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A positive Flow Cytometry XM increases AMR but not graft loss following HLA-incompatible kidney transplantation

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Background: Kidney transplantation in the presence of donor-specific HLA antibodies (DSA) is an option for difficult to match patients. Predicting the risk of rejection and/or worse outcomes remains a challenge.

Methods: National multi-centre case-control study included HLA incompatible (HLAi) kidney only transplant recipients (2011-2018) matched in a 1:2 ratio with HLA compatible (non-HLAi) controls (2015-2016). Match criteria included gender, age and donor source. HLAi was defined as the presence of DSA (DSA POS) identified by Luminex at time of transplantation irrespective of T and B-cell flow cytometry crossmatch (FCXM) status. Antibody mediated rejection (AMR), transplant- and patient survival were retrospectively analysed.

Results: Hundred-eighty patients were included in the study, of which sixty received an HLAi transplant. Mean age 46 years; 60% female, 25% received a live donor organ (cases vs controls; p=NS). Median cumulative Mean Fluorescence Intensity (MFI) at time of HLAi transplant was 3321 (IQR 1276 – 6675) which resulted in a positive FCXM in 25 (42%) recipients. All patients were CDC crossmatch negative. Forty-five (75%) HLAi recipients received lymphocyte depleting (LDa) induction therapy and 15 (25%) received an IL-2R antagonist (IL2Ra). Non-HLAi controls received IL2Ra induction. Mean follow up was 2.1 (SD±0.9) and 2.2 (SD±0.6) years for HLAi and non-HLAi respectively (p=NS).

DSA POS/FCXM POS transplantation carried an increased risk of AMR at 1 year (53%) compared to DSA POS/FCXM NEG transplants (26%) and non-HLAi transplants [(0%), p<0.001]. LDa induction was superior to IL-2Ra induction in preventing AMR at 1 year (43% vs 75%, p=0.06) in DSA POS/FCXM POS transplants, but not in DSA POS/FCXM NEG transplants (26% vs 29%, p=NS). Patients with HLA Class II DSA as predominant DSA had higher rates of AMR than patients with HLA Class I DSA (45% vs 28% AMR at 1 year, p=0.16). Graft survival at 1 year was 94% following HLA compatible transplantation, compared with 97% following DSA POS/FCXM NEG and 87% following DSA POS/FCXM POS transplantation (p=NS). Mortality risk was increased in the 2 years following HLAi transplantation (15% and 2% for HLAi and non-HLAi recipients respectively [p<0.001]); 46% and 0% of deaths were infection-related in each group.

Conclusion: In kidney transplantation, the presence of DSA and a positive FCXM carries the greatest risk of AMR, but not graft loss at 1 year compared to HLA compatible and DSA POS/FCXM NEG transplantation. Induction therapy consisting of a lymphocyte depleting agent improves AMR risk at 1 year in FCXM POS but not FCXM NEG transplants.