

18 December 2019

Dear Editor,

Thank you for your kind consideration of our manuscript entitled: Plasma Exchange in Patients with Acute and Acute-on-Chronic Liver Failure - A Systematic Review. We appreciate the valuable comments given by the reviewers and have encompassed it in our current draft of the manuscript.

Reviewer #1 Code 03471268:

In this systematic review, the authors provide a summary of currently available evidence for the use of plasmapheresis in ALF and ACLF. They described about transplant free survival, biochemical improvement, the volume of plasma exchange, duration of plasmapheresis and etiology of liver failure. The result from this study may provide the guide for therapy on ALF and ACLF. It is clear to show that the current situation of PE for ACLF and further research may be needed. I have some comments for their revision: 1) Abstract, Introduction, Methods and Discussion are well organized and easy to be understood; However, between Methods and Results, the inserted special section, "Mechanism of action of plasma exchange in liver failure" is not a normal. I think it might be better to move it into the "introduction" or "Discussion". 2) All figures and tables should be cited in main text no matter whether they are supplementary data or not. for example, Table 1 and Figure 2 are never mentioned in the text. 3) Table2 doesn't match the description in text.

Our response: Thank you for your review. We have removed the 'Mechanism of action' of plasmapheresis in ALF/ACLF. We have made the corrections to the figures and main texts as required.

Reviewer #2 Code 00005009:

No specific comments.

Our response: Thank you for your favourable review.

Reviewer #3 Code 00503215:

Nice review article. Can be improved with some figures particularly if possible with forest plot.

Our response: Thank you for your review. We have taken into consideration your suggestions and incorporated a forest plot to generate a pooled estimate of mortality in non-transplanted

ACLF patients, which showed a significant difference, favouring PE over SMT for patients with ACLF who were not transplanted. We have tried to contact corresponding authors for 30 day mortality figures for one of the studies, however to no avail.

Due to limited RCTs for ALF and missing critical information from the publication(s) itself, only a subgroup meta-analysis (Figure 2) was explored comparing mortality among non-transplanted ACLF patients who underwent PE based therapy vs SMT. We have tried contacted the respective authors since receiving the peer review comments, but again to no avail.

Lastly, we have incorporated comments from editor and made edits to the final manuscript.

Thank you for considering our manuscript and we look forward to your reply.

Regards, 

Eunice Tan and Guan-Huei Lee