

Dear Editor,

Please find enclosed our edited manuscript in Word format for the Invited Article entitled "Challenges in managing hepatitis C virus infection in cancer patients".

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We thank the reviewers for their constructive criticisms. The manuscript has been improved with revisions according to the suggestions of the reviewers. Their concerns and suggestions have been addressed thoroughly (please see the detailed list of revisions below). We highlighted all these changes in an additional copy of the manuscript.

(1) Question, reviewer number 1, "Challenges need to be briefly listed in the introduction?"

Answer: Challenges in HCV management of cancer patients are now listed in the introduction.

(2) Question, reviewer number 1, "A diagram or flow chart showing challenges in treatment of HCV at each stage of different cancers should be shown?"

Answer: A new figure (figure 1) has been included to diagram challenges in HCV treatment at different stages of cancer, and is discussed within the manuscript.

(3) Question, reviewer number 1, "The take-home message seems not clear?"

Answer: The conclusions have been modified to include a clear take home message.

(4) Question, reviewer number 1, "The cost-effect, as well as benefit-adverse evaluation, ideally with solid data support, are needed?"

Answer: We also have addressed the topics of cost-effectiveness and benefit-adverse reactions in the conclusion section.

(5) Question, reviewer number 2, "Second paragraph. Authors report a SVR of 41% of HCV cancer patients, and 41% of SVR in G1 pegIFN+RBV treatment, is not a rare rate, authors should clarify which patients did they study (genotypes) and which therapeutic treatment was used?"

Answer: We have modified the section on "Therapeutic challenges" to include the requested information. As we note in our retrospective study, none of the patients with G1 achieved SVR, and this is a poor response.

(6) Question, reviewer number 2, "Page 5. Citation 14 refers to a review, and when possible, it is recommended to quote the original manuscript?"

Answer: Review reference 14 has been replaced with the original article by Simmonds P, Bukh J, Combet C, et al. and we have included the requested additional reference by Smith DB, Bukh J, Kuiken C, et al. that most recently appeared in the October, 2013 online issue of *Hepatology* as suggested. These two new references (16 and 17) have been added to the manuscript.

(7) Question, reviewer number 2, "Authors mention "Occurrence of occult infection" as a first difference between HCV infected cancer patients compared to those without cancer. Since occult infection has not been demonstrated for HCV, this sentence should be excluded?"

Answer: We respectfully disagree with the reviewer on the occurrence of occult HCV infection. In clinical practice, HCV infection is diagnosed based on the presence of serologic markers of exposure. However, viremia can occur in patients with negative serologic markers, conditions described as occult HCV infection. For instance, occult viremia has been reported in up to 10% of high-risk

patients for HCV infection [Rai RR, et al. Prevalence of occult hepatitis B & C in HIV patients infected through sexual transmission. *Trop Gastroenterol*. 2007 Jan-Mar;28(1):19-23.]. Occult hepatitis C infection does occur in cancer patients, as we have seen in our institution and others have reported [Locasciulli A, et al. Hepatitis C virus serum markers and liver disease in children with leukemia during and after chemotherapy. *Blood*. 1993;82(8):2564-7]. Additionally, published guidelines for preventing infectious complications among HSCT recipients acknowledge this condition [reference 10 of our review]. Therefore, we added two new references to the article and respectfully decline the recommendation to append this aspect of our manuscript.

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

Sincerely,

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