



Date: August 11, 2014

**European LeukemiaNet Workpackage Meetings
at 19th Congress of EHA**

Milan, June 12-15, 2014

Coordinator: Prof. Dr. Rüdiger Hehlmann

Summary

The 19th EHA Congress took place from 12 to 15 June 2014 in Milan, Italy. In this context, the WP meetings of the European LeukemiaNet were held on June 12, 2014 in the Fiera Milano Congressi in Milan. The WP meetings were financially supported by the ESF-ELN research networking program. The ELN is grateful for the support.

One major goal of the WP meetings was to get the members of all ELN WPs face-to-face together and to have the opportunity to discuss new studies, ongoing studies and recommendations to common European trials.

Scientific content of and discussion at the workshops

On 12 June, each ELN-Workpackage had their meeting. Challenges and new directions in leukemia and related disease entities were highlighted during the workpackage meetings. Trials were presented and discussed. Each WP reported on the different projects and discussed future objectives and partially recommendations.

EURO-SKI meeting

Discussion of the Inner Circle of the Steering Committee on future analyses and planned amendment (Patient number ↑, 2nd stop)

CML (WP4)

EURO-SKI Study: *FX Mahon* and *S Saussele* gave a short update. EUTOS Population Based Registry: *M Baccarani* presented an update. 2978 newly diagnosed pts registered by 22 Study Groups in 20



European countries. Pregnancy registry: *E Abruzzese* presented a short report of Italian Pregnancy Registry. Metabolic side effects of TKIs: *J Mayr* proposed a prospective study. ELN Statistical Committee: *M Pfirrmann* presented contents of a workshop offered in February 2015.

Next WP4 meeting will take place at ASH in San Francisco early Sunday morning Dec 7.

CLL (WP7)

A General Meeting covered administrative issues including an update on three projects:

- The MRD Harmonisation Approach by Flow Cytometry – *A Rawstron and P. Ghia*
Under this collaborative effort a tube including a panel of 6 colour flow cytometry was validated among investigators and it is planned a comparison between flow cytometry and High Throughput Sequencing techniques to assess minimal residual disease. In addition, a survey is planned to send to all ERIC members to understand how investigators perform minimal residual disease in CLL in clinical practice
- ERIC Novel Mutation Project – *K Stamatopoulos and R Rosenquist*
Final results of mutation gene project was presented in more than 3000 patients and it was notified that the manuscript was recently accepted for publication in Leukemia, and further analysis is continuing.
- ERIC Accreditation in TP53 Mutation Analysis – *S Stilgenbauer and S Pospisilova*
Shipment of DNA samples were organised for analysis of TP53 mutations among ERIC investigators

MDS (WP8)

Four topics have been discussed during 2 meetings: EUMDS Registry, Triage-MDS (FP7), MDS-RIGHT: Horizon 2020 application and the MDS hematopoietic stem cell transplantation (HSCT) guidelines

MDS Registry

New website of the EUMDS Registry has been launched by the York Team. Information will be added and updated (work in progress).

Progress of studies within the EUMDs Registry

- EUMDS Registry: 17 Countries and 134 Centres are participating; 1623 patients registered
- Cytomorphology sub study: final analysis ongoing.



- Implementation of TRIAGE-MDS (FP7 project) with York and with Project Management is ongoing.
- del5q: synopsis will be circulated
- BM fibrosis proposal will be circulated
- Iron chelation: final analysis postponed to next year if insufficient events in September 2014.
- Demographics (IPSS-R) : paper rejected by JCO; it will be resubmitted to Haematologica
- Iron sub study: interim analysis on 112 patients ongoing; abstract to be submitted to ASH
- Kinetics of cytopenias EUMDS: Joint models will be used to address the issues of slow decline over time. Plan to submit abstract to ASH
- Prognostic model comparison: postponed until more molecular data are available
- Novel algorithmic diagnostic model based on available clinical and laboratory data obtained from blood sample: proposal will be circulated
- Treatment with erythropoietin stimulating agents (ESAs): final analysis completed; manuscript phase
- MDS and solid tumors: in total 164 patients in Registry with solid tumors; questionnaire for additional information will be circulated

TRIAGE-MDS: This FP7 application has been granted. The study had an official kick-off in Mannheim (February 2014). The Horizon 2020 proposal (MDS-RIGHT) will have an interaction with the progression of TRIAGE-MDS. Important issues are: 1) a good inventory of what DNA material is available (sequenced data and retrospective samples); and 2) integration of already available sequence data into EUMDS should be discussed.

MDS-RIGHT: Horizon 2020 application

In Mannheim (Feb 2014) PHC-17 was identified as the most relevant topic for our MDS population. A first stage proposal has been submitted March 11th. It passed the first stage successfully (May 14, 2014). The core team of MDS-RIGHT is situated in Nijmegen. 15 Partners will contribute to the project (proposal). The submission of the final application is planned August 19, 2014. Outcome is expected before the end of October.

MDS HSCT guidelines: scenario analysis discussion with expert panel

During the second expert panel meeting they discussed all relevant topics and scenarios. Discussion on the scenario was based on the evaluation of scenarios by 22 experts. Only scenarios without consensus



or with relevant remarks/suggestions by the experts have been discussed. The task force of the expert panel will review the report of this meeting. This will be followed by a second round of scenario evaluation by all expert panel members.

CMPD (WP9)

The inflammatory pathways, leukemia stem cell habitats and the bone marrow microenvironment in myeloproliferative neoplasms: myths and facts:

The WP9-colloquium comprised of a series of state-of-the art discussions led by globally-recognized leaders in the increasingly recognized field of inflammation and cancer, with a specific focus in the myeloproliferative neoplasms (MPN) and the cellular and molecular biology involved. The forum helped strategize optimal efforts to target candidate inflammatory pathways, MPN stem cell habitats and the bone marrow microenvironment. The relationship between the clonality of MPNs and inflammatory cytokines, bone marrow morphology, stem cell niches, the JAK-STAT pathway and MPN-specific symptom-burden and the recent observation of a durable survival benefit afforded by the only licensed JAK inhibitor, ruxolitinib, for patients with myelofibrosis, was a focus of much debate and deliberation.

The experts concurred that the colloquium accorded a unique platform to discuss methods to harmonize and develop optimal targeted therapies, such as interferons, JAK inhibitors, mTOR inhibitors, telomerase inhibitors, to target these unique components in efforts to improve the outcome of patients with MPNs further. The colloquium leadership considered it prudent to collate the various findings and produce a peer-reviewed independent manuscript shortly.

ELENAE Project

JL Steegmann announced that *J Cortes* had confirmed his participation in the panel, whereas *A Quintas-Cardama* was not able to continue, because he is working with Novartis. The discussion was centred mainly in vascular problems and diabetes. A general agreement was to have a formal meeting at ASH 2014. A draft will be prepared to be discussed in that venue. They did not exclude to have another meeting at ELN meeting in Berlin. The final form of the manuscript is in kind dispute. The aim is to send it to Blood or JCO, but other options such as Leukemia or Haematologica are sensible as well.



SCT (WP14)

During the annual European Hematology Association Meeting in Milan the WP14 held on June 12th a session on Stem Cell Transplantation from 10.45 to 12:45 (room Tourquoise 2). The randomized study hematopoietic cell transplantation versus chemotherapy in elderly patients with AML was updated. Patient accrual reached 151 patients for registration and 73 were randomized. No safety concerns were raised. The interim analysis will be done according to protocol in the fall 2014 according to events reported. This is the first randomized study in elderly patients with acute myelogenous leukemia and a related or unrelated donor. As a next topic the second allo study was discussed in detail by *T. Ruutu*. The manuscript has been submitted to JCO and we are hoping for acceptance. The results of the study were presented to the audience and factors influencing survival defined. Further analysis on the rule of complete remission before first autologous and second autologous in comparison to allogeneic was analysed by *S. Iacobelli*. This important study is a further evaluation of a randomized study performed at a European level comparing auto (auto) vs. auto allo related in more than 300 patients. The clinical trial and an update was published recently, now the significance of achieving CR before auto and before second SCT was analysed in detail using a new statistical tool named multistate analysis. The results obtained underline the importance of achieving CR before SCT, which now can be reached using new drugs able to increase CR rate. New information on the global survey for stem cell transplantation was given during the session. The manuscript on 1 million transplants since the beginning has been terminated and will be submitted to a top scientific journal. Now more than 60.000 stem cell transplants are performed annually around the world. Collections for the global survey in 2011 and 2012 were initiated. The discussion focused also on the recommendations on how to treat GvHD. A first paper was released by *T. Ruutu* some time ago. The suggestion was to check on how these recommendations did change the treatments in Europe. Discussion on how collect this information and the possibility to publish a second version evaluated. A further topic should analysed the cost of stem cell transplantation globally and analyse factors associated with expenses and alternative drugs. *S. Giebel* will lead this project.

The meeting closed on 12.45.

Assessment of results and impact of the workshops on the future direction of the field

The European LeukemiaNet Workpackage Meetings at 19th Congress of EHA highlighted upfront European research in leukemia. European clinical trials are important to gain a broad patient collective, to discuss and compare results and offer optimal treatment for patients. Important activities



include consensus decisions in clinical study endpoints, the setup of patient registries for all leukemias, common standardisation procedures and classification systems in diagnosis and follow up (molecular monitoring, cytogenetics, minimal residual disease assessment) but also harmonisation in data evaluation and reporting. The publication and continuous revision of recommendations is an important aspect in patients' healthcare. Cooperative research is the only way to cure leukemia.



Final Programme

Assignment of groups and rooms
19th Congress of the EHA, Milan, Thursday, June 12, 2014

TIME THURSDAY JUNE 12		Tourquoise 2	SCIENTIFIC WORKING GROUPS
8:00 – 10:00	EURO-SKI	ELENÆ Project	
Coffee break 10:00 – 10:45			
10:45 – 12:45		SCT (WP14)	
Lunch break 12:45 – 13:30			
13:30 – 15:30	CML (WP4)	CLL (WP7)	
Coffee break 15:30 – 16:15			
16:15 – 18:15	CMPD (WP9)	MDS (WP8)	
Official EHA Scientific Working Groups			
From 18:30			AML (WP5 + 12) ALL (WP6)

ADDRESS: MiCo, Viale Eginardo (Gate 2), Milan, Italy



WP4 meeting

**Thursday, June 12, 2014
13.30 – 15:30**

Room: Tourquoise 1
MiCo – Milano Congressi, Milan, Italy

Agenda

1. EURO-SKI

(Mahon, Saussele)

2. Update of the EUTOS population based registry

(Baccarani)

3. Horizon 2020: Application 2015 or later using EUTOS data.

(Baccarani, Hasford, Hehlmann, J Guilhot, Simonsson)

4. Pregnancy registry. Short report and prospect of a common publication

(Abruzzese, Chelysheva)

5. Prospective study on metabolic side effects of TKIs

(Mayr)

6. Contents of Workshop offered by the ELN Statistical Committee in February 2015

(Pfirrmann)

7. Next WP4 meeting (ASH Sunday morning)

8. Other topics



WP7 – CLL/ERIC - Meetings

Session 1. 35th General meeting of ERIC members

Chairpersons: E. Kimby and E. Montserrat

Date: Thursday, June 12, 2014

Time: 13:50 – 15:30

Venue: Room Tourquoise 2, MiCo congress center, Milan, Italy

Agenda

- General information *E. Montserrat*
- New ERIC website
- Project Updates:
 - Recurrent gene mutations in CLL – harmonization and future directions *R. Rosenquist*
 - The MRD Harmonisation Approach by Flow Cytometry *P. Ghia/A. Rawstron*
- Other issues

Session 2. ERIC symposium / EHA scientific working group session

Cellular origin and immune system in CLL

Chairpersons: E. Kimby and E. Montserrat

Meeting Organizer: Federico Caligaris-Cappio (Milan, Italy)

Date: Thursday, June 12, 2014

Time: 18:30 – 20:00

Venue: Room Amber 1 + 2, MiCo congress center, Milan, Italy

Agenda

- Cell origin of CLL *Ralf Kuppers (Essen, Germany)*
- The innate immune system in CLL *Martina Seiffert (Heidelberg, Germany)*
- The clinical implications of understanding immune deficiency and autoimmune phenomena in CLL *Carol Morena (Barcelona, Spain)*
- Harnessing the immune system to treat (cure?) CLL *Alan Ramsay (London, UK)*



WP8 - MDS - Meeting

**Thursday, June 12, 2014
16:15 – 18:15**

Room: Tourquoise 2
MiCo – Milano Congressi, Milan, Italy

Agenda

TOPIC: Consensus Meeting for guidelines for allogeneic SCT in MD

- 1. Welcome and Recap**
- 2. Summary of responses from expert panel**
- 3. Topics to discuss**
 - a. Controversial topics
 - b. Missing topics
- 4. Scenarios to discuss**
 - a. Absence of consensus
 - b. Missing scenarios
- 5. General remarks or suggestions**
- 6. Further planning**



WP9 - CMPD

**Thursday, June 12, 2014
16:15 – 18:15**

Room: Tourquoise 1
MiCo – Milano Congressi, Milan, Italy

Agenda

Chair: Tiziano Barbui

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| 1. Objectives and introductions | <i>Tiziano Barbui
Tariq Mughal</i> |
| 2. The clonal and systemic inflammation-mediated effects in MPNs | <i>Hans-Carl
Hasselbalch</i> |
| 3. Hematopathological appraisal of ‘inflammation and MPNs | <i>Hans-Michael
Kvasnicka
Radek Skoda</i> |
| 4. Role of NF-E2 in chronic inflammation and clonal evolution in MPNs | |
| 5. Potential clinical impact of targeting JAK-STAT pathways in MPNs | <i>Peter Valent</i> |
| 6. T-regs in MPNs | <i>Gianni Barosi</i> |
| 7. Lessons learned from clinical trials of interferons in MPN | <i>Heinz Gisslinger</i> |
| 8. Summary | <i>Tiziano Barbui
Tariq Mughal</i> |

