



ISBMT

Indian Society for Blood & Marrow Transplantation



Transplant in Hemoglobinopathies Who, When and How ?

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BMT Masterclass

13th & 14th Dec 2025

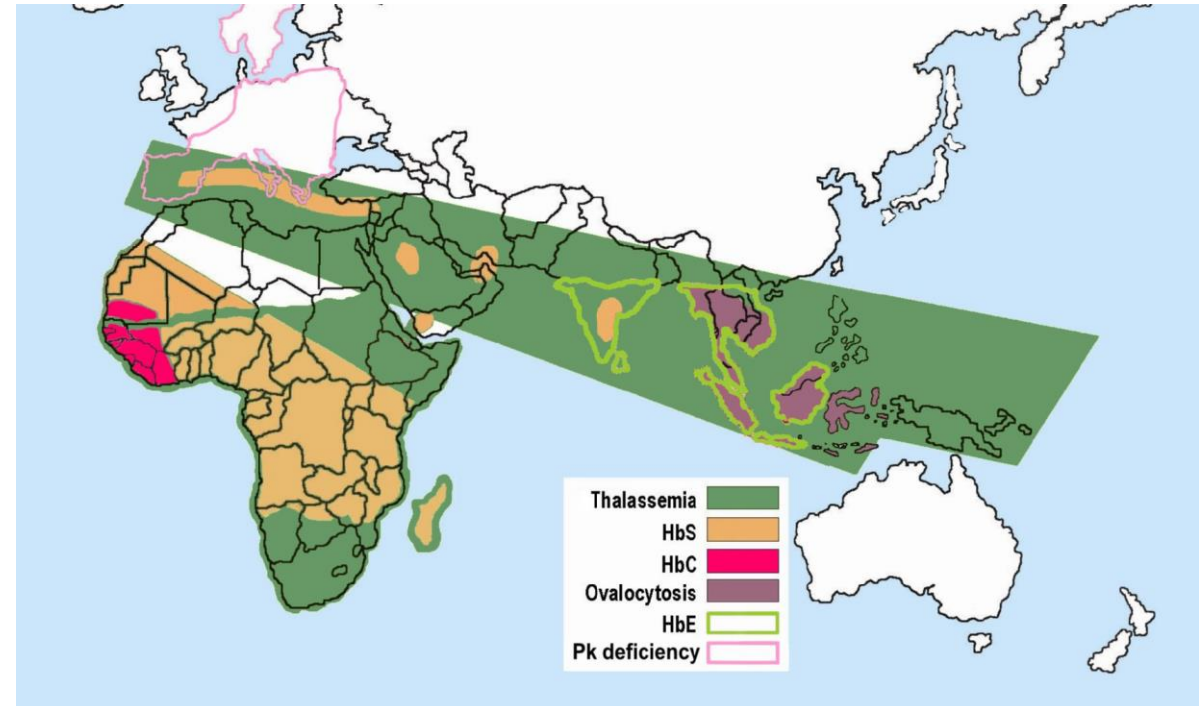
Overview

- Transplant
 - Disease characteristics
 - TDT vs Sickle
 - Conditioning regimens
 - MAC vs RTC vs RIC vs NMA
 - Donor source
 - GVHD prophylaxis
 - Expanding donor sources
- Data from India and guidelines

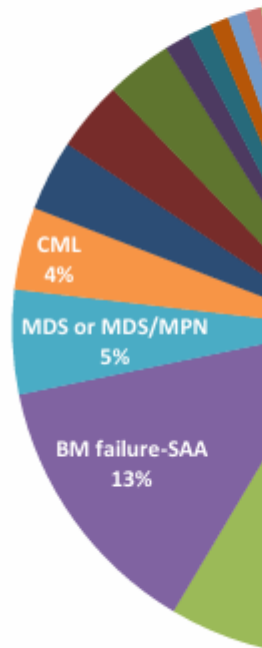


Magnitude

- Thal
 - 60000 born annually
 - India: 4 % (0.2 – 21%)
 - 10000 born annually
- Sickle
 - 300000
 - India: 3.3 – 9%
 - 20000 born annually
- Transplant is definitive cure



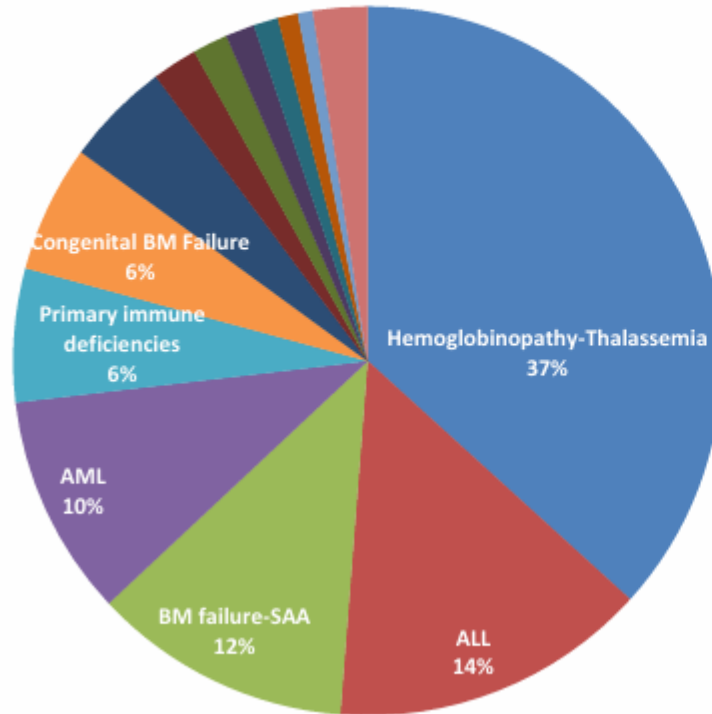
ISBMT REGISTRY 2012 to 2024 - Activity report Indications for Allogeneic SCT



Total HSCT units – 167

< 18 years

Pediatric (9695)



Total HSCT units – 167

Diagnosis	N	%
Hemoglobinopathy-Thalassemia	3561	36.7
ALL	1406	14.5
BM failure-SAA	1144	11.8
AML	979	10.1
Primary immune deficiencies	591	6.1
Congenital bone marrow failure	563	5.8
Hemoglobinopathy-other	464	4.8
MDS or MDS/MPN	199	2.1
Inherited metabolic disease	156	1.6
Hemophagocytic syndrome	128	1.3
CML	109	1.1
Other hematological disease	89	0.9
Other leukemia	66	0.7
others	240	2.5
Total	9695	100.0

Planning a transplant - Hemoglobinopathy

- **Hypercellular BM**
- **Alloimmunised**
- **Benign - No benefit of GVHD**
 - Donor availability



Rejection

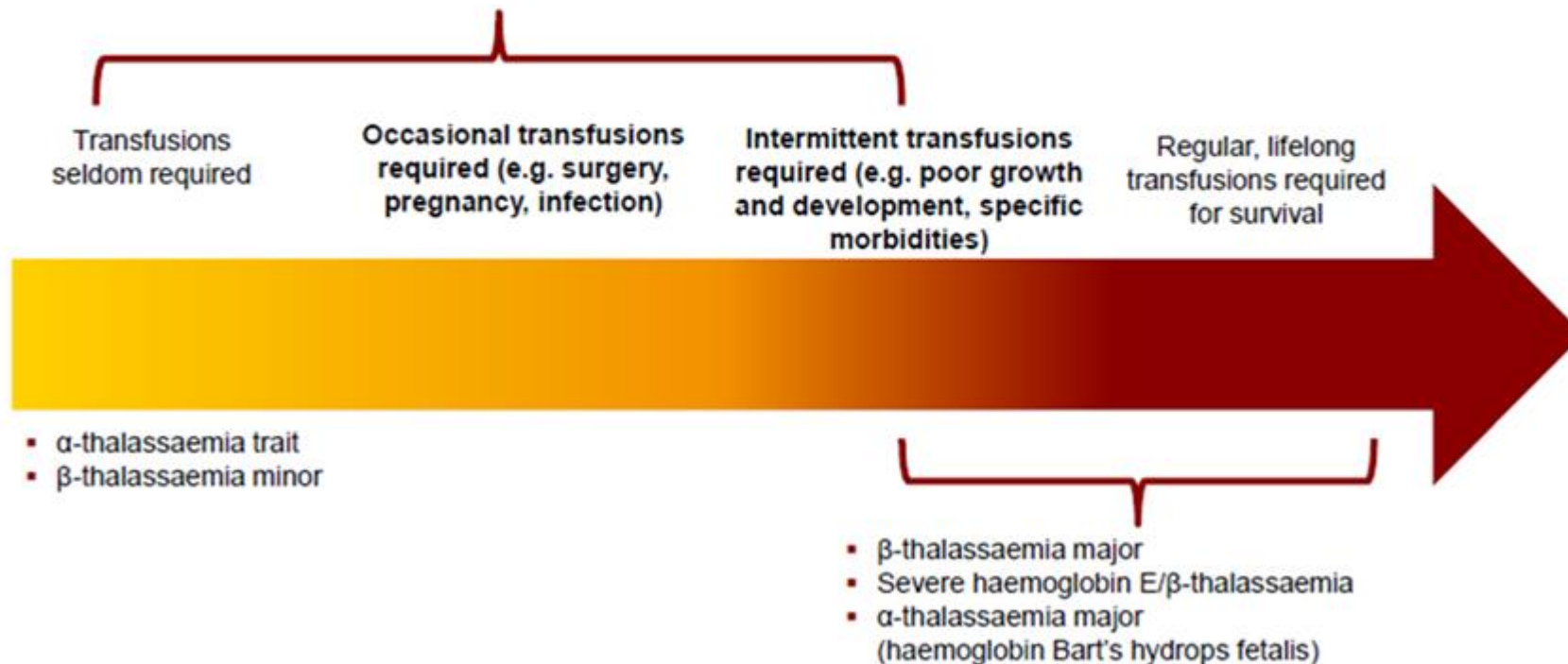
**Stable mixed donor
chimerism is OK !
30%
Stable Hb; asymptomatic**

- Host characteristics - Organ injury (iron overload vs vasculopathy)
- Prediction of natural history – **Supportive care VS HSCT**

Who ? : TDT – needs HSCT

Non-transfusion-dependent thalassaemias (NTDT)

- β -thalassaemia intermedia
- Mild/moderate HbE/ β -thalassaemia
- α -thalassaemia intermedia (HbH disease)



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BONE MARROW TRANSPLANTATION IN PATIENTS WITH THALASSEMIA

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DONATELLA BARONCIANI, M.D., CLAUDIO GIARDINI, M.D., PATRIZIA POLITI, M.D.,
SUZY MARIA TERESA DURAZZI, M.D., PIETRO MURETTO, M.D.,
AND FEDERICO ALBERTINI, M.A.

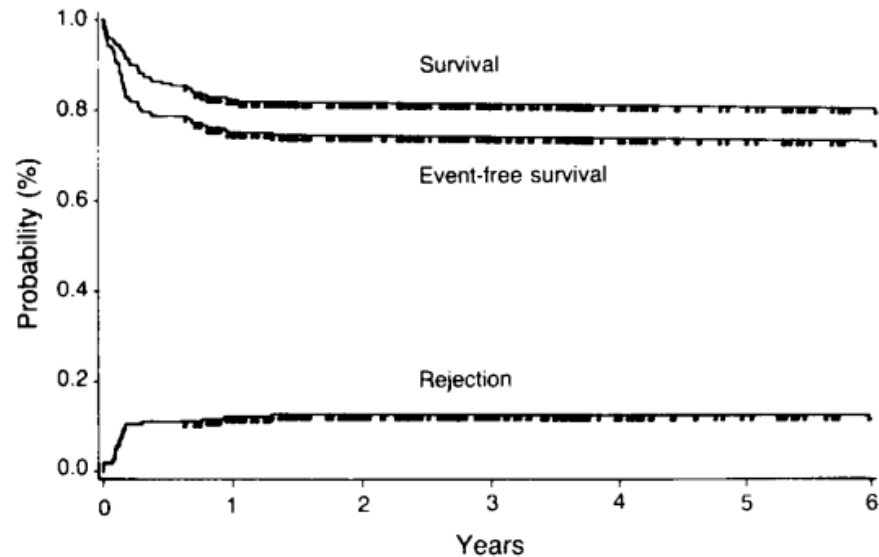


Figure 1. Probabilities of Survival, Event-free Survival, and Re-
currence in 222 Patients under 16 Years Old with Thalassemia
Treated with Allogeneic Marrow Transplantation.

An event was defined as rejection, the recurrence of thalassemia,
or death.

MARROW TRANSPLANT PROTOCOL for THALASSEMIA

Pescara

Hypertransfusion regimen (Hgb > 14)

DAYS	Treatment
-10	Acyclovir ⇔ 9 months
-9	Busulphan 3.25 mg / Kg
-8	Busulphan 3.25 mg / Kg
-7	Busulphan 3.25 mg / Kg
-6	Busulphan 3.25 mg / Kg
-5	Cyclophosphamide 50 mg / Kg
-4	Cyclophosphamide 50 mg / Kg
-3	Cyclophosphamide 50 mg / Kg
-2	Cyclophosphamide 50 mg / Kg
-1	Cyclosporine ⇔ day +365
0	BMT

OS and EFS

Table 2. Multivariate Analysis of Risk Factors.

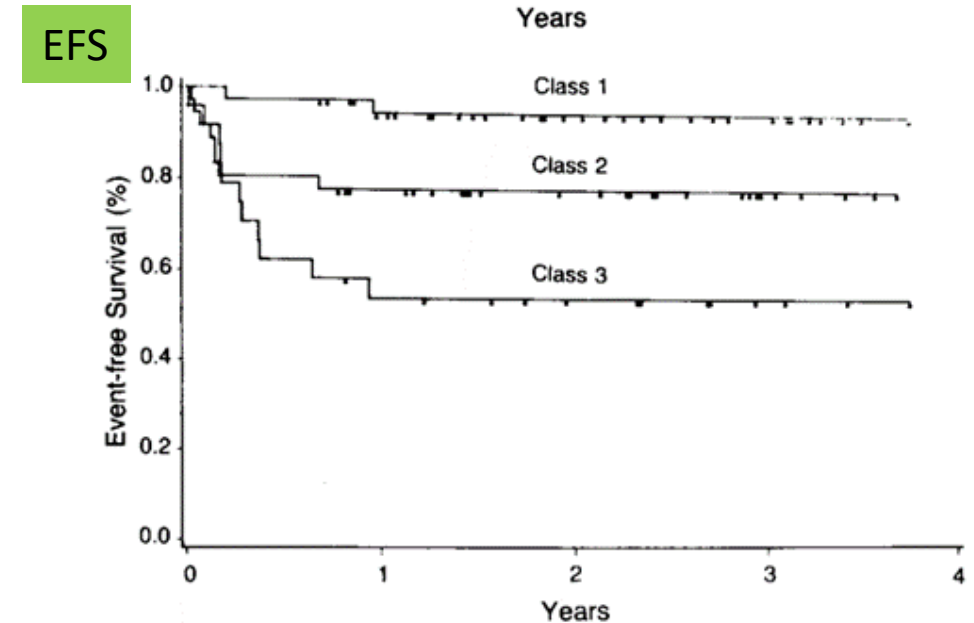
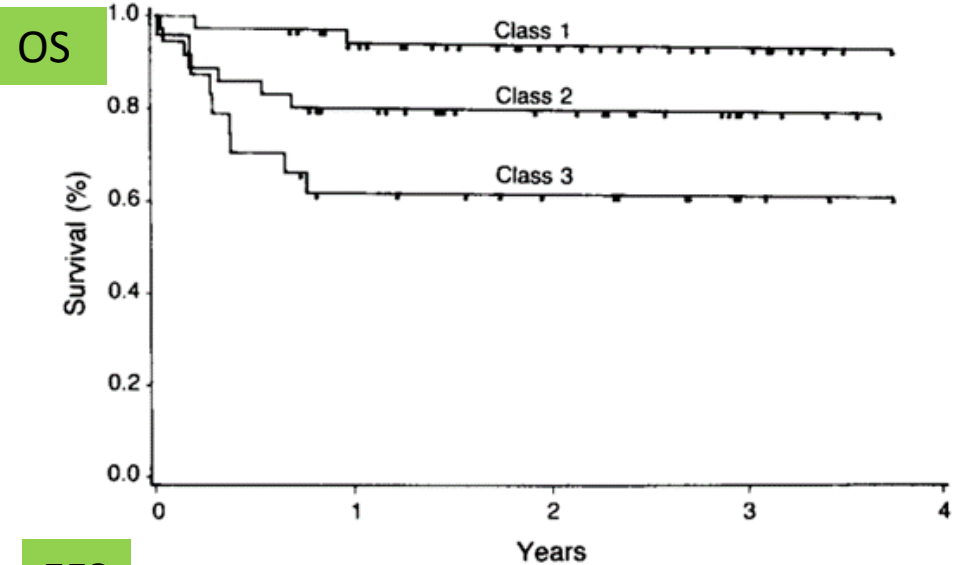
ADVERSE FACTORS	P VALUE	RELATIVE RISK*
Survival		
Hepatomegaly >2 cm	0.004	2.23 (1.14–7.74)
Portal fibrosis	0.03	1.92 (1.07–12.41)
Event-free survival		
Hepatomegaly >2 cm	0.0003	3.67 (2.11–11.39)

*Values in parentheses are 95 percent confidence intervals.

Table 3. Characteristics of Patients According to Class.

CHARACTERISTIC	CLASS 1 (N = 39)	CLASS 2 (N = 36)	CLASS 3 (N = 24)
Median age — yr (range)*	6.5 (1–13)	10.5 (3–15)	12 (5–15)
Regular chelation (no.)	26	12	1
Hepatomegaly (no.)	0	4	24
Portal fibrosis (no.)	0	32	24

*F = 14.69 by analysis of variance (Welch).



REVIEW

Stem cell transplantation in India

M Chandy

The Christian Medical College, Vellore, India



Table 1 Transplant activity in India (September 2005)

	<i>Autologous</i>	<i>Allogeneic</i>	<i>Total</i>
Christian Medical College Hospital, Vellore	117	522	639
Tata Memorial Hospital, Mumbai	90	178	268
All India Institute of Medical Sciences, New Delhi	144	66	210
Apollo Hospital, Chennai			159
Jaslok Hospital, Mumbai	49	19	70
Research and Referral Hospital of the Armed Forces, New Delhi	26	37	63
Sahayadri Hospital, Pune	7	59	66
Gujarat Cancer Research Center, Ahmedabad	32	0	32
			25
	-	-	-

Table 2 Indications for BMT—Christian Medical College Hospital, Vellore (October 1986–December 2006)

<i>Diseases</i>	<i>Patients</i>	<i>Transplants</i>	<i>BMT-1</i>	<i>BMT-2</i>	<i>BMT-3</i>
Thalassemia	218	227	218	9	—
AML	107	111	107	4	—
ALL	39	39	39	—	—
CML	91	99	91	7	1
Aplastic anemia	84	90	84	5	1
Fanconis anemia	8	10	8	1	1
Myelodysplasia	29	31	29	2	—
Miscellaneous	19	19	19	—	—
Total	595	626	595	28	3

Table 3 Outcome of allogeneic BMT for thalassemia Christian Medical College Hospital, Vellore (5-year Kaplan–Meier estimate of overall survival and EFS)

<i>Class</i>	<i>Number</i>	<i>Survival (%)</i>	<i>EFS (%)</i>	<i>Rejection (%)</i>
All patients	218	72.3 ± 3.1	65.3 ± 3.3	14.6
Class I	15	71.8 ± 11.98	71.8 ± 11.98	0
Class II	89	82.6 ± 4.1	78.3 ± 4.4	12.4
Class III	114	64.5 ± 4.6	54.6 ± 4.8	18.4

Vellore High risk

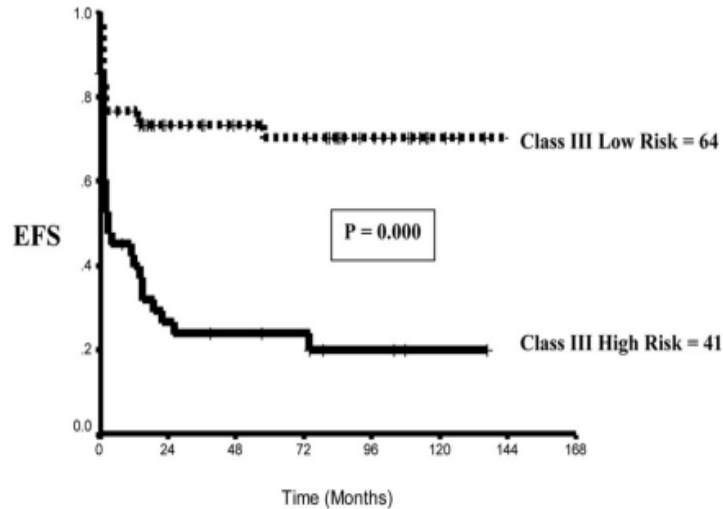


Figure 2. Comparison of 5-year EFS of Class III transplants in the high-risk group (n = 41) and rest of transplants in Class III (n = 64).

- Age ≥ 7
- Liver size ≥ 5 cms

A New Stratification Strategy That Identifies a Subset of Class III Patients with an Adverse Prognosis among Children with β Thalassemia Major Undergoing a Matched Related Allogeneic Stem Cell Transplantation

Vikram Mathews,¹ Biju George,¹ Uday Deotare,¹ Kavitha M. Lakshmi,¹ Auro Viswabandya,¹ Dolly Daniel,² Mammen Chandy,¹ Alok Srivastava¹

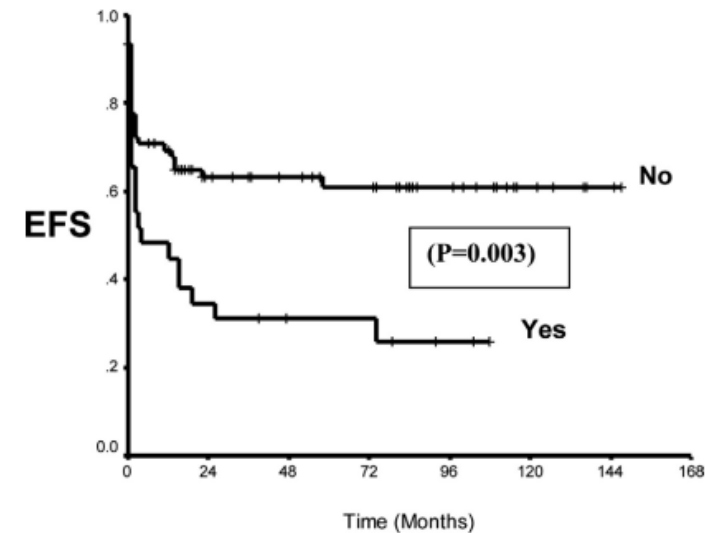
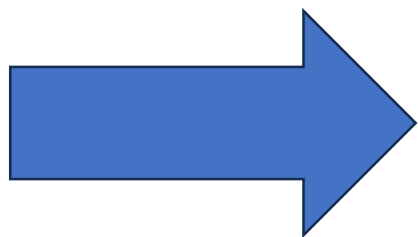
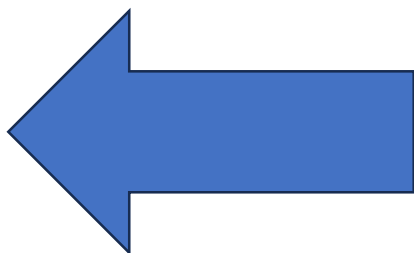


Figure 1. Comparison of 5-year EFS of Class III transplants who had a pretransplant splenectomy (n = 29) versus those who did not (n = 76).

Not all thal patients are same..... When HSCT ?



- Young
- Well transfused
- Well chelated



- Older
- Poorly transfused
- Iron overload



AGE as a factor affecting outcome

Group	OS	EFS
EBMT		
• < 14 yr	90	83
> 14 yr	82	74
CIBMTR		
• < 6 yr	90	86
6-15 yr	84	80
15-25 yr	63	63

Main challenges of increasing age.....

- Higher risk of rejection
- Higher risk of SOS
- **Solution ?**
 - IV Bu
 - PK monitoring
 - Avoids too little or too much Bu.....

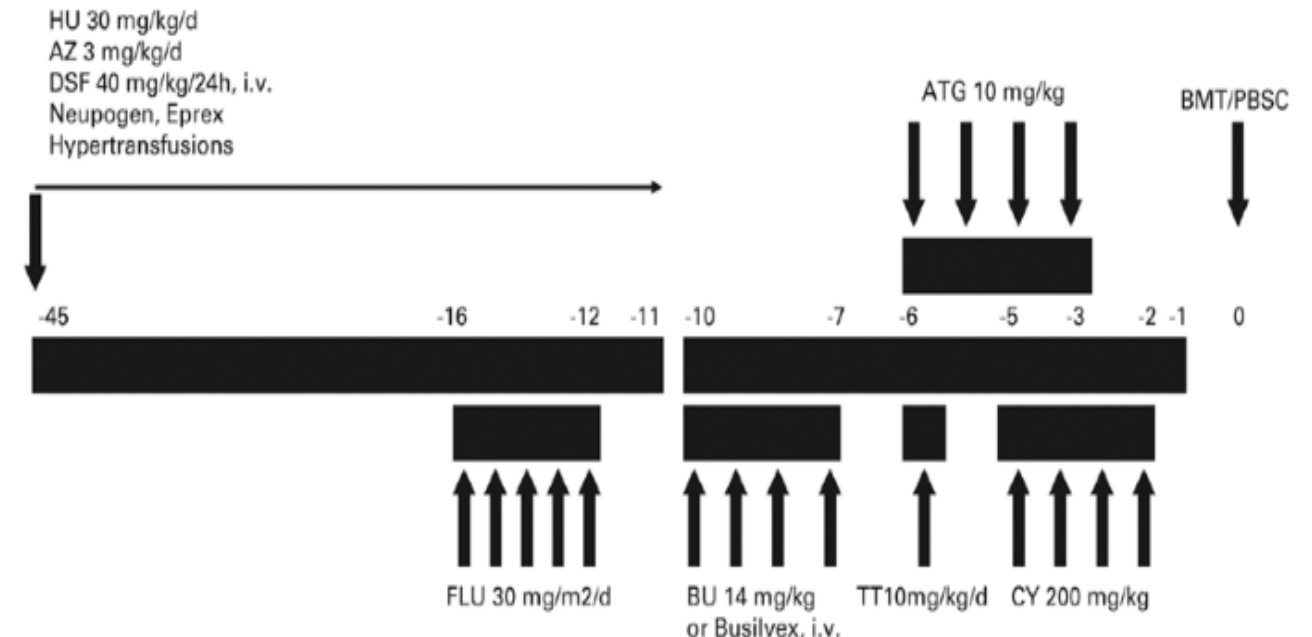
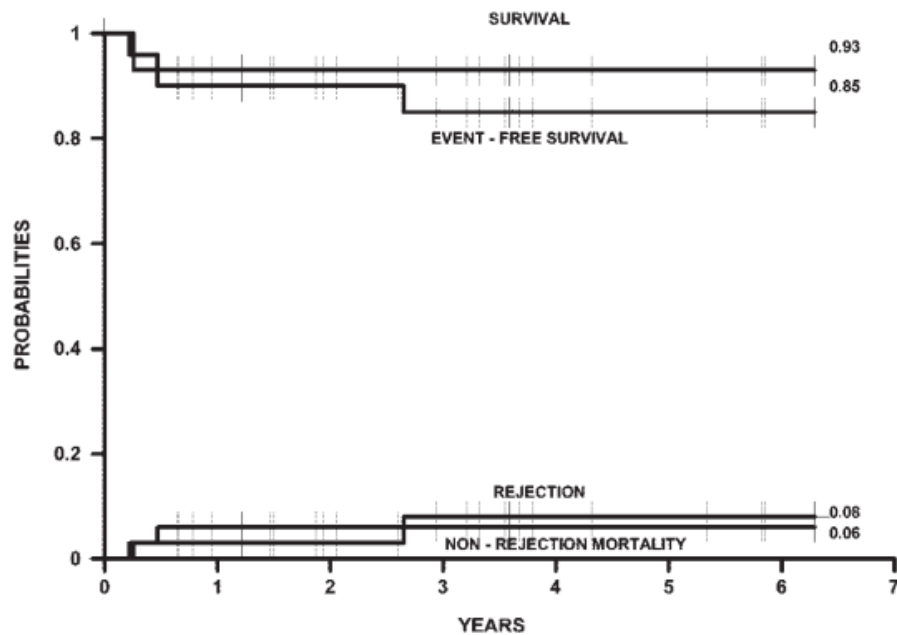
New approach for bone marrow transplantation in patients with class 3 thalassemia aged younger than 17 years

Pietro Sodani, David Gaziev, Paola Polchi, Buket Erer, Claudio Giardino, Emanuele Angelucci, Donatella Baronciani, Marco Andreani, Marisa Manna, Sonia Nesci, Barbarella Lucarelli, Reginald A. Cliff, and Guido Lucarelli

- 33 patients – Class 3
- Aim – reduce rejection
- Survival 93%



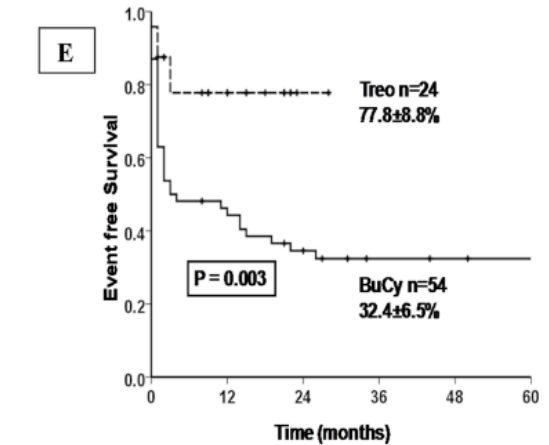
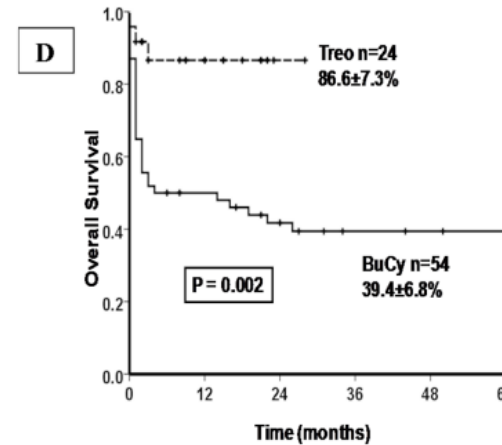
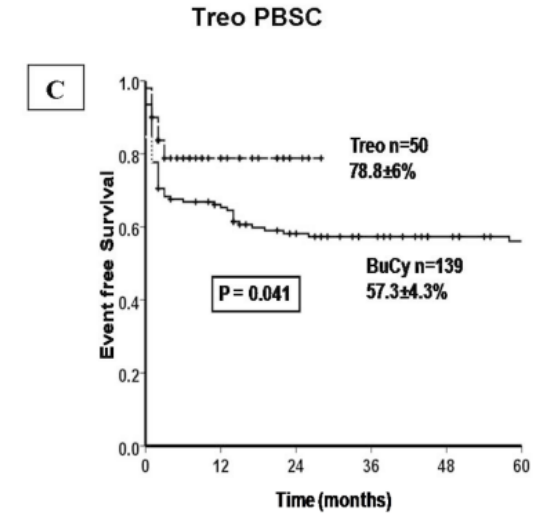
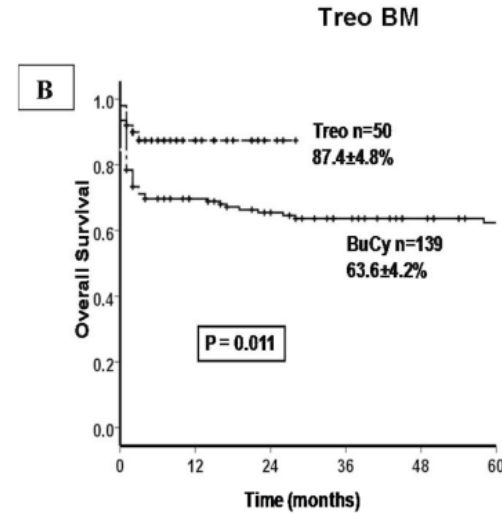
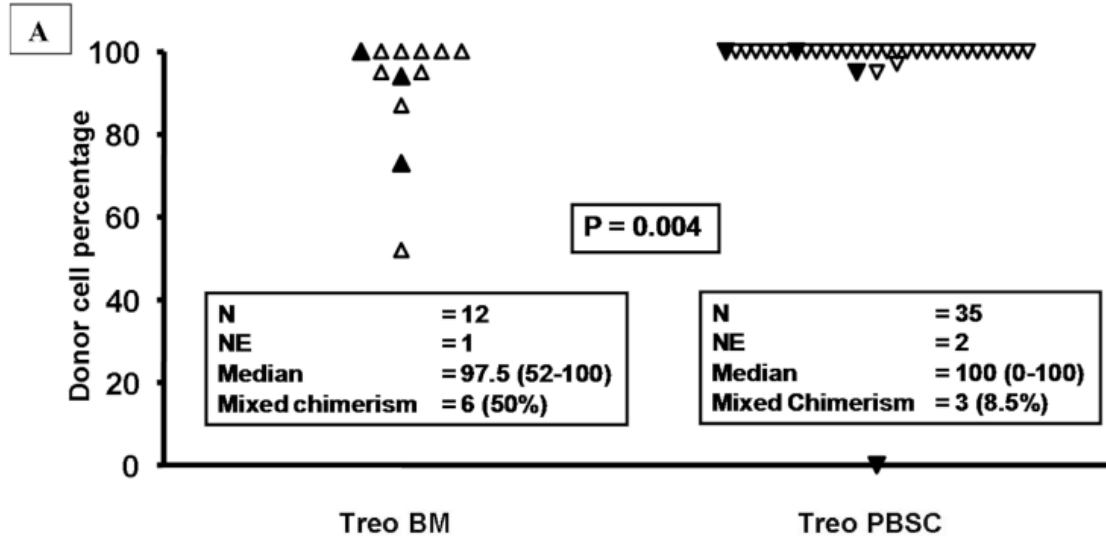
Protocol 26



Improved Clinical Outcomes of High Risk β Thalassemia Major Patients Undergoing a HLA Matched Related Allogeneic Stem Cell Transplant with a Treosulfan Based Conditioning Regimen and Peripheral Blood Stem Cell Grafts

Vikram Mathews*, Biju George, Auro Viswabandya, Aby Abraham, Rayaz Ahmed, Abhijeet Ganapule, Eunice Sindhuvi, Kavitha M. Lakshmi, Alok Srivastava

Department of Haematology, Christian Medical College, Vellore, India



Conditioning regimens

- **Bu / Cy**
 - Works well for younger patients
 - Less iron load
 - Risk of VOD – even with PK adjusted doses

- **Treo / Flu / TT**
 - Minimal risk of VOD
 - More mixed chimerism
 - ? Mucositis
 - Skin toxicity of TT



Matched Family versus Alternative Donor Hematopoietic Stem Cell Transplantation for Patients with Thalassemia Major: Experience from a Tertiary Referral Center in South India

Venkateswaran Vellaichamy Swaminathan¹, Ramya Uppuluri^{1,*}, Shivani Patel¹, Nikila Ravichandran¹, Kesavan Melarcode Ramanan¹, Lakshman Vaidhyanathan^{1,2}, Balasubramaniam Ramakrishnan¹, Indira Jayakumar^{1,3}, Revathi Raj¹

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- 2007-2018
- 264 kids (MRD 76% , MUD 22%)
- PBSC 61%, BM 38%, UCB 3%.

Table 1
Comparison of Events between Matched Related Donor versus Matched Unrelated Donor with Statistical Significance

Characteristic	Matched Related Donor (MFD + MSD), n (%)	Matched Unrelated Donor, n (%)	P Value
Total No.	206	58	
PRES	8 (3.8)	6 (10)	.107
Immune cytopenia	3 (1.4)	16 (27)	.0001
Viral reactivation	4 (1.9)	15 (26)	.0001
Acute GVHD	42 (20)	35 (60)	.0001
Chronic GVHD	36 (17)	24 (41)	.0003

Figure 2. Kaplan-Meier survival curve depicting overall survival of 95% and 90% with a median follow-up of 65 months in those who underwent transplantation less than and greater than 7 years of age, respectively.

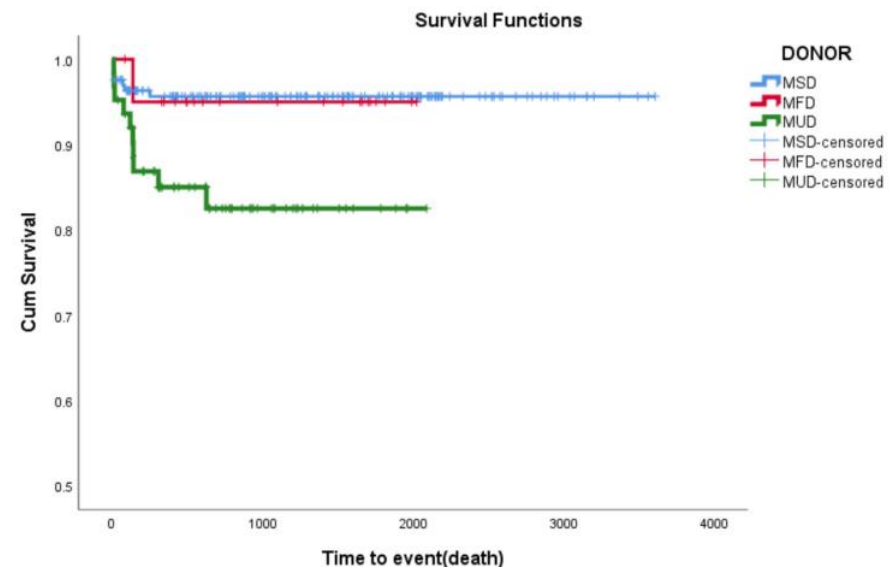


Figure 3. Kaplan-Meier survival curve depicting thalassemia-free survival of 96%, 94%, and 84% with a median follow-up of 65 months in the MSD, MFD, and MUD groups, respectively.

The problem of donors.....

- **MUD**

- Addition of ATG
- Higher risk of rejection
- Higher risk of GVHD
- Higher risk of viral reactivation

- Extra cost of MUD a barrier



Haploidentical

Hematopoietic Stem Cell Transplantation for Severe Thalassemia Patients from Haploidentical Donors Using a Novel Conditioning Regimen



Usanarat Anurathapan¹, Suradej Hongeng^{1,*}, Samart Pakakasama¹, Duantida Songdej¹,

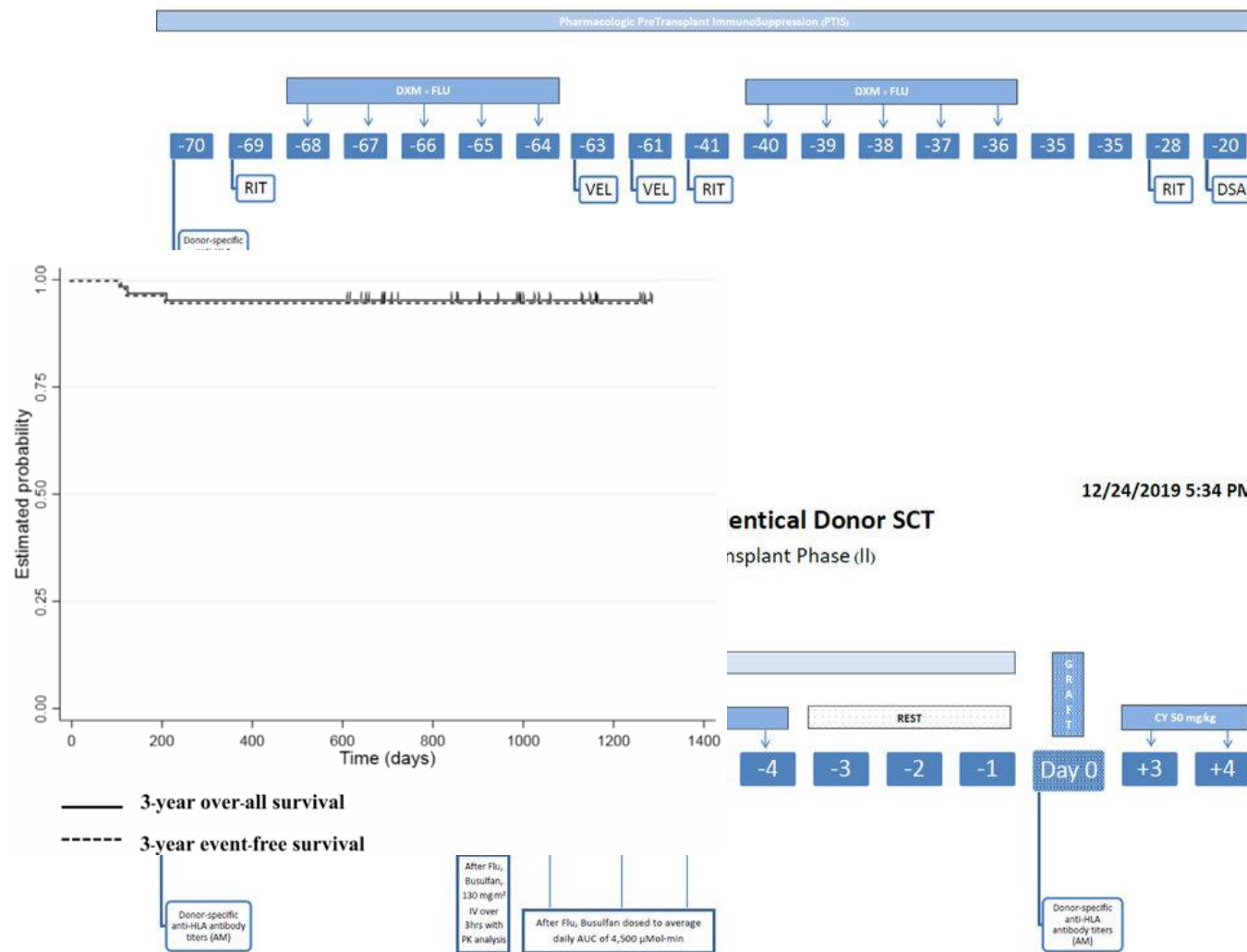
- PTIS – Flu / Dex
- Bu (PK) / Flu / ATG
- PTCy + Tac + MMF

- N = 83
- aGVHD (3/4)= 7%
- cGVHD (limited)= 40%

A)

Thalassemia, Haplo-Identical Donor Transplant

Pre-Transplant ImmunoSuppression Phase (I)



Can we use an available HAPLO.....

- **HAPLO**

- Inherent higher risk

- GVHD

- Rejection

- Viral reactivation

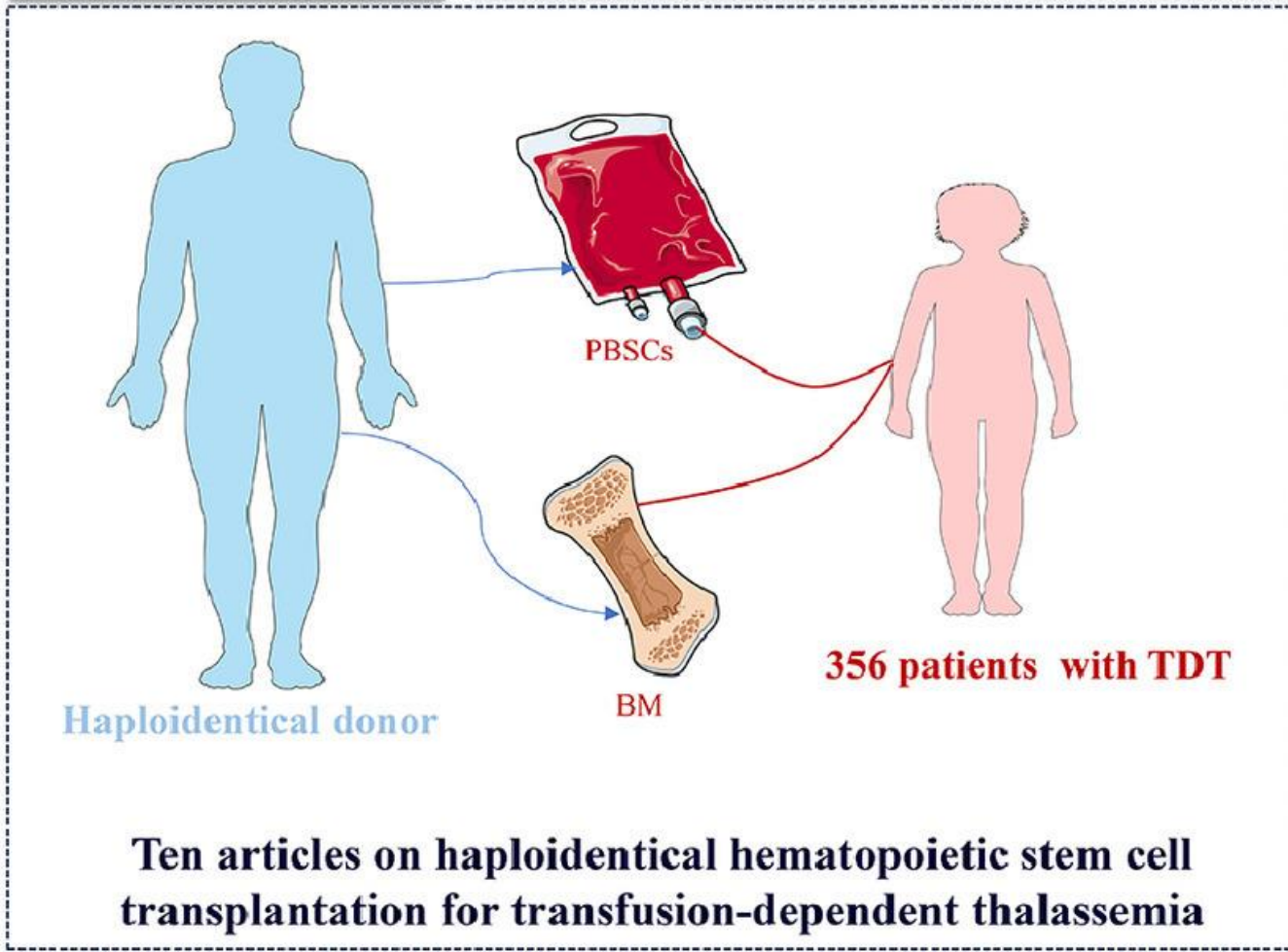
- Strategies for reducing risk of rejection

- PTIS

- T cell depletion

Haploidentical Hematopoietic Stem Cell Transplantation in Pediatric Transfusion-Dependent Thalassemia : A Systematic Review and Meta-analysis

Transplantation and Cellular Therapy 31(2025)



Survival

Overall Survival: 92.4%

Thalassemia-free Survival: 84.5%

Graft Failure: 8.1%

Transplantation Related Mortality: 7.4%

GvHD

Total aGvHD: 29.6%

Grade 3-4 aGvHD: 9.1%

Total cGvHD : 19.6%

Extensive cGvHD: 1.0%

No significant differences in these outcomes when comparing PTCy vs non-PTCY

EBV Reactivation: 22.6%

Sepsis: 9.4%

Invasive fungal diseases: 7.6%

Haplo Thal : PTCy vs T cell depletion

	PTCy	T cell deplete
Engraftment / GF	Excellent	Small risk of GF
GVHD	Higher cGVHD	Very low GVHD
Immune reconstitution	Earlier	Later (higher early infection rates)
Treatment toxicity (more related to conditioning)	Cystitis	Low
Cost/ availability	Low/ high	High / low

Thal HSCT : Long term outcomes

- Endocrine problems
 - growth delay, hypothyroidism, impaired pubertal development, diabetes
- Gonadal failure & infertility
 - Treo better than Bu
- **cGVHD** – skin/lung/eye
- Secondary malignancy

Sickle cell disease

- Evolution from restrictive indications to **early transplant**
 - Especially if MSD available
- Active BMA
- Varying degrees of iron overload
- Organ toxicity at HSCT
- Endothelial injury

Indication for HSCT - Evolving

- Classical indications:
 - Stroke (or abnormal TCD)
 - Recurrent vaso-occlusive crises or ACS
 - Sickle nephropathy
 - Pulmonary hypertension
 - Priapism refractory to therapy
 - Iron overload or poor access to care
- Early HSCT ***before*** organ toxicity especially if MSD available

American Society of Hematology 2021 guidelines for sickle cell disease: stem cell transplantation

Julie Kanter,¹ Robert I. Liem,² Françoise Bernaudin,^{3,4} Javier Bolaños-Meade,⁵ Courtney D. Fitzhugh,⁶ Jane S. Hankins,⁷ M. Hassan Murad,⁸ Julie A. Panepinto,⁹ Damiano Rondelli,¹⁰ Shalini Shenoy,¹¹ John Wagner,¹² Mark C. Walters,¹³ Teonna Woolford,¹⁴ Joerg J. Meerpohl,^{15,16} and John Tisdale⁶

- MSD HSCT if CNS/pain/ACS
- Early HSCT (<16 if CNS issues)
- Conditioning
 - TBI or chemo based
 - Children
 - MAC > RIC
 - Adults
 - NMA > RIC
- MUD – trials

Table 2. Summary of American Society of Hematology (ASH) Recommendations (R) for HSCT in Patients With SCD.

R1	The ASH guideline panel suggests HLA-matched related HSCT rather than standard of care (HU/transfusion) in patients with SCD who have experienced an overt stroke or have an abnormal transcranial Doppler ultrasound (TCD). When considering transplantation for neurologic injury, children younger than age 16 years who receive MSD HSCT have better outcomes than those older than age 16 years.
R2	For patients with frequent pain, the ASH guideline panel suggests using related matched allogeneic transplantation rather than standard of care.
R3	For patients with recurrent episodes of ACS, the ASH guideline panel suggests using matched related allogeneic transplantation over standard of care.
R4	For patients with SCD with an indication for HSCT who lack an MSD, the ASH guideline panel suggests using transplants from alternative donors in the context of a clinical trial.
R5	For allogeneic HSCT, the ASH guideline panel suggests using either total body irradiation (TBI) ≤ 400 cGy or chemotherapy-based conditioning regimens.
R6	a. For children with SCD who have an indication for allogeneic HSCT and an MSD, the ASH guideline panel suggests using myeloablative conditioning over RIC that contains melphalan/fludarabine regimen. b. For adults with SCD who have an indication for allogeneic HSCT and an MSD, the ASH guideline panel suggests nonmyeloablative conditioning over RIC that contains melphalan/fludarabine regimens.
R7	In patients with an indication eligible for HSCT, the ASH guideline panel suggests using allogeneic transplantation at an earlier age rather than an older age.
R8	The ASH guideline panel suggests the use of HLA-identical sibling cord blood when available (and associated with an adequate cord blood cell dose and good viability) over bone marrow (BM).

Sickle : HSCT Outcomes

- EBMT + CIBMTR
- 1,000 patients
- MSD 87%
- MAC 87%
- BM 84%
- 5-year EFS 91.4% (89.6%–93.3%)
OS 92.9% (91.1%–94.6%)
- GF : 23 pts
- Died of sepsis 7%
- Every 1 yr increment
- HR increases
 - GVHD – 4%
 - GF/Death – 10%
- Age > 16 yr
 - cGVHD – 2% increase HR
- **Early HSCT for symptomatic pts with MSD**
- **HSCT complications can exacerbate SCD-related organ damage**

Conditioning : Sickle

MAC: Bu+Cy+ATG

Bu+Flu+TT

Treo+Flu+TT

Younger patients !

Table 3. Myeloablative Conditioning Regimen in Patients With SCD.

	No.	Age range (years)	Graft source (N)	Donor (N)	Conditioning regimen	GvHD prophylaxis	Acute GvHD (grade II-IV)	Chronic GvHD	OS %	EFS %
Bernaudin et al. ²⁴	87	2-22	BM: 74 PB:1 UCB: 12	MRD	MAC: BU + CY ± ATG	CSA± MTX	20%	Limited: 11% Extensive: 2.4%	6 years: 93.1%	6 years: 86.1%
Panepinto et al. ²⁵	67	2-27	BM: 54 PB:9 UCB: 4	MRD	MAC: BU+CY	CSA+ MTX Tacrolimus T cell depletion Non	10%	22% Limited:9 patients Extensive: 3 patients	5 years: 97%	5 years: 85%
Strocchio et al. ²⁶	30	1.7-18.8	BM: 22 PB:1 UCB: 4 BM + UCB: 3	MRD: 24 MUD: 6	MAC: BU+Thio+Flu Treo+Thio+Flu ± ATG	CSA± MTX	7% in the Bu- and 0% in the Treo-group	7% in the Bu- and 0% in the Treo- group	100%	5-years: 93% MRD: 96% MUD: 83%
Krishnamurti et al. ²⁷	22	17-36	BM	MRD: 17 MUD: 5	MAC: BU+ Flu+ATG	CNI+MTX	18%	27%	1 year: 91% MRD: 94% MUD: 80%	1 year: 86% MRD: 94% MUD: 60%
Kogel et al. ²⁸	25	1-21	BM: 21 PB: 4	MRD: 17 MUD: 8	MAC: BU+CY Flu+Thio+Treo Flu+Thio+Alk	CSA + MTX CSA + MMF CSA Tacrolimus+MTX CSA + MMF+MTX	grade I-II: 8 patients	No	100%	88%
Dedeken et al. ²⁹	50	1.7-15.3	BM: 39 PB:1 UCB: 3 BM + UCB: 7	MRD	MAC: BU+CY± ATG	CSA + MTX CSA CSA+MMF	grade I-II: 12% grade III-IV: 10%	Mild in 10 patients	8 years: 94.1%	8 years: 85.6%
Bernaudin et al. ³⁰	234	2.2-28.9	BM: 195 PB:1 UCB: 30 BM + UCB: 8	MRD	MAC: BU+CY± ATG	CSA± MTX	20.1%	10.5%	97%	93.9%

Conditioning : Sickle – Role of RIC / NMA

- Adults
- SCD-mediated tissue damage endothelial activation inflammation
- Flu + Mel + TT/TLI
- Bu(2) + Flu + ATG +TLI
- Alem + TBI (300cGy)
- Target : Stable mixed chimerism

Table 4. Nonmyeloablative/RIC Conditioning Regimen in Patients With SCD.

	No.	Age range (years)	Graft source	Donor	Conditioning regimen	GvHD prophylaxis	Acute GvHD (grade II–IV)	Chronic GvHD	OS %	EFS %
Hsieh et al. ³⁷	30	17–65	PB	MRD	NMA: Alemtuzumab+TBI	Sirolimus	No	No	97%	87%
Saraf et al. ³⁵	13	17–40	PB	MRD	NMA: Alemtuzumab+TBI	Sirolimus	No	No	100%	92%
Al-Zahrani et al. ³⁶	18	14–39	PB	MRD	NMA: Alemtuzumab+TBI	Sirolimus	No	No	100%	88.9%
Ozdogu et al. ³¹	20	20–45	PB	MRD	NMA: Flu+CY+BU+TBI+ATG	Sirolimus	5%	No	100%	100%
Alzahrani et al. ³⁸	110	14–43	PB	MRD	NMA: Alemtuzumab+TBI	Sirolimus	skin grade I–II in 3 patients	NO	97%	87.3%
Krishnamurti et al. ³³	7	6–18	BM	MSD	RIC: BU(2)+Flu+ATG+TLI	CSA+MMF	Skin grade II in 1 patient	Limited skin in 1 patient	100%	86%

Sickle : Alternate donor

- T deplete and replete

- PTIS

- Lower EFS

Table 5. Haploidentical Hematopoietic Stem Cell Transplantation in Patients With SCD.

	No.	Age range (years)	Graft source (N)	Donor	Conditioning regimen	GvHD prophylaxis	Acute GvHD (grade II–IV)	Chronic GvHD	OS %	EFS %
Pawłowska et al. ⁴⁵	4	12–24	BM: 3 PB: 1	Haploidentical	BU+CY+ATG	PTCy+ Tacrolimus+ MMF	grade I GI in 1 patient.	Limited skin in 3 patients.	100%	100%
Foell et al. ⁴⁶	9	3–31	PB (CD3±CD19+ depleted)	Haploidentical	Flu+Thio+Treo+ATG	CSA+MMF	grade I–II: 56%	Moderate in 1 patient.	88%	88%
Cairo et al. ⁴⁴	19	3.3–20	PB(CD34+ selected)	Haploidentical	BU+CY+Thio+Flu+ATG+TLI	-	6.2%	6.7%	84%	84%
Wiebking et al. ⁴⁷	3	5–20	BM	Haploidentical	Alemtuzumab+Treo+Thio+Flu+CY	PTCy+ Tacrolimus+ MMF	grade I in 1 patient.	No	100%	100%
Foell et al. ¹²	25	3–31	PB: CD3/CD19-depleted (n = 19), TCRaβ/CD19-depleted (n = 6)	Haploidentical	Treo+Thio+Flu+ATG	CSA+MMF (12 patients)	grade I–II: 28%	16%	88%	88%
Frangoul et al. ⁴⁸	4	12.1–23.5	BM: 3 PB: 1	Haploidentical	Thio+Flu+ATG+CY+TBI	Sirolimus+ MMF	grade II: 100%	No	100%	100%
Bolaños-Meade et al. ⁴³	14	15–42	BM	Haploidentical	Flu+CY +ATG +TBI	PTCy+ Tacrolimus+ MMF	No	No	100%	57%
Fitzhugh et al. ¹³	12	20–56	PB	Haploidentical	Alemtuzumab +TBI	PTCy+ Sirolimus	grade I in 1 patient.	Limited ocular in 1 patient.	92%	50%
de la Fuente et al. ⁴⁹	15	7–40	BM	Haploidentical	NMA: Flu+CY+ Thio+ATG+TBI	PTCy+ Sirolimus+ MMF	grade III–IV in 2 patients.	Mild in 1 patient.	100%	93%
Saraf et al. ³⁹	8	20–38	PB	Haploidentical	Flu+CY+ Thio+ATG+TBI	PTCy+ Sirolimus+ MMF	grade II–IV in 2 patients.	Moderate in 1 patient.	87.7%	75%
Gluckman et al. ¹¹	144	Children (<16 y): 114 Adults (>16 y): 30	BM: 100 PB: 38 UCB: 6	MUD: 70 UCB: 6 Haploidentical: 68	Flu+Thio+Treo Flu+CY+Thio+TBI Bu+CY Flu+Mel+Thio ATG Alemtuzumab Ex vivo T-cell depleted or PTCy (Haploidentical)	CSA + MTX MMF + Sirolimus CSA + MMF Tacrolimus + MMF	24%	24%; Limited: 13 patients Extensive: 18 patients.	86% ± 3%;	72% ± 4%
Kharya et al. ⁵⁰	25	1–27	PB	MRD	PTIS AND Thio+Flu+ATG+CY+TBI	PTCy+ Sirolimus+ MMF	20%	Limited in 3 patients (skin, oral cavity and Liver)	88%	88%

Cellular Therapy

Efficacy and Safety of Allogeneic Hematopoietic Stem Cell Transplantation in Curing Sickle Cell Disease: A Systematic Review and Meta-Analysis of Single-Arm Studies

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- 58 studies (n=7931)
- OS 94%
- EFS 86%
- aGVHD 20%
- cGVHD 14%
- GF 9%
- Mortality 6%

Main factors affecting outcomes

Subgroup Analysis

Variable	Subgroup	Overall Survival			Event-Free Survival			Graft Failure			aGVHD			cGVHD			Mortality		
		Studies (n)	Event rate (%)	Difference (p-value)	Studies (n)	Event rate (%)	Difference (p-value)	Studies (n)	Event rate (%)	Difference (p-value)	Studies (n)	Event rate (%)	Difference (p-value)	Studies (n)	Event rate (%)	Difference (p-value)	Studies (n)	Event rate (%)	Difference (p-value)
Age	Pediatrics	16	94	0.3637	14	87	0.6970	13	7	0.6596	15	29	0.0284	14	15	0.1145	15	5	0.2677
	Adults	4	91		3	90		3	10		3	9		3	5		4	9	
Stem cell source	BMSC	17	93	0.4496	18	86	0.5060	18	10	0.9397	18	23	0.0011	17	12	0.0115	17	8	0.1566
	PBSC	12	94		9	88		11	10		10	7		10	3		12	6	
Conditioning regimen	MAC	20	94	0.1981	22	90	0.2497	20	5	0.0146	20	25	0.0218	20	14	0.0042	20	6	0.2233
	NMA	15	95		12	86		14	12		13	10		13	4		15	4	
	RIC	6	91		7	87		6	7		6	26		5	25		6	11	
Donor type	Haplo	7	92	0.0296	8	79	0.0224	8	16	0.0025	7	21	0.3336	7	15	0.0163	7	9	0.0404
	MRD	27	94		24	91		25	6		24	16		23	8		27	6	
	URD	2	87		n/a	n/a		2	14		2	24		2	40		2	16	
Year of publication	2010-2016	17	92	0.4393	17	86	0.7792	16	10	0.7236	15	23	0.4278	15	12	0.5875	17	8	0.4556
	2017-2025	40	94		34	87		36	9		37	19		35	14		39	6	

BM indicates bone marrow, PB = peripheral blood, NMA = non-myeloablative conditioning, MAC = myeloablative conditioning, RIC = reduced-intensity conditioning, MRD = matched related donor, Haplo = haploidentical donor, URD = unrelated donor, n/a = not available.

Sickle HSCT outcomes

Reversal and Improvement

- Vaso-occlusive crises (pain crises)
- Acute chest syndrome and transfusion dependence
- Chronic hemolysis
- Splenic function
- Prevention of new organ
- Quality of life and patient-reported

What often does not reverse fully

- Established ischemic brain injury (prior large infarcts) and fixed neurologic
- Avascular necrosis & established osteonecrosis
- Retinopathy
- Established pulmonary hypertension or severe chronic lung disease
- Established chronic kidney disease

Summary

- Common indication in India
- Excellent outcomes

- Early MSD HSCT
- Conditioning – RTC – Treo to reduce SOS
- Pre transplant preparation – esp in MUD / HAPLO
- PTCy or T deplete – both good outcomes; specific advantages

- Mainstay of curative treatment till Gene therapy established & accessible

Quiz 1

- In patients with **sickle cell disease (SCD)** post-HSCT, which level and lineage of donor chimerism is generally sufficient to **abrogate the sickle phenotype**?
 - A. $\geq 95\%$ whole blood donor chimerism
 - B. $\geq 80\%$ lymphoid donor chimerism alone
 - C. $\geq 20\text{--}25\%$ donor myeloid chimerism
 - D. Any detectable donor chimerism
 - E. Full donor erythroid chimerism only

Quiz 2

- Which of the following statements regarding **haploidentical HSCT for hemoglobinopathies** is **most accurate**?
- A. Outcomes are inferior to matched sibling transplants regardless of platform
- B. Post-transplant cyclophosphamide (PTCy) eliminates graft failure risk
- C. T-cell–depleted platforms have lower graft rejection than PTCy in thalassemia
- D. Graft rejection remains a key challenge, particularly in heavily transfused patients
- E. GVHD is the major cause of mortality in modern haploidentical transplants

Thank you !

