Introduction

Several reports indicated that HIV-1 infected people have lower bone mineral density (BMD) than general population, independently of traditional osteoporosis risk factors. Currently, Tenofovir Disoproxil Fumarate (TDF) is the most widely used antiretroviral because of its efficacy on both HIV and hepatitis B infections, and its favorable resistance profile, safety and availability as a coformulation with other antiretroviral drugs in once-daily pills. However, some reports indicated that TDF-including regimens were associated with greater loss of BMD than other regimens.

Objective

The aim was to identify factors associated with BMD and to assess the impact of TDF-including regimens on BMD evolution, in African patients starting a second line antiretroviral treatment (ART) and included in METABODY / ANRS 12250 (Cameroon, Burkina Faso, Sénégal).

Methods

Study design - METABODY / ANRS 12250 is an observational longitudinal study nested in the 2LADY / ANRS 12169 trial (ClinicalTrials.gov n° NCT00928187) [1].

Population - HIV-1-positive adults failing standard first-line ART from Yaoundé, Cameroon; Bobo-Dioulasso, Burkina Faso and Dakar, Sénégal.

2LADY intervention - 2LADY is a multicenter randomized, open-label, phase III trial that compared efficacy and safety of three second line combinations in Africa. Patients were randomized to receive either TDF/FTC + LPV/r, ABC + ddI + LPV/r or TDF/FTC + DRV/r.

Procedures - BMD was assessed by quantitative ultrasound (QUS) (Archies GE Healthcare) at baseline and every 24 weeks. QUS parameters include broadband ultrasound attenuation (BUA), a measure of the frequency-dependent attenuation of ultrasound, and speed of sound (SOS), reflecting the transmission velocity of ultrasound passing through soft tissue and bone tissue. At each visit, biological and clinical data were collected; 3 BMD repeated measurements were realized for each patient and the average of the two closest measures was used for the analysis.

Stiffness index (SI = 0.67BxBUA + 0.28xSOS – 420) [2] was used to evaluate BMD. Low BMD was defined according to International Society for Clinical Densitometry recommendations using QUS reference data from Nigeria (SI T-score < -1 in post-menopausal women and men age 50 and older, SI Z-score ≤ -2 in women prior to menopause and men younger than age 50).

Analysis - Mixed linear models with random effects were used to determine associated factors during the follow-up.

Ethics - Written informed consent was obtained from all patients. Study protocol was approved by the appropriate ethic committees and regulatory authorities and were conducted in accordance with the Declaration of Helsinki and Good Clinical Practices.

Results

Table 2. BMD associated factors in African patients during the first 96 weeks follow-up on a second line antiretroviral treatment

<table>
<thead>
<tr>
<th>Multivariable</th>
<th>β</th>
<th>95% Cl</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up (&lt;4 weeks)</td>
<td>-0.9</td>
<td>[-1.4, -0.4]</td>
<td>0.001</td>
</tr>
<tr>
<td>Age (per ten years)</td>
<td>-6.8</td>
<td>[-9.4, -4.1]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>-9.6</td>
<td>[-15.5, -8.8]</td>
<td>0.001</td>
</tr>
<tr>
<td>Baseline BMI</td>
<td>0.8</td>
<td>[0.3, 1.4]</td>
<td>0.014</td>
</tr>
<tr>
<td>Physical activity</td>
<td>-1.0</td>
<td>[-2.5, 0.6]</td>
<td>0.23</td>
</tr>
<tr>
<td>Duration of first line ART (&lt;36 months)</td>
<td>6.4</td>
<td>[0.6, 12.2]</td>
<td>0.07</td>
</tr>
<tr>
<td>(months)</td>
<td>≥ 72</td>
<td>2.5</td>
<td>[-4.4, 9.3]</td>
</tr>
<tr>
<td>Year of inclusion (2011 vs 2012)</td>
<td>2.3</td>
<td>[-2.6, 7.7]</td>
<td>0.35</td>
</tr>
<tr>
<td>Cameroon</td>
<td>10.9</td>
<td>[5.7, 16.1]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TDF exposure</td>
<td>1.7</td>
<td>[-4.1, 7.4]</td>
<td>0.57</td>
</tr>
<tr>
<td>LPV exposure</td>
<td>1.6</td>
<td>[-4.0, 7.2]</td>
<td>0.57</td>
</tr>
</tbody>
</table>

**Multivariable analysis shown**.

Figure 2. Mean BMD evolution by treatment groups

Evolution of BMD over time and associated factors (figure 2 & table 2)

After 96 weeks of second line therapy, a reduction of 7.3% of mean stiffness index was observed, compared to baseline. The factors associated with BMD during the follow-up were similar to those found at baseline. Neither treatment arm, nor TDF exposure was associated with loss of BMD over time.

Conclusions

BMD decreases after second line ART initiation in African patients independently of TDF exposition. Factors associated with BMD were age, sex, baseline BMI, study site and time of follow up. Our results do not suggest the need for systematic bone loss screening in HIV infected people in Africa. Screening procedures applied for the general population can be used.