Dear Editor,

Thank you for reviewing our manuscripts and offering us some very useful and appropriate comments. According to your advice, we have revised our manuscript quite intensively. We are attaching a point-by-point response to our reviewer's comments.

We hope that this revised version of our manuscript will be deemed suitable for publication in *World Journal of Clinical Cases.*
Yours faithfully,

Konstantinos Argyriou, M.D., Ph.D.,
Department of Gastroenterology
University Hospital of Larisa
E-mail: kosnar2@doctors.org.uk

Response to Reviewer #1:

Comments to Authors: this article can be a valuable reference study, helping clinicians to holistically understand how immunotherapy affects the pre-existing enteral disease in inflammatory bowel disease patients. It is an interesting manuscript. Authors succeed to present their idea in a clear way. Therefore, I have no corrections to do and the manuscript can be published unaltered.

Response to comment

We thank Reviewer#1 for his/her comment.

Response to Reviewer #2:

Specific Comments to Authors: Regarding the manuscript: Comment on "Disease exacerbation is common in inflammatory bowel disease patients treated with immune checkpoint inhibitors for malignancy" The authors commented for the published paper "Disease exacerbation is common in inflammatory bowel disease patients treated with immune checkpoint inhibitors (ICIs) for malignancy". They mentioned that the above study did not include endoscopic, histologic and radiologic data of the study population in the analysis and hence, it did not make a clinically meaningful differentiation between IMC (Immune checkpoint inhibitor-Mediated Colitis) and true IBD (Inflammatory Bowel Disease) exacerbation cases and suggested this shortcoming to be supplemented. I agree with their smart comments and they could be supported by the followings. - There is an emerging paradigm shift that recognizes the similarity between IMC and IBD, they have similar chronic pathology with similar predisposal to flares with certain triggers [1]. Thus, differential diagnosis between IMC and true IBD seems to be difficult clinically. - Because the number of subjects is limited due to the single center nature of the above study and the rarity of IBD preceding ICI therapy, the study results are vulnerable to the misclassification between IMC and true IBD. - As the risk factors for IMC cover a wide spectrum of variables such as medication history, preexisting autoimmune diseases, tumor type, combined ICI therapy, inflammatory cell levels, cytokines, gut microbiome, etc. [2,3], various other enteral diseases should all be carefully excluded before reaching a diagnosis of IBD exacerbation. I hope that my comments could be helpful for both authors and readers and appreciate for the patience of editors. (Referrences) [1] Tang L, Wang J, Lin N, Zhou Y, He W, Liu J, Ma X. Immune Checkpoint Inhibitor-Associated Colitis: From Mechanism to Management. Front Immunol. 2021 Dec 21;12:800879. [2]

Tran T, Tran NGT, Ho V. Checkpoint Inhibitors and the Gut. J Clin Med. 2022 11:824-836. [3] Oprescu AM, Tulin R, Slavu I, Venter DP, Oprescu C. Immune Checkpoint Inhibitor-Induced Gastrointestinal Toxicity: The Opinion of a Gastroenterologist. Cureus. 2021 Nov 27:19945.

Response to comment

In accordance with the reviewer's comment, we would like to thank the reviewer for his/her thoughtful comments. His/her suggestions were taken into consideration and we made the necessary adjustments. All references were reviewed accordingly.