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A WEB-BASED SYSTEM SUPPORTING STRATEGICAL DECISIONS IN WORLD WIDE URELATED DONOR SEARCH

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Most active unrelated stem cell donor registries in the world are participating in the cooperation of Bone Marrow Donors Worldwide (BMDW). Formally, BMDW is a service provided by the Dutch registry Europdonor collecting all data, providing them back to the contributors and making them directly accessible via a web based matching program. Unfortunately, HLA information is limited for many donors, in particular where DRB1 alleles are missing or only tested at low or intermediate resolution. We are using our own copy of the BMDW data to generate haplotypes frequencies per registry for HLA-A,B-,DRB1. HLA-A and B are analyzed using serological nomenclature and DRB1 using a resolution of 2 and 4 digits as far as the data for each registry permits. These haplotypes frequencies are used for a web based system prototyped in our intranet, which calculates the probability of finding a donor who is a match for HLA-A and B (serology) and for DRB1 (allele level) by performing subsequent test on partially typed donors. In the calculation of the conditional match probabilities the program correctly interprets all broad serological designations and multiple allele codes using the individual frequencies for each registry. Where there are test candidates in several registries, the system can also indicate which donors according to their origin or partial typing status are most likely to turn out to be matches. This provides a highly intelligent sorting of BMDW match lists. The program is currently implemented as a CGI-script using PERL and typically takes 5–20 seconds on a 1.5 GHz XEON including a full molecular BMDW match run. The program has immediately become an indispensable tool for the analysis of all difficult donor searches.

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COMPARABLE RESULTS OF UMBILICAL CORD BLOOD AND HLA MATCHED SIBLING DONOR HEMATOPOIETIC STEM CELL TRANSPLANT AFTER REDUCED-INTENSITY PREPARATIVE REGIMEN FOR ADVANCED HODGKIN'S LYMPHOMA

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The lower regimen-related toxicity of reduced-intensity conditioning (RIC) preparative regimens has extended the opportunity for allogeneic stem cell transplantation (alloSCT) and its potential graft-versus-lymphoma effect to patients with advanced Hodgkin's lymphoma (HL). In this pilot study, we compared the safety and efficacy of RIC alloSCT in 21 adults with chemosensitive primary refractory or relapsed HL using either umbilical cord blood (UCB-9) or matched sibling donors (MSD-12). Indications for RIC alloSCT were age >55 years with HLA matched sibling donor (19%), age >45 years with UCB donor (5%), extensive prior therapy including previous autologous stem cell transplant (ASCT) (67%), or major comorbidity (22%). Of the 14 patients who had failed prior ASCT, median duration of post-transplant CR was 11 months (range, 3–54). Patient demographics, disease characteristics at initial diagnosis, and at relapse prior to alloSCT were comparable except for a younger age in the UCB cohort (median 28 years vs 42 years for MSD, $P = .04$). Results are shown in Table 1. Neutrophil recovery occurred earlier in the MSD group. All patients had sustained donor engraftment by day +60. Cumulative incidence of grade III/IV acute graft-versus-host disease and 180-day treatment-related mortality were comparable. Two patients who underwent MSD alloSCT received donor-lymphocyte infusion for post-transplant relapse with resultant partial responses lasting 3 and 6 months. With a median follow-up of 17 and 24 months for the UCB and MSD groups, respectively, the 2-year progression-free survival (PFS) for UCB is 25% compared to 20% for MSD alloSCT. The median time to disease progression was 4 months for the UCB group and 6 months for the MD group; all relapses occurred within 1 year of alloSCT. Patients with relapsed disease or longer post-ASCT CR (≥12 months) were more likely to be alive and free of progressive disease than patients with primary refractory disease or short CR. Our results suggest comparable outcomes for RIC alloSCT using UCB or MSD source in adults with high-risk, advanced HL. Since many patients lack a matched sibling or unrelated donor, UCB grafts can provide an effective and safe alternative. In addition, alloSCT using RIC is associated with durable PFS in a selected subgroup of patients. Further studies are ongoing to identify patients who would benefit the most by this approach (Table 1).

Table 1. *Post-Transplant Outcomes*

		UCB (n = 9)	MSD (n = 12)	P-Value
Cell dose ($\times 10^7$ NC/kg)	Median (range)	3.8 (2.3–5.3)	10.0 (7.9–16.4)	<.01
HLA 1–2 antigen mismatch		9 (100%)	1 (8%)	<.01
Neutrophil engraftment (days)	Median (range)	10 (6–28)	7 (5–12)	.02
Complete donor chimerism	Day +21 Day +60	6 (67%) 9 (100%)	12 (100%) 12 (100%)	.06 -
Acute GVHD	Grade II–IV	6 (67%)	7 (58%)	.70
	Grade III–IV	3 (33%)	4 (33%)	.99
Chronic GVHD		1 (11%)	4 (33%)	.24
CR after alloSCT		8 (89%)	9 (75%)	.42
Treatment related mortality	100 days 180 days	1 (11%) 2 (22%)	2 (17%) 3 (25%)	.80 .88
Followup (months)	Median (range)	17 (4–51)	24 (9–53)	
2-year PFS (months)	(95% CI)	25% (0–55%)	20% (0–44%)	.67
2-year OS (months)	(95% CI)	51% (16–86%)	48% (19–77%)	.93

NC-nucleated cells; HLA-human leukocyte antigem; GVHD-graft-versus-host-disease; CR-complete remission; CI-confidence intervals.

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MOBILIZATION OF PERIPHERAL BLOOD CD34 STEM CELLS IN A HEAVILY PRE-TREATED PEDIATRIC MEDULLOBLASTOMA PATIENT USING AMD3100 AND G-CSF

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Autologous peripheral blood stem cell transplantation has been beneficial in the setting of recurrent medulloblastoma, however many of these patients are heavily pre-treated, making conventional mobilization of peripheral blood stem cells with G-CSF alone difficult. The recent development of AMD3100 as an inhibitor of the binding of SDF-1/CXCL12 to its receptor CXCR4 in the marrow stem cell compartment has resulted in significant enhancement in the mobilization of peripheral blood stem cells. This has met with considerable success in adults with phase III trials under way, however there is little pediatric experience with the use of AMD3100. We report here the use of AMD3100 to mobilize peripheral blood CD34 cells from a heavily pre-treated 11 year-old girl with recurrent medulloblastoma. DM was diagnosed with stage IV medulloblastoma in Feb 2004 and was treated with surgical resection, radiation, and maintenance chemotherapy including cisplatin, CCNU, and vincristine. Prior to her 5th cycle of chemotherapy she experi-