



September 1, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12415-review.doc).

Title: Predictors of kidney tubular dysfunction by adefovir for chronic hepatitis B

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 12415

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

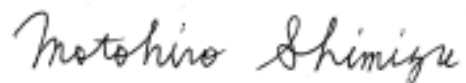
2 Revision has been made according to the suggestions of the reviewer

- (1) As suggested by reviewer #00070056, we described inclusion criteria for the "Study patients".
- (2) Based on the comment from reviewer #00013065 and #01560031, we added the information of NA other than ADV in the narrative (P5-last para); we did not assess the differences between ADV and each NA (but with/without ADV) because we focused on ADV-induced PKTD in the present study.
- (3) Based on the comment from reviewer #00070056, we clearly showed the dosage of ADV (10-mg daily) at the beginning of the MATERIALS AND METHODS and DISCUSSION sections.
- (4) Following the comment from reviewer #01560031, we described the symptom of osteomalacia of our subjects and cited references for the diagnosis of this complication (P8-the last sentence of "Patient characteristics" in the RESULTS section).
- (5) Based on the comment from reviewer #00013065, we described as follows: No significant difference was found between men and women (P8-last para).
- (6) Based on the comment from reviewer #02457523, we discussed the effect of lamivudine for the development of PKTD (P9-the last sentence).
- (7) Based on the comment from reviewer #00070056, we clarified that we did not perform histological evaluation in the present study (P10-2nd para).
- (8) Following the comment from reviewer #01560031, we suggested how to manage patients with PKTD in the DISCUSSION (P11-2nd para).
- (9) As suggested by reviewers #02457523 and #00013065, we emphasized the limited number of subjects used to evaluate the effect of SNPs as a study limitation (P11-3rd para).
- (10) Based on the comment from reviewer #01560031, we mentioned the different prevalence of HBV genotype between patients with/without ADV as a study limitation (P11-3rd para).
- (11) We did not test HDV coinfection in the present study because Japan is a non-endemic area of HDV. Therefore, we mentioned it as a study limitation (P11-3rd para). (Reply to the comment from reviewer #00013065)
- (12) As shown in "Patient characteristics" and Table 1, blood gas examination was performed for the entire study population. (Reply to the comment from reviewer #01560031)
- (13) We did not obtain data on HBV mutation; at present, detection is difficult in patients with low or undetectable HBV DNA levels. (Reply to the comment from reviewer #01560031)

3 References and typesetting were corrected

Thank you again for considering publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in black ink, reading "Motohiro Shimizu". The script is cursive and fluid, with the first name "Motohiro" and last name "Shimizu" clearly distinguishable.

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