Creating a Culture of Measuring What Matters : From Outcomes to Accountability

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Designation: Professor, Haematology

Organization: CMC Vellore

Data collection → Reduce risks → Reduced mortality

> "Outcome measurement is the single most important tool to drive innovation in health care delivery."
> Porter (2010)

Ethical behavior → Culture of responsibility → Patient centric decisions

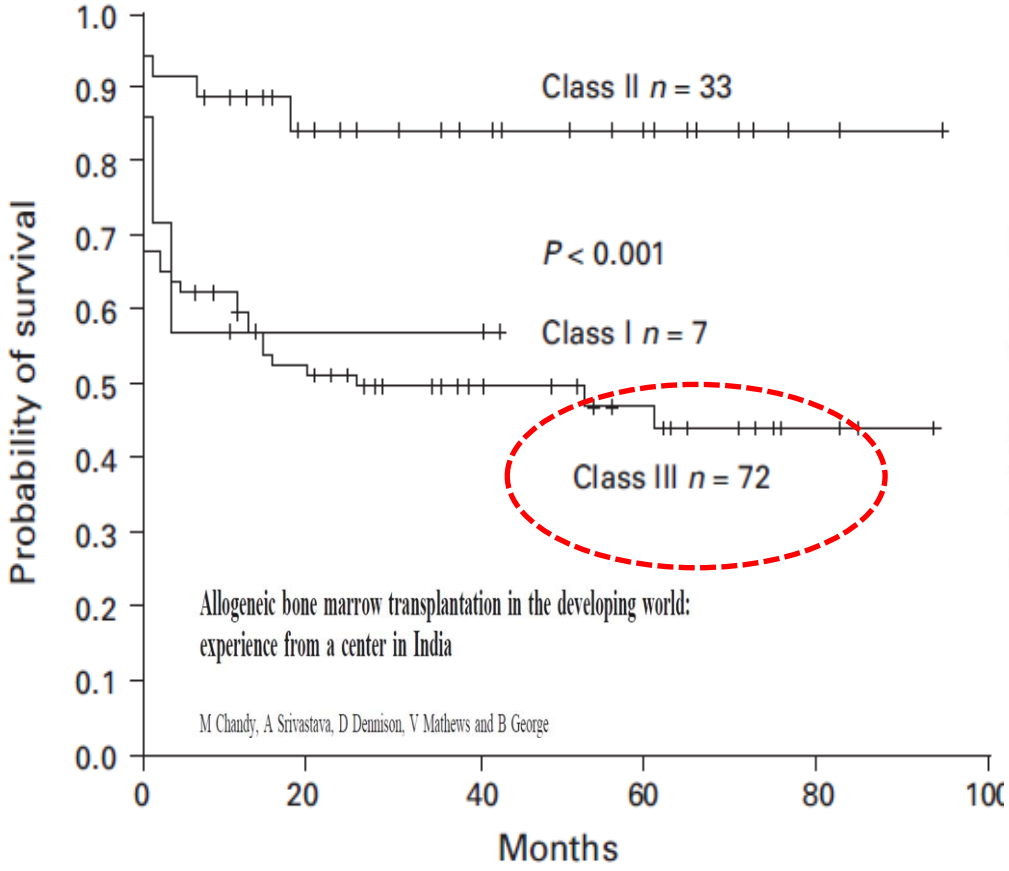
Cost effective treatment

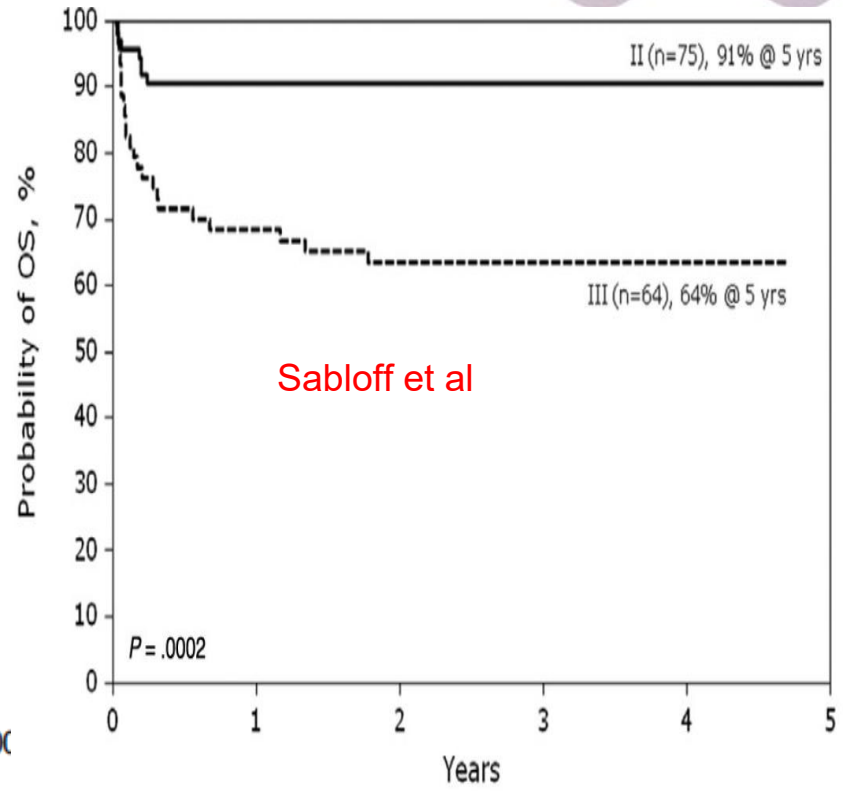
OUTCOMES

BMT in CMC started in 1986

BMT for Thalassemia in 1991

Analysis of data 2001





Sabloff et al

Figure 3. Probability of OS by Pesaro risk class.

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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

PLOS ONE 2013

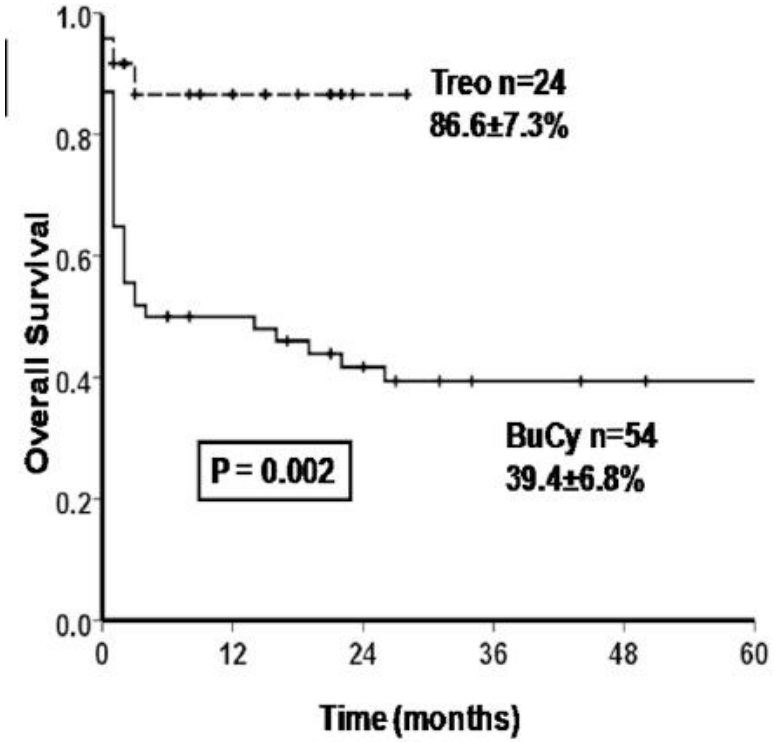
Vikram Mathews*, Biju George, Auro Viswabandya, Aby Abraham, Rayaz Ahmed, Abhijeet Ganapule, Eunice Sindhuvi, Kavitha M. Lakshmi, Alok Srivastava

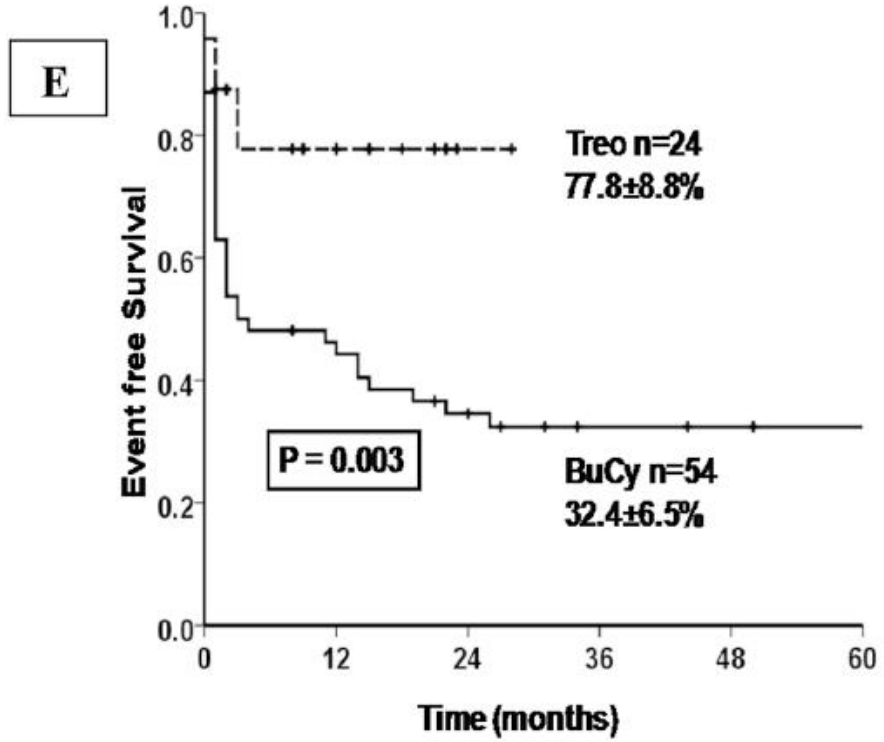
Department of Haematology, Christian Medical College, Vellore, India

Needed to find better treatment for Class III

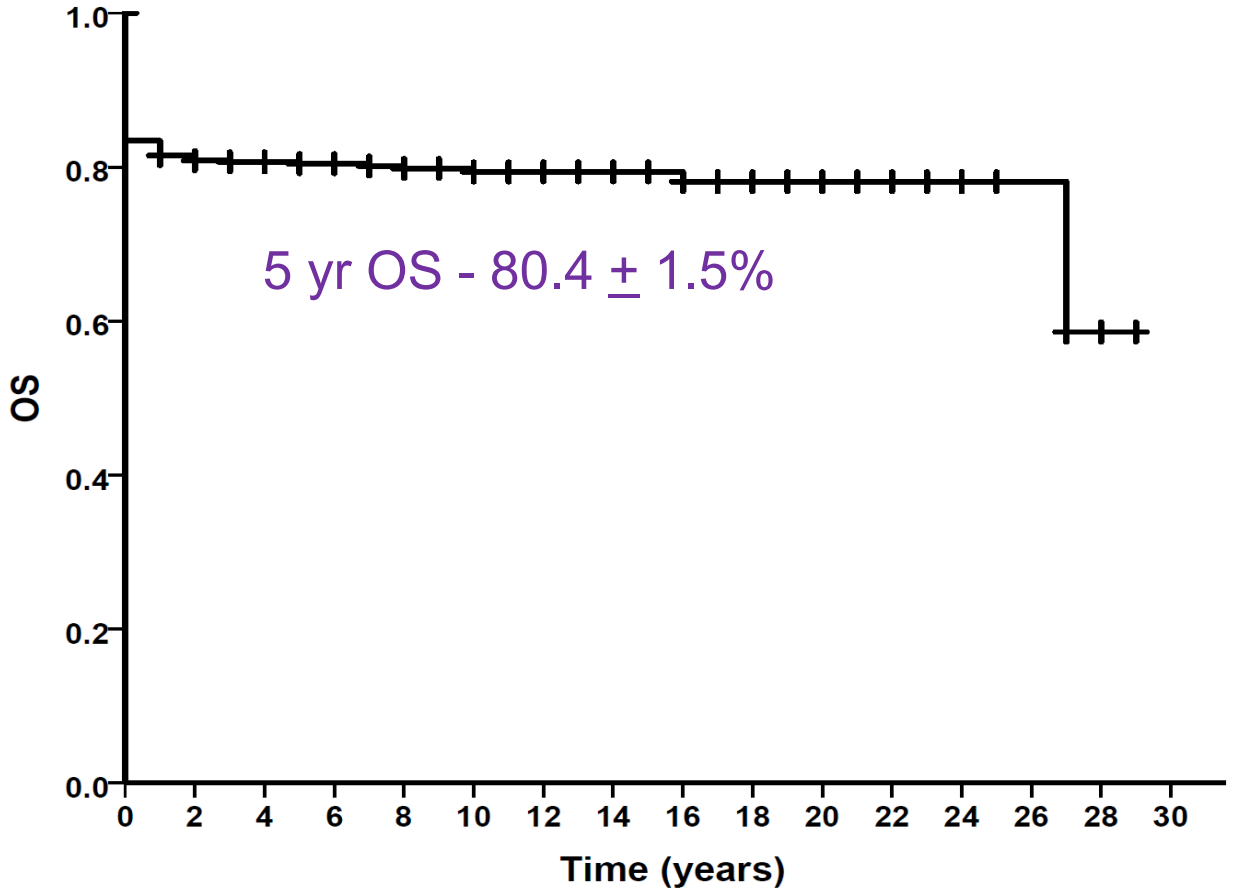
Analysed mortality - mainly RRT.

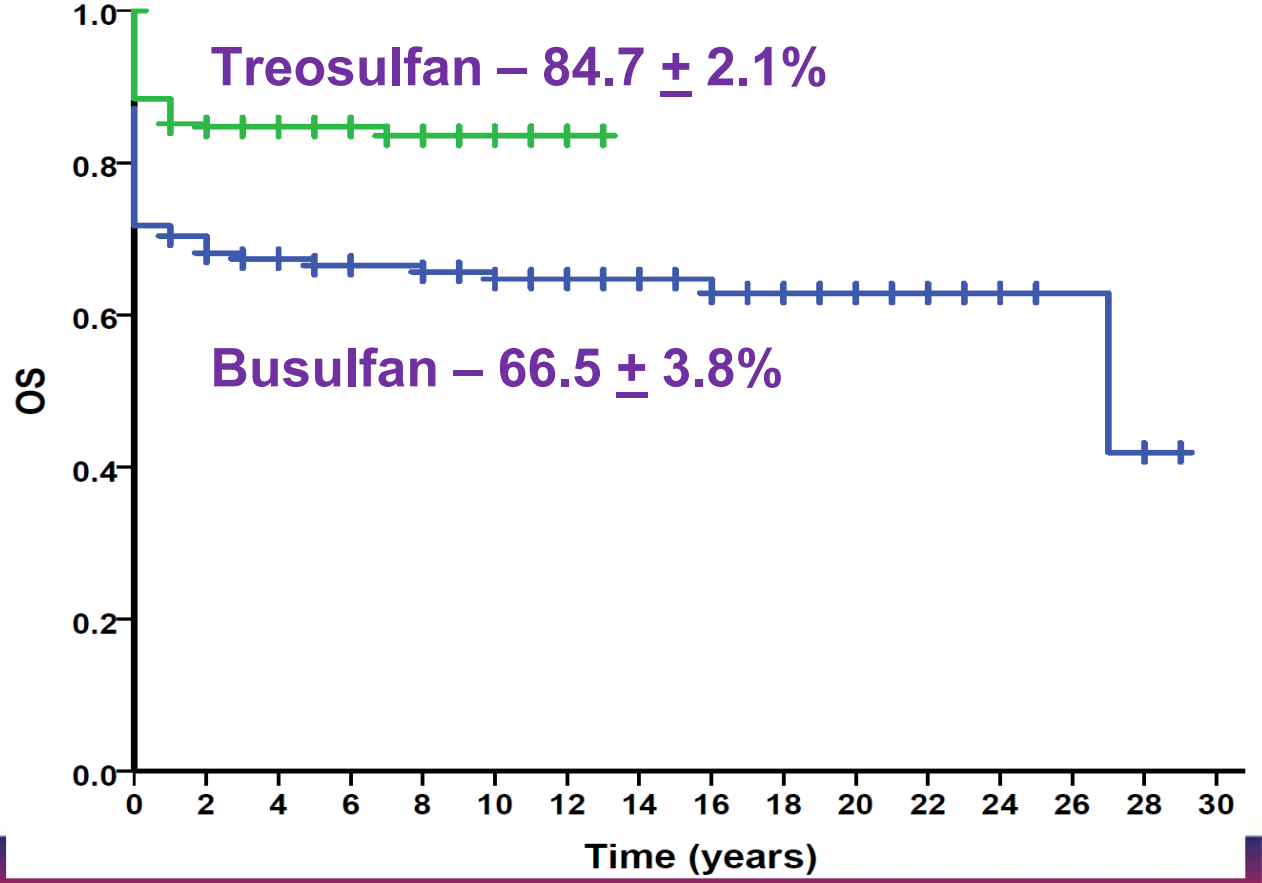
Designed new regimen using Treosulfan instead of Busulfan

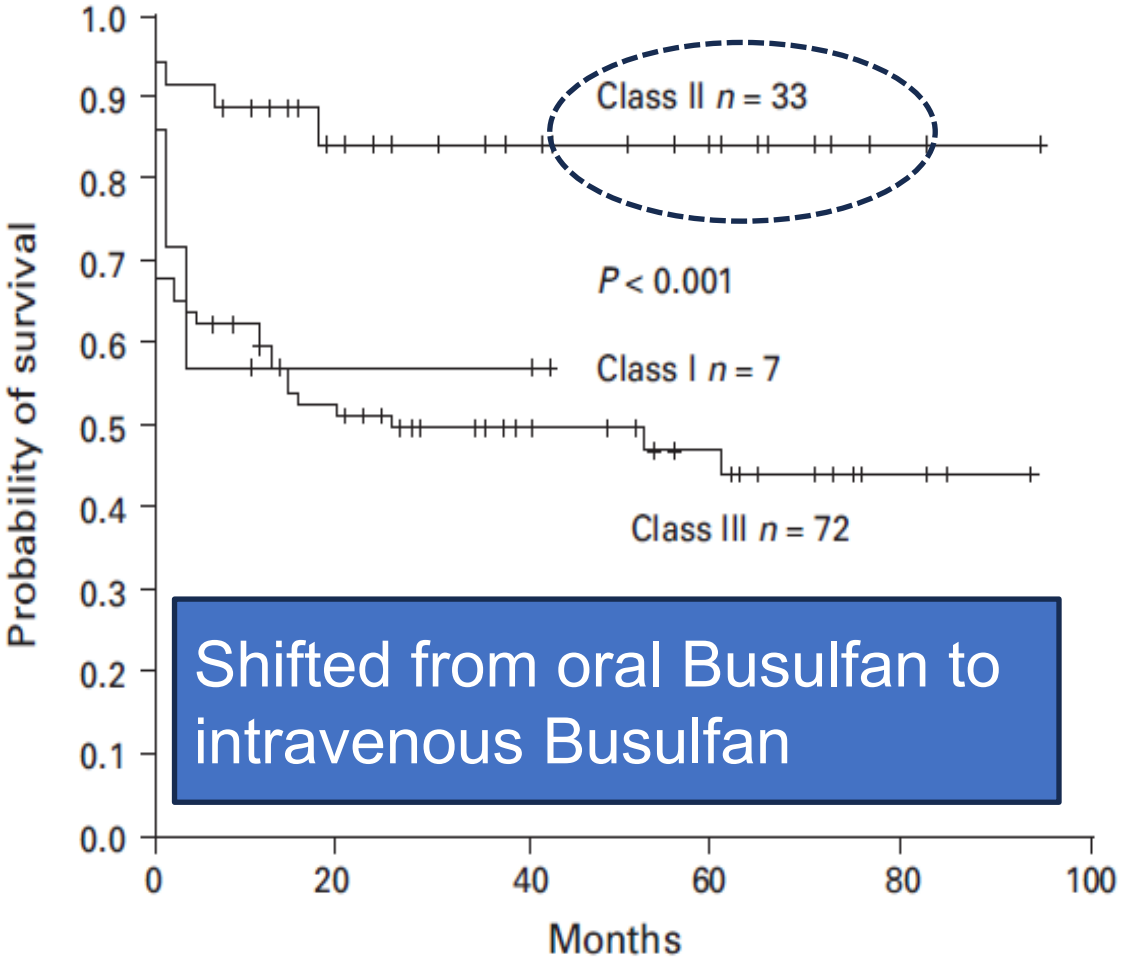




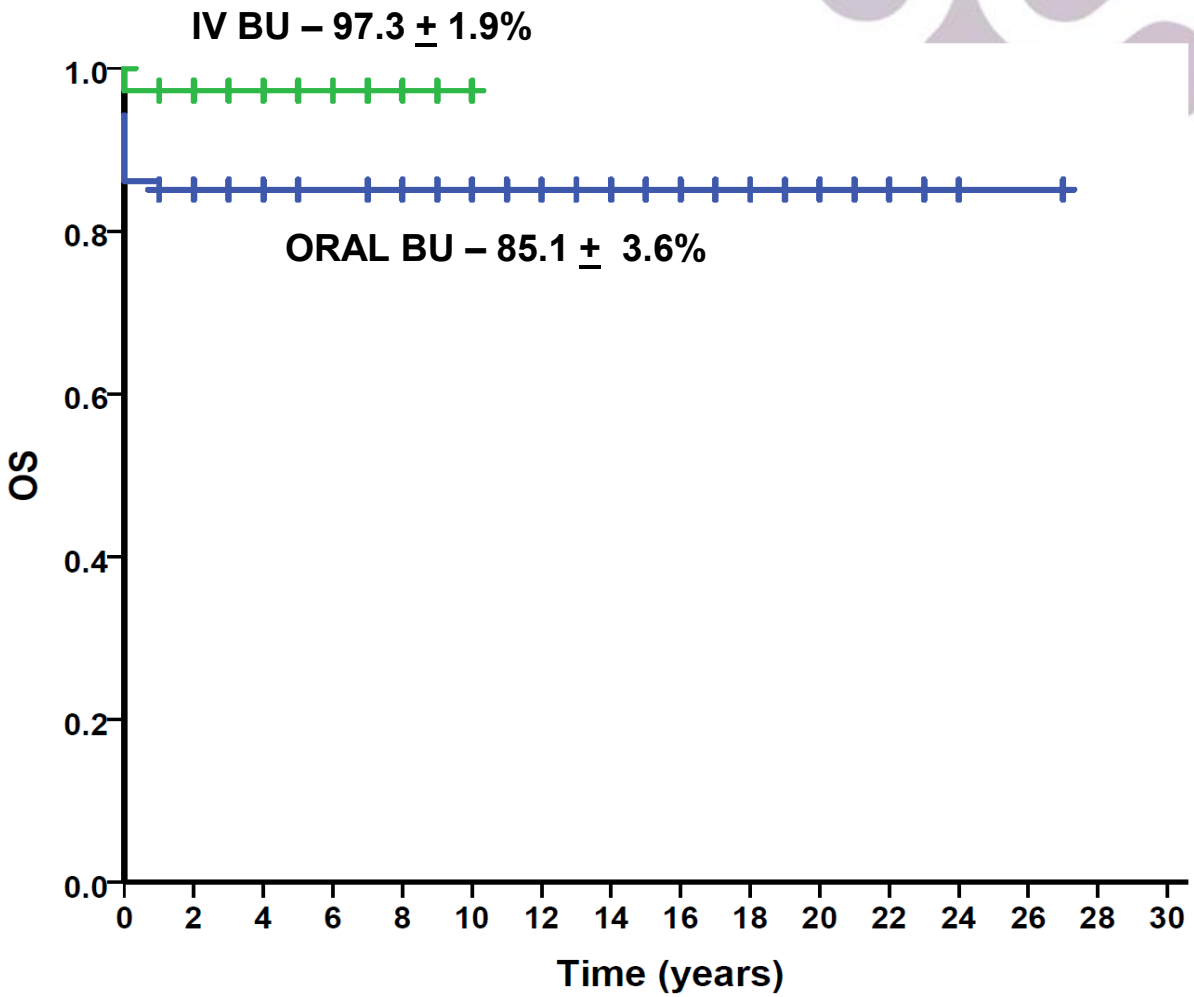
Overall Survival outcomes for Thalassemia between 1990 – 2025 [n = 743]







Shifted from oral Busulfan to intravenous Busulfan

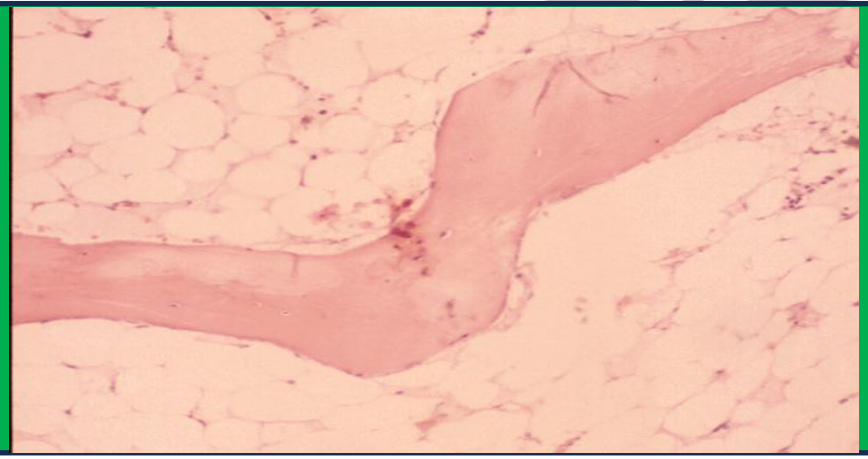


AA – characterized by pancytopenia + empty marrow.

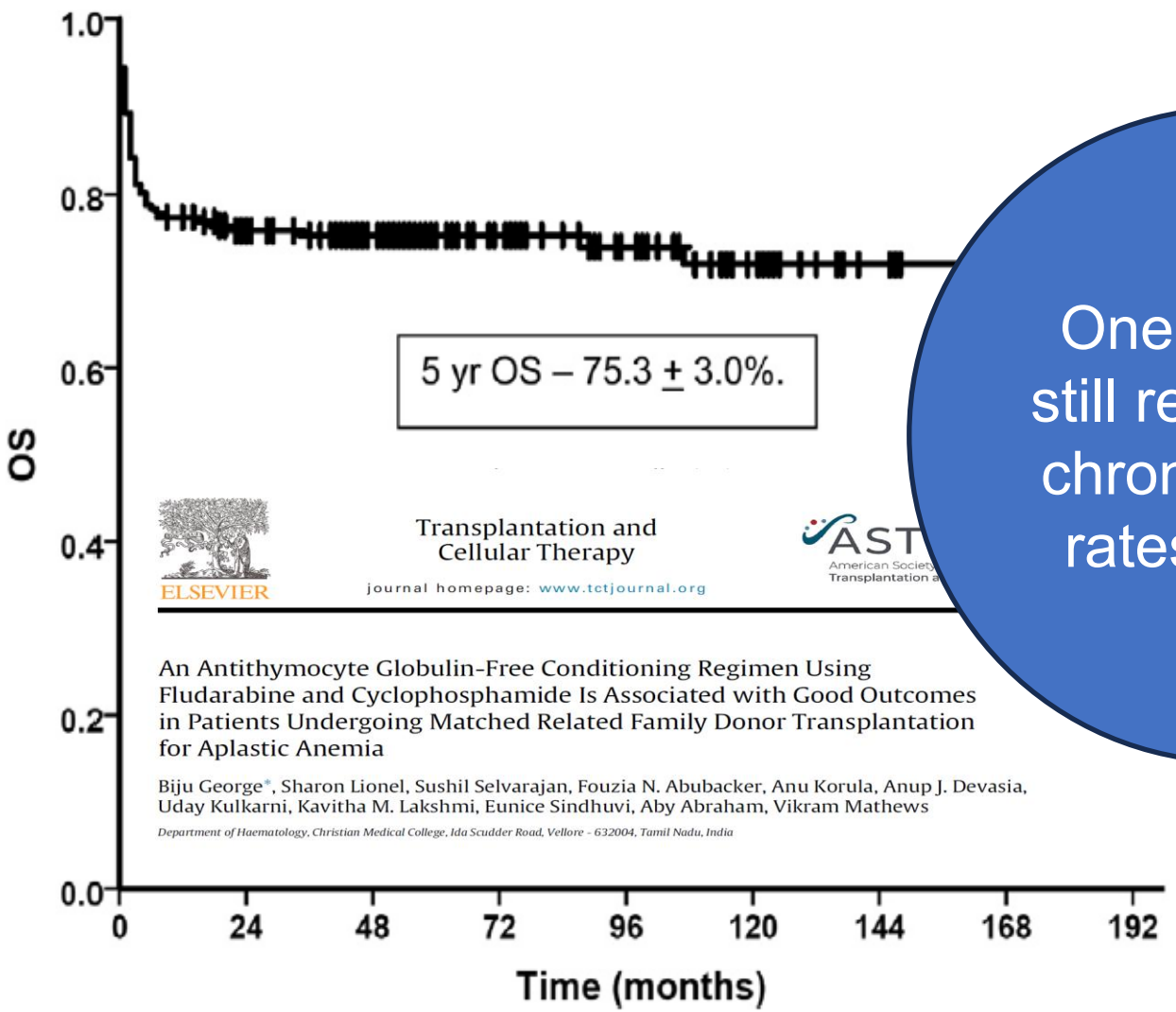
C/F - severe anemia, bleeding and infections.

80% of patients with SAA die within 1 year of Dx

First BMT in 1990



Conditioning regimen	Graft	Rejection	GVHD	Survival
Cy alone or Cy/ATG (26)	BM	26.3%	35%	52.8%
Flu/Bu/ATG (19)	PBSC 17 BM 2	10.5%	40%	57.8%
Flu/Cy (260)	PBSC 159 BM 11	4.1%	36.5%	75.1%



Transplantation and Cellular Therapy

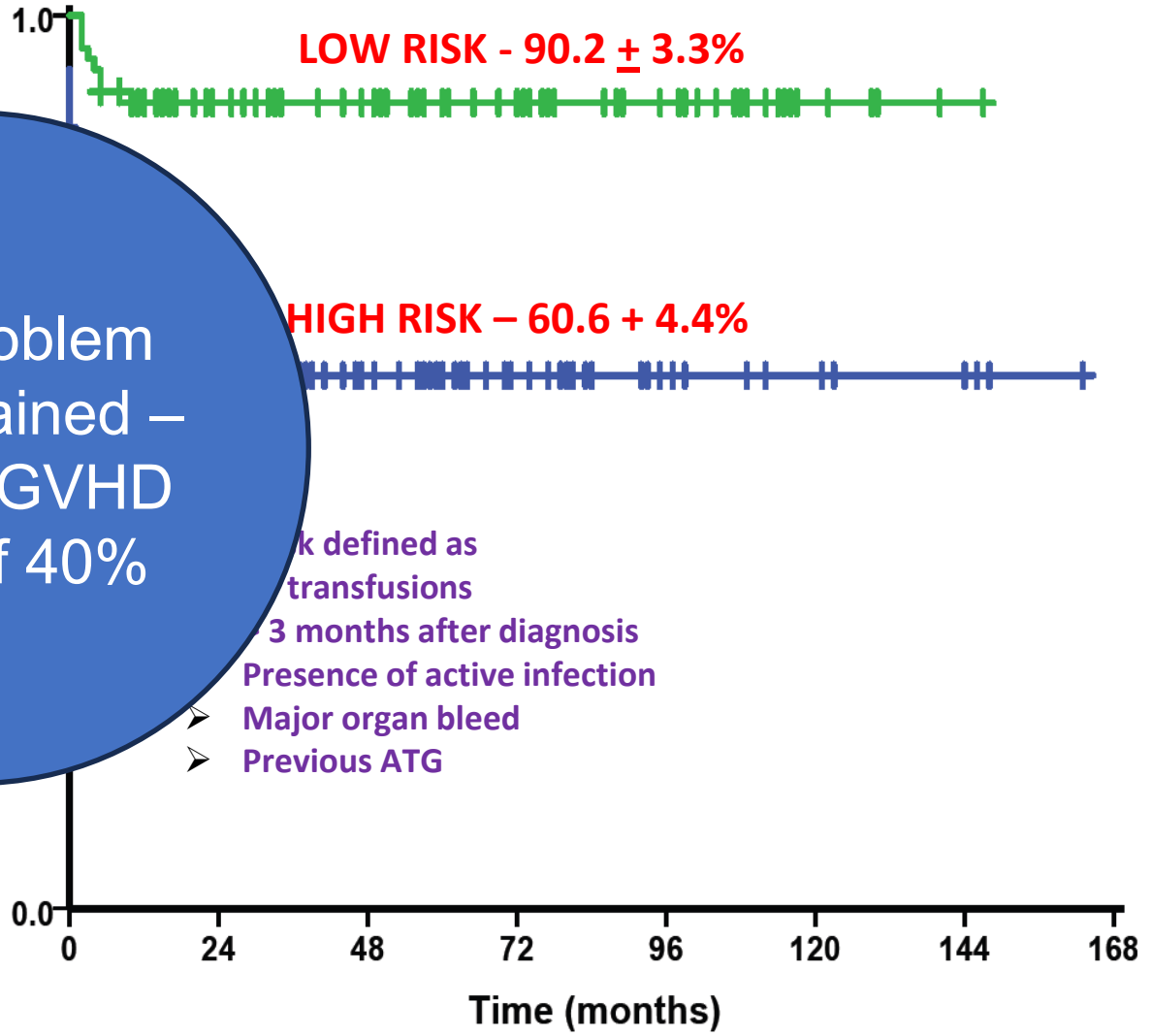
journal homepage: www.tctjournal.org

An Antithymocyte Globulin-Free Conditioning Regimen Using Fludarabine and Cyclophosphamide Is Associated with Good Outcomes in Patients Undergoing Matched Related Family Donor Transplantation for Aplastic Anemia

Biju George*, Sharon Lionel, Sushil Selvarajan, Fouzia N. Abubacker, Anu Korula, Anup J. Devasia, Uday Kulkarni, Kavitha M. Lakshmi, Eunice Sindhuvi, Aby Abraham, Vikram Mathews

Department of Haematology, Christian Medical College, Ida Scudder Road, Vellore - 632004, Tamil Nadu, India

One problem still remained – chronic GVHD rates of 40%



- k defined as
- transfusions
- 3 months after diagnosis
- Presence of active infection
- Major organ bleed
- Previous ATG

Table 4
Comparison of GVHD, Infections, and OS in Patients Receiving PTCY or Cyclosprine/MTX for GVHD Prophylaxis

Variables	MTX10 group	MTX15 group	PTCY group	*P*
Grades II-IV acute GVHD, %	53.8	37.1	22.2	.056
Grades III-IV acute GVHD, %	42.3*	11.1	11.1	.013*
No. assessable chronic GVHD	21	22	22	
CI of chronic GVHD, %	76.2*	63.6†	22.7	.0007* .013†
Median immunosuppression use, mo (range)	36.6 (9-82)	16.6 (8-34)	1.43 (0-7)	.000
NIH score for chronic GVHD				
Mild	2	8	2	
Moderate	10	6	3	.0005*
Severe	4	0	0	.456†
CI of moderate + severe, %	66.6*	27.2†	13.6	
Infections				
Bacterial	12 (40%)	6 (20%)	9 (30%)	.588
Viral	10 (33.3%)	7 (23.3%)	18 (60%)	.008
2-year OS, %, mean ± SD	69 ± 8.6	63.9 ± 9.5	65.9 ± 8.8	.922
2-year event-free survival, %, mean ± SD	3.3 ± 3.3%	12.7 ± 6.6%	42 + 9.3%	.000
Causes of death				
GVHD	3 (33.3%)	2 (20%)	2 (20%)	
Bacterial infection	6 (66.7%)	6 (60%)	1 (10%)	
Viral infections	0	0	4 (40%)	
Rejection	0	2 (20%)	2 (20%)	
Others	0	0	1 (10%) (candida)	

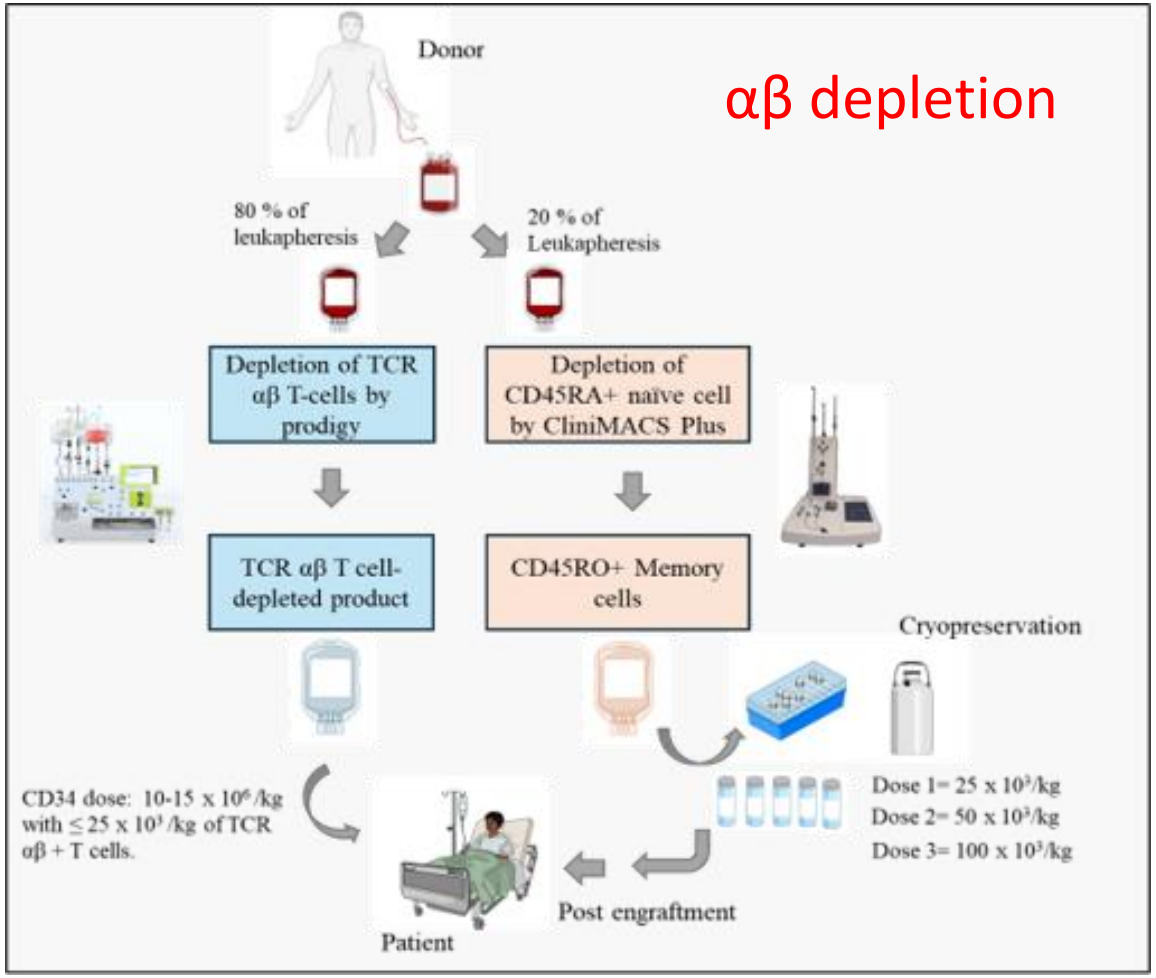
RCT comparing PTCy with CSA/MTx as GVHD prophylaxis

Clinical Trial Details (PDF Generation Date :- Wed, 19 Jun 2019 09:12:26 GMT)

CTRI Number	CTRI/2019/06/019765 [Registered on: 19/06/2019] - **Trial Registered Prospectively**
Last Modified On	19/06/2019
Post Graduate Thesis	No
Type of Trial	Interventional
Type of Study	Drug
Study Design	Non-randomized, Active Controlled Trial
Public Title of Study	Methods to reduce GVHD after bone marrow transplant for aplastic anemia
Scientific Title of Study	A randomized controlled trial comparing post transplant cyclophosphamide (PTCy) with cyclosporine and methotrexate (CM) as graft versus host disease (GVHD) prophylaxis and “early” versus “late” cyclophosphamide administration in patients undergoing matched sibling donor transplantation (SCT) for aplastic anemia.

Haplo-identical SCT – only 50% match needed.

Standard Rx approach more difficult in older pts - mortality



20 pts done
Mean age – 59 yrs
oldest 74 years

Survival presently 60% compared to 30% with standard approach.

Early 2000s

APML was a killer disease with 60 - 80% mortality

ATRA + chemo only Rx

Cost 10 – 12 lakhs

Reports from Varanasi about arsenic being used to treat

Obtained industrial grade arsenic – converted in Pharmacy to pharmaceutic grade

Obtained support from ICMR to conduct first clinical trial

Single-agent arsenic trioxide in the treatment of newly diagnosed acute promyelocytic leukemia: durable remissions with minimal toxicity

Handed over technology to a Pharma company to produce large scale arsenic – keep is cost effective for Indian patients

Cost of generic arsenic – Rs 400

In the word – 100 USD [Rs 6500]

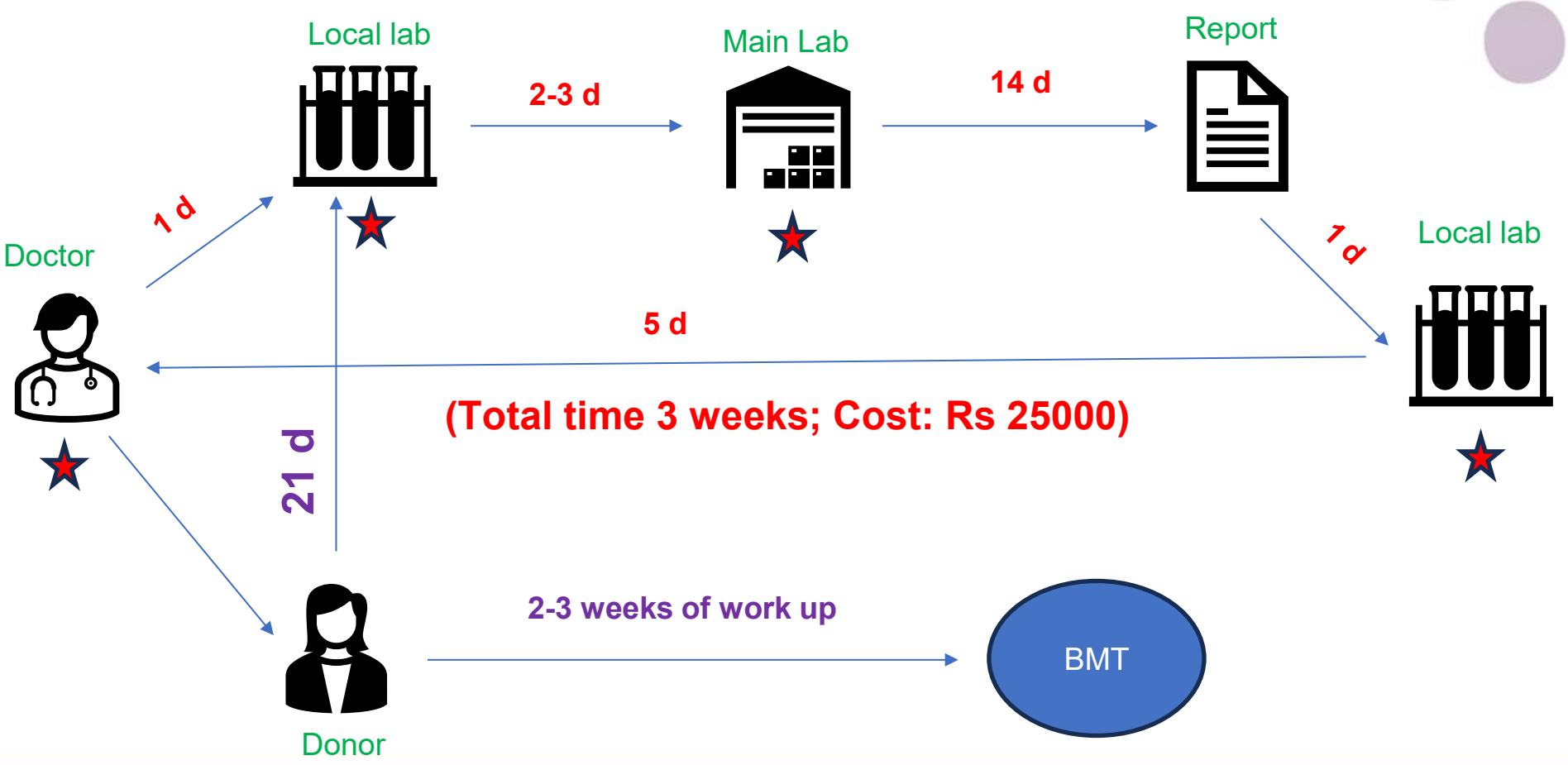
Second in the world to use arsenic for APML

Accountability occurs at multiple steps in a healthcare ecosystem

30 yr male SAA c/f - Has lung and liver fibrosis Suspecting DKC

Has fully matched brother for SCT

Need to send NGS to r/o DKC



Accountability - Timely accurate reporting and then appropriate action !!!

30 yr male SAA
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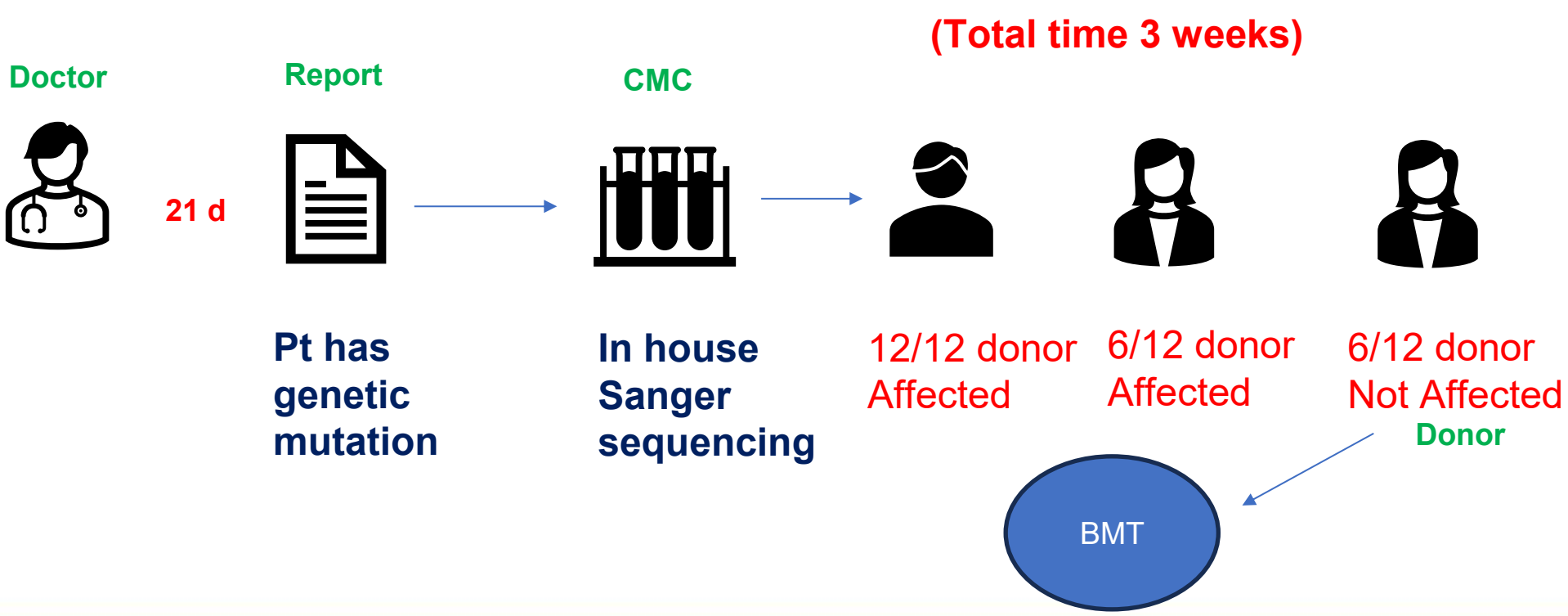

5 patients with transfusion dependent anemia and low blood counts – hypocellular bone marrow with fibrosis in BM– referred for BMT – NGS sent

MOLECULAR ANALYSIS BY NEXT-GENERATION SEQUENCING

Test Code	-
Test Category	Screening of multiple genes involved in germline predisposition to hematological malignancies by a focussed exome panel NGS
Sample type	Bone marrow in EDTA
Clinical Details	Triple-negative MPN - (Myelofibrosis)

NGS Result Summary

Gene/Transcript	CDS Variant	Amino acid/Exon	Mode of Inheritance	Zygosity	OMIM Phenotype	Clinical Significance
TBXAS1 (ENST00000448866.7)	c.1235G>A	p.Arg412Gln (Exon 11)	Autosomal Recessive	Homozygous	Ghosal hematodiaphyseal dysplasia (GHDD) (OMIM# 231095)	Likely Pathogenic

This mutation causes disturbances in the arachadonic acid pathway and is amenable to treatment with low dose aspirin

Date	11-04-2023	17-04-2023	25-04-2023	01-05-2023	08-05-2023	15-05-2023	22-05-2023	29-05-2023	25-07-2023	12-02-2024	25-06-2024
Hb Gm%	4.9	7.3	6.2	7.2	6.3	6.3	5.2	5.6	6.4	16.6	17.7
Retics %											
Total	5500		9900	9300		11200	9600	11800	8800	4600	5200
Blasts											
Promyelo / Myelocyte			- 12			-	-	-	-	-	-
Metamyelo / Bandforms			01 -			-	-	-	-	-	-
Neutrophils			52			42	47	44	64	39	45
Lymphocytes			29			53	50	51	29	53	47
Eosinophils / Basophils			1 - 2			1 - 0	0 - 0	1 - 0	1 - 0	1 - 0	1 - 0
Monocytes			3			4	3	4	6	7	7
NRBC			40/ 100 WBC						12.1	0.0	0.0
ANC			5148			4704	4512	5192	5632	1794	2340
Platelets /CU MM	29000		27000	28000	26000	22000	19000	19000	34000	122000	157000

CONCLUSIONS

- Studying outcomes are an important part of quality management.
- Helps in improving treatment pathways and ultimately patient survival
- Accountability is important for improving pathway care and ensuring appropriate times for providing diagnosis and treatment

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