Author’s response to reviews

Title: Hepatitis B Reactivation among 1962 Patients with Hematological Malignancy in Taiwan

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The Editor

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Thank you very much for your kindly attention to the manuscript titled "Hepatitis B Reactivation among 1962 Patients with Hematological Malignancy in Taiwan" by Dr Chen CY. We revised according to the reviewers’ comments point-by-point. We marked the revised sentences with underlined in the revised manuscript. We hope the manuscript could be suitable for publication in the BMC Gastroenterology.
Sincerely

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REV#1

1. Did the investigated patients with HBV reactivation demonstrated a different course in relation to different antiviral regimes, e.g. was outcome better in patients treated with entecavir?

Reply: Entecavir has trend (p=0.065) of less reactivation rate (32.8% vs 44.8%) than other antiviral agent. However, the limited cases were in use of tenofovir (n=4), adefovir (n=4), and telbivudine (n=12), so we did not presented this part in the article.

2. Did the authors check HBe and anti-HBe status? Was co-infection with hepatitis D excluded?

Reply: HBeAg and anti-HBe were checked in 174 (60.8%) and 133(46.5%) of 286 HBV carrier. Positive HBeAg and anti-HBe rate were 21.3% (37 / 174) and 80.4% (107/133). We described this information in the section of Result (Page 11, line 17-20). Patients with HIV were not enrolled in this study because we did not routine check anti-HDV in the clinical practices of hematology.

3. The authors state that presence of diabetes was a risk factor for HBV reactivation. An increased BMI (body mass index) may also go along with acute liver failure. Was increased BMI a risk factor for liver failure in the cohort?

Reply: Thank you for your suggestion. We did not collect the BMI results in this cohort, therefore, we could not predict the BMI as a risk factor for liver failure in this cohort.
1) This manuscript is worth for publication in the journal because it has made an important contribution in the field of Hepatitis B management for immunosuppressed patient population. This manuscript stated that type of the hematologic malignancy is not important for Hepatitis B reactivation. I believe that this is valuable for literature.

Reply: Thank you very much!

2) The authors did not give a data about Hbe status of the cohort. What is the rate of HBe negative Hbs Ag positive patients? They only defined chronic hepatitis B carrier status by the detection of HBs Ag positivity for 6 months. Although they did not stated that they measured Anti HBe antibody, did they have this data? Hbe status (Hbe Ag negative chronic hepatitis B) may be an independent factor for Hepatitis B reactivation.

Reply: HBe and anti-HBe were checked in 174 (60.8%) and 133 (46.5%) of 286 HBV carrier. Positive HBeAg and anti-HBe rate were 21.3% (37 / 174) and 80.4% (107/133). We described this information in the section of Result (Page 11, line 17-20).

3) Is there a sub analysis of which oral antiviral agent protects form reactivation? This statistical information can make their manuscript more attractive.

Reply: Entecavir has trend (p=0.065) of less reactivation rate (32.8% vs 44.8%) than other antiviral agent. However, the limited cases were in use of tenofovir (n=4), adefovir (n=4), and telbivudine (n=12), so we did not presented this part in the article.

4) They reiterated the results in the discussion (Page 17 line 29-35). I think this is not necessary. This part and similar sections can be eliminated from discussion.

Reply: Thank you very much for your suggestion. We had eliminated these results from the part of discussion.
5) One of the main conclusion is about the period of antiviral prophylaxis. 59 patient suffered form Hepatitis B reactivation although the received prophylaxis. What is the relationship between the discontinuation time of the prophylaxis and the reactivation for these 59 patients. Did they have the information about discontinuation time for these patients?

Reply: In the section of result, “There were 59 patients who developed HBV reactivation after a discontinuance period of antiviral agent primary prophylaxis, and the median length for HBV reactivation was 210 days (range 15–2349 days) after discontinuing the antiviral drug.” (Page 12, Line 18-21)

6) 41 patients had Hepatitis B reaction although they were not HBsAg positive. I understood that none of these patient were AntiHbc positive (Page 17 line 1 "All patients with HBV reverse seroconversion displayed negative anti-HBc serology"). But in Table 1 it was stated taht 19 of 41 HBs reverse seroconversion patient were AntiHbc positive and this was an independent factor for Hepatitis B reactivation in HBsAg negative group. How did authors define these patient as resolved hepatitis B? They were HBsAg negative and AntiHBc negative. Did they define this cohort with AntiHbs positivity and HBeAg positivity? I think it will be more appopriate for redefine the resolved Hepatitis B patients in the manuscript because they reach the conclusion that resolved Hepatitis B patient will not need prophylaxis when they receive chemotherapy or bone marrow transplantation for hematologic malignancy. This is an important theory and it conflicts with recommendation of major guidelines

Reply: The description of "All patients with HBV reverse seroconversion displayed negative anti-HBc serology" on Page 17 line 1 is not correct. Therefore, we delete the sentence. We add the description in the section of result, "Eighteen (43.9%) patients were positive anti-HBc at diagnosis of hematological malignancy, one patient (2.4%) was negative anti-HBc and others no data available. The only one patient with negative Anti-HBc was 56 year-old man, and he did not receive hepatitis B vaccine before.”(Page 14, Line 9-12)

7) In table 1 authors gave some p values below 0.05 (Age, Hbs Ag (+) at diagnosis, HBs Ag (-) positive seroconversion, Hepatitis C, Hepatocellular carcinoma, Allogeneic transplantation). What is the signficant p value fort this Table. There were more than two groups for this comparison? Do they execute a post hoc analyse for significant statistics.

Reply: Table 1 showed the demography of this cohort. P values below 0.05 is significant. We did not do post hos analysis in this table.