**PEER-REVIEW REPORT**

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

**Manuscript NO:** 78409

**Title:** Combination Strategies for Pharmacologic Treatment of Non-Alcoholic Steatohepatitis

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

**Peer-review model:** Single blind

**Reviewer’s code:** 06245556

**Position:** Peer Reviewer

**Academic degree:** DPhil

**Professional title:** Doctor

**Reviewer’s Country/Territory:** Australia

**Author’s Country/Territory:** United States

**Manuscript submission date:** 2022-06-24

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-06-25 10:55

**Reviewer performed review:** 2022-06-26 22:10

**Review time:** 1 Day and 11 Hours

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<tr>
<th>Scientific quality</th>
<th>[ ] Grade A: Excellent</th>
<th>[ ] Grade B: Very good</th>
<th>[Y] Grade C: Good</th>
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<th>Conclusion</th>
<th>[ ] Accept (High priority)</th>
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<td>[ ] Minor revision</td>
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<p>| Re-review          | [Y] Yes                   | [ ] No                         |</p>
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<th>Peer-reviewer statements</th>
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<td>Conflicts-of-Interest:</td>
<td>[ ] Yes  [Y] No</td>
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**SPECIFIC COMMENTS TO AUTHORS**

In this minireview the authors discuss the role of combination therapeutics in treating nonalcoholic steatohepatitis. Overall the review is informative and well-written but would benefit from a number of improvements. Introduction: - NASH definition, include other important factors such as excluding excessive alcohol consumption >20g/day women or >30g/day men, and excluding other causes of liver disease. -"Liver specific targets aimed at decreasing histologic inflammation or fibrosis such as farnesoid X receptor (FXR) agonists or peroxisome proliferator-activated receptor (PPAR) agonists." This is not a complete sentence and needs to be rephrased.

-Where is the figure mentioned in-text, figure 1, table 1 etc.? These are not included in the manuscript.

-"As such, it was no surprise that a previously terminated clinical trial attempted to combine the effects of pioglitazone and roflumilast, a potent anti-inflammatory drug used in chronic pulmonary disease trials. " Please could the authors clarify what they mean by this statement?
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Peer-review model: Single blind

Reviewer’s code: 03538879

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Chief Doctor, Professor

Reviewer’s Country/Territory: China

Author’s Country/Territory: United States

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Reviewer accepted review: 2022-06-27 02:53

Reviewer performed review: 2022-06-28 05:51

Review time: 1 Day and 2 Hours

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SPECIFIC COMMENTS TO AUTHORS

In this minireview, the authors discussed the current drug development pipeline of NASH, target pathways associated with NASH pathogenesis, and evaluated the multimodal combination strategy. Since NASH is a complex disease, the combination strategy might be superior to mono-therapeutic options, and represent new direction for NASH treatment.
RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer’s code: 06245556

Position: Peer Reviewer

Academic degree: DPhil

Professional title: Doctor

Reviewer’s Country/Territory: Australia

Author’s Country/Territory: United States

Manuscript submission date: 2022-06-24

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2022-07-28 11:19

Reviewer performed review: 2022-07-28 11:25

Review time: 1 Hour

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Peer-reviewer: Peer-Review: Y Anonymous | Onymous
SPECIFIC COMMENTS TO AUTHORS
The authors have made appropriate changes to the manuscript.