Breakthrough fungal infections were observed in 4 (6%) and 11 (15%) patients in the L-ampho B and the caspofungin groups, respectively (p = 0.2). Of all, 13 were due to *Aspergillus* spp while 1 *C. neoformans* CNS infection and 1 *B. capitatus* fungemia were observed in patients receiving caspofungin. Nine additional patients had a baseline fungal infection (4 in the L-ampho B group and 5 in the caspofungin group) and none of them had successful treatment. Resolution of fever during neutropenia was seen in 40 (66%) and 41 (56%) of patients in the L-ampho B and the caspofungin groups, respectively (p = 0.17). There was a trend towards higher premature discontinuation of therapy due to lack of efficacy or toxicity in the caspofungin group (27% vs 13%, p = 0.057). However, more patients survived at least 7 days after completion of therapy in the caspofungin group (92% vs 75%, p = 0.007). The overall success rate defined as the fulfilment of all 5 composite end points was achieved in 28 (46%) and 24 (33%) patients in the L-ampho B and the caspofungin groups, respectively (p = 0.16).

L-ampho B and caspofungin were both effective when given as empirical antifungal therapy for the treatment of PFN in patients undergoing allogeneic SCT. Differences between L-ampho B and caspofungin in overall success assessed by the 5-component end point were not statistically significant.

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RE-IMMUNIZATION PRACTICES AMONG SURVIVORS OF PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT

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Background: The number of Hematopoietic Stem Cell Transplants (HSCT) has increased over the past 25 years with higher rates of success and a large number of long-term survivors. Patients who undergo either an autologous or allogeneic HSCT experience profound immunosuppression from the conditioning regimen causing them to lose the immunity gained from previous vaccinations. Acknowledging the need for consistency among practices, the Centers for Disease Control and Prevention, Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation published guidelines regarding re-immunization post HSCT in 2000.

Purpose: The purpose of this study was to assess patient adherence to re-immunization guidelines after HSCT. Completeness, timeliness, factors influencing adherence and parental identification of barriers to re-immunization were also examined.

Methods: Patients who received an HSCT between 01/01/2001 and 12/31/2007 and were alive at time of recruitment were eligible for enrollment. Parents of eligible patients were contacted to participate in a phone survey assessing perceptions of and barriers to re-immunization. Vaccination data was abstracted using the Georgia Registry of Immunization Transactions and Services (GRITS), a state-wide mandatory reporting database for Georgia.

Results: Of the 271 patients transplanted during the designated time period, 98 met eligibility criteria and 58 completed the phone survey. Of the phone survey participants, 90% (N = 58) reported being told their child would need to be re-immunized post HSCT and 89% (N = 57) reported their child being up to date on immunizations to the best of their knowledge. Data in GRITS, however, showed that only 9% (N = 98) had completed all doses of 6 of the recommended vaccines (Hep B, HiB, MMR, Polio, PPV, DTaP/Td). On average patients who had received at least one post-HSCT vaccination completed 60% of the recommended doses (N = 87). Patients who received allogeneic transplants averaged 63% (N = 56) complete while patients who received autologous averaged 54% (N = 31) complete. The guidelines recommend patients begin re-immunization 365 days post HSCT. The average time to first immunization post HSCT was 639 days (median 512 days, range 195 – 2728 days).

Conclusion: Parents perceived their children to be more up to date with their re-immunizations than was found in GRITS data. Further education is needed for both parents and healthcare providers caring for these patients.

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BIOAVAILABILITY OF ORALLY ADMINISTERED VORICONAZOLE AND ITS ASSOCIATION WITH THE EFFECTS ON TACROLIMUS CONCENTRATION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Backgrounds: Although drug interaction between calcineurin inhibitors and voriconazole has been recognized, the interaction has not been fully evaluated in hematopoietic stem cell transplantation (HSCT) recipients. We have previously shown a notably wide variability in the effect of voriconazole administration on the concentration of calcineurin inhibitors in HSCT recipients, in whom voriconazole and calcineurin inhibitors were administered orally or intravenously (Bone Marrow Transplant 2009;44:371). In the present study, the drug interaction between voriconazole and tacrolimus was evaluated in HSCT recipients, when both were orally administered. In addition, bioavailability of voriconazole was evaluated and its association with the drug interaction was quantitatively assessed.

Patients & Methods: Twenty-two recipients of allogeneic HSCT who had already been on a steady dose of orally administered tacrolimus, and were started on voriconazole (orally 200 mg per body every 12 h) for the treatment or prophylaxis of fungal infection were evaluated. Conditioning were myeloablative in 12 patients, and reduced-intensity in 8 patients. The concentration/dose (C/D; (ng/ml)/(mg/kg)) ratio of calcineurin inhibitors was calculated before and 7–10 days after initiating voriconazole administration. The C/D ratios before and after voriconazole administration were compared, and increased rate (%) was calculated. The plasma level of voriconazole was measured by high-performance liquid chromatography.

Results: The median C/D ratio of tacrolimus significantly increased to 531.1 (ng/ml)/(mg/kg) (range, 127.8-759.2) after initiating voriconazole administration as compared with that before (169.6 (range, 128.6-541.3): $P < 0.001$). Median increased rate of C/D ratios were 196.8% with a range of -32.0% to 685.7%. The plasma level of voriconazole on the day of evaluating C/D ratio was 2.39±1.67 mg/ml, which was lower than 1.0 mg/ml in 4 patients and higher than 4.0 mg/ml in 3 patients. The increased rate of C/D ratio of tacrolimus did not correlate with the plasma level of voriconazole (r = -0.05, $P = 0.838$).

Conclusion: Orally administered voriconazole demonstrates a significant interaction with orally administered tacrolimus with a wide interindividual variability in the magnitude. A wide interindividual variability could not be explained by the difference in the bioavailability of voriconazole, and other mechanisms such as p-gp should be investigated.

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TREATMENT OF PARAINFLUENZA 3 INFECTION WITH DAS181 IN A PATIENT AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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Parainfluenza virus (PIV) infections are common after allogeneic SCT and can cause severe morbidity, yet there is no effective treatment. DAS181 is an investigational antiviral medication which is active *in vitro* and *in vivo* against PIV. It is a recombinant sialidase protein which removes sialic acid residues. Binding to these residues is the initial step in PIV infection. We report the first treatment of PIV3 infection with DAS181 in a SCT patient. A 63 year-old female with AML underwent a second SCT after primary graft failure. Conditioning included fludarabine and alemtuzumab, with tacrolimus as GVHD prophylaxis. After engraftment, her course was complicated by grade III skin GVHD which was treated with steroids and mycophenolate mofetil. Three months after her second SCT, she developed nasal congestion and cough and was found to have PIV3 infection. She was treated with bronchodilators and IVIG. There was no evidence of superinfection. She was admitted 6 weeks later for pancytopenia and worsening respiratory status thought to be from progressive PIV3 infection. Given her worsening status, we obtained an emergency IND from the FDA to administer DAS181.