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First line zidovudine/lamivudine/lopinavir/ritonavir leads to greater bone loss compared to nevirapine/lopinavir/ritonavir

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Abstract

Objective: We studied changes in bone mineral density (BMD) and bone turnover after initiation of combination antiretroviral therapy (cART) and the contribution of zidovudine/lamivudine (ZDV/3TC) in particular.

Design: Randomized clinical trial comparing lopinavir/ritonavir(LPV/r) + ZDV/3TC with LPV/r + nevirapine (NVP) in 50 cART-naive men.

Methods: Dual energy X-ray absorptiometry (DXA) and quantitative computed tomography scans (QCT) were performed at baseline and 3, 12, and 24 months after cART initiation. Serum 25-hydroxy-vitamin D3, parathyroid hormone (PTH), osteocalcin, and urine deoxypyridinoline (DPD)/creatinine ratio were measured.

Results: BMD decreased rapidly in both femoral neck and lumbar spine after cART initiation. BMD loss during 24 months measured by DXA, but not by QCT, was greater in the ZDV/3TC/LPV/r group compared to the NVP/LPV/r group [femoral neck: -6.3% ± 1.0% ($P < 0.0001$) compared to -2.3% ± 0.9% ($P = 0.01$), between-group $P = 0.0006$); lumbar spine: -5.1% ± 0.8% ($P < 0.0001$) compared to -2.6% ± 0.7% ($P = 0.0006$), between-group $P = 0.07$]. Osteocalcin [+1.60 ± 0.32 ($P < 0.0001$) and +1.81 ± 0.29 ($P < 0.0001$) nmol/l] and the urine DPD/creatinine ratio [+1.35 ± 0.44 ($P = 0.0029$) and +1.19 ± 0.38 nmol/mmol ($P = 0.0024$)] increased in both groups over 24 months, with no significant difference between groups. PTH increased to a greater degree in the NVP/LPV/r group [+2.0 ± 0.31 pmol/l ($P < 0.0001$)] compared to [+0.81 ± 0.33 pmol/l ($P = 0.021$) in the ZDV/3TC/LPV/r group].

Conclusion: BMD in both femoral neck and lumbar spine decreased rapidly after initiation of cART, in parallel to an increase in bone turnover. The greater bone loss in the ZDV/3TC/LPV/r group compared to the NVP/LPV/r group suggests that ZDV/3TC contributes to this process. The PTH increase does not explain this greater bone loss.

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