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Was the work presented in this abstract performed by a Transplant Nephrology Fellow enrolled in an AST accredited Fellowship Program? No.

Title: *In Vitro* C1q Binding is Associated with Acute Rejection Among Renal Transplant Recipients Who Develop Circulating Anti-HLA Antibodies: Preliminary Analysis of the NIH CTOT02.

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Body: We have recently demonstrated that the de novo development of anti-HLA alloantibodies (Abs) in kidney transplant recipients is associated with acute rejection. The C1q assay is a novel in vitro assay that differentiates complement from non-complement binding anti HLA-Abs. This report looks at possible associations between C1q positivity and acute rejection following the de novo development of anti-HLA Abs post transplantation.

756 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 60 months post transplant. 78 subjects who developed anti-HLA Abs were included in the present analysis, the rate of conversion to anti-HLA Ab+ occurred at a fairly constant rate throughout the post-transplant period. Anti-HLA Ab detection and the C1q assay were conducted using Luminex.

41 of 78 (53%) Ab+ subjects were C1q positive, with a predominance of class II Abs (26 (63%) class II with 11 (27%) class I, and 4 (10%) class I and II). The distribution of Ab+C1q+ subjects compared to Ab+C1q- subjects was not different according to whether they were directed against class I or II. 24/32 (75%) of C1q+ compared to 14/32 (44%) of C1q- antibodies were donor specific (p=0.01). Donor specificity of Ab could not be determined in 14 of the subjects as DQ testing was not universally available. Interestingly, the presence of *in vitro* C1q+ positivity was significantly more associated with acute rejection episodes than was C1q- negativity in anti HLA Ab+ subjects (39 vs. 16%; p=0.03). In particular, acute cellular rejection occurred more often in C1q+ subjects (32 vs. 11%; p=0.03), whereas there was no statistically significant difference in antibody-mediated rejection (15 vs. 8%; p=0.49).

This analysis indicates that C1q positivity is more often associated with donor specific Ab and that a high proportion C1q+ Ab+ subjects develop acute rejection, especially of the cellular type. Whether the ability of Ab to bind C1q *in vitro* is associated with poorer long-term outcomes will be the subject of further studies.