Supplemental Data

Table S1. Incidence of CRS after haploidentical HCT (n = 169)

	CRS Grade	N	%	Median (range)
CRS occurrence		98	58	
CRS max grade	1	65	38.5	
	2	31	18.3	
	3	1	0.6	
	4	1	0.6	
Days to CRS onset from HCT				1 (0-5)
Days to max CRS				3 (0-5)
Days to CRS resolution				5 (0-8)

Table S2. Multivariable analysis of predictors of clinical outcomes

		OS*				PFS				NRM**				Relapse			
		HR	95% CI		p-value	HR	95% CI		p-value	sHR	95% CI		p-value	sHR	95% CI		p-value
CRS	Yes vs No	0.92	0.51	1.66	0.78	0.70	0.43	1.15	0.16	1.18	0.46	3.03	0.73	0.53	0.30	0.94	0.03
Age	>=60 vs <60	1.35	0.73	2.49	0.34	1.31	0.77	2.24	0.32	2.05	0.75	5.60	0.16	1.01	0.50	2.03	0.98
Male Patient & Female Donor	Yes vs No	1.27	0.64	2.52	0.49	1.11	0.61	2.02	0.74	1.03	0.30	3.54	0.96	0.92	0.44	1.92	0.82
Conditioning Intensity	RIC vs MAC	1.42	0.64	3.15	0.39	1.05	0.54	2.06	0.89	0.66	0.23	1.94	0.45	1.52	0.56	4.16	0.42
HCT-CI	>=3 vs 0-2	1.97	1.15	3.35	0.013	1.86	1.18	2.92	0.007	4.66	2.03	10.69	0.0003	1.01	0.59	1.72	0.99
CMV serostatus	Pos. vs Neg.	1.16	0.66	2.02	0.61	1.07	0.66	1.73	0.78	1.40	0.49	4.04	0.53	0.91	0.53	1.59	0.75
MRD status	Yes vs No	1.38	0.72	2.62	0.33	1.50	0.85	2.64	0.16	0.88	0.31	2.48	0.81	1.77	0.84	3.74	0.13
Disease	AML vs Other	2.39	1.37	4.15	0.002	1.36	0.85	2.20	0.20	0.70	0.29	1.67	0.42	1.59	0.87	2.91	0.13
Year of transplant	>=2018 vs <2018	0.83	0.45	1.52	0.55	0.99	0.59	1.65	0.97	1.16	0.47	2.86	0.74	0.93	0.51	1.69	0.80
DRI	High/V high vs Low/Int	0.53	0.31	0.94	0.03	0.75	0.46	1.22	0.24	1.00	0.45	2.23	1.00	0.73	0.39	1.35	0.31
Cell source	PBSC vs BM	0.93	0.47	1.82	0.82	0.95	0.54	1.69	0.86	1.31	0.34	5.11	0.70	0.75	0.39	1.45	0.39

*Multivariable Cox model was used for OS and PFS **Fine and Gray model was used for non-relapse mortality and relapse. RIC: reduced intensity conditioning, MAC: myeloablative conditioning, HCT-CI: hematopoietic cell therapy comorbidity index, MRD: measurable residual disease at the time of transplantation, DRI: disease risk index, PBSC: peripheral blood stem cell, BM: bone marrow.

Table S3. Early immune reconstitution of NK cells post haploidentical HCT

		No CRS				CRS				
	month	N*	Med	Q1	Q3	N	Med	Q1	Q3	p-value
NK CELLS	1	28	45.1**	21.7	120.9	37	96.1	36.6	161.3	0.16
	2	41	153.1	103	241.9	43	119.7	82.6	230.6	0.15
	3	40	140.7	79.7	240.2	53	137.7	92.8	257.8	0.64
	6	32	140.9	105.8	239.8	58	142.6	78.8	251.7	0.99
	12	29	141.7	87.8	198.6	40	168.8	98.4	280.4	0.3
$CD56^{BRIGHT}$ NK	1	28	17.6	5	40.2	37	35.3	10.5	60	0.15
	2	41	41.6	15	78.1	43	28.7	15.2	43.8	0.07
	3	40	31.9	15.5	58.8	53	28.6	14.7	41.8	0.67
	6	31	24.5	15	53.3	58	18.1	7.6	42.7	0.09
	12	29	14.9	7.1	42.5	40	17.6	7.6	29.9	0.78
$CD56^{DIM}$ NK	1	28	11.2	4.7	46.6	37	27.4	6.9	56.5	0.21
	2	41	70.8	35.8	114.9	43	64.5	30.4	114	0.54
	3	40	79.3	38	121.7	53	73.1	47.8	131	0.62
	6	31	76.5	55.3	144.7	58	86.1	41.1	152.9	0.86
	12	29	88.9	52.9	132.1	40	119.5	53.6	191.4	0.14

*N is the number of samples available at each corresponding time point. ** The measured values derived from flow cytometry data are in cells/uL. Med: Median, Q1: first quartile, Q3: third quartile.

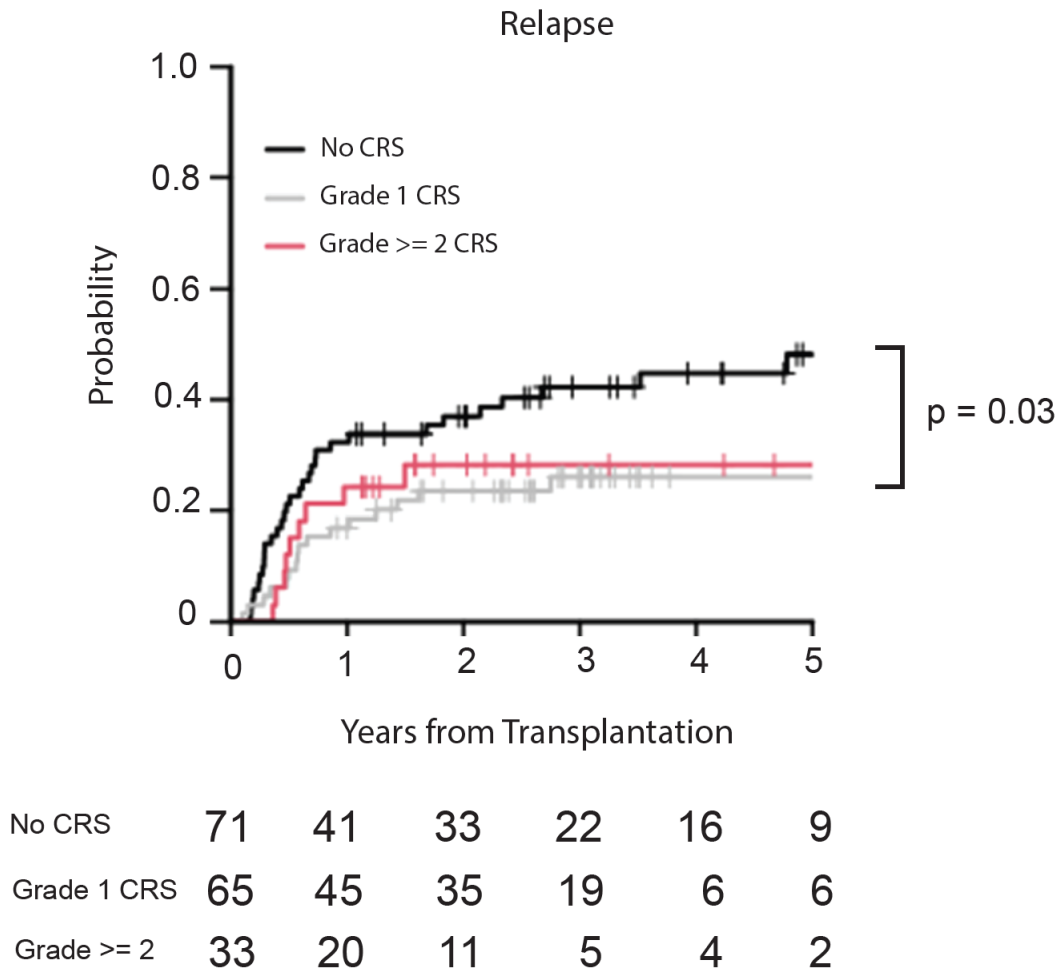

Figure S1. Association of CRS grade with cumulative incidence of post-haploidentical HCT relapse. Comparison of the 3-year cumulative incidence of relapse between grade 1 CRS and no CRS is shown.

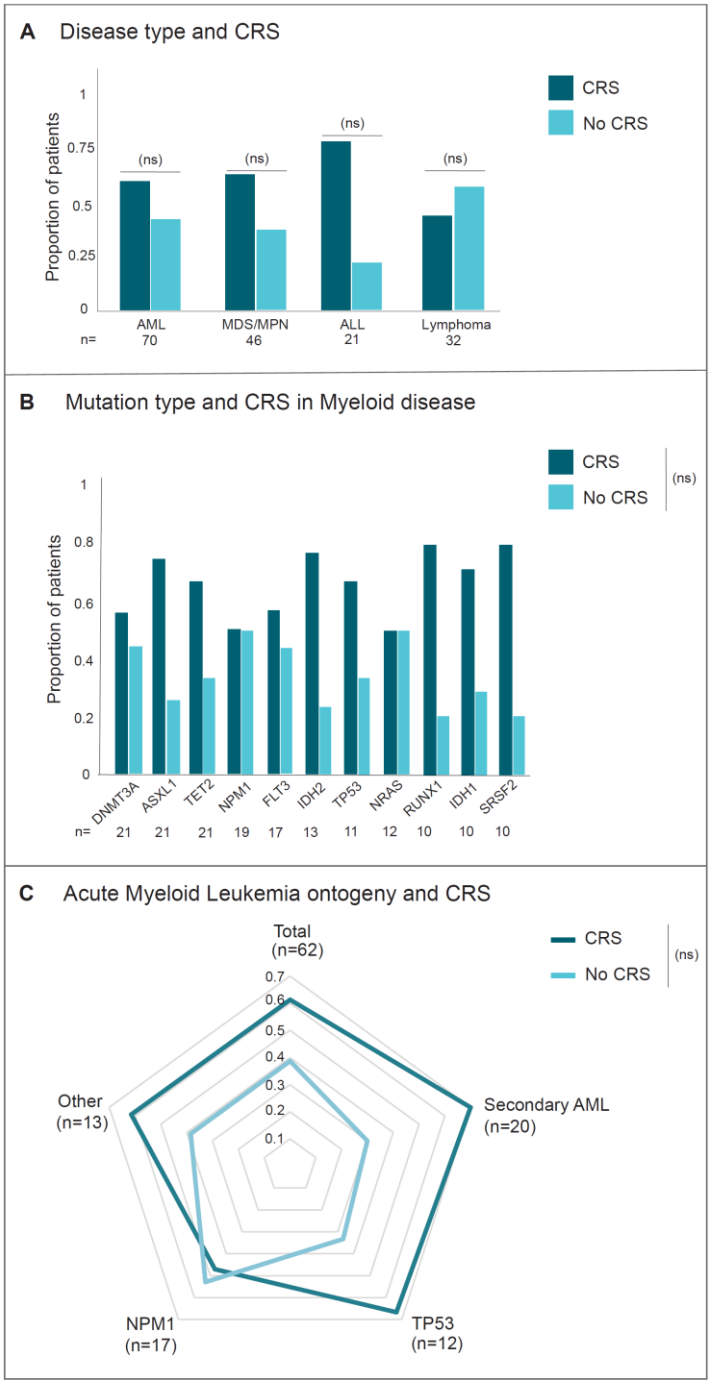

Figure S2. Incidence of CRS among disease type and burden at the time of haploidentical HCT. **A** Distribution of CRS among the distinct major disease groups represented in the HCT cohort. For each disease type, there was no association between CRS and disease type ($p > 0.05$, χ^2 test of independence). **B** Among patients with myeloid disease (MDS, MDS/MPN and AML) in the HCT cohort, gene mutations constitution at least 10% of the evaluable population are shown. For each gene mutation there was no association between CRS and mutation type ($p > 0.05$, Fisher's exact test). **C** Among patients with AML and available pre-HCT gene mutation data, distribution of CRS among the distinct leukemia ontogenies is shown. There was no association between myeloid disease ontogeny and post-HCT CRS ($p > 0.05$, χ^2 test of independence or Fisher's exact test where appropriate).

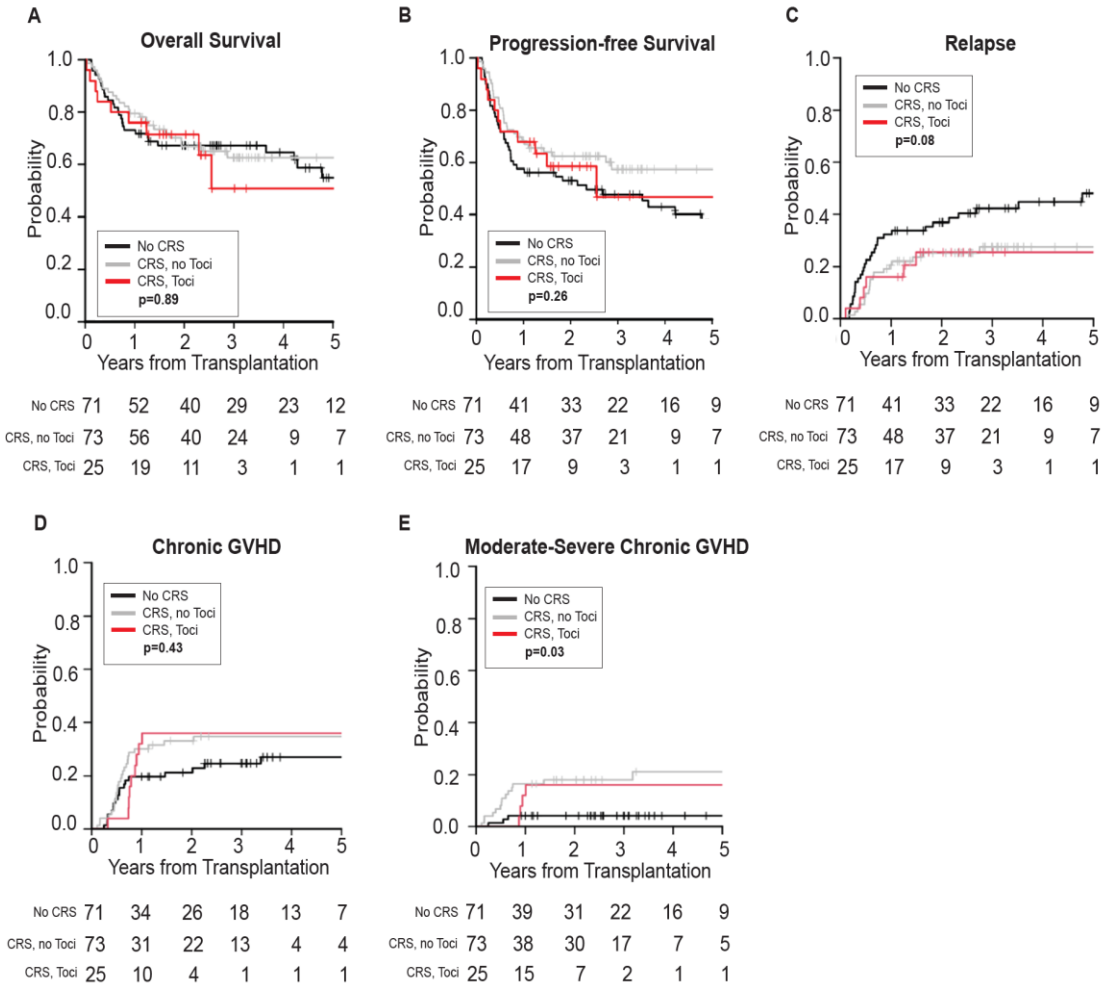

Figure S3. Post-haploidentical HCT outcomes following the development of CRS and treatment with tocilizumab. Kaplan-Meier curves are presented for **A** Overall survival, **B** Progression-free survival, with comparison shown between patients who developed no CRS (black), patients who developed CRS and were not treated with tocilizumab (gray), and patients who developed CRS and were treated with tocilizumab (red). Cumulative incidence of **C** Relapse, **D** Chronic GVHD, and **E** Moderate-severe chronic GVHD are presented, with comparison shown between the groups of patients who developed no CRS, CRS that was not treated with tocilizumab, and CRS that was treated with tocilizumab.

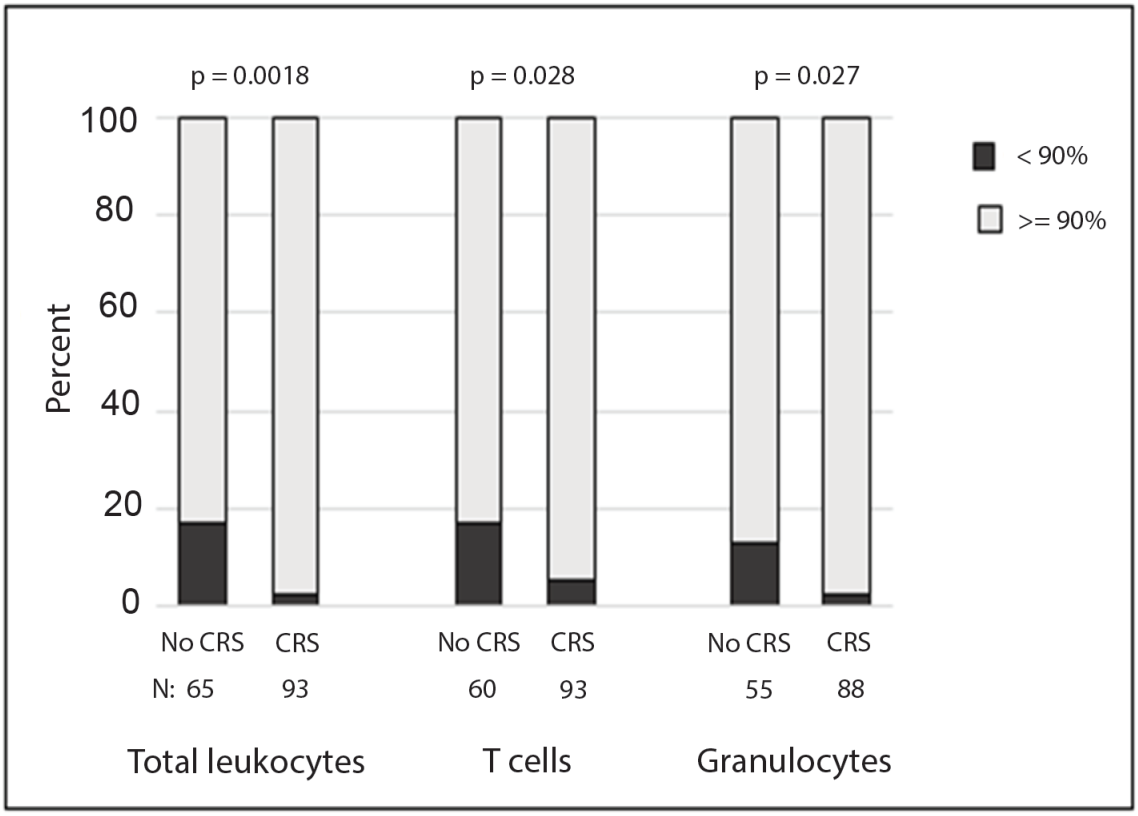

Figure S4. **Percent donor chimerism at 1 month post haploidentical HCT**. Shown are the percentages of patients in the subgroups who did and did not develop CRS, and who attained either >= 90% or < 90% total buffy coat leukocytes, T-cell, or granulocyte chimerism.

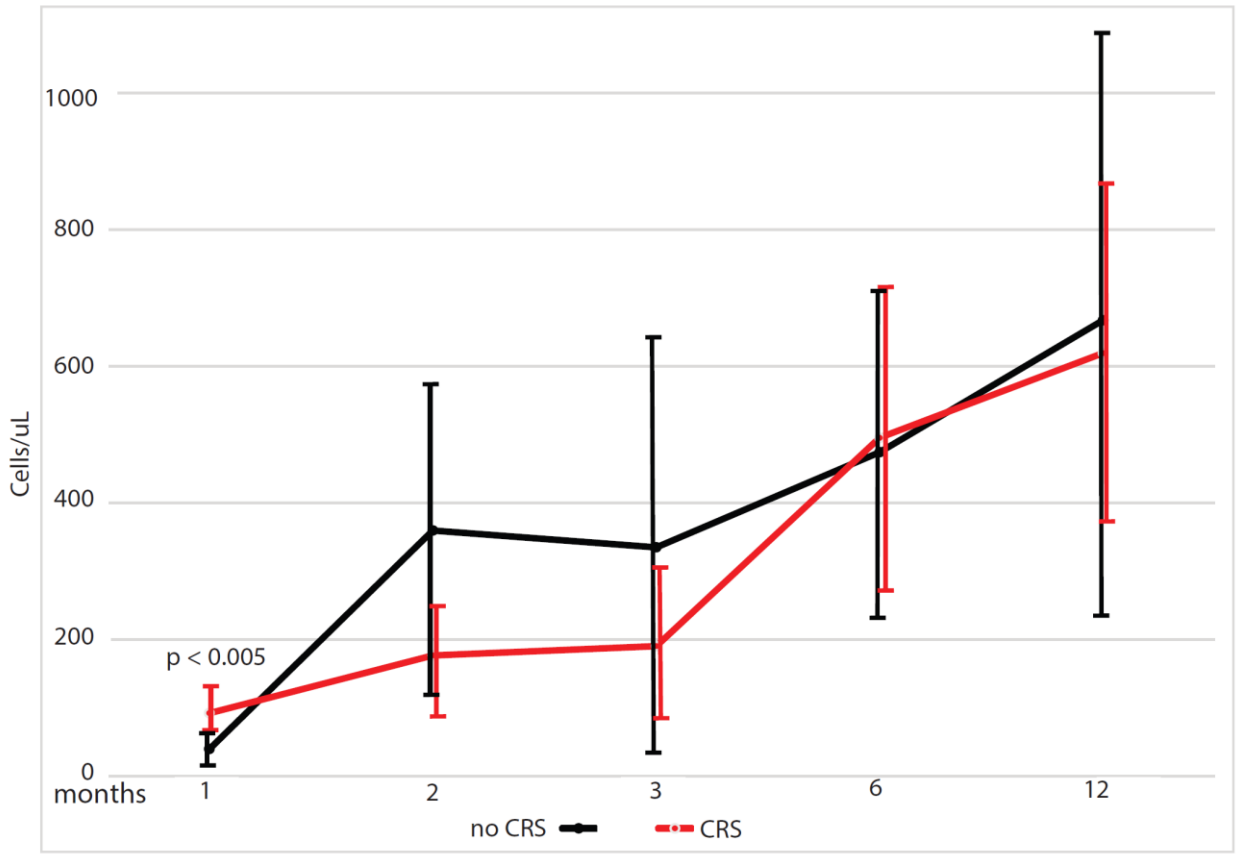

Figure S5. Immune reconstitution of CD8+ T-cells in patients who developed post haploidentical HCT CRS among patients who received PBSC grafts. Wilcoxon-signed-rank test was done for all paired comparisons, with all testing being two-sided with significance level of 0.05. The bars in all plots represent median values, with error bars representing the interquartile range between the 25% and 75% quartiles.

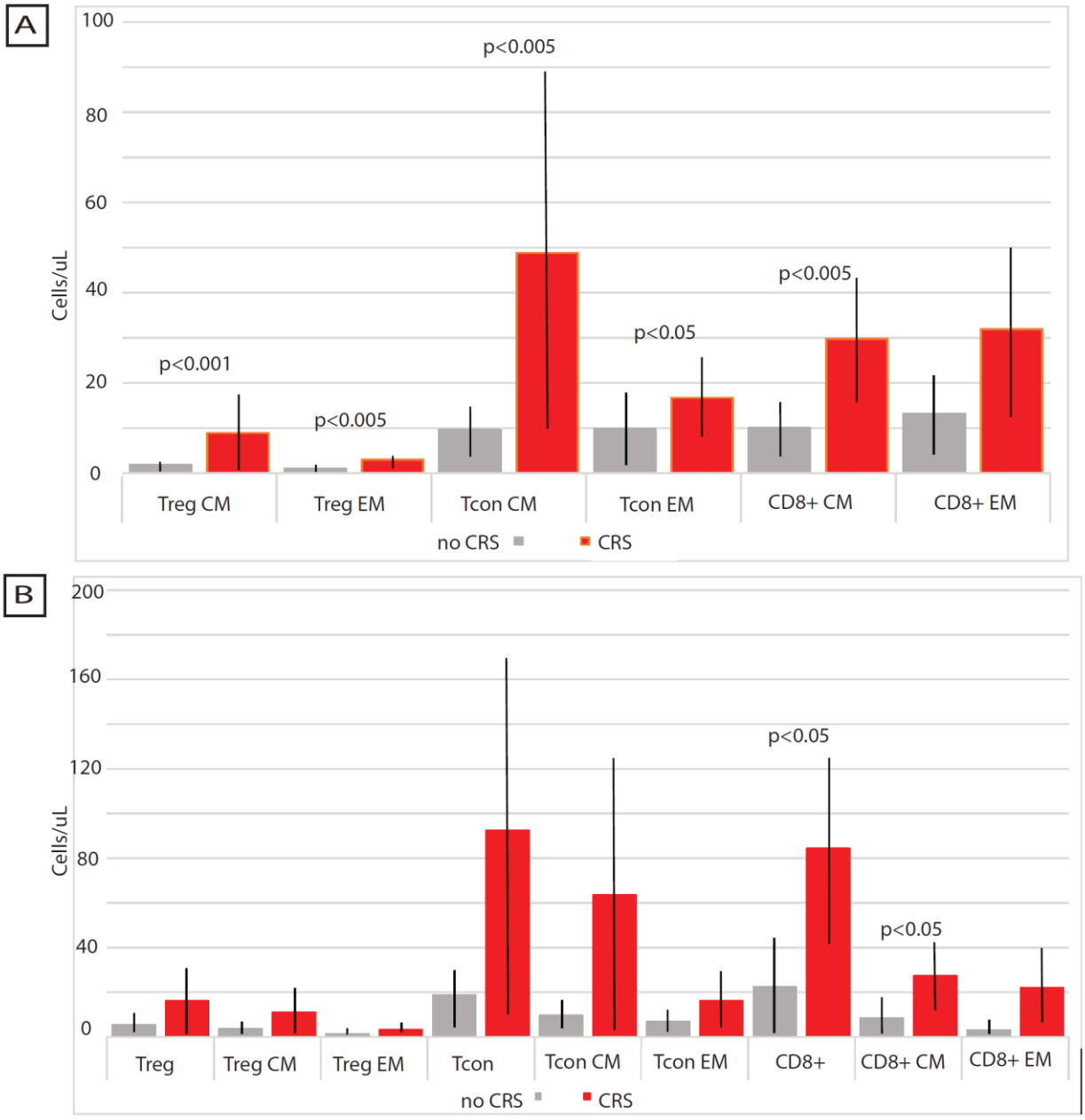

Figure S6. **Immune reconstitution of T-cell subsets at 1 month post haploidentical HCT. A** T-cell subset reconstitution among all patients who developed CRS (n = 37) compared to those who did not (n = 28). **B** T-cell subset reconstitution among patients who received PBSC grafts and developed CRS (n = 23) compared to those who did not (n = 7). CM: central memory, EM: effector memory. Wilcoxon rank-sum test was done for all group comparisons with all testing being two-sided with significance level of 0.05. The bars in all plots represent median values, with error bars representing the interquartile range between the 25% and 75% quartiles.