HLA-haploidentical hematopoietic stem cell transplantation in patients with sickle cell disease: results from the phase II DREP-HAPLO trial

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Abstract

We report the final analysis of the DREP-HAPLO multicenter phase II protocol, which evaluated haploidentical transplantation after a reduced-intensity conditioning regimen incorporating thiotepa, in children and adults with severe sickle cell disease (SCD). Twenty-two patients (median age, 17 years; range, 12-40) received a conditioning regimen consisting of 2 Gy total body irradiation, thymoglobulin, cyclophosphamide, fludarabine, and thiotepa, followed by T-cell–replete bone marrow infusion and graft-*versus*-host disease (GvHD) prophylaxis based on post-transplant cyclophosphamide. The primary endpoint, event-free survival, defined as survival without graft failure and without moderate-to-severe chronic GvHD, was 68.18% (95% confidence interval [95% CI]: 51.25%-90.70%) and 61.98% (95% CI: 44.07%-87.19%) at 1 and 4 years, respectively. Overall survival and rejection-free survival at 4 years were 90.15% (95% CI: 78.03%-100%) and 85.56% (95% CI: 71.63%-100%), respectively. Six patients (27%) developed moderate-to-severe GVHD. In most cases (4/6) GvHD resolved, leaving only two patients (9%) with persistent moderate-to-severe GvHD at their last follow-up. Eighty-five grade 2 to 4 infectious episodes were reported in 21 patients during the 24 months of follow-up, most of which were bacterial (38 cases). These data strengthen existing evidence supporting the feasibility of haploidentical transplantation in both pediatric and adult patients with severe SCD, demonstrating a very low rejection rate when thiotepa is incorporated into the conditioning regimen. Future efforts should focus on reducing chronic GvHD and infection rates.

Introduction

Sickle cell disease (SCD) is a severe inherited hemoglobinopathy associated with hemolytic anemia, recurrent vaso-occlusive episodes, and cumulative end-organ damage, leading to significantly impaired quality of life and premature mortality. To date, allogeneic hematopoietic stem cell transplantation (HSCT) remains the only established curative treatment for SCD. In children, myeloablative HSCT from an HLA-identical sibling donor offers an excellent rate of survival without disease.[1,2] In adult patients, non-myeloablative conditioning regimens have been developed to reduce toxicity while preserving curative potential.[3,4] Nonetheless, a major barrier to the widespread application of HSCT in SCD remains the limited availability of HLA-identical sibling donors.

Haploidentical transplantation has emerged as a compelling alternative, substantially expanding donor availability. Initial reduced intensity conditioning haploidentical transplant platforms using fludarabine, cyclophosphamide, thymoglobulin and 2 Gray total body irradiation with graft-*versus*-host disease (GvHD) prophylaxis based on post-transplant cyclophosphamide demonstrated favorable safety profiles, with low incidences of GvHD but rates of graft failure, approaching 50%.[5] To address this limitation, several modifications to the original post-transplant cyclophosphamide-based regimen have been investigated.[6-9] The approach of intensifying conditioning with thiotepa has been the most widely used.[10,11] We hereby report the final analysis of DREP-HAPLO a French multicenter phase II protocol, including both children and adults, which employs an approach of reduced intensity conditioning haploidentical transplantation with conditioning intensification with thiotepa.

Methods

Study design and participants

DREP-HAPLO is a prospective, multicenter phase II clinical trial (ClinicalTrials.gov: NCT03240731) designed to evaluate the efficacy and safety of haploidentical HSCT in patients with severe SCD. The trial was sponsored by the Centre Hospitalier Intercommunal de Créteil (France) and was approved by its institutional review board (N. ID-RCB: 2016-A00300-51). Eligibility criteria were patients aged from 7 to 40 years old with SCD (HbSS) or Sβ^0-thalassemia, with no available HLA-identical sibling donor. Patients were required to have at least one severe SCD-related complication, detailed in the *Online Supplementary Methods*. All collected data have been reviewed by the sponsor. During the course of the study, an independent Data Safety Monitoring Board met regularly to validate the continuation of the study and to analyze serious adverse events. All patients and donors gave informed consent.

Transplant modalities

Pre-transplant recipient management is detailed in the *Online Supplementary Methods*. Conditioning included thymoglobulin 4.5 mg/kg, thiotepa 10 mg/kg, cyclophosphamide 29 mg/kg, fludarabine 150 mg/m^2 and 200 cGy total body irradiation with testis shielding in males. GvHD prophylaxis included post-transplant cyclophosphamide (50 mg/kg on days +3 and +4), mycophenolate mofetil (day +5 through day +35); and sirolimus targeting (day +5 through day +365) after transplantation.[7] The source of stem cells was bone marrow in all recipients (*Online Supplementary Figure S1*).

Outcomes and definitions

The primary endpoint was 12-month event-free survival, defined as survival without rejection and without moderate-to-severe chronic GvHD. Secondary outcomes included overall survival, engraftment rates, graft rejection, rejection-free survival defined by survival without rejection, GvHD, infections, hemolysis markers, and chimerism. In accordance with the protocol, each participant had a 24-month follow-up, and the main outcome was also updated in October 2024. Graft failure was defined as donor total peripheral blood cell chimerism below 5%, low mixed chimerism was defined as 5%-50% donor blood cells, high mixed chimerism as 50%-95% donor blood cells and full donor chimerism as donor blood cells above 95%. The severity of adverse events, including infections, was recorded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Quality of life was assessed using the French version of the Pediatric Quality of Life Inventory Generic Core Scales, version 4.0 (PedsQL 4.0) self-report for patients under 18 years of age, and the EORTC QLQ-C30, version 3.0 self-report for patients aged 18 years and older. Scores were transformed to a 0–100 scale, with higher scores indicating better quality of life.[12,13]

Statistical analysis

Categorical variables were summarized as counts and percentages, and continuous variables as medians with interquartile ranges (IQR). Event-free survival, overall survival and survival without rejection were estimated using the Kaplan-Meier method. All statistical analyses were conducted using R software, version 4.4.3.

Protocol evolution

The original use of granulocyte colony-stimulating factor (G-CSF)–mobilized bone marrow was discontinued due to concerns about increased GvHD risk (2 of the 3 patients who received a G-CSF-primed bone marrow graft developed chronic GvHD). The protocol was planned to include 15 patients but the duration of inclusion was extended. Initial eligibility criteria included patients aged 13 years and older; this was subsequently revised to allow the inclusion of children aged 7 years and above.

Results

Study population

A total of 25 patients were enrolled across five French centers between September 2017 and April 2022. Three patients did not proceed to transplantation: one was considered a screening failure because he presented with cerebrovascular vasculopathy but had not initiated a transfusion program; one whose donor withdrew consent after enrollment; and one with a history of delayed hemolytic transfusion reaction contraindicating further transfusions. This resulted in 22 patients who proceeded to transplantation per protocol. The median age at transplantation was 17 years (IQR: 16–19; range, 12–40), 13 patients were under

18 years old at the time of their transplant and nine were over 18 years of age. Sixty-eight percent were females. SCD genotypes included HbSS (95%) and HbSβ⁰ (5%). Prior to transplantation, 86% had recurrent vaso-occlusive crises, 50% had experienced at least one acute chest syndrome and 50% had cerebral arterial stenosis. Delayed hemolytic transfusion reactions were reported in 14% of patients. Hydroxyurea had been administered to 77% of patients, and 73% of patients were on chronic red blood cell transfusions (9 by simple transfusions, 5 by erythrocytapheresis, and 2 who had received both modalities). Among these 16 patients, three had normal ferritin levels and did not undergo liver magnetic resonance imaging. Among the remaining 13, liver iron concentration was normal (<2 mg of iron per gram of liver tissue) in two patients, between 2 and 7 mg in eight patients, and between 7 and 10 mg in the remaining three patients. Patients experienced a median of five (IQR: 1–12) hospitalizations during the 3 years preceding transplantation. Most donors (N=19; 86%) were heterozygous for HbS (HbAS). The patients' characteristics are summarized in Table 1.

Outcomes

The primary endpoint, 1-year event-free survival, defined as survival without graft failure and without moderate-to-severe chronic GvHD was 68.18% (95% confidence interval [95% CI]: 51.25-90.70%). With a median follow-up of 4.25 years (IQR: 3.25–5.16 years), the 4-year event-free survival was 61.98% (95% CI: 44.07-87.19%). OS at 1 and 4 years were 95.45% (95% CI: 87.14-100%) and 90.15% (95% CI: 78.03-100%), respectively. Rejection-free survival rates at 1 and 4 years were 90.90% (95% CI: 79.66-100%) and 85.56% (95% CI: 71.63-100%), respectively (Figure 1). All patients achieved engraftment, but one patient (4.5%) aged 17 years at transplant, who received 2.67x10⁶ CD34⁺ cells/kg, experienced secondary graft failure, occurring at 4.5 months after the transplant in the context of severe acute respiratory syndrome coronavirus-2 infection. Two patients (9%) died: one, aged 19.7 years, from chronic GvHD (8 months after transplant) and the other, aged 16 years, from a late fulminant pneumococcal sepsis (31 months after transplant).

Hematopoietic recovery

The median time to neutrophil recovery was 21 days (IQR: 19–25). The median times from transplantation to the last red blood cell and platelet transfusions were 27 days (IQR: 19–35) and 24 days (IQR: 17–31), respectively. Median CD4⁺ T-cell counts were 0.4×10⁹/L at 3 months (IQR: 0.1–0.7) and 0.6×10⁹/L at 12 months (IQR: 0.4–1.0).

Graft-*versus*-host disease

Acute GvHD occurred in nine patients (40.9%): it was grade II in six (27.2%), grade III in two (9%), and grade IV in one (4.5%). Chronic GvHD was observed in eight patients (36%): it was mild in two (9%), moderate in three (13.5%), and severe in three (13.5%). The 2-year incidence of moderate-to-severe chronic GvHD was 27%. Two of the

Table 1. Patients' characteristics.

Characteristics	Values
N of patients	22
Age at transplant, years, median (range) [IQR]	17 (12-40) [16-19]
Female sex, N (%)	15 (68)
Sickle subtypes, N (%)	
HbSS	21 (95.5)
HbSβ⁰	1 (4.5)
Pre-transplant sickle-related complications, N (%)	
Recurrent vaso-occlusive crises	19 (86.3)
Acute chest syndrome	11 (50)
CNS disease	
Overt stroke	5 (22.7)
Arterial stenosis	11 (50)
Silent infarct	1 (4.5)
History of abnormal TCD	3 (13.5)
Moyamoya	4 (18.1)
Avascular necrosis	3 (13.5)
Sickle-related nephropathy	2 (9)
Presence of micro/macroalbuminuria	2 (9)
GFR <60 mL/min/1.73 m²	0
Tricuspid regurgitation velocity >2.5 m/s	0
Hospitalization	
Total N of hospitalizations during the last 3 years, median [IQR]	5 [1-12]
Prior treatment, N (%)	
Hydroxyurea	17 (77)
Regular exchange programs (>1 year)	16 (73)
Treatment-related complications, N (%)	
History of DHTR	3 (14)
Iron overload: ferritin >1,000 mg/L	10 (46)
Female donor to male recipient, N (%)	7 (32)
ABO recipient-donor type compatibility, N (%)	
Matched	10 (46)
Minor incompatibility	6 (27)
Major incompatibility	6 (27)
CMV serology: recipient/donor, N (%)	
Positive/positive	18 (82)
Positive/negative	2 (9)
Negative/positive	1 (4.5)
Negative/negative	1 (4.5)
Recipient positive EBV serology, N (%)	22 (100)
Donor hemoglobin phenotype, N (%)	
Hemoglobin AS	19 (86)
Hemoglobin AA	3 (14)
Sorror score, median [IQR]	1 [0-2]
G-CSF-primed bone marrow, N (%)	3 (14)
CD34⁺ cell dose infused, 10⁶/kg recipient, median (range)	2.67 (1.6-6.8)

IQR: interquartile range; CNS: central nervous system; TCD: transcranial Doppler ultrasonography; GFR: glomerular filtration rate; DHTR: delayed hemolytic transfusion reaction; CMV: cytomegalovirus; EBV: Epstein-Barr virus; G-CSF: granulocyte-colony stimulating factor.

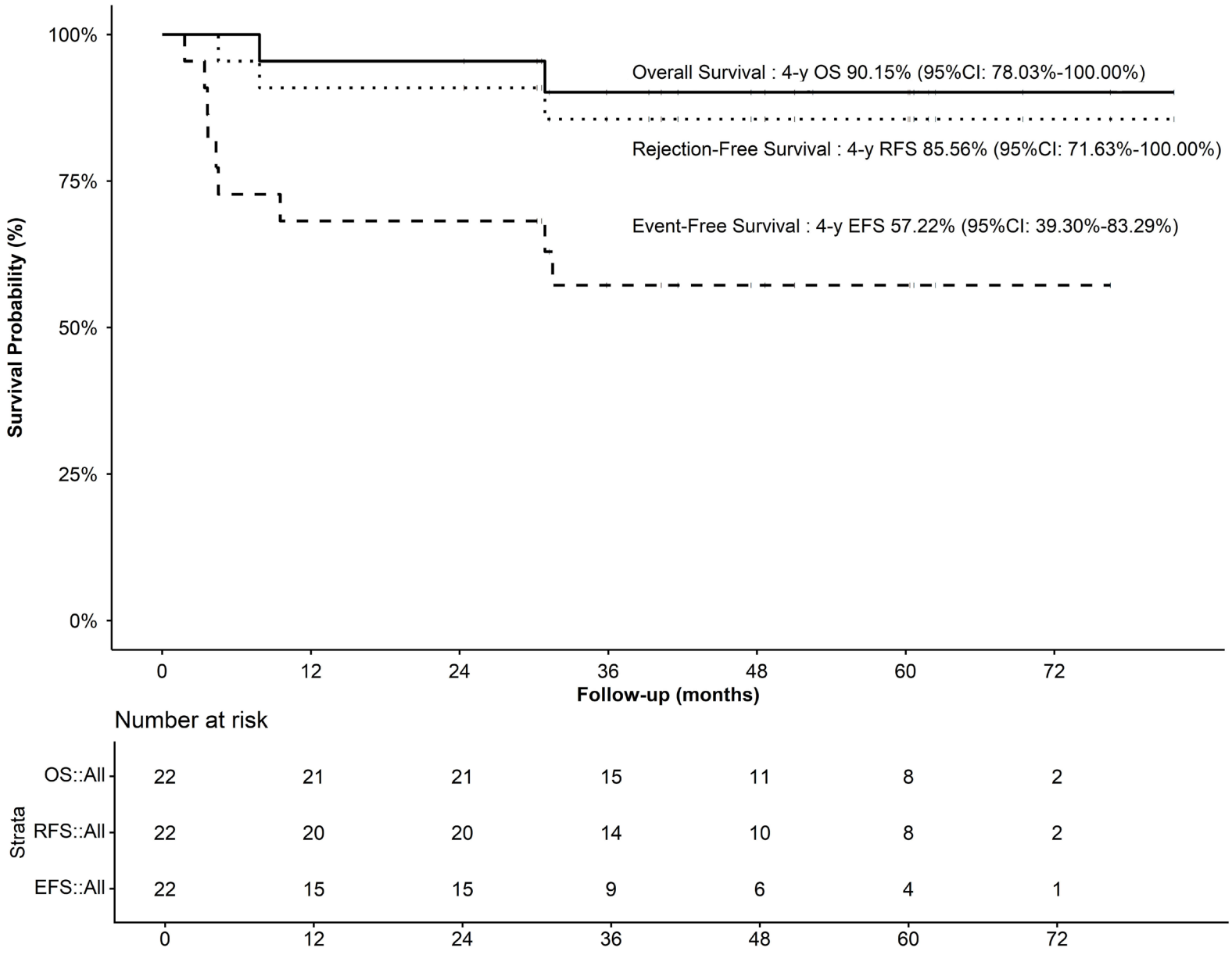

Figure 1. Post-transplant outcomes. Event-free survival was defined by survival without rejection and without moderate-to-severe chronic graft-*versus*-host disease. OS: overall survival; RFS: rejection-free survival; EFS: event-free survival; y: years; 95%CI: 95% confidence interval.

three patients who received G-CSF-primed bone marrow experienced chronic GvHD (moderate, N=1; severe, N=1). At the last follow-up, moderate-to-severe chronic GvHD was present in 9% of patients after resolution in four of the six initially affected cases. Only one patient continued to require systemic immunosuppressive therapy.

Infections

A total of 85 infectious episodes were reported in 21 patients within the first 24 months after transplantation: 51 were grade 2, 32 grade 3 and two were grade 4 according to the CTCAE version 5.0. Patients with grade II-IV acute GvHD or moderate-to-severe chronic GvHD presented a median of four (range, 0-7) infectious episodes *versus* three (range, 1-9) in patients without GvHD. The most common infections were bacterial (38 cases), mostly bloodstream infections or severe sepsis (29 cases). Among these, six episodes were caused by *Pseudomonas aeruginosa* and six by *Staphylococcus aureus*. In eight patients, the infection was linked to the central venous catheter. Two non-splenectomized patients experienced *Streptococcus pneumoniae* infections: one developed pneumonia and another, whose infection occurred after 24 months and was therefore not included in the main count, died from fulminant pneumococcal sepsis. This patient had discontinued pneumococcal prophylactic antibiotics and had received revaccination after transplantation; however, the sepsis was caused by pneumococcal serotype 24F, which was not covered by the vaccine. Four patients experienced BK virus-associated cystitis. Most infections occurred early after transplant with only 17.6% after day 100. No cases of cytomegalovirus disease or post-transplant lymphoproliferative disorder were observed. Infectious episodes are detailed in *Online Supplementary Table S1*.

Other post-transplant complications

Three patients (13.5%) developed posterior reversible encephalopathy syndrome, concomitant with corticosteroid therapy used for the management of GvHD or for treatment of macrophage activation syndrome. Macrophage activation syndrome occurred in two patients (9%), one of whom presented with disseminated human herpesvirus-6 infection.

No new SCD-related complications were reported after transplant. Although follow-up remains relatively short, no cases of myeloid malignancy have been identified to date.

Follow-up biological data

In the absence of rejection, hemoglobin levels rapidly normalized after transplant, and hemolytic markers were corrected by 3 months. A key biological marker of cure was the HbS level, which mirrored the donors' phenotype: 0% in the recipient of grafts from AA donors and <40% in those with AS donors. Among the 21 patients who did not reject their grafts, complete donor chimerism was observed in 19 patients at 2 years after the transplant and at the last follow-up (median, 34 months; IQR: 27-51). The remaining two patients exhibited mixed chimerism, 75% and 45%, respectively, at 24 months and 47% and 36%, respectively, at the last follow-up (57 and 52 months after transplant). Importantly, despite mixed chimerism, hemolytic markers remained normal, and HbS levels were similar to those of the donor (37.2% and 38.3% for an AS donor). (Table 2).

Quality-of-life reports

Self-reports were obtained prior to transplant from nine of the 14 patients younger than 18 years and from all eight adult patients. Data from one adult who died 8 months after transplant were not evaluable at 12 and 24 months. Two participants who turned 18 during follow-up initially completed the pediatric self-report and subsequently switched to the adult version. The analysis showed an improvement in total scores after transplant, with more pronounced gains in adolescent self-reports than in those of adults. Interestingly, pre-transplant physical scores were lower in adolescents than in adults, with substantial improvement observed in adolescents after transplant. In both groups, emotional scores improved after transplant. Fatigue remained a long-lasting symptom after transplant in adults. Pain scores showed only slight improvement, but most patients had been enrolled in a chronic transfusion exchange program prior to transplantation and, therefore, may have had relatively few pain crises at baseline (Table 3).

Discussion

This is the third multicenter phase II trial evaluating reduced-intensity haploidentical transplantation incorporating thiotepa in patients with severe SCD. The first study was an international collaborative consortium including both pediatric and adult patients across eight centers, totalizing 70 transplants with varying eligibility criteria.[10] The second was a prospective multicenter United States (US) study involving 42 patients over 15 years of age with severe SCD-related complications, such as cerebral vasculopathy, recurrent vaso-occlusive crises and acute chest syndrome.[11] As in previous studies, our findings confirm that adding thiotepa is critical for engraftment. The graft failure rate was notably low, with only one secondary graft failure (4.5%). While the consortium study observed a 25% rejection rate in patients under 18 years of age compared to 0% in adults, this was not confirmed in our cohort: among 13 patients under 18 years old at transplant and nine adults, a single rejection was observed in a 17-year-old patient. In the international consortium study, six of the eight patients who experienced graft rejection also had viral infections, supporting the hypothesis that infections may have contributed to rejection.[10] In the absence of rejection, 18 of 20 patients

Table 2. Biological evolution.

Parameters	Month 3	Month 12	Month 24
Patients evaluable, N	22	21	21
Hemoglobin, g/dL, median (IQR)	11 (10-12)	12.5 (10.7-13)	12.7 (11.2-14.4)
Reticulocyte count, g/L, median (IQR)	50 (37-74)	78 (62-110)	78 (58-104)
Total bilirubin, median (IQR)	3.75 (3-6.45)	5.3 (4-9)	7 (5-10)
LDH (IU/mL), median (IQR)	338 (276-392)	327 (233-434)	200 (170-250)
Haptoglobin (g/L), median (IQR)	1.19 (0.41-1.9)	0.85 (0.56-1.45)	0.47 (0.1-1)
Hemoglobin S, %, median (IQR) In AS donors, N=18 In AA donors, N=3	 28 (27-31) 0	 38 (32-38) 0	 39 (34-40) 0
Donor chimerism, % ≥95% 50-95% 20-50% 5-20% <5%	 100 0 0 0 0	 85.9 9.4 0 0 4.7	 85.9 4.7 4.7 0 4.7

IQR: interquartile range; LDH: lactate dehydrogenase.

Table 3. Quality of life.

In adolescents (N=14 at transplant) according to the PedsQL 4.0 self-report	**Physical score**	**Emotional score**	**Social score**	**School score**	**-**	**Total score**
Pre-transplant: N=9 (64%) Median (IQR)	48.44 (43.75-56.25)	65 (60-70)	72.5 (63.75-85)	52.5 (36.25-57.92)	-	55.98 (48.8-62.8)
M3: N=10 (71%) Median (IQR)	59.38 (56.25-84.38)	75 (55-93.75)	80 (65-100)	55 (40-75)	-	66.30 (48.9-85.9)
M6: N=10 (71%) Median (IQR)	62.50 (59.38-84.38)	60 (50-75)	85 (70-100)	62.50 (43.7-76.25)	-	66.30 (51.1-81.2)
M12: N=6 (43%) Median (IQR)	71.88 (62.50-78.12)	65 (55-85)	90 (90-95)	55 (55-56.25)	-	65.22 (64.1-77.2)
M24: N=3 (21%) Median (IQR)	90.62 (85.94-95.31)	90 (85-95)	95 (92.50-97.50)	72.5 (63.75-81.25)	-	87.5 (82.3-92.6)
In adults (N=8 at transplant) according to the EORTC QLQ-C30 self-report	**Physical score**	**Emotional score**	**Social score**	**Fatigue**	**Pain**	**Total score**
Pre-transplant: N=8 (100%) Median (IQR)	88.9 (77.7-91.6)	66.7 (58.3-91.7)	100 (66.7-100)	66.7 (47.2-77.8)	58.3 (29.7-83.3)	58.3 (54.2-66.7)
M3: N=6 (75%) Median (IQR)	83.3 (69.4-97.2)	58.3 (50.0-79.1)	100 (87.5-100)	38.9 (33.3-52.8)	50.0 (12.5-62.5)	62.5 (52.1-79.2)
M6: N=8 (100%) Median (IQR)	88.9 (77.8-88.9)	83.3 (66.7-83.3)	83.3 (83.3-100)	66.7 (55.5-66.7)	66.7 (66.7-83.3)	66.7 (64.6-77.1)
M12: N=9 (100%) Median (IQR)	94.4 (80.5-100)	83.3 (70.8-95.8)	66.7 (54.2-91.7)	61.1 (36.1-86.1)	66.7 (54.2-79.2)	66.7 (54.2-79.2)
M24: N=9 (100%) Median (IQR)	94.4 (88.9-100)	100 (87.5-100)	83.3 (70.8-83.3)	66.7 (50-75)	66.7 (54.2-79.2)	70.8 (54.2-81.2)

One adult who died 8 months after transplant was not evaluable at 12 and 24 months. Two adolescents who turned 18 during follow-up initially completed the pediatric self-report and subsequently switched to the adult version. IQR: interquartile range; M: months after transplant.

achieved sustained full donor chimerism at 2 years and last follow-up, with normalization of hemolysis and HbS levels matching those of the donor, suggesting disease cure. Notably, in the two patients with mixed chimerism, levels of 47% and 36% donor chimerism more than 4 years after transplant were sufficient to achieve complete resolution of hemolysis and to maintain HbS levels similar to those of their donors. Although longer follow-up is needed, there is hope that these patients are cured. Additionally, the high rate of full donor chimerism with this regimen suggests a low risk of malignant transformation.

Toxicity management remains a key challenge, particularly regarding transplant-related mortality and chronic GvHD. Our cohort showed a higher incidence of moderate-to-severe chronic GvHD than previously reported. No age-related correlation was identified (*data not shown*), but two out of three patients (66%) who received G-CSF–primed bone marrow developed moderate-to-severe chronic GvHD, compared to four of 19 (21%) among those receiving non-primed marrow. While most chronic GvHD cases resolved, one patient remained on systemic immunosuppression at last follow-up. These findings highlight the need for larger studies to assess chronic GvHD incidence in patients receiving non–G-CSF–primed marrow. If it is confirmed that the incidence of chronic GvHD remains significant, GvHD prophylaxis could be optimized through strategies such as increasing the antithymocyte globulin dose, which has been shown to reduce chronic GvHD incidence in children with SCD undergoing matched sibling transplantation, or adding abatacept, as explored in unrelated donor settings.[1,14]

The 4-year mortality rate of 9.8% observed in our study is considered acceptable given the underlying severity of disease in this cohort. This mortality rate must be weighed against the high cure rate achieved with HSCT. One pa-

tient died from pneumococcal sepsis. This patient was not splenectomized (*versus* 3 others); however, functional asplenia, nearly universal in adolescents and adults with SCD, complicates interpretation of infection-related mortality, as these patients are intrinsically at increased risk of severe pneumococcal infections regardless of transplant status. The incidence of infections was high, mainly due to bacterial infections, particularly bloodstream infections. Seven cases were clearly catheter-related, often in patients with poor venous access requiring prolonged central lines. More cases were likely underreported. Viral infections were mostly those expected after allografting, with frequent BK virus–associated cystitis. However, six patients developed less common infections such as disseminated adenovirus and human herpesvirus-6 requiring antiviral treatment, which are complications usually reported in patients with profound immunosuppression. This high rate of infections is consistent with data reported in the multicenter US trial and, notably, all eight deaths across both the US and consortium studies were attributed to infectious complications.[10,11] These findings underscore the critical need for effective infection prophylaxis and comprehensive supportive care in the post-transplant setting.

Although our cohort was smaller than those reported in the two previous studies, it represents the majority of haploidentical transplants performed in France for this indication during the study period, with data rigorously monitored by the sponsor. It reinforces, with longer follow-up, previously published findings and provides detailed information on post-transplant infections. We also provide quality-of-life outcomes which suggest that transplantation is associated with a progressive improvement in quality of life, an effect that appears more pronounced at 2 years in adolescents than in adults

The role of haploidentical transplantation in SCD is often compared to that of gene therapy. The main advantage of gene therapy is the absence of GvHD. However, haploidentical transplantation offers several benefits, especially better feasibility and lower cost. In our study, 17 out of 22 patients (77%) would not have qualified for a gene therapy trial because of cerebral vasculopathy requiring exchange transfusions or a history of transfusion-related complications. Gene therapy also requires a myeloablative conditioning regimen, which may not be suitable for some adults. In addition, the process is more complex, with a higher risk of manufacturing failure: in a recent report 24% of mobilized patients did not receive exagamglogene autotemcel gene therapy.[15] After haploidentical transplant, hemolysis resolves in almost all patients who do not reject their grafts, while it persists in about 50% of cases after LentiGlobin (lovotibeglogene autotemcel) or exagamglogene autotemcel therapy.[15,16] Thus, it has been shown that haploidentical transplantation can cure SCD, while gene therapy, so far, mostly improves it.

In conclusion, the data regarding the DREP-HAPLO protocol reinforce existing evidence supporting the feasibility of haploidentical transplantation in both pediatric and adult patients with SCD, and its potential to cure the majority of them. However, long-term follow-up is needed to assess data on sickle cell-related organ damage and fertility. Compared to results from prior studies, our findings suggest a trend toward a very low rejection rate, albeit with a higher incidence of chronic GvHD. A fair comparison of feasibility and outcomes between haploidentical transplantation and gene therapy should be conducted in similar patient populations, using standardized evaluation criteria.

Disclosures

No conflicts of interest to disclose.

Contributions

ND designed the study, recruited patients, contributed to the analysis, and wrote the manuscript. BB, CPa, NB, MOC, J-BA, and CPo recruited patients and critically revised the manuscript. EG analyzed the data. MG collected the data. CJ contributed to the study design, data curation and analysis.

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Data-sharing statement

Anonymized data are available upon reasonable request.

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