The dose of tenofovir alafenamide (TAF) is reduced from 25 to 10 mg daily when given with cobicistat (COBI) or ritonavir (RTV) due to the documented boosting effects of these drugs on tenofovir levels.

RTV-booster HIV protease inhibitors significantly increase tenofovir concentrations. However, no dose reduction has never being adopted for tenofovir disoproxil fumarate (TDF) when given with these drugs.

Consistent evidence is available in literature showing that patients exposed to high plasma tenofovir concentrations are at higher risk to experience TDF-related complications.

The less nephro- and/or bone toxicity observed with TAF versus TDF during registrative trials could have been driven, at least in part, by inappropriate dose selection for drugs comparison (no adoption of reduced TDF doses when given with boosters).

To investigate the effect of COBI on tenofovir plasma concentrations in real-life settings.

A cross-sectional analysis was conducted in HIV-positive patients receiving TDF-containing antiretroviral therapies for at least one month and with at least one assessment of tenofovir plasma trough concentrations.

Uni- and multivariate regression analyses were carried out considering tenofovir concentration as the dependent variable. A general linear model to analyze the effect of independent clinical variables on tenofovir concentrations was applied. Independent variables with p-values <0.20 at univariate analysis where introduced in the multivariate model.

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The importance of some clinical covariates (body weight, renal function, patients' age, gender) in predicting tenofovir overexposure was confirmed.

Co-administration with COBI resulted in significantly higher tenofovir concentrations compared with other antiretroviral regimens, including also RTV-boosted protease inhibitors.

The possibility that the lack of proper dose adjustment for TDF when given with COBI (or with RTV) could have introduced a bias in the comparison of safety between TAF and TDF during registrative trials cannot be ruled out.

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Aim of the study

Methods

Results 1: patients characteristics

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Pi/s</th>
<th>NNRTI/s</th>
<th>INI/s</th>
<th>ELV/COBI/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males (%)</td>
<td>212</td>
<td>176</td>
<td>46</td>
<td>76</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47±10</td>
<td>48±10</td>
<td>48±9</td>
<td>44±9</td>
</tr>
<tr>
<td>Body weight (Kg)</td>
<td>68±16</td>
<td>70±14</td>
<td>69±13</td>
<td>71±12</td>
</tr>
<tr>
<td>Tenofovir therapy (days)</td>
<td>164±120</td>
<td>180±112</td>
<td>144±115</td>
<td>45±680</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>0.9±0.3</td>
<td>0.9±0.2</td>
<td>0.9±0.3</td>
<td>1.0±0.2</td>
</tr>
<tr>
<td>Co-infections (%)</td>
<td>43%</td>
<td>23%</td>
<td>49%</td>
<td>23%</td>
</tr>
<tr>
<td>Viral load &gt;37 copies/mL (%)</td>
<td>21%</td>
<td>5%</td>
<td>14%</td>
<td>23%</td>
</tr>
<tr>
<td>CD4 count &lt;250 cells/mL (%)</td>
<td>12%</td>
<td>5%</td>
<td>17%</td>
<td>16%</td>
</tr>
</tbody>
</table>

Data were given as mean ± standard deviation. *p<0.05.

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