical education (CME).
- Provide useful information for patients and healthcare givers.

Team

- GLAM includes various professionals like biochemists, immunologists, cytogenetists, flowcytometrists, pathologists and hematologists. This diversity will contribute to broaden complementary visions.
- To date, the group is integrated by 155 colleagues from Latin America: Argentina, Bolivia, Brasil, Chile, Colombia, Costa Rica, Dominican Republic, Ecuador, El Salvador, Guatemala, Mexico, Panama, Paraguay, Peru, Uruguay and Venezuela.

Projects

MDS Survey

This survey aims to collect epidemiologic data in order to know the state-of-the-art of diagnostic and therapeutic tools in the region.

Training and Teaching

One of the most important projects is to organize scientific MDS meetings, workshops, symposiums, etc. in different Latin American countries.

MDS Common Registry

It is extremely necessary to develop a Latin American online MDS Registry in order to build a common database.

Subcommittees

Small and specialized working groups promote the participation and exchange of professionals' experiences. The following subcommittees are proposed: 1–Diagnostic, 2–Therapeutic strategies, 3–Pediatric MDS, 4–Hematopoietic Progenitor Cell Transplantation, 5–Secondary MDS, 6–Overlap syndromes.

Investigation and Clinical Trials

We are determined to encourage investigation and help to promote clinical trials in MDS throughout Latin America.

Patients, Relatives and Healthcare Givers Information and Support

GLAM´s web page will provide useful information about MDS to help groups of patients, relatives and healthcare givers.

CONTACT INFORMATION

info@mds-la.o

Uruguayan Society of Hematology (on behalf of GLAM)

COLONIA 1086 OF.404

Montevideo, Uruguay

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Myelodysplastic Syndromes – Just a Matter of Age?

Carolien M Woolthuis[1] and Christopher Y Park[2]

[1]Human Oncology and Pathogenesis Program, Memorial Sloan Kettering Cancer Center, New York, New York, US; [2]Departments of Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, New York, US

Abstract

The myelodysplastic syndromes (MDS) are primarily a disease of the elderly, but it is unclear whether aging itself is an independent contributor to the pathophysiology of these disorders. While the normal aged hematopoietic system and MDS share many features compared to young hematopoiesis, they also exhibit important differences. With the demonstration that mutations present in MDS can also be identified in healthy elderly individuals, it will be important to elucidate the differences and interactions between normal hematopoietic aging and MDS.

The myelodysplastic syndromes (MDS) represent a heterogeneous group of clonal hematologic disorders, characterized by inefficient hematopoiesis, myeloid dysplasia, and an increased risk for developing acute myeloid leukemia (AML).[1,2] In the majority of patients, morbidity and mortality are the result of progressive cytopenias, but transformation to AML is observed in approximately one-third of patients. MDS is highly associated with age, illustrated by an increase in the incidence with advancing age and a median age at diagnosis of 65–70 years.

While the pathophysiology of MDS is not fully understood, it is clear that it involves a multifactorial process that includes alterations in chromosomes, gene mutations, and changes in DNA methylation status in the hematopoietic cells.[1,2] Recent large-scale genome-sequencing studies have identified multiple recurrent gene mutations in MDS. These mutations affect genes involved in epigenetic regulation (e.g. DNMT3A, TET2, IDH1/2, EZH2, ASXL1)3 and RNA splicing (e.g. SF3B1, SRSF2, U2AF1, ZRSR2)4,5 among other pathways. In the majority of MDS cases more than one mutation can be detected.[6–8]

Since MDS occurs primarily in elderly patients, it has been hypothesized that hematopoietic aging itself is an important factor in the pathophysiology of MDS. Indeed, hematopoietic stem cells (HSCs) in normal aged individuals and MDS patients exhibit similar differences when compared to normal young adults, including an increased frequency, myeloid skewing with diminished lymphoid potential, and decreased erythroid output.[9–11]

However, whether age simply increases the probability of acquiring disease initiating mutations or whether cellular context itself contributes to disease pathogenesis is an unresolved question. Interest in this question has increased dramatically due to recent descriptions of clonal hematopoiesis in healthy elderly individuals. While the phenomenon of age-related clonal skewing in the bone marrow has been known for some time, the recent development of high-throughput genome sequencing has extended this observation by identifying presumed disease-initiating mutations in healthy individuals.[12–16] Indeed, the spectrum of mutations found in healthy elderly individuals with clonal hematopoiesis overlaps considerably with the mutations observed in MDS patients at diagnosis, including DNMT3A, TET2, and ASXL1 mutations. Blood-specific clonal mutations were identified in 5–6% of healthy people aged 70 years or older in one study16 and clonal hematopoiesis was observed in 10% of individuals aged 65 and older in another cohort.[13] The detection of a clonal mutation is associated with an increased risk for developing a hematologic malignancy. However, the majority of individuals with a detectable clonal mutation did not develop a hematologic disease and actually died from non-hematologic causes.[13,14]

This highlights the fact that the presence of a somatic clonal mutation is distinct from a diagnosis of MDS. In fact, it resembles more a condition like monoclonal gammopathy of undetermined significance (MGUS) , which is associated with increased risk of developing clinically relevant B-cell lymphoproliferations. Based on these insights it was recently proposed that in patients without hematologic alterations, detection of a clonal mutation in a gene also recurrently mutated in hematologic malignancies could be classified as a separate entity, termed clonal hematopoiesis of indeterminate potential (CHIP).[17] This would recognize this condition while preventing over-diagnosis and misinterpretation. It would also facilitate investigating the clinical meaning of detecting such mutations in the blood of a healthy person.[17,18]

CHIP arises when genetic alterations are acquired in HSCs, much like MDS. While previous studies in MDS demonstrated their HSC origin by showing that chromosomal abnormalities associated with disease (i.e. loss of 5q, 7 or gain of chromosome 8) are present in HSCs,[10,11,19–22] a more recent study demonstrated that MDS-associated mutations in SF3B1 are present in HSCs.[23] As previously described, there are several similarities between hematopoiesis in aging and MDS. However, there are also important differences. For instance, bone marrow dysplasia is not significant in

healthy elderly and ineffective hematopoiesis only occurs in the context of MDS. In addition, normal elderly and MDS patients demonstrate differences in hematopoietic progenitor composition as well as HSC gene expression profiles and DNA methylation.[11] Whether such differences are also present in CHIP HSCs when compared with elderly HSCs is an open question that will likely be the subject of future investigations.

Given that normal aged HSCs and MDS HSCs exhibit significant differences, some investigators have explored whether these differences might be due to alterations in the bone marrow microenvironment.[24] Although several recent studies have revealed that bone marrow stromal cells may functionally interact with malignant marrow cells to promote disease phenotypes and that cell-intrinsic changes in stromal cells may induce MDS-like disease,[25–27] more studies are required to elucidate whether aging is involved in these processes. In addition, investigating whether the presence of a mutation in a young or aged HSC results in the same hematopoietic phenotype would provide significant insights regarding the importance of the cellular context in which somatic mutations appear.

Overall, multiple recent studies have highlighted the differences between hematopoiesis in normal aging and MDS. The latter process clearly requires more than just age-related alterations, of which the specifics are currently being elucidated, and therefore now, the line between normal hematopoietic aging and MDS is largely a distinction based on clinical features. Given the significant overlap between these two states, finding features that are specific to each would be an attractive focus of future studies. A potential fruitful approach may be the evaluation of pediatric, nonfamilial MDS, which would allow researchers to distinguish between age- and disease-related alterations. In addition, to more directly address the contribution of aging to MDS pathogenesis, it will be important to use genetically accurate disease models, which may be induced at different ages to directly assess the influence of cellular age on disease characteristics. As such investigations are currently ongoing in various laboratories, we look forward to the results of these studies in the near future.

References

1. Ades L, Itzykson R, Fenaux P, Myelodysplastic syndromes, *Lancet*, 2014;383: 2239–52.
2. Tefferi A, Vardiman JW, Myelodysplastic syndromes, *N Engl J Med*, 2009;361: 1872–85.
3. Shih AH, Abdel-Wahab O, Patel JP, et al., The role of mutations in epigenetic regulators in myeloid malignancies, *Nat Rev Cancer*, 2012;12:599–612.
4. Papaemmanuil E, Cazzola M, Boultwood J, et al., Somatic SF3B1 mutation in myelodysplasia with ring sideroblasts, *N Engl J Med*, 2011;365:1384–95.
5. Yoshida K, Sanada M, Shiraishi Y, et al., Frequent pathway mutations of splicing machinery in myelodysplasia, *Nature*, 2011;478:64–9.
6. Haferlach T, Nagata Y, Grossmann V, et al., Landscape of genetic lesions in 944 patients with myelodysplastic syndromes, *Leukemia*, 2014;28:241–7.
7. Bejar R, Stevenson K, Bdel-Wahab O, et al., Clinical effect of point mutations in myelodysplastic syndromes, *N Engl J Med*, 2011;364:2496–506.
8. Papaemmanuil E, Gerstung M, Malcovati L, et al., Clinical and biological implications of driver mutations in myelodysplastic syndromes, *Blood*, 2013;122:3616–27.
9. Beerman I, Maloney WJ, Weissmann IL, et al., Stem cells and the aging hematopoietic system, *Curr Opin Immunol*, 2010;22: 500–6.
10. Pang WW, Pluvinage JV, Price EA, et al., Hematopoietic stem cell and progenitor cell mechanisms in myelodysplastic syndromes, *Proc Natl Acad Sci USA*, 2013;110: 3011–6.
11. Will B, Zhou L, Vogler TO, et al., Stem and progenitor cells in myelodysplastic syndromes show aberrant stage-specific expansion and harbor genetic and epigenetic alterations, *Blood*, 2012;120:2076–86.
12. Busque L, Patel JP, Figueroa ME, et al., Recurrent somatic TET2 mutations in normal elderly individuals with clonal hematopoiesis, *Nat Genet*, 2012;44: 1179–81.
13. Genovese G, Kahler AK, Handsaker RE, et al., Clonal hematopoiesis and blood-cancer risk inferred from blood DNA sequence, *N Engl J Med*, 2014;371:2477–87.
14. Jaiswal S, Fontanillas P, Flannick J, et al., Age-related clonal hematopoiesis associated with adverse outcomes, *N Engl J Med*, 2014;371:2488–98.
15. Shlush LI, Zandi S, Mitchell A, et al., Identification of preleukaemic haematopoietic stem cells in acute leukaemia, *Nature*, 2014;506:328–33.
16. Xie M, Lu C, Wang J, et al., Age-related mutations associated with clonal hematopoietic expansion and malignancies, *Nat Med*, 2014;20:1472–8.
17. Steensma DP, Bejar R, Jaiswal S, et al., Clonal hematopoiesis of indeterminate potential and its distinction from myelodysplastic syndromes, *Blood*, 2015; 126:9–16.
18. Malcovati L, Cazzola M, The shadowlands of MDS: idiopathic cytopenias of undetermined significance (ICUS) and clonal hematopoiesis of indeterminate potential (CHIP), *Hematology Am Soc Hematol Educ Program*, 2015;2015:299–307.
19. Nilsson L, Strand-Grundstrom I, Arvidsson I, et al., Isolation and characterization of hematopoietic progenitor/stem cells in 5q-deleted myelodysplastic syndromes: evidence for involvement at the hematopoietic stem cell level, *Blood*, 2000; 96:2012–21.
20. Nilsson L, Strand-Grundstrom I, Anderson K, et al., Involvement and functional impairment of the CD34(+)CD38(-)Thy-1(+) hematopoietic stem cell pool in myelodysplastic syndromes with trisomy 8, *Blood*, 2002;100:259–67.
21. Tehranchi R, Woll PS, Anderson K, et al., Persistent malignant stem cells in del(5q) myelodysplasia in remission, *N Engl J Med*, 2010;363:1025–37.
22. Woll PS, Kjallquist U, Chowdhury O, et al., Myelodysplastic syndromes are propagated by rare and distinct human cancer stem cells in vivo, *Cancer Cell*, 2014;25:794–808.
23. Mian SA, Rouault-Pierre K, Smith AE, et al., SF3B1 mutant MDS initiating cells may arise from the haematopoietic stem cell compartment, *Nat Commun*, 2015;6:10004.
24. Nakamura-Ishizu A, Suda T, Aging of the hematopoietic stem cells niche, *Int J Hematol*, 2014;100:317–25.
25. Bulycheva E, Rauner M, Medyouf H, et al., Myelodysplasia is in the niche: novel concepts and emerging therapies, *Leukemia*, 2015;29:259–68.
26. Cogle CR, Saki N, Khodadi E, et al., Bone marrow niche in the myelodysplastic syndromes, *Leuk Res*, 2015;39:1020–7.
27. Krause DS, Scadden DT, A hostel for the hostile: the bone marrow niche in hematologic neoplasms, *Haematologica*, 2015;100:1376–87.

PATIENTS & CAREGIVERS LIVING WITH MDS FORUMS

SPREADING THE NEWS WORLDWIDE

MARK YOUR CALENDAR FOR THE LOCATION NEAREST YOU!

FEBRUARY 25
in honor of Rare Disease Day
Las Vegas, NV
Gainesville, FL

APRIL 22
Chicago, IL
Seattle, WA

MAY 6
Valencia, Spain

SEPTEMBER 9
Buffalo, NY
Charleston, SC

OCTOBER 28
in honor of MDS World Awareness Day
Atlanta, GA
San Francisco, CA

NOVEMBER 18
San Antonio, TX
Iowa City, IA

Register Today
FOR OUR FREE EVENTS

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

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

JUNE 11, 2016
Copenhagen, Denmark

THANK YOU to Prof. Drs. Lars Kjeldsen, Kirsten Grønbaek, and Lone Friis, for the invaluable contribution you all made at our Copenhagen Patient Forum. 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 Danish speaking friends, the audio/visual taping of this event can be viewed here
http://www.mds-foundation.org/mds-patient-forum-copenhagen-denmark

MDS FUNDRAISING EVENTS

WORKING TOGETHER FOR MDS

COMEDY NIGHT IN MEMORY OF KAREN A. WENZEL

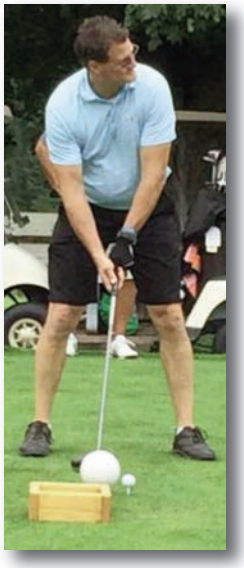
Karen A. Wenzel was a beloved wife and mother who lost her battle with MDS in 2006. Karen's son, Paul, has held many golf tournaments in her memory but this year decided to plan a special comedy night to support the MDS Foundation. Paul's hope is that this comedy event will be the first of many and will be a day to get family and friends together to remember his mother, and to help raise money and awareness for MDS.

Paul Wenzel with his mom, Karen

TOM "SHU" SHUEY MEMORIAL GOLF TOURNAMENT

In memory of his Dad, Timothy Shuey and his family held their second annual charity golf tournament on August 5. Tom Shuey passed away in 2014 after battling MDS.

He was an avid golfer and his son, Tim's biggest regret was missing his last opportunity to golf with him. This inspired Tim and his family to organize an annual golf tournament in his memory.

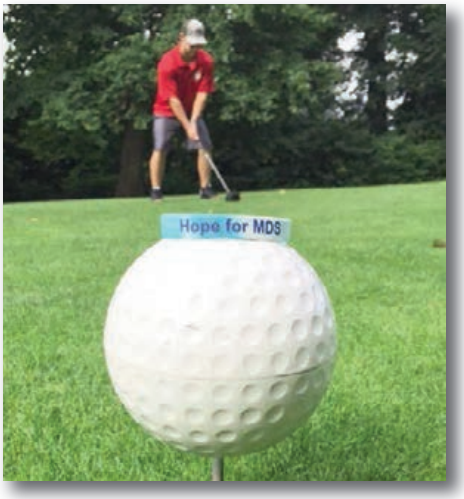


For years to come, they plan to keep Shu's memory in our hearts and minds, and continue to support the MDS Foundation.

#2forshu

Tim using his dad's golf club

Tom 'Shu' Shuey

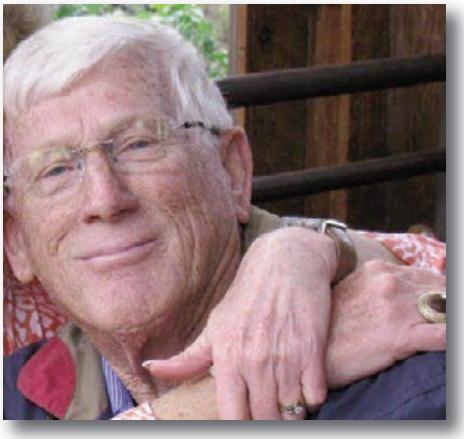


RUNNING FOR AWARENESS

Timothy Stohner ran the Naperville, Illinois Half-Marathon in memory of his father to help raise awareness about MDS and the MDS Foundation. He feels fortunate to have the opportunity to run this race and he encourages others to do the same.

MDS AWARENESS T-SHIRTS

Amber Cornell created MDS Awareness T-shirts in honor of her grandfather, Richard Pratt, who had MDS. He was her hero and best friend. All proceeds from the sale were donated to the MDSF.



MARIELLE THORSEN AND ERIC HALL WEDDING

On June 2, 2015, Marielle lost her grandmother, Irene Caso, to MDS. In lieu of favors at their wedding on July 29, 2016, her husband, Eric, and she donated to the MDS Foundation in honor and loving memory of her grandma. Marielle told us that she was the most beautiful, happiest, strongest, and above all, the most loving person in the world. Her husband and she were so happy to be able to include her grandmother in their wedding by donating to the MDS Foundation. "She was definitely with us on our wedding day, it was the most beautiful day; sun was bright and shining, warm air, and overall just perfect and best day ever. We hope that our donations will help to find a cure and further research for MDS."

BENEFIT CONCERT

In memory of her father, Anthony, Janna Pelle organized her second MDS Awareness & Benefit Concert with the Leave A Lasting Mark Concert Series at the Bitter End in New York City. This year's theme was the Talking Heads album, "Stop Making Sense"—because MDS doesn't make sense. Hopefully, with our dedicated work, research, awareness and fundraising, we will be able to make sense of this disease and find better treatments for the future. There was also a bone marrow drive made possible by Love, Hope, Strength at the concert. With over 20 performing artists participating, including herself, money was raised to support the MDSF.

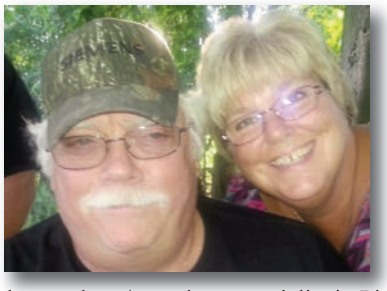
FUN RUN

Terry Tintor and her friends participated in the 'Light the Night' LLS Walk and wore MDS T-shirts that they created to increase MDS awareness.

ASHLEY PANEI MDS AWARENESS WALK

Ashley was just 29 when she passed away from MDS, and in lieu of flowers, the family asked that memorial contributions be made to the MDS Foundation. She was in remission from having ovarian cancer when she was diagnosed with MDS and needed a bone marrow transplant. Unfortunately, the disorder took her life before she was able to get the transplant. In Ashley's honor, her family will hold an annual walk in her memory to benefit the MDSF.

DAN LEWIS MEMORIAL GOLF DAY



Sue Lewis shares her husband's journey with MDS.

We didn't know how much our lives would change on August 23, 2015. My husband, Danny, had just had bloodwork done in order to have his prescriptions refilled. When the results came back, the doctors called and told us we needed to meet with them.

At our appointment on 8/23/2015, we were told that Dan had MDS. She suggested we meet with a hematology/ oncology specialist in Pittsburgh instead of our doctor here in Pymatumy. Once in Pittsburgh, they started the first round of chemotherapy. We then returned home to complete treatment in Meadville. Meanwhile, the doctors suggested we start testing family members for a bone marrow match. My brother-in-law was a suitable candidate. They ordered a biopsy which now sadly indicated that Dan's condition had progressed to leukemia. A ten day regiment of a much stronger dose of chemotherapy began. During this treatment, Danny developed an infection. The infection ultimately took his life on December 14, 2015.

Danny was a loving husband, a father of four (Dan, Jamie, Brandon, and a baby which they lost). He was a beloved son to Mary and Tom and a brother to Debbie, Diane, Dale, Donny, Duane, and Denise. He was a friend to many. Dan was a dedicated worker at Westinghouse/Siemens for 40 years. He loved hunting, fishing and any other outdoor activity. He definitely enjoyed a good beer!

Although he was a quiet man, you knew he meant business when he spoke up.

We chose to honor Dan at our golf outing on July 16, 2016. All that attended laughed and enjoyed the memories which were shared. This is what Danny would have wanted to be remembered with a smile, or in his case a smirk with a raised eyebrow over the edge of his glasses! Although we lost him way too early, he will forever be in our hearts.

We decided to make a donation to MDS with the profits from our golf outing so that more people are aware of this condition and research can only continue to improve treatment.

T-SHIRT FUNDRAISER FROM LOVING DAUGHTER

In memory of her Dad, Lee Kaasa, Caitlin Wohlmacher designed MDS Awareness t-shirts with all monies raised donated to the MDSF. Read Caitlin's dedication to her father.

My father was a family man that was devoted to taking care of those he loved. He loved children and animals and was an avid outdoorsman. His two most cherished hobbies were hunting and fishing. He also enjoyed target practice, mushroom picking, reloading his ammunition and working on his '29 Durant classic car. He sadly passed away from complications brought on by MDS in February of this year.

As a welder and rigger, my father worked in the shipyards around the Puget Sound for 42 years. One of his many jobs was to clean out cargo ships after they had transported crude oil. One chemical contained in crude oil is benzene. Sadly, the protection from benzene for workers exposed to it was mostly non-existent in the past, and contact would often burn their eyes and skin. Benzene is a known trigger for MDS. It was this benzene exposure that possibly contributed to my father's death.

My dad was never one to go to the doctor and due to this we didn't know he even had MDS. It had probably been developing for quite some time and the onset was slow enough that we chalked it up to getting older. Eventually, he had fallen too ill for it to be dismissed as aging. He was admitted to the hospital and bone marrow biopsies led to the detection of MDS. He was admitted 3 different times over the course of a month and would receive plasma infusions, platelets, blood transfusions and 24 hour a day dialysis treatment. In his final stay at the hospital, he was placed on a breathing tube after contracting pneumonia. My father was, and always had been, one to never give up; a big tough guy with a teddy bear heart. Alas, he took his last venture into the woods and passed away at 6:10 pm on February 16, 2016. He wouldn't have wanted us to stress, worry, or be distraught; but when you love someone with everything you have you grieve in the deepest way possible. I still cry almost every day and will never forget what has happened. As a father, husband, brother and grandfather, he was taken from us due to possible negligent safety practices in the workplace. My father will be missed and always in our hearts. We all cherish the memories of our loved ones and when they pass those memories become even more of a treasure.

ATV 'TRASH THE DRESS FOR MDS' BENEFIT IN MEMORY OF TAYLOR MOEN

Taylor

Shelly Guzek organized her second annual ATV wheeler ride and mud run on September 16 in memory of her son, Taylor Moen, who passed away October 26, 2014.

Taylor loved to ride 4-wheelers even during his struggle with MDS. Shelly wants to continue this event as an annual tradition adding some humor and making this a unique ride to give Taylor some good laughs up in heaven and for any of those who have lost a loved one to MDS.

MDS JOURNEY TO HOPE BRACELETS

Sandy Madrigal handcrafted her bracelets to draw attention to MDS. Her designs are dedicated to the loving memories of her mother, Betty and her sister, Linda. They were diagnosed with MDS just eight weeks apart. Both fought the disease bravely and with great dignity. Now she is doing what she can to continue their fight. Each bracelet is only $20.00 (plus S&H). A portion of the proceeds are donated to the MDS Foundation.

Women's Bracelet: Swarovski crystals, fine glass beads, antique Rhodium (a lead-free pewter), silver plated and sterling silver accents.

Men's Bracelet: Wooden and organic beads, silver plated accents and your choice of "HOPE" or "MDS" sterling block letters.

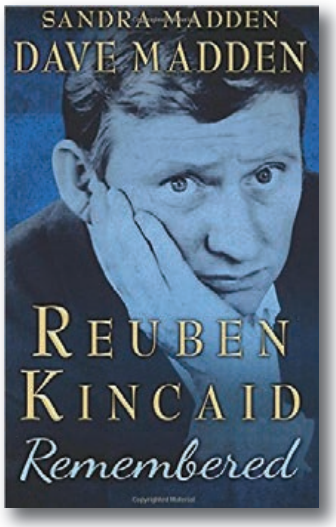
Women's Bracelet
Available in: Petite (7 inches), Small (7.25 inches, Medium (7.5 inches), Large (7.75 inches), and X-Large (8 inches)

Men's Bracelet
Available in: 7 inches, 8 inches

Order your bracelets at:
http://www.lovinkissescreations.com/mds.html

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

Look for more news as we get closer to the movie's release date now slated for January 2017. Yale Productions, the makers of this film, will be donating 5% of their campaign's donations, and 5% of the film's proceeds to the MDS Foundation.



REUBEN KINCAID *Remembered*

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

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

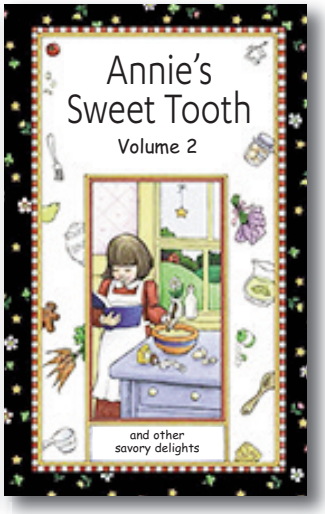
Each purchase of ***Reuben Kincaid*** *Remembered* will support the work of the MDS Foundation.

Available through Amazon at:

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

COOKBOOKS TO BENEFIT THE MDS FOUNDATION

Nancy Cosenza Nussbaum was looking for a way to pay tribute to her late sister, Ann Cosenza Hallberg, who passed away from MDS. As a result, she decided to publish a cookbook with recipes from family and friends, local restaurants, and some well-known bakers and chefs. For Nancy, continuing charitable work in her sister's name allows others to know her and become aware of MDS.



NEW! Annie's Sweet Tooth – Volume 2 – Now Available!

Thank you to Nancy Nussbaum for providing Volume 2 of *Annie's Sweet Tooth and other savory delights*! This edition is also dedicated to the memory of Nancy's sister, Ann Cosenza Hallberg.

Each cookbook is available for $10.00 + $3.00 shipping and handling and 100% of the proceeds are donated to the MDS Foundation. Don't miss out on the new collection of recipes and cooking tips – order your copy today!

To order, email Janice Butchko at jbutchko@mds-foundation.org or call 1.800.MDS.0839.

We are very grateful to families and friends of MDS patients who make generous donations in memory of their loved ones. We applaud all for your valiant efforts. THANK YOU SO MUCH!

Our work as a non-profit organization depends on public funding. If you would like to contribute in this way, or if you have a unique idea of your own, please contact us.

Update: Meeting Mackenzie's Donor

Joanne Curran
Kingston, Ontario, Canada

Last spring we shared with you the journey of our daughter being diagnosed with MDS, then receiving a successful bone marrow transplant. We also shared that this past December we learned the identity of her unrelated donor, Alex from Germany. He was 23 at the time he said "yes" to donate his marrow stem cells to save Mackenzie's life. In January we invited him to visit Canada and were thrilled when he accepted our invitation.

How do we put into words the emotions we felt on May 18, 2016 when, exactly 2 ½ years after Mackenzie's bone marrow transplant, we were finally able to meet Alex, the young man who selflessly saved her life?

At 4:30 pm, friends, family, friends from Canadian Blood Services, friends from Make-A-Wish Eastern Ontario, and news anchors watched, cheered, applauded and cried while Alex came down the escalator at the Ottawa Airport in Ontario, Canada. Mackenzie ran to him. The meeting between Alex and Mackenzie was very emotional.

We were next in line to embrace and thank Alex, who was instantly welcomed into our family. The day following this indescribable meeting, our family was invited to Parliament Hill in Ottawa to meet the Prime Minister which was an amazing honor. We were given a personal tour of Parliament Hill. Prime Minister Justin Trudeau thanked Alex personally for his gift of life.

Alex spent two weeks with our family. We made sure he was able to see some of the popular landmarks close to our home town of Kingston, Ontario. In addition to seeing Parliament Hill in Ottawa, his visit included: a cruise of the 1000 Islands, lunch and a tour of the CN Tower, a visit to Ripley's Aquarium in Toronto, a Carrie Underwood concert in Toronto, a visit to Niagara Falls, and finally a bi-plane ride over Ottawa.

During the two weeks Alex spent in Canada, he was asked often and was able to share with many, how simple the surgical stem cell donation actually was. He let everyone know he was asleep for the procedure and left the hospital the very next day – never requiring the pain medication he was given.

It was difficult to say goodbye to Alex after the 2 wonderful weeks we spent with him, but thanks to modern technology we are able to keep in touch. One day we hope to travel to Germany to visit Alex and his family, and to thank his parents for raising such a remarkable young man.

November 20, 2016 marked Mackenzie's 3rd bone marrow birthday. We celebrated this day as we do every day. We will forever be grateful to Alex for his gift of life.

If you are interested in viewing the wonderful meeting between Mackenzie and Alex, please feel free to google: "CTV Ottawa – Mackenzie meets bone marrow donor".

Parliament Hill: Prime Minister Justin Trudeau thanked Alex personally for his gift of life.

Fighting The Beast

Sandra Asher
San Antonio, Texas

It wasn't supposed to turn out this way. My strong, smart, handsome, motorcycle riding, Krav Maga trained, "never been sick" husband Mike is fighting for his life. In retirement, we should be exploring new places, learning about new things and enjoying new experiences after a lifetime of hard work. Going to see new doctors, learning about MDS and experiencing the yo-yo existence after diagnosis is not what we had in mind.

MDS is a beast. It has a vicious appetite and prefers sneaking up behind unsuspecting victims. The beast often disguises itself as something else and seems to take pleasure in confusing patient and doctor alike by causing different kinds of problems and wasting precious time until it shows enough of itself that a diagnosis can be made. After diagnosis it continues its cruel path, picking and choosing which victims will get more of its attention. MDS toys with many of its victims for years, playing with them like a yo-yo. Other times it prefers to suck the life out of someone quickly.

My husband, Mike, is a retired, 21 year Air Force pilot. We raised a family while moving around the country and were lucky enough to live and travel in Europe for 5 years. During the last years of his career, he was Deputy Commander of Basic Training for the U.S. Air Force which brought us to San Antonio, Texas. Lovely town, great Mexican food—we decided to stay after retirement.

Mike worked at a second career in management before retiring again. He became a volunteer in the Burn Unit at Brooke Army Medical Center and joined the Patriot Guard, providing security and motorcycle escort for our fallen military heroes. I continued my accounting day job and evenings as a fitness instructor with Mike as my roadie and unpaid assistant. He and I taught ballroom dance and loved to travel when my work would allow. Then I had a moderate brain stem stroke, followed six months later by breast cancer. Mike was

with me every step of the way, through rehab, treatments and surgeries. He took care of everything so I could concentrate on getting well. When the worst was finally over, we were ready to get back on track and start crossing things off our post-retirement bucket list. Instead, Mike collapsed, unresponsive in an elevator on his way to his volunteer job.

After a week of hospitalization, tests and consultations, we heard, "You have high risk MDS and have 1.6 years to live. There's no cure." WHAT? No, that can't be right, Mike has never been sick in his life. He doesn't even get colds. All of Mike's relatives on both sides live into their 80's and 90's. It's not fair! He should have 20 more years. How can he be dying? ***The beast had found a new victim.***

Our oncologist called in a colleague who ran the Bone Marrow Transplant Unit. He told us only about 10–15% of patients could qualify for a transplant, but he had reviewed the medical records and although Mike was 68, his extraordinary good health and lack of comorbidities meant he could be a good candidate. There was a glimmer of hope. His MDS was an aggressive type so the doctors wanted to get him to transplant within 3 months. We began a whirlwind of tests and evaluations. Mike said every doctor in the hospital had to sign off on the transplant except for OB/GYN! Mike asked me to be the detail person and his research assistant so I needed to know as much about MDS as possible…fast. I found good, solid, up to the minute information on the MDS Foundation website. They sent me some helpful resources like *100 Questions & Answers About Myelodysplastic Syndromes*. The more I learned, the less afraid and more confident I became that Mike might beat the beast.

The search for a donor began. Friends all over the country got cheek swabs. The ideal donor is 18–44 years old so fellow Chi Phi fraternity alumni at Georgia Tech set up a very successful Be The Match event for the fraternities and sororities on campus. His story was published in the national fraternity journal, educating and inspiring other chapters in the country to set up their own events. The doctors told us that there is only a 20–25% chance that a sibling (no older than 60) will be a match. Mike had a better chance finding an unrelated donor. He has one sibling, a 60 year old sister who decided to give it a try anyway. Her blood was drawn in Indiana where she lived and Fed Ex'd to our Texas doctors. She was a perfect 10/10 HLA match!! Lisa unselfishly came to San Antonio for more testing, preparation and donation of 8 million healthy stem cells. (Once frozen, they are viable for 10 years!)

Meanwhile, Mike began chemo. He was one of the lucky ones for whom Vidaza worked right away. The transplant was put on hold as long as the monthly chemo kept him stable. He had virtually no side effects and went through 13 cycles before the

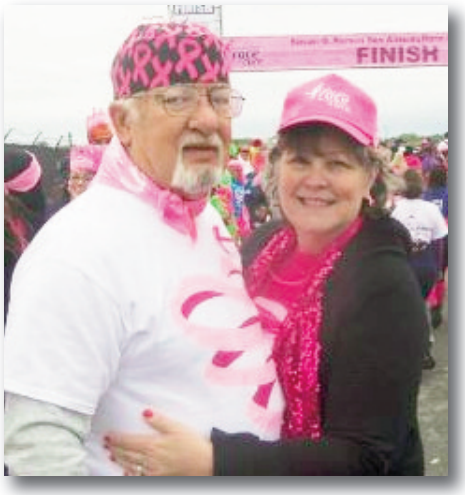
routine bone marrow biopsy showed the blast percentage had more than doubled! The doctor said it was important to have the transplant in the next 30 days because MDS at that stage can progress quickly. We were given 50/50 odds of making it through the year but were sure he would be one of the survivors.

The transplant went fine. Mike had a sore throat for two days…that's it! He went to the transplant unit gym most days, had an appetite and felt good. After a month he was released. His numbers climbed steadily, all getting into the normal range. We were thrilled! Mike had beaten the odds.

Around day +80 Mike's platelets started falling. In spite of medication changes, every few days. The lab results for the other two cell lines began to fall too. Chimerism testing showed he had dropped from 93% donor at day +58 to 23% donor. The transplant had failed.

Failed? How could that be possible? Everything was in his favor. His sibling match was perfect. He was in good physical shape going into the transplant. I made sure his nutrition and his environment were perfect. He never had a fever or infection. We followed our doctor's advice in every way. We did everything "right." It should have worked. I guess we forget about the 50-50 odds.

The bone marrow biopsy had more bad news. The MDS had relapsed. His blast percentage was the same as it had been before the transplant. I poured my broken heart out to others on the Facebook support group, and searched online for news about people who had survived a relapse. ***The beast was back.***



The doctors decided to try DLI (Donor Leukocyte Infusion), even though the chances of it working for a MDS patient are only about 30%. We were told acute GVHD was likely. Mike had a round of Vidaza first, standard before DLI. Although he'd never had problems in 13 prior rounds, this time his belly was bruised and sore, he felt awful, and his lab numbers kept falling. New tests showed that in less than a month, he had progressed to AML. The DLI was cancelled and the doctor said anything done at this point would be a Hail Mary. He wouldn't survive a second transplant. Mike was dying and there was nothing more they could do. Disbelief, anger, sadness, depression…we went through those and more.

Our doctor called a friend at MD Anderson Cancer Center in Houston and asked him to review the medical records. Could Mike qualify for a research trial? Although we were afraid of being told no and having our fragile hopes dashed again, we drove to Houston. After 10 days of tests he was accepted into a Phase I trial. He was given "salvage" chemo, meant to try to rescue patients with a poor prognosis and also began the research trial oral chemo. I could only see him through a window for weeks while he was in a protective environment. He got through the chemo but developed a serious complication called paralytic ileus that almost killed him. Not being able to touch him or even be close to him was awful, especially since he was in so much pain. The MD Anderson doctors saved his life. Mike doesn't remember most of that time, which is just as well. Thin and weak, he began to recover and could soon sit up if helped.

We spent 69 days at MD Anderson. Mike was 203 lbs when we arrived and 143 lbs when we left last week. For the next four months, we will go back one week a month for 4–5 days of inpatient chemo. He takes oral research trial chemo every day along with 11 other meds and is monitored 3 days a week at our local hospital for lab tests, blood, platelets, etc. Unless he is too tired, he can stand and shuffle along with a walker most days. Sometimes I have to pick him up after a fall. He has no fat or muscle left and is frustrated that he can't open a medicine bottle. But he is glad to be alive and has new hope because the last bone marrow biopsy showed he is in remission! Of course we know the beast could come back again, but for today, it's gone and we are daring to think about a future.

No, this isn't the way life was supposed to be at this stage of our lives. I never dreamed Mike would be in the fight of his life and I would be his full time caretaker. Thanks to my husband's care two years ago, I am physically able to take care of him now. We meant it 46 years ago when we promised "for better and for worse… in sickness and in health." Mike says we will dance again and I think I believe him.

Keep Calm and Get Educated

Celgene and Agios Announce Collaborations With Abbott For Diagnostic Identification of IDH Mutations in AML

SUMMIT, NJ and Cambridge, Mass. (Oct. 12, 2016) – Celgene Corporation (NASDAQ: CELG) and Agios Pharmaceuticals, Inc. (NASDAQ:AGIO) today announced each company has entered into collaboration agreements with Abbott (NYSE: ABT), a leader in diagnostic technologies, to develop and commercialize companion diagnostic tests on Abbott's m2000 RealTime System to identify isocitrate dehydrogenase (IDH) mutations in acute myeloid leukemia (AML) patients. Celgene is currently developing enasidenib (AG-221/CC-90007), an IDH2 mutant inhibitor, for the treatment of patients with relapsed or refractory AML who have an IDH2 mutation. Agios is developing AG-120, an IDH1 mutant inhibitor, for the treatment of patients with relapsed or refractory AML who have an IDH1 mutation.

IDH1 and IDH2 mutations occur in approximately 20% of AML patients. An article published online this week in the journal *Leukemia* (Medeiros, *Leukemia* 2016) concluded that advances in the understanding of the genetics underlying myeloid malignancies are driving an era of development for targeted treatments such as IDH mutant inhibitors. The authors recommend that IDH mutational analysis should become part of the routine AML diagnostic workup and repeated at relapse to identify patients who may be eligible for targeted investigational treatments currently under clinical study.

"AML is a complex and heterogeneous disease, making it difficult to treat," said Han Myint, MD, Vice President, Global Medical Affairs, Myeloid for Celgene. "IDH mutations lead to aberrant DNA methylation, causing a block in myeloid differentiation that leads to disease progression. Molecular profiling is important to identify genomic mutations which may have prognostic and potential treatment implications for patients with AML."

Abbott's m2000rt RealTime System, is a polymerase chain reaction (PCR) instrument designed to enable clinical laboratories to automate PCR and results analysis, simplifying the complex and manual steps often associated with molecular diagnostics. Both Celgene and Agios have incorporated this screening into clinical trial designs, including the recently initiated Phase 3 IDHENTIFY trial comparing enasidenib with conventional therapy in older patients with an IDH2 mutation and relapsed or refractory AML (NCT02577406).

"The field of personalized medicine is advancing at a rapid pace for a broad range of medical conditions, especially within hematology-oncology," said Chris Bowden, MD, chief medical officer at Agios. "Our collaboration with Abbott will provide a test to help identify AML patients with IDH mutations who are in need of treatment options."

The m2000 system has not been FDA cleared or approved for use with enasidenib or AG-120.

Enasidenib and AG-120 have not been approved for any use in any country.

MDS Patient Celebrates her Milestone 100 Year Birthday

Estelle celebrated her 100th birthday September 30th!

That's a remarkable milestone for a person with two kinds of cancer. Estelle was diagnosed with MDS (myelodysplastic syndromes) and smoldering multiple myeloma in late 2011. What's also remarkable is that there are cancer medications gentle enough for even a patient in her 90's to tolerate.

As Estelle herself has said, "I am amazed that I can take a drug that affects my system. That I'm so sensitive to. Pretty great."

Estelle now lives in San Francisco so she can be near her grandson and his family. She has had a difficult personal life with the loss of her husband and their two daughters, and in recent weeks she has slowed down considerably. But Estelle likes to say,

"It's hard some days to say hoop de la, everything is great. There are a lot of negatives. But the positives outweigh the negatives — and you have to recognize them. I'm lucky to be here."

This picture of Estelle was taken in February of this year.

Syros Announces First Patient Enrolled in Phase 2 Clinical Trial of SY-1425 in Genomically Defined Patients with Acute Myeloid Leukemia or Myelodysplastic Syndrome

CAMBRIDGE, Mass., September 22, 2016 – Syros Pharmaceuticals (NASDAQ: SYRS) announced today that the first patient has been dosed in the Phase 2 clinical trial of its lead drug candidate, SY-1425, a first-in-class selective retinoic acid receptor alpha (RARα) agonist, in genomically defined subsets of patients with relapsed or refractory acute myeloid leukemia (AML) or high-risk myelodysplastic syndrome (MDS) identified using a novel biomarker discovered by its gene control platform.

"This is an important milestone for Syros and for patients," said David A. Roth, M.D., Chief Medical Officer of Syros. "There has been little improvement in the treatment of AML and MDS for the past 20 years, and survival rates for these patients lag behind many other blood cancers. Treatment with SY-1425 represents a promising therapeutic strategy for subsets of AML and MDS patients with a novel biomarker that we discovered using our gene control platform. Our pioneering approach is designed to advance a new wave of medicines to control the expression of disease-driving genes in genomically defined subsets of patients to provide them with a profound and durable clinical benefit. Our goal is to rapidly advance this first-in-class therapy for these currently underserved patients."

Using its gene control platform, Syros discovered subsets of AML and MDS patients whose tumors have a highly specialized regulatory region of non-coding DNA, known as a super-enhancer, that is associated with the *RARA* gene, which codes for the RARα transcription factor. The super-enhancer is believed to lead to over-production of the RARα transcription factor, locking cells in an immature, undifferentiated and proliferative state. Syros further investigated this unique biology directly in patient tissues and conducted preclinical studies showing that the *RARA* super-enhancer is predictive of response to treatment with SY-1425 in preclinical models of AML. Based on that data, Syros is implementing a biomarker strategy for its Phase 2 trial that selects a subset of approximately 25 percent of AML and MDS patients who may respond to treatment with SY-1425.

"The prognosis for these patients is poor, and targeted approaches like SY-1425 offer hope for much-needed new therapies that attack the underlying biology of the disease and hopefully allow patients to live longer without the toxicities of traditional chemotherapy," said Rachel J. Cook, M.D., M.S., assistant professor of medicine at Oregon Health & Science University and an investigator in the trial. "We're pleased to have enrolled the first patient in this clinical trial and look forward to further investigating SY-1425 for this newly identified subset of AML and MDS patients."

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 MDS and AML patient populations:

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

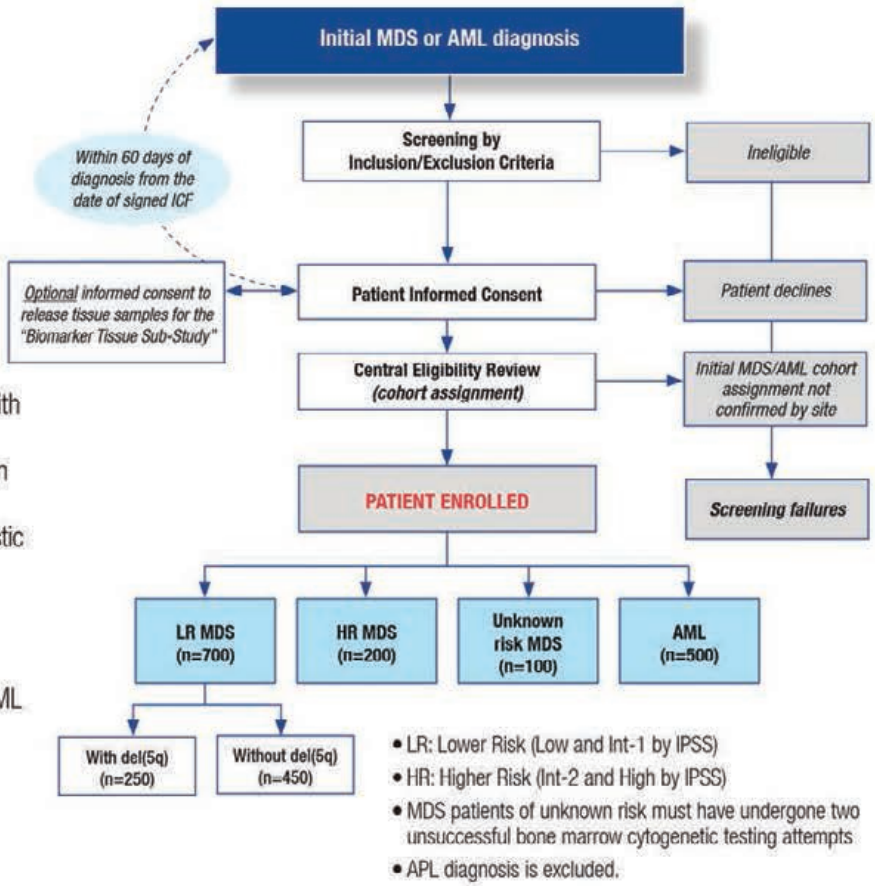
- Newly diagnosed,* primary or secondary MDS or AML
- MDS patients must be at least 18 years
- AML patients must be at least 55 years of age
- Patients must be willing and able to complete enrollment and follow-up HRQoL instruments, for which patients must be proficient in either English or Spanish

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

Note: Concomitant patient enrollment in other studies is permitted.

Physicians – you could be an Investigator if:

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



- LR: Lower Risk (Low and Int-1 by IPSS)
- HR: Higher Risk (Int-2 and High by IPSS)
- MDS patients of unknown risk must have undergone two unsuccessful bone marrow cytogenetic testing attempts
- APL diagnosis is excluded.

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

Celgene

The MDS Family: Coping and Caring Events

Rochelle Ostroff-Weinberg
Wynnewood, Pennsylvania

Coping and Caring Luncheon
White Dog Café
Philadelphia, PA, April 16, 2016

Have you felt overwhelmed by the demands of your MDS? Are you always faced with low stamina and high worry over what medication might restore your energy and health? Have you felt overwhelmed that MDS has taken over your life? And perhaps you are confused by the advice offered? These core concerns, too, were articulated by the MDS patients present. As each MDS patient at the table recounted a grippingly unique story, those voices and those stories embody common elements understood and embraced by every MDS patient.

Have you ever felt that everyone around you is focused on the unquestionably important needs of your spouse, stricken with MDS, leaving you in a lonely spot? Have you felt both helpless and hopeless as you try to cope with your life that has suddenly been metamorphosed into a world of complex medical demands, questions and concerns? Do you feel guilty if you express your needs, your fears and sense of overwhelmedness to others? These feelings that are expressed by so many spouses of MDS patients were clearly

heard around the table at this *Coping and Caring* White Dog luncheon event.

As we gathered at the table in an intimate setting at the White Dog Café, tenseness dissolved as folks began to feel comfortable opening up their hearts to the MDS community assembled to listen, understand and share. I sensed that it was the first time that Prue, eyes welling with emotion, had been given the opportunity to express to someone the challenges for her, as she carries the responsibilities of the MDS spouse. This poignant moment underscores the raison d'être of the *Coping and Caring* events.

The attendees represented a cross-section of the MDS Community:

Jeff and spouse Amy, regulars at the *Coping and Caring* events since its inception three years ago, experience the ability to breathe more easily than the others thanks to a successful bone marrow transplant. Jeff and Amy brought to the table hope and a unique empathy. They told their success story to hungry and appreciative ears. Both Amy and Jeff brought a beautifully special level of compassion to the table. We all surely beam in learning this wonderful detail, which Amy shared:

"Jeff's donor, Nicole, and her family visited us to celebrate the fifth anniversary of Jeff's bone marrow transplant!"

Ray and spouse Prue, both in their eighties, are courageously walking the MDS path at this point in their lives. Prue came to the table with an anxiety that I recognized all too well. Ray's attendance at the luncheon enabled him to provide critical MDS information — videos, websites — to Claudette and George, creating an important bond that results from gathering together at the Coping and Caring table. It is quite simply moving to witness the patient to patient, spouse to spouse outreach that takes place at each Coping and Caring event. Ray's desire to help another MDS patient jumps out at you, conveying the invaluable benefit of participation. Surely, it is not solely the concrete information exchanged, but an MDS patient or spouse learning that she, that he is not alone with the MDS challenge.

Claudette and spouse George attended for the first time, contributing their feelings and concerns. Of course, as they opened up to those gathered around them, what they express bears fruit: understanding, empathy and support. Claudette shared:

"The people present were so welcoming which made it easier to get involved in the discussion. I learned that MDS comes in many different forms, that educating oneself is important, and that MDS is not an immediate death sentence but requires time and attention. I was made aware of the availability of support groups, videos, and the MDS Foundation who provides much information. I learned so much from all of you. It is comforting to know that others have similar problems but are unselfishly willing to give support to others."

Continuing around the table, we come to **Mindy Greenstein**, author, national speaker and psychologist, who was the perfect guest presenter at this event, I am so grateful to Audrey Hassan of the MDS

Foundation for her dedicated energy to find outstanding presenters for each Coping and Caring event. And what exactly makes Mindy an ideal choice? Along with the credentials already mentioned, she is a psycho-oncologist and specialist in geriatric psychiatry at Memorial Sloan-Kettering in New York, who brought to the table a plateful of personal experiences germane to the situation of those in attendance, as well as deep knowledge and inspiring humanity. Each participant received a copy of her fascinating book, *Lighter as We Go: Virtues, Character Strengths, and Aging* (written in conjunction with Dr. Jimmie Holland). I was curious to learn her observations of what unfolded at the event. Here is some of what she shared:

"One theme from the book that seemed to have resonance is the way we learn from our experiences and gain in emotional strength over time. In my work, we help people recognize and build on their strengths to deal with adversity. The stories help me see that kind of resilience at work in real time, watching participants support each other by sharing the lessons they've learned from their own experiences. It was so heartening to hear everyone's stories, and see how much support they provide each other. Each story—whether patient's or family member's—is unique and yet, together, they speak to the vicissitudes of human resilience and how much we gain from each other."

Truly, who can be more genuinely understanding of the circumstances, the trauma or euphoria of those in the MDS Community than those who are living in the same reality? And it is they who can best benefit from hearing stories that replicate what they and what you are living and experiencing each and every day.

Coping and Caring Dinner Margate, NJ, July 30, 2016

We gathered once again for the Coping and Caring dinner in Margate, New Jersey. And Audrey Hassan found, once again, a terrific guest presenter, Jill Garaffa, who, as Audrey described, offered "an interactive and engaging program". As an occupational therapist, professional certified life coach and energy leadership master practitioner, Jill lent her knowledge on coping with the challenges of living day to day with this new normal – called MDS.

I want to thank everyone for making the voyage to my summer home in Margate. It was unquestionably a significant moment for me. I have given much reflection, since your departure, to all that you shared: your concerns and worries, your hopes and revelations. They gave and continue to give me pause.

I was struck poignantly by Pat, your remark that "nobody cares." That crying out is resonating in every red blood cell in my body, in every part of me. I heard that, as I hope all of us did, long after we separated. As I said in immediate response "I care." And I meant and I mean that with genuine feeling and sincerity. I so hope that you feel just a little bit less alone with this scary reality. Please let me say again, I care.

There is also, please note, a photo of Bob, my husband, in the hospital a few weeks before he died. Attached to his tower of infusions he is dancing to the music of the blues group, Muddy Waters. May this snapshot linger in your mind, may it be an inspiration to you to get up and dance, to get up and exercise, to get up and to stay up and to know that I, Rochelle Ostroff-Weinberg, am holding you up.

I am a Fred and Ginger fan. In spite of "silly" scenes and "silly" songs, there is brilliant wisdom to the messages behind

the fun. Here are some of the lyrics of one of my favs that is my mantra:

from *Swingtime*
Jerome Kern and Dorothy Fields

...Nothing's impossible, I have found.
For when my chin is on the ground,
I pick myself up, dust myself off,
Start all over again.
Don't lose your confidence if you slip.
Be grateful for a pleasant trip,
And pick yourself up; dust yourself off;
Start all over again...
Will you remember the famous men
Who had to fall to rise again.
So take a deep breath;
Pick yourself up; Dust yourself off;
Start all over again.

Sending love and caring, Rochelle

My Dad, My Hero

Lisa Evangelista
Laguna Hills, California

When I think about how my dad should have passed away, I think of him lying in a hospice bed, my mom, my sister and me at his side holding his hand. We would tell him we're so proud of him. He would say he's proud of us. He would smile calmly at us before taking his last breath, squeeze my mom's hand one last time and then go peacefully to where we cannot follow him. That's how I wished it had happened.

Flashback to over 25 years ago when my sister and I were young children growing up in Canada. Our dad seemed like a man of Herculean strength who could pull both of us around in our toboggans in the snow with one hand. He ran like a stallion alongside us when he taught us how to bike without training wheels. He had so much athletic prowess when he played basketball with us, we wished we could be as good as him when we grew up.

We relocated to the United States shortly before our teenage years at which time we developed a vague awareness of the generic maladies that perturbed our parents like hypertension and arthritis. Our dad wasn't Hercules anymore but most people our parents' age dealt with the same afflictions so it was "normal." In our college years, our dad was diagnosed with lupus and his overall health seemed to decline.

It wasn't until 2013 after a series of abnormal blood test results and a bone marrow biopsy that our dad's health seemed to actively take a different course. He was diagnosed with myelodysplastic syndromes or MDS for short. After becoming familiar with the condition, we began to understand why he bruised easily and why he required more Band-Aids when he got a cut. But he's always been a bleeder for years. Why is this diagnosis just happening now? I didn't know at the time, but this reflection is but one of many that will spark countless yet meaningless "what-ifs" over the course of the next three years.

MDS became either the intensely discussed or the eluded topic of conversation for my family. When we would talk about MDS, we would typically share what each of us had learned about the condition...

Since the diagnosis, blood tests, Procrit injections and blood transfusions become more frequent. Doctors, specialists, hematologists and other white coat cloaked oncologists assimilated themselves into his life and became fixtures of his weekly routine. Terms like dysplasia, acute myeloid leukemia and increasing blasts were integrated into our everyday vernacular.

In March 2015 his co-workers became concerned with his behavior at work. Normally talkative and social, my dad was withdrawn and unusually quiet. They said it was warm but he wore his parka all day in the office. He couldn't think straight and his speech became incomprehensible. They brought him to the emergency room where doctors identified his behavior was due to severely low hemoglobin and thrombocytopenia. This incident jumpstarted an outpatient chemotherapy program recommended by his hematologist where he would be administered Decitabine intravenously for five days out of every month. The treatment was going to increase and stabilize his blood cell count. When I asked him how his treatments were going, how he felt sitting in the room alongside other patients receiving chemotherapy, he used to deflect from talking about his personal experience and instead tell me about the books he was reading and what he learned from them during treatment. He wasn't being dismissive — he just didn't want us to worry.

MDS became either the intensely discussed or the eluded topic of conversation for my family. When we would talk about MDS, we would typically share what each of us had learned about the condition online, from friends, or in my sister's case, through the advice of the medically adept network of her colleagues at her medical center. Five to ten years survival after diagnosis. There is no specific cause. I'm not a candidate for bone marrow transplant. These were common expressions in our conversations. My dad was just being factual. After all, I have

never seen him angry or discouraged. Only upset when the Buckeyes let him down in championship games or disappointed when I brought home less than stellar report cards. Regardless, we stayed positive. Sometimes his blood test results yielded improvement. Sometimes they didn't. But it wasn't getting worse. And that's all we could hope for.

Almost exactly a year after being admitted to the emergency room by his colleagues, I received a startling phone call from my mom. My dad was being rushed to the hospital in an ambulance because he fell and hit his head but he doesn't remember how. He called her while she was at work and told her to come home because he was bleeding profusely. She found him lying on their bed, with blood-soaked sheets, in the midst of a setting resembling an atrocious crime scene—the carpet doused with pools of red, bloody prints stained the walls and closet doors. MDS patients may not produce enough mature platelets that form blood clots to stop bleeding. He continued to bleed from the gash on his head for over 24 hours.

Now our vocabulary expanded to terms like acute subdural hematoma, splenic laceration and intracerebral hemorrhage. He remained in the hospital for nine days. In those nine days my dad went through what seemed like a never-ending barrage of tests, assessments and therapies from a brand new pantheon of surgeons, oncologists, and intensivists. Throughout every exam, no matter how invasive or inconvenient, my dad obliged with utmost gentility and never complained of any pain or discomfort.

As soft-spoken and unassuming as he was, he was not a victim. He had MDS but he did not let it define him.

He was able to return home and by then, he had lost a significant amount of weight. His muscles had severely atrophied and he couldn't stay awake for more than three hours without a nap. He couldn't eat more than half of his usual portion size and couldn't walk without a cane. Cue the thoughts of saying goodbye in a hospice bed.

Days went by with little improvement in his physical condition. It was hard to accept how frail he had become. It was difficult to look at him without my eyes tearing up. But his cheery nature, his positive spirit, made it impossible to be sad around him.

The morning of May 7, 2016, three weeks after my dad was released from the hospital, he passed away. My mom found him unconscious on the floor of their living room. He stayed up the night before watching TV but never made it to bed. Emergency responders were unable to resuscitate him. I remember my mom's hysterical cries on the phone and knew then that was the day. No hospice bed. No calm smile. No one last goodbye.

In the days following his death, I found myself routinely explaining what MDS is to friends and family. I became quite capable of reciting definitions of MDS, and transforming what were sometimes awkward encounters with sympathizers into brief informational sessions on the condition. MDS is a genre of blood cancers. MDS is a condition in which the patient's bone marrow does not produce sufficient amounts of healthy blood cells. That's what MDS is.

It wasn't until after my dad passed away I began to think about what MDS was to him. A struggle that was present for the greater part of his life, an invisible enemy he showed up to fight every day. As soft-spoken and unassuming as he was, he was not a victim. He had MDS but he did not let it define him. Despite the physical complications and distress he endured because of MDS, he still found means to accomplish everything he wanted to in his lifetime, earn advanced degrees in science and business and receive numerous accolades. Despite the anxiety MDS brought him, he provided well enough for his family so we were able to grow up in an affluent area and celebrate our own achievements. He did this all on his own, never seeking recognition or praise. A man, who regardless of his achievements, successes and respected character, remained inconceivably humble. He truly transcends physical Herculean strength.

This story may not have the happiest ending. Or a resolution. But it has a hero. And with this story, I hope others who are affected by MDS are able to find the strength to carry on and live their lives as best they can. Just like my hero did.

What a Trip!

Shirley Bulloch
Midlothian, Virginia

Survivor! Advocate! Fighter! Determined! Researcher! Positive! These words describe me after my 16 year battle to survive MDS. I recorded everything in a journal and called it "Myelodysplasia – My Journey: Letters to a Friend". If I had started the journal today, it would be entitled, "Myelodysplasia – What a Trip".

I was referred to a hematologist in late May of 2000 to determine the cause of my extreme fatigue and dizziness. I had been treated with B12 injections for years for anemia, but the lab results indicated a problem with my hemoglobin. On June 1, 2000, Dr. Yogesh Gandhi performed a bone marrow biopsy. One week later, he called to inform me that I had myelodysplastic syndromes refractory anemia with ringed sideroblasts and megakaryocytes. This was the beginning of my trip. I asked him if I should cry, and he told me "No".

I have shed only a few tears, and I became very determined to fight and conquer this dreaded blood disease. I went home and "put my house in order", making plans for the future. Through my reading, I found that the prognosis was two to five years. I knew that I still had a lot to accomplish in life and the time would be much longer. I had just retired in 1999 as an educator at the age of 59, and we had completed a month long road trip to California. I was not going to spend my retirement getting ready to die, but to enjoy life.

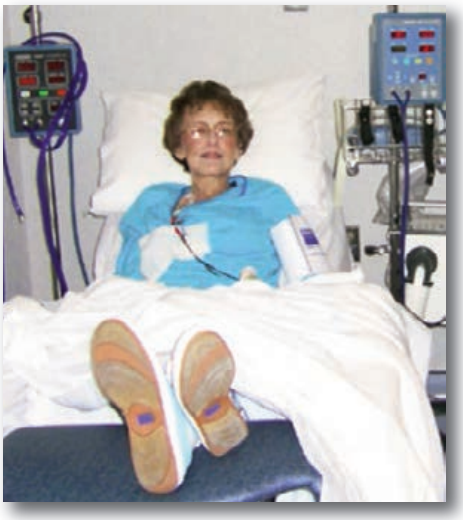
Shirley, Charlotte (donor), Patti, (supporter)

Be the Match Run/Walk 2012

At that time, I was considered too old for a transplant and would need to survive with transfusions and experimental treatments. My hematologist said that together, we would find a new method of treatment. While I continued to research everything, I received 2 units of packed red blood cells every 13 weeks gradually requiring the transfusions every 14 to 18 days. In May 2001, I had a portacath placed in my upper right chest to make the transfusions easier. This was the first of many portacaths between 2001 and 2012. The hematologist tried lenalidomide, amifostine, and Procrit®. I had adverse reactions to the lenalidomide and the amifostine. The Procrit® did not increase my red blood cell counts as my kidneys were producing sufficient erythropoietin (EPO). I was given medication to decrease the number of platelets and the MDS did not affect my white cell counts. None of these drugs provided me with any benefit.

I just knew that there would be positive outcomes in my future. In May of 2002 while surfing the net, I read the notes from the April 2002 Oncology Conference in Orlando, Florida about a clinical trial with a mini-peripheral stem cell transplant following four cycles of the experimental drug 5-azacitidine (now Vidaza®). One of the trials was conducted at Virginia Commonwealth University (formerly called Medical College of Virginia) Hospital in Richmond, just 25 miles from my home. 16 centers in the US were conducting the Phase II trials. On June 11, 2002, I had my first appointment with Dr. John McCarty. The steps to be part of the clinical trial were in motion – insurance approval, finding a sibling donor match, and having batteries of tests. My older sister was a match and I started the painful 5-azacitidine injections, three shots a day for seven days with three weeks off, and then a repeat of the cycle until I had completed four cycles. There were some delays while my white cells took their time in generating more cells. I spent one week in the hospital with pneumonia. Wow! I was the first in the nation with MDS to complete the Phase II trial with a pre-treatment of 5-azacitidine. On March 10, 2003, I was admitted to the bone marrow transplant wing, my new home until April 10, 2003. The second day of stem cell infusion was completed on March 15, 2003. To track the progress of the longest surviving MDS patient in that clinical trial, I have easy access by just looking in the mirror.

When you look at the big picture, it is easier to fight through each day with the nausea, weakness, and delays. It is easier to find some humor in each day as it is better to continue to laugh. I even put on makeup every morning and put rollers in my hair. Eating was the most difficult as was the need to continue the Desferal® pump, an iron chelation machine, used for getting rid of the iron overload caused by all the transfusions. As soon as my hemoglobin counts increased post transplant, it was no longer necessary to use the pump. Once during photopheresis, they removed a pint of blood and that reduced the iron level. I had one other phlebotomy, a self-performed one. I had hooked my port to a medication IV at home and must not have had it tightened correctly as I woke up in a pool of blood. My levels were checked the following day, and I apparently removed a pint of blood. The benefit was no more phlebotomies for iron overload. Now I have to laugh about that experience - I was only upset about ruining the comforter on my bed!



Photopheresis Treatment

Once the transplant was completed, the battles still continued with the consequences of the chemotherapy, radiation and the medications. The treatments included frequent bone marrow biopsies, liver biopsy for high liver enzymes (determined cause was one of the medications), photopheresis for skin graft vs. host disease (GVHD), breathing treatment with pentamidine as I was allergic to the bactrim. There were some downsides to the transplant. The chemo was low dose, so my plan for my hair to fall out and grow in curly didn't happen as my hair did not fall out. I had to eliminate one of my three favorites, chocolate. I always said I survived transfusions by eating peanut butter, special dark chocolate and colby jack cheese. I had to wear a mask when I took part in my favorite activity: shopping.

There were problems especially with the catheter for drawing blood. With one of them, I had to be in an infusion chair tipped all the way back with my feet in the air, in a contorted position, to get any blood. Eventually that had to be replaced. Between the release date and 2012, there were additional hospital stays. A few of the times, the doctors appeared grim. Not me though as I never thought about anything but survival. One hospital stay was a result of a reaction to prednisone which gave me drug-induced diabetes and took away my upper leg muscles. I had to use my arms to lift my legs in and out of bed. When taken off of the prednisone, the glucose levels returned to normal, but I had weeks of physical therapy in the hospital and at home to get me out of the wheelchair and walking. Until therapy was completed, I lived in the family room, used the lower level bedroom, and could not get up the three steps into the kitchen. So much for being independent! I had hospital stays for congestive heart failure and for lung GVHD. I had skin, mouth, and eye GVHD. I had photopheresis treatment for several years 2004–2009 to resolve the skin GVHD problems and special rinses for the mouth irritations. Photopheresis is the process of removing blood in cycles, separating the returning red cells immediately to the body, and then treating the white cells with ultraviolet A light and infused into the blood stream. I still cannot tolerate pepper or citrus. The eye GVHD led to three different surgeries on the lower eyelids. In 2007, I had a pacemaker implanted to regulate a slow heartbeat that had surfaced in 2001. As the result of the chemotherapy and radiation, mouth GVHD and the dry mouth syndrome, I have had major dental surgery. Also as a result of all of this, my kidneys have failed and I have been on peritoneal dialysis for two years. I conquered the cancer and the GVHD. I am successfully dealing with the dialysis. I refuse to let anything slow me down as I remain positive and find some humor in my experiences.

2009: Matthew and Grandma

I have laughed, enjoyed life, and we traveled from 2005–2011 in the motor home for weeks at a time because I could carry my sanitary lodging with me and prepare our own meals. We were able to travel to my sister's home in Arizona, to Pennsylvania Amish Country, Myrtle Beach, New Orleans, our home state of Michigan, and visits to our daughters in North Carolina and Georgia. We went gemming in North Carolina and Georgia. I developed a hobby of crafting clay jewelry and everyone I know has at least one piece of my jewelry. I have taken part in the *Be the Match Run/Walk*. Since the transplant in 2003, I have had an additional 13 years of marriage, two more grandsons, and I hope through my website (http://shirley.bulloch.org) that I have helped at least one person as 18,569 people have visited my site.

I have made "Shirley's Shawls of Hope" for in-hospital transplant patients, and in May performed Random Acts of Kindness in memory of my grandson who lost his battle against cancer on Mother's Day 2009, at the age of 13. Matthew was a big part of my life as we were both diagnosed in 2000, and through the following 9 years, we both traveled the road together. There was a special bond between us. We both had cancer – with mine being MDS and his a brain tumor. I continue my fight for both of us. I have one more goal. At the end of this summer, with the help of the MDS Foundation, I plan to help organize a support group in our area for post-transplant patients. I feel the need to do this as I have younger transplant friends that would benefit from sharing with others.

There have been many bumps in the road, even some roadblocks, but I have conquered them with my increased knowledge and determination. I am proud to be 76 years old and still maintain a positive attitude. By the way, September 26, 2012 was a memorable day. After many portacaths, I was finally deported. I am transfusion free and the only drug I am still taking related to the transplant is a daily Singulair as it apparently keeps the lung

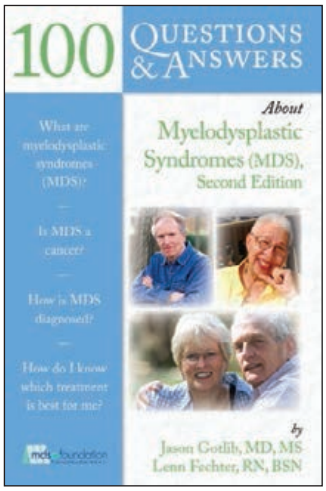
GVHD as non-symptomatic. I now have a dialysis port and do the dialysis at home while I sleep. I plan to still be here for another ten years doing what I love best…living.

If I had known the side effects of the transplant in 2003, my decision to have the transplant would have been the same. I was determined to beat cancer, not have it beat me. My nurses, doctors and people that know me well call me Dr. Shirley. My nurse calls me tenacious. I am just stubborn and determined. I must be part of the team involved in my care. The last 16 years have tested me as a person and in many ways made me stronger. Yes, there has been a lot of humor in this. I had the support of my husband, my family, my friends and the many doctors and nurses at North Hospital in the VCU-MCV Bone Marrow Clinic (Drs. John McCarty, Harold Chung, and Toor, Nurses Judy, Laura, and Carol and countless others) as well as the doctors and nurses in Photopheresis. It has been difficult to condense 16 years into a couple of pages. If you have any questions, please visit my website http://shirley.bulloch.org/ and send me an email. Bless each of you and keep fighting.

2016—16 years since my MDS diagnosis and 13 years post-transplant. The trip continues…

2009: Shirley and Ross, New Orleans

HAVE QUESTIONS ABOUT MDS?



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Living With MDS for More Than 10 Years Gives Hope

Niels Jensen
Slangerup, Denmark

I am one of the lucky ones! For more than 10 years I have now lived knowing that I have myelodysplastic syndromes (MDS). It has been a journey with some bumps along the road, some periods of anxiety, and many periods of joy. So how did it all start?

When Running for a Train or Bus Was Not an Option

Getting exhausted and out of breath for several minutes by just running a short distance to catch a train or bus on the way to or from work was the first symptom I noticed. But that was easy to adapt to — I simply stopped running to catch a bus or train. Instead, I walked slowly, and got on the next bus or train. With time other things popped up such as being unable to have a normal conversation for a few minutes after taking a set of stairs to the second floor. That I also adapted to. In early 2004, it was when my secretary noticed that I was unable to answer her after climbing the stairs to our office that I finally did something. She told me to pay my doctor a visit. I did!

My GP had no idea what was wrong, and sent me to the local regional hospital about 10 kilometers from my home in Slangerup. That was the start of a year of frequent hospital visits. I was 55 and that was — except for a couple of broken arms — my first real encounter with our health services. The approach used at the regional hospital was that you talked to a doctor, normally the same one at each visit, and he ordered some test, then you would get another appointment with the doctor to hear the results of the tests. If the results did not indicate what was wrong with you, then the doctor would order further tests, and you would get an appointment to hear the results of those tests. This went on for some months without an answer coming up.

Trying to Find the Straw That Broke my Breathing

At the time, I was taking a very low dosage of phenobarbital — a drug commonly used to prevent epileptic seizures. In the mid 1970's, I had 2 grand mal seizures. Initially I was put on Dilantin®, but that drug lowered my red blood cell count, and I was switched to phenobarbital. The regional hospital doctor found out that phenobarbital, which is sleep inducing, could sometimes also result in shortness of breath, which I experienced after just minor physical activity. Hence, I was sent to a neurologist to see if I could get off phenobarbital. The EEG showed that my brainwaves still had the features, which had caused my earlier grand mal seizures. Nonetheless, the neurologist recommended that I got off phenobarbital, since at the time I had not had a seizure for more than 15 years. So I did.

Some months later my shortness of breath was still very noticeable, and I returned to the regional hospital for a bone marrow biopsy to see if I had leukemia. Before I had the bone marrow biopsy, one of the nurses was kind enough to tell me that the procedure was like being kicked by a horse — something I have never experienced. However, it did not sound pleasant. I was lucky not to have leukemia. Then my visits to the regional hospital stopped, and some months went by. My wife told me that we men have to be reminded about everything and that it was time for me to see my GP again.

I attempted to phone the GP office one morning to tell about my breathing problems. This is only possible between 8AM and 9AM. After attempting to get through for a whole hour, and not having any success I went to the clinic, and told them. They just told me to try again the next morning. I was furious when I left the clinic, and started my journey to work using our good public transit system here in Denmark. As I reached the top of the stairs to my second floor office, my mobile phone started ringing. I was out of breath from climbing the stairs, but answered anyway. It was my GP, and she could immediately hear that something was wrong. The next day, I had an appointment to see her. When I saw her the next day, she sent me to a private heart specialist and she also planned to schedule an appointment for me to see a hematologist at the major regional hospital. It was getting close to Christmas 2004, and I had planned to conference trips in January — one to Okayama, Japan and one in Bialystok, Poland, so I asked her if she could make the appointment with the hematologist after February 1st next year. She said OK.

I had the appointment with the heart specialist before Christmas, and he told me that my heart was pumping fine, but that my red blood cell count was about half of normal. I told him that my GP was already attempting to get me an appointment with a hematologist, and I went on to have a nice Christmas with my wife and four children and two nice conference trips. It was May 2005 before I first saw the hematologist at the major regional hospital in Hillerød.

A Very Special Wedding Anniversary Gift

On my first visit, the hematologist told me that the other hospital had done a bone marrow biopsy, but had not ordered a chromosome analysis so he could not use that result. He then told my wife and I to go sit in the waiting room, while he found a nurse and a bed, so the bone marrow biopsy could be performed right there. That remark completely changed how I since have viewed getting a bone marrow biopsy: It was just another type of medical test, just a bit more complex than taking a blood sample. From that day on, there has always been someone with me when I go to see a hospital doctor. Our next appointment with the hematologist was on the morning of our 23rd wedding anniversary — July 8, 2005. We took the bus to the hospital, and after a short wait, we were sitting in the hematologist office. He told me that I had MDS, and that this was a chronic illness, which I would have to live with the rest of my life. He would give me Aranesp®, an EPO-like substance, and Neupogen®, a growth factor, in order to improve my blood counts. My wife also recalls him telling us the FAB category of my MDS. In the waiting room, a nurse instructed my wife on how to give the injections and I got my first EPO shot. The nurse also gave medication for the period until our next appointment in about two months' time, and told us that the rather expensive medication should be kept in a refrigerator. What a gift to start with on our anniversary celebration!

My wife took the bus back to our home in Slangerup to put the medication in our refrigerator, while I, due to my severe shortness of breath, waited in the shopping center Slotsarkaderne for her return. It was a nice summer day, and we started our celebration with a walk up and down the walking streets of Helsingør. For some time, we had planned to celebrate our anniversary with dinner at Jan Hurtigkarls restaurant in Ålsgårde on the northern shore island we live on, and a short train ride west of Helsingør. This place — now

closed — was known for serving a very nice gourmet dinner with accompanying wines, and you started with a before dinner drink right on the beach towards Kattegat. We had a very nice and unforgettable anniversary dinner in a restaurant overlooking the approach to Kronborg and Øresund on a beautiful summer day and evening. The question: "What is MDS?" had to wait until the next day.

What is this "MDS"?

The very next day, both my Anna and I spent most of the day in front of our two relatively new laptops. We searched the internet for information about MDS and found the MDS Foundation and the Medifocus site. We looked at the same websites, looked at the same survival curves, but interpreted the information very differently. I looked at a diagram, and thought: Great! After more than 10 years, 30% of RARS patients are still alive. However my wife looked at the same data and thought: Bad! After 3 years, 30% of RARS patients are dead. We both got the message that the only cure was a bone marrow transplant, which the hematologist did not even mention when informing me that I had MDS.

I also discovered, that in the summer of 2005, there was just one FDA approved drug, and it was neither Aranesp or Neupogen—although these were FDA approved for aplastic anemia, they were not approved for use by MDS patients. Why then did I get them? It turns out that the laws in Denmark allow doctors at major hospitals to treat patients with drugs approved for the treatment of related diseases. Aranesp was approved for aplastic anemia.

Based on her expectation for how long I would live with my chronic illness, my wife called our best friends from the time we lived and worked in Sarnia, Canada. Already in September — just as we took possession of our used VW Lupo 3L — they arrived at our home in Slangerup. We had a couple of wonderful days with more focus on memories than a chronic illness. And some excellent sightseeing in North Zealand.

In October 2005, during my second visit after diagnosis to the hematologist in Hillerød, my blood counts had not improved, and the hematologist told me that he could not do more for me, and that he would recommend that I got transferred to the Hematological Clinic at Rigshospitalet in Copenhagen.

In New Hands at a Very Specialized Hospital: Rigshospitalet

My first meeting with Rigshospitalet in November 2005 was a very positive experience. I was scheduled to talk with my new hematologist, Dr. Lars Kjeldsen, around 10 AM. He told me that my MDS according to the International Prognostic Scoring System (IPSS) was considered to be risk level intermediate-1, because all my blood counts, i.e. red cells, white cells, and platelets, were low. Then he went on to tell us that they were going to perform a number of tests on me in order to eliminate other diseases and confirm the results from the hospital in Hillerød. I was then given a list of three procedures to be performed that day, and a time to talk with Dr. Kjeldsen after lunch.

At that first meeting, my dose of Aranesp was almost doubled from 500 microgram every three weeks to 300 microgram every week. At the same time, the amount of Neupogen was increased from one injection per week to 2 or 3 injections per week. This programme was continued until the middle of 2007. The result was that eventually my red blood cell

count increased to about 75% of normal at the end of 2007 and 95% of normal at the end of 2008. During 2008, the dose of Aranesp and Neupogen was reduced until completely stopped towards the end of the year. During 2009 and 2010, my red blood cell count dropped to around 75% of normal, where it has remained until this day.

It is very nice to think back on the treatment I was offered back in 2005, and see that in 2013 an international clinical study was started to confirm the Scandinavian findings with this treatment. That is great especially in the light of Italian findings that many blood transfusions (an alternative method to treat MDS) are bad if you later need a bone marrow transplant. It is also great to look at the list of drugs which have been FDA approved for treatment of MDS: azacitidine in May 2004, lenalidomide in December 2005, decitabine in May 2006, and each year brings more new treatment options.

Bumps Along the Journey With MDS

In the initial years living with MDS, I was a bit careless. For example, during a trip to a conference in Prague in late August 2006, I was sitting 4 hours next to an open hotel window putting the finishing touches to my conference presentation. While I was at the conference with a rather bad cold, Anna enjoyed seeing some Unesco Heritage Sites in the Czech Republic. As we started our drive back towards Denmark, I was not feeling especially well. I was lucky to have such a good co-driver in my wife, and we made it back to Slangerup without a planned stopover. The next day my GP told me, that I had pneumonia. This was only my first encounter with pneumonia. Over the years, I have had two more.

Just one and a half months later, I encountered another bump. I was going to attend a meeting in Luxembourg, and since the doctor had made it clear that flying was not a good option at that time, we planned to drive to Luxembourg. When, after a stopover in Hameln, we arrived at our hotel outside Luxembourg City, I had a bath before dinner. While I was having my bath, Anna took one look at my leg, and said we had to go to a hospital. Anna had learned how to recognize the appearance of a blood clot, and she did not like what she saw on my leg. We drove to Centre Hospitalier du Luxembourg — thank you GPS. After a fairly short wait, I had a consultation with an English speaking doctor, who ordered some blood test. The test indicated a potential blood clot, and she requested that I come back the next morning for an ultrasound scan. The scan showed there was a blood clot in my lower left leg, and I was immediately put on clexane and told not to drive. My wife drove me to the DuPont site in Luxembourg, where my meeting about the BP Texas City refinery explosion and fire, was to take place. After the meeting, the drive back to Denmark started with Anna at the wheel, and me lying on the back seat with my leg high. Two days later we reached Slangerup, but unfortunately an ultrasound scan at the local regional hospital could not confirm the presence of a blood clot, so they did not put me on blood thinner. That was a mistake.

I hit the third bump in January 2007. I was taking the train from Roskilde through Hamburg and Bruxelles to London to attend a meeting of the EFCE Working Party on Loss Prevention in London at the offices of BP. It was a two day meeting and on the morning of the last day, a major storm was developing over England, North West France, Belgium, Holland and western Germany. As I left the BP offices, the wind was already so strong that two persons had to manage the building glass doors, and while waiting for the train to London a billboard left its stands and landed on the track. There were no more trains from that station that day, and hundreds of people scrambling to find alternative means of getting to London. Eventually, I found a bus to Heathrow and from there a bus to central London to catch my Eurostar train to Bruxelles. However, as I approached the Eurostar terminal station it was announced that all Eurostar services had been cancelled until next morning due to the storm over the Channel area. My return to Denmark was delayed by 24 hours, a good part of which I spent attempting to get some rest in the Eurostar terminal area. That was a bit of a challenge, due to the many people there and custodians wanting to do the normal morning cleaning.

So with a delay of 24 hours and almost no sleep for 48 hours, Anna picked me up at Roskilde. Sunday, we attended the baptism of my niece's first child and Monday I drove to work as usual. However, there was nothing usual about the trip home that evening. After passing through the forest between Farum and Lynge, I hit a curb between a left turning lane and straight lane in an intersection at Nymølle. A real bump. I had passed out. I can recall the drive through the forest, but not the approach to the intersection. The bump actually woke me up, and I stopped

the car on the other side of the intersection, waited for five to ten minutes, and drove home. I didn't say anything about the incident — no car damage and no injury to me or others — at the dinner table. However, that night I could not fall asleep, and finally in the middle of the night I told Anna what had happened. Then I fell asleep.

The very next morning I phoned my GP, who immediately said I was not to drive a car until further notice. Later that day, I was admitted to the local hospital, and subjected to 24/7 monitoring for heart problems. During the following days, they scanned my heart — nothing, they performed ultrasound of my legs — blood clot behind one knee, scanned my lungs — reduced capacity in both lungs. I was in the hospital for 10 days. Result: I was put on warfarin — permanently! And I could not drive a car for the next six months.

Another result was that my boss at the Department of Chemical Engineering at the Technical University of Denmark deemed that I could no longer be responsible for teaching a regular chemical engineering course. Teaching was about half of my job, the other half was being safety leader at the department, which had more than 200 persons and many experimental facilities. This confirmed a feeling, which I had even before my diagnosis, that my boss wanted to get rid of me. At the end of 2007, he succeeded partly due to this bump.

However, some of the biggest bumps I have experienced were chills. They have occurred twice. It starts with a feeling of tiredness, so I lay down to rest on our couch. Then I start shaking and feeling cold. The first time this happened, I just got some orange juice and slept for a few hours, and the chills were gone. The second time, Anna was home and she took action by calling the medical emergency number, telling them I had MDS and what was happening to me. Five minutes later, we were on our way to an off-hours consultation at the local hospital. The doctor examined me. She even googled the home page dkpsg.mds-and-you.info, and

concluded she had to admit me to the hospital in order to find out what was wrong. At that time, I had no fever based on both her observations and my own feelings.

Ten minutes later, I was lying in a bed in the admission unit, and a nurse asked if I had a fever. I said no. She measured my temperature, and it was 39.5 Celsius. We remembered a letter, which Dr. Lars Kjeldsen at Rigshospitalet had given to us years ago, about what to do if my temperature increased beyond 38.5 Celsius. Based on this letter, the local hospital contacted Rigshospitalet, and they told the local hospital to give me intravenous antibiotics twice and then follow up with bioclavid. That killed the fever, but to this day I don't know what caused it.

A few days later, I had a previously scheduled consultation with Dr. Lars Kjeldsen, and I told him about the event. He then told me and my wife, that one can die from these chills, and if it happens again, then call Rigshospitalet directly. Don't waste time with the medical emergency number.

Bumps Keep Coming on this Journey with MDS

In the fall of 2015, my wife noticed that my right eye was closing more and more. At the same time, I noticed that my night vision on the right was deteriorating, and in retrospect I should have gone to see an eye doctor. However, as other men I waited — until I had to take my mother, who is 93, to the eye doctor for a regular checkup. I got an acute appointment with the eye doctor on April 25th. Within two weeks I got an appointment at the eye clinic at the main hospital in Copenhagen. On May 11th I went there for a preliminary check-up, and after a 45 minute very careful check-up the eye doctor concluded, that whatever was pressing my right eye forward by about 6 millimeter could be related to my MDS. Then I was turned over to the hematologists, who quickly concluded, that in order to find out more about the thing behind my eye I needed an MRI-scan, so while my wife was enjoying the last day of her walk around Montenegro, I found myself to be a patient at the MDS Center of Excellence in Copenhagen. Within two hours my head was subjected to an MRI-scan. Although that procedure does not hurt in anyway, it is very noisy and after it I felt my balance was a bit messed up.

Although it was not said directly, it was quite clear to me that the doctors had a suspicion that my MDS had suddenly moved along and developed into AML or something of that nature. So I had a PET-CT scan to see if things had spread, and a triple bone-marrow biopsy with the

purpose of getting an update state of the bone-marrow, a sample next-gene sequencing and a sample that allowed the doctors to — if needed — treat me under a new protocol. After the Pentecost holiday — in Denmark, hospitals close for holidays—an eye biopsy was performed. During this appointment, the eye doctor removed as much material as possible from behind my eye. The risk here was that one could damage the main vision nerve connecting the eye with the brain, i.e., I could lose my sight in the right eye. Luckily this did not happen, and enough material was removed to allow my right peripheral vision to improve.

The initial pathological test on the sample from behind my eye did not show any lymphatic or leukemic development, so I was sent home to wait for the final analysis results. Finally on the afternoon of May 23rd, exactly four weeks after my initial examination by a local eye doctor, my hematologist recorded the following message on my answering service: "Niels, I have good news for you!" I phoned her back, and she told me that the pathologists had found nothing lymphatic or leukemic in the sample from behind my eye. My whole family and I could relax again. My wife and I celebrated the good news with a lunch in Tivoli the following day.

During the next four weeks, I think I talked with 4–5 eye doctors and 6–8 hematologists. All along, I felt as if there was a team behind the person relaying any information to me and that gave me a very comfortable feeling.

The Joys of Living with MDS

Living with MDS is not always a bed of roses. You regularly have to tell people that you walk with to slow down. It can be annoying, but something you easily get used to. The biggest joy are the MDS patients and professionals I have met internationally in connection with the MDS Life Beyond Limits campaign, at Celgene's Partners for Progress events, at Novartis Oncology meetings around Europe, and

last but not least the people behind the MDS Foundation. Participation in these international events has brought both learning and friendships.

Friendship like that of the late Kirby Stone, who after I met him in San Diego in connection with the MDS Life Beyond Limits Gala Photo Exhibition during the American Society of Hematology (ASH) Annual Congress held in 2011, shared a spreadsheet with his complete MDS-related medical data with me. Or the Belgian gentleman, who I met in Edinburgh and who later created an MDS Patient Support Group in Belgium. He said, "The decision to have a bone marrow transplant was easy. My doctor told me that if I did not have transplant then the chance that he would see me in six months' time was less than 5%". Statistics show that 30%–40% of MDS patients who get a bone marrow transplant are cured. Or Bergit Kühle, whom I also first met in San Diego, and then some years later in Berlin. She said, "When you get blood it should depend on how you feel, not on some arbitrary blood count measurement". Or the late Robert Weinberg, whom I also met in San Diego, and who lived with MDS for many years without his colleagues knowing it.

The pictures around this story are all taken by Ed Kashi during the *MDS Life Beyond Limits* photo campaign in the fall of 2011. It was fun to work with him during one and a half days of shooting photos of me and my family in and around Slangerup. Some of them were exhibited at ASH in San Diego, December 2011.

Soon Anna and I can celebrate our 34th anniversary with all of our four children — two boys and two girls — having finished their formal education and going on to new adventures around the world. You always hope for the best for your children. And I am happy to have shared many joyful moments with them over the past more than 10 years of living with MDS, especially during Christmas when they have all returned home.

I could go on to mention many more professionals I have met during the last 10 years, but I will stop here, and just finish with the words of the late Kirby Stone: "Living with MDS is about making every second count!"

PS: MDS does not consume my whole life. To mention some non-MDS activities, I am also active with photography and with new developments in functional modelling to improve plant operations and design.

UPDATE: *In our next newsletter, look for Niel's journey in creating MDS DK Patientstøttegruppe. As of the date of this publication, MDS DK Patientstøttegruppe has joined Lyle Patientforeningen for Lymfekræft og Leukæmi. The Danish MDS Support Group will continue under the umbrella of Lyle and will continue to arrange events directed towards MDS patients and their relatives. For the time being, the Danish language website will continue: http://dkpsg.mds-and-you.info Email niels.jensen@mds-and-you.info.*

Living With MDS...

Ryan Szanto
Ocala, Florida

I am 78 years old and have been an MDS patient for 19 years. My desire is to convey to you my experiences with MDS. I also hope my longevity with MDS will give you hope and encouragement.

During a routine wellness check, I was diagnosed with anemia in July, 1996. I was a very active, outdoor person and did not feel there was anything wrong with me, so I did nothing about it. The next year during another routine wellness check, the doctor wrote in red pen and circled: significant anemia. He recommended I see my primary care doctor. I saw her in August 1997, and had blood tests run over a five week period. I was told that they did not know what was wrong with me and recommended I see a hematologist/oncologist, which I did.

A bone marrow biopsy was performed and it was determined that my anemia was due to MDS. I saw this doctor once a week for a CBC (blood test) and Procrit® shots. During the next five years and 9 months, Procrit increased gradually from 30,000 to 80,000 units to keep my hemoglobin at a healthy level. In December 2005, I was switched from Procrit to bi-weekly Aranesp® injections. This was a blessing. The Aranesp dosage started at 300 mcg for 28 injections and now continues at 400 mcg. I have had a total of 238 injections as of April 2016.

In June 2001, I had my first blood transfusion of 2 units. As of April 2016, I have had 473 units of blood. By June 2004, I had iron overload. My ferritin level was 2,090. I started iron chelation with a drug called Desferal®, which is dispensed with an infusion pump into the stomach 12 hours a day, 5 days a week. I continued this treatment for 18 months.

In the fall of 2005, the MDS Foundation notified me that there was a new oral drug for iron overload called Exjade®. It was up for FDA approval in Washington, DC and I

was asked to testify as to why the drug should be approved. I was thrilled to go. It would be wonderful to get off that pump! I went with 14 other patients who also had iron overload as a result of chronic transfusions for MDS, Sickle Cell Anemia, and Thalassemia. Thankfully, it was approved. I started taking Exjade 1500 mg daily in January 2006. Hurray, this was another blessing! Every morning I dissolved the Exjade tablets in water and drank it.

In July 2015, I was informed of another new drug for iron overload called Jadenu®, which is a pill to swallow!!! Even Better than Exjade!!! In August, I started on 90 mg of Jadenu and I am currently taking 360 mg daily.

I took part in a drug trial at Moffitt Cancer Center in Tampa, Florida for Revlimid® in 2005, but unfortunately it did not help my MDS. I am not sorry I took part in the trial because it might benefit other patients later on by using my bone marrow for research.

During my first three years, I could not find any non-MDS specialists who knew anything about the disease. There also was not much research on this disease. The first research done was for high-risk MDS. I am classified as low-risk MDS, Refractory Anemia with Ringed Sideroblasts (RARS). Much research is now being done for all MDS types.

When I was first diagnosed, I was in denial for about 18 months. My family and I started researching MDS and I started talking with my doctor about my options. I realized my body was the temple of the Lord and I had a responsibility to take care of it. That is when my denial shifted to a positive attitude and I accepted my situation with God's help. I joined the MDS Foundation and through their Patient and Family Forums, a quarterly publication, and their website, I have learned so much about the disease. Doctors and Nurses attend the Forums and inform us of the latest information.

I have done several videos for the drug company who makes the iron chelation drugs I've been on. This involvement

caused me to realize how much I appreciate what is taking place to find better ways to deal with iron overload.

I took part in an MDS National Registry for 5 years that collected data on MDS patients to determine the differences and similarities in patients. What works and doesn't work.

Besides learning all that I can and getting involved, I have used my faith to pray for and encourage other patients. I ask God to put in my path anyone He wants me to talk with, pray for, or encourage every week when I go to the Oncology Center. I believe this involvement is what is keeping me going. My positive attitude and faith has been strengthened every day.

My wife and I are family-oriented. We attend all local family birthday parties, and go to gymnastic practices and competitions, T-Ball, baseball, volleyball, and soccer games, cheerleading, and homecoming events for our grandchildren. We cheer them on to let them know we are there for them and very proud of them. We also have the pleasure of having some of the local grandchildren spend the night with us. We take them to the skating rink,

Stay positive, be motivated, and get involved, especially by attending Patient and Caregiver Forums.

bowling, and to the park. I will admit there are times I do not feel my best, but I push myself to go to be a part of their lives.

To summarize, I would say have a good support system whether it be family, friends or church family and learn all that you can about MDS. One way is to join the MDS Foundation and go to their website to stay updated on the latest research. Stay positive, be motivated, and get involved especially by attending their Patient and Caregiver Forums. Ask questions of your doctors and nurses, and most of all, keep God as your pilot. Yes, it is true I have not been physically healed, but God has healed me spiritually and my spirit is what will live on for eternity.

May God Bless you now and forever.

DONATION

Hand-Made Mermaid Blanket to Benefit the MDS Foundation

MDS patient Ryan Szanto's wife, Gloria Szanto, has crocheted this beautiful mermaid blanket! She is offering to auction it off as a donation to the MDS Foundation!

If you are interested in purchasing this blanket with 100% of the proceeds being donated to the MDSF, please email ahassan@mds-foundation.org

MDS CENTERS OF EXCELLENCE

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

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

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

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

The following centers have qualified as MDS Centers of Excellence:

UNITED STATES

ARIZONA

Mayo Clinic Hospital
Scottsdale, Arizona
Raoul Tibes, MD, PhD
Lisa Sproat, MD

The University of Arizona Cancer Center
Tucson, Arizona
Ravi Krishnadasan, MD, FACP

CALIFORNIA

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

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

Moores Cancer Center at the University of California, San Diego
Rafael Bejar, MD, PhD
Peter Curtin, MD

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

UCLA Center for Health Sciences
Los Angeles, California
Gary J. Schiller, MD

University of Southern California Keck School of Medicine
Los Angeles, California
Casey L. O'Connell, MD

COLORADO

University of Colorado School of Medicine
University of Colorado Cancer Center
Aurora, Colorado
Daniel Aaron Pollyea, MD, MS

CONNECTICUT

Yale Cancer Center/ Smilow Cancer Hospital
Yale Univesity School of Medicine
New Haven, Connecticut
Steven D. Gore, MD

FLORIDA

All Children's Hospital
St. Petersburg, Florida
Gregory Hale, MD

Mayo Clinic
Jacksonville, Florida
James M. Foran, MD

Moffitt Cancer Center
Tampa, Florida
Alan F. List, MD

Sylvester Comprehensive Cancer Center
University of Miami
Miller School of Medicine
Miami, Florida
Stephen D. Nimer, MD

University of Florida Shands Hospital
Gainesville, Florida
Christopher R. Cogle, MD

GEORGIA

Emory Winship Cancer Institute
Emory University School of Medicine
Atlanta, Georgia
Amelia Langston, MD

The Blood and Marrow Transplant Program at Northside Hospital
Atlanta, Georgia
Asad Bashey, MD

ILLINOIS

Loyola University Chicago Cardinal Bernardin Cancer Center
Maywood, Illinois
Scott E. Smith, MD, PhD

Robert H. Lurie Comprehensive Cancer Center of Northwestern University
Feinberg School of Medicine
Chicago, Illinois
Olga Frankfurt, MD

Rush University Medical Center
Chicago, Illinois
Jamile Shammo, MD

University of Chicago Medical Center
Chicago, Illinois
Richard A. Larson, MD

INDIANA

Indiana University Simon Cancer Center
Indianapolis, Indiana
Larry Cripe, MD/Hamid Sayar, MD, MS

IOWA

The University of Iowa Hospitals and Clinics, Holden Cancer Center
Iowa City, Iowa
Carlos E. Vigil-Gonzales, MD

MARYLAND

Johns Hopkins University School of Medicine
Baltimore, Maryland
Amy Elizabeth DeZern, MD

University of Maryland Greenebaum Cancer Center
Baltimore, Maryland
Maria R. Baer, MD

MASSACHUSETTS

Dana-Farber Cancer Institute
Boston, Massachusetts
Richard M. Stone, MD/David P. Steensma, MD/Benjamin Ebert, MD, PhD

Massachusetts General Hospital Cancer Center
Boston, Massachusetts
Timothy Graubert, MD

Tufts University School of Medicine
Tufts Medical Center
Boston, Massachusetts
Kellie Sprague, MD

MICHIGAN

Barbara Ann Karmanos Cancer Institute, Wayne State University
Detroit, Michigan
Charles A. Schiffer, MD

William Beaumont Hospital Cancer Center
Royal Oak, Michigan
Ishmael Jaiyesimi, DO

MINNESOTA

Mayo Clinic
Rochester, Minnesota
Mark R. Litzow, MD

University of Minnesota Medical Center, Fairview University of Minnesota Medical School
Minneapolis, Minnesota
Erica D. Warlick, MD

MISSOURI

Washington University School of Medicine
Siteman Cancer Center
St. Louis, Missouri
John F. DiPersio, MD, PhD

NEBRASKA

University of Nebraska Medical Center
Omaha, Nebraska
Lori Maness, MD

NEW HAMPSHIRE

Dartmouth-Hitchcock Medical Center and Norris Cotton Cancer Center
Lebanon, New Hampshire
Kenneth R. Meehan, MD

NEW JERSEY

The Cancer Center of Hackensack University Medical Center
Hackensack, New Jersey
Stuart Goldberg, MD

NEW YORK

Albert Einstein Cancer Center/Albert Einstein College of Medicine of Yeshiva University
Bronx, New York
Amit Verma, MD

Columbia University Medical Center
New York, New York
Azra Raza, MD

Memorial Sloan-Kettering Cancer Center
New York, New York
Virginia M. Klimek, MD

Monter Cancer Center/NSLIJ Cancer Institute
Lake Success, New York
Steven L. Allen, MD

Icahn School of Medicine at Mount Sinai
New York, New York
Lewis R. Silverman, MD

New York Medical College/ Westchester Medical Center
Zalmen A. Arlin Cancer Center
Valhalla, New York
Karen Seiter, MD

Roswell Park Cancer Center
Buffalo, New York
Elizabeth Griffiths, MD/James E. Thompson, MD

University of Rochester Medical Center
Rochester, New York
Jane L. Liesveld, MD

Weill Medical College of Cornell University
New York Presbyterian Hospital
New York, New York
Gail J. Roboz, MD

NORTH CAROLINA

Duke University Medical Center
Durham, North Carolina
Carlos M. deCastro, MD

Wake Forest University School of Medicine
Comprehensive Cancer Center
Winston-Salem, North Carolina
Bayard L. Powell, MD

OHIO

Cleveland Clinic Foundation
Taussig Cancer Center
Cleveland, Ohio
Jaroslaw Maciejewski, MD, PhD
Mikkael Sekeres, MD, MS

The Ohio State Comprehensive Cancer Center, James Cancer Hospital and Solove Research Institute
Columbus, Ohio
Alison R. Walker, MD

PENNSYLVANIA

Allegheny Health Network Cancer Institute Western Pennsylvania Hospital
Pittsburgh, Pennsylvania
Salman Fazal, MD

Fox Chase Cancer Center
Philadelphia, Pennsylvania
Patricia Kropf, MD

University of Pennsylvania Cancer Center
Philadelphia, Pennsylvania
Selina Luger, MD

UPMC Cancer Center
Pittsburgh, Pennsylvania
Anastasios Raptis, MD/James M. Rossetti, DO

TENNESSEE

Vanderbilt University Medical Center
Nashville, Tennessee
Sanjay Mohan, MD/Michael R. Savona, MD

TEXAS

Cancer Care Centers of South Texas
San Antonio, Texas
Roger Lyons, MD

Texas Oncology, Midtown
Austin, Texas
Richard Helmer, III, MD

University of Texas MD Anderson Cancer Center
Houston, Texas
Guillermo Garcia-Manero, MD/Hagop Kantarjian, MD

University of Texas Southwestern Medical Center
Dallas, Texas
Robert H. Collins, Jr., MD, FACP

WASHINGTON

Fred Hutchinson Cancer Research Center
University of Washington
Seattle Cancer Care Alliance
Seattle, Washington
Joachim Deeg, MD/Elihu Estey, MD

WASHINGTON, DC

Georgetown University Hospital
Lombardi Comprehensive Cancer Center
Washington, D.C.
Catherine Broome, MD

George Washington University
VA Medical Center
Washington, D.C.
Charles S. Hesdorffer, MD

WISCONSIN

American Family Children's Hospital
University of Wisconsin Health
Madison, Wisconsin
Inga Hofmann, MD

Medical College of Wisconsin
Bone Marrow Transplant Program
Milwaukee, Wisconsin
Parameswaran Hari, MD

University of Wisconsin
Madison Medical School
Madison, Wisconsin
Mark B. Juckett, MD

OUTSIDE THE UNITED STATES

ARGENTINA

Sanatorio Sagrado del Corazón
Buenos Aires, Argentina
Marcelo Iastrebner, MD

ARMENIA

Muratsan University Hospital
Complex of Yerevan
State Medical University
Yerevan, Armenia
Gevorg Tamamyan, MD

AUSTRALIA

Peter MacCallum Cancer Institute
University of Melbourne
East Melbourne, Australia
John F. Seymour, MD

The Royal Melbourne Hospital
Parkville Victoria, Australia
David Ritchie, MD

University of Tasmania
Royal Hobart Hospital
Hobart, Tasmania, Australia

AUSTRIA

Hanusch Hospital
Medical University of Vienna
Vienna, Austria
Michael Pfeilstöcker, MD

Medical University of Vienna
Vienna, Austria
Peter Valent, MD

University Hospital of Innsbruck
Innsbruck, Austria
Reinhard Stauder, MD

BELGIUM

AZ Sint-Jan AV
Brugge, Belgium
Dominik Selleslag, MD

University Hospital Leuven
Leuven, Belgium
Marielle Beckers, MD, PhD
Michel Delforge, MD, PhD

BRAZIL

AC Camargo Hospital – Cancer Center
São Paulo, Brazil
Luiz Fernando Lopes, MD, PhD

Hospital das clínicas da Faculdade de Medicina da Universidade de São Paulo
São Paulo, Brazil
Elvira D. Rodrigues Pereira Velloso, MD, PhD

Universidade Federal de Ceará
Ceará, Brazil
Silvia Maria M. Magalhães, MD, PhD

Universidade Federal de São Paulo
São Paulo, Brazil
Maria de Lourdes Chauffaille, MD, PhD

CANADA

Princess Margaret Hospital
Toronto, Ontario, Canada
Karen Yee, MD

Toronto Sunnybrook Regional Cancer Centre
Toronto, Ontario, Canada
Richard A. Wells, MD

University of Toronto
Hospital for Sick Children
Toronto, Ontario, Canada
Yigal Dror, MD

CHINA

Guangdong General Hospital & Guangdong Academy of Medical Sciences
Guangzhou, China
Xin Du, MD, PhD

Institute of Hematology and Blood Diseases Hospital
Chinese Academy of Medical Sciences
Tianjin, China
Zhijian Xiao, MD

The First Affiliated Hospital of Soochow University
Jiangsu Institute of Hematology
Jiangsu Province, China
Suning Chen, MD, PhD

The Sixth Hospital Affliated to Shanghai Jiaotong University
Shanghai, China
Xiao Li, MD, PhD

CZECH REPUBLIC

Institute of Hematology & Blood Transfusion
Prague, Czech Republic
Jaroslav Cermák, MD, PhD

DENMARK

Odense University Hospital
The University of Southern Denmark
Odense, Denmark
Gitte Birk Kerndrup, MD

Rigshospitalet National University Hospital
Copenhagen, Denmark
Kirsten Grønbaek, MD
Lars Kjeldsen, MD, PhD

FRANCE

Centre Henri Becquerel
Rouen University School of Medicine
Rouen, France
Aspasia Stamatoullas, MD

Centre Hospitalier Universitaire (CHU) de Angers Service des Maladies du Sang
Angers, France
Norbert Ifrah, MD

Centre Hospitalier Universitaire (CHU) de Grenoble
Grenoble, France
Jean-Yves Cahn, MD

Centre Hospitalier Universitaire (CHU) de Limoges Hôpital Dupuytren
Limoges, France
Dominique Bordessoule, MD

Centre Hospitalier Universitaire (CHU) de Nancy
Nancy, France
Agnés Guerci-Bresler, MD, PhD

Centre Hospitalier Universitaire (CHU) de Tours – Bretonneau
Tours, France
Emmanuel Gyan, MD, PhD

Hôpital Avicenne/
University Paris XIII
Bobigny, France
Charikleia Kelaidi, MD

Hôpital Cochin/
University Paris V
Paris, France
Francois Dreyfus, MD

Hôpital Saint Louis/
University Paris VII
Paris, France
Pierre Fenaux, MD, PhD
Christine Chomienne, MD, PhD

Hôpital Saint-Vincent de Paul (Lille)
Lille, France
Christian Rose, MD

Institut Paoli-Calmettes
Marseille, France
Norbert Vey, MD

Service des Maladies du Sang
Hôpital Claude Huriez
Lille, France
Bruno Quesnel, MD

GERMANY

Georg-August-Universität Göttingen
Göttingen, Germany
Detlef Haase, MD, PhD

Hannover Medical School
Medizinische Hochschule Hannover
Hannover, Germany
Arnold Ganser, MD

Heinrich-Heine Universität Düsseldorf
University Hospital
Düsseldorf, Germany
Ulrich Germing, MD

Johann Wolfgang Goethe Universität
Frankfurt Main, Germany
Gesine Bug, MD

Klinikum Rechts der Isar
Technical University of Munich
Munich, Germany
Katharina Götze, MD

MLL Münchner Leukämielabor
Munich, Germany
Torsten Haferlach, MD

Rems-Murr-Klinik Winnenden
Winnenden, Germany
Stefani Parmentier, MD

St. Johannes Hospital
Heinrich-Heine Universität
Duisburg, Germany
Carlo Aul, MD, PhD
Aristotle Giagounidis, MD, PhD

University of Heidelberg
Medical Center
St. Lukas Klinik Solingen
Solingen, Germany
Ulrich Mahlknecht, MD, PhD

Albert-Ludwigs-Universität Freiburg
Freiburg, Germany
Michael Lübbert, MD, PhD

Universität Hamburg
Hamburg, Germany
Nicolaus Kröger, MD, PhD

Universitätsklinikum Carl Gustav Carus
Dresden, Germany
Uwe Platzbecker, MD

University Children's Hospital
Freiburg, Germany
Charlotte Niemeyer, MD

University of Cologne
Cologne, Germany
Karl-Anton Kreuzer, MD

University Hospital Mannheim
Mannheim, Germany
Wolf-Karsten Hofmann, MD

GREECE

Patras University Hospital
Patras, Greece
Argiris Symeonidis, MD

University of Athens Laikon Hospital
Athens, Greece
Nora Viniou, MD

University General Hospital Attikon
Athens, Greece
Vassiliki Pappa, MD

HUNGARY

Semmelweis University School of Medicine
Budapest, Hungary
Judit Várkonyi, MD, PhD

INDIA

Tata Medical Centre
Kolkata, India
Col (Dr.) Deepak Kumar Mishra, MD

Tata Memorial Hospital
Mumbai, India
Purvish Parikh, MD

IRELAND

Adelaide and Meath Hospital
Dublin, Ireland
Helen Enright, MD

ISRAEL

Tel-Aviv Sourasky Medical Center
Tel-Aviv, Israel
Moshe Mittelman, MD

Chaim Sheba Medical Center
Tel Hashomer, Israel
Drorit Grizim Merkel, MD

ITALY

Cancer Center – IRCCS Humanitas Research Hospital
Milan, Italy
Matteo G. Della Porta, MD

Centro di Riferimento Oncologico di Basilicata (CROB)
Rionero in Vulture (PZ), Italy
Pellegrino Musto, MD

Istituto di Ematologia Universita' Cattolica Sacro Cuore
Rome, Italy
Giuseppe Leone, MD

Policlinico Tor Vergata
Rome, Italy
Sergio Amadori, MD
Maria Teresa Voso, MD

S. Eugenio Hospital Tor Vergata University
Rome, Italy
Paolo de Fabritiis, MD
Pasquale Niscola, MD

University of Florence Azienda OSP Careggi
Florence, Italy
Valeria Santini, MD

University of Pavia School of Medicine Fondazione IRCCS Policlinico San Matteo
Pavia, Italy
Mario Cazzola, MD

JAPAN

Kyoto University Hospital
Kyoto, Japan
Akifumi Takaori, MD

Metropolitan Research Center for Blood Disorders Shin-Yurigaoka General Hospital
Kanagawa, Japan
Kiyoyuki Ogata, MD, FACP

Nagasaki University Hospital School of Medicine Atomic Bomb Disease Institute
Nagasaki City, Japan
Yasushi Miyazaki, MD

Saitama International Medical Center Saitama Medical University
Hidaka, Saitama, Japan
Akira Matsuda, MD

Tokyo Medical College
Tokyo, Japan
Kazuma Ohyashiki, MD, PhD

KOREA

Catholic Blood and Marrow Transplantation Center The Catholic University of Korea
Seoul, Korea
Yoo-Jin Kim, MD

Seoul National University Hospital Seoul National University College of Medicine
Seoul, Korea
Dong Soon Lee, MD, PhD

Yonsei Cancer Cetnre, Severance Hospital Yonsei University College of Medicine
Seoul, Korea
June-Won Cheong, MD, PhD

THE NETHERLANDS

Radboud University Nijmegen Medical Center
Nijmegen, The Netherlands
Saskia M.C. Langemeijer, MD

Vrije Universiteit Medical Center
Amsterdam, The Netherlands
Arjan A. van de Loosdrecht, MD, PhD

POLAND

Jagiellonian University Collegium Medicum
Kraków, Poland
Aleksander Skotnicki, MD, PhD

PORTUGAL

Hospital de Santa Maria
Lisbon, Portugal
Joao F. Lacerda, MD

SAUDI ARABIA

King Faisal Specialist Hospital & Research Centre
Riyadh, Saudi Arabia
Amr Hanbali, MD

King Khaled University Hospital King Saud University
Riyadh, Saudi Arabia
Ak Almomen, MD

SINGAPORE

Singapore General Hospital
Singapore
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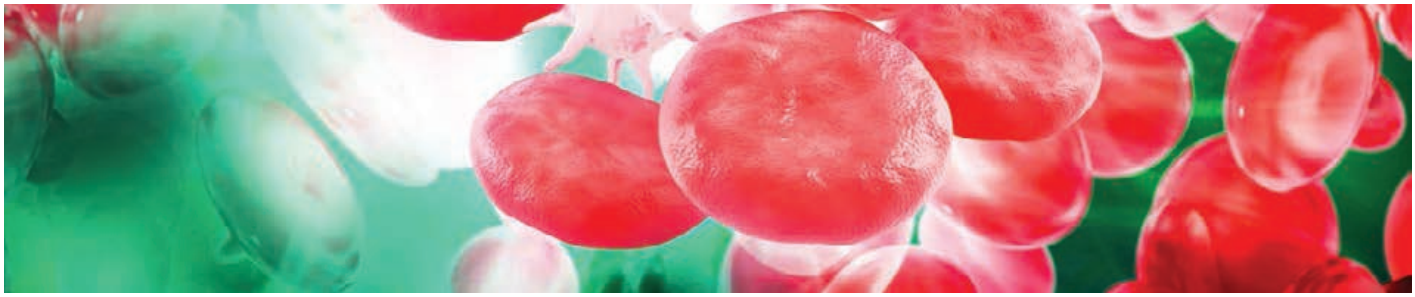

NEW CLINICAL STUDY IN MDS

PEVONEDISTAT-2001

A Phase 2, Randomized, Controlled, Open-Label, Clinical Study of the Efficacy and Safety of Pevonedistat Plus Azacitidine Versus Single-Agent Azacitidine in Patients with Higher-Risk Myelodysplastic Syndromes (MDS), Chronic Myelomonocytic Leukemia (CMML), and Low-Blast Acute Myelogenous Leukemia (AML).

Takeda Pharmaceuticals International Co. is currently enrolling patients for a Phase 2 clinical trial of 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 survival, event-free survival and response to treatment in people who take pevonedistat and azacitidine when compared to people who take single-agent azacitidine.

The study will enroll approximately 117 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 cycle:

- Pevonedistat 20 mg/m^2 and azacitidine 75 mg/m^2 combination
- Single-agent azacitidine 75 mg/m^2

All participants will receive azacitidine via the intravenous or subcutaneous route. Participants randomized to the combination arm will also 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 based on the Revised International Prognostic Scoring System (IPSS-R), a standard prognostic tool, or have CMML
- 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 (NCT02610777)

Contact: 1-877-674-3784; globaloncologymedinfo@takeda.com

Pevonedistat 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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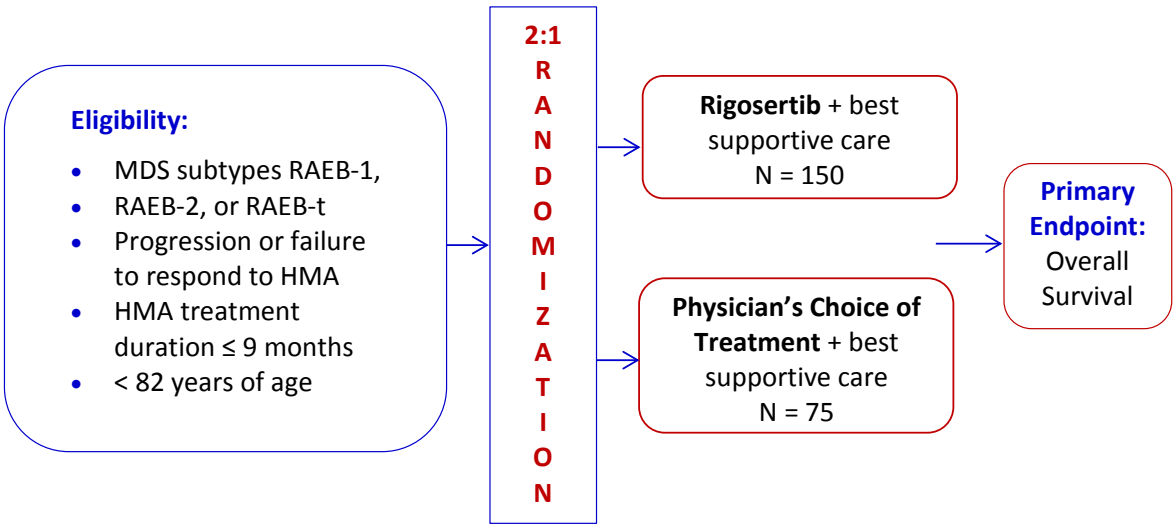
For MDS Patients

After HMA failure

INSPIRE
Phase 3 Trial

INternational Study of Phase III Intravenous RigosErtib

A Phase III, International, Randomized, Controlled Study of Rigosertib versus Physician's Choice of Treatment in Patients with Myelodysplastic Syndrome after Failure of a Hypomethylating Agent



Primary Endpoint: Overall survival

- in the intention-to-treat population, or
- in the subgroup with very high risk per the Revised International Prognosis Scoring System (VHR-IPSS-R)

International Trial:

- More than 100 trial sites

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

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

Rigosertib prior clinical data: Garcia-Manero G, et al. Lancet Oncology. 2016;17(4):496-508.

Rigosertib mechanism of action: Athuluri-Divakar et al., Cell. 2016;165,643–655

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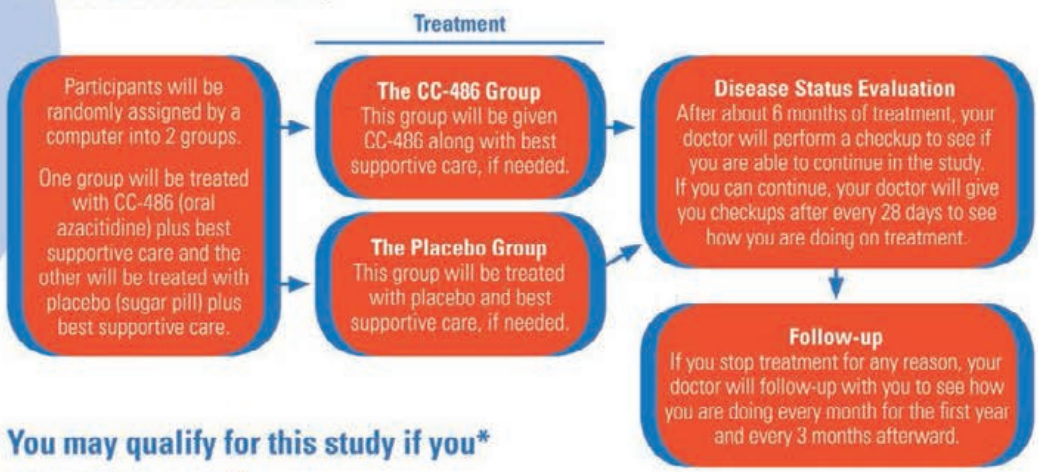
QUAZAR Lower-Risk MDS is a study for people with MDS who need blood transfusions due to low red blood cell counts (called anemia) and low platelet counts (called thrombocytopenia).

The QUAZAR MDS Study



You may qualify for this study if you*

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- Have been diagnosed with MDS
- Have low red blood cell counts and are dependent on blood transfusions
- Have low blood platelet counts

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NEW CLINICAL STUDY: IMerge Lower-Risk MDS

Current Status: Part 1 recruitment complete; Part 2 is not yet open for recruitment. For additional details, refer to the Geron press release (12Sep2016) at **http://ir.geron.com/phoenix.zhtml?c=67323&p=irol-newsArticle&ID=2201055.**

Janssen Research & Development, LLC is conducting a Phase 2/3 clinical study referred to as "IMerge", with the study drug Imetelstat, which is a first-in-class telomerase inhibitor. With its novel mechanism of action, Imetelstat may provide clinical benefit to MDS patients. In this study, Imetelstat is administered as a 2-hour intravenous infusion every 28 days.

IMerge is a study for people with MDS who need blood transfusions due to anemia (low red blood cell counts). People with low or intermediate-1 risk MDS that has relapsed or is refractory to Erythropoiesis-Stimulating Agents (ESAs) treatment are enrolled in the study. This study is being conducted at multiple hospitals and institutions around the world, in approximately 80 sites globally.

For more information about this clinical study, please visit

www.clinicaltrials.gov (NCT02598661)