

ANSWERING REVIEWERS



Title : All show, no go: HBV and HCV reactivation in immunosuppressed patients with IBD

Name of Journal: *World Journal of Gastroenterology*

Author: Stefano Sansone, Maria Guarino, Fabiana Castiglione, Antonio Rispo, Francesco Auriemma, Ilaria Loperto, Matilde Rea, Nicola Caporaso, Filomena Morisco.

Dear Editor,

Attached you will find the revised manuscript in Word format (manuscript 5932).

We thank the reviewers for their helpful comments. We have followed their suggestions and believe that the revised version of the manuscript has improved..

The modifications in the text are highlighted in yellow. We trust that the new version of the manuscript is suitable for publication in the *World Journal of Gastroenterology*.

ESPS Manuscript NO: 5932

Point-by point response to reviewers comments.

1. *The authors should indicate the definition of HBV or HCV reactivation*

Definition of HBV and HCV reactivation significantly differ among cited articles. We have specified it in the manuscript (see line 83-86)

2. *Thiopurines have little effect for induction of remission in IBD, so these drugs are not usually used in steroid-refractory IBD? Calcineurin inhibitors are used as a first-line therapy for severe steroid-refractory UC as well as TNF alpha antagonists.*

We thank the revisor for the appropriate comment. We have changed the text as suggested (see line 101-107)

3. *Comparison of the prevalence of HBV and HCV infection between IBD patients and the general population in other countries than Western European ones should be also indicated.*

We appreciate the suggestion; the information required has been reported in lines 140 and 154-158 of the manuscript

4. *Immunosuppressive therapy and risk of reactivation in HBsAg positive patients. The authors described that there is only one case of IBD in which fulminant hepatic failure occurred during conventional immunosuppressive therapy. However, Loras et al. reported 6 cases of HBV reactivation resulting in severe hepatic failure, in most of which TNF alpha antagonists were not administered.*

We have modified the sentence “notably there is only one case of IBD in which fulminant hepatic failure occurred during conventional immunosuppressive therapy (11)..” with “Notably, only a few cases of HBV reactivation during conventional immunosuppressive therapy (prednisone and azathioprine), resulting in fulminant hepatic failure has been reported in the literature (11, 60)”. See also line 209-211

5. *Immunosuppressive therapy and risk of reactivation in HBsAg negative/HBcAb positive carriers.*

According to Table 1, in 2 patients with IBD, HBV reactivation from occult carrier occurred during immunosuppressive therapy, although the authors described only one case has been reported.

We apologize for the error in table 1 at prof stage. Only one case of HBV reactivation from an occult carrier has been described in IBD patients. The HBsAg status of the patient reported from Zeitz et al. was not described in the paper (see table 1, last line)

6. *Screening and vaccination. The HBV vaccination coverage significant differs not only among European countries but also among other countries in the world.*

We have implemented the information with the vaccination coverage in China (see also line 284-289)

7. *Tables. The authors should place citation numbers in tables*

Done.

8. *On page 6 sentence: In this perspective, the deficiency of umoral response to infection caused by the immunosuppressive/chemotherapeutic drugs plays a crucial role. umoral ? ---> It need to be corrected*

We have changed the sentence: "In this perspective, the deficiency of umoral response to infection caused by the immunosuppressive/chemotherapeutic drugs plays a crucial role" with "in this perspective, the deficiency of immune response to infection caused by the immunosuppressive/chemotherapeutic drugs plays a crucial role" (see also line 167-169)

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

Sincerely yours,

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