News from the MDS-RIGHT Study • For all MDS Stakeholders

NEWSLETTER

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MDS RIGHT

Providing the right care to the right patient with MyeloDysplastic Syndrome at the right time

MDS-RIGHT General Assembly Meeting,
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MDS EUROPE
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Welcome from the Project Co-ordinator

Prof. Theo de Witte, MD PhD [CO], Radboud university medical center, NL

Dear friends of MDS-RIGHT, dear readers!

It is my pleasure to welcome you on behalf of the MDS-RIGHT consortium to the second issue of our electronic project newsletter. Since its inception in May 2015, the 15 European partners involved in our 5-year research project have made great strides in evaluating and comparing the effectiveness of existing healthcare interventions for elderly patients affected by lower-risk myelodysplastic syndromes (MDS) and anaemia (a shortage of red blood cells).

While it is still too early for drawing final conclusions, the MDS-RIGHT study is well on track and has already started improving the guidance for MDS diagnosis and treatment. There is no doubt that this project will make a difference by facilitating better patient care, treatment compliance and a more effective use of healthcare resources.

This newsletter will not only update you on the progress during the second phase of the project (months 19-36). In her interview, Prof. Hellström-Lindberg also shares unique insights into the art of developing and providing evidence-based interactive guidance for MDS patient management. And in the last section of this newsletter, you will be introduced to the new MDS Manifesto.

I hope you will enjoy reading this newsletter and I invite you to visit us online and to join the discussion at **https://mds-europe.eu/community**!

Guidance on the Guidelines

Interview with Prof. Eva Hellström-Lindberg, Practice Guideline Development Work Package Leader

Prof. Eva Hellström-Lindberg, MD PhD, Karolinska Institutet, SE

MDS-RIGHT: *We are looking forward to the launch of the first version of the interactive MDS online guidelines! What are the main benefits of this new patient management tool?*

Eva Hellström-Lindberg: There are many benefits, but I think that the most important one is that we will be able to provide all physicians in Europe, specialists in haematology as well as internists, and doctors in training a very handy tool for gaining access to how MDS patients are diagnosed, how prognosis is established, and how treatment is chosen based on this work-up.

In other words, this tool serves to elevate the median and lower level for correct management rather than to educate MDS specialists.

Another major benefit is that these guidelines will be open to everyone. This means they will be accessible also to other health professionals, policy makers and MDS patients.

MDS-RIGHT: *What kind of evidence is used for the online guidelines and how is it integrated?*

Eva Hellström-Lindberg: The guidelines use the same system for evidence and recommendation level as all published guidelines.

The advantage of the online format is that new evidence can be more quickly introduced than with the usual scenario where a guideline is first published in a scientific journal.

MDS-RIGHT: *How are country-specific issues addressed – and what about the existing national MDS guidelines?*

Eva Hellström-Lindberg: The existing national MDS guidelines can be accessed also via the MDS-Europe website. By clicking on the flag of a specific country you will either come to the relevant MDS website for that specific country or to a preferred guideline. We will work more on this section during the next year.

Naturally there are differences between countries with regard to investigational procedures and specific therapies that are available for MDS patient management.

MDS-RIGHT: *Will the new guidelines cover all aspects of MDS diagnosis, prognosis and treatment?*

Eva Hellström-Lindberg: In the end, yes: the new guidelines will cover all aspects of MDS diagnosis, prognosis and treatment.

We have started with the diagnostic and prognostic guidelines and let them go public first. We aim to also have the therapeutic MDS guidelines released by May 2019.

MDS-RIGHT: *Who will have access to the guidelines – and is it planned to have them in different formats (also for patients/caregivers) and languages?*

Eva Hellström-Lindberg: As mentioned before, the MDS-RIGHT guidelines will be open to anyone who would like to read English, including patients.

We have good experience from the Nordic MDS Group with the Nordic guidelines, which have been openly accessible for many years.

Of course, this will not be sufficient for patients who have difficulties both with the language and the medical terms, but our experience is that many patients actually print out and bring them to their doctor and ask for further information.

The MDS-RIGHT guidelines are also written in a concise and well-structured format, with clear bullets. What is more, we have endeavoured to make the language of the online guidelines as simple as possible. They are meant to function on desktop computers as well as on smartphones and tablet computers.

We also have plans to address patients in a more direct way in the future, but not during the current project.

MDS-RIGHT: *How frequently are you going to update the guidelines after finalization of the first version – and what approach do you have in mind?*

Eva Hellström-Lindberg: First, we will include new data that are derived from the other MDS-RIGHT work packages and from other large international collaborative efforts. In particular, data on molecular profiles, quality of life and co-morbidities will be important contributions. I foresee that within two years we will have a new diagnostic-prognostic model. Then, large clinical trials of new drugs, if they hold high quality, may influence treatment decisions and algorithms.

We will first ask different international groups to feedback directly into the system. Then we will create an editorial board that regularly, at least every six months, reviews the content and checks if new information should be included and if some information needs to be removed.

MDS-RIGHT: *Looking at guideline development in general, what is your most important piece of advice?*

Eva Hellström-Lindberg: My most important piece of advice is that you should try to make it as simple as possible, but still make sure that what you include is correct and accepted by everyone. And if there are disagreements, in some cases disclose that there are two views on certain aspects.

Remember, we do not write these guidelines for ourselves as MDS experts, but for colleagues seeing these patients amongst many other patients with different diagnoses.

Also, young colleagues are probably the best to use guidelines. I am happy that we have created a junior faculty that now actively helps us to format this first version. I would like to see this group grow and be more active in the future.

MDS-RIGHT: *Thank you very much!*

Updates from the Work Package Leaders

Prof. Andrea Manca, PhD, University of York, UK

Work Package 1 – Health care interventions

The second phase of the MDS-RIGHT project was used to continue with the evaluation of the impact of healthcare interventions (HCI) and prognostic factors on established core outcomes (overall and progression-free survival) and new outcomes, including health-related quality of life (HRQoL), trans-fusion density, and the decline of cytopenias (shortages of cells). All results will be integrated into MDS treatment recommendations.

The quantification and analysis of health care resource utilisation (HCRU) is also ongoing, using data obtained through the **European MDS Registry** and country-specific unit cost data.

Making sure that no aspects of clinical management in MDS patients are overlooked, a series of additional activities have been carried out to assess also the cost-effectiveness of alternative MDS treatment strategies.

Prof. Joop Jansen, PhD, Radboud university medical center, NL

Work Package 2 – Diagnostics and bioinformatics

To inform recommendations for the use of genetic screening for clinical decision making, newly developed bioinformatic pipelines were used for collecting MDS-specific genetic and clinical data and for assessing the clinical relevance of genetic mutations with regard to disease progression,

treatment outcome and HRQoL.

Mutational analysis was performed on the DNA (molecules carrying genetic information) of more than 1,000 MDS patients and several scientific papers on this topic have been published.

In addition, a phenotypic/physical characterisation of MDS cells by flow cytometry (FCM, a method for analysing cell surface markers) was conducted for hundreds of MDS patients, allowing further analyses. Furthermore, procedures were put in place for securely transmitting, storing and linking the aggregated data to the clinical and outcome data.

Prof. Reinhard Stauder, MD MSc, Medizinische Universität Innsbruck, AT

Work Package 3 – HRQoL issues in patients with anaemia

Activities to enable implementation and cross-cultural validation of the MDS-specific QUALMS (Quality of Life in Myelodysplasia Scale) questionnaire in the EUMDS Registry population were continued. The integration of the QUALMS within the EUMDS Registry has been completed. The QUALMS questionnaire was translated into many different languages and the corresponding data collection is ongoing.

Activities to identify HRQoL measures for MDS and their integration into a new MDS-specific core outcome set (COS) were continued and two related online Delphi surveys were initiated to inform consensus on the definition of the core outcomes. A scientific article on this topic is in preparation.

Using the EUMDS Registry dataset, the identification and statistical analysis of predictors for low HRQoL are ongoing. What is more, a number of activities geared towards providing HRQoL adapted treatment strategies for each of the mutational MDS-subtypes are being conducted.

Prof. Luca Malcovati, MD PhD, Università Degli Studi di Pavia, IT

Work Package 4 – Treatment outcome prediction

Building on the EUMDS dataset and on data generated by Work Package 2 on genetic abnormalities in MDS, the analysis of newly identified molecular defects with potential prognostic value is ongoing. In addition, relevant statistical methods for developing robust clinical/molecular prognostic models for response to specific treatment modalities were defined.

Activities to identify new biological MDS subgroups that might be good candidates for the development of new categories of targeted therapies were continued. New statistical methods are applied to identify homogenous subgroups and early treatment response indicators.

Furthermore, activities to assess whether unexplained anaemia in the elderly (AoE) is an early or mild manifestation of MDS and a cause of undertreatment were also continued, using biological samples from more than 650 elderly anaemic individuals selected from the Dutch **LifeLines** reference population.

Prof. Eva Hellström-Lindberg, MD PhD, Karolinska Institutet, SE

Work Package 5 – Practice guideline development

For the development of new dynamic web-based evidence-based guidelines, European guideline development working groups of MDS experts have been established. International MDS guidelines, newly published evidence and initial data from the other Work Packages were evaluated and the contents of 13 dedicated web-based guideline sections were drafted, divided into a 'Diagnostic and Prognostic' section and a 'Therapeutic' section. New scenarios and cases have been used to address country-specific issues.

The technical implementation of the corresponding dynamic online tool in responsive design (for PC, tablet, smartphone etc.) is ongoing. In parallel, a panel of external haematologists-in-training and junior specialists was set up for reviewing and pretesting demo versions on the **MDS-Europe** website.

The 'Patient management' section with the online guidelines version 1.0 is planned go live in the autumn of 2018.

Prof. Pierre Fenaux, MD PhD, Groupe Francophone des Myélodysplasies, FR

Work Package 6 – Dissemination, exploitation, communication

Following the establishment of a multi-stakeholder MDS competence network, the **MDS-Europe** website was further expanded and its content management system and security settings upgraded. For example, the 'Resources' section now also includes MDS clinical trials and registries, and the 'Community' section offers regular MDS stakeholder articles and opportunities for online discussion.

In addition, a dedicated 'MDS-RIGHT Workspace' section was set up to allow selected user groups to download and share project documents and tools, including a comprehensive set of public relations (PR) guidelines. A set of MDS multi-stakeholder and European media mailing lists was developed for disseminating project newsletters, announcements, press releases etc.

A press release was distributed around the international multi-stakeholder meeting on '**European Perspectives on MDS Patient Management**', held on 3 May 2017 in Valencia, Spain. The essence of this meeting is also reflected in the **MDS Manifesto** (see page 5).

Prof. Theo de Witte, MD PhD [CO], Radboud university medical center, NL

Work Package 7 – Project management/consortium

In addition to the overall day-to-day management and process monitoring of the MDS-RIGHT project, numerous meetings were planned and organised, such as regular core team meetings, general assembly meetings and scientific meetings, to name but a few, each meeting involving conscientious documentation and follow-up.

Where possible, partner support has been provided with regard to project implementation (e.g., dissemination) or amendments. Uniform and proper reporting to the European Commission is ensured by means of a centralised communication structure that is co-ordinated by the Project Manager.

In parallel to the MDS-RIGHT project, the EUMDS Registry has further evolved and now holds information on over 2,460 eligible MDS patients. EUMDS core activities (patient enrolment, data collection, management, quality assessment, training, organisation of meetings, project dissemination etc.) will continue during the course of the MDS-RIGHT project. Activities are underway to ensure the continuation and expansion of the EUMDS Registry structure and activities beyond 2020.

News and Announcements

Be part of the community and join the online discussion!

All MDS stakeholders are encouraged to visit the Community section of the MDS-Europe website, where different stakeholders present their views and everybody is invited to comment on a great variety of interesting MDS topics, including diagnostics, MDS treatment challenges, quality of life, nursing etc. **Visit us and leave your comment!** And if you would like to contribute an article, please do get in touch: **https://mds-europe.org/community**

MDS Manifesto – Sign the call to improve the care for patients with MDS!

The **MDS Manifesto** is a joint public written declaration issued by the MDS stakeholder community. It specifies in general terms what needs to be done to address the key issues the MDS community is faced with. The text reflects the major concerns and needs expressed by various MDS stakeholder groups at the first MDS-RIGHT multi-stakeholder meeting in May 2017.

The MDS Manifesto is meant to unite the MDS community behind a clear joint statement. Therefore, MDS-RIGHT encourages all parties committed to improving the care of MDS patients to **co-sign and further disseminate** this Manifesto. The joint declaration may also be translated into other languages and can be used for local, national or international MDS advocacy purposes.

The signatories of the Manifesto call on European and national authorities, governments, research institutions, professional societies, patient groups, and the pharmaceutical and bio-technology industries to help increase research efforts and improve the diagnosis and care of people affected by MDS by addressing the following **five key needs:**

3 **More, and better, affordable and accessible treatment options**

2 **More international and patient-centred collaborative clinical research**

4 **Improved diagnosis and professional guidance for patient management**

1 **Increased laboratory research and analysis of real-world datasets**

5 **Enhanced collaboration and better patient information, advocacy and involvement**

To access the full text of the MDS Manifesto, download a copy for your own advocacy purposes and find out how your organisation or institution can easily support this call by co-signing it, please visit **https://mds-europe.eu/manifesto**.