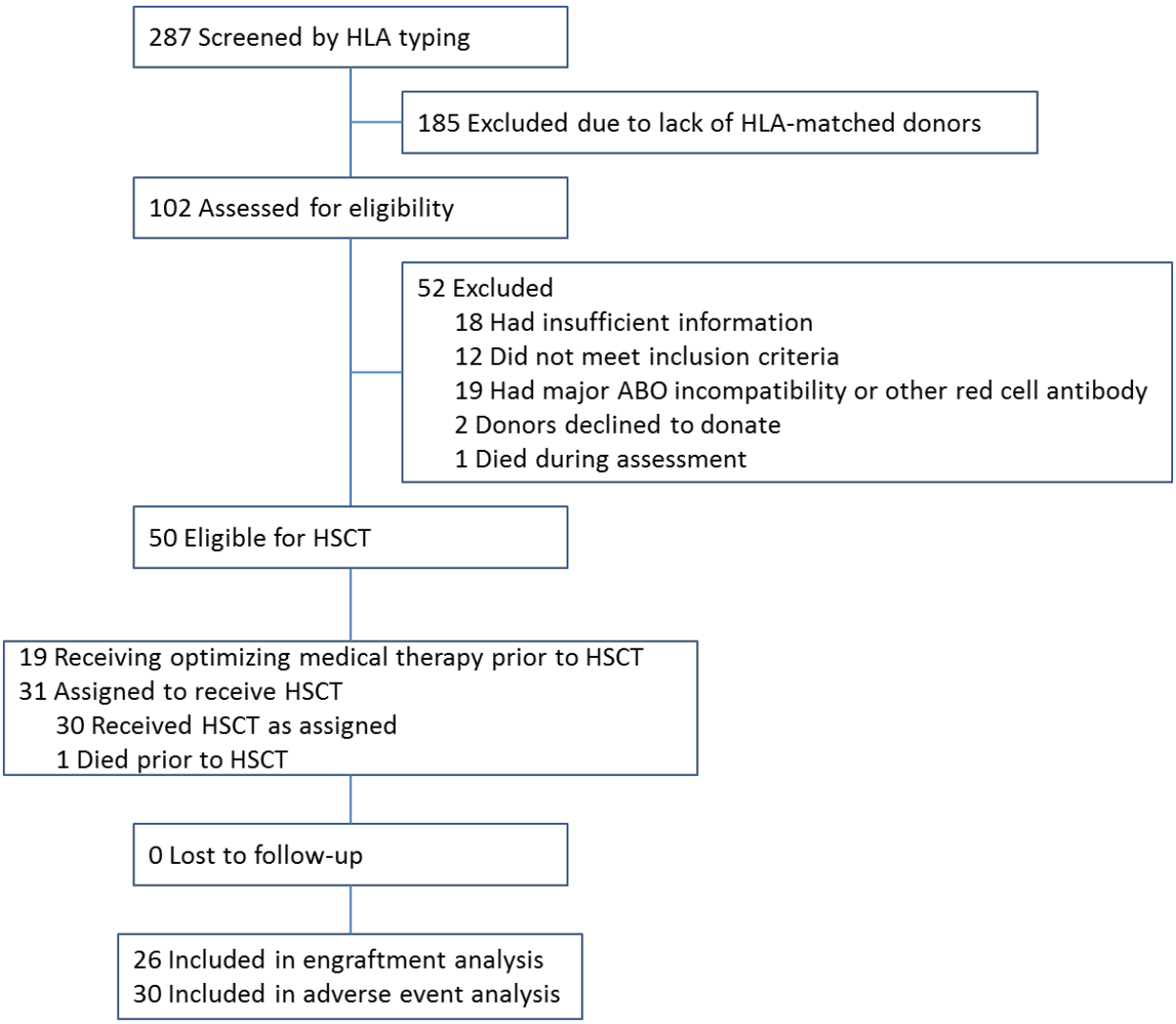
Supplementary Online Content

Hsieh MM, Fitzhugh CD, Weitzel RP, et al. Nonmyeloablative HLA-matched sibling allogeneic hematopoietic stem cell transplantation for severe sickle cell disease. *JAMA*. doi:10.1001/jama.2014.7192

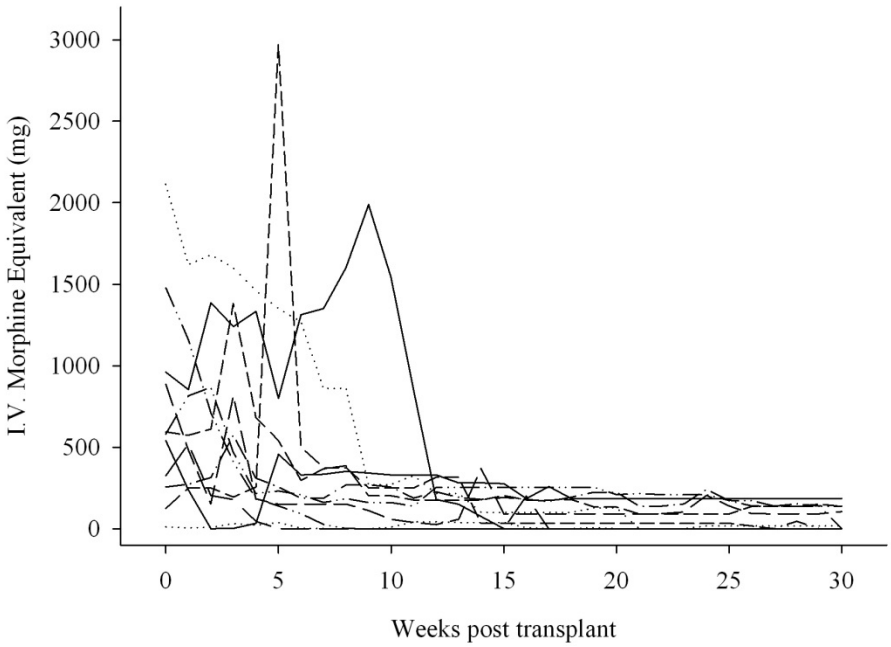
This supplementary material has been provided by the authors to give readers additional information about their work.

Supplemental Figure 1. Study Enrollment.



We are a transplant referral center and received many mail-in samples from within and outside the continental United States from patients and families who wanted to know their human leukocyte antigen (HLA) typing status. As a result, it was logistically easier to first perform the testing, then to request detailed medical information to determine eligibility when there is a match. HLA typing was performed in 287 patients and approximately 2 donors per patient, and 6/6 match was found in 102 patients. The medical care to prepare for transplantation included optimization of hydroxyurea, iron chelation, and treatment of concurrent co-morbidities (such as are proteinuria, renal insufficiency, avascular necrosis, or anticoagulation). During this optimization process, 19 patients were still in various stages of pre-transplant preparation, and could receive transplant when their health has been optimized. Four patients with secondary graft failure were not included in the engraftment analysis.

Supplemental Figure 2. Narcotic use post-transplant.



Mean intravenous morphine equivalent doses of narcotics per week of each patient (N=11) with respect to time after HSCT.

Supplemental Table 1A. Selected transplant parameters in patients with engraftment or with graft failure.

	Long term engraftment (N=26)	Graft failure (N=4)	
Median age (range)	28.5 years (17-65)	27.5 years (16-31)	P = 0.11*
Median CD34+ dose per kilogram of recipient body weight (range)	14.6 x 10^6 cells ($5.5 – 26.2 \times 10^6$)	13.2 x 10^6 cells ($10.3 – 31.7 \times 10^6$)	P = 0.80*
Median CD3+ dose per kilogram of recipient body weight (range)	3.5 x 10^8 cells ($1.6\text{-}9.4 \times 10^8$)	6.3 x 10^8 cells ($2.8\text{-}7.6 \times 10^8$)	P = 0.23*
Mean Pre-HSCT ferritin	1532 mcg/L (39-4666)	1621 mcg/L (152-3926)	P = 0.92^
Red cell alloimmunization (history of or presence of red cell antibody pre-HSCT)	6 of 26 patients	1 of 4 patients	P = 0.55#

*Wilcoxon rank test; ^ t-test; # Fisher's exact test.

Supplemental Table 1B. Percent of donor chimerism at early time points post-HSCT.

	Long term engraftment (N=26)			Graft failure (N=4)		
	1 month	2 month	3-4 month	1 month	2 month	3-4 month
Median % CD14/15 (range)	100 (67-100)	100 (90-100)	100 (80-100)	97 (67-100)	85 (0-99)	0 (N/A)
N	26	26	26	4	4	3
Standard error	1.21	3.42	6.24	45.1	33.6	0
95% CI	(94.7, 99.7)	(87.7,100)[a]	(71.0, 96.7)	(0, 100)[b]	(0, 100)[b]	N/A
Median % CD3 (range)	12.5 (0-91)	7 (0-55)	8 (0-33)	13 (0-27)	0 (0-2)	0 (N/A)
N	26	26	25	4	4	3
Standard error	24.7	16.8	9.95	7	0.25	0
95% CI	(0, 75.0)[c]	(0, 48.0)[c]	(0, 31.1)[c]	(0, 36.3)[c]	(0, 1.3)[c]	N/A

*N/A, not applicable; [a] upper bound is truncated to 100; [b] both upper and lower bound are truncated to 0 and 100, respectively; [c] lower bound is truncated to 0.

Supplemental Table 1C. Red cell alloimmunization, minor ABO incompatibility, and engraftment status.

Patient number	History of red cell antibodies	Minor ABO and Rh mismatch (recipient/donor)	Engraftment
7	Yes	No	Yes
9	Yes	No	Yes
13	Yes	No	Yes
17	Yes	No	Yes
20	Yes	No	Yes
28	Yes	Yes, (O+ / O-)	Yes
27	Yes	Yes, (B+ / O+)	No
6	No	Yes, (B+ / O+)	Yes
12	No	Yes, (A+ / A-)	Yes
16	No	Yes, (B+ / O+)	Yes
19	No	Yes, (B+ / O+)	Yes
25	No	Yes, (A+ / O+)	Yes

Supplemental Table 1D. Fetal hemoglobin (HbF) data among patients with graft failure.

Patient number	Age at HSCT	HbF, 1 month pre-HSCT	Pre-HSCT hydroxyurea	HbF, 6 month post-HSCT	HbF, 12 month post-HSCT	HbF, most recent	Post-HSCT hydroxyurea
4	16	24.6%	Yes	35%	26.8%	17.5% (6 years)	Yes
14	25	22%	Yes	18.5%	15%	22.8% (4 years)	Yes
15	31	10.8%	Yes	26.5%	24%	20.2% (4 years)	Yes
27	30	13%	Yes	6%	N/A	N/A	No

N/A, not available; most recent, at the most recent follow-up post-HSCT (median 4 years, range 4-6).

Supplemental Table 2. Summary of Serious Adverse Events (SAEs)

Type of serious adverse events (SAEs)	Number	Subtotal
Related to femoral catheter placement	3 (all in donors)	3
Death	Pre-transplant, cause: cardiac, 1 Post-transplant, cause: intracranial bleeding from previous moyamoya disease after relapse of sickle cell disease, 1	2
Other pain	Narcotic withdrawal, 2 Other arthralgia and/or myalgia, 5 Avascular necrosis, 1 Priapism, 1	9
Infection	C. difficile, 2 Babesia, 1 Skin abscess, 1 Malaria, 1 Pneumonia, 1	6
Abdominal pain	Gastric ulcer, 1 Pancreatitis, 1 Hernia, 1 Not specified, 3	6
Related to sirolimus	Arthralgia, 2 Pneumonitis, 2 Fever, 1	5
Transplant rejection	4	4
Others	Rhabdomyolysis, 1 Deep vein thrombosis, 2 Bleeding: hematuria, 1; compartment syndrome, 1 Hypotension, 1 Muscle weakness, 1	7
		42

As of October 25, 2013 (over 10 year accrual period), there were a total of 42 reported SAEs, which includes all hospitalizations. Three of them were from donors, and all were related to femoral catheter placement for stem cell collection. One SAE was a death from a recipient who died from cardiac arrhythmia prior to transplant. The remaining 38 SAEs were from 30 transplant recipients; 5 recipients had 21 SAEs combined. The details are summarized in the accompanying table.