

IELSG

INTERNATIONAL EXTRANODAL LYMPHOMA STUDY GROUP

TRIALS COORDINATION CENTRE: ONCOLOGY INSTITUTE OF SOUTHERN SWITZERLAND

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NEWSLETTER 13

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PRIMARY CNS LYMPHOMA: THE NEXT UNDERTAKING HAS BEGUN

The workshop on PCNSL, held during the Lymphoma Conference in Lugano in June 2002, provided further evidence that an international collaborative effort is needed to answer the most pressing questions on PCNSL treatment. During the last ASH conference in Philadelphia a preliminary meeting has been held to explore the possibility of setting up an effective international co-operation.

During the meeting there has been a unanimous agreement about the formation of an international collaborative group for the study of PCNSL. It was emphasized the need of an international collaborative group since PCNSL is a rare tumour and involves many clinical disciplines. There was a consensus that this PCNSL collaborative group would function under the sponsorship of the IELSG.

This collaborative group should be organized around a set of research concepts. The first step has been the preparation, under the direction of Dr. Ferreri, of a Consensus Paper based on the Lugano workshop on PCNSL, which has been sent to JCO. The development of one or more phase II clinical trials, the creation of a tissue bank and of a patient/case registry were also proposed.

An Executive Committee devoted to develop goals and provide governance for the group has been constituted together with an Advisory Committee of senior leaders to provide guidance and advice.

The details concerning these committees and also a number of scientific subcommittees devoted to focus on specific topics can be found in the minutes of the Philadelphia meeting on the IELSG web site.

Of course, the conclusions of the Philadelphia meeting are a challenge for the IELSG. At the next IELSG meeting in Ascona we want to properly discuss the issue of PCNSL. For this reason you can find below a summary of the results of our retrospective studies (page 2) and the proposals of clinical studies are described in the program of the Meeting (page 3).

THE FORTHCOMING ASCONA MEETING

You finally find the program below. A pathology review session is also planned in Locarno on Thursday and Friday, March 6th and 7th. The opening of the pathologists' meeting will be on Thursday, 3:00 p.m. We will make you know as soon as possible more detailed information.

You find attached the Registration Form (page 5) for participating to the IELSG Meeting (clinicians and pathologists). The deadline has been deferred to February 15th 2003. Please send it back soon!

Best wishes

E. Zucca, A. Conconi, F. Cavalli, C. Morinini, M. Trovesi

SUMMARY OF THE IELSG 7 STUDY AND PROPOSALS FOR IELSG MEMBERS

by A. Ferreri, Milan, I

THE IELSG 7 STUDY

The IELSG 7 study is a retrospective analysis of clinical and pathological data of an international series of 378 immunocompetent patients with primary central nervous system lymphoma (PCNSL) treated at 23 cancer centres, from 5 countries, which actively participate in the IELSG activities. The final results of the analysis of the clinical data have been recently reported in three papers regarding therapeutic management and results, intraocular lymphoma and prognostic factors. The main conclusions of this study are:

- 1) Chemo-radiotherapy is superior to radiotherapy alone.
- 2) High-dose methotrexate (HD-MTX) is the most effective drug.
- 3) In patients treated with HD-MTX, the addition of high-dose cytarabine was associated with better outcome.
- 4) In these patients, intrathecal chemotherapy was not correlated to outcome.
- 5) In patients reaching complete remission after receiving HD-MTX-based chemotherapy, consolidation radiotherapy did not improve survival.
- 6) Cases of intraocular lymphoma showed a similar survival to the rest of PCNSL.
- 7) Chemotherapy combined with ocular irradiation resulted in better ocular-disease control and survival.
- 8) Age, PS, LDH serum level, CSF protein concentration, and involvement of deep regions of the brain were independently predictors of response and survival. These variables were used to design a prognostic score useful for distinguishing risk groups.

IELSG PROSPECTIVE TRIALS

The IELSG is planning a multicenter international randomized trial in PCNSL, which will be performed within an International Cooperative PCNSL Study Group created during the last Lugano Congress. The program of the IELSG for the next years regards the assessment of the superiority of polychemotherapy with respect to monochemotherapy with HD-MTX. This comparison should be developed by a phase II randomized trial with two arms: A) monochemotherapy with MTX 3.5 g/m², and B) the same MTX dose associated with cytarabine 2 g/m² twice a day, for 2 days; both arms followed by RT. These have been chosen on the bases of a large meta-analysis [Reni M. *et al.* IJROBP 51(2):419-425, 2001] and of the IELSG#7 study [Ferreri AJM, *et al.* Neurology 58(10):1513-20, 2002]. The IELSG prognostic scoring system [Ferreri AJM, *et al.* J Clin Oncol 21:266-272, 2003] will be used as stratification parameter. This protocol will ideally start before June 2003. With a P0 of 20% and a P1 of 40%, a total number of 33 patients per arm is required (two sided test, type I error 5%, power 80%). If the study question will be considered important and the accrual will be fast and high, this randomized phase II trial might be transformed in a phase III trial.

The identification of new active drugs in phase I/II trials in relapsed or refractory PCNSL must receive high priority. Then, a concomitant open non-randomized phase II trial, assessing idarubicin 25 mg/m² ev, every 3 weeks, as salvage monochemotherapy in relapsed and refractory patients might be sponsored by the IELSG. With a P0 of 10% and a P1 of 30%, a total number of 25 patients are required (two sided test, type I error 10%, power 90%). If active, idarubicin will be subsequently incorporated in a new experimental first-line chemotherapy regimen. This could be a winning strategy to delineate, in a few years, a more efficient chemotherapy regimen against PCNSL.

VI IELSG ASCONA MEETING: PROVISIONAL PROGRAM

FRIDAY MARCH 7, 2003

14.30 - 15.00

Registration at Centro Stefano Franscini, Monte Verità, Ascona

OPENING OF THE MEETING *E. Zucca, Bellinzona CH*

15.00 - 16.15

OVERVIEW OF THE STATUS OF THE ONGOING RETROSPECTIVE IELSG STUDIES

- IELSG 11 Retrospective evaluation of localized primary cutaneous B-cell lymphomas
S. Cortelazzo, Bergamo, I
- IELSG 12 Chromosome 11Q amplification in primary extranodal diffuse large B-cell lymphomas
F. Bertoni, London, UK
- IELSG 14 A retrospective evaluation of primary bone lymphoma
D. Christie, Tugun, AU
- IELSG 15 A retrospective international study of primary lymphoma of the breast
G. Martinelli, Milan, I
- IELSG 16 RT-PCR detection of the t(11;18) translocation as a predictor of outcome in extranodal marginal lymphoma of MALT type
F. Bertoni, London, UK
- IELSG 17 Multi-institutional retrospective analysis of intravascular lymphomatosis
M. Ponzoni, Milan, I
- IELSG 18 Retrospective international survey on primary effusion lymphomas
A. Conconi, Novara, I
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16.15 - 17.00

BEYOND THE WOTHERSPOON SCORE *C. Capella, Varese, I*

Report of the IELSG Workshop on the pathological criteria for the post-treatment evaluation of gastric MALToma

COFFEE BREAK

17.15 - 17.45

THE BIG UNDERTAKING I

The ongoing prospective clinical trials

- IELSG 4 Prospective randomized trial of chemotherapy vs chemotherapy plus irradiation in diffuse large-cell gastric lymphoma
G. Martinelli, Milan, I
- IELSG 19 Multicenter randomized trial of Chlorambucil versus Chlorambucil plus Rituximab in extranodal marginal zone B-cell lymphoma of mucosa associated lymphoid tissue (MALT lymphoma)
E. Zucca, Bellinzona, CH
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IELSG 10 A phase II study of R-CHOP, with intrathecal methotrexate followed by radiotherapy, in patients with primary testicular non-Hodgkin's lymphoma: to be finished! *U. Vitolo, Torino, I*

17.45 - 18.45

THE BIG UNDERTAKING II

CNS Lymphoma studies: where we are and where we want to go

- Report of a Philadelphia meeting ended with the creation of a CNS Lymphoma Intergroup Committee *F. Cavalli, Bellinzona, CH*
 - Proposal for a IELSG clinical study to be activated soon. *A. Ferreri, Milan, I*
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19.30 DINNER

20.45 - 21.45

EDUCATIONAL LECTURE I

Extranodal T- cell lymphomas *J.Vose, Omaha, USA*

SATURDAY MARCH 8, 2003

8.15 - 9.00

NEW PROPOSALS

- IELSG retrospective survey of Head and Neck lymphomas. *S. Cortelazzo, Bergamo I*
 - Gastric irradiation for MALT lymphoma: proposal for a retrospective study *G. Ryan, Merlbourne, AU*
 - An "External proposal": The F2 study in follicular lymphoma. *M. Federico, Modena, I*
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9.00 - 10.00

EDUCATIONAL LECTURE II

Everything you always wanted to know about microarrays and proteomics (but were afraid to ask) *F. Cotter, London, UK*

10.00 - 12.45

PLENARY DISCUSSION

How the Group can face the present challenges *F. Cavalli, Bellinzona, CH*

12.45 - 13.00

CLOSING REMARKS *F. Cavalli, Bellinzona, CH*

IELSG

INTERNATIONAL EXTRANODAL LYMPHOMA STUDY GROUP

REGISTRATION FORM - SIXTH IELSG ANNUAL MEETING ASCONA (SWITZERLAND) MONTE VERITÀ - March 7- 8, 2003

1 Registration Form for each participant

Name

clinician pathologist other

Institution (full address)

Contact phone

Fax

E-mail

I will attend the IELSG Ascona Meeting (March 7- 8, 2003)

Hotel accommodation is required yes no If yes specify:

single room double room shared with
(we suggest you, when possible, to share your room with a colleague)

Date of arrival Date of departure

PATHOLOGISTS' SECTION

We cannot accommodate more than 20 participants. Therefore registration might be limited to one person for each institution. Please register early.

I will attend the IELSG Pathology Review Session in Locarno (March 6- 7, 2003)

Hotel accommodation is required yes no If yes specify:

single room double room shared with
(we suggest you, when possible, to share your room with a colleague)

Date of arrival Date of departure

REGISTRATION CLOSING DATE: February 15, 2003

Please send back this filled Form to the IELSG coordination centre
by e-mail ielsg@ticino.com or Fax N. ++41 91 811 91 82