



**Newsletter Issue 24**  
**June 2020**





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## 1. Message from the Chair



### Welcome to the June 2020 EUMDS newsletter

The human world, and especially the world of older persons, is going through dramatic changes and challenges. It is clear that all of us involved in the EUMDS registry - patients and caregivers, research nurses, data managers, research staff and physicians - are affected by the consequences of the COVID-19 pandemic.

- Patients do not dare to leave home and avoid visits to hospitals and other health facilities.
- Clinical research activities have been limited or put on hold in many hospitals so clinical staff could commit their efforts to the increased demand for clinical care. New inclusions of patients in the EUMDS Registry this year (76 as of 1 June) do not seem dramatically low, however this number has dropped heavily during the second quarter of this year. To get more insight in the consequences of the pandemic on MDS care, we would like to monitor all new patients during the COVID-19 pandemic, also those patients who have died prematurely during the first 6 months after diagnosis. We will put together a proposal in July how to address and to study these issues properly.
- Our annual meeting in Mannheim has been skipped due to travel restrictions, but we plan a dedicated video meeting in September. Details will follow before the end of August.

The good news is that our team managed to submit a new grant application for Horizon 2020 "Digital transformation of real-world datasets to improve understanding and management of chronic anaemia and the associated complex chronic conditions in older persons (DI-CAP)". We will hear before the end of October 2020 the outcome of this application.

We are pleased that we can continue the EUMDS Registry beyond 2020 and looking forward to continue the success of the EUMDS Registry together.

Theo de Witte  
Coordinator, EUMDS Steering Committee



## 2. Updated EUMDS website

We recently launched the updated EUMDS website. Featuring a refreshed visual design that automatically adapts to the screen size on any device. The new site also includes a comprehensive list of EUMDS-related publications, abstracts and other publications and for the first time also lay summaries).

Access to the database is still via the website, but you are now able to login using the link at the top right. This will also give you access to 'Study information', 'Documents', 'Announcements' and 'FAQs' - these links will appear in the left-hand navigation menu.

In the Documents section, you have access to the Progress and Interim reports. The Interim report March 2020 provides an extensive overview of the data available in the Registry.

If you experience any difficulties using the new website or if you have any feedback, please get in touch (enquiries@eumds.org).

**European Myelodysplastic Syndromes (MDS) Registry**

Welcome to the European Myelodysplastic Syndromes Registry (EUMDS)

The European MDS Registry (EUMDS) is a prospective multicentre European Registry for newly diagnosed patients with Myelodysplastic Syndromes (MDS). Newly diagnosed patients with Acute Myeloid Leukaemia (AML) with 20-30 percent marrow blasts (former RAEB-I), and Chronic Myelomonocytic Leukaemia (CMML) are also eligible for participation in this Registry.

Members of participating centres may login or register to access the database using the links in the left-hand menu or buttons below.

- About EUMDS
- Publications
- Newsletters
- Protocol summary

**Publications**

Search: All fields | Any

The European MDS Registry (EUMDS) is a prospective multicentre European Registry for newly diagnosed patients with Myelodysplastic Syndrome (MDS) initiated by members of the LeukemiaNet MDS working group. Since its inception in 2008, the EUMDS has evolved into a valuable source of information on more than 2500 MDS patients, collected in over 140 hospitals in 16 European countries and Israel. Initially, the Registry only MDS (FPS low and intermediate-1), but has been extended to also include patients with High Risk MDS since July 2017.

**Study objectives**

The objectives of the EUMDS Registry are:

- Register to collect and analyse demographics, disease management and treatment outcomes
- Study to perform observational studies concerning relevant MDS-related research questions in the fields of pathogenesis, diagnostic prognostication, treatment, Health Related Quality of Life (HRQL) issues, health economics and risk stratification for MDS treatment
- Share to share all study results with the community involved in MDS and its treatment: patients, medical specialists, health care pro pharmaceutical companies, health care regulators and health insurance companies

The ultimate goal is to better patients lives, by improving diagnosis, treatment and quality of life.

**Data collection**

A wide range of data is collected, for example:

- Demographic data
- Performance scores
- MDS history

**Frequently asked questions**

Answers to the most commonly asked questions about the EUMDS Database

- A new user needs login details to access the database - what should they do?
- At follow-up my patient has an ongoing concomitant disease recorded at the previous visit - how do I enter this into the database?
- Can I practise using the database?
- Cytogenetics have not been done, can the patient still be entered?
- How do I convert my laboratory values from microkatals/l (µkat/l) into international units (IU/l)?
- How do I enter a new follow-up visit?
- How do I enter ongoing MDS treatments or iron chelation therapy?
- I am entering data for a repeat visit and the patient has not had a bone marrow biopsy - what should I do?
- I cannot enter the missing date value 01/01/1900 - what should I do?
- I cannot remember my password - what should I do?
- I cannot unlock a visit - what is wrong?
- I do not have a value to enter in a field - why can't I leave it blank?
- I have entered a patient into the wrong centre - how do I change this?
- I have entered the date of inclusion for a patient incorrectly - how can I change this?
- I have one or more dates missing - what should I enter?
- I have tried to enter a value and a red exclamation mark has appeared - what does this mean?
- I need to update data for concomitant diseases or treatments and the boxes are greyed out and unselectable - what should I do?
- My password is not working - what can I do?
- My patient has a CMML diagnosis. Can I include them in the registry?



### 3. New grant application

The quantity and quality of the EUMDS Registry data are becoming more and more relevant. This is reflected by the rapidly increasing number of presentations and publications by our consortium. In addition, the research projects TRIAGE-MDS, MDS-RIGHT and HTx contribute substantially to our ongoing and planned studies.

Activities of TRIAGE-MDS are being continued and extended as part of the MDS-RIGHT. HTx has just started in 2019 and the first 2 studies have been identified recently, including a study on iron chelators. Work is progressing well, and also MDS-RIGHT will be completed this year.

To gain additional funding for our research activities, a new grant application to the Horizon 2020 program has recently been submitted (Di-CAP). This project will focus on chronic anemia and the associated complex chronic conditions (CCC) in older persons, addressing the interaction between individual CCC, the potential contribution of multiple shared pathogenic mechanisms, and shared therapeutic effects and the gap between RWD and RCT data.

This project will provide improved understanding of pivotal molecular, inflammatory, and immune mechanisms playing a role in progression of the MDS clone as well as non-resilient aging and contribute to more effective and repurposed interventions. Quite a few of the recently developed sub studies will contribute to our knowledge in this field and will support our chance to a successful grant application.

Typical examples of these new studies are: Cardiovascular Biomarkers in Lower-risk MDS, the impact of anti-depressive drugs (serotonin antagonists) on outcome of MDS, the role of metformin on progression of MDS, and the role of hypomethylating agents on auto-immune diseases.



## 4. MDS-RIGHT progress

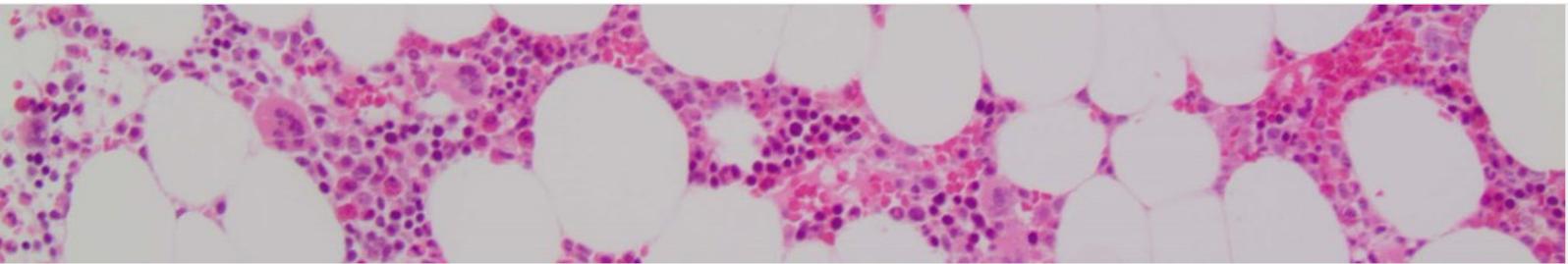
The third period activities of the MDS-RIGHT have been completed successfully, thanks to a productive scientific meeting at the Steigenberger airport hotel at October 2019 and the input of all participants, relentlessly stimulated by Corine van Marrewijk.

The MDS-RIGHT participants are working to achieve its final goal. The official completion of the project was scheduled at the end of April 2020, however, due to the COVID-19 challenges and restriction, it was necessary to request a prolongation of MDS-RIGHT for another 6 months until the end of October 2020. This extension will allow us to complete several studies, especially the studies integrating the molecular and clinical data collected and harmonised in the TRIAGE and MDS-RIGHT project. These studies are ongoing on an integrated dataset of more than 1000 patients.

The HRQoL group showed a new core outcome set with predictors for low quality of life (HRQoL). This information will be integrated with the biological (molecular) subtypes to aid the development of new clinical guidelines and cost-effective analysis.

The burden of MDS on HRQoL has been assessed by comparing HRQoL within participants of the LifeLines cohort and the EUMDS Registry. This study shows a clear MDS-specific impact on quality of life independent of red blood cell transfusions and anaemia (manuscript in preparation).

MDS-RIGHT has successfully translated the existing European MDS guideline (Malcovati et al. Blood 2013) into an interactive online guideline (see next item). All results of the MDS-RIGHT project will be integrated.



## Patient management

This is a recently developed section of the website; as such, we welcome comments from our users on content, design and functionality. If you have any

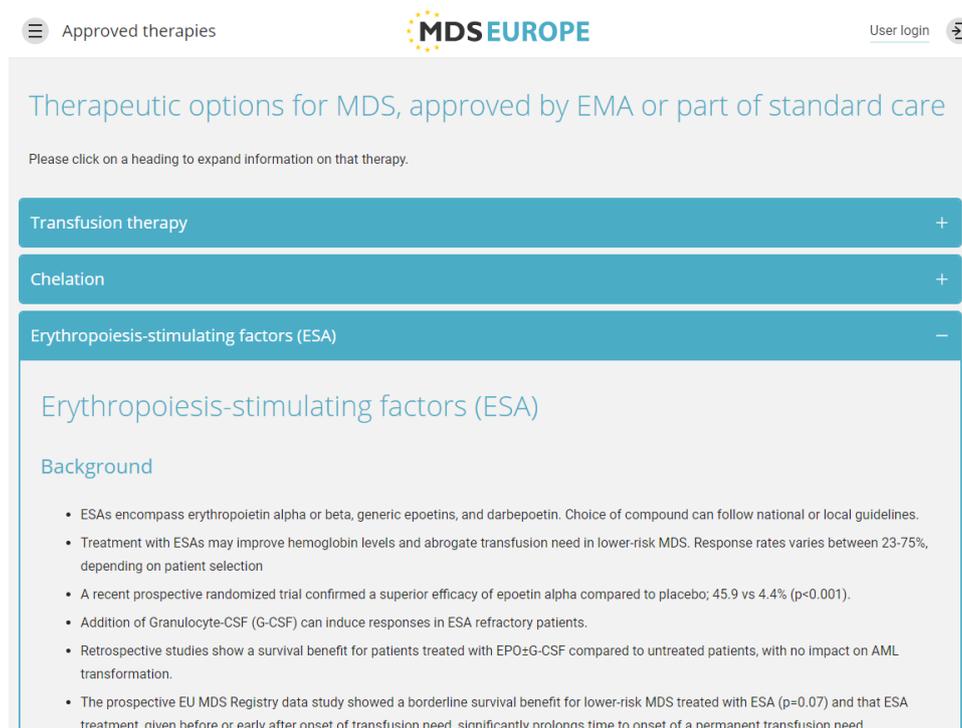
### 5. Interactive MDS online guidelines

The MDS-RIGHT interactive online guidelines are open to anyone (<https://mds-europe.eu/management>).

The guidelines use the same system for evidence and recommendation level as other published guidelines. The advantage of the online format is that information about new evidence and recently approved treatments can be made available to caregivers and patients without the usual route of publication in a scientific journal. However, it is essential that everything that is added to or removed from the guidelines undergo consensus decision in the guideline committee.

There are many benefits to interactive online guidelines for patient management, the most important being that we are able to provide all physicians in Europe, specialists in haematology as well as internist and doctors in training, a 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, the online guidelines serve to elevate the median and lower level for correct management, rather than to educate MDS specialists.

The guidelines are written in a concise and well-structured format, with clear bullets. We have good experience from the Nordic MDS Group with the Nordic guidelines and many patients actually print out and bring them to their doctor and ask for further information.



The screenshot shows the MDS EUROPE website interface. At the top, there is a navigation bar with a menu icon, the text "Approved therapies", the MDS EUROPE logo, and a "User login" link with a home icon. Below the navigation bar, the main content area is titled "Therapeutic options for MDS, approved by EMA or part of standard care". A sub-header reads "Please click on a heading to expand information on that therapy." Below this, there are three expandable sections: "Transfusion therapy" (expanded), "Chelation" (collapsed), and "Erythropoiesis-stimulating factors (ESA)" (collapsed). The "Erythropoiesis-stimulating factors (ESA)" section is expanded, showing a heading "Erythropoiesis-stimulating factors (ESA)" and a sub-heading "Background". The background section contains a list of bullet points:

- ESAs encompass erythropoietin alpha or beta, generic epoetins, and darbepoetin. Choice of compound can follow national or local guidelines.
- Treatment with ESAs may improve hemoglobin levels and abrogate transfusion need in lower-risk MDS. Response rates varies between 23-75%, depending on patient selection
- A recent prospective randomized trial confirmed a superior efficacy of epoetin alpha compared to placebo; 45.9 vs 4.4% (p<0.001).
- Addition of Granulocyte-CSF (G-CSF) can induce responses in ESA refractory patients.
- Retrospective studies show a survival benefit for patients treated with EPO±G-CSF compared to untreated patients, with no impact on AML transformation.
- The prospective EU MDS Registry data study showed a borderline survival benefit for lower-risk MDS treated with ESA (p=0.07) and that ESA treatment, given before or early after onset of transfusion need, significantly prolongs time to onset of a permanent transfusion need.



## 6. Publications

Four manuscripts of EUMDS sub studies or collaborative studies have been submitted to peer-reviewed journals:

- Hoeks M, Bagguley T, van Marrewijk C, Smith A, Bowen D, Culligan D, Macheta M, Symeonidis A, Garelius HKG, Spanoudakis M, Langemeijer S, Roelofs R, Wiegerinck E, Tatic A, Killick S, Panagiotidis P, Stanca O, Hellström-Lindberg E, Čermák J, van der Klauw M, Wouters H, van Kraaij M, Blijlevens N, Swinkels DW, de Witte T, on behalf of the EUMDS Registry Participants. **Toxic iron species and oxidative stress in lower-risk myelodysplastic syndrome patients: course of disease and effects on outcome.**  
[Submitted: Leukemia]
- de Witte T, Malcovati L, Fenaux P, Bowen D, Symeonidis A, Mittelman M, Stauder R, Sanz G, Čermák J, Langemeijer S, Hellström-Lindberg E, Germing U, Holm MS, Mądry K, Tatic A, Almeida AM, Savic A, Mandac Rogulj I, Itzykson R, Hoeks M, Garelius HG, Culligan D, Kotsianidis I, Ades L, van de Loosdrecht AA, van Marrewijk C, Yu G, Crouch S, Smith A. **Novel dynamic outcome indicators and clinical endpoints in MDS developed during the first 10 years of the EUMDS Registry: the MDS-RIGHT project perspective.**  
[Submitted: Haematologica]
- Oster HS, Crouch S, Smith A, Yu G, Abu Shrkhihe B, Baruch S, Kolomansky A, Ben-Ezra J, Naor S, Fenaux P, Symeonidis A, Stauder R, Čermák J, Sanz G, Hellström-Lindberg E, Malcovati L, Langemeijer S, Germing U, Holm MS, Mądry K, Guerci-Bresler A, Culligan D, Sanhes L, Mills J, Kotsianidis I, van Marrewijk C, Bowen D, de Witte T, Mittelman M. **Clinical and Lab Parameters may rule out and assist in the Diagnosis of MDS.**  
[Submitted: Leukemia]
- Stojkov K, Silzle T, Stussi G, Schwappach D, Bernhard J, Bowen D, Čermák J, Dinmohamed AG, Eeltink C, Eggmann S, Fenaux P, Germing U, Haschke M, Hellström-Lindberg E, Heger M, van de Loosdrecht AA, Passweg J, Pfeilstöcker M, Platzbecker U, Malcovati L, Almeida AM, Mittelman M, Morgenthaler C, Steensma D, Santini V, Stauder R, Symeonidis A, Schär S, Maddox C, de Witte T, Bohlius J, Bonadies N, the Swiss MDS Study Group, the Swiss Group of Clinical Cancer Research (SAKK). **Guideline-Based Indicators for Adult Patients with Myelodysplastic Syndromes.**  
[Submitted: Blood Advances]



## 6. Meeting calendar

Due to the COVID-19 pandemic, the MDS-RIGHT GA & EUMDS SC meeting (Mannheim 2020) and the Second stakeholder meeting have been postponed.

New dates will be set as soon as the situation has sufficiently stabilized and allows us to meet again.



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