



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastroenterology*

**Manuscript NO:** 96898

**Title:** Beyond the gluten-free diet: Innovations in celiac disease therapeutics

**Provenance and peer review:** Invited manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 07930157

**Position:** Peer Reviewer

**Academic degree:** N/A

**Professional title:** N/A

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2024-05-17

**Reviewer chosen by:** Yu-Fei Wei

**Reviewer accepted review:** 2024-08-12 08:41

**Reviewer performed review:** 2024-08-12 16:30

**Review time:** 7 Hours

<b>Scientific quality</b>	<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 Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

This review encompasses comprehensive data on drug therapy trials for non-dietary treatment in celiac disease. The authors included all the phase 2 trials in their analysis. They provided also a very useful synoptic table for these trials according to different drug mechanisms of action. The paper is well written, references accurate. Few suggestions to improve the paper: Chapter 1. Current Challenges in Celiac Disease Management “Secondly, gluten-free products, to be more tasty, are often high in fat and sugar content and low in fibers, vitamins, and minerals increasing, on one hand, the risk of obesity and metabolic syndrome and on the other the risk of deficiencies (16, 17) “ Please consider adding to this part also a theoretical risk for mycotoxins from corn and arsenic from rice exposure in those who have a diet restricted only to few carbohydrate sources. Please consider these references for these issues PMID: 24694905 and PMID: 28223206 Different preparations of this enzyme are already available over the counter, but their ability to digest gluten peptides can be different and, in some cases, inferior to the pure enzyme (40). Few words of caveat should be written about the risk of CeD patients taking these over-the-counter medications at the time being. When



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summarizing data on the modulators of the tight junctions, a few words about a zonulin-independent constitutional alteration of the permeability in celiac patients and first degree relatives of CD patients (PMID: 31921880 and PMID: 26535478 ) and an alteration of zonulin in the very early phases of celiac disease (PMID: 38062791) might be noteworthy to mention. Please rephrase: "This study aims to evaluate the efficacy of TAK-101 in reducing gluten-related symptoms and immune activation in adult CD patients following a GFD undergoing gluten challenge and WAS expected to be completed by May 2024 Please rephrase: ... "its primary completion date was expected in May 2024 (Table 2).