	HLA-DPB1 matching			
Biological models	matched	1 mm	2 mm	Total
TCE3.1				
matched	257	0	0	257
non-permissive	0	157	154	311
permissive	0	269	72	341
TCE3.2				
matched	257	0	0	257
non-permissive GvH	0	93	84	177
non-permissive HvG	0	64	70	134
permissive	0	269	72	341
TCE4.1				
matched	257	0	0	257
non-permissive	0	239	195	434
permissive	0	187	31	218
TCE4.2				
matched	257	0	0	257
non-permissive GvH	0	139	106	245
non-permissive HvG	0	100	89	189
permissive	0	187	31	218
Expression				
matched	257	0	0	257
R-high,D-high	0	48	0	48
R-high,D-low	0	129	0	129
R-low,D-high	0	61	0	61
R-low,D-low	0	109	0	109
not classified	0	78§	227	305
PIRCHE I				
0	254	170	36	460
1-3	3*	185	124	312
>3	0	71	66	137
PIRCHE II				
0	254	134	22	410
1-10	1*	158	100	259
>10	2*	134	104	240

mm: mismatch; GvH: mm in graft versus host direction; HvG: mm in host versus graft direction; R: recipient; D: donor.

§: including 2 donor/recipient pairs with expression level not available and 76 pairs with a mismatch in the HvG direction only.

*: 12/12 matched with the presence of an HLA-DRB3/4 mismatch.

Supplementary table 1. Distribution of HLA mismatches according to the different biological models

		OS (N=909; events=378)*					TRM (N=909, events=154)*					aGVHD≥3 (N=832, events=86)*					cGVHD (N=813, events=288)*				
HLA-DPB1 matching	**Categories**	**events/n**	**HR**	**95% CI**		**p**	**events/n**	**HR**	**95% CI**		**p**	**events/n**	**HR**	**95% CI**		**p**	**events/n**	**HR**	**95% CI**		**p**
Classical matching.1	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	1 mm	174/426	0.85	0.66	1.09	0.19	69/426	1.01	0.66	1.56	0.96	40/385	1.25	0.72	2.17	0.43	149/376	1.09	0.83	1.45	0.53
	2 mm	101/226	1.02	0.77	1.35	0.90	54/226	1.58	1.01	2.47	***0.05***	27/203	1.50	0.83	2.71	0.18	65/207	0.95	0.68	1.33	0.76
Classical matching.2	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	1 mm bidirectional	115/266	0.89	0.68	1.17	0.41	41/266	0.98	0.61	1.58	0.94	25/247	1.22	0.66	2.24	0.52	99/237	1.17	0.86	1.58	0.32
	1 mm GvH	27/84	0.63	0.41	0.96	***0.03***	12/84	0.82	0.42	1.61	0.57	8/78	1.18	0.52	2.70	0.69	32/74	1.08	0.71	1.65	0.71
	1 mm HvG	32/76	0.97	0.64	1.45	0.87	16/76	1.39	0.75	2.59	0.30	7/60	1.45	0.61	3.44	0.41	18/65	0.83	0.49	1.39	0.48
	2 mm	101/226	1.02	0.77	1.35	0.89	54/226	1.58	1.01	2.48	***0.05***	27/203	1.50	0.83	2.71	0.18	65/207	0.95	0.68	1.33	0.77
TCE3.1	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	non-permissive	125/311	0.86	0.66	1.13	0.28	58/311	1.21	0.78	1.89	0.39	32/278	1.31	0.74	2.32	0.36	99/278	1.06	0.79	1.44	0.69
	permissive	150/341	0.94	0.73	1.21	0.63	65/341	1.20	0.78	1.85	0.42	35/310	1.37	0.78	2.40	0.27	115/305	1.03	0.77	1.39	0.83
TCE3.2	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	non-permissive GvH	65/177	0.78	0.57	1.07	0.12	32/177	1.20	0.73	1.99	0.48	18/160	1.31	0.69	2.50	0.42	55/156	1.00	0.70	1.42	1.00
	non-permissive HvG	60/134	0.97	0.70	1.35	0.87	26/134	1.23	0.72	2.10	0.45	14/118	1.31	0.65	2.64	0.46	44/122	1.16	0.79	1.68	0.45
	permissive	150/341	0.94	0.73	1.22	0.64	65/341	1.20	0.78	1.85	0.42	35/310	1.37	0.78	2.40	0.27	115/305	1.03	0.77	1.39	0.83
TCE4.1	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	non-permissive	183/434	0.87	0.68	1.11	0.27	86/434	1.21	0.79	1.84	0.38	45/390	1.32	0.77	2.27	0.32	146/387	1.09	0.82	1.44	0.57
	permissive	92/218	0.97	0.73	1.29	0.84	37/218	1.20	0.74	1.94	0.46	22/198	1.38	0.75	2.56	0.31	68/196	0.97	0.70	1.36	0.87
TCE4.2	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	non-permissive GvH	92/245	0.75	0.56	1.00	***0.05***	43/245	1.03	0.64	1.65	0.91	22/223	1.11	0.60	2.06	0.74	87/219	1.06	0.77	1.45	0.73
	non-permissive HvG	91/189	1.05	0.79	1.40	0.74	43/189	1.47	0.92	2.37	0.11	23/167	1.63	0.88	3.03	0.12	59/168	1.13	0.80	1.59	0.50
	permissive	92/218	0.98	0.74	1.30	0.87	37/218	1.20	0.74	1.94	0.46	22/198	1.39	0.75	2.57	0.30	68/196	0.97	0.70	1.36	0.87
Expression	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	R-high,D-high	20/48	1.05	0.64	1.72	0.84	11/48	1.77	0.85	3.69	0.13	8/45	2.99	1.30	6.88	***0.01***	18/39	1.69	0.99	2.87	0.05
	R-high,D-low	43/129	0.75	0.52	1.08	0.12	19/129	1.11	0.62	1.99	0.73	12/118	1.32	0.64	2.74	0.46	36/114	0.88	0.59	1.31	0.52
	R-low,D-high	30/61	0.80	0.53	1.20	0.28	6/61	0.44	0.18	1.08	0.07	2/57	0.46	0.11	2.01	0.30	27/57	1.18	0.76	1.85	0.46
	R-low,D-low	46/109	0.77	0.54	1.10	0.15	17/109	0.84	0.46	1.55	0.58	11/103	1.22	0.58	2.57	0.61	50/99	1.29	0.90	1.86	0.17
PIRCHE I	0	192/460	1.00		-		72/460	1.00		-		38/422	1.00		-		143/405	1.00		-	
	1-3	127/312	0.86	0.69	1.08	0.19	55/312	0.92	0.65	1.32	0.66	34/291	1.17	0.73	1.88	0.52	113/284	1.11	0.86	1.42	0.43
	>3	59/137	1.06	0.79	1.42	0.72	27/137	1.34	0.85	2.09	0.21	14/119	1.29	0.69	2.42	0.42	32/124	0.64	0.43	0.94	***0.02***
PIRCHE II	0	171/410	1.00		-		57/410	1.00		-		32/377	1.00		-		120/363	1.00		-	
	1-10	105/259	0.86	0.67	1.10	0.23	45/259	1.04	0.70	1.55	0.84	29/244	1.38	0.83	2.29	0.22	98/238	1.31	1.00	1.72	***0.05***
	>10	102/240	0.96	0.75	1.23	0.73	52/240	1.46	1.00	2.14	0.05	25/211	1.21	0.70	2.08	0.50	70/212	0.87	0.65	1.18	0.37

*: the number of patients/events for the regressions with expression is N=604/242, 604/84, 579/191, 564/52, 539/205 and 558/212 for OS, TRM, aGVHD≥2, aGVHD≥3, cGVHD and relprog, respectively. **: patients with non-malignant disorder are excluded from analyses on relapse.

events: number of events in the risk category for the specified outcome, n: number of patients in the risk category for the specified outcome.

0.05 > p ≥ 0.01 are shown in bold and italic, p<0.01 are shown in bold, italic and underlined. GvH: mm in graft versus host direction; HvG: mm in host versus graft direction; R: recipient; D: donor.

Significant co-variables retained for OS: type of diagnosis, status of disease, co-morbid conditions and graft manipulation.

Significant co-variables retained for TRM: type of diagnosis, status of disease, co-morbid conditions, graft manipulation and transplant center.

Significant co-variables retained for aGVHD: HLA-DRB3/4/5 matching, graft manipulation and transplant center.

Significant co-variables retained for cGVHD: age of patient, status of disease, graft manipulation and transplant center.

Significant co-variables retained for relprog: EBMT risk score, graft manipulation and transplant center.

Supplementary table 2. Multivariable analyses for several HSCT outcomes and association with each HLA-DPB1 matching model

HLA-DPB1 matching	Categories	OS (N=909; events=378)*					TRM (N=909, events=154)*					aGVHD≥3 (N=832, events=86)*					cGVHD (N=813, events=288)*				
		events/n	HR	95% CI		p	events/n	HR	95% CI		p	events/n	HR	95% CI		p	events/n	HR	95% CI		p
TCE3.1 & PIRCHE II	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	non-permissive, no PIRCHE II	24/55	0.87	0.55	1.36	0.53	20302	0.85	0.39	1.88	0.70	5/50	1.05	0.39	2.83	0.92	22/48	1.21	0.75	1.96	0.43
	non-permissive, PIRCHE II	101/256	0.86	0.65	1.14	0.30	50/256	1.30	0.82	2.05	0.26	27/228	1.38	0.76	2.50	0.30	77/230	1.03	0.75	1.42	0.87
	permissive, no PIRCHE II	45/101	1.01	0.71	1.45	0.94	18/101	1.14	0.63	2.06	0.67	8/86	1.21	0.53	2.76	0.66	24/88	0.80	0.51	1.28	0.35
	permissive, PIRCHE II	105/240	0.92	0.70	1.21	0.53	47/240	1.22	0.77	1.93	0.40	27/224	1.43	0.79	2.59	0.23	91/217	1.12	0.82	1.53	0.48
TCE4.1 & PIRCHE II	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	non-permissive, no PIRCHE II	44/99	0.88	0.61	1.26	0.47	17/99	0.99	0.54	1.80	0.96	9/87	1.19	0.54	2.63	0.67	36/86	1.12	0.75	1.67	0.59
	non-permissive, PIRCHE II	139/335	0.87	0.67	1.13	0.30	69/335	1.28	0.83	1.97	0.27	36/303	1.37	0.78	2.40	0.28	110/301	1.08	0.80	1.45	0.63
	permissive, no PIRCHE II	25/57	1.13	0.73	1.77	0.58	21064	1.14	0.53	2.41	0.74	4/49	1.05	0.36	3.09	0.93	10/50	0.63	0.33	1.23	0.18
	permissive, PIRCHE II	67/161	0.93	0.68	1.26	0.62	28/161	1.22	0.73	2.03	0.46	18/149	1.49	0.78	2.85	0.23	58/146	1.07	0.76	1.52	0.69
Expression & PIRCHE II	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	R-high, no PIRCHE II §	8/13	NI	NI	NI	NI	4/13	NI	NI	NI	NI	2/12	NI	NI	NI	NI	1/11	NI	NI	NI	NI
	R-high, PIRCHE II	55/164	0.75	0.53	1.04	0.08	26/164	1.16	0.68	1.98	0.58	18/151	1.65	0.86	3.17	0.13	53/142	1.05	0.73	1.50	0.80
	R-low, no PIRCHE II	19/45	0.73	0.44	1.19	0.21	5/45	0.51	0.19	1.35	0.18	2/42	0.60	0.14	2.59	0.50	20/39	1.25	0.76	2.07	0.38
	R-low, PIRCHE II	57/125	0.80	0.58	1.11	0.19	18/125	0.75	0.41	1.37	0.35	11/118	1.12	0.53	2.38	0.77	57/117	1.25	0.89	1.78	0.20
Expression & TCE3.1	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	R-high, non-permissive	34/96	0.79	0.53	1.17	0.24	15/96	1.16	0.61	2.21	0.64	10/86	1.52	0.70	3.28	0.29	32/82	1.19	0.78	1.81	0.43
	R-high, permissive	29/81	0.86	0.57	1.31	0.49	15/81	1.39	0.74	2.60	0.30	10/77	1.92	0.89	4.16	0.10	22/71	0.89	0.55	1.44	0.63
	R-low, non-permissive	14/38	0.58	0.33	1.02	0.06	2/38	0.29	0.07	1.22	0.09	0/36	0.00	0.00	.	0.97	15/36	1.23	0.70	2.15	0.48
	R-low, permissive	62/132	0.85	0.62	1.17	0.32	21/132	0.79	0.44	1.41	0.43	13/124	1.25	0.62	2.55	0.53	62/120	1.26	0.89	1.77	0.19
Expression & TCE4.1	matched	103/257	1.00		-		31/257	1.00		-		19/244	1.00		-		74/230	1.00		-	
	R-high, non-permissive	39/105	0.80	0.55	1.17	0.25	17/105	1.17	0.63	2.17	0.62	11/95	1.50	0.71	3.17	0.29	35/90	1.18	0.79	1.77	0.43
	R-high, permissive	24/72	0.86	0.55	1.35	0.52	13/72	1.40	0.73	2.71	0.32	9/68	2.06	0.93	4.58	0.08	19/63	0.86	0.52	1.43	0.56
	R-low, non-permissive	39/95	0.68	0.47	0.99	***0.04***	12/95	0.53	0.26	1.06	0.07	5/89	0.71	0.26	1.93	0.51	41/87	1.18	0.80	1.74	0.39
	R-low, permissive	37/75	0.92	0.63	1.35	0.68	11/75	0.96	0.48	1.93	0.90	8/71	1.29	0.56	2.95	0.56	36/69	1.34	0.89	2.01	0.16

*: the number of patients/events for the regressions with expression is N=604/242, 604/84, 579/191, 564/52, 539/205 and 558/212 for OS, TRM, aGVHD≥2, aGVHD≥3, cGVHD and relprog, respectively. **: patients with non-malignant disorder are excluded from analyses on relapse.

events: number of events in the risk category for the specified outcome, n: number of patients in the risk category for the specified outcome.

$0.05 > p \geq 0.01$ are shown in bold and italic, $p<0.01$ are shown in bold, italic and underlined. R: recipient; D: donor.

§: not interpretable (NI) because of the very small number of patients in this group.

Significant co-variables retained for OS: type of diagnosis, status of disease, co-morbid conditions and graft manipulation.

Significant co-variables retained for TRM: type of diagnosis, status of disease, co-morbid conditions, graft manipulation and transplant center.

Significant co-variables retained for aGVHD: HLA-DRB3/4/5 matching, graft manipulation and transplant center.

Significant co-variables retained for cGVHD: age of patient, status of disease, graft manipulation and transplant center.

Significant co-variables retained for relprog: EBMT risk score, graft manipulation and transplant center.

Supplementary table 3. Multivariable analyses for several HSCT outcomes and association with combined biological models

Supplementary Figure 1

Distribution of the number of PIRCHE I and II according to classical matching, TCE and expression. The number of donor/recipient pairs included in each group is indicated above the boxplots (more details in Table 2). Each dot indicates the number of potential binders predicted by the PIRCHE algorithm in a given donor/recipient pair. The color of the dot represents the matching status between donor and recipient at HLA-DPB1 (i.e. 0, 1 or 2 mismatches) and HLA-DRB3/4/5 (i.e. absence or presence of a mismatch). The models TCE3.1 and TCE4.2 were chosen among the four alternative TCE models investigated in this study to illustrate the distribution of potential binders in permissive and non-permissive (total, HvG or GvH) mismatched groups. Similar distributions were observed for TCE3.2 and TCE4.1 (data not shown). HvG: incompatibility in the host versus graft direction, GvH: incompatibility in the graft versus host direction, TCE: T-Cell Epitopes, PIRCHE: Predicted Indirectly ReCognizable HLA Epitopes, mm: mismatch.

Supplementary Figure 2

Selected Kaplan Meier (KM) plots for single HLA-DPB1 models and acute GVHD ≥ 2.

Supplementary Figure 3

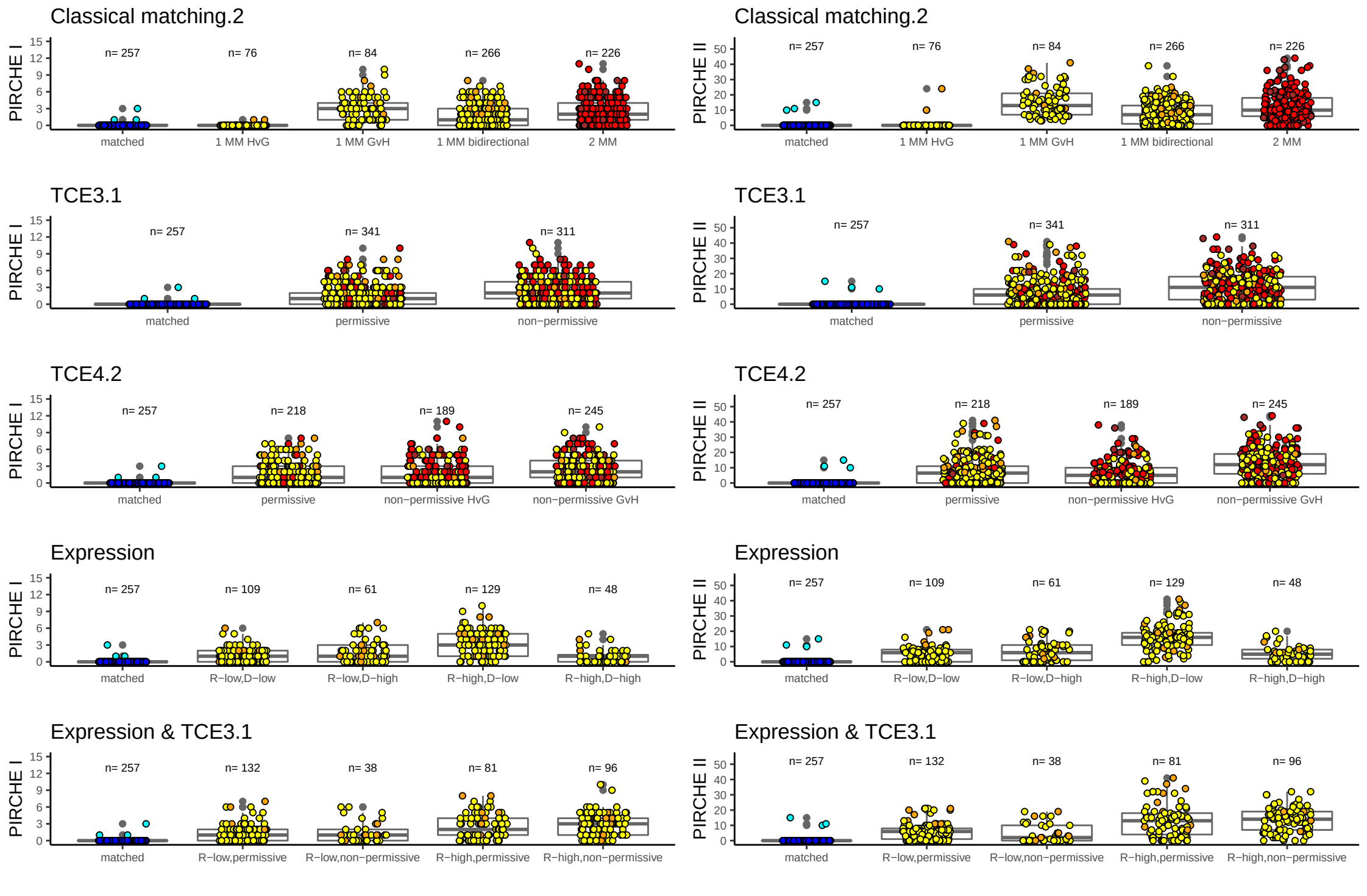
Selected Kaplan Meier (KM) plots for single HLA-DPB1 models and relapse/progression.

Supplementary Figure 4

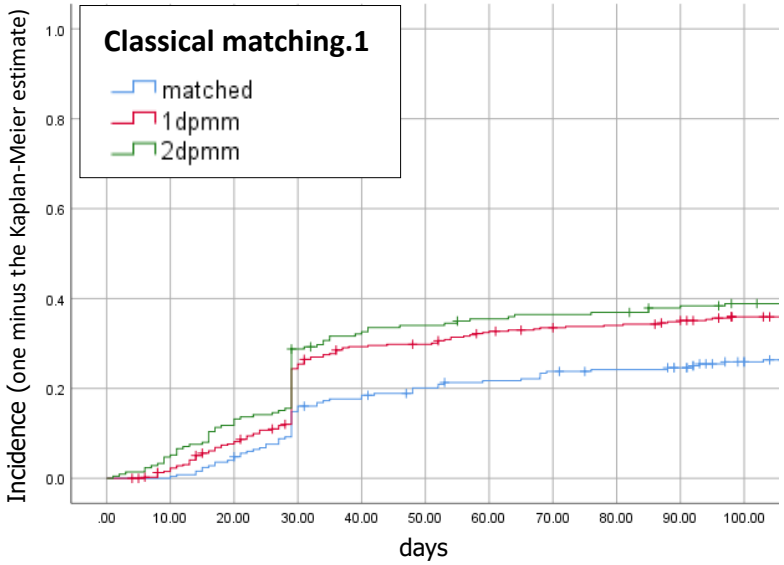
Kaplan Meier (KM) plots for the five combined HLA-DPB1 models and acute GVHD ≥ 2.

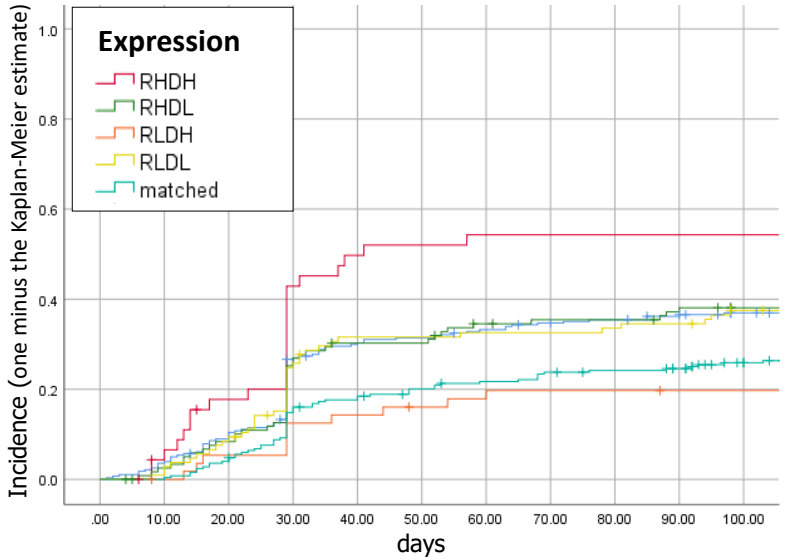
Supplementary Figure 5

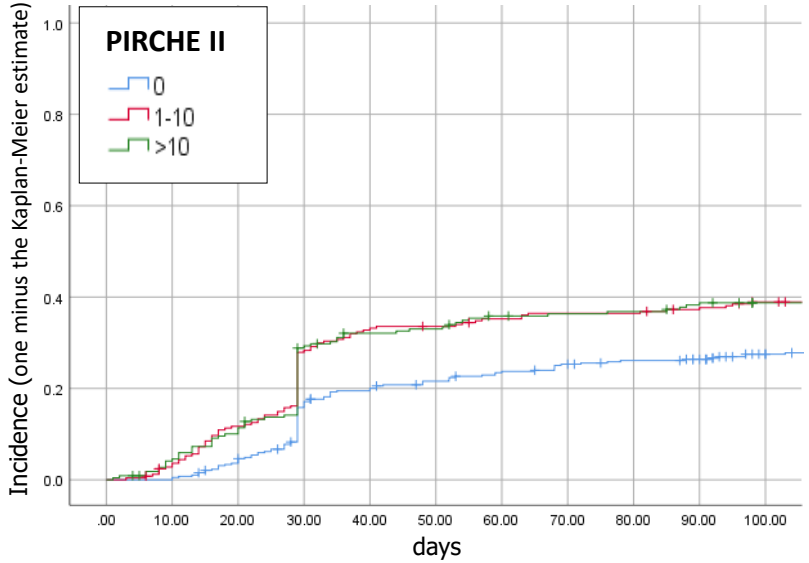
Kaplan Meier (KM) plots for the five combined HLA-DPB1 models and relapse/progression.

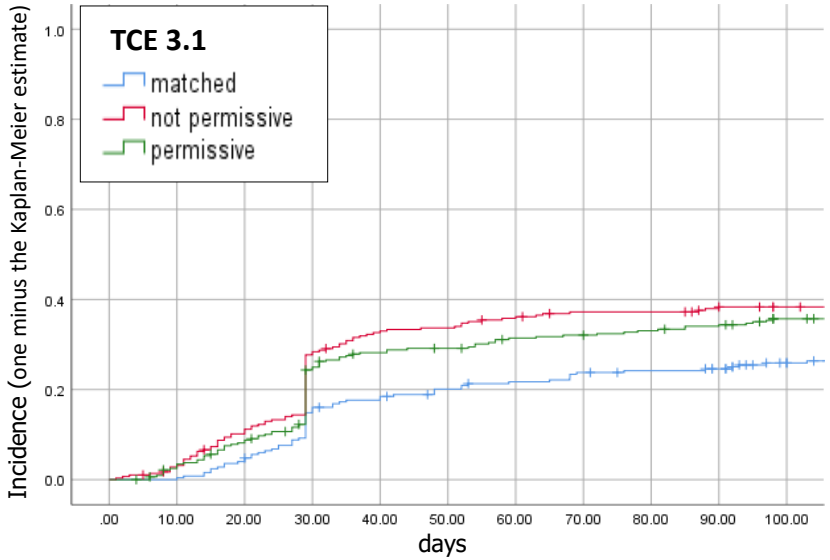

Classical matching.2
PIRCHE I
n= 257
n= 76
n= 84
n= 266
n= 226
matched
1 MM HvG
1 MM GvH
1 MM bidirectional
2 MM
Classical matching.2
PIRCHE II
TCE3.1
n= 341
n= 311
permissive
non−permissive
TCE4.2
n= 218
n= 189
n= 245
non−permissive HvG
non−permissive GvH
Expression
n= 109
n= 61
n= 129
n= 48
R−low,D−low
R−low,D−high
R−high,D−low
R−high,D−high
Expression & TCE3.1
n= 132
n= 38
n= 81
n= 96
R−low,permissive
R−low,non−permissive
R−high,permissive
R−high,non−permissive
0 DPB1 mm & no DRB345 mm
1 DPB1 mm & no DRB345 mm
2 DPB1 mm & no DRB345 mm
0 DPB1 mm & a DRB345 mm
1 DPB1 mm & a DRB345 mm
2 DPB1 mm & a DRB345 mm

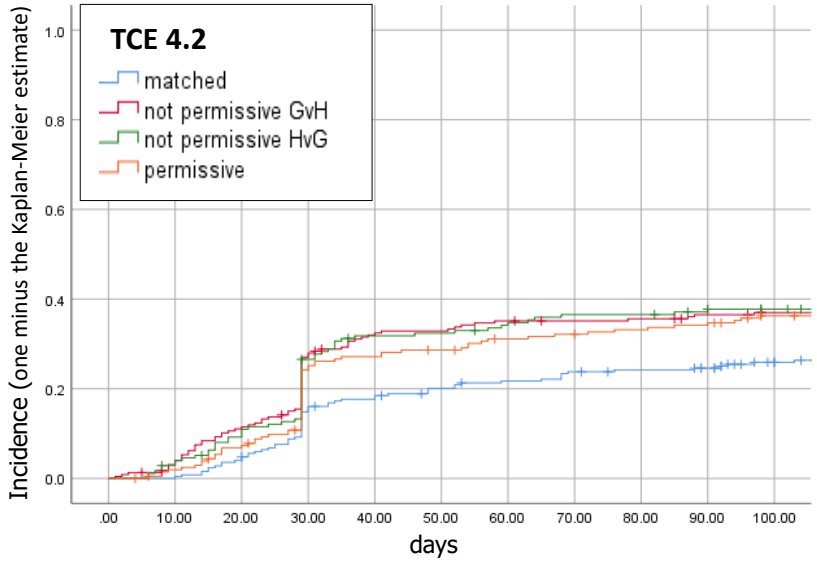
Acute GVHD ≥ 2


Classical matching.1
matched
1dpmm
2dpmm
Incidence (one minus the Kaplan-Meier estimate)
days

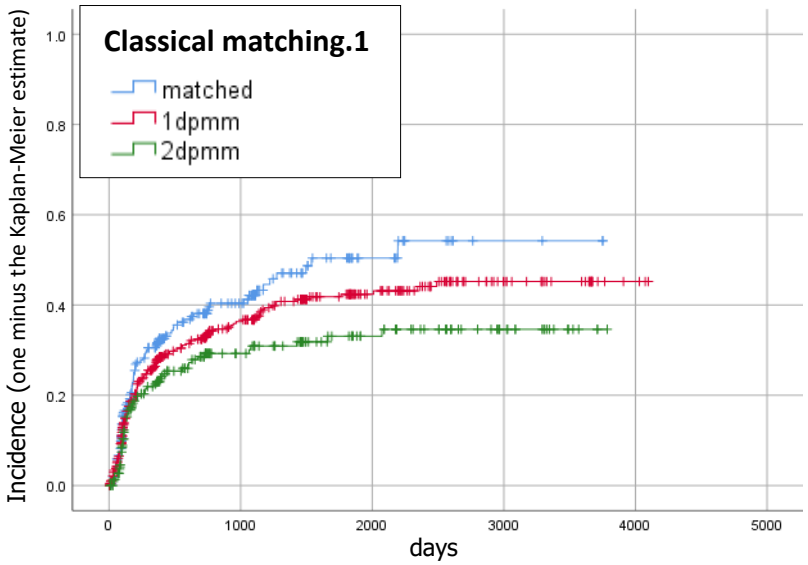

Expression
RHDH
RHDL
RLDH
RLDL
matched
Incidence (one minus the Kaplan-Meier estimate)
days

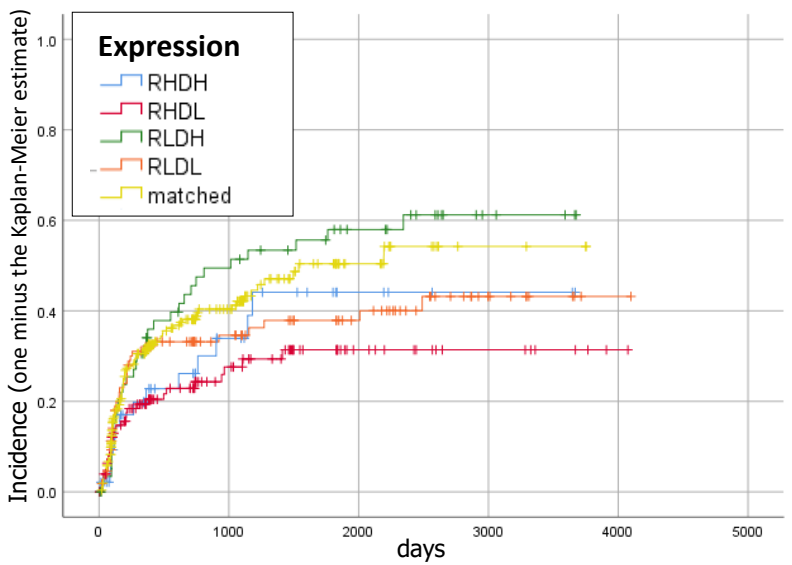

PIRCHE II
0
1-10
>10
Incidence (one minus the Kaplan-Meier estimate)
days

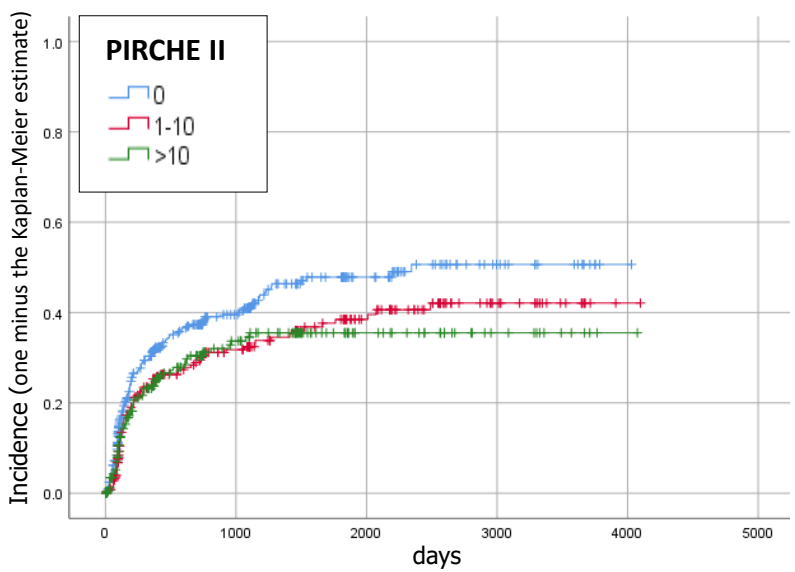

TCE 3.1
matched
not permissive
permissive
Incidence (one minus the Kaplan-Meier estimate)
days

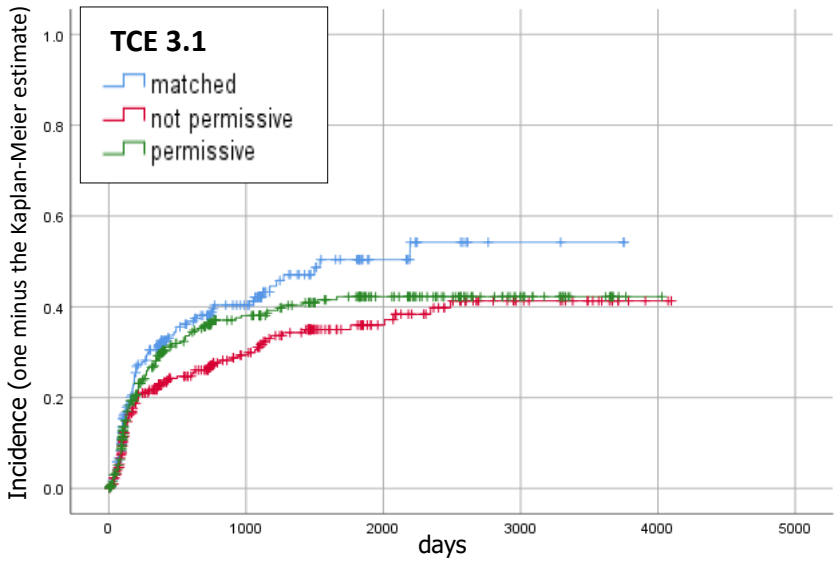

TCE 4.2
matched
not permissive GvH
not permissive HvG
permissive
Incidence (one minus the Kaplan-Meier estimate)
days

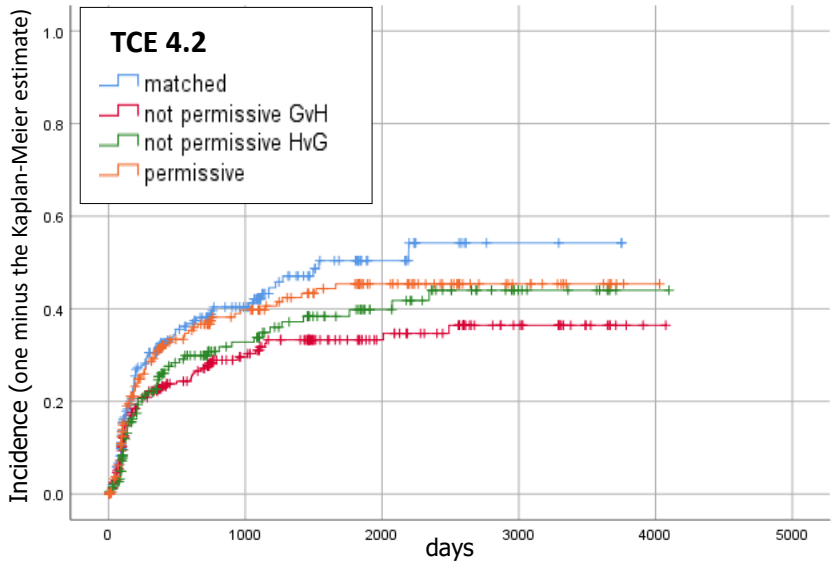
Relapse/progression



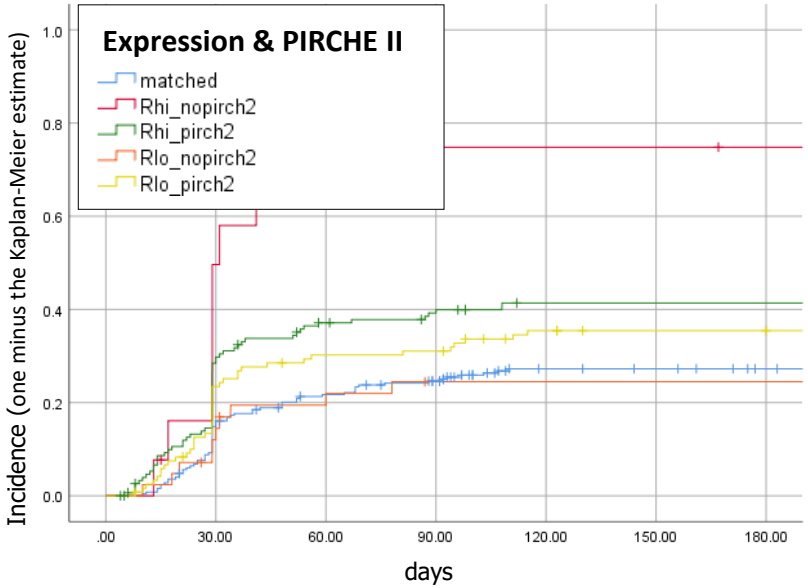


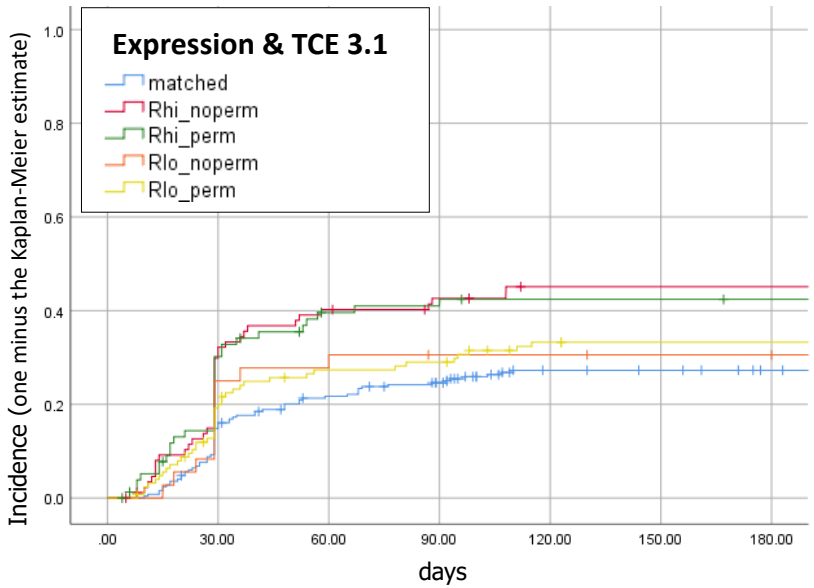


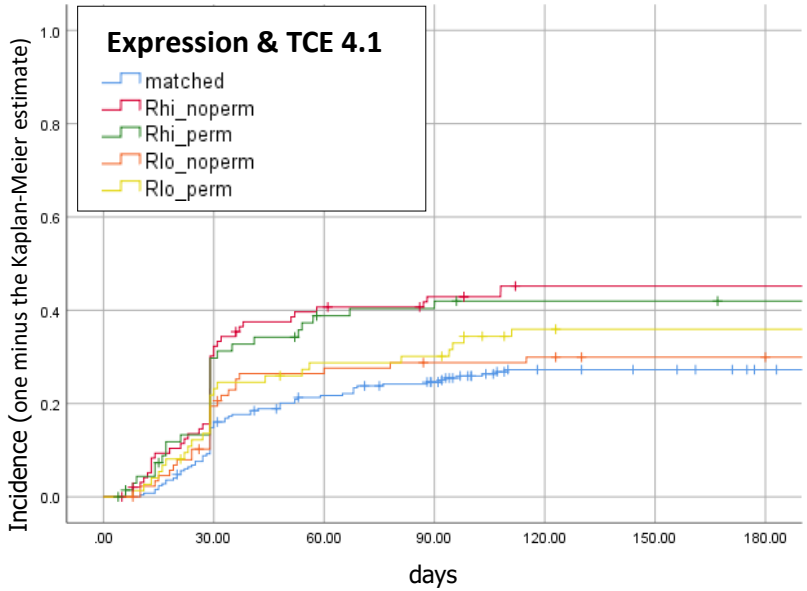




Acute GVHD ≥ 2


Expression & PIRCHE II
matched
Rhi_nopirch2
Rhi_pirch2
Rlo_nopirch2
Rlo_pirch2
Incidence (one minus the Kaplan-Meier estimate)
1.0
0.8
0.6
0.4
0.2
0.0
.00
30.00
60.00
90.00
120.00
150.00
180.00
days


Expression & TCE 3.1
matched
Rhi_noperm
Rhi_perm
Rlo_noperm
Rlo_perm
Incidence (one minus the Kaplan-Meier estimate)
1.0
0.8
0.6
0.4
0.2
0.0
.00
30.00
60.00
90.00
120.00
150.00
180.00
days


Expression & TCE 4.1
matched
Rhi_noperm
Rhi_perm
Rlo_noperm
Rlo_perm
Incidence (one minus the Kaplan-Meier estimate)
1.0
0.8
0.6
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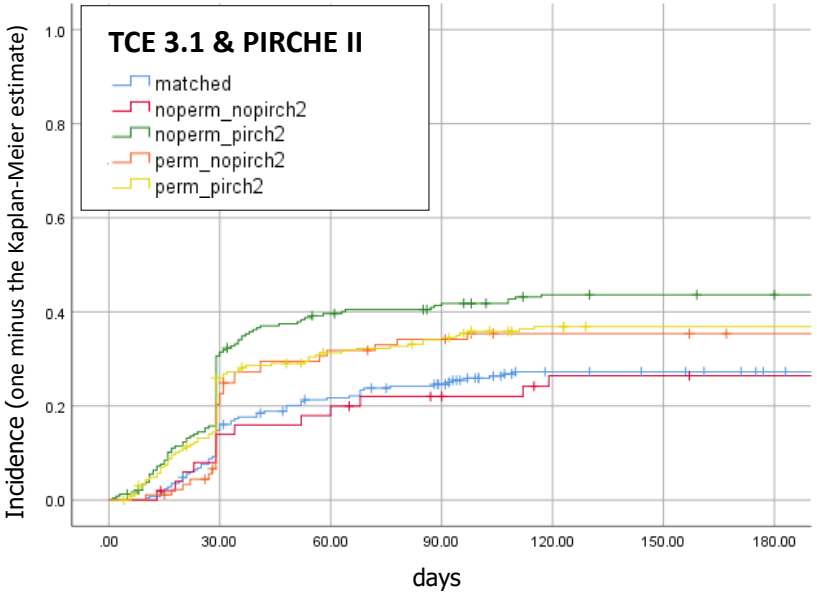
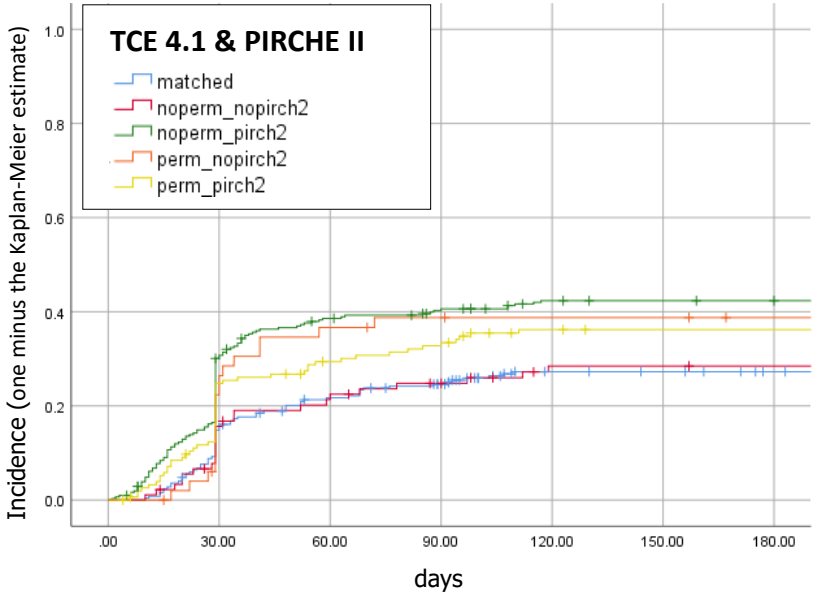
0.2
0.0
.00
30.00
60.00
90.00
120.00
150.00
180.00
days


TCE 3.1 & PIRCHE II
matched
noperm_nopirch2
noperm_pirch2
perm_nopirch2
perm_pirch2
Incidence (one minus the Kaplan-Meier estimate)
1.0
0.8
0.6
0.4
0.2
0.0
.00
30.00
60.00
90.00
120.00
150.00
180.00
days


TCE 4.1 & PIRCHE II
matched
noperm_nopirch2
noperm_pirch2
perm_nopirch2
perm_pirch2
Incidence (one minus the Kaplan-Meier estimate)
1.0
0.8
0.6
0.4
0.2
0.0
.00
30.00
60.00
90.00
120.00
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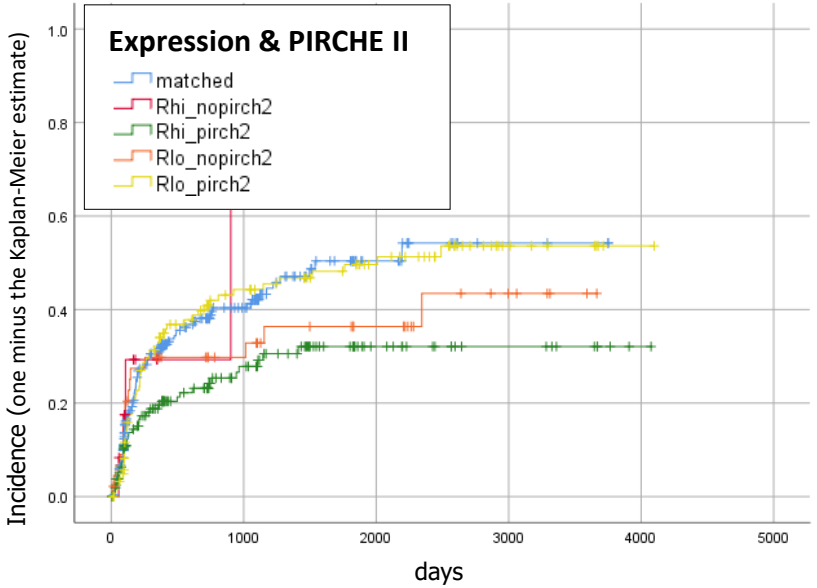
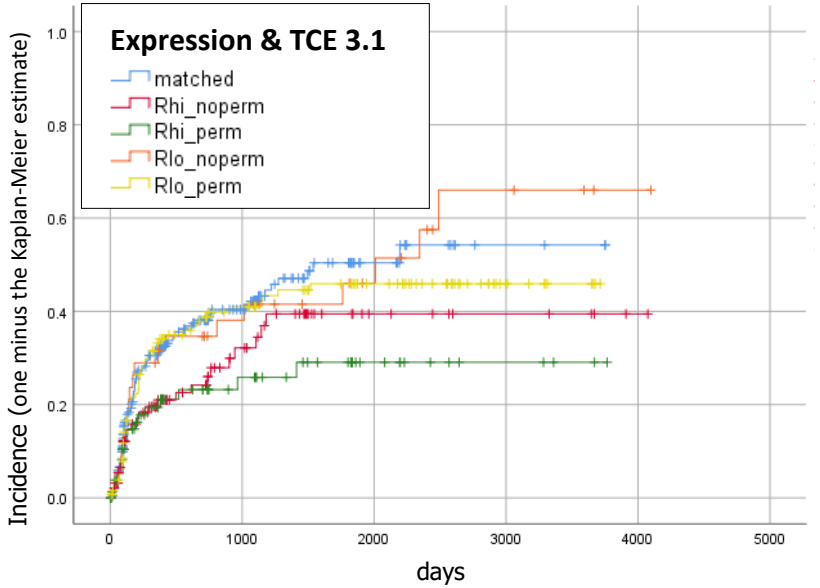
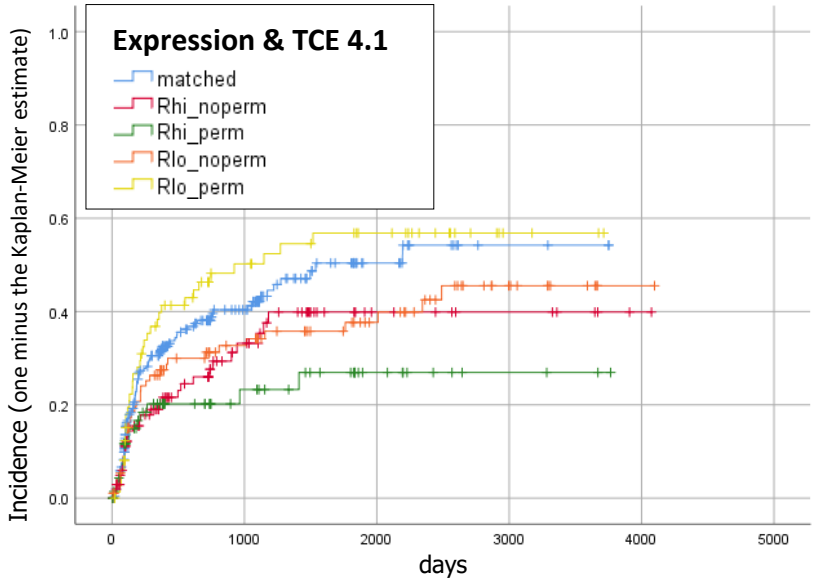
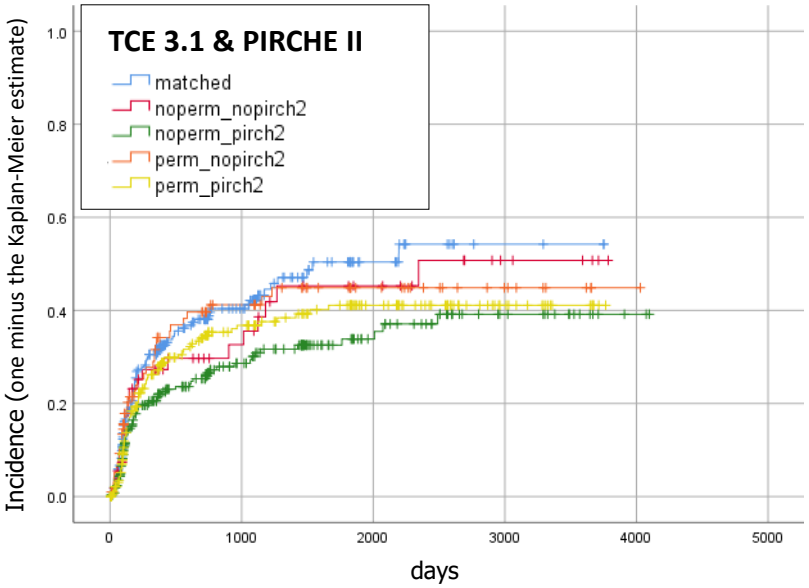
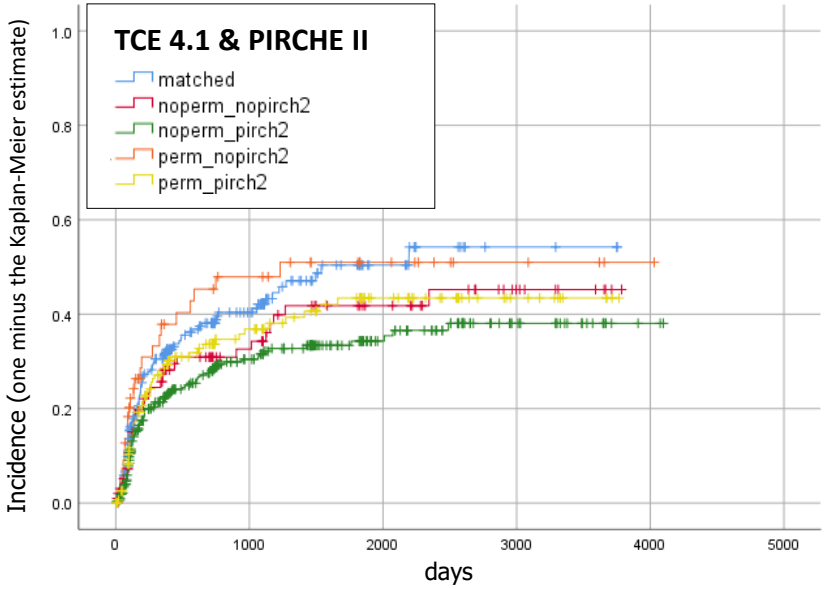
days

Relapse/progression