



# Introduction to ECIL

*from ECIL1 to ECIL 4*



# **The ECIL is the European Conference on Infections in Leukemia**

**The ECIL is a common initiative of:**

- the Infectious Diseases Working Party of the EBMT**
- the Infectious Diseases Group of the EORTC**
- the Supportive Care group of the European LeukemiaNet**
- the International ImmunoCompromised Host Society**

*The slide sets are available on the websites of these 4 organizations*



## **ECIL 1: Juan-les-Pins, France, Sept 30-Oct 1st, 2005**

59 experts from 24 European countries, one from Australia

## **ECIL 2: Juan-les-Pins, Sept 28-29th, 2007**

53 experts from 24 European countries, one from Australia

## **ECIL 3: Juan-les-Pins, France, Sept 25-26th, 2009**

57 experts from 18 European countries, 2 from Russia

## **ECIL 4: Sept 9-10th, 2011**

53 experts from 18 European countries, one from Russia



# Objectives

- **Elaborate European guidelines on prophylaxis, and treatment of infectious complications in leukemic patients**
- **Obtain information about what are current management strategies in Europe**
- **Favor communication between groups**
- **Define new areas of clinical research**



# **ECIL 1 - 2005: Six topics**

- I      Fluoroquinolone prophylaxis in neutropenic patients**
- II     Aminoglycosides in febrile neutropenia**
- III    Glycopeptides and other anti-Gram+ antibiotics in febrile neutropenia**
- IV    Empirical antifungal treatment for persistent fever in neutropenic patients**
- V     Antifungal prophylaxis**
- VI    Antifungal therapy (*Aspergillus* and *Candida*)**



# ECIL 2 – september 2007

- **Three topics of ECIL1 were updated:**
  - Empirical antifungal therapy
  - Antifungal prophylaxis
  - Antifungal treatment
- **Two new topics were addressed:**
  - Management of Herpes virus infections:  
HSV, VZV, CMV and HHV6 and 7, EBV
  - Management of other viral infections:  
Respiratory viruses, Influenza virus  
Polyoma, Parainfluenza virus



# ECIL 3 – september 2009

<b>UPDATES</b>	<i><u>Leaders</u> and group members</i>
<b>Empirical Antifungals</b>	<i><u>O Marchetti</u>, C Cordonnier , T Calandra,</i>
<b>Antifungal prophylaxis</b>	<i><u>J Maertens</u>, O Cornely, P Frère, W Heinz, C Lass-Flörl</i>
<b>Antifungal therapy</b>	<i><u>R Herbrecht</u>, B Gachot, U Fluckiger, P Ribaud, A Thiebaut</i>
<b>CMV, HHV6 and EBV</b>	<i><u>P Ljungman</u>, R de la Camara, D Engelhard, H Einsele, P Reusser, J Styczynski, K Ward</i>
<b>New ECIL 3 topics</b>	
<b>Zygomycosis</b>	<i><u>G Pettrikos</u>, A Skiada, F Lanternier, A Groll, Raoul Herbrecht, L Pagano, S Zimmer, O Lortholary</i>
<b>Classical diagnostic procedures of IFI</b>	<i><u>J Bille</u>, M Arendrup, E Dannaoui, C Kibbler, M Ruhnke, C P Heussel</i>
<b>Non-invasive diagnostic procedures for Aspergillus</b>	<i><u>S Bretagne</u>, P Verweij, J Loeffler, J Maertens, P Donnelly, RM Barnes, T Lernbecher, L White, M Cuenca-Estrella</i>
<b>Non-invasive diagnostic procedures for yeasts</b>	<i><u>C Viscoli</u>, M Mikulska, T Calandra, M Sanguinetti, J Ponton, D Poullain</i>
<b>βeta-D glucane</b>	<i><u>O Marchetti</u>, F Lamothe, M Cruciani, E Castagnola, O Lortholary, M Richardson</i>

# ECIL 4 – September 2011

<b>UPDATES</b>	<i><u>Leaders</u> and group members</i>
<b>Antifungal prophylaxis</b>	<i><u>J Maertens</u>, O Cornely, A Tanase, W Heinz, C Lass-Flörl</i>
<b>Antifungal therapy</b>	<i><u>R Herbrecht</u>, B Gachot, U Fluckiger, P Ribaud, A Thiebaut</i>
<b>CMV, HHV6 and EBV</b>	<i><u>P Ljungman</u>, R de la Camara, D Engelhard, H Einsele, P Reusser, J Styczynski, K Ward</i>
<b>New topics</b>	
<b>Respiratory viruses</b>	<i><u>P Lungman</u>, M Boeckh, H Einsele, D Engelhard, T Feuchtinger, H Hirsch, S Matthes-Martin, R Martino, B Mohty, P Shaw, K Ward</i>
<b>Bacterial resistance in the hematology ward</b>	<i><u>M Akova</u>, D Averbuch, C Cordonnier, I Gyssens, G Klyasova, W Kern, D Livermore, M Mikulska, P Munoz, C Orash, M Tumbarello, C Viscoli</i>
<b>IFI anf antifungal treatment in children</b>	<i><u>A Groll</u>, E Castagnola, S Cesaro, JH Dalle, D Engelhard, W Hope, T Lernbecher, E Roilides, J Styczynski, A Warris</i>



# METHODS (I)

**1 – Questions proposed by the organization committee and redefined by each group**

**2 – Population explored:** Leukemic, neutropenic ( $<500/\text{mm}^3$ ), Auto- and Allo SCT recipients

**Key words:** *leukemia, neutropenia ... MeSH*

**Sources:** *Medline, PubMed, Cochrane Library, Abstracts of ASH, ICAAC, ASCO, ECMID, and EBMT (limited to the 4 previous years for abstracts).*

**3 – Endpoints:** overall mortality, infection-related mortality, breakthrough infections, safety, emergence of resistant organisms, costs  $\pm$  others/group. Eventually redefined according to the topic



# METHODS (II)

## 4 – Literature review:

**Randomized trials, meta-analyses, open studies ,  
review articles, treatment guidelines**

## 5 – Grading the level of evidence and level of recommendation:

### **CDC grading system**

*Please note that the grading system used for the ECIL guidelines has been  
changed at ECIL 3 in 2009 (see the next 2 slides)*

## 6 – Presentation, discussion in plenary session, and revision of the guidelines till consensus



# CDC Grading system used for ECIL 1 and ECIL 2, and update of ECIL 3

Quality of evidence	Strength of recommendations
<p><b>I Evidence from at least one well-executed randomized trial</b></p> <p><b>II Evidence from at least one well-designed clinical trial without randomization; cohort or case-controlled analytic studies (preferably from more than one center); multiple time-series studies; or dramatic results from uncontrolled experiments</b></p> <p><b>III Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports from</b></p>	<p><b>A Strong evidence for efficacy and substantial clinical benefit</b>  <i><b>Strongly recommended</b></i></p> <p><b>B Strong or moderate evidence for efficacy, but only limited clinical benefit</b>  <i><b>Generally recommended</b></i></p> <p><b>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</b>  <i><b>Optional</b></i></p> <p><b>D Moderate evidence against efficacy or for adverse outcome</b>  <i><b>Generally not recommended</b></i></p> <p><b>E Strong evidence against efficacy or of adverse outcome</b>  <i><b>Never recommended</b></i></p>



# CDC Grading system used from ECIL3

Quality of evidence	Strength of recommendations
I Evidence from $\geq 1$ properly randomized, controlled trial	A <b>Good evidence</b> to support a recommendation for or against use
II Evidence from $\geq 1$ well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from $>1$ center); from multiple time-series studies; or from dramatic results from uncontrolled experiments	B <b>Moderate evidence</b> support a recommendation for or against use
III Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	C <b>Poor evidence</b> to support a recommendation



# Publications subsequent to ECIL meetings <sup>(1/2)</sup>

## Following ECIL1

The first European Conference on infections in leukaemia: Why and how? C. Cordonnier, T Calandra. Eur J Cancer 2007; Suppl. 5,.

Quinolone prophylaxis for bacterial infections in afebrile high risk neutropenic patients. G Bucaneve, E Castagnola, C Viscoli, L Leibovici, Francesco Menichetti. Eur J Cancer 2007; Suppl. 5, 5-12.

The need for aminoglycosides in combination with b-lactams for high-risk, febrile neutropaenic patients with leukaemia . L Drgona, M Paul, G Bucaneve, T Calandra, F Menichetti. Eur J Cancer 2007; Suppl. 5. 13-22

Primary antifungal prophylaxis in leukaemia patients..J Maertens, P Frere, C Lass-Flörl, W Heinz, O Cornely. Eur J Cancer 2007; Suppl. 5. 43-48

Empirical use of anti-Gram-positive antibiotics in febrile neutropaenic cancer patients with acute leukaemia. Alain Cometta\*, O. Marchetti, T. Calandra. Eur J Cancer 2007; Suppl. 5. 23-31

Empirical antifungal therapy in neutropenic cancer patients with persistent fever. Guidelines of the ECIL1 conference..O Marchetti, C Cordonnier, T Calandra.. Eur J Cancer 2007; Suppl. 5. 32-42.

European guidelines for the treatment of invasive candida and invasive aspergillus infections in adult haematological patients. R Herbrecht, U Fluckiger, B Gachot, P Ribaud, A Thiebaut, C Cordonnier. Eur J Cancer 2007; Suppl. 5., 49-59.

## Following ECIL 2

Management of CMV, HHV6, HHV7 and Kaposi-sarcoma herpesvirus infections in patients with hematological malignancies including stem cell transplantation.

P Ljungman, R De La Camara, C Cordonnier, H Einsele, D Engelhard, P Reusser, J Styczynski, K Ward for the ECIL BMT, 2008, Aug;42(4):227-40).

Management of HSV, VZV, and EBV infections in patients with hematological malignancies and after SCT : guidelines from the Second European Conference on Infections in Leukemia.. J Styczynski, P Reusser, H Einsele, R de la Camara, C Cordonnier, KN Ward, P Ljungman, D Engelhard, for the ECIL. BMT 2009; 43:757-770



# Publications subsequent to ECIL meetings (2/2)

## Following ECIL3

European guidelines for antifungal management in leukemia and hematopoietic stem cell transplant recipients: Summary of the ECIL3 – 2009 Update

J Maertens, O Marchetti, R Herbrecht, O A. Cornely, U Flückiger, P Frère, B Gachot, W J. Heinz, C Lass-Flörl, P Ribaud, A Thiebaut, C Cordonnier. BMT, 2011 May;46(5):709-18.

The use of mannan antigen and anti-mannan antibodies in the diagnosis of invasive candidiasis: recommendations from the 3rd European Conference on Infections in Leukemia (ECIL-3).

M. Mikulska, T. Calandra, M. Sanguinetti, D. Poulain and C. Viscoli, on behalf of the third ECIL Critical Care 2010;14(6):R222.

ECIL recommendations for the use of biological markers for the diagnosis of invasive fungal diseases in leukemic patients and hematopoietic stem cell transplant recipients

O Marchetti, F Lamoth, M Mikulska, C Viscoli, P Verweij, S Bretagne, and the ECIL laboratory working groups. BMT 2011 Sep 19. doi: 10.1038/bmt.2011.178. [Epub ahead of print]

ECIL 3 Classical diagnostic procedures for the diagnosis of Invasive Fungal Diseases in patients with Leukemia

M Cavling Arendrup, Chris Kibbler, E Dannaoui, M Ruhnke, CP Heussel, J Bille. BMT 2012 Jan 9. doi: 10.1038/bmt.2011.246. [Epub ahead of print]

Diagnosis and treatment of zygomycosis: Guidelines from the 3rd European Conference on Infections in Leukemia

A Skiada, F Lanternier, A H Groll, L Pagano, S Zimmerli, R Herbrecht, O Lortholary, G Petrikos. *Submitted*

Beta-Glucan antigenemia for the diagnosis of invasive fungal infections in patients with hematological malignancies: A systematic review and meta-analysis of cohort studies

F Lamoth et al., M Cruciani, C Mengoli, E Castagnola, O Lortholary, M Richardson, O Marchetti. Clin Infect Dis. 2011 Dec 23. [Epub ahead of print]



# On behalf of the Organization Committee of the ECIL 4 meeting

*C Cordonnier, T Calandra, M Akova, S Cesaro, P Donnelly H Einsele,  
A Groll, R Herbrecht, P Ljungman, J Maertens, O Marchetti, C Viscoli*

WE SINCERELY THANK ...

**The sponsors of ECIL1, 2005:** *Astellas Pharma, BMS, Gilead Sciences, Glaxo Smith Kline, Merck Sharp&Dohme, Pfizer, Schering Plough, Wyeth and Zeneus Pharma*

**The sponsors of ECIL 2, 2007:** *Astellas Pharma, Cephalon, Gilead Sciences, Glaxo Smith Kline, Merck Sharp&Dohme, Novartis, Pfizer, and Schering Plough*

**The sponsors of ECIL 3, 2009:** *Astellas Pharma, Gilead Sciences, Merck Sharp&Dohme, Pfizer, and Schering Plough*

**And the sponsors of ECIL4, 2011:** *Astellas Pharma, Gilead Sciences, Merck Sharp&Dohme, Novartis, and Pfizer*

**And KOBE, Groupe GL Events, Lyon, for organizing the conferences**



**4<sup>th</sup> European Conference on Infections in Leukemia**