If PB CD34 was < 10/μL on day 5, plerixafor (0.24 mg/kg sc) was administered in the evening 5 and apheresis was commenced the next day. If daily yield was < 0.5 × $10^6$CD34/kg, plerixafor was added. In Dec 2009, the algorithm was changed to Plerixafor-2. The dosing of G-CSF and plerixafor remained the same, however the thresholds changed to if day 4 PB CD34 < 10 for single or <20/μL for multiple transplants, plerixafor was added. If day 1 yield was <1.5 × $10^6$ CD34/kg, or any subsequent daily yield was < 0.5, plerixafor was added.

In the 3 time periods, Jan-Dec 2008, there were 327 mobilization attempts in 286 patients, Feb-Nov 2009, 228 mobilization attempts in 224 pts, and Dec 2009-June 2010, 101 attempts in 100 pts. Costs of the mobilization and collection included drugs costs (cyclophosphamide, G-CSF, GM-CSF and plerixafor), apheresis and cryopreservation. Supportive care costs of transfusions, antibiotics, hospitalizations, nursing costs and patients personal costs were not included. The details of the results are outlined in the table. Plerixafor-2 shows a statistical improvement PBSC collections, increased number of patients reaching minimum and optimal goals, less days of apheresis and total days of mobilization/collection.

In conclusion, although the earlier identification of ineffective PBSC mobilization and initiation of plerixafor (Plerixafor-2) increases the costs of PBSC mobilization, more patients are able to achieve the minimum and optimal goals of CD34 collection, failure rates, number of days of apheresis and total days of mobilization/collection are lower. It is unclear if upfront mobilization with plerixafor + G-CSF would result in further benefit.

**Table 1. Results of Mobilization and Collection**

| | Baseline 2008 | Plerixafor-1 | Plerixafor-2 | P value |
|---|---|---|---|---|
| **Patients** | 286 | 224 | 100 | |
| **Mobilization Attempts/ Remobilizations** | 327/ 41 (14%) | 228/ 4 (2%) | 101/ 1 (1%) | |
| **CD34 collected - x$10^6$/kg** | | | | |
| Median | 5.34 | 6.04 | 7.72 | <0.001 |
| Range | 0-25.8 | 0.1-28.2 | 1.48-29.3 | |
| Mean | 5.66 | 6.86 | 8.16 | |
| **Collections >4 x$10^6$/kg (%)** | 223 (68%) | 185 (81%) | 93 (92%) | <0.001 |
| **Collections >2x$10^6$/kg(%)** | 261 (80%) | 212 (93%) | 99 (97%) | <0.001 |
| **Mobilization Failures** | 66 (20%) | 16 (7%) | 1 (1%) | <0.001 |
| **Days of Apheresis** | | | | |
| Median | 2 | 3 | 2 | 0.002 |
| Range | 0-11 | 1-12 | 1-9 | |
| Mean | 2.6 | 3.1 | 2.5 | |
| **Total Days of Mobilization/ Collection** | | | | |
| Median | 8 | 8 | 6 | |
| Range | 4-28 | 4-25 | 4-22 | |
| Mean | 9 | 8.9 | 7.2 | <0.001 |
| **Total Cost per patient** | | | | |
| Median | $12 500 | $12 500 | $21 000 | <0.001 |
| Minimum | $3000 | $5000 | $5500 | |
| Maximum | $146 750 | $93 500 | $89 750 | |
| Mean | $17 300 | $21 686 | $20 695 | |
| **Plerixafor Use** | 29 # (9%) | 94 (41%) | 60 (59%) | |
| Days- Median | 5 | 3 | 2 | <0.001 |
| Range | 1-10 | 1-8 | 1-9 | |
| Mean | 5 | 3.3 | 2.6 | |
| **Bone Marrow Harvest*** | 3 | 0 | 0 | |

#All remobilizations were on the compassionate use protocol. Costs were based on current pricing of plerixafor;
*Cost of bone marrow harvest not inclusded in costs per patient.

# GVH/GVL

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### A NOVEL ROLE FOR LYMPHOCYTE EXPRESSION OF THE CYCLIN-DEPENDENT KINASE 5 (Cdk5) IN THE GENERATION OF ALLOGENEIC T CELL RESPONSES AFTER BMT

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Cdk5 is a ubiquitously expressed serine/threonine kinase. Cdk5 and its obligate partners p35 and p39 are required for neuronal development and migration. Activation of the Cdk5/p35 complex is associated with inflammatory disorders, but the contribution of Cdk5 activity to T cell activation has not been explored. Using a mouse BMT model (B6 → B6D2F1), we reveal a critical role for Cdk5 in the induction of GVHD. TCR stimulation leads to a rapid induction of Cdk5/p35 expression and function, and Cdk5 activity is increased in the spleen and intestine of mice with GVHD. To study the role of Cdk5 in T cells, we generated chimeric mice ($Cdk5^{-/-}$C) by reconstituting irradiated B6 mice with hematopoietic progenitors from the liver and spleen of E16.5 $Cdk5^{+/+}$ and $Cdk5^{-/-}$ littermate embryos; germ line deletion of the Cdk5 gene is embryonically lethal. BMT using B6 $Cdk5^{-/-}$C donors and lethally irradiated F1 hosts resulted in a dramatic reduction in mortality (25% vs. 92%) and systemic GVHD ($p < 0.01$) compared to mice receiving B6 $Cdk5^{+/+}$C BMT. Similar findings were seen in GVHD across an isolated MHC-II mismatch, but were less apparent in a MHC class I disparate model, suggesting that Cdk5 was functioning primarily through $CD4^+$ T cells. Mixing studies in the B6→F1 model showed that CDk5 expression in purified T cells (compared to BM) was predominantly responsible for reduced GVHD, and while a survival advantage was maintained in GVL experiments, $Cdk5^{-/-}$C BMT was associated with more leukemic deaths. Functional characterization of $Cdk5^{-/-}$C T cells showed modest reductions in T cell proliferation to host antigens, but no differences in cytokine production or CTL activity. However, donor splenic T cell numbers were markedly reduced on days 7, 10 and 14 after $Cdk5^{-/-}$C BMT ($p < 0.01$), findings that were associated with reductions in day 7 serum IFNg levels. Further studies showed that Cdk5 phosphorylates the actin modulator Coronin 1a on threonine 418. Activated $Cdk5^{-/-}$ T cells lack this post-translational modification, exhibit defective TCR-induced actin polarization and reduced migration towards CCL-19. Co-migration studies using flow cytometry and intravital microscopy revealed significant reductions in homing of $Cdk5^{-/-}$C T cells (CD4 > CD8) to spleen and lymph nodes, but once entered, the migration speed of $Cdk5^{-/-}$ T cells was not altered. Collectively, our data define a novel role for Cdk5 in lymphocyte biology and allogeneic T cell responses after BMT.

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### VALIDATION OF THE NATIONAL INSTITUTES OF HEALTH (NIH) CONSENSUS CRITERIA FOR CHRONIC GVHD (cGVHD) STAGING CORRELATED WITH ESTABLISHED INDICATORS OF DISEASE SEVERITY AND PROGNOSIS

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**Background:** In 2005, the NIH Consensus Project proposed the cGVHD severity score to standardize clinician evaluation and staging of cGVHD. This analysis was conducted to validate NIH scoring variables as adequate determinants of disease severity.

**Methods:** 189 adults were enrolled on the prospective NCI cross-sectional cGVHD natural history study between 2004-2010. Median age was 46 yrs (18–70), median time from transplant was 35 mos