Infectious Diseases Working Party

Chair: Simone Cesaro – Verona, Italy
Secretary: Jan Styczynski – Bydgoszcz, Poland

Gram-Negative Bacteremia in HSCT Recipients

EBMT/IDWP Non-interventional Prospective Study
February 2014 – July 2015

Study update week 8, 2015

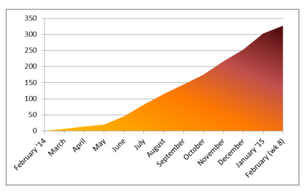
Brief overview of the study

There is a significant increase in resistant bacteria emerging in HSCT recipients. These resistant bacteria may be associated with increased mortality and the treatment options are limited. To provide the currently best empirical coverage and to control the growing resistance, knowledge of trends in antibiotic susceptibility as well as risk factors is essential. For this reason we are performing a non-interventional prospective multicentre study (NIS) among EBMT centres.

We aim to collect a minimum of 365 episodes of Gram-negative bacterial infections by following all transplant recipients of the participating centres over a 1 year period. The background information about the transplantations is collected via the standard MED A form. Data on all the episodes of Gram-negative bacteria blood stream infections are collected prospectively from the initiation of the conditioning treatment until the end of the first 6 months after the HSCT (or death or lost follow-up, if they occur earlier). Data on the patients who will develop a Gram-negative infection are reported using a special MED C form and includes data on the pathogen and antimicrobial susceptibility of the pathogen, presence of certain risk factors at the time and before infection, treatment and outcome. The responsibility of centres participating in this NIS will be to fill the MED C form within 3 months of the Gram-negative bacteremia episode.

Recruitment

Recruitment of centres in the study is going well. **95 EBMT centres** have agreed to participate. Together they expect to perform over 6500 transplants (autologous and allogeneic) within one year, which means that there is a good chance we will be able to collect the required minimum of **365 episodes**.



306 patients have been included in the study at this moment . The first episode of gram-negative bacteremia was registered on February 12th, and we have received 325 more episodes since. We expect that the registration of episodes will remain up to speed until the end of the study period.

Study MED C form

It is advised to have one person in your centre responsible for tracking the episodes.

For all participating centres: Your study period has started and you can submit your gram-negative bacteremia cases of patients who received HSCT after your start date to the IDWP Data Office via the MED C form within 3 months of the Gram-negative bacteremia episode.

For each separate episode a new form should be completed.
Please use the study manual while completing the form
For certain questions it is difficult to derive the meaning from the questionnaire itself. The manual has been created to properly define those issues, in order to avoid inconsistency in the answers from the different participating centres.

Med A registration

Please be reminded that we will need the Med A data for all your transplanted patients in the study period, not only for the patients with a case of gram-negative bacteremia. Please make sure the Med A data of the study period is entered into ProMISe as soon as possible.

Contact

When you need help or if you would like to contact us about any aspect of the study please send an e-mail to Jennifer Hoek at the IDWP Data Office in Leiden, Netherlands, via idwpebmt@lumc.nl.

Publications

Per Ljungman, Ronald Brand, Jennifer Hoek, Rafael de la Camara, Catherine Cordonnier, Hermann Einsele, Jan Styczynski, Katherine N Ward, Simone Cesaro for the IDWP of the EBMT. Donor CMV status influences the outcome of allogeneic stem cell transplantation; a study by the European Group for Blood and Marrow Transplantation. Clinical Infectious Diseases. **Clin Infect Dis 2014; 59:473-81**

Groll AH, Castagnola E, Cesaro S, Dalle JH, Engelhard D, Hope W, Roilides E, Styczynski J, Warris A, Lehrnbecher T; **Fourth European Conference on Infections in Leukaemia (ECIL-4): guidelines for diagnosis, prevention, and treatment of invasive fungal diseases in paediatric patients with cancer or allogeneic haemopoietic stem-cell transplantation.** Fourth European Conference on Infections in Leukaemia; Infectious Diseases Working Party of the European Group for Blood Marrow Transplantation (EBMT-IDWP); Infectious Diseases Group of the European Organisation for Research and Treatment of Cancer (EORTC-IDG); International Immunocompromised Host Society (ICHS); European Leukaemia Net (ELN). **Lancet Oncol. 2014;15: e327-40**.

Mikulska M, Viscoli C, Orasch C, Livermore DM, Averbuch D, Cordonnier C, Akova M. Aetiology and resistance in bacteraemias among adult and paediatric haematology and cancer patients. Fourth European Conference on Infections in Leukemia Group (ECIL-4), a joint venture of EBMT, EORTC, ICHS, ELN and ESGICH/ESCMID . **J Infect. 2014;68:321-31**

Bontant T, Sedlaçek P, Balduzzi A, Gaspar B, Cesaro S Einsele H, Peters C, Dalle JH. Survey of CMV management in pediatric allogeneic HSCT programs, on behalf of the inborn errors, infectious diseases and pediatric diseases working parties of EBMT. **Bone Marrow Transplant. 2014; 49: 276-9**

New Studies

Current Treatment of HCV Infection After HSCT

The availability of novel therapies with DAAs might prompt clinicians caring for HCV-positive HSCT recipients to prescribe the treatment more frequently and possibly earlier after HSCT. Since numerous possible therapeutic combinations exist, the choice of the most appropriate one is not straightforward. It depends not only on its efficacy and toxicity, but also on availability (both through healthcare system and in expanded access programs), and cost.

This non-interventional prospective study will focus on treatment strategies in HCV-positive HSCT recipients. The main focus will be the rate of treatment, the combination of drugs chosen, the length of treatment and the outcome. This study might provide additional data compared to previous older cohorts in the area of non-invasive assessment of fibrosis, HCV-RNA levels and genotyping.

In order to get as much data as possible on HCV treatment, patients with chronic HCV infection regardless of the time from transplant will be included.

All HCV-positive patients cared for during the observation period, both after autologous and allogeneic HSCT, irrespective of the time of transplant.

Patients data will be collected at baseline (first visit during the observation period), including data on HCV infection. HCV-positive patients follow-up data will be asked every 12 months until 24 month after the end of the observation period.

A digital Feasibility Survey has been sent to all EBMT centres in March 2015. Please complete the Survey as soon as possible.

A paper copy of the Survey is also available at the EBMT booth in the congress centre.

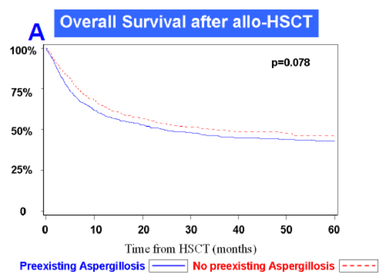
****

Impact of Pre-Existing Invasive Mould Infections on Allo-SCT

We are planning to conduct a prospective non-interventional study to assess clinical outcome of patients with – and without – history of pre-existing invasive aspergillosis undergoing SCT.

Background and Rationale

In patients with pre-existing invasive aspergillosis allo-SCT is feasible without progression of fungal infection.[1] However, the influence of invasive mould infections on transplant related complications and on long term survival has not been investigated in a larger patient cohort under current conditions.
Recently the IDWP and ALWP performed a retrospective analysis on the impact of pre-existing aspergillosis on allo-HSCT outcome.[2] In summary, there was a trend towards impaired outcome of allo-HSCT in patients with prior IA but there was no significant impact on important allo-HSCT transplant outcomes, such as survival, GVHD and relapse. The data suggest that a history of IA should not generally be considered a contraindication for allo-HSCT (Figure A). To be able to more precisely investigate the impact of IA on allo-HSCT, a non-interventional prospective study is needed.



[1]Martino et al for the EBMT ID WP, Blood. 2006 Nov 1;108(9):2928-36. [2]Penack et al., Blood; ASH Abstracts, Dec 2014.

Study population

First allo-SCT in patients with acute leukaemia, MDS or lymphoma given stem cell grafts.
Cohort 1: History of probable or proven invasive aspergillosis
Cohort 2: History of possible invasive aspergillosis
Cohort 3: No history of invasive aspergillosis

Study period:

One year inclusion + One year follow up.

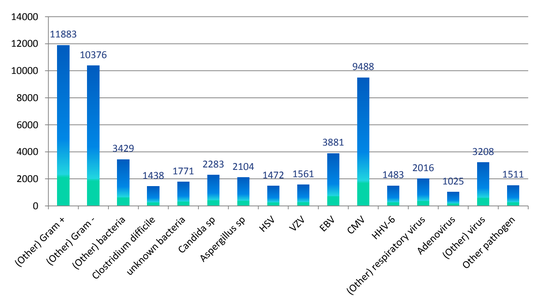
A digital Feasibility Survey will be sent to all EBMT centres in April 2015.

A paper copy of the Survey is already available at the EBMT booth in the congress centre.

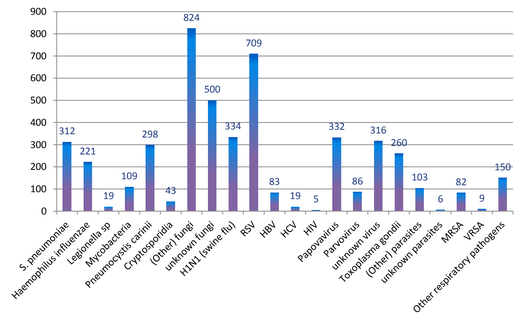
Numbers in the registry

Counts of different pathogen registered in the EBMT registry since the year 2008

Infections >1000 cases registered



Infections <1000 cases registered



Contact

Simone Cesaro
Chair IDWP
Simone.cesaro@ospedaleuniverona.it

Jan Styczynski
Secretary IDWP
jstyczynski@cm.umk.pl

Jennifer Hoek
Study Coordinator IDWP
idwpebmt@lumc.nl