Author's response to reviews

Title: Survival in patients with stage IV noncardia gastric cancer - the influence of DNA ploidy and Helicobacter Pylori infection.

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To
BMC Cancer
Editorial Office

Dear Dr Soong

Please find enclosed the revised version of our article entitled “Survival in patients with stage IV noncardia gastric cancer – the influence of DNA ploidy and Helicobacter Pylori infection”. We appreciate the careful review and thoughtful comments from the editorial board and the reviewers. We have given careful consideration to each specific point raised by the reviewers and modified our manuscript accordingly. All the corrections have been highlighted with yellow in the amended manuscript.

We hope that our work will now be considered suitable for publication in BMC Cancer.

Reviewer Dr Daniele Marrelli:

1. Tables 1 and 2 of the manuscript have been amended to indicate that “abdominal metastases” indeed refer to peritoneal dissemination.
2. We substituted the albumin values to normal/low instead of no/yes, as suggested.
3. We converted all time values in months both in text and in figures/tables.
4. MST values in Table 2 are depicted in months.
5. The role of palliative gastrectomy in advanced gastric cancer is still controversial. We amended the background section by adding a sentence referring to the ongoing trial (Japan/Korea, KGCA01/JCOG0705) which aims to address this important point and kindly provided by Dr Marelli (page 4, para 2). A citation was also added (Fujitani et al, Jpn J Clin Oncol 2008, 38(7):504-506)
6. We agree with the reviewer that the prognostic factors identified by our analysis, meaning liver metastases, PS and DNA index can be assessed preoperatively and may help select patients for palliative gastrectomy. However, this notion should be further strengthened by prospective data. We amended our manuscript by adding the paragraph “Based on our analysis, the high DNA content (DNA Index) along with the poor PS and the presence of liver metastasis have evolved as independent predictors of survival in patients with Stage IV gastric adenocarcinoma treated with palliative gastrectomy and systemic chemotherapy. Since all these three variables can be assessed in preoperative biopsies, they may serve as a prognostic tool in order to preoperatively select patients eligible for palliative gastrectomy; however, prospective studies are needed to confirm this hypothesis” in the discussion section (page 12-13).
7. We performed all the suggested changes in the reference list.
8. Same as 7.

Reviewer Dr Masaki Aizawa

1. According to our analysis H. Pylori infection was not correlated with survival. However the exploration of a putative association was one of the main aims of our study and this is the reason we included “H. Pylori” in the title of the manuscript.
2. Only patients with biopsy proven noncardia gastric adenocarcinoma were included in our study. This is described in the methods section and further highlighted throughout the manuscript, according to the reviewer’s suggestion.
3. Despite the fact that seven variables were identified as significant in univariate analysis only three of them proved of significant weight after multivariate analysis in our group of patients. We cannot offer any solid biological reason to explain our finding that DNA index performed better than the other serological factors (CRP, albumin, CA19-9, CA72-4). We speculate that DNA index refers to an intrinsic feature of the tumor while the other markers may be affected by various extratumoral factors (smouldering infection, aberrant systemic immune response etc).

4. We omitted at least a paragraph in the discussion section (pages 13-15) concerning *H. pylori* infection, according to the reviewer’s suggestion. The omissions are highlighted in yellow.

5. In our study high DNA index was associated with poor outcome. We suggest that high DNA index will adversely affect survival after palliative gastrectomy but only a new, randomized study will safely answer whether DNA ploidy will affect management decisions, mainly to give or not chemotherapy.

6. (Minor essential revision): The cut-off values of albumin and CRP were added in Tables as suggested.

Yours sincerely,

Stavros Sougioultzis, MD