Sirs, In the debate on the use of nucleotide/nucleoside analogues in chronic hepatitis B (CHB), recent guidelines have pointed out that drug-resistant mutations are more frequent with lamivudine, telbivudine or adefovir. For this reason, only entecavir or tenofovir is recommended as first-line monotherapy.1, 2

As there are no head-to-head comparisons between entecavir and tenofovir, we performed a network meta-analysis of randomised trials, which was focused on patients with compensated liver disease. The end-point of our analysis was the rate of virological response at 1 year. Our meta-analytical methods were the same as those of a previous study3, 4 (see also our Data S1).

A total of two trials were suitable for our analysis.5 Figure 1 summarises its main results. The direct comparison of entecavir vs. adefovir (1 trial) was associated with a response rate ratio (RRR) of 3.07 [95% confidence interval (CI): 1.41–6.69] with a number need to treat [NNT] of 3 (95% CI: 1–17). Likewise, the direct comparison of tenofovir vs. adefovir (1 trial) had a RRR of 5.71 (95% CI: 3.35–9.73) and a NNT of 1 (95% CI: 1–3). Using the data of these direct comparisons, our network meta-analysis generated a RRR for the indirect comparison of tenofovir vs. entecavir of 1.86 (95% CI: 0.72–4.78) with a NNT of 3 (95% CI: 1–∞). These results clearly show that no difference in effectiveness exists between tenofovir and entecavir.

In conclusion, differences in effectiveness between these two agents are not demonstrated by our analysis, and are very unlikely to exist. As a result, other factors (mainly related to patient characteristics) must guide the

Figure 1 | Multiple comparisons among entecavir, tenofovir and adefovir evaluated by network meta-analysis. Analysis of the rates of virological response at 1 year in HBeAg-positive patients evaluated according to NNT (Panel A) and response rate ratio (Panel B). Both graphs show two direct comparisons (solid line) and one indirect comparison (dotted line); all direct comparisons show superiority of the active treatment while no difference is found in the head-to-head comparison between entecavir and tenofovir. Statistical calculations according to the ITC software (Ottawa, 2009); graph plotted as described by Fadda et al.6 Symbols: ‘+’indicates which treatment is favoured at levels of statistical significance, and vice versa for ‘−’; ‘="”‘ denotes comparisons showing no significant difference; ‘t’ indicates which treatment is favoured by a trend in cases of no significant difference.

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decision of which treatment is more appropriate for each individual patient.

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**SUPPORTING INFORMATION**
Additional Supporting Information may be found in the online version of this article:

**Data S1.** First-line monotherapies for chronic hepatitis B: indirect comparison between entecavir and tenofovir.

**REFERENCES**


