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x 2 and fludarabine 25 mg/m<sup>2</sup>/d x 5 (FluCy) for NMAT. Methotrexate 5 mg/m<sup>2</sup> on days +1, +3 and +6, mycophenolate mofetil day -1 to +60 and tacrolimus day -1 to off by +180 was the GvHD prophylaxis regimen in 90%. Patient characteristics at NMAT included: male (n = 24), female (n = 16), median (range) age 52 (21-71) yrs, KPS 90-100 (n = 12), KPS 50-80 (n = 28), NHL (n = 12), AML (n = 10), HL (n = 8), MDS (n = 5), ALL (n = 2), MM (n = 2), PLL (n = 1), HLA-matched related donor (n = 14), 7/8 HLA-mismatched related donor (n = 1), HLA-matched unrelated donor (n = 15), HLA-mismatched unrelated donor (n = 9 at 9/10 and n = 1 at 8/10), complete remission (CR, n = 11), no prior CR (n = 12), and relapsed disease (n = 17). Prior transplants included autologous (N = 19) and allogeneic (N = 2). The TRM cumulative incidence at Day +100 and 1-yr post NMAT was 13% (CI 1-25%) and 34% (CI 17-51%) respectively. Overall, TRM deaths were due to infection (n = 8), GvHD (n = 2), regimen-related toxicity (n = 2), hemorrhage (n = 1). OS estimates at Day +100, 1-yr, and 3-yrs post NMAT were 80% (CI 68-92%), 43% (CI 27-58%), and 19% (CI 7-32%) respectively. OS was improved in patients with KPS 90-100 (1 yr OS 58% vs. 36%, p = 0.04) but worse in recipient/donor CMV +/- vs. other combinations (1 yr OS 8% vs. 59%, p = 0.001). PFS at Day +100, 1-yr, and 3-yrs was 65% (CI 50-80%), 25% (CI 12-38%), and 14% (CI 3-25%) respectively. Patients with advanced disease, defined by CIBMTR criteria http://www.cibmtr.org/ReferenceCenter/Slides Reports/SummarySlides/pages/index.aspx, had Day +100 PFS 54% (CI 24-74%) with PFS 21% (CI 6-40%) at both 1-and 2-yrs. FluCy has a low rate of TRM and is curative in about 1/5 of advanced disease patients. Identification of pre-NMAT factors, which predict for long term survival after FluCy may allow for appropriate patient selection for FluCy versus alternative NMAT regimens.

# 380

# BOOSTER INFUSION OF T-CELL DEPLETED, CD34+ ENRICHED, DONOR CELLS RESULTS IN SUSTAINED COUNT RECOVERY FOR PATIENTS WITH POOR GRAFT FUNCTION FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION

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Poor graft function following allogeneic stem cell transplantation (ASCT) is defined by cytopenias in the presence of complete donor engraftment. Infusion of unselected donor hematopoietic stem cells (HSC) can improve cytopenias but may increase graft versus host disease (GVHD). Here we conducted a single institution prospective study to investigate the feasibility of using "booster" infusions of Tcell depleted, CD34+ enriched donor peripheral blood mononuclear cells mobilized using G-CSF +/- plerixafor to improve the blood counts and decrease transfusion requirements in patients with poor graft function following ASCT. Patients age >18 years who were at least 60 days post ASCT with persistent cytopenia (Platelets <20,000/mm<sup>3</sup> or ANC <500,000/mm<sup>3</sup>, transfusion dependent or inadequate response to hematopoietic growth factors > 30 days) with no reversible etiology were included in the study. Only patients with donor chimerism of  $\geq$ 90% were included in the study. To date we have enrolled a total of 6 patients (1 unrelated, 5 related), Age range 25-68 (mean 56.5), Male: Female ratio 1:1. One related donor withdrew consent after enrolling. All 5 patients had platelet counts below 20,000 /mm3 and were platelet transfusion dependent with 1 patient also requiring RBC transfusions. Unrelated donor stem cell were mobilized using standard NMDP guidelines and related using GCSF+Plerixafor (GCSF 10 mcg/Kg SC x 5 days followed by plerixafor 320 mcg/Kg IV four hour prior to mobilization). CD34+ cells were selected from the leukapharesis product using CliniMACS (Miltenyi) and infused to the recipient without conditioning. All products contained >99% CD34+ cells with <0.01% T-cells. A median of 12.5x106 (range 3.1x106 -23.9x106) CD34+ cells per patient were obtained. No donor or recipient toxicity related to the procedure or worsening of GVHD was observed. 4 patients achieved transfusion independence with sustained response in 3 (follow up 7-365 days). Median time to platelet recovery was 26 days (range 14-62). 2 patients died (1 disease relapse, 1 unexplained cause). This study shows the feasibility of administering booster' CD34+ selected cells from donor for poor graft function following ASCT, with minimal toxicity and durable response. A larger study to evaluate efficacy is warranted.

# ALLOGENEIC TRANSPLANTATION IN ADULT ALL: CLINICAL EQUIPOISE IN CANADA

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**Introduction:** Adults with acute lymphoblastic leukemia (ALL) in first complete remission (CR1) may be treated with chemotherapy or allogeneic hematopoietic stem cell transplantation (alloHCT). The MRC/ECOG trial1 demonstrated a survival benefit to standard risk patients with a matched sibling donor (MSD). However, pediatric inspired chemotherapy, reduced intensity conditioning (RIC), and alternative stem cell sources have renewed controversy about the role of alloHCT in CR1. We hypothesized that Canadian physicians who treat adult ALL would demonstrate wide practice variation.

**Methods:** Physician members of the Canadian Blood and Marrow Transplant Group (CBMTG) and hematologists at all universitybased medical centres in Canada were contacted via email with a validated electronic survey in May 2011.

Results: 69 of 173 physicians surveyed responded(40%). The majority of respondents worked at centres that saw fewer than 20 adult ALL patients annually. While there was high agreement with alloBMT in CR1 high risk cytogenetics or induction failure after a single chemotherapy course (91.7% and 87.5%, respectively), only 45.9% and 19.3% felt that age >35 and T cell immunophenotype would be indications for alloHCT in CR1. High WBC (>30 for B-Cell, >100 for T-Cell) was felt to be an indication for alloHCT by 81.2% of respondents. Respondents felt that the presence of minimal residual disease (MRD) was a strong indication for alloHCT (63.8% agree), although most (66.7% agree) did not have access to MRD testing. Most (96%) felt that a well matched unrelated donor was an acceptable alternative to a MSD. There was uncertainty about the role of cord blood as an appropriate cell source (53.2% agree) and the utility of reduced intensity alloHCT (RIC alloHCT) (41% agree). The strongest agreement was on the role of AlloHCT in Philadelphia positive ALL (98% agree).

**Conclusions:** In Canada, there is substantial disagreement about indications for alloHCT in adult ALL in CR1. Respondents felt that alloHCT was particularly helpful in high-risk patients, contradicting the results of the MRC/ECOG study. The t(9;22) was felt to be a strong indication for transplant. Consensus was lacking on the use of cord blood or RIC alloHCT. Although MRD testing was thought to be a useful guide to planning therapy, it was not widely available. Equipoise exists on the role of alloHCT in CR1 in ALL, suggesting further trials in this area are needed.

1 – Goldstone et al, Blood, 2008.

# 382

# SELF COLLECTION OF NASAL SWABS FOR DIAGNOSIS OF RESPIRATORY VIRUSES IN IMMUNOCOMPETENT VOLUNTEERS AND HEMATOPOIETIC STEM CELL TRANSPLANT (HCT) RECIPIENTS

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**Background:** We previously developed a method for self collection of nasal swab samples and demonstrated that self-collected swabs were sensitive (sensitivity 96%) compared with staff-collected nasal washes (sensitivity 88%) for detection of respiratory viruses (RVs) by PCR in 152 collections from immunocompetent volunteers with new upper respiratory infections (URIs). Our self-collection method employed saline spray delivered by a metered spray bottle and a polyurethane foam swab, but many current protocols advocate use of dry respiratory swabs. In the present study, we compare collection of swabs with and without use of saline spray in both immunocompetent volunteers and HCT recipients.

**Methods:** Immunocompetent volunteers with new URI completed a symptom survey and performed self collection in one naris using saline spray and a polyurethane foam swab ("wet"), and in the opposite naris using a swab alone ("dry"). HCT recipients with a documented virologically-positive URI completed a symptom survey and collection procedure within 1 week of initial diagnosis; these subjects were followed weekly as feasible until negative. Swabs

#### Table. Number of virus detections, average PCR C<sub>T</sub> values, and sensitivity of PCR for detection in wet versus dry swab collections

	Negative Swab Pairs N	Virus Detections: Positive Wet & Dry N (Ave. C <sub>T</sub> Value Wet; Dry)	Virus Detections: Positive Wet, Negative Dry N (Ave. C <sub>T</sub> Value)	Virus Detections: Positive Dry, Negative Wet N (Ave. C <sub>T</sub> Value)	% Sensitivity	
					Wet Swabs	Dry Swabs
Immunocompetent Controls (N = 106 collections)						
All virus detections <sup>#</sup>	28	78 (27.1; 27.2)	10 (34.6)	3 (34.3)	97	89
+ Rhinorrhea (n = 83)*	18	65 (26.8; 26.8)	7ª (35.4)	3 <sup>b</sup> (34.3)	96	91
- Rhinorrhea (n = 22)*	9	13 (28.9; 29.4)	3° (32.8)	0	100	81
HCT Patients ( $N = 105$ collections)			( )			
All virus detections#	20	69 (28.2; 28.4)	14 (33.5)	12 (32.8)	87	85
+ Rhinorrhea (n = 66)	9	48 (27.5; 27.8)	8 <sup>d</sup> (32.5)	7 <sup>e</sup> (33.0)	89	87
- Rhinorrhea (n = 39)	11	21 (29.9; 29.7)	6 <sup>f</sup> (35.9)	5 <sup>g</sup> (32.4)	84	81

<sup>#</sup>Total N is greater than number of paired swab collections because of multiple virus detections in some swabs.

\*I survey was blank for rhinorrhea and omitted. Discordant virus detections.

<sup>a</sup>Adenovirus (AdV) x3, parainfluenza (PIV) 3, PIV4, coronavirus (HCoV)/rhinovirus (HRV) co-infection.

<sup>b</sup>HRV x2, bocavirus.

<sup>c</sup>Influenza A, AdV, HCoV.

<sup>d</sup>respiratory syncytial virus (RSV) x2, PIV3 x2, HRV x2, AdV, HCoV.

<sup>e</sup>PIV3, PIV1, HCoV, HRV x4.

<sup>f</sup>RSV, PIV3 x2, HCoV x2, AdV.

<sup>g</sup>RSV x2, HRV x3.

were stored at ambient temperature, and PCR testing was performed for 12 RVs (positive value = threshold cycle  $[C_T] < 40$ ).

**Results:** Samples were collected during 106 URIs in 70 immunocompetent persons; 3 subjects were < 6 yo (parent performed). Counting all positive respiratory virus detections as true positives, sensitivity was 88/91 = 97% for wet swabs and 81/91 = 91% for dry (Table). Among 30 HCT recipients aged > 6 yo, 105 paired samples were collected during 30 URIs (median 3 samples/patient, range 1-9). Sensitivity was 83/95 = 87% for wet swabs and 81/95 =85% for dry. In both populations, discordant results were associated with higher average C<sub>T</sub> values (i.e., lower viral load), and discordance was highest in samples collected from HCT recipients. Dry swabs, in particular, appeared to perform better in subjects with rhinorrhea than without. A subset of 73 immunocompetent subjects rated the self collected swabs simple (96%) and comfortable (88%); no epistaxis occurred with any collection.

**Conclusion:** Our method of foam swab self-collection of nasal secretions is simple, comfortable, and safe among HCT recipients. Discordance between wet and dry swabs increased with lower viral load. Overall, the wet swab appeared to increase sensitivity for respiratory viral detection in both immunocompetent subjects and HCT patients.

### 383

#### ALLOGENEIC STEM CELL TRANSPLANTATION FOR SICKLE CELL ANEMIA (SCA) AT MSKCC: A SINGLE INSTITUTION SERIES

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**Background:** Allogeneic hematopoietic stem cell transplantation (SCT) is the only proven cure for children with sickle cell anemia. SCT is considered for high risk patients with SCA who have an HLA-matched sibling donor.

**Methods:** We reviewed medical records of 13 children (1.4 -19.2 years, 8 females and 5 males) who received allogeneic SCT from matched sibling donors from 1994-2010 for SCA at Memorial Sloan-Kettering Cancer Center (MSKCC).

**Results:** Indications for HSCT were: stroke (n = 3), acute chest syndrome (n = 6), multiple vaso-occlusive crises (n = 10), and allo-immunization (n = 3); nine patients had more than one risk factor. Donors were heterozygous for sickle cell (n = 9) or with normal hemoglobin (n = 4). All patients received marrow grafts while one patient received combined marrow and cord blood grafts. Nine patients received standard cytoreduction with Busulfan/Cyclophosphamide. Three other regimens were used in an attempt to decrease toxicity and improve chimerism. They were Busulfan/Fludarabine (n = 2), Busulfan/Cyclophosphamide/Fludarabine (n = 1) and

Busulfan/Melphalan/Fludarabine (n = 1). GvHD prophylaxis included cyclosporine (CSA) and methotrexate (MTX) (n = 9), tacrolimus and MTX (n = 2), or other (n = 2). All 13 patients engrafted. With a median follow-up of 10.2 years (range 0.9-17.6 years), twelve of 13 patients are alive and well. One patient died of interstitial pneumonitis on day +77 post SCT. No patient developed acute GvHD. Two patients developed de-novo limited chronic GvHD, which resolved. Donor chimerism included 100% (n = 5), 76-97% (n = 5) while two patients recipients of Bu/Cy regimen had 35% and 50% donor cells. Six of 7 evaluable patients showed evidence of splenic function recovery post transplant. Late effects analysis included evaluation of gonadal function revealing 6 of 8 females with ovarian dysfunction.

**Conclusions:** This single institution based SCT series for SCA is consistent with multi-institutional series results, showing a very good outcome following Busulfan based myeloablative regimen. Future directions include the improvement of donor chimerism, and the late effects of treatment including that of gonadal function.

#### 384

#### FAVORABLE OUTCOMES IN ELDERLY AND HIGH-RISK PATIENTS WITH AML AND MDS FOLLOWING T-CELL DEPLETED REDUCED INTENSITY CONDITIONED ALLOGENEIC STEM CELL TRANSPLANTATION

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For patients with high-risk acute myeloid leukemia(AML), myeloablative conditioning(MAC) followed by allogeneic hematopoietic stem cell transplantation(allo-HSCT) offers the best chance of longterm disease free survival.Retrospective analysis comparing reduced intensity conditioning(RIC) and MAC suggest that early OS and PFS rates are comparable where increased relapse rate(RR) is offset by reduced non-relapse mortality(NRM). In AML patients receiving a RIC regimen, very high RR has been observed in patients with poor risk cytogenetics. We analyzed outcomes of 70 consecutive adult patients with AML or MDS(CR1 or CR2 at time of allo-HSCT) who received Fludarabine(150mg/m2), Melphalan(140mg/m2) Alemtuzumab(CAMPATH)(20-100mg)(FMC) RIC regimen.Median age at transplant was 56 yrs(range 17-70).29 had a HLA identical sibling donor and 41 an unrelated donor(29 matched;12 mismatched).Stem cell source was PBSC in 66 and BM in 4 patients.43 patients were in CR1 and 27 were in CR2.Median follow up of live patients was 32 months(range 12-119).OS and PFS at 3 yrs was 55% and 53%.100-day and 3-yr NRM rates were 10% and 24%.3-yr RR was 25% and median time to relapse was 6.2 months (range