

Comparison of outcomes of hematopoietic stem cell transplantation without chemotherapy conditioning by using matched sibling and unrelated donors for treatment of severe combined immunodeficiency

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Background: Patients with severe combined immunodeficiency disease who have matched sibling donors (MSDs) can proceed to hematopoietic cell transplantation (HCT) without conditioning chemotherapy.

Objective: We sought to determine whether the results of HCT without chemotherapy-based conditioning from matched unrelated donors (URDs), either from volunteer adults or umbilical cord blood, are comparable with those from MSDs.

Methods: We performed a multicenter survey of severe combined immunodeficiency transplantation centers in North America, Europe, and Australia to compile retrospective data on patients who have undergone unconditioned HCT from either URDs (n = 37) or MSDs (n = 66).

Results: Most patients undergoing URD HCT (92%) achieved donor T-cell engraftment compared with 97% for those with

MSDs; however, estimated 5-year overall and event-free survival were worse for URD recipients (71% and 60%, respectively) compared with MSD recipients (92% and 89%, respectively; $P < .01$ for both). URD recipients who received pre-HCT serotherapy had similar 5-year overall survival (100%) to MSD recipients.

The incidences of grade II to IV acute and chronic graft-versus-host disease were higher in URD (50% and 39%, respectively) compared with MSD (22% and 5%, respectively) recipients ($P < .01$ for both). In the surviving patients there was no difference in T-cell reconstitution at the last follow-up between the URD and MSD recipients; however, MSD recipients were more likely to achieve B-cell reconstitution (72% vs 17%, $P < .001$).

Conclusion: Unconditioned URD HCT achieves excellent rates of donor T-cell engraftment similar to that seen in MSD recipients, and reconstitution rates are adequate. However, only

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a minority will have myeloid and B-cell reconstitution, and attention must be paid to graft-versus-host disease prophylaxis. This approach might be safer in children ineligible for intense regimens to spare the potential complications of chemotherapy. (J Allergy Clin Immunol 2014;■■■:■■■-■■■.)

Key words: Severe combined immunodeficiency, hematopoietic cell transplantation, sibling donors, unrelated donors, umbilical cord blood, conditioning, serotherapy

Severe combined immunodeficiency (SCID) diseases are a heterogeneous group of genetic disorders that impair T- and B-cell function and when untreated lead to early death caused by recurrent infections. Although gene therapy has had some success in recent years and enzyme replacement therapy can restore immunologic function for patients with adenosine deaminase (ADA)-deficient SCID, the most successful treatment for SCID has been allogeneic hematopoietic cell transplantation (HCT).¹ Because of the absence of functional T cells in patients with typical SCID, graft rejection is rare, even when immunoablative conditioning is omitted.² The major exception to this rule is in natural killer (NK)-positive SCID phenotypes, where NK cells have been shown to be capable of mediating rejection of HLA-mismatched donors unless maternal engraftment is present and the mother is used as the donor.³⁻⁵

An HLA-matched sibling donor (MSD) is always the preferred stem cell donor, with overall survival (OS) rates exceeding 90%, especially when the transplantation is performed before opportunistic infections develop.^{6,7} MSD transplantations are typically performed without any conditioning chemotherapy because the immune system of a patient with SCID is generally incapable of mediating rejection of the donor stem cells.⁸ Unfortunately, most patients do not have MSDs, in which case either a haploidentical family member or an HLA-matched adult unrelated donor (URD) or umbilical cord blood (UCB) unit can be used as the stem cell source.^{1,9} Traditionally, many haploidentical HCTs have been performed without pre-HCT conditioning,^{3,6,10} whereas the majority of URD or UCB recipients have been conditioned with myeloablative doses of chemotherapy,^{7,11,12} making direct comparisons difficult.⁹

Given the advances in HLA-typing technology, we hypothesized that a closely matched URD or UCB unit could approximate the situation of an MSD and thus be used to perform successful transplantations in patients with SCID without the need for cytotoxic conditioning, thereby sparing patients the potential risk of early and long-term complications of chemotherapy. However, reports describing URD or UCB HCTs for patients with SCID without the use of conditioning chemotherapy are few and have small numbers.¹³⁻¹⁶ Therefore to test this hypothesis, we have assembled a cohort of 37 patients in North America, Europe, and Australia who have undergone unconditioned URD or UCB HCTs for treatment of SCID and compared their engraftment rates, complications, and immunologic outcomes with those of a contemporaneous cohort of 66 recipients of unconditioned MSD HCT undergoing transplantation at the same centers.

METHODS

Patient identification

The Primary Immune Deficiency Treatment Consortium (PIDTC) consists of 33 centers in North America with a special interest in patients with primary

Abbreviations used

ADA:	Adenosine deaminase
aGVHD:	Acute graft-versus-host disease
BM:	Bone marrow
cGVHD:	Chronic graft-versus-host disease
DCLRE1C:	DNA cross-link repair 1C
EFS:	Event-free survival
GVHD:	Graft-versus-host disease
HCT:	Hematopoietic cell transplantation
IEWP-EBMT:	Inborn Errors Working Party of the European Blood and Marrow Transplant Society
IL2RG:	Interleukin receptor common γ chain
JAK3:	Janus kinase 3
LIG4:	Ligase 4
MSD:	HLA-matched sibling donor
OS:	Overall survival
PIDTC:	Primary Immune Deficiency Treatment Consortium
RAG:	Recombination-activating gene
SCID:	Severe combined immunodeficiency
TNC:	Total nucleated cell
TRM:	Transplant-related mortality
UCB:	Umbilical cord blood
URD:	Unrelated donor

immunodeficiencies. The Inborn Errors Working Party of the European Blood and Marrow Transplant Society (IEWP-EBMT) consists of more than 30 centers with a specialty in HCT for patients with primary immunodeficiencies. A retrospective questionnaire-based analysis of 37 children with SCID who had undergone URD (adult or UCB) transplantation without conditioning other than serotherapy was undertaken through a query of all members of the PIDTC and the IEWP-EBMT. Data from some URD¹³ and MSD^{17,18} recipients have been previously published. URD HCTs were performed between July 1993 and November 2012 in 8 PIDTC and 8 IEWP-EBMT centers, with a median year of HCT of 2007. A contemporaneous control cohort of 66 nonconditioned MSD HCT recipients from the same centers was also identified, although with a median HCT year of 2002. When required, participating centers obtained informed consent from parents before HCT to use blinded information for scientific purposes in accordance with the Declaration of Helsinki. Data were gathered and stored anonymously.

Summarized details of presenting characteristics are shown in Table I, whereas individual details can be found in Table E1 (URD recipients) and Table E5 (MSD recipients) in this article's Online Repository at www.jacionline.org. Patients with interleukin receptor common γ chain (*IL2RG*), Janus kinase 3 (*JAK3*), or *ADA* defects were classified as NK⁻, and patients with recombination-activating gene (*RAG*), DNA cross-link repair 1C (*DCLRE1C*), or Ligase 4 (*LIG4*) mutations were classified as NK⁺, whereas actual numbers were used to classify those without a molecular diagnosis by using a threshold of greater than or less than $100 \times 10^6/L$. Twenty-nine URD recipients had NK⁻ forms of SCID, including 21 with *IL2RG* mutations, 7 with either mutations in the *ADA* gene or undetectable levels of ADA, and 1 with an undefined mutation. Eight patients had NK⁺ forms of SCID, including 2 with *RAG2* deficiency, 1 with *DCLRE1C* deficiency, 1 with *LIG4* deficiency, and 3 with undefined mutations. Of the 66 MSD recipients, 48 had NK⁻ SCID, including 20 with mutations in *IL2RG*, 3 with *JAK3* deficiency, 23 with *ADA* deficiency, and 2 with undefined mutations. Eighteen had NK⁺ forms of SCID, including 6 with mutations in a *RAG* gene, 5 with *DCLRE1C* mutations, and 7 with undefined mutations. All met the agreed definition of SCID from the PIDTC with very low T-cell numbers and absent proliferative response to PHA.¹⁹ Both cohorts had an equal percentage of patients who met the criteria for leaky SCID, with reduced numbers of CD3⁺ T cells for age (>300 but $<1000/\mu L$ up to 2 years), absence of maternal engraftment, and less than 30% of the lower limit of normal T-cell function (as measured by response to PHA).²⁰

Two (29%) of 7 URD recipients and 7 (30%) of 23 MSD recipients received treatment with PEG-ADA before HCT, which was withdrawn 1 to 8 weeks

TABLE I. Summary of clinical and immunologic characteristics at the time of SCID diagnosis

	MSD				URD: adult or umbilical cord blood			
	IL2RG/JAK3	ADA	Other*	Overall	IL2RG/JAK3	ADA	Other*	Overall
Genotype, no.	20/3 (35%)	23 (35%)	20 (30%)	66	21/0 (57%)	7 (19%)	9 (24%)	37
Leaky	0	0	5 (20%)	5 (8%)	2 (10%)	0	1 (11%)	3 (8%)
Days at diagnosis, median (range)	130 (0-414)	34 (0-490)	108 (0-851)	82 (0-851)	184 (0-426)	30 (11-200)	109 (2-947)	121 (0-947)
Sex (male/female)	21/2	11/12	14/6	46/20	21/0	2/5	6/3	29/8
Diagnostic trigger: FH/NBS	6 (26%)	2 (9%)	7 (35%)	15 (23%)	4 (19%)	1 (14%)	2 (22%)	7 (19%)
Diagnostic trigger: Infection	17 (74%)	21 (91%)	13 (65%)	50 (77%)	17 (81%)	6 (86%)	7 (78%)	30 (81%)
Immunologic data, median (range)								
ALC ($\times 10^6/L$)	1610 (486-3,102)	250 (0-1,540)	975 (38-16,054)	759 (0-16,054)	1,760 (272-8,200)	200 (60-380)	1,200 (210-3,267)	1,100 (60-3,267)
CD3 ($\times 10^6/L$)	15 (0-504)	12 (0-455)	112 (0-8,076)	20 (0-8,076)	10 (0-605)	5 (0-56)	17 (0-510)	9 (0-605)
CD4 ($\times 10^6/L$)	12 (0-82)	5 (0-134)	73 (0-2,935)	12 (0-2,936)	2 (0-553)	5 (0-31)	0 (0-421)	2 (0-553)†
CD8 ($\times 10^6/L$)	0 (0-490)	5 (0-172)	31 (0-5,079)	5 (0-5,079)	4 (0-194)	0 (0-22)	0 (0-49)	3 (0-194)
B cells ($\times 10^6/L$)	1193 (336-3,015)	10 (0-1,201)	23 (0-1,440)	NA	1494 (5-7,786)	2 (0-22)	20 (0-1,486)	NA
NK cells ($\times 10^6/L$)	24 (0-215)	52 (0-340)	586 (5-7,848)	NA	20 (0-415)	15 (0-88)	445 (50-1,200)	NA
PHA (% of control)	0 (0-11)	0 (0)	0 (0-60)	0 (0-60)	0 (0-10)	0 (0)	0 (0-3)	0 (0-10)
Presence of TME‡	7/21 (33%)	1/20 (5%)	7/17 (41%)	15/58 (26%)	2/18 (11%)	0/7 (0%)	1/8 (13%)	3/33 (9%)

ALC, Absolute lymphocyte count; FH, family history; NA, not applicable; NBS, newborn screen; TME, transplacental maternal engraftment.

*See the [Methods](#) section for details.

† $P < .05$ compared with sibling donor recipients.

‡Not all patients were tested.

before HCT. The median age at diagnosis for the URD recipients was 121 days (range, 0-947 days), whereas the MSD recipients were given a diagnosis at a median of 82 days of age (range, 0-851 days; $P = .18$). Similar percentages of URD recipients (19%) and MSD recipients (23%) were given diagnoses based on family history or newborn screening, whereas the others were brought to clinical attention because of the presence of 1 or more opportunistic infections. Whether the inciting infection had resolved by the time of HCT was not able to be reliably determined. Transplacentally transferred maternal T cells were detected in 9% (3/33) of tested URD recipients and 15 (26%) of 58 MSD recipients ($P = .061$). The URD and MSD recipients were very similar in terms of their immunologic data at the time of diagnosis, with the exception that the URD recipients had a statistically lower median number of CD4⁺ T cells ($2 \times 10^6/L$; range, $0-553 \times 10^6/L$) compared with the MSD recipients ($12 \times 10^6/L$; range, $0-2936 \times 10^6/L$; $P = .04$).

Transplantation characteristics

Summarized details of transplantation characteristics are shown in [Table II](#), whereas individual details can be found in [Table E2](#) (URD recipients) and [Table E6](#) (MSD recipients). The MSD HCTs were almost exclusively done with bone marrow (BM) as the stem cell source (97%), whereas 19 of the URD recipients received cells from an adult donor (16 from BM and 3 from peripheral blood stem cells that were *ex vivo* CD34 selected), and a UCB unit was used in 18 patients ($P < .0001$). The median cell doses administered to the URD BM recipients were a total nucleated cell (TNC) count of $4.8 \times 10^8/kg$ (range, $2-10 \times 10^8/kg$), CD34⁺ cell count of $6.1 \times 10^6/kg$ (range, $2.5-20 \times 10^6/kg$), and CD3⁺ cell count of $4.5 \times 10^7/kg$ (range, $3.4-72 \times 10^7/kg$). This did not significantly differ from the BM cell doses given to the MSD recipients: TNC count of $5.5 \times 10^8/kg$ (range, $0.7-12.6 \times 10^8/kg$), CD34⁺ cell count of $8.4 \times 10^6/kg$ (range, $0.8-29.1 \times 10^6/kg$), and CD3⁺ cell count of $3.7 \times 10^7/kg$ (range, $0.02-37.1 \times 10^7/kg$). URD UCB recipients received a median TNC count of $13 \times 10^7/kg$ (range, $4-26 \times 10^7/kg$), with a CD34⁺ cell count of $5 \times 10^5/kg$ (range, $2-17 \times 10^5/kg$) and a CD3⁺ cell

count of $2.1 \times 10^7/kg$ (range, $0.1-9.2 \times 10^7/kg$). HLA-typing methods ranged over time from evaluating 6 loci (HLA-A, HLA-B, and HLA-DR) in 35% of patients to 12 loci (HLA-A, HLA-B, HLA-C, HLA-DR, HLA-DQ, and HLA-DP) in 16% of patients. All but 1 of the adult URDs and 14 of 18 UCB donors were fully matched by the criteria in place at the time of HCT (86%), whereas 3 of the sibling donors were mismatched at 1 locus, and the remaining 95% were fully matched ($P = .13$).

The only conditioning used before HCT was serotherapy in the form of anti-thymocyte globulin or alemtuzumab in 14 (38%) of 37 URD recipients and 2 (3%) of 66 MSD recipients ($P < .0001$), although this was typically administered for its ability to serve as prophylaxis against graft-versus-host disease (GVHD).²¹ Because no cytotoxic chemotherapy was used for any of these HCTs, we designate them as being nonconditioned. Other pharmacologic GVHD prophylaxis regimens varied and ranged from none to a single calcineurin inhibitor, such as cyclosporine or tacrolimus alone; 2 agents (calcineurin inhibitor plus either methotrexate, corticosteroids, or mycophenolate mofetil); or 3 agents. The majority (65%) of URD recipients received 2 to 3 agents compared with only 14% of sibling HCTs ($P < .0001$), whereas only 1 URD HCT was performed without any GVHD prophylaxis (3%) compared with 59% of sibling donor HCTs ($P < .001$). Acute GVHD (aGVHD) and chronic GVHD (cGVHD) were graded by local investigators.

Chimerism and immune reconstitution

Chimerism was measured in PBMCs, T cells (CD3⁺), B cells (CD19⁺ or CD20⁺), and/or myeloid cells (CD15⁺ or CD33⁺). Donor T-cell engraftment was defined as the detection of any amount of donor DNA in either whole blood or separated CD3⁺ cells. Given variations in detection limits of the various chimerism laboratories, 5% was set as the threshold amount of myeloid or B-cell chimerism required to be considered clinically relevant. NK cell chimerism was not evaluated. Immune reconstitution of T-cell (CD3, CD4, and CD8), naive T-cell (CD4/CD45RA), B-cell, and NK cell numbers; quantitative immunoglobulins; and T-cell function (through a

TABLE II. Summary of unconditioned HCT characteristics

	MSD				URD: adult umbilical cord blood			
	IL2RG/JAK3	ADA	Other*	Overall	IL2RG/JAK3	ADA	Other*	Overall
Genotype, no.	20/3	23	20	66	21/0	7	9	37
Days from diagnosis to HCT, median (range)**	23 (1-153)	27 (12-86)	32 (12-1389)	25 (1-1389)	56 (25-281)	31 (16-40)	55 (16-111)	49 (16-281)†
Donor match‡								
“Complete”	21 (91%)	23 (100%)	19 (95%)	63 (95%)	17 (81%)	7 (100%)	8 (89%)	32 (86%)
≥1 Known mismatches	2 (9%)	0	1 (5%)	3 (5%)	4 (19%)	0	1 (11%)	5 (14%)
Stem cell source								
BM	21 (91%)	23 (100%)	20 (100%)	64 (97%)	9 (43%)	1 (14%)	6 (67%)	16 (43%)†
Umbilical cord blood	2 (9%)	0	0	2 (3%)	9 (43%)	6 (86%)	3 (33%)	18 (49%)†
PBSC (TCD)	0	0	0	0	3 (14%)	0	0	3 (8%)†
Serotherapy administered	0	0	2 (10%)	2 (3%)	10 (48%)†	1 (14%)	3 (33%)	14 (38%)†
GVHD prophylaxis agents§								
Ex vivo TCD	4 (17%)	0	1 (5%)	5 (7%)	3 (14%)	0	0	3 (8%)
None	16 (70%)	17 (74%)	6 (30%)	39 (59%)	1 (5%)†	0	0	1 (3%)†
1	2 (9%)	6 (26%)	5 (25%)	13 (20%)	3 (14%)	2 (29%)	4 (45%)	9 (24%)
2	1 (4%)	0	8 (40%)	9 (14%)	6 (29%)†	4 (57%)†	3 (33%)	13 (35%)†
3	0	0	0	0	8 (38%)†	1 (14%)	2 (22%)	11 (30%)†

PBSC, Peripheral blood stem cells; TCD, ex vivo T-cell depletion.

*See the Methods section for details.

**Excluding patients treated with ADA enzyme replacement therapy before HCT.

† $P < .05$ compared with sibling donor recipients.

‡As defined by era of HCT.

§Including pre-HCT serotherapy.

proliferative response to PHA) were measured at approximately 1 year after HCT, shown in Table E3 (URD recipients) and Table E7 (MSD recipients) and at the most recent follow-up, shown in Table E4 (URD recipients) and Table E8 (MSD recipients). Clinical freedom from gammaglobulin replacement therapy was used as a surrogate for B-cell function. An effectively normal immune system was defined as a CD4 count of greater than $400 \times 10^6/L$,²² PHA of greater than 50% of the control value, and freedom from gammaglobulin replacement.

Statistical analysis

Descriptive statistics were calculated as medians and ranges for quantitative variables or frequencies and percentiles for categorical variables. Comparisons between groups were done by using the nonparametric Mann-Whitney test for quantitative variables and the Fisher exact test for categorical variables. Kaplan-Meier curves were used to analyze survival rates, with the log-rank test used to compare survival between different groups. Cumulative incidence functions considering death from any cause or the need for a conditioned second HCT as competing events were used to estimate other end points. Transplant-related mortality (TRM) was defined as any death from a cause (eg, an infection) not present at the time of cell infusion. Age of less than 3.5 months was analyzed for effect of survival because of previous data showing that this is a biologically relevant time point.⁶ Analyses were done with NCSS 8 software (NCSS, Kaysville, Utah). Significant differences are defined as a P value of .05 or less.

RESULTS

Excluding patients who received ADA enzyme replacement therapy before HCT, patients were treated with HCT from a URD at a median of 49 days (range, 16-281 days) from diagnosis, with a median of 62 days for an adult URD compared with 42 days for a UCB unit ($P = .08$). This was significantly longer than the interval between diagnosis and HCT when an MSD was available, which took a median of only 25 days (range, 1-1389 days; $P < .001$). Similarly, median age at the time of URD HCT was greater at 182 days of life (range, 40-996 days) compared with a median

of 132 days of life (range, 1-2240 days) at the time of MSD HCT ($P = .03$).

Engraftment

All but 1 URD recipient (who died 9 days after HCT from ongoing infectious respiratory failure) and 1 MSD control subject (who died 16 days after HCT from cytomegalovirus-related pneumonitis) survived at least 1 month after unconditioned HCT and were therefore considered evaluable for engraftment, need for second cell infusion, and GVHD. As shown in Table III, initial donor T-cell engraftment was seen in 97% of MSD recipients and 94% of URD recipients ($P = .61$). Of the URD recipients, the NK^- patients universally engrafted donor T cells (28/28) compared with 75% (6/8) of NK^+ patients ($P = .04$).

A similar number of MSD recipients (15%) and URD recipients (19%) ultimately required additional infusions of donor cells to treat inadequate immune reconstitution ($P = .78$). This was done as a nonconditioned boost in 9% of MSD recipients and 8% of URD recipients ($P = 1$), whereas fully conditioned second HCTs were eventually performed in 6% of MSD recipients and 11% of URD recipients ($P = .45$). Conditioned second HCTs were more common in patients with NK^+ forms of SCID undergoing URD HCT (38% vs 4% for NK^- patients, $P = .04$). The use of serotherapy might have been associated with a higher need for second cell infusion (28% vs 13% for no serotherapy) but did not reach statistical significance ($P = .39$).

Chimerism was not uniformly evaluated, although the majority of tested MSD recipients (86% [38/44]) and URD recipients (100% [15/15]) had high-level (>90%) donor CD3⁺ engraftment ($P = .32$, Table IV). At the time of last follow-up, B-cell or myeloid chimerism of greater than 5% was detected in 48% of the MSD recipients compared with 50% of the URD recipients ($P = 1$), with no significant differences between molecular subtypes. Patients who underwent conditioned second HCTs were excluded from this analysis.

TABLE III. Clinical outcomes after unconditioned HCT

	MSD			URD: adult or umbilical cord blood				
	Overall	NK ⁻	NK ⁺	Overall	NK ⁻	NK ⁺	No serotherapy	With serotherapy
Donor T-cell engraftment*	63/65 (97%)	45/46 (98%)	18/19 (95%)	34/36 (94%)	28/28 (100%)	6/8 (75%)	22/22 (100%)	12/14 (86%)
Second HCT required*	10/65 (15%)	5/46 (11%)	5/19 (26%)	7/36 (19%)	4/28 (14%)	3/8 (38%)	3/23 (13%)	4/14 (28%)
Unconditioned boost	6/65 (9%)	3/46 (7%)	3/19 (16%)	3/36 (8%)	3/28 (11%)	0/8 (0%)	2/23 (9%)	1/14 (7%)
Conditioned	4/65 (6%)	2/46 (4%)	2/19 (11%)	4/36 (11%)	1/28 (4%)	3/8 (38%)†	1/23 (4%)	3/14 (21%)
TRM*	2/65 (3%)	2/46 (4%)	0/19 (0%)	6/36 (17%)‡	3/28 (11%)	3/8 (38%)	6/22 (27%)	0/14 (0%)
aGVHD*								
Any grade	21/63 (33%)	20/46 (43%)	1/17 (6%)†	22/34 (65%)‡	18/28 (64%)	4/6 (67%)	16/22 (73%)	6/12 (50%)
Grade II-IV	14/63 (22%)	13/46 (28%)	1/17 (6%)	17/34 (50%)‡	14/28 (50%)	3/6 (50%)	14/22 (64%)	3/12 (25%)
Grade III-IV	3/63 (5%)	3/46 (7%)	0/17 (0%)	8/34 (24%)‡	6/28 (21%)	2/6 (33%)	7/22 (32%)	1/12 (8%)
cGVHD*	3/62 (5%)	2/45 (4%)	1/17 (6%)	11/28 (39%)‡	8/24 (33%)	3/4 (75%)	8/17 (47%)	3/11 (27%)
Alive at last follow-up	60/66 (91%)	43/47 (92%)	17/19 (89%)	27/37 (73%)‡	22/29 (76%)	5/8 (63%)	13/23 (56%)	14/14 (100%)
Alive without conditioning	56/66 (85%)	41/47 (87%)	15/19 (79%)	23/37 (62%)‡	21/29 (72%)	2/8 (25%)†	12/23 (52%)	11/14 (79%)

*Of evaluable patients (see the Results section).

† $P < .05$ compared with NK⁻ phenotypes.‡ $P < .05$ compared with sibling donor recipients.

TABLE IV. Summary of survivors' immune reconstitution at 1 year and at last follow-up after unconditioned HCT

	MSD				URD: adult or umbilical cord blood			
	IL2RG/JAK3	ADA	Other*	Overall	IL2RG/JAK3	ADA	Other*	Overall
No. evaluable: 1-y from HCT (± 1 mo)	19	21	19	59	16	5	3	24
CD3 ($\times 10^6/L$)	3,428 (1,751-9,287)	1,008 (364-2,500)	744 (27-5,698)	1,764 (27-9,287)	2,153 (66-4,673)†	572 (540-2,144)	1,414 (421-3,233)	1,767 (66-4,673)
CD4 ($\times 10^6/L$)	1,766 (921-2,653)	405 (132-1,330)	330 (17-3,773)	585 (17-3,773)	1,241 (21-3,027)	293 (272-530)	853 (308-2,221)	692 (21-3,027)
CD4/CD45RA (%)	33 (17-78)	14 (3-22)	8 (1-82)	21 (1-78)	57 (9-94)	55 (8-80)	26 (19-32)	55 (8-94)
CD8 ($\times 10^6/L$)	1,180 (444-6,302)	370 (194-1,114)	298 (8-6,646)	764 (8-6,646)	770 (45-2,350)	207 (192-1,503)	541 (189-857)	550 (45-2,350)
B cells ($\times 10^6/L$)	1,200 (30-2,571)	50 (9-333)	5 (0-1,155)	NA	280 (0-3,602)	25 (22-30)	150 (11-333)	NA
NK cells ($\times 10^6/L$)	142 (47-392)	40 (0-602)	260 (125-804)	NA	52 (0-297)	43 (10-78)	251 (184-291)	NA
PHA (%)	79 (8-100)	76 (58-100)	48 (16-100)	59 (8-100)	100 (69-100)	86 (72-100)	85 (85)	100 (69-100)
Off gammaglobulin	13 (68%)	16 (76%)	8 (47%)	37 (63%)	1 (6%)	1 (20%)	0 (0%)	2 (8%)*
No. evaluable at last follow-up	20	20	17	57	16	5	2	23
Time to last follow-up (y)	5.5 (1-14.4)	6.3 (2-17.1)	7.5 (1.6-18.9)	6.9 (1-18.9)	4.3 (1-19)	2.5 (1.1-12.3)	2.8 (1.6-3.9)	3.9 (1-19)
CD3 ($\times 10^6/L$)	2,230 (1,190-9,287)	1,720 (578-4,440)	1,000 (230-2,606)	1,814 (230-9,287)	1,864 (315-4,210)	1,328 (593-6,017)	6,091 (383-10,790)†	1,574 (315-10,790)
CD4 ($\times 10^6/L$)	1,302 (458-2,653)	1,065 (298-3,330)	432 (140-1,640)	944 (140-3,330)	943 (144-2,330)	506 (272-1,105)	3,623 (247-6,999)†	840 (144-6,999)
CD4/CD45RA (%)	60 (17-80)	13 (2-17)	11 (3-71)	19 (2-80)	43 (4-94)	8 (4-41)	26 (0-51)	35 (0-94)
CD8 ($\times 10^6/L$)	982 (468-6,302)	757 (220-2,040)	313 (140-1,026)	772 (220-2,040)	575 (80-1,853)	613 (199-4,851)	2,007 (570-3,443)	580 (80-4,851)
B cells ($\times 10^6/L$)	460 (347-1,879)	180 (36-750)	24 (0-395)	NA	399 (0-3,602)	47 (30-137)	1,017 (338-1,696)	NA
NK cells ($\times 10^6/L$)	85 (0-392)	131 (0-1025)	115 (37-524)	NA	29 (0-194)	98 (10-363)	306 (274-338)	NA
PHA (%)	100 (66-100)	100 (46-100)	86 (47-100)	100 (46-100)	100 (65-100)	72 (72)	85 (85)	100 (65-100)
Off gammaglobulin	16 (80%)	18 (90%)	10 (59%)	44 (77%)	4 (25%)	2 (40%)	1 (50%)	7 (30%)*
Donor myeloid >5%	7/16 (44%)	8/15 (53%)	7/15 (47%)	22/46 (48%)	6/13 (46%)	2/4 (50%)	1/1 (100%)	9/18 (50%)

NA, Not applicable.

*See the Methods section for details.

† $P < .05$ compared with sibling donor recipients.

GVHD

As shown in Table III, despite the greater number of GVHD prophylaxis agents used in the URD recipients, the incidence of any grade of aGVHD was significantly higher: 22 (65%) of 34 evaluable URD recipients compared with 21 (33%) of 63 sibling donor recipients ($P = .005$). Grade II to IV aGVHD was seen in 17 (50%) of 34 URD recipients compared with only 14 (22%) of 63

sibling donor recipients ($P < .01$), whereas grade III to IV aGVHD was seen in 8 (24%) of 34 URD recipients compared with only 3 (5%) of 63 sibling recipients ($P = .02$). For both the MSD recipients and the URD recipients, the year of HCT, the presence of known HLA mismatches, or the number of agents used for GVHD prophylaxis did not predict subsequent aGVHD (see Table E9 in this article's Online Repository at www.jacionline).

org). However, the use of serotherapy in the URD recipients demonstrated a trend toward being protective from grades II to IV aGVHD, with an incidence of 64% (14/22) in those not receiving serotherapy compared with 25% in those given serotherapy (3/12, $P = .07$). For the URD recipients, there was no difference in the incidence of grade II to IV aGVHD between recipients of BM (43%) versus other stem cell sources (55%, $P = .73$) nor an effect of cell dose administered (data not shown). URD recipients with any grade aGVHD trended to have an increased incidence of B-cell or myeloid chimerism (64%), including 2 patients with 100% donor chimerism in all cell lines, compared with those patients who never had any aGVHD (14%, $P = .07$), likely because of a graft-versus-marrow effect. This association of GVHD and donor chimerism was not seen in the MSD recipients, possibly because of a lower degree of alloreactivity and incidence of aGVHD.

cGVHD was rare in the evaluable MSD recipients (5%) and significantly higher in the URD recipients (33%, $P < .001$). For the URD recipients, there was no difference in the incidence of cGVHD between recipients of BM (38%) versus UCB (38%) versus peripheral blood stem cells (50%, $P = 1$) nor was there an effect of cell dose administered (data not shown). The use of serotherapy in URD recipients resulted in a lower incidence of cGVHD (27% vs 47% in those not given serotherapy); however, this did not reach statistical significance ($P = .43$).

Survival

Causes of death are listed in Tables E2 and E6. For the MSD recipients, this included progression of pre-existing problems/infections ($n = 4$), probable sepsis ($n = 1$), and GVHD ($n = 1$). For the URD recipients, this included progression of pre-existing problems/infections ($n = 4$), intraoperative complication ($n = 1$), or GVHD ($n = 5$) for a TRM of 3% in the MSD recipients compared with 17% in the URD recipients ($P = .02$). Possibly because most TRM was related to GVHD, in the URD recipients the use of serotherapy trended toward being protective from TRM (0%) compared with that seen in those who did not receive serotherapy (27%, $P = .06$), although this might also be due to preferential selection of serotherapy in patients without infection at time of HCT.

As shown in Fig 1, of the MSD recipients, 57 patients are alive (median follow-up, 6.9 years; range, 1-18.9 years) without a conditioned second HCT, for an estimated 5-year event-free survival (EFS) of 89% (95% CI, 81% to 97%). This was significantly better than in the URD recipients, among whom only 23 patients are alive (median follow-up, 3.9 years; range, 1-19 years) without a conditioned second HCT, for an estimated 5-year EFS of 60% (95% CI, 44% to 77%; $P < .01$). In the MSD recipients 3 of 4 patients who underwent conditioned second transplantations were long-term survivors, as were all 4 URD recipients. Therefore the estimated 5-year OS for the MSD recipients was 92% (95% CI, 85% to 98%), which is significantly better than for the URD recipients, whose estimated 5-year OS was 71% (95% CI, 56% to 87%; $P < .01$). Among recipients of the same donor source, there was not a significant difference in OS between those with NK⁻ and NK⁺ SCID (Table III).

In the URD recipients the use of serotherapy resulted in an estimated 5-year EFS of 71% (95% CI, 42% to 100%) compared with those not receiving serotherapy (38%; 95% CI, 13% to 62%), but this did not reach statistical significance ($P = .18$), likely because there was a slight trend toward more patients in the

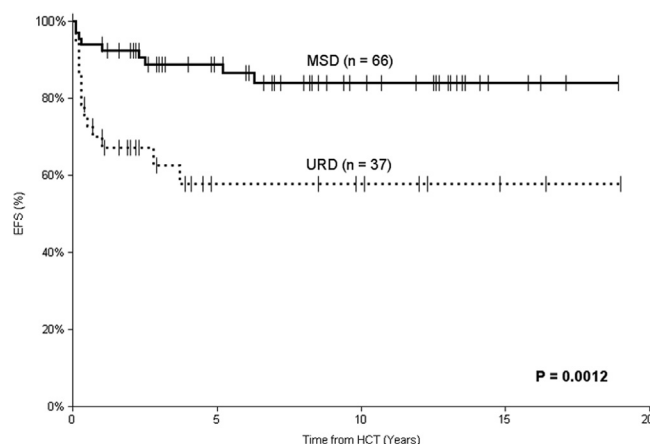


FIG 1. EFS after unconditioned HCT for SCID comparing MSDs with URDs, with death and conditioned second HCT as events.

serotherapy group requiring a conditioned second transplantation (21% vs 4%, $P = .14$). However, because all patients undergoing retransplantation survived, the use of serotherapy was associated with a significantly superior estimated 5-year OS of 100% (95% CI, 75% to 100%) compared with those patients who did not receive serotherapy (51%; 95% CI, 25% to 77%; $P < .01$; Fig 2). Those receiving a URD HCT before 3.5 months of age had similar outcomes (5-year OS of 69%; 95% CI, 39% to 99%; $n = 12$) compared with those undergoing transplantation after 3.5 months of age (5-year OS of 72%; 95% CI, 54% to 90%; $n = 25$; $P = .75$), as did those given diagnoses in the absence of infection (5-year OS of 75%; 95% CI, 33% to 100%; $n = 7$) compared with those undergoing transplantation after an infection (5-year OS of 70%; 95% CI, 54% to 86%; $n = 30$; $P = .38$). URD HCTs performed in the early period (1993-2007) had an estimated 3-year OS of 65% (95% CI, 42% to 87%) compared with 80% (95% CI, 62% to 98%) for those done more recently ($P = .42$). There was no difference in 5-year OS depending on the cell source of the URDs.

Immune reconstitution

As shown in Table IV, T-cell reconstitution was similar between the survivors of unconditioned HCTs from an MSD and a URD. The median CD3 count at 1 year after HCT was $1764 \times 10^6/L$ (range, $27-9287 \times 10^6/L$) from an MSD compared with $1767 \times 10^6/L$ (range, $66-4673 \times 10^6/L$) from a URD ($P = .55$), and this lack of difference persisted at the time of last follow-up ($P = .57$). Subgroup analysis demonstrated that *IL2RG*-defective patients had higher CD3 counts at 1 year after HCT from an MSD compared with from a URD ($P < .01$), although the difference was less evident at the time of last follow-up ($P = .07$). Similarly, there was no difference in the median CD4 count at either 1 year after HCT ($P = .58$) or the time of last follow-up ($P = .74$). At the time of last follow-up, 4% (2/57) of MSD recipients had very poor CD4 reconstitution ($<200 \times 10^6/L$) compared with 4% (1/23) of URD recipients ($P = 1$), whereas 12% (7/57) of MSD recipients and 26% (6/23) of URD recipients had borderline ($200-400 \times 10^6/L$) CD4 counts ($P = .18$). Naive CD4/CD45RA counts were not always measured, but there was no apparent difference in the median percentage at the time of last follow-up between those undergoing

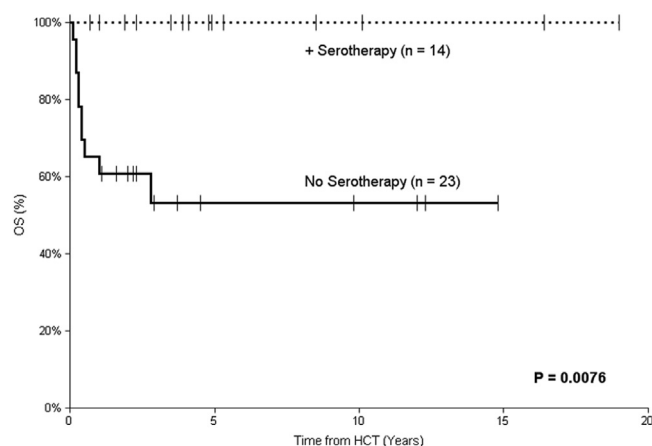


FIG 2. OS after unconditioned HCT for SCID using an URD comparing the use of pre-HCT serotherapy for GVHD prophylaxis with no serotherapy.

MSD control HCT (19%; range, 2% to 80%) and URD recipients (35%; range, 0% to 94%; $P = .51$).

Despite the lack of difference in the percentage of patients with detectable myeloid or B-cell chimerism between the MSD recipients and the URD recipients, there were significantly more MSD recipients with clinical freedom from gammaglobulin replacement at both 1 year after HCT (63% vs 8%, $P < .001$) and the time of last follow-up (77% vs 30%, $P < .001$). The URD recipients only achieved gammaglobulin replacement independence in the setting of donor myeloid or B-cell chimerism, whereas these outcomes were not linked in the MSD recipients, possibly because of incomplete testing of lineage-specific chimerism in these patients (19% had neither myeloid nor B-cell chimerism tested) or testing methods with limited sensitivity for microchimerism. Patients with NK^- forms of SCID undergoing MSD HCT were more likely to recover B-cell function (85% [35/41]) than those with NK^+ forms of SCID (56% [9/16], $P = .03$), whereas there were too few NK^+ patients undergoing URD HCT to compare. The URD stem cell source used did not affect gammaglobulin independence (25% for non-UCB vs 36% for UCB, $P = .67$).

An effectively normal immune system was seen in significantly more MSD recipients (72% [41/57]) compared with URD recipients (26% [6/23]) who survived without a conditioned second HCT ($P < .001$).

DISCUSSION

The data presented here represent the largest cohort of patients to be reported with SCID undergoing URD (including UCB) HCT without conditioning chemotherapy. Because most patients who undergo URD HCT receive chemotherapy-based conditioning,²³ the majority of this retrospective cohort is likely composed of a selected group of patients who were deemed too sick to undergo chemotherapy. Despite this selection bias, the majority of patients engrafted donor T cells (94%) and subsequently survived (5-year OS, 71%), although some patients were not able to reverse their pre-HCT problems/infections in time. This survival rate is comparable with what has been reported in large multicenter trials for URD HCT (primarily with conditioning), with the IEWP-EBMT reporting a 10-year OS of 66%¹⁰ and the PIDTC soon to report a 5-year OS of 64% (S.-Y. Pai, personal

communication). Furthermore, T-cell immune reconstitution in survivors of unconditioned URD HCTs was generally adequate and comparable with that seen in recipients of unconditioned MSD HCTs. Therefore we have demonstrated that chemotherapy before URD (or UCB) HCT is not always required for patients with SCID because of deficiencies in IL2RG, ADA, and possibly even some NK^+ genotypes, as long as the primary goal is donor T-cell reconstitution. Up to 20% of recipients of unconditioned HCTs require repeat HCTs, either as unconditioned boosts or with conditioning chemotherapy. Although this is a limitation of this approach, the need for repeat HCTs has also been reported after conditioned HCTs.⁷

However, important differences remain between URD and MSD HCT, especially with respect to the high rates of GVHD seen after URD HCT, which contributed to 5 of the 6 deaths not related to progression of a pre-HCT problem. Of note, in many URD recipients the development of GVHD was linked with the achievement of at least modest amounts of donor myeloid or B-cell chimerism, likely from a direct immunologic attack on the recipients' BM.^{24,25} Although likely of ultimate benefit to the patient because it correlated with freedom from gammaglobulin replacement, this "graft-versus-marrow" effect is not a reliable or safe method to achieve 100% donor chimerism. The high rate of GVHD seen in this cohort is likely multifactorial because the lower number of GVHD prophylactic agents administered, the stem cell source, and the presence of known HLA mismatches were not predictive of GVHD, although the failure to use pre-HCT serotherapy trended toward increased GVHD. We found that the use of anti-thymocyte globulin was associated with an improved OS in the URD recipients. Although this might be a direct protective effect from excessive alloreactivity, it is also possible that the use of serotherapy was simply a surrogate marker for healthier patients whose infections were under control at the time of HCT because many clinicians avoid using serotherapy in an actively infected patient as a result of concerns of slower T-cell recovery.

It should be noted that 43% of patients either received a known HLA-mismatched donor or underwent URD HCT in an era when HLA typing was more limited than is currently used and that future analyses confined to only to those with 10/10 (or 12/12) HLA allele-matched donors might demonstrate lower rates of GVHD. One potential method to decrease these rates of GVHD might be to use more aggressive *in vivo* T-cell depletion with alemtuzumab,²⁶ although this could delay post-HCT T-cell recovery,²⁷ and both URD recipients in this cohort who received alemtuzumab eventually underwent a fully conditioned second HCT. Another possibility would be to use a relatively less-toxic pre-HCT chemotherapeutic agent, such as the mAb rituximab or the nonalkylating fludarabine, with the goal of eliminating antigen-presenting host B cells that might contribute to the development of subsequent GVHD.^{28,29} Furthermore, it should be noted that the majority of patients in this cohort underwent URD HCT after receiving a diagnosis of 1 or more opportunistic infections, and it has been shown that the presence of certain infections (especially cytomegalovirus³⁰ and HHV-6³¹) after HCT is linked to the subsequent development of GVHD, presumably through the release of inflammatory cytokines. Therefore it is possible that this high rate of GVHD might become less of a problem as more patients are identified through newborn screening and proceed to well-matched HCT in the absence of a severe opportunistic infection. However, if B-cell recovery is linked to a graft-versus-marrow effect, efforts to improve GVHD

prophylaxis might result in decreased rates of complete T- and B-cell immunologic recovery.

In addition to GVHD and subsequent TRM leading to poorer survival for the URD recipients, the other major difference with survivors of unconditioned MSD HCT was the relative lack of freedom from clinical gammaglobulin replacement. Most surviving MSD recipients (77%) were able to stop gammaglobulin, and 72% were considered to have “complete” immune reconstitution (to the limits of this retrospective analysis), with normal CD4⁺ T-cell counts and clinical gammaglobulin independence. Conversely, only 30% of surviving URD recipients were off gammaglobulin, and only 26% had “complete” T- and B-cell reconstitution, although this degree of B-cell recovery from an unconditioned URD HCT is similar to what has been reported for IL2RG-deficient patients undergoing nonconditioned haploidentical HCT (34%, also tightly linked to donor B-cell engraftment).³² In the URD recipients B-cell recovery was tightly linked to myeloid engraftment; however, this was not the case for the MSD recipients, despite the lack of an agent to produce space in the BM niches. The exact mechanism behind this interesting dichotomy remains to be elucidated.

For patients with non-SCID primary immunodeficiencies, all of whom undergo pre-HCT conditioning chemotherapy, advances in HLA typing during a relatively modern era of 2000-2005 have allowed URD HCT to produce equivalent outcomes to MSDs.¹⁰ However, for patients with SCID, the outcomes were worse for URD HCTs compared with MSD HCTs.¹⁰ Some of this might be attributable to the delay in time from SCID diagnosis (typically through the presence of a severe opportunistic infection) to the time of HCT that is required for the URD search process (a median of 24 additional days for this cohort), during which time the patient's infection might worsen. However, another factor could be the use of conditioning chemotherapy, which is used far more frequently in the recipients of URD HCT compared with MSD HCT and appears in our cohort to be unnecessary to successfully achieve donor T-cell engraftment. Data from the PIDTC demonstrate that for patients with SCID undergoing transplantation from 2000-2009, the use of chemotherapy-based conditioning was associated with inferior survival when an active infection was present at the time of HCT (S.-Y. Pai, personal communication). Although advances in individualized drug dosing and other supportive care techniques have made the use of conditioning chemotherapy safer, there is still a finite risk of fatal end-organ toxicity, such as liver sinusoidal obstruction syndrome,³³ which does not occur in nonconditioned HCTs. The only TRM in the URD recipients of this cohort resulted from GVHD or an unusual iatrogenic intraoperative complication. This implies that improved GVHD prophylaxis strategies could eventually enable nonconditioned HCT to become safer than a conditioned HCT.

This study is limited by the retrospective nature of the cohort, and therefore it is possible that a positive selection bias was introduced by a lack of participation from centers that have performed unconditioned URD/UCB HCTs and found poor outcomes, although the majority of surveyed centers replied that they had no eligible patients to contribute to this cohort.

Furthermore, we do not have data on the kinetics of T-cell reconstitution or on some newer methods of monitoring the robustness of T-cell reconstitution after HCT, such as T-cell receptor V β family diversity by spectratyping or T-cell receptor excision circles, and it is possible that these might identify immune defects in the URD recipients that are not present in the MSD recipients.

Finally, we did not directly compare the clinical outcomes and immune reconstitution in patients with SCID undergoing URD HCT with or without pre-HCT conditioning because this was not the objective of this study and we believe that a significant selection bias might exist, with “healthier” patients allowed to receive conditioning chemotherapy and “sicker” patients given an unconditioned URD/UCB HCT as a last-ditch effort to salvage the patient.³⁴ This selection bias can only be eliminated through either a randomized prospective clinical trial or potentially by means of prospective analysis of sufficient numbers of uninfected patients given diagnoses based on a family history or newborn screen result, as the PIDTC is attempting in North America.²³

In conclusion, our data demonstrate that in patients with SCID lacking MSDs but in whom a well-matched adult URD or UCB can be located in a timely fashion, HCT can proceed without the use of conditioning chemotherapy in a fashion akin to common practice with an MSD, especially in the typical (nonleaky) NK⁺ subtypes included in this cohort (ie, mutations in *IL2RG* and *ADA*). If successful, such an approach would spare patients the potential short-term toxicity and long-term sequelae of conditioning chemotherapy. However, this approach is currently fraught with high rates of aGVHD and cGVHD, and therefore careful consideration of the optimal GVHD prophylaxis regimen (based on the severity of ongoing opportunistic infections) is required. In addition, although this approach can produce adequate long-term donor T-cell reconstitution, it has a much lower success rate of achieving normal B-cell function (30%) than when conditioning chemotherapy is used (roughly 85%).⁸ Therefore novel methods to improve donor myeloid and B-cell engraftment are still needed, such as antibody-based targeted therapy of hematopoietic stem cells.^{35,36} In those rare patients in whom T-cell reconstitution is insufficient or those patients in whom normal B-cell function is desired, a subsequent conditioned HCT can still be considered in the future after the patient has recovered from their opportunistic infections and/or organ function has improved and matured.³⁷

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Clinical implications: Patients with certain subtypes of SCID can have donor T-cell (and occasionally B-cell) reconstitution after URD HCT without conditioning chemotherapy, thereby potentially sparing short- and long-term toxicities.

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TABLE E1. Individual characteristics at the time of diagnosis of SCID for patients undergoing URD HCT

Case no.	Sex	Age (d)	Race/ ethnicity	ALC ($\times 10^6/L$)	CD3 ($\times 10^6/L$)	CD4 ($\times 10^6/L$)	CD8 ($\times 10^6/L$)	B cells ($\times 10^6/L$)	NK	PHA	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	TME	Diagnostic trigger	Mutation
IL2RG SCID																
1	M	0	White	620	6	4	3	355	26	NT	820	0	0	0%	Family history	c.355delG
2	M	110	White	272	253	166	90	5	8	NT	520	24	7	0%	Paraflu3, Lymphoma	IVS3-11bp C>G
3	M	271	White	1661	124	3	49	1528	0	2%	330	67	20	0%	PCP	c.284 (del2): a-g
4	M	169	White	682	6	0	0	613	6	NT	400	19	0	0%	Thrush, PNA, perianal abscess	c.1-3318_594+455del5157
5	M	270	White	1700	605	553	52	605	415	10%	104	28	0	0%	RSV, PCP	c.129 (+5) G>A
6	M	228	White	300	0	0	0	160	100	NT	357	36	0	0%	PCP, Paraflu, Astro	11-bp deletion from intron 4 to first 6 bp of exon 5
7	M	25	Hispanic	780	0	0	0	1096	45	0%	320	14	0	0%	Newborn screen	c.822-840del119
8	M	426	White	8200	321	89	194	7786	25	0%	10	14	0	84%	VZV	p.Q81X
9	M	0	White	847	8	0	8	NT	NT	NT	NT	NT	NT	0%	Family history	NR
10	M	120	White	1836	293	36	110	1468	73	2%	400	23	0	25%	Thrush	c.640C>T
11	M	274	White	4914	49	9	4	4766	0	NT	80	34	0	0%	RSV, hMPV, norovirus	c.509T>C
12	M	185	White	2100	0	0	0	2000	0	0%	NT	NT	NT	0%	PCP, RSV	NR
13	M	149	White	2065	4	2	6	2034	64	0%	93	0	0	0%	Thrush, influenza B	delc.772, changing 3' splice site
14	M	209	White	930	37	9	9	893	NT	1%	572	14	7	NT	RSV, Paraflu, <i>Staphylococcus aureus</i> bacteremia	NR
15	M	97	White	2900	3	2	3	433	8	0%	576	35	0	0%	Adeno, Paraflu, rotavirus	NR
16	M	157	Asian	1760	18	0	0	1707	0	NT	426	36	7	NT	Thrush, RSV	c.633A>T
17	M	328	White	1100	0	0	0	1090	0	NT	330	38	0	0%	PCP	c.268T>C
18	M	0	White	1970	60	10	40	1520	20	NT	801	5	0	0%	Family history	c.822_823delCAins dup833_845
19	M	229	White	2170	0	0	0	2130	20	NT	658	0	0	0%	PCP	c.670C>T
20	M	184	White	2870	10	1	1	2840	3	NT	801	21	0	0%	PCP	c.854G>A
21	M	236	White	2180	240	170	70	1610	220	0%	NT	NT	NT	NT	PCP	c.720G>T
ADA SCID																
1	F	200	Hispanic	170	56	31	22	22	88	0%	49	0	0	0%	PCP, rotavirus	p.L107P + p.C262Y
2	F	74	White	200	0	0	0	0	0	NT	776	5	0	0%	RSV	NR, level = 0
3	F	30	White	350	14	12	3	0	0	NT	684	8	0	0%	PCP, Paraflu3	NR, level = 0
4	M	24	White	380	9	6	3	2	76	NT	280	5	0	0%	PCP	NR, level = 0
5	F	68	White	60	0	0	0	9	28	0%	200	8	0	0%	PNA	NR, level = 0
6	M	11	Asian	250	5	5	0	3	9	NT	840	0	0	0%	Family history	c.256-258 ins T
7	F	23	Asian	200	4	1	0	2	15	NT	370	17	25	0%	PNA	NR, level = 0
Other SCID																
1	M	2	White	1200	0	0	0	0	1200	NT	NT	NT	NT	0%	Family history	Unknown
2	M	38	White	1720	17	0	0	860	757	0%	1360	47	0	0%	PNA	Unknown
3	F	121	White	210	0	0	0	0	210	NT	120	NT	NT	0%	Influenza A, FTT	RAG2; c.1643C>T
4	F	947	White	1670	0	0	0	1486	167	0%	0	14	0	0%	Paraflu3, HHV-6, ALL	Unknown
5	F	302	White	3267	510	421	49	23	699	NT	NT	NT	NT	0%	PCP, mycobacteria	Unknown
6	M	5	Middle Eastern	400	0	0	0	0	390	NT	927	0	0	0%	Family history → CMV	Artemis; NR

(Continued)

TABLE E1. (Continued)

Case no.	Sex	Age (d)	Race/ ethnicity	ALC ($\times 10^6/L$)	CD3 ($\times 10^6/L$)	CD4 ($\times 10^6/L$)	CD8 ($\times 10^6/L$)	B cells ($\times 10^6/L$)	NK	PHA	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	TME	Diagnostic trigger	Mutation
7	M	11	Middle Eastern	1200	189	101	25	0	781	0%	131	3	3	100%	Family history	RAG2; NR
8	M	147	White	660	173	120	20	20	445	3%	41	172	0	0%	PCP	LIG4; compound heterozygous
9	M	109	White	660	30	10	10	550	50	0%	NT	NT	NT	NT	PCP, CMV, Paraflu	Unknown

ALC, Absolute lymphocyte count; ALL, acute lymphoblastic leukemia; CMV, cytomegalovirus; F, female; FTT, failure to thrive; HHV-6, human herpes virus 6; hMPV, human metapneumovirus; M, male; NK, Natural Killer; NR, not reported; NT, not tested; Paraflu, parainfluenza; PCP, *Pneumocystis jirovecii*; PNA, pneumonia; RSV, respiratory syncytial virus; TME, transplacental maternal engraftment; VZV, varicella zoster virus.

TABLE E2. Individual HCT characteristics for patients undergoing URD HCT

Case no.	Year of HCT	Days from diagnosis	Serotherapy dose (mg/kg)	GVHD prophylaxis	Source	Matching	TNC ($\times 10^8$ /kg)	CD34 ($\times 10^6$ /kg)	CD3 ($\times 10^7$ /kg)	aGVHD	cGVHD	Second HCT	Alive	Cause of death
IL2RG SCID														
1	1993	46	rATG/10	CSA/MTX	BM	6/6	5.5	NT	NT	Grade II	No	No	Yes	
2	1997	66	None	CSA	BM	6/6	7.4	4.4	NT	Grade II	No	No	Yes	
3	2004	64	rATG/40*	CSA/steroids	BM	10/10	5.6	10	4.5	Grade II	No	No	Yes	
4	2006	42	None	CSA	BM	10/10	3	4.1	4.3	Grade II	NE	Boost (D+21)	No	aGVHD (D+103)
5	2006	74	rATG/9	CSA/steroids	BM	10/10	10	NT	NT	0	No	No	Yes	
6	2008	86	rATG/10	CSA	BM	12/12	NT	20	NT	0	No	No	Yes	
7	2011	54	rATG/8	CSA/MMF	BM	12/12	2.9	5.9	72	0	No	Boost (D+48)	Yes	
8	2012	34	rATG/10	TAC/MTX	BM	10/10	4.1	6.1	NT	0	No	No	Yes	
9	2012	47	hATG/100	TAC	BM	10/10	5.4	8.1	NT	Grade I	Yes	Boost (D+40)	Yes	
10	2003	281	None	CSA	PBSC (TCD)	9/10 (C)	1.1	10	10	Grade IV	NE	No	No	aGVHD (D+77)
11	2010	60	None	CSA/MMF	PBSC (TCD)	10/10	0.1	10	0.02	Grade II	Yes	Full (D+113)	Yes	
12	2010	48	None	CSA	PBSC (TCD)	10/10	NT	10	0.01	0	No	No	Yes	
13	1996	155	hATG/90	CSA/steroids	UCB	6/6	2.6	NT	NT	Grade III	Yes	No	Yes	
14	2000	43	None	CSA/steroids	UCB	6/6	1	0.5	NT	Grade I	Yes	No	Yes	
15	2002	28	hATG/120	CSA	UCB	6/6	0.8	0.9	NT	0	No	No	Yes	
16	2004	25	None	None	UCB	5/6 (A)	2.3	0.1	NT	Grade II	Yes	No	No	cGVHD (D+362)
17	2008	64	rATG/10	CSA	UCB	12/12	0.4	0.4	NT	Grade I	No	No	Yes	
18	2008	43	None	CSA	UCB	11/12 (DP)	1.3	1.7	2.1	Grade III	No	No	Yes	
19	2010	56	None	CSA/steroids	UCB	10/10	0.9	0.5	0.4	Grade III	Yes	No	Yes	
20	2010	78	None	CSA/MMF/steroids	UCB	10/10	0.8	0.3	0.4	Grade II	Yes	No	Yes	
21	2011	74	None	CSA/MMF/steroids	UCB	8/10 (A+DQ)	1.1	0.3	0.1	0	NE	No	No	Ongoing Neuro (D+39)
ADA SCID														
1	2011	530†	rATG/8	CSA/MMF	BM	12/12	4	2.5	46	Grade I	Yes	No	Yes	
2	2000	20	None	CSA	UCB	6/6	1.3	0.7	6.3	0	No	No	Yes	
3	2002	40	None	CSA/steroids	UCB	6/6	2	0.6	NT	Grade III	No	No	No	Ongoing Paraflu (D+166)
4	2002	16	None	CSA	UCB	6/6	1.3	0.4	NT	0	No	No	Yes	
5	2006	31	None	CSA/steroids	UCB	10/10	1.6	0.5	6.3	Grade III	NE	No	No	Ongoing Neuro (D+101)
6	2010	32	None	CSA/MMF	UCB	10/10	3	1	9.2	Grade II	No	No	Yes	
7	2011	62†	None	CSA/MMF	UCB	10/10	2.4	0.9	6.2	0	No	No	Yes	
Other SCID														
1	1995	67	None	CSA	BM	6/6	4	NT	NT	Grade I	Yes	No	No	cGVHD, AIHA, ITP (D+1024)
2	1998	100	None	CSA	BM	6/6	NT	14	15.5	0	NE	No	No	IntraOp (D+71)
3	2005	96	Campath/1	CSA/MTX	BM	10/10	3.3	3.7	NT	0	NE	Full (D+90)	Yes	
4	2009	49	None	CSA/MTX	BM	12/12	6.4	7	3.5	Grade II	No	No	Yes	
5	2011	44	None	TAC	BM	10/10	2	4.2	3.4	Grade III	Yes	No	Yes	

(Continued)

TABLE E2. (Continued)

Case no.	Year of HCT	Days from diagnosis	Serotherapy dose (mg/kg)	GVHD prophylaxis	Source	Matching	TNC ($\times 10^8$ /kg)	CD34 ($\times 10^6$ /kg)	CD3 ($\times 10^7$ /kg)	aGVHD	cGVHD	Second HCT	Alive	Cause of death
6	2012	111	None	CSA	BM	10/10	9	6.8	NT	Grade III	Yes	No	No	cGVHD, RSV (D+145)
7	1998	55	rATG/20	CSA/MTX	UCB	6/6	1.5	NT	NT	NE	NE	Full (D+241)	Yes	
8	2007	33	Campath/1	CSA	UCB	5/6 (A)	1.3	0.4	NT	NE	NE	Full (D+139)	Yes	
9	2010	16	None	CSA/steroids	UCB	10/10	0.6	0.2	0.9	NE	NE	No	No	Ongoing respiratory failure (D+9)

AIHA, Autoimmune hemolytic anemia; *CSA*, cyclosporine; *hATG*, horse anti-thymocyte globulin; *ITP*, idiopathic thrombocytopenic purpura; *MMF*, mycophenolate mofetil; *MTX*, methotrexate; *NE*, not evaluable; *NT*, not tested; *Paraflu*, parainfluenza; *PBSC*, peripheral blood stem cells; *rATG*, rabbit anti-thymocyte globulin; *RSV*, respiratory syncytial virus; *TAC*, tacrolimus; *TCD*, T-cell depletion.

*Fresenius.

†PEG-ADA before HCT.

TABLE E3. Individual immunologic data at 1 year after URD HCT

Case no.	ALC ($\times 10^6/L$)	CD3 ($\times 10^6/L$)	CD4 ($\times 10^6/L$)	CD8 ($\times 10^6/L$)	B cells ($\times 10^6/L$)	NK cells ($\times 10^6/L$)	CD4/CD45RA	PHA	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	Receiving immunoglobulin
IL2RG SCID												
1	5,916	4,673	2,839	1,656	946	297	9%	100%	NT	8	53	Yes
2	3,365	3,161	1,632	1,394	68	136	NT	NT	671	85	0	Yes
3	3,354	3,250	940	2,350	0	40	NT	100%	573	50	7	Yes
5	1,820	839	401	201	912	36	70%	100%	NT	NT	NT	Yes
6	4,000	3,520	2,310	930	330	140	57%	NT	373	34	0	Yes
7	2,960	2,516	1,362	770	397	0	94%	100%	870	31	9	Yes
8	6,300	2,604	1,241	1,250	3,602	120	57%	69%	482	31	7	Yes
9	1,031	979	381	526	0	0	NT	75%	NT	0	0	Yes
11	2832	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	No
12	5,388	2,186	3,027	1,460	1,460	99	68%	NT	540	60	18	Yes
13	337	66	21	45	151	120	50%	100%	1283	253	50	No
15	2,600	764	402	361	248	52	16%	NT	840	9	0	Yes
17	5,100	3,910	2,580	1,280	1,150	30	60%	NT	501	37	0	Yes
18	2,560	2,120	1,410	560	280	80	88%	NT	839	42	45	Yes
19	520	460	360	60	30	5	32%	NT	479	0	10	Yes
20	490	420	270	80	40	10	24%	NT	929	27	138	Yes
ADA SCID												
1	2,210	2,144	530	1,503	22	44	8%	72%	663	NA	NA	Yes
2	830	NT	NT	NT	NT	NT	NT	NT	301	86	50	No
4	580	540	277	214	28	42	80%	NT	781	29	20	Yes
6	640	551	309	192	0	78	55%	100%	410	40	0	Yes
7	636	593	272	199	30	10	NT	NT	950	14	4	Yes
Other SCID												
1	590	421	308	189	11	184	19%	NT	NT	NT	NT	Yes
3	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	Yes
4	2,080	1,414	853	541	333	291	NT	85%	NT	34	35	Yes
5	4,560	3,233	2,221	857	150	251	32%	NT	1130	46	6	Yes
7	1,300	623	496	114	13	458	0%	NT	880	7	3	Yes
8	520	120	109	21	16	390	NT	3%	NT	NT	NT	Yes

Values in boldface and italics are after conditioned second HCT (not counted in Table IV).

ALC, Absolute lymphocyte count; NA, not applicable; NT, not tested.

TABLE E4. Individual immunologic data at last follow-up after URD HCT

Case no.	ALC (× 10 ⁶ /L)	CD3 (× 10 ⁶ /L)	CD4 (× 10 ⁶ /L)	CD8 (× 10 ⁶ /L)	B cells (× 10 ⁶ /L)	NK cells (× 10 ⁶ /L)	CD4/ CD45RA	PHA	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	Receiving immuno- globulin	PBMC chimerism	CD3 chimerism	B-cell chimerism	Myeloid chimerism	Other complications
IL2RG SCID																	
1	1,909	1,798	355	1,101	111	9	4%	65%	643	38	0	Yes	NT	99%	0%	0%	None
2	2,928	2,249	1,059	1,069	400	48	43%	100%	8.7	88	0	No	NT	100%	18%	16%	None
3	908	742	314	423	139	22	NT	100%	3820	40	7	No	28%	99%	100%	12%	AIHA, AI neutropenia, bacterial infections, Hepatitis B
5	1,800	919	362	226	804	29	NT	100%	NA	124	54	Yes	4%	NT	NT	NT	None
6	1,000	315	144	154	70	40	35%	100%	429	63	24	Yes	77%	NT	NT	1%	None
7	2,960	2,516	1,362	770	397	0	94%	100%	870	31	9	Yes	41%	97%	9%	5%	None
8	6,300	2,604	1,241	1,250	3,602	120	57%	69%	482	31	7	Yes	NT	100%	NT	0%	None
9	1,031	979	381	526	0	0	NT	75%	NT	0	0	Yes	74%	NT	NT	NT	FTT
11	2,397	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	No	100%	NT	NT	NT	TTP
12	4,000	3,159	1,046	1,853	1,072	0	71%	NT	820	74	65	Yes	78%	100%	2%	0%	None
13	1,800	1,165	502	569	389	194	NT	100%	1010	135	69	No	100%	100%	100%	100%	None
14	2,700	1,930	1,360	550	460	NT	NT	74	NT	29	7	Yes	25%	NT	NT	NT	None
15	2,500	764	402	361	248	52	16%	NT	1067	83	0	Yes	NT	NT	0%	NT	None
17	10,000	3,150	1,440	1,540	700	40	35%	NT	482	82	39	No	71%	NT	NT	31%	None
18	5,070	4,210	2,330	1,670	710	100	86%	100%	832	29	32	Yes	NT	100%	12%	0%	None
19	2,890	2,310	1,620	580	400	29	77%	100%	NA	60	0	Yes	NT	100%	NT	0%	Pneumatosi, NTM bacteremia
20	1,150	1,070	840	80	3	10	8%	NT	NA	28	14	Yes	NT	100%	NT	0%	Vertebral fractures
ADA SCID																	
1	6,140	6,017	1,105	4,851	0	61	8%	72%	884	22	0	Yes	6%	98%	35%	1%	CMV
2	1,760	1,277	408	650	47	363	4%	NT	610	61	76	No	NT	NT	NT	NT	Pneumonitis
4	1,570	1,328	506	613	137	98	8%	NT	730	55	138	No	NT	96%	91%	14%	Pneumonitis
6	1,690	1,574	981	353	48	98	41%	NT	870	31	0	Yes	NT	95%	NT	0%	Pneumonitis, nephrotic syndrome
7	636	593	272	199	30	10	NT	NT	950	14	4	Yes	NT	100%	NT	0%	None
Other SCID																	
3	2,110	1,393	781	570	338	338	NT	85%	NT	98	66	No	100%	100%	100%	100%	Seizures
4	12,474	10,790	6,999	3,443	1,696	274	51%	NT	1,970	21	14	No	100%	100%	100%	100%	None
5	525	368	247	63	5	84	0%	NT	NT	NT	NT	Yes	NT	NT	NT	NT	None
7	1,190	757	467	201	257	127	12%	NT	1430	30	88	Yes	56%	NT	NT	6%	None
8	4,360	2,566	1,846	634	189	156	75%	100%	NT	0	0	Yes	100%	NT	NT	NT	None

Values in boldface and italics are after conditioned second HCT (not counted in Table IV).

AI, Autoimmune; AIHA, autoimmune hemolytic anemia; ALC, absolute lymphocyte count; CMV, cytomegalovirus; FTT, failure to thrive; NT, not tested; NTM, nontuberculous mycobacteria; TTP, thrombotic thrombocytopenic purpura.

TABLE E5. Individual characteristics at the time of diagnosis of SCID for patients undergoing MSD HCT

Case no.	Sex	Age (d)	Race/ethnicity	ALC (× 10 ⁶ /L)	CD3 (× 10 ⁶ /L)	CD4 (× 10 ⁶ /L)	CD8 (× 10 ⁶ /L)	B cells (× 10 ⁶ /L)	NK cells (× 10 ⁶ /L)	PHA	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	TME	Diagnostic trigger	Mutation
IL2RG and JAK3 SCID																
1	M	57	White	1,656	34	23	11	1,424	30	2%	850	0	0	0%	Family history	p.Glu109
2	M	5	White	800	16	16	0	336	24	NT	710	80	0	0%	Family history	c.676C>T
3	M	242	White	2,496	20	15	5	2,172	17	0%	460	0	0	0%	Rotavirus	NR
4	M	0	White	NR	0	0	0	NR	NR	0%	NR	NR	NR	0%	Family history	NR
5	M	90	White	1,530	245	15	153	1,193	8	0%	NR	NR	NR	+	HSV, PNA	NR
6	M	209	White	930	37	9	9	865	0	0%	572	14	7	NT	RSV, Paraflu, <i>S aureus</i> sepsis	NR
7	M	186	White	1,410	8	8	0	1,120	20	0%	362	109	14	+	Skin abscesses, GVHD	p.S225R
8	M	130	African	1,938	504	17	165	1,345	215	11%	18	22	116	+	Paraflu, GVHD	c.691G>A
9	M	30	African	2,301	449	46	318	1,719	21	2%	225	0	0	+	Enterovirus	c.269del7
10	M	209	White	1,610	0	0	0	1,562	0	NT	NR	NR	NR	0%	PNA	NR
11	M	209	White	NR	NR	NR	NR	NR	NR	NT	NR	NR	NR	+	Paraflu, thrush	NR
12	M	0	White	1,880	130	10	150	850	60	NT	NR	NR	NR	0%	Family history	NR
13	M	414	Hispanic	1,763	10	5	5	1,739	14	1%	7	61	0	NT	<i>Aspergillus</i> and <i>Enterococcus</i> species	c.806del23
14	M	158	Asian	1,224	12	0	0	1,187	0	0%	426	36	7	0%	RSV, <i>Enterobacter</i> species PNA	c.633A>T
15	M	60	Asian	620	0	0	0	560	20	0%	NR	NR	NR	0%	CMV, thrush	NR
16	M	134	Caribbean	3,000	650	50	490	1,780	130	NT	0	0	0	100%	PNA	c.215G>A
17	M	198	White	486	13	12	0	361	87	NT	40	0	0	0%	hMPV, norovirus	c.437T>C
18	M	0	White	726	0	0	0	0	30	NT	90	0	0	0%	Family history	NR
19	M	0	White	1,067	14	11	0	990	53	NT	730	18	0	0%	Family history	Exon 3 IVs3+1G>C
20	M	162	White	2,784	0	0	0	2,728	28	NT	790	26	0	0%	PCP	c.545G>A
21	F	106	White	915	146	82	46	613	101	NT	0	128	0	0%	CMV, PCP	JAK3; NR
22	F	106	White	1,730	13	13	0	1,249	13	NT	0	0	0	0%	PCP, vaccine polio	JAK3; NR
23	M	202	Asian	3,102	40	30	0	3,015	43	NT	1,100	0	0	1%	PCP, rotavirus, BCG	JAK3; NR
ADA SCID																
1	F	9	Asian	NR	NR	NR	NR	NR	52	NT	NR	NR	NR	0%	Family history	NR
2	M	30	Asian	350	67	4	63	7	147	0%	NR	NR	NR	0%		NR
3	M	34	Asian	200	158	134	24	10	26	NT	NR	NR	NR	0%	PNA	NR
4	F	60	African	410	70	33	37	25	45	0%	NR	NR	NR	0%		NR
5	M	30	White	1,540	92	15	77	1,201	185	0%	NR	NR	NR	0%		NR
6	M	383	Hispanic	300	60	10	50	20	10	0%	406	11	NT	NT	Candidemia, PCP, CMV	NR, level = 0
7	M	20	White	30	5	5	2	8	9	0%	381	40	0	0%	Interstitial pneumonitis	NR, level = 0
8	F	0	Asian	170	6	4	0	3	132	0%	332	0	0	0%	Family history	NR, level = 0
9	F	74	White	369	4	0	0	15	339	0%	168	10	0	0%	ParvoB19, H. flu	NR, level = 0
10	F	63	White	660	455	59	172	26	60	0%	NR	NR	NR	+		NR
11	F	48	White	640	13	1	5	13	115	NT	NR	NR	NR	0%	CMV pneumonitis	NR
12	F	21	White	110	NR	NR	NR	NR	NR	NR	NR	NR	NR	0%		NR
13	F	31	White	200	10	0	0	NT	NT	NT	417	3	5	NT	<i>Pseudomonas</i> species	NR, level = 0
14	M	49	Middle Eastern	378	8	2	4	4	102	NT	218	7	0	0%	RSV, rotavirus	c.164_172del9
15	M	28	African	470	10	10	0	30	340	0%	NR	NR	NR	0%	Cytopenias, rash	NR
16	M	20	Asian	0	0	0	0	0	0	NT	NR	NR	NR	0%	PNA	NR
17	M	34	Asian	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0%	PNA	NR, level = 0
18	M	490	Middle Eastern	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0%	PNA	NR, level = 0
19	M	88	White	300	240	60	170	30	30	0%	1,570	85	37	0%	Skin abscesses	NR, level = 0

(Continued)

TABLE E5. (Continued)

Case no.	Sex	Age (d)	Race/ethnicity	ALC (× 10 ⁶ /L)	CD3 (× 10 ⁶ /L)	CD4 (× 10 ⁶ /L)	CD8 (× 10 ⁶ /L)	B cells (× 10 ⁶ /L)	NK cells (× 10 ⁶ /L)	PHA	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	TME	Diagnostic trigger	Mutation
20	F	194	African	200	140	120	40	10	30	NT	NR	NR	NR	0%	PNA	NR
21	F	165	African	30	2	1	5	8	8	0%	NT	0	0	NT	Paraflu, rotavirus	NR, level = 0
22	F	122	White	41	0	0	0	0	36	NT	820	0	0	0%	RSV, BCG	c.648G>A
23	F	18	White	190	12	9	2	4	168	0%	NT	NT	NT	0%	Interstitial pneumonitis	c.646G>A
Other SCID																
1	M	0	Hispanic	147	0	0	0	0	144	0%	170	18	26	0%	Family history	Artemis; c.326C>T
2	M	0	Native American	500	0	0	0	0	500	0%	NT	NT	NT	0%	Family history	Artemis; c.597C>A
3	M	76	Native American	2,574	283	219	64	52	2,239	0%	100	0	0	14%	GVHD	Artemis; c.597C>A
4	M	367	Hispanic	759	457	125	332	7	240	NT	361	40	284	+	Aspergillosis, <i>Pseudomonas</i> species	RAG2; c.217C>T
5	F	101	Asian	16,054	8,076	2,935	5,079	0	7,848	NT	0	9	0	+	CMV, ParaFlu3, BCG	Artemis; NR
6	M	156	Asian	1,324	0	0	0	0	1,324	0%	89	9	0	0%	Paraflu3, BCG	RAG1; c.2146C>T
7	M	147	Asian	1,120	4	4	0	2	960	NT	NR	NR	NR	NT	PNA, thrush	RAG1; NR
8	M	194	Middle Eastern	1,634	392	180	180	0	1,095	NT	93	0	0	0%	RSV, H. flu	RAG1; g.1455C>T
9	M	0	White	690	18	16	2	2	667	0%	NT	0	NT	0%	Family history	RAG1; c.1303A>G
10	M	0	Asian	950	304	133	152	38	504	NT	NR	NR	NR	0%	Family history	RAG1; NR
11	F	63	White	38	7	7	0	26	5	0%	190	NT	NT	+	CMV	Artemis: Exon1del + Exons1-3del
12	F	141	Middle Eastern	1,000	0	0	0	0	980	0%	490	0	0	0%	PCP	Unknown
13	M	150	White	400	90	47	47	20	300	NT	220	42	25	75%	Diarrhea	Unknown
14	F	125	White	360	133	86	32	58	166	0%	NR	NR	NR	+	NR	Unknown
15	M	110	White	140	34	25	9	46	57	1%	179	8	287	NT	Family history	Unknown
16	M	851	Middle Eastern	1,376	248	179	69	757	248	60%	NT	7	0	0%	Enterovirus, BCG, <i>Cryptosporidium</i>	Unknown
17	F	106	Asian	390	70	60	10	120	250	0%	NR	NR	NR	0%	FluA, rotavirus	Unknown
18	M	6	Asian	2,610	310	210	30	1,440	780	0%	NR	NR	NR	+	Family history	Unknown
19	M	510	Middle Eastern	2,401	432	120	192	624	1,200	8%	NT	36	13	0%	Bronchitis	Unknown
20	F	15	Asian	1,630	410	310	70	330	820	0%	NR	NR	NR	NT	Family history, Omenn syndrome	Unknown

ALC, Absolute lymphocyte count; CMV, cytomegalovirus; F, female; H. Flu, Haemophilus influenza; hMPV, human metapneumovirus; HSV, herpes simplex virus; M, male; NR, not reported; NT, not tested; Paraflu, parainfluenza; PCP, *Pneumocystis jirovecii*; PNA, pneumonia; RSV, respiratory syncytial virus; TME, transplacental maternal engraftment; VZV, varicella zoster virus.

TABLE E6. Individual HCT characteristics for patients undergoing MSD HCT

Case no.	Year of HCT	Days from diagnosis	Serotherapy dose (mg/kg)	GVHD prophylaxis	Source	Matching	TNC ($\times 10^8/\text{kg}$)	CD34 ($\times 10^6/\text{kg}$)	CD3 ($\times 10^7/\text{kg}$)	aGVHD	cGVHD	Second HCT	Alive	Cause of death
IL2RG and JAK3 SCID														
1	1993	3	None	None	BM	6/6	10.7	NT	NT	0	No	No	Yes	
2	1994	11	None	None	BM	8/8	9	NT	NT	Grade I	No	No	Yes	
3	1995	36	None	None	BM	8/8	3.3	NT	NT	Grade II	No	No	Yes	
4	1998	1	None	None	BM	6/6	3.5	4.9	0.1	0	No	No	Yes	
5	2000	153	None	None	BM	6/6	NT	NT	NT	Grade I	No	No	Yes	
6	2000	43	None	CSA/steroids	UCB	6/6	10.3	5.4	NT	Grade I	No	No	Yes	
7	2001	23	None	None	BM	10/10	4.9	10.7	0.5	Grade II	No	No	Yes	
8	2001	14	None	TCD	BM	8/8	2.2	8.2	0.3	0	No	No	Yes	
9	2002	30	None	TCD	BM	10/10	14	13	0.5	0	No	No	Yes	
10	2002	17	None	None	BM	6/6	NT	10.7	3.8	Grade II	No	No	Yes	
11	2002	17	None	None	BM	6/6	NT	9.8	3.5	0	No	No	Yes	
12	2003	15	None	None	BM	6/6	NT	11.4	9.5	0	No	No	Yes	
13	2004	16	None	TCD	BM	10/10	8	4.6	1.8	Grade II	No	No	Yes	
14	2004	24	None	None	UCB	5/6 (A)	23.2	9.7	NT	Grade III	Yes	No	No	cGVHD and RSV (day +362)
15	2007	55	None	None	BM	6/6	7.5	8.4	7	Grade III	Yes	No	Yes	
16	2009	74	None	None	BM	10/10	4	3.3	NT	0	No	No	Yes	
17	2009	20	None	TCD	BM	12/12	6.3	6.5	8.8	0	No	No	Yes	
18	2010	17	None	CSA	BM	12/12	5	7.1	1.7	0	No	No	Yes	
19	2012	34	None	CSA	BM	11/12 (DP)	2.6	9.3	5.5	Grade II	No	No	Yes	
20	2012	18	None	None	BM	10/10	5.4	16.3	6.5	NE	NE	Full (D+23)	Yes	
21	1996	61	None	None	BM	10/10	4.9	NT	NT	Grade I	No	No	Yes	
22	1996	61	None	None	BM	6/6	5.1	NT	NT	Grade II	No	No	Yes	
23	2009	47	None	None	BM	10/10	2.4	7.7	0.2	0	No	No	No	Probable sepsis (day +928)
ADA SCID														
1	1993	14	None	None	BM	6/6	NT	NT	NT	0	No	No	Yes	
2	1994	86	None	None	BM	6/6	NT	NT	NT	0	NE	No	No	Metabolic (day +96)
3	1994	14	None	None	BM	6/6	NT	NT	NT	0	No	No	Yes	
4	1995	121*	None	None	BM	6/6	NT	NT	NT	0	No	No	Yes	
5	1996	195*	None	None	BM	6/6	NT	NT	NT	0	No	No	Yes	
6	1998	386*	None	CSA	BM	6/6	5	NT	NT	0	No	No	Yes	
7	1998	19	None	None	BM	10/10	10	NT	NT	Grade II	No	No	Yes	
8	1999	32	None	None	BM	10/10	5	NT	NT	0	No	No	Yes	
9	1999	12	None	None	BM	10/10	6.8	11.4	8.3	Grade I	No	No	Yes	
10	1999	24	None	None	BM	6/6	NT	NT	NT	0	No	No	Yes	
11	2001	15	None	None	BM	6/6	NT	NT	NT	NE	NE	NA	No	CMV (day +16)
12	2002	26*	None	CSA	BM	6/6	NT	NT	NT	Grade III	No	No	Yes	
13	2002	30	None	None	BM	10/10	2	2.92	1	Grade I	No	Full (D+2310)	Yes	
14	2002	18	None	None	BM	8/8	12.6	5	NT	0	No	No	Yes	
15	2004	45	None	None	BM	10/10	NT	NT	NT	Grade II	No	No	Yes	
16	2006	21	None	None	BM	10/10	NT	NT	NT	Grade II	No	Boost (D+343)	Yes	
17	2006	65	None	CSA	BM	10/10	NT	NT	NT	0	No	No	Yes	

(Continued)

TABLE E6. (Continued)

Case no.	Year of HCT	Days from diagnosis	Serotherapy dose (mg/kg)	GVHD prophylaxis	Source	Matching	TNC ($\times 10^8/\text{kg}$)	CD34 ($\times 10^6/\text{kg}$)	CD3 ($\times 10^7/\text{kg}$)	aGVHD	cGVHD	Second HCT	Alive	Cause of death
18	2007	30	None	None	BM	10/10	NT	NT	NT	0	No	No	Yes	
19	2007	38	None	None	BM	10/10	6.2	2.5	NT	0	No	Boost (D+237)	Yes	
20	2008	279*	None	CSA	BM	10/10	NT	NT	NT	0	No	Boost (D+211)	Yes	
21	2009	30	None	None	BM	10/10	4.4	NT	NT	Grade I	No	No	Yes	
22	2010	37*	None	CSA	BM	12/12	5.6	7.2	2.4	Grade II	No	No	Yes	
23	2011	37*	None	CSA	BM	12/12	3	10	3.1	0	No	No	Yes	
Other SCID														
1	1998	13	None	CSA/MTX	BM	6/6	11.8	NT	NT	0	No	No	Yes	
2	1998	17	None	CSA/MTX	BM	6/6	7.3	NT	NT	0	No	No	Yes	
3	1999	19	None	CSA/Steroids	BM	6/6	6	NT	NT	0	No	No	Yes	
4	2002	12	None	TCD	BM	8/8	0.7	0.8	0.02	0	Yes	Boost (D+586)	Yes	
5	2002	35	None	CSA	BM	12/12	12	16	31.7	0	No	No	Yes	
6	2004	20	None	None	BM	10/10	7.2	5.6	29	0	No	No	Yes	
7	2005	29	None	None	BM	10/10	6.9	14.8	NT	0	No	Boost (D+2311)	Yes	
8	2006	87	None	CSA	BM	5/6 (A)	4.4	NT	NT	0	NE	Full (D+89)	Yes	
9	2007	15	None	CSA/MTX	BM	10/10	7.5	29.1	9	0	No	No	Yes	
10	2010	41	None	None	BM	10/10	8.6	18.4	4.4	0	No	Full (D+837)	No	Unknown (day +1002)
11	2011	64	Campath/1.2	None	BM	10/10	1.4	8.3	1.12	0	No	Boost (D+71)	Yes	
12	1998	25	None	None	BM	6/6	NT	7.3	NT	0	No	No	Yes	
13	1998	56	None	CSA/MTX	BM	6/6	2	NT	NT	0	No	No	Yes	
14	2000	12	None	CSA	BM	6/6	NT	NT	NT	0	No	No	Yes	
15	2000	18	hATG/90	CSA	BM	6/6	6.9	9.9	NT	0	No	No	Yes	
16	2002	1389	None	None	BM	8/8	10	NT	NT	0	No	No	Yes	
17	2004	40	None	CSA/MMF	BM	10/10	NT	3.6	11.8	0	No	No	Yes	
18	2005	47	None	None	BM	10/10	NT	NT	NT	Grade II	No	No	No	Unknown (day +1916)
19	2006	160	None	None	BM	10/10	1.8	NT	NT	0	No	No	Yes	
20	2010	60	None	CSA	BM	10/10	NT	8.5	5.6	0	No	No	Yes	

CMV, Cytomegalovirus; CSA, cyclosporine; hATG, horse anti-thymocyte globulin; MMF, mycophenolate mofetil; MTX, methotrexate; NA, not applicable; NE, not evaluable; NT, not tested; rATG, rabbit anti-thymocyte globulin; RSV, respiratory syncytial virus; TCD, T-cell depletion.

*PEG-ADA before HCT.

TABLE E7. Individual immunologic data at 1 year after MSD HCT

Case no.	ALC ($\times 10^6/L$)	CD3 ($\times 10^6/L$)	CD4 ($\times 10^6/L$)	CD8 ($\times 10^6/L$)	B cells ($\times 10^6/L$)	NK cells ($\times 10^6/L$)	CD4/CD45RA	PHA	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	Receiving immunoglobulin
IL2RG and JAK3 SCID												
1	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NR
2	6,142	4,361	2,580	1,167	1,536	553	NT	NT	610	40	10	No
3	4,736	3,078	2,179	758	1,373	142	NT	NT	300	61	51	No
4	NR	4,140	1,783	NR	NR	NR	NR	NR	NR	NR	NR	No
5	NR	3,040	1,820	NR	NR	NR	NR	NR	NR	NR	NR	No
6	2,335	1,751	1,191	444	537	47	NT	8%	NT	29	7	Yes
7	4,720	2,440	1,460	850	2,020	210	NT	100%	550	28	0	Yes
8	6,180	3,955	2,559	1,267	2,126	80	78%	99%	514	103	114	No
9	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NR
10	5,690	3,700	2,110	1,480	1,710	170	NR	NR	NR	NR	NR	No
11	7,270	4,940	2,620	2,250	1,890	220	NR	NR	NR	NR	NR	No
12	5,480	4,270	1,750	2,300	1,100	50	NR	NR	NR	NR	NR	No
13	4,248	3,428	2,014	1,160	599	115	55%	59%	605	67	9	No
15	2,810	2,390	1,210	1,180	30	280	NR	NR	NR	NR	NR	No
16	5,600	3,500	1,600	1,600	1,200	170	75%	NT	580	85	34	No
17	6,100	3,390	1,646	1,451	2,571	93	21%	NT	1,150	22	13	Yes
18	2,390	1,769	921	824	561	47	33%	NT	820	27	12	Yes
19	2,200	1,981	1,083	793	83	52	42%	NT	600	7	4	Yes
20	5,375	2,956	1,827	1,075	2,150	161	74%	NT	610	72	17	No
21	10,449	9,287	2,653	6,302	1,879	221	17%	NT	1750	116	21	No
22	4,736	3,680	1,766	2,012	834	392	20%	NT	1,380	128	97	No
23	2,456	1,966	1,025	889	423	57	26%	NT	870	68	44	Yes
ADA SCID												
1	NR	1,008	405	NR	NR	NR	NR	NR	NR	NR	NR	No
3	NR	1,659	NR	NR	NR	NR	NR	NR	NR	NR	NR	No
4	NR	1,279	570	NR	NR	NR	NR	NR	NR	NR	NR	No
5	NR	2,030	577	NR	NR	NR	NR	NR	NR	NR	NR	No
6	1,780	1,246	463	694	249	231	NT	100%	NT	99	14	No
7	2,000	1,274	404	626	14	97	NT	NT	1,050	30	0	Yes
8	1,960	1,814	716	1,114	144	82	NT	NT	800	101	45	No
9	2,582	1,764	593	958	333	358	NT	NT	397	33	17	No
10	NR	2,360	368	NR	NR	NR	NR	NR	NR	NR	NR	No
12	NR	760	240	NR	NR	NR	NR	NR	NR	NR	NR	No
13	400	364	132	214	9	20	7%	NT	893	36	25	Yes
14	1,824	985	383	474	73	602	22%	58%	520	52	14	No
15	620	500	250	240	40	20	NR	NR	NR	NR	NR	No
16	810	640	280	370	30	40	NR	NR	NR	NR	NR	No
17	NR	730	330	NR	NR	NR	NR	NR	NR	NR	NR	No
18	NR	2,500	1,330	NR	NR	NR	NR	NR	NR	NR	NR	No
19	800	730	460	250	50	20	NT	NT	721	24	15	Yes
20	620	520	240	240	30	10	NR	NR	NR	NR	NR	No
21	864	597	280	257	106	84	20%	76%	793	133	31	No
22	974	772	510	194	157	30	3%	NT	810	0	23	Yes
23	2,322	2,256	1,214	851	47	0	NT	NT	890	13	0	Yes

(Continued)

TABLE E7. (Continued)

Case no.	ALC (× 10 ⁶ /L)	CD3 (× 10 ⁶ /L)	CD4 (× 10 ⁶ /L)	CD8 (× 10 ⁶ /L)	B cells (× 10 ⁶ /L)	NK cells (× 10 ⁶ /L)	CD4/CD45RA	PHA	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	Receiving immunoglobulin
Other SCID												
1	1,560	744	450	248	0	682	NT	100%	NT	29	45	Yes
2	470	244	103	141	5	174	NT	46%	NT	11	0	Yes
3	488	326	189	122	4	158	NT	31%	NT	NT	NT	Yes
4	468	27	17	8	0	400	NT	49%	NT	8	115	Yes
5	9,043	8,157	1,559	6,646	0	804	1%	NT	843	11	16	Yes
6	936	743	278	348	0	187	4%	100%	854	17	14	Yes
7	NR	160	80	NR	NR	NR	NR	NR	NR	NR	NR	Yes
8	4,180	1,463	502	794	2,132	543	39%	43%	800	91	67	<i>No</i>
9	590	354	136	212	12	207	NT	31%	NT	21	NT	Yes
10	480	250	100	50	0	230	NR	NR	NR	NR	NR	NR
11	NT	NT	NT	NT	747	NT	NT	NT	NT	NT	NT	No
12	1,500	1,020	290	770	30	470	NT	NT	644	44	23	No
13	600	490	330	140	0	90	NT	NT	720	49	0	Yes
14	NR	2,250	1,460	NR	NR	NR	NR	NR	NR	NR	NR	No
15	2,835	NT	NT	NT	NT	NT	NT	NT	372	59	85	No
16	1,558	997	374	608	374	125	12%	16%	1010	26	32	No
17	2,630	2,000	950	1,000	260	290	NR	NR	NR	NR	NR	No
18	NR	1,800	520	NR	NR	NR	NR	NR	NR	NR	NR	NR
19	7,700	5,698	3,773	1,309	1,155	616	82%	97%	960	191	282	No
20	2,170	1,320	630	520	330	350	NR	NR	NR	NR	NR	No

Values in boldface and italics are after conditioned Second HCT (not counted in Table IV).

ALC, Absolute lymphocyte count; NR, not reported; NT, not tested.

TABLE E8. Individual immunologic data at last follow-up after MSD HCT

Case no.	ALC ($\times 10^6/L$)	CD3 ($\times 10^6/L$)	CD4 ($\times 10^6/L$)	CD8 ($\times 10^6/L$)	B cells ($\times 10^6/L$)	NK cells ($\times 10^6/L$)	CD4/ CD45RA	PHA	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	Receiving immuno- globulin	PBMC chimerism	CD3 chimerism	B-cell chimerism	Myeloid chimerism	Other complications
IL2RG SCID																	
1	3,172	2,632	1,586	856	347	95	70%	NT	1540	200	170	No	NT	NT	NT	NT	Warts
2	3,608	2,417	1,335	938	1,010	0	54%	66%	470	26	80	No	NT	100%	NT	0%	None
3	2,162	1,578	713	735	454	65	65%	100%	740	51	89	No	NT	NT	NT	NT	None
4	NT	1,650	470	NR	NR	NR	NR	100%	NR	NR	NR	No	52%	NR	NR	NR	Warts
5	2,710	2,220	1,270	NR	330	80	NR	100%	NR	NR	NR	No	34%	100%	5%	0%	None
6	2,700	1,930	1,360	550	460	0	NT	74%	NT	29	7	Yes	NT	NT	NT	NT	None
7	2,383	1,890	1,113	727	419	62	NT	100%	921	107	169	No	5%	99%	6%	NT	BCG, immune pancytopenia
8	3,750	3,116	1,616	1,297	589	128	67%	100%	1080	95	206	No	NT	NT	11%	NT	Transaminitis
9	1,520	1,190	458	468	248	33	73%	100%	743	57	155	No	NT	NT	29%	NT	None
10	2,200	1,690	700	NR	350	90	NR	100%	NR	NR	NR	No	33%	100%	0%	0%	None
11	2,250	1,600	540	NR	450	140	NR	100%	NR	NR	NR	No	44%	100%	0%	0%	NR
12	2,840	2,240	850	NR	430	NR	NR	100%	NR	NR	NR	No	67%	100%	0%	0%	None
13	4,950	4,069	1,752	1,284	822	149	73%	100%	604	41	6	No	NT	NT	18%	NT	Transaminitis
15	3,590	2,960	1,500	NR	790	160	NR	NR	NR	NR	NR	No	30%	100%	18%	NR	None
16	6,000	4,300	1,800	2,100	1,200	380	80%	NT	810	190	60	No	64%	NT	NT	3%	None
17	5,266	3,650	1,837	1,358	1,566	0	28%	NT	920	33	27	Yes	NT	99%	4%	1%	None
18	2,977	1,901	836	1,026	989	37	16%	NT	770	33	41	Yes	NT	94%	0%	0%	None
19	2,200	1,981	1,083	793	83	52	42%	NT	600	7	4	Yes	NT	100%	NT	0%	CMV pneumonitis
20	5,375	2,956	1,827	1,075	2,150	161	74%	NT	610	72	17	No	100%	100%	100%	100%	None
21	10,449	9,287	2,653	6,302	1,879	221	17%	NT	1,750	116	21	No	50%	90%	10%	50%	Engraftment syndrome
22	4,736	3,680	1,766	2,012	834	392	20%	NT	1,380	128	97	No	NT	80%	10%	10%	Engraftment syndrome
ADA SCID																	
1	NR	NR	1,452	1,280	NR	33	NR	NR	NR	NR	NR	No	14%	NR	NR	NR	None
3	NR	2,760	1,630	1,050	580	470	NR	100%	NR	NR	NR	No	45%	100%		34%	NR
4	NR	2,140	1,630	660	110	340	NR	100%	NR	NR	NR	No	60%	NR	NR	NR	NR
5	NR	4,440	3,330	2,040	750	220	NR	100%	NR	NR	NR	No	23%	100%	54%	0%	NR
6	2,150	1,613	796	774	194	301	NT	NT	NT	99	14	No	53%	88%	82%	22%	None
7	2,169	1,886	803	831	213	45	13%	NT	670	61	115	No	NT	92%	60%	10%	None
8	1,847	1,547	944	493	152	111	2%	NT	890	142	111	No	NT	88%	26%	3%	None
9	2,582	1,764	593	958	333	358	NT	NT	397	33	17	No	NT	NT	NT	NT	Neurologic damage
10	NR	2,000	1,600	740	180	100	NR	100%	NR	NR	NR	No	18%	95%	30%	24%	NR
12	NR	1,720	1,320	600	190	150	NR	NT	NR	NR	NR	No	32%	100%	59%	0%	NR
13	700	646	273	329	28	21	3%	NT	894	18	44	No	NT	NT	NT	NT	None
14	2,440	1,171	512	561	122	1,025	13%	46%	670	49	27	No	NT	100%	NT	0%	None
15	NR	1,380	1,190	510	100	10	NR	NT	NR	NR	NR	No	33%	100%	5%	0%	Hearing loss
16	NR	1,370	990	NR	NR	NR	NR	NR	NR	NR	NR	No	NR	100%	0%	0%	NR
17	NR	600	1,140	NR	NR	NR	NR	NR	NR	NR	NR	No	NR	100%	NR	NR	NR
18	NR	2,390	1,240	NR	NR	NR	NR	NR	NR	NR	NR	No	NR	84%	NR	5%	None

(Continued)

TABLE E8. (Continued)

Case no.	ALC ($\times 10^6/L$)	CD3 ($\times 10^6/L$)	CD4 ($\times 10^6/L$)	CD8 ($\times 10^6/L$)	B cells ($\times 10^6/L$)	NK cells ($\times 10^6/L$)	CD4/ CD45RA	PHA	IgG (mg/dL)	IgM (mg/dL)	IgA (mg/dL)	Receiving immuno- globulin	PBMC chimerism	CD3 chimerism	B-cell chimerism	Myeloid chimerism	Other complications
19	4,300	3,830	1,420	1,720	220	220	NT	NT	667	32	66	No	NT	89%	35%	0%	Seizures
20	NR	1,190	330	NR	NR	NR	NR	NR	NR	NR	NR	No	NR	100%	NR	0%	None
21	754	578	298	170	94	54	17%	100%	855	113	51	No	NT	NT	NT	NT	None
22	794	723	368	220	36	27	6%	NT	470	16	30	Yes	NT	100%	0%	0%	HCM
23	2,572	2,459	980	936	78	0	16%	NT	1060	17	0	Yes	NT	100%	NT	0%	None
Other SCID																	
1	2,360	1,864	1,109	755	0	472	3%	95%	812	NT	NT	Yes	8%	98%	NT	1%	Chronic lung disease
2	1,940	1,397	407	989	0	524	NT	47%	NT	7	11	Yes	28%	96%	NT	1%	None
3	540	439	248	140	4	81	NT	61%	NT	NT	NT	Yes	6%	92%	7%	0%	None
4	720	559	305	294	1	37	5%	86%	NT	0	0	Yes	NT	NT	NT	NT	None
5	2,073	1,939	906	1,026	0	128	3%	NT	1,310	0	7	Yes	NT	94%	NT	0%	None
6	1,051	861	492	255	18	161	3%	NT	1,140	18	82	Yes	NT	97%	0%	0%	None
7	NR	230	140	NR	NR	NR	NR	NR	NR	NR	NR	Yes	NR	100%	NR	0%	NR
8	3,096	2,198	1,300	867	279	681	18%	100%	860	65	81	<i>No</i>	100%	100%	100%	100%	Chronic lung disease
9	610	403	146	256	13	115	20%	77%	644	56	66	No	9%	90%	58%	1%	None
11	3,132	2,606	1,431	955	395	113	36%	100%	1,370	31	33	No	NT	100%	100%	63%	None
12	1,000	480	230	220	170	340	NT	NT	1,150	40	125	No	NT	98%	81%	NT	None
13	1,197	728	410	278	87	387	52%	NT	1,270	72	NT	No	37%	NT	NT	6%	Hypothyroidism
14	1,510	1,250	690	NR	170	50	NR	NR	NR	NR	NR	No	35%	42%	NR	19%	NR
15	1,200	1,140	288	588	24	24	16%	NT	375	48	133	No	NT	99%	57%	NT	None
16	1,081	768	432	313	216	65	4%	58%	1,120	34	153	No	NT	95%	NT	2%	EBV PTLD
17	1,960	1,650	900	NR	140	100	NR	100%	NR	NR	NR	No	52%	100%	NR	0%	NR
19	3,216	2,508	1,640	772	418	225	71%	100%	920	138	183	No	NT	100%	NT	0%	None
20	NR	1,890	820	NR	NR	NR	NR	NR	NR	NR	NR	No	NR	100%	NR	NR	None

Values in boldface and italics are after conditioned second HCT (not counted in Table IV).

ALC, Absolute lymphocyte count; CMV, cytomegalovirus; HCM, hypertrophic cardiomyopathy; NR, not reported; NT, not tested; PTLD, post-transplant lymphoproliferative disease.

TABLE E9. Additional analysis of risk for grade II or greater aGVHD

	MSD	P value	URD	P value
Year of HCT				
Before median	15% (5/34)		53% (9/17)	
After median	31% (9/29)	.14	47% (8/17)	1
Known HLA mismatches				
Yes	100% (2/2)		75% (3/4)	
No	20% (12/61)	.05	47% (14/30)	.6
No. of anti-GVHD agents (non-ATG)				
None	26% (10/39)	.36	100% (1/1)	1
1	25% (3/12)	1	38% (5/12)	.72
2	0% (0/7)	.33	50% (8/16)	1
3	NA		50% (1/2)	1
<i>Ex vivo</i> TCD	20% (1/5)	1	67% (2/3)	1

ATG, Anti-thymocyte globulin; NA, not applicable; TCD, T-cell depletion.