UK NEQAS
International Quality Expertise

Histocompatibility
& Immunogenetics

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Interpretive Educational Scheme (iED)
Clinical Scenario 2/2017 – Haematopoietic Stem Cell Transplantation

Dispatched on 7th February 2017

Summary of Results

A total of 49 responses were received.

1) Please select 3 potential donors for this patient.

As the table below shows, Donor A was the most popular 1st choice donor with 33/49 (86.7%) participants selecting this donor. However, Donor B was the overall most popular choice of donor with 44/49 (89.8%) participants selecting it as one of their 3 choices.

Donor	Number of Participants			
	1st Choice	2nd Choice	3rd Choice	Total
A	33	6	2	41
B	13	23	8	44
C	0	3	16	19
D	0	0	3	3
E	1	0	4	5
F	0	1	2	3
G	0	13	12	25
H	2	3	2	7

The following table summarises the responses given by participants for selecting each donor.

Reason for selection		Donor							
		A	B	C	D	E	F	G	H
Donor	Male		✓	✓			✓		✓
	Female					✓		✓	
	Young age		✓	✓		✓	✓	✓	✓
	CMV match								✓
	ABO match	✓						✓	

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	Reason for selection	Donor							
		A	B	C	D	E	F	G	H
HLA	Potential 10/10 match/No mismatch identified	✓							
	Potential 9/10 match		✓	✓	✓			✓	✓
	ABDR matched	✓				✓			
	HLA-A mismatch preferred over B or DRB1 mismatch		✓	✓					
	HLA-B mismatch preferred over A or DR mismatch					✓			
	DRB1 high resolution match		✓						
	Permissive HLA-B mismatch							✓	
	Mismatch at HLA-B better than Mismatch at DR					✓		✓	
	B*41:01 mismatch often associated with C*17:01							✓	
	Likely Cw and DQ match			✓					
	Already typed for 5 loci		✓					✓	
	Potential 8/10 match							✓	
	Potential 7/8 match						✓		
	Linkage disequilibrium between HLA-DQ and HLA-DR	✓					✓		
	Expect it to be difficult to find a match to HLA-A*02:02		✓						
	Strong association between/tight linkage between HLA-B and HLA-C locus	✓					✓		
	High chance to obtain a A*23:01		✓						
	Probably African origin/haplotype	✓	✓						
	Potential 10/10 match/no mismatch in GvH direction			✓					✓
	Potential 9/10 match in HvG direction								✓
	1 A mismatch in GvH direction, potential fully matched in HvG direction.			✓					
Registry	Reliable/well established registry		✓					✓	
	Accredited registry					✓		✓	
	NMDP			✓					
	Poor experience with registry	✓							

Please note: ✓- indicates 'reason' was submitted by one or more participants relating to that donor. Other reasons may also apply.

Suggestions for further information required and testing the lab would perform included:

- Extended donor HLA typing, various combinations of loci and resolution, including:
  - High resolution/allelic/2nd field HLA-A*, B*, C*, DRB1*, DQB1*, DPB1*
  - Low resolution/1st field HLA-C* and DQB1*
- Confirm donor CMV on current sample
- ABO testing
- Weight of donor and family medical history
- Sex and age of donor if not provided
- Donor pregnancy information
- HLA antibody test recipient serum for donor specific antibodies

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2) After further typing, one donor found with 9/10 match at 2nd field (mismatch DRB1), with CMV mismatch. Would you recommend using this donor?

Yes	n= 13 (26.5%)
No	n= 33 (67.3%)
Did not answer	n= 3 (6.1%)

Explanations included:

- Not recommended according to guidelines
- Danger of reactivation of CMV
- Avoid HLA and CMV mismatch combinations if possible
- High risk patient due to age and disease
- More information required
- Explore alternative options
- Mismatch at DRB1 unacceptable
- Unlikely to find better match, urgency to transplant
- Recommend if only donor available
- CMV not considered in adult patients/not a risk as CMV positive patient

3) Would you recommend investigating an alternative transplant option for this patient?

Yes	n= 45 (91.8%)
No	n= 3 (6.1%)
Did not answer	n= 1 (2.0%)

Explanations included:

- Patient has AML, better to find CMV matched haplo donor
- Would perform a cord search
- Investigate siblings/children for suitability as haplotype donor
- Cord search may increase time taken to find donor (clinical urgency – AML can have small window of opportunity) and may struggle to get adequate cell count
- Study extended family (cousins, uncles, aunts…)

4) Which family member would you select as the donor of choice?

Brother	n= 14 (28.6%)
Son	n= 13 (26.5%)
Daughter	n= 21 (42.9%)
Did not answer	n= 1 (2.0%)

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Explanations included:

- Daughter:
  - 6/10 match
  - 7/12 match
  - CMV positive/match
  - High DPB1 DSA MFI permissive/could give high cell dose and DLI if required
  - DP antibody incompatibility irrelevant/less concern than Class I DSA
  - Plasmapheresis could be used to remove antibody
  - Better KIR B content score
  - Age/Young
  - Gender match/female

- Son:
  - Age/Young
  - CMV positive/match
  - Male
  - Low level MFI (A*68:01) would be low risk, unlikely to give positive crossmatch
  - Assuming heavier as male, therefore higher cell dose
  - Bw4 KIR ligands mismatch

- Brother:
  - No DSA (whereas DSAs to children)
  - Older patient likely to have reduced intensity conditioning – antibodies may cause problems post-transplant
  - DSA most important factor in haploidentical transplant
  - Male

5) Would you recommend any further testing to be performed on the relatives and the patient prior to transplant?

Yes	n= 47 (95.9%)
No	n= 2 (4.1%)

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Explanations included:

- Blood group of donor
- Red blood cell antibody screen
- KIR typing of recipient
- Repeat antibody testing
- Confirmatory HLA typing (donor and recipient)
- Monitor recipient HLA antibody levels
- Screen recipient for HPA/HNA antibodies
- Virology (IDMs)
- Standard donor evaluation to confirm fitness
- Minisatelites to follow chimerism post-transplant
- DPA1* type for all family members
- DRB3/4/5 type
- Re-test brother CMV
- C1q testing
- Weight and relevant medical history
- Crossmatch (CDC and Flow) relatives and patient
- Donor pregnancies

6) The Consultant decides to go ahead with the daughter. By day +28 the neutrophil count of the patient has not risen above 0.4x109/L. What post-transplant monitoring would you recommend?

Explanations included:

- Chimerism analysis to monitor engraftment
- HLA antibody testing to check DSA level
- Virology – especially BK and CMV
- HNA antibody screen (exclude potential cause of neutropenia)
- Respiratory viruses
- Confirm disease status
- Consider plasma exchange and DLI
- Consider adjusting immunosuppression
- Consider testing for granulocyte antibodies
- Check for MRD
- C1q screen
- CD34 boost from donor
- Immunophenotyping of lymphocytes