14th International Donor Registry Conference & WMDA Meetings

25 – 29 June, 2024 – Cape Town, South Africa

All patients & donors matter

Dr Tanya Glatt

ABO Incompatibility in Bone Marrow Stem Cell Transplants: A bloo perspective

Introduction

1. Define and classify ABOi HSCT

2. Special considerations for an ABOi HSCT
   - **Registry**
   - **Clinical facility**
   - **Collection facility**
   - **Processing facility**
   - **Transfusion service**

3. Blood product support and outcome measures

Introduction

- A patient receiving blood products needs to receive **ABO compatible blood pro**
- Stem cells do not express ABO antigens and therefore **allogeneic stem cell tra** **ABO matched**
- ~50% of MUD HSCT are ABO mismatched
- ~15% of MRD HSCT are ABO mismatched
- ABO mismatch HSCT does not have worse overall survival – or does it?
- BUT ABO-incompatible HSCT do have special considerations…
- AND there are RBC, plasma and platelets in HSCT products
- Individual pt: may **require prolonged product support**

Types of ABO-I HSCT:

1. Major – recipient has antibodies to donor RBCs
2. Minor – donor has antibodies to recipient RBCs
3. Bidirectional both major and minor

ABO Blood Group System

	ANTIGENS (on red cells)	ANTIBODIES
Group A	A	
Group B	B	
Group O	-	An
Group AB	A+B	

- Antibodies develop to antigens of the ABO blood group system in people lacking t antigens
- These are **naturally** occurring (person doesn't have to be exposed to the antigen antibody)
- Naturally occurring antibodies develop in the first 6 months of life (possibly due to antigens found in the environment)

Types of ABO-I HSCT:

1. Major – recipient has antibodies to donor RBCs
   - Recipient: group O and Donor: group A, B, AB
   - Recipient: group A or B and Donor: group AB

2. Minor – donor has antibodies to recipient RBCs
   - Recipient: group A, B, AB and Donor: group O

3. Bidirectional both major and minor
   - Donor A, recipient B or
   - Donor B, recipient A

Major ABO-i

Major ABO-i: RISKS

1. Haemolysis at the time of HSCT infusion –may be severe
2. Delayed haemolysis due to production of antibodies by residual host lymphocyte
3. Delayed RBC engraftment –may require ongoing RBC transfusions
4. Pure red cell aplasia (PRCA) –rare

NB: clinical manifestations depend on the amount of RBC and also the amou
(antibody titer)

Amount RBC:

- bone marrow collections have a lot of RBCs (equivalent of one unit of red cells)

Management: Major ABO-I HSCT prior to transplant

PRE-EMPTIVE!

1. Need to know antibody titer of the patient
2. Need to know the amount of RBC in the graft

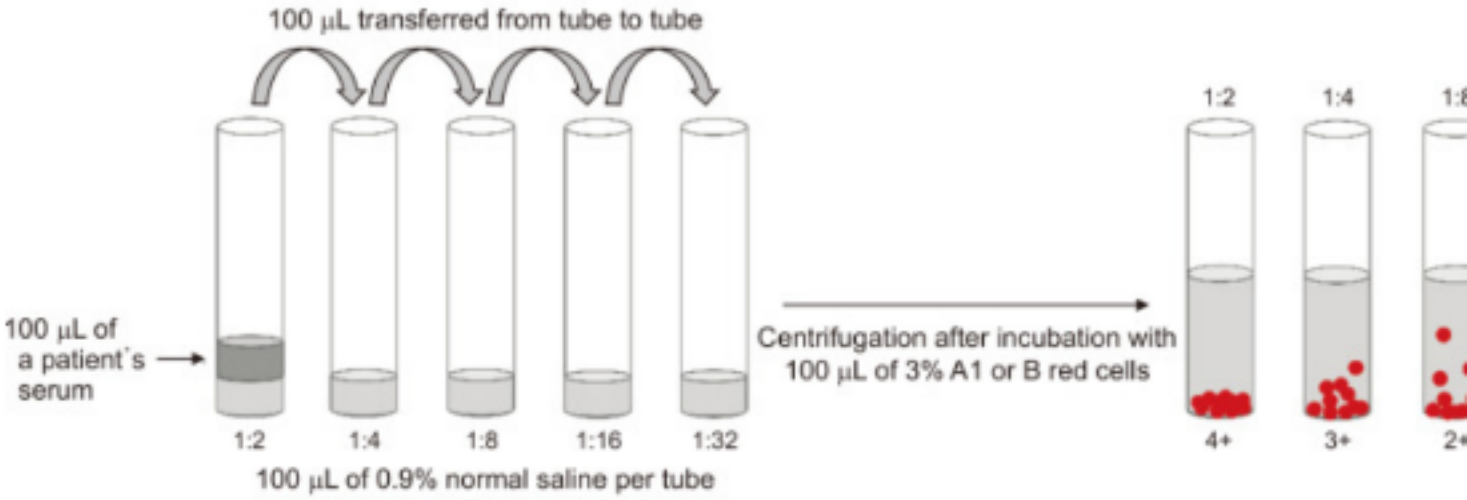
Titer level **≤1:32** or RBC volume of graft **<20ml (0.2 -0.5 ml/kg)**– may NOT require

If titer ≥64 and RBC vol >20ml, consider further management

1. remove red cells from the graft before it is infused
2. remove antibodies from the patient - plasma exchange or immunoadsc

NB: consider loss of stem cells

Antibody titer testing



A schematic description of isoagglutinin titer measurement using the conventional tube method. The isoaggl
the endpoint that shows agglutination with two-fold dilution. Each laboratory sets its own cutoff (trace or 1+
protocol.

titers don't predict entirely but do give a guide

Minor ABO-i

Minor ABO-i

- Donor antibodies to patient antigens
- All HSCT sources contain plasma: cord blood, apheresis, BM (BM product can cont

Donor	Recipient
Non-AB	AB
B or O	A
A or 0	B

Minor ABO-i

Complications: Haemolysis of **recipient RBC (acute or delayed)**

Management: **PRE-EMPTIVE**

- Decrease volume of plasma in the product prior to infusion
- Carefully monitor recipient for clinical and lab signs of haemolysis post trans

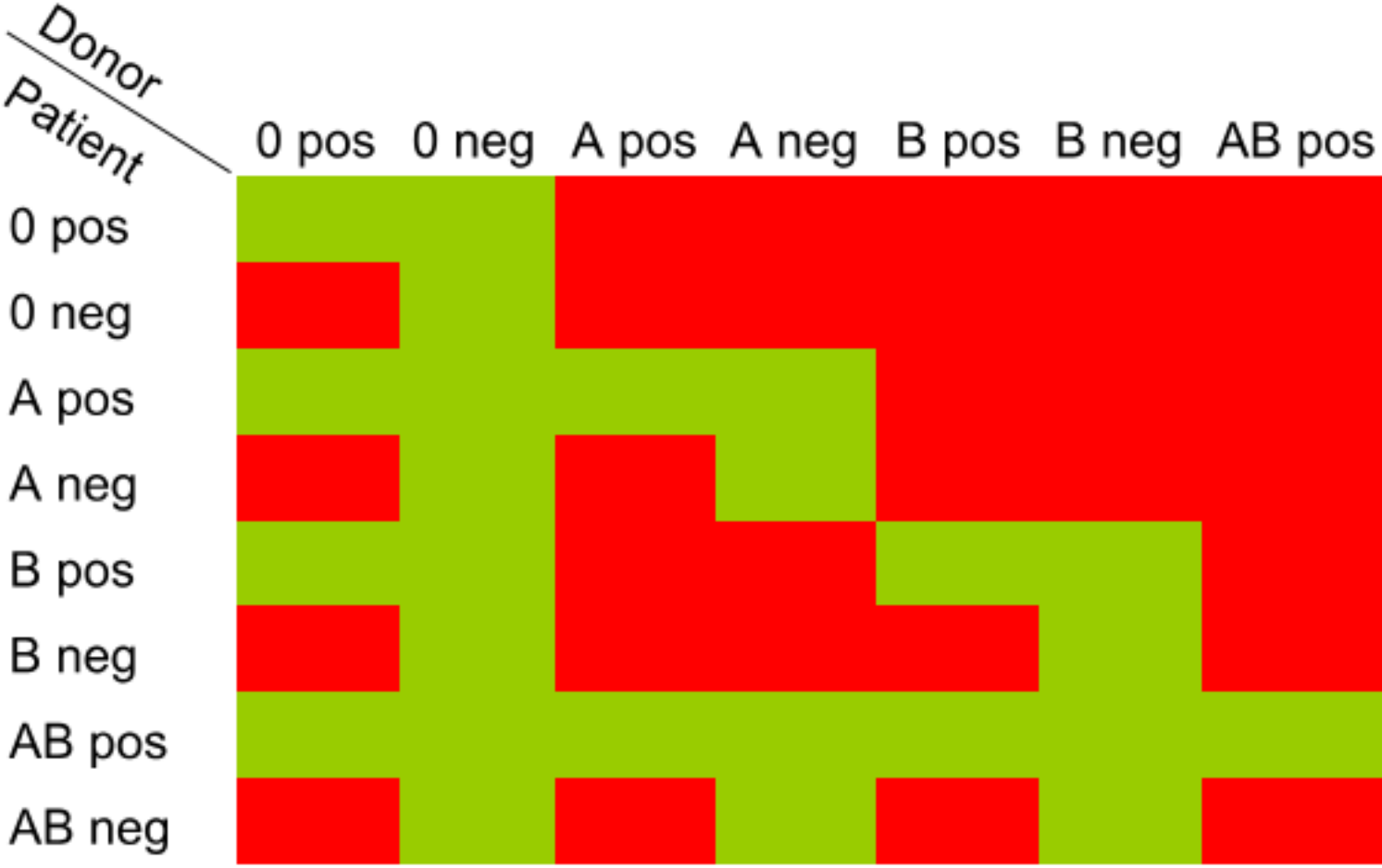
if the donor titer level is **≤1:128: may not need to do anything; if donor titer is **≥1**
reduction

TABLE 1. Types of ABO incompatibility, potential adverse consequences, and recommended in

	Major	Minor
Definition	• Recipient isoagglutinins (anti-A, anti-B, anti-A,B) incompatible with donor RBCs	• Recipient RBCs incompatible with donor isoagglutinins.
Donor-recipient ABO pairs	• Group A, B, and AB donor and Group O recipient • Group AB donor and group A or B recipient	• Group O donor and group A, B, or AB recipient
Potential adverse consequences	• Immediate hemolysis • Delayed RBC engraftment • PRCA	• Immediate hemolysis • Passenger lymphocyte syndrome causing delayed hemolysis
Recommended interventions	• RBC reduction if >30 mL RBC and/or if recipient isoagglutinin titers >32 • Transfuse ABO appropriate blood products	• Plasma reduction • Close clinical and laboratory observation, between Days +5 and 15 after HPC transplantation for hemolysis (e.g., Hb/Hct, LDH, bilirubin, hemoglobinemia) Transfuse ABO appropriate blood products
Additional or alternate interventions that may be performed	• Recipient's isoagglutinins removal before transplantation via TPE or immunoadsorption	• Replacement of recipient RBCs with donor type v RBC exchange (rarely), rituximab

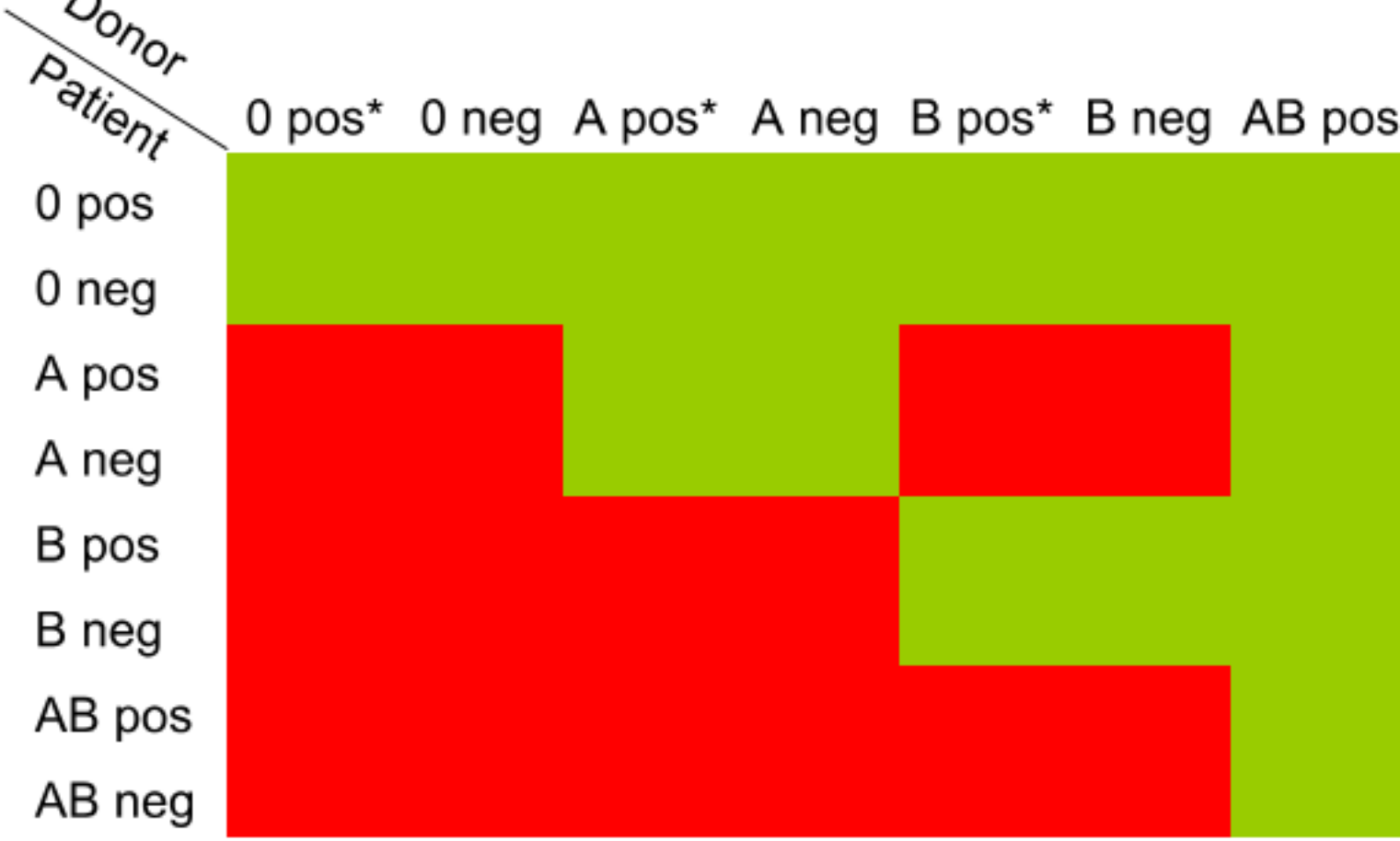
BLOOD PRODUCT SUPPORT IN ABO-I HSCT

Blood transfusion: RBCs



Neyrinck & Vrielink - Jan 2017

Blood transfusion: Plasma



BLOOD PRODUCT SUPPORT –three phases of HSCT

Phase 1:

- Before the transplant

Phase 2:

- From infusion of stem cells to engraftment / **recipient RBC no longer detect**ed (fu
  donor type -forward and reverse grouping look donor)

Phase 3:

- Post engraftment phase

1. ABO antibodies to the donor ABO group are undetectable in the 'standard' reverse g
and/or B cells using either polyspecific AHG or anti-IgG (major ABO incompatibility onl
2. Negative DAT
3. **Complete conversion to donor group**: no mixed field seen using the patient's cell
tests with anti-A or anti-B (in practice this can only be demonstrated if there have been
the last 3 months).

BLOOD PRODUCT SUPPORT

Phase 1:

- Give **recipient-compatible blood group**

BLOOD PRODUCT SUPPORT

Phase 3:

- Give **donor-compatible red cells, plt and FFP**

BLOOD PRODUCT SUPPORT

Phase 2:

- **EBMT guidelines**: **Group O RBC, group AB plasma and PLT**

- **NHSBT guidelines:**
- **Major** ABO incompatibility
  - RBC: red cells of **recipient's** ABO group or **group O**
  - Platelets and FFP: platelets and plasma of **donor** ABO group

- **Minor** ABO incompatibility:
  - RBC: red cells of **donor** ABO group
  - Platelets and FFP: platelets and plasma of **recipient** ABO group

- **Bidirectional** ABO incompatibility:
  - RBC: group O
  - Platelets and FFP: give group AB plasma and recipient group platelets.

BLOOD PRODUCT SUPPORT

TABLE 2. Transfusion support for patients undergoing ABO-incompatible allogeneic HP

Recipient	Donor	Phase I, all components	Phase II		
			RBCs	First-choice PLTs	Next-choice PLTs†
O	A	Recipient	O	A	AB; B; O
O	B	Recipient	O	B	AB; A; O
O	AB	Recipient	O	AB	A; B; O
A	O	Recipient	O	A	AB; B; O
A	B	Recipient	O	AB	A; B; O
A	AB	Recipient	A	AB	A; B; O
B	O	Recipient	O	B	AB; A; O
B	A	Recipient	O	AB	B; A; O
B	AB	Recipient	B	AB	B; A; O
AB	O	Recipient	O	AB	A; B; O
AB	A	Recipient	A	AB	A; B; O
AB	B	Recipient	B	AB	B; A; O

* From Szczepiorkowski et al.[43]

† PLTs should be selected in the order selected.

BLOOD PRODUCT SUPPORT

Selecting Appropriate Blood Products for Recipients of ABO/Rh Mismatched S Cell Transplants

APPROPRIATE ABO GROUPS FOR TRANSFUSION, IMMEDIATELY POST-TRANSPLANTATION

	Donor	Recipient	Red cells	Platelets	FFP
Major ABO incompatibility	A	O	O	A	A
	B	O	O	B	B
	AB	O	O	A	AB
	AB	A	A*	A	AB
	AB	B	B*	B	AB
Minor ABO incompatibility	O	A	O	A	A
	O	B	O	B	B
	O	AB	O	A	AB
	A	AB	A*	A	AB
	B	AB	B*	B	AB
Bidirectional ABO Incompatibility	A	B	O	B	AB
	B	A	O	A	AB

* group O red cells may also be used

- Every centre performing ABOi HSCT must have transfusion protocols for docto

OUTCOMES OF ABO
HSCT

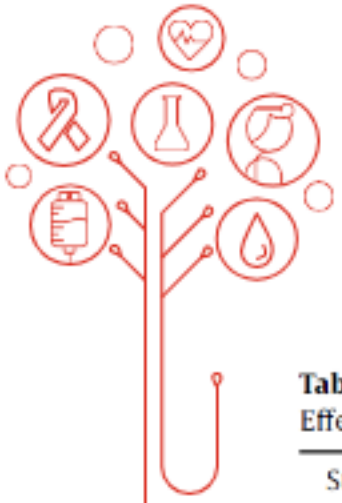


Table 2
Effect of ABO Incompatibility on Recipient Survival and Incidence of Graft-versus-Host Disease

Study Authors	Year	Survival after ABO-Incompatible HCT Transplantation			Risk of Graft-
		Major	Minor	Bidirectional	
Kimura et al. [3]	2008	Decreased	Decreased	No difference	Increased wit
Helming et al. [13]	2007	No difference*	No difference*	No difference*	No difference
Erker et al. [15]	2005	No difference	Decreased	Decreased	No difference
Kim JG et al. [12]	2005	No difference	No difference	No difference	No difference
Stussi et al. [14]	2002	Decreased	No difference	No difference	Increased wit
Benjamin et al. [18]	1999	Decreased†	Decreased†	No difference	No difference
Bacigalupo et al. [19]	1988	—	—	—	Increased wit
Benisnger et al. [41]	1982	No difference	—	—	No difference
Buckner et al. [17]	1978	—	No difference	—	No difference

RR indicates relative risk.

* Pediatric patients.

† Only in patients being treated for acute myeloid leukemia or myelodysplastic syndrome. A difference was not observe were treated for chronic myelogeneous leukemia.

Garrett S. Booth [1,*], Eric A. Gehrie [1], Char

Of course, especially in patients at high risk for
engraftment (eg, those with myelofibrosis) and th
received multiple RBC transfusions, selection of A
compatible HCT donors is optimal. **However, A**
incompatibility generally exerts less impact o
than other donor-recipient relationships, such
source, degree of HLA matching, status of expos
and other infectious disease, and most likely, don
gender, and parity.

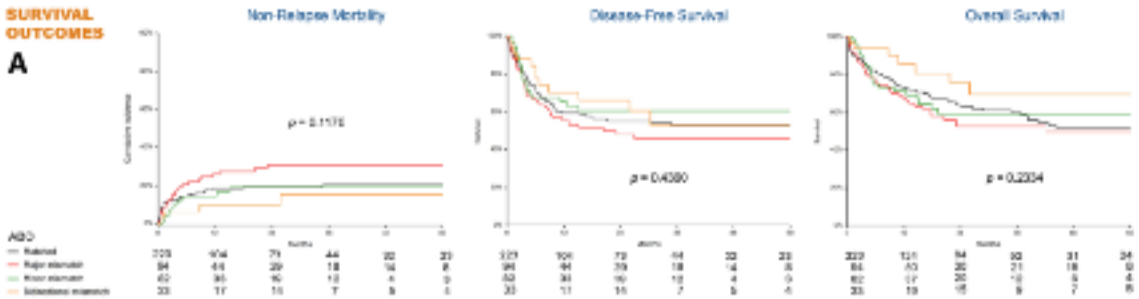
Overall, major ABO mismatch does NOT seem
consistent effect on other major outcomes aft
HSCT, such as incidence of acute or chronic G
rate, and overall survival, regardless of the ster

ABO Mismatch in Allogeneic Hematopoietic Stem Cell Transplant: Effect on Short- and Long-term Outcomes

Caterina Giovanna Valentini, MD, PhD,[1] Elisabetta Metafuni, MD, PhD,[1] Lorenzo Gallo, MD,[2] Sabrina Giammarco, MD, PhD,[1] Nicoletta Orlando, BSc, PhD,[1] Maria Bianchi, MD, PhD,[1] Simona Sica, MD, PhD,[1,2] Andrea Bacigalupo, MD, PhD,[1,2] Patrizia Chiusolo, MD, PhD,[1,2] and Luciana Teofili, MD, PhD[1,3]

Transplantation DIRECT ■ 2021

432 adult patients with acute leukemia a
lymphoma , MDS, AA, MM



No significant effect of any ABO mismatches was found at univariate analysis

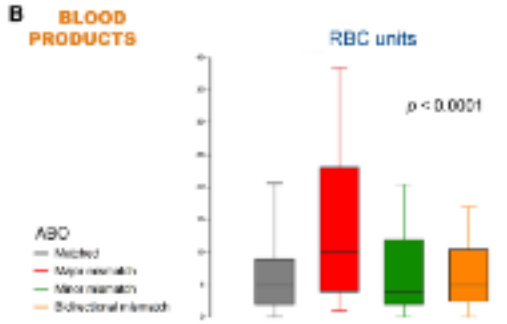


FIGURE 2. Cumulative incidence of transfusion discontinuation according to transfusions. B. Transfusion requirements in different ABO match groups. R.T.

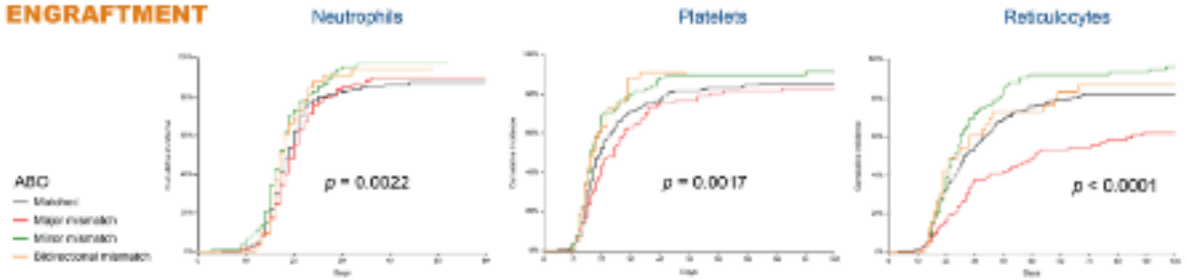


FIGURE 1. Cumulative incidence of neutrophil, platelet, and reticulocyte engraftment in different ABO match groups.

The reticulocyte engraftment was significantly impaired in major ABO-I transplants for both BM and PBSC source

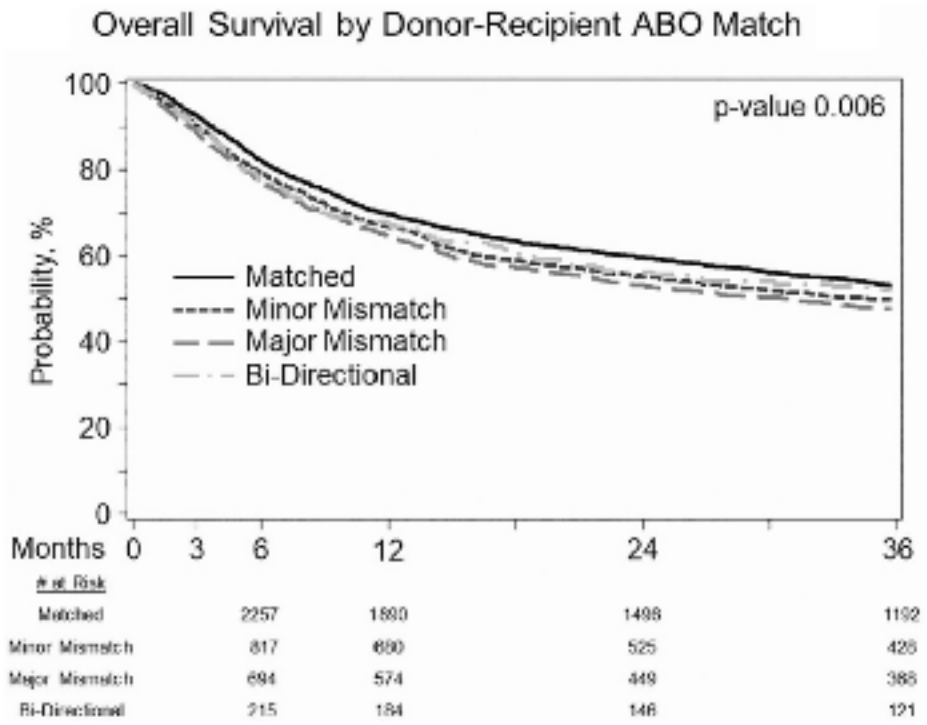
ABOi HSCT:

- Delayed RBC engra
- More RBC requirer
- BUT: NO effect on

Association of ABO mismatch with the outcomes of allogeneic hematopoietic cell transplantation for acute leukemia

Guru Subramanian Guru Murthy[1] | Brent R. Logan[1,2] | Stephanie Bo-Subait[3] | Amer Beitinjaneh[4] | Steven Devine[2] | Nosha Farhadfar[4] | Lohith Gowda[5] | Shahrukh Hashmi[7,8] | Hillard Lazarus[9] | Sunita Nathan[10] | Akshay Sharma[11] | Jean A. Yared[12] | Heather E. Stefanski[3] | Michael A. Pulsipher[13] | Jack W. Hsu[6] | Galen E. Switzer[14] | Sandhya R. Panch[15] | Bronwen E. Shaw[1]

Am J Hematol. 2023;98:606–619.



- 4946 patients with ALL/ AML MUD/ MRD
- 55.4% were ABO matched, 20.8% had a
  had a major mismatch, 5.6% had a bidir
- Multivariable analyses: compared to ma
  was associated with worse overall su
  engraftment, and **higher primary graft**
- **Relapse, acute and chronic GVHD we**
  associated with ABO status.
- Older recipient age was associated with
  relapse mortality.
- **donor–recipient ABO status is indepe**
  survival and other post transplantation
  leukemia.
- This underscores the importance of **con**
  donor selection algorithms and its im

ABOi HSCT outcomes - In summary

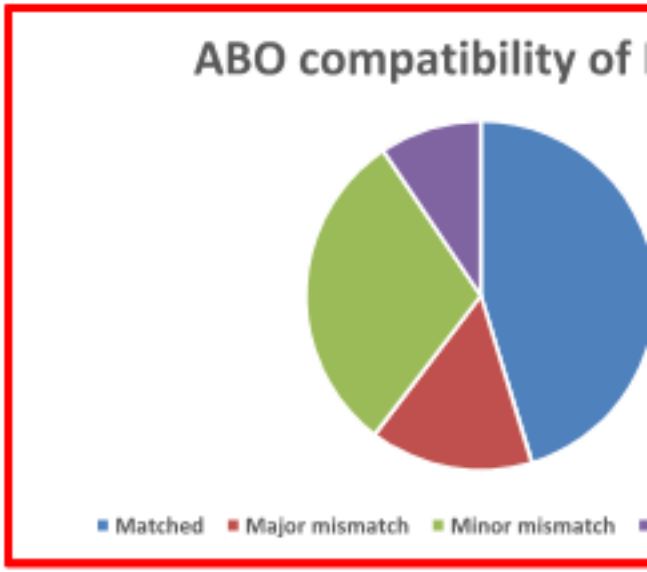
The heterogeneity of

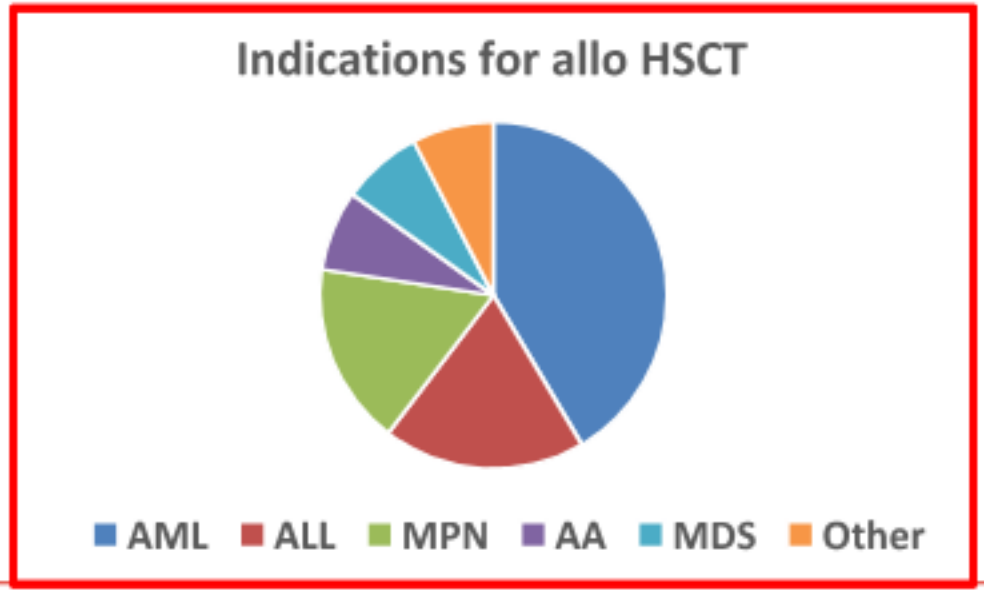
1. underlying diseases
2. patient age
3. variations in transplant practice and GVHD prophylaxis

adds to the complexity of interpreting outcome results and making conclusive f
ABOi versus ABO-compatible HSCT

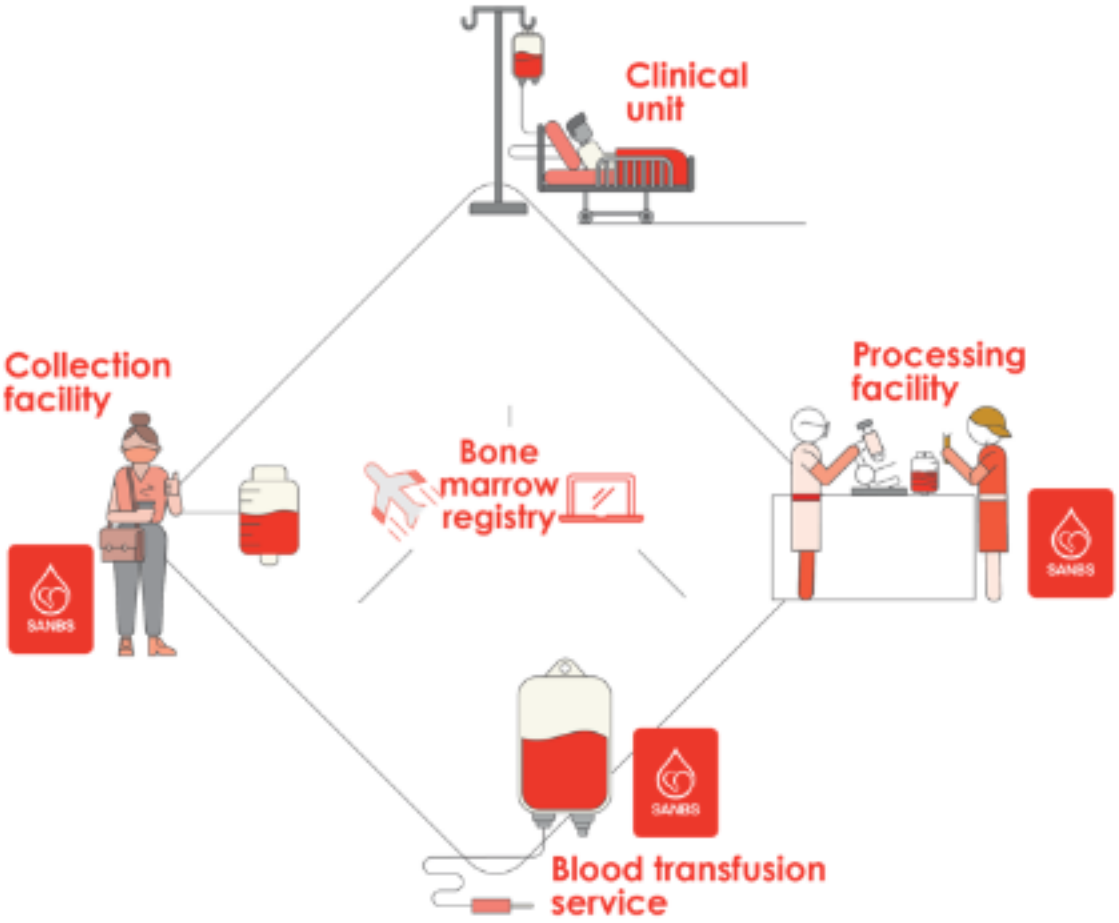
The SANBS experience –collection/ processing facility

- Two year period
- 53 allogeneic HSCT grafts:
  - MRD -45%
  - MUD -51%
  - Haploidentical <4%
- 29 grafts were ABO mismatched (**55%**): 8 major, 16 minor and 5 bidirectional.





- No ABOi HSCT recipient had
  (versus 1 ABO matched HSC
- 1 ABOi HSCT recipients had
  engraftment –minor mismatc
  matched)
- one-year mortality, graft-vers
  relapse rates and blood prod
  being assessed with clinical f



1. **ABO incompati**
contraindication t
and internationally

2. We need to **iden**
HSCTs EARLY so
managed - Further
as appropriate. AB
a routine part of pa

3. Team effort - **Co**
team, registry, proc
transfusion service

"Spectacular achievement is always preceded by unspectacular preparation" -Robe

Thank you.

Tanya.glatt@sanbs.org.za