

KIR B donors improve the outcome for AML patients given reduced intensity conditioning and unrelated donor transplantation

Supplemental Tables 1-3

Supplemental Table 1. Previous vs. Current Cohort. Demographics and Outcomes	JI Cohort 1988-2009	Current Cohort 2010-2016	
Conditioning Intensity	MAC (100%)* N = 1532	RIC (40%) N = 1083	MAC (60%)** N = 1579
Recipient Age (median) % over age 60	38 3%	64 71%	49 18%
Male (%)	55%	49%	52%
HLA allele match 8/8 (%) 7/8 (%) >1 allele mismatch (%)	92% 7% 1%	87% 13% 0%	84% 16% >1%
Poor Risk Cytogenetics	25%	19%	19%
KPS <90	32%	45%	30%
Graft Source: PBSC (%)	47%	92%	81%
Donor Age (median)	34	28	29
Advanced Disease status (%)	32%	1%	2%
Recipient CMV Seropositive (%)	54%	65%	67%
GVHD Prophylaxis TAC +/- others (%) CSA +/- others (%)	51% 46%	83% 17%	92% 8%
KIR B/x Donors (%)	67%	69%	69%
Follow-up of Survivors Median (range) months	60 (3-240)	38 (6-99)	44 (2-98)
Outcomes			
Overall Survival at 5 years (95% CI)	32 (30-34)	39 (36-43)	49 (46-52)
DFS at 5 years (95% CI)	29 (26-31)	35 (32-39)	46 (43-38)
Relapse at 3 years (95% CI)	34 (32-37)	34 (31-36)	29 (27-31)
NRM at 1 year (95% CI)	27 (25-29)	16 (14-18)	15 (13-16)
Donor KIR Bx association with outcomes in C1/x recipients	HR KIR Bx vs. AA*	HR KIR Bx vs. AA	HR KIR Bx vs. AA**

Relapse	0.70 (0.56-0.87) P=0.0018	0.78 (0.62-0.98) P=0.037	0.96 (0.78,1.19) P=0.73
DFS	0.78 (0.67-0.91) P=0.0015	0.85 (0.72-0.99) P=0.04	1.07 (0.89,1.29) P=0.46

*from Cooley, et al. (10)

**in current MAC recipients no influence of KIR genotype was seen, in C1/x or others.

Supplemental Table 2. Multivariate Analysis

2A. Reduced Intensity Conditioning						
Overall Survival						
Factor	N	Event	HR	HR Low	HR Upper	P
Donor KIR haplotype	*0.069
AA	336	197	1.00	.	.	.
BX	730	388	0.85	0.71	1.01	0.069
HLA matched alleles	0.0056
7/8	146	100	1.00	.	.	.
8/8	920	485	0.69	0.53	0.90	0.0056
Cytogenetics	*0.050
Disease status	*0.030
Early	838	447	1.00	.	.	.
Intermediate	219	130	1.19	0.98	1.44	0.079
Advanced	9	8	2.72	1.13	6.54	0.025
Recipient age	0.089
Recipient CMV status	0.052
GVHD prophylaxis	*0.037
ATG/ alemtuzumab	0.84
No ATG/ alemtuzumab	619	334	1.00	.	.	.
ATG alone	404	225	1.03	0.83	1.29	0.75
alemtuzumab alone	43	26	1.13	0.70	1.83	0.62
HLA-DP mismatch	0.49
Fully matched	178	109	1.00	.	.	.
Mismatch	874	307	1.12	0.89	1.41	0.34

2B. Myeloablative Conditioning						
Overall Survival						
Factor	N	Event	HR	HR Low	HR Upper	P
Donor KIR haplotype	*0.61
AA	491	229	1.00	.	.	.
BX	1066	504	1.05	0.88	1.24	0.61
HLA matched alleles	0.0007
7/8	245	134	1.00	.	.	.
8/8	1312	599	0.71	0.58	0.87	0.0007
Cytogenetics	*0.0023
Disease status	*<.0001
Early	1152	529	1.00	.	.	.
Intermediate	373	181	1.17	0.99	1.38	0.058
Advanced	32	23	2.52	1.71	3.71	<.0001
Recipient age	0.0014
Recipient CMV status	0.14
GVHD prophylaxis	*<.0001
ATG/ alemtuzumab	0.044
No ATG/ alemtuzumab	936	443	1.00	.	.	.
ATG alone	590	275	1.01	0.85	1.18	0.95
alemtuzumab alone	31	15	0.44	0.23	1.85	0.015
HLA-DP mismatch	0.52
Fully matched	265	141	1.00	.	.	.
Mismatch	1270	593	0.97	0.80	1.18	0.77

Missing	13	9	1.29	0.63	2.65	0.49
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Missing	19	10	0.96	0.47	1.96	0.91
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Factor	N	Event	HR	HR Low	HR Upper	P
Donor KIR centromeric regions	0.20
AA	485	279	1.00	.	.	.
AB	483	259	0.87	0.73	1.03	0.1030
BB	98	47	0.80	0.58	1.10	0.1613
HLA matched alleles	0.0085
7/8	146	100	1.00	.	.	.
8/8	920	485	0.70	0.53	0.91	0.0085
Cytogenetics	0.046
Disease status	*0.027
Early	838	447	1.00	.	.	.
Intermediate	219	130	1.20	0.99	1.45	0.0633
Advanced	9	8	2.72	1.12	6.63	0.0273
Recipient age	0.11
Recipient CMV status	0.071
GVHD prophylaxis	*0.036
ATG/ alemtuzumab	0.82
No ATG/ alemtuzumab	619	334	1.00	.	.	.
ATG alone	404	225	1.03	0.83	1.27	0.82
alemtuzumab alone	43	26	1.15	0.72	1.84	0.56
HLA-DP Mismatch	0.47
Fully matched	178	109	1.00	.	.	.
Mismatch	874	307	1.12	0.89	1.40	0.34
Missing	13	9	1.31	0.65	2.61	0.45
Stratified variables: Karnofsky Performance score						

Factor	N	Event	HR	HR Low	HR Upper	P
Donor KIR centromeric regions	0.96
AA	747	358	1.00	.	.	.
AB	647	300	0.99	0.83	1.19	0.9481
BB	163	75	1.03	0.82	1.29	0.8126
HLA matched alleles	0.0007
7/8	245	134	1.00	.	.	.
8/8	1312	599	0.71	0.58	0.87	0.0007
Cytogenetics	0.0022
Disease status	*<.0001
Early	1152	529	1.00	.	.	.
Intermediate	373	181	1.17	0.99	1.38	0.0627
Advanced	32	23	2.54	1.72	3.75	0.0000
Recipient age	*0.0013
Recipient CMV status	0.14
GVHD prophylaxis	*<.0001
ATG/ alemtuzumab	*0.038
No ATG/ alemtuzumab	936	443	1.00	.	.	.
ATG alone	590	275	1.01	0.86	1.18	0.92
alemtuzumab alone	31	15	0.44	0.23	0.84	0.0023
HLA-DP mismatch	0.96
Fully matched	268	141	1.00	.	.	.
Mismatch	1270	593	0.97	0.80	1.18	0.79
Missing	19	10	0.96	0.47	1.96	0.91
Stratified variables: Karnofsky Performance score						

Adjusted multivariate analysis for the endpoints shown stratified as indicated.

*Represents overall p value for the variable group; **Bolded p values** are independently significant $p < 0.05$

Supplemental Table 3 Individual Donor KIR B Genes: Influence on Outcome.

Table 3A. Donor KIR B genes and Relapse, DFS and Survival

RIC					MAC				
Relapse					Relapse				
Donor KIR Group	N	RR	95% CI	P	Donor KIR Group	N	RR	95% CI	P
KIR A/A	334	1			KIR A/A	490	1		
KIR B/x with 2DS1+	381	0.75	(0.60-0.95)	0.016	KIR B/x with 2DS1+	601	0.96	(0.77-1.21)	0.74
KIR B/x with 2DS2+	558	0.73	(0.57-0.93)	0.010	KIR B/x with 2DS2+	780	0.94	(0.77-1.14)	0.51
KIR B/x with 2DS3+	287	0.61	(0.47-0.79)	0.0001	KIR B/x with 2DS3+	412	1.00	(0.78-1.28)	0.99
KIR B/x with 2DS5+	292	0.77	(0.61-0.98)	0.037	KIR B/x with 2DS5+	485	1.00	(0.80-1.24)	0.97
KIR B/x with 2DL2+	554	0.72	(0.56-0.93)	0.010	KIR B/x with 2DL2+	775	0.93	(0.77-1.13)	0.48
KIR B/x with 2DL5+	489	0.70	(0.56-0.87)	0.0016	KIR B/x with 2DL5+	757	0.97	(0.79-1.19)	0.76
KIR B/x with 3DS1+	369	0.75	(0.60-0.95)	0.016	KIR B/x with 3DS1+	589	1.03	(0.83-1.28)	0.77
DFS					DFS				
Donor KIR Group	N	RR	95% CI	P	Donor KIR Group	N	RR	95% CI	P
KIR A/A	334	1			KIR A/A	489	1		
KIR B/x with 2DS1+	381	0.87	(0.73-1.03)	0.10	KIR B/x with 2DS1+	600	1.06	(0.90-1.26)	0.47
KIR B/x with 2DS2+	557	0.80	(0.66-0.97)	0.020	KIR B/x with 2DS2+	778	1.07	(0.90-1.26)	0.44
KIR B/x with 2DS3+	287	0.76	(0.62-0.92)	0.0054	KIR B/x with 2DS3+	412	1.09	(0.89-1.33)	0.42
KIR B/x with 2DS5+	292	0.86	(0.72-1.03)	0.10	KIR B/x with 2DS5+	484	1.05	(0.89-1.24)	0.58
KIR B/x with 2DL2+	554	0.80	(0.66-0.97)	0.025	KIR B/x with 2DL2+	773	1.08	(0.91-1.27)	0.39
KIR B/x with 2DL5+	489	0.83	(0.69-0.99)	0.037	KIR B/x with 2DL5+	756	1.07	(0.91-1.25)	0.40
KIR B/x with 3DS1+	369	0.85	(0.71-1.01)	0.066	KIR B/x with 3DS1+	588	1.11	(0.94-1.31)	0.20

Supplemental Table 3 A.

RIC					MAC				
Survival					Survival				

Donor KIR Group	N	RR	95% CI	P	Donor KIR Group	N	RR	95% CI	P
KIR A/A	336	1			KIR A/A	491	1		
KIR B/x with 2DS1+	381	0.91	(0.75-1.10)	0.31	KIR B/x with 2DS1+	605	1.02	(0.86-1.22)	0.80
KIR B/x with 2DS2+	557	0.82	(0.67-1.00)	0.055	KIR B/x with 2DS2+	784	1.05	(0.88-1.26)	0.58
KIR B/x with 2DS3+	287	0.81	(0.65-1.01)	0.056	KIR B/x with 2DS3+	414	1.03	(0.83-1.28)	0.78
KIR B/x with 2DS5+	292	0.88	(0.72-1.09)	0.24	KIR B/x with 2DS5+	488	1.02	(0.84-1.23)	0.85
KIR B/x with 2DL2+	554	0.82	(0.67-1.01)	0.058	KIR B/x with 2DL2+	779	1.06	(0.88-1.28)	0.52
KIR B/x with 2DL5+	489	0.86	(0.71-1.05)	0.13	KIR B/x with 2DL5+	762	1.03	(0.87-1.22)	0.75
KIR B/x with 3DS1+	369	0.89	(0.73-1.08)	0.24	KIR B/x with 3DS1+	594	1.06	(0.89-1.27)	0.51

Bolded p values are independently significant $p < 0.05/7 = 0.007$

Table 3B. Donor KIR B genes in Recipients with C1/x and Outcome

RIC with Recipient C1/x					MAC with Recipient C1/x				
Relapse					Relapse				
Donor KIR Group	N	RR	95% CI	P	Donor KIR Group	N	RR	95% CI	P
KIR A/A	302	1			KIR A/A	405	1		
KIR B/x with 2DS1+	329	0.72	(0.56-0.94)	0.014	KIR B/x with 2DS1+	512	0.94	(0.73-1.23)	0.66
KIR B/x with 2DS2+	486	0.74	(0.57-0.95)	0.020	KIR B/x with 2DS2+	665	0.95	(0.76-1.19)	0.64
KIR B/x with 2DS3+	240	0.60	(0.45-0.78)	0.0002	KIR B/x with 2DS3+	357	0.93	(0.68-1.25)	0.62
KIR B/x with 2DS5+	250	0.76	(0.58-0.99)	0.043	KIR B/x with 2DS5+	413	1.01	(0.77-1.31)	0.95
KIR B/x with 2DL2+	482	0.73	(0.57-0.95)	0.020	KIR B/x with 2DL2+	662	0.95	(0.75-1.18)	0.63
KIR B/x with 2DL5+	418	0.70	(0.56-0.88)	0.0021	KIR B/x with 2DL5+	646	0.93	(0.73-1.20)	0.59
KIR B/x with 3DS1+	317	0.74	(0.57-0.95)	0.018	KIR B/x with 3DS1+	502	1.00	(0.77-1.29)	0.99
DFS					DFS				
Donor KIR Group	N	RR	95% CI	P	Donor KIR Group	N	RR	95% CI	P
KIR A/A	302	1			KIR A/A	404	1		

KIR B/x with 2DS1+	329	0.87	(0.73-1.03)	0.11		KIR B/x with 2DS1+	511	1.04	(0.84-1.27)	0.73
KIR B/x with 2DS2+	486	0.80	(0.66-0.97)	0.027		KIR B/x with 2DS2+	663	1.08	(0.89-1.32)	0.43
KIR B/x with 2DS3+	240	0.75	(0.60-0.93)	0.0081		KIR B/x with 2DS3+	357	1.06	(0.83-1.35)	0.64
KIR B/x with 2DS5+	250	0.88	(0.73-1.07)	0.20		KIR B/x with 2DS5+	412	1.05	(0.86-1.30)	0.62
KIR B/x with 2DL2+	482	0.80	(0.66-0.98)	0.031		KIR B/x with 2DL2+	660	1.09	(0.90-1.33)	0.38
KIR B/x with 2DL5+	418	0.84	(0.70-1.01)	0.057		KIR B/x with 2DL5+	645	1.05	(0.87-1.28)	0.62
KIR B/x with 3DS1+	317	0.86	(0.72-1.02)	0.085		KIR B/x with 3DS1+	501	1.07	(0.88-1.32)	0.50
Survival						Survival				
Donor KIR Group	N	RR	95% CI	P		Donor KIR Group	N	RR	95% CI	P
KIR A/A	304	1				KIR A/A	406		1	
KIR B/x with 2DS1+	329	0.88	(0.72-1.06)	0.18		KIR B/x with 2DS1+	515	1.02	(0.82-1.26)	0.86
KIR B/x with 2DS2+	486	0.80	(0.65-0.98)	0.029		KIR B/x with 2DS2+	667	1.08	(0.88-1.32)	0.47
KIR B/x with 2DS3+	240	0.75	(0.59-0.96)	0.022		KIR B/x with 2DS3+	357	1.03	(0.80-1.32)	0.83
KIR B/x with 2DS5+	250	0.87	(0.70-1.08)	0.20		KIR B/x with 2DS5+	416	1.04	(0.83-1.30)	0.74
KIR B/x with 2DL2+	482	0.79	(0.64-0.97)	0.025		KIR B/x with 2DL2+	664	1.09	(0.88-1.35)	0.43
KIR B/x with 2DL5+	418	0.83	(0.68-1.02)	0.075		KIR B/x with 2DL5+	649	1.03	(0.84-1.27)	0.75
KIR B/x with 3DS1+	317	0.86	(0.71-1.05)	0.15		KIR B/x with 3DS1+	505	1.07	(0.86-1.32)	0.56

Bolded p values are independently significant $p < 0.05/7 = 0.007$