

ANSWERING REVIEWERS

February 19, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 16521-review.doc).

Title: Voriconazole and the liver

Author: Romeo-Gabriel Mihăilă

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 16521

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

Reviewers comments and recommendations:

02462024: Please review and improve the written English as it is difficult to follow Please state more clearly what your aims are for this article There is too much concentration on pharmacology and not enough on the association with the liver.

03022391: The effect of voriconazole on the liver is a useful topic to review, but the poor fluency of the article makes it difficult to follow. It appears that good articles were chosen and the organization is fine. Unfortunately, the sentence structures are awkward and make the text difficult to follow.

00002314: This is an interesting narrative review focusing on liver damage by voriconazole. MAJOR POINT The English style and grammar need extensive revision by a native speaker because they compromise the pleasure of reading this nice contribution OTHER POINTS The author may want to consider these aspects: a) is damage by voriconazole mainly due to cytotoxic damage to the hepatocyte or to cholestasis or mixed? b) what is the role of autoimmunity in causing damage when no clearcut dose-dependence is found (as in this case)?

02991558: A well written manuscript clearly answering the questions associated with Voriconazole and its negative effects on the liver.

00188507: This is a well written invited review describing the use of voriconazole. The manuscript is well written and can be accepted as its current form.

Corrections and additions

This article is written for clinicians who use voriconazole. Starting from pharmacological data, the aim of this literature synthesis is that to find explanations and to establish correlations with clinical manifestations that may occur during its use.

Therefore, among the liver side effects of voriconazole, jaundice, including the cholestatic one, is more common while hepatomegaly or hepatitis occurs less frequently. It rarely induces liver failure and very rarely hepatic coma. So the liver damage produced by voriconazole is mainly due to cholestasis, and more rarely can be cytotoxic or mixed.

Voriconazole is not involved in the appearance of autoimmune hepatitis, but an increase in the levels of immunosuppressive drugs (cyclosporine or tacrolimus) used in patients after solid organ transplants or with autoimmune disorders was reported during coadministration with this antifungal drug. One of five such patients developed a moderate increase in hepatic enzymes. This combination of drugs requires immunosuppressive dose adjustment (by its reducing)[16].

I reviewed the entire article and I corrected the topic (the sentence structure and fluency) and grammatical expression. The corrected sentences and the additions are in red.

Thanks to all the reviewers for the recommendations made and I assure them of my entire gratitude.

3 References and typesetting were corrected

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

Sincerely yours,



Romeo-Gabriel Mihăilă, MD, PhD

Faculty of Medicine

Lucian Blaga University of Sibiu

Sibiu, str Lucian Blaga, 2A

550169, Romania

romeomihaila@yahoo.com

Telephone: +40269 215050. Fax: +40269 218365.