Low Bone Mineral Density among Ugandan HIV infected patients on failing first line Antiretroviral Therapy; a sub-study of the EARNEST trial

(Poster No 784)

Bonnie Wandera[1], Agnes Kiragga[1] , Fred Semitala[1], Jayne Ellis[1], Robert Colebunders[3], Nicholas Paton[4], Andrew Kambugu[1], Philippa Easterbrook

1-Infectious Diseases Institute Makerere University Kampala Uganda , 2- School of Medicine Makerere University ,Kampala Uganda , 3-Institute of Tropical Medicine Antwerp Belgium 4-MRC-Clinical trials unit, London

Background

Both HIV infection and some Antiretroviral Therapy(ART) drugs may accelerate bone demineralization although most data comes from developed settings *Yin et al, Osteoporos Int **2005**, Brown et al AIDS **2006**..*

Patients failing ART maybe at increased risk of low bone mineral density (BMD) due to prolonged ART exposure and uncontrolled vireamia *Brown et al J Acquir Immune Defic Syndr **2009**.*

There is limited data on bone health among HIV infected patients in sub-Saharan Africa partly due to lack of access to Dual energy x-ray absorptiometry (DXA) scans.

Objective

To determine the baseline prevalence of low BMD (both osteopenia and osteoporosis) and factors associated with low BMD among patients failing first-line ART in Kampala, Uganda.

Methods

This was a sub-study of the Europe-Africa Research Network for Evaluation of Second-line Therapy (EARNEST) Trial - a large randomised trial of three different second line ART strategies in protease inhibitor – naïve patients at initiation of second line ART after first-line virological treatment failure.

Eligibility criteria were: aged at least 18 years, 12 months of continuous 2NRTI + NNRTI-based regimen, good adherence to ART, naïve to PI therapy plus established treatment failure defined by modifiedWorld Health Organisation (WHO) 2006 criteria .

Subjects were enrolled from 3 clinics in Kampala Uganda collecting data on ART treatment, age, Body mass index (BMI), alcohol use, physical activity and dietary calcium intake were collected using a standardized interviewer administered questionnaire.

BMD was measured at the beginning of secondline(baseline) using Discovery Hologic DXA scan at the lumbar spine and proximal femur .

Osteopenia was defined as T-score between −1.0 and −2.5. Osteoporosis T-score ≤ -2.5 while low BMD was defined as T-score < -1.

Multivariable Logistic regression analyses were used to identify factors independently associated with low BMD (T-score < -1) separately at the lumbar spine and the proximal femur .

Results

A total 181/1200 EARNEST participants were enrolled into the BMD sub-study.

Table 1: Descriptive characteristics of BMD sub-study participants at randomisation to second-line ART in Kampala Uganda.

Characteristic	Median (IQR):
Age (years)	35 (31 – 41)
Female gender n (%)	125 (69%)
Post menopausal, n(%)	16 / 125 (13%)
Waist – hip ratio	0.9 (0.8 – 0.9)
BMI (kg/m2)	21.9 (19.9 – 24.5)
Years on 1st line ART	3.7 (2.7 – 5.0)
Exposed to tenofovir, n (%)	30 (16.7%)
CD4+ cell count (cells/μL)	67 (35 – 151)
HIV RNA (Log10 copies/mL)	4.9 (4.5 – 5.3)

Table 2: Bone mineral density outcomes of subjects enrolled in the BMD sub-study at randomisation to commence second-line ART in Kampala Uganda.

Body Part	Lumbar spine	Proximal femur
BMD in g/cm2, Median (IQR)	0.94 (0.86 – 1.03)	0.91 (0.83 – 0.99)
Osteopenia n/N, (%)	75/175, (42.9%)	42/176 (23.7%)
Osteoporosis n/N, (%)	14/175, (8%)	2/176 (1.1%)

Table 3: Multivariable logistic regression results of factors associated with low BMD (both Osteopenia and osteoporosis) at randomisation to second-line ART in Kampala Uganda.

Variable	Adjusted odds ratio for Lumbar spine (95%CI)	Adjusted odds ratio for Proximal femur(95%CI)
BMI (kg/m2), Ref= 20 – 24.9		
< 20	3.48; (1.08-11.2), p=0.04	4.12; (1.51-11.3), p=0.005
≥30	0.42; (0.20-0.88) , p=0.02	0.39; 0.14-1.07, p=0.070
Tenofovir in first line ART	2.23; (0.95-5.28), p=0.06	not significant.

Conclusions

In this first study of ART experienced subjects in Sub-Saharan Africa, about half of Ugandan patients with virological failure in Kampala had evidence of osteopaenia at the lumbar spine and 8% had osteoporosis at initiation of second-line ART. Low BMD was more prevalent at the lumbar spine compared to the proximal femur.

Low BMI (<20kg/m2) was associated with a > 3 fold increase in the odds of a low BMD at both the Lumbar spine and proximal femur, and Tenofovir had a two fold increase at only the lumbar spine (of borderline significance) at switch to second-line ART following virological failure.

Lower cost strategies for evaluation of bone health are needed. In view of limited access to DEXA scan technology in these settings, careful clinical evaluation is important, especially in patients with low BMI and those receiving Tenofovir.

Acknowledgement: Study subjects and EARNEST trial staff at Joint Clinical research center, Nsambya and Infectious Diseases Institute.

Funding : Vlaamse Interuniversitaire Raad (VLIR) and the Wellcome Trust