Newsletter Issue 19
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1. Message from the Executive Committee

Welcome to December 2017 EUMDS newsletter

The amended protocol (v5.1) continues to be implemented, and high-risk MDS patients are now being recruited. The routine collection of genomic data coupled with expanded quality of life information (QUALMS) will markedly enhance the analysis of outcomes for MDS patients, incorporating a more contemporary dataset. We encourage you to collect the optional dataset where feasible, including healthcare resource utilisation data. Such data from real-world sources like EUMDS will prove invaluable for comparative and cost-effectiveness analyses and, therefore, for market access of new drugs approved for MDS in Europe in the future.

Analysis of red cell transfusion, iron parameters and iron chelation within EUMDS is nearing completion, which together may create a new narrative for discussion of the clinical relevance of these interventions. The publication of the labile plasma iron data is the first of a series of provocative and interesting manuscripts.

We are grateful for all of your efforts with recruitment which continues to be strong, reflecting a widespread interest in this programme. As we indicated in Valencia we welcome your input in proposing sub studies and joining the substudy teams for studies that interest you.

David

David Bowen
on behalf of the EUMDS Executive Committee

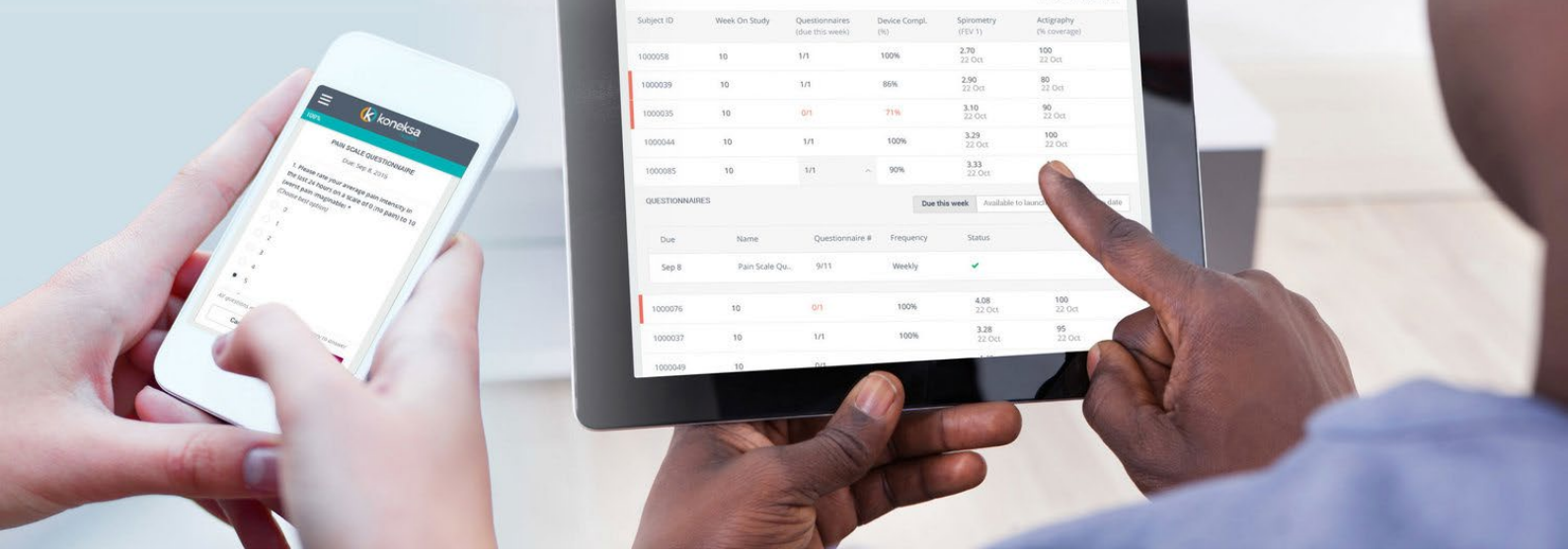
2. MDS RIGHT meeting, Milan

In the MDS-RIGHT project (Horizon2020), EUMDS Registry data is used to address several important research questions, aiming to improve MDS Care. Various EUMDS partners are involved in MDS-RIGHT and gathered in Milan in October this year, to discuss the progress in the 6 scientific work packages of this study.

Amongst others, the meeting focused on the importance of the QUALMS questionnaire as well as defining and prioritizing relevant molecular research questions. To allow us to draw valuable conclusion from these research questions correlating genotype of the patient with the clinical manifestations of MDS, collection of molecular samples and molecular data within EUMDS – as previously mentioned – is of great importance.

A specific highlight of interest during the meeting was the updating and improving the current (European) MDS guidelines, guiding medical specialists through the diagnostic and treatment process. The current guidelines are published in Blood (2013) by Luca Malcovati et al, the national PI of EUMDS for Italy. He is involved in the update process, guided by Eva Hellström-Lindberg (national PI of Sweden). The update does not only concern content, but also format: developments are ongoing to make the guidelines available for mobile devices like smart phones and tablets in an interactive format. We expect this to be available in the first half of 2018.

This meeting will be followed by a next MDS-RIGHT General Assembly meeting on February 1st in Amsterdam, the Netherlands. The EUMDS Steering Committee will meet on February 2nd at the same venue.



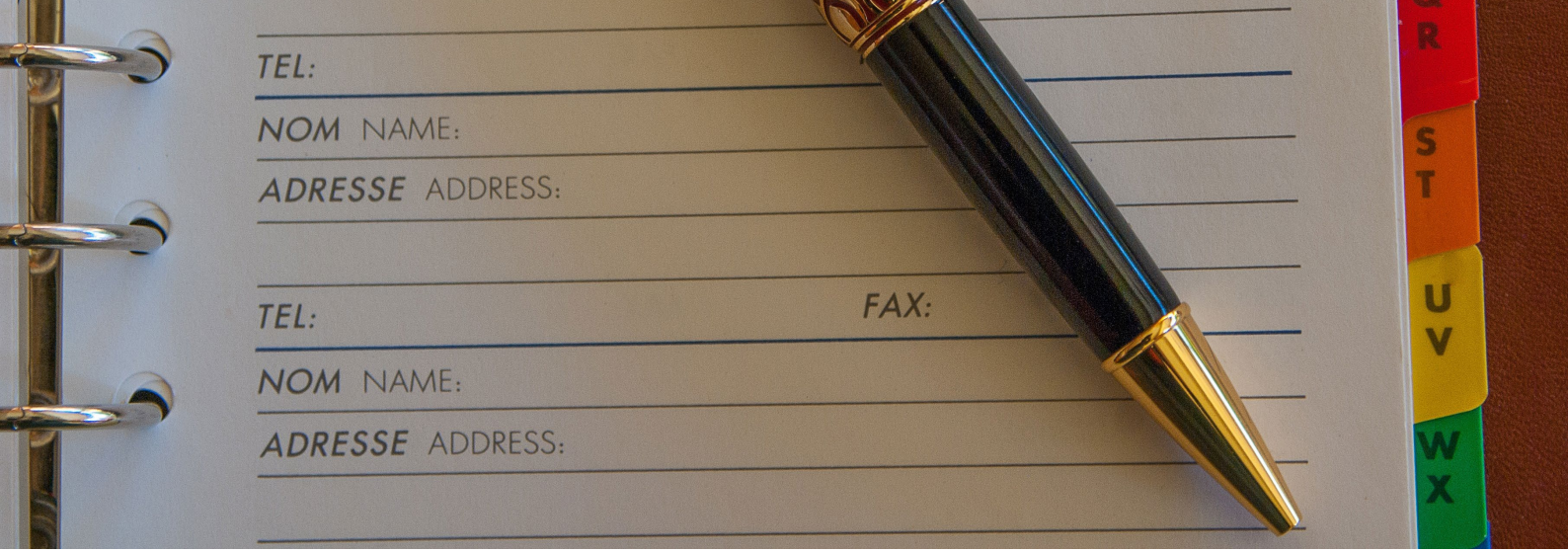
3. QUALMS questionnaire

Quality of Life in Myelodysplasia (QUALMS) is a questionnaire assessing quality of life, specifically for MDS patients. This questionnaire has been introduced in the EUMDS registry as part of the new protocol V5.1 (not all countries, see below for available languages) and comprises 38 questions that allows scoring of physical and emotional burden, benefit finding, and total QUALMS score.

The questionnaire may be used as an app for Apple tablets. This app saves time for data entry, thus the costs for the tablet are redeemed quickly. In addition, EQ-5D may be entered using the same app via tablet. Answers are transferred automatically from the tablet to the EUMDS database. When using the paper version, the answers have to be entered manually to the database.

The QUALMS questionnaire is currently available in English, Dutch, French, German, Italian, Korean, Portuguese, Russian, and Spanish. Additional translations are currently ongoing. Prerequisite for the application of QUALMS is ethical approval of the amended version of the protocol (v5.1) and the updated EUMDS case report forms.

We encourage the assessment of patients with this novel MDS specific questionnaire, ultimately aiming to consider and integrate disease-specific symptoms and patient perspectives.



4. Centre contact details and affiliation information

We are happy that the centre contact information has been completed for several centres in France and the Netherlands. **We ask all sites that have not yet completed the data, do so as soon as possible.** Complete and up-to-date contact information for all participating sites is important to improve communication, but among others also for acknowledgment of contributions in the output that we are generating as a project.

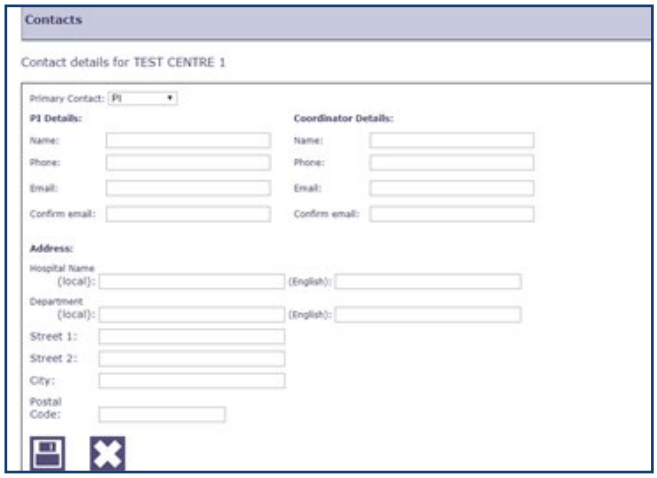
Contact information of the 'Local Principle Investigator' as well as 'Local Study Coordinator' should be completed by one person with a registered log-in for each participating site (or the country coordinator), and should be kept up to date.

Local sites that have more than one clinical investigator for EUMDS should add the clinical investigator serving as primary contact as Principle investigator and can add the other clinical investigators as described in the next paragraph. Because centre contact information is also used for affiliations, we ask you to provide the formal local as well as English names of the hospital and the department.

Additional local staff involved in the EUMDS Registry who want to receive Newsletters and other EUMDS communications, but do not have a registered log-in can be added at 'Administrator email addresses for centre'.

How to access, enter or edit centre contact details

1. Click Centre Administration on the home screen
2. Click Edit contact addresses for centre
3. Complete the form
4. Return to home screen
5. Click Administrator email addresses for centre to add further local staff who would like to receive EUMDS communications



5. From the monitor: Karnofsky score

After almost 1 year of being the monitor for the EUMDS registry, I would like to share some of my findings.

Overall the sites that I have visited have high quality data entry and have a well structured, up-to-date ITFs.
However, the data that is most often missing in the database (and source files) is the Karnofsky performance status (or other equivalent like ECOG).

In protocol v5.1 the Karnofsky performance status is part of the core outcome set and is instrumental in the statistical analysis. Therefore, please encourage everyone at your site who is responsible for Karnofsky score collection to do so **and record it in the source files**.

Peter

Peter Karel,
EUMDS Monitor

Karnofsky status:

Able to carry on normal activity and work; no special care needed	100	Normal - no complaints; no evidence of disease
	90	Able to carry on normal activity; minor signs or symptoms of disease
	80	Normal activity with effort; minor signs or symptoms of disease
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed	70	Care for self; unable to carry on normal activity or do active work
	60	Requires occasional assistance, able to care for most personal needs
	50	Requires considerable assistance and frequent medical care
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly	40	Disabled, requires special care and assistance
	30	Severely disabled; hospital admission is indicated although death not imminent
	20	Very sick; hospital admission is necessary; active supportive treatment necessary
	10	Moribund; fatal processes progressing rapidly
	0	Dead

6. Substudies update

Overview of substudies

During the investigators meeting in Valencia in May 2017 many investigators expressed their interest in planned and ongoing studies within the EUMDS registry and would like to be updated regularly.

An overview 'in a nutshell' of ongoing sub studies:

- **Demographics**
- **ESA**
- **Cytomorphology**
- **HRQoL**
- **Iron sub study**
- **Iron chelation**
- **Transfusions**
- **BM metaphases**
- **Kinetics of cytopenias**
- **MDS and solid tumors**
- **del5q**
- **BM fibrosis**
- **TRIAGE-MDS (FP7)**
- **MDS-RIGHT (H2020)**
- **Auto-immune disorders**
- **Thyroid disorders)**
- **Metformin**
- **del20q**
- **Non invasive diagnostics**
- **SF3B1**
- **Diabetes**

Publications

In addition to the ESA paper, this year two more articles have been published/ accepted for publication:

- de Swart L et al. Cytomorphology review of 100 newly diagnosed lower-risk MDS patients in the European LeukemiaNet MDS (EUMDS) registry reveals a high inter-observer concordance. Ann Hematol. 2017 Jul;96(7):1105-1112 PMID: 28526957

- de Swart L et al. Labile plasma iron levels predict survival in patients with lower-risk Myelodysplastic syndromes. Haematologica 2017 Nov (online)

Another four articles have been submitted for publication in various scientific journals.

Presentations

At ASH-2017 in Atlanta, Raphael Itzykson presented the Kinetics of Cytopenia and Marlijn Hoeks the Iron Chelation sub studies. Posters were presented for the Transfusion (de Witte), Non-invasive diagnostics (Oster/ Mittelman), and Diabetis (Symeonidis) sub studies.

Interested?

If you are interested in initiating a new sub study or if you would like to join an existing sub study, please contact the national PI of your country. If you do not have the contact details of your national PI, please contact project management: Karien.croezen@radboudumc.nl.

7. Substudy in the spotlight: Non-invasive diagnosis of MDS

Professor Moshe Mittelman, national P.I., Israel

Anyone who treats MDS and especially anyone who suffers from MDS knows that the diagnosis is made with a bone marrow (BM) examination. While it is not the worst of examinations, it is still invasive and painful. We are advancing our work to see if we can diagnose MDS non-invasively for at least some of the patients. We have been developing models that incorporate clinical, demographic and laboratory data. We know that there are characteristics that are associated with patients who have MDS. For example, they are usually 60-70+ years old and their red blood cells have a relatively high mean corpuscular volume (MCV). Can we use these and other data to help discriminate between patients with and without MDS?

In our initial study, we built a statistical (logistic regression – LoR) model using the data from 48 MDS (BM proven) patients and 63 (BM ruled-out) control patients, and we found that in approximately 50% of the patients, we could diagnose or rule out MDS with 80-85% accuracy. We then validated the results with 40 additional patients. In about half of the patients we could perhaps avoid a BM examination. For the rest of the patients, the invasive examination would still be needed in order to make a definitive diagnosis.

At this time, we are working closely with the EUMDS registry and the team at York University, incorporating the data of hundreds of MDS patients from the registry and a similar number of controls from the Tel Aviv Sourasky Medical Center, and examining the ability of an LoR model as well as a gradient boosted (GB) model to make or rule out the diagnosis.

The initial results are very encouraging and exciting. We believe that this work will further improve the non-invasive diagnostic model for MDS. The work will be presented at the 2017 meeting of the American Society of Hematology (ASH) this December.

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