

March 6, 2013

ESPS 6944

Dear Dr Lian-Sheng Ma,

We are pleased to submit the revised version of our review article entitled “**Natural history, treatment and prevention of hepatitis C recurrence after liver transplantation: past, present and future**” for publication in the *World Journal of Gastroenterology*.

The manuscript has been modified according to the reviewer’s comments as follows. We have enclosed a detailed letter responding to each of the comments. All the revisions in the text are underlined.

We look forward to hearing from you, and thank you for your consideration.

Sincerely yours.

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Reviewer 1

The present manuscript reviews the natural history of HCV recurrence after liver transplantation, including risk factors for disease progression, and on antiviral therapy. The authors suggested possible ways to improve final long-term results of liver transplantation for HCV-related liver disease. Comments: This is a diligent review study of the results and management of HCV-related liver disease undergoing liver transplantation. The manuscript was generally well written with some innovative ideas and concepts.

We are really grateful to the reviewer for this kind comment.

Reviewer 2

The review article of Dumortier et al. presents an adequate overview of the current literature and knowledge of natural history, treatment and prevention of recurrent hepatitis C after liver transplantation. However some changes and additional comments are required to improve the importance and significance of the article:

1. Title and subtitles do not accurately reflect the therein described topics, particularly the partitions in “past, present and future” are not convincing: I would recommend the following changes: Title such as: “Natural history, treatment and prevention of hepatitis C recurrence after liver transplantation: past, present and future” Subtitles such as: a) “Natural history of HCV recurrence after LT” b) “Treatment of HCV recurrence after LT: past and present” c) “Treatment and prevention of HCV recurrence after LT: future perspectives”

This has been modified.

2. Section “Natural history...”: The authors should add a comment on what could be the best way to treat an acute rejection in the setting of HCV recurrence after LT and more importantly they should focus on the clinical and histopathological difficulties to differentiate between acute rejection and HCV recurrence after LT (amongst others see Regev et al. Liver Transplantation, Vol 10, No 10 (October), 2004: pp 1233–1239).

This point has been added.

3. Section “Treatment of HCV...”:

a) The authors should discuss the virological response rates of Boceprevir vs. Telaprevir as reported in the paper of Coilly et al. (ref. 102) in comparison to the results obtained by Pungapong et al. (ref. 101).

These contradictory results can probably be related to patients-related differences since these two cohorts report preliminary experiences in an open-label design. This has been added.

b) The article of Werner et al. (Liver Transpl. 2012 Dec;18(12):1464-70) should be cited (first full paper publication on safety, efficacy and drug-drug interactions in patients receiving Telaprevir triple therapy after LT).

This has been added.

c) The article of Fontana et al. (Am J Transplant. 2013 Jun;13(6):1601-5) should be cited (first case report in interferon free DAA therapy of FCH after LT).

It was already cited (Ref 124). A sentence has been added.

4. Section "Prevention of HCV...":

a) To reinforce the really important point of the impact on morbidity and mortality during emerging HCV treatments also the publication of Deuffic-Burban et al. (Gastroenterology 2012; 143:974-985) should be mentioned and cited.

This has been added.

b) At the end of this or the previous section a comment or may be a recommendation should be given to the readership how to treat HCV after LT under the current circumstances/current therapeutic availabilities (e.g. ...refuse therapy and await new drugs?, ...treatment only in special patients?, ...dual or triple therapy?,...preference for TVR or BOC?)

We agree that some recommendations could help the readers at the present time of major therapeutic advances (but also open questions!!). Nevertheless, because of the lack of available data in LT recipients, and because of the unknown date of availability of new generation DAA, we believe we can not do pertinent recommendations by now. We only suggest that TVR and BOC will probably no longer be used in LT patients.

5. Please check again the manuscript carefully for some typing errors.

We did our best to correct all typing errors.

6. Beyond that, also a careful language polishing should be made by a native speaker.

Of course, we accept all modifications able to improve language during the editorial

process.