

12 June 2016

To: Editors-in-Chief,  
World Journal of Gastroenterology

**Submission of a revised review**

On behalf of all authors, I would like to submit a revised version of the revised review titled 'Management of hepatocellular carcinoma with portal vein tumor thrombosis: Review and update at 2016' (ID: 02462657).

Below please find the point-to-point replies to reviewers' comments. We also highlighted corresponding changes in the submitted file. Thank you for your kind attention.

Yours sincerely,  
Dr. Stephen L. Chan  
Department of Clinical Oncology  
The Chinese University of Hong Kong

## Point-to-point responses to reviewers

### Reviewer 1

1. Grammatical error in Page 4 line 5: However, biopsy procedures are not frequently conducted in real-life situation for work-up of PVTt because of a small but potentially life-threatening complications including bleeding and injures to bile ducts or hepatic arteries.

Response: The sentence was modified to ‘however, biopsy procedures are not frequently conducted in clinical practice to confirm PVTt because of concern about life-threatening complications such as injuries to bile ducts or hepatic arteries.

2. Typing error in Page 4 line 13: transarterial

Response: It was changed to transarterial.

3. Confusion expression in Page 7 line 9: The 3- and 5-year survival rates were 35.3% and 41.8% respectively in the Vp3 group and 21.2% and 20.9% respectively in the Vp4 group

Response: It was modified to ‘The 3- and 5-year survival rates in vp3 and vp4 group were 35.3% and 41.8%, and 21.2% and 20.9%, respectively.’

4. There are only OS data but DFS data in: Page 7 line 21: The 1-, 3- and 5-year overall survival rates were 50%, 12.5% and 12.5% respectively in Group 2 and 28.6%, 14.3% and 14.3% respectively in Group 3. Again, the two approaches had no significant difference in terms of overall survival and disease-free survival

Response: It was modified to ‘The 1-year DFS rates were 24.3, 0, and 14.3 %, respectively. The 3-year DFS rates were 14.3, 0, and 14.3 %, respectively. The 5-year DFS rates were 10.7, 0, and 14.3 %, respectively.’

5. The interpretation for EACH study and the reason for adoption of FOLFOX are not so correct in Page 14 line 13: The overall study fails to demonstrate

statistically significant difference between the two regimens but FOLFOX4 was found to have a small survival benefits in the subgroup population of Chinese patients [69, 70]. As a result, FOLFOX4 has been considered a standard treatment in China, where sorafenib is not widely available.

Response: We have removed the final statement.

#### Reviewer 2

1. This paper reviewed recent data on the management of HCC with PVTT, providing information for clinical practice, however it is similar with a recently published paper entitled 'Treatment of hepatocellular carcinoma with portal venous tumor thrombosis: A comprehensive review' by Han et al.

Response: As compared to the review by Han et al., our review paper has additional aspects as follows: 1) discussion on the option of surgery in the treatment of PVTT; 2) discussion on various classification systems for PVTT; 3) the need of multidisciplinary team for the management of PVTT; 4) the role of portal vein stenting in the management of PVTT. Further, even in contents with similar heading such as

2. The format of the tables should be unified.

Response: It has been unified.

#### Reviewer 3

1. Please include references for the following studies: 1) A PVTT confined to the hepatic lobe harboring the HCC (ipsilateral PVTT) is usually resected when a hepatectomy is conducted to remove the HCC. 2) For the management of PVTT extending to the portal vein bifurcation or the main or contralateral portal vein, different approaches have been advocated. En-bloc resection including the bifurcation with or without the main portal vein and/or the contralateral portal vein is believed to produce good oncological outcomes. 3) TACE is repeated every 8 to 12 weeks, and

the treatment is to be stopped when there is progressive disease, extrahepatic disease, severe life-threatening complication, or evidence of liver failure or decompensation (serum total bilirubin >50umol/L, gross ascites uncontrollable with diuretics, or hepatic encephalopathy) (include references).

Responses: Corresponding references have been added.

2. The study by University of Hong Kong (ref 22) is randomized? Please specify

Responses: It is a randomized study. Amendment has been made in the revised manuscript for clarification.