Newsletter European MDS Registry

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From the chairman

This newsletter of the EUMDS registry will be devoted to new developments in our Registry study. The amended protocol will incorporate new issues, like inclusion of all sub categories of MDS and related disorders, collection of material for genetic analyses, more data on treatment modalities and health economics. The aim is to collect data on at least 3000 low-risk and 1,000 high-risk MDS patients. It is clear that for the execution of the full study we need additional funding from various sources, including the EU and pharmaceutical patrons. Therefore, we have developed various patron levels.

Data collected within the EUMDS Registry have been used in many projects and sub studies developed within the EUMDS Registry. The first study has been published in the British Journal of Haematology; another study has been submitted for publication and the third study will be submitted in a few months. We are happy that Alex Smith could extend her team with new collaborators to facilitate the progress and output of our projects.

More and more countries, sites and scientists are participating in the Registry. Therefore, we modified the organizational structure of the EUMDS registry and nominated an executive committee for the daily coordination of the registry.

I would like to thank you all for your continuous effort in this project and your involvement!

Theo de Witte

Accrual

Thanks to the efforts of all participants, we have reached the target of 2000 patients before the end of 2015. Thank you all for your commitment and dedication!

As the chairman already indicated, our new target is 4000 MDS patients. Currently, 2048 patients from 17 countries have been included in the EUMDS registry. By the end of 2016 we hope to have reached 2.300 included patients.

New protocol

As mentioned in the previous newsletter the current version (2.2) of the protocol has been modified and has been approved by the Steering Committee in February.

The amendment of the protocol is necessary, to maintain the high standard of the database and to keep our scientific approach up-to-date. One of the major changes is the collection of genetic material; genetic insights are of major importance to understand the mechanisms underlying MDS and therefore to 'personalize' treatment of MDS-patients.

The following major changes are made in the new protocol:

- Inclusion of **new sub categories** of MDS (IPSS intermediate-2 and high risk, AML with 20-30 % marrow blasts – formerly RAEB-t and CMML)
- **New recruitment target**: 3000 lower-risk MDS and 1000 higher-risk patients.
- **Extension of recruitment period** *at least* until May 1st, 2020

- **Extension of the follow up** until withdrawal for any reason, or termination of the registry (up to 12 years of follow-up, *or beyond*)
- Besides serum samples, also **genetic samples** will be collected
- **Modified informed consent form**, including collection of genetic material and explanation of 'unsolicited findings'.
- **Re-consent information and consent form** for all living patients still participating in the registry.
- Addition of a **withdrawal form**
- **Modified CRF**

The patient information and informed consent form has been revised to cover the changes in the protocol. Final versions will be sent to the Operational Team (OT) member of your country as soon as possible. In every country the updated documents have to be amended to fit national or local requirements and submitted for ethical or regulatory approval. The OT-member of your country will initiate this procedure and they will be in contact with you for implementation in your hospital.

Please, feel free to contact your OT-member or the overall project management team in case you have comments or questions about the implementation of the new protocol.

Rationale for genetic research

In today's medicine, a 'trial-and-error'-approach in treating patients is commonly used in order to find the treatment that is most effective for that particular patient. In the field of MDS, developments show that genetic research enhances the understanding of MDS and its treatment options considerably. By gaining more insight into the genetic mechanisms underlying MDS, treatment can be improved – either by better targeting current treatments or by developing new treatment modalities – and the 'trial-and-error'-strategy might be exchanged for *a more personalized approach*: therapy with the right drug at the right dose in the right patient. This will lead to more cost-effective and accurate medicine, benefiting both patient and society.

The addition of collection of genetic samples from diagnosis (like EDTA-blood, isolated DNA or BM-aspirate) will be a valuable asset for the Registry. This will enable us to provide a scientific contribution to the evolution of 'personalized medicine' for MDS-patients.

For patients to be included according to the new protocol, these samples can be collected prospectively. Unfortunately, this is no option for already included patients. For these patients we would need to rely on materials collected at diagnosis for other purposes (e.g. stored clinical samples). Therefore, we would like to ask participating sites to try to retrieve (clinical) samples that could be used for genetic research, after patients have given re-consent.

Sub study in the spotlight: Metformin Study

Bone marrow failure and progression to acute myeloid leukaemia (AML) are the main risks of lower-risk MDS. If MDS-cells develop into AML cells, this will be accompanied by other biological cell characteristics. For example, AML cells need more energy and are likely to be more dependent on glucose. Therefore, we hypothesize that the anti-diabetic drug metformin could affect the progression of MDS to AML by lowering blood glucose levels.

In order to investigate this, we need to know which patients with MDS and diabetes actually use metformin. Until now, this data has not been collected in such detail. For all patients identified with diabetes in the EUMDS Registry, you will receive a small questionnaire to ask whether your patient used metformin and at which dose. Further, we like to know whether your patient also used insulin or other anti-diabetic agents.
The outcome of this study could be that treatment with a cheap, widely used and well tolerated agent (metformin) reduces the risk of progression of MDS to AML.