

## Format for ANSWERING REVIEWERS



February 20, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: **8964-review.doc**).

**Title:** Age-related differences in response to peginterferon alfa-2a/ribavirin in patients with chronic hepatitis C infection

**Author:** Claudia Roeder, Sabine Jordan, Julian Schulze zur Wiesch, Heike Pfeiffer-Vornkahl, Dietrich Hueppe, Stefan Mauss, Elmar Zehnter, Sabine Stoll, Ulrich Alshuth, Ansgar W. Lohse, Stefan Lueth

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 8964

We thank the reviewers for the thorough review and excellent suggestions to the current study. In the short time span we have clarified all of the reviewers' queries and added several points to the discussion section as recommended by the reviewers. We think that the quality of the manuscript has definitely increased. Below please find a point to point response to the reviewers' critiques:

### **Reviewer #1 (02861260):**

1. Table 1 Please provide patient race distribution because host genetic factor influence virologic response.

We added the patient race distribution into table 1 and stated in III. Results that there were no differences in racial distribution in both age groups with the vast majority of patients being caucasian.

2. Please explain about the reason why non response is high in elderly patients. "Treatment response in patients with GT 1 was substantially lower in patients  $\geq 60$  years (23.7% vs. 43.7%;  $p < 0.001$ ).“ Please explain about the reason for a continuous decline in SVR rate over age.

We added to the discussion section that we could show that age is an independant factor for SVR. The reason therefor remains unknown. We discussed the influence of altered IFN-immunomodulation and pharmacokinetics in elderly patients.

The continuous decline in SVR over age might be due to a marked influence of those factors even becoming more apparent with longer duration of therapy in older patients and genotype 1 infections.

**Reviewer #2 (00053634):**

1. As rate of cirrhosis is higher in patients aged  $\geq 60$  years than those  $< 60$  years, it is necessary to perform a logistic regression analysis to assess the independent role of age in impacting SVR rate and tolerability. It is not clear to me whether a logistic regression analysis has been performed or has not.

We have added a new table (table 6) with a multivariate logistic regression analysis showing that age and stage of liver disease (fibrosis stage 4 vs. other fibrosis stage) are independent factors of treatment response.

2. In introduction the authors correctly state that incidence of HCV infection is declining- However, they should acknowledge that patients undergoing hemodialysis, surgery, endoscopies, tattooing as well as homosexual men and intravenous drug users still remain at risk of acquiring HCV infection.

In introduction section we added that despite of declining incidence of HCV infection intravenous drug abuse together with sexual behavior (Men Who have Sex with Men) as well as tattooing remain main risk factors for infection. Iatrogenic infections are decreasing but do still occur occasionally. We also integrated some references as suggested.

3. The field of HCV therapies is moving very rapidly and authors should mention in introduction that the first interferon-free therapies were approved at the end of 2013 by FDA for HCV genotypes 2 and 3 patients and cite these references.

We edited this very important point and integrated the new antiviral therapies into the discussion part. We mentioned the approval of the nucleotide NS5B polymerase inhibitor Sofosbuvir as the first interferon-free therapy and cited the correspondent references.

We hope to have edited the very helpful reviewers comments satisfactory and thank them again for the thorough review.

Sincerely yours,

Dr. Stefan L  th

Revisions due to editor suggestions:

- Format Author affiliations changed
- Core Tip added
- Author contributions added
- Abstract revised
- Section Comments added
- References: PMID added
- Please find editable tables and source data for figures in separate files