Author's response to reviews

Title: Retrospective comparison between a regular and a split-dose protocol of 5-fluorouracil, cisplatin, and mitoxantrone for the treatment of far advanced hepatocellular carcinoma

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Version: 2 Date: 17 February 2010

Author's response to reviews: see over
Dear Miss Deepali Singhal and Dr Zhao-Chong Zeng,
Thank you very much for your letter of Feb 4, 2010 and interest in our manuscript. My colleagues and I greatly appreciate the comments and suggestions from the Editor and the Reviewers.

We have revised our manuscript along the lines indicated by the Editor and the Reviewers. All changes were marked in red in the revision. The following are the point-by-point responses to the comments:

Editor comments:
The distribution of HCC patients receiving various forms of treatment in our institute was given as requested (page 4, lines 8-13).
English was polished using a commercial Editing Service (ATS Medical Editing Solutions; by Steven R. Kaufman).

Reviewer 1 (Dr Tianshu Liu)
1. The reviewer asked for the representativeness of the patients selected in this study. This information is added to the Method/Patients section (page 4, lines 8-13).
2. The disadvantage and possible selection bias in this retrospective study is discussed as requested (page 11, lines 6-10 and 19-22).
3. The clinical applicability of the split-dose FMP therapy is discussed (page 11, lines 18-22).
4. The reviewer possibly misread the data. In fact, split-dose group has significantly lower risk of toxicity (Table 4).
5. These patients all had main portal vein thrombosis and/or extrahepatic metastasis and were therefore not suitable for further TACE or RFA treatment (see Method/patients).

Reviewer 2 (Dr Jason Chia-Hsien Cheng)
1. Dr Jason Cheng clearly understood the current difficulty in treating advanced HCC patients. He pointed out that the key value of the present study was to offer a possible choice of chemotherapy with acceptable disease control and yet lower
toxicity profile. We appreciated very much his careful reading and review. The side effects of anthracyclin-based chemotherapy regimen and etoposide-containing regimen were discussed as suggested (page 10, lines 16-24).

2. The possible reason why HCV is a good prognostic marker is discussed as suggested (page 12, lines 2-6).

3. The hazard ratios of other non-significant factors in multivariate analysis were provided as requested (page 8, lines 17-22).

4. Albeit odd, HCCs in younger age do have a poorer prognosis in Taiwan. This has been reported in a large-scale study (reference 23). We have cited this paper and discussed this interesting observation (page 11, lines 2-5).

5. The method to select the control group as well as the possible bias was discussed as suggested (page 11, lines 6-10). The overall median survival in untreated terminal HCC patients reported in this study was consistent with that observed in a large-scale study (reference 21).

6. The limitation of our study and the fact that most patients received only one cycle of treatment were discussed (page 11, lines 18-22). More comprehensive randomized controlled study should be done before we can conclude that the split-dose protocol is indeed beneficial for terminal HCC patients (added to Discussion; page 11, lines 20-22).

We hope the paper is acceptable now.
Thank you again for handling our paper.

Sincerely,

Chau-Ting Yeh, MD, PhD