HLA identical sibling transplant outcomes according to age in patients with sickle cell disease

Barbara Cappelli, MD[1,2], Karina Tozatto-Maio, MD[1,2,3], Fernanda Volt, MSc[1,2], Annalisa Paviglianiti, MD[1,2], Alina Ferster, MD[4], Sophie Dupont, MD[5], Belinda Pinto Simões, MD, PhD[3], Amal Al-Seraihy, MD[6], Mahmoud Aljurf[7], Cristina Belendez, MD[8], Susanne Matthes, MD[9], Nathalie Dhedin, MD[10], Corinne Pondarre, MD[11], Jean-Hugues Dalle, MD, PhD[12], Yves Bertrand, MD[13], Jean Pierre Vannier, MD[14], Mathieu Kuentz, MD[11], Patrick Lutz, MD[15], Gerard Michel, MD[16,17], Hanadi Elayoubi, MD[1,2], Benedicte Neven, MD[18], Josu de la Fuente, FRCP, PhD, FRCPath[19,20], Marco Zecca, MD[21], Said Y. Mohamed, MD[7], Peter Bader, MD, PhD[22], Annalisa Ruggeri, MD[1,2,23], Francoise Bernaudin, MD[11] and Eliane Gluckman[1,2] on behalf of Eurocord -Monacord and the Paediatric Diseases Working Party of EBMT

[1]Monacord, Centre Scientifique de Monaco, Monaco, Monaco [2]Eurocord, Hopital Saint Louis, Paris, France [3]Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, Brazil [4]Hematology/Oncology, Hôpital Universitaire des Enfants Reine Fabiola, Université Libre de Bruxelles, Brussels, Belgium [5]Cliniques Universitaires Saint Luc, Brussels, Belgium [6]Paediatric SCT Program, King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia [7]Oncology Center, King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia [8]Hospital Univ.Materno Infantil Gregorio Marañon, Madrid, Spain [9]St. Anna Children's Hospital, Vienna, Austria [10]Department of Hematology, University Hospital Saint-Louis, PARIS, France [11]Centre Hospitalier Intercommunal Créteil, Créteil, France [12]Pediatric Hematology Department, Robert Debre Hospital, Paris, FRA [13]Institute of Hematology and Oncology Pediatrics, University Hospital of Lyon, Lyon, France [14]Institut de Recherche et d'Innovation Biomédicale, Faculté de Médecine-Pharmacie, Unité Mixte de Recherche U 1234 (PANTHER) Physiopathologie, Autoimmunité, Maladies neuromusculaires et Thérapies régénératrices, Rouen, France [15]Centre Hospitalier Universitaire de Strasbourg, Strasbourg, France [16]EA 3279, Aix-Marseille University, Marseille, FRA[17]Department of Pediatric Hematology, Aix Marseille University, Marseille, France [18]Necker Children's Hospital, Assistance Publique-Hôpitaux de Paris, Paris, France [19]Department of Paediatrics, St. Mary's Hospital, London, United Kingdom [20]Centre for Haematology, Imperial College London, London, United Kingdom [21]Pediatric Hematology Oncology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy [22]Department for Children and Adolescents; Division for Stem Cell Transplantation and Immunology, University Hospital Frankfurt, Frankfurt, Germany [23] Hôpital Saint Antoine, Service d'Hématologie Clinique et de Thérapie cellulaire, Paris, France*

Background:

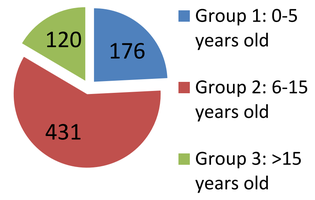
Hematopoietic stem cell transplant (HSCT) from an HLA identical (HLAid) sibling donor is a well-established curative therapy for sickle cell disease (SCD). However, the ideal age to perform HSCT in SCD patients remains controversial. We report the outcomes after HLAid sibling HSCT for SCD according to patient's age at the time of HSCT as well as their pre-transplant characteristics.

Methods:

- Retrospective, registry based analysis on HLA identical sibling HSCT 727 patients (children and adults)
- HSCT performed from 1986-2015 in 98 EBMT centres (73% France, Belgium, UK, Italy)
- 3 age groups (0-5 years, 6-15 years, >15 years)
- Primary endpoint: 3-year overall survival (OS) according to age group.

Patient and donor Characteristics:

Patient Characteristics (%)	Age 0-5 years	6-15 Years	>15 Years
Follow Up, median, months (range)	56 (3-346)	37 (0.3-323)	32 (0.5-304)
Age, median, years (range)	4.3 (1-6)	9.8 (6-15)	17.4 (15-39)
Weight, median, kg (IQ range)	17 (14-19)	29 (23-37)	53 (47-64)
Hb genotype*:			
HBSS	95	92	84
HBSβO	4	5	11
Other	1	3	5
Received >20 RBC units transfusions pre HSCT*	36	46	60
RBC immunisation *	6	13	16
Use of HU *	37	60	77
Performance Status pre-HSCT*:			
>80%	99	98	94
≤80%	1	2	6



Patient/Donor (P/D) Characteristics*	
Donor age at transplant, median, years (range)	9 (1-47)
Donor Trait (%)	44
P/D sex match (%):	49
Equal	23
Patient F/Donor M	28
Patient M/Donor F	
P/D ABO match (%):	65
Compatible	16
Minor incompatible	5
Bi-directional incompatible	14
Major incompatible	
P/D CMV serology (%): P+/D+	58
P-/D+	11
P+/D-	17
P-/D-	14

Risk factors

Pre HSCT Risk factors (%)*		Age 0-5 years	Age 6-15 years	Age >15 years
Abnormal transcranial doppler		60	57	27
Previous stroke		40	49	42
Previous acute chest syndrome (ACS)		40	49	42
Previous vaso-occlusive crisis (VOC)		70	79	85
Previous priapism		3	5	48
Previous osteonecrosis		3	11	30
Number of organs/ systems involved in SCD complications:	1	59	43	34
	2	30	38	28
	3	11	19	39

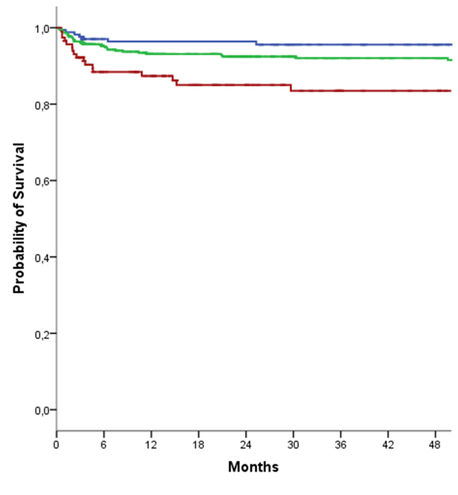
Main Indication for HSCT*	Age 0-5 years	Age 6-15 years	Age >15 years
1st	CNS vasculopathy	VOC	VOC
2nd	VOC	CNS vasculopathy	ACS
3rd	ACS	ACS	CNS vasculopathy

* % of evaluable patients

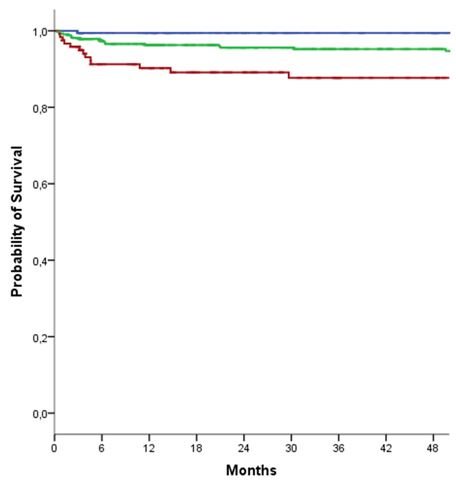
Results:

Cell Source/Conditioning regimen %		Age 0-5 years	Age 6-15 years	Age >15 years	p
Stem cell source:	BM	74	85	78	
	PBSC	3	4	20	<0.001
	CB	23	11	2	
Conditioning Regimen# :	RIC	3	4	17	<0.001
	MAC	97	96	83	
In vivo T-cell depletion:	ATG	69	79	77	<0.001
GVHD Prophylaxis:	CSA + MTX	50	68	66	
	CSA + MMF	5	7	6	
	CSA ± other	43	24	18	
	Other	2	1	10	

3 year EFS



3 year OS



Age 0-5 years Age 6-15 years Age >15 years

 # MAC: BuCy=78%, TreoTTFlu+/-Cy = 8% and BUFLU+/-Cy = 7%; **RIC**: BU-FLU=24%,FluMelTT=24%, FluMel=17%, AlemtuzumabTBI=10%

Outcomes	Age 0-5 years	Age 6-15 years	Age >15 years	p
Neutrophil engraftment (only for BM) @60d	97%±2	98%±1	98%±2	0.432
acute GvHD @100d	9%±2	18%±2	17%±4	0.022
chronic GvHD @3 yrs	9%±2	12%±2	20%±4	0.006
Chimerism(%): §				
Full donor	65	65	46	0.006
Mixed chimera	32	32	49	
Autologous	3	3	5	
3- year EFS	96±2%	92±1%	84±4%	0.001
3- year OS	99±1%	95±1%	88±3%	<0.001

§Subset of 405 patients with available chimerism

Conclusions:

Patients transplanted at a young age have a better 3-year OS and 3-year EFS, with lower incidence of aGvHD and cGvHD. These findings outline the importance of early referral to HSCT for SCD patients. Strategies to further evaluate patient/disease characteristics, HSCT and donor factors that may influence survival and adverse events could help improve HSCT outcomes.

There are no conflicts of interest to disclose.
For more information please contact us at: monacord@centrescientifique.mc