# Transplanting blood group incompatible kidneys: potential utilisation of A2 donors

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## Introduction

We were asked by the Chair of KAG to consider whether utilisation of A2 deceased donor kidneys would be worthwhile in the UK, following recent reports from this approach in the US. In the UK, the Hammersmith group carried out 2 or 3 such transplants over a decade ago, with low titre recipients and no additional induction therapy or antibody removal (personal communication Prof Warrens). A recent report[1] suggested that a third of pediatric patients on the deceased donor waiting list had low anti-A or anti-B titres, and could therefore undergo a deceased donor blood group incompatible (ABOi) transplant, and although this approach was ratified by the Pediatric KAG, to our knowledge no such transplants have occurred. This paper summarises the current evidence for the use of A2 deceased donor kidneys for ABOi transplants, and assesses the potential value of this approach.

## Background

The use of A2 deceased donor kidneys for transplantation without antibody removal is well described, and is based on the lower expression of the A2 antigen, in combination with low anti-A titres in the recipient.[2,3]

In the US, the OPTN changed its policy in 2002 to allow transplantation of A2 or A2B kidneys from deceased donors into group B recipients[4]. The aim was to increase transplantation rates in group B recipients, and recipients were required to have anti-A IgG titre levels of less than 1 in 8. Titres were repeated at 3 monthly intervals, and 2 consecutive low titre results were required to enter the scheme. Interestingly, 42% of candidates were excluded due to a high first titre, and of the remainder 84% had a consistently low titre. Thus one might estimate that around a half of group B recipients could benefit from this approach.

Over a decade, there were 101 such transplants, and there was no significant difference in 1 or 3 year graft survival, when compared with compatible deceased donor transplants. However, there was no attempt to match the groups and antibody-mediated rejection rates were not reported.

Subsequently, in 2014 the OPTN extended the approach to formally incorporate this approach into the national allocation scheme[5]. No data is yet available from this period.

## Rationale

The longer waiting time for Group B candidates, and the high proportion of ethnic minorities amongst these patients, are well-known and will not be considered in further detail here. An increase in transplant rates for these patients would clearly be attractive, assuming this did not significantly disadvantage other groups. There are two further groups who could be considered: the Group O or B highly sensitised (CRF>85%) deceased donor candidates, who number 19% and 27% of those waiting respectively, and the NKSS, which already allows blood group incompatible transplantation for HLAi pairs.

Between 14 and 20% of A donors would be expected to be A2.[5] Assuming a cut-off of anti-A titres of 1 in 16, 3% of Group O but 68% of Group B waiting list recipients would be eligible for a deceased donor A2 transplant.[6]

**Practical considerations**

The first issue is the acceptable titre level. 4 centres in the UK use a level of 1 in 4 for the level on the day of transplant in their ABOi living donor transplant programmes, 2 decide on a case by case basis, and the remainder use 1 in 8[7]. However, many centres do not subtype for A2; at Guys, when this was done a level of 1in 16 was considered acceptable. It would therefore seem reasonable to consider eligibility for a deceased donor A2 kidney at 1 in 8 or less, with individual centres able to set local criteria as lower.
The OPTN/UNOS requires 2 tests to confirm the A subgroup[5]. This may be difficult, but subgrouping should be possible in all hospitals. Out of hours testing may be challenging in some centres. It would also be important that donor subgroup be tested on pretransfusion blood samples.
Titres may vary over time, so regular titre measurement would be important, as with HLA antibodies in the context of virtual cross-matching. It would seem reasonable to adopt a similar approach as the US, and require 2 titres of 1 in 8 or less, prior to inclusion. KAG may wish to consider whether all candidates for such a programme should have titres measured in a central laboratory, given the tremendous variation in titre measurement, as reported to the LDKT 2020 Strategy group[8].

**Efficacy**

The two key questions are firstly whether this approach would significantly benefit Group B or O recipients, and secondly whether it would disadvantage other patients.
Lisa Mumford is currently modelling the effects both within the deceased donor allocation scheme, and the NKSS.

**References**

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