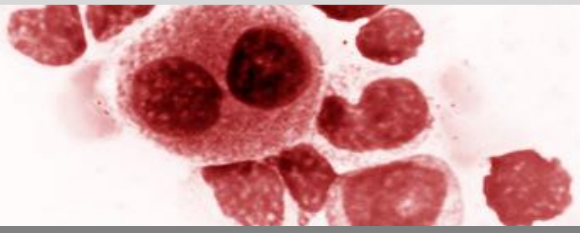
MDS Newsletter

Issue # 04
December 2014



Motivation und Mission

The goal of the MDS Newsletter is to promote new knowledge and to support the exchange of information in the clinical research, diagnostics and therapy of myelodysplastic syndromes (MDS).

The newsletter is particularly directed towards clinicians, scientists and industry developers of therapies for MDS.

Your MDS Newsletter team

Implementation of Flow Cytometry in the Diagnosis of Myelodysplastic Syndromes and its additive Value for Prognosis

Although cytomorphology is the mainstay in the diagnosis of myelodysplastic syndromes (MDS) it may be ambiguous, especially in cases with low blast counts and mild dysplastic features. In particular, in cytopenic patients with normal or inconclusive morphology and normal cytogenetics, additional diagnostic markers are necessary. Flow cytometry (FC) can play a key role.[29,30] Flow cytometry has been introduced as an important co-criterion in the diagnosis of MDS. Moreover, it has been recommended recently as a tool in the diagnostic work-up of MDS if performed according to the guidelines as defined by the International and European LeukemiaNet (ELNet) Working Party on Standardization of FC in MDS (IMDSFlow)[1-4,30]. ELNet reports describe recommendations on implementation of FC (i.e. technical issues as sample preparation, instrument set-up and quality assessment, acquisition of data and gating strategy); IMDSFlow also proposes minimal FC? criteria for the diagnosis and prognostic evaluation of MDS and other cytopenias.[2,3]

Analysis of bone marrow cells by FC can identify specific aberrations in both immature and maturing compartments among different hematopoietic lineages. Since, MDS comprises a heterogeneous group of myeloid neoplasms, it is unlikely that a single specific marker can discriminate MDS from other cytopenias. Hence, the presence of multiple aberrancies has a higher predictive value for MDS than single aberrancies.[5-8] In line with this, current WHO2008 recommendations recognize the presence of three or more FC aberrancies as indicative of MDS in at least two cell lineages.[9,30]

As demonstrated in a multicenter study on behalf of the ELNet, application of only four parameters enables to distinguish low-risk MDS without other specific markers (i.e. cytogenetics or ring sideroblasts) from non-clonal cytopenias.[10] The key parameters within this score are: i) an increase in CD34+ myeloid progenitor cells within bone marrow nucleated cells (≥2%); ii) a decreased percentage of progenitor B cells within the CD34+ compartment (≤5%); iii) a decrease or increase of CD45 expression level on myeloid progenitor cells as compared to lymphocytes as a reference (≤4 or ≥7.5) and iv) a decrease in SSC of neutrophils as compared to lymphocytes (≤6). The presence of two or more of these aberrancies identified 70% of low-risk MDS cases with a specificity of 93%.[10] Assessment of FC aberrancies of myeloid progenitor cells and the maturing myelomonocytic compartment can add valuable information.[5,11] Furthermore, FC analysis of erythroid dysplasia might provide supplementary information, particularly within low-risk MDS.[12-14] Few applications are available for FC analysis of the megakaryocytic lineage but no standardized approach is yet available.[15] The next paragraphs summarize current recommendations for FC analysis in MDS. Of note, evaluation of dysplasia by FC necessitates knowledge of expression levels in age-matched normal and appropriate pathological bone marrow controls.

Evaluation of dysplasia in the immature myeloid progenitor compartment

The immature cell compartment is very heterogeneous. Therefore, beyond the classic CD45dim/SSClow/intprofile, >>>

Disclaimer

Publisher / responsible according to §5 TMG:
GMIHO
Gesellschaft für Medizinische Innovation – Hämatologie und Onkologie mbH
Managing Director:
Claus-Peter Held

Address:
GMIHO mbH
Alte Jakobstraße 77,
10179 Berlin
Phone:
+49 351.25933-280
Fax:
+49 351.25933-289
Email: info@gmiho.de
https://www.gmiho.de

registered at Berlin-Charlottenburg District Court
(Amtsgericht)
HRB 101719 B

VAT-ID
DE 250223501

Editors:
Silke Gloaguen
Denise Lippmann

Layout:
Denise Lippmann

Photo credits:
Cover: © Prof. Dr. med. Uwe Platzbecker
Figure. 1:
© Arjan A. van de Loosdrecht, MD, PhD
Figure. 2-5:
© Michael Schmidt
Figure. 6: © Dr. med. Martin Wermke
Figure 7: © ECTU-Network

>>> antibody combinations such as CD45/CD34/CD117/HLA-DR and CD45/CD34/CD123/HLA-DR are instrumental to identify myeloid progenitor cells (CD45dim and SSClow/int) among other populations that show overlapping CD45 and SSC features (e.g. B cell precursors, plasma cells, monoblasts, basophils, erythroblasts and plasmacytoid dendritic cell precursors).[2] Observed aberrancies in the immature myeloid compartment in MDS are an abnormal intensity or lack of expression of CD45, CD34, CD117, HLA-DR, CD13, CD33, asynchronous presence of CD11b, and/or the expression of lineage infidelity markers such as CD5, CD7 or CD56.[5,7,11,12,16-19]

Evaluation of dysplasia in the neutrophil compartment

Maturing neutrophils are identified by their $CD45^{int}SSC^{int\text{-}bright}$ profile. Other markers such as CD33, CD64, HLA-DR and CD11b are useful in distinguishing monocytes and hypogranular neutrophils. Neutrophils display diminished CD33 and CD64 expression, heterogeneous to bright CD11b and mostly lack HLA-DR as compared to CD33bright, HLA-DR+ and CD11b+ monocytes. One of the most frequently reported FC aberrancies in the maturing neutrophil compartment is a decreased SSC reflecting hypogranularity.[2] Next to decreased SSC, dysplastic neutrophils can display aberrant expression levels of certain antigens or an aberrant relationship among two or more antigens, e.g. aberrant relationships between CD13 and CD11b and/or CD13 and CD16 and between CD15 and CD10.[2,3]

Evaluation of dysplasia in the monocytic compartment

Morphological assessment of dysmonopoiesis in MDS is difficult unless there is marked monocytosis. By FC, monocytes can be defined based on their CD45 expression (intermediate-bright), SSC (intermediate) and additional markers such as HLA-DR, CD11b, CD64, CD36, CD33 and CD14. The use of CD14 alone may underestimate the percentage of monocytic cells particularly when immature forms are present. Aberrancies of interest in the monocytic lineage are an abnormal distribution of maturation stages, abnormal relationships of HLA-DR and CD11b, abnormal intensity of CD13 and overexpression of CD56. CD56 (and CD2) may even contribute to discriminate chronic myelomonocytic leukemia (CMML) from MDS/ myeloproliferative neoplasms.[20,21]

Evaluation of dysplasia in the erythroid compartment

The erythroid population can be defined by its dim to negative CD45 expression and low FSC and SSC properties. Commonly applied markers are CD45, CD71, CD235a, CD36, CD117, and CD105. One of the most frequently observed aberrancies (80% of low-risk MDS) is an increased number of erythroid progenitors associated with a larger proportion of immature erythroid cells (CD117+ or CD105+). Furthermore, abnormal relationship of CD71 vs. CD235a and/or decreased expression of CD36 is observed.[7,12-14,22] Currently, a large data set is under evaluation within IMDSFlow to further define the optimal parameters to identify dyserythropoiesis in MDS versus pathological controls.

Flow cytometry and prognosis of MDS

Thus far, the only validated prognostic FC score is the FC scoring system by Wells et al.[5,8,19,23] This flow score weighs the percentage of myeloid progenitor cells and their aberrancies and the amount of aberrancies in the maturing myelomonocytic compartment. A higher flow score is related to worse clinical outcome. In clinical practice, WHO classification, International Prognostic Scoring System (IPSS and IPSS-revised) and WHO-based Prognostic Scoring System (WPSS) are all well validated and applied routinely.[9,24-26] Interestingly, within these validated risk groups flow scores are rather heterogeneous. This implies that FC can identify patients with different prognosis within validated risk categories (see figure). Indeed, we recently confirmed that higher flow scores identify patients at higher risk within the current low IPSS and IPSS-R risk categories.[31] The impact on clinical decisions is not yet known but is focus of ongoing research.

Application of flow cytometry in predicting and monitoring treatment response

Flow cytometric analysis of MDS **>>>**

>>> bone marrow samples can identify subgroups in low and int-1 risk MDS with distinct clinical behaviour regarding transfusion dependency and progression to advanced disease.[19,31] Moreover, the absence of aberrant myeloid progenitors as assessed by FC in combination with low endogenous erythropoietin levels is predictive for response to growth factor treatment.[27] In addition, aberrant marker expression on myeloid progenitor cells identifies patients who may not benefit from treatment with hypomethylating agents such as azacitidine in intermediate-2 and high risk MDS.[28] Patient specific aberrant flow profiles can be applied in monitoring MDS during treatment. For instance, the specific flow signatures that is recognized within the specific cytogenetic subgroup of MDS with isolated del(5q). This flow signature facilitates monitoring MDS during treatment with lenalidomide.

Concluding remarks

Flow cytometric analysis is recommended as tool for diagnosis of MDS when performed according to the ELNet guidelines.[2,3]. Noteworthy, FC in MDS should only be applied as part of an integrated diagnostic approach. Results from FC analysis can add to identification of patients with better or even worse clinical course not predicted by current risk scoring models. Current investigations focus on the role of FC in monitoring the course of the disease in untreated (low risk) MDS patients and in the selection of patients who might benefit from new drugs in low and high risk MDS.

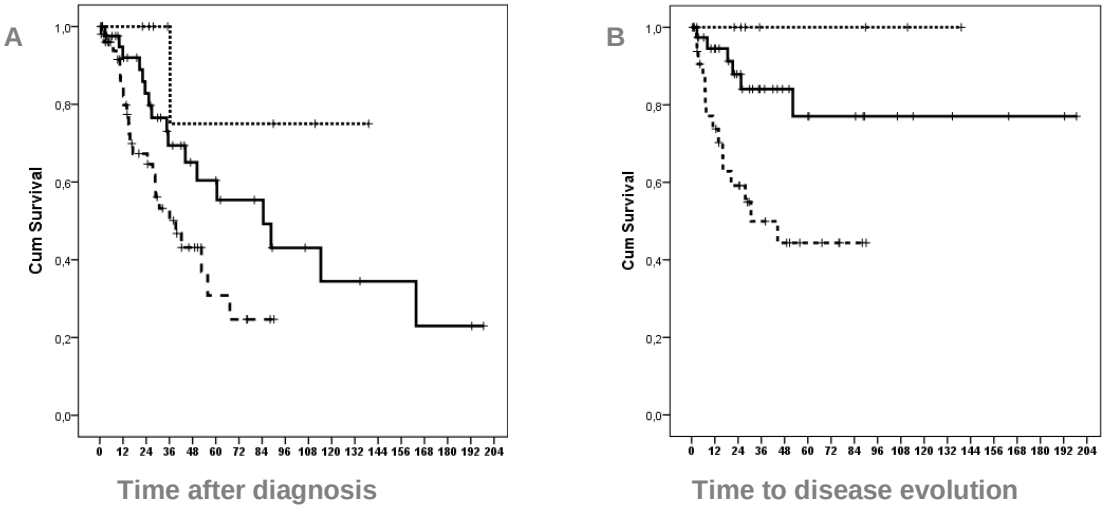


Figure 1: Overall survival and time to disease progression within the IPSS-R cytogenetic subgroup by FCSS. Overall survival (A)(n=104) and time to disease progression (B)(n=82) were significantly better in patients with flow scores of 0-1 points (dotted line) or 2-3 points (solid line), compared with patients with ≥4 points (broken line), p<0.001. (data depicted from: Alhan C, Westers TM, Cremers EM, Cali C, Witte BI, Ossenkoppele GJ, van de Loosdrecht AA. High flow cytometric scores identify adverse prognostic subgroups within the revised international prognostic scoring system for myelodysplastic syndromes. Br J Haematol. 2014 Oct;167(1):100-9 with minor modifications).

Acknowledgements

We would like to thank all participants of the IMDSFlow and Dutch MDS FC working groups for providing input in the development of the ELNet guidelines for the assessments of FC in MDS.

Authors: Arjan A. van de Loosdrecht, MD, PhD, Canan Alhan, MD, Eline Cremers, MD, Theresia M. Westers, PhD. Department of Hematology, Cancer Center Amsterdam, VU University Medical Center, Amsterdam, The Netherlands.

Article adapted from the MDS-Foundation Spring newsletter 2013; 19:issue 1.

All correspondence to: Arjan A. van de Loosdrecht, MD, PhD; Department of Hematology, Cancer Center Amsterdam, VU University Medical Center; De Boelelaan 1117; 1081 HV, Amsterdam; The Netherlands. Tel: +31-20-4442604; Fax: +31-20-4442601. E-mail: a.vandeloosdrecht@vumc.nl

References

(1) Valent P, Horny HP, Bennett JM, Fonatsch C, Germing U, Greenberg P, et al. Definitions and standards in the diagnosis and treatment of the myelodysplastic syndromes: Consensus statements and report from a working conference. Leuk Res 2007 Jun;31(6):727-36.

(2) van de Loosdrecht AA, Alhan C, Bene MC, Della Porta MG, Drager AM, Feuillard J, et al. Standardization of flow cytometry in myelodysplastic syndromes: report from the first European LeukemiaNet working conference on flow cytometry in myelodysplastic syndromes. Haematologica 2009 Aug;94(8):1124-34.

(3) Westers TM, Ireland R, Kern W, Alhan C, Balleisen JS, Bettelheim P, et al. Standardization of flow cytometry in myelodysplastic syndromes: a report from an international consortium and the European LeukemiaNet Working Group. Leukemia 2012 Jul;26(7):1730-41.

(4) Malcovati L, Bowen D, Cermak J, et al. Diagnosis and treatment of primary myelodysplastic syndromes in adults. Recommendations from the European Leukemia Net. Blood. 2013 Oct 24;122(17):2943-64. doi: 10.1182/blood-2013-03-492884.

(5) Wells DA, Benesch M, Loken MR, Vallejo C, Myerson D, Leisenring WM, et al. Myeloid and monocytic dyspoiesis as determined by flow cytometric scoring in myelodysplastic syndrome correlates with the IPSS and with outcome after hematopoietic stem cell transplantation. Blood 2003 Jul 1;102(1):394-403.

(6) Arroyo JL, Fernandez ME, Hernandez JM, Orfao A, San Miguel JF, Del Canizo MC. Impact of immunophenotype on prognosis of patients with myelodysplastic syndromes. Its value in patients without karyotypic abnormalities. Hematol J 2004;5(3):227-33.

(7) Malcovati L, Della Porta MG, Lunghi M, Pascutto C, Vanelli L, Travaglino E, et al. Flow cytometry evaluation of erythroid and myeloid dysplasia in patients with myelodysplastic syndrome. Leukemia 2005 May;19(5):776-83.

(8) Scott BL, Wells DA, Loken MR, Myerson D, Leisenring WM, Deeg HJ. Validation of a flow cytometric scoring system as a prognostic indicator for posttransplantation outcome in patients with myelodysplastic syndrome. Blood 2008 Oct 1;112(7):2681-6.

(9) Brunning R, Orazi A, Germing U, LeBeau MM, Porwit A, Baumann I, et al. Myelodysplastic syndromes/neoplasms. In: Swerdlow et al., editor. WHO classification of Tumours and Haematopoietic and Lymphoid Tissues.Lyon: IARC; 2008.

(10) Della Porta MG, Picone C, Pascutto C, Malcovati L, Tamura H, Handa H, et al. Multicenter validation of a reproducible flow cytometric score for the diagnosis of low-grade myelodysplastic syndromes: results of a European LeukemiaNET study. Haematologica 2012 Aug;97(8):1209-17.

(11) Tang G, Jorgensen JL, Zhou Y, Hu Y, Kersh M, Garcia-Manero G, et al. Multi-color CD34(+) progenitor-focused flow cytometric assay in evaluation of myelodysplastic syndromes in patients with post cancer therapy cytopenia. Leuk Res 2012 Aug;36(8):974-81.

(12) Stetler-Stevenson M, Arthur DC, Jabbour N, Xie XY, Molldrem J, Barrett AJ, et al. Diagnostic utility of flow cytometric immunophenotyping in myelodysplastic syndrome. Blood 2001 Aug 15;98(4):979-87.

(13) Della Porta MG, Malcovati L, Invernizzi R, Travaglino E, Pascutto C, Maffioli M, et al. Flow cytometry evaluation of erythroid dysplasia in patients with myelodysplastic syndrome. Leukemia 2006 Apr;20(4):549-55.

(14) Mathis S, Chapuis N, Debord C, Rouquette A, Radford-Weiss I, Park S, Dreyfus F, Lacombe C, Béné MC, Kosmider O, Fontenay M, Bardet V. Flow cytometric detection of dyserythropoiesis: a sensitive and powerful diagnostic tool for myelodysplastic syndromes. Leukemia. 2013 Oct;27(10):1981-7.

(15) Sandes AF, Yamamoto M, Matarraz S, Chauffaille ML, Quijano S, Lopez A, et al. Altered immunophenotypic features of peripheral blood platelets in myelodysplastic syndromes. Haematologica 2012 Jun;97(6):895-902.

(16) Ogata K, Nakamura K, Yokose N, Tamura H, Tachibana M, Taniguchi O, et al. Clinical significance of phenotypic features of blasts in patients with myelodysplastic syndrome. Blood 2002 Dec 1;100(12):3887-96.

(17) Stachurski D, Smith BR, Pozdnyakova O, Andersen M, Xiao Z, Raza A, et al. Flow cytometric analysis of myelomonocytic cells by a pattern recognition approach is sensitive and specific in diagnosing myelodysplastic syndrome and related marrow diseases: emphasis on a global evaluation and recognition of diagnostic pitfalls. Leuk Res 2008 Feb;32(2):215-24.

(18) Matarraz S, Lopez A, Barrena S, Fernandez C, Jensen E, Flores J, et al. The immunophenotype of different immature, myeloid and B-cell lineage-committed CD34+ hematopoietic cells allows discrimination between normal/reactive and myelodysplastic syndrome precursors. Leukemia 2008 Jun;22(6):1175-83.

(19) van de Loosdrecht AA, Westers TM, Westra AH, Drager AM, van der Velden VHJ, Ossenkoppele GJ. Identification of distinct prognostic subgroups in low- and intermediate-1-risk myelodysplastic syndromes by flow cytometry. Blood 2008 Feb 1;111(3):1067-77.

(20) Xu Y, McKenna RW, Karandikar NJ, Pildain AJ, Kroft SH. Flow cytometric analysis of monocytes as a tool for distinguishing chronic myelomonocytic leukemia from reactive monocytosis. Am J Clin Pathol 2005 Nov;124(5):799-806.

(21) Lacronique-Gazaille C, Chaury MP, Le GA, Faucher JL, Bordessoule D, Feuillard J. A simple method for detection of major phenotypic abnormalities in myelodysplastic syndromes: expression of CD56 in CMML. Haematologica 2007 Jun;92(6):859-60.

(22) Lorand-Metze I, Ribeiro E, Lima CS, Batista LS, Metze K. Detection of hematopoietic maturation abnormalities by flow cytometry in myelodysplastic syndromes and its utility for the differential diagnosis with non-clonal disorders. Leuk Res 2007 Feb;31(2):147-55.

(23) Chu SC, Wang TF, Li CC, Kao RH, Li DK, Su YC, et al. Flow cytometric scoring system as a diagnostic and prognostic tool in myelodysplastic syndromes. Leuk Res 2011 Jul;35(7):868-73.

(24) Greenberg P, Cox C, LeBeau MM, Fenaux P, Morel P, Sanz G, et al. International scoring system for evaluating prognosis in myelodysplastic syndromes. Blood 1997 Mar 15;89(6):2079-88.

(25) Greenberg PL, Tuechler H, Schanz J, Sanz G, Garcia-Manero G, Sole F, et al. Revised international prognostic scoring system for myelodysplastic syndromes. Blood 2012 Sep;20;120(12):2454-65.

(26) Malcovati L, Germing U, Kuendgen A, Della Porta MG, Pascutto C, Invernizzi R, et al. Time-dependent prognostic scoring system for predicting survival and leukemic evolution in myelodysplastic syndromes. J Clin Oncol 2007 Aug 10;25(23):3503-10.

(27) Westers TM, Alhan C, Chamuleau MED, van der Vorst MJDL, Eeltink C, Ossenkoppele GJ, et al. Aberrant immunophenotype of blasts in myelodysplastic syndromes is a clinically relevant biomarker in predicting response to growth factor treatment. Blood 2010 Mar 4;115(9):1779-84.

(28) Alhan C, Westers TM, van der Helm LH, Eeltink C, Santini V, Ossenkoppele GJ, et al. Absence of Aberrant Myeloid Progenitors by Flow Cytometry Is Associated with Favorable Response to Azacitidine in Int-2 and High Risk Myelodysplastic Syndromes. Cytometry B Clin Cytom. 2014 May;86(3):207-15.
(29). van de Loosdrecht AA, Westers TM. Cutting edge: flow cytometry in myelodysplastic syndromes. Natl Compr Canc Netw. 2013 Jul;11(7):892-902.
(30). Porwit A, van de Loosdrecht AA, Bettelheim P, Brodersen LE, Burbury K, Cremers E, Della Porta MG, Ireland R, Johansson U, Matarraz S, Ogata K, Orfao A, Preijers F, Psarra K, Subirá D, Valent P, van der Velden VH, Wells D, Westers TM, Kern W, Béné MC.Revisiting guidelines for integration of flow cytometry results in the WHO classification of myelodysplastic syndromes-proposal from the International/European LeukemiaNet Working Group for Flow Cytometry in MDS. Leukemia. 2014 Sep;28(9):1793-8.
(31). Alhan C, Westers TM, Cremers EM, Cali C, Witte BI, Ossenkoppele GJ, van de Loosdrecht AA. High flow cytometric scores identify adverse prognostic subgroups within the revised international prognostic scoring system for myelodysplastic syndromes. Br J Haematol. 2014 Oct;167(1):100-9

3. French-German MDS Workshop / 2. EMSCO Annual Meeting in Dresden

For the third time French and German MDS experts were meeting on the 10th and 11th September 2014 in order to discuss the latest developments in MDS diagnosis and therapy in their respective countries. As last year's meeting had been organized by the French MDS group in Paris, this time it was Germany's turn to host the event. More than 80 participants were therefore welcomed in Dresden by the two chairs Prof. Pierre Fenaux (Paris) and Prof. Uwe Platzbecker (Dresden). This year, it was a great pleasure to notice that the conference starts to raise interest beyond the French and German borders as participants from Italy, Spain, The Czech Republic, The Netherlands as well as Switzerland were present.

Figure 2: Prof. Uwe Platzbecker welcomes the participants of the 3rd French-German MDS Workshop / 2nd EMSCO Annual Meeting

At the beginning of the meeting, two trials – the DACOTA and the EUROPE trial – were presented. These two trials are the first ones to be carried out in common between the French and the German MDS study groups and they are coordinated under the common EMSCO label. Furthermore, the first day of the conference was complemented by scientific talks on immunotherapeutic approaches, the utility of mouse models and an update and review of the WHO and IWG diagnostic and response criteria.

The second day focused on current clinical research activities in both lower and higher risk MDS. In the lower risk sessions topics such as molecular aspects, iron chelation, ESAs as well as MRD guided treatment were addressed. In addition, Prof. Ulrich Germing from Düsseldorf presented MDS registry experiences on both national and European levels.

Figure 4: Prof. Ulrich Germing during his talk on MDS registries

In the higher risk sessions AZA first line trials as well as approaches for patients failing on AZA were discussed and trials investigating allogeneic stem cell transplantation were presented. To conclude the meeting colleagues from Italy, Spain and the Netherlands gave a snapshot overview of clinical trials in their respective countries. **>>>**

Figure 5: Group photo of the 3rd French-German MDS Workshop / 2nd EMSCO Annual Meeting

Figure 3: Prof. Gerhard Ehninger during his talk on immunotherapeutic approaches in myeloid neoplasms

>>> We are now looking forward to the next meeting in Marseille, France, which will be hosted by Prof. Norbert Vey on the 17th and 18th September 2015 and a big thank you for the successful outcome of this year's event goes to all organizers, speakers, and participants as well as our supporters Novartis, Celgene, Boehringer-Ingelheim, Janssen, Lilly, Roche and Amgen.

Author: S. Gloaguen

The 3rd French-German MDS Workshop / 2nd EMSCO Annual Meeting was supported by:

Reinforced cooperation of German Early Clinical Trial Units – an opportunity for new MDS therapies

Early clinical trial units (ECTUs or phase I units) are highly specialised clinical entities for the conduction of new and experimental tumour therapies.

Such therapeutic units are essential for translational research in medicine and they are an important component of modern comprehensive cancer centers. Phase I units have benefits for both academic research and patient care.

Whilst early clinical trial units have been established already 15 years ago in the US, there are only few active phase I units in Germany. One of them is the ECTU located at the University Hospital Carl Gustav Carus in Dresden.

An important prerequisite for the safe conduction of phase I trials is the presence of the necessary infrastructure. Besides sufficient specialised personnel and adequate technical equipment, there is a need for immediate access to intensive care.

Figure 6: Early Clinical Trial Unit - UCC Dresden

Furthermore, the administrative handling of phase I trials can be a challenge. At first, it is not always easy to acquire phase I trials, which are attractive for both the patients and the ECTU. This requires good contacts and cooperative relationships with the pharmaceutical industry and contract research organizations, which have grown over years. The GWT-TUD GmbH has these contacts and has extensive experience with contract management for clinical trials. Quick turnaround yet thorough contract review as well as efficient contract negotiations have proven to be a true advantage.

The ECTU of the university cancer center (UCC) in Dresden has therefore decided to cooperate with the GWT-TUD GmbH and currently conducts 4 phase I trials on behalf of the GWT.

In order to increase the attractiveness of Germany for the pharmaceutical industry and to strengthen the international competitiveness of the German ECTUs, a national ECTU network is planned to be set up based on this Dresden model, which will be coordinated by the GWT-TUD GmbH. The ECTUs of Würzburg, **>>>**

>>> Munich, Rhein/Ruhr and Dresden have already started to group themselves accordingly.

In the focus of this network are not only common negotiations with sponsors but primarily the implementation of uniform standards and processes as well as comparable prices for clinical research. Furthermore, the initiative aims at a clearly higher number of patients and at using synergetic effects regarding the planning and conduction of trials with, besides others, a special focus on MDS and AML.

The central task of the GWT as the coordinating body of the network is the management and implementation of all administrative processes, including contract management. Thus, there is only one central point of contact for the pharmaceutical companies and they directly sign the contracts with the GWT for the corresponding trials. The GWT then incorporates the ECTUs via individual service agreements. This means: better quality and therefore increased interest of the pharmaceutical industry to place trials in Germany based on transparency of all the processes.

For haematologic diseases as MDS - for which there currently is only a limited number of therapeutic options available - clinical trials in early phases can represent important opportunities for the participating patients. Through an active and internationally competitive ECTU network, the number of active phase I trials in Germany can be enhanced in this indication and thus offer more MDS patients the option to benefit from advances in clinical research.

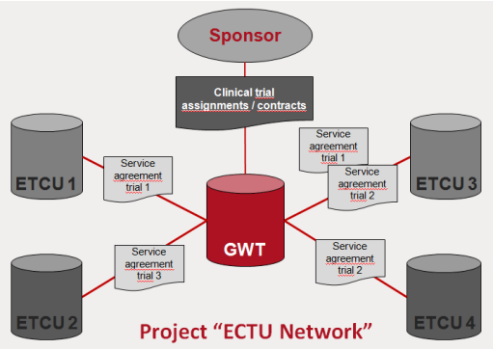


Figure 7: ECTU Network

Author: D. Lippmann

Young Dresden Researcher Awarded GMIHO-DGHO Doctoral Scholarship

With a project outline on the optimisation of therapies for patients suffering from myelodysplastic syndromes (MDS) or acute myeloid leukaemia (AML), Julia Eckoldt from Dresden has been awarded this year's joint doctoral scholarship of the company GMIHO – Innovation in Haematology and Medical Onclogy – and the German Society for Haematology and Medical Oncology (DGHO). The purpose of the medical student's thesis, which is supervised by Prof. Dr. U. Platzbecker and Dr. M. Wermke, is to show how the therapy of patients who have had a stem cell transplantation can be improved. For this purpose, over 130 patients will be examined in a clinical study at five study sites in Germany.

"Study on the Significance of Systemic, Hepatic and Labile Plasma Iron of MDS and AML Patients for the Clinical Course and Immune Constitution after an Allogenic Stem Cell Transplantation" is the full title of the successful project outline. In a prospective study, Julia Eckoldt intends to examine the course of patients' therapies in order to obtain new findings on the dynamics, biology and clinical consequences of systemic iron overload. Julia Eckoldt is currently studying medicine at the Faculty of Medicine Carl Gustav Carus in Dresden. Her scholarship started on the 1st of October, at the beginning of the new semester. She presented her project outline at the annual DHGO conference, which has taken place from the 10th until the 14th of October in Hamburg, to international experts at a poster discussion on Monday, 13th October.

With their doctoral scholarship, GMIHO and DGHO support young researchers in the field of clinical research in Germany. The scholarship holders receive a monthly grant of 800 EUR over one year. In addition, the costs for attending conferences etc. are covered. The doctoral scholarship is awarded once a year. Students of medicine and doctoral students may apply by submitting a project outline no later than the 30th of June. The DHGO has set up a special website for this purpose.

An independent body of experts consisting of three physicians who are **>>>**

>>> actively involved in clinical research evaluates the applications according to a scoring system. The proposal with the highest score is awarded the scholarship.

GMIHO was founded by the DGHO in Berlin in 2000 as a provider of services for researching physicians. Since 2012 the company is part of the GWT-TUD GmbH.

Author: A. Klopsch

Overview of event recommendations

ESH International Conference on «Practical Problems» in Diagnosis and Management of MDS and MDS/MPN
15. bis 16 März 2015, Paris- Frankreich

13th International Symposium on Myelodysplastic syndromes
29 April 2015, Washington, D.C. – USA
Mehr Informationen: http://mds.kenes.com/

MDS experts presented: Prof. Arjan van de Loosdrecht - VU University Medical Center Amsterdam, Netherlands

Arjan van de Loosdrecht is Professor of Hematology at VU University Medical Center in Amsterdam (VUmc). He passed Medical School at the same University in 1989. After a scientific laboratory training in Cell Biology, Immunology and Hematology he received PhD graduation at the Department of Hematology (VUmc) on the thesis "Monocyte mediated cytotoxicity in acute myeloid leukaemia; Mechanisms and clinical implications". In 1995 he graduated in Immunology (MSc). From 1993-1998 he performed a clinical training in Internal Medicine followed by a Hematology Fellowship (Department of Internal Medicine and Hematology at the Groningen University Medical Center, Groningen, The Netherlands).

Since 2000, he is a staff member at the department of Hematology, VU University Medical Center in Amsterdam. The department has a leading role in the implementation of flow cytometry in minimal residual disease detection in acute myeloid leukaemia (AML) and in diagnostic and prognostics in myelodysplastic syndromes (MDS) using immunophenotypical methods in prospective clinical protocols within the HOVON/SAKK collaborative groups.

He is author of over 150 peer-reviewed papers published in national and international journals particularly in the field of hematology and immunology. His particular scientific experiences and interests are on translational hematology. He is project leader of the preclinical and translational immunotherapy programmes in AML and MDS and Principle Investigator of clinical (translational) programmes dealing with the treatment of MDS. His research has focused on immune surveillance mechanisms in AML and MDS. With respect to MDS, he is chair of the MDS WG within HOVON, chair of the MDS Working Group of the Dutch Society of Cytometry and the ELN WP8 (subgroup flow-cytometry) on the implementation of flow-cytometry in MDS and chair of the database sharing committee of the IWG-PM (IPSS-revised) in MDS.

The structure of the study coordinating office EMSCO (European Myelodysplastic Syndrome Coordinating Office) is supported by

Baxter