changed between the two time periods. Also, the use of PBSC instead of BMSC increased (P=0.0001). In order to evaluate the relative importance of these factors a multivariate analysis will be performed. **Conclusion:** The pronounced improvement in TRM during recent years seem to be multi factorial however, an improved donor selection strategy is probably the main cause.

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IMPROVEMENT OF MATCHED SIBLING DONOR ENGRAFTMENT WITH SIROLIMUS ADDED TO A NON-MYELOABLATIVE CONDITIONING REGIMEN

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Non-myeloablative regimens extend the benefit of allogeneic hematopoietic transplantation to many otherwise ineligible patients. Anti-tumor effects are however thought not to occur for most patients until full donor chimerism is achieved. We have recently added sirolimus to an established conditioning regimen in an attempt to optimize engraftment and anti-tumor effects while minimizing morbid GVHD. We compare results of two sequential studies conditioning patients with hematological malignancies with cyclophosphamide (days −7 and −6) and fludarabine (days −7 through −3) prior to matched sibling peripheral blood stem cell transplantation. All received tacrolimus and methotrexate immunoprophylaxis. 9 patients were enrolled in the initial study, and 6/9 also received Campath 1H 20 mg IV on day −7 of the regimen. The second study has treated 10 patients with sirolimus added to the immunosuppression and adjusted to 5–15 ng/ml beginning on day −7 (no Campath was given on this study). Tacrolimus has been tapered off in this protocol between days 30–45, but sirolimus has continued. Graft versus host disease occurred prior to day 100 in 5/9 patients on protocol 1 and 2/10 patients on protocol 2. In all cases GVHD was controllable and no patient has died of transplant related causes. In both protocols all patients showed some degree of donor engraftment by RFLP or XY FISH analysis by day 30. Mean fractional peripheral blood donor chimerism values through day 180 are given in the table below. There is no significant interaction between treatment and time (p-value=0.8579), hence the engraftment curves for the two protocols are parallel. Based on a repeated measures analysis using general F-statistics, there is a significant treatment effect, with patients on the second protocol showing an average of 18% higher engraftment (p-value=0.0281). While follow-up is shorter for patients on Protocol 2, 8/10 patients are beyond 180 days from transplant and the other two have both achieved >0.98 fractional donor engraftment. We conclude that our second protocol, using sirolimus with early tapering of tacrolimus, appears to yield more rapid and complete donor chimerism (Table).

Donor Fractional Whole Blood Chimerism

	Day 15	Day 30	Day 100	Day 180
Protocol 1	**0.51**	**0.75**	**0.82**	**0.81**
Protocol 2 with Sirolimus	**0.72**	**0.88**	**0.99**	**1.00**

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IMATINIB ONLY FOR MOLECULAR RELAPSE IS NOT SUFFICIENT TO ACHIEVE A DURABLE COMPLETE CHIMERIC STATUS AND MOLECULAR REMISSION AFTER ALLO HCT IN CML

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Background: Allogeneic hematopoietic cell transplantation (AlloHCT); today, is still the only treatment modality that provides cure for CML. But relapses after AlloHCT are still an ongoing problem. In most of these patients donor lymphocyte infusions (DLI) are effective to achieve molecular remission (MR). Post DLI aplasia and GVHD are the most important reasons of morbidity and mortality in these patients. Imatinib is a tyrosine kinase inhibitor and blocks CML progenitor cell proliferation. The effect of imatinib on relapse after AlloHCT has been investigated in a few studies including patients with chronic and accelerated phase CML. In this study we aimed to analyze the effect of imatinib on post AlloHCT molecular relapse. **Patients and Method:** Imatinib was applied 400 mg/day p.o. at least for six months to 11 patients; transplanted from their HLA identical siblings with molecular relapse. Patients were monitored closely with ATM Multiplex PCR for chimerism and RQ-PCR (LightCycler, Roche Diagnostics) for bcr-abl/G6PDH. **Results:** Eleven of the patients were under imatinib treatment for more than 6 months. Seven of the 11 patients responded to imatinib. At the end of the sixth month except two patients all of them had donor type chimerism. Periorbital edema developed in 4 of the patients, and none of the patients had Gr 3–4 GIS and hematologic side effect. After cessation of the drug five patients had durable MR and complete chimeric (CC) status. Two patients with second molecular relapse and mix chimeric status after imatinib, and four patients with primary imatinib resistance received DLI. After median 12 (6–20) months follow up, imatinib sensitive 5 patients were in continuing MR, imatinib sensitive two patients with second relapse were in MR and CC after DLI. One of the imatinib refractory patients was lost after DLI induced acute GVHD in MR, The remaining patients did not achieve MR. One patient is still receiving DLI, IFN and imatinib. **Conclusion:** Imatinib treatment for molecular relapse after AlloHCT has acceptable adverse event profile and provides over 60% MR rate but this response was not durable as in DLI; 25% of the patients experience second relapse early after cessation of the drug. DLI may achieve MR in 50% of the primary imatinib resistant patients. Concerning the in vitro effect if imatinib on T cell functions there is an urgent need for prospective studies comparing DLI and imatinib ± DLI with close follow up of chimerism.

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CAN WE CONSIDER FLUDARABINE/ FULL DOSE I.V. BUSULFAN A REDUCED INTENSITY CONDITIONING REGIMEN?

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In this study we analyzed 22 patients who received an allogeneic HSCT from matched related (n=17) or unrelated (n=5) donors, and were conditioned with FLU/BU (fludarabine 30 mg/m^2/d × 4 days followed by single dose i.v. busulfan 3.2 mg/kg/d × 4 days) (n=12) or with the FLU/MEL (fludarabine 30 mg/m^2/d × 5 days and melphalan 70 mg/m^2/d × 2 days) (n=10) RIC regimen. Median age was 26 yrs (range: 19–51) in the FLU/BU group and 47 yrs (range: 22–57) in the FLU/MEL group (p=0.02). High risk patients were 8/12 in the FLU/BU group (7 AML in relapse, 1 CML-AP) and 3/10 in the FLU/MEL group (2 resistant NHL and 1 HD). GVHD prophylaxis was FK-506/MTX and in 9/12 FLU/BU cases (including 5 MUD) Thymoglobulin was added. All FLU/MEL and 6/12 FLU/BU patients received PBSC (median nr. CD34$^+$ cells: 5.0 and 5.9 × 10^6/kg, respectively), while 6 FLU/BU received marrow cells (median nr. CD34$^+$ cells: 1.58 × 10^6/kg). Median time to ANC >500 was comparable in PBSC FLU/BU (d14, range: 11–20), and PBSC FLU/MEL (d12, range: 10–15) patients, while it was longer in bone marrow FLU/BU (d 22, range: 17–37) patients (p= 0.01 and p=0.001, respectively). Time to Plt >20K was d 12 (range: 10–16) in the PBSC FLU/MEL group and d 20 (range: 17–37) in the bone marrow FLU/BUS group. Four of 6 PBSC FLU/BU patients did not have severe thrombocytopenia (<20K) after transplant. Mucositis > grade 2 was never observed. Median length of stay in the hospital after transplant was 17 days (range: 13–37) in PBSC FLU/MEL, 23 days (range: 18–42) in PBSC FLU/BU and 30 d (range: 22–38) in bone marrow FLU/BU. Median chimerism levels on d30 after transplant were: 100% in FLU/MEL and 95% (1 rejection) in FLU/BU. Median follow-up for patients currently alive is 254 days (range: 145–628) in the FLU/BU group and 636 days (range: 429–715) in the FLU/MEL group. Acute GVHD grade II-IV was seen in 1 FLU/BU patient after DLI and in 1 FLU/MEL patient. Chronic GVHD is

present in 2/6 FLU/BU and 4/9 FLU/MEL evaluable patients. Six of 12 patients in the FLU/BU died of relapse (n=4) and/or infection (n=2, 1 within d100) and 3 of 10 patients in the FLU/MEL died of relapse. In conclusion, since in allogeneic PBSC transplantation the FLU/BU regimen seems to have a myelotoxicity comparable to FLU/MEL, it could be used in allotransplant for elderly patients and may represent a platform for donor lymphocyte infusions in high risk patients.

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ALEMTUZUMAB IMMUNOTHERAPY PROVIDES EFFECTIVE CYTOREDUCTION PRIOR TO ALLOGENEIC STEM CELL TRANSPLANTATION FOR REFRACTORY LYMPHOPROLIFERATIVE DISORDERS

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Introduction: The optimal cytoreductive therapy for refractory chronic lymphoproliferative disorders prior to allogeneic stem cell transplantation is not well defined. Immunotherapy may represent an alternative cytoreductive strategy in chemotherapy refractory disease. We assessed the role of alemtuzumab (anti-CD52, CAMPATH) immunotherapy in reducing disease bulk pretransplant in a pilot single center clinical protocol. **Patients and Methods:** Patients with CLL and lymphoplasmacytic lymphoma (LPL) refractory to at least two prior lines of chemotherapy, age less than 65 years, and adequate organ function received alemtuzumab monotherapy 30 mg. intravenously thrice weekly for 8–12 weeks. Molecular, hematologic, and radiological responses were measured. Transplantation conditioning consisted of Fludarabine/Melphalan or BEAM. **Results:** Between 10/2002 and 10/2004, 7 patients (6 refractory CLL, 1 refractory LPL) received alemtuzumab cytoreduction and allogeneic stem cell transplantation. All patients had received prior fludarabine or alkylator therapy; 1 had received rituximab. High-risk cytogenetic markers (p53 or Rb1 deletions) were present in 4 of 6 CLL patients, as assessed by FISH. Marrow involvement decreased from a mean of 80% pre-alemtuzumab to 15% post; 3 patients attained complete marrow clearance. Hematologic remission following alemtuzumab was achieved in 4 of 6 CLL patients. Partial (3/7) or complete (4/7) molecular remission was achieved in all patients after immunotherapy. Four patients exhibited partial radiologic responses; 3 were unchanged. Adverse effects were rare (CMV viremia in 2 patients; moderate cytopenias requiring brief therapy interruption in 4). All 7 patients proceeded to allogeneic stem cell transplantation (4 MRD, 3 MUD), one in clinical relapse. Neutrophil engraftment was rapid (less than 20 days); one patient had delayed platelet engraftment. Although early to assess long-term disease response, 4/4 evaluable patients have achieved a complete molecular, hematologic, and radiologic response at 6 months post-transplant; one patient remains in complete remission at 2 years. One patient died of sepsis at 3 months. **Conclusion:** Alemtuzumab immunotherapy is an effective cytoreductive regimen for chemotherapy-refractory lymphoproliferative disorders prior to allogeneic stem cell transplantation, and bears testing in a larger multi-centre Phase II/III protocol.

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THE FREQUENCY OF EARLY COMPLICATIONS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) WITH MYELOABLATIVE (MA) AND NON-MYELOABLATIVE (NMA) CONDITIONING REGIMEN

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The frequency of early complications (before 100 days) of HSCT was measured on 38 patients (pts) with hemoblastosis, underwent allogeneic HSCT (allo HSCT) from HLA-matched related donors (median age 24.4 ± 1.8). Conditioning regimens were myeloablative in 28 patients (73.7%, median age 21 ± 2.0) and consist Bu+Cy, and NMA in 10 patients (26.3%, median age 29.9 ± 3.6), consist of Flu+Bu+ALG or Flu+Bu+Alkeran. In group of MA HSCT 13 patients had CML, 9 - ALL, 5 - AML and 1 - MDS. In group of NMA HSCT 6 patients had CML, 2 - ALL, 1 - AML, 1 - MDS. The frequency of bacterial infectious complications in NMA HSCT group was 21.4% and in MA HSCT group 20% ($p>0.05$). The frequency of febrile neutropenia was significantly lower in NMA HSCT group: 30% and 67,8% respectively ($p<0.05$). Viral complications was observed in 14 (50%) patients in group of MA HSCT and in 5 patients (50%) in NMA group. 8 pts (28.6%) in MA group developed CMV viremia and 4 pts (40%) in NMA group ($p>0.05$). Herpes simplex infection was diagnosed in 6 pts (21.4%) in group of MA HSCT and in 1 pt (10%) in NMA HSCT group ($p>0.05$). Hemorrhagic complications were observed in 14 patients with MA HSCT (50%) and in 4 (40%) with NMA HSCT ($p>0.05$). Acute graft versus host disease (GVHD) grade 2–4 was observed in 5 patients with MA HSCT (17.8%) and in 1 pt (10%) in group of NMA HSCT ($p>0.05$) and chronic GVHD was developed in 9 pts in MA HSCT group and in 1 pt in NMA HSCT group ($p>0.05$). The toxicity of conditioning regimens (only grade 3–4 were considered) for cardiovascular system was significant lower for NMA HSCT group: 1 pt (10%) and 11 pts (39.2%), ($p<0.05$). The toxicity for digestive system was lower in NMA HSCT group too: 5 pts (50%) and 28 (100%) respectively ($p<0.05$). The for respiratory system (7.1% and 0% respectively, $p>0.05$), urogenital system (25% and 20% respectively, $p>0.05$), and hepar (46.3% and 40% respectively, $p>0.05$) had no significant differences between two groups. 1 pt in group NMA HSCT had veno-occlusive disease (10%) and no cases in group MA HSCT ($p>0.05$). The engraftment of stem cells was achieved in 100% cases as in MA as NMA HSCT groups (25.5 ± 4.5 and 20.5 ± 1.2 days respectively, $p>0.05$). We conclude, that there are no differences between patients groups with MA and NMA HSCT in spite of engraftment kinetics, the frequency of infectious complications, the frequency of acute and chronic GVHD. But the use of NMA HSCT accompany note lower toxicity on cardiovascular and digestive systems.

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UNRELATED CORD BLOOD TRANSPLANTATION WITH MYELOABLATIVE CONDITIONING FOR ADULT PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

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Background: Umbilical cord blood (CB) has been rapidly established as an alternative source of stem cells to bone marrow or peripheral blood for unrelated allogeneic hematopoietic stem cell transplantation. However, concern about the engraftment failure probably due to low number of stem cells has limited its use particularly for adult patients. We report the results of unrelated cord blood transplantation (CBT) for 8 adult patients with hematological malignancies. **Patients and Methods:** Patients with hematological malignancies without a suitable related donor were eligible. Conditioning consisted of total body irradiation (TBI; 120 cGy) followed by high-dose cytarabine (3 g/m^2 × 8) for myeloid malignancies, and TBI (120 cGy) followed by high-dose cytarabine (2 g/m^2 × 4) and cyclophosphamide (60 mg/kg × 2) for lymphoid malignancies. For acute graft-versus-host disease prophylaxis, tacrolimus (0.03 mg/kg) and short-term methotrexate (15 mg/m^{2}on day 1, 10 mg/m^{2}on days 3, 6) were given. All patients received G-CSF infusion starting on day 1 until neutrophil recovery was obtained. Cord blood unit was selected according to the nucleated cell number (more than 2.0 × 10^7/kg) and HLA compatibility (less than serological 2-loci mismatches). **Results:** Eight patients were enrolled. Median age was 39 years (range, 20–58), and median number of cryopreserved nucleated cells in the CB unit was 2.9 × 10^7/kg (range, 2.0–4.7 × 10^7/kg). Their diagnoses were AML in 3 (2nd CR, 2; primary induction failure (PIF), 1), Ph1+ ALL (1st CR) in 2, advanced MDS in 2, and CML (2nd CP) in 1. All patients achieved engraftment with full donor chimerism. Acute GVHD occurred in 5 patients, and the grading was grade I in 2 and grade II in 3 patients. Chronic GVHD occurred only in 2 patients. No transplant-related mortality was observed, and overall survival was 100% with a median follow-up 14.7 months (range, 6.1–33.8 months). One patient with AML (PIF) relapsed 13 months after