

defined as: urgent LT, LT in patients undergoing hemodialysis, re-transplantation, early urgent surgical complications after LT (including vascular), patients needing  $\geq 40$  units of blood cell components or derivatives. All documented invasive fungal infections were considered. Patients who died intraoperatively or within 1 week after LT were excluded.

**Results** Of all the patients included in the study, 26 died intraoperatively and 21 patients during the follow-up period. Of the remaining, 99 (20%) were considered to be at high risk for fungal infection. These patients presented a higher MELD score (19.5 vs 14.2,  $p < 0.001$ ), higher CTP score (12.1 vs 6.9,  $p > 0.001$ ), more frequent acute kidney injury (AKI $\geq 2$  21% vs 10%,  $p < 0.001$ ) and greater need for vasopressors intraoperatively (67% vs 14%,  $p < 0.001$ ).

61 of them (61.6%) received prophylaxis with AnfoBlip. 8 fungal infections were detected (7 *Candida albicans* and 1 *Candida tropicalis*), 5 in the high risk group without prophylaxis and 1 in the high risk group with prophylaxis. In one patient AnfoBlip was discontinued due to worsening renal function.

**Conclusion** The introduction of prophylaxis with AnfoBlip after LT in selected patients decreases the incidence of invasive fungal infections. Nonetheless we observed that not all patients at higher risk received this prophylaxis.

## P181

### Evaluation of the pattern of antifungal therapy prescription after liver transplantation

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**Objective** To evaluate the antifungal therapy prescription after liver transplantation (LT) Design: retrospective, non-interventional study, with a 1-year follow-up.

**Patients and Methods** All patients who underwent LT during January 2008 and December 2012 (n = 490; mean age  $47.4 \pm 12.4$  years, 68.5% male, mean MELD  $15.1 \pm 4.1$ , mean CTP score  $7.7 \pm 3.3$ ) were included for enrollment. Patients were further separated in prophylaxis group, considered at high risk and receiving antifungal therapy within the first 10 days after LT, and patients receiving any other antifungal therapy afterwards, up to the end of the follow-up period. All documented invasive fungal infections were considered. Patients who died intraoperatively or within 1 week after LT were excluded.

**Results** From the total of enrolled patients, there were 26 intraoperative deaths and another 32 patients died during the follow-up period. Ninety nine were considered at high risk for fungal infection and, of them, 61 (61.6%) received prophylaxis with AnfoBlip, at a standard dose of 100 mg/day. During this period, a total of 8 fungal infections were detected (7 by *Candida albicans* and 1 by *Candida tropicalis*), 5 in the high risk group without prophylaxis and 1 in the high risk group who received prophylaxis period. After this period antifungals were prescribed to other 19 patients. The most prescribed antifungal class was azoles (15), followed by liposomal Amphotericin B and echinocandins (2). Prescriptions were mostly performed during readmissions (14) or in outpatient follow-up. In this period, only 3 fungal agents were detected, all *Candida albicans*.

**Conclusion** Initial prophylactic treatment of antifungal invasive infection after LT in high risk patients during the study period covered only 61% of the eligible patients; after this period, the prescriptions are performed empirically, mostly not supported by microbiological results but upon a higher clinical suspicion of the in-charge physician.

## P182

### Invasive aspergillosis in patients with hematological malignancies in Czech and Slovak Republics: fungal infection database (find) analysis (2001–2011) – an update

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**Objectives** "Fungal InfectioN Database" (FIND) represents international database of invasive fungal infections in Czech and Slovak hematooncological departments. FIND - *aspergillus* covers all case of invasive aspergillosis (IA) in participating centers since 2001.

**Methods** The goal of our retrospective analysis was to evaluate incidence, early diagnostic procedures and effect of antifungal therapy in proven and probable IA that occurred in 16 institutions participating in FIND database between 2001–2011. Till 2009 we followed EORTC/MSG 2002 and from 2010 EORTC/MSG 2008 criteria in evaluation of IA diagnosis and therapy response.

**Results** 256 probable and 58 proven IA (91% isolated pulmonary IA, IPA) have been documented. Prolonged and profound neutropenia (61%) and long-term use of corticosteroids (28%) were identified as the major risk factors of IA. 68% pts. had consecutive positivity of serum-galactomannan (S-GM) (OD index  $> 0.5$ ). 83% pts. with IPA and bronchoalveolar lavage (BAL) had positive GM in BAL fluid (OD index  $> 0.5$ ). In pts. with IPA only 7.6% BAL fluids and 8.4% sputum samples had positive microscopic result for filamentous fungi and 2.2% BAL fluids and 1.8% sputum samples had positive culture for *Aspergillus* spp. The primary antifungal therapy of IA was used in 89% pts. - 41% voriconazole (VORI), 7% echinocandins (ECHINO), 23% VORI+ECHINO, 7% amphotericine B deoxycholate (C-AMB) and

9% lipid-based AMB (LBA). Overall RR to primary therapy of IA was 46% - VORI 55%, VORI+ECHINO 54%, C-AMB 35%, LBA 39%, ECHINO 25%. There was a statistically significant difference in overall RR to targeted therapy in pts. with neutrophil count <0.1 and >1.0 x10<sup>9</sup>/l at the end of therapy (21% vs. 71%). The overall mortality rate was 61%, with 39% attributable to IA.

**Conclusion** On the basis of our analysis we confirm typical risk factors for IA and critical role of S-GM and CT for early diagnosis and prompt start of antifungal therapy of IA. A reasonable treatment response was achieved using VORI, VORI+ECHINO or LBA in primary therapy of IA. We have confirmed neutropenia at the end of antifungal therapy as the major predictive factor for therapeutic response.

On behalf of CELL - The Czech leukemia study group for life.

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**Galactomannan determination for diagnosis of invasive aspergillosis in different groups hematological patients in Saint-Petersburg, Russia**

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**Objectives** To analyze the utility of galactomannan (GM) test for the diagnosis of invasive aspergillosis (IA) in patients with hematological malignancies in St. Petersburg, Russia.

**Methods** The study included 728 samples: 480 serum, 164 bronchoalveolar lavage fluid (BAL) and 15 cerebrospinal fluid (CSF) from 351 hematological patients with IA in 19 hospitals in St. Petersburg in 1998–2012 yy. Diagnosis of IA was based on EORTC/MSG 2008 criteria. Detection of GM was performed with "Platelia Aspergillus EIA" (Bio-Rad). The test was considered as positive with a cut-off of ≥0.5 (serum, CSF) and ≥1.0 (BAL). BAL and CSF were examined by direct microscopy with calcofluor white and culture.

**Results** Test "Platelia Aspergillus EIA" was positive in serum of 65.0% of patients invasive aspergillosis: in 62.8% - pulmonary aspergillosis, 57.7% - Aspergillus sinusitis and 73% - central nervous system aspergillosis. Direct microscopic examination of BAL, sputum, cerebrospinal fluid and discharge from sinuses was positive in 28% of cases. Aspergillus spp. were isolated in 26% of cases. Level of GM index in samples differed: in serum was 0,5 - 2,7, CSF - 0,5 - 2,0, and in BAL - 1,0–7,5.

Sensitivity of GM test in BAL were higher, than in serum on 12.9% at similar specificity (83% vs. 86.0%). The positive results of GM test in BAL samples and serum samples correlated with positive results of microscopy and culture of BAL in 60% and 30%, respectively. In hematological patients with IA a higher level GM index (2, 0–7,5) was found in the BAL samples more frequently along with a positive microscopy than with positive mycological culture.

**Conclusion** This study indicates that GM test in serum, BAL and CSF has a significant impact on the diagnostics of IA in patients with hematologic malignancies. The sensitivity of "Platelia Aspergillus EIA" test was higher than that of classical mycological methods and depends on the type of biological specimen.

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**Epidemiology and outcome of mucormycosis in hematopoietic stem cell transplant recipients**

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**Background** In recent years mucormycosis (M) has become an important cause of morbidity and mortality in allogeneic hematopoietic stem cell transplant (allo-HSCT) recipients. This study focuses on etiology, clinical forms and outcome of M and factors which influence on overall survival (OS) in allo-HSCT recipients.

**Methods** 14 pts with M after allo-HSCT were included in 2009–2013 yy. Baseline patient characteristics and treatment are outlined in Table 1. EORTC/MSG 2008 diagnostic criteria of proven and probable invasive fungal disease (IFD) were used.

**Results** Incidence of M was 2.4% (14/582, allo-HSCT 2009–2012). There were 6 proven (43%) and 8 probable (57%) cases of M in 14 pts with predominantly acute leukemia (71%). Median date of M onset after allo-HSCT was D + 105 (14–449). One case of M was diagnosed post-mortally. Main clinical forms of M were pulmonary 79%, rhinocerebral 7%, subcutaneous/osteomyelitis 7%, and bowel 7%. In 79% pts bronchoscopy was performed, in 100% cases it was informative for the diagnosis. In 57% of cases diagnosis was confirmed by culture. Etiologic agents of M were Rhizopus spp. (75%), Rhizomucor spp. (12.5%), Mucor spp. (12.5%), and L. corymbifera (12.5%). In 50% cases M was diagnosed after or with invasive aspergillosis (IA). 12-week OS after diagnosis of M was 31%, 6-months OS in - 31%, and 1-year OS - 23%.

**Table 1**

Baseline patient characteristics with mucormycosis (n = 14)	
Variable	
<b>Demographic characteristics</b>	
Age, years - Median, range	21 (4-48)
Sex - Male/Female	10/4
<b>Underlying disease</b>	
Diagnosis	
Acute leukemia, Acute myeloid leukemia/Acute lymphoblastic leukemia	5/4
Others	4
<b>Status at the moment of HSCT</b>	
Remission/Relapse or without remission	8/9
<b>Transplant characteristics</b>	
Hematopoietic stem cells (HSC) source	
Bone marrow (BM)	8
Peripheral blood (PBSC)	9
Type of donor	
Unrelated matched/ Unrelated mismatched	7/1
Family matched/ Haploidentical	3/3
Conditioning regimen (CR)	
Myeloablative (MAC)	3
Reduced intensity (RIC)	11
Secondary alloHSCT	2
Antifungal prophylaxis	
Primary - fluconazole/ voriconazole	7/2
Secondary - voriconazole/ posaconazole	3/2
<b>Mucormycosis characteristics</b>	
Clinical forms (isolated and/or in combination)	
Pulmonary	11
Rhinocerebral	1
Subcutaneous/osteomyelitis	1
Bowel	1
<b>Treatment of mucormycosis</b>	
Combination antifungals base on Amphotericin B/lipid forms	3/3
Caspofungin	2
Posaconazole	4
Monotherapy	8
Posaconazole	2
Lipid complex amphotericin B	1
Amphotericin B deoxycholate	2
Caspofungin	1
Voriconazole	2