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Presentation Title: Continuous Antiretroviral Therapy (ART) Decreases Bone Mineral Density: Results from the SMART Study

Keywords: bone mineral density,antiretroviral therapy,randomized trial

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Background: HIV-infected adults have lower bone mineral density (BMD) than the general population and may experience more fractures. We evaluated the role of ART. **Methods:** In the SMART trial, HIV+ patients with CD4 counts > 350 cells/mm^3 were randomized to continuous ART (Viral Suppression [VS] group) or CD4-guided intermittent ART (Drug Conservation [DC] group). In 214 patients, hip and spine BMD were measured annually by dual-energy x-ray absorptiometry (DXA) and trabecular BMD of the spine by quantitative computed tomography (qCT). We compared treatment groups for change in BMD using longitudinal models and, in the main SMART study, for incidence of passively reported fractures using Cox regression. In the VS cohort, we evaluated associations of BMD decline with cumulative ART use. **Results:** Patients (98 randomized to the VS and 116 to the DC group; median 44 years, 19% female, 73% on ART, 12% with osteoporosis, median t-scores -0.5 [femur], -0.9 [spine qCT], and -0.7 [spine DXA]) were followed for a mean of 2.4 years. In the VS group, patients received ART for 93% of follow-up time, compared with 37% in the DC group. BMD declined by 0.9% per year (femur), 2.9% (spine qCT) and 0.4% (spine DXA) in the VS group, and significantly less in the DC group. Estimated DC minus VS group differences in mean BMD change from baseline through follow-up were 1.4% (95% CI 0.5 to 2.3; p=0.002) at the femur, 2.9% (95% CI 0.7 to 5.1, p=0.01) for spine qCT, and 1.2% (95% CI 0.02 to 2.3, p=0.05) for spine DXA. No consistent drug-specific association with BMD decline was found. In the main study (n=5472, mean 2.8 years of follow-up), 10 patients in the VS and 2 in the DC group reported fractures as grade 4 adverse events (hazard ratio 4.9 [95% CI 1.1 to 22.5]; p=0.04). **Conclusions:** Continuous ART is associated with decline in BMD and possibly more fractures relative to intermittent, CD4-guided ART. Intermittent ART is not recommended due to increased risk of AIDS and death observed in the SMART study.