

Dear Friends,

Please find below the 46th NEWSLETTER of the International Extranodal Lymphoma Study Group.

1. Last annual meeting

The last IELSG Annual Meeting was held in Bellinzona, on March 21-22, 2014.

Sixty-five haemato-oncologists, radio-oncologists, pathologists and basic research scientists from all over the world joined the meeting and discussed ongoing and future trials.

We want to thank all of you for your contribution.

Both days of the meeting were closed by excellent education lectures. On March 21, prof. Gianluca Gaidano from Novara on "Post-transplant extranodal lymphoproliferative lesions", and on March 22 Dr. Astrid Pavlovsky from Buenos Aires on "PET-based treatment of Hodgkin Lymphoma: present evidence and future developments".

2. An important IELSG publication

On May 5 the results of the IELSG 26 study ([¹⁸F]Fluorodeoxyglucose Positron Emission Tomography Predicts Survival After Chemoimmunotherapy for Primary Mediastinal Large B-Cell Lymphoma: Results of the International Extranodal Lymphoma Study Group IELSG-26 Study, Martelli M, Ceriani L, Zucca et al.) were published in the Journal of Clinical Oncology. The paper was accompanied by an editorial (Hamlin PA. Evolving Treatment Paradigms for Primary Mediastinal Diffuse Large B-Cell Lymphoma. J Clin Oncol. 2014 May 5) which acknowledged and applauded the IELSG efforts to improve the management of PMLBL.

3. Current status of the IELSG trials

The total accrual of prospective, retrospective and biological IELSG trials has now reached more than 6300 patients.

Ongoing clinical studies

IELSG 39 – International prospective phase 2 trial addressing the efficacy of first-line Chlamydomphila 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. At present, accrual is only open in Italy where 18 of the 30 expected patients have been enrolled.

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 IELSG 38 trial will 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 will be the first study to assess a maintenance treatment with rituximab in this patient population. Based on the statistical design, approximately 100 patients will be enrolled in the study.

The study is activated in all the participating countries (Switzerland, Italy and France) and 7 patients have been enrolled up to now (3 in Italy, 3 in France and 1 in Switzerland).

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)

116 patients have been enrolled in the IELSG 37 up to now in Canada, Italy, Norway, Sweden, Switzerland, UK and Ukraine and we welcome the activation also of Buenos Aires (Argentina) and Mayo Clinic (USA) in May 2014.

The protocol has recently been amended and sent to the competent authorities in order to implement the most current knowledge on post treatment PET scans deriving from the IELSG 26 trial: in fact, data analysis from IELSG 26 indicated that patients with a Deauville score of 3 (residual FDG uptake > mediastinal blood pool and ≤ liver) had a clinical outcome identical to that of patients with Deauville score 2 (i.e., FDG uptake below the mediastinal blood pool one). Using the Deauville score 3 as cut-point (uptake ≤ liver) increases specificity and maintains sensitivity in identifying patients who are at risk of failure. Based on this, the sample size was recalculated and 540 patients will have to be registered (instead of more than 700) in order to reach the required number of 376 responding patients to be randomized.

IELSG 36 – BRISMA – Bendamustine and Rituximab for the treatment of Splenic Marginal Zone Lymphoma. A phase II prospective study

The IELSG 36 study will assess safety and efficacy of the combination of Bendamustine and Rituximab as a first line treatment in patients with splenic marginal zone lymphoma.

The accrual of this study is open in France and Italy and 52 patients have now been enrolled.

IELSG 32 – Randomized phase II trial on primary chemotherapy with high-dose Methotrexate and high-dose Cytarabine with or without Thiotepa, and with or without Rituximab, followed by brain irradiation vs. high-dose chemotherapy supported by autologous stem cells transplantation for immunocompetent patients with newly diagnosed primary CNS lymphoma
The IELSG 32 randomized study in patients with primary CNS lymphoma has had a very good accrual (216 at first randomization) and the goal of 104 evaluable patients at the second randomization will be reached before the end of July 2014.

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

The phase II IELSG 30 study, after the recall of Depocyte, was recently re-opened in Italy. Thirty-one patients have been enrolled and the first efficacy results are awaited.

4. Next activities

New IELSG prospective trials

Several trial proposals were presented and discussed, among those the most important were:

CNS lymphoma - Two PCNSL studies will follow the IELSG 32: IELSG 42 “MARIETTA” on CNS relapses of aggressive lymphoma and IELSG 43 “MATRIX” on newly diagnosed CNS. Both trials were presented by Andrés Ferreri, on behalf of the European PCNSL Collaborative Group (EPCG).

MALT lymphoma - The IELSG 19 study of chemotherapy-naïve MALT lymphoma showed that the combination of Rituximab and Chlorambucil produces superior EFS and PFS in comparison with either Rituximab or Chlorambucil as single agents.

While the IELSG 38 study is currently ongoing plans for a future randomized trial in MALT lymphoma were discussed during the meeting. A decision was made that before planning the conduct of a big randomized trial, further analysis of clinical and biological data from the IELSG 19 patients will be performed to tailor a sound treatment approach for patients with marginal zone lymphoma. Several interesting options such as combinations of antibiotics and immunomodulators, new drugs or new CD 20 antibodies were discussed

Additionally it was accepted that an effort should be done in the future prospective trials of the IELSG to collect tumor tissue from participating patients that could be used for subsequent genetic analyses.

Next meeting

The next meeting will be held in London (UK) on March 27-28, 2015. More details will follow as soon as possible.

Kind regards

F Cavalli, E Zucca, A Conconi, A Stathis, R Gianascio, N Ielmini, J De Jong, E Porro