

Dear Friends,

Please find below the 49<sup>th</sup> NEWSLETTER of the International Extranodal Lymphoma Study Group.

### IELSG further expands collaboration

At the beginning of April, during the meeting “*Avances en linfoma: Linfomas extranodales y linfomas T*”, which took place in Santiago (Chile), the participants expressed their intention to widen the cooperation on lymphoma research and management either by joining the IELSG studies, or by starting the T-Cell Lymphoma Project coordinated by Prof. Massimo Federico.

In this context, during the annual meeting of the Brazilian Association of Hematology (ABHH), which was held in Sao Paulo a few days later, ABHH became a member of the IELSG. We will therefore now explore the possibilities of opening at least a few centers for the IELSG 37 study. Perhaps, we will also be able to find room for some retrospective epidemiological studies, particularly on extranodal T-cell lymphomas which might have some particular characteristics in Latin America. We have planned to meet again in San Diego at ASH, hoping by then to have some concrete proposals, also on behalf of ABHH.

### Current status of the IELSG trials

The total accrual of prospective, retrospective and biological IELSG trials has now reached more than 6'700 patients.

### Ongoing prospective clinical studies

#### **IELSG 30 – A phase II study of R-CHOP with intensive CNS prophylaxis and scrotal irradiation in patients with primary testicular diffuse large B-cell lymphoma**

Thanks to the first efficacy results of the IELSG 10 study, the sample size has been increased in January 2015 to 54 patients. Only 9 patients are now missing to reach the study's goal: we expect to complete the accrual by the end of this year.

#### **IELSG 37 – A randomized, open-label, multicenter, two-arm phase III comparative study assessing the role of involved mediastinal radiotherapy after Rituximab containing chemotherapy regimens to patients with newly diagnosed Primary Mediastinal Large B-Cell Lymphoma (PMLBCL)**

Two hundred fifty seven patients have been enrolled in this study: 185 in Italy, 21 in Ukraine, 21 in the UK, 10 in Switzerland, 6 in Norway, 3 in Sweden, 4 in Canada, 2 in Poland and 1 in the US.

We are currently waiting for the activation of other centers in Europe (Czech Republic and Portugal).

The amendment of the study protocol that allows the accrual of patients without baseline PET is already active in some centers and we hope we will soon have its approval for all participating centers.

#### **IELSG 39 – International prospective phase II trial addressing the efficacy of first-line *Chlamydomoeta psittaci*-eradicating therapy with protracted administration of Doxycycline followed by eradication monitoring and antibiotic re-treatment at infection re-occurrence in patients with newly diagnosed Ocular Adnexal Marginal Zone Lymphoma (OAMZL)**

The IELSG 39 study will assess the role of prolonged Doxycycline treatment and re-treatment in case of *Clamydophila psittaci* re-infection in patients with ocular adnexal marginal zone lymphoma. The study is open in Italy and at present, 43 of the expected 44 patients have been enrolled.

**IELSG 42 – An international phase II trial assessing tolerability and efficacy of sequential Methotrexate-Aracytin-based combination and R-ICE combination, followed by high-dose chemotherapy supported by autologous stem cell transplant, in patients with systemic B-cell lymphoma with central nervous system involvement at diagnosis or relapse (MARIETTA regimen)**

Aim of the IELSG 42 study is to evaluate the efficacy and feasibility of a new sequential combination of HD-MTX-AraC-based chemoimmunotherapy, followed by R-ICE regimen, and by high-dose chemotherapy supported by ASCT. The study is already open in Italy (where 22 patients have been included) and will soon be active in the UK. An amendment has recently been submitted to the competent authorities and we are planning to have activate centers also in Czech Republic, France, Germany, Israel, Italy, Spain, Switzerland and the Netherlands.

**IELSG 43 – High-dose chemotherapy and autologous stem cell transplant or consolidating conventional chemotherapy in primary CNS lymphoma - randomized phase III trial (MATRix)**

The aim of this randomized phase III trial is to optimize the treatment of patients with PCNSL less than 70 years old by comparing HDT and ASCT to an optimized non- stem-cell supported consolidating therapy. The study has been open for accrual since June 2014 and, according to the study design, 250 patients will be included into the study.

This is the first randomized trial in PCNSL which will probably give an answer to the question whether high-dose-chemotherapy within the first-line treatment is superior to conventional therapy as consolidation after intensified immunochemotherapy in newly diagnosed PCNSL at the highest level of evidence.

The study is open in Germany (81 patients enrolled) and will be soon approved in Denmark and Italy. The end of trial is expected in 2017.

## New prospective trials

**IELSG 40 – A phase II Trial addressing feasibility and activity of Clarithromycin plus Lenalidomide combination: A full oral treatment for patients with relapsed/refractory mucosa-associated lymphoid tissue lymphoma (CLEO)**

The CLEO trial is a single arm, two-stage, phase II trial for the treatment of MALT lymphoma with Clarithromycin and Lenalidomide. Patients with gastric or extragastric disease are eligible at first or greater relapse after prior radiotherapy, chemotherapy or immunotherapy. The planned number of evaluable patients is 30 in stage one and 32 in stage two (total number of evaluable patients 62).

The study is expected to open in Austria, Italy, Spain and Switzerland later this year.

## Clinical trial with completed accrual

**IELSG 38 – A phase II study of Chlorambucil in combination with subcutaneous Rituximab followed by a maintenance therapy with subcutaneous Rituximab in patients with extranodal marginal zone B-cell lymphoma of mucosa associate lymphoid tissue (MALT lymphoma)**

The aim of the IELSG 38 trial is to assess the safety and efficacy of the Chlorambucil plus Rituximab combination using a new formulation of Rituximab given subcutaneously, followed by a two-year maintenance treatment with subcutaneous Rituximab. This is the first study to assess a maintenance treatment with Rituximab in this patient population.

The accrual is complete and data analysis has already been started.

## Ongoing retrospective studies

### IELSG 17 – Multi-institutional retrospective analysis of intravascular lymphomatosis

Sixty-eight patients have been enrolled in 15 countries: 33 in Italy, 7 in Spain, 4 in Australia, 3 in France Greece, Hungary, Israel and in the Netherlands, 2 Argentina and Switzerland, 1 in Belgium, Germany, Poland, Sweden and US.

**The next meeting will be held in Stuttgart (Germany) on March 17-18, 2017.  
Save the date!**

More details will follow soon.

Kind regards from the Operational Office

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**CAREER DEVELOPMENT**

Seminar 1:  
CCL & IOSI course

Module 1:  
Basic research  
epidemiology, pathology

Module 2:  
Principles of diagnostics,  
management & clinical  
trials

Module 4:  
Lymphoma  
subtypes II

Attendance  
Seminar 3:  
CCL course

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*THIRD COHORT 2017-18*

*The European School of Oncology in co-operation with Ulm University is presenting a structured Certificate of Competence in Lymphoma Programme, an academically recognised curriculum of studies, that was developed with the contribution of internationally recognised physicians and scientists in the field of haemato-oncology.*

**Chairs:**  
J.O. Armitage, US  
M. Bergmann, DE  
F. Cavalli, CH  
S. Stilgenbauer, DE

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