

January 27, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8358-review.doc).

Title: Current status of predictive biomarkers for neoadjuvant therapy in esophageal cancer

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Name of Journal: *World Journal of Gastrointestinal Pathophysiology*

ESPS Manuscript NO: 8358

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) English is very poor with grammatical mistakes throughout the article. A professional help is required to improve English.

; We apologize for grammatical mistakes. We corrected several mistakes. This article had received English editing by a professional. We attach a certificate of professional English editing.

(2) Most of the article mentions the biomarkers and quotes one study with mentioning the result to be significant. I feel it is very important to quote sensitivity, specificity, positive and negative predictive value as well as accuracy of these biomarkers. A table (may be for each of the seven category) with these parameters (wherever available) will certainly improve the quality of paper.

; We appreciate this valuable comment. We added the sensitivity, specificity, positive and negative predictive value as well as accuracy of these biomarkers in table1.

(3) Squamous cell carcinoma and adenocarcinoma of esophagus are actually two diseases with different behavior and response to CRT. Any article clubbing two diseases together is not appropriate. Though authors have mentioned this (albeit mildly), this needs to be emphasized and analysis of data needs to be done accordingly.

; We agree this comment. We added a description about this inadvisability (line 435).

(4) Unfortunately majority of data is based on single study on a relatively small group of patients. The data where same markers have been compared is limited to only 2 sets of markers (out of 23). Here again these studies have given contradictory results i.e. Reference 67 and 68 contradicts the result of results of Ref 66 on EGFR and Reference no 67, 72 and 71 contradicts the result of Reference 70 regarding p 53 – these data make the biomarkers role doubtful and this needs to be emphasized.

; We agree this comment. We think that the limited number of cases and institute is one of the major problems of the current biomarker development. We described about this problem in Chapter 4.

(5) Study 21 deals with breast cancer and this should be clearly mentioned on page 8.

; We apologize for this insufficient description. We added information about study 21 (line 139).

(6) First line of abstract should be deleted.

; We deleted first line of abstract.

(7) Author needs to compare techniques of performing various biomarkers in terms of availability, cost, ease and reproducibility of methodology.

; We agree that the description about this matter is important. However, this is very difficult consideration because it is greatly depend on the testing situation such as the characters of operators and the size of institutes. It may also depend on the subjects and materials. These issues are quite general issues in biomarker studies for any diseases and interesting for debate, however we do not think that our paper is a good place for it.

(8) Some of recent references should be included e.g. a. Philips RE et al, Dis Esophagus 2013; 26 : 299 b. Minato T et al, Ann Surg Oncol 2013 ; 20 : 209 c. Okamoto H et al, World J Surg Oncol 2013; March 1 d. Zhang SS et al, Ann Surg Oncol 2013; 20: 2919 e. Slotta et al al Br J Cancer 2013; 109: 370

; We appreciate introduction of these references. One reference (d. Zhang SS et al, Ann Surg Oncol 2013; 20: 2919) has been already included in this review. We added one reference (e. Slotta et al al Br J Cancer 2013; 109: 370). However, other references describe about prognostic biomarkers or negative data about predictive biomarkers. Therefore, we don't include in this review.

(9) Mention of uselessness of miRNAs (page 13) in differentiating pancreatic adenocarcinoma from chronic pancreatitis is irrelevant, since this review addresses the issue of biomarkers differentiating responsive malignancies from resistant malignancies.

; We deleted a description about pancreatic adenocarcinoma. We added a description about ongoing clinical trials of miRNA instead.

(10) Reference (most of them) have used inappropriate abbreviation for journal's name such as American Journal of Surgery, Annals of surgical Oncology; The New England Journal of Medicine. Page numbers should be complete e.g. Ref No 3; Page number should be 538-543 and not 538-43. This is as per World Journal format.

; We apologize for this incorrect format. References and typesetting were corrected.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastrointestinal Pathophysiology*.

Sincerely yours,

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## TITLE OF THE PAPER

Current status of biomarkers for predicting the response to neoadjuvant therapy in esophageal cancer

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