ZOLEDRONIC ACID IS SUPERIOR TO TDF-SWITCHING FOR INCREASING BONE MINERAL DENSITY IN HIV-INFECTED ADULTS WITH OSTEOPENIA: A RANDOMISED TRIAL

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Background: Tenofovir disoproxil fumarate (TDF) reduces bone mineral density (BMD) and probably increases fracture risk in HIV-infected adults. Proven strategies for improving BMD in HIV-infected adults on TDF are either TDF switching or bisphosphonate therapy; which strategy is superior is unknown.

Methods: We randomised virologically-suppressed, HIV-infected adults on TDF-based antiretroviral therapy with low BMD (T score <-1.0 at hip or spine by dual-energy x-ray absorptiometry [DXA]) to either switch TDF or to continue TDF and receive intravenous zoledronic acid (ZOL) 5mg every 12 months. Calcium (all patients) and vitamin D (if serum 25OH vitamin D was <50 nmol/L) were supplemented. The primary study outcome was change in lumbar (L1-L4) spine BMD at 24 months by intention-to-treat analysis. Secondary outcomes included femoral neck and total hip BMD, fractures, safety, and virological failure (confirmed viral load ≥400 copies/mL).

Results: We randomised 87 patients (44 to TDF switch and 43 to ZOL): mean age 50 years (SD 11), 96% men, mean TDF duration 5.9 years (SD 3.1), 22% on a boosted PI, mean spine and hip T scores -1.6 and -1.3, respectively. TDF switches were mostly to abacavir (62%) or raltegravir (19%). Adherence to each strategy was high: four switch patients (10%) recommenced TDF at a median of 9 months; 98% of ZOL doses were administered. Mean spine BMD changes at 24 months were 7.4% (SD 4.3%) with ZOL vs. 2.9% (4.5%) with TDF-switching (mean difference 4.4%, 95%CI 2.6-6.3; p<0.001). Mean left femoral neck BMD changes were 4.1% (3.8%) and 2.1% (4.6%), respectively (mean difference 2.0%, 95%CI 0.2-3.8; p=0.03). Mean left total hip BMD changes were 4.6% (2.6%) and 2.6% (4.0%), respectively (mean difference 1.9%, 95%CI 0.5-3.4; p=0.009). There was 1 fracture in the ZOL group (1 patient) and 7 separate fracture events in the TDF switch group (4 patients). Serious adverse events occurred in 9 (19%) ZOL patients and 6 (14%) TDF-switch patients; none was related to study drugs or procedures. Virological failure occurred in 1 TDF-switch patient and no ZOL patient.

Conclusions: ZOL is more effective than TDF switching at increasing BMD in osteopenic adults on TDF, and may result in fewer fractures.

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