



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Cases

**Manuscript NO:** 63502

**Title:** Prevention of hepatitis B reactivation in patients requiring chemotherapy and immunosuppressive therapy

**Reviewer's code:** 03476530

**Position:** Peer Reviewer

**Academic degree:** FRCP (C), MD

**Professional title:** Associate Professor

**Reviewer's Country/Territory:** Canada

**Author's Country/Territory:** Taiwan

**Manuscript submission date:** 2021-01-29

**Reviewer chosen by:** Jin-Lei Wang

**Reviewer accepted review:** 2021-03-05 04:09

**Reviewer performed review:** 2021-03-06 22:36

**Review time:** 1 Day and 18 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



**Baishideng  
Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**https://**[www.wjgnet.com](http://www.wjgnet.com)

#### **SPECIFIC COMMENTS TO AUTHORS**

Good overall review on this topic. Good effort in developing the algorithm, but it did not include all the factors needed to be considered before making a decision on starting on prophylaxis anti-viral. E.g. for those with HBsAg + and anti-HBc, those with normal ALT and HBV DNA 2000, it seems like treatment is recommended without considering the potency/duration of immunosuppression. Individuals needing a low dose of steroids for very short term or methotrexate might not necessarily need prophylaxis if they have no fibrosis, low HBV DNA and ALT. In the table, I would suggest specifying what "general immunosuppressants" in the low risk group, giving some examples will help the readers.



### PEER-REVIEW REPORT

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**Title:** Prevention of hepatitis B reactivation in patients requiring chemotherapy and immunosuppressive therapy

**Reviewer's code:** 03488219

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Canada

**Author's Country/Territory:** Taiwan

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**Reviewer chosen by:** Jin-Lei Wang

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** bpgoffice@wjgnet.com  
**https://**www.wjgnet.com

## SPECIFIC COMMENTS TO AUTHORS

A well written comprehensive review on hepatitis B reactivation in patients requiring chemotherapy. General comments: It would be helpful to have a conclusion at the end of each immunosuppressive medication/disease state section to summarize the recommendations with regards to HBV prophylactic therapy. eg: HCC: Due to high incidence of HBVr, it is recommended to initiate antiviral therapy in all patients with HBV related HCC undergoing chemoradiation, locoregional or systemic therapy.

Below are a list of points within the manuscript that should be clarified: Page 6: "In patients with resolved HBV infection, 27 (8.2%) developed HBVr after chemotherapy [32]. Of the patients without prophylactic nucleos(t)ide therapy, 10.8% had HBVr while only 2.1% patients had HBVr if prophylactic nucleos(t)ides were given [32]" Please elaborate on the study (reference 32). Patient population, total N, type of immunosuppression received, and total number who received prophylaxis and proportion in each group with HBVr Page 7 "corticosteroids at a daily dose of  $\geq 20$  mg for  $\geq 4$  weeks" Please state "dosage equivalent to prednisone 20mg daily" " Because HBsAg-negative patients with NHL frequently present a direct HBV infection of lymphocytes, chronic antigenic stimulation and associated B-cell proliferation [22]." This is verbatim from reference 22 which is a review article itself. It is a vague sentence and needs to be clarified. Please refer to the original article cited in reference 22 and clarify. Page 9 - under Rheumatologic diseases The introduction of tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) inhibitors and other biological agents increase the risk of HBVr in these patients [49]." Please quantify the increased risk - by how much? What is the treatment recommendation for this group? Page 10 Please define "pre-emptive therapy" - at what point should one initiate therapy? How often to monitor, etc . . . You need to clearly state the difference between primary prophylaxis (initiate therapy



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7041 Koll Center Parkway, Suite  
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**Telephone:** +1-925-399-1568  
**E-mail:** bpgoffice@wjgnet.com  
**https://**www.wjgnet.com

before chemotherapy) and pre-emptive therapy. Please clarify the section under “Moderate-risk patients (1-10%)” In whom would you recommend pre-emptive therapy and who should get prophylactic therapy? “Given the fact that screening for HBV before chemotherapy and immunosuppressive therapy with prophylactic antiviral agents could significantly decrease the occurrence of HBVr, the screening rates remain relatively low in non-HBV endemic countries such as the United States (17%) and Canada (14% to 31%), as well as in China (17%), one of the HBV endemic countries [63-65]” Need to clarify this sentence. The way it reads now it appears that China is a non-endemic country. Page 11 “A computerized order entry-based alert system (e-REMINDER) and a therapeutic control system (e-CONTROL) achieved . . .” Please provide more information on this study. Where was this program? What was the total N? Study design etc . . . Table 2: Please note that anti-CD20 antibodies is synonymous with B-cell depleting agents. Both terms are used in the table. Fig 1. HBsAg- negative and anti-HBc positive pts who receive high risk IMS – can Lam be used in this population? Do they need to start therapy 7 days in advance? Can you provide a reference for the 7 day advanced treatment initiation? “Monitor HBsAg, HBV DNA levels and ALT every 3-6 months until after completing anti-HBV therapy for 12 months” Is this monitoring frequency reasonable for all levels of risk? ie q6months in a pt with moderate risk of HBVr?



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Canada

**Author's Country/Territory:** Taiwan

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**Reviewer chosen by:** Han Zhang (Online Science Editor)

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**Reviewer performed review:** 2021-04-13 23:51

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

### SPECIFIC COMMENTS TO AUTHORS



**Baishideng  
Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA

**Telephone:** +1-925-399-1568

**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)

**https://**[www.wjgnet.com](https://www.wjgnet.com)

Thank you for responding to my enquires. Well done!