Table 1
Daily Micafungin Antifungal Prophylaxis Results

Observations	Number (%) or Median (Range)
Total patients	28
Duration (days)	37 (3-94)
Average dose - start (mg/kg/day)	2.1 (0.8-4.3)
AST	
Baseline elevation	7 (25)
End elevation	7 (25)
Increase ≥ 2x baseline	17 (61)
ALT	
Baseline elevation	11 (39)
End elevation	10 (36)
Increase ≥ 2x baseline	19 (68)
Total Bilirubin	
Baseline elevation	0
End elevation	4 (14)
Increase ≥ 2x baseline	24 (86)
Creatinine	
Baseline elevation	1 (4)
End elevation	1 (4)
Increase ≥ 2x baseline	10 (36)

296

Alternate Day Micafungin Antifungal Prophylaxis in High Risk Pediatric Patients Undergoing Hematopoietic Cell Transplantation (HCT)

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Background: Disseminated fungal infection is a major cause of morbidity and mortality in children undergoing HCT. Prophylaxis with amphotericin B can be limited by renal toxicity. Oral triazoles can be limited by poor absorption, large interindividual pharmacokinetic (PK) variability, and hepatic toxicity, leading to interruptions in therapy and breakthrough infections. Micafungin has potential advantages, due to its better safety profile, specifically in terms of hepatic and renal toxicity, and lack of drug-drug interactions with common medications used in the HCT setting.

Both animal and adult human data suggest that alternate day dosing schedule can be effective. In a PK study in pediatric HCT patients, we have previously shown detectable and protective Micafungin levels at 48 hours after the dose (Mehta et al, 2010). Here we report our clinical experience of use of alternate day micafungin (3 mg/kg) in high risk pediatric patients undergoing HCT.

Methods: A total of 33 infants and children with various hematological and immune deficiency disorders undergoing HCT were reviewed retrospectively. The median age was 5 years (range 0.5-20). None of the patients had a history of prior fungal infection.

Results: Results are described in Table 1. Eleven patients were started on alternate day Micafungin after sustaining liver dysfunction from voriconazole, liver graft vs. host disease (GVHD), disseminated viral infection and/or veno-occlusive disease. Three patients developed liver dysfunction while on alternate day micafungin from similar causes. In all these patients, continuation of micafungin did not worsen liver dysfunction, which in fact improved in most patients over time. Two patients developed breakthrough fungal infection during alternate day micafungin prophylaxis. One patient had been on micafungin for 8 weeks and another for 14 weeks at the time of developing breakthrough candida line infection and esophagitis respectively. Of note, both these patients had refractory liver and gastrointestinal GVHD and were significantly immunocompromised from multiple immune suppressive therapies for their GVHD.

Conclusion: We conclude that, alternate day micafungin prophylaxis is safe and well tolerated; specifically even in patients with baseline liver dysfunction, without additional liver toxicity. This provides a simple prophylaxis regimen that can be administered for prolonged duration to patients undergoing HCT even on an outpatient basis.

Table 1
Alternate day Micafungin Antifungal Prophylaxis: Results

Observations	Number or Median (Range)
Total number of patients	33
Total weeks of alternate day Micafungin	10 (4-28)
Liver profile trends during Micafungin prophylaxis	
Baseline ALT	49 (15-164)
Baseline AST	51 (15-1080)
Baseline direct bilirubin	0.1 (0-4.3)
Highest ALT	138 (26-491)
Highest AST	105 (37-900)
Highest direct bilirubin	0.2 (0-9)
End of therapy ALT	98 (20-190)
End of therapy AST	52 (18-156)
End of therapy direct bilirubin	0.1 (0.1-8.9)
Breakthrough fungal infection	2
Patient 1	*Candida albicans* fungal esophagitis - confirmed by culture
Patient 2	Line infection - culture positive for *Candida glabrata*

297

Changing Trends in the Use of Surgical Biopsy for Diagnosis of Pulmonary Disease in Hematopoietic Cell Transplant Recipients

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Introduction: Historically, diagnosis of enigmatic pulmonary disease after hematopoietic cell transplant (HCT) has required lung biopsy. Recent improvements in laboratory diagnostics and therapies for fungal infections have led to changes in how clinicians approach pulmonary abnormalities. We examined temporal trends in the use of lung biopsy after HCT.

Methods: We retrospectively reviewed patients who underwent their first allogeneic HCT at the Fred Hutchinson Cancer Research Center between the years 1993-1997 and 2003-2007. Data on lung biopsies were abstracted from a prospectively collected database of all recipients from these two cohorts (NEJM 2010). Outcome data were analyzed using Fisher's exact test. Hazards for lung biopsy for the two cohorts were determined using a Cox-proportional hazards model with death and relapse considered competing risks.

Results: A total of 50/1418 (3.5%) patients underwent 52 post-HCT surgical lung biopsies during 1993-1997 compared

with 21/1148 (1.8%) patients and 21 biopsies in the 2003-2007 cohort. The median time to biopsy post-HCT was 72 days (IQR 32-89) for the early cohort and 97 days (IQR 33-119) for the more recent cohort, for an overall biopsy incidence of 0.052 and 0.02 per 1000 patient days, respectively. Patients in the 2003-2007 cohort were less likely to undergo a lung biopsy (HR 0.52, CI 0.28-0.98, $P = .04$) when compared to patients in the 1993-1997 cohort. Although a similar number of patients underwent a bronchoscopy between the two cohorts (272/1418 [19.2%] vs. 243/1148 [21.1%], $P = .22$), more patients in the early cohort underwent lung biopsy without antecedent bronchoscopy (26/52 [50%] vs. 18/21 [86%], $P = .007$). Infections were a more common finding at biopsy in the early cohort (35/1418 vs. 8/1148, $P < .001$), but the number of biopsies demonstrating non-infectious lesions was similar between the two cohorts (17/1418 vs. 13/1148, $P = .85$). Fungal infections were the major infectious etiology in both cohorts (30/35[85%] vs. 5/8 [63%], $P = .15$), but there was a significant reduction in the number of *Aspergillus* species found at biopsy between the cohorts (29/52 vs. 1/21, $P < .001$). A similar number of patients underwent biopsy with a therapeutic intent in the two cohorts (8/52 [15%] vs. 3/21 [14%]); all of those who underwent therapeutic biopsy in the 2003-2007 cohort had documented *Mucorales* species.

Conclusions: Surgical evaluation of lung disease in HCT recipients significantly declined over a decade between 1993-1997 and 2003-2007. This decreased incidence of lung biopsies between these two cohorts was related to a reduction in the number of biopsies for post-transplant infections, particularly for those due to aspergillosis. We speculate that this decline is related to the introduction of galactomannan testing and the increased use of empiric therapy with extended-spectrum azoles.

298

Building Resiliency in New Nurses

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Background: The Bone Marrow Transplant Unit of Cincinnati Children's Hospital Medical Center is a crucial care and stressful unit. The nurses not only care for complex patients with an array of co-morbidities, but also therapeutically support the family. This may lead to an increased workload and increased stress levels on nurses, which can potentially cause burnout and turnover. Resiliency training has been shown to decrease stress levels and improve positive outlook in stressful work environments (Pipe et al. 2012; Steinhart et al. 2008; Burton et al. 2010; Sood et al. 2011). There is a gap in the literature regarding specific interventions to help new nurses cope with the stressors of a critical care environment. Research Question Do newly hired nurses who receive resiliency training in addition to standard orientation improve nurse job satisfaction scores and decrease job turnover? Purpose/Intervention The purpose of this project is to improve the well-being and job satisfaction of the new staff nurses on the Bone Marrow Transplant Unit at CCHMC. Using principles founded in positive psychology, an education program will be implemented into the orientation schedule of newly hired nurses. Job satisfaction scores and stress levels will be monitored before the educational program and at 6 months and 1 year post. Data will be collected to determine the efficacy of the additional education throughout the orientation period.

299

Invasive Fungal Infections in Recipients of Hematopoietic Stem Cell Transplants: Results From a Single Center Retrospective Analysis

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Background: The purpose of our study was to evaluate the incidence and outcome of Invasive Fungal Infections (IFI) among patients who underwent autologous or allogeneic Hematopoietic Stem Cell Transplantation (HSCT) at our BMT-Unit.

Methods: This cohort-retrospective study,conducted during 02/1994 to 09/2012, involved HSCT patients admitted to our BMT-Unit, who developed IFI.The IFI were classified according to the modified EORTC/MSG criteria.

Results: Among 369 patients who underwent HSCT(88 allogeneic HSCT recipients and 281 autologous HSCT recipients), IFI occurred in 38 patients (overall incidence 10,3 %). 34 episodes (9,2 % of all patients) were due to molds, and 4 (1 %) were due to yeasts. 27 episodes (30,6 %) occurred among the allogeneic HSCT recipients, and 11 (3,9%) occurred among the autologous HSCT recipients (RR 7.83, 95%CI 3.92-16.21). Etiological agents were Aspergillus (31 episodes), Candida (3 episodes), Rhodotorula (1 episode), Fusarium (1 episode), Scedosporium (1 episode), Zygomycosis (1 episode). The incidence of Aspergillosis was 25 % and 3,2 % among allogeneic and autologous HSCT recipients respectively (RR 7.80, 95%CI 3.58-17.75). The incidence of Candidiasis was 2,2 % and 0,3% among allogeneic and autologous HSCT recipients respectively (RR 6.38, 95% CI 0.45-177.57). The overall mortality rate for IFI was 5,7% among allogeneic HSCT recipients and 1 % among autologous recipients (RR 5.32,95% CI 1.13-27.79), whereas the attributable mortality rate for IFI registered in our population was 21% (18,5 % for allogeneic HSCT recipients and 27,2 % for autologous HSCT recipients (RR 0.67,95% CI 0.16-3.34). The attributable mortality rate for aspergillosis was 22,6 % (18,2 % and 33,3 % for allogeneic and autologous HSCT recipients, respectively, RR 0.54,95%CI 0.12-2.81), and the rate for Candida IFI was 0 %.

Conclusions: IFI represents a common complication for allogeneic HSCT recipients.Aspergillosis is the most frequently detected IFI in these patients. Conversely, autologous HSCT recipients rarely develop aspergillosis. Candidemia was observed less often than aspergillosis among both allogeneic and autologous HSCT recipients.

300

A Single Daily Ultra Low-Dose of Oral Acyclovir Is Sufficient to Prevent the Occurrence of Herpes Zoster Post Hematopoietic Stem Cell Transplantation: Interim Results of a Prospective Randomized Trial

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