SP685 **HLA CLASS II ANTIBODIES AT THE TIME OF KIDNEY TRANSPLANTATION AND CARDIOVASCULAR OUTCOME: A COHORT STUDY**

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INTRODUCTION AND AIMS: The immune system is directly involved in the pathogenesis of atherosclerosis and coronary artery disease but its role in cardiovascular disease after transplantation remains uncertain. The negative role of especially class II donor specific antibodies (DSA) on kidney graft outcome is well-recognized. Recently, high panel reactive antibodies (PRA) at the time of transplantation and class II DSA 6 months post transplantation were associated with worse cardiovascular outcome in kidney transplant recipients. Our hypothesis was that pre-formed HLA class II antibodies at the time of transplantation were associated with worse cardiovascular outcome after kidney transplantation.

METHODS: We conducted a single-center, observational retrospective cohort study including 1114 kidney transplant recipients transplanted between January 2003 and December 2016. Data on the presence of HLA class II antibodies at the time of transplantation were available in 827 subjects. The primary outcome of interest was a composite of time to major adverse cardiac and cerebrovascular events and all-cause mortality (MACCE) with up to 15 year follow-up. Secondary outcomes were a composite of cardiac and cerebrovascular events with or without cardiovascular mortality. We designed a multivariable Cox proportional hazard regression model with adjustment for potential confounders including age, sex, PRA and re-transplantation as well as for polyclonal induction, diabetes and baseline cardiovascular disease at time of transplantation. We registered the incidence of biopsy proven acute rejection (BPAR) and graft loss for separate subgroup analysis.

RESULTS: The mean age of the patients (62% male) was 52 ($\pm$13) years with a mean follow-up of 5.4 ($\pm$3.3) years. One hundred and sixteen patients (14%) had HLA class II antibodies at the time of transplantation. Sixty-seven patients (8.1%) received polyclonal antibodies as induction therapy. BPAR occurred in 120 patients (14.7%) and graft loss in 59 patients (7.3%) with no statistical difference in incidence between patients with or without class II HLA antibodies. Seventy-eight patients (9.7%) had adverse cardiac and cerebrovascular events and 83 (10%) died during follow-up. The primary outcome analysis revealed an adjusted hazard ratio (aHR) of MACCE in those with versus without class II HLA antibodies of 1.71 (95%CI of 1.13 to 2.60). The increased aHR due to class II HLA positivity was confirmed in a subgroup analysis in patients without BPAR or graft loss with an aHR of respectively 2.03 (95%CI of 1.29 to 3.18) and 1.97 (95%CI of 1.25 to 3.12). The secondary outcome analysis showed an aHR of 1.92 (95%CI of 1.11 to 3.3) and an aHR of 1.85 (95%CI 1.06-3.2) for cardiac and cerebrovascular events respectively with and without cardiovascular mortality.

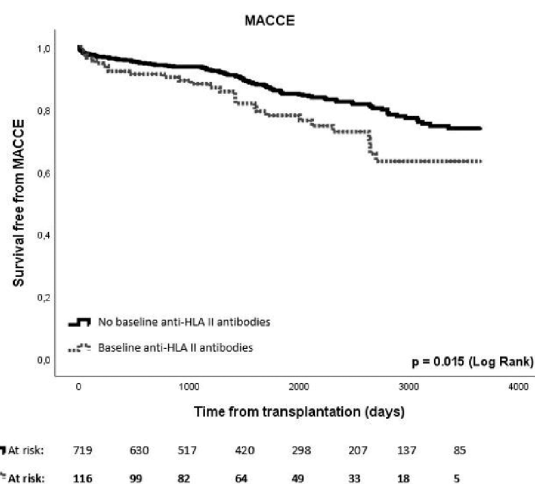|		MACCE					
At risk:	719	630	517	420	298	207	137	85
At risk:	116	99	82	64	49	33	18	5

Figure: Kaplan-Meier survival curves for MACCEs in kidney transplant recipients with or without anti-HLA II antibodies at time of transplantation. MACCE = major adverse cardiac and cerebrovascular event, indicating acute coronary syndrome, coronary revascularization, transient ischemic attack, cerebrovascular accident or all-cause mortality.

CONCLUSIONS: Previous sensitization against HLA class II antigens is associated with unfavorable long-term cardiovascular outcome in kidney transplant recipients independent of effects on graft function.