Combination of Non-HLA and HLA-DSA Antibodies Identifies Liver Transplants Recipients With Highest Risk for Fibrosis Progression and Mortality

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Recent data has shown an increased risk of fibrosis progression in HCV viremic liver transplant (LT) recipients with HLA DSA in serum. However, the role of non-HLA DSA and the interaction between HLA and non-HLA DSA remains unknown in LT patients. Methods: 535 HCV-viremic primary liver allograft recipients at Baylor University Medical Center between 1/00 to 4/09 had their prospectively collected pre-transplant serum tested retrospectively for the following alloantibodies: Class I & II HLA DSA (MFI>5000), Angiotensin II Type-1 Receptor (AT1R) DSA (>19 U/mL), and Endothelin-1 Type A receptor (ETAR) DSA (>23 U/mL). Results: Preformed DSA were found in the following patients: Class I &/or II HLA DSA alone (69), AT1R (76), ETAR (64), HLA DSA with AT1R (13), HLA DSA with ETAR (12). Fibrosis progression to the composite endpoint of METAVIR stage 2-4 or death caused by liver allograft failure was markedly accelerated in patients with the combination of a preformed HLA and non-HLA DSA compared to patients with either none or 1 DSA (Figure 1; p=0.01). Similar findings were seen when each HLA DSA was combined with AT1R (p=0.04) or ETAR (p=0.04). Stepwise multivariable analysis, controlling for donor and recipient race, recipient age, CMV infection, sustained virologic response, and induction therapy, showed the combination of a preformed non-HLA and HLA-DSA had a HR=2.33 (p=0.01) of advanced fibrosis or liver related death. Conclusions: The combination of a preformed non-HLA (either AT1R or ETAR) and HLA DSA was associated in multivariable modeling with the highest hazard ratio for METAVIR stage 2-4 or liver related death of

any other single variable.