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Correspondence

Letter: Cardiovascular risk of tenofovir disoproxil fumarate or tenofovir alafenamide fumarate in patients with chronic hepatitis B: More questions than an answer – author's reply

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Keywords: Antiviral agent; Tenofovir; Lipid

Dear Editor,

We would like to express our gratitude to Cheng and Yu for their insightful comments on our study.[1] Tenofovir disoproxil fumarate (TDF) has been associated with lipid-lowering effects in chronic hepatitis B (CHB) patients.[2-5] However, after switching to tenofovir alafenamide (TAF) from TDF, lipid profiles showed changes, including gradual increases in total cholesterol, low-density lipoprotein, and triglycerides, and a progressive decrease in high-density lipoprotein.[2,6] Another study showed that switching from TDF to TAF was associated with weight gain, derangements of lipid profile, and increased insulin resistance in patients with CHB.[7] The underlying mechanisms behind these differing effects remain elusive. Therefore, concerns have arisen regarding the long-term cardiovascular (CV) risk implications of these changes, motivating our study.

Cheng and Yu note that, while the association between long-term TDF or TAF treatment and changes in lipid profiles may contribute to CV risk to some extent, traditional CV risk factors such as smoking, hypertension, diabetes, and steatotic liver disease remain paramount determinants, as demonstrated in our study. We completely agree with this notion. Nevertheless, evaluating the long-term CV risk between the two treatments in CHB patients is essential due to the lack of conclusive evidence from previous studies, which primarily focused on surrogate markers rather than hard clinical outcomes, which was the primary outcome of our study.

As Cheng and Yu pointed out, it might be premature to conclude whether the CV risk in patients treated with either TDF or TAF is "beneficial", "neutral", or "detrimental" based on limited evidence. In particular, without knowing the exact underlying mechanism for outcomes, drawing firm conclusions may be challenging. However, a Korean study demonstrated that TAF treatment did not lead to significant changes in lipid profiles when compared to untreated patients with CHB and non-CHB patients, suggesting that TAF may not exacerbate lipid profiles.[8] Additionally, in our study, we com-

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pared total cholesterol levels in patients on TAF to untreated patients with CHB, revealing no significant difference between the two groups. This may indicate that concerns about changes in lipid profiles when switching from TDF (known for its lipid-lowering effects) to TAF (considered lipid-neutral) may be somewhat exaggerated, despite lipid profiles beginning to return to their baseline.

While acknowledging the necessity of long-term TDF or TAF use, controlling metabolic risk factors, such as steatotic liver disease, is crucial for reducing liver-related morbidity and mortality in these patients. Additionally, further research is needed to elucidate the underlying mechanisms driving differential metabolic impacts between the two treatments, emphasizing the importance of well-designed prospective studies to validate our findings.

Authors' contribution

H Hong and J Choi were responsible for the acquisition, analysis, and interpretation of data, and statistical anlaysis. H Hong and J Choi drafted and approved the manuscript.

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Conflicts of Interest

J Choi has received a research grant from Gilead Sciences. H Hong has nothing to disclose.

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Abbreviations:

TDF, tenofovir disoproxil fumarate; CHB, chronic hepatitis B; TAF, tenofovir alafenamide; CV, cardiovascular