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Non-myeloablative human leukocyte antigen-matched related donor transplantation in sickle cell disease: outcomes from three independent centres

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Summary

Non-myeloablative haematopoietic progenitor cell transplantation (HPCT) from matched related donors (MRD) has been increasingly utilized in sickle cell disease (SCD). A total of 122 patients received 300 cGy of total body irradiation (TBI), alemtuzumab, unmanipulated filgrastim-mobilized peripheral blood HPC and sirolimus. The median follow-up was four years; median age at HPCT was 29 years. Median neutrophil and platelet engraftment occurred on day 22 and 19 respectively; 41 patients required no platelet transfusions. Overall and sickle-free survival at one and five years were 93% and 85% respectively. Age, sex, pre-HPCT sickle complications, ferritin and infused HPC numbers were similar between graft failure and engrafted patients. Mean donor myeloid chimaerism at one and five years post HPCT were 84% and 88%, and CD3 was 48% and 53% respectively. Two patients developed grade 1 and 2 skin graft-versus-host disease (GVHD) with no chronic GVHD. Median days of recipients taking immunosuppression were 489; 83% of engrafted patients have discontinued immunosuppression. Haemoglobin, haemolytic parameters and hepatic iron levels improved post HPCT. Pulmonary function testing, hepatic histology and neurovascular imaging remained stable, suggesting cessation of further sickle-related injury.

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Author contributions

MA, MD, DR, JT, SS and MH designed this collaborative effort. MA, MD, BA, AS, SS and MH collected data. MA, NJ, SS and MH did the analyses and wrote the manuscript.

Conflicts of interest

SLS receives research funding from Pfizer, Novartis and Global Blood Therapeutics and serves on advisory committees for Novartis and GBT. The other authors have nothing to declare.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Fourteen patients had children. In this largest group of adult SCD patients, this regimen was highly efficacious, well-tolerated despite compromised organ functions pre HPCT, and without clinically significant GVHD.

Keywords

sickle cell disease; allogeneic transplantation; sirolimus; alemtuzumab; matched related donor

Introduction

Sickle cell disease (SCD) is an inherited red-cell disorder, characterized by life-long manifestations of acute and chronic complications, and leading to accumulation of organ injury and early mortality.¹ For many years, hydroxycarbamide was the only disease-modifying treatment,^{2,3} and recently L-glutamine,⁴ voxelotor,⁵ and crizanlizumab⁶ expanded this short list of sickle-specific treatments. The arrival of these new agents has generated much enthusiasm; however, whether they improve survival remains to be determined. Curative therapy by myeloablative conditioning haematopoietic progenitor cell transplant (HPCT) from human leukocyte antigen-matched related donors (HLA-MRD) was initially reported and later replicated in larger paediatric multi-centre studies with event-free survival as high as 98%.^{7–10} Many individuals with severe SCD do not have a MRD, and improvements in haploidentical HPCT^{11–13} and autologous gene therapy¹⁴ have broadened the donor options to make transplantation more accessible.

Adults with SCD are increasingly recognized to have organ injury in two or more organ systems in addition to the bone marrow.¹⁵ This pattern is distinctly different in children. Many children with prior sickle-related cerebral infarct can tolerate myeloablative doses of chemotherapy (such as busulfan or cyclophosphamide, with or without anti-thymocyte globulin), but the majority of adults with severe disease have compromised organ function and likely cannot. Their reduced function in various organs, including the lungs (moderate or severe obstructive and/or diffusion defect), liver (bilirubin >5 mg/dl with and without fibrosis), or kidneys (estimated glomerular filtration rate <60 ml/min/1.73 m²), puts them at risk for chemotherapy-induced toxicities. There were efforts to use different agents or lower doses, but higher rates of graft-*versus*-host disease (GVHD) or transplant-related mortality were observed.¹⁶ To address this critical need, we developed a non-myeloablative conditioning regimen for these individuals, with the goal of improving safety, achieving mixed chimaerism and tolerance induction.^{17,18} After expanding accrual, overall and disease-free survival were >95% and 87%, respectively, with a median follow-up of 3.4 years.¹⁹ Other transplant centres began adopting this low-intensity approach in both adult and paediatric SCD patients.^{20,21}

Here we report combined results from three independent centres, the National Heart, Lung and Blood Institute in Bethesda, Maryland (NHLBI), the University of Illinois at Chicago (UIC), and the King Abdulaziz Medical City in Riyadh, Saudi Arabia (KAMCR), employing the identical chemotherapy-free non-myeloablative conditioning regimen. These results

included a large proportion of adults with SCD, focusing on haematologic, cerebrovascular, pulmonary and hepatic outcomes as these organs are most frequently affected in SCD.

Methods

Patients were identified and enrolled to separate institutional/ethics review board-approved studies ([NCT00061568](#) NHLBI; [NCT01499888](#) UIC; RC16/135/R KAMCR) and gave informed consent. Patients met inclusion criteria if they had a sickle-related complication not ameliorated by hydroxycarbamide (e.g. frequent vaso-occlusive crisis, acute chest syndrome, or recurrent priapism) or an end-organ damage from SCD (stroke, renal insufficiency/proteinuria, hepatopathy,²² or tricuspid regurgitant jet velocity ≥ 2.5 m/s or avascular necrosis of multiple joints.^{23–25} Pre-conditioning use of hydroxycarbamide, red-cell exchange, and/or hypertransfusion was per institutional practice (see the Supporting information). Conditioning regimens included alemtuzumab (1 mg/kg divided over five days), 300 cGy of total body irradiation (TBI), sirolimus and infusion of unselected filgrastim-mobilized peripheral blood HPC (Figure S1).

Laboratory and testing results were collected pre HPCT and annually post HPCT as per institutional standard procedures.^{26–28} Patients who had at least one year of post-HPCT data as of September 30, 2019 were included for post-HPCT comparative analyses. Discontinuation of immunosuppression began at one year post HPCT and when CD3 chimaerism was $>50\%$.

Pre- and post-transplant data for forced expiratory volume in the first second (FEV1), diffusion capacity of carbon monoxide (DLCO) and ferritin were analyzed by regression models (Supporting information).

Results

Patient characteristics

A total of 122 patients received MRD HPCT from 2004 through 2019 (Table I, Tables SI and SII). Male patients comprised 59%. The median follow-up for the entire cohort was four years (range 0.6–15). Median overall age at HPCT was 29 years, and 48% were 30 years and older.

Engraftment and haematologic improvement

Median neutrophil and platelet engraftment occurred on day 22 (range 8–39) and 19 (6–42) respectively. Platelet transfusions was not required for 41 (34%) patients. Markers of hemolysis improved toward the normal range within the first month post HPCT (Table II). Total haemoglobin levels increased steadily through day 100 and plateaued between one and two years. An improvement in haemoglobin concentration was also observed in the subgroup of ABO-mismatched patients (pre HPCT: 97 g/l, one year post HPCT: 121 g/l, $n = 6$).

The primary end-point was engraftment rate at one year, which was 87%. GVHD/relapse-free survival (GRFS) was also 87%. Overall survival was 98% at one year post HPCT and

93% at five years (Table SII). Peak donor myeloid chimaerism was achieved by day 30 and sustained beyond day 100. Donor CD3 chimaerism increased gradually and plateaued between one and two years (Fig 1, Table II).

Graft failure

There were 16 patients (13%) who experienced graft failure (Fig 2), defined as complete loss of donor cells or restarting sickle-specific therapy. Thirteen occurred between month two and six post HPCT and three occurred as late as near or beyond one year. The proportion of patients with graft failure was: NHLBI 14%, UIC 13% and KAMCR 11%. Pre-HPCT age, sex, sickle complications, ferritin, CD34 or CD3 cell number and day of engraftment in these patients did not differ from those in engrafted patients, except that there was a trend for priapism ($P=0.11$) and nephropathy ($P=0.06$) history in those with graft failure. Two patients from UIC did not take their post-HPCT medications regularly. There were three patients with delayed autologous recovery (NHLBI-14 and 37, KAMCR-30; Supporting information).

Five patients underwent repeat transplantation: three at NHLBI (#2, 4, 37), one at UIC (#16) and one at KAMCR (#30) (Fig 2, Figure S2).

Graft-versus-host disease and immunosuppression

There were two patients with presumed skin GVHD occurring before day 100 (grade 1 and 2); in both the condition was resolved with topical corticosteroids. Median days of recipients taking immunosuppression was 489. Eighteen of 106 (17%) engrafted patients were still taking immunosuppression because their follow-up was relatively short (12%) or their donor CD3 chimaerism had not reached >50% (8.2%). Donor chimaerism remained stable after discontinuing immunosuppression.

Viral reactivation or infections

Although intermittent detection of cytomegalovirus (CMV) viral genome was common within the first 100 days post HPCT (e.g. 51% of the NHLBI and 90% of KAMCR cohorts), only 11 patients (9%) met criteria for treatment (Table III). Intermittent detection of Epstein-Barr virus (EBV) viral genome was common (e.g. 49% of the NHLBI and 25% of KAMCR cohort), but only one patient received pre-emptive treatment for rising EBV copies shortly after graft failure. That patient did not have any lymphadenopathy or symptoms. Several episodes of herpetic reactivation occurred within three years post HPCT (Table III). One patient displayed BK viruria; no patients had adenovirus or BK virus detected in the blood.

Pre-malignant or malignant conditions post HPCT

No solid tumours were identified in this combined cohort to date, although the follow-up for many patients was short. Two patients developed myelodysplastic syndromes (MDS). One (UIC-16) had a prior transplant using fludarabine and melphalan-based regimen from MRD at age 18, and had graft failure three months after the first HPCT. That patient underwent a second transplant using this regimen from the same donor 15 years later. Four months later, that patient experienced graft failure a second time and had autologous recovery.

MDS with complex cytogenetics developed 2.5 years later. The second patient (NHLBI-37) was 37 years old at the time of transplant, and also had graft failure four months post transplant. His autologous recovery took four months; then MDS with complex cytogenetics and TP53 mutation developed 2.5 years after graft failure. A third patient (NHLBI-46) developed chronic myelogenous leukaemia (CML) at 3.5 years post HPCT when he had an increasing leukocyte count with left shift, increasing percent sickle haemoglobin and declining donor myeloid chimaerism. His CD3 chimaerism was stable despite the drop in myeloid chimaerism, suggesting his CML was recipient in origin.

Deaths

There were seven deaths (5.7%) and five were among those with graft failure (Fig 2). Two died of sickle-related complications after relapse: intracranial bleeding from pre-existing moyamoya disease (NHLBI-27) and acute chest syndrome (UIC-15). One had marrow aplasia and died of sepsis before a planned second transplant (KAMCR-30). Two patients with MDS (NHLBI-37 and UIC-16) died of intracranial bleeding prior to donor cell engraftment during the re-transplant process. Among those with successful grafts, two experienced sudden death. One was 35 years old, was seven years post HPCT and healthy, and no specific cause of death was identified (NHLBI-16). The other was the oldest patient who developed pancytopenia four years post HPCT at age 69 (NHLBI-13). Diagnostic testing could not be completed prior to the sudden death.

Pulmonary function

Overall, FEV1 and forced vital capacity (FVC) were similar pre and through five years post HPCT ($P = 0.16$ from the regression model for the hypothesis of no difference in mean annual values post transplant relative to baseline; Table II and Fig 3). Prior to transplant, 53% of patients had FEV1 in the normal range (80% of predicted); 21% had mild (70–79%), 15% moderate (60–69%), 9% moderately severe (50–59%) and 2% severe reduction (<50%). Post HPCT, the proportion of individuals with moderate, moderately severe and severe defects decreased (Fig 3a, b). Pre transplant, carbon monoxide diffusion capacity (DLCO) was normal in <5% of the patients, nearly half had a mild diffusion defect (60–79% predicted), and the other half had a moderate defect (40–59%). DLCO also remained stable for up to five years post HPCT ($P = 0.36$; Table II). Six-minute walk test distances also improved in the first year post HPCT, and remained stable up to five years (data not shown).

Hepatic function

Ferritin, a surrogate marker of iron burden in the liver, was elevated prior to transplant (range 46–24 949). Approximately half had levels below <1 000 ng/ml, 42% were 1 000–5 000 and 4% were >5 000. The proportion of patients with ferritin <1 000 increased over time to 70%. The regression model hypothesis indicated a significant reduction after transplant ($P = 0.002$). Post-HPCT use of iron chelation and/or large-volume phlebotomy were used to reduce iron burden at the discretion of treating providers.

Brain imaging findings

All the patients had magnetic resonance imaging and angiography pre HPCT; the NHLBI cohort had post-HPCT imaging annually up to three years, then as clinically indicated. Pre HPCT, six patients had parenchymal small-vessel disease without motor or sensory sequelae, consistent with silent cerebral infarct; four patients had asymptomatic angiographic abnormalities that required no vascular intervention; and four patients had both types. Up to three years post HPCT, all patients had stable parenchymal and/or vascular abnormalities and they remained asymptomatic. One KAMCR patient had vasculopathy pre HPCT. She had intracranial bleeding two years post HPCT with no identifiable risk factors for bleeding. That patient has since recovered, is alive and without neurologic sequelae.

Fertility outcome

There were 21 pregnancies from seven men and seven women (NHLBI and KAMCR). One male patient received assisted reproductive medications for azoospermia which led to a healthy girl. He had two additional children without further assistance. The other pregnancies were uncomplicated and resulted in healthy live births except for three elective abortions.

Discussion

This report combines results from three independent centres and highlights several notable differences from previous myeloablative MRD HPCT outcomes by several groups.^{16,29} Our data comprise the largest group of older adult patients with SCD, with only 9% <18 years of age. Many of them have overlapping overt organ injuries: 26% had moderate or greater reduction in FEV1; half had a moderate defect in DLCO; 20% had total bilirubin levels between 5 and 10 (85–170) or >10 mg/dl (171 µmol/l); two were on haemodialysis; and two had liver cirrhosis. While older patients typically had more compromised organ function, there were also young adults with advanced organ damage: nine patients (7.4%) were <30 years old with pre-HPCT total bilirubin levels >5 mg/dl (85 µmol/l) and one of the two patients on haemodialysis was <30 years old. Yet all tolerated this low-intensity regimen well: one- and five-year overall survival was 98% and 93%; sickle-free survival was 88% and 85% respectively.

Generally, filgrastim-mobilized peripheral blood HPC from MRD has been avoided due to reported higher rates of acute and chronic GVHD.²⁹ However, alemtuzumab given at day -7 depleted T cells *in vivo* and was detectable for several weeks post infusion, and sirolimus dramatically reduced GVHD to 2% (acute only), which was limited in presentation and easily treatable with first-line therapy. No chronic GVHD occurred. Alemtuzumab also did not lead to higher rates of viral complications.

Importantly, all patients intentionally achieved mixed chimaerism. With the criteria for discontinuing immunosuppression at one year and >50% CD3 donor chimaerism, a median of 489 days taking immunosuppression was expected. This timing also corresponded with patients' chimaerism stabilizing between 18 and 24 months. At the latest visit, 83% had discontinued immunosuppression. There were no changes in chimaerism or new onset of

GVHD after ceasing immunosuppression.^{30,31} A recent report using this regimen in children showed successful outcome and all have stopped immunosuppression.²¹ In the NHLBI cohort 16 patients had near 10 years or longer follow-up, stable mixed chimaerism remained in all. A mixed lymphocyte reaction occurred in a subset of NHLBI patients from one month to two years post HPCT.³² There was higher proliferation, indicating more reactivity between host and recipient cells, during the first six months post HPCT than at later timepoints. These experimental data at early timepoints suggest that immunosuppression could be discontinued earlier than one year post HPCT.

The graft failure rate was 13% in our cohort, and no pretransplant factor was identified to correlate with graft failure, consistent with reports using myeloablative conditioning.³³ While there was a trend for priapism and sickle nephropathy, the significance is unclear. Since alemtuzumab was detectable one month post HPCT, those with graft failure had more robust autologous recovery beginning at month two. Unfortunately, two patients had MDS about three years after graft failure. Both had clinical risk factors for low stem-cell reserve and haematopoietic stress, favouring acquisition of pro-survival mutations. One patient had two HPCTs, and the other patient had a very slow autologous recovery after graft failure. This low frequency of pre-malignant and malignant conditions post transplant is consistent with the current literature.^{34–36}

Patients with SCD are known to have abnormal pulmonary function testing, with a restrictive defect more common than an obstructive or mixed one. Having lower FEV1 was previously shown to be associated with early mortality.³⁷ This pattern was observed in this combined cohort at the pre-HPCT timepoint. The stability of spirometry, diffusion capacity, and the six-minute walk test over five years post HPCT indicated that the radiation did not add to the pre-existing restrictive lung defects and there was no subclinical chronic GVHD. Our results were similar to those in a recent report which documented the stability of lung function after myeloablative transplant.³⁸ Our results also compared favourably to those of the Cooperative Study of Sickle Cell Disease, in which pulmonary function tests (PFTs) were performed in a large group of patients without transplantation. They showed that DLCO was inversely correlated with increasing age, equivalent to a decline of 1% per year.³⁹

There were 14 patients among the NHLBI cohort with abnormal cerebrovascular imaging pre HPCT, and no new parenchymal or vascular lesions were detected post HPCT. These findings are consistent with recent results showing transcranial Doppler velocity improved more significantly after myeloablative HPCT than with continuation of chronic red-cell exchange.⁴⁰ These stable neuro-imaging results suggest our non-myeloablative HPCT has halted further sickle-related neuro-injury. Furthermore, it is also important to highlight the subclinical vasculopathy in these patients. Three of the seven deaths were due to intracranial haemorrhage. One patient had relapsed SCD with moyamoya and a normal platelet count; the other two were undergoing repeat HPCT, and bleeding occurred before platelet recovery despite attempts to keep platelet counts >50 k/μl. This higher haemorrhagic propensity was initially recognized in the multi-centre transplant study using myeloablative HPCT in children, which changed the platelet transfusion threshold from 20 k/μl to 50 k/μl whenever feasible.⁹

There are several limitations in these analyses. Since each centre accrued to individual protocols with varied funding sources or insurance coverage, there were differences in the post-transplant testing. Furthermore, the leukocyte chimaerism were not performed in a central laboratory, thus these results could vary across the transplant centres. Also, pulmonary function testing was performed per institutional practice and normalized to standards determined by each department. Minor variations in the percentage of predicted values were likely present as well.

In summary, alemtuzumab, low-dose TBI and sirolimus were applied to the largest group of adult patients with SCD; half of them were older than 30 years old. The overall results were equally efficacious across centres, safe in those with compromised organ functions, and with no clinically significant GVHD. Additional studies are under way to improve the long-term engraftment rate and to ascertain if immunosuppression can be discontinued earlier or in those with CD3 chimaerism <50%.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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<i>n</i>	96	89	74	46	30	24
Cumulative % off IS	1	36	68	75	79	83

Fig 1.

Donor white cell chimaerism. Percent donor T cells (CD3) and myeloid cells (CD14/15), means $\pm$ standard errors, are shown with timepoints after haematopoietic progenitor cell transplant (HPCT). Number of patients and cumulative percent who have discontinued immunosuppression (IS) are shown in the accompanying table.

Fig 2.
Transplant outcome after haematopoietic progenitor cell transplant (HPCT).

Fig 3.

Pre- and post-haematopoietic progenitor cell transplant (HPCT) pulmonary function testing. Forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC) are shown as percent of predicted values in healthy controls. Normal is 80% of predicted; mild reduction, 70–79%; moderate, 60–69%; moderately severe, 50–59%; and severe, <50%. [Colour figure can be viewed at wileyonlinelibrary.com]

Table I.Patient demographic and clinical characteristics ($n = 122$).

Characteristic	<i>n</i> (% or range)
Sickle subtypes	
HbSS	101 (83%)
HbSC	5 (4%)
HbS/ β -thalassaemia ⁺	1 (1%)
HbS/ β -thalassaemia ⁰	15 (12%)
Median age in years (range)	29 (10–65)
30 years or older	59 (48%)
40 years or older	21 (17%)
Sex	72 (59%) male, 50 (41%) female
Median follow-up duration in years	
NHLBI (2004–2019, $n = 57$)	6.9 (0.6–14.9)
UIC (2011–2019, $n = 30$)	4.1 (0.6–7.9)
KAMC-R (2016–2019, $n = 35$)	2.5 (1.5–4.8)
Pre-transplant sickle-related complications	
Vaso-occlusive crisis (2 or more hospital admissions or IV infusion clinic visits per year)	107 (88%)
Acute chest syndrome (at least one hospital admission per year)	43 (35%)
Sickle-related hepatopathy, with or without iron overload (direct bilirubin >0.4 mg/dl [6.84 μ mol/l] or ferritin >1000 mcg/l)	41 (34%) total bilirubin 5–10 mg/dl or 85–170 μ mol/l: 19 (16%); >10 mg/dl or 171 μ mol/l: 5 (4.1%)
Avascular necrosis (2 or more joints)	38 (31%)
Tricuspid regurgitant jet velocity ≥ 2.5 m/s (Bethesda and Chicago cohorts only)	25 of 87 (29%)
Presence of red cell auto- or alloantibodies	31 (25%)
Priapism (2 or more episodes requiring injection medication or medical care per year)	17 of 72 (24%)
Stroke (includes overt and silent)	26 (21%)
Cerebrovasculopathy (identified on brain imaging)	18 (15%)
Sickle related nephropathy (biopsy proven, presence of proteinuria, or estimated GFR <60 ml/min)	8 (7%, including 6 patients with eGFR <60 ml/min, 2 of which on hemodialysis)
Pre-transplant therapy	
Hydroxyurea (Hydroxycarbamide)	111 (91%)
Folic acid	114 (93%)
Red cell transfusions	
Periodic	63 (52%)
Regular exchange programs	20 (16%)
Narcotics	
Short acting	107 (88%)
Long acting or scheduled	28 (23%)
Iron chelation	23 (19%)
Prior haematopoietic cell transplant	2 (1.6%)
Additional recipient-donor testing	
Median donor cell dose	

Characteristic	<i>n</i> (% or range)
CD34+	12·3 9 10 ⁶ /kg (range 4·1–41·2)
CD3+	2·56 9 10 ⁸ /kg (0·36–9·37)
ABO blood type compatibility	
Matched	94 (77%)
Minor or Rh mismatch	23 (19%)
Major mismatch	5 (4%)
Cytomegalovirus IgG status (recipient/donor)	
Positive/positive	85 (70%)
Positive/negative	10 (8%)
Negative/positive	10 (8%)
Negative/negative	17 (14%)
Proportion of donors with	
Sickle trait (HbAS)	67 (55%)
Haemoglobin C trait (HbAC)	2 (1·6%)

HbS, sickle haemoglobin; NHLBI, National Heart, Lung and Blood Institute in Bethesda, Maryland (NHLBI); UIC, University of Illinois at Chicago (UIC); KAMC-R, King Abdulaziz Medical City in Riyadh, Saudi Arabia.

Table II.

Transplant outcomes.

	Pre-HPCT	1 year post	2 year post	3 year post	4 year post	5 year post
Haemoglobin (g/l)						
Male	95 ± 2 (n = 69)	135 ± 3 (n = 68)	143 ± 3 (n = 56)	138 ± 4 (n = 36)	141 ± 5 (n = 18)	140 ± 5 (n = 15)
Female	88 ± 2 (n = 48)	121 ± 3 (n = 44)	126 ± 3 (n = 33)	124 ± 3 (n = 23)	126 ± 4 (n = 15)	125 ± 4 (n = 11)
Reticulocyte count (k/μl)	241 ± 12.5 (n = 113)	108 ± 6.5 (n = 97)	105 ± 8.5 (n = 76)	92.6 ± 9.1 (n = 55)	101 ± 13.5 (n = 33)	101 ± 11.7 (n = 26)
Total bilirubin (mg/dl)	2.9 ± 0.2 (n = 116)	0.7 ± 0.1 (n = 111)	0.9 ± 0.1 (n = 89)	0.7 ± 0.1 (n = 60)	0.6 ± 0.1 (n = 34)	0.7 ± 0.2 (n = 25)
Lactate dehydrogenase (units/l)	357 ± 14 (n = 114)	220 ± 7.6 (n = 99)	200 ± 7.3 (n = 88)	209 ± 12 (n = 54)	186 ± 9 (n = 30)	190 ± 14 (n = 25)
FEV1 (% predicted)	82.0 ± 1.6 (n = 117)	81.2 ± 1.5 (n = 89)	82.6 ± 1.7 (n = 64)	80.5 ± 2.2 (n = 37)	79.2 ± 2.3 (n = 30)	81.4 ± 2.1 (n = 24)
DLCO (ml/mm Hg/min)	17.7 ± 0.68 (n = 98)	18.8 ± 0.72 (n = 78)	23.0 ± 1.55 (n = 57)	23.7 ± 2.72 (n = 36)	20.4 ± 1.02 (n = 30)	20.1 ± 1.02 (n = 24)
Ferritin (ng/l)	1634 ± 345 (n = 78)	1122 ± 164 (n = 83)	935 ± 172 (n = 65)	834 ± 172 (n = 37)	1196 ± 239 (n = 24)	893 ± 214 (n = 24)

Mean ± standard errors are shown. HPCT, haematopoietic progenitor cell transplant; FEV1, forced expiratory volume in the first second; DLCO, diffusion capacity of carbon monoxide.

Table III.

Viral reactivations post-transplant.

Type	n (%)
CMV reactivation requiring treatment	11 (9%)
CMV IgG status (recipient/donor)	Positive/positive 8 Positive/negative 3
EBV reactivation requiring treatment	1 (1%)
HSV infection or reactivation	2 (1.6%)
VZV reactivation	12 (9.8%)
BK viruria	1 (1%)

CMV, cytomegalovirus; EBV, Epstein–Barr virus; HSV, herpes simplex virus; VZV, varicella zoster virus.