

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 79986

Title: Current status of novel biologics and small molecule drugs in the individualized treatment of inflammatory bowel disease

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04091850

Position: Editorial Board

Academic degree: DSc, MD, PhD

Professional title: Chief Doctor, Professor

Reviewer's Country/Territory: Denmark

Author's Country/Territory: China

Manuscript submission date: 2022-09-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-10-11 04:18

Reviewer performed review: 2022-10-17 12:45

Review time: 6 Days and 8 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 Grade E: Do not publish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 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: [<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

The manuscript presents an overview of new developments regarding biologics and small molecule drugs for use in the treatment of inflammatory bowel disease. Besides it depicts new ways to go as far as combination therapy with these drugs are concerned. In general the manuscript is of interest and I think many colleagues will find it useful. For the most part it is well written and well disposed and the English language is good with only minor corrections needed.

Specific comments: Many different drugs are described. To provide the readers with a better overview a table could be suggested naming the different drugs, their immunological targets and relevant references.

Abstract: The sentence starting with "Additionally, identifying the subgroup..." should be corrected in that the word "pattern" should be removed and it may seem as though it would be more correct to use the word "responding" instead of sensitive.

Introduction: I would prefer to start with the statement that "The inflammatory bowel diseases ulcerative colitis (UC) and Crohn's disease (CD) are progressive inflammatory diseases..."

Emerging (correct the spelling) biologics and SMDs in IBD: It is mentioned that the efficacy of monotherapies is limited to 15-40% compared to placebo. I think it would be advisable to split the response into induction phase and long time effects. Likewise it could be suggested to put in a few words on end-points (clinical response/remission, endoscopic response/remission).

Anti-TNF agents: Here it should be added that immunogenicity is also a problem and that it can be partly overcome by adding immunomodulators.

Anti IL 12/23 agents: Data regarding Gusulcumab should be added.

JAK inhibitors: It is not evident that filgotinib and upadacitinib have better safety profiles than tofacitinib.

In general I think that information on safety



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issues/concerns regarding all the actual drugs described in the manuscript is too scarce. Safety is a very important concern when using these drugs. Current status of biological combinations in IBD An excellent and interesting part of the manuscript. I think a sentence or two should be added addressing the fact that practical all knowledge on the effect of combination of drugs stems from data on patients rather resistant to therapy and who may have failed several lines of monotherapy. This is important when you evaluate the treatment results. The sentence "A better understanding of the pathology..." should read "understanding of the pathophysiology". What can we do to improve the response to DTT: I think this part of the manuscript could be shortened without loss of important information. One could get the impression that TDM measurements and biomarkers are tools used when applying DTT which is not true. In fact all the information given regarding TDM are derived from studies done in patients on monotherapy. For that reason it should be clarified that TDM and biomarkers are only tools suggested to could play a role in the management of patients treated with a DTT principle. Besides the description og TDM seems to be a little too optimistic. In fact in clinical studies it has been somewhat difficult to prove its superiosity compared with conventional approaches. In fact international guidelines only advocates to use it in a reactive setting while the value of TDM is not settled in a proactive set up. Could the above mentioned points be addressed I think the manuscript would be welcomed among most gastroeterologists with an interest in IBD.

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Reviewer's code: 05685534

Position: Peer Reviewer

Academic degree: PhD

Professional title: Chairman, Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: China

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Reviewer chosen by: Dong-Mei Wang

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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
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SPECIFIC COMMENTS TO AUTHORS

The manuscript is well written , comprehensive , described an up to date revision of the evolution of the small molecules and biological therapies of inflammatory bowel disease ; the abstract is competent and inclusive , and manuscript is well categorized and organized some typo errors in the manuscript (attached)