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## NEWSLETTER 22

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### HIGHLIGHTS FROM THE 9th IELSG ANNUAL MEETING HELD IN ROME ON FEBRUARY 17-18, 2006

Dear Colleagues and friends,

The recent meeting held in Rome gave us, as usual, the opportunity to review the ongoing studies, to compare our experiences and to discuss novel proposals and strategies for the future of the group. 91 persons from 15 countries attended the meeting. Here is a summary of the main topics addressed.

#### ONGOING CLINICAL STUDIES

*IELSG 10: A phase II study of R-CHOP, with intrathecal methotrexate followed by radiotherapy in patients with primary testicular non-Hodgkin's lymphoma.*

52 patients have already been enrolled in the study. However only 44 had systemic chemoimmunotherapy with R-CHOP whilst the first 8 patients had CHOP only. It has been decided to continue the accrual until a total number of 50 evaluable patients treated with R-CHOP will be reached.

In the meanwhile a discussion has been started about the possibility of a novel study in this setting. Since the preliminary analysis of this ongoing trial seems to suggest that the IELSG 10 strategy can reduce but probably not eliminate the risk of CNS relapses it has been suggested that the design of any future study should be aimed to an improvement of the CNS prophylaxis. A general agreement was achieved on the idea that the next study should test either the use of Depocyte instead of intrathecal Methotrexate or the inclusion of medium (-high) dose systemic Methotrexate. A more detailed proposal will be prepared and will circulate soon.

*IELSG 20: Randomized phase II trial on primary chemotherapy with high-dose methotrexate, alone or associated with high-dose cytarabine, followed by response- and age-tailored radiotherapy for immunocompetent patients with newly diagnosed primary central nervous system lymphoma*

40 patients entered from May 2004 to February 2006 with a very good accrual rate. The median age of the enrolled patient is 57 years and an interim analysis of the first 38 treated patients is ongoing according to the protocol.

*IELSG 24: A Phase I Study of Intrathecal Rituximab in Patients with Lymphomatous Meningitis*

The phase I study on the intrathecal administration of Rituximab has not enrolled any patient thus far. The study was initially opened only at a few centers (Bellinzona and St. Gallen in Switzerland, Bergamo and Milan - HSR - in Italy). However some administrative and regulatory obstacles prevented the distribution of the drug in the Italian centers and later the Bergamo center renounced to participate. With the aim to finally start enrolling patients, the Novara center has been added in Italy along with an additional study center in Aviano. The IELSG Assembly in Rome decided, with the agreement of Roche International (which is providing the study agent), to open two additional study sites in Germany, namely Homburg and Bielefeld. To further improve the chance of a rapid patient accrual, also HIV-positive patients can now be entered in this study. We do hope that these move will allow the study to be properly performed.

*IELSG 25 A+B: Phase II Study of VELCADE™ in patients with extranodal marginal zone B-cell lymphoma of MALT-type pretreated with one or more prior systemic therapy regimen*

The studies are evaluating the activity and toxicity of Bortezomib in extranodal marginal zone lymphomas. A total of 12 patients have been enrolled thus far, 6 in each study. The discussion was focused on the fact that for the group would be very important to have soon some preliminary information on response rates and feasibility of such a treatment in marginal zone lymphomas before any plan about future controlled studies. Indeed, the combination of Velcade and Rituximab in marginal zone lymphoma seems biologically and scientifically sound but it has never been studied in this setting.

## NOVEL CLINICAL STUDIES TO BE ACTIVATED

*IELSG 26: A clinico-pathologic study of primary mediastinal B-cell lymphoma*

The study on the diagnostic and prognostic utility of PET scan in primary mediastinal lymphoma has been approved and all the IELSG members are solicited to start the study approval procedures with their regulatory agencies and Ethical Committees. The study is not testing any novel therapeutic approach and has been designed as a “no-profit” trial. For this reason a study-specific insurance has not yet been stipulated. It will be considered, however, if deemed necessary by Ethical Committees and regulatory agencies. The protocol will be provided upon request to [ielsg@ticino.com](mailto:ielsg@ticino.com).

*IELSG 27: A Clinico-pathological phase II study with translational elements to investigate the possible infective causes of MALT lymphoma of the ocular adnexae with particular reference to Chlamydia species and the effects of treatment with tetracycline*

This study will address the geographic variability of the association between Chlamydia infection and ocular adnexa lymphoma as well as the utility of a first line therapy with antibiotic alone. The protocol is available and will be provided upon request to [ielsg@ticino.com](mailto:ielsg@ticino.com). All IELSG members (groups and institutions) can now start the regulatory procedures for study activation in each country.

## RANDOMIZED TRIAL IN MALT LYMPHOMA

Updated details on the accrual of the IELSG 19 randomized study of Chlorambucil vs. Chlorambucil plus Rituximab in extranodal marginal zone lymphomas were presented. This study had completed the planned accrual in October 2005. The discussion was mainly focused on the opportunity of re-open the accrual in this trial after a major amendment to add a Rituxan alone arm to the already existing two study arms. Randomization can then continue on a 1:1:5 ratio.

The statistical and scientific adequacy of this design was confirmed by the statisticians at Roche. Since in most countries the study was not officially closed, it should be possible to re-start patient accrual after the approval of such an amendment by the local Ethical Committees and regulatory agencies. The amendment is in preparation and will be sent soon to the study principal investigators in each country.

## ONGOING AND FUTURE CLINICO-PATHOLOGICAL STUDIES AND MANUSCRIPTS IN PREPARATION

The assembly was updated on the situation of several retrospective clinico-pathology surveys that the group has undertaken. In particular the analysis of diffuse large B-cell lymphoma in the head and neck district (IELSG 23), the study on primary bone lymphoma (IELSG 14) and the study on primary diffuse large cell lymphoma of the breast (IELSG 15) have been completed and the manuscripts are in preparation. The analysis of low grade primary lymphoma in the breast is planned in the next months. The study of intravascular lymphoma is still ongoing and a collaboration with Japanese colleagues to better define the diagnostic criteria for this peculiar entity has begun with a fruitful workshop held in Locarno in December 2005.

A novel retrospective clinico-pathological study on lung lymphoma has been also approved: a detailed protocol with the data-collection forms will be available soon.

## A VIRTUAL TISSUE BANK FOR PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA

The availability of material for Primary Central Nervous System Lymphomas (PCNSL) is extremely limited. To overcome this problem, multi-institutional collaborations are mandatory. With the financial support of Oncosuisse, within the International IELSG and in collaboration with the International PCNSL Collaborative Group (IPCG), a virtual tissue bank has been set up for residual PCNSL tissue, which could be used for forthcoming biological studies on PCNSL.

The database backend runs on a dedicated server within the IELSG premises.

Records consist of 24 data fields describing (anonymously) patient, pathology and availability of samples. The patient is identified only by a local histology number.

Database access restrictions have been set according to different user types.

The virtual tissue bank is accessible via the IELSG website ([www.ielsg.org](http://www.ielsg.org)) with any web-browser and any operating system. After having read and signed the virtual tissue bank policies, pathologists willing to share their archival material receive strictly personal usernames and passwords. Submitters have access to all their data and to summarized data from the whole database. Importantly, the actual histological materials remain at the local Institutions. Access to all the data in the virtual tissue bank is available only to the curators of the database and to the IELSG data-managers. Investigators willing to perform research on PCNSL can

submit a research project to the IELSG; each project will be evaluated for material availability and for scientific relevance. Further information can be requested to F. Bertoni (frbertoni@mac.com) and M. Ponzoni (ponzoni.maurilio@hsr.it).

#### LAST BUT NOT LEAST

The election of Prof. Jim Armitage from the University of Nebraska in the IELSG Board of Directors has been approved by the Assembly. Jim has been an important friend of IELSG since the beginning of our story as witnessed by the homepage of our website. And we are looking forward to collaborating with him. His participation to the Board of Directors will be surely valuable and very fruitful.

The Czech National Lymphoma Study Group application for the IELSG membership has been approved by the Assembly. Dr. Marek Trneny and the scientific secretary of the Group Dr. Ingrid Vasova will be the contact persons. We do hope that the Group can take part to our ongoing and future clinical studies.

#### ACKNOWLEDGEMENTS

We want again to thank Maurizio Martelli for the excellent organization of the meeting in Rome as well as Beatriz Martinez Delgado and Thomas Rüdiger for their brilliant educational talks. We also thanks and are indebted with Cristina Morinini, Monica Bertini and Oxanna Lopez (our new data-manager!) not only for the excellent contribution they gave to the meeting organization but also for their conduction and for the important everyday work, which is keeping the IELSG alive.

F. Cavalli, E. Zucca