Supplemental Data

Table S1

	Included Patients (N=463)	Excluded Patients (N=427)	P-value	Total (N=890)
Age (y)				
			0.00472	
Median [IQR]	12.1 [5.6, 16]	10.0 [4.8, 15.5]		11.0 [5.1, 15.8]
Treatment center				
MSK	227 (49.0%)	45 (10.5%)	<0.001	272 (30.6%)
PMC	149 (32.2%)	53 (12.4%)		202 (22.7%)
SJCRH	87 (18.8%)	329 (77.0%)		416 (46.7%)
Gender				
Male	274 (59.2%)	230 (53.9%)	0.126	504 (56.6%)
Female	189 (40.8%)	197 (46.1%)		386 (43.4%)
Diagnosis				
ALL	202 (43.6%)	157 (36.8%)	0.0173	359 (40.3%)
AML	171 (36.9%)	187 (43.8%)		358 (40.2%)
MDS	41 (8.9%)	22 (5.2%)		63 (7.1%)
NHL	17 (3.7%)	20 (4.7%)		37 (4.2%)
Other	32 (6.9%)	41 (9.6%)		73 (8.2%)
Cell source				
BM	155 (33.5%)	193 (45.2%)	<0.001	348 (39.1%)
Cord	120 (25.9%)	50 (11.7%)		170 (19.1%)
PBSC	188 (40.6%)	184 (43.1%)		372 (41.8%)
HLA matching				
Matched	245 (52.9%)	182 (42.6%)	<0.001	427 (48.0%)
Mismatched	214 (46.2%)	190 (44.5%)		404 (45.4%)
Missing	4 (0.9%)	55 (12.9%)		59 (6.6%)
Conditioning regimen				
Only chemotherapy	282 (60.9%)	227 (53.2%)	0.0235	509 (57.2%)
Chemotherapy and TBI	181 (39.1%)	200 (46.8%)		381 (42.8%)
Ex vivo TCD				
No	271 (58.5%)	270 (63.2%)	0.194	541 (60.8%)
Yes	192 (41.5%)	156 (36.5%)		348 (39.1%)
Missing	0 (0%)	1 (0.2%)		1 (0.1%)
Serotherapy				
No	212 (45.8%)	222 (52.0%)	0.0747	434 (48.8%)
Yes	251 (54.2%)	205 (48.0%)		456 (51.2%)
Year				
			<0.001	
Median [Min, Max]	2015 [2008, 2019]	2013 [2008, 2019]		2014 [2008, 2019]

Table S1. Demographics and transplant characteristics of included and excluded patients. *P*-values calculated comparing included and excluded patients, using two-sample *t*-test for continuous data and Chi-square test for categorical data.

Supplemental Data

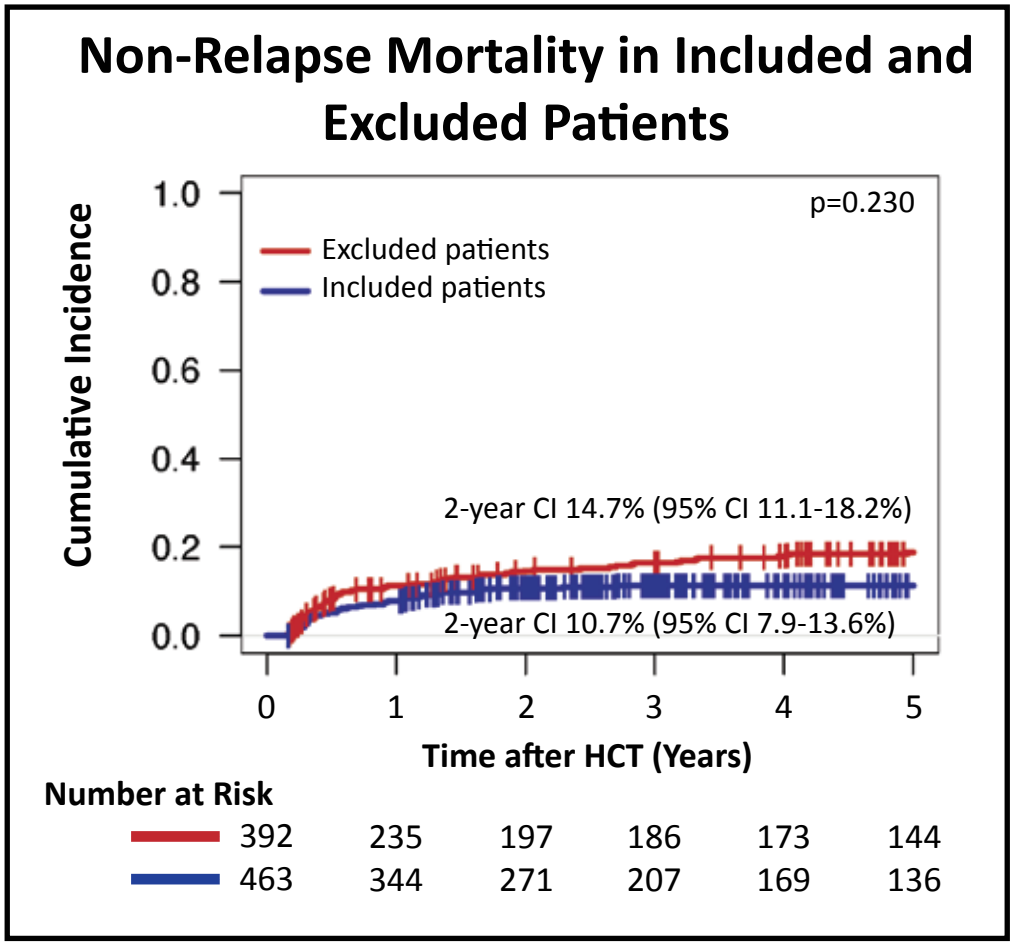

Figure S1. Non-relapse mortality by patients included versus excluded from our CD4 > 50 cells/μL and B Cell > 25 cells/μL analyses. Patients who died before the median time to CD4 and B cell IR were excluded. No significant difference was found between the cumulative incidence of NRM between the two groups (p=0.230 by multivariable Fine-Gray method).

Multivariable Cox Proportional Hazard Analysis for Non-Relapse Mortality

Variable		N	Hazard ratio	p
Age	0–3 years	69	Reference	
	3–10 years	119	0.49 (0.18, 1.37)	0.175
	10–18 years	206	0.80 (0.31, 2.11)	0.657
	>18 years	65	0.23 (0.06, 0.88)	0.031
Diagnosis	ALL	201	Reference	
	AML	169	0.66 (0.32, 1.36)	0.263
	Other	89	0.62 (0.28, 1.36)	0.232
Source	BM	153	Reference	
	Cord	120	0.86 (0.33, 2.19)	0.746
	PBSC	186	2.29 (0.60, 8.78)	0.228
HLA_match	Matched	245	Reference	
	Mismatched	214	1.74 (0.85, 3.57)	0.132
Conditioning	Only chemotherapy	278	Reference	
	Chemo and TBI	181	0.73 (0.37, 1.46)	0.376
TCD_Serotherapy	None	165	Reference	
	Only TCD	44	0.46 (0.08, 2.57)	0.376
	Only Serotherapy	103	1.33 (0.61, 2.91)	0.476
	Both	147	0.34 (0.07, 1.58)	0.170
CD4_Bcell_IR	None	33	Reference	
	Only CD4IR	85	0.26 (0.11, 0.62)	0.002
	Only B–cell IR	72	0.44 (0.18, 1.08)	0.072
	Both CD4 and B–cell IR	269	0.06 (0.03, 0.16)	<0.001
HCT_Year	Before 2015	225	Reference	
	2015 or after	234	0.54 (0.28, 1.03)	0.060

Variable		N	Hazard ratio	p
Age	0–3 years	71	Reference	
	3–10 years	120	0.43 (0.16, 1.14)	0.088
	10–18 years	207	0.64 (0.27, 1.55)	0.325
	>18 years	65	0.19 (0.05, 0.69)	0.012
CD4_Bcell_IR	None	33	Reference	
	Only CD4IR	86	0.30 (0.13, 0.66)	0.003
	Only B–cell IR	72	0.40 (0.18, 0.88)	0.023
	Both CD4 and B–cell IR	272	0.07 (0.03, 0.16)	<0.001
HCT_Year	Before 2015	228	Reference	
	2015 or after	235	0.64 (0.36, 1.14)	0.128

Table S2. Multivariable Cox Proportional Hazard Analysis for NRM. CD4 and B cell immune reconstitution were found to be predictors of decreased risk of NRM in multivariable analyses (left panel). Age above 18 years was also found to be predictive of NRM in this cohort. Since there were 54 events of NRM, to control for overfitting, analyses were also run including less covariates (see methods), leading to similar results (right panel).

Supplemental Data

Multivariable Cox Proportional Hazard Analysis for Relapse (Full Cohort)

Variable		N	Hazard ratio	p
Age	0–3 years	69	Reference	
	3–10 years	119	0.71 (0.38, 1.31)	0.27
	10–18 years	206	0.89 (0.50, 1.58)	0.68
	>18 years	65	0.32 (0.13, 0.81)	0.02
Diagnosis	ALL	201	Reference	
	AML	169	1.24 (0.77, 2.02)	0.38
	Other	89	0.80 (0.44, 1.47)	0.48
Source	BM	153	Reference	
	Cord	120	1.24 (0.67, 2.29)	0.50
	PBSC	186	1.38 (0.54, 3.50)	0.50
HLA_match	Matched	245	Reference	
	Mismatched	214	0.89 (0.55, 1.45)	0.64
Conditioning	Only chemotherapy	278	Reference	
	Chemo and TBI	181	0.99 (0.59, 1.66)	0.96
TCD_Serotherapy	None	165	Reference	
	Only TCD	44	0.87 (0.27, 2.80)	0.82
	Only Serotherapy	103	1.12 (0.67, 1.90)	0.66
	Both	147	0.84 (0.32, 2.25)	0.73
CD4_Bcell_IR	None	33	Reference	
	Only CD4IR	85	0.48 (0.18, 1.30)	0.15
	Only B–cell IR	72	0.57 (0.21, 1.56)	0.27
	Both CD4 and B–cell IR	269	0.76 (0.32, 1.81)	0.54
HCT_Year	Before 2015	225	Reference	
	2015 or after	234	0.63 (0.41, 0.97)	0.03

Variable		N	Hazard ratio	p
Age	0–3 years	69	Reference	
	3–10 years	119	0.68 (0.38, 1.23)	0.21
	10–18 years	206	0.87 (0.51, 1.49)	0.62
	>18 years	65	0.32 (0.13, 0.76)	0.01
Diagnosis	ALL	201	Reference	
	AML	169	1.28 (0.83, 1.95)	0.26
	Other	89	0.81 (0.45, 1.44)	0.46
HLA_match	Matched	245	Reference	
	Mismatched	214	0.97 (0.65, 1.45)	0.88
CD4_Bcell_IR	None	33	Reference	
	Only CD4IR	85	0.50 (0.19, 1.33)	0.17
	Only B–cell IR	72	0.58 (0.22, 1.55)	0.27
	Both CD4 and B–cell IR	269	0.78 (0.33, 1.84)	0.57
HCT_Year	Before 2015	225	Reference	
	2015 or after	234	0.63 (0.42, 0.94)	0.02

Table S3. Multivariable Cox Proportional Hazard Analysis for Relapse in Full Cohort. CD4 and B cell immune reconstitution were not found to be a predictor of relapse in the full cohort in multivariable analyses. Only age > 18 years and transplant after 2015 were found to be predictive factors for relapse (left panel). Since there were 116 events of relapse, to control for overfitting, analyses were also run including less covariates (see methods), leading to similar results (right panel).

Multivariable Cox Proportional Hazard Analysis for Relapse (AML)

Variable		N	Hazard ratio	p
Age	0–3 years	31	Reference	
	3–10 years	35	0.66 (0.24, 1.85)	0.429
	10–18 years	80	0.86 (0.37, 1.99)	0.722
	>18 years	23	0.25 (0.05, 1.26)	0.093
Status	CR1	94	Reference	
	CR2 or more	58	1.11 (0.52, 2.39)	0.791
	Active disease	17	3.58 (1.46, 8.78)	0.005
Source	BM	34	Reference	
	Cord	59	1.12 (0.40, 3.12)	0.830
	PBSC	76	3.65 (0.90, 14.89)	0.071
HLA_match	Matched	76	Reference	
	Mismatched	93	1.30 (0.62, 2.71)	0.492
Conditioning	Only chemotherapy	132	Reference	
	Chemo and TBI	37	1.05 (0.29, 3.80)	0.941
TCD_Serotherapy	None	63	Reference	
	Only TCD	23	0.43 (0.07, 2.87)	0.387
	Only Serotherapy	30	2.48 (1.02, 6.00)	0.045
	Both	53	0.31 (0.07, 1.38)	0.124
CD4_Bcell_IR	None	9	Reference	
	Only CD4IR	29	0.21 (0.04, 1.10)	0.065
	Only B–cell IR	24	0.27 (0.06, 1.21)	0.087
	Both CD4 and B–cell IR	107	0.24 (0.06, 0.92)	0.038
HCT_Year	Before 2015	74	Reference	
	2015 or after	95	0.35 (0.16, 0.78)	0.011

Variable		N	Hazard ratio	p
Status	CR1	95	Reference	
	CR2 or more	59	1.16 (0.58, 2.35)	0.67
	Active disease	17	5.37 (2.41, 11.96)	<0.001
CD4_Bcell_IR	None	9	Reference	
	Only CD4IR	29	0.22 (0.05, 0.96)	0.04
	Only B–cell IR	24	0.26 (0.06, 1.12)	0.07
	Both CD4 and B–cell IR	109	0.25 (0.07, 0.88)	0.03
HCT_Year	Before 2015	75	Reference	
	2015 or after	96	0.43 (0.22, 0.84)	0.01

Table S4. Multivariable Cox Proportional Hazard Analysis for Relapse in AML Patients. Combined CD4 and B cell immune reconstitution were found to be a predictor of Relapse in AML patients in multivariable analyses. Active disease and transplant before 2015 were also found to be predictive for increased risk of relapse (left panel). Since there were 46 events of relapse, to control for overfitting, analyses were also run including less covariates (see methods), leading to similar results (right panel), although in this case CD4 immune reconsitution alone was found to be a predictor of relapse as well, indicating that these analyses might need more power and a larger AML cohort to confirm this effect.

Supplemental Data

Multivariable Cox Proportional Hazard Analysis for Relapse (ALL)

Variable		N	Hazard ratio	p
Age	0–3 years	27	Reference	
	3–10 years	63	0.78 (0.24, 2.50)	0.677
	10–18 years	81	0.93 (0.28, 3.02)	0.899
	>18 years	28	0.51 (0.12, 2.16)	0.364
Status	CR1	97	Reference	
	CR2 or more	102	3.21 (1.51, 6.83)	0.002
Source	BM	73	Reference	
	Cord	45	2.09 (0.77, 5.62)	0.146
	PBSC	81	1.01 (0.26, 3.98)	0.992
HLA_match	Matched	114	Reference	
	Mismatched	85	0.68 (0.32, 1.43)	0.305
Conditioning	Only chemotherapy	77	Reference	
	Chemo and TBI	122	0.60 (0.30, 1.22)	0.160
TCD_Serotherapy	None	66	Reference	
	Only TCD	19	1.91 (0.35, 10.56)	0.457
	Only Serotherapy	45	0.60 (0.22, 1.62)	0.311
	Both	69	1.95 (0.47, 8.14)	0.361
CD4_Bcell_IR	None	15	Reference	
	Only CD4IR	37	0.75 (0.07, 7.66)	0.808
	Only B–cell IR	33	1.51 (0.18, 13.02)	0.707
	Both CD4 and B–cell IR	114	2.84 (0.36, 22.15)	0.319
HCT_Year	Before 2015	106	Reference	
	2015 or after	93	0.70 (0.36, 1.37)	0.303

Variable		N	Hazard ratio	p
Status	CR1	97	Reference	
	CR2 or more	103	2.78 (1.46, 5.27)	0.002
CD4_Bcell_IR	None	15	Reference	
	Only CD4IR	37	0.86 (0.09, 8.25)	0.894
	Only B–cell IR	33	2.50 (0.31, 20.37)	0.391
	Both CD4 and B–cell IR	115	3.92 (0.53, 28.84)	0.179

Table S5. Multivariable Cox Proportional Hazard Analysis for Relapse in ALL Patients. CD4 and B cell immune reconstitution were not found to be a predictors of Relapse in ALL patients in multivariable analyses. Only complete remission 2 or more was found to be predictive for increased risk of relapse (left panel). Since there were 43 events of relapse, to control for overfitting, analyses were also run including less covariates (see methods), leading to similar results (right panel).

Multivariable Cox Proportional Hazard Analysis for Acute GvHD Grade II-IV

Variable		N	Hazard ratio	p
Age	0–3 years	69	Reference	
	3–10 years	119	0.70 (0.40, 1.23)	0.211
	10–18 years	206	0.50 (0.29, 0.85)	0.010
	>18 years	65	0.44 (0.22, 0.87)	0.019
Diagnosis	ALL	201	Reference	
	AML	169	1.38 (0.88, 2.16)	0.158
	Other	89	0.96 (0.59, 1.58)	0.882
Source	BM	153	Reference	
	Cord	120	1.31 (0.75, 2.27)	0.339
	PBSC	186	3.16 (1.27, 7.87)	0.013
HLA_match	Matched	245	Reference	
	Mismatched	214	1.01 (0.64, 1.59)	0.979
Conditioning	Only chemotherapy	278	Reference	
	Chemo and TBI	181	0.92 (0.58, 1.46)	0.716
TCD_Serotherapy	None	165	Reference	
	Only TCD	44	0.44 (0.15, 1.30)	0.138
	Only Serotherapy	103	0.50 (0.31, 0.82)	0.006
	Both	147	0.15 (0.05, 0.41)	<0.001
CD4_Bcell_IR	None	84	Reference	
	Only CD4IR	74	0.17 (0.11, 0.27)	<0.001
	Only B–cell IR	69	0.10 (0.05, 0.19)	<0.001
	Both CD4 and B–cell IR	232	0.02 (0.01, 0.04)	<0.001
HCT_Year	Before 2015	225	Reference	
	2015 or after	234	0.77 (0.53, 1.13)	0.179

Variable		N	Hazard ratio	p
Age	0–3 years	71	Reference	
	3–10 years	120	0.68 (0.39, 1.18)	0.169
	10–18 years	207	0.50 (0.30, 0.82)	0.006
	>18 years	65	0.44 (0.23, 0.84)	0.013
Diagnosis	ALL	202	Reference	
	AML	171	1.43 (0.97, 2.10)	0.073
	Other	90	0.96 (0.59, 1.55)	0.861
Source	BM	155	Reference	
	Cord	120	1.32 (0.84, 2.09)	0.232
	PBSC	188	2.62 (1.17, 5.84)	0.019
TCD_Serotherapy	None	167	Reference	
	Only TCD	45	0.50 (0.19, 1.32)	0.160
	Only Serotherapy	104	0.50 (0.31, 0.80)	0.004
	Both	147	0.18 (0.07, 0.45)	<0.001
CD4_Bcell_IR	None	85	Reference	
	Only CD4IR	74	0.18 (0.11, 0.28)	<0.001
	Only B–cell IR	69	0.10 (0.05, 0.19)	<0.001
	Both CD4 and B–cell IR	235	0.02 (0.01, 0.04)	<0.001
HCT_Year	Before 2015	228	Reference	
	2015 or after	235	0.79 (0.56, 1.13)	0.201

Table S6. Multivariable Cox Proportional Hazard Analysis for Acute GvHD Grade II-IV. CD4 and B cell immune reconstitution, as well as age and use of serotherapy were found to be predictors associated with decreased risk of aGvHD grade II-IV in multivariable analyses. Since there were 138 events of aGvHD grade II-IV, analyses were also run including less covariates (see methods), leading to similar results (right panel).

Supplemental Data

Multivariable Cox Proportional Hazard Analysis for Extensive Chronic GvHD

Variable		N	Hazard ratio	p
Age	0–3 years	69	Reference	
	3–10 years	117	1.27 (0.25, 6.49)	0.772
	10–18 years	204	1.68 (0.35, 8.10)	0.517
	>18 years	65	2.04 (0.38, 11.06)	0.409
Diagnosis	ALL	201	Reference	
	AML	165	0.73 (0.28, 1.90)	0.519
	Other	89	0.90 (0.34, 2.36)	0.825
Source	BM	152	Reference	
	Cord	120	0.62 (0.17, 2.21)	0.457
	PBSC	183	1.44 (0.27, 7.64)	0.669
HLA_match	Matched	244	Reference	
	Mismatched	211	1.55 (0.62, 3.91)	0.349
Conditioning	Only chemotherapy	277	Reference	
	Chemo and TBI	178	0.83 (0.34, 2.01)	0.681
TCD_Serotherapy	None	163	Reference	
	Only TCD	42	0.60 (0.08, 4.75)	0.631
	Only Serotherapy	103	0.60 (0.19, 1.88)	0.381
	Both	147	0.39 (0.07, 2.35)	0.306
CD4_Bcell_IR	None	33	Reference	
	Only CD4IR	84	0.34 (0.10, 1.11)	0.073
	Only B–cell IR	72	0.29 (0.08, 1.05)	0.059
	Both CD4 and B–cell IR	266	0.16 (0.05, 0.49)	0.001
HCT_Year	Before 2015	225	Reference	
	2015 or after	230	0.51 (0.23, 1.15)	0.105

Variable		N	Hazard ratio	p
CD4_Bcell_IR	None	33		Reference
	Only CD4IR	85	0.44 (0.15, 1.33)	0.146
	Only B–cell IR	72	0.33 (0.10, 1.08)	0.066
	Both CD4 and B–cell IR	269	0.17 (0.06, 0.49)	0.001

Table S7. Multivariable Cox Proportional Hazard Analysis for Extensive Chronic GvHD. Combined CD4 and B cell immune reconstitution was found to be a predictor of decreased risk of extensive cGvHD in multivariable analysis. The p-value for CD4 and B cell immune reconstitution seperately did not reach significance at a threshold of 0.05, but the confidence interval is clearly not centered around 1, suggesting there might be a lack of power, secondary to low number of events (31), rather than a lack of effect (left panel). Due to the low number of events, multivariate analyses were also done including less covariates, to make up for overfitting (right panel), indicating similar results.