was 49 years (range, 21–71 years). Ten patients underwent a sibling transplantation (5 standard regimen, 5 reduced intensity), and 11 underwent an unrelated transplantation (5 standard regimen, 6 reduced intensity); graft T-cell depletion was done in 15 patients (Campath-1H in 7, OKT3 in 8). Neutropenia was observed in 5 patients, resolving in all of them. VGC was discontinued temporarily in these 5 patients until they recovered from neutropenia. Four of them received concomitant mycophenolate mofetil. No adverse effects were otherwise reported. The median follow-up after transplantation is 12 months. Six patients died during the study, from disease progression (2 patients), fungal infection (1 patient), or GVHD (3 patients). None of the 21 patients experienced CMV reactivation or disease while on VGC. **Conclusions:** These early results suggest that VGC has a role in the posttransplantation setting, and that further evaluation of VGC in CMV prophylaxis or preemptive therapy is needed.

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ACTUALIZING A WELLNESS PROGRAM AND WELLNESS ROOM IN THE ONCOLOGY SETTING: GETTING A PROGRAM THROUGH A LARGE INSTITUTION

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The Clinical Center (CC) of the National Institutes of Health (NIH) is a hospital solely dedicated to conducting biomedical research. Participation in the rigors of a phase I or II clinical trial requires inner strength, support, and ability to follow through with the demands of research. Nurses on the Oncology, Experimental Transplantation Unit at the CC acknowledge the special needs of their patients, caregivers, and staff, and strive to find ways to lessen the impact of these demands. A group of oncology nurses at the CC formed a Complementary and Alternative Medicine (CAM) Cancer Nursing Interest Group. A review of the literature reveals that a focus on patients' psychological, social, physical, and spiritual needs promotes improved quality of life in oncology patients. The CAM Interest Group recognized the importance of integrative therapies as one strategy to assist patients in dealing with their chronic illness. This presentation outlines the development and inception of a wellness program to aid patients in dealing with chronic illness using integrative therapies such as relaxation therapy, guided imagery, and a "room for silence."

The "plan-do-check-act" model serves as our conceptual model for development and evaluation of the program. Benchmarking with preeminent institutions nationwide, and identification of key stakeholders within the institution, as well as the National Cancer Institute (NCI) and the National Center for Complementary and Alternative Medicine (NCCAM), was instrumental in the development of the program.

With visionary nursing leadership and extensive collaboration with the CC interdisciplinary team, the program has been incorporated and follows the credentialing guidelines proposed by the CC's Integrative Medicine Taskforce. Self-care, empowerment, healing versus curing, relaxation, and comfort are emphasized, and an examination of theories and models is used for health education and promotion. Dedicated space has been allocated for a "room for silence," which is designed for meditation, prayer, imagery, and journaling. Patients and staff evaluate the wellness program on an ongoing basis and changes are incorporated based on feedback.

Incorporating a wellness program fosters improved patient outcomes, enhances quality of life for oncology patients, and serves as a model for integrative care.

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URSODIOL-BASED PROPHYLAXIS FOR VENO-OCCLUSIVE DISEASE (VOD): A RETROSPECTIVE RISK-BASED REVIEW OF OUTCOMES FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION

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A total of 307 sequential patients allografted at our institution over the past decade were evaluated retrospectively to study treatment-related hepatotoxicity, and prevention thereof, following the use of various ursodiol-based VOD prophylaxis regimens. The patient group comprised 178 males and 129 females, median age 42 years. There were 227 related and 80 unrelated donors, 271 matched and 36 mismatched. Diagnoses included acute leukemia in 129 patients (42%), chronic leukemia in 89 patients (29%), lymphoma in 37 patients (12%), myelodysplasia in 21 patients (7%), myeloma in 15 patients (5%), aplastic anemia in 10 patients (3%), and other in 6 patients (2%). A total of 158 patients (51%) received TBI, 112 patients (36%) received busulfan, and 37 patients (12%) received methotrexate. All patients whose bilirubin exceeded 2.0 mg/dL postgrafting (166 patients; 54%) were evaluated for cause. The mean day (D) of maximal bilirubin elevation for this group was D+19. Non-VOD causes included regimen-related toxicity in 57 patients (34%), GVHD in 50 patients (30%), infection/sepsis/multiorgan dysfunction in 19 patients (12%), and ABO-realted hemolysis in 18 patients (11%). The diagnosis of VOD was made by criteria described previously. VOD accounted for the cause of hyperbilirubinemia in 23 patients in this subset of 166 patients (14%). Of the total group of 307 patients, 164 patients (53%) received VOD prophylaxis, 38 patients (23%) received oral ursodiol (Urso) alone (600–900 mg/day), 69 patients (42%) received IV Urso + heparin (Hep)(800 U/hr), 54 patients (33%) received SQ Urso + Lovenox (Lov)(40 mg/day), and 3 patients (2%) received Hep alone. Overall, 23 patients (7.5%) developed VOD, with only 7 patients dying due to VOD (2.3%). The incidence of VOD was not significantly different for +/− Urso (7.5% vs 7.6%), +/− Lov (7.4% vs 7.5%), +/− Hep (11.1% vs 6.4%; $P = .18$); +/− Urso + Lov (7.4% vs 7.5%), and +/− Urso + Hep (7.2% vs 7.6%). Data were also analyzed for the effect of 7 known risk factors for VOD: age > 40 years, unrelated donor, preparative regimen including busulfan or TBI, baseline AST, methotrexate for GVHD prophylaxis, and history of liver disease. Risk factors (f) for VOD occurred as follows: 0(f), 5 (2%); 1(f), 90 (29%); 2(f), 150 (49%); 3(f), 54 (17%); 4(f), 8 (3%). The occurrence of VOD (%) correlated with the number of risk factors (f) pregrafting: 0(f), 0/5 (0%); 1(f), 5/90 (6%); 2(f), 10/150 (7%); 3(f), 7/54 (13%); 4(f), 1/8 (12%). The overall incidence of VOD, and related death, is lower in this series than historical reports. The benefit of ursodiol-based prophylactic regimens appears to be greatest in patients with 2 or fewer VOD-related risk factors.

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VORICONAZOLE (VOR) IS SAFE AND EFFECTIVE AS PROPHYLACTIC ANTIFUNGAL THERAPY FOR ALLOGENEIC STEM CELL TRANSPLANTATION (AT)

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Background: Despite fluconazole (FLU) prophylaxis in AT, invasive fungal infection (IFI) continues to cause significant morbidity and mortality. VOR is a second-generation triazole with broad-spectrum activity. Since August 2002, VOR has been used as antifungal prophylaxis at UCSF Medical Center. The goals of this study were to evaluate the incidence of IFI up to d100 and assess safety and organ toxicity (OT). **Methods:** The records of patients receiving VOR prophylaxis from August 2002 to May 2004 were reviewed. Demographics, conditioning, stem cell source, HLA status, laboratory and radiology results, OT, and survival were analyzed. All patients were hospitalized throughout AT. Tacrolimus and MTX +/− MMF were used for GVHD prophylaxis. VOR (4 mg/kg twice a day IV/PO) was administered through day +100 post-AT. EORTC criteria were used to assess for IFI. **Results:** A total of 72 patients were identified (44 males and 28 females, mean age 54 years [range, 19–70]). Of these, 41 patients received low-intensity conditioning and 31 received myeloablative therapy. PBSCs were used more frequently than BM (60 vs 12). Sibling donors were used for 37 patients; unrelated donors, for 35 patients. The 100- and 180-day TRM rates were 8% and 13%. The incidence of grade II-IV aGVHD was 16%. Two patients (3%) developed definitive IFI (1 mucor and 1 aspergillus plus scedosporium). No probable IFIs were identified. Both patients with definitive IFI died, 1 from grade IV GVHD and 1 from

multiorgan failure. No unexpected OT was noted. Fifty-four of the 72 patients (75%) received VOR until day 100 without interruption. The reasons for VOR discontinuation were increased LFTs in 11 patients, prolonged QTc in 2, and suspected resistant IFI in 2. The LFT increases were transient. The median total bilirubin, alkaline phosphatase, and AST values were 1.3 mg/dL, 134 U/L, and 34 U/L, respectively. Eight patients developed total bilirubin $>$ 6 mg/dL, and 3 had VOD. Four patients restarted VOR following improved LFTs. No significant cardiac toxicity was noted, despite a QTc of $>$ 500 msec in 10 patients. The mean increase in QTc after starting VOR was 34 msec (n = 36). The mean peak creatinine level was 1.5 mg/dL. Four patients required HD. Engraftment did not appear to be adversely affected, with means of 14 days to ANC $>$ 0.5/μL and of 20 days to platelets $>$ 50×10^3/μL. VOR did uniformly increase serum tacrolimus levels, necessitating a 60% reduction in tacrolimus dosing. **Conclusions:** VOR appears safe and effective as prophylaxis for AT. Tacrolimus levels must be closely monitored. A randomized trial comparing VOR to FLU in AT is warranted.

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ANTIFUNGAL PROPHYLAXIS WITH VORICONAZOLE IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION RECIPIENTS

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Background: Invasive fungal infection (IFI) remains a major cause of morbidity and mortality in recipients of allogeneic hematopoietic stem cell transplantation (HSCT). In many transplantation centers, *Aspergillus* has been the leading cause of death from fungal infections. Voriconazole is a triazole with broad-spectrum antifungal activity against several molds, including *Aspergillus*. In our institution, voriconazole was instituted as antifungal prophylaxis in July 2002. Before the institution of voriconazole, invasive aspergillosis (IA) was the most commom fungal infection in our allogeneic HSCT population, with 3 years of surveillance revealing a cumulative incidence of proven or probable IA of 12%. **Methods:** From July 2002 to March 2004, 40 adult patients undergoing allogeneic HSCT received oral voriconazole 200 mg every 12 hours from initiation of the preparative regimen until at least posttransplantation day 100. After day +100, voriconazole was continued in patients requiring corticosteroids for therapy of GVHD. Intravenous voriconazole was allowed in patients not able to take oral medications. All these patients were at high risk for *Aspergillus* infection. Diagnoses included myeloid malignancies in 23 patients, lymphoid malignancies in 16, and renal cell cancer in 1. Median patient age was 47 years. Some 75% of the patients had advanced disease, and 50% received an unrelated donor transplant. T-cell depletion was achieved using either OKT3 or Campath-1H in 75% of the patients. GVHD requiring high-dose corticosteroids occurred in 50% of the patients. **Results:** Voriconazole had to be discontinued in 1 patient due to hallucinations; this patient developed and died from IA. Three cases of candidemia caused by *Candida glabrata* were diagnosed (all 3 cases caused by voriconazole-resistant organisms). Disseminated zygomycosis was identified and caused the death of 2 patients at days 25 and 196 after transplantation. **Conclusions:** In this high-risk patient population, only 1 case of IA was diagnosed. This compares favorably with historical **results:** However, 2 cases of disseminated zygomycosis were diagnosed. Our experience raises concern regarding the changing epidemiology of IFI as practices using prophylactic antifungal agents evolve.

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PHARMACOKINETICS OF HIGH-DOSE WEEKLY AMBISOME (LIPOSOMAL AMPHOTERICIN B) ANTIFUNGAL PROPHYLAXIS IN PEDIATRIC BONE MARROW TRANSPLANTATION (BMT) PATIENTS

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Background: Disseminated fungal infection is a major cause of morbidity and mortality in children undergoing BMT. Prophylactic oral triazoles are limited by poor absorption, interindividual variation in metabolism, and hepatic toxicity. Ambisome is shown to produce higher plasma and tissue concentrations and has a better safety profile than the parent drug amphotericin B; however, it requires frequent intravenous administration. Both animal (murine models for *Candida/Histoplasma*) and human (adult) data show measurable plasma and tissue levels at 7 days after a single dose (2–20 mg/kg) of Ambisome. We hypothesized that weekly high-dose Ambisome will provide adequate fungal prophylaxis for immunocompromised children. This dosing schedule will improve compliance and broaden the applicability of Ambisome to a larger patient population. **Methods:** A total of 14 children (M/F ratio 2:1, age $<$10 years [mean age, 3.3 years]) with various hematologic conditions, metabolic disorders, and immunodeficiency syndromes at risk for invasive fungal infection received once-a-week intravenous Ambisome prophylaxis at the dose of 10 mg/kg given over 2 hours. Blood samples were drawn for phrmacokinetic (PK) measurements around the first and the fourth weekly doses. PK analysis of single-dose and steady-state data was conducted using standard noncompartmental methods. Individual plasma trough concentrations were determined by visual inspection of the plasma concentration time profiles. The area under the plasma concentration versus time curve ($AUC_{0-\infty}$) was determined using the log-linear trapezoidal rule. Total body clearance (CL), volume of distribution (Vz), and terminal half-life (T½) were calculated using standard equations. **Results:** Ambisome was well tolerated at this dosage. Half-life measured in this pediatric population appears to be shorter than reported in adults (45 hours vs 152 hours). Volume of distribution and clearance were higher compared to adult reports and correlated positively with body weight (r^2 = 0.62 for Vz; r^2 = 0.28 for Cl). Plasma levels at 7 days (Cmin) were not significantly different after the first and fourth doses, suggesting no accumulation over the course of therapy. **Conclusions:** Our data show measurable plasma levels present 7 days after the dose. Adult studies show tissue concentrations $>$ 10-fold higher than plasma concentrations, suggesting that once-weekly dosing, as described in this study, likely provides useful protection against fungal infection.

Table 1. *Pharmacokinetic Parameters After Weekly Ambisome (10 mg/kg)*

Parameters (Unit)	After Single Dose (n = 12)	After Multiple Doses (n = 9)
T½ (h)	45.44 (15.43)	58.94 (26.42)
Day 7 plasma trough (Cmin; mg/L)	0.23 (0.14)	0.51 (0.46)
$AUC_{0\text{-}INF}$ (hr · mg/L)	157.51 (71.71)	230.08 (132.67)
Vz (L/kg)	4.29 (1.01)	4.97 (2.96)
Cl (L/hr/kg)	0.0742 (0.0341)	0.0669 (0.0442)

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EVALUATION OF ANTIBIOTIC CYCLING AND PROPHYLAXIS FOR NEUTROPENIC FEVER WITHIN A BLOOD AND MARROW TRANSPLANTATION UNIT

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Background: Bacterial resistance to antibiotics is an increasing problem and associated with significant morbidity and mortality. Patients undergoing HSC transplantation and treatment for hematologic malignancy are at high risk of infection. We evaluated whether rotating the empiric antibiotics for patients who develop neutropenic fever in this setting resulted in decreased emergence of resistant organisms and decreased vancomycin use. **Methods:** Within the BMTU, all patients with neutropenic fever were empirically treated with piperacillin plus gentamicin (intermittent dosing) from January 1999 to February 2002. From March 2002 through June 2004, 3 antibiotic regimens were cycled every 8