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Donor *KIR B* Genotype Improves Progression Free Survival of Non-Hodgkin lymphoma Patients Receiving Unrelated Donor Transplantation

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Abstract

Donor killer immunoglobulin-like receptor *(KIR)* genotypes associate with relapse protection and survival after allotransplantation for acute myelogenous leukemia. We examined the possibility of a similar effect in a cohort of 614 non-Hodgkin lymphoma (NHL) patients receiving unrelated donor (URD) T-cell replete marrow or peripheral blood grafts. Sixty four percent (n=396) of donor-recipient pairs were 10/10 allele HLA-matched; 26% were 9/10 allele matched. Seventy percent of donors had *KIR B/x* genotype; the others had *KIR A/A* genotype. NHL patients receiving 10/10 HLA-matched URD grafts with *KIR B/x* donors experienced significantly lower relapse at 5 years (26%; CI 21–32% vs. 37%; CI 27–46%, p=0.05) compared with *KIR A/A* donors, resulting in improved 5 year progression-free survival (PFS) (35%; CI 26–44% vs. 22%; CI 11–35%; p=0.007). In multivariate analysis, use of *KIR B/x* donors associated with significantly reduced relapse risk (RR 0.63, p=0.02) and improved PFS (RR 0.71, p=0.008). The relapse protection afforded by *KIR B/x* donors was not observed in HLA-mismatched transplants,

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V.B., D.J.W, J.S.M and S.C. contributed to the study design, analyzed and interpreted data and wrote the manuscript. S.R.S and M.D.H contributed to the study design, sample procurement, data management and manuscript editing. T.W. performed the biostatistical analyses for the study. E.T and M.L. performed KIR genotyping. S.G.E.M, L.A.G, and P.P. reviewed and edited the manuscript.

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and was not specific to any particular *KIR-B* gene. Selecting 10/10 HLA-matched and *KIR B/x* donors should benefit patients with NHL receiving URD allogeneic transplantation.

Keywords

non-Hodgkin lymphoma; KIR; allogeneic transplantation; genotype; NK cells

Introduction

Allogeneic hematopoietic cell transplantation (HCT) can cure non-Hodgkin lymphoma (NHL) through the combination of chemotherapy and immune mediated graft-versus-lymphoma (GvL) responses.[1] Long-term survival ranges from 30 to 70%, relapse being the major cause of treatment failure for all NHL histologic subtypes.[2,3] The mechanisms of tumor escape from GvL are poorly understood, but analyses of patients with acute myeloid leukemia (AML) after unrelated donor (URD) HCT reveal the importance of donor killer-cell immunoglobulin-like receptor *(KIR)* genotype in effective GvL responses.[4–6] NK cells reconstitute promptly after HCT, and express inhibitory KIRs that interact with class I HLA-C1 (ligand for KIR2DL2/3), HLA-C2 (ligand for 2DL1) and HLA-Bw4 epitopes (ligand for 3DL1) to regulate NK cell education and function.[7] NK cells also can express activating KIRs 2DS1, 2DS2, 2DS3 and 2DS5 to co-regulate antitumor effects by binding to HLA-C2 (2DS1) or neo-ligands on tumor cells. Individuals vary in the number of *KIR* genes contained in their genome. *KIR* genes are closely linked on chromosome 19q and inherited as haplotype A or B from each parent. The main difference between group A and B haplotypes is that group B contains variable numbers of activating *KIR* genes, while group A has a fixed gene content of inhibitory but no activating *KIR*. About 70% of the population has at least one *KIR B* haplotype. The haplotypes combine to give the *A/A* and *B/x* (*A/B* or *B/B*) genotypes.[8] The *KIR B* genotype can be further defined by a *KIR B* content score determined by the number of centromeric and telomeric motifs containing B-haplotype defining genes (permissible values 0–4). HLA and KIR genes segregate on different chromosomes (6 and 19) and are inherited independently. Although donor selection is guided by HLA matching, we hypothesized that donor *KIR* interactions with recipient HLA might influence clinical outcomes. Our previous studies showed that *KIR B/x* donors, and not *KIR A/A* donors improve leukemia-free survival in AML.[4–6] The impact of *KIR* polymorphism on relapse and survival of patients with NHL after allo-grafting is unknown. In the current study, we investigated NHL patients receiving allogeneic URD HCT to determine the influence of donor *KIR* genotype and individual *KIR B* genes on clinical outcomes.

Patients and Methods

We studied 614 adults (age >18 years) with NHL who underwent T-cell replete URD HCT between 1990 and 2009 facilitated by the National Marrow Donor Program (NMDP). The outcome data were collected at the Center for International Blood and Marrow Transplant Research (CIBMTR). The study protocol was approved by the Institutional Review Board of the NMDP in accordance with the Declaration of Helsinki. Stored donor samples were

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obtained from the CIBMTR Research Repository and genotyped for *KIR*.[9] *KIR* gene content was assessed, allowing each donor to be designated as either *KIR A/A* or *B/x* genotype.

Statistical Analysis

Progression-free survival (PFS) and overall survival (OS) were evaluated with Kaplan-Meier estimates.[10] Relapse, non-relapse mortality (NRM) and acute graft-versus-host disease (GVHD) were evaluated using the cumulative incidence function. Clinical variables were tested for the proportional hazard assumption and were adjusted as needed through stratification. Stepwise forward-backward selection was performed to build multivariate Cox proportional hazards models with a threshold of 0.05 for model entry. Donor *KIR* genotype, the primary variable of interest was forced into the model and adjusted for clinical variables. Other clinical variables analyzed were donor source, GVHD prophylaxis, conditioning regimen, HLA-match, time from diagnosis to transplant, histology group, disease status, in vivo T-cell depletion, age and KPS. To adjust for multiple testing, variable with $p<0.01$ were considered statistically significant.

Results

Patients, disease and transplant characteristics

The ages of the 614 NHL patients ranged from 19–72 with a median of 50 years. Follicular lymphoma was the most common histology, followed by mantle cell lymphoma, diffuse large B-cell lymphoma and T cell NHL; Burkitt/lymphoblastic lymphomas were excluded (Table 1). Almost all patients were Caucasians and 62% had chemosensitive lymphoma prior to transplant. Most patients were at least 1.5 years from diagnosis to transplant, 41% received myeloablative conditioning regimens and 63% received filgrastim mobilized peripheral blood stem cell (PBSC) grafts. The donor *KIR* genotype frequencies reflected those of a general Caucasian population; 30% were *KIR A/A* (n=183) and 70% were *KIR B/x* (n=431) with *KIR-B* content scores of 1 (n=243), 2 (n=140) or ≥3 (n=48). We found no correlation between KIR *B/x* and donor ethnicity (Caucasian vs other 71% vs 68%; p=0.4). Two-thirds of the donor-recipient pairs were 10/10 allele matched at *HLA-A, -B, -C, -DRB1* and *-DQB1* (n=396); the rest were 1 (n=158) or ≥2 HLA allele (n=60) mismatched. Fully matched recipients were older (52 versus 48 years, p=0.0053), more of them received reduced intensity conditioning (RIC) (62% versus 52%, p=0.011), and received PBSC grafts (69% versus 53%, p=0.0003) vs HLA mismatched transplant recipients. There were no significant differences for other clinical variables (Table 1). We than compared 10/10 HLA matched donor-recipient pairs by donor *KIR* genotype and found similar patient and graft characteristics in patients with *KIR A/A* vs *KIR B/x* donors (Table 1).

Impact of *KIR* genetics on transplant outcomes

In the 10/10 HLA-matched HCT cohort (n=396), *KIR B/x* donor grafts resulted in less relapse at 5 years after transplantation (26% [95% CI 21–32%]) compared to *KIR A/A* donors (37% [27–46%]; p=0.05). This relapse protection translated into improved PFS (*KIR B/x* 35% [95% CI 26–44] versus (*KIR A/A* 22% [95% CI 11–35%]; p=0.007) (Figure 1A/B). After adjusting for important clinical variables, *KIR B/x* donors conferred significant

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protection against relapse (HR 0.63 [95% CI 0.43–0.92]; p=0.02) and improved PFS (HR 0.71 [95% Cl 0.55–0.91]; p=0.008) compared to *KIR A/A* donors. In evaluating the protection conferred by individual genes of the *KIR B* haplotype (*KIR2DS2, 2DS5, 2DL2, 2DS1, 3DS1, 2DS3*, and *2DL5*), we found that each *KIR* gene was associated with a similar degree of protection against relapse (RRs 0.68–0.79; Figure 1C). Thus individual centromeric and telomeric *KIR B* genes had similar influences on transplant outcomes and donor with ≥3 *KIR B* genes conferred the best PFS compared to *KIR A/A* donors (RR 0.47; 95%CI 0.27–0.81; p=0.007). The protective effect of *KIR B/x* donors was not observed for our cohort of HLA-mismatched transplants (RR 1.49 [95% CI 0.87–2.55; p = NS). Donor *KIR* genotypes had no effect on 1 year non-relapse mortality (*KIR B/x* vs *KIR A/A* Hazard ratio (HR) 0.8 (95% CI 0.55–1.11); p=0.17), grade II-IV acute GVHD (HR 1.06; 95%CI 0.82–1.38; p=0.67) or chronic GVHD (HR 0.91; 95%CI 0.71–1.15; 0.42). Despite the effect on PFS, HCT recipients had similar OS when transplanted with *KIR B/x* versus *KIR A/A* donors (10/10 HLA matched cohort: HR 0.8 (95%CI 0.61–1.06); p=0.12; entire population: HR 0.9 (95%CI 0.74–1.1); p=0.4)). This likely reflects the growing number of immune options available to patients after receipt of an allograft

Clinical factors affecting transplant outcomes

Main factor associated with improved OS of entire population (n=614) in adjusted multivariate regression was RIC conditioning (HR 0.57 [95% CI 0.42–0.77]; p=0.0008). Shorter OS was associated with chemotherapy-resistant disease (HR 1.6 [95% CI 1.08–2.40]; p=0.02), histology other than follicular lymphoma (HR 1.74–2.06; p=0.0001), and using ≥2 locus HLA-mismatched donors (≤8/10 match HR 1.46 [95%CI 1.06–2.01]; p=0.02; 9/10 match HR 1.09 [95%CI 0.81–1.47; p=0.57). TRM was better with RIC conditioning (HR 0.6; 95% CI 0.5–0.8; p=0.001) and follicular lymphoma histology (HR 0.5; p=0.03) and was not influenced by 9/10 HLA match, GVHD prophylaxis and *KIR* status (*KIR B/x* HR 0.97; 95%CI 0.74–1.27; p= 0.81). HCT using donors with ≥2 locus HLA-mismatch had increased TRM (HR 1.5 (95%CI 0.99–2.26; p=0.056). Factors associated with increased relapse were chemotherapy resistance (HR 1.57; p=0.001), in vivo T cell depletion (HR=1.53; p=0.006), histology other that follicular lymphoma (HRs1.66–1.88; p=0.02) and ≥2 locus HLA mismatch (≤8/10 match HR 1.8, p=0.016; 9/10 match HR 1.19; p=0.3). There were no interactions between the in vivo T cell depletion and <10/10 HLA mismatch. Adjusted incidence of grade III-IV acute GVHD was reduced with tacrolimus-other (mostly MTX) GVHD prophylaxis (HR 0.64 [HR 0.38–1.07] compared to tacrolimus-MMF (HR 1.0) and CSA-containing regimen (HR 1.19 [0.71–1.99; overall p=0.012). Use of tacrolimus-other and CSA-based GVHD prophylaxis resulted to similar OS (HR 0.6 [0.46–0.8]) and HR 0.72 [0.53–0.97]). Overall mortality was increased after tacrolimus-MMF combination (HR 1.0; p=0.0014). In adjusted multivariate regression, the 10/10 HLA-matched cohort *KIR B/x* donors were associated with improved PFS and less relapse. Chemo-resistance, lymphoma histology other than follicular lymphoma and <1.5 years from diagnosis to transplant resulted in inferior PFS (Table 2). Relapse was increased by chemo-resistance, shorter time to HCT and use of in vivo T cell depletion (Table 2).

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Discussion

The importance of donor *KIR* genotypes has been mainly studied in AML where benefit has been reported using haploidentical or matched URD donors. [4–6,11–14]. Here we report a similar benefit conferred by *KIR B/x* donors after 10/10 HLA-matched URD HCT for mature lymphoid malignancies. Using fully HLA-matched *KIR B/x* donors lowered relapse by 11% and resulted in significantly better PFS in NHL patients. These effects can potentially be explained by augmented cytolytic function and graft-versus-lymphoma alloreactivity of donor NK cells containing activating *KIR*. This is consistent with findings in AML by our group and others, as well as new findings in pediatric ALL. [3,6,14–20] While *KIR B/x* donors conferred significant improvement in PFS and relapse, we noted lack of impact on OS which likely reflects the efficacy of post-transplant therapies and effective immune interventions used in NHL patients who experience post-transplant relapse.[21]

Graft versus tumor effects are delivered by both NK cell and T cell responses against residual malignancy.[15] It is also clear that differential NK cell and T cell susceptibility is governed by HLA class I expression, NK cell receptor repertoires, and NK cell receptor ligands on targets. The balance between donor-derived T and NK cells may regulate the relative anti-tumor response between these cell types. NK cell alloreactivity in a transplant setting was first recognized in AML patients in absence of T cells with HLA-haploidentical donors and grafts prepared with CD34 selection.[16] The impact of genetic polymorphisms of *KIR* was subsequently reported by several groups showing protective effects of donor *KIR B/x* genotype in T-cell replete URD HCT in adult AML but not ALL.[3,6,14] The favorable influence of specific activating *KIR2DS1* or *KIR2DS2* on transplant outcomes in AML was confirmed by several groups in different transplant settings [12,14,17], but data on the benefit of *KIR* in lymphoid malignancies is scarce. After URD HCT for AML, we showed that donors with increasing number of *KIR B* defining motifs (≥2) contribute to the protective effect. However, in NHL, we find that a donor *KIR* gene content score of at least 1 is protective. The protective effect is enhanced ≥3 *KIR B* defining motifs, and is not limited to any one specific activating *KIR* gene.

Many reports showed that clinical impact of *KIR* genetics differ between transplant procedures. In some reports, activating KIR genes have no effect on relapse, yet do result in lower TRM and improved OS using sibling donors.[18,13] The difference between AML and ALL outcomes may be a result of more pronounced HLA-C and HLA-B downregulation on AML and pediatric ALL blasts than adult ALL blasts potentially causing resistance again NK cell mediated cytolysis.[20] Similarly to pediatric ALL, lymphomas variably down regulate HLA class I molecules, particularly HLA-B and C, which engage inhibitory KIR on alloreactive NK cells.[22–24] For example EBV-transformed B-cell lines which completely lack HLA class I are particularly sensitive to NK mediated killing.[25] Indeed, relapse protection, irrespective of disease, perhaps combines cancer mediated downregulation of inhibitory HLA class I alleles with expression of potential neo-ligands for activating KIR on NK cells from *KIR B/x* donors.[26] This will require detailed study as most of these ligands are not yet established.

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The finding is that the benefit of a *KIR B/x* donor in NHL is limited to the HLA-matched URD HCT setting was unexpected. While it is plausible that altered reconstitution of alloreactive T cells versus NK cells may be dependent on HLA matching, it must be noted that recipients of HLA-mismatched grafts also more frequently received myeloablative conditioning and bone marrow grafts which can alter immune reconstitution, and matched grafts were more often T cell depleted in vivo. It is possible that alloreactive T cells dominant in HLA mismatched URD HCT for NHL mediate GvL, masking a smaller NK cell mediated effect. In contrast, an HLA matched donor with less HLA differences may have less T cell GvL and increase the importance of *KIR B/x* donor-mediated NK cells in this setting.

Our study confirmed the importance of established favorable prognostic factors for survival such as chemosensitive disease and follicular lymphoma histology. Other notable variables impacting OS in this series were RIC and adverse impact of tacrolimus-MMF GVHD prophylaxis. While RIC conferred a major reduction in TRM leading to improved survival; this contrasts with several prior studies analyzing mixed NHL histologies in which RIC also resulted to higher relapse rates for more aggressive NHL and offset the survival benefit.[27,28] These discrepancies likely reflect the disease and patient heterogeneity of respective cohorts. Recipients of ≤8/10 matched grafts experienced higher relapse rate; however these 60 patients more often had aggressive NHL including T cell and NK cell lymphoma (50% vs 34%) compared to matched donor HCT and given small size of this subset, this data requires caution in inferring conclusions. Another interesting finding is the impact of GVHD regimen on survival. While survival after tacro-other (mostly MTX) and CSA-based combinations was similar, tacrolimus-MMF combination was associated with increased grade 3–4 acute GVHD and inferior survival. Inferior efficacy of tacrolimus-MMF may be explained by inadequate MMF levels; indeed data on MMF dosing and pharmacokinetics with tacrolimus is limited and warrants future investigations.[29,30]

In conclusion, our data suggest that patients with lymphoma benefit with relapse protection after HLA-matched URD HCT when using donors with *KIR B/x* haplotypes. This effect is broadly seen with the presence of an activating *KIR* gene and is not limited to a specific *KIR*. While prospective validation is merited, selecting a *KIR B/x* donor from amongst available HLA 10/10 allele-matched donors should benefit NHL patients in whom allografting with an unrelated donor is the best treatment option.

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Highlights

1. Donor *KIR* genetics influences graft-versus-lymphoma responses.
2. HLA-matched *KIR B/x* donors improve progression free survival.
3. *KIR B/x* donors benefit non-Hodgkin lymphoma patients undergoing matched unrelated transplantation.

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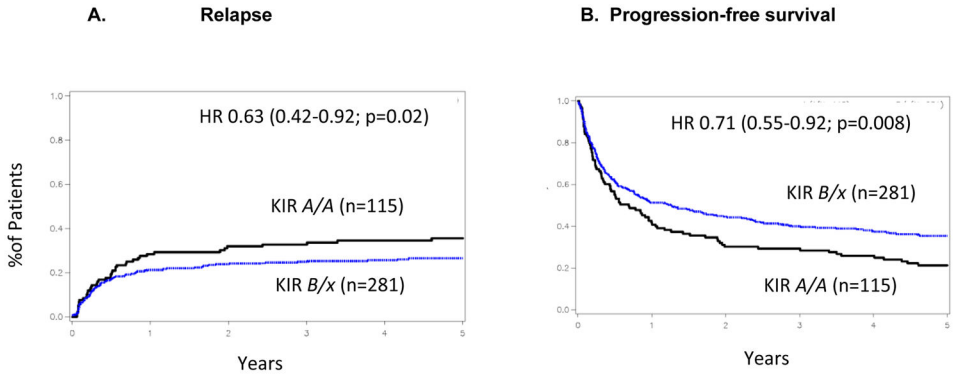

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Progression-free survival				
Donor KIR groups	n	Relative Risk	95%CI	p
KIR A/A B =0	115	1.0		
KIR B/x B≥1	281	0.71	0.55-0.91	0.008
B =1	160	0.68	0.51-0.91	0.01
B =2	92	0.84	0.61-1.15	0.27
B = 3 or 4	29	0.47	0.27-0.81	0.007
KIR B A/A	115	1.0		
KIR B/x with 2DS2	224	0.7	0.53-0.91	0.014
KIR B/x with 2DS5	119	0.74	0.55-1.01	0.093
KIR B/x with 2DL2	224	0.7	0.54-0.91	0.014
KIR B/x with 2DS1	146	0.75	0.56-1.00	0.067
KIR B/x with 3DS1	146	0.79	0.59-1.05	0.1
KIR B/x with 2DS3	109	0.68	0.50-0.94	0.07
KIR B/x with 2DL5	195	0.68	0.52-0.9	0.015

Figure 1. *KIR B/x* donors confer relapse protection and superior progression-free survival for NHL patients receiving 10/10 HLA-matched unrelated donor HCT

Adjusted cumulative incidence curve for relapse (A) and Kaplan Meier curve for progression-free survival (B) are shown for transplants involving donors of different *KIR* genotype (*A/A* vs. *B/x*). (C) The table lists the relative risks [RR] for PFS given by multivariate models that compared *KIR A/A* to *KIR B/x* donors based on their *B* gene content (1, 2, and 3 or 4 *KIR B* content elements). Also shown are comparisons between different subsets of *KIR B/x* donors including each of the 7 *KIR B* genes. Most donors with *KIR B/x* genotypes have more than one *KIR B* gene.

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Table 1

Patient, Disease and Transplant Characteristics: HLA mismatched and HLA matched Cohort. HLA-matched donor HCTs are compared by donor *KIR* genotype.

Category	HLA Mismatch n=218	HLA Match n=396	P-value	HLA Match		P-value
				KIR A/A n=115	*KIR B/x* n=281	
Age			**0.0053**			**0.079**
Median (years)	48	52		49	52	
Race			**0.0017**			**0.57**
Caucasian	194 (89%)	380 (96%)		112 (97%)	268 (95%)	
Karnofsky Score			**0.055**			
90–100	131 (60%)	264 (67%)		73 (63%)	191 (68%)	**0.64**
≥80	75 (35%)	101 (25%)		33 (29%)	68 (24%)	
Missing	12 (5%)	31 (8%)		9 (8%)	22 (8%)	
Lymphoma subset			**0.060**			
Follicular lymphoma	60 (28%)	113 (29%)		36 (30%)	77 (27%)	**0.91**
Diffuse Large B-cell	36 (17%)	65 (16%)		17 (15%)	48 (17%)	
Mantle cell lymphoma	28 (13%)	81 (21%)		22 (20%)	59 (21%)	
T cell lymphoma	26 (12%)	60 (15%)		18 (15%)	40 (15%)	
Other non-Hodgkin lymphoma	68 (30%)	77 (19%)		22 (20%)	57 (20%)	
Chemosensitivity			**0.58**			**0.31**
Chemosensitive Relapse/PIF	86 (39%)	155 (39%)		40 (35%)	115 (41%)	
Untreated Relapse/PIF	21 (10%)	27 (7%)		9 (8%)	18 (6%)	

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Category	HLA Mismatch n=218	HLA Match n=396	P-value	HLA Match		P-value
				KIR A/A n=115	*KIR B/x* n=281	
Complete Remission[#]	47 (22%)	97 (25%)		25 (22%)	72 (26%)	
Chemoresistant Relapse/PIF[&]	64 (29%)	117 (29%)		41 (35%)	76 (27%)	
CMV Serostatus			**0.18**			**0.25**
Donor −/recipient−	71 (33%)	133 (34%)		37 (32%)	96 (34%)	
Donor +	78 (36%)	117 (29%)		30 (26%)	87 (31%)	
Donor −/recipient+	64 (29%)	141 (36%)		48 (42%)	93 (33%)	
Unknown	5 (2%)	5 (1%)		0	5 (2%)	
Conditioning Intensity			**0.011**			**0.77**
Myeloablative	104 (48%)	149 (38%)		42 (37%)	107 (38%)	
Reduced Intensity	114 (52%)	247 (62%)		73 (63%)	174 (62%)	
GVHD Prophylaxis			**0.63**			**0.15**
Tacrolimus + MMF	37 (17%)	72 (18%)		27 (23%)	45 (16%)	
Tacrolimus +/− others	102 (47%)	199 (50%)		54 (47%)	145 (51%)	
CSA containing	76 (35%)	122 (31%)		32 (28%)	90 (32%)	
Other prophylaxis	3 (1%)	3 (1%)		2 (2%)	1 (1%)	
In vivo T cell depletion			**0.68**			**0.64**
No	149 (89%)	282 (81%)		80 (69%)	202 (72%)	
Yes	69 (11%)	114 (19%)		35 (31%)	79 (28%)	
***HLA match-A, B, C, DRB1* and *DQB1*[1,2]**			**<0.0001**			

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Category	HLA Mismatch n=218	HLA Match n=396	P-value	HLA Match		P-value
				KIR A/A n=115	*KIR B/x* n=281	
10/10 allele matched	0 (0%)	396 (100%)		115 (100%)	281 (100%)	**0.32**
9/10	158 (72%)	0				
8/10	44 (20%)	0				
<8/10	16 (7%)	0				
Year of Transplant			**<0.0001**			**0.32**
1990–2000	61 (28%)	55 (14%)		17 (15%)	38 (13%)	
2001–2005	90 (41%)	164 (41%)		41 (35%)	123 (44%)	
2006–2009	67 (31%)	177 (45%)		57 (50%)	120 (43%)	
Interval from diagnosis to transplant			**0.40**			**0.49**
<= 1.5 years	93 (43%)	155 (39%)		42 (37%)	113 (40%)	
> 1.5 years	125 (57%)	241 (61%)		73 (63%)	168 (60%)	
Graft type			**0.0003**			**0.36**
Bone marrow	103 (47%)	124 (31%)		40 (35%)	84 (30%)	
PBSC	115 (53%)	272 (69%)		75 (65%)	195 (70%)	
Donor *KIR* genotype[$]			**0.69**			
KIR A/A	68 (31%)	115 (30%)		115 (100%)	0	
KIR B/x	150 (69%)	281 (70%		0	281 (100%)	

[#]Complete remission 1 (CR1) included MCL (n=19); peripheral T cell (n=18); FL (n=7); DLBCL (n=9), composite lymphoma (n=2).

[&]PIF included FL (n=19); DLBCL (n=18); immunoblastic NHL (n=4); T cell lymphoma and other (n=27); MCL (n=7)

[$]15 KIR genes typed: 2DL1, 2DL2, 2DL3, 2DL4, 2DL5, 2DP1, 2DS1, 2DS2, 2DS3, 2DS4, 2DS5, 3DL1, 3DL2, 3DL3, 3DP1, 3DS1,

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Table 2

Multivariate analysis for PFS and relapse for patients undergoing 10/10-matched unrelated donor HCT for NHL.

Variable	Hazard ratio	95% confidence intervals	p-value
Progression free survival			
KIR genotype			0.0075
KIR A/A	1.0		
KIR B/x	0.71	0.55–0.91	
Disease status			0.002
Chemo sensitive	1.0	0.87–2.83	
Chemo resistant	1.41	0.84–2.35	
Complete Remission	0.74	0.43–1.27	
Lymphoma subset			0.014
Follicular lymphoma	1.0		
Diffuse large B cell	1.68	1.14–2.48	
Mantle cell lymphoma	1.61	1.12–2.3	
T cell lymphoma +other	1.62	1.16–2.3	
Interval from Dx to HCT			0.013
≤ 1.5 year	1.0		
>1.5 year	0.73	0.56–0.94	
Relapse rate			
KIR genotype			0.018
KIR A/A	1.0		
KIR B/x	0.63	0.43–0.92	
Disease status			0.039
Chemo sensitive	1.0		
Chemo resistant	1.08	0.53–2.2	
Complete remission	0.51	0.24–1.09	
T cell depletion in vivo			0.0037
No	1.0		
Yes	1.75	1.20–2.55	
Interval from Dx to HCT			
≤ 1.5 year	1.0		0.0003
>1.5 year	0.49	0.33–0.72	