

Thank you for taking your time to review our manuscript. We addressed the reviewer's comments in the manuscript and revised it. The changes are marked in blue in the revised manuscript. Three references are added. Our answers are appended below.

Reviewer #1: I would like to thank the authors for presenting this important topic. I have some notes regarding the manuscript.

*Abstract: The keywords are very broad and do not reflect the topic.* – The keywords are changed.

*The core tip includes many unexplained abbreviations.* – The abbreviations are explained.

*Introduction: Please rewrite this sentence to be more clear: "It is graded from 1 to 5 with grade 1 being the mildest and grade 5 representing death."* – We rephrased this sentence. "It is graded from 1 to 5 with grade 1 representing mild symptoms and grade 5 patient's death related to ICIs induced colitis."

*The authors mention: "Prompt diagnosis and management of ICIs induced colitis is crucial for optimal outcome">>>why diagnosis should be prompt considering that most of the differential diagnoses (except infection) will also require steroids i.e. same management? - ICIs toxicities leading to fatal outcomes tend to occur early in the disease course and evolve rapidly. Although the first line of treatment is steroids similar to other colitis, it should be escalated to infliximab if the symptoms persist or recur. Moreover, ICIs should be permanently discontinued for patients with grade 4 colitis. Please refer to clinical presentation and treatment section of the manuscript.*

*The subtitle "Interval" please clarify of what? e.g. Interval from drug infusion to colitis.* - Correct, we changed the subtitle in the revision

*The authors stated, " Overall mortality rate associated with ICIs induced colitis is 5% (225/3905). Sixty percent (135/225) of the fatality was from CTLA-4 inhibitor, 25.8% (58/225) from anti PD-1 or PD-L1 and 14.2% (32/225) from combined therapy">> is that a meta-analysis or an original study, kindly clarify in the text to know the significance of the numbers stated.- It is a meta-analysis. It is clarified in the revision.*

*Could the authors clarify whether in the 5% mortality, the incidence increases with severity of the colitis or is unrelated? 5% mortality is the general death rate regardless of the grades of*

colitis. The authors did not analyze the correlation between the death rate and grades of colitis. This is clarified in the revised text.

There are a lot of subtitles without enumeration and sometimes get confusing, please enumerate. – *The subtitles are enumerated.*

*The authors didn't state the pathophysiology and risk factors of the ICI induced colitis in details; I think this is important before stating treatment options.* – Agree. Pathophysiology is added in the revised text. The risk factors of ICIs induced colitis are included in the “Incidence” paragraph, including the types of ICIs regimen, cancer type, and race.

*Please add the following reference and state the differences in aim if possible (as there is a lot of similarities in the topic and presentation); Reference: Som, A., Mandaliya, R., Alsaadi, D., Farshidpour, M., Charabaty, A., Malhotra, N., & Mattar, M. C. (2019). Immune checkpoint inhibitor-induced colitis: A comprehensive review. World journal of clinical cases, 7(4), 405–418. <https://doi.org/10.12998/wjcc.v7.i4.405>* - The reference is added as #6. While the subject is similar, the strength and difference of our review compared with Som et al’s is that we provide detailed histological differential diagnoses and supply ample microscopic images. The difference in aim is added in the end of the Introduction of the revised text.

## 2 Editorial Office's comments

1) Science Editor: The manuscript describes a Review of differential diagnosis and management of immune checkpoint inhibitor-induced colitis. The topic is within the scope of the WJGO. (1) Classification: Grade C and Grade B;

(2) Summary of the Peer-Review Report: This important topic; however, some major adjustments in the text are necessary. The questions raised by the reviewer should be answered; - **Answered**

(3) Format: There are 5 figures; (4) References: A total of 65 references are cited, including 24 references published in the last 3 years;

(5) Self-cited references: There is 1 self-cited reference. The assistant editor require the upload of Non-Native Speakers of English Editing Certificate by a native English speaker or a professional editing company. – **The author Dr. Daniel Cho is a native English Speaker. Therefore we believe this is not applicable.** Conflict-of-Interest Disclosure

Form and Copyright License Agreement must be requested. This is an invited manuscript. The "Author Contributions" section is missing. Please provide the author contributions. - **Provided**. The authors did not provide original pictures. Please provide the original figure files. Please prepare and arrange the figures using Power Point.- **Provided**. Re-Review: Not Required. Recommendation: Transfer to World Journal Of Experimental Medicine.

2) Editorial Office Director:

3) Company Editor-in-Chief: I recommend the manuscript to be published in the World Journal of Experimental Medicine.