ABACAVIR INDUCED ALLOREACTIVITY: RELEVANCE TO KIDNEY TRANSPLANTATION FOR HIV POSITIVE INDIVIDUALS

D'Orsogna L[1,2], Almeida C[1], van Miert P[3], Zoet Y[3], Anholts J[3], Chopra A[4], Watson M[4], Witt C[1], John M[5], Claas F[3].

1. Department of Clinical Immunology and Pathwest, Fiona Stanley Hospital, Perth, Australia
2. School of Medicine, University of Western Australia, Perth, Australia
3. Department of Immunohaematology and Blood Transfusion, Leiden University Medical Centre, Leiden, the Netherlands
4. Institute for Immunology and Infectious Disease, Murdoch University, Perth, Australia
5. Department of Clinical Immunology and Pathwest, Royal Perth Hospital, Perth, Australia

Introduction: Abacavir administration is associated with drug induced hypersensitivity reactions in HIV+ individuals expressing the HLA-B*57:01 allele. However the immunological effects of abacavir administration in an HLA-B57 mismatched transplantation setting has not been studied. We hypothesized that abacavir exposure could induce *de-novo* HLA-B57 specific allorecognition.

Materials and Methods: HIV-specific CD8 T cell clones were generated from HIV+ individuals, using single cell sorting based on HIV peptide/HLA tetramer staining. The T cell clones were assayed for alloreactivity against a panel of single HLA expressing cell lines (SALs), in the presence or absence of abacavir. Cytokine assay, CD137 upregulation and cytotoxicity were used as readout.
Results: Abacavir exposure can induce *de-novo* HLA-B57 allorecognition by HIV-specific T cells. A HIV Gag RK9/HLA-A3 specific T cell did exhibit IFNγ production, CD137 upregulation and cytolytic effector function against allogeneic HLA-B57, but only in the presence of abacavir. Allorecognition was specific to the virus-specificity, HLA restriction and TCR TRBV usage of the T cell.

Conclusion: We provide proof-of-principle evidence that administration of a drug could induce specific allorecognition of mismatched HLA molecules in the transplant setting. We suggest that HIV seropositive recipients of an HLA-B57 mismatched graft should not receive abacavir until further studies are completed.