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June 2010

NEWSLETTER

2010 UPCOMING CONFERENCES

2-4 July, 2010 - Lisbon, Portugal
HAEMATOLOGICAL MALIGNANCIES IN THE ELDERLY
Chairs : L. Balducci, P. Fenaux, J.-L. Harousseau
Local organizer : L. Ribeiro

24-26 September, 2010 - Washington, DC, USA
CHRONIC MYELOID LEUKEMIA - Biological Basis of Therapy
Organizers: J.M. Goldman, J. Cortes, T. Hughes
Co-Organizers: : P. Hari, T. Holyoake, F.-X. Mahon, D. Perrotti, J. Radich

24-26 September, 2010 - Rhodes
ESH - EUROCORD - NETCORD - CORD BLOOD WORKSHOP
Organizing Committee: E. Baudoux, A. Fassas, E. Gluckman, D. Sotiropoulos

30 September-2 October, 2010 Albufeira, Portugal
MYELOPROLIFERATIVE DISORDERS
Chairs: T. Barbui, A.R. Green, H. Pahl, R. Skoda, W. Vainchenker

14-18 October, 2010 - Cascais, Portugal
MECHANISMS OF CELL DEATH AND DISEASE: Advances in Therapeutic Intervention and Drug Development
Chairs: T.J. McDonnell, J.A. Hickman, K.M. Debatin

28-30 October, 2010 - Tunis, Tunisia
An update on
HAEMATOLOGICAL MALIGNANCIES, from bench to bedside
Chairs: P. Fenaux, B. Medded, G. Salles

4-7 November, 2010 – Marseille, France
WORLD CORD BLOOD CONGRESS
Chair : E. Gluckman
Scientific Committee: W. Arcese, H.E. Broxmeyer, J. Kurtzberg, F. Locatelli, A. Madrigal, V. Rocha, G. Sanz, E.J. Shpall, S. Takahashi, J. Wagner
Local Organizer: C. Chabannon

5-7 November, 2010 - Cascais, Portugal
ESH-EHA - Type I tutorial
DIAGNOSTIC WORK UP FOCUS ON ACUTE MALIGNANCIES
Chairs: B. Bain, W. Erber, R. Foà, G. Zini

2011 UPCOMING CONFERENCES

1-2 April - Brussels
ESH-ENERCA TRAINING COURSE ON HAEMOGLOBIN DISORDERS
Laboratory Diagnosis and Clinical Management
Chair : P. Aguilar-Martinez, Y. Beuzard, B. Gulbis, D. Loukopoulos, S.L.Thein

April
ESH-EBMT TRAINING COURSE ON BLOOD AND MARROW TRANSPLANTATION
Chairs : J. Apperley, E. Carreras, E. Gluckman, T. Masszi

15-18 September - Rome
WORLD CORD BLOOD CONGRESS
Chair : E. Gluckman

22-25 September - Estoril
ESH- ICMLF INTERNATIONAL CONFERENCE ON CHRONIC MYELOID LEUKEMIA
Chairs : J. M Goldman, J. Cortes, T.P. Hughes

October - Mumbaï
ESH INTERNATIONAL CONFERENCE ON LEUKEMIAS
Chair : J.M. Goldman

October
ESH-EHA SCIENTIFIC WORKSHOP ON ACUTE MYELOID LEUKEMIA
Chairs : B. Löwenberg, H. Döhner

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FROM THE PRESIDENT

ESH LEADERSHIP ROTATION

The new ESH by laws call for regular rotation of the members of the Executive and Scientific committees.

I take this opportunity to thank the Committee members who are now stepping down or changing position.

ESH is indebted to Gérard Schaison, co-founder of ESH and to Dieter Hoelzer. As Vice-Presidents of the school, their skill and devotion have guided ESH to maturity.

My sincere thanks to Magnus Bjorkhölm whose fine chairmanship of the ESH Scientific Committee is reflected in many projects and tools that have become well-known signatures of the school's scientific and educational quality.

I am very pleased and proud to announce that Bob Löwenberg has accepted to lead the Scientific Committee for a term of 3 years, renewable. Bob has also accepted to participate in the direction of the school as a member of the Executive Committee.

A warm welcome to Christine Chomienne and Vanderson Rocha who have joined the Executive Committee, respectively in the role of Secretary and Treasurer.

My thanks and gratitude go to all new ESH Committees. Together, we shall do our best to serve you well by making the educational opportunities you need available to you.

Eliane Gluckman,
ESH President

FROM THE CHAIRMAN OF THE SCIENTIFIC COMMITTEE

The European School of Haematology (ESH) is now in its 24th year. As the incoming chair of the Scientific Committee, I am very happy to be able to take an active part in the future development of the school. It is also a pleasure for me at the personal level to join the ESH Executive Committee.

I have enjoyed a relationship with ESH over many years in various roles including chairing and participating as a speaker in many ESH educational meetings and workshops, and serving as a member of the ESH Scientific Committee.

While I look forward to contributing to the next generation of challenges, I also wish to express my gratitude to those members of the Scientific Committee who have recently stepped down. I extend special thanks to my predecessor Magnus Bjorkhölm who has served as chair of the Scientific Committee for the past 6 years. ESH educational programmes and postgraduate training courses are well known throughout the world and there is no question that the school's reputation has developed still further during Magnus's tenure, as demonstrated by a continuously increasing level of participation in ESH programmes.

Future challenges for ESH include maintaining and wherever possible enhancing our programme palette and our reputation for innovation. We also aim to involve junior faculty in ESH activities. In this respect the initiatives to develop joint activities (co-organizing meetings) with partner scientific societies and professional organizations in the field of haematology will be further advanced and shaped according today's needs. Examples of some of these fruitful collaborations are the joint activities with EBMT and EHA. Other societies have also expressed interest in developing similar cooperation with the school. ESH is fully prepared to contribute its extensive experience to these collaborative projects, to create attractive, new opportunities by pooling expertise and know-how with colleagues who share our sincere clinical and scientific interest in haematology.

The School is constantly working to improve its service to colleagues and trainees and we are therefore very receptive to your spontaneous recommendations. Evidently, we depend on your input and we welcome your suggestions regarding ESH programmes and organization.

Bob Löwenberg
Chair, Scientific Committee

FROM THE NEW SECRETARY OF THE SCIENTIFIC COMMITTEE

I am very happy and honoured to be part of the new ESH Executive Committee. As a lecturer and a clinician in Haematology, I have always counted on ESH training courses, at first for myself and now for my students and assistants.

ESH is able to constantly adapt to the overwhelming increase in knowledge arising in our rapidly evolving scientific field and to translate it into valuable educational opportunities. The School's new organizational structure set up this year, is yet another example of this. The new extensive Scientific Board includes members from a variety of disciplines, European countries and European haematology organizations and societies. It provides the structure required to pursue the School's mission and to coordinate future training activities throughout Europe. It will be my pleasure to contribute to this new setting, with Eliane Gluckman and Bob Löwenberg.

Christine Chomienne
ESH, Secretary,
Executive Committee

FIRST INTERNATIONAL CONFERENCE ON HAEMATOLOGICAL MALIGNANCIES IN THE ELDERLY

Chairs: **L. Balducci, P. Fenaux, J.L Harousseau**

2-4 July 2010 - Lisbon, Portugal

This ESH conference on haematological malignancies in the elderly will be organized in association with the International Society of Geriatric Oncology (SIOG). It is open to physicians and nurses working in the field of haematology, oncology, gerontology and geriatrics. It will be an opportunity for interdisciplinary cross-fertilization.

Due to increased longevity, haematological malignancies are seen with increasing frequency in elderly patients. While the prognosis of most haematological malignancies has improved over the last 2 decades with better treatments and better supportive care, in many cases it remains to be seen how these clinical breakthroughs can be applied to the elderly patient population.

Physiological age does not always reflect chronological age. The physiological age of elderly patients, as a group, has improved over time and it may now be possible to deliver somewhat more aggressive treatments to these patients than before. All the same, equally effective but less myelosuppressive new treatments are generally preferred in this age range.

The scientific programme will address the physiology and pathophysiology of ageing and the consequences of cytopenias. It will also discuss how functional capacities, co-morbidities and quality of life should be analyzed in elderly patients. The management of the main types of haematological malignancies in the older individual will be addressed in detail.

The webcasted conference will subsequently be available on the ESH website.

For further information and to register : www.esh.org

Pierre Fenaux
Member,
ESH Scientific Committee

OPEN CALL FOR APPLICATIONS 2011-2012 to CHAIR / ORGANIZE an ESH INTERNATIONAL CONFERENCE or an ESH INTERNATIONAL TRAINING COURSE

Interested clinicians and scientists are welcome to apply to chair and develop the scientific programme of an ESH International Conference or an ESH Training Course in 2011 or 2012.
ESH International Conferences are high-level scientific meetings including topics in either or both clinical or basic science whereas ESH International Training Courses have a more educational focus.
ESH International Conferences are to 2,5 day meetings starting on a Friday afternoon and ending on Sunday before lunch. ESH International Training Courses are full immersion 3-day meetings.
To apply, please follow the two-step procedure involving a Pre-Call and a Call for applications available on the ESH website **WWW.ESH.ORG**

Regulatory News: *Upon the initiative of Senator Marie-Thérèse Hermange, 90 French senators have submitted a proposal for new legislation which would contribute to promote and organize collection, conservation and research on umbilical cord blood. One important aspect of this bill is its proposal to change the status of umbilical cord blood from one of post-operative waste to therapeutic ressource.*

A chain of solidarity linking the vocational actors, the general public, and EU policy makers to improve patient outcomes

Two healthy Cord Blood Transplantation recipients today and the scientific pioneers who made it possible.

The European School of Haematology is very pleased to be one of the fifteen international partner organizations in the European Commission funded Eurocord-Ed project. The three-year project is now in its second successful year and the forty members of the consortium submitted the project's mid-term report to the European Commission at the end of April 2010. The mid-term report provided the opportunity to explain the importance of cord blood technology to the lay public, vocational actors, and to policy and decision makers at the EU level. The consortium members also took this opportunity to recount the story of the first umbilical cord blood stem cell transplantation and to encourage all interested individuals to visit the Eurocord-Ed platform at www.eurocord-ed.org

In 1988, the parents of a very sick American child accepted that their little boy should travel to Paris to become the first recipient of a cord blood stem cell transplantation. In doing so, they saved his life and allowed him to become the fully recovered adult, husband and father he is today. Twenty-two years later, cord blood transplantation is used to treat a broad range of clinical, life-threatening disorders.

The procedure to harvest stem cells from the umbilical cord after birth is totally safe and painless for both the mother and the child. And yet, families are not well informed that the donation of an umbilical cord can save lives. The umbilical cord and the precious stem cells it harbours are generally simply discarded.

To improve this situation, it is necessary to raise awareness through a chain of solidarity linking the general public to the vocational actors involved in the field and to healthcare decision makers. It is also essential to promote communication between the vocational sectors active in cord blood technology and clinical applications and to provide lifelong learning tools to improve and harmonize professional knowledge and skills.

Eurocord-Ed is an on-line project for vocational learning in the fields related to cord blood technology and clinical applications.It aims to be an easily accessible lifelong training tool for the many vocational sectors involved in cord blood technology and clinical applications, and to foster communication and exchange between vocational actors and vocational sectors who are separated by constraints notably linked to geographical setting and language. It is also designed to be a resource for healthcare policy makers.

As a resource for lifelong learning, Eurocord-Ed offers new, easily accessible opportunities to improve knowledge and skills. Webcasted scientific, technical and clinical conferences, Standard Operating Procedures, articles, links to publications, information on upcoming conferences and seminars, information on regulatory and ethical issues can all be found on Eurocord-Ed. Video demonstrations of technical procedures, interactive case study sessions and Meet the Expert Forums are in preparation and will be available soon. By the end of the project, Eurocord-Ed should be a very diverse, multilingual resource for all individuals professionally engaged in the field.

The Eurocord-Ed Consortium and website will be a source of reliable, expert information and counsel for healthcare policy decision makers. The website should also serve as a validated source of information for the general public, with interesting potential economic spin-offs. The field is evolving very rapidly at the international level with strong investment on all continents. Eurocord-Ed will contribute to the visibility of Europe in this highly competitive international arena.

The Eurocord-Ed Consortium is led by Eliane Gluckman who performed the first cord blood transplantation worldwide. She is also the founder of Eurocord, the European organization for clinical activities in the field of cord blood. The Consortium includes representatives of major European organizations, including the European Organization for Blood and Marrow Transplantation, Netcord (the organization that federates accredited cord blood banks) and the European Haematology Association.

It also includes the European School of Haematology, the only European organization entirely devoted to lifelong learning in the field. Cord blood banks, universities, public research organizations and three SMIs are also implicated in the project. The individuals involved in the direction of Eurocord-Ed are all internationally recognized experts in their fields.

To ensure that the project develops according to identified needs, it calls for continuing quality control on the part of those who use the website. Steps are now being taken to make open calls for contributions, along side those made by the members of the Consortium itself. These contributions will be peer-reviewed by the Consortium members and by outside experts when appropriate, before being made available on Eurocord-Ed.

The Eurocord-Ed Consortium strongly believes that this novel lifelong learning tool will contribute to improve and harmonize professional knowledge and skills. It will also promote cross-disciplinary fertilization and exchange, thus contributing to develop human potential and technological means and to accelerate progress. Main -streaming activities should help to raise political awareness of the importance of progress in this field, to meet current therapeutic needs and to prepare for future clinical challenges. Ultimately, it is the patient who stands to benefit from this collective effort.

Does iron chelation therapy improve survival in patients with myelodysplastic syndromes?

Commentary by Dr Frank Fox (Düsseldorf, Germany) and Dr Rafael Duarte (Barcelona, Spain)

This article was submitted by Novartis, ESH Bronze Institutional Partner

Myelodysplastic syndromes (MDS) are characterized by ineffective erythropoiesis, peripheral-blood cytopenias, Depending on a number of risk factors: the median survival ranges from less than 6 months for patients with high-risk MDS to over 5 years for those with low-risk disease[1]. Most patients receive regular transfusions of red blood cells to counteract the effects of anaemia, and therefore patients with a high transfusion burden are at risk of developing iron overload. Transfusion dependence and increased serum ferritin levels (>1,000 ng/mL) are associated with poor survival outcomes in MDS patients[2–4]. At the Annual Meeting of the American Society of Hematology (ASH) in December 2009, new data were presented that suggest that ICT may prolong survival in patients with MDS. The following is a brief summary of the main findings presented at ASH 2009. Dr Frank Fox (Düsseldorf, Germany) and Dr Rafael Duarte (Barcelona, Spain) provide expert commentary on the implications of this research.

Iron chelation therapy and survival: matched-pair analysis

Dr Frank Fox and colleagues at the Heinrich Heine University in Düsseldorf, Germany, conducted a matched-pair analysis to determine the influence of ICT on survival outcomes in patients with MDS and iron overload (serum ferritin[3] 500 ng/mL)[5]. A total of 93 patients with various types of MDS undergoing long-term ICT were matched with 93 controls from the Düsseldorf MDS Registry who received supportive care only. Patients were matched according to age at diagnosis, gender, MDS type by World Health Organization (WHO) classification, and International Prognostic Scoring System (IPSS) score.

Patient characteristics

Most of the patients in each group had lower-risk MDS (Low or Intermediate-1), according to IPSS score, and only 17% of patients in each group had Intermediate[2] (14%) or High-risk MDS (3%). All classes of MDS were represented in each group. The most common classification was refractory cytopenia with multilineage dysplasia (n = 41 in each group). At baseline, the median serum ferritin level was higher in the ICT group (1,954 ng/mL) than the non-ICT group (945 ng/mL). Chelation therapy consisted of deferoxamine (n = 54), deferasirox (n = 32), or deferiprone (n = 5); 12 patients received deferoxamine followed by deferasirox and 4 received combined therapy with deferoxamine plus deferiprone.

Survival outcomes

The median duration of ICT with deferoxamine and deferasirox was 39 months and 28 months, respectively. Median survival was significantly longer in ICT patients than in matched controls who received no ICT (74 months vs 49 months; p = 0.002; Figure 1). The risk of AML transformation 2 years after diagnosis, however, was similar in both groups (10% and 12%, respectively).

Conclusion:

These data provide further evidence that ICT improves overall survival in MDS patients.

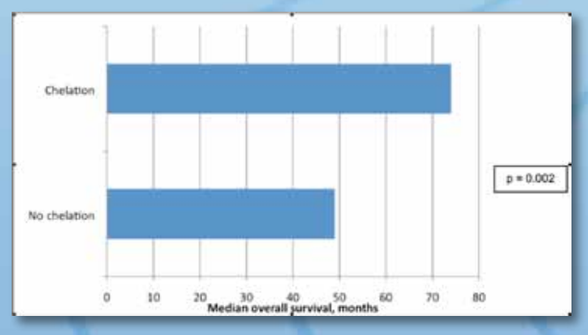

Figure 1. Median overall survival in MDS patients with iron overload (serum ferritin ≥ 500 ng/mL) who received iron chelation therapy (n = 93) or supportive care only (n = 93) in a matched-pair analysis. Data from Fox F, et al. [5].

Commentary:

What prompted this study?

Dr Fox: A link between transfusion dependence and shorter survival times has been clearly established in patients with MDS [2–4],but it is less clear whether the poorer outcomes were due to the more aggressive underlying disease that required transfusions, or the increased risks associated with transfusion therapy itself, including iron overload. A study reported by Leitch et al. provided the first hint that reducing iron levels with ICT may improve survival in patients with lower-risk MDS,[6] and a subsequent study by the Groupe Francophone des Myélodysplasies (GFM) also found a strong correlation between ICT and survival.[7] We conducted a matched-pair analysis using our MDS patient registry in Düsseldorf to determine the effects of long-term ICT on survival.

What were the main findings from this study?

Dr Fox: This was the first matched-pair analysis to assess the impact of ICT on survival in patients with MDS. The main finding was that median survival was significantly longer in patients who received ICT than in those who did not (74 months vs 49 months; p < 0.002).

Dr Duarte: The study presented by Dr Fox builds upon the findings from previous studies (including a study by the Spanish Registry of MDS presented by Dr Sanz at ASH 2008)[4], which indicated that transfusion dependence and iron overload are associated with poor outcomes in MDS[2,3,8].While many of these studies were relatively small, our study was a large, retrospective analysis involving over 2,000 patients with MDS[4]. The results confirmed that transfusion dependence was associated with poor outcomes and showed that iron overload was an independent prognostic factor for not only survival, but also AML transformation (Table 1). The study by Dr Fox and colleagues represents an important step forward in our understanding of the effects of ICT in MDS, and brings us closer to defining ways in which we can improve daily practice in a manner that could have a meaningful impact on patient outcomes (Table 1).

How does ICT lead to improved survival?

Dr Fox: The beneficial effects of ICT are attributed primarily to its ability to remove iron from tissue, thereby reducing organ damage and dysfunction that could lead to clinical complications, such as cardiac death. One of the major limitations of our study was the lack of data on the cause of death. Differences in the cause of death between patients who received ICT and their matched controls may have provided an indication of exactly how ICT influenced survival. A significant decrease in cardiac death, for example, would have supported the hypothesis that cardiac iron overload is a significant cause of death in MDS that can be reversed by ICT. A recent analysis of causes of death in patients with lower-risk MDS revealed that most patients (84%) died due to disease-related problems, such as infection (38%), AML transformation (15%), or haemorrhage (13%) [9]. Of the 43 patients who died of causes not directly related to MDS, the most common cause was cardiovascular events (44%).

Dr Duarte: In addition to the data presented by Dr Fox, several other noteworthy presentations related to iron overload in MDS were given at ASH 2009. For example, Mattiuzzi and colleagues reported that increased serum ferritin levels prior to transplantation are associated with an increased risk of infections – including bacterial and fungal infections – in patients with higher-risk MDS or AML[14].Other studies have confirmed that increased iron load prior to transplantation negatively affects outcomes[15–17]. Given these findings, the next step is to determine the best way to reduce the risk of infections in patients receiving transplants. While ICT is typically considered after transplantation, it may be beneficial to lower iron levels prior to transplantation. The more proactive use of ICT in this setting may avoid the toxic effects of excess iron, including infections.

Table 1: Effect of transfusion dependence and iron overload on the risk of death or AML transformation in 902 patients with MDS. (Data from Sanz G, et al.)[4].

	Overall Survival, hazard ratio (p value)	AML-Free Survival, hazard ratio (p value)
Transfusion dependence*	7.20 (< 0.001)	2.90 (< 0.001)
Iron overload†	2.11 (< 0.001)	1.57 (0.04)

*Defined by the WPSS criteria as: at least 1 red blood cell transfusion every 8 weeks over a period of 4 months [3].

†Defined as serum ferritin > 1,000 ng/mL.

AML = acute myeloid leukaemia; MDS = myelodysplastic syndromes; WPSS = WHO classification-based Prognostic Scoring System.