



# Haematopoietic stem cell transplants from Matched Unrelated Donors (MUD)

J Thomson, D Brittain, D Reynders, L Burger, H  
Duvenhage.

*Faerie Glen Haematopoietic Stem Cell Transplant Unit  
Pretoria*

# Background



- IBMTR 50 000 transplants/annum
- Number of donors donor registry world wide increasing
- Number of MUD transplants increasing

# Background



57 Allogeneic SCT

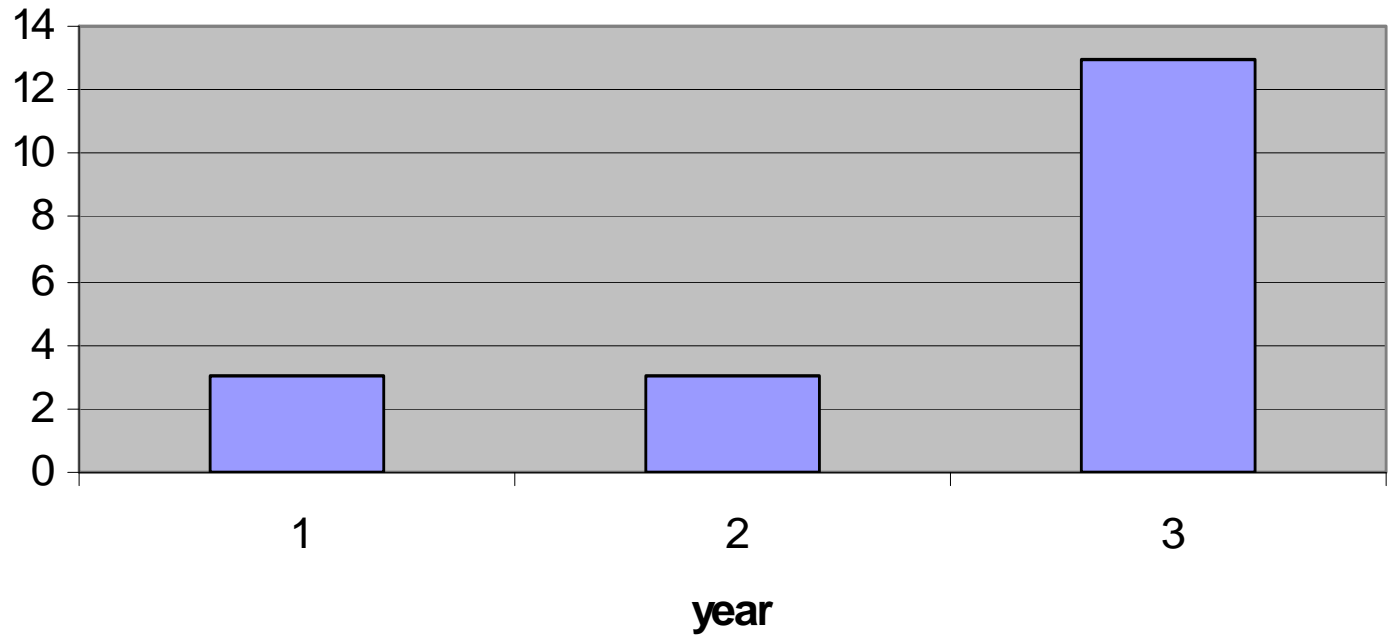
38 Sibling

19 MUD

# Background



**Incidence of unrelated stem cell transplants**



# Background



- Limited number of resources
  - Blood products
  - Human
  - Financial
- Variability in outcome
- Patient selection

# Background



- Recipient risk factors
  - Age, comorbidity, performance status, cytomegalovirus (CMV) status
  - Disease considerations: diagnosis, stage, and cytogenetic risk.
  - Prior chemotherapy regimens,
  - Patient race and IL10 promoter polymorphism

# Background

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- Donor factors
  - Level of HLA mismatch
  - Donor gender, relation, age, and KIR genotype also affect outcome.

# Background



These factors must all be considered in relation to one another when selecting whether to recommend patients for transplant.





# Risk SCORE

## ■ EBMT:

- 1 [redacted] "early phase" (e.g. acute myeloblastic leukemia [AML] in CR1) – 0 points, 'intermediary level (e.g. AML in CR2) – 1 point, 'advanced illness" (e.g. AML resistant to treatment) – 2 points
- 2 [redacted] <20 years old – 0 points, 20–40 years old – 1, >40 years old – 2 points
- 3 [redacted] <12 months/>12 months – 0 or 1 point
- 4 [redacted] – 0, from unrelated donor – 1 point
- 5 sex of the donor: female for male recipient

# Aim



- Retrospective Audit
- To validate the risk score according to the EBMT for TRM in our patient population
- Guidelines

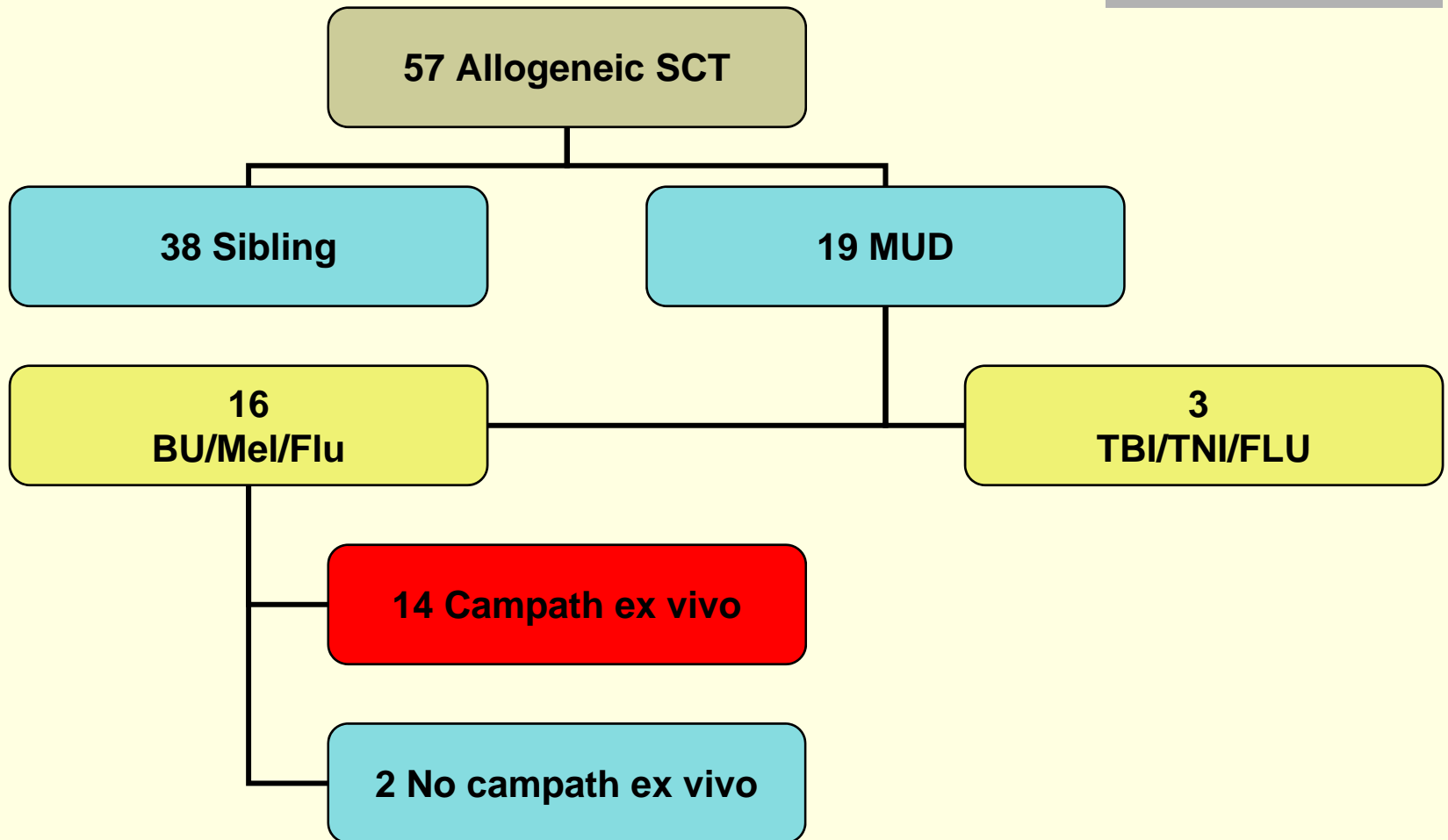
# Methods

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- August 2006 – January 2009
- Allogeneic stem cell transplant from MUD

# Patient Population



# Methods



## ■ Preconditioning:

- Busulphan IVI 0.8mg/kg/QID x day -8,-7,-6
- Melphalan 150mg/m<sup>2</sup> day -5
- Fludarabine 40mg/m<sup>2</sup> day -5,-4,-3
- Campath-1H in the bag 5-12mg
- ATG 1.5 mg/kg Day -5,-4,-3, -2
- Cyclosporin 3mg/kg IVI

Day -7 -5

Bu 0.8mg/kg/qid

Day -4

MEL 150/m<sup>2</sup>

Day -4 -2

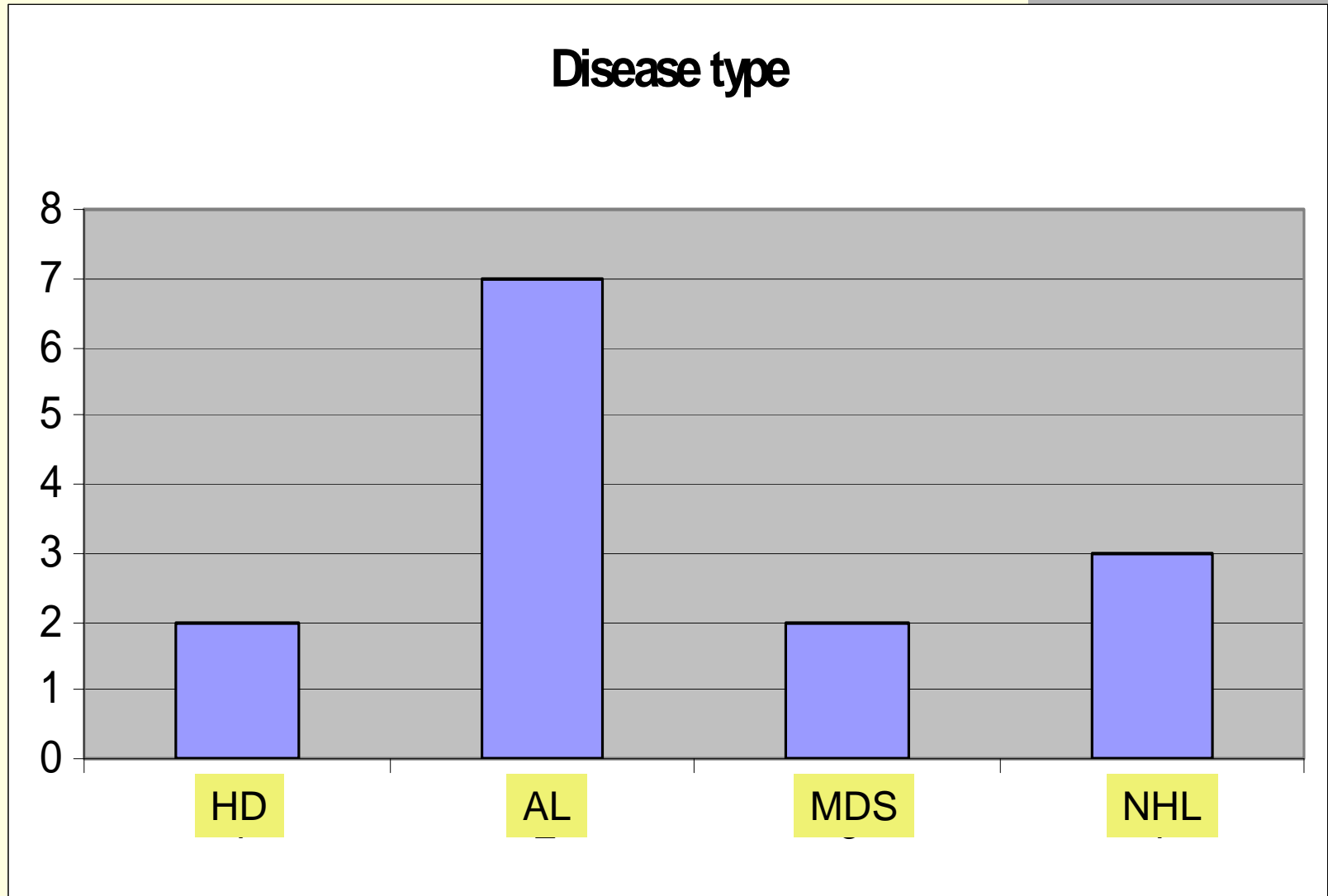
FLU 40mg/m<sup>2</sup>

# Methods



- Post transplant treatment
  - Tacrolimus prophylaxis for 3 months
  - Valacyclovir 1g t.d.s p.o.
  - Bactrim prophylaxis
  - SHS weekly
  
- Weekly viral monitoring to 3 months

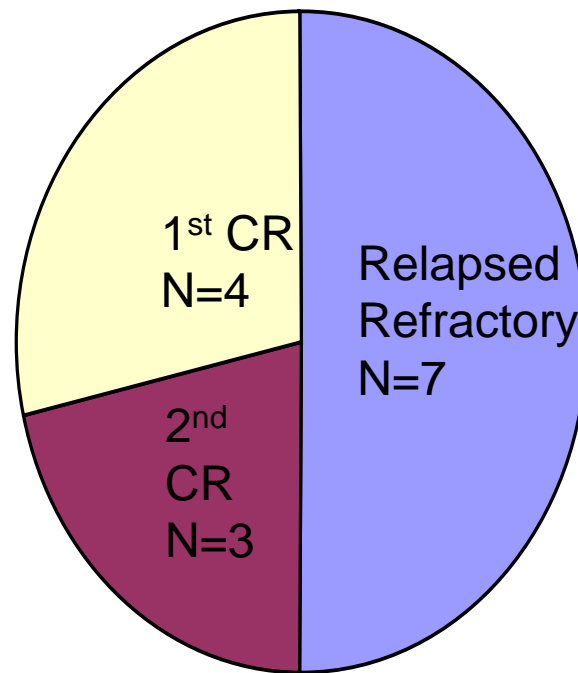
# Patient Population



# Disease Status



## Disease status

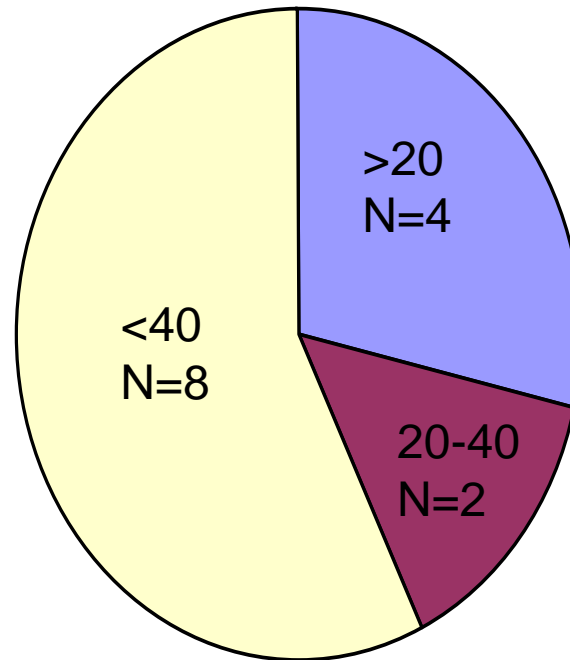




# AGE



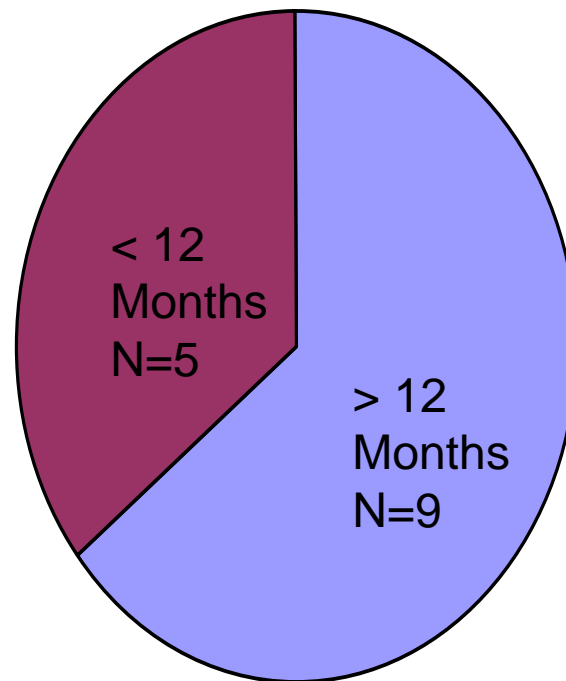
Age



# TIME TO TRANSPLANT



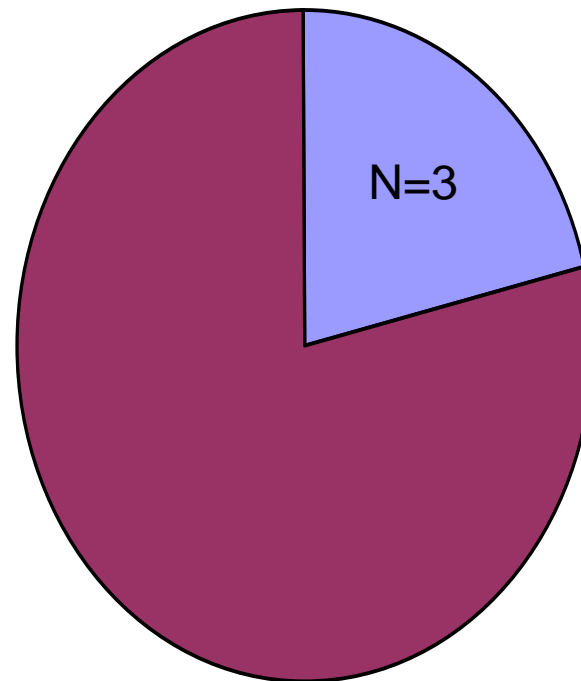
**Time to transplant**



# FEMALE TO MALE



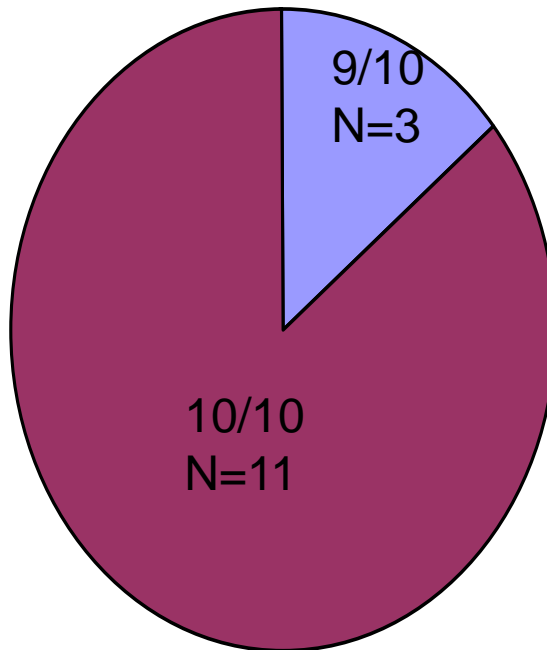
**Female to male**



# HLA Matching



## HLA



# Results



- Stem cell dose:
  - 2 – 9 x10<sup>6</sup> cells/kg
  - Mean 6 x 10<sup>6</sup> cells/kg
  
- Campath-1H dose:
  - 5-12 mg in the bag
  - Mean 8mg

# Results



- Engraftment:

- Time to

- NAC > 0.5 10 days (8-11)
    - PI > 20 11 days (9-13)
    - (One patient did not engraft platelets)
    - Donor chimerism 11/11 100% donor at 3 months

# Results



<u>Toxicity</u>	<u>n=14</u>
■ Nausea and vomiting	7
■ Mucositis Grd II	7
■ Mucositis Grd III	2
■ Septicaemia	2
■ Veno-occlusive disease	0
■ DAH	3
■ CMV	6
■ Invasive Aspergillosis	2
■ PTLPD	1

# Results



## GVHD

■ <u>Acute</u>	<u>n=14</u>
■ <u>GR I</u>	3/14
■ <u>GR II</u>	6/14
■ <u>GR III-IV</u>	0/14
Total Grd II – IV	(42%)
■ <u>Chronic GVHD</u>	
■ 5/11 – (30%) – 2 DIED of extensive GVHD	
■ Aspergillus	
■ GIT Bleed	
■ 2 received DLI	



# Relapse rate



- 3 Patients relapsed
  - 2 Leukaemia- complex cytogenetic
  - 1 HD - refractory
  
- 1 DLI
  - Grd III GVHD (liver,gut,skin) attained CR

# Results



- Treatment related mortality according to risk score

Risk score 1-2  
N=6  
TRM day 100  
0%

Risk score 3-5  
N=5  
TRM day 100  
20%

Risk score >5  
N=3  
TRM day 100  
60%

# Discussion



- EBMT do not recommend allogeneic transplant in patients with a risk score  $> 5$
- Small numbers
- Validated at our unit

# Conclusion



- MUD allo SCT increasing
- Should be performed on patients with risk score 2-3
- Those with a risk score  $> 5$  should not be transplanted
- Donor factors should also be considered
- High risk patients should be transplanted in first CR

# Acknowledgement

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- Nursing and supportive staff involved in the transplant unit
- SABMR – support in recruiting donors
- Laboratory support
- SANBS – blood product support