News from the MDS-RIGHT Study • For all MDS Stakeholders

# NEWSLETTER



MDS RIGHT

Providing the right care to the right patient with MyeloDysplastic Syndrome at the right time

MDS-RIGHT Kick-off Meeting, Vienna, Austria, 11 June 2015

MDS EUROPE mdseurope.eu

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European Commission
Horizon 2020

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# Welcome to MDS-RIGHT!

MDS-RIGHT is a European research project focusing on the anaemia (a shortage of red blood cells) of elderly patients with lower-risk myelodysplastic syndromes (MDS), and comparing the effectiveness of existing healthcare interventions in this situation.

MDS are a group of increasingly prevalent blood cell disorders leading to a failure of the bone marrow to produce healthy blood cells. MDS are usually complicated by severe anaemia, affecting 50 to 70,000 mainly elderly Europeans and impacting their quality of life and survival. MDS care is complex and challenging. Available interventions in the elderly generally do not cure MDS, but aim to ameliorate related symptoms and to improve quality of life. MDS under- and overtreatment is a growing financial burden both on patients and on healthcare systems across Europe.

About 25% of lower-risk MDS patients develop acute myeloid leukaemia (AML), a blood cancer. The MDS-RIGHT study uses data from the **European MDS Registry** (>2,200 patients from 16 European countries and Israel) and the **Dutch LifeLines** reference population (>14,000 elderly individuals). As a result, better guidance for MDS diagnosis and treatment will facilitate better patient care and treatment compliance, and a more effective use of healthcare resources.

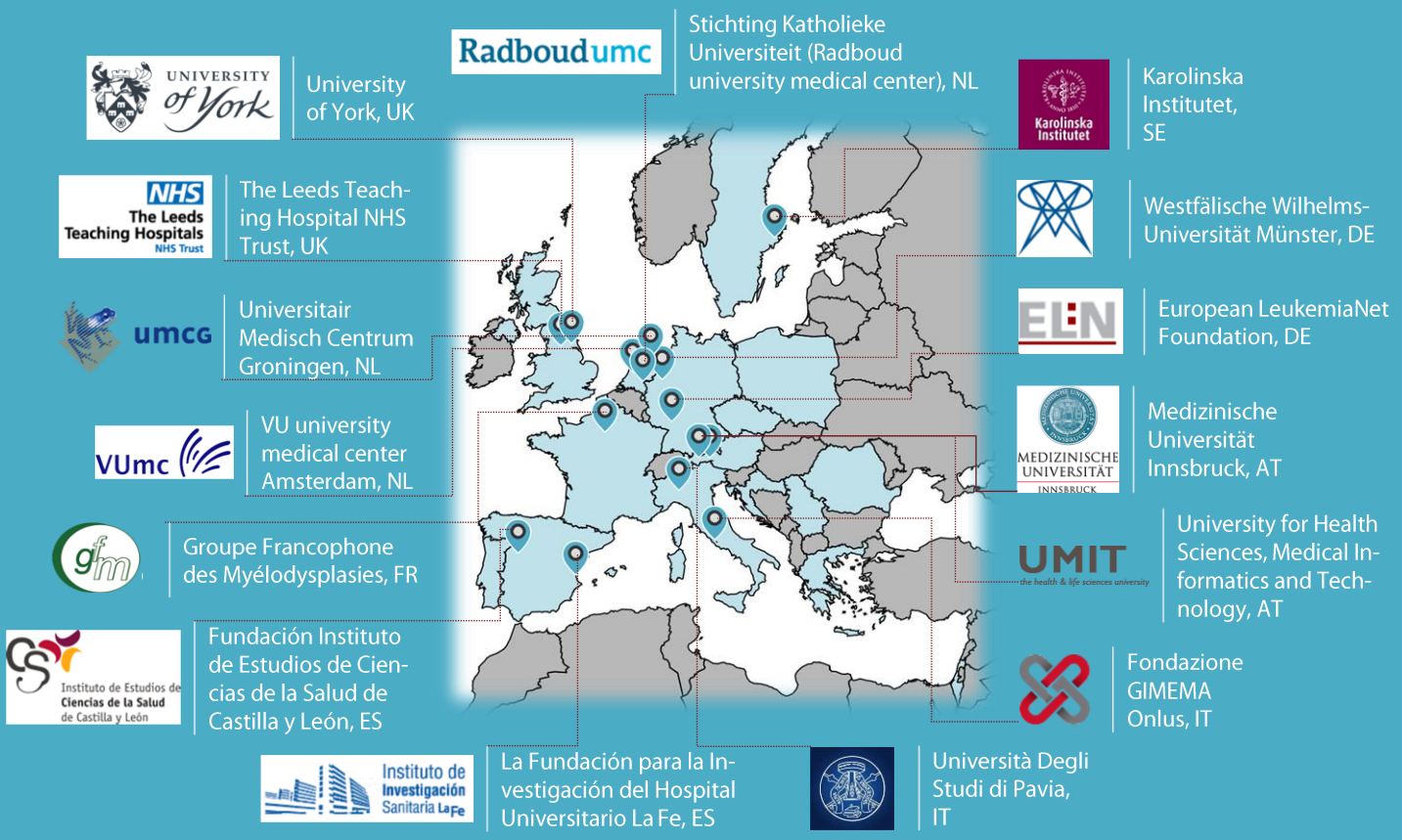
MDS-RIGHT is a 'Personalising Health and Care' study that is funded by the European Commission. The 5-year project started in May 2015. It is coordinated by the Radboud university medical center at Nijmegen, the Netherlands. The collaborative work of the MDS-RIGHT research consortium is organised in seven highly interacting and interdependent work packages, involving 15 project partners from eight European countries.

**For a detailed outline of MDS-RIGHT and its objectives and expected impacts, or to get in touch, please visit: https://mds-right.eu/.**

## Main MDS-RIGHT Objectives

- To compare outcomes, costs and approaches to the diagnosis and treatment of MDS and anaemia of the elderly (AoE)
- To assess genetic and epigenetic abnormalities (heritable changes in the set of an individual's genetic information) in MDS and AoE
- To develop more effective and safer evidence-based, tailored interventions for elderly patients with lower-risk MDS and AoE

## MDS-RIGHT Partners



# Work Packages and Progress

| Work Package 1<br>Health care interventions | Work Package 2<br>Diagnostics and bioinformatics | Work Package 3<br>HRQoL issues in patients with anaemia | Work Package 4<br>Treatment outcome prediction | Work Package 5<br>Practice guideline development | Work Package 6<br>Dissemination, exploitation, communication | Work Package 7<br>Project management/ consortium |
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| ➔ Perform data management, HTA (health technology assessment) and statistical analysis on efficacy, cost and quality of life (QoL) | ➔ Introduce new scientific techniques into the diagnostic approach of lower-risk MDS patients and healthy controls within this project | ➔ Analyse health-related quality of life (HRQoL) issues in AoE, based on the EUMDS registry and the Dutch LifeLines reference population | ➔ Focus on existing and new core outcome sets (COS) and develop new and better treatment-outcome prediction models | ➔ Analyse ethical, legal and policy issues as well as social and user-acceptance and produce evidence-based clinical practice guidelines | ➔ Interact with stakeholders and end-users to generate acceptance and facilitate the endorsement and uptake of MDS-RIGHT guidelines | ➔ Focus on project management and consortium co-ordination, as well as on monitoring the observational trials within this project |
|  <br>Prof. Andrea Manca, PhD, University of York, UK<br>WP Leader |  <br>Prof. Joop Jansen, PhD, Radboud university medical center, NL<br>WP Leader |  <br>Prof. Reinhard Stauder, MD MSc, Med. Universität Innsbruck, AT<br>WP Leader |  <br>Prof. Luca Malcovati, MD PhD, Università Degli Studi di Pavia, IT<br>WP Leader |  <br>Prof. Eva Hellström-Lindberg, MD PhD, Karolinska Institutet, SE<br>WP Leader |  <br>Prof. Pierre Fenaux, MD PhD, Groupe Francophone des Myélodysplasies, FR<br>WP Leader |  <br>Prof. Theo de Witte, MD PhD [CO], Radboud university medical center, NL<br>WP Leader |

## Progress Update

**MDS-RIGHT is well on track. During the first 18 months, a solid basis has been provided for achieving the expected impacts of the 5-year project:**

**1.** A core dataset containing demographic, diagnostic and prognostic information, treatment history, laboratory measurements, HRQoL and outcome (disease progression free survival (PFS) and overall survival (OS)) has been extracted from the European MDS Registry (EUMDS), including a mapping of MDS treatment pathways.

A detailed health economic statistical analysis plan was developed and, as a first step, the impact of healthcare interventions, including iron chelation (removing iron from the body) on OS (poster at ASH 2016) and of erythropoiesis (red blood cell formation)-stimulating agents (ESAs) on PFS and OS, was analysed. A related scientific manuscript was published (JIM 2016).

In addition, a data collection strategy was developed for quantifying the utilisation and the costs of healthcare resources for the management of lower-risk MDS patients, including hospital and outpatient visits, primary care appointments, medicines, dosage, mode of administration, dosing schedule and other parameters.

**2.** A central 'bioinformatic pipeline' for data collection and quality assessment has been established, and clinical (disease progression, outcome and HRQoL) and genetic data are being integrated to enable a comprehensive genetic analysis in lower-risk MDS patients. Two scientific manuscripts related to the bioinformatic pipeline are published and one is in preparation.

Proper DNA (molecules carrying genetic information) samples have been collected and analysed, in order to validate the diagnostic and prognostic impact of frequently occurring molecular mutations.

The collection and transfer of additional DNA samples will continue, to allow the definition and identification of patients whose DNA will undergo methylation profiling (the analysis of cell mechanisms for controlling how genetic information is converted to a protein), in addition to analysing for MDS-related gene mutations.

Furthermore, a phenotypic/physical characterisation of MDS cells by flow cytometry (FCM, a method for analysing cell surface markers) is underway and will allow additional MDS-related analyses.

**3.** To be able to analyse health-related quality of life (HRQoL) issues in anaemia of the elderly (AoE), several preparatory steps have been taken to implement and validate cross-culturally an MDS-specific QUALMS (QoL in Myelodysplasia Scale) questionnaire in the EUMDS Registry.

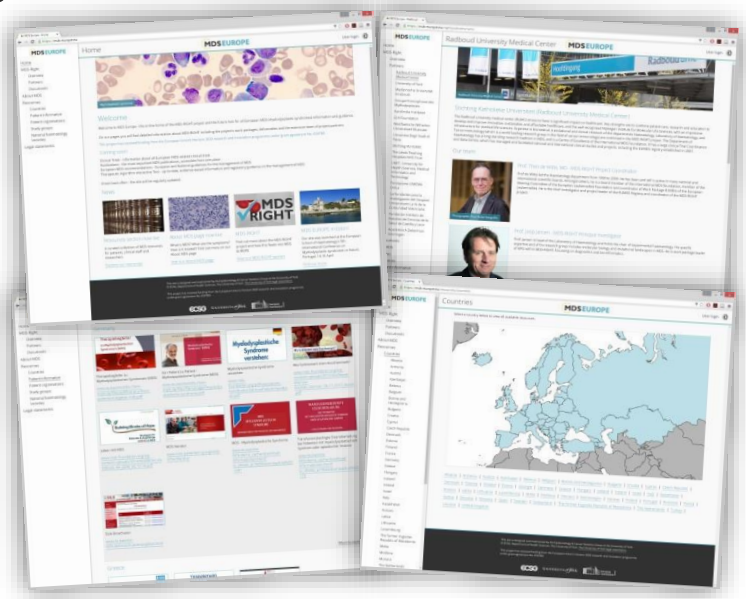
To provide an overview of the most frequently used outcomes among MDS studies and to initiate the establishment of MDS-specific core outcome sets (COS), more than 1,300 MDS patient- and clinically relevant outcomes that fall into 25 major categories were evaluated and stratified for clinical intervention groups. In addition, relevant patient-reported outcomes (PROs), including symptoms, activity limitations, and patient satisfaction, are being identified and categorised, based on systematic scientific literature reviews and on international surveys.

In parallel, a first analysis of HRQoL in lower-risk MDS patients registered in EUMDS has been performed to evaluate the HRQoL impairment in lower-risk MDS in comparison to reference populations. A related scientific manuscript is in preparation.

**4.** Relevant statistical methods for analysis have been defined for the identification of molecular defects with prognostic value and for the development of new predictive models for response to specific treatment modalities integrating clinical and molecular variables.

In addition, statistical methods for the identification of genetically defined MDS subtypes that may benefit from novel targeted treatments have been defined, with the aim to identify biologically homogeneous patient subgroups with respect to the variables of interest.

Relevant samples from more than 400 individuals with AoE have been identified and selected from the LifeLines reference population. The first samples have been sequenced to gain insights into the frequency of molecular abnormalities in (unexplained) AoE in a general population, and to elucidate the relation between unexplained AoE, age-related clonal haematopoiesis (the formation of blood cells derived from one abnormal stem cell) and MDS. The analysis will help to identify molecular characteristics with a positive predictive value for MDS, and to validate the mutational analysis of peripheral blood cells as a diagnostic tool in individuals with unexplained blood cytopenia (a shortage of cells).



**5.** Relevant approved MDS guidelines/recommendations have been evaluated and uploaded on the newly developed **MDS-Europe** online platform. The website will be regularly updated, whenever new relevant guidelines/recommendations or updated versions are published. In addition, the general international MDS guidelines (Blood 2013) were updated, in particular with regard to allogeneic (genetically different) haematopoietic (blood building) stem cell transplantation (HSCT). HSCT scenarios for MDS patients were developed and the impact of individual components of the current MDS prognostic scoring systems was analysed.

A manuscript on the 'Recommendations for the use of HSCT in MDS' was published (Blood 2017). Furthermore, synergies with other research projects (LeukemiaNet, Swedish Cancer Society, Swedish Research Council) have led to additional MDS-related publications.

A comprehensive outline and a format for a dynamic, interactive MDS guidelines online tool for healthcare providers were developed for implementation on the MDS-Europe online platform. The tool will allow the continuous integration of new evidence generated by MDS-RIGHT. The online tool is planned to be extended also for use by patients and regulatory agencies.

**6.** A detailed plan for the dissemination, exploitation and communication of study results and a comprehensive catalogue of MDS collaborative groups, documents and contacts have been developed to create a European multi-stakeholder MDS competence network for sharing MDS information and knowledge.

A corresponding **website** was developed in responsive design (for PC, tablet, smartphone etc.) as the central hub of the multi-stakeholder network, including an **MDS-RIGHT project section**. The platform will be continuously expanded, offering access to MDS-related resources, research groups, patient and professional organisations, information on clinical trials, registries, scientific publications, practice recommendations, links, news and events, and a dedicated MDS community section with a moderated blog for continuous MDS stakeholder interaction.

In addition, template materials and PR guidelines, project updates via partner newsletters (EUMDS, European LeukemiaNet), information exchange at consortium meetings and continuous visibility around international scientific congresses have been used for generating awareness and endorsement across European MDS stakeholder groups.

**7.** The progress of the MDS-RIGHT project is continuously monitored by the project management and also by each individual project partner. Parallel to MDS-RIGHT, the EUMDS Registry has evolved substantially with regard to the number of lower-risk MDS patients enrolled, data collection and other aspects. The co-ordination, overall management and process monitoring of all activities carried out within the EUMDS Registry and the MDS-RIGHT project require the frequent organisation of regular project conferences and meetings in different formats, as well as continuous and seamless day-to-day communications with and between all project partners involved in the closely interacting and interdependent work packages and also with many external parties and with the EU Commission as the funding agency.

To ensure that all EUMDS Registry and MDS-RIGHT activities are always performed in a consistent fashion and in accordance with existing regulations, project partners are continuously supported with regard to project-related contractual or legal negotiations and required and obligatory reporting and documentation, also through the ongoing provision, review and approval of project-related formats and templates.

# News and Announcements

## Your Opportunity to Engage in Multi-Stakeholder Discussions

The **Community section** of the **MDS-Europe website** now offers a dedicated English-language online platform for continuous MDS stakeholder interaction to facilitate the exchange of views on different aspects of MDS management and research. The new multi-stakeholder platform has been set up as a blog that is moderated by MDS-RIGHT.

**All MDS stakeholders** are encouraged to express their views on the topics raised in the blog, by posting their comments, thus generating a continuously expanding online dialogue on a variety of important subjects. The blog is not intended for discussing personal or individual questions concerning MDS diagnosis or treatment.

## Join Us for the First MDS-RIGHT Multi-Stakeholder Meeting in Valencia!


**All stakeholders** interested in advancing the cause of MDS research, diagnosis, treatment and care are invited to attend the first MDS-RIGHT multi-stakeholder meeting: **European Perspectives on MDS Patient Management on 3 May 2017 from 16.00-18.00 hrs CET in Valencia, Spain**.

Held right before the opening of the MDS 2017 International Symposium, which you may already plan to attend, this meeting offers the unique opportunity to obtain new insights and exchange views directly with other MDS stakeholder groups, including medical researchers, doctors, nurses, MDS patient advocates, regulators, health technology assessment (HTA) experts, industry representatives and others.

Listen to our expert speaker panel and discuss about challenges and solutions concerning, for example, MDS treatment access, reimbursement, testing, clinical practice recommendations, Quality of Life, ageism, and patient information, to name but a few. Learn more about the progress of the MDS-RIGHT research project and get an exclusive first-hand demonstration of a new interactive online tool supporting MDS patient management in real time.

See you in Valencia!


Guillermo Sanz (ES)
Co-chair


Theo de Witte (NL)
Co-chair

The MDS-RIGHT meeting flyer, including the meeting programme and other information, can be downloaded by clicking **here**. **For free meeting registration, click here**. (Important: The MDS-RIGHT meeting is held in conjunction with the 14th International Symposium on MDS (MDS 2017), but it is not part of the MDS 2017 programme. The MDS-RIGHT meeting does not necessitate registration for MDS 2017. Registration for MDS 2017 is not free of charge and should be done via the **MDS 2017 website**.)