Background: Bone mineral density (BMD) decreases by 2-4% in the first 2 years of antiretroviral therapy (ART). The decline is 1-2% greater with tenofovir (TDF) than other nucleos(t)ide reverse transcriptase inhibitors (NRTI). The effects of maraviroc (MVC) on BMD are unknown. We investigated a novel regimen containing MVC in a randomized, double-blind, placebo-controlled study.

Methods: Subjects were randomized to MVC with darunavir/ritonavir and tenofovir/emtricitabine (n=130) or TDF with darunavir/ritonavir (n=130) and tenofovir eradication. Subjects were baseline-matched on CD4 count; ART status; and age. Subjects received MVC (150 mg once daily [QD]) or tenofovir (300 mg QD) stratified by baseline VL < and ≥100,000 copies/mL and age < and ≥30 yrs. All subjects received darunavir (800 mg QD) and emtricitabine (200 mg QD). Plasma HIV-1 RNA <50 copies/mL was used as the endpoint for virologic success. Baseline and week 24 bone mineral density (BMD) scans were performed. After 24 weeks, subjects were randomized to continue receiving MVC/TDF or switch to placebo. Subjects were followed for 24 additional weeks. Apheresis and densitometry results were in line with bone loss component TDF-based therapy with no apparent difference in virologic efficacy. MVC may be an option to attenuate early bone-loss.

Results: Entry, Week 4, 16, 24, 36, 48
- Dual-energy X-ray absorptiometry (DXA) scan of the left hip and lumbar spine (1.0-1.4) – Baseline and week 24
- Central reading of a Tufa Body Composition Analysis Center
- Plasma HIV-1 RNA (Abbott RealTime Assay, lower limit of detection 40 copies/mL)
- Active hepatitis B infection – History of bone fragility fracture
- New hormonal therapy within 6 months, steroids within 30 days
- Current or prior use of bisphosphonates, teriparatide, raloxifene, denosumab
- History of bone fragility fracture
- Any major NRTI or darunavir-resistance mutation
- Active HBV infection; and CrCl <50 mL/min

Eligibility criteria:
- HIV-1 infected, men and women, 18 years and older
- Antiretroviral treatment-naïve
- CD4 count <350 cells/mm³
- TDF; median of +234 (131,327) vs. +188 (94,304) cells/mm³, p=0.036.
- Decline in hip and lumbar spine BMD from baseline to week 48 was less with MVC than TDF.
- At week 48, CrCl was >90 mL/min in 90%MVC, 91% TDF. All results were similar with ITT analyses. Both regimens were well-tolerated. Grade 3 adverse events (AE) were more common with MVC (28%) than TDF (20%); MVC had fewer grade 4 AEs than TDF (7% vs. 10%).

Conclusions:
- Initiating ART with QD MVC, FTC and DRV/RTV resulted in less bone loss compared to TDF-based therapy with no apparent difference in virologic efficacy. MVC may be an option to attenuate early bone-loss.

Statistical analysis:
- Baseline and week 24 BMD scans were performed. After 24 weeks, subjects were randomized to continue receiving MVC/TDF or switch to placebo. Subjects were followed for 24 additional weeks. Apheresis and densitometry results were in line with bone loss component TDF-based therapy with no apparent difference in virologic efficacy. MVC may be an option to attenuate early bone-loss.

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