Author's response to reviews

Title: Phase I Study of Miriplatin combined with Transarterial Chemotherapy using CDDP powder in Patients with Hepatocellular Carcinoma

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Version: 2 Date: 1 September 2012

Author's response to reviews: see over
Dear Professor Timothy Shipley and Reviewers:

Thank you and reviewers for a thorough review of our manuscript entitled “Phase I Study of Miriplatin combined with Transarterial Chemotherapy using CDDP powder in Patients with Hepatocellular Carcinoma” (MS: 1430136757311736) by Kenya Kamimura. The thoughtful comments from the reviewers are greatly appreciated. In preparing for revision, we have carefully studied reviewers’ comments and incorporated many of their suggestions into the revised manuscript. For your convenience, we have marked our changes in blue in the revised manuscript. We hope this revised manuscript is now acceptable for publication in *BMC Gastroenterology* as an original research paper.

Thank you for consideration.

Sincerely yours,

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Dear Reviewers:

Thank you very much for your thoughtful comments and suggestions. In preparing for revision, we have carefully studied your comments and incorporated many of your suggestions into the revised manuscript. The following are point-to-point response to your comments. For your convenience, we have marked the changes made in the manuscript in blue.

**Reviewer #1**

*Kamimura and coworkers have conducted a phase I dose-escalating study using transarterial chemotherapy that utilized CDDP powder (DDP-H) in combination with miriplatin for the treatment of unresectable hepatocellular carcinoma (HCC). In their cohort of 9 patients no dose-limiting toxicity was observed. A partial response was obtained in 1 patient while four showed stable disease.*

**Response:** We are grateful to this reviewer for the positive comments.

1. *In the abstract a disease control rate of 40% is reported while in table 3 this number ranged between 50% and 66%. This should be clarified.*

   **Response:** We have corrected the mistake in the abstract.

2. *In the patients selection criteria it is stated that “no other therapeutic treatment was found to be effective” while the minimal interval to the previous treatment was only 4 weeks. Apparently, 8 out of 9 patients had received CDDP therapy before where a 4-week interval is certainly too short to convincingly assess disease progression. Thus, the authors should state the interval to the previous therapy for each patient and clarify the individual treatment history.*

   **Response:** We described “an interval of 4 weeks or more since previous therapy” as patient selection criteria. Therefore, the actual shortest period from the previous therapy was 12-weeks. To clarify these points, we have modified Table 1 and added information about the previous therapy and the interval to it to make this point clearer.

3. *The introduction is far too lengthy and should be more focused on the literature that is available on the subject.*

   **Response:** We have modified and deleted sentences to focus our point in the manuscript

4. *In figure 2 tumor marker levels are shown for each dosing group. It would be more informative, however, if individual levels were shown possibly arranged according to radiological response.*

   **Response:** The figure 2 and its legend were modified with information of individual radiological response.
5. *The manuscript needs the thorough attention of a native speaker.*

**Response:** We have asked a native speaker to edit our language and attached the certificate.

**Reviewer #2**

*Overall, the results are clearly presented and the manuscript is well written. Previous studies from Japan have already compared the efficacy of miriplatin with cisplatin and observed a comparable short-term efficacy, but slightly better tolerability for miriplatin. The study presented here indicates that both drugs can also be safely administered together, which might lead to a better tumor control.*

*His manuscript describes image-guided, intravascular hydrodynamic injection of plasmid DNA into the muscle of pigs. The transfection efficiency obtained is quite impressive with 70% to 90% of the muscles in the targeted limb being transfected.*

**Response:** We thank this reviewer for recognizing the significant value of our work.