product, StemEx demonstrates its feasibility as a quality alternative stem cell source for allogeneic HSCT.

GRAFT PROCESSING

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MORE ACCURATE DETERMINATION OF BLOOD VOLUME ALLOWS FOR A HIGH CORRELATION OF PRE-APHERESIS PERIPHERAL BLOOD AND FINAL APHERESIS PRODUCT CD34+ CELL COUNTS

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The final apheresis product CD34+ cell count is used to determine if more apheresis procedures are necessary to collect sufficient hematopoietic stem cells for autologous (auto) peripheral blood stem cell transplantation. Flow cytometric analysis of CD34+ cells can take several hours. A more timely way to predict apheresis product CD34+ cell counts may help determine if further cytokines are necessary or if apheresis catheters can be removed, and improve the efficiency of patient (pt) care. We performed a retrospective review of all pts undergoing auto peripheral blood (PB) stem cell mobilization with G-CSF alone, G-CSF and plerixafor, or with chemotherapy (chemo) followed by G-CSF, from July 2010 through May 2011 who underwent PB stem cell collection on the COBE Spectra cell separator. Linear regression models were used to formulate pt blood volume (BV) based on the pre-apheresis CD34+ cell count per micro liter of blood, the final apheresis product CD34+ cell counts, and the amount of blood processed during the apheresis procedure. This calculated BV is expressed by the formula BV = 82.5(pts weight in Kg) + 793. We then prospectively evaluated the next consecutive pts who underwent stem cell mobilization and apheresis in June and July 2011. Twenty-seven apheresis collections were done on 26 pts. The PB CD34+ cell count/ul was multiplied by 1000 and this product was multiplied by the calculated BV and then divided by the pts weight [(PBCD34+ cell count x 1000) x BV]/Kg to determine the predicted apheresis product CD34+ cell count, which was then compared to the actual apheresis product final CD34+ cell count. On the first day of collection the mean for the predicted product CD34+ cell count was 4.98 x 10^6 +/- 3.1 x 10^6, and the actual apheresis product CD34+ cell count was 4.61 x 10^6 +/- 2.90 x 10^6 (Pearson correlation r value of 0.913 and a p value <0.001). There was no significant difference in the correlation between pts mobilized with G-CSF alone, G-CSF and plerixafor or after chemo and G-CSF. In conclusion, a more accurate determination of pt BV allowed for a high degree of correlation on the first day of PB stem cell collection between the predicted product CD34+ cell count and the actual apheresis product CD34+ cell count. An accurate prediction of the final apheresis product CD34+ cell count may allow for less cytokine use, quicker removal of catheters, and more efficient disposition of patients.

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CXCL12 G801A POLYMORPHISMS DO NOT PREDICT RESPONSE TO MOBILIZATION BY PLERIXAFOR IN NORMAL ALLOGENEIC STEM CELL DONORS

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Several reports suggest that G→A transition at position 801(G801A) in the 3' untranslated region (3'UTR) of CXCL12 in donors mobilized with G-CSF can predict for response to mobilization. It is unknown if this polymorphism impacts mobilization with the CXCR4 antagonist plerixafor. We hypothesized that the AA polymorphism would show increased stem cell mobilization in response to plerixafor.

Methods: A cohort of 55 donors enrolled in a phase I/II clinical trial evaluating IV plerixafor mobilization were evaluated. 21 donors in the phase I portion were mobilized with IV plerixafor at increasing doses (0.08, 0.16, 0.24, 0.32, 0.40, 0.48mg/kg) in a 3+3 design followed by one week wash out then mobilization and apheresis collection with 0.32 mg/kg subcutaneous plerixafor. 34 donors in the phase II portion of the trial were mobilized with 0.32mg/kg plerixafor IV. The G801A polymorphism in the 3'UTR of the CXCL12 gene was analyzed in peripheral blood mononuclear cells isolated from phase I and II donors. Final collected CD34/Kg recipient weight on day 1, CD34/liter apheresis on day 1, and reaching goal collection of >2x10e6 CD34/kg recipient weight were used as the dependent variables in determining mean differences based on genotype and for univariate analysis.

Results: A total of 55 allogeneic donors were mobilized (female/male = 25/30; age range 12 – 67 years, median 50 years). In total 54 were evaluable for genotyping. The frequency of genotypes in the combined cohort of 54 individuals was: GG = 38(69.1%), AG = 14(25.5%), AA = 2(3.6%). There was no detectable difference in the mean number of CD34 cells/L apheresis on day 1 of collection by CXCL12 genotype (p = 0.78, ANOVA, CD34/liter log10 scale). Mean CD34 cells/L apheresis (log10 scale) was: GG = 7.021 (95% CI 6.936, 7.107), AG = 7.028 (95%CI 6.883, 7.172), AA = 6.892 (95%CI 6.524, 7.260). The probability of collecting at least 2x10e6 CD34 cells/Kg recipient weight on day 1 was not affected by CXCL12 genotype (logistic regression, p = 0.74). The proportion of patients with a successful collection on day 1 in each group was: GG = 64.86 (95%CI 47.46, 79.79), AG = 53.85 (95%CI 25.13, 80.78), AA = 50 (95% CI 1.26, 98.74).

Conclusion: These results suggest that unlike what has been reported for normal allogeneic stem cell donors mobilized with G-CSF, plerixafor mobilization yield is not affected by the CXCL12 3'UTR G801A polymorphism.

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RELATIONSHIPS AMONG COMMONLY USED MEASURES OF CORD BLOOD POTENCY, ALDHBR CELL CONTENT, AND COLONY FORMING CELL CONTENT IN CORD BLOOD UNITS PRIOR TO CRYOPRESERVATION: TOWARDS AN IMPROVED METRIC FOR POTENCY OF BANKED CORD BLOOD

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Despite adequate total nucleated cell (TNC) dosing, engraftment delays and failures remain a significant issue for patients undergoing cord blood (CB) transplantation. We have shown before that post-thaw colony forming units (CFU) better predicted engraftment compared to TNC and CD34+. However, the CFU assay is not standardized and results take weeks. Aldehyde dehydrogenase (ALDH), an enzyme expressed in stem and progenitor cells (ALDHbr cells), is detected by a rapid functional, flow-based intracellular assay. In this study, we explored statistical relationships among TNC, mononuclear cell count (MNC), CD34+, ALDHbr cells and CFU in a large cohort of fresh CB units (CBU) prior to cryopreservation. Our ultimate goal is to identify the best parameter(s) to predict potency as defined by successful engraftment.

Methods: Post-processed TNC, MNC, CD34+ and CFU content were routinely enumerated on fresh CBUs donated to the Carolinas Cord Blood Bank for public (n = 5268) or directed use (n = 14) from 9/07-7/09. Aldecount® (Aldagen, Inc) was used to measure ALDHbr content. Statistical relationships were established.

Results: The median TNC, CD34+, MNC, ALDHbr and CFU content were: 11.8x10^8(range, 2.9-55.5x10^8), 3.36 x10^6(range, 0.17-98.2x10^6), 5.5x10^8(range, 1.7-20.0x10^8), 4.3x 10^6(0-36.6x10^6) and 34.0x10^5(range, 0.6-193.3x10^5), respectively. Significant correlations existed among measured parameters (Table 1). By standardizing univariate models, we were able to rank using AIC values. CFU was best predicted by TNC (AIC = 11,501) followed closely by ALDHbr (AIC = 12,012) and, to a lesser degree, MNC (AIC = 12,412) and CD34+ (AIC = 12,612). Multivariate results were similar (data not shown). Ratios of ALDHbr and CD34+ to CFU were 1.36:1 and 1.09:1, respectively, whereas the ratio of TNC to CFU was 332:1.