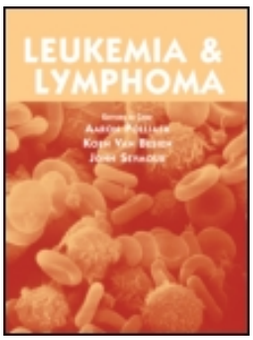

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REVIEW

Report on the First International Workshop on interim-PET scan in lymphoma

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Abstract
An international workshop, under the auspices of Groupe d'Etude des Lymphomes de l'Adulte (GELA) took place in Deauville, France, in April 3–4, 2009. The European experts with a published or personal experience on interim-PET in lymphoma were invited to the meeting. The aim of the workshop was twofold: (1) to reach a consensus on simple, reproducible criteria for interim-PET interpretation in Hodgkin lymphoma and diffuse large B-cell lymphoma (DLBCL), and (2) to launch two or more international validation studies, in an attempt to validate these rules. We concisely report here the minutes of the meeting and the conclusions/statements that have been reached.

Keywords: *Lymphoma and Hodgkin disease, prognostication, chemotherapeutic approaches*

Introduction

During the past 4 years the interim-PET scan performed in patients with lymphomas has emerged as a powerful prognostic tool in predicting treatment outcome particularly in Hodgkin lymphoma (HL) and diffuse large B-cell lymphoma (DLBCL). In a recent meta-analysis, the sensitivity of interim-PET ranged from 65 to 100% in HL and between 50% and 100% in DLBCL. The specificity reported was 94–100% for HL, and 73–100% for DLBCL [1]. In most of these studies interim-PET emerged as the most powerful prognostic tool, when compared with other well-established clinical parameters, such as the International Prognostic Score in HL or the International Prognostic Index (IPI) in DLBCL [2,3]. However, the major drawback in the reported literature appeared to be related to the lack of uniform and reliable criteria for interim-PET scan interpretation. The relatively wide range of sensitivity and specificity reported and mentioned above, appear to depend on the different sets of criteria used for PET scan interpretation employed by the different groups.

In some studies a new gray-zone area, defined as 'minimal residual uptake' was introduced for these equivocal scan interpretations, but the boundaries of this area were not always strictly defined [4]. In other reports the criteria suggested by the International Harmonization Project [5] were used, despite the fact that they were only proposed (and basically used) for the end-treatment PET response assessment. In this respect it is of interest to note that several clinical trials in HL: (a) the H10 cooperative study from the Group pour l'Étude del Lymphomes de l'Adulte (GELA), the European Organisation for Research and Treatment of Cancer (EORTC) and the Gruppo Italiano Studio Linfomi (GISL); (b) the Risk-Adapted Therapy for Hodgkin Lymphoma (RATHL) study from the British Medical Council

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This workshop was held at Deauville, France from April 3–4, 2009, under the auspices of the GELA.

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(BMC) and GISL; (c) the HD 0801 study from the Intergruppo Italiano Linfomi (IIL); (d) the HD0607 study from the Gruppo Italiano Terapie Innovativo Linfomi (GITIL); (e) the HD18 study from the German Hodgkin Lymphoma Study Group (GHSG) and at least two trials in DLBCL, the PETAL study (Essen group) and the GELA LNH073B) study have recently been launched, aiming to assess the clinical impact of early chemotherapy intensification, based on the results of interim-PET scan, performed very early on during treatment. In almost all these studies, interim-PET was planned to be performed after only two courses of chemotherapy (PET-2). Today all authors who were able to demonstrate the prognostic relevance of the outcome of interim-PET in lymphoma feel the full responsibility together with the international scientific community for the consequences of their assumptions and agree that an effort should be made to standardize these criteria in order to attempt to reproduce these results on a worldwide basis.

Because of these considerations, in late 2008 an international meeting was planned, open to both nuclear medicine physicians and haematologists, with a personal or published experience in this field. These experts were invited to the First International Workshop on interim-PET scan in lymphoma which took place during the annual GELA meeting in April 3–4, 2009 in Deauville, France, with a twofold purpose: (1) to reach a consensus on simple, reproducible criteria/standards for interim-PET interpretation, and (2) to launch two or more international validation studies (IVS), in an attempt to validate these standards, as it had been done for end-treatment PET results as in the 2007 international harmonization study [5].

In addition, invited people were also asked to report their opinions on the proposal of two different sets of criteria and rules for interim-PET interpretation performed in HL and DLBCL, respectively. This was based on the assumption that the cellular architecture and physiopathology of the neoplastic tissue is different in these two lymphoma subsets. As an example, in the former the neoplastic Reed-Sternberg (RS) cells account for less than 1% of the overall cellularity of the neoplastic tissue, whereas in the latter they contribute for more than 90% of the total cell population. In HL, bystander, non-neoplastic lympho-mononuclear cells produce a cytokine network that ensures the immortalization of RS cells and works as an amplifier of the PET detection power. This non-neoplastic cellular compartment is switched-off very early by chemotherapy: this phenomenon is also known as 'metabolic CR' [6]. On the other hand, in DLBCL a progressive fraction of the neoplastic cells are lysed by the chemotherapy and the percentage of the cell destruction is predictive of the final response to the chemotherapy. For these reasons a visual assessment seems preferable in HL whereas a quantitative approach by SUX_{MAX} measurement seems more appropriate in DLBCL. Consequently, it seems best to plan and perform two separate IVS for these two different lymphoma subsets.

Participants

The following experts were invited and attended the meeting:

Hematologists

Marc André (GELA), Charleroi, Belgium, Pauline Brice (GELA), Paris, France, Olivier Casasnovas (GELA), Dijon, France, Ulrich Dührsen, Essen, Germany, Andrea Gallamini, Cuneo, Italy, Corinne Haioun (GELA) Creteil, France, Andreas Huettmann, Essen, Germany, Martin Hutchings, Copenhagen Denmark, George Mikhaeel, London, United Kingdom, Franck Morschauser (GELA), Lille, France, Nicolas Mounier (GELA), Nice, France, Aaron Polliack, Jerusalem, Israel, Laurie Sehn, Vancouver, Canada, Teruhiko Terasawa, Nagoya, Japan, Josée Zijlstra, Hovon, Amsterdam, Nederland.

Nuclear medicine physicians

Stéphane Bardet (GELA), Caen, France, Alberto Biggi, Cuneo, Italy, Ronald Boellaard, Amsterdam, Netherlands, Emmanuel Itti (GELA), Créteil, Paris, France, Françoise Kraeber Bodéré, Nantes, France, Michel Meignan (GELA), Créteil, Paris, France, Stefan Müeller Essen, Germany, Michael O'Doherthy, London, United Kingdom, Thierry Vander Borght (GELA) UCL, Yvoir, Belgium, Pierre Vera (GELA), Rouen, France.

This consensus meeting was a 2-day event. During the first day the experts attended two separate sessions – Group 1 consisted of nuclear medicine physicians, and Group 2 consisted of clinicians (Haematologists and Oncologists). Group 1, chaired by Michel Meignan discussed how to reach a consensus for the interpretation criteria, and Group 2, chaired by Andrea Gallamini, discussed the issue of the IVS. Both groups then met together at the end of their separate sessions in order to report their conclusions.

We provide here a brief point-by-point summary of the conclusions reported at the end of the first day.

First day

Group 1

Statement 1 (general).

- The use of interim-PET to assess early response is increasing.
- It is therefore necessary to standardize response criteria for the interim setting.
- The published criteria until now were not intended for interim analysis of response.
- The criteria should be simple, reproducible, easy to implement, and relevant for prognosis.
- These criteria should be validated as soon as possible in a large cohort of patients.

Statement 2 (methodology).

- A baseline PET/CT should always be performed prior to initiation of therapy.
- An interim-PET must be performed early on during induction chemotherapy.
- Preservation of the continuous nature of the data is recommended instead of just reporting a binary decision (i.e. either an ordinal visual score or SUV data).

Statement 3 (interpretation).

- A visual analysis using a 5-point scale should first be applied.
- The preferable reference scale should be the mediastinum and the liver.

Statement 4 (scoring).

The 5-point scale.

1. No uptake.
2. Uptake $\leq$mediastinum.
3. Uptake $>$ mediastinum but $\leq$liver.
4. Uptake moderately more than liver uptake, at any site.
5. Markedly increased uptake at any site and new sites of disease.

Statement 5 (cutoff).

- For categories 2–4, correction methods by means of the SUV_{max} should be investigated.
- For therapeutic decisions, this should be determined according to the clinical strategy planned (consider lymphoma subtypes, and the decision for (de)-escalation of therapy).

Group 2

Statement 1 (purpose of international validation study).

- To validate the results of previously published studies in HL and DLBCL.
- To investigate the consensus criteria on an international cohort of patients with lymphoma who are currently being collected.
- To assess the inter-observer variability using the proposed consensus criteria.

Statement 2 (methods).

- Cases are and will be collected retrospectively.
- Patients are only eligible if interim-PET/CT was performed after two cycles of chemotherapy.
- Patients wereexcluded if clinical decisions are based on interim-PET/CT results alone.
- A baseline PET/CT is mandatory.
- Only PET/CT technology is allowed.

Statement 3 (Hodgkin lymphoma).

- The 5-point visual assessment is applied as proposed at this consensus meeting.
- A cohort of ABVD-treated advanced-stage patients with HL has already been collected to validate previous results.
- This cohort is soon to be expanded for assessment of consensus criteria, including all clinical stages of disease.
- Assessment of the additional value of SUV analysis.

Statement 4 (diffuse large B-cell lymphoma).

- The 5-point visual assessment is applied as proposed at this consensus meeting.
- Assessment of the additional value of SUV analysis, as proposed recently by the GELA group [3].
- Stratified analysis according to therapy (14- *vs.* 21-day schedules, with and without rituximab) and prognostic score (IPI).

Proposed timetable for the HL-IVS

- May 2009: close accrual of cases.
- September 2009: all PET-CT images and clinical data collected.
- February 2010: end of analysis.
- April 2010, First report of results at Menton meeting in France.
- PET/CT review panel: Sally Barrington, Alberto Biggi, Martin Hutchings, Michel Meignan and any interested colleague from other participating centres with significant contribution of patients.

A schedule for the DLBCL-IVS will be defined very soon.

Second day

During the GELA plenary session the following presentations were given:

Laurie Sehn (Vancouver): an overview of the role of the prognostic factors in lymphoma.

Josée Zijlstra and Ronald Boellaard (Amsterdam): Experience in aggressive DLCL and SUV_{max} computation.

Teruhiko Terasawa (Boston): an exhaustive meta-analysis of the prognostic role on interim-PET in HL and DLCL from the literature-focused on the methodology of the various studies.

Andrea Gallamini (Cuneo): the Italian-Danish experience in advanced-stage HL, the on-going IVS.

Michel Meignan (Paris): the GELA experience in interim-PET in aggressive DLBCL and the quantitative approach to PET interpretation in these settings.

Ulrich Duhrsen (Essen): preliminary results of PETAL study, based on quantitative Interim-PET interpretation and early chemotherapy escalation in patients with DLCBL: a positive interim scan compared with a standard arm in which no therapy change was allowed according to PET results.

The reports of the second day will be published later in Leukemia & Lymphoma. Before the end of the session Michel Meignan and Andrea Gallamini presented summaries of the results of the Friday workshop (see above). Finally, it was decided that the Second International Workshop on Interim-PET in Lymphoma will be held on April 8 and 9, 2010 in Menton (France).

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References

1. Terawsawa T, Lau J, Bardet S, et al. Fluorine-18-fluorodeoxyglucose positron emission tomography for interim response assessment of advanced-stage Hodgkin's lymphoma and diffuse large B-cell lymphoma: a systematic review. J Clin Oncol 2009;27:1906–1914.
2. Gallamini A, Hutchings M, Rigacci L, et al. Early interim 2-[18F]fluoro-2-deoxy-Dglucose positron emission tomography is prognostically superior to international prognostic score in advanced-stage Hodgkin's lymphoma: a report from a joint Italian-Danish study. J Clin Oncol 2007;25:3746–3752.
3. Itti E, Lin C, Dupuis J, et al. Prognostic value of interim 18F-FDG PET in patients with diffuse large B-cell lymphoma: SUV-based assessment at 4 cycles of chemotherapy. J Nucl Med 2009;50:527–533.
4. Hutchings M, Mikhaeel NG, Fields PA, et al. Prognostic value of interim FDG-PET after two or threecycles of chemotherapy in Hodgkin lymphoma. Ann Oncol 2005;16: 1160–1168.
5. Juweid ME, Stroobants S, Hoekstra OS, et al. Use of positron emission tomography for response assessment of lymphoma: consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma. J Clin Oncol 2007; 25:571–578.
6. Kostakoglu L. Early prediction of response to therapy: the clinical implications in Hodgkin's and non-Hodgkin's lymphoma. Eur J Nucl Med Mol Imaging 2008;35:1413–1420.