Supplemental Material

Supplemental Table S1

KIR2DS4 genotype

Classifier	N pos AML pts (N total AML pts)	Portion of pos AML pts	N pos control (N total control)	Portion of pos control	P-value	Adjusted p-value
KIR2DS4 **full-length and truncated version**						
KIR2DS4 f/f	266 (1689)	0.157	7710 (51890)	0.149	0.328	1.000
KIR2DS4 f/v	310 (1689)	0.184	10546 (51890)	0.203	0.051	0.204
KIR2DS4 v/v	893 (1689)	0.559	27121 (51890)	0.523	0.642	1.000
Others°	220 (1689)	0.130	6513 (51890)	0.126	0.589	1.000

° … ambiguous sequencing results (no allele information, new alleles, …)

Supplemental Table S2

See excel file

Supplemental Table S3

KIR-ligand groups: HLA-class I ligands C1, C2, Bw4-80I, and Bw4-80T

Classifier	N pos AML pts (N total AML pts)	Portion of pos AML pts	N pos control (N total control)	Portion of pos control	P-value	Adjusted p-value
HLA-C ligands for *KIR2DL1, 2DL2, 2DL3* | overall chi square test p-value = 0.012						
C1/C1	608 (1678)	0.362	19838 (50312)	0.394	0.009	0.027
C1/C2	833 (1678)	0.496	24241 (50312)	0.482	0.249	0.746
C2/C2	237 (1678)	0.141	6233 (50312)	0.124	0.037	0.112
HLA-B ligands for *KIR3DL1* | overall chi square test p-value = 0.042						
Bw4-80I/Bw4-80I	64 (1685)	0.038	1274 (50999)	0.025	0.001	0.007
Bw4-80I/Bw4-80T	113 (1685)	0.067	3510 (50999)	0.069	0.816	1.000
Bw4-80I/Bw6	331 (1685)	0.196	10296 (50999)	0.202	0.605	1.000
Bw4-80T/Bw4-80T	77 (1685)	0.046	2311 (50999)	0.045	0.988	1.000
Bw4-80T/Bw6	454 (1685)	0.269	13624 (50999)	0.267	0.856	1.000
Bw6/Bw6	646 (1685)	0.383	19984 (50999)	0.392	0.499	1.000

Supplemental Table S4

KIR/KIR-ligand counts and scores tested as ordinal category or dichotomized.

Classifier	N pos AML pts (N total AML pts)	Portion of pos AML pts	N pos control (N total control)	Portion of pos control	P-value	Adjusted p-value
inhibitory KIR/KIR-ligand count (Boelen *et al.*)						
1	229 (1676)	0.137	7743 (49898)	0.155	0.042	0.169
2	615 (1676)	0.367	17644 (49898)	0.354	0.272	1.000
3	588 (1676)	0.351	17915 (49898)	0.359	0.508	1.000
4	244 (1676)	0.146	6596 (49898)	0.132	0.120	0.481
inhibitory KIR/KIR-ligand score (Boelen *et al.*)						
0.5	2 (1676)	0.001	33 (49898)	0.001	0.729	1.000
0.75	165 (1676)	0.098	5742 (49898)	0.115	0.039	0.390
1.0	62 (1676)	0.037	1968 (49898)	0.039	0.657	1.000
1.5	30 (1676)	0.018	749 (49898)	0.015	0.394	1.000
1.75	415 81676)	0.247	12665 (49898)	0.254	0.585	1.000
2.0	170 (1676)	0.101	4230 (49898)	0.085	0.018	0.184
2.5	90 (1676)	0.054	2356 (49898)	0.047	0.242	1.000
2.75	460 (1676)	0.274	14572 (49898)	0.292	0.126	1.000
3.0	38 (1676)	0.022	987 (49898)	0.020	0.455	1.000
3.75	244 (1676)	0.145	6596 (49898)	0.132	0.120	1.000
Inhibitory KIR/KIR-ligand matches (Rafei *et al.*) | overall chi square test p-value = 0.355						
Inhibitory Favorable[$]	629 (1581)	0.398	17283 (42171)	0.410	0.355	
Inhibitory Unfavorable	952 (1581)	0.602	24888 (42171)	0.590		
Activating KIR/KIR-ligand matches[§] (Rafei *et al.*) | overall chi square test p-value = 0.128						
Activating Favorable[#]	618 (1584)	0.390	17274 (42171)	0.410	0.128	
Activating Unfavorable	966 (1584)	0.610	24897 (42171)	0.590		

$ … <3 inhibitory KIR/KIR-ligand matches; # … ≥1 activating KIR/KIR-ligand match;

Supplemental Table S5

KIR/KIR-ligand counts and scores tested as a continuous variable.

Coefficient	Estimate (log odds change)	N total AML pts	N total control	P-value
Continuous inhibitory KIR/KIR-ligand count including KIR3DL1 (Boelen _et al._)				
Functional iKIR Count (continuous)	-0.045	1679	49898	0.094
Inhibitory Score (continuous)	-0.049	1679	49915	0.076
Additive inhibitory / activating KIR/KIR-Ligand Model (Krieger et al.)				
wKIR Score (continuous)	-0.034	1581	42171	0.478
ImKIR-Score (continuous)	-0.045	1581	42177	0.298

Continuous models by Boelen _et al._ and Krieger _et al._, individually fitted logistic regression models with patient / control label as response, and the score or count as the single continuous explanatory variable.

Supplemental Table S6.

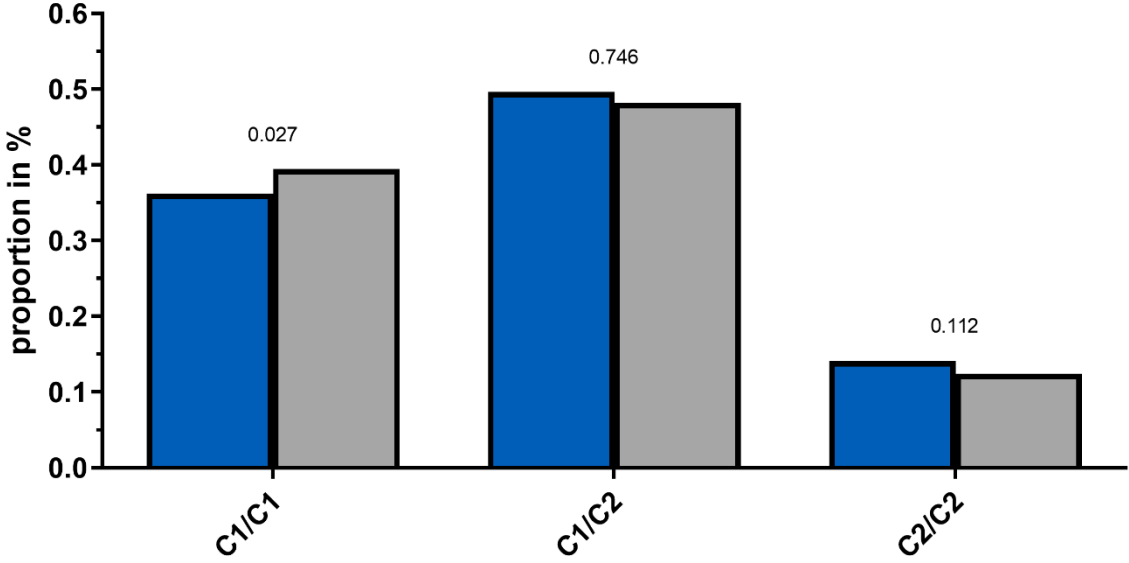KIRs and their ligands considered for the calculation of the respective model.

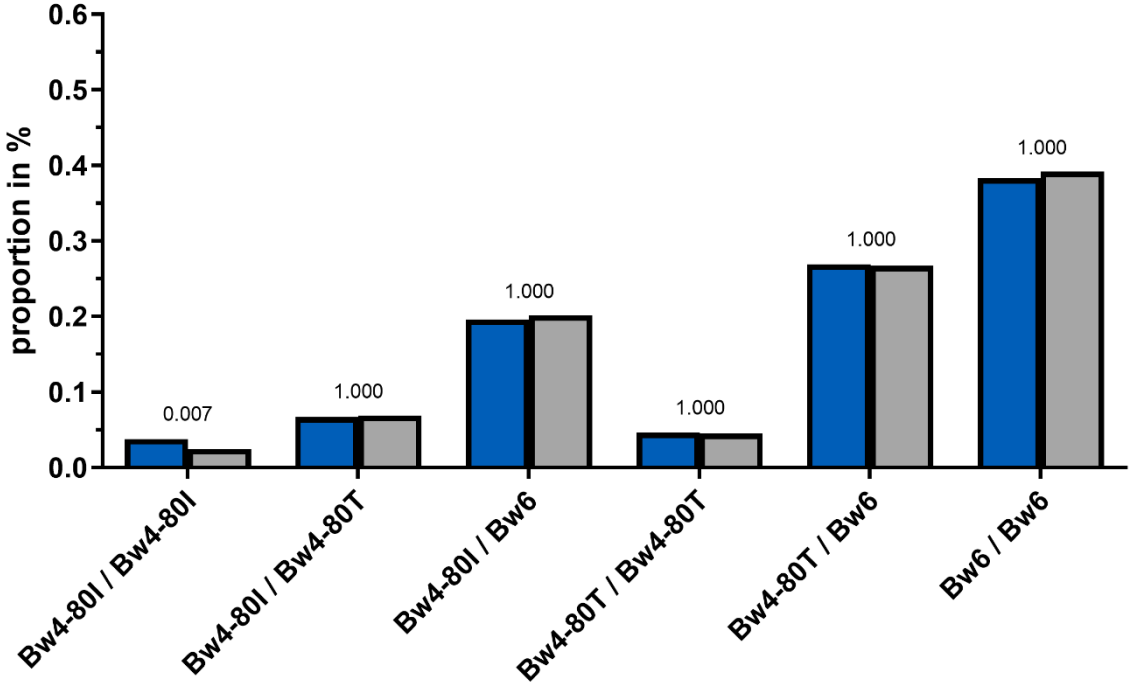|	KIR/KIR-ligand model published by…					
	Venstrom *et al.*, NEJM, 2012	Boudreau *et al.*, J Immunol, 2016	Boudreau *et al.*, JCO, 2017	Boelen *et al.*, Sci Immunol, 2018	Rafei *et al.*, J Clin Oncol. 2019	Krieger *et al.*, BBMT, 2019
Inhibitory KIR	KIR ligand					
KIR2DL1				C2	C2	C2
KIR2DL2				C1 (strong) C2 (weak)	C1, B46:01, B73:01	C1
KIR2DL3				C1	C1, B46:01, B73:01	C1
KIR3DL1		Bw4 80-I/T	Bw4 80-I/T	Bw4	Bw4	Bw4
KIR3DL2					A3, A11	A3, A11
Activating KIR	KIR ligand					
KIR2DS1	C2/C2 (hyporesp.) C1+ (responsive)		C2/C2 vs C1+		C02:02, C04:01, C05:01, C06:02, C17:01, C18:02	C2
KIR2DS2					A11:01	A11
KIR2DS4					C01:02, C02:02, C05:01, C14:02, C16:01, A11:01, A11:02	A11
KIR2DS5						C2
KIR3DS1					B27:05, Bw4 80-T	

Supplemental Figure S1

Frequencies of *KIR2DS4* genotypes. Blue columns are displaying frequencies of patients with AML and gray columns are displaying the control group. Adjusted p-values are depicted above the pairs of columns. f … full-length; v…truncated variant
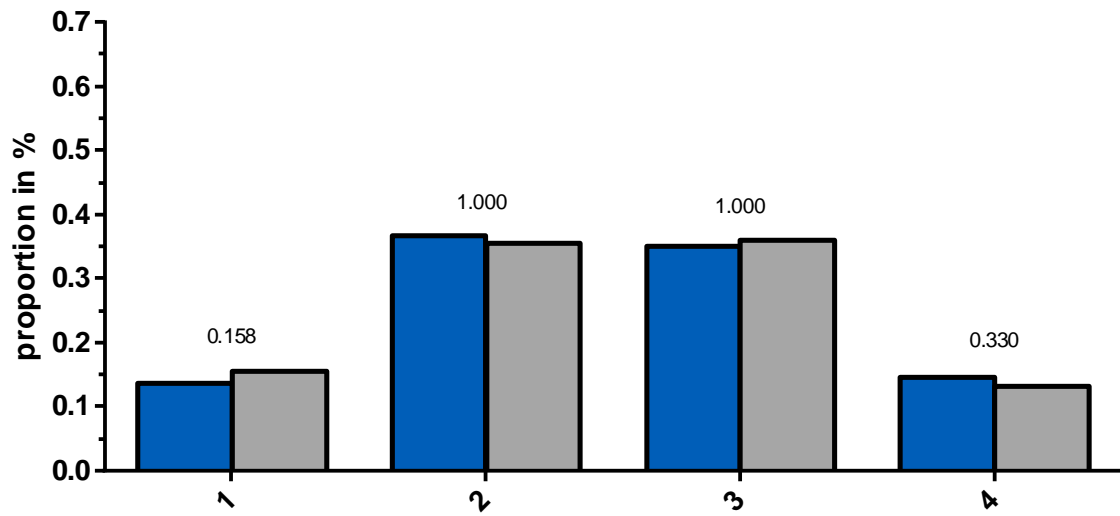
Supplemental Figure S2

Frequencies of *HLA-C1/C2* KIR ligands. Blue columns are displaying frequencies of patients with AML and gray columns are displaying the control group. Adjusted p-values are depicted above the pairs of columns.
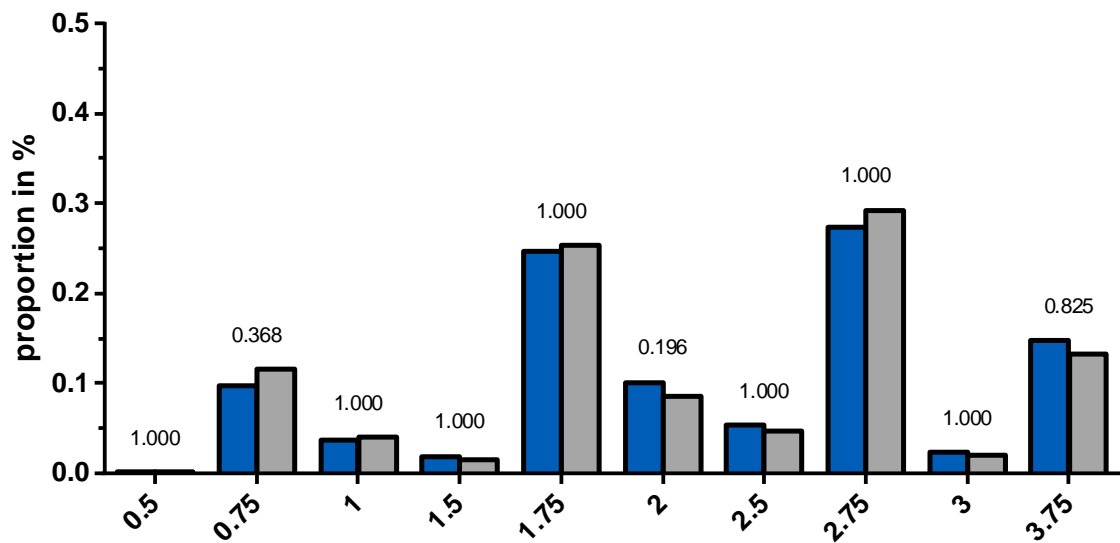
Supplemental Figure S3

Frequencies of *HLA-Bw4/Bw6* KIR-ligands. Blue columns are displaying frequencies of patients with AML and gray columns are displaying the control group. Adjusted p-values are depicted above the pairs of columns.
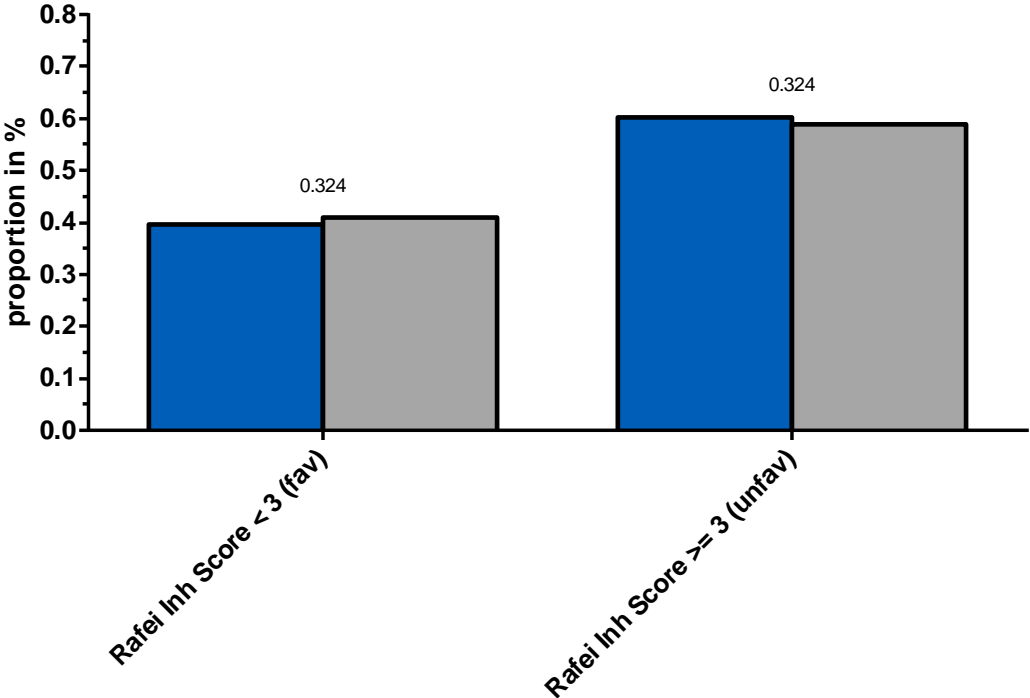
Supplemental Figure S4

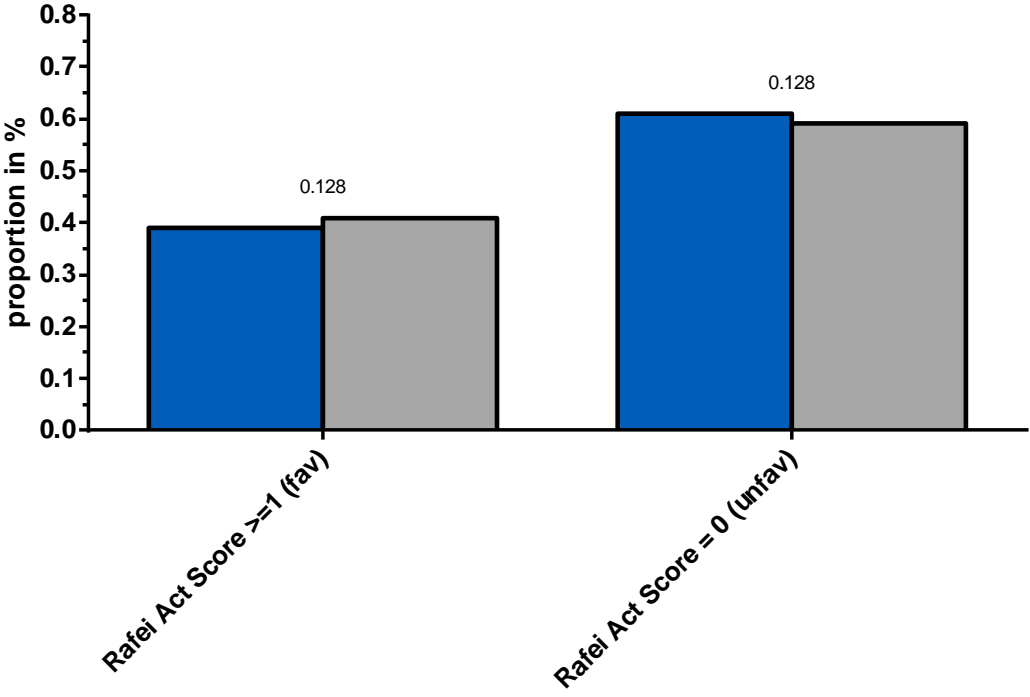A) Inhibitory KIR/KIR-ligand count (Boelen *et al.*)

B) Inhibitory KIR/KIR-ligand score (Boelen *et al.*)

C) Inhibitory KIR/KIR-ligand matches (Rafei *et al.*)

D) Activating KIR/KIR-ligand matches (Rafei *et al.*)

Frequencies of scores according to four additive KIR/KIR-ligand models. Inhibitory KIR/KIR-ligand count (A), and inhibitory KIR/KIR-ligand score (B), both according to Boelen *et al*. (1), including KIR3DL1/HLA-Bw4 and considering KIR2DL2 and KIR2DL3 separately. Inhibitory (C) and activating (D) score by Rafei *et al*. (2) with an unfavorable inhibitory score defined by the presence of ≥3 inhibitory KIR/KIR-ligand matches, and an unfavorable activating score defined by the absence of activating KIR/KIR-ligand matches, the truncated version of KIR2DS4 is not considered as an activating KIR. Blue columns are displaying frequencies of patients with AML and gray columns are displaying the control group. Adjusted p-values are depicted above the pairs of columns.

References

1.   Boelen L, Debebe B, Silveira M, Salam A, Makinde J, Roberts CH, et al. Inhibitory killer cell immunoglobulin-like receptors strengthen CD8+ T cell–mediated control of HIV-1, HCV, and HTLV-1. Sci Immunol. 2018;3:eaao2892.

2.   Rafei H, Fernández-Viña M, Carmazzi Y, Moore B, Willis D, Basar R, et al. Role of killer cell immunoglobulin-like receptor (KIR)-ligand interactions to prevent relapse in patients (pts) receiving matched unrelated stem cell transplant (SCT) for acute myeloid leukemia (AML). J Clin Oncol. 2019;