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Author response to: Increasing frequency of gene copy number aberrations is associated with immunosuppression and predicts poor prognosis in gastric adenocarcinoma

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Dear Editor

Thank you for your interest in our study[1]. We have not stratified our analyses by treatment because the initial statistical analysis showed no significant treatment interaction for chromosomal instable (CIN) status and overall survival. The KCCH gastric cancer (GC) patients were either treated with surgery or surgery plus adjuvant chemotherapy. Therefore, pathological or radiological tumour regression grade could not be assessed. For the palliatively treated patients, information on radiological tumour response was not available and survival time was used as the surrogate measure of 'chemotherapy response'.

Although others suggested that patients with CIN GC experienced the greatest benefit from adjuvant chemotherapy, formal statistical analyses for treatment interaction were not conducted in previous studies. Therefore, it remains to be clarified whether the improved survival in CIN patients treated with adjuvant chemotherapy is due to the prognostic effect of CIN or a potential predictive effect of CIN.

Another study demonstrated, in biopsies before patient treatment with neoadjuvant chemotherapy followed by resection, that a high 'global LOH rate' was related to tumour response. This study used a different methodology (fractional allelic loss) to establish 'chromosomal instability' and investigated a different clinical setting. Therefore, their results cannot be directly compared. Finally, in patients receiving neoadjuvant chemotherapy, the CIN classification as reported was close to our methodology; unfortunately, a formal statistical analysis for treatment interaction was not conducted. Our results suggested a higher CIN frequency in stage IV GC. We, therefore, included the TNM stage in our multivariable Cox regression model and demonstrated that CIN was a poor prognostic biomarker independent of TNM staging. We agree that there are conflicting results about the potential relationship between CIN and response to chemotherapy which deserves further exploration ideally by a large multicentre series of patients undergoing the same clinical treatment, using the same molecular assay and an appropriate statistical methodology.

Reference

1. Silva ANS, Saito Y, Yoshikawa T, Oshima T, Hayden JD, Oosting J *et al.* Increasing frequency of gene copy number aberrations is associated with immunosuppression and predicts poor prognosis in gastric adenocarcinoma. *Br J Surg* 2022;**109**:291–297

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