none has detectable bcr/abl transcripts in blood or marrow. One patient (CML-CP3) with cytogenetic relapse at D + 118 had a fourth remission after withdrawal of immunosuppression and continued imatinib but developed hematological relapse at D + 429. **Conclusions:** We conclude that imatinib therapy can be safely prescribed early after myeloablative allogeneic HCT at a dose-intensity comparable to that used in general oncology. Preliminary efficacy data are encouraging and worthy of further study (Table1).

Table 1. *Patient Characteristics and Outcomes*

	ALL (n = 12)	CML (n = 6)
Pretransplant characteristics		
Disease phase, *N*	CR1 *10*, CR2 *2*	AP *2*, CP2 *2*, CP3 *2*
Patients with MRD[1] present, *N*	*9*	*6*
Median age, *years* (range)	36 (5–49)	45 (36–62)
Related donor, unrelated donor, *N*	*5, 7*	*2, 4*
Peripheral blood, marrow, cord blood, *N*	*8, 3, 1*	*4, 1, 0*
Posttransplant outcomes		
Imatinib therapy start day, median (range)	28 (24–39)	29 (25–36)
Imatinib therapy, *days of,* median (range)	183 (3–381)	243 (89–353)
Average daily imatinib doses, *milligrams*		
≤Day 90, median (range)	400 (212[2]–400)	400 (novariance)
>Day 90, median (range)	400 (250[2]–550)	400 (novariance)
Survival, *days,* median (range)	214 (27–600)	511 (130–627)
Molecular remission/completed therapy, *N/N*	*4/4*	3/4
Molecular remission/continue Imatinib, *N/N*	*8/8*	*2/2*

[1]MRD = minimal residual leukemia by cytogenetic and/or molecular methods.

[2]Two children did not receive 400 mg per day but received close to 340 mg/m^2/day.

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DIFFERENCES IN THE PHENOTYPE AND IN VIVO ANTI-TUMOR ACTIVITY OF WT1 SPECIFIC AND EBV-SPECIFIC T-CELLS GENERATED IN VITRO FOR ADOPTIVE IMMUNOTHERAPY

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Our studies in SCID mouse/human tumor xenograft models have demonstrated that T cells sensitized with autologous EBV BLCL in vitro will, following intravenous transfer into mice bearing tumors varying in HLA type and expression of EBV antigens, selectively accumulate in EBV+ tumors co-expressing the T cell's HLA restricting allele, and will proliferate and persist in these tumors through there complete regression. In contrast while T cells sensitized against WT1 peptides presented by peptide-loaded autologous DCs or EBV BLCL in vitro also exhibit HLA-restricted accumulation in WT1+ tumor xenografts and induce significant inhibition of tumor growth, they persist only for periods of 8 days following adoptive transfer. By day 15, the T cells were no longer detectable in the tumors, following which the regrowth of WT1 expressing tumors was again observed. Accordingly, we compared T cells sensitized in vitro with autologous EBV BLCL alone or with EBV BLCL loaded either with the pool of overlapping 15-mers spanning over WT1 sequence or transduced to express WT1. Antigen-specific T cells were then characterized as to their specificity and HLA restriction. Antigen-reactive T cells were then isolated on the basis of IFNγ production in response to secondary restimulation with APCs bearing targeted peptides and the appropriate restricting HLA alleles and evaluated for their phenotype and tumor-specific activity. Both CD4+ and CD8+ EBV-specific T cells exhibited HLA-restricted lysis of EBV+ tumor cells while the CD8+ WT1 specific T cells consistently lized WT1 tumors bearing HLA restricting HLA class I allele. The CD4+ T cells were not cytotoxic. The WT1-specific and EBV-specific CD4+ T cells did not differ in phenotype. However, while CD8+ T cells specific for EBV expressed an effector memory phenotype ($CD3^+$ $CD8^+$ $CCR7^-$ $CD45RA^+$ $CD45RO^+$ $CD62L^+$ $CD25^+$), the WT1 specific CD8+ T cells were predominantly of a central memory type ($CD3^+$ $CD8^+$ $CCR7^+$ $CD45RA^-$ $CD45RO^+$ $CD62L^+$ $CD25^+$). These studies suggest that T cells generated against WT1 in vitro may be relatively deficient in effector memory T cells required to induce complete tumor regression in vivo.

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HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FOR MALIGNANCIES USING UMBILICAL CORD BLOOD UNITS (UCB) THAT WERE NOT RED BLOOD CELL DEPLETED

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Cell dosage is a limiting factor for UCB HSCT, especially for adult patients. Most UCB banks practice red cell depletion (RCD) techniques to save storage space, which incur significant nucleated cell loss after processing. One method of minimizing cell loss and still reduce volume after processing is to deplete plasma (PD), but not the red blood cells. Not washing UCB after thawing also minimizes cell loss. A large, racially diverse PD UCB inventory of 18,000 units is now available on stem cell registries. A retrospective analysis was performed on 70 patients with malignancies without prior HSCT who were transplanted during remission with PD UCB. There were 28 ALL, 16 AML, 8 CML, 7MDS/RA/RAEB, 3 JMML, and 8 others. Of the ALL/AML/CML cases with available information, there were 19 1CR/CP, 10 2CR, and 9 3CR/CP. The median age of patients was 5.8 years old (range 0.5–54); median weight 23 kg (range 5–84); male 63%. Transplant characteristics indicated a median # HLA ABDR matches of 5.0 (11-6/6; 23-5/6; 27-4/6; 8-/6; 1-/6;) median pre-freeze TNC dose 6.4×10^7/kg; median post-thaw TNC dose as reported by TC 5.3×10^7/kg; median pre-freeze CD34 dose 2.5×10^5/kg; transplants outside of U.S. 24%; double unit transplant 14%; nonmyeloablative 7%. Forty-seven percent of the transplanted UCB were washed post-thaw (W), 33% were infused without post-thaw wash (NW), with 20% of the units without available post-thaw data. Median time to engraftment for ANC 500 (n = 66), platelet 20K (n = 52), and 50K (n = 50) were 24 days (range 7–49 days), 53 days (range 15–94 days), and 63 days (range 37–132 days), respectively. Median time to engraftment for W versus NW were 28 versus 23 days for ANC500, and 55 versus 49 days for platelet 20K, respectively. The unadjusted cumulative incidence (C.I.) of ANC500 and platelet 20K and 50K engraftments are 93 ± 3%, 76 ± 6%, and 75 ± 6%, respectively. The incidence of reported grade II-IV and III-IV acute GVHD were 37% and 20%, respectively. Twelve percent developed limited chronic GVHD and 15% developed extensive chronic GVHD. With a median follow-up of 282 days (range 50–1263 days), the Kaplan-Meier estimates of 1-year TRM, OS and relapse-free survival were 20 ± 6%, 67 ± 6%, and 59 ± 7%, respectively. These results demonstrate that HSCT using unrelated PD UCB can be performed safely and effectively in patients with malignancies, and post-thaw wash may not be necessary.

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OUTCOME OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION AFTER ADDING HIGH-DOSE CYTARABINE TO THE CONVENTIONAL Cy/TBI CONDITIONING REGIMEN FOR THE TREATMENT OF PHILADELPHIA-CHROMOSOME-POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA

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Philadelphia-chromosome-positive (Ph+) acute lymphoblastic leukemia (ALL) accounts for 3–5% of childhood ALL, and allogeneic hematopoietic stem cell transplantation (HSCT) is considered to be the best way to cure the relatively rare and aggressive subtype of ALL. Cytarabine is an effective agent in both lymphoid and myeloid leukemia, and high-dose cytarabine (HDC) has been used to treat patients with ALL who had relapsed or had been refractory to the standard induction chemotherapy. From this point of view, we postulated that the addition of HDC to the standard conditioning regimen might decrease the relapse rate through more effective eradication of residual leukemia before transplant. So, we investigated the feasibility of HDC-containing conditioning for the treatment of children with Ph+ ALL. Between February 2002 and May 2005, 10 consecutive patients with Ph+ ALL, including one who had presented with CML in lymphoid blastic phase, aged 3.5–12.8 years (median age 9.4 years) received allogeneic HSCT at our two cooperative institutions. The median time from diagnosis to transplant was 6 months (range, 3–10 mo). Two patients (20%) were not in CR1 at transplant. The sources of stem cells were as follows: unrelated bone marrow (n = 5), unrelated cord blood (n = 4), matched sibling bone marrow (n = 1). The conditioning regimen included HDC (3 g/m^2/dose every 12 h × 4 doses, total 12 g/m^2), cyclophosphamide (60 mg/kg/day × 2 days, total 120 mg/kg), and total body irradiation (TBI). TBI was delivered in 2 different manners according to the each institutional guideline (1000 cGy/3 Fr/3 day, n = 5; 1320 cGy/11 Fr/4 day, n = 5). Cyclosporine with or without other agents was used for GVHD prophylaxis. The neutrophil recovery was attained in all recipients at a median of 20.5 days (range, 11–44 days) and the platelet engraftment also occurred in all patients at a median of 26.5 days (range, 13–148 days). Grade 2-4 and grade 3-4 acute GVHD were developed in 4 (40%) and 2 (20%) patients, respectively. Three patients (30%) developed chronic GVHD (2 limited, 1 extensive). All but one patient are alive disease-free with a median follow-up of 21 months (range, 4–39 months). There was no relapse and the only event was a chronic pulmonary GVHD with bronchiolitis obliterans leading to death in 1 patient. The 3-year estimated event-free survival was 83.3%. In conclusion, our results suggest that adding HDC to the standard Cy/TBI conditioning is feasible in allogeneic HSCT for pediatric patients with Ph+ ALL.

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ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) IN ADULTS WITH ACUTE MYELOID LEUKEMIA (AML) – A SINGLE PROGRAM EXPERIENCE

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From 1/00 to 4/05, 93 patients (pts) with AML underwent allo HSCT at the VU/VA SCT program. Variables including donor type, stem cell source, regimen intensity, and degree of HLA matching were analyzed for their effect on OS and TTP. Median age at transplant was 47 (19–66). 85 pts (91%) had poor risk disease, defined as prior MDS or MPD (n = 17), poor-risk cytogenetics (n = 6), refractory disease (n = 4), relapsed disease (n = 15), history of chemotherapy and/or radiotherapy for a prior malignancy (n = 4), CR2 (n = 35), or requiring >1 cycle of induction to achieve CR1 (n = 4). Regimens were either full-dose (BuCy and CyTBI) or reduced-dose (FluBu, FluBuTBI, or FluTBI). Of the 93 pts, 62 (67%) had matched related donors (MRD) and 31 (33%) had unrelated donors (URD). Both groups (MRD vs URD) were similar in disease risk (87% vs 100% high risk), degree of HLA matching (98% vs 77% fully matched), and regimen intensity (79% vs 77% full-dose) but differed significantly in stem cell source with MRD 95% PBSC and URD 71% BM, $P < .001$. Day 100 mortality was 11% for MRD versus 29% for URD, and all pts surviving to day 30 engrafted (ANC >500). Median OS was 10.8 months and was not significantly affected by donor type, regimen intensity, or pt age. OS was significantly higher in pts with fully-matched donors (median 12.9 months vs 2.4 mos, $P = .027$) and in pts without high-risk disease (median not reached vs 8.0 months, $P = .040$). There was also a trend towards improved survival of pts receiving PBSC versus BM (median 13.4 mos vs 6.7, $P = .062$). Interestingly, pts receiving full-dose regimens were more likely to die of relapse than transplant-related mortality (TRM) (30 relapse vs 16 TRM), while pts receiving reduced-dose regimens had more TRM than relapse deaths (3 relapse vs 9 TRM, $P = .02$), which may be accounted for by the higher median age of the reduced-dose group (56 vs 43). Of the 93 pts, 35 (38%) are alive with a median follow-up of 18.0 mos (5.5–61.8), 35 (38%) have died of relapse, and 23 (25%) TRM. TTP was 31.4 months with censorship of pts with TRM. OS at 36 months was 33%. Using a Cox-proportional multivariate model, only disease risk approached significance with a hazard ratio of 3.6 ($P = .079$). These results highlight the need for better anti-leukemic regimens and indicate that allo HSCT is most beneficial to pts who have chemotherapy-responsive disease and few risk factors for TRM, but can still salvage approximately 1/3 of patients with poor risk disease.

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THE EARLY REFERRAL FOR REDUCED-INTENSITY STEM CELL TRANSPLANTATION IN PATIENTS WITH Ph1 (+) CHRONIC MYELOGENOUS LEUKEMIA IN CHRONIC PHASE IN THE IMATINIB ERA: RESULTS OF THE LATIN AMERICAN COOPERATIVE ONCOHEMATOLOGY GROUP (LACOHG) PROSPECTIVE, MULTICENTER STUDY

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Using a reduced intensity stem cell transplantation (RIST) schedule, 24 patients with Ph1 (+) chronic myelogenous leukemia (CML) in first chronic phase were prospectively allografted in 4 Latin American countries: Mexico, Brasil, Colombia, and Venezuela, using HLA-identical siblings as donors. Median age of the patients was 41 years (range 10–71); there were 8 females. Patients received a median of 4.4 × 10^6/Kg CD34 cells. Median time to achieve above 0.5 × 10^9/L granulocytes was 12 days, range 0–41, whereas median time to achieve above 20 × 10^9/L platelets was also 12 days, range 0–45. Twenty two patients are alive 81 to 830 (median 497) days after the RIST. The 830-day probability of survival is 92%, whereas median survival has not been reached, being above 830 days. Eleven patients (46%) developed acute graft-versus-host disease (GVHD), whereas 7 of 23 (30%) developed chronic GVHD. Two patients died 43 and 210 days after the RIST, one as a result of sepsis and the other one of chronic GVHD. The 100-day mortality was 4.4 %, whereas the transplant-related mortality was 8%. RIST for patients with CML in chronic phase seems as an adequate therapeutic option.

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ADDITION OF RITUXIMAB TO HYPER-CVAD IN THE TREATMENT OF CD20-POSITIVE ADULT ACUTE LYMPHOCYTIC LEUKEMIA (ALL)

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Hyper-CVAD (fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate-cytarabine has proven to be an effective regimen in the treatment of adult ALL. Addition of the anti-CD20 monoclonal antibody rituximab to standard chemotherapy regimens has shown significant benefit in the treatment of lymphoma and leu-