

Reply to the reviewers

All improved parts are written in red letters.

3. Scientific quality

Reviewer #1

In this series of the patients, Hazard Ratio in the patients with cirrhosis in HCV virus infection were not cited in most of the patients, so regrettably, we cannot compare the HBV and HCV groups of patients.

Reviewer #2

- 1) Why was only ALT considered in hepatic inflammation ? Why was aspartate aminotransferase (AST) not considered ? ;

We previously demonstrated the strong association between high serum alanine aminotransferase (ALT) levels (≥ 80 international units (INU) annual average) and the development of HCC in patients with HCV-LC (Child Stage A) by long-term observation lasting about 7 years (Cancer 1999;86:589-595).

In this series of the study, we also investigated the association between sustained high (≥ 80 INU) serum aspartate aminotransferase levels (AST) and HCC development, but the association was so strong as ALT. Moreover, many studies have demonstrated a close association between severe inflammation as estimated by higher serum ALT level and initiation of HCC development (Scand J Gastroenterol 2006;41:1078-1094; Scand J Gastroenterol 2009;44:1340-1348).

Additionally, all studies in this study cited Hazard ratio of ALT as a predictor of inflammation.

Why ALT was adopted in this series of the study was cited in the the "Introduction"

- 2) In this study, we intended to evaluate the pure effects of inflammation for hepatocarcinogenesis in HBV and HCV infection. So, we excluded the patients treated by Interferon, nucleoside analogues (HBV) and DAA (HCV). Please understand the situation.
- 3) The patients with co-existing liver diseases such as alcoholic liver

diseases or fatty liver diseases were also excluded in this study, (we describe that in the “Materials and Methods”.

- 4) Flow diagrams to document the number of articles were added in the “Materials and Methods”, (Table 1 and 2).

4. Language polishing

We have sent our manuscript to the dignified English polishing company in Kyoto City in Japan.

5. Abbreviations

- (1) Title: spell out any abbreviation in the tittle
- (2) Running title: shorten the running title to no more than 6 words
- (3) Abbreviation are defined upon first appearance in “Abstract”, “Core tip”, “Main text”, “Article Highlights”, and “Figures ”.