Title: Inflammation and microbial translocation in primary HIV infection and the effect of short course antiretroviral therapy

Abstract:

Background: Microbial translocation is associated with immune activation in chronic HIV-1 infection and may provoke endothelial dysfunction. We examined the relationship between surrogate markers of microbial translocation, endothelial activation and immune activation in Primary HIV-1 infection (PHI) and assessed whether short course ART given in PHI impacts on these biomarkers after stopping treatment.

Methods: Plasma samples from 90 UK and Australian SPARTAC participants recruited within 6 months of HIV seroconversion and randomised to 12 or 48 weeks ART, or no ART, were analysed for surrogate markers of microbial translocation (LPS-Binding Protein (LPB), soluble CD14 and Endotoxin Core Antibody (EndoCab) at baseline and week 60. Results were correlated with markers of inflammation, coagulation and endothelial activation (IL-6, D-dimer, soluble tissue factor, ICAM-1) and CD4 and CD8 T-cell activation (CD38 and HLA DR) using Spearman rank correlations. Biomarker levels at week 60 and change from baseline were compared between arms using linear regression analyses. Samples from 30 healthy controls were also analysed at a single time point and compared to SPARTAC week 0 and 60 using Mann-Whitney U tests.

Results: At SPARTAC week 0, no relationship was seen between T cell activation and markers of microbial translocation. However at week 60, sCD14 and EndoCab correlated with CD4 T-cell activation (e.g. sCD14 and CD4 HLADR% rho=0.4, p<0.001; EndoCab and dual CD4 CD38 HLADR% rho=0.3, p=0.01) and LBP weakly correlated with CD8 T-cell activation. No difference was seen between SPARTAC arms at week 60 comparing those who received either 12 or 48 weeks ART and those randomised to no ART. LBP and sCD14 were raised in SPARTAC patients compared to healthy controls at week 0 and week 60 (p<0.001 for sCD14; p=0.002 at week 0, p=0.02 at week 60 for LBP).

Conclusion: Surrogate markers of microbial translocation were raised in HIV+ve patients compared to healthy controls. In SPARTAC, these markers were associated with T cell activation at week 60 but not at seroconversion. 48 weeks of ART did not impact LPS activity at 60 weeks after PHI, 12 weeks after treatment interruption; this analysis was however limited by small numbers.