ANSWERING REVIEWERS

31th December, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 03253495-edited).

Title: LYMPHOCYTE-TO-MONOCYTE RATIO PREDICTS SURVIVAL AFTER RADIOFREQUENCY ABLATION FOR COLORECTAL LIVER METASTASES

Author: Antonio Facciorusso, Valentina Del Prete, Nicola Crucinio, Gaetano Serviddio, Gianluigi Vendemiale, Nicola Muscatiello

Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:

1 Very good and interesting study focusing on use of biomarkers used to predict efficacy of locoregional treatment. Though that I am not an expert in statistics, methodology appears to be correct, the rationale of the study is convincing, and results are useful in clinical practice. I think the article should be published.
RE: We are glad for the appreciation and the interest of the reviewer towards our work. Thank you!

2. In this study, the authors tested the correlation between LMR and survival in patients with colorectal liver metastasis treated by RFA. The results confirmed the feasibility of using LMR as a novel predictor of outcome for CLM patients. The authors stated in the second paragraph in page 11 that "……confirmed the independence of lymphocyte-to-monocyte ratio from other baseline features". What are these baseline features that were excluded? As all patients were undergone primary colorectal tumor resection before RFA and received systemic chemotherapy, how could you exclude the influence of resection and chemotherapy on the OS of the cohort?
RE: The sentence "….confirmed the independence of lymphocyte-to-monocyte ratio from other baseline features" means that we excluded with logistic regression analysis the direct correlation between LMR and other baseline factors, _not_ the influence of previous treatments on patient survival (which in fact cannot be excluded but was homogenous throughout the study population since _all_ the included patients had undergone resection of primary tumor and had received systemic chemotherapy before RFA). Aim of the regression analysis was then to exclude collinearity between LMR and other clinical-tumoral baseline parameters, where collinearity in statistics indicates a phenomenon in which two or more predictor variables in a multiple regression model are highly correlated, meaning that one can be linearly predicted from the others with a substantial degree of accuracy. In this situation coefficient estimates of the multiple regression may change erratically in response to small changes in the model or the data. Notably, one of the baseline assumptions underlying regression analysis in medical statistics is the absence of collinearity.
We hope to have adequately addressed the point raised by the reviewer.

Thank you again for considering our manuscript for publication in the *World Journal of Gastroenterology.*

Sincerely yours,

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