

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 76518

Title: Comment on “Disease exacerbation is common in inflammatory bowel disease patients treated with immune checkpoint inhibitors for malignancy”

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05665395

Position: Peer Reviewer

Academic degree: MD

Professional title: Director, Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Greece

Manuscript submission date: 2022-03-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-20 10:31

Reviewer performed review: 2022-03-22 12:30

Review time: 2 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC 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.

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Title: Comment on “Disease exacerbation is common in inflammatory bowel disease patients treated with immune checkpoint inhibitors for malignancy”

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03740440

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: Greece

Manuscript submission date: 2022-03-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-21 17:38

Reviewer performed review: 2022-04-06 08:06

Review time: 15 Days and 14 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
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Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

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. (References) [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.