

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

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 Grade E: Do not publish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 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 type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" 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

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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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 performed review: 2022-06-28 05:51

Review time: 1 Day and 2 Hours

Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input 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 checked="" type="checkbox"/> Accept (High priority) <input 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

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

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
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have made appropriate changes to the manuscript.