

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 70516

Title: Cost-effective low-coverage whole-genome sequencing assay for the risk stratification of gastric cancer

Responses for reviewer's, Science editor's and Company editor-in-chief's comments

Reviewer's code: 05721372

Comment:

I find useful to add some comments about the different types of gastric cancer and their determination. It is mandatory, in such a complex subject, to add more recent references. Differential diagnosis should be related, including GIST (cite: Ceausu M, Socea B, Ciobotaru VP, et al. A multidisciplinary approach in the diagnostic challenge of GIST. *Exp Ther Med*. 2021 Oct;22(4):1063. doi: 10.3892/etm.2021.10497.) Multimodal therapy and complications should be addressed. One of the main surgical complications is anastomotic fistula (Radulescu D, Baleanu VD, Padureanu V, et al. Neutrophil/Lymphocyte Ratio as Predictor of Anastomotic Leak after Gastric Cancer Surgery. *Diagnostics (Basel)*. 2020 Oct 9;10(10):799. doi: 10.3390/diagnostics10100799.) English language editing is needed.

Author's response:

The authors appreciate for the comments from the reviewer. It should be noted the red mark in the manuscript represents new addition.

According to the comment from reviewer, we have edited manuscript to a professional English language editing company to polish the manuscript further. We have revised in the manuscript according to the suggestions form the reviewer (line 251-256). The corresponding contents have been revised in the latest version manuscript uploaded and named 70516-Supplementary-Material-revision.docx.

251 advances in diagnosis and treatment, the 5-year OS remains poor. Moreover, gastrointestinal stroma
252 tumor is a rare but highly curable cancer and has a satisfactory prognosis with a 5-year OS ranging
253 from 60–85% [18, 19]. Notably, multimodal complications associated with radical gastrectomy during
254 perioperative period should be addressed. Anastomotic fistula, one of the main surgical complications
255 that raises the risk of local recurrence and worsens the overall prognosis, has been reported to be
256 positively correlated with the neutrophil/lymphocyte ratio [20]. The traditional morphology-based

- 419 18 Ceausu M, Socea B, Ciobotaru VP, Constantin VD, Enache S, Enache V, Bancu A, Socea LI,
420 Serban D, Predescu D, Smarandache CG, Ceausu Z. A multidisciplinary approach in the
diagnostic challenge of GIST. *Exp Ther Med* 2021; **22**(4): 1063 [PMID: 34434277 PMCID:
PMC8353641 DOI: 10.3892/etm.2021.10497]
423 19 Call J, Walentas CD, Eickhoff JC, Scherzer N. Survival of gastrointestinal stromal tumor
424 patients in the imatinib era: life raft group observational registry. *BMC Cancer* 2012; **12**: 90
425 [PMID: 22429770 PMCID: PMC3364851 DOI: 10.1186/1471-2407-12-90]
426 20 Radulescu D, Baleanu VD, Padureanu V, Radulescu PM, Bordu S, Patrascu S, Socea B,
427 Bacalbasa N, Surlin MV, Georgescu I, Georgescu EF. Neutrophil/Lymphocyte Ratio as
428 Predictor of Anastomotic Leak after Gastric Cancer Surgery. *Diagnostics (Basel)* 2020; **10**(10)
429 [PMID: 33050137 PMCID: PMC7601164 DOI: 10.3390/diagnostics10100799]



Science editor

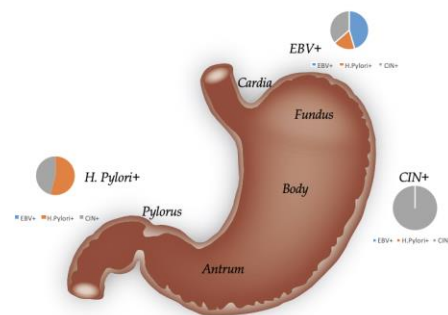
Comment:

Specific Comments To Authors: The manuscript elaborated a low-coverage whole-genome sequencing assay for the risk stratification of gastric cancer. I find it an interesting study. Figure 3 the picture quality is poor. Is there any copyright? The table uses a three-line table. What is the difference between the classification proposed by the author and other different types of gastric cancer and their diagnosis? Scientific Quality: Grade C Language Quality: Grade B Recommendation: Conditional acceptance.

Author's response:

The authors appreciate for this suggestion. We have redrawn and improved the quality of Figur3. The corresponding Figure 3 has been revised in the latest version manuscript uploaded and named 70516-Supplementary-Material-revision.docx.

1.



2. We have made corrections in the corresponding tables of the manuscript according to the Science editor's comments. These tables (table1 and table2) were all revised in a three-line form. The corresponding contents have been revised in the latest version manuscript uploaded and named 70516-Supplementary-Material-revision.docx.

3. We further evaluated the difference between the classifications proposed in our study (molecular subtypes: EBV+, *H. pylori*+, and CIN+ types) and Borrmann type, a classic gastric cancer classification widely used currently. Prognostic analysis was chosen as a pointcut to compare the two different classifications (molecular type and Borrmann type). As a result, patients with different molecular subtypes showed

distinct prognoses by long rank test ($p=0.019$), in which CIN+ patients were found to have the worst survival with a median OS less than 500 days. However, no significant difference was founded among the Borrmann types ($p=0.078$) (Figure 5). It may indicate that the molecular subtypes in our study have advantages in guiding the prognosis of patients with gastric cancer. However, more clinical evidences are needed to support this argument owing to the limited sample sizes in this study (line 152, 232, 237-239, 280-286). The corresponding contents have been revised in the latest version manuscript uploaded and named 70516-Supplementary-Material-revision.docx.

280 suggest a different treatment approach for each GC subtype, which may require further research. In
281 addition, patients with different molecular subtypes showed distinct prognoses by long rank test
282 ($P=0.019$), in which CIN+ patients were found to have the worst survival with a median OS less than
283 500 days. However, no significant difference of OS was found among the Borrmann types ($p=0.078$),
284 a classic GC classification widely used currently. It may indicate that the molecular subtypes in our
285 study have advantages in guiding the prognosis of patients with GC. Nonetheless, owing to the limited
286 sample sizes in this study, additional clinical evidence is needed to support this argument.

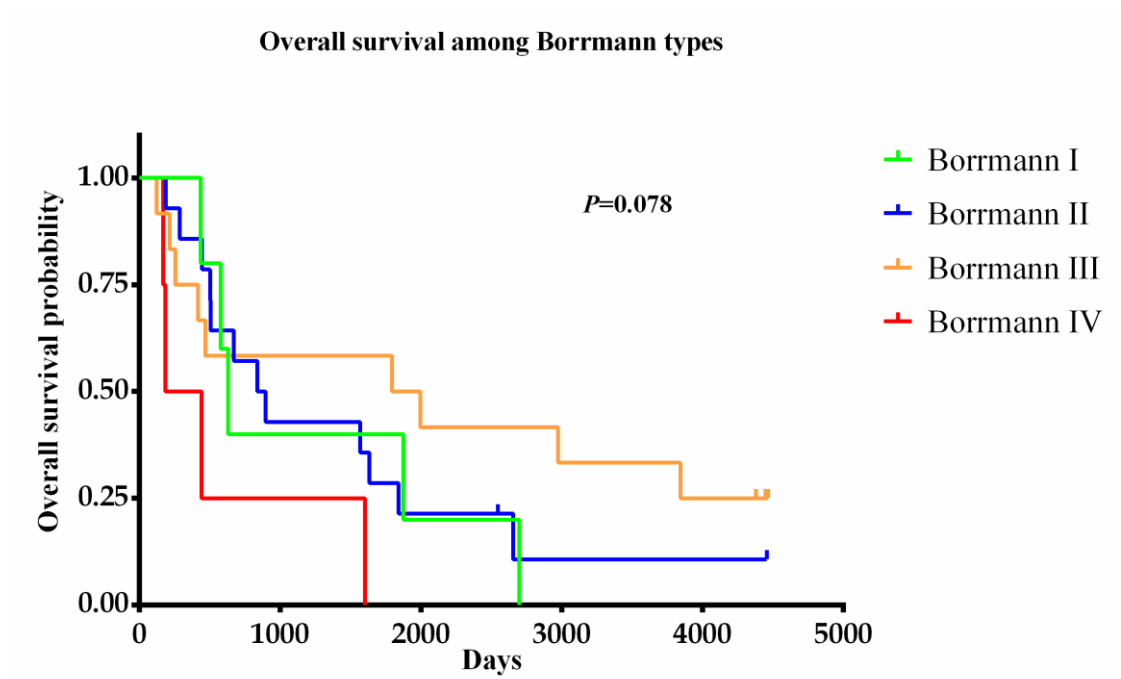


Figure 5: Overall survival among Borrmann types of gastric cancer.

Company editor-in-chief:

Comment:

I recommend the manuscript to be published in the World Journal of Gastrointestinal Oncology. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Author's response:

According to the comment from Company editor-in-chief, we have edited manuscript to a professional English language editing company to polish the manuscript further.

