possibly improving its PK exposure through ritonavir-fluconazole co-boosting. The prolonged half-life of fluconazole (31–34 h), allowing once daily administration, would add only a reasonable extra pill burden to the patients while providing a more potent antiretroviral action.

Transparency declarations

None to declare.

References


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Sir,

A significant improvement of survival of people infected with HIV has been observed since the introduction of HAART in clinical practice.1 Several toxicities have arisen such as lipo-dystrophy, insulin resistance, diabetes, dyslipidaemia and also abnormalities of bone metabolism such as osteopenia/osteoporosis and osteonecrosis.2–4 HIV infection, a prolonged use of protease inhibitors (PIs), lactic acidosis, lipodystrophy, immune reconstitution, nutritional and hormonal factors and prior AIDS-related wasting are all factors that can contribute to these abnormalities.5,6

No data are at the moment available on the frequency and on the predictive factors of osteopenia/osteoporosis in HIV-infected subjects receiving a non-nucleoside-reverse-transcriptase-inhibitor (NNRTI)-based HAART.

This observational prospective study involved 89 consecutive HIV-infected subjects aged between 30 and 50 years; patients with pathological or toxic conditions potentially affecting bone metabolism such as hypogonadism, hyper- or hypothyroidism and hypocortisolism, bed rest period >1 month, drug/alcohol abuse, neoplasia, chronic diarrhoea or absorption dysfunction, body mass index (BMI) < or >20% normal ranges (19.1–25.8 for women and 20.7–26.4 for men), chronically treated with corticosteroids, levotyroxine, lithium or oestrogens, and women in menopause or amenorrhoea were excluded. We included in the study both naive and HAART-treated subjects. Patients receiving antiretroviral treatment were naive for PIs and were receiving a stable, first-line, NNRTI-based HAART for at least 2 years with HIV-RNA < 50 copies/mL in the previous 6 months.

All subjects underwent dual energy X-ray absorptiometry (DEXA) scans (Hologic, QDR 4500 Delphi system, Bedford, MA, USA) in antero-posterior lumbar spine (L1-L4) and left hip sites to evaluate mean bone mineral density (BMD), total mean T-score and Z-score. DEXAs were performed at the same radiological centre by a single radiologist, and WHO criteria were considered for the diagnosis of osteopenia/osteoporosis. Written informed consent was obtained from all participants, and the study was conducted in adherence with local drug regulations, guidelines on ‘Good Clinical Practice’ and the principles of the Declaration of Helsinki.

Comparisons between categorical groups were performed by χ² and Wilcoxon tests. Potential predictive factors of osteopenia/osteoporosis were evaluated by a multivariate regression logistic analysis. Variables included in the model were gender, age, risk factors for HIV infection, CDC stage, hepatitis C virus (HCV) serostatus, BMI, lipodystrophy, CD4 cell count at DEXA, months since first HIV-positive test and use of NNRTI-containing HAART. A similar analysis was repeated including only NNRTI-treated subjects to evaluate the role of NNRTI-based HAART duration in the occurrence of osteopenia/osteoporosis.

Table 1 summarizes demographic and clinical characteristics of the subjects included in the study: 47 were naive and 42 were NNRTI-treated. As expected, naive patients had a lower duration of HIV infection and a lower CD4 cell count than NNRTI-treated patients. Median duration of HAART was 41 months.

Non-nucleoside-reverse-transcriptase-inhibitor-based HAART and osteoporosis in HIV-infected subjects

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(IQR: 32–49); efavirenz was used by 27 subjects and nevirapine by 15; the most prescribed nucleoside backbone was zidovudine plus lamivudine (n = 36).

A total of 46 (51.7%) subjects, 23 in each group, had abnormal findings at DEXA: 35 (39.3%) had osteopenia and 11 (12.4%) had osteoporosis. Among naïve subjects, 18 had osteopenia and 5 had osteoporosis; among NNRTI-treated subjects 17 had osteopenia and 6 had osteoporosis (P = not significant).

In the multivariate analyses on the whole cohorts predictors of osteopenia/osteoporosis were older age (OR: 1.18, 95% CI: 1.05–1.33, P < 0.01 for each additional year) and low BMI (OR: 0.68, 95% CI: 0.54–0.85, P < 0.01 for each additional unit). The use of NNRTI-containing HAART was not associated with osteopenia/osteoporosis (OR: 1.30, 95% CI: 0.64–3.36, P = 0.26). When considering only NNRTI-treated subjects, older age (OR: 1.93, 95% CI: 1.10–3.36, P = 0.02 for each additional year) and low BMI (OR: 0.43, 95% CI: 0.19–0.95, P = 0.03 for each additional unit) were confirmed to be predictive of osteopenia/osteoporosis; in this subgroup also a more prolonged exposure to NNRTI seemed predictive (OR: 2.48, 95% CI: 0.96–6.42, P = 0.06 for each additional year).

The presence of osteopenia/osteoporosis is a frequent finding in HIV-infected individuals, and its pathogenesis remains unexplained. The role of both HIV infection itself and HAART has been considered. In one of the first reports, Tebas et al. found that PI-containing regimens were associated with a higher risk of osteopenia/osteoporosis; in a more recent study, the rate of osteopenia and osteoporosis was comparable between naïve and HAART-treated patients, and in both these populations BMD was lower than in healthy controls. However, in the present study the groups were not well balanced for age and BMI, both factors potentially related to bone abnormalities. In a previous report on an unselected population, we found that both higher HIV-RNA and HAART duration were predictors of osteopenia/osteoporosis. In this study, antiretroviral treatments were heterogeneous, and the role of specific drug classes was not evaluated.

To our knowledge, this is the first report evaluating the presence of osteopenia/osteoporosis in NNRTI-treated subjects. Traditional risk factors for osteopenia/osteoporosis, such as low BMI and older age, were also predictive in the HIV population; NNRTI-treated subjects did not seem at higher risk than naïve subjects. However, when restricting the analysis to NNRTI-treated individuals, those with a more prolonged exposure to NNRTI seemed at higher risk of osteopenia/osteoporosis. This finding needs to be confirmed in studies with a longer follow-up.

To date, the presence of osteopenia/osteoporosis in HIV-infected subjects is of particular concern. Overall, our data suggest that this condition is not higher in NNRTI-treated than in naïve subjects; however, when considering only NNRTI-treated subjects, a more prolonged NNRTI exposure seems to correlate with osteopenia/osteoporosis.

### Transparency declarations

None to declare.

### References