The Royal College of Pathologists
Pathology: the science behind the cure

Histocompatibility and Immunogenetics audit template

Date of completion	(To be inserted when completed)
Name of lead author/ participants	(To be inserted)
Specialty	Histocompatibility and Immunogenetics
Title	An audit of compliance with level 1 recommendations of BSHI Guidelines on HLA matching and donor selection for haematopoietic progenitor cell transplantation (HPCT).
Background	British Society for Histocompatibility and Immunogenetics (BSHI) have published updated guidance on best practise for HLA matching and donor selection for haematopoietic progenitor cell transplantation in 2021 (Little *et al.*, *Int J Immunogenet.* 2021;48:75–109) This audit will review compliance with some of the level 1 recommendations made in the guidelines.
Aim & objectives	To assess if HLA matching and donor selection service for haematopoietic progenitor cell transplantation is compliant with the 2021 Guideline
Standards & criteria	Criteria range: 100% or, if not achieved, there is documentation that explains the variance. The audit standards are based on the recommendations given in the 2021 BSHI Guideline: HLA matching and donor selection for haematopoietic progenitor cell transplantation.
Method	Sample selection: All patients undergoing haematopoietic progenitor cell transplantation over a minimum period of 3 months. Information collection method: from laboratory and clinical records (electronic and paper). Data to be collected on proforma (see below).

Results	(To be completed by the author) The results of this audit show the following compliance with the standards: Period covered: Number of transplants performed: Number of transplants assessed:		
	Investigation		**% compliance**
	1	The H&I lab is accredited by EFI and UKAS.	
	2	HLA typing definitions as described by Nunes et al., (2011) and within the guideline were used in reports.	
	3	Alternative progenitor cell donors (single mismatched unrelated donor/ umbilical cord blood (UCB) / haploidentical) were considered early in the donor search when a patient was identified as unlikely to have an HLA matched unrelated donor.	
	4	HLA typing of patients and all donors (matched and mismatched, related, unrelated and cord) proceeding to transplant was carried out at high resolution for HLA-A, B, C (exons 2 and 3 minimum) and DRB1, DQB1 and DPB1 (exon 2 minimum).	
	5	A 10/10 high or UHR/allele resolution HLA-A, -B, -C, -DRB1 and –DQB1 matched unrelated donor was selected over a mismatched donor.	
	6	Where a 10/10 matched unrelated peripheral blood stem cell (PBSC) or bone marrow donor was not available a single mismatch at HLA-A, B, C, DRB1 or DQB1 was selected with mismatches at DQB1 preferred.	
	7	Amino acid mismatches within the ARD were avoided when in mismatched donors.	
	8	Shortlisted UCB units met the minimum threshold required for a single UCB transplant (UCBT), (>3x10^7/kg recipient weight). In non-malignant conditions, especially bone marrow failure syndromes, or in cases where the HLA match was <6/8, the total nucleated cell (TNC) threshold was increased to >5.0 x 10^7/kg. When the patient's weight indicated that a double UCBT was required, a minimum TNC of >3.5 x 10^7/kg was maintained with the minimum TNC required for each unit being 1.5 x 10^7/kg. Preference was given to the best HLA matched UCB with TNC in excess of this minimum threshold.	
	9	UCB units with HLA match ≥4/8 in adults and ≥5/8 in children (non-malignant disease) are selected.	
	10	For single UCBT, UCB units with minimum CD34+ cell dose	

		≥1.5x10^5/kg were selected; and for double UCBT, units with minimum CD34+ cell dose ≥1.0x10^5/kg each were selected.	
	11	Red blood cell (RBC) replete UCB units with Haematocrit of >40% were avoided.	
	12	All patients and selected donor/UCB unit(s) had their HLA types confirmed on a sample independent to the first HLA type, prior to commencement of transplant work-up.	
	13	Donors that are cytomegalovirus (CMV) matched with the patients were selected (when there is a choice).	
	14	Younger donors were preferentially selected.	
	15	Homozygosity and novel HLA alleles identified within DNA extracted from patients with a high frequency of circulating tumour cells were confirmed by family studies or using DNA extracted from non-diseased cells.	
	16	Individuals actively involved in the provision of a donor selection service undertake continuing professional development (CPD) and the service is directed by a Royal College of Pathologist Fellow and Consultant in H&I.	
	17	Testing for HLA antibodies detects antibodies reactive with HLA-A, B, C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1 and DPB1 gene products.	
	18	The clinical urgency was made available to the individual performing the related and unrelated donor search.	
	19	HLA typing of regions outside the ARD to achieve Ultra High Resolution (UHR) or allelic level typing was performed.	
	20	When a choice of otherwise equally matched donors was available, non-permissive HLA-DPB1 mismatches were avoided. Patient HLA-DP expression levels were also be considered.	
	21	HLA-DRB3, DRB4, DRB5 typing was performed and, if a choice of otherwise equally matched donors was available, mismatches for these were minimised.	
	22	Additional testing for HLA-DPA1 and DQA1 was undertaken if indicated by patient's HLA antibody status.	
	23	Recipients receiving an HLA mismatched donor transplant had HLA alloantibody testing performed to ensure selection of donors, against whom the patient may have antibodies, was avoided.	
	24	If donor specific antibodies (DSA) were detected, the risk was further defined by determining the complement binding ability and / or by performing a crossmatch between the patient and donor as agreed with the transplant team.	
	25	Major ABO incompatibilities were avoided when there was a choice of donors.	
	26	Male donors were preferentially chosen when the patient has multiple donor options.	

	27	A back-up donor option was identified.	
	Comments:		
Conclusion	(To be completed by the author)		
Recommend-ations for improvement	Present the results with recommendations, actions and responsibilities for action, and a timescale for implementation. Assign a person(s) responsible to do the work within a timeframe. Some suggestions: • Highlight areas of practice that are different • Present findings. • Suggestions for improvements to this audit template and for improvements to the Guideline cited, send to the RCPath SAC for H&I		
Action plan	(To be completed by the author – see attached audit action plan proforma)		
Re-audit date	(To be completed by the author)		
Reference	BSHI Guideline: HLA matching and donor selection for haematopoietic progenitor cell transplantation, Little *et al*., *Int J Immunogenet.* 2021; 48:75–109		

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Data collection proforma

This form should be completed for each case included in the audit.

Audit reference: Case number: *(local identifier):*

Laboratory: Date(s):

Person completing form:

This document can be formatted to suit the laboratory's quality management system e.g Q-Pulse

Recommendation		1 Yes	2 No	3 N/A	Comments / notes about the case	4 If column 2 ticked, was there documentation to explain the variance?	5 Compliant with guideline if column 1 ticked or an appropriate explanation from column 4.
1	The H&I lab is accredited by EFI and UKAS.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**

Recommendation		1 Yes	2 No	3 N/A	Comments / notes about the case	4 If column 2 ticked, was there documentation to explain the variance?	5 Compliant with guideline if column 1 ticked or an appropriate explanation from column 4.
2	HLA typing definitions as described by Nunes et al., (2011) and within the guideline is used in reports.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
3	Alternative progenitor cell donors (single mismatched unrelated donor/ umbilical cord blood (UCB) / haploidentical) were considered early in the donor search when a patient was identified as unlikely to have an HLA matched unrelated donor.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
4	HLA typing of patient and donors (matched and mismatched, related, unrelated and cord) proceeding to transplant was carried out at high resolution for HLA-A, B, C (exons 2 and 3 minimum) and DRB1, DQB1 and DPB1 (exon 2 minimum).					**Yes No** **Comments:**	**Yes No N/A** **Actions:**

Recommendation		1 Yes	2 No	3 N/A	Comments / notes about the case	4 If column 2 ticked, was there documentation to explain the variance?	5 Compliant with guideline if column 1 ticked or an appropriate explanation from column 4.
5	A 10/10 high or UHR/allele resolution HLA-A, -B, -C, -DRB1 and –DQB1 matched unrelated donor was selected over a mismatched donor.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
6	Where a 10/10 matched unrelated peripheral blood stem cell (PBSC) or bone marrow donor was not available a single mismatch at HLA-A, B, C, DRB1 or DQB1 was selected with mismatches at DQB1 preferred.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
7	For mismatched donor transplants, amino acid mismatches within the ARD were avoided.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**

Recommendation		1 Yes	2 No	3 N/A	Comments / notes about the case	4 If column 2 ticked, was there documentation to explain the variance?	5 Compliant with guideline if column 1 ticked or an appropriate explanation from column 4.
8	Shortlisted UCB units met the minimum threshold required for a single UCB transplant (UCBT), (>3x10^7/kg recipient weight).					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
9	In non-malignant conditions, especially bone marrow failure syndromes, or in cases where the HLA match was <6/8, the total nucleated cell (TNC) threshold was increased to >5.0 x 10^7/kg.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
10	When the patient's weight indicated that a double UCBT was required, a minimum TNC of >3.5 x 10^7/kg was maintained with the minimum TNC required for each unit being 1.5 x 10^7/kg. Preference was given to the best HLA matched UCB with TNC in excess of this minimum threshold.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**

11	UCB units with HLA match ≥4/8 in adults and ≥5/8 in children (non-malignant disease) are selected.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
12	For single UCBT, UCB units with minimum CD34+ cell dose ≥1.5x10^5/kg were selected; b) For double UCBT, units with minimum CD34+ cell dose ≥1.0x10^5/kg each were selected.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
13	Red blood cell (RBC) replete UCB units with Haematocrit of >40% were avoided.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
14	All patients and selected donor/UCB unit(s)					**Yes No**	**Yes No N/A**

	had their HLA types confirmed on a sample independent to the first HLA type, prior to commencement of patient transplant conditioning.					**Comments:**	**Actions:**
15	Donors that are cytomegalovirus (CMV) matched with the patients were selected (when there is a choice).					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
16	Younger donors were preferentially selected.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
17	Homozygosity and novel HLA alleles					**Yes No**	**Yes No N/A**

	identified within DNA extracted from patients with a high frequency of circulating tumour cells were confirmed by family studies or using DNA extracted from non-diseased cells.					**Comments:**	**Actions:**
18	a) Individuals actively involved in the provision of a donor selection service undertake continuing professional development (CPD) b) the service is directed by a Royal College of Pathologist Fellow and Consultant in H&I.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
19	The clinical urgency was made available to the individual performing the related and unrelated donor search.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
20	HLA typing of regions outside the ARD to					**Yes No**	**Yes No N/A**

	achieve Ultra High Resolution (UHR) or allelic level typing was performed.					**Comments:**	**Actions:**
21	a) When a choice of otherwise equally matched donors was available, non-permissive HLA-DPB1 mismatches were avoided. b) Patient HLA-DP expression levels were also considered.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
22	HLA-DRB3, DRB4, DRB5 typing was performed and, if a choice of otherwise equally matched donors was available, mismatches for these were minimised.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
23	Additional testing for HLA-DPA1 and DQA1 was undertaken if indicated by patient's HLA antibody status.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
24	a) Recipients receiving an HLA mismatched					**Yes No**	**Yes No N/A**

	donor transplant had HLA alloantibody testing performed. b) Donors were selected to avoid patient HLA antibodies.					**Comments:**	**Actions:**
25	Testing for HLA antibodies detects antibodies reactive with HLA-A, B, C, DRB1, DRB3, DRB4, DRB5, DQA1, DQB1, DPA1 and DPB1 gene products.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
26	If donor specific antibodies (DSA) were detected, the risk was further defined by determining the complement binding ability and / or by performing a crossmatch between the patient and donor as agreed with the transplant team.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
27	Major ABO incompatibilities were avoided when there was a choice of donors.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
28	Male donors were preferentially chosen when the patient has multiple donor options.					**Yes No** **Comments:**	**Yes No N/A** **Actions:**
29	A back-up donor option was identified.					**Yes No**	**Yes No N/A**

						Comments:	**Actions:**

Audit action plan

An audit of compliance with level 1 recommendations of BSHI Guidelines on

HLA matching and donor selection for haematopoietic progenitor cell transplantation

Audit recommendation	Objective	Action	Timescale	Barriers and constraints	Outcome	Monitoring