Dear sir/ madam,

I am submitting a revised version of my article entitled: "The landscape of *BRIP1 (FANCJ)* molecular lesions in gastrointestinal cancers from published genomic studies" for consideration for publication at World Journal of Gastroenterology.

All reviewers' comments have been taken into consideration in the revision. A list of the reviewers' comments (in red) and my answers follow below:

This manuscript provides the review of our current knowledge as to the role of BRIP1 expression in gastrointestinal cancer. Based on the published genomic data, the conclusion is that the higher BRIP1mRNA expression is associated with the improved OS as compared with lower BRIP1mRNA expression in gastric cancer. These findings suggest that cancers with up-regulated BRIP1 may have a less aggressive course due to a better ability to repair DNA lesions. Hence, the combination therapies with immune checkpoint inhibitors and PARP inhibitors offer an interesting avenues requiring further exploration.

I thank the reviewer for his/ her insightful comment.

This manuscript is well preparation and written with more innovation.

I thank the reviewer for his/ her kind comment.

This is very interesting paper. I ask some questions. 1. Previous studies of esophageal squamous cell carcinoma have shown a high frequency of allelic loss on chrosome 13q, infrequent somatic mutations in BRCA2, and a suggested association between a positive family history (FH +) of upper gastrointestinal cancer and germline BRCA2 mutation. Please tell me about BRIP1 in esophageal squamous cell carcinoma with family history ,and without family history. 2. In page 8, author write that "increased expression of BRIP1 mRNA was associated with improved survival in patients with gastric carcinomas compared with patients whose cancers expressed lower BRIP1". Please tell the criteria of increased expression of BRIP1 and lower expression of BRIP1.Moreover,pleae tell me the relationship between BRIP1 and TNM.

1. Unfortunately no data on family history is available in the genomic studies that form the basis of the current study.

2. A clarification of the criteria of the classification of BRIP1 expression has been added in the text. Higher expression was expression above the median expression among the patients in the series and

lower expression means expression below the median in the series. This clarification had already been included in the legend of figure 5.

The analysis has included all TNM stages but similar results (HR=0.64) have been observed when only patients with localized disease have been included in the analysis. A phrase has been added in the penultimate paragraph of the results.

Major comment: This manuscript deals with BRIP1 (FANCJ) molecular lesions in gastrointestinal cancers and also provides future research perspectives. Specific comments: "Introduction", first paragraph, and "Discussion", first paragraph: "quadraplex" -> quadruplex. "Results", penultimate paragraph: "aneuploidy scores in BRIP1 amplified GI tumors was variable" -> aneuploidy scores in BRIP1 amplified GI tumors were variable. "Discussion", second paragraph: "Main findings include the low frequency of BRIP1 defects in GI cancers and a significance association of BRIP1 mutations with defects of MSI/ polymerase ε and δ1 genes and the mutator phenotype" – do you mean "a significant association of BRIP1 mutations with defects of MSI/ polymerase ε and δ1 genes and the mutator phenotype"? Figure legend 3 should be shortened. Reference list: DOIs/PMIDs are not provided.

“quadruplex” was corrected in both places. The phrases “aneuploidy scores in BRIP1…” and “Main findings include….” were also corrected. I thank the reviewer for his/her diligence.

The legend of Figure 3 was shortened as suggested by the reviewer.

A list of the references with DOIs / PMIDs has been added below the original reference list for the editorial office to review.

Thank you for your consideration.

Sincerely,

Ioannis A. Voutsadakis, MD, PhD