Reviewer’s report

Title: Long-term outcomes after nucleos(t)ide analogues discontinuation in chronic hepatitis B patients with HBeAg-negative

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Reviewer: Yun-Fan Liaw

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The authors followed 66 HBeAg-negative CHB patients with HBsAg loss or achieving sustained undetectable HBV DNA levels and discontinued NUCs therapy. They found no relapse in HBsAg loss patients, and 29.7% of the 64 patients with maintained undetectable HBV DNA demonstrated evidence of relapse. No significant factor was found for relapse.

This study addressed an important clinical issue in CHB therapy. However, the study has several major problems.

1. The study included patients treated with different Nuc, each in small number of patient and the majority (64%) used the least potent one (ADV).
2. The definition of relapse is not clear. Since all patients had had maintained undetectable HBV DNA (< 200 IU/mL) before stopping therapy, how do you define an increase of HBV DNA level of 1 log10 IU/mL? Do you mean > 2000 IU/mL?
3. After stopping therapy, the patients were evaluated at least every 3 months. What were included for evaluation?
4. The relapse rate is very low when compared with 56% in a study with LAM (ref 9) and 61.4% in 1yr in a study with ADV (Ha M et al Arch Virol 2012;157:285-290). In addition, a time to relapse of 36 (12-48) weeks was much longer than that in the above mentioned 2 studies. The later was not mentioned and the reason(s) of the discrepancy were not discussed. They seemed to suggest that longer consolidation therapy was responsible. Unfortunately, duration of consolidation was not shown to be a factor for relapse in the current study (Table 5).
5. The reference list is incomplete (other studies on stopping therapy in HBeAg-negative CHB) or irrelevant (ref 10 and 11).

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests