



## Antiretroviral therapy options in people living with HIV at risk of or with osteoporosis

Comment on “Diagnosis, prevention, and treatment of bone fragility in people living with HIV: a position statement from the Swiss Association against Osteoporosis”

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With great interest we read the manuscript of the Swiss Association against Osteoporosis on the diagnosis, prevention, and treatment of bone fragility in people living with HIV (PLWH) [1]. This manuscript adds enormously to the care of PLWH, providing the first concise recommendations in this group of people with an excess risk for osteoporosis based on current knowledge [2].

We do, however, want to raise attention towards the algorithm of Biver et al. for PLWH under antiretroviral therapy (ART) that could be mistaken by readers who are primarily looking at the algorithm while not reading the whole manuscript: while in the full-text, the authors recommend to switch PLWH with osteoporosis or osteopenia with certain risk factors to a tenofovir disoproxil fumarate (TDF)-free ART (seemingly in general), their algorithm in Fig. 2 advises to switch to a “tenofovir alafenamide (TAF)-equivalent.” We think that this is only one option. We do agree that it has been shown that switching patients from TDF- to TAF-containing regimens does not only lead to a decline in bone formation markers but also leads to an increase in bone mineral density (BMD) as assessed by dual-energy x-ray absorptiometry (DXA) [3–6]. A recent meta-analysis could confirm that switching from TDF to TAF seems to be beneficial in terms of the incidence of fracture in PLWH on ART regimens

including a pharmacoenhancer (“booster,” ritonavir, or cobicistat), while there was no clear benefit for PLWH on other TDF-containing ART regimens [7]. However, it seems to be the absence of TDF rather than the presence of TAF that leads to an increase in BMD and a potential reduction of fracture risk following discontinuation of a TDF-ART: a more favorable profile towards surrogate markers of osteoporosis and fracture has also been demonstrated in other TDF-free ART regimens when compared with TDF-containing therapies in both, the setting of switch of virologically suppressed patients as well as therapy-naïve PLWH [8–12]. Additionally, we do not think that a switch to a TAF-based regimen has to be to the equivalent of the previous TDF regimen, particularly in patients on efavirenz or boosted regimens, drugs that have also been attributed to unfavorable properties concerning bone health [13, 14].

For treatment-naïve PLWH, we think that the recommendation should be to use TDF-free regimens (as recommended in Fig. 2) that are not restricted to TAF- or abacavir-containing regimens (as recommended in the text) but also includes new therapeutic strategies such as dual regimens (like dolutegravir and lamivudine) which have shown non-inferiority to standard triple therapy with an overall positive profile concerning bone health [12].

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## Compliance with ethical standards

**Conflicts of interests** Sebastian Noe, Hans Jaeger, and Eva Wolf have received honoraria and/or travel grants from Gilead Sciences, GlaxoSmithKline, Hexal, Janssen, MERCK SHARP & DOHME, and ViiV Healthcare.

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