

Supplementary information to the manuscript

Reticular Dysgenesis: International Survey on Clinical Presentation,

Transplantation and Outcome

Table S1: Bone marrow morphology before HSCT reported in 26 patients with Reticular Dysgenesis.

Bone marrow morphology	patients
reports	26/32
cellular hyperplasia	5/26
cellular hypoplasia	9/26
abnormal myelopoiesis with developmental arrest (promyelocytes)	22/26
abnormal lymphopoiesis	9/26
abnormal megakaryopoiesis	3/26
abnormal erythropoiesis	4/26

Abnormalities described in myelopoiesis in addition to promyelocytic developmental arrest include: increased percentage of myeloblasts and signs of dysplastic maturation; abnormalities described in erythropoiesis include: dysplastic maturation, hyper- or hypoplasia; abnormal megakaryopoiesis was described as: hyperplasia and dysplastic maturation with micromegakaryocytes.

Table S2: Details of HSCT in 31 patients with Reticular Dysgenesis

patient number	age at HSCT (mo)	donor	HLA match	stem cell source, graft manipulation	chemotherapy	sero-therapy	GvHD-prophylaxis	engraftment	aGvHD	cGvHD	follow up after most recent Tx	Outcome/ cause of death
2a	0.5	MSDb	6/6	BM, none	-	atmab	-	no	no	no	n.a.	primary graft failure -> 2 nd Tx
2b	3.3	MSDs	6/6	BM, none	-	ATG	-	yes	skin 2	no	23.4 y	a&w, hearing aid
3	4.4	MFD	6/6	BM, none	Mel80 Flu125	no	CSA, MTX	yes	no	no	7.9 y	a&w, hearing aid
4	7.0	MFD	11/12	BM, none	Bu16 Cy200	no	CSA, MTX	yes	skin 4	no	3.0 y	a&w, hearing aid
5	2.2	MFD	10/10	BM, none	Bu20 Flu140	no	CSA	yes	skin 2	no	8.0 y	clonic seizures, speech delay, brain malformations (lipoma, agenesis of corpus callosum), hearing aid
6a	4.2	MFDf	10/10	BM, none	Treo36	no	CSA	yes	skin 3	no	n.a.	secondary graft failure (3mo) -> 2 nd Tx
6b	9.8	MFDf	10/10	BM, none	Bu20.4 Mel140	no	CSA	yes	no	no	3.8 y	a&w, hearing aid
7	1.3	MFD	10/10	BM, none	Treo42	atmab	CSA, MMF	yes	no	no	2.1 y	a&w, cochlear implant
8	4.7	MUD	12/12	BM, none	Bu20 Cy200	ATG	CSA	yes	skin 1	no	11.0 y	a&w, hearing aid
9a	8.0	UCB	8/10	UCB, none	αCD45 Cy1200* Flu150	atmab	CSA, MMF	yes	skin 2	no	n.a.	secondary graft failure -> 2 nd Tx
9b	42.8	MSD	10/10	BM, none	Bu19.2 Cy200	no	CSA, MTX	yes	no	no	1.2 y	a&w, hearing aid
10	1.8	UCB	10/10	UCB, none	Bu16Cy200	atmab	CSA	yes	no	no	7.4 y	a&w, hearing aid (CI)
11a	1.7	UCB	6/6	UCB, none	Treo1500**Flu100	no	CSA, steroids	yes	no	no	n.a.	secondary graft failure (2mo)-> 2 nd Tx
11b	8.4	UCB	5/6	UCB, none	Bu320*Cy200	ATG	CSA, steroids	yes	no	no	6.0 y	a&w, hearing aid (CI)
12	5.2	UCB	4/6	UCB, none	Bu16Cy200	ATG	MTX, tacrolimus	yes	no	no	5.0 y	a&w, hearing aid
13	3.7	UCB	6/6	UCB, none	BuCy (dosage n.r.)	atmab	CSA, steroids	yes	skin 2 (pre)	gut	3.1 y	a&w, hearing aid (CI)
14	6.1	UCB	5/6	UCB, none	Bu16Cy200	ATG	CSA	yes	gut 2	extensive	3.4 y	alive & on immunosuppression (CSA + steroids)
15	3.5	MMUD	9/10	BM, none	Bu***Cy200	ATG	CSA, MTX, steroids	yes	gut 3	no	died d +31	VOD, multiorgan failure
16a	1.5	MMFDm	3/6	BM, SBL/SE	-	-	-	T only	no	no	n.a.	primary graft failure -> 2 nd Tx
16b	8.3	MMFDm	3/6	BM, SBL/SE	Bu12 p.o.	-	-	T only	no	no	n.a.	primary graft failure -> 3 rd Tx
16c	10.3	MMFDm	3/6	BM, SBL/SE	-	-	-	T only	no	no	died d +76	invasive pulmonary aspergillosis
17	3.5	MMFDm	3/6	BM, SBL/SE	-	atmab	-	no	no	no	died d +59	encephalitis
18a	1.3	MMFDm	3/6	BM, SBL/SE	-	ATG	-	no	no	no	n.a.	primary graft failure -> 2 nd Tx

18b	2.5	MMFDm	3/6	BM, SBL/SE	TBI 7Gy Cy120	ATG	-	yes	no	no	1.0 y	a&w, hearing unknown
19a	2.1	MMFDm	3/6	PBSCs, CD34+/CD2-	-	ATG	CSA steroids	T only	liver (pre)	liver (pre)	n.a.	primary graft failure -> 2 nd Tx
19b	10.5	MMFDm	3/6	PBSCs, CD34+/CD2-	Cy200	ATG	CSA	T only	liver (pre)	liver (pre)	died y +1.7	pneumonia (leukopenia)
20a	9.5	MMFDm	3/6	BM, CD34+	-	-	-	no	no	no	n.a.	primary graft failure -> 2 nd Tx
20b	15.4	MMFDf	3/6	BM, CD34+	Bu16 Cy200	ATG	-	no	no	no	died d +34	aplasia, pulmonary disease
21a	2.5	MMFDm	4/8	BM, SBL/SE	Cy200	ATG	-	no	no	no	n.a.	primary graft failure -> 2 nd Tx
21b	4.0	MMFDm	4/8	BM, SBL/SE	Bu16 Cy200	ATG	-	yes	no	no	16.4 y	a&w, hearing aid (CI)
22	1.8	MMFDm	3/6	PBSCs, CD34+/CD3-	Bu8	ATG	-	yes	no	no	4.4 y	a&w, hearing aid (CI)
23	1.9	MMFDm	3/6	BM, SBL/SE	Bu16 Cy200	-	-	yes	no	no	17.1 y	a&w, hearing aid
24	2.4	MMFDm	3/6	BM, SBL/SE	Bu16 Cy200	-	-	yes	skin 2, liver 2	liver	died y +0.5	GvHD, liver failure
25	5.1	MMFDm	3/6	BM, CD2-/CD7-/CD19-	Bu8 Cy150	-	-	n.r.	no		died d +15	interstitial pneumonia
26a	1.8	MMFDm	5/6	BM, CD34+/CD3-	Bu8 Cy200	-	-	yes	skin 3, gut 3	no	n.a.	secondary graft failure and MDS -> 2 nd Tx
26b	74.0	MMFDm	5/6	BM, CD34+/CD3-	Bu16 Cy200	-	-	yes	no	no	died y +1.0	relapse MDS
27	1.9	MMFD	3/6	BM, CD34+	Bu8 Cy200	-	-	yes	no	no	17.0 y	a&w, hearing aid
28	2.1	MMFDm	3/6	PBSC, CD34+/CD2/3-	Bu16 Cy120	-	CSA	yes	skin 2 (pre)	no	12.9 y	a&w, hearing aid (CI)
29a	1.1	MMFDf	6/12	BM, CD34+	Bu16 Cy200	ATG	CSA	no	no	no	n.a.	primary graft failure -> 2 nd Tx
29b	10.1	MMFDm	6/12	BM, CD34+	-	no	-	no	no	no	n.a.	primary graft failure -> 3 rd Tx
29c	13.1	MMFDm	6/12	BM, CD34+	Bu16 Cy200	atmab	-	no	no	no	died d +25	systemic adenovirus infection
30a	2.8	MMFDm	3/6	BM, CD34+	Bu16 Cy200	ATG	-	yes	no	no	n.a.	secondary graft failure and MDS -> 2 nd Tx
30b	32.8	MMFDm	3/6	BM, CD34+	Bu25 Cy200	-	-	yes	no	no	died y +5.2	glioma
31a	11.1	MMFDm	3/6	BM, CD34+	Bu16 Cy50	-	-	no	no	no	n.a.	primary graft failure -> 2 nd Tx
31b	12.5	MMFDf	3/6	BM, CD34+	-	ATG	-	yes	skin 2, gut 2	no	0.5 y	a&w, hearing aid (CI)
32	1.8	MMFDm	3/6	PBSCs, CD34+	Bu12.8 Flu100	ATG	CSA	yes	no	no	9.1 y	a&w, hearing aid (CI)

Abbreviations: Repeat transplants are indicated with "a", "b" or "c" after the patient number; d: day; y: year; n.a.: not applicable; n.r.: not reported; MSD: matched sibling donor; MSDb: matched sibling donor, brother; MSDs: matched sibling donor, sister; MFD: matched family donor; MUD: matched unrelated donor; MMUD: mismatched unrelated donor; MMFD: mismatched family donor; MMFDf: mismatched family donor, father; MMFDm: mismatched family donor, mother; BM: bone marrow; PBSC: peripheral blood stem cells; UCB: unrelated cord blood; SBL/SE: soy bean lectin/ sheep erythrocyte agglutination;

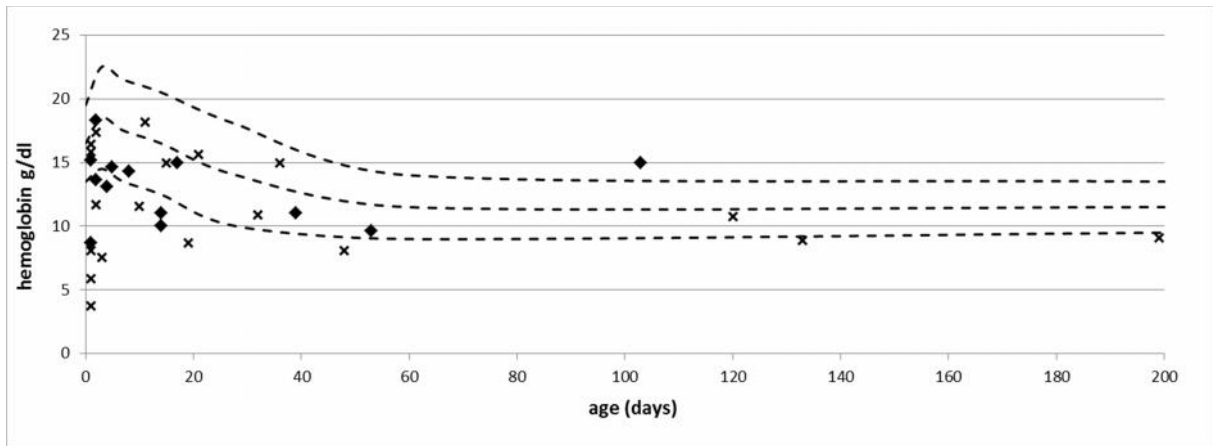
ATG: anti-thymocyte globulin; atmag: alemtuzumab; Tx: transplantation; CI: cochlear implant; a&w: alive and well; TBI: total body irradiation; α CD45: anti-CD45 antibody; Bu: Busulfan dosage given in mg/kg intravenous application if not indicated by p.o.: per os; Cy: cyclophosphamide dosage given in mg/kg; Flu: fludarabine dosage given in mg/m²; Treo: treosulfan dosage given in g/m²; Mel: melphalan dose given in mg/m²; CSA: cyclosporine A; MTX: methotrexate; MMF: mycophenolate mofetil; T only: only T cells of donor origin were detected; pre: GvHD was present before transplantation and is most probably due to an alloreaction caused by persisting maternal cells; MDS: myelodysplastic syndrome; VOD: venoocclusive disease; *busulfan dosage given in mg/m²; **treosulfan dosage given in mg/kg; ***targeted Bu 800-1200 μ mol*min/L;

Table S3: Non-hematological outcome of long-term survivors

patient	age at most recent clinical evaluation	weight	height	Lansky scale	education	neurological	
						learning disability suspected	gross motor deficit
no.	date (years)	kg (percentile)	cm (percentile)		special needs or support beyond hearing disability		
2	28.1	53 (10-25 th)	151 (<3 rd)	100	lower secondary education without graduation, apprenticeship	no	no
3	11.0	37.2 (25-50 th)	142 (25-50 th)	100	no	no	no
4	8.7	22 (4 th)	127 (10-25 th)	70	special school	autistic behaviour	no
5	5.0	14 (<3 rd)	102 (<3 rd)	n.a.	n.a.	seizures, developmental delay, agenesis of corpus callosum	n.a.
6	4.6	14.1 (<3 rd)	102 (3-10 th)	100	regular kindergarten	no	no
7	5.0	15.7 (3-10 th)	106 (10-25 th)	100	regular kindergarten	learning disability, special support at school	n.a.
8	3.5	14 (25-50 th)	n.a.	n.a.	n.a.	n.a.	n.a.
9	11.0	30 (10 th)	135 (10 th)	100	no	no	no
10	13.3	35.7 (9 th)	157 (50 th)	100	normal schooling	no	no
11	10.5	26.7 (3-10 th)	136 (3-10 th)	100	school for hearing impaired	no	no
12	8.7	22.4 (3-10 th)	124 (3-10 th)	100	school for hearing impaired	no	no
13	3.3	15 (38 th)	100 (28 th)	n.a.	normal schooling	no	n.a.
14	7.0	18.1 (3 rd)	98 (3 rd)	100	normal schooling	learning disability, special support at school	no
18	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
21	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
22	7.5	23 (25-50 th)	118 (3-10 th)	100	kindergarten for hearing impaired	no	no
23	17.0	81.5 (90-97 th)	180 (50-75 th)	100	finished school for hearing impaired	no	no
27	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
28	12.9	32.6 (3-10 th)	148 (10-25 th)	100	normal schooling	no	no
31	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
32	12.07	30 (3 rd)	145 (10-25 th)	100	normal schooling	no	no

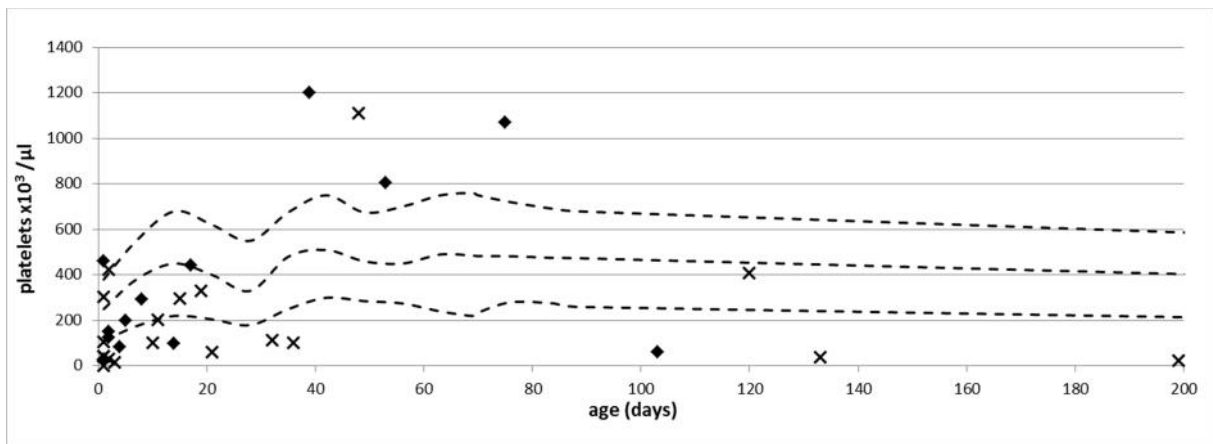
Abbreviations: n.a.: data not available.

Figure S1: Hemoglobin levels at presentation.



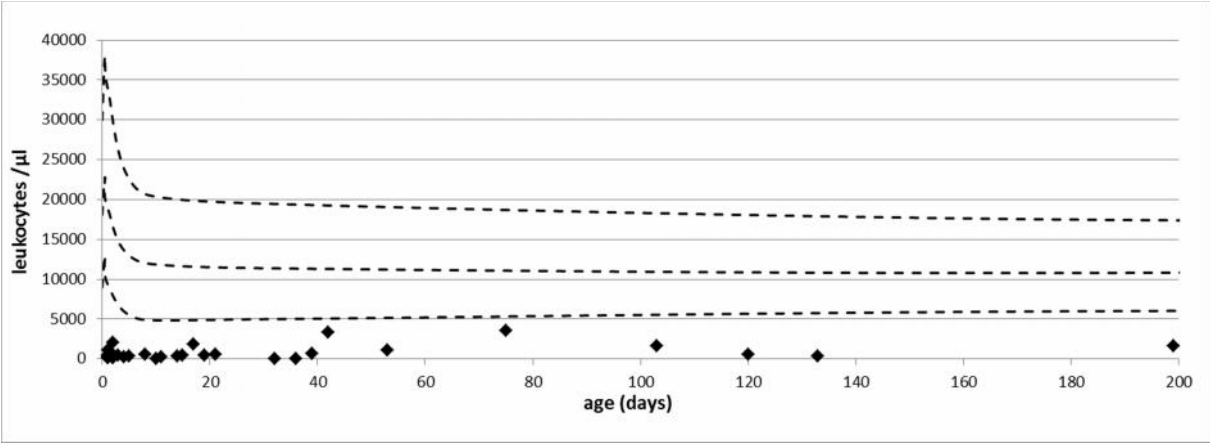
The patients with a bacterial sepsis are marked with crosses, the patients without signs of sepsis are marked with diamonds. Dotted lines indicate the age related mean and the 5th and 95th percentile of values found in normal controls.¹

Figure S2: Platelet counts at presentation.



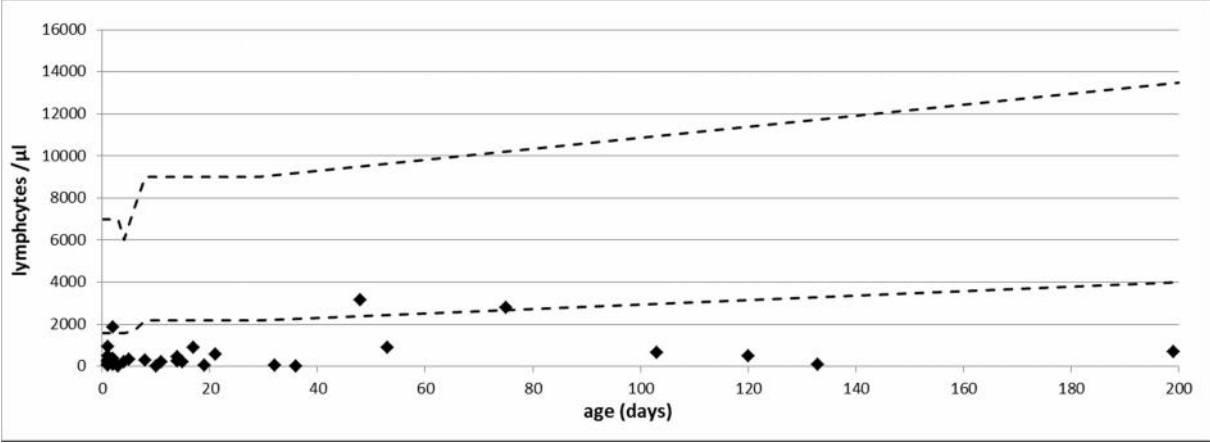
The patients with a bacterial sepsis are marked with crosses, the patients without signs of sepsis are marked with diamonds. Dotted lines indicate the age related mean and the 5th and 95th percentile of values found in normal controls.²

Figure S3: Leukocyte counts at presentation.



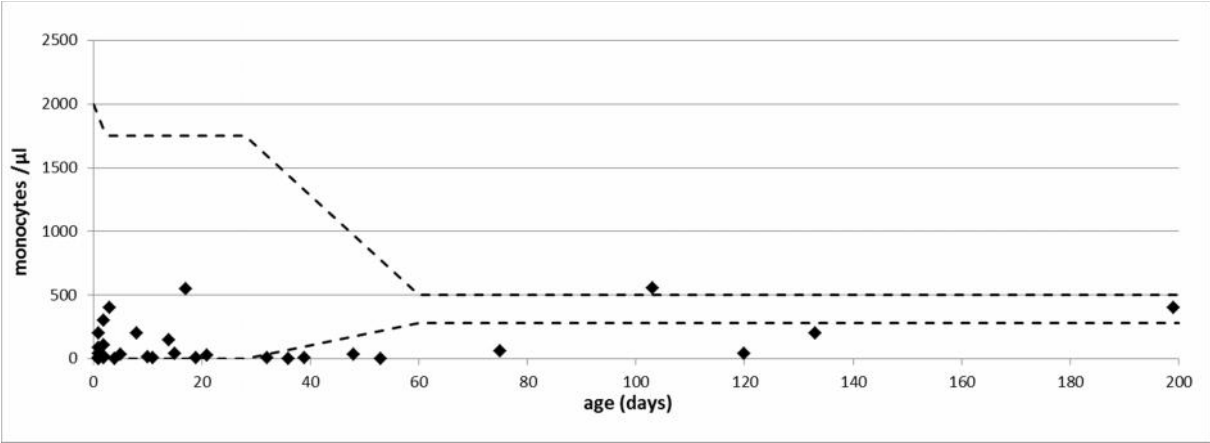
Dotted lines indicate the mean and age related 5th and 95th percentile of values found in normal controls. ¹

Figure S4: Lymphocyte counts at presentation.



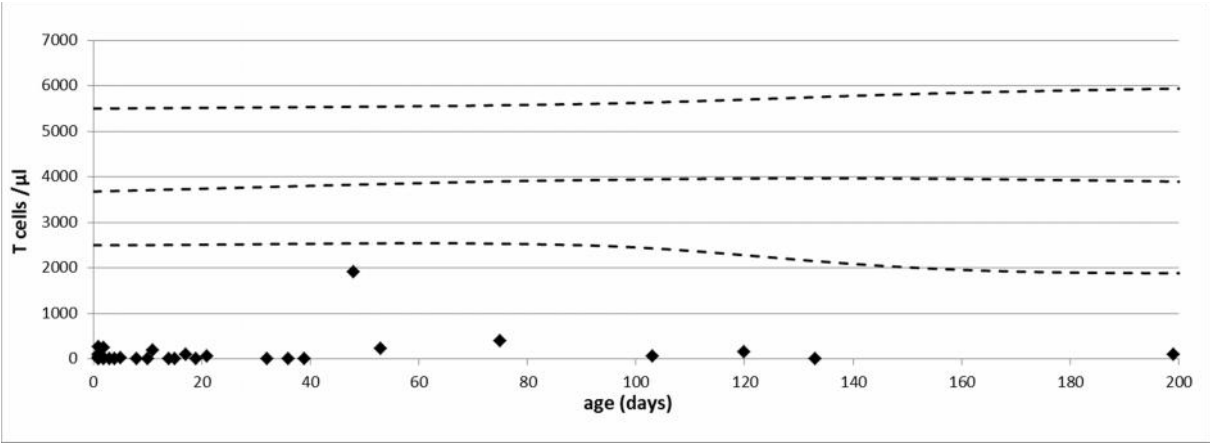
Dotted lines indicate the age related 5th and 95th percentile of values found in normal controls. ³

Figure S5: Monocyte counts at presentation.



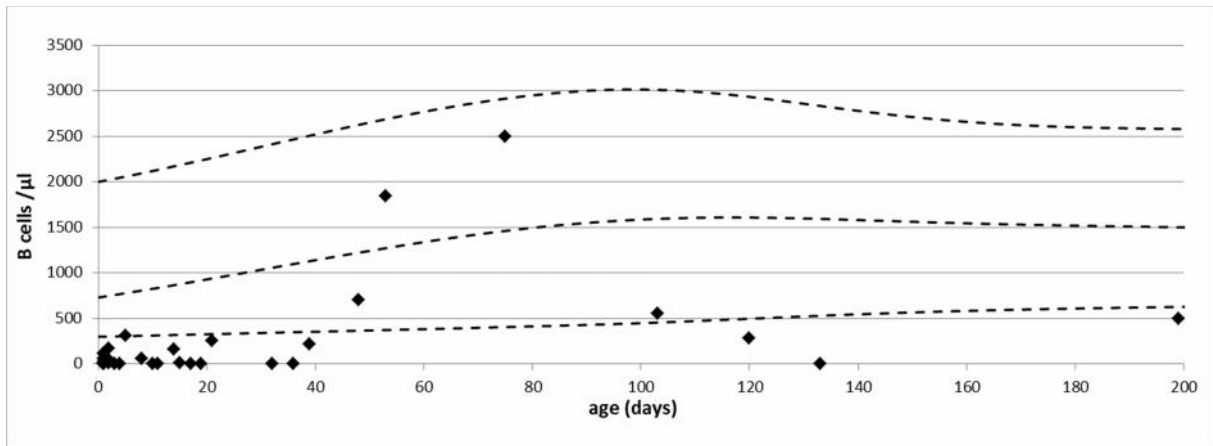
Dotted lines indicate the age related 5th and 95th percentile of values found in normal controls.³

Figure S6: T-cell counts at presentation.



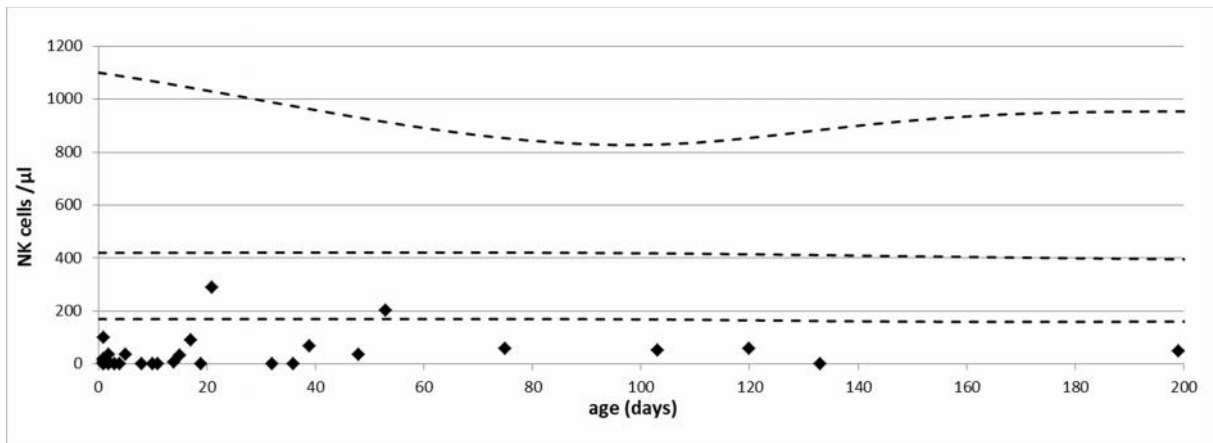
Dotted lines indicate the age related median as well as the 5th and 95th percentile of values found in normal controls.⁴

Figure S7: B-cell counts at presentation.



Dotted lines indicate the age related median as well as the 5th and 95th percentile of values found in normal controls.⁴

Figure S8: NK-cell counts at presentation.



Dotted lines indicate the age related median as well as the 5th and 95th percentile of values found in normal controls.⁴

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4. Shearer WT, Rosenblatt HM, Gelman RS, et al. Lymphocyte subsets in healthy children from birth through 18 years of age: the Pediatric AIDS Clinical Trials Group P1009 study. *J Allergy Clin Immunol.* 2003;112(5):973-980.