



## STATISTICAL SUB COMMITTEE

Minutes of the meeting held on 2<sup>ND</sup> December 2005, Université Pierre et Marie Curie, Paris

**Participants:** Myriam Labopin (Chair); Antonella Santucci ;Carmen Canals ;Carmen Ruiz ;Emmanuelle Polge ;Irina Ionescu ;;Kim Champion;Richard Szydlo;Ronald Brand;Sandrine Katsahian;Simona Iacobelli;Stefan Suci;Ulrike Pötschger;Vanderson Rocha;David Pacheco; Samey Benedicte

Absent persons: Jean-Yves Mary , Ann Dickinson, Vincent Levy

**Presentation of the statistical subcommittee :** Myriam welcomed all the participants. This meeting constituted the first one of the committee, and its aim was to discuss the plans and future of the statistical subcommittee. The history of the statistical subcommittee was summarized. It was created in June 2004 by the EBMT board.

**1. Members:** The first point of this meeting was to update and complete the list of the members. Myriam asked each participant to complete the participation form and to indicate if they wanted to be a member and their field of interest.

At the end, 12 persons agreed to be a member:

- old members: M Labopin, Ronald Brand, Simona Iacobeli, Stefan Suci, Richard Szydlo
- New members (field of interest):
  - o E polge (responsible for reporting to the RSC)
  - o D Pacheco (Quality of data)
  - o I Ionescu (clinical input)
  - o V Rocha(clinical input)
  - o A Santucci (education methodology)
  - o S Katsahian (methodology)
  - o U Pötschger (methodology)
  - o J Y Mary (methodology)
  - o V Levy (clinician input)

The responsibilities of each member remained to be defined during next meetings according to their field of interest.

The proposal made by Myriam was that statisticians will be responsible for coordination, organisation of the meetings, search for fundings, implementation of the web site and education. Datamanagers and clinicians would be responsible for coordination with other committees,improvement of the data quality and homogeneity of the studies

### **2. Summary of what has been already done in 2004-2005:**

[a] A letter has been sent in June 2004 to all chairpersons in order to know the persons responsible for data analysis within the different WPs. Two different issues were raised:

- the problem of working parties without any dedicated statistician (late effect, TBI, pediatrics, infectious diseases...)
- The fact that nobody involved in statistics was working full time
- 3 WPs never answered: Autoimmune disease, Immunobiology, Infection diseases

[b] The EBMT web site has been implemented with the statistical guidelines and has given the possibility for each EBMT member to contact a statistician for advices:

The majority of requests were generated by clinicians and WP chairpersons, who were asking for:

- Help in competing risk analyses: condition to be used, software, training
- Assistance for the redaction of the protocols for clinical prospective trials
- Review of the methodology of scientific papers already written

The number of requests remained low (about 15 per year).

[c]- Two meetings have been organized. This first was the annual statistical symposium within the EBMT meeting in Prague in March 2005, the second was a new workshop during the ESH-EBMT meeting in Lisboa in May 2005. During this meeting; Richard and Myriam asked the participants to tick 2 or 3 problems that they would like to go through. People were mainly interested in methodology of survival analysis.[d] - A proposal for an ongoing statistical research position has been submitted to the board. Its aims was to develop statistical models to study center effect and to take into account time dependent covariates using competing risk analysis. The project has been rejected after an expert review in september 2004 and no official letter was communicated by the EBMT board.

Carmen suggested that it is important to:

- Emphasize the existence of the statistical subcommittee on the front page of the EBMT web site.
- Report the activity of the EBMT statistical subcommittee to the board
- Implement the next EBMT news with the presentation of the subcommittee

### **4. Objectives of the statistical subcommittee:**

Two objectives have been already defined:

#### **[a] To give a statistical help and information to all EBMT members**

In order to better understand what is expected within the EBMT, Myriam made a proposal for a survey asking all EBMT members what they would like us to do. This proposal was accepted and Myriam will

circulate a preliminary questionnaire (including a list of propositions) to all the members of the subcommittee in January.

**(b) To standardize the approaches to statistical analyses**

The main issue was the lack of communication between statisticians, WPs and subcommittees.

In order to improve exchanges, a proposal was the establishment of a "web forum" that would allow the better communication among all members of the statistical subcommittee.

Each member would be in charge of informing the others of what has been done within each WP in terms of methodology used either for retrospective or prospective trials (statistical methods of each synopsis). Such a "forum" would be accessible to each of the statistical subcommittee members and statisticians involved in analysing BMT data.

The different steps would be the following

- Myriam will contact again each WP chairperson to get at least the name of a contact (even a local statistician) responsible for analysing the data.
- Then, a survey will be done in order to know:
  - o Who accept to participate
  - o Who is interesting in answering the questions, etc
- Ronald will ask for a budget in order to develop such a "forum" and will look for its feasibility

If such a forum can be created, the cooperation of one person of the IBMTR would be important. Myriam will contact Mary Horowitz.

**5. Budget:**

No financial help has been accepted from the board until now except 2500 euros for refunding the accommodation for this meeting. Each year, 3 or 4 speakers are invited for the statistical symposium during the annual EBMT meeting.

For 2006, it seems reasonable to ask again 2500 euros for refunding such a meeting.

The question of sponsors was raised by Ronald.

Carmen suggests that Myriam would contact Fiona in order to approach companies. Antonella proposed to contact SPSS in Italy.

**6. Specific meeting on statistics next years:**

Two meetings are already planned:

- the Annual statistical symposium in Hambourg

ESH-EBMT training course : The ESH has invited Myriam for another workshop in 2006 in Poland. Myriam is waiting for more detailed information on what is expected and if it is possible or not to organise a session with more than 2 statisticians.

The organisation of another specific meeting on statistics did not seem realistic in 2006. Moreover, the intended audience is not well defined (the survey should help for this definition) and it is not possible to ask for specific financial help from the board without any detailed project.

The possibility to organize training courses in statistics in the future have been discussed:

- One possibility would be to take advantage of the training courses for datamanagers during the annual congress, but Carmen pointed that clinicians are attended clinical sessions and that it seems not possible to add training course during the congress (not enough time). So she would be in favor of the organisation of such "workshop" out of the congress
- Another possibility would be a joint meeting with EORTC which organized each year one day formation called "statistics for non statisticians". Stefan Suciuc will tell us about this possibility.

**7. Problem of the data quality and standardisation**

[a] Data quality: Myriam told that only 20% of transplants are reported via MEDB (35% according to Carmen). This must be checked. Whatever, the consequence is a population selection which can concern either patients, centres, and sometimes period within the same center.

In order to better understand this issue:

- A report of missing data concerning major variables for statistics (endpoints, prognostic) should be done
- Carmen suggested to make a recommendation to the board on:
  - o Items which are never used by statisticians
  - o MEDB items which are always necessary for statistical analyses and to propose to add them to MEDA

Such a report could only be done after consulting all the statisticians responsible for analyses within WPs

[b] Another problem concerns patients included in prospective clinical trials. Theoretically, minimum essential data should be reported for these patients. However, for some specific studies, MEDA information allows to determine the arm in a trial (ex: mini vs maxi...) and patients are not reported.

[c] Regarding standardisation of the methods in prospective trials, Carmen indicated that the randomisation is not centralized, and Kim said that the statisticians are generally "local" statisticians. A need for coordination is therefore important also for prospective trials.

[d] A quality control of the data via some audit of the centres have already been planned.

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### **8. Program of the next statistical symposium in Hambourg.**

The major issue is that intended audience will be clinicians and that the presentations have to be well adapted in order to be well understood (no formulaes...). Carmen and Ronald insisted on the need for improving information for EBMT centers on the existence of this statistical symposium. They suggested that Myriam would contact Jane Apperley in order to ask her to present the statistical committee and symposium during the opening session and to underline that this statistical symposium will focus on very practical problems and is addressed to clinicians.

Moreover, a common mailing with Kim will be done to inform all members about the statistical symposium and the session on good clinical practice in February.

The program planned is the following:

Statistical symposium (Tuesday 16.30 to 18.30)

**Title: Methodological and Statistical issues in design & analysis of clinical trials and data from the ProMISe MED-AB data base**

**Subtitle: Basic explanations, tips & tricks for clinicians and data managers**

Chairs: M Labopin, R Brand

Program:

[a] Methodology of clinical trials: the 10 commandments

Speakers: Stefan Suciu, Jean-Yves Mary

Definition of endpoints

Comparison of (sub)groups and (statistical tests/models)

Sample size and power

Design & conduct of Interim analyses

Definition of 'intent to treat' and 'per protocol' analyses

[b] Data extraction from the MEDAB-database using Promise and survival analysis in SPSS and the new Statistical Portal (R):

Speakers: R Brand, Henk Jan van der Wijk

guidelines and examples in SPSS

demonstration of analysis via the Statistical Portal interface to R

[c] Centre effect in retrospective and prospective studies.

Speaker: Sandrine Katsahian **10. Next meeting**

The next statistical SC meeting is scheduled to take place at the EBMT 2006 congress in Hamburg, on Tuesday 21 March from 8.00 to 9.00AM.