

13 January 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 15661-edited VP).

Title: Hepatitis B reactivation in the setting of chemotherapy and immunosuppression – prevention is better than cure

Author: Venessa Pattullo

Name of Journal: World Journal of Hepatology

ESPS Manuscript NO: 15661

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

Reviewer 73008

1. In the paragraph 2: lack of references for the explanation of both HBV mechanisms of hepatocytes damage.

RESPONSE: A reference has been added as requested.

Suhail M, Abdel-Hafiz H, Ali A, Fatima K, Damanhour GA, Azhar E, Chaudhary AG, Qadri I. Potential mechanisms of hepatitis B virus induced liver injury. *World J Gastroenterol* 2014; **20**(35): 12462-12472 [PMID: 25253946 PMCID: 4168079 DOI: 10.3748/wjg.v20.i35.12462]

2. The references in the text should be corrected to WJG instructions to authors.

RESPONSE: The references have been corrected to WJG instructions. A handful of references do not have available DOIs on their home journal websites or are not available digitally.

3. HBV genotype in Mediterranean is D; genotypes B and C are rare in Caucasians.

RESPONSE: The statement in the introduction has been amended to reflect reviewer's comment (see page 10).

"HBV reactivation appears to correlate with HBV genotypes C and B, prevalent in East Asia (but rare in Caucasians)".

Reviewer 52899

1. In table 2, risk estimates of HBVr should be evaluated on the basis of dividing patients into HBsAg positive and HBsAg negative/anti-HBc positive, as summarized in table 2 in American Gastroenterological Association Institute Technical Review on Prevention and Treatment of Hepatitis B Virus Reactivation During Immunosuppressive Drug Therapy.

RESPONSE: The manuscript table 2 has been amended to add the risk estimates of HBVr according to the serological status as per the AGA technical guidelines table 2.

2. The grading of severity degree of HBVr is recommended to be introduced in the third part "Definitions of HBV reactivation and associated clinical endpoints".

RESPONSE: The proposed grading system (by Hoofnagle) has been detailed in section 3 "Definitions of HBV reactivation and associated clinical endpoints".

“Consensus is needed as to a grading of the severity of biochemical hepatitis and associated clinical symptoms for the purposes of reporting in future studies. A 5-point grading system was proposed at a recent single topic conference¹⁶:

- (1) without change in ALT level (silent)
- (2) increased ALT level without jaundice (mild)
- (3) increased ALT level and concomitant jaundice (moderate)
- (4) jaundice and signs of liver failure (severe),
- (5) fatal.”

3. The serial number of some subheadings in the manuscript was incorrect and should be revised.

RESPONSE: The subheading numbering has been corrected.

4. There are several typographical errors.

RESPONSE: The typographical errors have been corrected.

Yours sincerely,

Dr Venessa Pattullo