

**Protocol of the 9th Meeting of the  
EUROPEAN RESEARCH INITIATIVE ON CLL (ERIC)**  
(ELN Breakfast Meeting)

**Time:** Sunday Dec 11<sup>th</sup> 2005, **8:00 a.m. 10:00 a.m.**

**Location:** Hotel Ritz Carlton, 181 Peachtree Street, Atlanta (downtown), USA

**Participants:** ca. 100

**Ad TOP 1: M. Hallek**

Welcome of participants, update on funding status: just in December 2005 the EU launched funding money for the ELN. ERIC was funded with approx. 30.000 € for the period month 19-30 (which is finished summer 2006). The money will be split for the support of the research committees/groups in the UK (MRD harmonization, Andy Rawstron), in France (Florence Cymbalista, ZAP70 harmonization), for administrative efforts in Cologne (secretary office) and for future harmonization projects.

**Ad TOP 2: U. Jäger (please find attached the slides from U. Jäger)**

ERIC Research Committee, coordinated by U. Jäger: the EU is calling for research projects for the next EU frame program FP7. If we want to emphasize the importance, support and funding of CLL research, we have to initiate and define new important CLL research projects. Most importantly we have to get in touch with our country representatives for the EU frame program and try to lobby for our CLL projects – if possible. Besides that U. Jäger is coordinating the submission of project applications to the EU. Find attached a very short word-file prepared by U. Jäger, where you can quickly insert your project proposal/idea. Uli Jäger will collect the proposals and submit them as complete announcement to the EU. **PLEASE SUBMIT YOUR PROJECT PROPOSALS UNTIL JANUARY 25<sup>th</sup> 2006 TO ULI JÄGER (Ulrich.Jaeger@meduniwien.ac.at).** Projects/ideas will be discussed in Heidelberg in Feb 2006.

**Ad TOP 3: Harmonization of ZAP 70**

The harmonization of ZAP 70/CD38 analysis is coordinated by Florence Cymbalista and Remi Letestu in Paris/France. 4 different methods of measurement are available in relation to normal lymphocytes or more specific to normal B cells. So far it could be shown that analysis is feasible for 24 hours after sampling with a maximum of delay up to 48 hours. Next plan is to further exchange probes between the participating institutes/centers and set up a standard protocol, which should be published soon as it is done for MRD harmonization:

The harmonization of MRD analysis was coordinated and successfully completed by the cooperation of different MRD groups. ERIC could represent a forum for these groups. Andy Rawstron (UK) had presented the data on harmonized MRD diagnostics already in Stockholm (EHA) and is currently preparing a manuscript for publication.

**Ad TOP 5: Harmonization of cytogenetics**

Harmonization of cytogenetics will be one of the major focuses of the current research activities within ERIC.

Cytogenetics: Unfortunately D. Oscier got not much response with the p53 questionnaire up to now. Future plan is to collect and follow up p53 cases by clinical studies. Newly launched clinical studies must include p53 analysis. In the upcoming meeting in Heidelberg results of current phase II studies regarding p53 patients should be collected and presented to discuss how we should handle these patients in the future (next phase III generation).

Hartmut Döhner volunteers to coordinate the harmonization of p53 analysis between European countries. Probes between all interested countries/institutes will be exchanged especially for 17p- analysis. Interested countries/participants should contact Hartmut Döhner

in Ulm/Germany. Most difficult and interesting is to set the right threshold or cutoff for the diagnosis of 17p deletion. Goal is to set up a publishable standard protocol for 17p analysis and result interpretation (like in the MRD harmonization project).

### **Ad TOP 6: European CLL Survey – Vincent Levy**

Vincent Levy (Paris/France) suggested the initiation of an European-wide survey on clinical practice in CLL patients with the recordation of how CLL patients are treated within or without clinical studies. This could be done by vignettes and collection of information about patients in Europe excluded from studies. The aim of the study would be to evaluate the quality of patient's treatment and conception of a detailed common survey. The suggestion of Vincent was very well appreciated by the ERIC community. It was decided, that all European CLL study groups shall discuss this projects within their groups and how they can contribute to it. The project will be integrated into the future deliverables for the upcoming funding period of ERIC. Vincent will present a more detailed plan on the next steps in Heidelberg, Feb 2006. A short description of the project by Vincent Levy:

*Randomized controlled trials are accepted to be the research design of choice to evaluate the effectiveness of health care interventions and are commonly used to evaluate cancer treatments. However, it has been reported that only 5 to 10% of adults patients are included in clinical trials, with selected patients, selected physicians and selected treatments<sup>(1)</sup>.*

*We propose to perform a prospective multisite European internet-based survey on CLL practice.*

*The study will be conducted among the physicians actively engaged in treating CLL patients, participating or not to clinical trials and from all types of medical structures (from private practice to large tertiary centers). Each National CLL cooperative group (or National Hematological Society) will be asked to provide the names and e-mail addresses of their members.*

*Four vignettes will be realized by a team of European experts, selecting 4 common medical conditions in CLL practice.*

*Vignettes are a valid tool for measuring clinical practice<sup>(2)</sup>. They can be used for diverse clinical settings, diseases, physician types, and situations in which case-mix variation is a concern. They are inexpensive and easy to use. Vignettes are particularly useful for comparing quality among and within sites and may be useful for longitudinal evaluations of interventions intended to change clinical practice.*

*These vignettes will be randomly proposed to the physicians. Results will be analysed in collaboration with the statistical team (Pr S Chevret, INSERM U 717, Paris).*

*Results should help in the analysis of the factors of non participating in clinical trials, the conception of common European trials, and finally in the quality of care of patients.*

For more information :

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#### *References*

(1) Tournoux *et al.* Cancer. 2005 Dec 7;106(2):258-270.

(2) Peabody *et al.* Ann Intern Med. 2004 Nov 16;141(10):771-80.

### **Addendum: Platform on phase I/II clinical trials in CLL**

At the last meeting in Stockholm Vincent Levy also presented a project idea on the creation of a European platform for phase I/II trials to improve performance, recruitment and outcome quality of these studies, find here a short summary on this project by Vincent Levy:

*Early clinical trials design in cancer therapeutics has changed little in 20 years <sup>(1)</sup>. They are distinct from therapeutics evaluations in other medical disciplines. (i) First, the risk association with treatments dictate that they be evaluated in cancer patients only, (ii) second dose response relationships are essential to the understanding of potential therapeutic benefit and toxic side effects, (iii) third, determining the specificity of therapeutic value for subsets of patients is essential to the development of effective therapies <sup>(2)</sup>.*

*Comparing with large randomised collaborative phase III trials, early clinical trials are frequently neglected, of poor methodological quality, and with poor accrual. On the other hand new drugs and new treatment strategies are emerging, necessitating new biological and statistical technologies (early prognostic factors, surrogates of efficacy, new statistical designs).*

*Our objective is to make the inventory in Europe of available platforms /centers with ongoing phase I/II trials in CLL, the number of patients treated, in order to initiate collaboration, share information to ensure that there is no duplication of effort or wasted time in parallel discussions about the same trial or development of the same agent. This survey should be the first step for the creation of a network of expertise and a trial structure for academic investigators and pharmaceutical industry.*

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#### *References*

- (1) Eisenhauer *et al.* J. Clin. Oncol. 2000, vol 18, N°3 (February), 684-692.  
(2) Teicher BA, Andrew PA (Eds). anticancer Drug Development Guide (2<sup>nd</sup> ed.). Humana Press 2004.

#### **Next Meeting:**

- **ELN Annual Symposium Jan 31- Feb 01 2006**
- **Location: Heidelberg, Germany**
- **Invitation with forms for registration was sent out by email or can be reached at the ERIC office in Cologne (M. Buchner, phone: +49-221-478-3988).**

#### **Topics for Heidelberg:**

- **ERCC: Basic research projects now and in future, especially for the EU frame program FP7**
- **Harmonization of cytogenetics: status**
- **European trials for acquisition and surveillance of 17p- cases: results from phase II trials from different European countries**
- **European survey on CLL treatment: next steps**
- **Update on diagnostic and treatment guidelines in CLL**
- **Further meetings in Amsterdam (EHA), Orlando (ASH)**