March 19, 2016

Manuscript ID: ; 25074 revision

To Dr. Damian Garcia-Olmo, Stephen C Strom, Andrzej S Tarnawski

Editors-in-chief, World Journal of Gastroenterology

Manuscript title: **Usefulness of portal vein pressure for predicting the effects of tolvaptan**

Dear Dr. Damian Garcia-Olmo, Stephen C Strom, Andrzej S Tarnawski

We were pleased to read the fair assessment of the reviewer and the encouraging comments by members of the Editorial board. We believe that adequate modifications were successfully made in our revision, taking into consideration the comments raised by the expert reviewer. We also carefully proofread the revision including the text, tables and figures.

We take this opportunity to express our gratitude to the reviewer for their useful and critical remarks. Their comments allowed us to identify areas in our manuscript that needed modification and clarification.

We hope that the revision is now acceptable for publication in *World Journal of Gastroenterology*.

Sincerely Yours,

Professor Damian Garcia-Olmo, Stephen C Strom, Andrzej S Tarnawski
Science Editor Ya-Juan Ma,

Dear Professor Ya-Juan Ma,

We would like to thank the editor and the reviewer for examining our manuscript entitled, " Usefulness of portal vein pressure for predicting the effects of tolvaptan" (Manuscript ID 25074). We have reviewed the reviewers' comments and submitted responses as listed below:

Response to Reviewer

In Methods the authors should describe the methodology used in the study better because the main part of the study seems to be an analysis of the responders and non responders to tolvaptan administration, but in the section on "Effects of tolvaptan, biochemical tests, and urinalysis" and in '"Association between HVPG and the effect of tolvaptan" the groups are divided by other concepts which make it difficult to read and understand the paper.

→As suggested, we provided more information about differences between responders and non-responders in the Result Section as follows.

Differences in background factor according to responses for tolvaptan

Next, based on previous clinical studies using tolvaptan, patients with a body weight decrease of 2 kg or greater from the baseline were regarded as responders. On the other hand, patients with decreases of less than 2 kg or increases from the baseline were regarded as non-responders. We analyzed differences in background factor according to responses for tolvaptan. HVPG (P=0.045) and serum hyaluronic acid (P=0.017) were detected as useful factors. All other characteristics factors did not have the significant difference between both groups (Table 2).

In addition, we stated Table 2 about differences between responders and non-responders for tolvaptan..

Hepatic edema should be changed to liquid retention or severe liquid retention and hyponatremia should be used instead of hyposodiumemia.

→As suggested, we rewrote some words that the reviewer pointed.

In the second paragraph in the "Introduction" albumin reinfusion should be

included in the treatment of refractory ascites.
→As suggested, we rewrote and added 'albumin reinfusion' in the treatment of refractory ascites.

The concept of uncontrollable hepatocellular carcinoma should be better explained, because there are 12 patients with hepatocellular carcinoma included in the group of patients studied.
→As suggested, we provided and explained about uncontrollable hepatocellular carcinoma in the Method Section as follow.
(a) uncontrollable hepatocellular carcinoma, such as the Barcelona clinic liver cancer (BCLC) stage D. BCLC stage D is end-stage hepatocellular carcinoma in a patient with disturbed liver function (Child-Pugh C) and/or performance status 3-4, and with an average predicted survival of 3 months.

In "Results. Patients" there are some figures which should be revised. The authors state that "The daily dosages of furosemide and spironolactone before the administration of tolvaptan were 20 (range 20-160)"; if the mean is 20 the range is incorrect or vice-versa.
→As suggested, we added mean daily dosages of furosemide and spironolactone instead of median daily dosages of furosemide and spironolactone in the text and Table1 as follows.
The daily dosages of furosemide and spironolactone before the administration of tolvaptan were 37.0 ±29.5 mg and 43.4 ±26.8 mg, respectively.

In the printed version the legend of Figure 1 is divided by the characteristics of the patients included in the study.
→As suggested, we rewrote figure legend.

We would like to submit our revised manuscript for consideration and hope you will agree that our study is of enough scientific relevance to justify publication.

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