We would like to take this opportunity to express our sincere thanks to the reviewers who identified areas of the manuscript that needed corrections or modification and for their careful review. Based on the instructions provided in the decision letter and comments provided by the reviewers, we have carefully revised the manuscript.

Manuscript NO: 45968.

Our responses to the reviewers' comments are as follows:

Response to the Reviewer 1(ID:02533177)

Thank you for reviewing our manuscript. We appreciate your acceptance of our manuscript.

Response to the Reviewer 2(ID:01438231)

Thank you for reviewing our manuscript. Our responses to your comments are as follows:

1) A major issue with this study is the small sample size (n=41) and the fact that almost all the subjects were male. In fact, analysis was performed on the basis of gender in tables 2 and 3. Since only 3 subjects were female, how can this data be meaningful?

Response to 1)

Thank you for your valuable comment. We have indicated that a previous study has reported that the relationships between ADAMTS13:AC and other parameters

are not associated with any gender bias in the Discussion section (page 16 and 17, lines 381–385). We believe that the difference in gender had no effects in our study.

2) In the Introduction, the authors discuss HCC, ADAMTS13 and sorafenib, but do not really explain how they are related to one another. Why would they think that ADAMTS13 and vWF would be useful biomarkers for sorafenib response?

Response to 2)

Thank you for your valuable comment. In the Introduction section, we have indicated that previous studies have reported that the imbalance of ADAMTS13 and VWF is associated with angiogenesis through VEGF that is in turn associated with LC and HCC development and that the imbalance of ADAMTS13 and VWF might be associated with sorafenib treatment efficiency because VEGF is inhibited by sorafenib (page 7, lines 154–158).

3) In the intro they state "Furthermore, blood coagulation cascade was demonstrated to be associated with cancer development". They do not discuss this association any further. Are they suggesting that vWF and ADAMTS13 levels/activity affect coagulation and affect tumor progression? This should be presented more clearly in the intro

Response to 3)

Thank you for your valuable comment. Based on your comment, we have included a description that the imbalance of ADAMTS13 and VWF are associated

with hypercoagulability as well as cancer development in the Introduction section (page 7, lines 159 and 161).

4) Also, they state "…we investigated the relationship between ADAMTS13 and VWF in patients with HCC receiving sorafenib treatment…" It is a minor detail, but I am guessing they mean ADAMTS13 and vWF levels. Or activity?

Response to 4)

Thank you for your valuable comment. According to your suggestion, we have made the relevant revisions in the Introduction section and have indicated plasma ADAMTS13 and VWF levels (page 7, line 165–167).

5) VEGF levels are measured and analyzed, but the exact significance of these measurements is unclear? Is it another biomarker?

Response to 5)

Thank you for your valuable comment. The patients with VEGFR-2, AFP, DCP, and AFP-L3% levels were not different between the low and high VWF:Ag/ADAMTS13:AC ratio groups and between the low and high ADAMTS13:AC groups. We have included this clarification in the Results section (page 12, lines 283 and 285; page 13, lines 301 and 303). In addition, we have indicated that the change in VEGF during sorafenib treatment is associated with the prognosis of patients with HCC receiving sorafenib treatment in the Discussion section (page 15, lines 343–345). We believe that the relationship between VEGF and VWF:Ag/ADAMTS13:AC ratio and between VEGF and

ADAMTS13:AC is important in our study.

Response to the Reviewer 3(ID:03270412)

Thank you for reviewing our manuscript. We are pleased to know that our manuscript has been considered for publication and for your acceptance of our manuscript. Our responses to your comments are as follows:

1) Ramicirumab has effective increased AFP level patients. Is there any correlation between VEGFR2 and increased AFP patients?

Response to 1)

Thank you for your valuable comment. We have indicated that DCP was directly correlated with VEGF ($r = 0.503$, $p < 0.05$). However, DCP was not correlated with VEGFR-2, and AFP or AFP-L3% was not correlated with VEGF or VEGFR-2 in the Results section (pages 11, lines 244–247).

We hope and believe that the revised manuscript is accepted for publication and look forward to the publication of our manuscript in *World Journal of Gastrointestinal Oncology*.

Sincerely,

Hiroaki Takaya