Development of circulating anti-HLA antibodies is associated with acute rejection: Interim Analysis of CTOT02

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Body: The clinical characteristics and the impact of development of anti-HLA alloantibodies (Abs) in renal transplant recipients is not well defined. This report looks at possible associations between Ab development, clinical characteristics, allograft histology at time of Ab development, and acute rejection following Ab conversion.

Over 750 subjects have been enrolled in the screening phase of the NIH CTOT-02/CCTPT-02 study, a multi-center prospective trial where unsensitized kidney transplant recipients are screened for development of *de novo* anti-HLA Abs up to 48 months post transplant. Subjects were divided into those who developed anti-HLA antibodies (Ab+) and those who did not (Ab-) as detected by Luminex. Ab+ subjects were offered treatment with anti CD20 therapy.

92 (15%) subjects developed Abs, at a fairly constant rate throughout the study period. 26, 51 and 15 subjects developed class I, II or both I & II Abs respectively. Mean time of Abs development was 18±10 months post transplant. Compared to Ab- subjects, Ab+ subjects were younger (36±18 vs. 43±17; $p<0.01$) and had lower serum creatinine (SCr) (1.3±0.5 vs. 1.4±0.5; $p=0.03$) at enrollment. There was no evidence of an association between Ab development and gender, donor type or DGF status. SCr at time of Ab conversion in Ab+ subjects was similar to the last SCr at follow-up in Ab- subjects (1.5±1.8 vs. 1.4±0.6; $p=0.65$). The proportion of subjects who developed acute rejection (AR) was higher in the Ab+ group (14 vs. 3%; $p<0.01$); most of the AR (77%) were noted after Ab development, at a mean time of 4.8±4.8mo post conversion. Moreover, biopsies in 7/18 Ab+ subjects prior to treatment showed evidence of acute rejection.

This interim analysis of CTOT-02 reveals unexpected differences in the baseline characteristics and a high proportion of subclinical and clinical rejection associated with anti-HLA Abs.