



Haematopoietic stem cell transplants from Matched Unrelated Donors (MUD)

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Background



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

Background



57 Allogeneic SCT

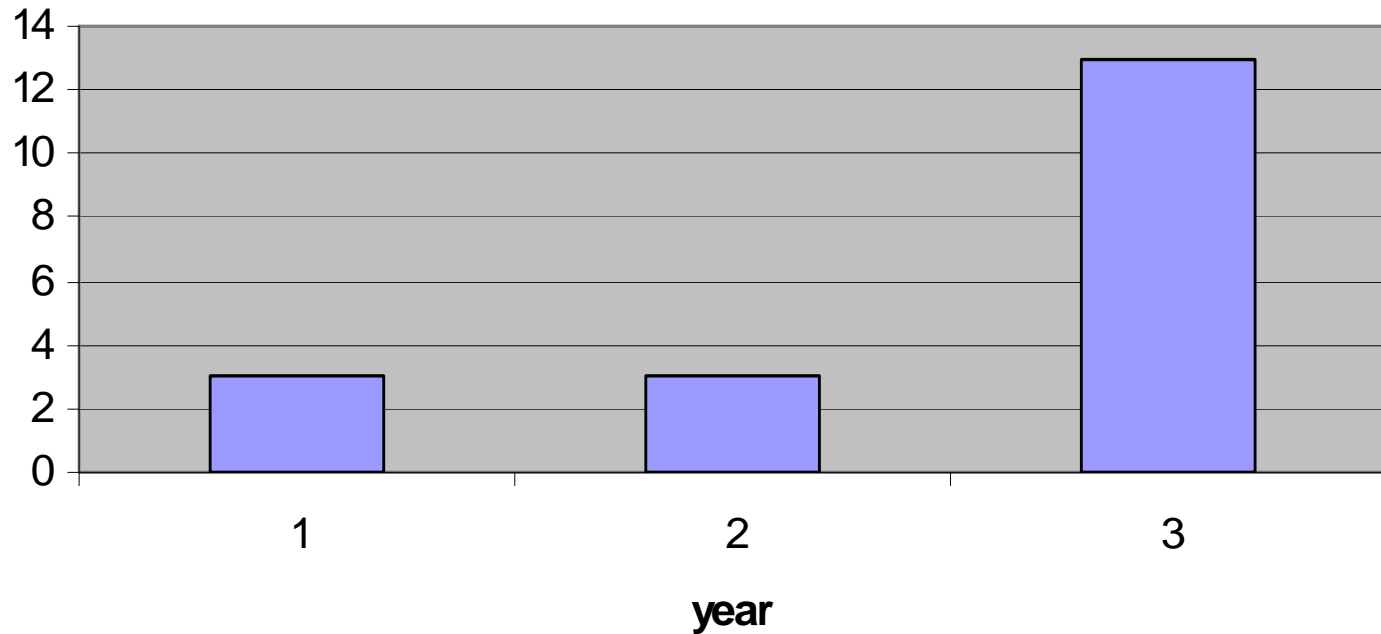
38 Sibling

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



- 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



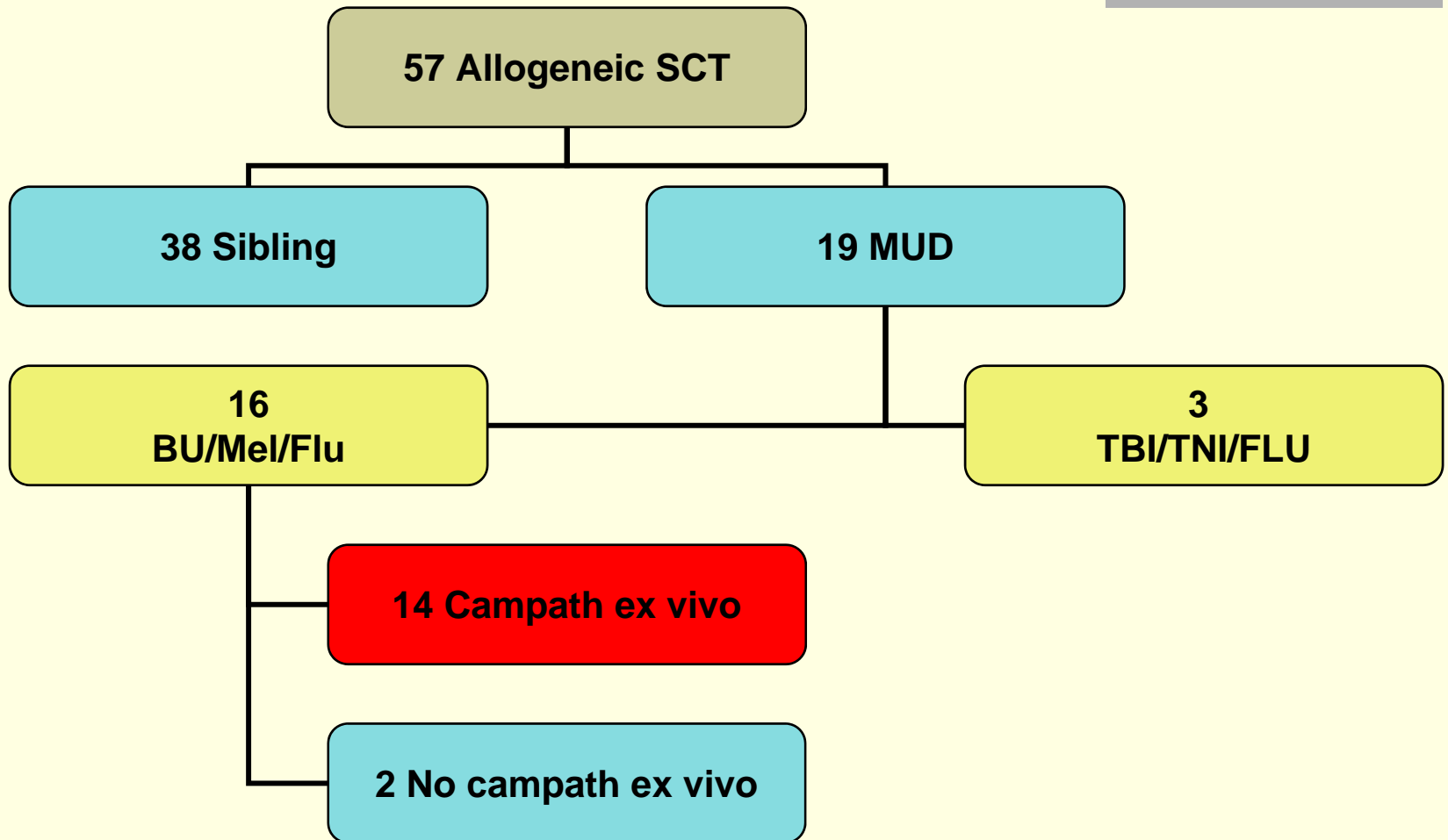
- Retrospective Audit
- To validate the risk score according to the EBMT for TRM in our patient population
- Guidelines

Methods



- 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/m² day -5
- Fludarabine 40mg/m² 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/m²

Day -4 -2

FLU 40mg/m²

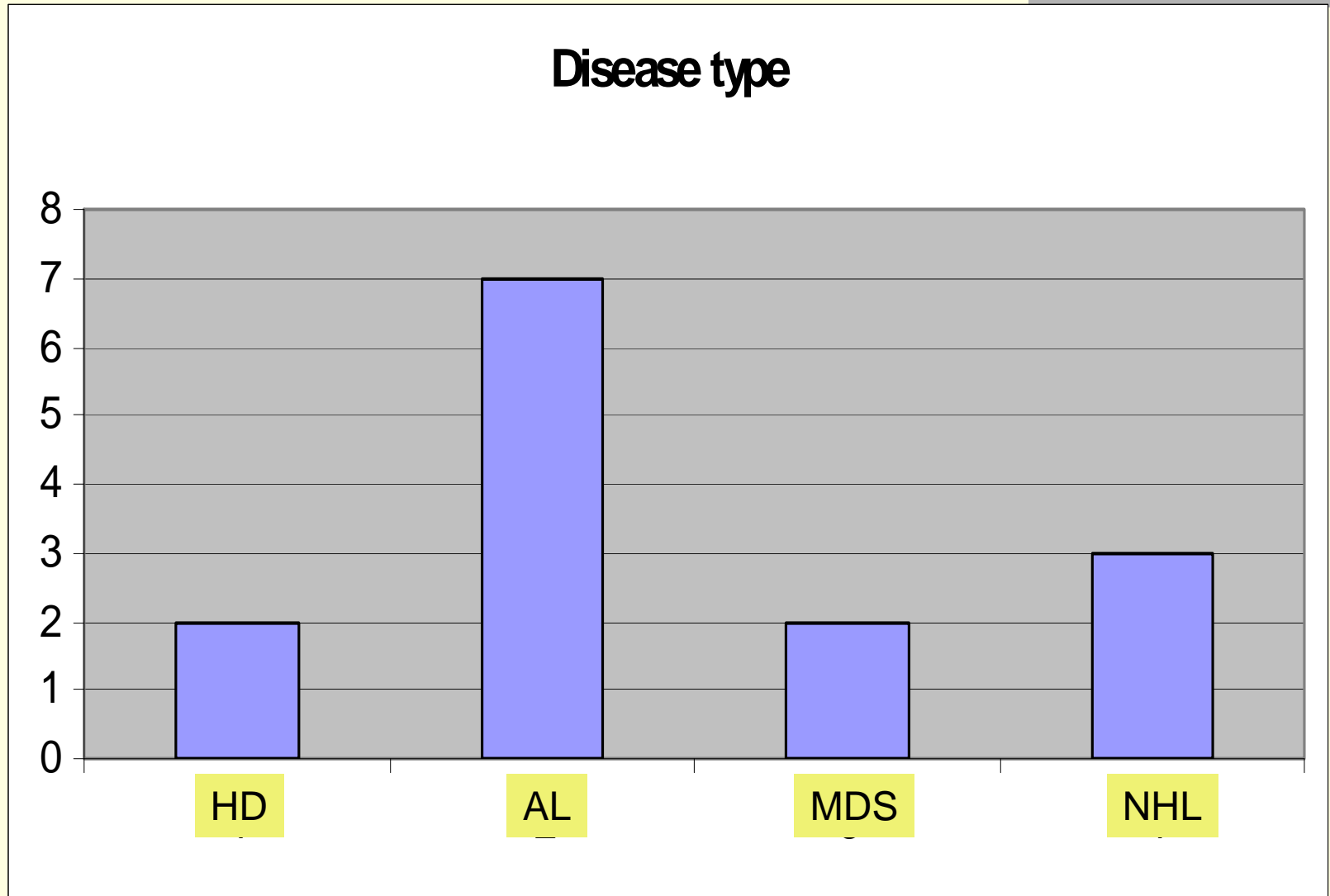
Methods



- 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

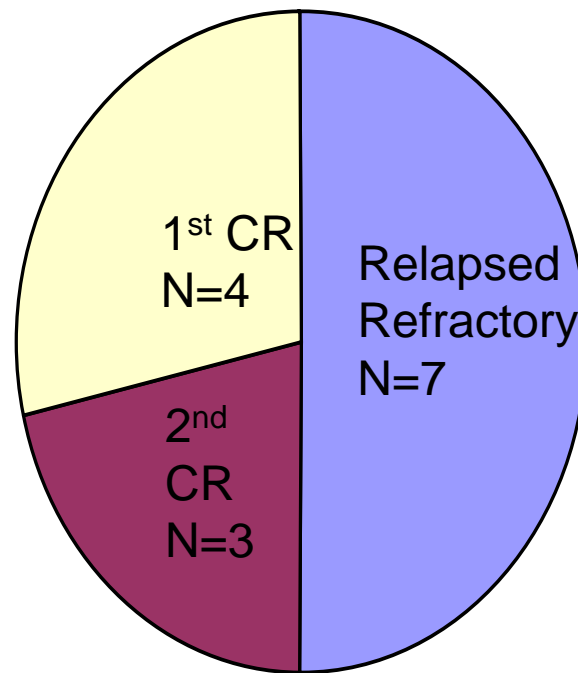
Patient Population



Disease Status



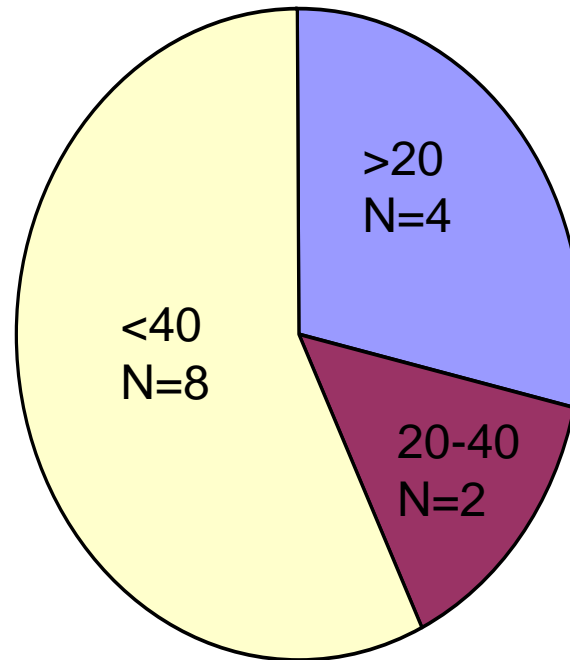
Disease status



AGE



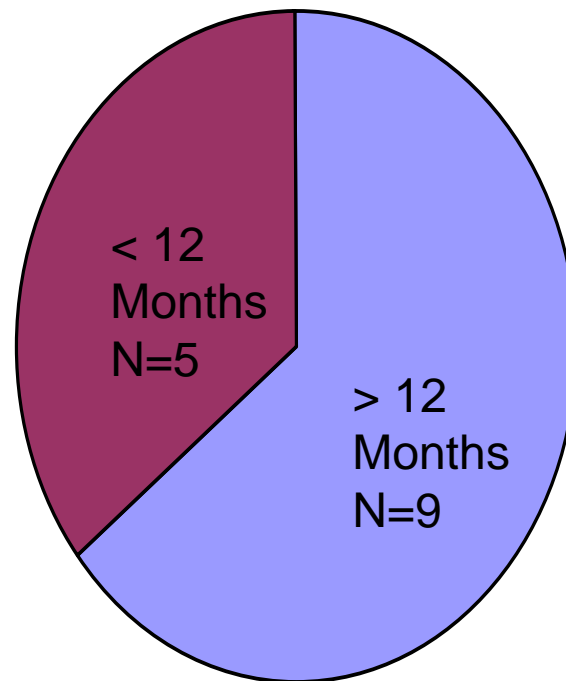
Age



TIME TO TRANSPLANT



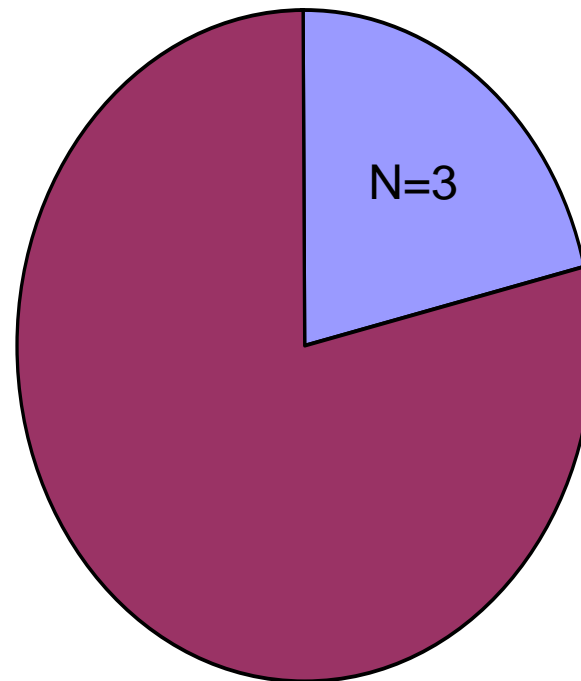
Time to transplant



FEMALE TO MALE



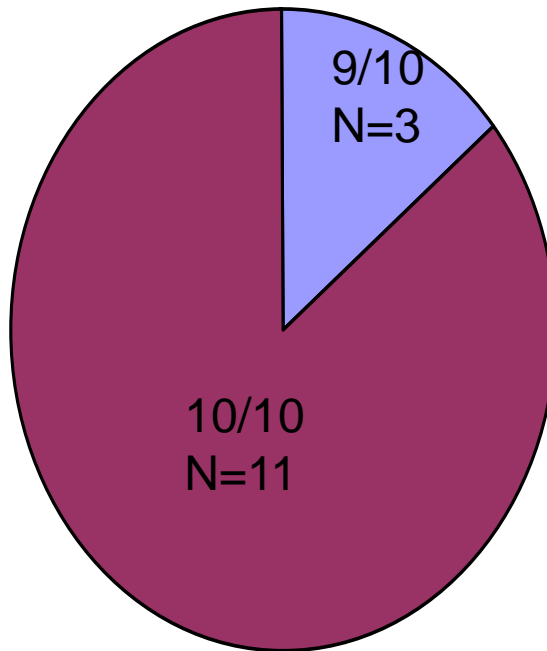
Female to male



HLA Matching



HLA



Results



- Stem cell dose:
 - 2 – 9 x10⁶ cells/kg
 - Mean 6 x 10⁶ 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



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