

## Poster Session I

Age, malignancy, and cell dose had no impact on OI. The median values for major leukocytes were; WBC:  $0.7 \times 10^6/\mu\text{l}$ , T cells:  $63/\mu\text{l}$ , NK cells:  $47/\mu\text{l}$ , B cells:  $0/\mu\text{l}$ , CD4+T cells:  $42/\mu\text{l}$ , %CD4+ T cells: 66%. Both the OI+ and OI- group had comparable WBC, CD3+, CD4+ T cells, NK lymphocytes, or DC1, DC2 subsets. Strikingly, 44% of circulating T cells were in cell cycle (KI-67+) and ~10% were entering apoptosis (activated Caspase-3+), regardless of OI status. Only ~16% preserved the CD45RA+/CD62L+ phenotype of the infused graft. We conclude that in lymphopenic UCBT recipients even undetectable viral infections may induce T cell maturation towards effector CD8+ Tc1 cells as soon as 2-3 weeks after UCBT allowing early identification of those at risk for clinical OI (Table 1).

*Differences in Lymphocyte Reconstitution Between Those Who Will Develop Opportunistic Infections (OI) or Not*

Variable	OI+ Median Value	OI- Median Value	P-Value
% CD8+ T cells	39	28	.04
% CCR-5+ T cells	85	56	.005
% CD8+/CD57+/CD28-	6	2.8	.027
<b>Abs</b>			
CD8+/CD57+/CD28-	1.3	0.4	.017
% IFN $\gamma$ + T cells	35.1	12.2	.006
% CD4+/IFN $\gamma$ + T cells	14	10	.017
% CD8+/Perforin+ T cells	48	26	.019
MFI of BCL-2 in T cells	76	54	.036

Absolute values in microliter.

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**FACTORS AFFECTING IMMUNOLOGIC RECOVERY AFTER NONMYELOABLATIVE CONDITIONING**

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**Background/Methods:** We investigated factors affecting immune recovery after nonmyeloablative (NM) conditioning in 94 pts given PBSC from HLA-matched related (MRD, n = 51) or unrelated (URD, n = 43) donors after 2 Gy TBI +/- fludarabine. Postgrafting immunosuppression (IS) consisted of mycophenolate mofetil (MMF), given TID for 40 days followed by a 56 day taper in URD recipients, and BID for 28 days in MRD recipients) and cyclosporin. Univariate and multivariate analyses were performed to determine factors affecting counts of CD4 T cells, naive CD4 T cells, CD8 T cells, B cells, and frequency of CMV-specific CD4 T-helper cells (among CMV seropositive pts or CMV-seronegative pts with CMV-seropositive donors; determined by lymphoproliferation (CMV- $\Delta$ CPM)) on days 30, 80, 180, and 365 after HCT. **Results:** In multivariate analyses, URD recipients had lower counts of CD4 T cells, naive CD4 T cells, CD8 T cells, and CMV- $\Delta$ CPM than MRD on day 30 after HCT. This delay in CMV-specific immune reconstitution was accompanied by increased frequency of CMV-reactivation (and increased use of preemptive antiviral therapy [PET]) among CMV-seropositive pts or CMV-seronegative pts with CMV sero-positive donors given URD grafts (cumulative incidence [CI] 61%) compared with MRD (33%) recipients the first 100 days after HCT. This did not lead to increased CMV disease among URD recipients (1 episode) compared with MRD recipients (1 episode), demonstrating that PET was similarly effective in preventing CMV diseases in both groups. Higher donor age was associated with lower counts of naive CD4 T cells, suggesting that most naive CD4 T cells derived from transplanted naive CD4 T cells rather than through neo-generation. As seen in pts given myeloablative conditioning, CMV-seropositive patients had higher levels of CD8 T cells after HCT. Further, lower levels of T cells and CD34+ cells in the grafts, as well as acute GVHD, impaired immune recovery of naive CD4 T cells and B-cells (Table 1). **Conclusions:** Despite similar NM

conditioning regimens, immunologic recovery was delayed among URD recipients in comparison to MRD recipients, either because of increased/extended postgrafting IS or the greater degrees of antigenic disparities between donors and recipients. This resulted in a higher incidence of CMV-infection and increased use of PET. Other factors associated with immune recovery were donor age, patient CMV-serostatus, number of CD34 and T cells in the graft, as well as acute GVHD (Table 1).

**Table 1. Multivariate Analyses of Factors Affecting Immune Recovery After NM Conditioning\***

Cell Subset	Day After HCT	Factor(s) Associated With Lower Cell Subset Counts
CD4 T-cell	30	URD vs MRD (P = .06)
CD4 T-cell	80	URD vs MRD (P = .003); High donor age** (P = .006)
CD4 T-cell	180 & 365	MRD vs URD (P = .035)
Naive CD4 T-cell	30	URD vs MRD (P < .001); High donor age** (P = .001)
Naive CD4 T-cell	80	Low # of CD34 cells transplanted (P = .006); Grade II-IV acute GVHD (P = .007)
Naive CD4 T-cell	180 & 365	High donor age** (P = .003); Pt CMV seropositive (P = .03)
CD8 T-cell	30	URD vs MRD (P < .001)
CD8 T-cell	80	Pt CMV seronegative (P = .018)
CD8 T-cell	180 & 365	Pt CMV seronegative (P = .06)
B-cell	30	Low no. of CD34 cells transplanted** (P = .022); Low # of T-cells transplanted** (P = .039)
B-cell	80	Low no. of T-cells transplanted** (P = .002); Grade II-IV acute GVHD (P = .08)
B-cell	180 & 365	Grade II-IV acute GVHD (P = .031)
CMV- $\Delta$ CPM $\dagger$	30	URD vs MRD (P = .007)
CMV- $\Delta$ CPM $\dagger$	80	URD vs MRD (P = .008); Low no. of T-cells transplanted** (P = .02)
CMV- $\Delta$ CPM $\dagger$	180 & 365	Low no. of T-cells transplanted** (P = .01)

\*Other factors assessed were pt age, prior chemotherapy or not, day 28 T-cell chimerism, extensive chronic GVHD; \*\*continuous linear variable;  $\dagger$ analyses restricted to CMV seropositive pt or donor.

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**SIGNIFICANCE OF LYMPHOCYTE CONTRIBUTION POST PROCESSING IN CORD BLOOD TRANSPLANTATION**

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In cord blood transplantation, engrafting cell populations include hematopoietic stem/progenitor cells. Naive and antigen-specific T and B cells mediate protective immune responses as well as graft-versus-host reactions. Total Nucleated Cell Dose (TNC) has consistently been shown to correlate with recipient outcome. A major complication, including death, in post transplant recovery is infection. In this preliminary analysis, we attempt to determine the significance of the lymphocyte contribution with regard to infection control post cord blood infusion. The outcomes of 318 single cord blood unit transplants have been evaluated. Recipients were assigned to groups based on the percentage of lymphocytes post processing. The overall mean was 30%. Group 1 consists of recipi-