

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 80237

Title: Role of the combination of biologics and/or small molecules in the treatment of patients with inflammatory bowel disease

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05205634

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Brazil

Author's Country/Territory: Argentina

Manuscript submission date: 2022-09-22

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-09-22 12:03

Reviewer performed review: 2022-09-22 12:20

Review time: 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 Grade E: Do not publish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 checked="" type="checkbox"/> Yes <input type="checkbox"/> No

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

Minor revisions: please include some references: PMID: 35134323 - here the authors are studying Guselkumab (phase 2 trial in CD) however in one are they have Ustekinumab. please add this reference Please add the Sonic study in the references. It was a study that evaluated in 2010 IFX vs IFX + AZA and AZA - it an important historical study to be added. PMID 20393175 please check if the right name is Clostridoides instead of Clostridium (the name was recent changed) Safety section: please use the full name followed by the abbreviation (IMID : immune mediated inflammatory disease) Nevertheless, in this series, these complications developed only in patients with Crohn's disease. Importantly, no case of reactivation of herpes zoster has been reported in any publication The correct is Nevertheless, in this series, these complications developed only in patients with CD. Importantly, no case of reactivation of herpes zoster has been reported in any publication Nu further comments.

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Peer-review model: Single blind

Reviewer's code: 03476357

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Argentina

Manuscript submission date: 2022-09-22

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Reviewer accepted review: 2022-09-22 14:43

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Review time: 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
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Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**Peer-reviewer
statements**Peer-Review: [☒] Anonymous [☐] OnymousConflicts-of-Interest: [☐] Yes [☒] No**SPECIFIC COMMENTS TO AUTHORS**

This interesting mini-review explores a particularly hot topic in management in IBD, namely the use of combination biologic therapies. The introduction is clear as is the definition of dual therapy. The description broken down by efficacy and safety is excellent as is the sectorization of the data in pediatric patients. The quality of the figures is acceptable. Table 1 is well done.

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Peer-review model: Single blind

Reviewer's code: 01587889

Position: Editorial Board

Academic degree: MD, MSc, PhD

Professional title: Associate Professor, Consultant Physician-Scientist

Reviewer's Country/Territory: United States

Author's Country/Territory: Argentina

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Reviewer accepted review: 2022-09-22 01:36

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input 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

**Peer-reviewer
statements**

Peer-Review: [☒] Anonymous [☐] Onymous

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

Balderram et al. is a mini-review summary of the results of different combinations of advanced drugs in patients suffering from IBD, both in adults and in the pediatric population. In addition, the safety profile of different combinations of dual newer recently approved treatments, the application of new biomarkers and artificial intelligence, and clinical trials to establish effectiveness given the fact that about 40% of patients are refractory to current different treatments with an increase need for hospitalization and surgery. Dual therapy includes two distinct scenarios in IBD therapy in which a) refractory active luminal disease without extraintestinal manifestations, and b) patients with IBD in remission, but with active extraintestinal manifestations or immune-mediated inflammatory diseases. There are multiple pathways of inflammatory activity activated in patients with IBD, and for this reason, treatment with monotherapies may not be sufficient for the management of all patients. The sequencing of biologics or small molecules in patients in remission is a strategy that probably results in a better cost balance. The development of new molecules and the implementation of new strategies are necessary to achieve a better control of IBD activity in patients who are refractory to currently available treatment. The numbers of therapeutic trials described in studies including 2 or more IBD patients are shown in fig. 1 and also published data on efficacy and adverse events are presented in table 1 which includes 2 or more adult or pediatric IBD patients with use of combination therapy. Good job.