

Review Form 3

Journal Name:	International Research Journal of Gastroenterology and Hepatology
Manuscript Number:	Ms_IRJGH_121988
Title of the Manuscript:	Resmetirom in the Treatment of Noncirrhotic Non-Alcoholic Steatohepatitis: An In-Depth Review
Type of the Article	Review Article

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PART 1: Review Comments

Compulsory REVISION comments	Reviewer's comment	Author's Feedback (Please correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<p>Please write a few sentences regarding the importance of this manuscript for the scientific community. Why do you like (or dislike) this manuscript? A minimum of 3-4 sentences may be required for this part.</p>	<p>Non-alcoholic steatohepatitis (NASH) is a progressive form of non-alcoholic fatty liver disease (NAFLD) associated with steatosis, hepatocellular injury, inflammation and fibrosis. As a liver-directed, selective THR-β agonist, resmetirom could promote intrahepatic lipid catabolism, improve mitochondrial function, and reduce LDL cholesterol levels. This review summarizes resmetirom for the treatment of NASH, including the pharmacology, pharmacokinetics, clinical studies, dosing, and adverse effects according to literature search between 2010 and 2024.</p>	
<p>Is the title of the article suitable? (If not please suggest an alternative title)</p>	<p>Yes</p>	
<p>Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here.</p>	<p>The abstract of the article is comprehensive</p>	
<p>Are subsections and structure of the manuscript appropriate?</p>	<p>Please add 7.2 effectiveness and adverse effect of a multimodal approach with other medications</p>	
<p>Please write a few sentences regarding the scientific correctness of this manuscript. Why do you think that this manuscript is scientifically robust and technically sound? A minimum of 3-4 sentences may be required for this part.</p>	<p>This review is timely and interesting, and the conclusion is supported by substantial evidence. Nevertheless, I have several comments and suggestions that should be addressed before publication. These comments are found below.</p> <ol style="list-style-type: none"> 1. This review discusses the efficacy and safety and adverse events of resmetirom in the therapeutic effects of MASH. It needs further research, particularly regarding ethnic and sex differences, age difference. 2. Resmetirom expands the medication options available to treat patients with NASH. As occurs in many chronic conditions, combination therapy might lead to better outcomes. '7 Dosage and Administration of Resmetirom' on page 8. the authors should provide its effectiveness and adverse effect of a multimodal approach with other medications 	
<p>Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.</p> <p>:-</p>	<ol style="list-style-type: none"> 3. On page 4, the authors mention 'Metabolically, resmetirom is primarily metabolised by CYP2C8, with minimal involvement of other cytochrome P450 enzymes.' I do not agree with this. In fact, Sun et al (PMID: 38789494) showed that resmetirom treatment markedly reduced cytochrome P450 8B1 (CYP8B1) expression in both NASH mouse models. This should be corrected. 4. Bile acids (BAs) play key roles in regulating nutrition absorption and systemic energy homeostasis. NASH is associated with bile acid metabolism, intestine fat absorption and fat oxidation. Please refer to these references (PMID: 33098092, PMID: 33655500) and added to Figure 2 Key molecular pathways involved in the advancement of NASH. 	

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Minor REVISION comments		
Is the language/English quality of the article suitable for scholarly communications?	Yes	
<u>Optional/General</u> comments		

PART 2:

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Are there ethical issues in this manuscript?	<i>(If yes, Kindly please write down the ethical issues here in details)</i>	

Reviewer Details:

Name:	Shuwei Hu
Department, University & Country	Northeast Ohio Medical University, China