0.8 mg/kg often failed to achieve our target AUC of 1150–1350. Fifteen AML/MDS patients receiving 0.8 mg/kg had a mean AUC of 1059 (822–1653), with 12 AUCs < 1150. Subsequently, our routine starting dose of IV Bu was changed to 0.9 mg/kg.

Methods: We performed a retrospective review of AML and MDS patients from an IRB approved HIPAA compliant database established for the collection and analysis of Bu PK. Data from two groups of Bu patients treated between 1998 and 2008 were analyzed. Fifty-eight patients were treated with oral Bu (1 mg/kg) and fifty-eight patients were treated with IV Bu (0.9 mg/kg). Bu AUC was determined for the first dose and adjustments were made on subsequent doses to target an AUC of 1150–1350.

Results: Median age for IV and oral Bu patients was 42 (18–68) and 47 (23–67), respectively (p = 0.0049). The mean terminal half-life ($T_{½}$) was 186 minutes (131–253) for IV Bu and 181 minutes (110–305) for oral Bu (p = NS). Mean AUCs were 1115 (777–1569) for IV Bu patients and 1260 (654–2019) for oral Bu (p = 0.0094). Seventeen (29.3%) patients in each group achieved AUCs within our target of 1150–1350. Thirty-four (58.6%) IV Bu patients had AUCs < 1150 compared to twenty (34.5%) oral Bu patients (p = 0.0092). Eight (13.8%) IV Bu patients had AUCs >1350 compared to twenty-one (36.2%) oral Bu patients (p = 0.0053).

Conclusions: While first dose PK analysis showed similar $T_{½}$ for IV and oral Bu, the AUCs achieved with 0.9 mg/kg IV Bu are lower than with 1mg/kg oral Bu dosing. First-dose AUC from recipients of IV Bu had a lower variance than AUC from recipients of oral Bu. Despite changing our starting IV Bu dosing from 0.8 mg/kg to 0.9 mg/kg, the majority of patients still require therapeutic drug monitoring with dose adjustments to obtain our desired target AUC of 1150–1350.

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A RETROSPECTIVE ANALYSIS OF RISK FACTORS THAT INFLUENCE INTRAVENOUS BUSULFAN KINETICS IN ADULT PATIENTS

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Busulfan (Bu) is a bifunctional alkylating agent that is a common component of conditioning regimens prior to hematopoetic stem cell transplantation (HSCT). Bu pharmacokinetics, either with area under the curve (AUC) or average concentration at steady state (C_{ss}), can be utilized to evaluate efficacy and prevent adverse effects such as hepatic veno-occlusive disease (VOD). Pharmacokinetic models that predict Bu levels were historically performed with q 6 hour oral dosing in the pediatric population and used a limited linear regression model. Since the advent of intravenous (IV) Bu, a consistent pharmacokinetic modeling system based on specific patient parameters has not emerged. Likewise, current Bu pharmacokinetics models may not be accurate in adult patients or with once-daily dosing schedules. We will report a retrospective study of approximately 300 patients and present a predictive pharmacokinetic model for appropriate AUC with once-daily IV Bu in adult patients. Our model will be based on first dose kinetic analyses. We will also evaluate currently published risk factors that may influence IV Bu kinetic parameters using univariate, multivariate and stepwise Cox regression analyses. Age, race, gender, disease state, disease status at time of transplantation, number of previous chemotherapy regimens, renal and hepatic function at time of transplant and graft source will be evaluated. Long-term outcomes to be examined include overall mortality, probability of survival, development of acute and chronic graft versus host disease (GVHD), development of VOD and days until neutrophil and platelet engraftment. Statistical model design and specific data results will be presented at the 2009 ASBMT Annual Conference.

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AN ANALYSIS OF TOXICITIES AND TIME TO ENGRAFTMENT ASSOCIATED WITH THREE DISTINCT MELPHALAN TREATMENT SCHEMAS IN PATIENTS WITH MULTIPLE MYELOMA RECEIVING AUTOLOGOUS HEMATOPOETIC STEM CELL TRANSPLANTATION

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At MD Anderson Cancer Center, the standard-of-care preparatory regimen in patients with multiple myeloma receiving an autologous stem cell transplant is melphalan 200 mg/m^2 given over two days with one day of rest prior to transplant. The primary objective of this study is to determine if differences exist in the severity of toxicities in patients with multiple myeloma who receive melphalan as a preparatory regimen in three distinct treatment schema. The secondary objective of this study is to ascertain the differences in time to engraftment in this population. Toxicities, defined as nausea, vomiting, diarrhea, renal and hepatic dysfunction, were graded using the NCI-CTCAE. Pain secondary to mucositis was recorded based on the use of patient-controlled analgesia. We performed a retrospective review in patients who received one of the following preparatory regimens: arm 1) melphalan 200 mg/m^2 over days -3 and -2, arm 2) melphalan 200 mg/m^2 over day -2, or arm 3) melphalan 200 mg/m^2 over days -2 and -1. This review included patients over the age of 18 in first remission or with primary refractory disease who received autologous transplantation within 12 months of diagnosis. Patients who received prior transplantation were excluded from this review. 164 patients were identified from the institutional database for data collection and 100 patients were selected at random for this interim analysis. The majority of patients identified were male, <65, ISS stage of I-II, and had an ECOG performance status of 0–1. With respect to the primary endpoint, no statistically significant differences were observed in the severity of toxicity when comparing the treatment schemas (nausea: p = 0.55; vomiting: p = 0.46; diarrhea: 0.52, Kruskal-Wallis test and PCA use secondary to mucositis: p = 0.82, Fisher's exact test). With regard to time to engraftment, the actual difference between the arms was approximately 1 day, yet the comparison between the three groups was statistically significant (p<0.001, log-rank test). We concluded that differences between the three treatment schemas in the severity of toxicities were neither statistically nor clinically significant; the differences in time to engraftment were not clinically significant. Based on the interim analysis, this review demonstrates the potential for melphalan to be administered in any one of three distinct treatment schemas without resulting in adverse effects on toxicity and time to engraftment.

Results

	Arm 1 (N=44)	Arm 2 (N=37)	Arm 3 (N=19)
Grade 3-4 Toxicity	n (%)	n (%)	n (%)
Nausea	2 (4.5%)	1 (2.7%)	0
Vomiting	2 (4.5%)	0	0
Diarrhea	0	2 (5.4%)	0
Serum creatinine	0	0	0
Total bilirubin	0	1 (2.7%)	0
Pain	5 (11.4%)	4 (10.8%)	1 (5.3%)
Time to engraftment (median)	10 days	11 days	10 days

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SUCESSFUL OUTCOME AFTER ACCIDENTAL HIGH DOSE CYTARABINE (HIDAC) INFUSION SEVEN DAYS POST UNRELATED DONOR (UD) CORD BLOOD (CB) STEM CELL TRANSPLATION (SCT)

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Introduction: The complex regimens of allogenic SCT increase the risk of medication errors. We report an accidental HIDAC infusion post UD-CBSCT and the patient outcome.

Case Report: A 24 year old heavily pretreated female with history of relapsed philadelphia (Ph) positive acute lymphoblastic leukemia received a 4/6 matched UD-CBST. The patient received a preparatory regimen of fludarabine 30 mg/m2 on days -7 to -3, melphalan 70 mg/m2 on day -3 and -2, and antithymocyte immunoglobulin 10mg/kg on days -4 and -2. Graft versus host disease (gvhd) prophylaxis consisted of tacrolimus (level 5 -15 ng/ml) and mycophenolate