ART Reduces T Cell Activation and Immune Exhaustion Markers in HIV Controllers

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Abstract

BACKGROUND: Despite low or undetectable plasma HIV RNA, many HIV controllers (HCs) have associated viral replication and varied systemic inflammation. We assessed the effect of ART on HIV suppression and immune activation. Methods: In a prospective, open-label study of RPV/FTC/TDF in ART-naive HIV controllers with viral loads <400 copies/mL, we measured week 48 changes in CD4+ T-cell counts, viral loads, and inflammation-related cytokines. Results: Forty-five HCs completed 48 weeks of ART and were analyzed, before ART, with undetectable viral loads, 40 had higher CD4 counts than those with associated viral loads (median 585 copies/mL vs. <50 copies/mL), and 36 had lower sCD160 levels (2.2% ± 3.9%, vs. 3.9% ± 5.9%). RPV/FTC/TDF was well tolerated, resulting in a modest, but significant improvement in sCD160 levels. The proportion of CD4+ T cells with activated memory phenotype increased only in ART-naive controllers, and no changes were observed in ART-controllers. One year of ART reduced T cell activation and markers of immune exhaustion in HIV controllers, with further increases in CD4-counts after two years of ART. ART was well tolerated and did not affect adverse effect status when discontinued. These results provide additional support for ART in ART-naive controllers.

Background

- HIV controllers suppress HIV in the blood to low levels without antiretroviral treatment (ART) and represent a natural model of a functional HIV cure.
- HIV controllers are reported to have higher levels of chronic inflammation, and increased rates of cardiovascular disease and hospitalization.
- We performed a prospective, open-label trial to assess the effect of RPV/FTC/TDF on HIV suppression, un-associated viral replication, immunity, inflammation, markers of quality of life in HIV controllers.

Objectives

1. Evaluate changes in CD4+ and CD8+ T-cell activation after initiation of RPV/FTC/TDF in ART-naive HIV controllers.
2. Assess changes in viral load and T-cell count after ART initiation.
3. Determine changes in markers of inflammation and immune exhaustion.
4. Evaluate the tolerability of ART and change in quality of life.

Methods

1. Study Design
   - We performed a prospective, open-label study of RPV/FTC/TDF in ART-naive HIV controllers.
   - Key inclusion criteria: (1) ART-naive, (2) At least 2 viral loads <500 copies/mL, for at least 2 months, (3) No severe immunological or extrasomatic complications.

2. Study Outcomes
   - Changes in CD4+ T-cell counts and viral loads after ART initiation.
   - Changes in markers of inflammation and immune exhaustion.
   - Evaluation of ART tolerability and change in quality of life.

3. Study Procedures
   - ART initiation: All participants were randomized to ART (RPV/FTC/TDF) or control (no ART).
   - Outcome measures: Changes in CD4+ T-cell counts, viral loads, and inflammation-related cytokines.

Results

- ART was well-tolerated and Improved quality of life.
  - RPV/FTC/TDF was well-tolerated and improved self-reported quality of life (QoL) as measured by the EQ-5D-5L questionnaire (QoL change: 0.27 -0.42).

- ART Reduces Levels of Immune Activation and Exhaustion in HIV-1 Controllers
  - RPV/FTC/TDF had no significant effect on CD4+ counts (Figure 8).
  - ART was associated in a significant decline in %CD160+ cells (35% ± 46% at 24 weeks (±7% ± 49% at 48 weeks after ART initiation) (2%), P=0.017).

- After ART initiation, several markers of immune exhaustion (%CD160+, %HLA-DR+ in CD4+ and CD8+ T cells) decreased in CD4+ T cells, but increased in CD8+ T cells (Figure 6).

- There were no significant changes in levels of HIV-1 DNA or CA-DNA with ART (Figure 4).

- While ART, 15% of participants had an increase in CD8+ T-cell activation (≥6% copies/mL), as compared to 94% of participants after 24-48 weeks on ART (Figure 3).

- These results provide additional support for ART in HIV controllers.

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