Editorial: does TAF have a better or worse safety profile than TDF, to treat hepatitis B? Authors' reply

We thank Dr Hill for providing his thoughtful discussion on our narrative review of data related to switching patients with chronic hepatitis B (CHB) to tenofovir alafenamide (TAF).\(^1,2\) As highlighted by Dr Hill, this is not a systematic review, but summarises data from clinical trial and real-world settings to provide an overview of how TAF is being used in clinical practice and the efficacy and safety profiles observed following switch. There is value in conducting systematic reviews given the stringent criteria applied; however, when compared with HIV, there are limited data available with TAF in CHB: 330 patients were switched from tenofovir disoproxil fumarate (TDF) to TAF in CHB clinical trials,\(^3,4\) whereas the meta-analysis cited by Dr Hill in HIV included 2809 subjects.\(^5\) Given that guidelines recommend switching to TAF in some patients,\(^6\) we believe that this narrative review provides a useful resource of data until meta-analyses and systematic reviews are conducted.

There are several reasons why patients with CHB may switch therapy, including cost, but few publications provide these details. Economic factors were beyond the scope of this article given the limited information available.

For TAF, the focus of safety analyses in clinical trials has been on renal or bone complications given that it may be administered over a long time. The significantly smaller reductions in bone mineral density and improvements in renal function seen in CHB trials\(^3,7,8\) resulted in guidelines recommending TAF or entecavir over TDF in specific circumstances, including in patients at risk of renal or bone complications.\(^6\) A consequence of these recommendations is that many of the real-world studies included in the review focus on these parameters when reporting safety data.\(^1\) However, where available, additional safety data are described, including lipids.

In HIV and CHB, TAF is associated with a neutral lipid profile while TDF shows a lipid-lowering effect\(^9\) and these differences were apparent in CHB studies.\(^3,7,8\) The changes in low-density lipoprotein (LDL) cholesterol and urine glucose in CHB studies shown by Dr Hill can be misleading. The percentage of patients with LDL cholesterol >300 mg/dl was higher for TAF versus TDF but this mostly occurred in patients with a history of dyslipidaemia, a raised value at baseline or both.\(^7,8\) The percentage of patients with urine glucose >250 mg/dl was higher with TAF versus TDF.\(^7,8\) However, non-fasting serum glucose >250 mg/dl was higher in TAF-treated Hepatitis B e antigen (HBeAg)-negative patients (4% vs. 1%),\(^7\) but not significantly different between groups in HBeAg-positive patients (3% vs. 2%).\(^8\) Additionally, a preliminary analysis of the Phase 3 TAF versus TDF studies showed no increased risk of cardiovascular disease with TAF.\(^10\) Cardiovascular risk should, therefore, be assessed to allow linkage to appropriate care, but the data do not support limiting the use of TAF based on lipid changes.

Our review did not aim to answer the question of which therapy has the better safety profile; however, it does provide data to support the concept of switching to TAF in CHB patients based on individual clinical needs.

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