Author’s response to reviews

Title: Association between HER2 status in gastric cancer and clinicopathological features: a retrospective study using whole-tissue sections

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Cover letter
Response to Revision 1

Date : 27th September 2015

To : Matteo Fassan, M.D., Ph.D.
Editor, BMC Gastroenterology

Dear Editor Matteo Fassan,

We would like to thank you once more and also the reviewers for their time and comments on our revised paper “Association between HER2 status in gastric cancer and clinicopathological features: a retrospective study using whole-tissue sections” (BMGE-D-15-00063R1).

We appreciate the opportunity to submit our revised manuscript containing changes according to reviewers' more recent suggestions. We have uploaded two documents: a “Revised Manuscript” incorporating the new revised changes, which are highlighted in the text, and a “Cover Letter” with a point-by-point description of changes, based on each reviewer’s comment, detailed as follow:
Reviewer reports:

“Dysplastic epithelia can be characterized by a ‘real’ HER2 overexpression (http://www.ncbi.nlm.nih.gov/pubmed/22882541). This has been confirmed by the use of different antibodies and also by CISH/SISH. Please, check and modify your assertion ‘Non specific staining was seen in both metaplastic and dysplastic epithelium, despite the nature of the metaplasia or the degree of the dysplasia.’ Or (at least) put an appropriate comment to the Discussion section.”

We completely agree with the reviewer’s suggestion and therefore we have decided to modify our assertion in the Results section and also to add a sentence to clarify this point in the Discussion section:

- Line 222: “This pattern of expression was seen in both metaplastic and dysplastic epithelium, despite the nature of the metaplasia or the degree of the dysplasia. Nuclear expression was frequently seen among diffuse type carcinomas, but all these immunostained areas were not taken into account for the scoring of the HER2 immunohistochemical profile.”

- Line 328: “In fact, HER2 staining of dysplastic epithelium has been correlated to gene amplification by ISH [43]. Although there were no difficulties in distinguishing HER2-positive neoplastic cells from those areas, we stress that the staining of the latter must not be considered when scoring HER2 expression.” [43] Fassan M, Mastracci L, Grillo F, Zagonel V, Bruno S, Battaglia G, et al. Early HER2 dysregulation in gastric and oesophageal carcinogenesis. Histopathology. 2012;61:769-76.

Yours truly,

Renato Santos Laboissière, M.D.