Newsletter Issue 23
October 2019

Contents

1. Message from the Chair

Welcome to the October 2019 EUMDS newsletter

We are living in an exciting and challenging time. The world is changing rapidly and creating unknown forces, including climate changes and nationalistic emotions. However, the EUMDS Registry will survive with the help of our management teams in York and Nijmegen.

New members have joined our teams, because we had to say goodbye to Karien Croezen and Peter Karel. Thank you, Karien and Peter, for all your help and dedication - we will miss you.

We celebrated the first 10-year existence of the EUMDS Registry with a lively symposium in Nijmegen, followed by Louise de Swart's thesis defense publicly attended by many members of the EUMDS Registry consortium. The progress on the various studies is remarkably well with four submissions planned before the end of the year.

To enable successful completion of the activities related with the health care resource evaluation, we hope you are willing to complete the survey (see next paragraph).

We have organized another MDS-RIGHT and EUMDS Registry scientific meeting at Schiphol Airport on October 10th and 11th, 2019.

The success of the EUMDS Registry reflects your commitment and dedication throughout all these years. The steering committee is very grateful for all your contributions and we are looking forward to continue the success of the EUMDS Registry together.

Theo de Witte
Coordinator, EUMDS Steering Committee

2. Healthcare resource use survey

The EUMDS Registry, holding Real World Data on more than 2600 MDS patients from 16 European countries and Israel, is well suited to evaluate MDS practice. In many countries evaluation of clinical practice is no longer limited to effectiveness of treatments (in general or in sub groups of patients), but also require robust assessments of the costs resulting from treatments received by patients. Therefore, 'Health care resource use' data collection has been added to the EUMDS in 2017.

As the amount of individual patient 'Health care resource use data' recorded so far in the EUMDS database is currently not enough to perform the anticipated cost-effectiveness analyses, two online surveys have been developed in order to quantify key parameters in the cost-effectiveness model: one in relation to the 'Use of pharmaceuticals' and another for 'Health care resource use more broadly'.

These two surveys have been circulated to EUMDS participant (via the national coordinating teams) and MDS-RIGHT partners in April. We had many more responses for the 'Use of pharmaceuticals' compared to the broader survey. So far, we received 13 responses to the survey on 'Health care resource use more broadly' providing cost information on 9 countries.

To allow proper quantification key parameters, we require multiple responses for each country participating in the Registry. It is important that we receive data from all countries participating in EUMDS! Regretfully, we have not received any response from Croatia, Denmark, Germany, Israel, Italy, Poland, Romania and Sweden. For the other countries (Austria, Czech Republic, France, Greece, Netherlands, Serbia, Spain, United Kingdom) we wish to receive several more responses.

By means of this newsletter, we would like to invite all clinical experts involved in treatment of MDS (also if you are not contributing to the EUMDS Registry) to complete this survey:

https://www.surveymonkey.co.uk/r/8C8653T

If you have questions, please contact: thomas.patton@york.ac.uk for support or to provide you with a PDF copy.

If you are a clinician involved in treatment of MDS, we look forward to receiving your response to the survey!

3. Celebrating 10 years of EUMDS - symposium (12 June)

The Registry celebrated its 10-year anniversary last June the 12th with a symposium in Nijmegen. The symposium was successful and informative. Around 40 local, national and international colleagues attended the symposium. A clear overview of various achievements was presented and ways to move further with the Registry were discussed.

David Bowen presented the history of the EUMDS Registry. He highlighted some lessons we learnt from the Registry, including using blood investigations only in individuals with cytopenias of unknown origin, the impact of Health-related Quality of Life in patients with lower risk MDS measured by the EQ5D and the novel QUALMS instruments and the addition of novel prognostic data, including molecular and FCM data. Finally, he presented European MDS Network platform MDS-Europe (https://mds-europe.eu/) with recently updated guidelines, a working project progressing well.

Eva Hellström-Lindberg stressed that ESA treatment should be initiated in patients with anemia as soon as possible after diagnosis of MDS before the development of transfusion dependency. Treatment of anemia with ESA in patients with MDS is only reimbursed in many European countries after the development of transfusion dependency. This policy is counterproductive because the response to ESA treatment is remarkably superior in untransfused patients.

Krzysztof Mądry presented the most recent data on the causes of death in the patients within the EUMDS Registry. The relative survival of these MDS patients compared to a European reference group indicated that MDS-related causes of death play a significant role in the decreased survival of these MDS patients. Patients diagnosed with RARS and del5q have a higher rate of fatal infections when compared to other MDS subtypes. Infections are the most frequent cause of death (24% of known causes of death), but the incidence of fatal infections decreases over time after diagnosis.

Moshe Mittelman presented an overview of their work on noninvasive diagnosis of MDS (no bone marrow necessary) coordinated by Howard Oster. They have developed a statistical model with 10 demographic and blood variables that could properly diagnose or exclude MDS in 84% of the 501 investigated cases. This means that for most individuals with unexplained anemia/cytopenia MDS can be diagnosed or ruled out without a bone marrow examination. They developed a web app which is accessible in this stage of development: shiny.york.ac.uk/mds

On behalf of Raphael Itzykson, Theo de Witte presented the outcome of the cytopenia kinetics study. He clearly showed that 25% drop in platelets over the first six months of follow-up has independent poor prognostic value in lower-risk MDS. He demonstrated that evaluation of platelet drops and red blood cell transfusion dependency (RBC-TD) at 6 months after diagnosis provides a universal, costless and robust prognostic classifier in MDS. However, the causality link between RBC-TD and worsening of cytopenias warrants further investigation.

Karin König updated the ongoing health related quality of life (HRQoL) studies in EUMDS and focused on longitudinal changes of HRQoL in lower-risk MDS and preliminary data on the impact of red blood cell transfusion (RBCT) and ESA on the HRQoL over time. In general, the dimensions usual activities, self-care and mobility are getting worse over time, but anxiety/depression is improving over time. Both ESA treatment and RBC-TD have an impact on HRQoL, but additional analyses are necessary to translate these longitudinal observations in more solid data.

Louise de Swart gave an overview of the transfusion studies. She used the new and less spikey outcome parameter 'Transfusion dose density' to allow the incorporation of longitudinal changes of transfusion intensity in the evaluation of the impact of transfusions on outcome. She concluded transfusion dependency may be considered as an indicator of inferior progression-free survival, even at relatively low transfusion dose densities of <0.75 units per month or <3 units per 16 weeks as defined in the revised IWG.

Marlijn Hoeks suggested that based on her chelation studies in the EUMDS Registry iron chelation therapy may improve overall survival in lower-risk MDS patients. In addition, a hematological response occurred in a subgroup of patients after starting iron chelation therapy. This large cohort of patients with prospectively collected 'real life' data provides data widely generalizable to the elderly, LR-MDS patient population. Confounding by indication, a common problem in observational studies, is maximally reduced by using the propensity-score matched method in this study.

Finally, Saskia Langemeijer, described our plans to increase the contribution of the Dutch expert centers and the planned activities within the EUMDS Registry. She mentioned the eight recently published studies in international scientific journals and the currently ongoing studies which will lead to another five publications within one year. She concluded that our consortium is very strong in developing brilliant ideas, but Time and Money will continue to be a challenge for the future of our group.

Louise de Swart thesis defence

Louise de Swart defended her thesis successfully after the symposium June 12th, 2019. The title of her thesis was: Patients with lower-risk myelodysplastic syndromes: in scope of iron related complications.

Louise's thesis focused on data reported in the EUMDS Registry concerning transfusion practice, transfusion effects and the consequences of the iron overload and toxicity associated with regular RBCT . She expanded the knowledge on key players of iron metabolism in LR-MDS and demonstrated for example that transferrin saturation can serve as a useful clinical tool in identifying patients prone to developing toxic iron complexes like labile plasma iron (LPI). In addition, she concluded that LPI and RBCT dependency, even at relatively low intensities, may be considered as indicators of poor prognosis for progression free survival in this patient population.

Published work from her thesis that included the EUMDS Registry data were: Validation of IPSS-R (Br J Haematol 2015); Cytomorphology high inter-observer concordance (Ann. Hematol. 2017); Prognostic impact suboptimal number of analysed metaphases (Leuk Res. 2018); Labile Plasma Iron (Haematologica 2018); RBCT dose density prognosis (Haematologica 2019).

4. Introductions

Rosalie Lubbers
Project Officer

Dear all,

My name is Rosalie and I recently started as the new project officer at the EUMDS registry. Here, I will continue the activities of Karien Croezen.

Besides my work at the Registry, I am currently also finishing my PhD thesis at the Leiden University Medical Center: Complement Biology in Health and Disease.

At the moment I am finding my way in all the information and documents that belong to the Registry. I am very excited to contribute to the Registry and to be part of such a large collaboration.

Els Meeuwsen
Monitor

Dear all,

As the new monitor of the EUMDS Registry I want to introduce myself. My name is Els Meeuwsen and I have started working within the project management team in Nijmegen on July 1st. I will continue the activities of Peter Karel who as you may know left the EUMDS project.

Currently, I am getting familiar with the Registry and I am impressed. Not only by the large amount of unique data available and the large number of sites participating in the Registry but also by the 10 years the Registry already exist.

I am really looking forward to working with you and to contribute to the quality of the EUMDS Registry.

Best regards
Els

5. Meeting calendar

- October meeting (MDS-RIGHT Sci & EUMDS SC): **10 October 12:00** – 11 October 13:00, Amsterdam
- ASH Breakfast meeting: **8 December 2019** 6:00-10:00, Orlando

Dates proposed, but final date to be confirmed:

- MDS-RIGHT GA & EUMDS SC meeting: either **Monday 30 March 2020** OR **Wednesday 1 April 2020**, Mannheim (in conjunction with the ELN meeting in Mannheim 31 March 2020)
- Second stakeholder meeting: proposal to organize in conjunction with either:
  - ESH MDS meeting, Mandelieu **23-25 April 2020**
  - EHA 2020, Frankfurt **11-14 June 2020**

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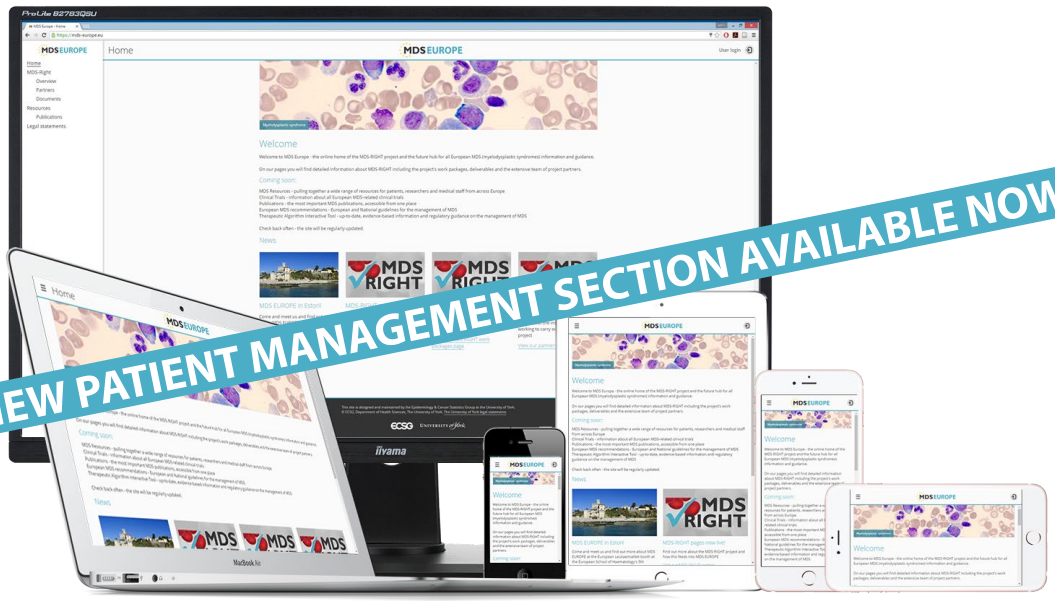

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