

Protocol of the 12th Meeting of the EUROPEAN RESEARCH INITIATIVE ON CLL (ERIC) in Orlando, Sunday Dec 10th 2006

TOP 1: Welcome and introduction, business part of ERIC as incorporated association (Michael Hallek, Cologne)

Michal Hallek welcomed all participants.

Election of the new ERIC board:

As new board of ERIC for a 2 years term in office the following members have been elected with the absolute majority by show of hands:

Chairman: Daniel Catovsky (although he could not be personally present the majority of members agreed to elect him in his absence)

Vice-Chairman: Eva Kimby (Stockholm)

Chairmen of the subcommittee on basic research:

Due to his additional duties as EHA board member Uli Jäger (Vienna) stepped back. As new head and vice-head/co-chair Paolo Ghia (Milan) and Florence Cymbalista (Paris) have been elected.

Chairmen of the subcommittee on clinical research:

As head of the subcommittee on clinical research John Gribben (London) was elected, as co-chair Michael Hallek (Cologne).

Secretary and Treasurer:

As secretary and treasurer the following persons have been confirmed to stay in office:

Secretary: Carmen Schweighofer (Cologne)

Treasurer: Gerassimos Pangalis (Athen)

It was common consensus that all formal commitments of ERIC i.e. correspondence and reporting with/to the ELN should stay in the Cologne office so far.

TOP 2: Current status of the 7th EU frame program (U. Jäger, Vienna)

Uli Jäger reported that in the current proposal of the future 7th EU frame program unfortunately CLL research was not specifically considered. The current project manuscript of the frame program will be sent around to all members. Some of the projects though may be compatible to allow some partial focus on CLL, i.e. (see FP7 framework proposal):

- novel testing strategies.. (p.16)*
- molecular epidemiological studies.... (p.18)*
- non-coding RNAs, omics, genomic instability, novel cancer screening (p.33)*
- targeted drug delivery, role of inflammation, epidemiology of*
- gene-environment interactions... (p.34)*
- cancer registries, Latin America... (p.35)*

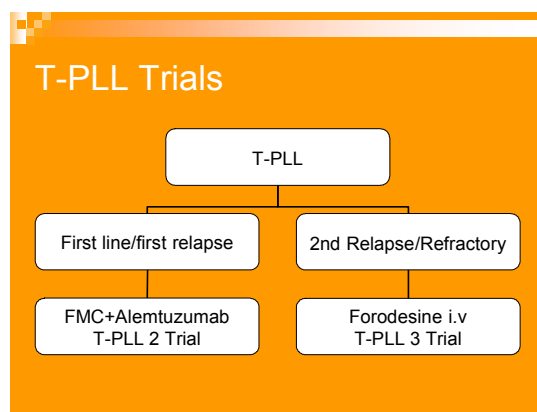
All members should give feedback to Uli Jäger about their thoughts and interests how there might be connections to CLL research and how there might be further lobbying and participation in the EU frame program in the participating countries.

TOP 3: Future treatment of PLL (M. Herold/F. Davi)

M. Herold (Erfurt) presented the current status and first data on the PLL-1 trial (chemotherapy with fludarabine + cyclophosphamide (FC) in patients with B-PLL, pre-treatment allowed except FC). 21 pts have been included, OR in 11 of 21. Median OS 32 months in responders vs 7 months in non-responders. The protocol was amended in 2004 for offering FC-Rituximab as therapeutic regimen. So far no pt has been enrolled into the amended protocol due to the rarity of the disease. M. Herold was asking for generating a European cooperative trial effort to improve progress in this trial protocol and in B-PLL treatment. Several members showed interest by hand sign in a combined European effort between PLL-treating centres in different countries. It was decided that interested members will get in touch and exchange further information.

TOP 4: ERIC European initiative on T-PLL trials (G. Hopfinger)

Georg Hopfinger (Vienna) presented data on the T-PLL studies 1-3, currently carried out in Germany and Austria as effort of the German CLL study group. Due to the rarity of the disease and increasing difficulties in the accomplishment of such small studies according to the new pharmaceutical law (i.e. sponsor must provide trial medication, ethical approval, monitoring etc.) a European initiative on the treatment of T-PLL was suggested to be created. The majority of the members agreed to launch an ERIC based effort but there were disagreements in therapeutic regimens to be used (alemtuzumab in combination with alkylators vs purinanaloga). It was decided to find a potential consensus strategy by direct exchange and comparison of data/experience and protocols by the currently T-PLL treating centres (Austria – Germany – UK).



Proposal of future T-PLL trials by Georg Hopfinger

TOP 5 & 7: Future p53 research in the context of ERIC & harmonization of FISH analysis (R. van Oers, A. Kater (Amsterdam), S. Pospisilova (Brno), S. Stilgenbauer (Ulm))

Correlation of p53 genetic mutation and functionality is currently of great interest since p53 dysfunction is the strongest independent predictor for aggressive disease, resistance to chemotherapy and early death in CLL. The group of A. Kater/R. van Oers suggested a MLPA-like test as assay for future p53 functional analysis, preliminary data were presented. Future questions to be answered are: Which (combination of) markers are most sensitive to detect p53 function? Which cut-off level of FISH data (%11q-/17p-) correlates with p53 function? Does measuring p53

function detect patients with dysfunctional p53 and normal FISH? For collection of more data by MLPA-testing blood samples of CLL patients with 11p-or 17p-deletion or clinical resistance to fludarabine would be required. To be able to collect enough patient material this was asked to be launched i.e. as a European initiative on behalf of ERIC.

Further data on p53 mutational analysis were presented by Sarka Pospisilova from Brno (Czech Republic) with the same aim of creating a common initiative on p53 research in CLL.

Stephan Stilgenbauer (Ulm) summarized that there are a lot of p53 assays developed and multiple experiences collected throughout different groups and countries. To ensure a straight forward future strategy in p53 research it was decided that a specific European workshop on p53 mutational analysis should be launched at one of the next ERIC meetings. There all interested researches should have the opportunity for more detailed exchange and discussion of their data and experiences (for more information/organization responsible: S. Stilgenbauer, N.N). It was also decided to contact CRC researchers for participation in this workshop.

TOP 6: *ERIC consensus & review board on IGHV mutational analysis (P. Ghia, Milan)*

Paolo Ghia presented the current status of the ERIC review board on IGHV mutational analysis. First recommendations on IGHV analysis have been published as editorial in Leukemia (Leukemia. 2007 Jan; 21(1):1-3). To make the effort accessible and helpful to everybody dealing with IGHV mutations a webpage has been created in cooperation with G. Strache (ERIC office Cologne/Munic, www.ericll.org/projects/IGVHMutationalAnalysis.php), where IGHV sequences may be uploaded and reviewed. A specific workshop for all researchers interested in IGHV mutational analysis was announced: "Educational Workshop on Immunoglobulin Gene Analysis in Chronic Lymphocytic Leukemia" in Uppsala/Sweden on June 14-15 2007. For more information and registration: www.igccl.com.

TOP 8: *Harmonization of ZAP70 analysis - status (F. Cymbalista/R. Letestu, Paris)*

Florence Cymbalista reported that the sample data from the participating centers are still being analyzed. It was generally stated that currently multiple labs try to apply ZAP70 testing being not aware of quality standards or requirements. To improve quality control of ZAP70 analysis throughout Europe and proceed with the harmonization (goal: recommendation of a standardized analysis procedure) it was planned to carry out a second specific workshop on this topic for interested researchers in 2007 (for further information Florence Cymbalista/Paris may be contacted).

TOP 9: *Harmonization of MRD analysis in CLL - news (CLL MRD Group, A. Rawstron, Leeds)*

Andy Rawstron reported that the results on harmonization of CLL MRD analysis are now accepted for being published in Leukemia soon. One of the major achievements throughout the year has been the establishment of the MRD-web page (www.mrd-cll.org), where MRD operating procedures and quality control analyses (including data

submission) are offered. Interested people can get registered there. In case of difficulties or errors in dealing with the web page the MRD group should be contacted. Future collaborative work will include the QC scheme with developing a simpler screening analysis and checking for feasibility of a 6- colour assay.

TOP 10: *European survey on CLL treatment: next steps (V. Levy, Paris) Vincent Levy (Paris/France) gave an update about the status of the planned European-wide survey on clinical practice in CLL patients. The aim of the survey is the recordation of how hemato-oncologists treat CLL patients European wide - within or without clinical studies. The survey will be carried out by the spread of vignettes offering 4 CLL virtual patient cases (2 CLL pts of young age, 2 of old age) to clinicians who will be requested to document their personal solutions for these cases. Current problems to be solved are: future funding has to be clarified (first funding application in France was defeated, several companies communicated their interest in the data). A list of corresponding physicians in the project is planned to be completed in spring 2007.*

TOP 11: **Next meeting: Heidelberg/Germany on Jan 30-31 2007 (at the General Assembly of the ELN), info: www.ericll.org**