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EFFICACY OF PEGFILGRASTIM (PF) FOR NEUTROPHIL RECOVERY AFTER AUTOLOGOUS STEM CELL TRANSPLANT (ASCT)

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Background: Daily filgrastim or sargramostim are commonly used to decrease the time to neutrophil engraftment (NE) after ASCT. Since a single 6 mg dose of PF has been shown to be as effective as daily filgrastim (F) in decreasing the duration of neutropenia after standard chemotherapy, this study explored the effectiveness of a single dose of PF after high dose chemotherapy and ASCT in adults with multiple myeloma (MM) or lymphoma (L). **Methods:** Originally 5 patients (pts) were enrolled in a pilot study to determine the efficacy, safety, and kinetics of PF given on day +5 after stem cell infusion. After efficacy and safety was demonstrated in these patients the standard protocol was changed to use PF on day +3 after ASCT. In total 16 pts have received PF after conditioning with melphalan (200 mg/m2) for MM (n = 6) or Rituxan BEAM (n = 6) or Rituxan-TBI-Cyclophosphamide (n = 4). A retrospective comparison was also made to 60 pts who had received sargramostim(SM) for NE after ASCT in the previous 12 months. **Results:** All pts treated with PF had engraftment of neutrophils and platelets. The median time to NE to ANC > 500 was 8.5 days (range 7–11) and to ANC > 1000 was 9.3 days. Average CD34 cells infused were 4.9×10^6/kg. The median time to platelet engraftment was 11.8 days (range 3–21). There were no adverse events associated with PF. The retrospective analysis of 60 patients treated with SM resulted in median time to NE of 11 days (range 9–14) with a median of 8 days of SM administration (range 6–11). **Conclusions:** A single dose of 6 mg PF administered SQ on days +3 to +5 after ASCT is safe and results in rapid neutrophil engraftment that appears to be at least comparable to daily SM. All patients preferred the single injection. The platelet engraftment time also appeared to be rapid. PF is a reasonable option in pts receiving ASCT.

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DESCRIPTIVE ANALYSIS ON THE ROLE AND OUTCOMES OF PSYCHOLOGICAL EVALUATION AND INTERVENTION IN PATIENTS UNDERGOING STEM CELL TRANSPLANT

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Background: Mental health problems often go undiagnosed and can complicate the management of patients (pts) after stem cell transplantation (SCT). In 2004, we established a clinical service with defined providers who focused on the mental health needs of the SCT patients. Prior to this time pts were referred to available community providers as needs were identified. This descriptive retrospective study evaluates the practical utilization of psychological and psychiatric services in the first year of this program and the role of mental health providers in a large SCT program. **Results:** 172 pts underwent SCT in the 1-year period designated for data analysis. Of these pts, 55 (32%) were referred for psychological services that included evaluation and therapeutic intervention by a clinic psychologist. Of the pts referred for psychological services, the average age was 47 years, with 26 males and 28 females. Twenty-four were Caucasian, 15 were Hispanic, and 1 was African American. Pts were referred for evaluation by SCT physicians, primarily for mood symptoms. These symptoms indicated depression, anxiety, or poor general coping. Other reasons for referral included smoking cessation, prior history of psychiatric illness, family issues, steroid-related mania, cognitive changes, panic disorder, "denial" of illness, and family dysfunction. DSM-IVR diagnoses included major depressive disorder (14), mood disorder related to diagnosis and treatment (13), dual diagnosis, either with nicotine dependence, drug or alcohol dependence with concurrent mood disorder (12), and bipolar type disorder unrelated to medications (7). Diagnosis was deferred for 6 patients. Three patients received adjustment related diagnoses. Twenty-four (40%) pts evaluated by the psychologist were referred for further evaluation for psychiatric medications by a psychiatrist or psychiatric clinical nurse specialist. Thirty-one pts were placed on medications. Pts were followed throughout their pre- and post-transplant course for an average of 6.4 sessions. Referrals for services increased throughout the first year of the program. **Conclusions:** Results of this retrospective study reflect the utilization of psychological services provided in the first year of services. The number of moderate to severe psychiatric diagnoses denotes the importance of the availability of psychological services. The study establishes a need for continued prospective research in this population with a focus on detection and development of useful interventions.

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BACTERIAL CONTAMINATION OF PLATELET CONCENTRATES: INACTIVATE OR SCREEN?

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Background: Platelets (PLTs) are stored under conditions that favor bacterial growth and therefore bacterial contamination is considered a serious problem in transfusion. Most frequent indications for repeated PLT transfusions are neutropenic patients during ablative chemotherapy and the incidence of non-fatal transfusion transmitted sepsis in these patients may be under diagnosed. This study compares efficacy of bacterial screening (BacT/Alert) versus pathogen inactivation (INTERCEPT) of PLT concentrates before transfusion. **Material and Methods:** 7 species of bacteria (*Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus agalactiae*, *Klebsiella pneumoniae*, *Escherichia coli*, *Propionibacterium acnes*, and *Clostridium perfringens*) were inoculated at three different concentration levels (1–10, 10–100, 100–1000 CFU/PLT unit) into double-dose PLTs. After inoculation the units were divided and one of the paired units was treated with INTERCEPT. Samples were taken from both units on day 1, 2, and 5 of storage and inoculated into culture bottles (BacT/Alert) to detect bacteria. PLTs were considered negative if no bacterial growth was detected after 120 hours of culture. **Results:** For untreated PLTs seeded with 100–1000 CFU/unit of bacteria cultures were positive in 86% of units before day 5. Inoculation with 1–10 CFU/unit or 10–100 CFU/unit resulted in negative cultures in 71% and 43% of units by day 5, respectively. All PLTs contaminated with bacteria and treated with INTERCEPT remained negative through day 5 regardless of species, level of contamination, and sampling time. **Conclusions:** Bacterial detection using cultures may fail to detect low levels of bacteria typically associated with platelet contamination at time of collection and processing. Failure to detect bacteria will result in the release of contaminated platelet products with "test negative-to-date" status. In contrast, inactivation of bacteria is capable of preventing release of contaminated platelet components.

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DIAGNOSIS OF CENTRAL VENOUS CATHETER-RELATED THROMBUS BY TRANSESOPHAGEAL ECHOCARDIOGRAPHY

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Thrombus at the tip of central venous catheters is a problem frequently seen in patients receiveing intensive chemotherapy. Because many catheter-related thrombi are asymptomatic, the true incidence of this complication is difficult to assess and is likely underestimated. The major complication of the thrombus is pulmonary embolism. The thrombus incidence observed by TEE in asymptomatic patients is reported 12.5%. Our aim was to assess the frequency of central venous catheter-related thrombus before catheter removal in patients with hematolog-

ical diseases by using TEE and to assess if the D-dimer test can predict the presence of a central venous catheter-related thrombus. We assessed 37 patients with various hematological diseases (18 AML, 8 NHL, 6 ALL, 2 MM, 1 HL, 1 primary amiloidosis, and 1 MDS). Mean age was 37 years. Mean time with catheter was 2.66 months. Fourteen of thirty-seven patients were transplanted. Thrombus was found in 8 of 37 patients (21.6%). Thrombus incidence in transplanted group was 28.57% (4/14). Thirty-four of the patients (91.9) were asymptomatic. No relation was found between thrombus and D-dimer levels (P = .071). The time with catheter was not related with the presence of thrombus also (P = .328). Our findings showed that TEE is a useful method in evaluating the presence of thrombus at the tip of central venous catheters, so it can be useful for the prediction of complications due to thrombus before catheter removal. D-dimer shows tendency to be useful in predicting the presence of a thrombus.

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ATYPICAL MYCOBACTERIUM INFECTIONS IN PEDIATRIC PATIENTS UNDERGOING RELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

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Atypical mycobacterium infections are uncommon in children undergoing HSCT compared to solid organ transplant recipients or HIV patients, though more prevalent than in the general population. Improvements in laboratory diagnostic methods have led to more accurate and timely identification of mycobacterium isolates. Diagnosis of non-tuberculus mycobacterium (NTM) infection in immunocompromised children is difficult due to non-specific, diverse clinical manifestations. We report 3 pediatric patients who underwent related donor HSCT from 2002 to 2005 and developed definite NTM infections in the setting of fever of unknown origin. Patient 3 was transplanted at Fred Hutchinson Cancer Research Center, received donor lymphocyte infusion at CMH and was re-grafted at Washington University Medical Center. CD4 counts were >200/μl at the time of diagnosis. Of note, the CD4 count had just recovered in patient 2 as has been reported in patients with AIDS developing atypical mycobacterium osteomyelitis. All patients were immunosuppressed at the time of NTM diagnosis. Aggresive local treatment such as debridement followed by bone grafting and insertion of appropriately coated antibiotic beads was essential for treatment of NTM osteomyelitis. Patient 3 underwent a second transplant and an alemtuzumab-based reduced intensity conditioning regimen without NTM prophylaxis and did not reactivate infection. Outcomes of NTM disease were all favorable after appropriate antimicrobial therapy. Susceptibility testing of isolates with MIC was very helpful in choosing appropriate outpatient treatment. The combination of newer macrolides, ethambutol, rifabutin, and fluoroquinolones appears to have greater in vivo activity and to provide improved eradication of bacteria compared to single agents. Concomitant surgical debridement and removal of the central venous catheter when indicated was essential. We conclude: (1) NTM infection can cause fever of unknown origin in HSCT patients. (2) NTM infection can be successfully treated in the outpatient clinic with antimicrobials chosen according to susceptibility testing of patient isolates. (3) Local treatment such as catheter removal, excisional biopsy, and surgical debridement are critical and can be performed without delayed wound healing or the necessity of skin grafting in the setting of active skin GVHD. (4) Subsequent second HSCT can be performed without prophylaxis provided that the prior NTM infection has been adequately treated (Table 1).

Table 1. *Patient Characteristics and Outcomes*

Category	Pt. 1	Pt. 2	Pt. 3
Diagnosis	SCID	AML	IPEX
Age at HSCT	6 months	16 years	2 years
Stem Cells and Match	maternal PBSC, 3 of 6	maternal PBSC, 3 of 6	BM, 6 of 6 sister
Preparation	Flu/ATG	Flu/TBI/Melphalan/ ATG	1: Flu/TBI; 2: Campath/Flu/ Melphalan
GVHD prophylaxis/ treatment	TCD	TCD	1: Tacrolimus, MMF; 2: Tacrolimus, steroid
Vital Status	alive	alive	alive
Engraftment	full donor chimerism	full donor chimerism	1: mixed chimerism; 2: mixed chimerism
GVHD	grade II acute	grade II acute	none
A. Mycobacterium site	central line, lung	tibia	subcutaneous
Species	M. chelonae/ abscessus	M. avium complex	M. chelonae/abscessus
Evaluation	blood culture, CT scan, lung biopsy	CT scan, MRI, bone aspiration	CT scan, MRI, excisional biopsy
Onset	+6 months	+39 days	+22 months
Treatment & Outcome	catheter removal, ciprofloxacin, azithromycin, linezolid × 6 wks; resolved	azithromycin, ethambutol, linezolid × 8 months, debridement, bone graft with antibiotic beads	surgical excision; cefoxitin, azithromycin, linezolid × 8 months

Abbreviations: SCID, common gamma chain X-linked severe combined immunodeficiency; AML, acute myelogenous leukemia; IPEX, immune dysregulation, polyendocrinopathy, enteropathy, X-linked; PBSC, peripheral blood stem cells; BM, bone marrow; Flu, fludarabine; ATG, anti-thymocyte globulin; TBI, total body irradiation; TCD, T-cell depletion; MMF, mycophenolate mofetil

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A PHASE I SAFETY, TOLERABILITY, PHARMACOKINETIC, AND PHARMACODYNAMIC ASSESSMENT OF VELAFERMIN IN PATIENTS WITH ACTIVE ORAL MUCOSITIS

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Velafermin (CG53135-05) or recombinant human fibroblast growth factor-20 (rhFGF-20) protein is under investigation for the treatment of active oral mucositis (OM). OM is a commonly occurring side effect of high-dose chemotherapy (HDCT) in patients (pts) undergoing autologous hematopoietic stem cell transplant (AHSCT) and in leukemia pts receiving CT. Pharmacology studies demonstrated that treatment of velafermin to animals with active OM for 2, 3, or 4 consecutive days resulted in a significant reduction in duration of clinically relevant OM compared with animals in the vehicle treated control group. Previous clinical studies showed that velafermin was generally well tolerated as a single dose regimen up to 0.2 mg/kg dose level. The objectives of this Phase I trial are to evaluate the safety, tolerability and pharmacokinetics (PK) of velafermin when administered as three daily doses via intravenous (IV) infusion to pts who develop oral mucositis after receiving HDCT. OM and diarrhea status are evaluated using the World Health Organization (WHO) grading system. Approximately 9–12 pts receiving AHSCT following myeloablative CT or leukemia pts receiving CT, age 18 years and older, are to be enrolled when Grades 1 or 2 OM is observed. Velafermin treatment is initiated within 24 hours after OM is observed. Three pts will be treated at each dose level based on tolerability and recruitment parameters. Pts will receive velafermin at 0.03, 0.1, or 0.2 mg/kg/day for 3 consecutive days. Pt follow-up will be continued for approximately 60 days following infusion of velafermin. The 3 pts in the first cohort receiving 0.03 mg/kg tolerated multiple doses of velafermin well with no complaints or adverse events (AE) during or immediately after infusion. Dose escalation deci-