

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 76029

Title: Liver regeneration as treatment target for severe alcoholic hepatitis

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05266907

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: United Kingdom

Author's Country/Territory: Croatia

Manuscript submission date: 2022-02-26

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-03-11 09:13

Reviewer performed review: 2022-03-11 09:59

Review time: 1 Hour

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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 Grade E: Do not publish |
| Language quality | <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 |
| Conclusion | <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 |
| Re-review | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
| Peer-reviewer | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous |

statements

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

SPECIFIC COMMENTS TO AUTHORS

A good review of the literature, with a focus on G-CSF and stem cells. I only have minor comments. Structurally, I would be tempted to discuss G-CSF and stem cells first, as these are discussed in detail, and are the focus of the review, then mention the other experimental treatments which are covered superficially with far less detail. Otherwise, in the introduction, I would not say that AH is usually accompanied by ascites and HE, as although it can be it is certainly not always accompanied by these. AH is also a spectrum - non-severe AH with a mDF <32 is much less likely to be accompanied by additional symptoms of hepatic decompensation. AH usually occurs in patients with advanced fibrosis or cirrhosis, those without significant fibrosis are a minority. Consequently, I am not sure I would say 'sometimes in occur in the presence of fibrosis or cirrhosis'. In the conclusion I think it is important to note that the results of the G-CSF trials in ACLF cannot be directly extrapolated to AH given the heterogeneity in the ACLF cohorts.

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Reviewer's code: 01047363

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Switzerland

Author's Country/Territory: Croatia

Manuscript submission date: 2022-02-26

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-04-28 06:47

Reviewer performed review: 2022-05-02 12:21

Review time: 4 Days and 5 Hours

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|---------------------------|---|
| 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 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 |
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statementsConflicts-of-Interest: [] Yes [**Y**] No**SPECIFIC COMMENTS TO AUTHORS**

This is a very good and objective overview of the liver regeneration problem in decompensated ALD and in particular in AH. The topic is well presented and the data as well. Such a comprehensive review on this important topic is welcome. One comment, however: I suggest the authors should insist more on alcohol relapse in the period following AH (a quite frequent situation) with a considerable negative impact on liver regeneration with regards on the effect of ethanol itself on cellular proliferation cycles. The limitations are clearly presented, due to the small number of good quality clinical data, and the heterogeneous protocols of proregenerative strategies administration. This publication will be important for basic scientists and clinicians who want to have a good overview of the problem.