

Format for ANSWERING REVIEWERS



April 11, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12131-review.docx).

Title: New treatments for chronic hepatitis C: an overview for paediatricians

Author: Giuseppe Indolfi, Daniele Serranti, Massimo Resti

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 7857

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

- (1) *This review is interesting and the subject is very hot, since there are a lot of new drugs and new future protocol. However there are 2 problems: 1. This study is a bit superficial regarding the new drugs (post PI drugs) and the new protocols. 2. The pediatric point of view is missing, although there is a problem since such new drugs are naturally tried in adults, however i would expect a little more regarding the potential and danger of such drugs in children*
- (2) *The review discusses emerging therapies for the treatment of hepatitis C. As there are no studies available in the pediatric population, the review depends upon the adult studies with possible implications for the pediatric population. I think it is important for the pediatric gastroenterologists and hepatologists to keep in touch with the emerging therapies and the paradigm shift in the treatment of hepatitis C. Few comments*

Page 4. "Early viral response (EVR), defined as undetectable plasma HCV RNA 12 weeks after the end of treatment". It is not clear that authors want to mention early virological response 12 weeks after starting treatment (EVR) or end of treatment response (ETR)?

The sentence has been corrected.

Page 7: "A recent clinical trial showed that 100% of previously untreated genotype 2 and 3 patients achieved SVR with sofosbuvir plus ribavirin regimen [23]." In fact responses are no so good for genotype 3 in all studies. Recommended duration of therapy for this genotype is 24 weeks, longer than genotype 1. In The Valence study presented at AASLD 2013, 24 week therapy of sofosbuvir with ribavirin resulted only in 60% SVR in treatment experienced cirrhotic patients with genotype 3

More information about sofosbuvir efficacy in genotype 3 has been added in the NS5B inhibitors section.

- (3) *1. Please report in a new paragraph, the role of liver biopsy in paediatric HCV patients, for the diagnosis and to provide the antiviral treatment.*

A statement on the role of liver biopsy in paediatric HCV patients has been inserted in the introduction paragraph.

2. Report also in another paragraph the host factors that can influence the SVR (e.i. insulin resistance, obesity, liver steatosis, IL-28B, etc).

Information about host factors that can influence SVR has been added in the SOC section.

3. The recent NASPGHAN practice guidelines on the diagnosis and management of HCV infection in infants, children, and adolescents is not cited and reported in the text (J Pediatr Gastroenterol Nutr. 2012 Jun;54(6):838-55).

The recently published NASPGHAN guidelines have been mentioned.

- (4) *Thank you for this very interesting paper. In fact, in view of the huge amount of new therapies available in the very new future (sofosbuvir has granted FDA and also EMA authorization few days ago and Daclatsvir is already on EMA process) pediatricians should be advised on the changes in the approach to HCV treatment in order to correctly manage their young patients. However, a general section on HCV in pediatric patients i.e. burden of HCV in this peculiar setting of patients and prognosis are warranted. Moreover, I suggest to enclose a general description of the virological categories (RVR, EVR) and their role as stopping rule. Their high predictive role in obtaining eradication is the results of an impressive number of paper in adults HCV patients and are a precise guide for clinicians to met futility rule and avoid side effects and reduce the costs.*

A general description of virological categories has been added. Their predictive role has been analyzed.

Please, state more in detail about the safety profile and side effects as well as the significant drug-drug interaction related to telaprevir and Boceprevir.

Statement on side effects and drug-drug interactions related to Telaprevir and Boceprevir has been added in the NS3-4A section.

A brief suggestions about the management of side effects as well as the role of counseling with the parents is suggested

Statement on the role of counseling with parents in the management of treatment side effects has been added in the SOC section.

- (5) *In this review, the authors described traditional and new drugs in the treatment for chronic HCV. The title named " a guide for pediatricians", actually, cause there are too little evidences of HCV treatment in children, the authors talked too little about the use of new drugs in children. So, the title and contents is not consistence and too far from guide.*

Title has been changed.

In the efficacy of PEG-IFN plus ribavirin regimen treatment part, the references is too limited, just talk about viral genotypes and EVR, as we known, the 4 weeks viral response and IL-28B SNP are also very important for SVR.

The role of RVR and IL-28B SNP as SVR predictors has been explained in the SOC section.

3 References and typesetting were corrected

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

Sincerely yours,

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