Outcomes according to age at transplant with an HLA identical sibling for sickle cell disease

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Background:

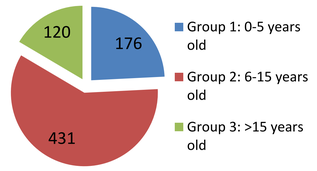
Hematopoietic stem cell transplant (HSCT) from an HLA identical (HLAid) sibling donor is a well-established curative therapy for sickle cell disease (SCD). However, the ideal age to perform HSCT in SCD patients remains controversial. We report the outcomes after HLAid sibling HSCT for SCD according to 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 (%):	Equal	49
	Patient F/Donor M	23
	Patient M/Donor F	28
P/D ABO match (%):	Compatible	65
	Minor incompatible	16
	Bi-directional incompatible	5
	Major incompatible	14
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

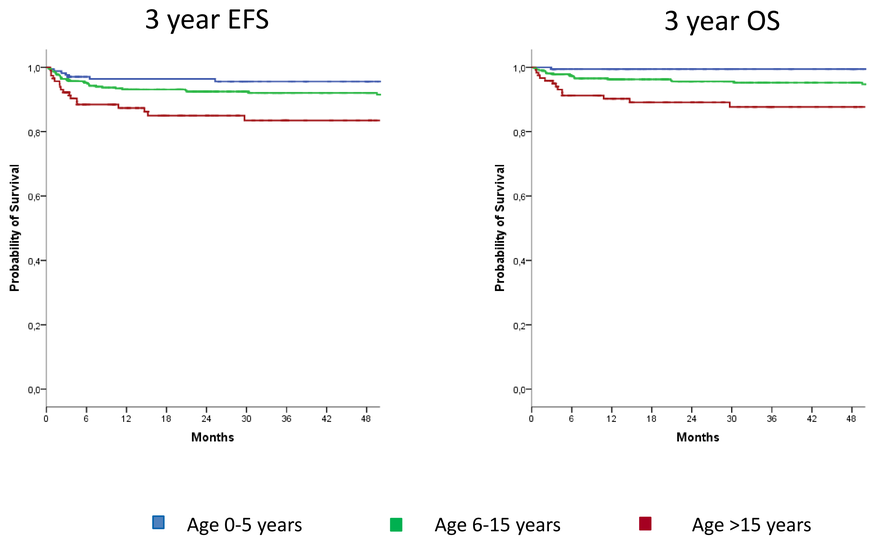
Results:

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	

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 pre HSCT, HSCT and donor factors that may influence survival and adverse outcomes could help improve HSCT results.

There are no conflicts of interest to disclose.
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