Minutes of European LeukemiaNet MDS workpackage Meeting during EHA meeting Stockholm, June 3 2005

Present: A. Giagounidis (Duisburg), D. Bowen (Dundee/Leeds), M. Lübbert (Freiburg), E. Hellström-Lindberg (Stockholm), M. Cazzola (Pavia), J. Jansen (Nijmegen), L. Malcovat (Pavia), F. Onida (Milan), P. Bernasconi (Pavia), R. Gologan (Boekarest), R. Invernizzi (Pavia), S. Levison-Keating (Nijmegen), J. Boultwood (Oxford), J. Cermak (Prague), T. Berg (Freiburg), F. Ficara (Torino) T. Wainscoat (Oxford), J. Sanz (Spain), N. Esoof (Oxford), S. Kahlenberg (Genzyme), L. Ballart (Genzyme), S. Maeser (Genzyme), W-K. Hofmann (Berlin), T de Witte (Nijmegen), P. Fenaux (Paris)

Agenda:
-1- Agenda & Incoming letters
-2- Proposal for diagnostic guidelines: E. Hellström-Lindberg
-3- Development of programme for new therapeutic guidelines MDS & management hypothetical patients: M. Cazzola/D. Bowen
-4- Clinical trial list website: T de Witte
-5- Interaction development new clinical trials: P. Fenaux
-6- Role of LeukemiaNet in accreditation new clinical trials: A. Ganser
-7- Organisation International Registry: D. Bowen/P. Bernasconi
-8- Proposal for organisation sample banking: J. Jansen
-9- Cooperation with AML: M. Lübbert
-10-Minutes 4rd MDS-WP meeting Heidelberg 1/2-2-05 and steering committee in Nagasaki, Japan, May 12, 2005
-11- Date new meeting: September in Pavia?

-1- Incoming letters:
Proposal of Dr. Jean-Loup Huret for collaboration on cases with rare chromosome aberrations. In principle there is agreement that collaboration is beneficial, especially in case of rare aberrations.

Letter will be posted on the WEB-site.

-2- Proposal for diagnostic guidelines: E. Hellström-Lindberg
In April 2005 an international working group has discussed morphological definitions of MDS subgroups (Portugal). This discussion has continued during a full day meeting at the MDS symposium in Nagasaki. Relevant adjustments in the classification and diagnostic guidelines will be incorporated in our guidelines: Germing/Hellström

In addition, the guidelines of the MDS WP should be harmonized with the existing guidelines from the MDS Foundation.

This proposal refers to clinical trials, where extensive diagnostic assessments are being performed to be confident on inclusion. However, the guidelines embedded within LeukemiaNet should be more restricted. A balance should be reached in what appears realistic to perform for the majority of centres.

The diagnostic and prognostic procedures proposed by Hellström have been discussed in detail. Bowen will give feedback on this discussion to Hellström (see also: details below).

Adaptations to the guidelines should be ready before the end of June.

Case reports could be published in the on-line section of Haematologica/the hematology Journal, and posted on the WEB site of the MDS foundation and LeukemiaNet.
The forms that will be used will be harmonized with the framework of the LeukemiaNet Registry

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-3- Development of program for new therapeutic guidelines MDS & management hypothetical patients:

Subcommittee: Bowen, Cazzola, Fenaux, de Witte, Gattermann, Ganser

Methodology: Scenario based and systematic literature review (Evidence and consensus-based). It is the aim to develop more than 20 hypothetical cases.

Time schedule
•The first draft should be finished before the end of 2005, in mid-july specific requests will be sent around to people with expertise on specific topics.
•Two face-to-face meetings (linked to other meetings) will be required to evaluate evidence and discuss management of hypothetical cases.
•Preparatory meeting in Stockholm, EHA: Cazzola presents agenda/format of first meeting and review of literature.
•The level of detail is discussed (Hellstrom) .
•Even if some drugs are not available in some countries, they might be incorporated in the guidelines. This will be further discussed.
•With Salamanca, matters concerning flowcytometry/immunophenotyping will be discussed (Cazzola).
•First meeting will be in Madrid: October 22?; combine with fifth leukemiaNet meeting?
•Second meeting at ASH?

-4- Clinical trial list website: T de Witte

1) List groups that have been active up to now (to website)
2) Identify formal representatives of groups (to website)
3) Formalize interactions on trials

Aims:
1) Comparing outcome of different trials
2) Common control arm for different trials: fewer patients needed for control arm. This is an ambiguous issue and needs to be discussed further.

LeukemiaNet is not a trial group, however it represents a platform to develop trials.

Identification of (new) drugs/treatment modalities potentially interesting for treatment of MDS patients
Activities:
•List of new drugs (phase I, II, III) with involved groups/scientists/pharmaceutical companies/potential translational activities.
•Development of new protocols.

-6- Role of LeukemiaNet in accreditation new clinical trials: A. Ganser

The possible development of Standard Operating Procedures for the Certification of MDS Treatment Protocols has been discussed. The general impression at this moment is that for the coming years this should not be a priority, as there seems to be little added value to the review systems that are already in place. It is decided to leave this matter for the time being.

-7- Organisation International Registry: D. Bowen/P. Bernasconi

Different MDS datasets: distributed by mail:

Med A = core dataset, mandatory data (including clinical intervention named) intended for MDS registry, including population-based registries and national registries.
Med B = dataset related to diagnostic guidelines
Med C = dataset related to clinical / translational studies.

Database structure:
Structured in such a way that data from population based registries, clinical trials and national registries can be separated from each other.
Bowen will make an inventory of the software system/requirements necessary for the development of the MDS database structure. This database structure should allow electronic conversion of the existing databases into the central database structure similar to the Promise EBMT structure (Ronald Brand).

Informed consent issue:
De Witte: EBMT uses anonymous data. No consent is required from the patient.
Bowen: If the sample bank will be linked to the MDS registry, probably, an informed consent is required. Include the question whether the patient has signed a general consent.

Bowen will keep track of the development of IT structure in WP3 and 17. In addition he will look into the legal issues of European registry, ownership and informed consent.

-8- Proposal for organisation sample banking: J. Jansen

In several places local archives exist, but these differ in content.
Therefore, it is hard to combine samples from different centres for collaborative studies.

Aim: to facilitate collaborative studies.

1) Centralized database: property of samples remains with the participating centres.
2) Consensus protocols: allowing combining samples with uniform quality.
3) Standardize time of collection: diagnosis-CR-AML.
4) Cell type: bone marrow/ blood, granulocytes.
5) Standardize what to store: viable cells, RNA, DNA, protein (serum).
6) Overview of research interests (including Haferlach initiative).

Joop Jansen distributed a questionnaire. In general people have responded positively to the questionnaire that was sent around. J. Jansen will sent around proposals for laboratory guidelines, to be amended by all participants. In addition to RNA, DNA, viable cells and serum, the possibility to enclose biopsies will be regarded. The database will be

incorporated/linked to the registry. Legal issues concerning sample banking (like informed consent) will be addressed (see 7: Registry)

-9- Cooperation with AML: M. Lübbert

Activity list from joint meeting in Heidelberg:
• to exchange MDS diagnostic guidelines to the AML work package for comments. Probably we can develop guidelines for "myeloid diseases'' (MDS and AML included, CML excluded).

•Hellström/Lübbert will send the diagnostic guidelines to the AML WP. RAEBT should be reported as a separate entity (RAEBt/AML) within the AML WP.

•Burnett: Proposes to enrol both AML and MDS patients in an AML protocol and to compare biological/disease related factors between these two groups

•Define shared criteria of response for AML and MDS, including the Cheson criteria?

•It is important to ensure that from MDS patients that are incorporated in larger AML trials, the % blasts and dysplasia are well documented in order to allow evaluation later on.

•In addition, if MDS patients are included in larger AML trials, it is important that these patienrts are stratified according to to known MDS risk factors, not only on morphology.

-11- Date new meeting: October 26-27 Madrid ?

Conclusions:

•LeukemiaNet MDS Work Package has started to function
•All major European MDS groups and experts participate actively
•Cooperation with MDS Foundation guaranteed through European Board members
•Interaction diagnostic and biologic groups stimulated from the beginning
•First contacts with pharmaceutical companies have been established formally

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Action Items from MDS WP meeting Stockholm, June, 3, 2005

Action	Coordinator	Target Date
Proposal for financial office in Hannover	Ganser	June 2005
Exchange MDS **diagnostic guidelines** to the AML work package for comments and harmonization	Hellström/Lübbert	May 2005
Harmonize **diagnostic guidelines** with the existing guidelines from the MDS Foundation	Hellström	
Presentation final draft **diagnostic guidelines** on website LN	Germing, Mufti, Hellström	August 2005
Therapeutic guidelines: Seek agreement from British Committee for Standards in Haematology	Bowen	May 2005
Therapeutic guidelines: Send specific requests to people with expertise on specific topics	Cazzola	July 2005
Therapeutic guidelines: Prepare two face-to-face meetings to evaluate evidence and discuss management of hypothetical cases:	Cazzola	Oct. 2005 Dec. 2005
Therapeutic guidelines: First draft finished.	Cazzola, Bowen	Dec. 2005
MDS trials: List of new drugs (phase I, II, III) with involved groups/scientists/pharmaceutical companies/potential translational activities.	Fenaux	June 2005
MDS trials: Development of new protocols	De Witte	
MDS registry: Define final datasets Med A, Med B, Med C.	Bowen, Bernasconi, Hellström	Sept. 2005
MDS registry: Check legal issues of European registry, ownership and informed consent.	Bowen	Oct. 2005
MDS registry: List features existing databases and work out details of IT structure similar to the Promise EBMT, which can integrate these population based databases.	Bowen, Bernasconi	Oct. 2005
Sample banking: sent around proposals for laboratory guidelines, to be amended by all participants.	Jansen	August 2005
Translational research related to Revlimid study:	Hofmann, Jansen	