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Editorial

The first European conference on infections in leukaemia: Why and how? ☆

The first European conference on infections in leukaemia (ECIL-1) was organised under the auspices of four groups or society involved in the understanding and management of infectious complications in patients with leukaemia or who have undergone stem cell transplantation: the Infectious Diseases Working Party of the European Group for Blood and Marrow Transplantation (EBMT), the Infectious Diseases Group of the European Organisation for Research and Treatment of Cancer (EORTC), the Supportive Care Group of the European LeukaemiaNet (ELN) and the International Immunocompromised Host Society (ICHS). The objective of the Conference was to elaborate guidelines – i.e. recommendations – for the management of bacterial and fungal infections in adult population of high-risk immunocompromised patients. The Conference took place on September 30th–October 1st, 2005 in Juan-les-Pins, France and gathered 59 experts from 24 European countries, Israel and Australia, composed of primarily of haematologists, oncologists, infectious diseases specialists, microbiologists and clinical trials specialists. The manuscripts published in this issue of the Journal present a summary of the main results of the European Consensus Conference and provide guidelines on prophylaxis and treatment of infectious complications occurring in patients with acute leukaemia and recipients of haematological stem cell transplantation.

This meeting has been, in many aspects, a tremendous experience of sharing practices, expert opinions and at the same time, a unique opportunity for intense discussion on the gap that sometimes exists between evidence-based medicine and real life practices. Clinical relevance or applicability is sometimes much more difficult than might have been foreseen. Comprehensive review of the literature on practices that may at first glance not have changed for decades always shed new light on *a priori* or beliefs which after all may not be evidence-based. In this respect, it is always good to challenge dogmas. This kind of exercise also is useful to take a fresh look at issues already broadly discussed in the literature. We are fully aware of the fact that guidelines by definition have rather short life-expectancies. We will update these recommendations at ECIL-2 in September 2007, due to the availability of new data in some of the addressed topics at ECIL1.

1. Methodology of the conference

The Organizing Committee selected a series of topics to be addressed during the Conference. Considering the large number of questions of potential interest in the field, the Organizing Committee elected to limit the spectrum of themes to be covered to the following topics:

Bacterial infections: (1) fluoroquinolone prophylaxis for the prevention of bacterial infections in neutropenic patients, (2) need for aminoglycosides antibiotics as part of the initial empirical antibiotic regimens in febrile neutropenic patients and (3) need for anti-Gram-positive antibiotics for the treatment of suspected Gram-positive infections in febrile neutropenic patients.

Fungal infections: (1) antifungal prophylaxis for the prevention of invasive mycosis, (2) empirical antifungal therapy in patients who remained febrile after broad-spectrum antibiotics therapy and (3) therapy of invasive aspergillosis and of invasive candidiasis.

For each of these six topics, a list of questions and assignments was established as the starting point for discussion by the Working Groups. Each Working Group consisted of 3–6 international experts chosen on the basis of their expertise on the selected topics and who worked under the leadership

☆ The ECIL-1 is a common initiative of the following groups or organizations: Infectious Diseases Working Party of the European Blood and Marrow Transplantation Group (EBMT-IDWP), Infectious Diseases Group of the European Organization for Research and Treatment of Cancer (EORTC-IDG), European Leukaemia Net (ELN)(EU Grant number: LSHC-CT-2004), and International Immunocompromised Host Society (ICHS).

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Table 1 – Quality of evidence and Strength of recommendations according to the CDC grading system

Quality of evidence	Strength of recommendations
I Evidence from at least one well-executed randomised trial	A Strong evidence for efficacy and substantial clinical benefit: Strongly recommended
II Evidence from at least one well-designed clinical trial without randomisation; cohort or case-controlled analytic studies (preferably from more than one centre); multiple time-series studies; or dramatic results from uncontrolled experiments	B Strong or moderate evidence for efficacy, but only limited clinical benefit: Generally recommended
III Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports from expert committees	C Insufficient evidence for efficacy; or efficacy does not outweigh possible adverse consequences (e.g. drug toxicity or interactions) or cost of chemoprophylaxis or alternative approaches: Optional
	D Moderate evidence against efficacy or for adverse outcome: Generally not recommended
	E Strong evidence against efficacy or of adverse outcome: Never recommended

of a designated Group leader. The Working Group were formed six months prior to Conference to allow sufficient time for thorough review of the literature and preparation of recommendations.

The Groups were asked to use Medical Subject Heading (MeSH) terms (http://www.nlm.nih.gov/mesh/MBrowser.html) as keywords to search articles published until the date of the conference, in Medline, PubMed or Cochrane databases. Neutropenia was defined as a polymorphonuclear neutrophil (PMN) count <500/mm^3, or <1000/mm^3 expected to drop <500 within 48 h. High risk patients were defined as those expected to have a severe (<100/mm^3) and prolonged (>7 days) neutropenia. Existing guidelines and systematic reviews were also reviewed. Abstracts presented during the period 2002–2005 at annual meetings of the American Society of Hematology, Interscience Conference on Antimicrobial Agents and Chemotherapy, European Society of Clinical Microbiology and Infectious Diseases, American Society of Clinical Oncology, European Group for Blood and Marrow Transplantation were also screened. Articles and abstracts presented or published between September 30 and December 31st, 2005 were not included in the review presented at the conference, but analysed at the initiative of each Working Group, and provisionally graded, pending an update of these guidelines. Analyses focussed primarily on the following end-points: overall survival, cause-specific survival, adverse events, development of antimicrobial resistance and costs whenever this information was available. Quality of evidence and strength of recommendation were graded according to the Centers for Diseases Control grading system (Table 1).

1.1. *Conference, participants and questionnaires*

The participants in the conference were chosen according to their active participation to the EORTC Infectious Diseases Group, the IDWP EBMT, and the ELN group, for their expertise on the topics, and in a balanced representativity of the different European countries in these groups. In order to obtain information about treatment practices in European countries, a questionnaire was developed and mailed to all Conference participants in the summer of 2005. The questionnaire consisted of 8–14 questions per topic, focusing on first or second line strategy, and routine practice. The six topics chosen for the conference were covered. Thirty-eight of the 53 (72%) questionnaires sent to participants not belonging to pharmaceutical companies ($n = 6$) were returned and analysed by Marianne Paesmans, from the EORTC Infectious Diseases Group in Brussels, and we all thank Marianne for her help.

At the meeting, the Working Groups were asked to present an executive summary of the literature review, results of the analyses of the questionnaires and treatment recommendations that were presented in a question and answer format. The recommendations were discussed and critiqued by the Conference participants in plenary session. Treatment recommendations were revised on site by the Working Groups based on the comments made during the plenary session and discussed again in a second plenary session until consensus was reached among participants about quality of evidence and grading of recommendations.

1.2. *Articles*

Each of the articles published in this issue of the *Journal* were written by the Working Groups and reviewed by the one or two chairpersons assigned to this specific part of the plenary session and by members of the Organizing Committee. Modifications were circulated electronically and subsequently agreed upon as part of an iterative process until consensus was reached.

We do hope these guidelines will help the clinician to make rational, evidence-based choices. However, as mentioned in some of these manuscripts, we do not find always the rational for our choices, and need to develop prospective trials each time possible when the answer to an important question is not available in the literature. We also hope to have created, through the ECIL, a new way to share our choices, and recognise our doubts in the management of these patients.

Conflict of interest statement

Catherine Cordonnier has received grants and research supports from Pfizer, Merck Sharp Dohme-Chibret, Gilead, Schering Plough and has been a consultant for Gilead, Schering Plough, and Zeneus Pharma.

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