

ANSWERING REVIEWERS

January 11, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5763-review.doc).

Title: Hepatic Flares in Chronic Hepatitis C: spontaneous exacerbation versus superinfection by other hepatotropic viruses

Authors: Evangelista Sagnelli, Caterina Sagnelli, Mariantonietta Pisaturo, Nicola Coppola

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5763

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

-Reviewer n.1

All typing and grammatical errors found by Reviewer n. 1 have been eliminated.

The discrepancy in the introduction section between the reported rate of spontaneous eradication of HCV infection and the references has been removed

-Reviewer n.2

Reviewer: GENERAL COMMENT – Very little has previously been published on hepatic flares in those with HCV infection. On these grounds, this submission deserves full attention for publication. However, the

manuscript may be improved to a substantial extent by major restyling affecting the very structure of this submission.

This article is chiefly centered on infective etiologies of flares and its scope should be widened as much as possible.

Answer: In agreement with the reviewer we have restyled the structure of the manuscript. The scope of the article, mainly centered on viral etiologies in the old manuscript, has been extended also to other etiologies in the new manuscript.

Reviewer: SPECIFIC COMMENTS Abstract, core tip and introduction – The Authors need to discuss shortly whether and how flares worsen the natural course of treated and untreated disease.

Answer: In the abstract, core tip and introduction of the new manuscript we have discussed briefly the unfavorable action of flares on the natural course of the treated and untreated disease.

Reviewer: Introduction – This section is very confused. The Authors may be willing to re-write it. First, describe the virus; next go to the epidemiology; next discuss the natural history of untreated and treated disease. Define flares. Omit “older and more recent”. “scientific data”-? change to “published data”

Answer: this section has been re-written according to the suggestion of the reviewer. We have also changed the “older and more recent... scientific data” to “published data”

Reviewer: Table 1 –The use of a Table in the introduction is quite unusual. The title of this table is unclear. The Authors might be willing to divide such a table into three sections a) evidence from prospective studies; b) cross-sectional studies; c) case reports. Once such a table is modified, findings from individual studies do need to be duplicated in the text. The various sections might be willing to comment on a) estimated prevalence of flares; b) risk factors for their occurrence; c) diagnosis and management.

Answer: Table 1, reported in the introduction section in the old manuscript, is mentioned in the single chapters in the new manuscript. The title of this table has been modified and the table divided in sections as suggested by the reviewer. Considering the interesting suggestion of the reviewer to focus on the management of patients, we have introduced two Figures (Figure 1 and 2) in the new manuscript, reporting some flow charts for patients' management. The findings from individual studies reported in the text refer to data we think of particular interest for the readers.

Reviewer: Section on viral infections “a practice recommended by several international and national healthcare institutions but which remains poorly applied.” Please provide references.

Answer: we have provided such references.

Reviewer: The scope of this article needs to be widened. For instance: based on personal experience and literature studies, could the authors comment on a) prevalence and risk factors for flares in viremic vs. SVR HCV patients ? b) host factors predisposing to flares, with particular reference to steatosis, endocrine derangements and metabolic conditions ? c) occurrence of flares during anti-HCV treatment: IFN toxicity or concurrent autoimmune liver disease ? d) Any practical suggestion on schedules of monitoring HCV patients: which patients are at increased risk and how often should they be monitored?

Answer: Following the suggestion of the reviewer, the scope of the article has been widened. As mentioned above, the two new Figures in the new manuscript are flow charts for patients' management.

3 References and typesetting have been corrected

We hope our manuscript is now worthy of publication in the *World Journal of Gastroenterology*.

Sincerely yours,

Prof Evangelista Sagnelli