European Society for Blood and Marrow Transplantation

Infectious Diseases Working Party

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

Gram-Negative Bacteremia in HSCT Recipients

Preliminary results on part of cohort November 2015. (Analysis on complete cohort ongoing).

PI: Dina Averbuch and Dan Engelhard

Introduction:
We report on resistance rate in Gram-negative rods (GNR) in HSCT patients, risk factors for resistance and mortality in bacteremia episodes caused by resistant vs. sensitive GNR.

Patients and methods:
Data on all episodes of GNR bacteremia since the initiating of conditioning and during 6 months after the HSCT were collected prospectively by a special form, containing information on pathogen, antimicrobial susceptibility, the risk factors, treatment and outcome. Background patient demographic and clinical data were obtained using MED A form of ProMise. Four patterns of resistance were assessed: to quinolones, non-carbapenem beta-lactams (at least one of ceftazidime, cefepime or piperacillin-tazobactam); carbapenems (at least one of meropenem/imipenem/doripenem); multidrug resistance (MDR, at least 1 agent in ≥3 any antimicrobial categories).

Countries participating in the gram-negative bacteremia study at time of preliminary analysis.

Results:
444 patients (median age at SCT 51 years, range 0.5-73; 267 males) developed 485 episodes of GN bacteremia in 58 HSCT centers from 23 countries. 181 patients underwent autologous, 263 allogeneic HSCT (65% of them received myeloablative conditioning). The stem cells sources were: 343 peripheral blood, 72 bone marrow, 10 both, 18 cord blood, 1 missing. Neutropenia <500 and <100 cells/mm^3 was present in 77% and 72% of episodes, respectively; breakthrough bacteremia occurred in 61%; GVHD (43 acute and 8 chronic, allo-HSCT) in 17% of episodes. Resistance to fluoroquinolones was recorded in 53%, to non-carbapenem beta-lactam in 47%, to carbapenems in 16%, MDR in 54% of isolates.
30-days mortality was 15% (61/401); in 84 episodes this information was unavailable. Mortality according to resistance pattern was as follows: in those resistant vs. sensitive to non-carbapenem beta-lactam: 21% vs. 9%, p=0.002; in carbapenem-resistant vs. sensitive: 40% vs. 10%, p<0.001; in MDR vs. non-MDR: 21% vs. 8%, p= p<0.001.

Conclusion:
The emergence of antibiotic resistance represents a major obstacle to successful outcome of GN bacteremia after HSCT, especially in case of carbapenem-resistance.

Presentation at EBMT 2016
Monday, April 4, 2016 / Room B4 / 15:45 – 15:55 & Tuesday, April 5, 2016 / Room 3F / 16:55 – 17:15

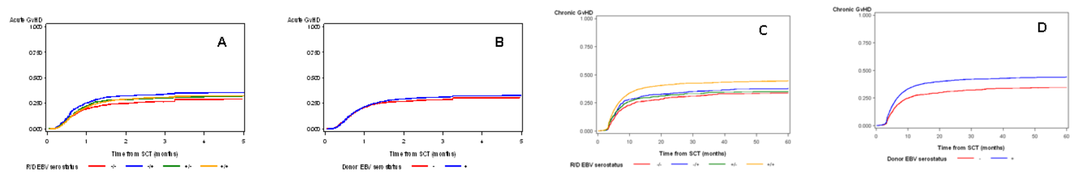
Impact of donor EBV on GvHD

PI: Jan Styczynski

PURPOSE: We investigated the effect of Epstein-Barr virus (EBV) serostatus on the overall outcome of allo-HSCT.

PATIENTS AND METHODS: The study included 11,364 allogeneic peripheral blood or bone marrow transplant patients carried out between 1997 and 2012 for acute leukemia. We analyzed the impact of donor and recipient EBV serologic status on overall survival, relapse-free survival, relapse incidence, non-relapse mortality and incidence of graft-versus-host disease (GVHD) after allogeneic hematopoietic stem cell transplant (allo-HSCT).

RESULTS: Patients receiving grafts from EBV-seropositive donors had the same overall survival as patients grafted from EBV-seronegative donors (hazard ratio [HR], 1.05, 95% confidence interval [CI], 0.97-1.12; P=0.23). Seropositive donors also had no influence on relapse-free survival (HR=1.04, 95%CI, 0.97-1.11; P=0.31), relapse incidence (HR=1.03, 95%CI, 0.94-1.12; P=0.58), and non-relapse mortality (HR=1.05, 95%CI, 0.94-1.17; P=0.37). However, in univariate analysis recipients receiving grafts from seropositive donors had a higher risk of chronic GVHD (40.8% vs 31.0%; P<0.0001; HR=1.42, 95%CI, 1.30-1.56) than those with seronegative donors. When adjusting for confounders higher risk was identified for both acute and chronic GVHD. In seronegative patients with seropositive donor HR was 1.30 (95%CI, 1.06-1.59; P=0.039) for chronic GVHD. In seropositive patients with seropositive donors HR was 1.24 (95%CI, 1.07-1.45; P=0.016) for acute and 1.43 (95%CI, 1.23-1.67; P<0.0001) for chronic GVHD. Seropositive patients with seronegative donors did not have an increased risk of GVHD.



Impact of recipient (R)/donor (D) or Donor EBV serostatus on: (A,B) the 100-day cumulative incidence of acute GVHD after stem cell transplantation (SCT); (C,D) the 2-year cumulative incidence of chronic GVHD.

CONCLUSIONS: Our data suggest that donor EBV status significantly influences development of acute and chronic GVHD after allo-HSCT.

Paper accepted for publication in Journal of Clinical Oncology

Meetings

2015

ECIL 6
September 2015, Sophia Antipolis, France
European Conference on Infections in Leukaemia
www.kobe.fr/ecil

Fall meeting
October 2015, Verona , Italy
Infectious Diseases Educational Course & business meeting

2016

EBMT Valencia
Business meeting
Monday, 4th April 2016 , Valencia, Spain / 07:00 - 09:00 / Room 3C
Working Party Session
Tuesday, 5th April, 2016, Valencia, Spain / 15:45 - 17:45 / Room 3F

Fall meeting
October 2016, Madrid, Spain
Infectious Diseases & Complications and Quality of Life Educational Course

Visit http://www.ebmt.org/Education for information on upcoming educational events

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Recruiting studies

Current Treatment of HCV Infection after HSCT

PI: Malgorzata Mikulska

The availability of novel therapies with oral directly acting antivirals (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.

Inclusion criteria:
All HCV-RNA positive patients cared for between December 2015 and November 2017, who underwent HSCT (auto or allo) from any time to May 2017 .

Data collection (besides MED A):
Patients not on treatment: 1 baseline form, 1 follow-up form at end of study.
Patients on treatment: 1 treatment form, 1 follow-up form 6 months after the end of treatment (EOT).

When interested in participation, please contact the IDWP Data Office: idwpebmt@LUMC.NL

Pneumocystis Jirovecii Pneumonia (PcP) after allogeneic HSCT

PI: Christine Robin

The study is open to EBMT centres using BAL for the diagnosis of PcP.
You may participate even when you have no pneumocystis PCR on site.

The study aims at identifying risk factors, timing and diagnostic methods of PcP after allogeneic HSCT within the EBMT. It consists of a prospective 12-months collection of new PcP cases occurring in the 24 months following an allogeneic HSCT. PcP is defined by any positive specific criteria in BAL (cytology or IF or PCR), whatever the clinical presentation and whether the patient has been treated or not. We will ask you for each PcP case to fill a specific short MedC. The IDWP data office will identify in your centre 2 control cases for one case of PcP and you will be asked to fill a short Med C for each of these controls. MED A registration of these patients is required.

The number of cases per EBMT centre during the last years is very low (0 up to 7 in very big centres) and this study represents few work for the centres, but may provide major information if most EBMT centres participate. We aim to collect 100 cases.

Study period:
01 March 2016 – 28 February 2017 + 90 days follow up.

Inclusion criteria of the PcP cases:
- Allogeneic HSCT within the previous 24 months.
- New case (first onset) of PcP documented in a BAL fluid, whatever the positive diagnostic test (cytology or IF or PCR) and whatever the presentation and treatment
- Any age
- Pre-or post-transplant informed consent to enter the data in the EBMT registry.

Exclusion criteria of the PcP cases:
- Autologous HSCT.
- Allogeneic HSCT recipient transplanted more than 24 months before the onset of PcP.
- Second episode of PcP since allogeneic HSCT (patients diagnosed with PcP before allogeneic HSCT are not excluded).

When interested in participation, please contact the IDWP Data Office: idwpebmt@LUMC.NL

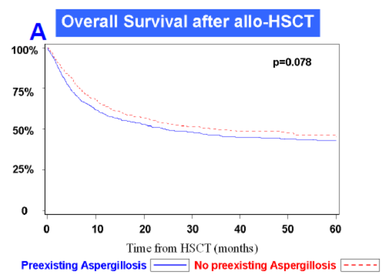
Starting soon

Impact of Pre-Existing Invasive Aspergillosis on Allo-SCT

PI: Olaf Penack

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 (IA) 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., Bone Marrow Transplant. 2015 Oct 26. doi: 10,1038/bmt.2015,237, [Epub ahead of print].

Study population
First allo-SCT in patients with acute leukaemia, MDS or lymphoma given stem cell grafts.
Cohort 1: History of proven/probable IA
Cohort 2: Non history of proven/probable IA or possible mycosis

Study period:
One year inclusion + One year follow up. **Planned start date May 1st, 2016**

Data collection:
All patients: (new) MED A; Patient Registration Form
Cohort 1: Aspergillus Form , study follow-up (MED C)

Please complete the participation form via the QR-code:
Or contact the IDWP data office for participation in the study: idwpebmt@LUMC.NL.