Persistent immune activation despite suppressive HAART is associated with higher risk for viral blips in HIV-1 infected individuals

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Background: Viral blips are thought to represent random biological variations around a steady state of residual HIV viremia and to lack clinical significance. However, blips may be the consequence of shedding from activated immune cells and persistent immune activation has recently been linked with increased morbidity and mortality. We aimed to assess the association of persistent immune activation and the occurrence of blips.

Methods: HIV infected patients from our outpatient cohort who developed a blip after having been on fully suppressive HAART for at least 180 days were matched with patients without blips according to duration of time of complete viral suppression (CVS), age, sex, and CDC stage. Domain averaged areas under the curve for CD3+, CD4+, CD8+, CD3+HLADR+, CD4+CD45RA+, CD16+CD56+CD3-, and CD19+ cells, as well as CRP levels were calculated from first date of CVS until index date and included in conditional logistic regression models. Adherence to HAART was assessed by measuring prescribed NNRTI or PI plasma levels in a sample of 57 patients.

Results: 82 Patients with a viral blip were matched with 82 controls. Mean age at blip was 47.2(SD 12.1) years, 80.5% of patients were male and 42.7% had CDC stage C disease in both groups. Viral blips occurred after a median of 14 months (IQR 8-34) of CVS. In the logistic regression, activated CD3+HLA-DR+ lymphocytes (OR 1.39 per 100 cells/µl,[95%CI1.12-1.72],p=0.003) and HAART initiation after 2007 (vs. before 2001, OR 0.23[0.08-0.69],p=0.005) were significantly associated with viral blips. In 7/23(30%) specimens from patients with blips and 13/34(38%%) controls, drug levels were below therapeutic concentration (p=0.55).

Conclusion: The occurrence of viral blips after suppressive HAART was associated with persistently elevated markers of T cell activation. Blips were not explained by decreased drug levels and may identify a subset of patients with higher immune activation and increased risk for HIV disease progression.