No impact of early intensified antiretroviral therapy on gut immune reconstitution

Summary

HIV infection is characterized by reduced mucosal Th22 and Th17 cell numbers and function, which contribute to microbial translocation and inflammation. Standard antiretroviral therapy (ART) is slow to reverse these mucosal defects, and the resulting persistent inflammation is linked to serious non-AIDS illnesses (SNAs). We examined whether ART intensification with maraviroc and raltegravir during early HIV infection would accelerate the resolution of gut immune dysfunction, microbial translocation, and SNA biomarkers. Twenty-two participants documented to have acquired HIV a median of 4 months ago were enrolled. Prior to ART initiation, gut Th22 cell numbers and Th17 polyfunctionality were reduced compared to controls, and plasma LPS and D-dimer levels were elevated. At 48 weeks after ART initiation, overall gut Th22 cell numbers were restored, but plasma LPS and D-dimer levels were lowered, despite gut Th17 function remaining unchanged, and blood D-dimer levels had actually increased. ART intensification had no impact on gut CD4 T cell immune subsets (Th1, Th17 and Th22 cells), microbial translocation (LPS), or SNA biomarkers (D-dimer and IL-6) assessed.

Methods

ART-naive men with early documented HIV infection were randomized 1:1 in a double-blind manner to receive standard ART (tenofovir/efavirenz + lopinavir/ritonavir) with either raltegravir (400 mg/day) and maraviroc (150 mg/day), or placebo, for 48 weeks (NCT01154673). In a predefined substudy, paired blood and stool samples were collected from participants at baseline and week 48, and from ART-naive controls. Microbial CD4 T cell immunology (Th1, Th17, Th22 cells), and blood markers of microbial translocation (LPS), immune activation (ICD14) and SNA (IL-6 and D-dimer) were assessed.

Results

- Gastrointestinal Th22 cell numbers and Th17 polyfunctionality were markedly reduced compared to HIV-uninfected controls before and after ART compared to HIV-uninfected controls.
- The frequency of gut Th17 and Th22 cells were similar between the standard and intensive ART arms at baseline and week 48. Similarly, there was no added benefit with intesnsified ART in gut and blood CD8 T cell immune activation or with plasma SNAs.

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