**Background**

- HIV persistence in reservoirs constitutes a barrier for HIV eradication.
- The male genital tract (MGT) constitutes a separate reservoir for HIV.
- HIV persistence in reservoirs constitutes a barrier for HIV eradication.
- The capability of ARV drugs to penetrate into the MGT is a key factor for achieving HIV suppression in this reservoir and also for preventing sexual transmission of the virus.

**Results**

- Extracellular TFV concentrations and intracellular TFVdp concentrations

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>TFV Concs.</th>
<th>TFV SP</th>
<th>TFV DP</th>
<th>Truvada (FTC + TDF)</th>
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</thead>
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<td>TFV sp (ng/mL)</td>
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**Patients and Methods**

- **Primary Objectives:**
  - To evaluate TFV concentrations in seminal plasma (SP) and intracellular TFV-diphosphate (TFV-DP) concentrations in seminal mononuclear (SMC) of HIV-1 infected men receiving ART with TAF/FTC/EVG/COBI.
  - To evaluate TFV concentrations in seminal plasma (SP) and intracellular TFV-DP concentrations in seminal mononuclear (SMC) of HIV-1 infected men receiving ART with TAF/FTC/EVG/COBI.

- **Secondary Objectives:**
  - To evaluate TFV suppression in SP after switching ART from TDF/FTC/EVG/COBI to TAF/FTC/EVG/COBI.
  - To evaluate changes in seminal quality after switching ART from TDF/FTC/EVG/COBI to TAF/FTC/EVG/COBI.

- **Eligibility criteria:**
  - HIV-1 infected adult (21-65 years old) men on stable ART with TDF/FTC/EVG/COBI (≥23 months) and blood plasma HIV-1 RNA suppression <40 copies/mL (≥6 months).

- **Procedures:**
  - ART was switched to TAF/FTC/EVG/COBI.
  - At baseline, and 12 weeks post-switch, TFV concentrations in SP and blood plasma (BP); TFV-DP concentrations in SMC and peripheral blood mononuclear cells (PBMC); and HIV-1 RNA in SP and BP were evaluated.

- **Drug concentrations were measured at the end of the dosing interval (C24h) using a validated liquid chromatography-tandem mass spectrometry (LC-MS/MS) method.**

- **HIV-1 RNA was determined by real-time PCR.**

- **Semen quality was assessed according to WHO guidelines 2010 in semen analyses performed before switching and 12 weeks after switching to TAF/FTC/EVG/COBI.** The results of the semen quality tests were evaluated and interpreted by an expert.

- **Statistical analysis:**
  - Data are presented as median (range). Statistical analysis was performed by the nonparametric Wilcoxon signed-rank test.

**Antiviral efficacy**

- All patients had HIV-1 RNA <40 copies/mL in both BP and SP at baseline and 12 weeks after switching to TAF.

- With TAF, TFV C24h was 11.9-fold higher in SP compared to BP.

- TFV C24h achieved in SP was significantly lower with TFV in comparison to TDF dosing but 9.6-fold higher than the TFV EC50 for wild type HIV-1 (11.5 ng/mL).

- In contrast, median TFVsp in SMC achieved with TAF was 6% of TFVsp in PBMC. Although the TFVsp SMC/PBMC ratio was significantly lower in TAF compared to TDF (5.66, range 0.01-1.41, vs. 0.27, range 0.04-4.85, p<0.002), TDF/FTC achieved in SP with TAF and TDF were comparable.

- Median TFVdp C24h in SMC was below the TFVdp EC50 (36.7 fmol/million CD4 cells) with both TAF and TDF. However, the majority of the lymphocyte population in SMCs is monocyte derived and data from previous studies indicates that competing endogenous nucleotide pools are lower in comparison with CD4+ T lymphocytes. In addition TFV interacts synergistically with FTC and EVG/COBI. Taking into account these considerations, TFVdp concentrations below the TFV EC50 in CD4+ T cells does not mean low efficacy in SMC.

**Conclusions**

1. **Seminal extracellular and intracellular TFV distribution differs between TAF and TDF.**

2. Nevertheless, both TFV formulations plus FTC/FTC/EVG/COBI maintained HIV-1 RNA suppression in semen.

3. Differences in MGT distribution between TAF and TDF are not associated with clinically relevant differences in semen quality. Larger studies are needed to elucidate any potential different effect of TAF and TDF on semen quality.

**References:**


**Acknowledgments:**

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