

July 21st, 2016

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 27067-review.doc).

**Title:** "Efficacy and safety of tenofovir in Chronic Hepatitis B: Australian real world experience"

**Author:** Lovett G., Nguyen T., Iser D.M., Holmes J.A., Chen R., Ryan M., Demediuk B., Shaw G., Bell S.J., Desmond P.V., Thompson A.J.

**Name of Journal:** *World Journal of Hepatology*

**ESPS Manuscript NO:** 27067

On behalf of all authors, I would like to thank you and the reviewers for your thoughtful comments on our initial submitted manuscript. We believe we have addressed your questions point by point in the attached pages of this cover letter and response, and we have made changes to the manuscript where indicated and appropriate. Also submitted, as requested, are two versions of the revised manuscript; one with changes highlighted, the other a clean or unmarked version.

Thank you again for your careful review and consideration of our revised manuscript. We look forward to your responses. We believe we have addressed all your concerns and recommendations which have resulted in an improved manuscript.

Sincerely yours,



Grace Lovett, BMedSci, MD  
41 Victoria Pde Fitzroy  
St Vincent's Hospital Melbourne  
Melbourne, Victoria  
3068 Australia  
Fax: +61-3-92313590  
E-mail: [grace.lovett@svhm.org.au](mailto:grace.lovett@svhm.org.au)

Reviewer 2860590:

- The space between the words should be reviewed throughout the manuscript.
- Please get a native English speaker to check the English used in the paper. Various sentences should be reviewed due to grammatical error.

**Response: Thank you, this has been corrected throughout the manuscript. A native English speaker has reviewed syntax.**

- Statistics: Were the data distributed normally?
- Results: The p-value should be described in the main text and in the tables. The results should be described in a more concise and substantial manner.
- Please, the discussion should be focused on the data of the current study.

**Response: Thank you, these issues have been addressed throughout the manuscript. A clinician trained in biostatistics was involved in designing and supervising the analyses. Comparisons between groups for demographic, clinical and virological data were performed using the Wilcoxon signed pair test for continuous data, appropriate for both parametric and non-parametric data, and Fisher's exact / Chi square test for categorical data. The predictor variables considered in the Cox models were normally distributed (ALT and HBV DNA levels were log-transformed for normality).**

Reviewer 11429:

This is a well-designed and well-written real life data study of tenofovir treatment for hepatitis B. The weakness of the study is its retrospective design, limited patient number and limited follow-up time. Although the data is coming from a real world setting, it is not original, and do not contribute to current knowledge and practice.

**Response: We acknowledge these limitations. However, this is the first dataset described in an Australian population. It has local relevance. Furthermore, the population is unique for the breadth of ethnicity and HBV genotypes included (A-D), which is of more general interest. Studies from Europe and Asia are dominated by genotype A/D (Europe) and genotype B/C (Asia), limiting cross genotype comparisons. The tenofovir registration studies included mainly Western genotype A/D individuals, as have most of the real world data - there are limited data including Asian patients. The safety data are reassuring for the clinic. Despite tenofovir's short patent life, the data remain very clinically relevant as tenofovir DF will remain a low cost alternative to the next generation compound tenofovir alafenamide. These points have been included in the discussion.**