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Suppl Table 1: Conditioning regimens

conditioning	total per group n=		n=
MAC	19	BU*/Flu	5
		BU/CY	4
		BU/Flu/TT	4
		Flu/mel/TT	3
		Flu/TBI	1
		Treo/Flu/TT	2
Reduced Toxicity	23	BU**/Flu	12
		Treo (36-42g/kg)/Flu	11
RIC/NMA	18	BU < 8 mg/kg/low CY	5
		Flu/Mel	5
		Flu/Mel/RIT	1
		reduced Treo/Flu	3
		reduced Treo/Flu/RIT	2
		Flu/RIT	1
		Flu	1

MAC denotes myeloablatice conditioning, RIC: reduced intensity conditioning, BU: busulfan, Flu: fludarabine, CY: cyclophosphamide, TT: thiotepa, TBI: total body irradiation, Treo: treosulfan, RIT: radio-immunotherapy, BU* : myeloablative dose of busulfan as defined by IEWP guidelines; BU**: reduced dose of busufan as defined by IEWP guidelines: BU* administered under therapeutic drug monitoring (TDM), i.e. AUC >80 mg*h/L (doses >12mg/kg); BU** administered under TDM: 60-70 mg*h/L.

Suppl Table 2 V(D)J recombination activity by genetic variants in *RAG1* or *RAG2* genes in cohort of hypomorphic RAG deficient patients

affected gene	allele 1	% VDJ activity	allele 2	% VDJ activity	functionality by class
RAG1	p.R108X	1,8	p.R404Q	1,2	3
RAG1	p.R108X	1,8	p.R108X	1,8	3
RAG1	p.R507Q	10,1	p.R507Q	10,1	3
RAG1	p.R410W	0,0	p.R507Q	10,1	3
RAG1	p.R561H	5,2	p.R759C	17,2	3
RAG1	p.K86VfsX33	2,7	p.K86VfsX33	2,7	3
RAG1	p.N855S	11,7	p.K992E	9,1	3
RAG1	p.K86fsX33	2,7	p.R559S	1,0	3
RAG1	p.R229L	7,3	p.G319X	1,6	3
RAG1	p.K86VfsX33	2,7	p.K86VfsX33	2,7	3
RAG1	p.R841W	10,0	p.R841W	10,0	3
RAG1	p.I956T	3,5	p.I956T	3,5	3
RAG1	p.R716Q	0,0	p.N855S	11,7	3
RAG1	p.R975W	3,7	p.R778Q	2,3	3
RAG1	p.H612R	6,3	p.H612R	6,3	3
RAG1	p.M183R	23,1	p.V779M	1,3	3
RAG1	p.R108X	1,8	p.R108X	1,8	3
RAG1	p.R507Q	10,1	p.R507Q	10,1	3
RAG1	p.T708A	24,7	p.E669K	0,2	3
RAG1	p.R314W	24,3	p.R737H	0,2	3
RAG1	p.E193K	48,4	p.E193K	48,4	2
RAG1	p.R142X	9,0	p.T477S	72,5	2
RAG1	p.R973H	32,0	p.R973H	32,0	2
RAG1	p.S480G	60,1	p.S480G	60,1	2
RAG1	p.K86fs*	2,7	p.M573K	27,7	2
RAG1	p.R112L	42,1	p.H735Q	0,2	2
RAG1	p.H375D	40,4	p.Y562C	0,0	2
RAG1	p.R410W	0,0	p.H375D	40,4	2
RAG1	p.R474H	57,8	p.R559S	1,0	2
RAG1	p.R112H	41,0	p.R410W	0,0	2
RAG1	p.W204X	0,4	p.W522C	41,6	2
RAG1	p.W522C	41,6	p.R975Q	57,9	2
RAG1	p.C363Y	45,3	p.R396C	0,6	2
RAG1	p.R973C	0,0	p.W522C	41,6	2
RAG1	p.R108X	1,8	p.W522C	41,6	2
RAG1	p.R112H	41,0	p.C328Y	16,0	2
RAG1	p.W204X	0,4	p.W522C	41,6	2
RAG1	p.A472BV	0,4	p.H612R	134,0	1
RAG1	p.R474C	109,2	p.Y768X	0,0	1
RAG1	p.R410Q	0,0	p.H612R	134,0	1
RAG1	p.R474C	109,2	p.K983NfsX9	0,1	1

affected gene	allele 1	% VDJ activity	allele 2	% VDJ activity	functionality by class
RAG1	p.K86VfsX33	2,7	p.H612R	134,0	1
RAG1	p.R474C	109,2	p.R624H	0,0	1
RAG1	p.R474C	109,2	p.K983NfsX9	0,1	1
RAG1	p.R474C	109,2	p.K983NfsX9	0,1	1

affected gene	allele 1	% VDJ activity	allele 2	% VDJ activity	functionality by class
RAG2	p.S447C	9,9	p.S447C	9,9	3
RAG2	p.G35A	22,1	p.A456D	0,1	3
RAG2	p.A456V	19,5	p.A456V	19,5	3
RAG2	p.G35A	22,1	p.G35A	22,1	3
RAG2	p.407X	2,9	p.p.407X	2,9	3
RAG2	p.N173S	47,5	p.E437K	0,9	2
RAG2	p.T77N	21,7	p.G451A	27,6	2
RAG2	p.G451A	66,3	p.I210T	57,6	2
RAG2	p.Y453R	0,6	p.P305R	30,9	2
RAG2	p.P305R	30,9	p.M459L	30,8	2
RAG2	p.G35V	0,4	p.M322T	55,1	2

1 (green) = normal/possibly reduced: at least one allele >75%; 2 (yellow) = reduced: at least one allele >25-75%; 3 (orange) = severely reduced: both alleles <25%.

Suppl Table 3: Autoimmune manifestations before HSCT and outcome after HSCT

Autoimmune manifestations:		Outcome after HSCT
Autoimmune cytopenia (n= 50 in 33 patients)		*resolved*
	AIHA n= 21	
	ITP n= 15	
	AI neutropenia n= 13	
	Pure Red blood cell aplasia n= 1	
Other autoimmune manifestations (n= 41 in 21 patients)		
SKIN:	Dermatitis n= 7	resolved n= 5, NA n= 2
	Vitiligo n= 7	resolved n= 1, improved n= 2, stable n= 2, NA n= 1
	Alopecia areata n= 6	resolved n= 4, NA n= 2
NEURO-MUSCULAR SYSTEM:		
	Myositis n= 3	improved n= 1, NA n= 2
	Myasthenia gravis n= 2	resolved n= 1, NA n= 1
	Arthritis n= 1	NA
	AI encephalitis n= 1	non active at HSCT
	Fascitis n= 1	NA
GASTRO-INTESTINAL TRACT:		
	Colitis n= 7	resolved n= 5, NA n= 2
	duodenitis n= 1	resolved
	panceatitis n=1	resolved
OTHERS	Uveitis n= 1	relapse after HSCT, then resolved
	interstitial lung disease n= 1	resolved
	Glomerulonephritis n= 1	NA
	Intra-cerebral vasculitis n= 1	resolved

Numbers of autoimmune manifestations per patient: n=16: one manifestation per patient; n=17: two; n=3: three; n=3: four; n=4: five.

Suppl Table 4: Details on organ damage prior HSCT

organ damage at HSCT	n	etiology	n
lung	30	chronic bronchitis	6
		bronchiectasia	6
		bronchiectasia and restrictive disease	1
		restrictive disease	2
		obstructive and restrictive disease	3
		pneumonitis	1
		post viral pneumonitis (mosaic attenuation)	1
		immune pneumonitis	1
		sequelae following severe/recurrent infections	2
		granulomatous–lymphocytic interstitial lung disease (GLILD)	1
		not otherwise specified	6
liver	10	viral hepatitis (CMV, varicella)	3
		cryptosporidium/sclerosing cholangitis	1
		recurrent infections	1
		severe hepatitis with CD8+ infiltration	1
		chronic hepatitis	1
		hepatic granuloma	1
		iron overload	1
		cholestasis (post hemophagocytic lymphohistiocytosis)	1
kidney	6	post-dialysis nephropathy (following life-threatening varicella infection)	1
		autoimmune glomerulonephritis with sclerosis	1
		tubular injury following recurrent hemolysis (intermittent hematuria, low grade proteinuria)	1
		not otherwise specified	3
other	9	enterocolitis	4
		peridontitis/recurrent mouth ulcers, recurrent episodes of diarrhea	1
		persistent norovirus infection	1
		pancreatitis	1
		persistent steroid-induced diabetes	1
		epilepsy (cerebral vasculitis)	1

Suppl Table 5: Details of T-cell depleted grafts

patient ID	4	7	10	27	41	43	49	69	22	25	26	38	42	52	68
EBMT CIC	204	204	913	201	243	209			201	201	201	243	243		
sex	f	m	f	f	m	f	m	f	m	m	f	m	f	f	f
RAG 1 or 2	1	1	2	2	1	1	1	1	1	1	1	2	2	1	1
age (mo) 1st symptom	8.5	17.5	18	11.5	12.5	10	66.5	16	16.5	63	150	18	NA	2	6
age at HSCT (y)	8.5	8.5	2.7	1.5	2.3	1.5	16.8	3.2	3	16.8	10	7.3	2.8	0.8	1.1
active infection at HSCT	y	y	y	y	y	y	y	y	n	n	n	n	n	n	n
donor	MUD	MMFD	MMFD	MMUD	MMFD	MMFD	MMFD	MUD	MUD	MUD	MUD	MMUD	MMFD	MMFD	MFD
conditioning	RIC	MAC	RTC	MAC	RTC	RTC	RTC	MAC	MAC	MAC	MAC	RIC	RIC	RTC	MAC
type of T-cell depletion	CD34	TCRab	TCRab	CD45RA	CD34	CD34	CD34	TCRab	CD45RA	CD45RA	CD45RA	CD34/addback	TCRab	TCRab	TCRab
serotherapy	ATG	ATG	ATG	ATG	none	alemtuz.	alemtuz.	ATG	alemtuz.	alemtuz.	ATG	alemtuz.	ATG	ATG	ATG
donor cell engraftment	100	0	NA	85	100	100	100	NA	100	100	100	NA	100	35	NA
autoimmunity pre HSCT	0	1	1	0	1	1	1	1	0	1	1	1	0	0	0
autoimmunity resolved post HSCT	NA	NA	NA	NA	y	NA	NA	NA	NA		improved	NA	NA	NA	NA
granuloma pre HSCT	1	0	0	0	0	0	0	0	1	1	0	0	0	0	0
granuloma resolved post HSCT	y	NA	NA	NA	NA	NA	NA	NA	y	y	NA	NA	NA	NA	NA
new onset/relapse autoimmunity	n	NA	NA	y	n	NA	NA	NA	y	y	y	NA	n	NA	NA
AI entity										sclerosing cholangitis	myositis				
AI entity									AIHA	AIHA	Basedow				
survival	n	n	n	y	n	n	n	n	y	n	y	n	y	n	n
time to death post HSCT (mo)	26	9	0.3	NA	41	6	2	0	NA	46	NA	0	NA	7	1
cause of death	GvHD/inf.	graft fail.	sepsis	NA	encephalitis	infection	p. hemorrhage	infection	NA	autoimmunity	NA	viral infection	NA	infection	infection

alemtuz=alemtuzumab

NA=not applicable

p.=pulmonary

**Suppl Table 6**: OS – variable importance for OS (random forest)

Variable	Variable importance
> 12 months between birth and diagnosis	0.1320875
VDJ-activity > 75% in at least one allel	0.2224135
age at HSCT < 3.5 years	0.3164747
autoimmunity and/or granuloma at HSCT	0.3902234
infection prior to HSCT	0.5286125
active autoimmunity and/or granuloma at HSCT	0.6836633
active infection at HSCT	0.9210747
organ damage prior to HSCT	**1.1368471**
mismatched family donor (MMFD)	**1.7044517**
T-cell depletion	**2.3940849**

Suppl Table 7: Determinants for Immunglobulin (Ig) substitution

| Variable		Ig substitution, n(%) no	yes	OR (univariable)*
infection prior to HSCT	no	11 (29.7)	1 (9.1)	-
	yes	26 (70.3)	10 (90.9)	4.23 (0.68-82.44, p=0.193)
autoimmunity prior to HSCT	no	15 (40.5)	1 (9.1)	-
	yes	22 (59.5)	10 (90.9)	6.82 (1.13-131.86, p=0.081)
organ damage prior to HSCT	no	18 (48.6)	4 (36.4)	-
	yes	19 (51.4)	7 (63.6)	1.66 (0.43-7.24, p=0.475)
age at transplantation < 3.5 years	no	19 (51.4)	6 (54.5)	-
	yes	18 (48.6)	5 (45.5)	0.88 (0.22-3.42, p=0.852)
myeloablative conditioning (MAC)	no	25 (67.6)	8 (72.7)	-
	yes	12 (32.4)	3 (27.3)	0.78 (0.15-3.27, p=0.746)
reduced intensity conditioning (RIC)	no	25 (67.6)	8 (72.7)	-
	yes	12 (32.4)	3 (27.3)	0.78 (0.15-3.27, p=0.746)
reduced toxicity conditioning (RTC)	no	24 (64.9)	6 (54.5)	-
	yes	13 (35.1)	5 (45.5)	1.54 (0.38-6.10, p=0.536)

* OR = Odd's ratio (95% confidence interval)

age distribution at HSCT
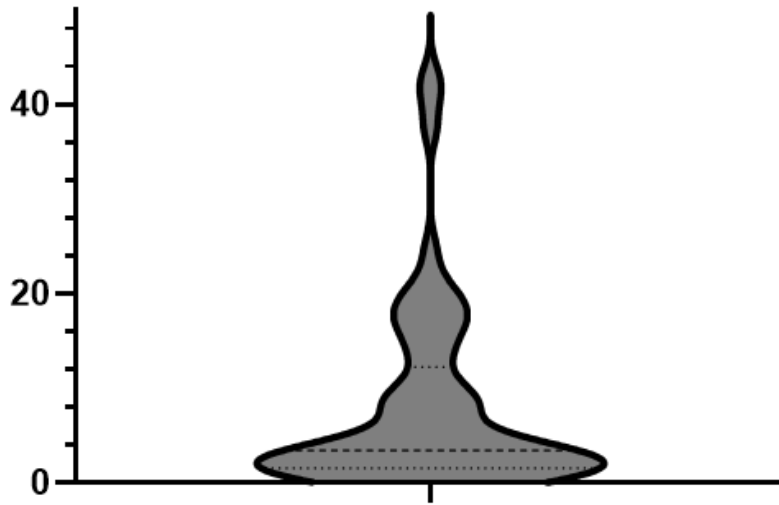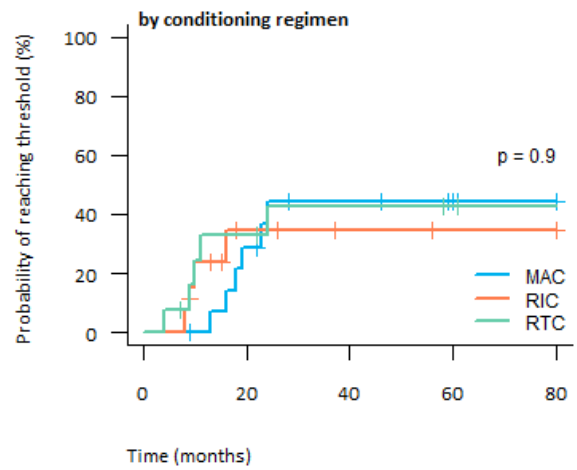
Suppl Figure 1 – Violin plot of age distribution at HSCT
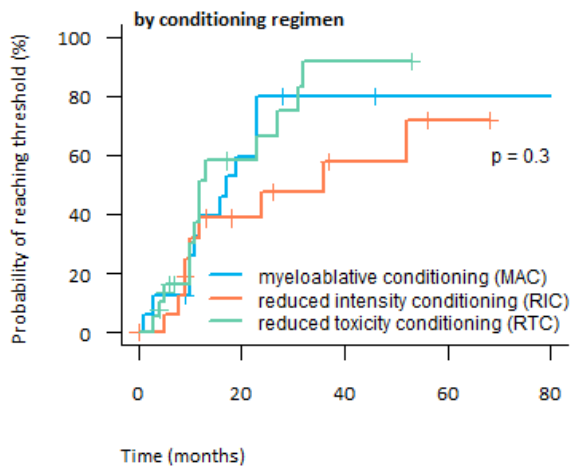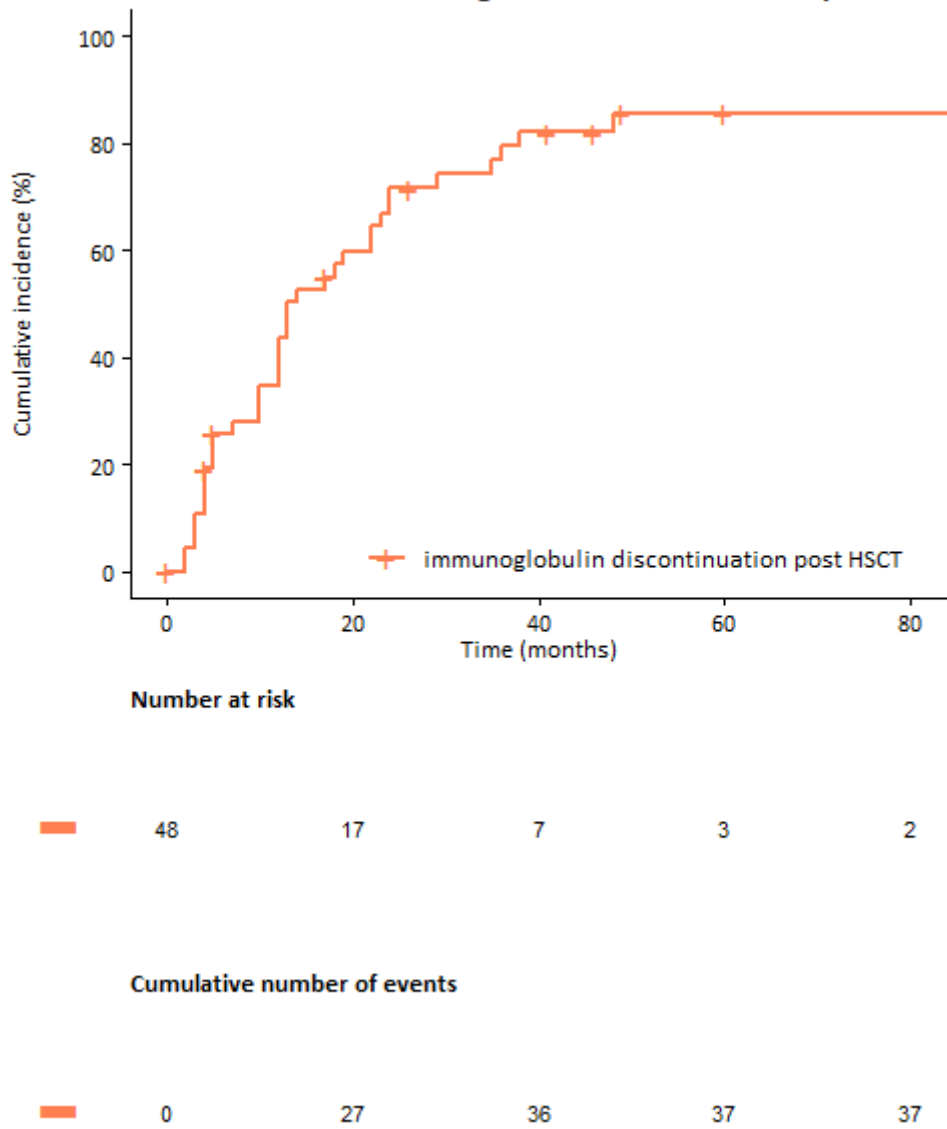
Suppl. Figure 2 - T-cell reconstitution by Conditioning regimen, **A**: age-adapted CD4^{+} T-cells, **B**: age-adapted CD45RA^{+} T-cells.

Suppl Figure 3– Cumulative incidence of immunoglobulin discontinuation post HSCT.