European Registry for Myelodysplastic Syndromes

Coordinators: Professor Carlo Bernasconi / Dr David Bowen

Draft proposals

Introduction

The EU 6th Framework LeukemiaNet Network of Excellence provides a real opportunity to develop a large registry of patients with MDS, from a variety of existing disparate sources. The goals of this registry will be many, varied and will include:

1. Demographic epidemiological study, including gender differences, temporal changes, and identification of rare, previously unrecognised disease entities.
2. Molecular epidemiological / pathological study: easy identification of samples from selected subtypes of MDS available in Biobanks
3. Improved definition of response predictors by combining data from several studies of the same drugs (including meta-analyses).
4. Extrapolation of patient selection within clinical trials to the "real world" of population-based demographics: interaction with Pharma.
5. Derivation / validation of new prognostic scoring systems based on unselected patient cohorts with high quality follow up data

These opportunities also present many challenges, which must be recognised and appropriately addressed. Some of these may prevent the optimal model, and may include

1. Data protection: determined by a EU Directive. If patient identifier data (patient names) are not transferred, this will comply (EBMT Office written directive). Patient consent is likely to be required.
2. Quality control: diagnostic consistency, accuracy of database records.
3. Scientific and legal ownership of data from individual registries: this will need to be handled sensitively, with a series of rules to allow access to data within the European registry, ensuring that the owners of the individual database consent to these projects. A Steering Committee will need to be established.

An overarching single database should be built, into which data are fed from three separate sources. Investigators contributing their data to the central registry must remain free to publish independently from their own registries. Clear restrictions will be defined for access to these datasets, as determined by a Steering Committee. Each source will be easily separated within the database. These three sources are as follows:

1. Clinical trial patients
2. Regional population-based registries
3. National registries + databases from tertiary referral centres

Clinical Trials

Lead: Eva Hellström-Lindberg

This first phase of the registry project will collate clinical and laboratory data from all non-commercial clinical trials for MDS in Europe, retrospectively from 1996, and prospectively from January 2004. Retrospective studies will include those of ATG,

haematopoietic growth factors, hypomethylating agents and intensive chemotherapy / SCT.

Aims

- Define common datasets for baseline data
- Define datasets for patients on treatment, including common timepoints for evaluation
- Review response criteria
- Define data protection laws for data transfer
- Meta-analysis of individual therapeutic modalities
- Establish trial-based Biobanks for study of response predictors

Population-based registries

Lead: Ulrich Germing / David Bowen

Second phase of the project: to combine all comprehensive population-based registries.

Population-based registries are essential to describe the true demographics of MDS, as exemplified by the long-standing Dusseldorf database. Whilst this database is large, there are at least two smaller established comprehensive population databases in Europe (Dundee, Cote d'Or), and one in development (Avicenne, Paris), which could add considerably to total numbers of cases.

These registries will hold more detailed clinical and laboratory data than the clinical trial / national registries. Follow up will be more complete and comprehensive. These data combined with tissue storage will provide a powerful resource for biological studies.

Other comprehensive registries will be identified and assessed for completeness of registration, before consideration is given to adding these to the larger registry.

Aims

- Define common datasets, including classification systems etc..
- Define data protection laws for data transfer
- Describe demographics of MDS, including age / sex distribution and temporal changes in incidence.
- Provide data to Pharma concerning the proportion of FAB / WHO subtypes in unselected populations, in order to assess markets for drug development, and aid with trial recruitment targets
- Development and / or validating of new prognostic scoring systems: it is likely that these cohorts will be less selected than the IPSS and that follow up will be more complete.
- Parallel tissue storage (Biobanking) with central catalogue of available samples held within the registry.
- Consideration should be given to establishing a "healthy control" cohort of samples within each registry region for molecular epidemiology study (single nucleotide polymorphisms)

It is unlikely that this registry would be meaningful to study:

- Geographical variation in incidence of MDS throughout Europe
- Environmental epidemiology of MDS

National / Referral Centre registries

Lead: Carlo Bernasconi

The Italian MDS Registry (RISMD) provides the model for a national registry. By their nature, these registries will initially invite voluntary registration and therefore cannot be comprehensive. A limited dataset is required to ensure continued recruitment. A similar registry is now well established in France (GFM registry), soon to combine digital slide images with clinical and laboratory data.

Government-funded national MDS registries are in the final phases of planning in Scotland and Sweden. Provided these are quality controlled, they will be all inclusive and more sustainable than those national registers relying on voluntary registration, but most likely will contain fewer data.

Several major European MDS Centers of Excellence collect data for tertiary referrals (e.g. Kings College, Nijmegen). Biobanks have also been established in some centres. These patients are selected but will have high quality data at least at referral. It is likely that follow up data are more incomplete for this patient population.

Aims

- Define common core datasets
- Define data protection laws for data transfer
- Register large numbers of patients, facilitating the study of rarer subgroups of MDS
- Develop large Biobanks for biological study.

Timelines

Months 1-12

1. Distribute questionnaire survey of existing registries within Europe: target at least one MDS-interested Haematologist from each European country.
2. Define common datasets for clinical trials database
3. Collate data from clinical trials retrospectively from 1996, and prospectively from January 2004.

Months 12-24

1. Define common datasets for population-based database
2. Collate population-based data
3. Define common datasets for national registries
4. Commence collation of national registry data

Location of European Registry

To be discussed. It would be reasonable to locate the registry on a server within one of the coordinator's centres, namely Pavia, Dundee or Dusseldorf. The advice / collaboration of Ronald Brand at EBMT (Leiden) would allow development of web-based data transfer in parallel with the ProMISe system.

[If the registry were to be based in Dundee, the MDS WP would need to provide short-term funding for development of this project. The members of WP 8 will have to decide how best to spend the EU LeukemiaNet resource assigned to our WP.]

Funding requirements

Programmer 0.5 WTE 2 years: 2080 person hours….!!

STRUCTURE OF EUROPEAN MDS REGISTRY: PROPOSAL