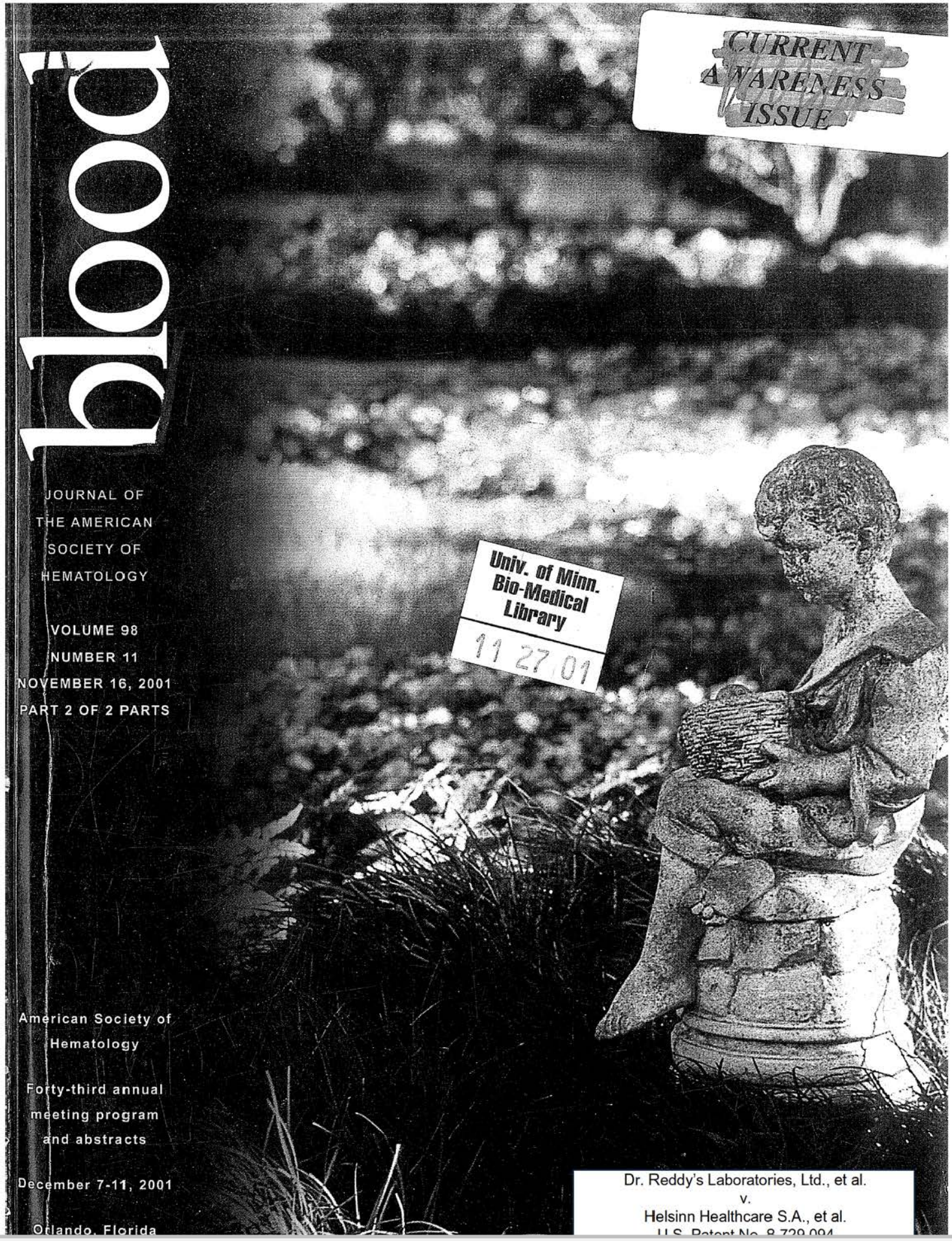

Abstract# 5167

Outcomes of Stem Cell Transplant Recipients Requiring Mechanical Ventilation and Cared for in the Bone Marrow Transplant Unit. Omanlyi Omotoso*, Hanna Khoury, Doug Adkins, William Blum, Manuel Iregui*, Peter Westervelt, Ravi Vij, Randy Brown, Lawrence Goodnough, John DiPersio. *Bone Marrow Transplantation and Leukemia, Washington University School of Medicine, St. Louis, MO, USA.*

The outcome of stem cell transplant (SCT) recipients admitted to the medical intensive care unit (MICU) has been well documented with reported survival rates of 10-18% (Ann Int Med 1996; 125:625). We sought to determine, in a single centre, the outcomes of SCT recipients requiring intubation and mechanical ventilation and who were nursed in designated ICU rooms within the BMT unit. Between May 1996 and March 2001, 1,269 patients received SCT at Washington University in St-Louis, and 59 (4.6%) required intubation and mechanical ventilation. Patients characteristics were as follows: median age was 46 years (range, 19-66); diagnoses included acute and chronic leukemias (n=25, 42%) and non-leukemic malignancies (n=34, 58%). Twenty patients (34%) received autologous SCT, while 21 (36%) received allogeneic SCT from a matched sibling donor and 18 (30%) from a matched unrelated donor. TBI was included in the conditioning in 68% (n=40). Median time from SCT to intubation was 19 days (range, 0 -1351), and median duration of intubation was 5 days (range, 1-38 days). Infectious complications (sepsis, pneumonia) were the most common indications for intubation (94%). Kaplan-Meier estimates for survival 1 month, 3 months and 1 year post-intubation were 25%, 24% and 21%, respectively. Variables associated with poor outcomes were analyzed. The presence of hyperbilirubinemia (serum bilirubin >3mg/dl) or renal dysfunction (creatinine >2 mg/dl) 24 hours prior to intubation, or an APACHE III score > 75 determined 24 hours post-intubation were associated with a 0% extubation rate and survival. Only 1/18 unrelated donor transplant recipient survived. In summary, our results show that the management of SCT recipients requiring intubation and mechanical ventilation is feasible in the BMT unit and is associated with a similar survival to patients transferred to the MICU. Nursing these patients in the BMT unit offers family members uninterrupted access to the patient, comparable outcomes to those observed in the MICU and continuous accessibility to BMT trained health care personnel.

Abstract# 5168

Pediatric Hematopoetic Stem Cell Transplantation (HSCT) in the Chilean Public Health System: Initial Experience. J. Palma*, C. Mosso*, M. Campbell*, C. Salgado*, L. Vargas*, A. Becker*, P. Advis*, J. Quintana*, H. Garcia*, V. Beresi*. (Intr. by Gaston K. Rivera) *PINDA (Programa Infantil Nacional de Drogas Antineoplasicas) and Hospital Luis Calvo Mackenna, Santiago, Chile.*

The national pediatric oncology cooperative group in Chile, PINDA, was founded 14 years ago. Initially, HSCT was not available to patients locally. With combined efforts from PINDA and St. Jude Children's Research Hospital in Memphis, TN, USA, in October 1999 a transplant unit was opened at Hospital Luis Calvo Mackenna, a public pediatric center with affiliation to the University of Chile. Eligible for transplantation, at no cost to their families, were all children treated at PINDA institutions. We report results for the initial 21 HSCT procedures performed: 18 allogeneic (17 matched-sibling and one haplotype-matched parent), and 3 autologous. Median age at the time of HSCT was 6 years (0.5-17 years). Diagnoses included CML (n=2), AML CR 1, 2 (n=4), ALL CR 1, 2, 3 (n=4), Hodgkin (n=1), neuroblastoma IV (n=1), severe aplastic anemia (n=6), Kostman syndrome (n=1), and SCID (n=1). Chemotherapy was given as preparative regimen in 9 allogeneic and 2 autologous HSCT; chemotherapy and total body irradiation in 5 and with total nodal irradiation in an additional 5 cases. The median CD34 cell count was 2.64 x 10^6/kg (range, 1.31 to 7.2x10^6/kg) when marrow cells were infused and 5.68 x 10^6 (range, 3.26 to 9.09x10^6) when peripheral blood cells were used. Heparin prophylaxis for venoclusive disease (VOD) was given to all patients from day -7 to +21 and cyclosporine was administered to patients who received allogeneic HSCT. Neutrophil counts were recovered at a median time of 19.3 days (range, 9-34), platelets 19 days (range, 12-42) and reticulocyte counts were >1% at 17.4 days (range, 11-34). Only 4 children had documented bacteremia, 3 developed grade III-IV graft vs. host disease, and no patient had VOD or required mechanical ventilation. There were no transplant related deaths. One patient died following disease relapse. All other patients are clinically well. Fifteen of 15 patients showed donor engraftment as indicated by molecular testing. Costs with up to 2 years of follow-up were $20,000 for autologous and $40,000 for allogeneic cases. The ongoing results show acceptable rates of morbidity and mortality and an encouraging outcome. Since these results are comparable to those obtained at international centers, we demonstrate that HSCT can be successfully performed, and at reduced costs, within the public health system of developing nations.

Abstract# 5169

An Interesting 5-HT_3 Receptor Antagonist Antiemetic for Patients Undergoing Chemotherapy-Based Conditioning Regimens? Gaia Piraccini*,[1] Randall Stolz*,[2] Munetetsu Tei*,[3] Steve Chernoff*,[4] (Intr. by John C. Byrd) *[1]Helsinn Healthcare SA, Lugano, Switzerland; [2]GFI Pharmaceutical Services, Evansville, IN, USA; [3]School of Medicine, University of Tokyo, Tokyo, Japan; [4]US Micron, Lenexa, KS, USA.*

Palonosetron is a potent, highly selective 5-HT_3 receptor antagonist with a strong binding affinity, long half-life and a low incidence of side effects. It does not exist as a racemic mixture as do other 5-HT_3 antagonists but rather as a single stereoisomer. Five Phase I studies evaluated the pharmacokinetic and metabolic profile of palonosetron. Two studies used the IV formulation with dose ranges of 0.3-90 mcg/kg, while two studies used the oral formulation with dose ranges of 3-90 mcg/kg. The fifth study used [^{14}C]-palonosetron to 50% of the drug with 40% found unchanged in the urine. The most interesting characteristic however, is the long half-life. The elimination half-life is about 40 hours, which is longer than any other available 5-HT_3 receptor antagonist (range 5.5-9 hours). There were no unexpected treatment emergent adverse events, nor were there any serious adverse events seen in the 173 subjects evaluated for safety. The most common adverse events were headache and constipation (6% and 11% respectively over the placebo rate), generally mild to moderate. Adverse events were not dose related. The strong binding affinity coupled with the chemical characteristics of the molecule may explain its high potency. Similarly, since a long duration of action may result from the long half-life and strong binding affinity, a Phase II dose ranging study was initiated. The study was designed to evaluate approximately 150 patients receiving highly emetogenic chemotherapy. Patients were assigned to one of five (5) dose groups of IV palonosetron while undergoing highly emetogenic chemotherapy including cyclophosphamide. Patients were evaluated for efficacy including duration of action, safety and pharmacokinetics for prevention of both acute emesis as well as emesis occurring on days 2-7. The encouraging pharmacokinetic results from five Phase I trials of palonosetron provided a basis to design the previously described Phase II dose ranging trial. This trial would evaluate the potential benefit of palonosetron for the prevention of nausea and vomiting in patients, including those receiving multi-day stem cell transplantation conditioning regimens.

Abstract# 5170

Effect of Bowel Preparation in Patients Undergoing HDSCT in a Community Hospital Setting. Anastasios Raptis,[1] Oscar Ballester,[2] Bradford Tan*,[1] Patti Wilcox*,[1] James Grutsch*,[1] Brian Braun*.[1] *[1]Bone Marrow Transplant Program, Midwestern Regional Medical Center, Zion, IL, USA; [2]Bone Marrow Transplant Program, Albany Medical Center, Albany, NY, USA.*

Infection is an important complication of patients undergoing high dose chemotherapy and stem cell transplantation (HDSCT), contributing significantly to the morbidity and mortality associated with the procedure. In an effort to reduce the prevalence of developing bacterial infection in this group of patients, physicians at MRMC-CTCA developed a protocol using the product GoLYTELY®(GT) to prepare the patient's bowel prior to stem cell transplantation. We evaluated the hypothesis that the GT treatment reduced the prevalence of positive bacterial cultures. At MRMC-CTCA 141 patients underwent HDSCT between September of 1994 and December of 2000. Forty-four patients received one gallon of GT once, one day prior to initiation of high dose chemotherapy (group A). Ninety-four of the patients received no GT (group B). There was no difference in the age distribution between group A and group B, 48 and 50.2 respectively (Median test two tailed p = 0.37).Patients with the following diagnoses received HDSCT at our institution; breast cancer 73 (51.5%), non-Hodgkin's lymphoma 30 (21%), multiple myeloma 19 (13.7%), and ovarian cancer 12 (8.5%), AML 2 (1.4%), CLL 2 (1.4%), Hodgkin's lymphoma 1 (0.96%), small cell lung cancer 1 (0.71%), and testicular cancer 1 (0.71%). GT treatment was initiated in June of 1999. Prior to the use of GT, the prevalence of positive cultures was 67% (63 positive cultures in 94 patients). Following the use of GT the rate of positive cultures fell to 47.7% in the 44 GT patients (21 positive cultures in 44 patients), a statistically significant difference (2-tail Fisher's Exact Test p = .0396). GT, as expected, had no effect on the prevalence of viral (3.2% vs. 2.3%) and fungal infections (3.2% vs. 2.3%). In these patients 21 had positive gram-negative cultures and sixty-two had positive gram-positive cultures. GT did not significantly reduce the prevalence of gram-negative strains, 17 % to 11.2 % (Fisher's exact test 2 tailed p = 0.455), but there was significant reduction in the prevalence of gram-positive strains from 60.6% to 42.2 % (Fisher's exact 2 tailed p = 0.066). The hospital stay for group A patients was 23 days, while in group B patients it was 19.5 days (Kruskal-Wallis P = 0.077). Clinically, time to leukocyte engraftment was not significantly different between the A and B groups, 13.2 days versus 12.4 days. The median time to platelet engraftment for group A was 15 days and group B was 12 days(Kruskal-Wallis two tailed p= 0.006). Seventeen patients died within one hundred days of stem cell transplantation. We evaluated the effect of GT on survival to one year. There was no survival difference between group A and group B patients (Two tailed Log Rank p = 0.88), where 74% of the group A and 70% of the group B patients achieved one-year survival. Finally, the prevalence of non-prophylactic antibiotic therapy was unaffected by the use of GT and the median time on non-prophylactic antibiotics was identical between the two groups, 13 days. We conclude that the use of GT significantly reduced the incidence of gram-positive bacterial cultures in the study population as compared to those that did not receive GT. In addition, the use of GT is linked to a longer time to platelet engraftment.

Abstract# 5171

The Influence of Amifostine of the Immune-Reconstitution after Conventional- and High-Dose Chemotherapy in Patients with Germ Cell Tumor. Oliver O. Rick*,[1] Joerg J. Beyer*,[2] Stefan S. Serke*,[3] Nimrod N. Schwella*,[3] Wolfgang W. Siegert.[1] *[1]Charite Berlin, Oncology/Hematology, Berlin, Berlin, Germany; [2]Universitaetsklinikum Marburg, Hematology/Oncology, Marburg, Hessen, Germany; [3]Charite Berlin, Hematology/Oncology, Berlin, Berlin, Germany.*

We assessed the influence of amifostine on immune-reconstitution after conventional-dose (CDCT) and high-dose chemotherapy (HDCT) followed by autologous peripheral blood progenitor cell (PBPC) rescue in patients with germ cell tumor (GCT). Fourty patients were treated with one day cycle of 175 mg/qm paclitaxel, 5 g/qm ifosfamide (TI) plus 10 µg/kg/day granulocyte-colony stimulating factor (G-CSF) to mobilize PBPC, followed by 3 cycles of CDCT with 175 mg/qm paclitaxel, 6 g/qm ifosfamide, 100 mg/qm cisplatin (TIP) plus 5 µg/kg/day G-CSF and one course of HDCT with 1,5 g/qm carboplatin, 2.4g/qm etoposide, 450 mg/qm thiotepa (CET) plus PBPC rescue and 5 µg/kg/day G-CSF. All patients were randomized to receive an absolute dose of 500 mg amifostine (group A, n= 20)