

Reply to reviewers' comments:

Dear Editor-in-Chief,

We thank you for the opportunity to revise our manuscript (64350) now entitled "**Long-term albumin infusion in decompensated cirrhosis: a review of current literature**".

Our point-to-point responses to the editor and reviewers are as below. The revised version of the manuscript is attached for your review.

Editor's comments:

Comment 1: The "Author Contributions" section is missing. Please provide the author contributions

Response 1: Thank you for the comment. We had included the author contribution section in the title page in our revised manuscript in page 2, para 4 as below:

"Author contribution

Study concept and design: WYJ; Systematic review of literature: WYJ, CYJ; Drafting the manuscript: WYJ, CYJ; Critical review of the manuscript: RK, ATL; All authors read and approved the final manuscript"

Comment 2: The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s)

Response 2: The grant approval letter has been uploaded in the system

Comment 3: PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout.

Response 3: Thank you for the comment. We had revised the referencing format as advised.

Reviewer 1's comments:

Comment 1: This is a comprehensive review. Authors had better discuss the limitation of human albumin supply. If positive results in long-term albumin, amount of albumin will be necessary for decompensated cirrhotic patients. The supply by blood donation might be limited.

Response 1: We thank the reviewer for the comment. We agree and had revised our manuscript in page 15 para 3 line 9-11 as below:

"Meanwhile, the positive result of long-term albumin infusion may increase the global demand for intravenous albumin particularly among decompensated cirrhosis patients"

Comment 2: How about the cell-free concentrated ascites reinfusion therapy (CART) in cirrhotic patients?

*Response 2: Thank you for the comment. We agree that the use of cell-free concentrated ascites infusion therapy (CART) is interesting. The current review focus on albumin infusion among patients with decompensated cirrhosis. While albumin was not used in CART therapy, the data of CART among cirrhosis patients with ascites is emerging. We had included a brief discussion on CART based on the reviewer's suggestion in **page 15, para 2, line 11-13** as below:*

"Meanwhile, the cell-free concentrated ascites reinfusion therapy (CART) may be a novel alternative to intravenous albumin infusion in patients with ascites ^[76], however more data is required to evaluate the efficacy and safety of CART, particularly among cirrhosis patients with refractory ascites."

Comment 3: What meant 'IV albumin'? Was 'IV albumin' different from 'albumin'?

*Response 3: Thank you for pointing out our mistake. We had revised intravenous (IV) albumin to albumin infusion to ensure consistency in our reporting in our revised manuscript in **page 9 para 3, line 1 and line 5** as below:*

"Even though albumin and terlipressin infusion achieves reversal of HRS-AKI in up to 60% of patients, it may not eventually result in reduced mortality."

"Based on two of the recent meta-analyses, there is no conclusive survival benefit of albumin and vasoconstrictor infusion in HRS-AKI when compared to placebo [55-56]."

Page 12, para 1, line 1 as below:

"The current societal guidelines do not endorse the use of long-term albumin infusion for either the treatment or prevention of HE in patients with decompensated cirrhosis"

Reviewer 2's comments:

Comment 1: The review is well done and the issue is discussed with balance and adequate criticism. The table is complete and also the references are exhaustive. The study merits to be published as it is

Response 1: We sincerely thank the reviewer for the time and commitment to improve our manuscript.

We hope that our revised manuscript is now acceptable for publication in your esteemed journal.

Warmest regards,

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