SUPPLEMENTAL DATA

Ree examining Risk of Repeated HLA Mismatch in Kidney Transplantation

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Supplement Table 1: Classification of RMM where first and second donor had unresolved split/broad antigen typings with the potential to be a RMM						
Coding: *A= Broad Antigen Typing* *B,C= Split Antigen Typing corresponding ONLY to Broad Antigen A* *Z= Antigen not related to A, B, C* *For all recipients: if at least 1 RMM, RMM was assigned*						
Recipient	Donor 1 Typing	Donor 1 equivalents	Donor 2 Typing	Donor 2 equivalents	Classified	N
DONOR ANTIGENS FULLY RESOLVED						
Z	B	n/a	B	n/a	RMM	n/a
Z	B	n/a	C	n/a	NOT RMM	n/a
RECIPIENTS NOT SHARING BROAD/SPLIT POTENTIAL MM WITH SUBSEQUENT DONORS						
Z	A	B,C	A	B,C	RMM	440 (11%)
Z	B	B	A	B,C	RMM	
Z	A	B,C	B	B	RMM	
RECIPIENTS SHARING A BROAD/SPLIT POTENTIAL MM WITH SUBSEQUENT DONORS						
A	A	B,C	A	B,C	NO RMM	157 (2%)
A	A	B,C	B	B	NO RMM	
A	B	B	A	B,C	NO RMM	
TOTAL PATIENTS WITH POTENTIAL FOR MISCLASSIFICATION BASED UPON BROAD/SPLIT ASSUMPTIONS						597 (4%)

Rationale for classification of associated Broad/Split antigens

Broad antigens were serologically detected through complement dependent antibody-antigen interactions using earlier HLA typing methodologies. The fact that they were detected as "broad" despite now knowing that two or more "split" antigens may be uniquely identified within a given broad group, is due to the fact that the split antigens share many common epitopes/eplets with each other (and typing sera antibodies would bind to these common epitopes leading to detection of these different antigens as "one").

For recipients who do not share a split/broad antigen corresponding to subsequent donor(s') broad/split antigens (n=440)

A second mismatch from a shared split antigen from the same broad as the first donor (or vice versa), whereas not a clear RMM at the split level is still plausibly immunologically higher risk than a second transplant with a completely dissimilar antigen, given the emerging data that repeat epitopes/eplets are major drivers of immunologically deleterious outcomes). (References 9,11 main text) Therefore we chose to classify second transplants where a split antigen in one or both donors was not fully resolved (and were distinct from broads/splits in the recipient), as RMM to identify this greater potential for immunologic risk.

For recipients who share a broad antigen corresponding to subsequent donor(s') broad/split antigens (n=157)

For similar epitope based reasons, this was classified as NOT a RMM as the repeated antigens even if mismatched are more similar to the recipient than an unrelated antigen not part of the broad group.

We acknowledge the potential for misclassification in both directions. Sensitivity analysis excluding the 597 recipients (4%) in whom this potential is present was performed for the final model and shows no significant change to the HR. (Supplement Table 2)

Supplement Table 2. Cox proportional hazards model for all cause graft loss and death censored graft loss. EXCLUDING 597 RECIPIENTS WITH UNRESOLVED BROAD ANTIGENS		
≥1 Repeat Mismatch	**All Cause Graft Loss Hazard Ratio (95% CI)**	**Death Censored Graft Loss Hazard Ratio (95% CI)**
Original Model Excluding n=597	1.03 (0.96, 1.09) 1.04 (0.97,1.11)	1.03 (0.96, 1.11) 1.04 (0.96, 1.13)
Above models adjusted for: Age, Sex, Race, Cause of ESRD, Donor Age, Donor type, Duration of first graft survival, HLA match for 2nd graft, PRA for 2nd graft, induction, immunosuppression, and year of transplant.		

Supplement Figure 1. Univariate All Cause Graft Loss Kaplan Meier Survival Analyses for Class II RMM with and without nephrectomy, and Class I RMM

Note that the Kaplan Meier Analysis is unadjusted and does not account for the other covariates included in the Cox Model (Table 5) (age, sex, race, cause of ESRD, donor age, donor type, duration of first graft survival, HLA match for 2nd graft, PRA for 2nd graft, induction, immunosuppression, and year of transplant)