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## 1. BACKGROUND

- Antiretroviral therapy (ART) is not curative, and the persistence of viral reservoirs forms the major obstacle to an HIV cure.
- Replenishment by residual virus replication despite ART has been proposed as a potential mechanism of HIV persistence.
- In recent years, there has been a clear trend towards ART regimens that include fewer drugs (e.g., dual instead of triple therapy).
- **In this study, we evaluated the possible increase in viral replication and reservoir replenishment in blood and tissue upon ART simplification with DTG/3TC and the impact of this simplification on chronic immune activation/exhaustion and inflammation.**

## 2. METHODS

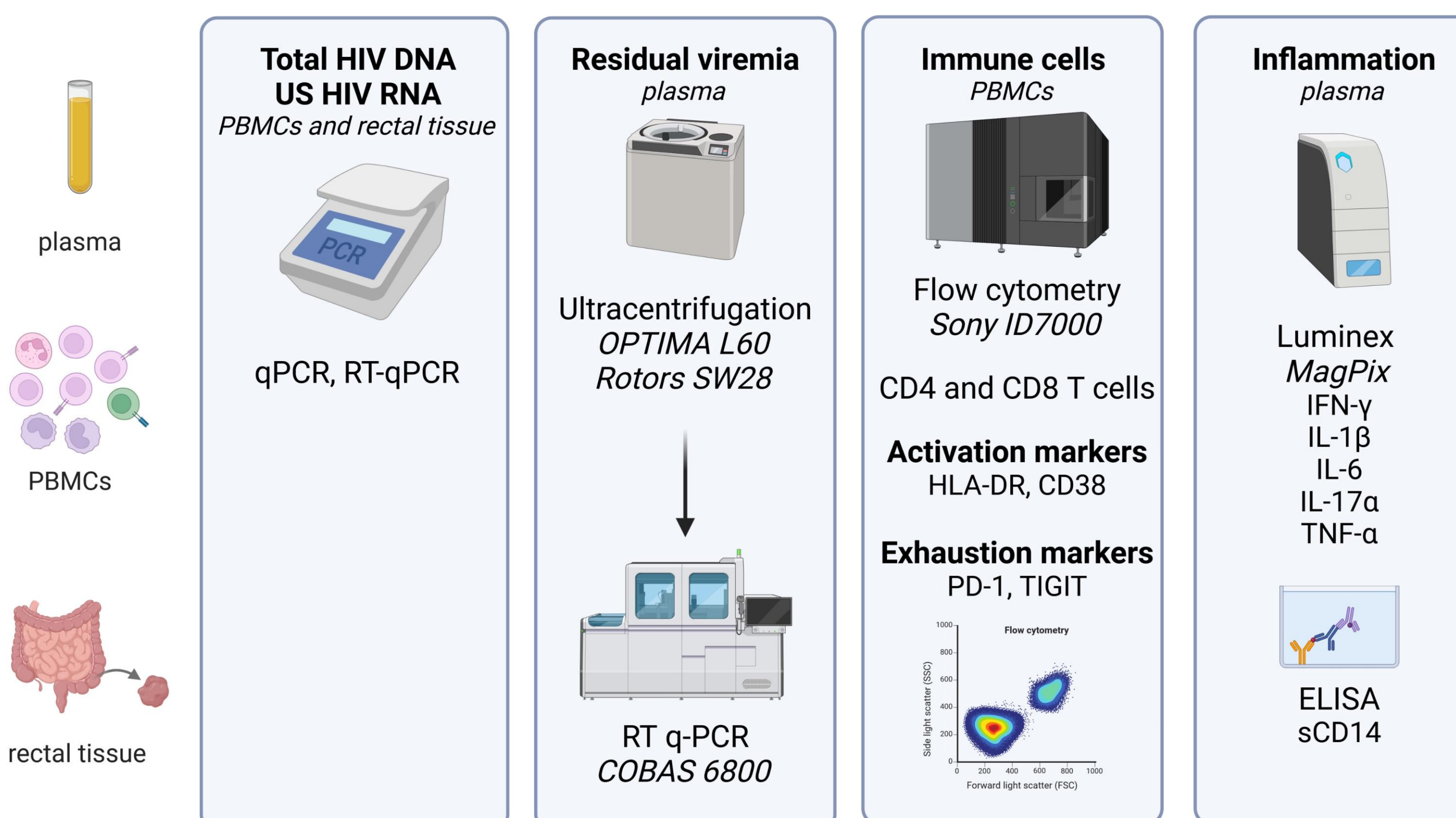
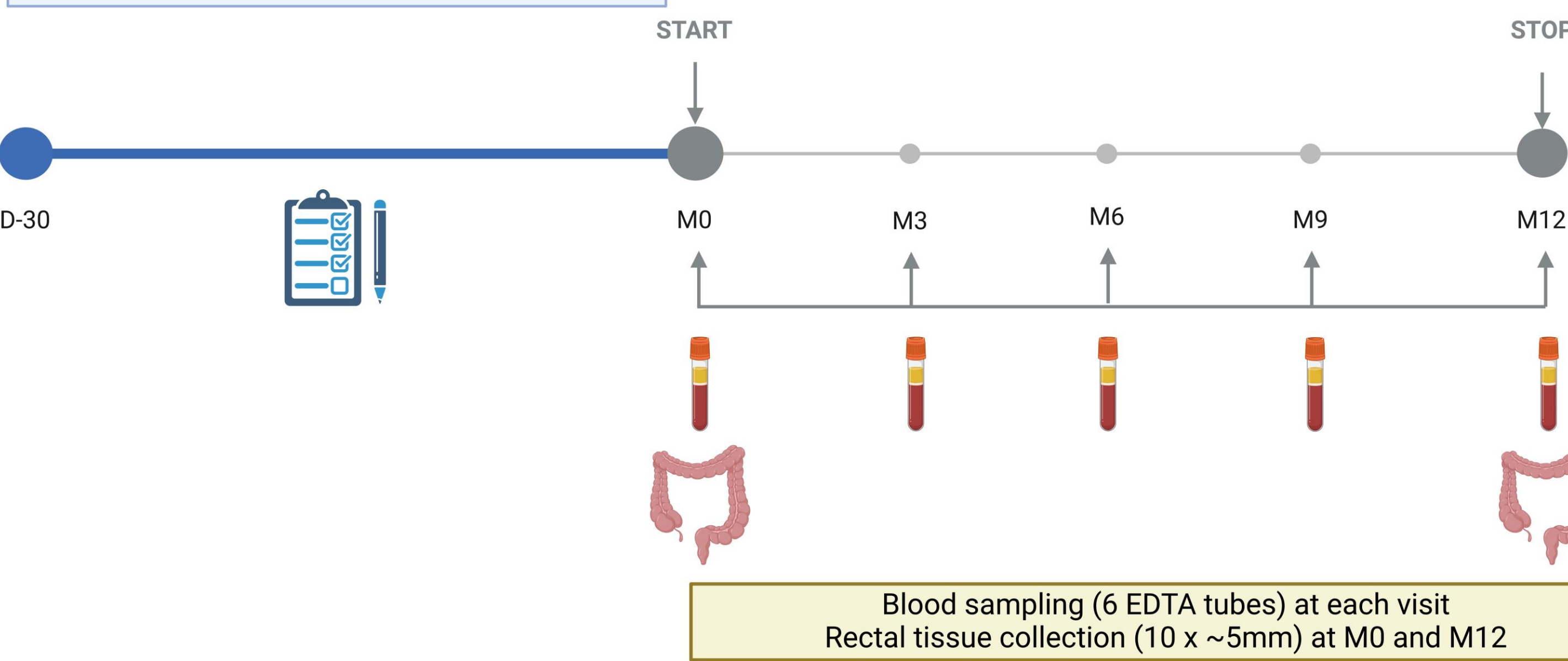
### Screening phase

### Phase 3 randomized and controlled clinical trial n=36

- People living with HIV-1 (PLWH)
- ≥ 18 years of age
- Receiving ART (DTG/ABC/3TC) for more than 2 years
- HIV-1 RNA <20 cop/mL for ≥ 24 months prior to screening
- Absolute CD4+ T lymphocyte count >200/mm<sup>3</sup>

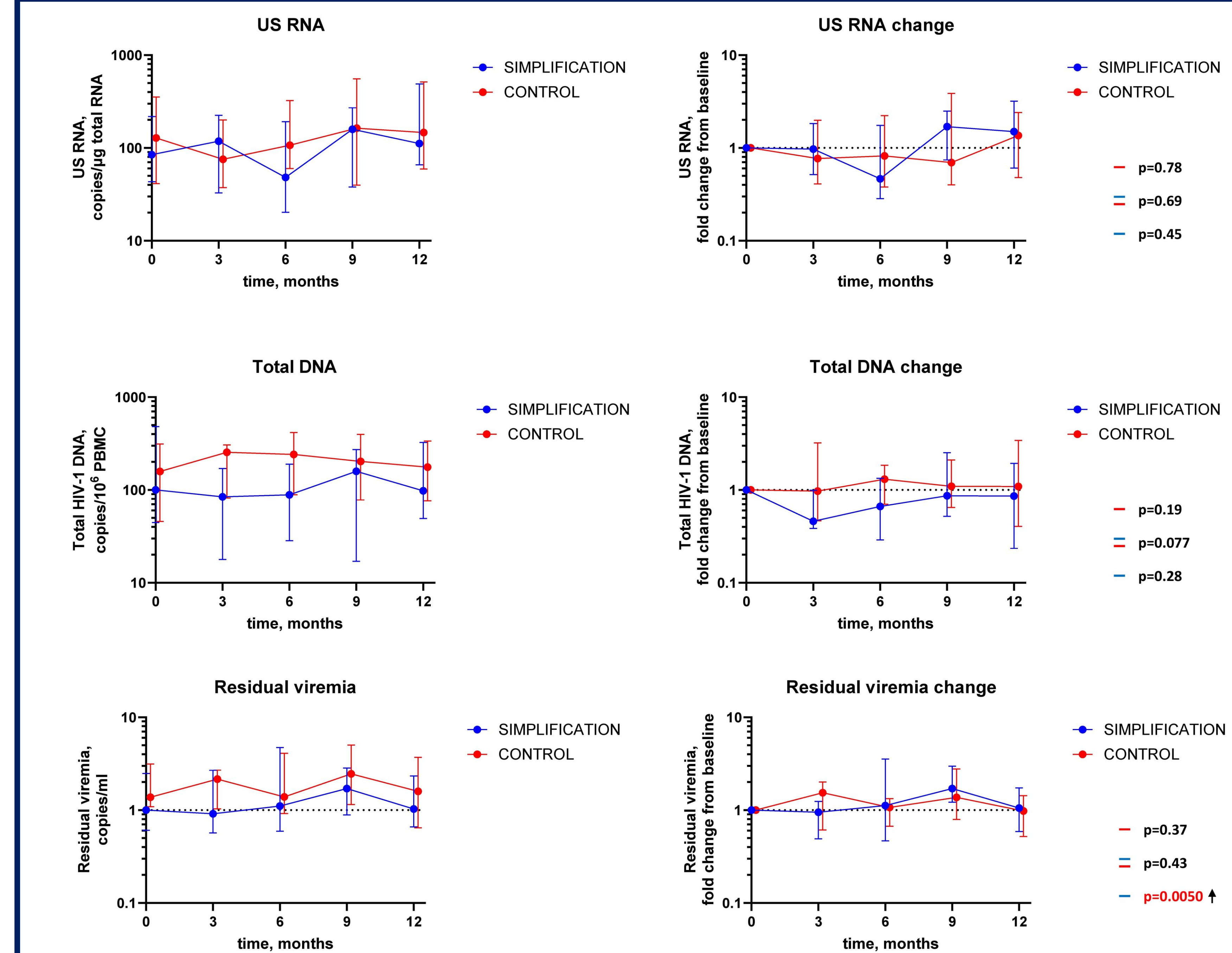
**Simplified group**  
DTG 50mg/3TC 300mg  
n=18

**Control group**  
DTG 50mg/ ABC 600mg/3TC 300mg  
n=18



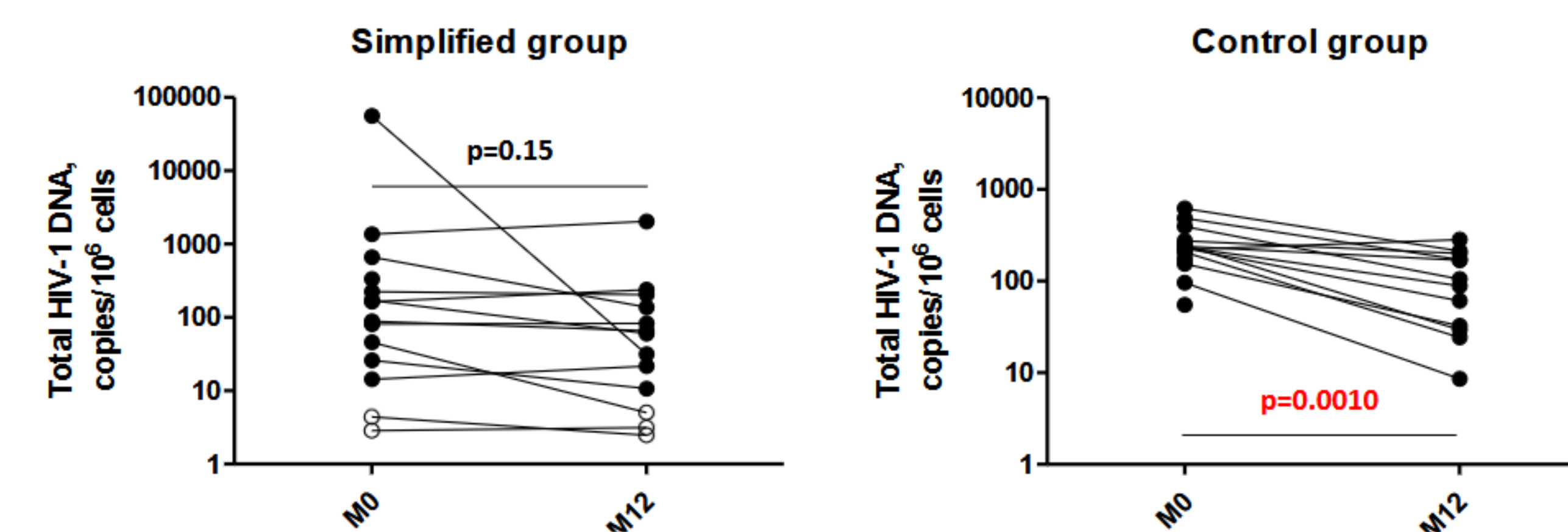
## 3. RESULTS

### Objective 1: Does DTG/3TC switch impact HIV reservoir or residual viremia



**Figure 1. Virological markers during ART simplification.**

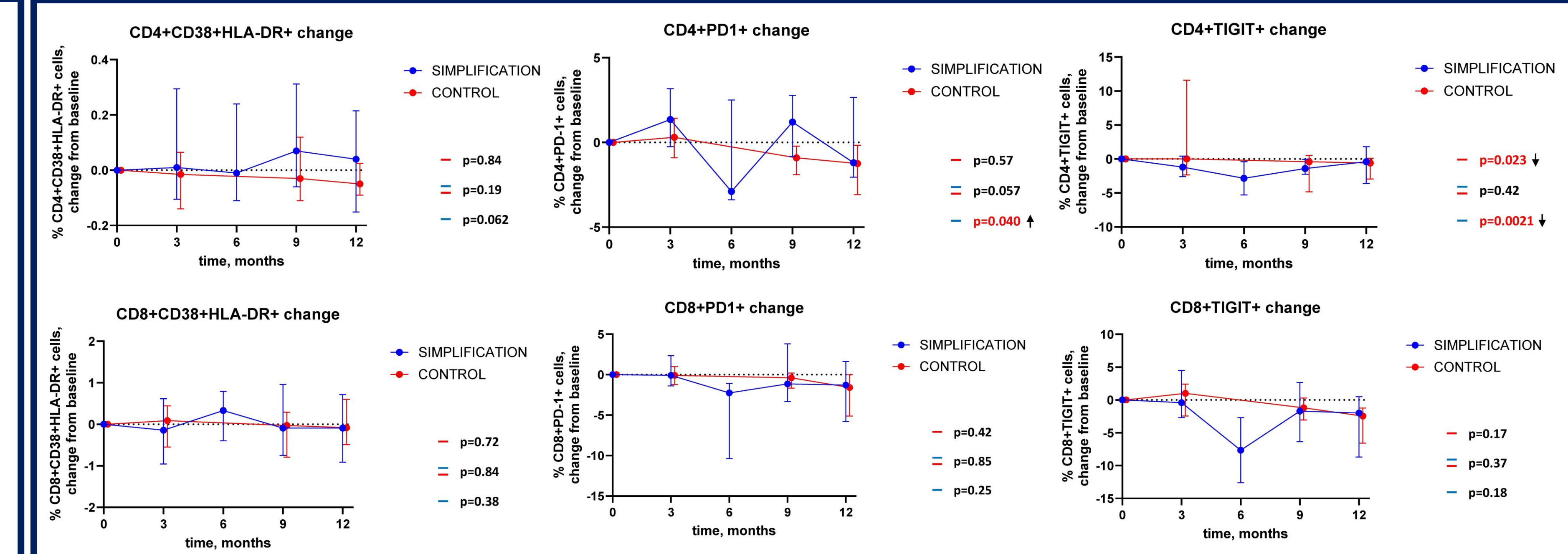
Left panels: median (IQR) concentrations of US HIV RNA, total HIV DNA in PBMCs and residual viremia. Right panels: fold change of US HIV RNA, total HIV DNA in PBMCs and residual viremia from baseline to months 3, 6, 9 and 12 of the study in the simplified (blue) and control (red) groups.



**Figure 2. Change of total HIV DNA in rectal tissue during ART simplification.**

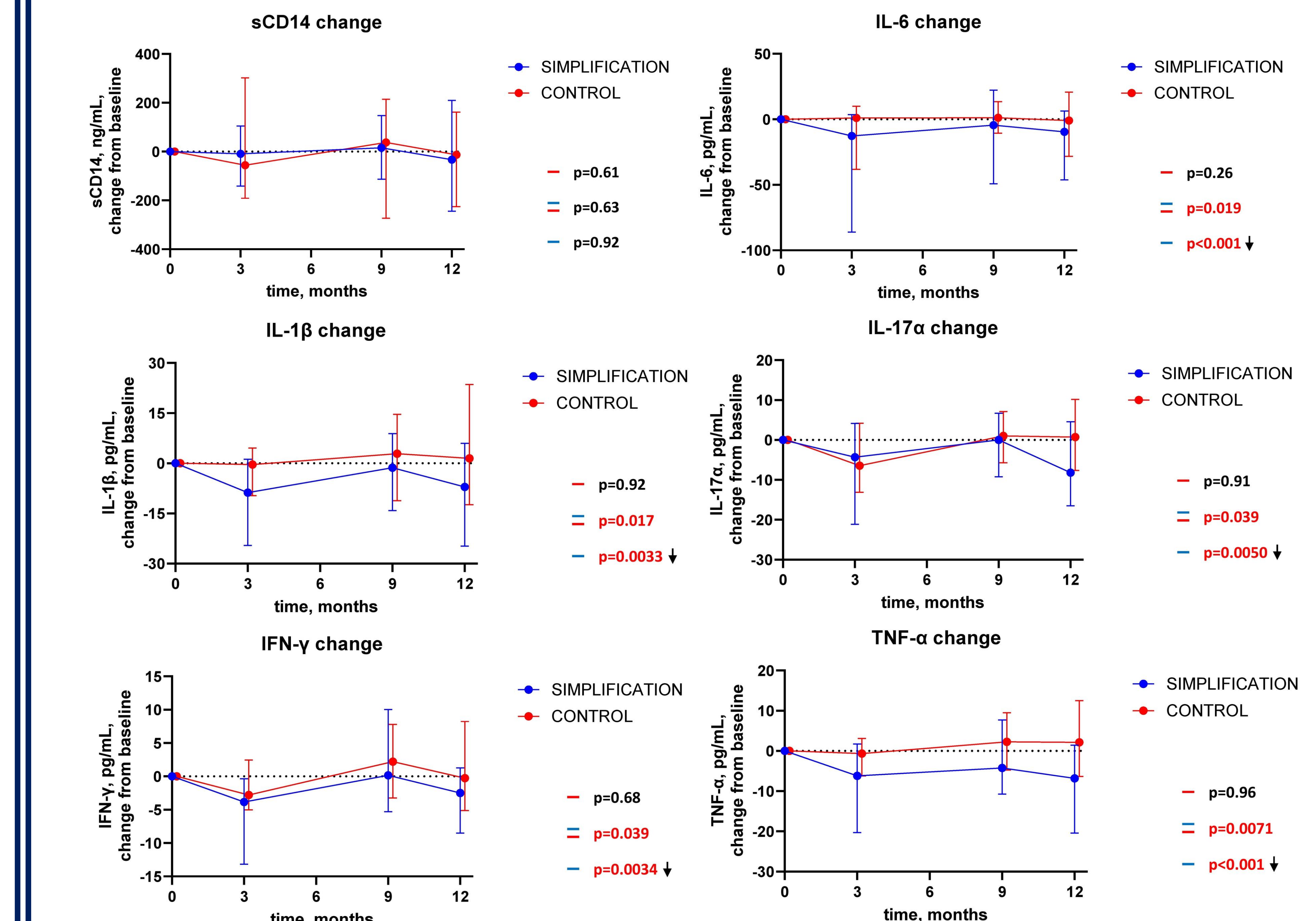
Change of total HIV DNA in rectal tissue in the simplified group and in the control group between month 0 and month 12.

### Objective 2: Does DTG/3TC switch impact immune activation or inflammation?



**Figure 3. T-cell activation and exhaustion during ART simplification.**

Graphs show changes of CD4+ cell markers (above) and CD8+ cell markers (below) from baseline to months 3, 6, 9 and 12 of the study in the simplified (blue) and control (red) groups. Median values and IQRs are shown.



**Figure 4. Biomarkers of inflammation during ART simplification.**

Changes of concentrations of sCD14, IL-6, IL-1β, IL-17α, IFN-γ and TNF-α from baseline to months 3, 6, 9 and 12 of the study in the simplified (blue) and control (red) groups. Median values and IQRs are shown.

**Switching to DTG/3TC maintained plasma viral load suppression, didn't measurably impact HIV persistence markers in blood or tissue, and reduced systemic inflammation. These findings support the use of DTG/3TC in PLWH.**