Introduction Persistent systemic immune activation despite effective HIV treatment may be revealed by measuring plasma 'biomarker' levels. Here we investigate three established biomarkers within a well-characterised HIV cohort.
Methods Plasma sCD14, sCD163 and CXCL10 levels were measured by ELISA methods in 475 consecutive patients with documented CVD risk (age, ethnicity, gender, smoking, blood pressure, BMI, fasting metabolic profile), as well as HIV treatment history and immunological/virological outcomes, and analysed using multiple regression analysis.
Results All biomarkers were reduced with higher CD4 counts ($p < 0.05$), but showed distinct associations with virological response: CXCL10 strongly correlated with viral load ($p < 0.001$), sCD163 was significantly reduced among 'aviremic' patients only ($p = 0.02$), while sCD14 was unaffected by virological status under 10000 cpms ($p > 0.2$) however sCD14 was increased if HIV RNA viral load was >10000 cpm ($p = 0.003$). The choice of HIV treatment did not affect CXCL10, however, higher sCD163 was associated with PI's ($p = 0.05$) and lower sCD14 was associated with integrase inhibitors ($p = 0.02$). Several CVD risk factors were associated with sCD163 (age, ethnicity, HDL, BMI), with a favourable influence of Framingham score <10% ($p = 0.04$). Soluble CD14 levels were higher among smokers ($p = 0.002$), with no effect of other CVD risk factors, except age ($p = 0.045$), or overall Framingham score.
Conclusion These biomarkers reveal remarkably distinct associations, with levels of CXCL10 most readily explained by routinely monitored variables (viral load, CD4 counts), while sCD163 levels appear to reflect a deeper level of virological suppression as well as the influence of CVD risk factors. Levels of sCD14, which have been linked to overall mortality risk, are least associated with routinely monitored variables, with evidence of specific effects of smoking and integrase inhibitor therapy that warrant further investigation.
Disclosure of interest statement None to disclose.

O21.3 PRE-THERAPY INFLAMMATION/COAGULATION ACTIVATION AND LONG-TERM CD4 RESPONSE TO ANTIRETROVIRAL THERAPY

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Background Pre-antiretroviral therapy (ART) inflammation/coagulation activation biomarkers predict clinical outcomes, but whether they predict CD4 response to ART initiation is unknown.
Methods Study cohort was a subset of 2 international trials, SMART (evaluating continuous versus interrupted ART) and FIRST (evaluating 3 first-line ART regimens with ≥2 classes). At the start of follow-up (baseline), participants had to be ART-naïve/off ART, have C-reactive protein (CRP), interleukin-6 (IL-6) and D-dimer measured and be (re)initiating ART. Using random effects linear models, we assessed the association between quartiles of each of the baseline biomarker and change in CD4 to up to 24 months after ART-initiation. Analyses adjusted for baseline CD4, study arm, follow-up time and other known confounders. Sensitivity analyses included separate analyses by trials and excluding the interrupted ART arm in SMART.
Results Overall, 1084 individuals (659 from SMART (26% ART naïve) and 425 from FIRST) met the eligibility criteria, providing 8264 CD4 measurements. 75% were male with the mean age of 42 years, 37% and 47% were white and black respectively, and 10% and 33%, respectively, were hepatitis B and C positive. The median (inter-quartile range) baseline CD4 (cells/mm^3) were 360 (265–473) overall and 416 (350–530) and 100 (22–300) in SMART and FIRST, respectively. All of the biomarkers were inversely associated with baseline CD4 in FIRST but not in SMART. Curves of CD4 change over time by pre-ART biomarker quartiles significantly overlapped for all biomarkers. In adjusted models, there was no significant relationship between baseline biomarker levels and mean change in CD4 (P for trend: CRP: 0.97; IL-6: 0.25 and D-dimer: 0.29). Sensitivity analyses yielded similar results.
Conclusion Pre-ART inflammation/coagulation activation markers do not predict CD4 response to ART. These biomarkers appear to influence the risk of clinical outcomes through mechanisms other than by blunting long-term CD4 gain.
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O21.4 DECREASED CELLULAR ENERGY IN THE BRAIN FRONTAL WHITE MATTER IS ASSOCIATED WITH PAST IMMUNOSUPPRESION IN CHRONIC HIV INFECTION

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Background Long-term brain neurochemical changes are not clearly understood in HIV-infected adults who are ageing and are otherwise clinically stable.
Methods Forty men (mean age = 54 ± 7), 20 HIV-infected (70% with historical AIDS, nadir CD4 ≤350, all on antiretroviral treatment and virally suppressed), and 20 demographically comparable HIV-uninfected controls were enrolled into a prospective observational cohort study. All underwent standard neuropsychological testing to determine the level of neurocognitive performance over an 18-month period, and a proton magnetic resonance spectroscopy scan of the brain frontal white matter to assess *in vivo* neurochemical information. Clinically relevant neuropsychological change over the study period was determined using neurocognitive norms for change. Major brain metabolites: Creatine, N-Acetyl Aspartate, Choline, Glutamate/Glutamine and Myo-Inositol were fitted in jMRUI in reference to water. Brain metabolites' change was determined using linear regression with a time effect, a group effect and a time*group interaction effect. Data were randomly selected from the larger baseline cohort (N = 120) for this preliminary analysis.
Results Over the 18 months period, neurocognitive performance change did not differ between HIV-infected and controls. Creatine significantly decreased in the HIV-infected compared to the controls ($p < 0.03$). Myo-Inositol and Glutamate/Glutamine increased as a function of time ($p < 0.0001$) but equally in both groups. When adjusting our analyses for age, we corroborated an age*group effect ($p < 0.03$) on reduced N-Acetyl Aspartate in the HIV-infected participants, while the decreasing Creatine