effects included nausea, vomiting, diarrhea, dizziness and lightheadedness following doses 1 and 2. The patient underwent AuSCT and achieved neutrophil engraftment on day +13 and platelet engraftment on day +20.
Observations: Peak concentrations were proportional to dose. AUC increased over the 3 days suggesting accumulation. Estimated clearance on HD was 3-3.7 fold higher than clearance off HD. Cl/F and V/F after dose 1 was comparable to published values while T1/2 is longer. Maximum 40mg dose was effective and tolerated. Plerixafor and filgrastim stimulated mobilization of HSC in the actively dialyzed patient is feasible, well tolerated and results in adequate numbers of functional cells for use in AuSCT.

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LONG TERM ENGRAFTMENT IS ASSOCIATED WITH SURVIVAL AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN MULTIPLE MYELOMA

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The correlation with long term engraftment on outcomes after autologous transplantation is largely unknown. We conducted a retrospective analysis of 214 patients who underwent auto-SCT for multiple myeloma from 1990 – 2009 and correlated long term engraftment of PBSC autografts (median CD34 dose 4.49; range 1.77-81.96) with outcomes. Patients who received maintenance therapy were not included in this analysis, and patients who relapsed prior to assessment of engraftment were also excluded. Optimal engraftment was defined by NCI CTCAE grade 1 criteria for cytopenias (ANC $\geq$ 1,500/mm^3, platelets $\geq$ 75,000/mm^3, and hemoglobin $\geq$ 10g/dL). The median age was 57 (range 31-76), and the median follow-up was 2.9 years. At day 100, 40% of patients achieved optimal engraftment, and 34% of patients had maintained these optimal engraftment levels at 1 year. There were no significant differences in gender, age, number of prior therapies, myelotoxic therapies (melphalan, lenalidomide, or radiation), and CD34 dose between patients with optimal vs sub-optimal engraftment. Cytogenetics and ISS stage from diagnosis were not available in the majority of patients. Performance status (KPS <90%) was associated with poor engraftment at day 100 but not 1 year.

Engraftment at day 100 was not associated with outcome. However, patients with optimal engraftment at 1 year were observed to have improved 3 year overall survival (89% vs 69%, p = 0.05) but not progression free survival (61% vs 62%). In our series, the majority of patients did not achieve optimal long term engraftment after auto-SCT in myeloma, and there appears to be a correlation of impaired long term engraftment with a deleterious effect on overall survival. Further analysis in larger data sets and other hematologic malignancies to confirm this finding and to identify factors predictive of long term engraftment is ongoing.

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PHASE IIA, OPEN-LABEL, RANDOMIZED, PHARMACOKINETIC COMPARATIVE, CROSS-OVER STUDY OF MELPHALAN HCL FOR INJECTION (PROPYLENE GLYCOL-FREE) AND ALKERAN FOR INJECTION FOR MYELOABLATIVE CONDITIONING IN MULTIPLE MYELOMA PATIENTS UNDERGOING AUTOLOGOUS TRANSPLANTATION

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Background: Though high-dose melphalan and autologous transplantation is a standard procedure in transplant eligible multiple myeloma patients. The marketed formulation of melphalan, Alkeran for Injection (Alkeran), has marginal solubility and limited chemical stability upon reconstitution. Alkeran uses propylene glycol as a co-solvent, which has been reported to cause complications including renal dysfunction and arrhythmias. Propylene Glycol-Free Melphalan HCL for Injection (PG-free Melphalan) is a reformulation of Alkeran. It incorporates Captisol®, a specially modified cyclodextrin, to replace the co-solvents and improve stability. This abstract summarizes the ultimate findings from this study after enrollment of all planned patients.
Methods: This is a phase IIa, open-label, randomized, cross-over design bioequivalence study. In this study, both the compartmental and non-compartmental pharmacokinetics (PK) of PG-free Melphalan and Alkeran were assessed in the same MM patients undergoing transplantation. Patients received both drug products in alternating dosing day fashion and were their own control for PK comparison. Furthermore, the safety and tolerability of high-dose melphalan HCL and rates of myeloablation and subsequent engraftment were determined in all patients.
Results: 24 patients, 11 females and 13 males, were enrolled between 2/4/2010 and 05/16/2011 at The University of Kansas Medical Center and Cancer Center. All patients achieved myeloablation followed by successful engraftment. Median time to myeloablation was 6 days post the start of preparative regimen (range 3-8 days). Median time to neutrophil engraftment was day +9.5 post transplant (range: 9-12). No additional toxicities were reported with PG-free Melphalan. The following events occurred more frequently ($\geq$2 difference) when Alkeran was given first (edema, headache, dysguesia, rash, bundle branch block,) and the following events occurred more frequently ($\geq$2 difference) when PG-free Melphalan was given first (dizziness). PK analysis showed PG-free Melphalan was bioequivalent with Alkeran and also revealed that Cmax and AUC were somewhat higher after PG-free Melphalan.
Conclusions: PG-free Melphalan resulted in successful myeloablation and subsequent engraftment with no immediate infusion-related toxicity and no additional overall transplant-related toxicity. PG-free Melphalan was bioequivalent to Alkeran while also demonstrating a marginally higher systemic drug exposure.

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AN INNOVATIVE APPROACH TO AUTOLOGOUS STEM CELL COLLECTION IN THE PEDIATRIC PATIENT

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Autologous stem cell collection in the pediatric patient can be a challenging and expensive endeavor. Our institution has created a novel, systematic procedure that has created a safe and efficient collection. Using outpatient Interventional Radiology, we place two turbo flow PICC lines with imaging –guided percutaneous technique centrally in patients that are greater than 30 kg. In patients under 30 kg, we are able to use double lumen broviacs or a single turbo flow PICC and the existing central line (I.e. single lumen mediport or broviac). Collection then takes place in our outpatient Apheresis Center without sedation of the patient. We have successfully collected more than 54 pediatric patients, with differing diagnoses, using these methods since the end of September 2008. We have had no documented line infections of the temporary PICC lines. This method allows for the pediatric patient to remain an outpatient, with a low morbidity procedure, but optimizing the stem cell collection process.

CLINICAL CELLULAR THERAPY

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THE USE OF BONE MARROW DERIVED MESENCHYMAL STROMAL CELLS FOR TREATMENT OF PATIENTS WITH MULTIPLE SCLEROSIS AND NEURODEGENERATIVE DISORDERS – ACHIEVEMENTS AND FUTURE GOALS

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Future treatment of multiple sclerosis (MS) aims at restoring myelination and neurological functions as well as re-induction of self-tolerance. We studied the role of mesenchymal stromal stem cells (MSC), known to be anti-inflammatory on the one hand and