Newsletter Issue 20
April 2018

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1. Message from the Chair

Welcome to April 2018 EUMDS newsletter

The registry has been extended to include high-risk MDS and other subgroups. Although the transitional phase of extending our Registry to high-risk MDS and other subgroups has not been completed yet, it is rewarding to see that we have already included more than 50 of these patients.

We have completed our new CRF, including the health care utilisation data for the MDS-RIGHT project. We are glad that we can reimburse separately for reporting these additional data, since these data are very important and unique

Our Registry is enjoying an attractive number of publications this year: three articles have been published and three additional manuscripts are either on the desk of the editors or about to be submitted to high ranking journals.

This rewarding success has been achieved by your commitment. The steering committee is grateful for your dedication and we are looking forward to continue collaborating with you all.

Theo de Witte
EUMDS Chair

2. Health care resource utilisation data

Andrea Manca and Tom Patton, University of York

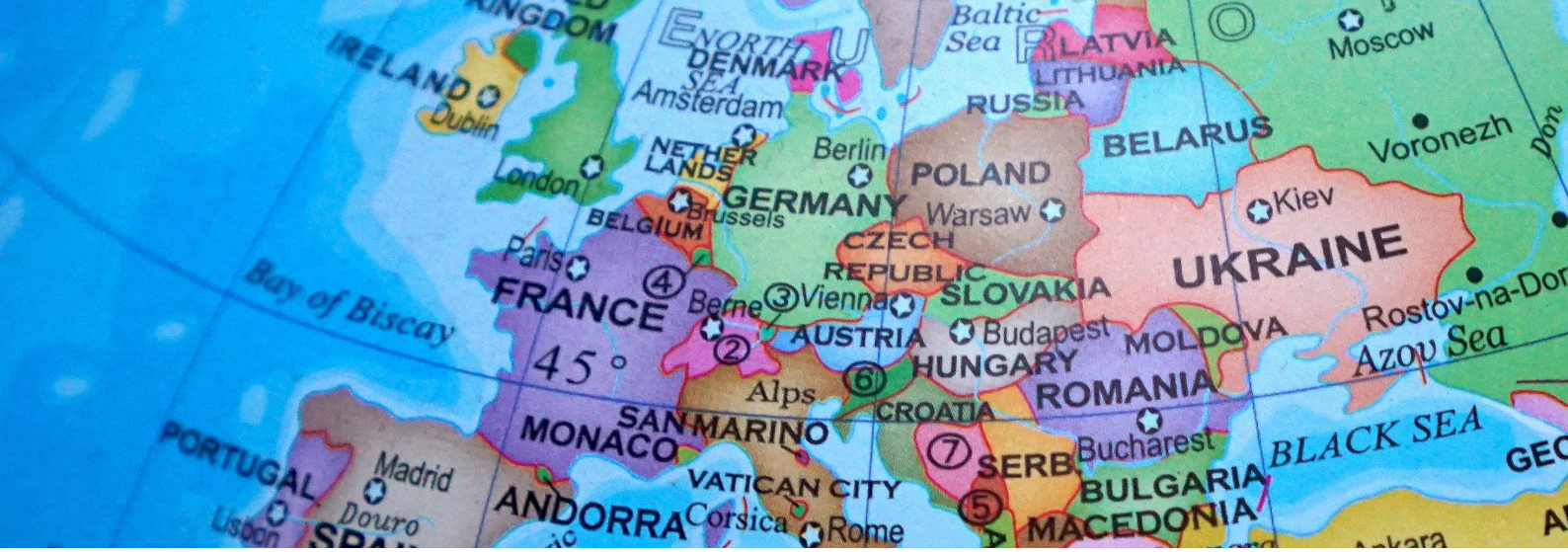
One of the main objectives of the EUMDS Registry is to generate evidence on (lower-risk) MDS patients in the 'real life' setting, among others to identify what treatments patients receive in healthcare systems throughout the participating countries. Many countries nowadays require robust assessments of the costs and health outcomes resulting from treatments received by patients. This is to ensure an efficient use of the limited resources available.

The quality of these assessments depends critically on the accurate collection of clinical and economic real-world data. To this end, the Steering Committee of the EUMDS Registry decided that additional information on health care resource utilisation (HCRU) by patients would substantially increase the overall value of the Registry. In 2017, the CRF were updated to include additional items on hospitalisations, emergency care visits, outpatient visits and primary care appointments.

The collection of HCRU data in EUMDS has started, albeit slowly. We would like to motivate all participants to collect HCRU data within our Registry by emphasizing its importance. The HCRU data will inform our research activities aiming to quantify MDS-related health care costs according to patient and country characteristics (as part of MDS-RIGHT work package 1).

It is important that data on health care visits are collected in patients across all of the countries involved in the registry, because we know that clinical practice varies across countries, as well as the availability of specific treatments and this can influence how patients are managed. This information will allow us to reflect differences in the way that health care services are financed and delivered across the participating countries. Without country-specific data on patient contacts with the health care system, it will be extremely difficult to deliver these results that are both empirically robust and meaningful to local policy and clinical decision makers.

Taking all of these factors into consideration, we would strongly urge all colleagues involved in the collection of data for the EUMDS registry to complete the items on health care resource utilisation. The new visit fees will be allocated to the data sections that have been completed, and there will be a specific amount for reported HCRU data.



3. Accrual

Corine van Marrewijk, Radboud University Medical Centre

We are proud of what the EUMDS Registry has already achieved thanks to the joint efforts of all participants. Since 2008 the EUMDS Registry has steadily evolved to a valuable dataset, currently containing information on 2376 patients (fig 1) and over 12000 visits. Since the extension to the General EUMDS Registry in July 2017, eighty patients (7 countries) have been registered with Higher-risk MDS or one of the other diagnostic groups (fig 2).

We have now reached a stage that the Registry is generating relevant data (6 publications and over 35 conference abstracts) contributing to the optimization of management of patients with MDS.

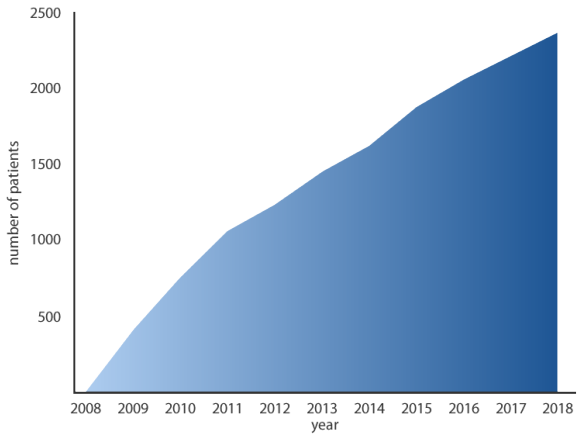


Fig 1: cumulative inclusion - overall

We are grateful for your continuing commitment and the perseverance during the previous years. We are confident that the Registry will continue at the same or increased pace with the recent financial amendments, upcoming new contracts and the completion of implementation of protocol V5.1 in all countries.

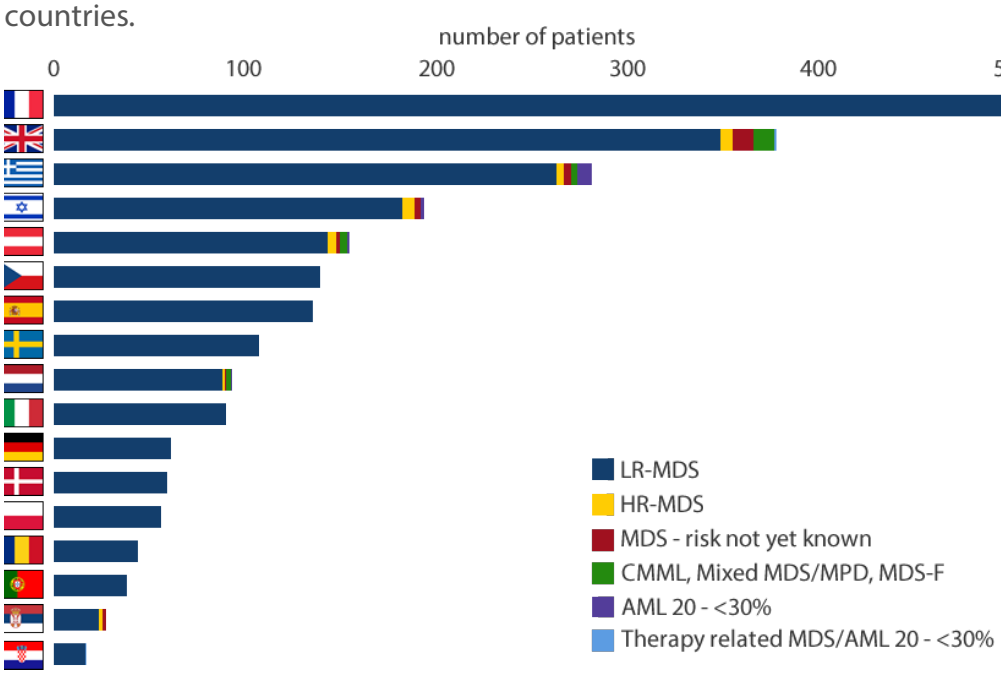


Fig 2: inclusion by country and diagnostic group

4. EUMDS@ASH - kinetics of cytopenias

Raphael Itzykson, Saint-Louis Hospital, Paris

The prognosis of patients with 'lower-risk' myelodysplastic syndromes remains heterogeneous. Lower hemoglobin, platelet and neutrophil counts at diagnosis have long been known to predict a worse outcome.

In this study, we wondered whether analyzing the change in those parameters over the first months of follow-up could provide additional information on their risk of disease progression and death. We notably wondered whether looking at the kinetics of these simple blood parameters could identify patients with poorer outcome before their levels in platelets or neutrophils reached the thresholds usually considered to carry prognostic significance.

We did not study the changes in hemoglobin levels, because these are likely to fluctuate in the large proportion of patients who receive blood transfusions. We thus looked at the drop in platelets and neutrophils over the first six months of follow-up after diagnosis and inclusion in the registry.

We found that more than 20% of patients had lost more than one fourth of their platelets over this 6-month observation period. Intriguingly, platelet counts dropped faster in patients receiving red blood cell transfusions. Importantly, a drop in platelets greater than 25% compared to the count at diagnosis was predictive of increased risk of progression to acute myeloid leukemia, and shorter survival, even when accounting for other known prognostic factors.

Altogether, this study suggests that close inspection of platelet counts during the first six months of follow-up, even in patients retaining seemingly normal platelet counts, can help identify patients with a worse prognosis, potentially requiring a specific management and surveillance.

5. EUMDS@ASH - iron chelation

Marlijn Hoeks, Leiden University Medical Centre

Red Blood Cell Transfusions (RBCT) contain about 200-250 mg of iron per bag, which is a hundredfold of the daily needed amount of iron to maintain iron homeostasis. Transfusion-dependent MDS patients are therefore at risk for development of secondary iron overload, which is associated with morbidity and even mortality. Many previous studies suggested an improved overall survival after treatment of iron chelation therapy; a treatment to excrete the excess of iron. However, those studies suffered from serious methodological problems. The aim of our study within the EUMDS registry was to assess the effect of iron chelation therapy on overall survival.

We compared chelated patients with a contemporary, non-chelated control group, that met eligibility criteria for starting chelation therapy (having received ≥15 RBCT; or ≥1 RBC unit per month in six consecutive months; or a ferritin level of >1000 µg/L) with two different statistical methods. From 2200 included patients, 689 patients were eligible for using iron chelation therapy according to the predefined criteria. From these patients, 198 received iron chelation therapy and 491 did not receive iron chelation therapy.

The hazard ratio (HR) for overall survival for chelated patients, adjusted for relevant confounders in the Cox model was 0.50 (95%CI 032-0.79) and in the propensity-score matched analysis 0.43 (95%CI 0.27-0.66). The results of this study suggest that iron chelation therapy may improve overall survival in lower-risk MDS patients.

6. Posters@ASH

In addition to the presentations already mentioned, various EUMDS posters were also approved for presentation at ASH:

- The impact of diabetes mellitus as comorbid condition, in patients with lower-risk MDS
- Can we diagnose MDS without bone marrow examination? A proposed EUMDS based non-invasive model
- Impact of red blood cell transfusion density on progression-free survival in lower-risk MDS patients included in the European LeukaemiaNet MDS (EUMDS) registry

7. Ongoing and new studies within EUMDS

Theo de Witte, Radboud University Medical Centre

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.

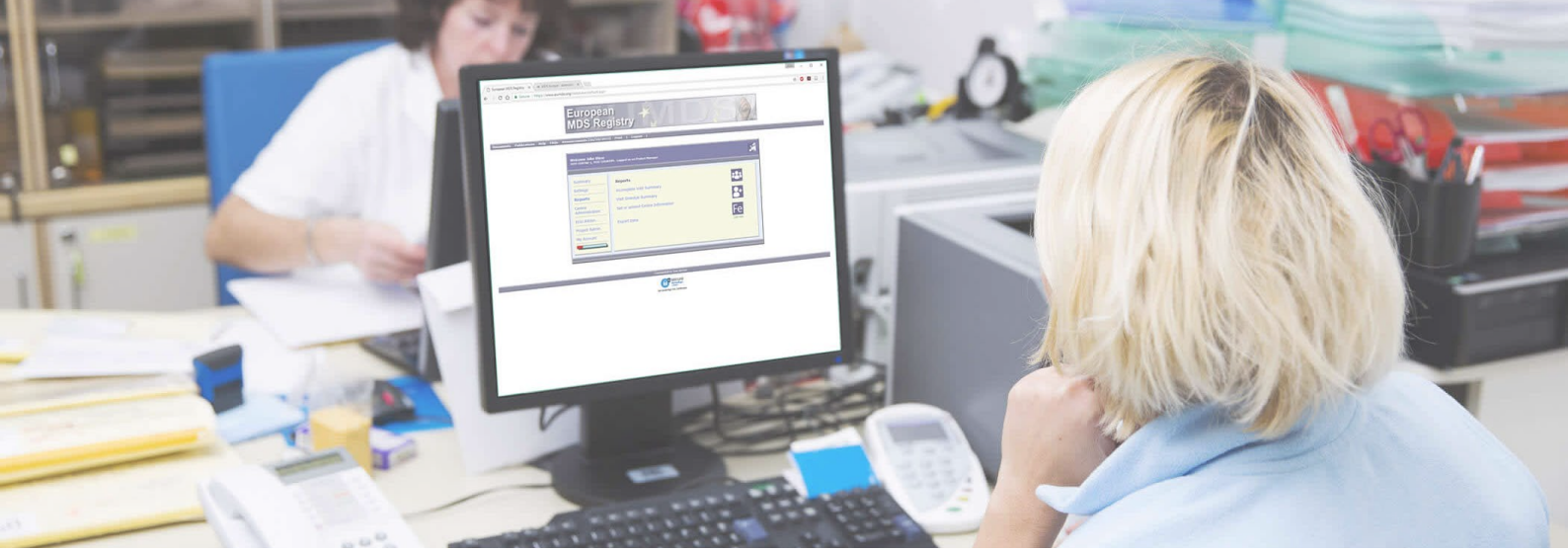
In addition, the ongoing research projects (TRIAGE-MDS and MDS-RIGHT) contribute substantially to our ongoing and planned studies. Both projects are progressing well, but they will be completed within the next 2 years. Therefore, a new grant application to the Horizon 2020 program is being developed.

This project will focus on the ever increasing pro-inflammatory status and immune suppression associated with MDS specific gene mutations during progression of the MDS clone and several frequently occurring co-morbidities.

Quite a few of the recently developed 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 low-risk MDS
- the impact of antidepressive drugs (serotonin antagonists) on outcome of MDS
- the role of metformin on progression of MDS
- the role of hypomethylating agents on auto-immune diseases.



8. Database updates

John Blase, University of York

A series of minor updates have recently been made to the EUMDS database and to the data we are asking you to collect:

1. For each patient, you will now be required to confirm which version of the study protocol they were included under (either 2.2 or 5.1). This will change various options available to you throughout the database, so please ensure you enter this data accurately. For example, patients included under protocol 2.2 become ineligible once disease progression is recorded in the database whilst progression is not recorded for patients included under protcol 5.1.

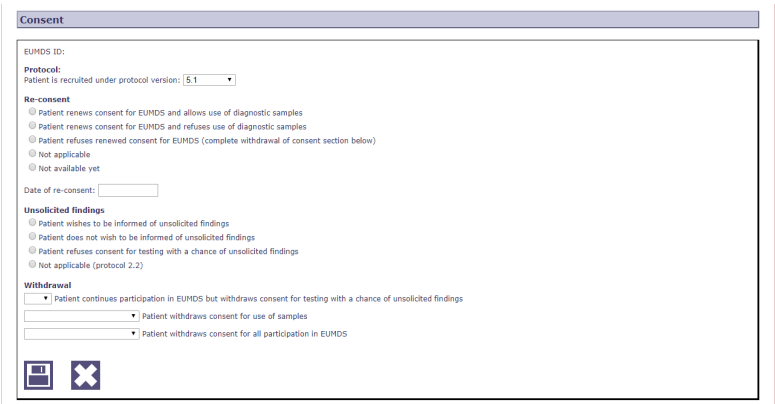
2. The consent status for each patient is now required at the registration visit - the items of consent are different depending on the protocol the patient was included under.

3. Consent and re-consent data items have been removed from the Biological Samples section and given their own section in the database.

4. Biological Samples data has been moved to the Core Data section of the patient summary screen.

5. Detailed information can now be recorded for intensive chemotherapy and stem cell transplant at follow-up visits (*not* registration) in the MDS Treatment section.

6. Updated CRFs have been issued to reflect these changes and can be found in the Documents section of the database.



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