Materials and Methods: We retrospectively analyzed all patients (n = 64) from January 1, 2009 to December 31, 2009 at our institution undergoing allogeneic SCT for hematologic malignancies. PLT refractoriness was defined as a clinical requirement for platelet crossmatching. Clinical outcomes studied included day 100 and one year survival, platelet and neutrophil engraftment and acute GVHD incidence. Risks of death and GVHD were compared between groups with logrank tests and were estimated with the Kaplan-Meier method. Number of days to platelet or neutrophil engraftment was compared with the Wilcoxon rank-sum test.

Results: Allogeneic SCT was performed in 64 patients including three pediatric patients. 10/64 (16%) patients demonstrated PLT refractoriness. Patients with PLT refractoriness had higher risk of acute GVHD (Grade I-IV) as compared to non refractory patients (p = 0.046). Excluding patients without platelet engraftment due to early death, patients with pretransplant PLT refractoriness (n = 9) had delayed PLT engraftment, median (IQR) = 27 days (19.5-64.50) compared to non-refractory patients (n = 52), median (IQR) = 19 days (16-23) (p = 0.01). However, there was no significant differences in terms of overall survival, GVHD grade II-IV or time to neutrophil engraftment

Conclusions: PLT refractoriness may be associated with increased incidence of acute GVHD and delayed platelet engraftment resulting in longer platelet transfusion support. A larger study is planned to confirm these findings.

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RADIOTHERAPEUTIC TECHNIQUES IN ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT (HCT)

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Radiotherapy (RT) is used as an antineoplastic and immunomodulatory therapy prior to allogeneic HCT. The practice of incorporating RT as part of HCT varies widely across centers worldwide. The present study explores the use of RT in 14,920 allogeneic HCT recipients (total body irradiation [TBI], N = 14,696, and total lymphoid irradiation [TLI], N = 402) reported to the Center for International Blood and Marrow Transplant Research between 1995 and 2010. TBI was performed in 335 reporting centers in 42 countries. The median age of TBI recipients was 33 years and the median age increased from 31 to 39 years during the period (p<0.0001). TBI was most commonly use in HCT for acute lymphocytic leukemia (87%) and in patients with prior central nervous system (CNS) leukemia involvement (76%, p<0.001). Shielding was used in 52% of patients, commonly for lungs (72%) and eyes (14%). The median dose of TBI was 12 Gy, with most patients receiving 2 fractions per day (60%, p<0.0001), for total of 6 doses (34%, p<0.0001). Myeloablative TBI doses (>8 Gy) decreased from 94% to 63% during the period (p<0.001). Conversely, reduced intensity and non-myeloablative (RI/NMA) TBI doses increased from <1% to 36% (p<0.001). TBI was most frequently combined with cyclophosphamide (97%) in myeloablative regimens and fludarabine (68%) in RI/NMA regimens. 11% of patients who received TBI also received RT within 14 days of starting conditioning; treatment was directed at the CNS (35%) and gonads (41%). TLI was performed in 70 centers in 22 countries. The median age for TLI recipients was 37 years and the median age increased from 29 to 56 years during the period. The most common indications for TLI was severe aplastic anemia (SAA) (23%) and acute myeloid leukemia (AML) (19%). TLI for SAA decreased from 47% to 0% while TLI for AML increased from 11% to 40% during the period. The median TLI dose was 6 Gy, with most patients receiving 6 fractions (41%). 4% of patients who received TLI also received RT within 14 days of starting conditioning; treatment was most often directed at the spleen (47%). RT practices in HCT changed during the past 16 years. There was a significant decrease use of myeloablative TBI and increase in RI/NMA TBI. Similarly, TLI practices changed towards a RI/NMA approach, being applied more frequently in older patients for treatment of malignant diseases.

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PREDICTIVE FACTORS FOR ADVERSE OUTCOMES AFTER USE OF DONOR CELL INFUSION (DCI) IN PATIENTS WITH RELAPSED HEMATOLOGICAL MALIGNANCIES TREATED WITH ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (AlloHCT)

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DCI is administered after AlloHCT to enhance the graft-versus leukemia effect and thereby induce remission in patients (pts) with relapsed hematological malignancies. The purpose of this retrospective study was to identify risk factors for post-DCI progression and mortality.

We identified 47 pts with hematological malignancies who received DCI from 02/1996 to 07/2011 for disease relapse. We analyzed variables such as pts baseline demographics, malignancy type, donor relationship, type of AlloHCT, presence of GVHD, duration of post-transplant remission, use of remission induction chemotherapy prior to DCI and DCI cell dose.

Among pts treated with DCI, 36 (77%) had myeloid malignancies. Myeloablative regimen was used in 36 pts (77%) and 35 pts (74%) had HLA-identical sibling donor transplant. 45 pts (96%) had grade <2 aGVHD and 40 pts (85%) had limited or no cGVHD. Median time of post-transplant relapse was 6.0 months (range, 0.9-84.6) and the median time from transplant to DCI therapy was 7.8 months (range, 2.3- 114). DCI was used once in 89% of pts and it was preceded with chemotherapy in 35 of 45 pts (78%). Median CD34 and TNC doses for the first DCI were $2.0x10^6$ and $3.9x10^8$ respectively. The rate of post-DCI grade 3-4 aGVHD was 2% vs. 17% for extensive cGVHD. With a median follow-up of 40.8 months (range, 2.3-174.1), 38 pts (77%) had died and 29 (62%) relapsed. Relapse was the most common cause of death (n = 25, 69%) after DCI. Although pts who received unrelated DCI tended to have less post-DCI relapses (42% vs. 69%), deaths (50% vs. 86%) or fatal events due to relapse (50% vs. 73%), the numbers were too small to detect statistically significant differences between groups. Recursive partitioning analysis indicated that pts who had disease relapse within 20 months after transplant (n = 39) were at higher risk of post-DCI relapse, worse OS and RFS. Multivariable analysis demonstrated that a bone marrow cell source was associated with poor OS (HR = 2.6; 95% CI 1.3-5.6, p = 0.01) compared to peripheral blood, and that post-transplant disease relapse within 20 months was an adverse predictor for post-DCI relapse (HR = 5.2; 95% CI 1.2-22.3, p = 0.025), OS (HR = 5.5; 95% CI 1.6-18.5, p = 0.006) and RFS (HR = 3.5; 95% CI 1.2-9.9, p = 0.02).

With long follow-up we demonstrated that disease relapse within 20 months of AlloHCT portends poor clinical outcome despite DCI, but for patients with longer remission duration, DCI can result in long-term progression free survival.

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ALLOGENEIC STEM CELL TRANSPLANTATION (SCT) IN ADULT ALL PATIENTS IN CR1: RESULTS OF UNRELATED DONORS ARE COMPARABLE TO SIBLING DONORS?

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In the German Multicenter ALL Studies, patients (pts) with Ph+ ALL (very high risk, VHR), with high risk ALL (HR), e.g. B lineage

ALL with leukocytes >30/nl at diagnosis and/or delayed CR (>4 weeks), pro B-ALL or complex karyotype, T lineage ALL (prae T-ALL, mature T-ALL) and standard risk ALL (SR-ALL) with molecular persistence or relapse are candidates for SCT in CR1. Pts with siblings have a 25% probability (prob) of an HLA identical sibling. Pts without an HLA identical sibling have a chance of 80% to find a compatible unrelated donor.

Here, we report our single centre data on SCT from sibling and unrelated donors. High resolution HLA typing class I+II was done since 01/2006. Between 2006 and 2010, 36 pts with ALL, CR1 underwent SCT. 12 pts had a sibling donor, 14 pts an HLA identical unrelated donor (MUD) and 10 pts an HLA compatible unrelated donor (MMUD). All HLA mismatches were in class I, 9/10 pairs had 1 mismatch (HLA-C antigen 4, HLA-A antigen 3, HLA-B allele 2) and 1/10 pairs had 2 mismatches (HLA-C antigen and HLA-B allele). Median age was 43 (18-67) years (yrs), not different between sibling or unrelated SCT. Indication for SCT: 14/36 pts belonged to the VHR group, 19/36 pts to the HR group and 3/36 pts of the SR group had molecular relapse. All pts were transplanted in CR1 (bone marrow <5% blasts). Conditioning was myeloablative (MAC) in 30/36 pts (12 Gy TBI and VP 16 or CY 29, other 1) and in 6/36 pts reduced intensity (RIC). Pts with unrelated donors received antithymocyte globuline (ATG) (60mg/kg in MAC, 40mg/kg in RIC).

Results: 25/36 pts are alive in CR (median f/u 40 months, 7-66), 11/36 pts died 8 months (0.5-24) after SCT. Causes of death: leukemia 3, infection ±GvHD 6, other 2. Prob of OS for all pts (36) at 4 yrs is 0.65, 0.82 for SCT with sibling donors, 0.52 for MUD-SCT, 0.56 for MMUD-SCT. The differences were not significant. Prob of LFS is 0.59 for all pts, in pts with sibling donors 0.82, after MUD-SCT 0.49 and 0.44 after MMUD-SCT. Prob of NRM for all pts was 0.26, in sibling SCT 0.18, in MUD-SCT 0.34 and in MMUD-SCT 0.26.

Conclusion: In ALL, CR1 SCT after MAC and with a sibling donor is still the gold standard (OS 0.82). In unrelated donor SCT we found no difference in survival between HLA identical or 1 antigen mismatched donor-recipient pairs. It has to be discussed if dose reduction of ATG in MUD-SCT might improve the results by decreasing NRM and relapse post SCT.

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NONABLATIVE CONDITIONING REGIMEN FOR CD20+ B-CELL LYMPHOID MALIGNANCIES: SHOULD CONDITIONING REGIMENS BE INDIVIDUALIZED TO OPTIMIZE TRANSPLANT OUTCOME?

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Background: Allogeneic stem cell transplantation (allo-SCT) is limited by transplant-related-mortality (TRM), primarily mediated by graft-versus-host disease (GVHD). Disease specific preparative regimens that offer acceptable graft-versus-host disease (GVHD)-associated morbidity and TRM are preferred. The B-cell lymphoma specific nonablative (NST) regimen fludarabine, cyclophosphamide and rituximab (FCR) is reportedly safe and effective, however most reported data are from single institution.

Methods: Twenty six pts with recurrent CD20+ B-cell lymphoid malignancies received FCR NST allo-SCT between March 2008 and May 2011. The conditioning regimen consisted of fludarabine (30 mg/m2 daily for 4 days), cyclophosphamide (750 mg/m2 daily for 3 days) and rituximab (375 mg/m2, day-13,-6,+1,+8). This was followed by either related (n = 18) or unrelated donors (n = 8) allo-SCT. All patients received tacrolimus and mini-methotrexate GVHD prophylaxis (rATG for unrelated donor allo-SCT).

Results: The median age of pts at transplantation was 59 years (range 41-64). Ten pts had CLL, 7 MCL, 3 DLBCL, 3 FL and 3 transformed-lymphoma. At diagnosis, 20 (77%) pts had stage IV disease. Twenty three pts (88%) received ≥3, 14 (54%) ≥4 regimens and 4 (15%) had prior autologous-SCT. Nine (35%) pts were in complete remission pre-SCT following salvage therapy. At the time of analysis, 17 pts were alive with an estimated 2-year OS and PFS of 63%, and non-relapse mortality (NRM) 25%. Grade II-IV aGVHD occurred in 8 (31%) pts and chronic GVHD in 6 (24%) pts (extensive = 3). Causes of death includes progressive disease 4, aGVHD 2 (both after receiving DLI for mixed chimerism with residual disease), infection 1 and others 2 (substance abuse, leucoencephalopathy). Only 6 pts required re-hospitalization within 100 days of SCT, (average 10 days; range, 3-18).

Conclusion: Our data suggests nonablative FCR conditioning regimen is safe and effective in heavily pre-treated B-cell lymphoid malignancies. While our conclusion is limited by the small sample size, this suggests the need for larger prospective studies to validate the efficacy of FCR and to compare it with other reduced-intensity conditioning allo-SCT in B-cell malignancies. We recommend that FCR allo-SCT be considered early and novel strategies (radioimmunotherapy, tandem auto-allo-SCT) be incorporated and evaluated to major cause of failure, particularly in heavily pre-treated pts.

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EBV-POSITIVE LYMPHOPLASMACYTIC LYMPHOMA: A HIGHLY AGGRESSIVE POST TRANSPLANT LYMPHOPROLIFERATIVE DISORDER WITH MULTIORGAN INVOLVEMENT

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Post transplant lymphoproliferative disorder (PTLD) is a heterogeneous disease ranging from benign polyclonal proliferation of B cells to monoclonal B cell proliferation. Its cumulative incidence is about 1% with most cases observed during the first year. Most cases are associated with Epstein-Barr virus (EBV) infection. Indolent lymphomas are not considered part of PTLD in the WHO 2008 classification.

Here we describe two cases of EBV related post transplant lymphoplasmacytic lymphoma (LPL) with multiorgan failure and aggressive course. The first patient was an EBV positive 28-year old male with refractory Hodgkin's lymphoma following autologous transplant. The second was an EBV negative 57-year old male with relapsed peripheral T-cell lymphoma, otherwise non-specified. They underwent matched unrelated allogeneic transplant after being conditioned with fludarabine, busulfan and ATG. They received methotrexate and cyclosporine for GVHD prophylaxis. On Day +20 post transplant, the first patient presented with fever, nausea, diarrhea, and bilateral cervical lymphadenopathy. He had pancytopenia, elevated liver enzymes, and acute renal failure. Bone marrow aspirate and biopsy findings were consistent with monomorphic LPL with normal cytogenetics. Biopsies of a cervical lymph node, duodenum and a colonic mass revealed the same histology. Serum protein immunofixation (SPIF) showed biclonal IgG kappa and lambda, IgA kappa and biclonal IgM lambda gammopathy. EBV PCR was $0.597x10^6$ copies/ml. He was treated with immunosuppression tapering, cyclophosphamide and rituximab with no evidence of improvement. The second patient presented with fever on day +35 post transplant. He had cervical, retroperitoneal and inguinal lymphadenopathy, splenomegaly, as well as pancytopenia, elevated liver enzymes and acute renal failure. Bone marrow aspirate and biopsy revealed a monomorphic LPL. SPIF showed biclonal IgG kappa paraprotein with lambda chains. EBV PCR was $1.38x10^6$ copies/ml. He was treated with immunosuppression tapering and rituximab but his condition deteriorated rapidly.

We described two cases of EBV driven post transplant LPL with profound protein abnormalities and multiorgan failure despite indolent morphology. Although indolent lymphomas are not considered part of PTLD, clinicians must be aware of this presentation. Severity of cases and lack of response to treatment should further bring into discussion the role of EBV load regular monitoring in patients at risk.

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SENSITIVE REAL-TIME PCR CHIMERISM ASSAY FOR HSCT MONITORING

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Chimerism testing, or the measurement of the percent of recipient and donor hematopoietic cell origin, is a standard of care for HSCT recipients. For leukemic recipients, the quantification of chimerism