

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

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Supplementary data.

Methods :

- *Inclusion criteria.* Patients were required to have at least one severe SCD-related complication including: cerebral vasculopathy with arterial stenosis with abnormal magnetic resonance angiogram (MRA) despite extended transfusion therapy; history of acute chest syndrome (ACS) or vaso-occlusive crises (VOCs) despite hydroxyurea therapy pulmonary hypertension (mean pulmonary artery pressure >25 mmHg, by right heart catheterization); tricuspid regurgitant velocity ≥ 2.5 m/s with left ventricular ejection fraction (LVEF) <55%; severe transfusion difficulties or alloimmunization; renal damage (albuminuria/creatininuria ratio >30 mg/mmol), or estimated creatinine clearance <80 mL/min/1.73m²); history of acute hepatic sequestration with hepatic failure; need for chronic red blood cell (RBC) transfusions during at least one year.
- *Exclusion criteria.* Patients with the following criteria were excluded: ECOG performance status >1, forced expiratory volume and forced vital capacity <50%, NYHA class ≥ 2 pulmonary hypertension, conjugated bilirubin >50 μ mol/L, creatinine clearance <30 mL/min/1.73m², LVEF <45%, anti-HLA donor-specific antibodies (DSA), active human immunodeficiency virus infection, uncontrolled severe infections, pregnancy or lactation, legal incapacity.
- *Pre-Transplant recipient management.* Patients received red cell transfusions or erythrapheresis to maintain hemoglobin S (HbS) levels below 30% during the three months preceding transplant. Chelation therapy aimed a hepatic iron concentration (MRI-based) below 10 mg/g liver tissue and cardiac T2* MRI values above 12 milliseconds, before transplant. For patients with poorly controlled pain, a specialized pain consultation was conducted pre-transplant: optimization of analgesia was prioritized to ensure clinical stability during hospitalization. For male patients, sperm cryopreservation was recommended prior to hydroxyurea initiation. Female patients were referred to reproductive biology consultation and offered ovarian tissue or oocyte cryopreservation. In patients with a history of alloimmunization or delayed hemolytic transfusion reactions, preemptive immunosuppressive

treatment and secure availability of compatible red blood cell units were required before proceeding.

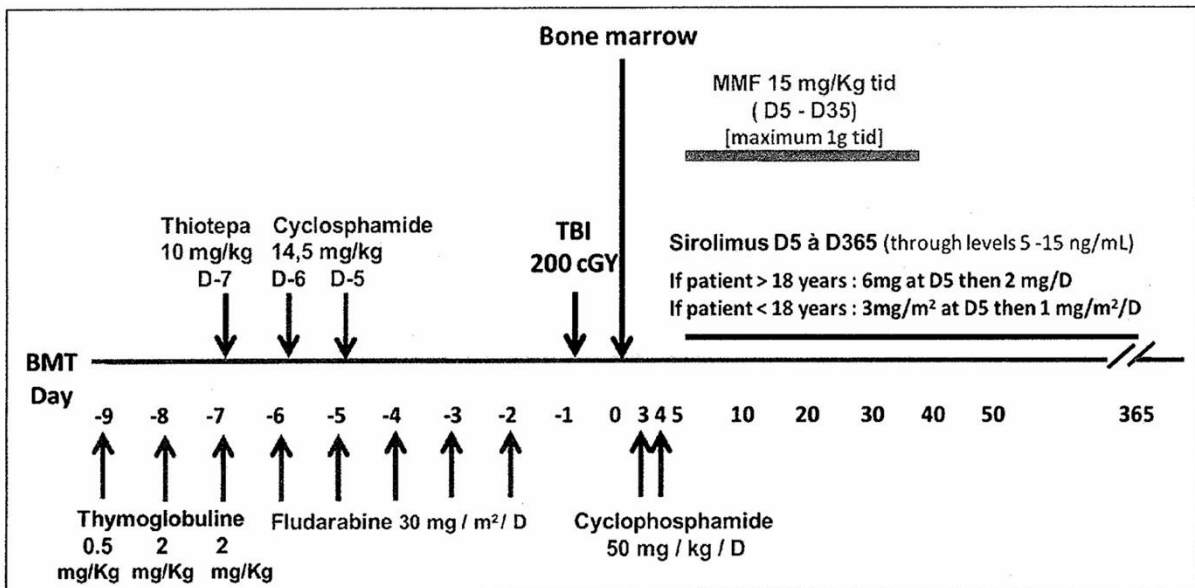
- Definitions : Neutrophil recovery was defined as three consecutive days with neutrophil count above $0.5 \times 10^9/L$; platelet recovery as three consecutive days with platelet count above $50 \times 10^9/L$. Acute GVHD (aGVHD) and cGVHD were defined and staged as previously reported.^{1,2}

1. Przepiorka D, Weisdorf D, Martin P, et al. 1994 consensus conference on acute GVHD grading. Bone Marrow Transplant. 1995; 15(6):825-828.

2. Vigorito AC, Campregher PV, Storer BE, et al. Evaluation of NIH consensus criteria for classification of late acute and chronic GVHD. Blood. 2009;114(3):702-708.

Results:

- **Supplemental Figure 1:** Transplant modalities. D : day. BMT bone marrow transplantation. TBI : total body irradiation.tib : three times in a day. MMF : mycophenolate mofetil.



➤ **Supplemental Table 1**

Table 1 : Infections grade 2-5 during the first 24 months post-transplant	
	Number (%)
Total episodes	85 (100)
Severity	# episodes (%)
- Grade 2	51 (60)
- Grade 3	32 (37.6)
- Grade 4	2 (2.3)
- Grade 5	0
Number of episodes by patient	# patients (%)
- 0	1 (4.5)
- 1	4 (18.1)
- 2	3 (13.6)
- 3	3 (13.6)
- ≥ 4	10 (45.4)
Infection timing	# episodes (%)
- Before day 30	36 (42.3)
- From day 30 to day 100	33 (38.8)
- After day 100	15 (17.6)
- Missing data	1 (1.1)
Infection and GVHD	
(acute grade II-IV or chronic moderate to severe)	# episodes
- Episodes number in 10 pts with GVHD : median (range)	4 (0-7)
- Episodes number in 12 pts without GVHD: median (range)	3 (1-9)
Infection site	# episodes (%)
- Bacteremia or severe sepsis/ fungemia	29 (34.1)
- Pneumonitis	5 (5.8)
-Urinary tract infection [BK virus cystitis]	10 (11.6) [4]
-Ear, nose, and throat infection	4 (4.7)
-Gastrointestinal tract	5 (5.8)
-Osteomyelitis	1 (1.1)
- Viral replication without clinical disease	20 (23.5)*
- No documented infection site	11 (12.9)
Pathogen type	# episodes (%)
-Bacterial	38 (44.7)
• Pseudomonas aeruginosa	6
• Escherichia coli	5
• Other Gram-negative bacilli	11
• Staphylococcus aureus	6
• Streptococcus pneumoniae	1
• Clostridium difficile	2
• Other bacteria	7
- Viral	29 (34.1)
• Cytomegalovirus (CMV)	8
• Epstein-Barr virus (EBV)	4
• BK virus	4
• Adenovirus	2
• SARS-CoV-2	1
• HSV/VZV	5
• HHV-6	5
- Fungal	4 (4.7)
• Pneumocystis jirovecii	1
• Geotrichum capitatum	1
• Candida spp.	2
-Non-microbiologically documented infections	14 (16.5)

: number. HSV: herpes simplex virus. VZV: varicella zoster virus
 SARS-CoV-2: severe acute respiratory syndrome coronavirus2.
 * related to CMV (n=8), EBV (n=4), HHV-6 (n=5), adenovirus (n=2), SARS-CoV-2(n=1).