of the treatment are. The content domain of a patient-reported instrument to measure the symptom burden of cGVHD should include questions about the severity of numerous symptoms and how those symptoms have interfered with normal functioning. Symptom burden should be measured longitudinally to capture changes in symptom burden over time. Clinicians caring for patients with cGVHD should reduce uncertainty as much as possible by offering clear explanations and should support patients in appropriate efforts at self-care to relieve symptoms.

PHARMACY

467 CLONAZEPAM PLUS LEVETIRACETAM (CL) FOR THE PREVENTION OF BUSULFAN-INDUCED SEIZURES: A SINGLE CENTER EXPERIENCE

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High dose busulfan (>1 mg/kg) used in hematopoietic stem cell transplant (HSCT) conditioning regimens is associated with a decrease in seizure threshold which can result in partial or generalized seizures in up to 10% of people without a previous seizure history. Phenytoin is the most frequently used agent to prevent seizures. Though this is an effective therapy, the frequent side effects and significant risk for drug interactions from phenytoin make it a suboptimal agent for this purpose. There is no preferred anti-seizure prophylaxis for phenytoin allergic or intolerant patients. A retrospective review was performed of a single center experience using CL in 46 consecutive patients receiving a variety of inpatient and outpatient busulfan-containing regimens to assess it for side effects and efficacy. The patients received the CL regimen over a 13 month period beginning July, 2006. Clonazepam 0.5 mg and levetiracetam 500 mg where given together orally twice daily, beginning the evening before busulfan therapy initiated until discontinuation on the morning after the final busulfan dose was given. All patients were adults, 20 female/26 male, aged 22–75 years (mean 52, median 56) morning after the final busulfan dose was given. All patients were prophylaxis for phenytoin allergic or intolerant patients. A retrospective review was performed of a single center experience using CL in 46 consecutive patients receiving a variety of inpatient and outpatient busulfan-containing regimens to assess it for side effects and efficacy. There were 12 patients treated with CL vs. 34 treated with phenytoin. There were 2 patients reporting mild sedation and 1 patient had their levetiracetam dose reduced to 250 mg twice daily for confusion. When compared to the prior 104 patients receiving the same variety of conditioning regimens with phenytoin anti-seizure prophylaxis, fewer side effects were seen, with equal anti-seizure benefits and a limited risk for drug interactions using the CL regimen. The CL regimen is now the preferred therapy for busulfan seizure prophylaxis for the transplant center.

468 METHOTREXATE AND PIPERACILLIN/TAZOBACTAM VERSUS METHOTREXATE AND CEFTAZIDIME: A LOOK AT TIME TO ENGRAFTMENT AND SIDE EFFECT PROFILES IN HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS

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Many HSCT patients receive methotrexate for GVHD prophylaxis. Commonly, methotrexate is given on days +1, +3, +6, and variably +11. Most patients develop fever during this time period and empiric antibiotics are started.

In June 2006, our institution’s SOP changed the empiric antibiotic for fever for ceftazidime to piperacillin/tazobactam. Penicillin derivatives interact with antineoplastic doses of methotrexate by competing for renal tubular binding sites. Methotrexate toxicity may include severe mucositis, marrow suppression, renal dysfunction, and hepatotoxicity. Smaller doses of methotrexate, like those used for GVHD prophylaxis, have not been investigated. We evaluated side effects in patients who may have prolonged methotrexate exposure caused by piperacillin/tazobactam co-administration.

We examined 36 patients over two years who received methotrexate for GVHD prophylaxis, comparing patients who received cephalosporins with those receiving piperacillin/tazobactam. The cephalosporin group included 23 patients (14 females, 9 males), from July 1, 2005 to June 30, 2006. Average time to engraftment (the first of three consecutive days with ANC > 500) was 18.25 (range 12–22) days for matched unrelated donor (MUD) transplants, 11.9 (9–20) for matched sibling (MS) transplants, and 16.33 (14–19) for mismatched related transplants; overall average for this group was 16.04 days to engraft. The piperacillin/tazobactam group included a total of 13 patients (11 males, 2 females), from July 1, 2006 to June 30, 2007. MUD transplants averaged 20.2 (16–23) days, and MS transplants 17.4 (15–22) overall average was 18.7 days to engraft. Average days antibiotics overlapped methotrexate was 2.17 and 5.46 for cephalosporin and piperacillin/tazobactam groups, respectively. No significant differences in transaminases, bilirubin, and serum creatinine were noted.

In summary, only a difference in time to engraftment was found, with the piperacillin/tazobactam group taking 2.66 days longer. This study is limited by small sample size and potential confounding variables. Mucositis severity could not be compared in this retrospective study, but would be of interest for future studies. Based on this small, retrospective single institution study, we conclude that a major interaction between small doses of methotrexate and piperacillin/tazobactam is not seen.

469 HIGH RATE OF REVACCINATION IN ALLOGENEIC AND EARLY AUTOLOGOUS STEM CELL TRANSPLANTATION — RESULTS OF A SINGLE CENTER COMPLIANCE TRACKING SURVEY

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Background: Hematopoietic stem cell transplants (HSCT) have increased over the past 25 years. With improving HSCT outcomes, the number of long-term survivors has grown. HSCT recipients lose their memory immune response against common vaccine-preventable infections and suffer from life-threatening late infectious complications. Revaccination is an important strategy for reducing the risk of preventable infections after HSCT.

Materials and Methods: After the implementation of an annual post transplant clinic, compliance with revaccination recommendations of the Infectious Disease Working Party of the EBMT (BMT 2005) was analyzed. Initially letters were sent to patients greater than 1 year post transplant inviting them to visit the clinic. The goal of the annual clinic was to educate HSCT recipients, identify complications, and recommend therapy for long-term post-transplant issues. Patients were encouraged to bring their immunization records to their appointments. Data were collected from January 2006 until August 2007 utilizing patient histories and computer data base documentation tools for the clinic. Schedules were generated based on the recommendations of the Infectious Diseases Working Party of the EBMT.

Results: 42 subjects, 27 autologous and 15 allogeneic, attended annual clinic during this time period. 27 patients had initiated the recommended vaccination schedule and/or elected to start or continue the re-immunization schedule after attending the clinic. Fifteen patients declined vaccinations (11 autos and 4 allos) for various reasons including time out from transplant (median 10 years), 1 completed recommended series, 1 due to immunosuppressive therapy, and 1 with history of adverse reaction to vaccine excipients. Patients declining full revaccination were encouraged to maintain standard revaccinations such as yearly influenza shots and ten year diphtheria/tetanus boosters. There were no toxicities associated with revaccination.

Conclusion: Education and
implementation of post HSCT revaccination was well received by patients. A high proportion of allogeneic and early autologous HSCT recipients successfully underwent revaccination.

**470 SUCCESSFUL TECHNOLOGICAL IMPLEMENTATION AT AN INNER CITY MEDICAL CENTER**

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Computerized order entry offers the potential of reduced medical errors arising from prescribing or administration. Our medical center has recently rolled out a new computerized system. This system does not provide chemotherapy specific ordering. The Pediatric HSCT program at University of Miami/Jackson Holtz Children's Hospital has been utilizing a dedicated chemotherapy specific commercially available system for outpatient chemotherapy prescribing for the last four years. This system is one of the few computerized systems available specifically for chemotherapy. We have recently implemented computerized order entry for inpatient HSCT. Standardized order templates for chemotherapy (TBICY, BUCY, CampFluMel, etc) were created in an attempt to diminish prescribing and administration errors. The protocols were flagged for high alert medications (ganciclovir, neupogen, ATGAM) in an attempt to diminish administration errors (protocol violations). A nursing flowsheet and extensive nursing in-service was implemented simultaneously. Since implementation in the inpatient setting we have observed significantly fewer deviations. Novel technologies have the potential to diminish medical errors and improve overall patient care.

**PHARMACY ORAL**

**471 AN APREPIVANT CONTAINING REGIMEN CONTROLS THE DELAYED NAUSEA AND VOMITING ASSOCIATED WITH HIGH-DOSE MELPHALAN FOLLOWED BY AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION IN PATIENTS WITH MULTIPLE MYELOGMA**

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**Background:** Aprepitant is approved for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic chemotherapy. It has not, however, been studied in patients receiving high-dose melphalan prior to an autologous peripheral blood stem cell transplantation (PBSCT). The principal objective was to determine the ability of an aprepitant containing regimen to prevent delayed vomiting 24–120 hours after the administration of high-dose melphalan followed by an autologous PBSCT in patients with multiple myeloma (MM). **Methods:** The study period was from days +1 through +3. Eligibility criteria included age ≥ 18 years, diagnosis of MM undergoing an autologous PBSCT utilizing melphalan as the preparative regimen and serum aminotransferases and t. bilirubin <2 x upper limit of normal. Twenty-five patients received a melphalan dose of 200 mg/M² and one received 140 mg/M² on day -1. Treatment consisted of aprepitant 125 mg orally d -1 followed by 80 mg orally for 2 days (days 0 and +1); ondansetron 16 mg orally d -1: dexamethasone 12 mg orally d -1 followed by 8 mg daily orally for 5 days (days 0 to +3) with breakthrough medications as needed. Patients were evaluated for the frequency of emetic episodes, the need for break-through antiemetic medication and the mean nausea score in 24-hour increments beginning 24 hours after treatment and continuing until 120 hours. The nausea score was determined using a linear analog scale (0–10). A complete response was defined as no more than one emetic episode during the evaluation period. **Results:** A total of 26 patients (17 male, 9 female) were enrolled in the study. Of these patients, 25 (96%) were complete responders and 24 (92%) had no documented emetic episodes during the study period. One patient (4%) had 1 emetic episode and 1 patient (4%) had 2 emetic episodes. Some degree of nausea was reported by 23 of 26 patients and the mean nausea score for the entire group over the study period was 0.7 (range 0–10). All but 3 patients required some breakthrough antiemetic therapy, primarily with promethazine. When compared with historical results, the aprepitant containing regimen provided better control than palonosetron alone, ondansetron alone or ondansetron/dexamethasone. **Conclusion:** This aprepitant containing regimen appeared to control the delayed nausea/vomiting associated with high-dose melphalan in the PBSCT setting and has now become the standard of practice in this group at our institution.

**472 PRE-TRANSPLANT BUSULFAN TEST DOSE IS A RELIABLE ALTERNATIVE TO FIRST BUSULFAN IV DOSE FOR PHARMACOKINETICS STUDIES IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION**


In this study we tested the efficacy of a test dose of IV busulfan in targeting blood levels of this drug during the conditioning regimen prior to an allogeneic hematopoietic stem cell transplant. We analyzed blood samples of 23 patients undergoing allogeneic hematopoietic stem cell transplantation with a busulfan-based conditioning regimen. Patients received a test dose of busulfan at 0.8 mg/kg as a 60 minute intravenous infusion. Serial blood samples were drawn at eight time points— from 15 minutes before dose to 6 hours after dose completion. Pharmacokinetics (PK) studies were then performed at the Seattle Cancer Care pharmacokinetics laboratory. The conditioning dose of busulfan was calculated by multiplying the test dose in mg/AUC × 4800. After the first conditioning dose of busulfan was administered, the same procedure was repeated to test busulfan PK. If the busulfan AUC was therapeutic (between 4800 μM×min and 5200 μM×min) then the same dose was continued, otherwise the third and fourth doses of busulfan were adjusted proportionally.

The test dose of 0.8 mg/kg intravenous did not have any hematological side effects. The mean historic dose (solely based on weight) was 3.2 ± 0.1 mg/kg and the mean dose based on the test dose was 3.5 ± 0.5 mg/kg (p = 0.02). In 17 patients we also analyzed PK after the first day of conditioning regimen. AUC values of busulfan calculated from test dose and from day 1 dose were not different (p = 0.15). The mean dose of busulfan based on test dose was 3.5 ± 0.5 mg/kg while the final dose based on day 1 busulfan PK was 3.6 ± 0.7 mg/kg (p = 0.9). Two CML patients who were on dasatinib and nilotinib had unusually high AUCs of 6065 and 5920 μM×min respectively suggesting a possible drug interaction between busulfan and tyrosine kinase inhibitors. Our study suggests that pre-transplant busulfan test dose reliably predicts the actual conditioning dose and can be safely utilized to target desirable AUC.

Test dose of busulfan can be conveniently performed anytime before transplant and therefore can safely replace the first dose PK at centers where quick busulfan assay cannot be performed.

**473 RABBIT ATG (THYMOSOLUBIN R) PHARMACOKINETICS IN PEDIATRIC PATIENTS RECEIVING A MATCHED UNRELATED DONOR BONE MARROW TRANSPLANTATION**


**Objective:** The pharmacokinetics of active and total rabbit ATG (rATG) were determined in children with hematologic malignancies receiving a matched unrelated donor (MUD) bone marrow transplantation (BMT). **Methods:** 13 pediatric patients (n = 13) undergoing MUD HSCT with a non-T-cell depleted graft received a conditioning regimen of 12 Gy TBI, thiopeta (5 mg/kg q12h × 2 doses day-4) and cyclophosphamide (60 mg/kg × 2 days -3, -2). GVHD prophylaxis consisted of cyclosporine and methotrexate.