



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

*Name: Dr. Biju George*

*Designation: Professor, Haematology*

*Organization: CMC Vellore*



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



Cost effective treatment

**OUTCOMES**

BMT in CMC started in 1986

BMT for Thalassemia in 1991

Analysis of data 2001

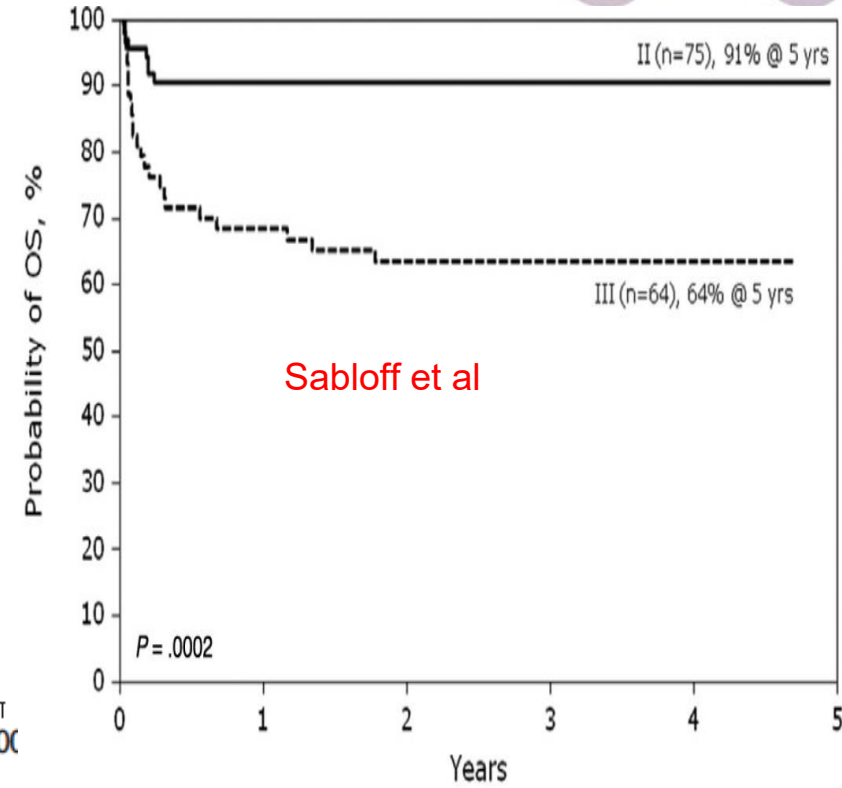
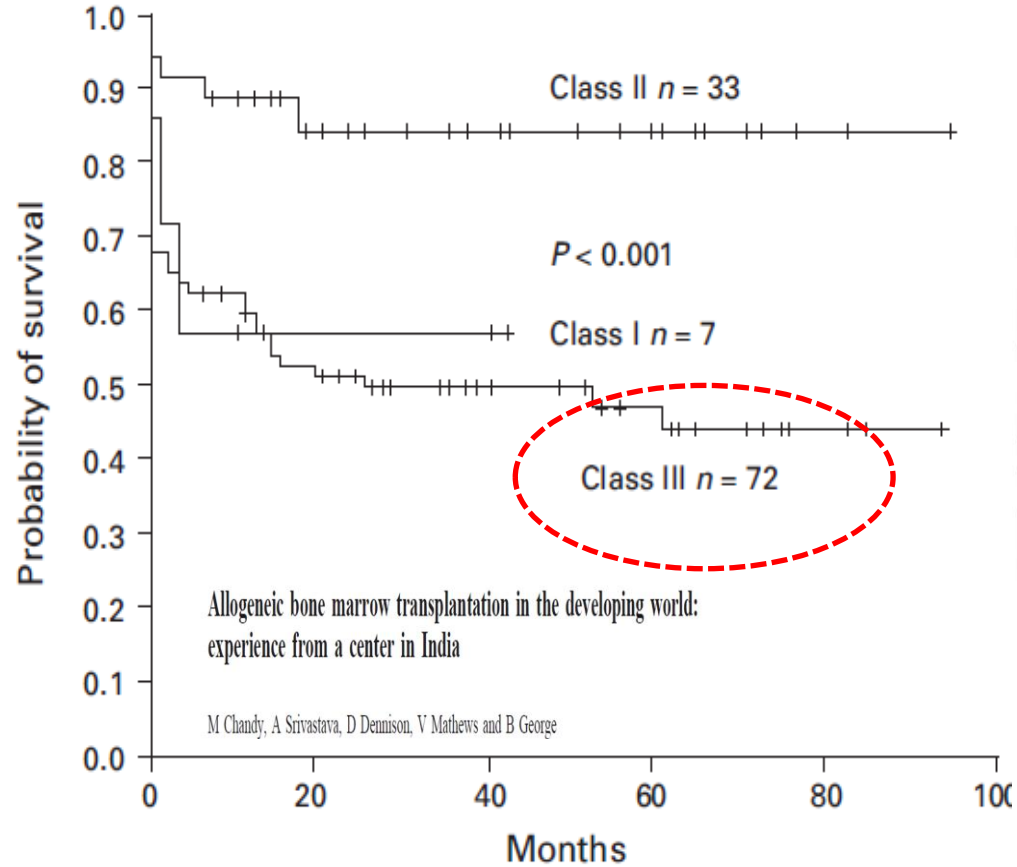


Figure 3. Probability of OS by Pesaro risk class.

# Improved Clinical Outcomes of High Risk $\beta$ 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*

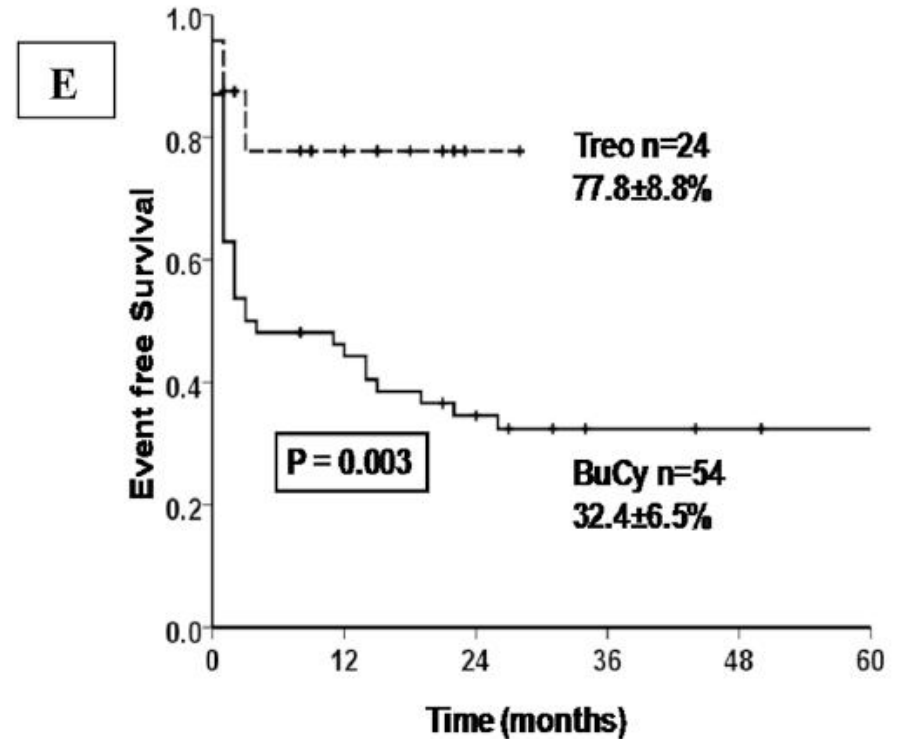
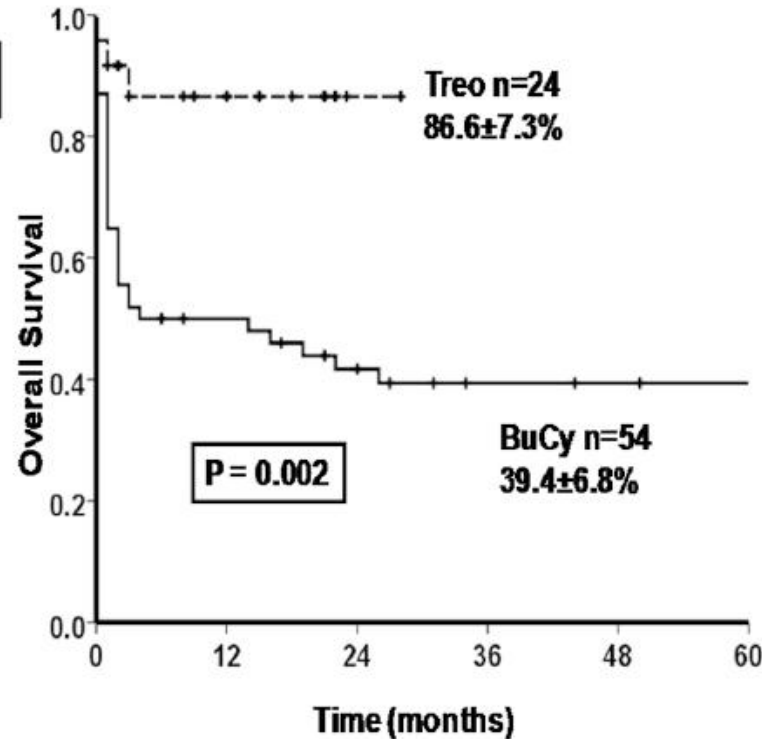
Vikram Mathews\*, Biju George, Auro Viswabandya, Aby Abraham, Rayaz Ahmed, Abhijeet Ganapule, Eunice Sindhuvi, Kavitha M. Lakshmi, Alok Srivastava

Department of Haematology, Christian Medical College, Vellore, India

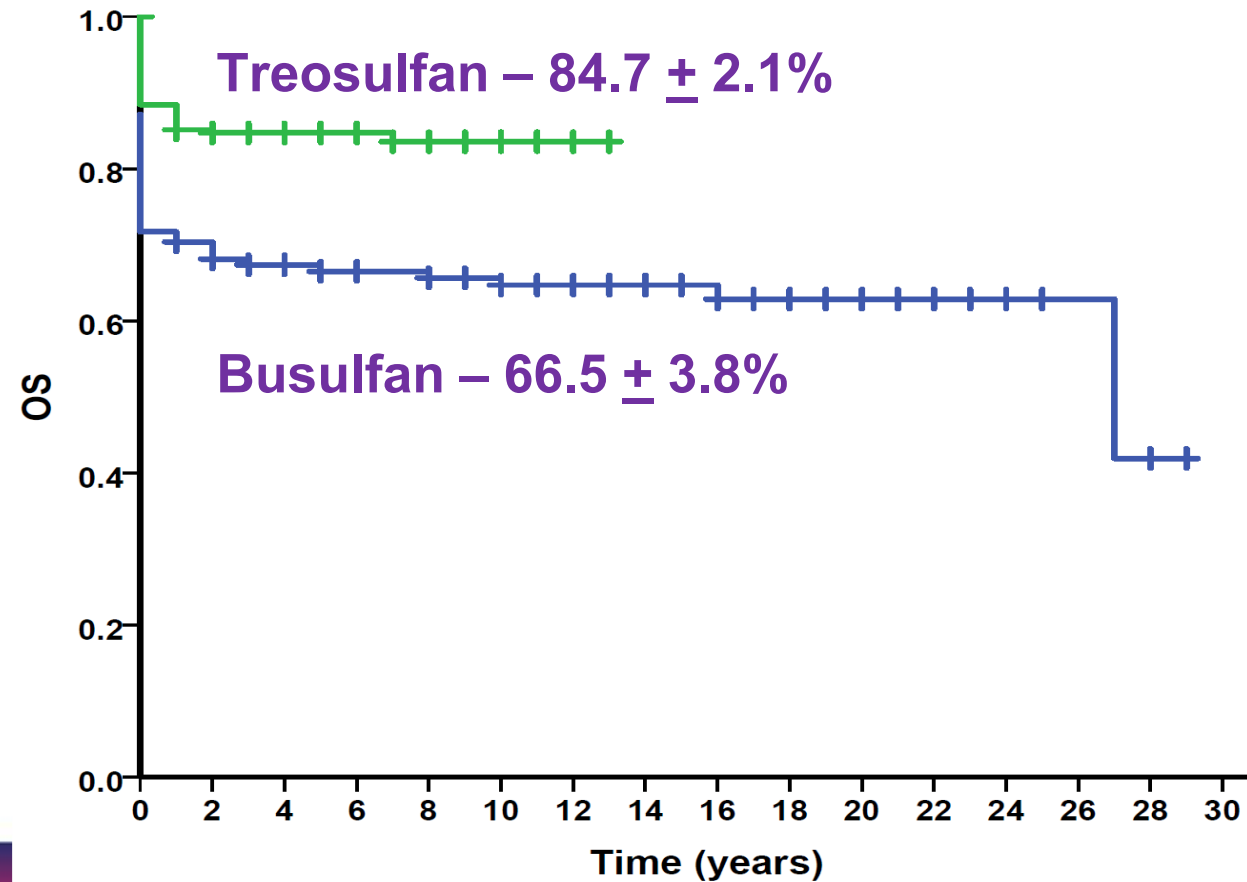
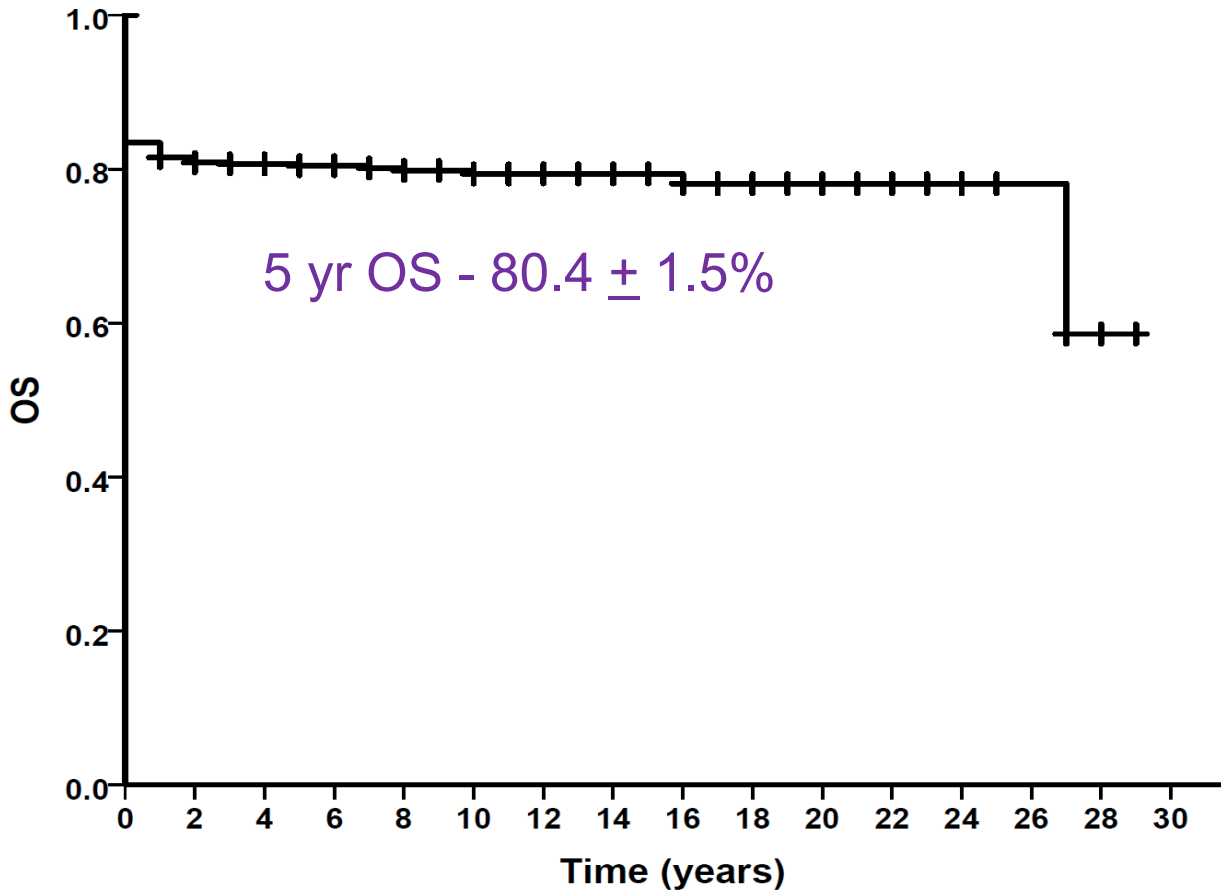
Needed to find better treatment for Class III

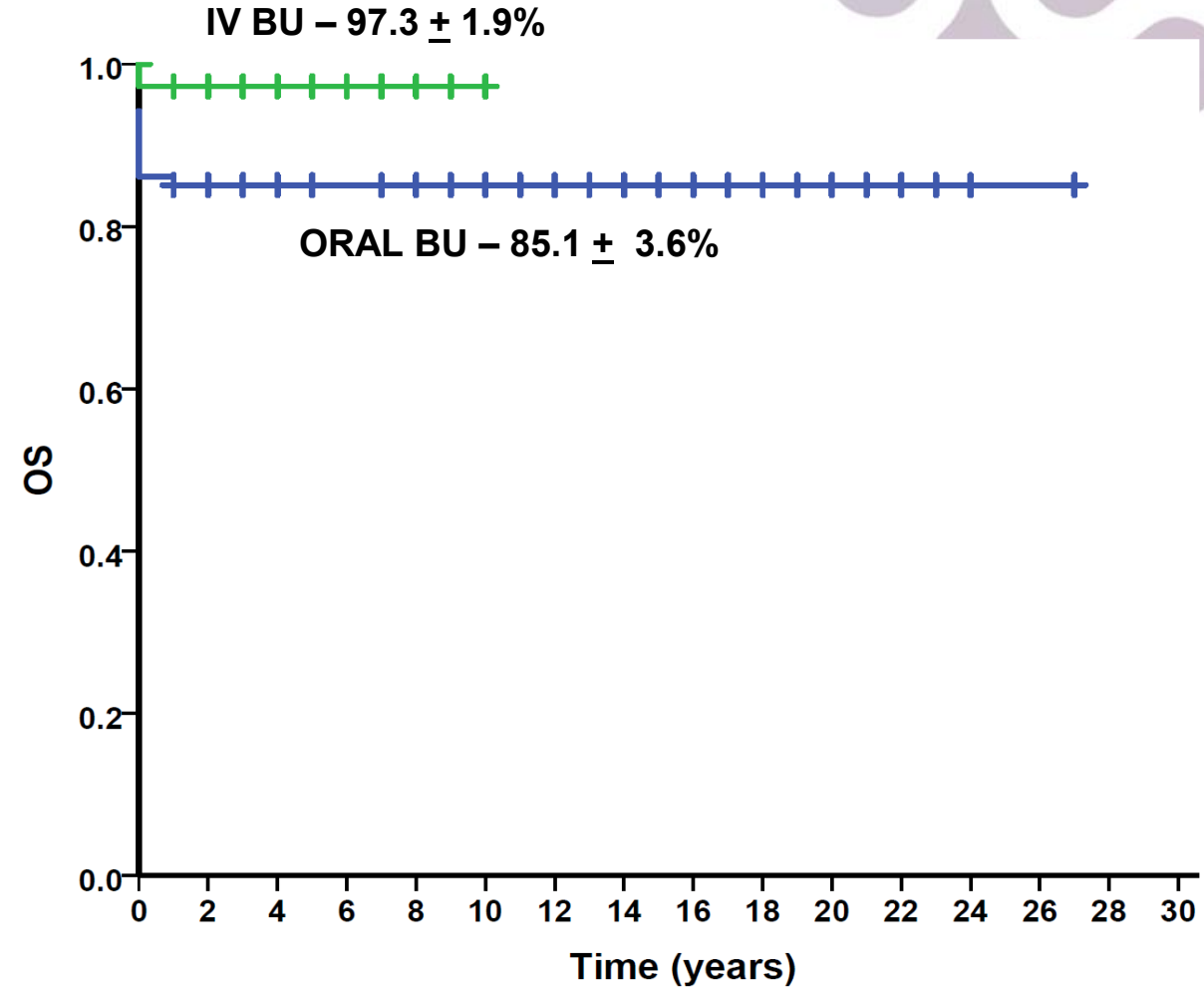
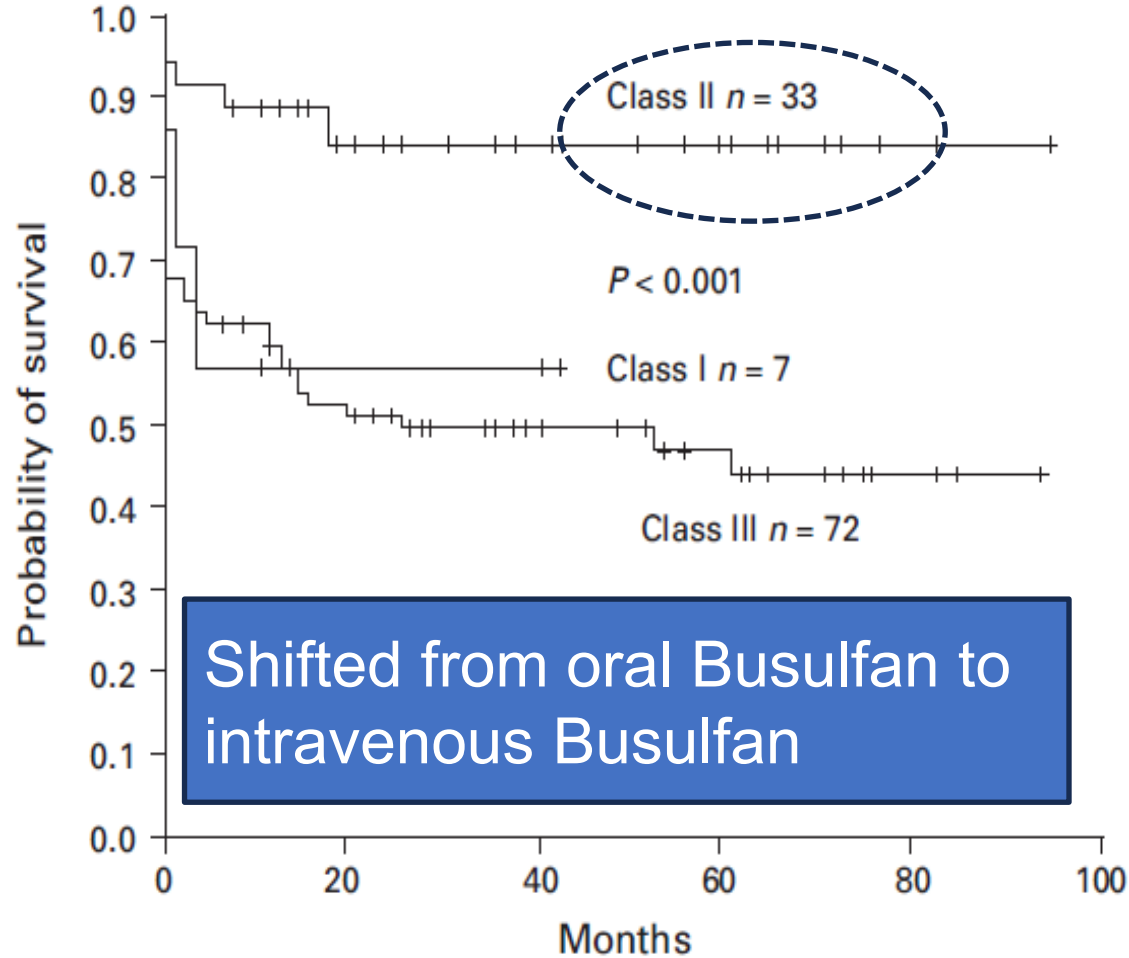
Analysed mortality - mainly RRT.

Designed new regimen using Treosulfan instead of Busulfan



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



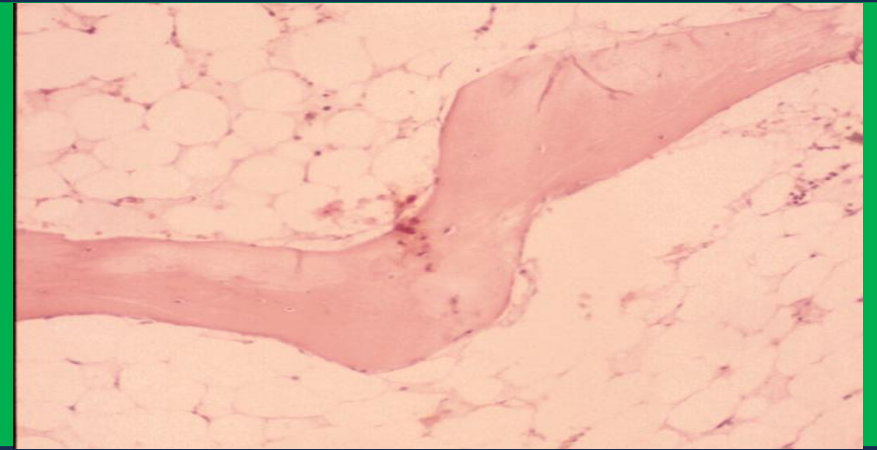


AA – characterized by pancytopenia + empty marrow.

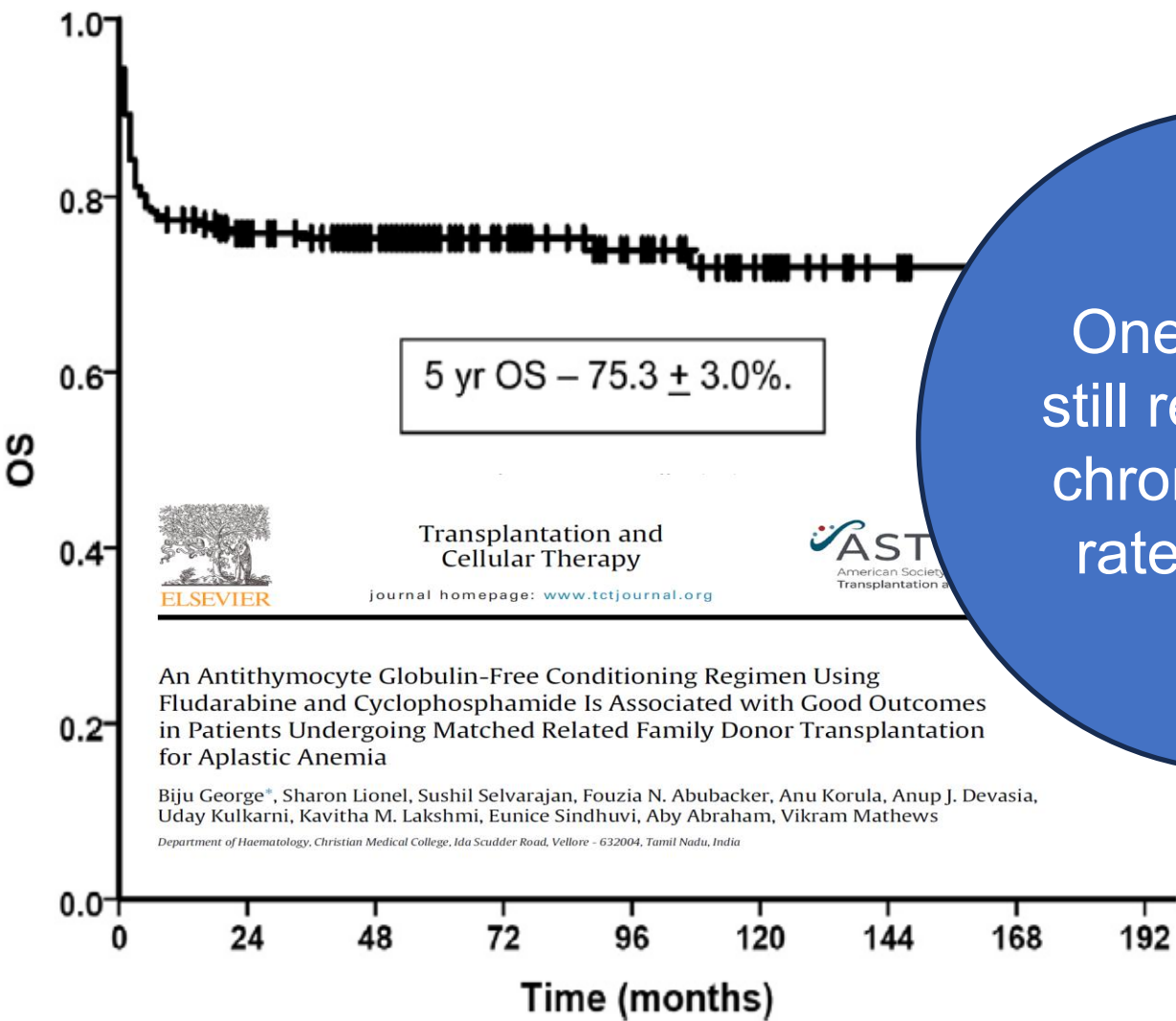
C/F - severe anemia, bleeding and infections.

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

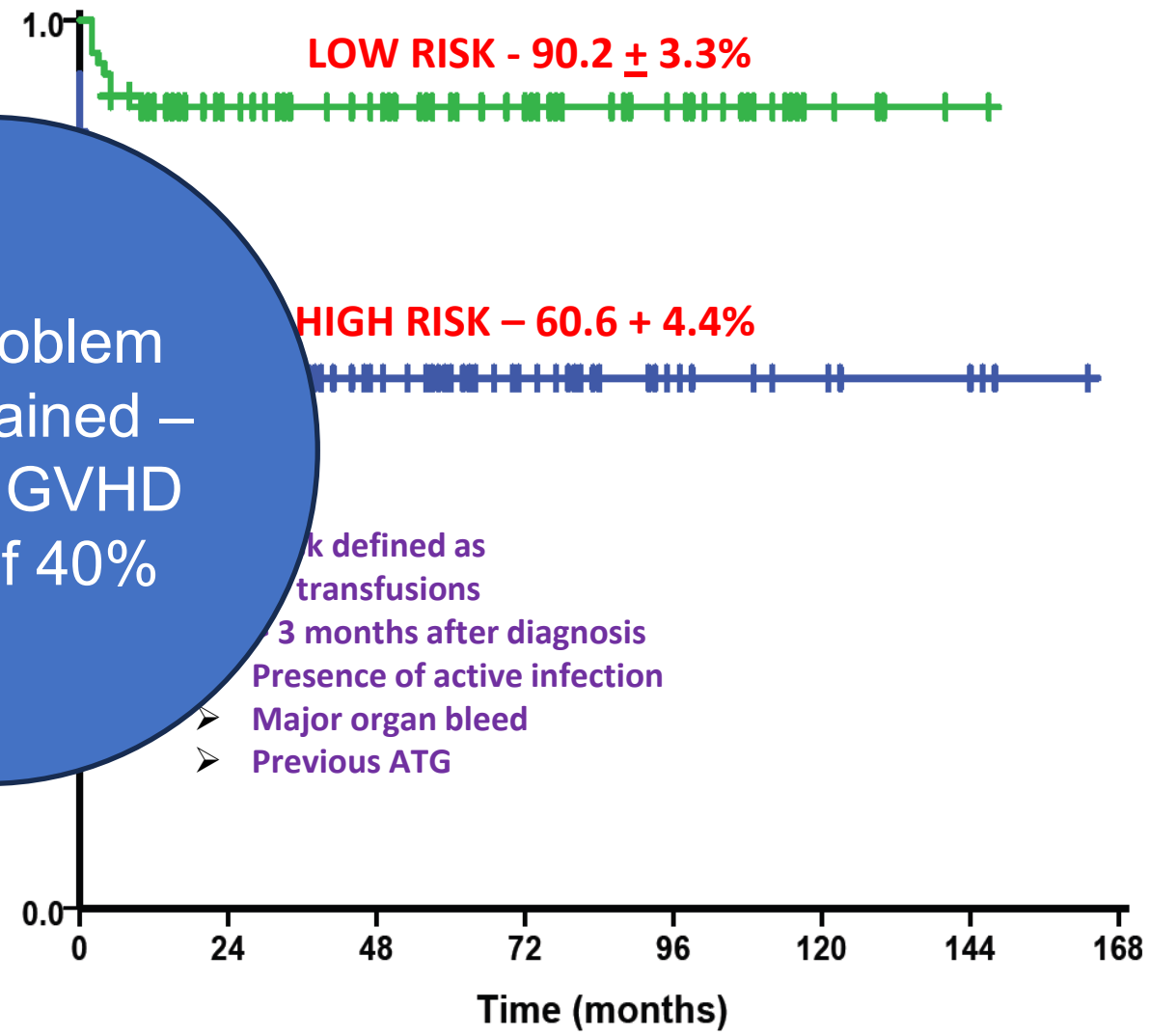
First BMT in 1990



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%



One problem still remained – chronic GVHD rates of 40%



**Table 4**  
Comparison of GVHD, Infections, and OS in Patients Receiving PTCY or Cyclosporine/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 <sup>†</sup>	22.7	.0007* .013 <sup>†</sup>
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 <sup>†</sup>
CI of moderate + severe, %	66.6*	27.2 <sup>†</sup>	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)	



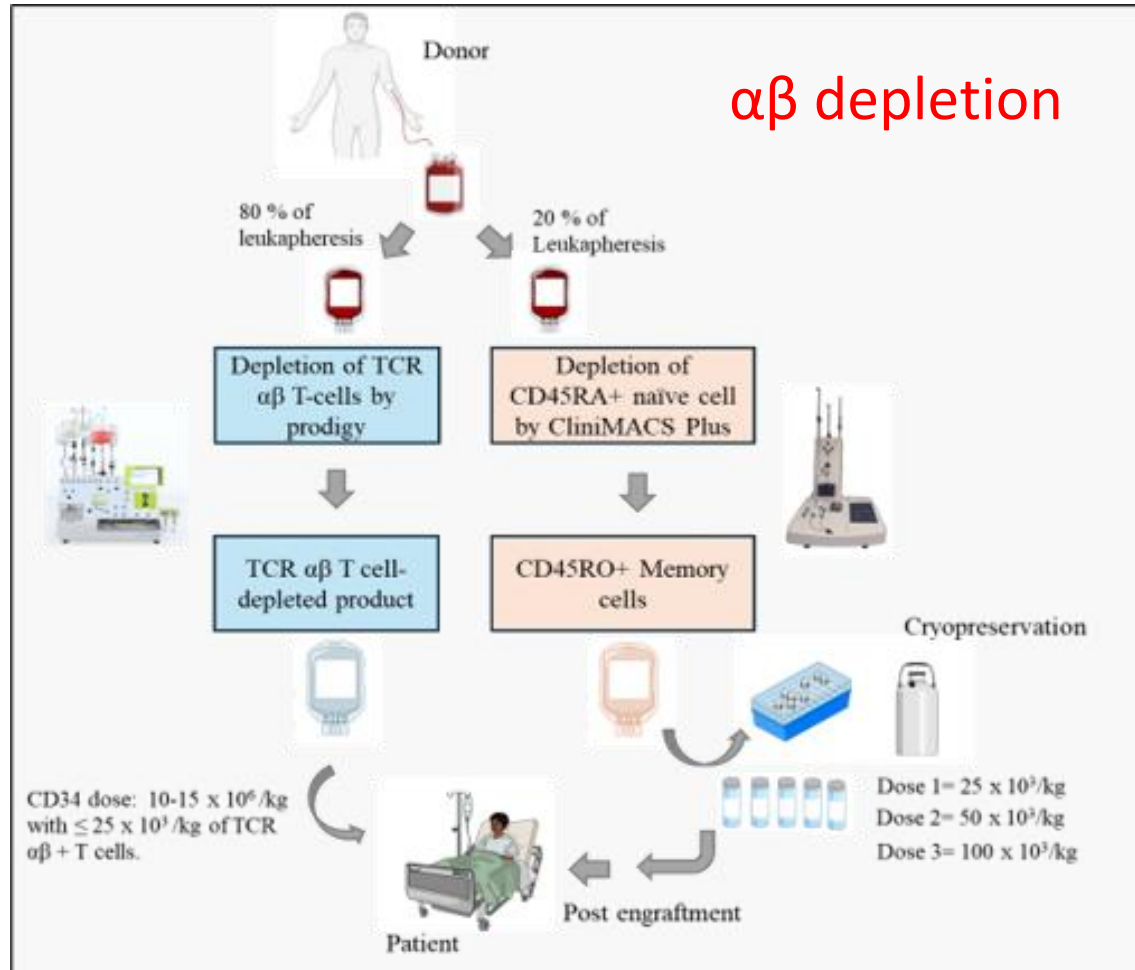
# RCT comparing PTCy with CSA/MTx as GVHD prophylaxis

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

<b>CTRI Number</b>	CTRI/2019/06/019765 [Registered on: 19/06/2019] - <b>Trial Registered Prospectively</b>
<b>Last Modified On</b>	19/06/2019
<b>Post Graduate Thesis</b>	No
<b>Type of Trial</b>	Interventional
<b>Type of Study</b>	Drug
<b>Study Design</b>	Non-randomized, Active Controlled Trial
<b>Public Title of Study</b>	Methods to reduce GVHD after bone marrow transplant for aplastic anemia
<b>Scientific Title of Study</b>	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

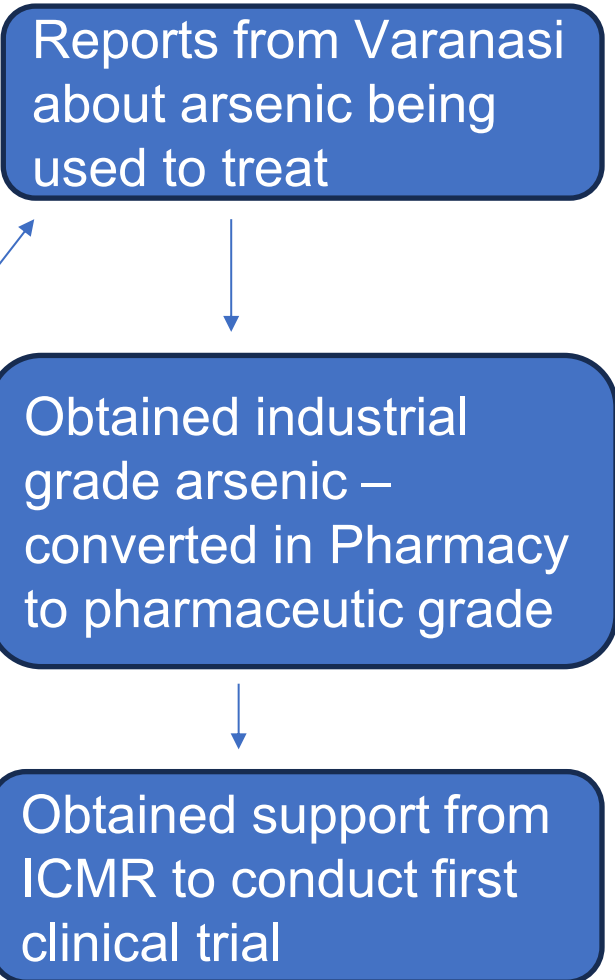


20 pts done  
 Mean age – 59 yrs  
 oldest 74 years

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



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]

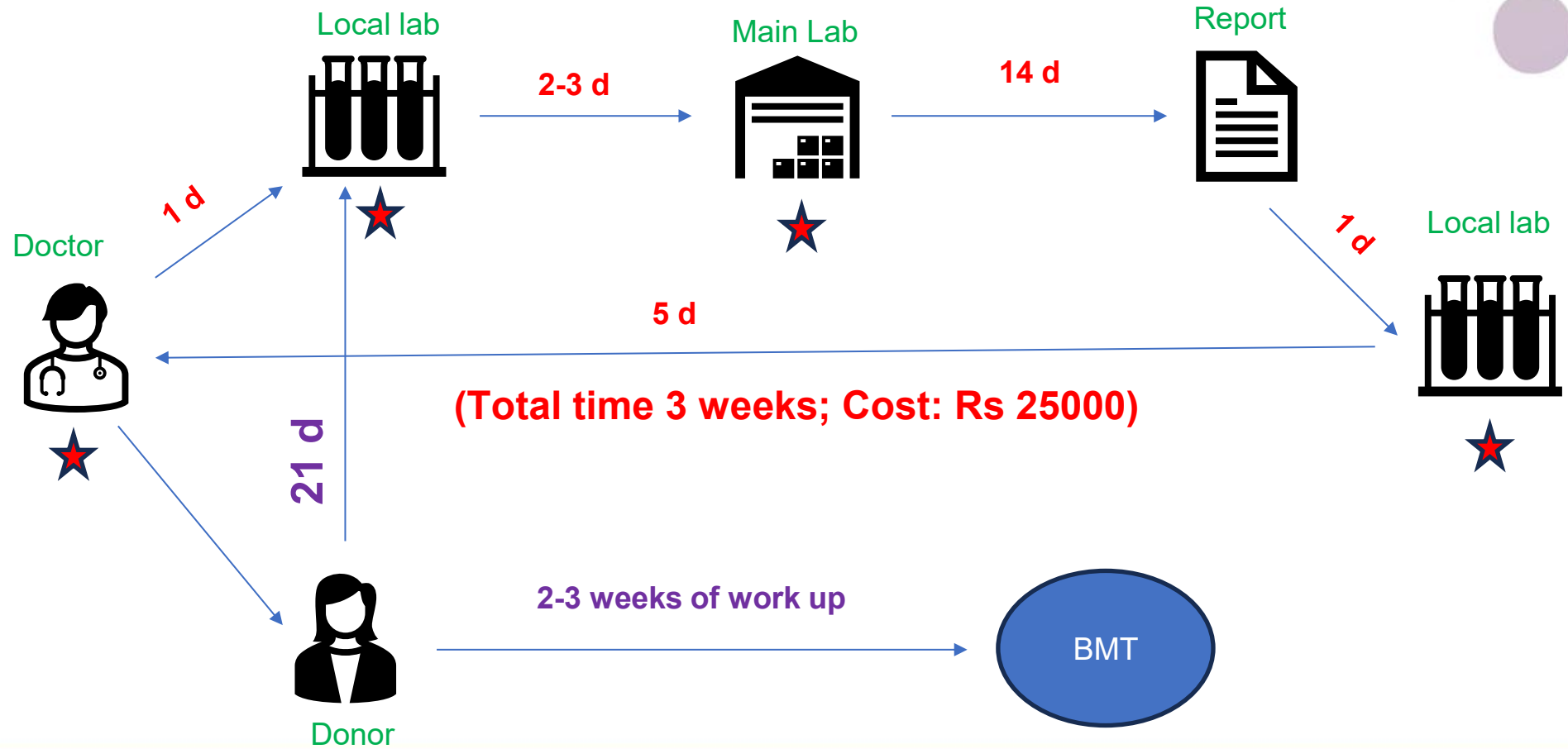
Second in the world to use arsenic for APML

## 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  
 c/f - Has lung and  
 liver fibrosis  
 Suspecting DKC

Has fully matched  
 brother for SCT

Need to send NGS  
 to r/o DKC

Doctor



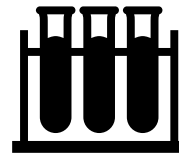
21 d

Report



Pt has  
 genetic  
 mutation

CMC



In house  
 Sanger  
 sequencing

(Total time 3 weeks)



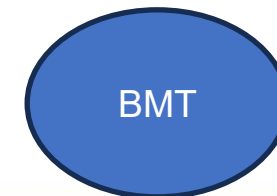
12/12 donor  
 Affected



6/12 donor  
 Affected



6/12 donor  
 Not Affected  
 Donor



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**

Reporting Date: 20/05/2023	
<b>Test Code</b>	-
<b>Test Category</b>	Screening of multiple genes involved in germline predisposition to hematological malignancies by a focussed exome panel NGS
<b>Sample type</b>	Bone marrow in EDTA
<b>Clinical Details</b>	Triple-negative MPN - (Myelofibrosis)

**NGS Result Summary**

Gene/Transcript	CDS Variant	Amino acid/Exon	Mode of Inheritance	Zygoty	OMIM Phenotype	Clinical Significance
<i>TBXAS1</i> (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



CHRISTIAN MEDICAL COLLEGE VELLORE, RANIPET CAMPUS