ANSWERING REVIEWERS

Mar. 25, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 9336-revised.doc).

Title: Clinical efficacy of tolvaptan for treatment refractory ascites in liver cirrhosis patients

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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) We have added related materials at discussion parts in revised manuscript about FDA´s warning on tolvaptan in patients with liver diseases from all reviewers. January 2013 , the U.S. FDA has issued a warning for using tolvaptan because of the potential risks of liver injury found in tolvaptan treatment of autosomal dominant polycystic kidney disease (ADPKD) clinical trials. The study found 3 of 1445 cases of patients was significantly higher serum bilirubin and ALT in tolvaptan group. In ADPKD clinical trail, however, the dose (120 mg/d,3years) of tolvaptan. However,in cirrhostic patients , the dose was 15mg/day for 7-14day of treatment hyponatremia or ascites in this study. Tharefore, talvoptan proving this dosage and length of therapy, do not affects liver function in patients with preexisting liver disease, such as liver cirrhosis in published papers.

(2) About data, we have added liver function(ALT/AST) and MELD in results at revised manuscript. Because there is no standard of weighing machines and very bad nutrition in these subjects .so, we don`t analyse weight.On the other hand, in this study,these are all critically ill patients, the 3-month survival rate is less than 50% . so, we only follow- up one month. We will take a long-term follow-up in next study program.

(3)In China clinical practice,it is rare that using high dose diuretic (400 mg of spironolactone and 160 mg of Furosemide) because of more SAE in chinese patients. The refractory ascites was regarded if

ascites were not satisfactorily controlled after a patient had received either: (1) sodium intake restrictions (< 6 g/day), intermittent albumin infusion (10–20 g/per treatment) and high doses of diuretics (more than 160 mg/day furosemide and 200 mg/day spironolactone) for 1 week, or (2) therapeutic paracentesis (3000–5000 mL per treatment) for 2 weeks.So, the definition for refractory ascites was minor revised. This may be considered as Chinese guideline in the future. The Spiranolactone is available in 20 mg pills in China which were difference in USA

(4) The renal parameters (BUN,Cr) were described in Adverse events parts. About 20% of all patients had received paracentesis before using tolvaptan.

(5) The figure was revised according to editor`suggestion.

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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