Reviewer’s report

Title: Lower ribavirin biodisponibility in patients with HIV-HCV coinfection in comparison with HCV monoinfected patients

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Reviewer: Monica Basso

Reviewer’s report:

The submitted manuscript by Hatu et al. entitled “Lower ribavirin biodisponibility in patients with HIV-HCV coinfection in comparison with HCV monoinfected patients” investigated ribavirin plasma exposure after a single dose of ribavirin (600 mg) and they reported a lower drug exposure in patients with HIV infection. This information may be of interest for the tailoring of antiviral treatment of this category of patients, mostly if immunological recovery under antiretroviral therapy is not optimal. Nevertheless, this study is primarily of pharmacokinetic interest rather than clinical.

Major compulsory revisions

Please describe the ribavirin dose modifications prescribed to HIV-HCV patients on the basis of the early bioavailability data.

A. Background

1. Third paragraph: “RBV doses must be adapted to body weight“. Please specify that the topic is antiviral treatment in HIV-HCV coinfection: according to EASL guidelines (Journal of Hepatology 2014), naïve HIV negative patients with genotype 2 and 3 HCV infection can be treated with ribavirin fixed dose (800 mg daily) if they have no unfavorable cofactors.

2. Page 4, last line: please add a reference on lower bioavailability of drugs in HIV patients.

B. Methods

1. Patients: all treated patients were included in the study? Please specify.

2. Statistical analysis. First line: median and range is preferred to “medians”.

C. Results

Specify if all patients are Caucasian. African Americans are reported to have a less cumulative ribavirin exposure in the work by Runyan et al (Am J Gastroenterol. 2012; 107: 1675–1683), with a different study design.

HCV treatment status at baseline (described in table 1): does it correlate with lower ribavirin biodisponibility?.

D. Discussion

Please comment the correlation between HCV treatment status at baseline and ribavirin biodisponibility.
Last paragraph: detectable HIV viremia can be due to drug resistance or to a slow response to antiviral therapy, moreover these patients received only a single ribavirin dose: in my opinion you have no data to evaluate adherence.

E. Tables

Table 1. Please check: age range “(23-74)”, hemoglobin level “(8.2-17.2)”, men hemoglobin level “(8.3-17.2)” of HCV monoinfected patients. Add the exact p value, even not significant, related to AST, ALT, HCV RNA and men hemoglobin level. Explain the virological characteristics of the group “RBV treatment naïve”: are they nonresponders or relapsers to interferon monotherapy or naïve to antiviral therapy and why do you analyze them separately? Add the explanation of the following abbreviations: MDRD, AST and ALT.

Table 2. Add the exact p value, even not significant. Modify NRTI and NNRTI in nucleoside reverse transcriptase inhibitors and nonnucleoside reverse transcriptase inhibitors respectively.

Table 3. Add the exact p value, even not significant.

Minor Essential Revisions

B. Methods

1. Patients: please specify the reasons to exclude co-infected patients not in antiviral treatment from the study.

2. Patients: last paragraph. Most HIV positive patients (20/23) had a plasma HIV viremia lower than 50 copies/ml. This parameter is better described as percentage of patients with undetectable HIV viremia rather than as HIV RNA absolute value, both in the text and in table 2.

C. Results. ninth paragraph. See the previous comment.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests