

Title: Silent development of *de novo* anti HLA antibodies following transplantation is associated with histological changes in the allograft. Interim report on behalf of the CTOT-02/CCTPT-02 study.

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Body: The clinical relevance of monitoring solid organ recipients for the development of anti-HLA alloantibodies (Abs) is unknown and the importance of class I vs. II Abs remains unclear. Over 650 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 post transplant. The aim of this report is to look at possible associations between Abs and gender, donor type, induction, HLA mismatch (MM) and DGF and correlate development with concurrent histology. Abs were detected by Luminex and the analysis was performed using log-rank statistics and univariate cox model.

49 subjects developed Abs: 22, 35 and 8 subjects developing class I, class II or both class I & II Abs. Unexpectedly, among the 75 zero MM subjects, 6 developed Abs, but only against class I (HR 2.9; p=0.03 vs. at least 1MM). Female gender was associated with class II conversion (HR 1.9; p=0.05). There was a trend for an association between class II conversion and the use of any induction therapy (p=0.09). This association was not confounded by MM status; 94% of subjects with zero MM received induction therapy, similarly to MM subjects. There was no association between Ab development and donor type or DGF. Biopsy results were available for 12 subjects prior to randomization to the treatment phase of the study. 5/12 showed evidence of borderline/acute rejection; all positive for class II, none for class I Abs (p=0.01).

This interim analysis of CTOT-02 suggests important differences in the baseline characteristics and the clinical impact associated with anti-HLA Abs. Longitudinal and mechanistic studies are underway to characterize the immunological profile and clinical outcome post-Ab conversion.