

# INCIDENCE OF HLA-C MISMATCHES IN "FAVOURABLY MATCHED" RENAL TRANSPLANT PATIENTS MATCHED FOR HLA-B SPECIFICITIES



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**Table 1. Donors' HLA-B/C "haplotypes", designated on HLA-B type, matched and mismatched for HLA-C with their recipients**

HLA B type	Total no. of B/C haplotypes	No. Cw matched	No. Cw mismatched
B5	7	1	6
B7	33	30	3
B8	47	47	0
B12	42	25	17*
B14	1	1	0
B15	2	2	0
B16	2	2	0
B17	5	3	2*
B18	3	3	0
B22	3	2	1
B27	1	0	1
B35	5	2	3
B37	1	1	0
B40	10	8	2**

\* 1 case associated with HLA-B split mismatch

\*\* 2 cases associated with HLA-B split mismatch

## Introduction

The allocation of cadaveric donor kidneys within the UK is founded on a scheme involving mismatching for HLA-A, B and DR only. Thus, HLA-C only influences allocation when HLA-C typing is coincidentally available on a cadaveric donor and the patient is registered with an "unacceptable" HLA-C specificity.

Matching for HLA-C may be important in renal graft survival and HLA-C antibodies can cause hyperacute rejection. It is often assumed that, due to strong linkage disequilibrium between HLA-B and C, matching for HLA-B will usually result in an HLA-C match.

Accordingly, to assess the highest level of HLA-C matching in cadaveric donor renal transplantation we HLA-C typed a group of donor/recipient pairs who were HLA-B matched using UKTSSA matching criteria.

## Methods

HLA-C typing was performed on 81 first graft donor/recipient pairs transplanted between 1985 and 1999. All had a UKTSSA HLA-A,B,DR mismatch grade of 000 (n=39) or 100 (n=42).

Typing was done by PCR-SSP at the "split specificity" level (Cw1-Cw18) as a minimum resolution. The degree of HLA-C mismatching was assessed at the "split" level and, using local HLA-B/C linkage disequilibrium data, the likely HLA-B/C haplotype(s) responsible for the HLA-C mismatch were established for each transplant pair.

## Results

A total of 32 of the 81 pairs (39.5%) were mismatched for at least one HLA-C "specificity" (35.9% of the 000 mismatched group and 42.9% of the 100 mismatched group) - Table 1. There was no significant difference in the level of HLA-C mismatching between the two mismatched groups  $p > 0.25$ .

The incidence of HLA-C mismatches was high where HLA-B5 and/or B12 was present. HLA-B5 was seen in association with Cw1, 4, 6, 14 and 15 resulting in an HLA-C mismatch in 6 of the 7 (85.7%) HLA-B5 positive cases. Similarly, HLA-B12 was seen in association with Cw3, 4, 5, 6, 7, and 16 and caused an HLA-C mismatch in 17 of the 42 (40.5%) HLA-B12 positive cases

Conversely, the incidence of HLA-C mismatches was low where HLA-B7 or B8 was present. HLA-C mismatching was seen in 3/33 (9.0%) of B7 positive and 0/47 of B8 positive cases. HLA-B7 was seen with Cw3, 7, and 12 while B8 was seen only with Cw7.

The associations of HLA-B/C haplotypes possessing B12 and/or B5 with an HLA-C mismatch and B7 and B8 with no HLA-C mismatches were significant (all p values  $< 0.01$ ).

Of the 32 mismatched donor/recipient pairs the HLA-B/C haplotypes with B5 and B12 caused 65.7% of the 35 instances (3 cases of two mismatches) of an HLA-C mismatch. There were 4 examples of an HLA-C mismatch with an HLA-B split mismatch. However, none possessed HLA-B5 and only one involved a B12 haplotype.

Notably, three HLA-B7 (n=33 in total) and three B35 haplotypes (n=5) caused an HLA-C mismatch due to uncommon associations with Cw12 (n=2 each) and Cw3 (n=1 each).

## Comments

Overall, almost 40% of HLA-B matched donor/recipient pairs will have at least one HLA-C mismatch.

The presence of some phenotypes, including B5 and B12, will result in up to 85% of transplants being HLA-C mismatched.

In HLA-B sensitised patients the definition of HLA-C antibodies can be difficult. This study shows how poor HLA-C antibody definition can lead to positive cross-matches even in "favourably matched" pairs. This may result in kidneys being "bounced". HLA-C typing is not mandatory for cadaveric donors even though there are recipients who have HLA-C specific antibodies. This suggests that all cadaveric kidney donors and sensitised renal patients should be HLA-C typed and that HLA-C matching should be included in the cadaveric kidney allocation process.