

Response Letter

Dear Editor,

Thank you for your letter regarding our manuscript entitled " **A Systematic Review About the Efficacy and Safety of Argatroban in the Treatment of Acute Ischemic Stroke (no. 69152)**" and for your time and effort in considering our revision. We appreciate the helpful and positive comments from you and the reviewers. We have carefully considered the comments and revised the manuscript accordingly. The following is a point-by-point response to all comments and a list of changes we have made to the manuscript.

Reviewer #1:

1. Please can the authors indicate if there are gender differences in these studies, in particular in adverse events (bleeding)?

Reply:

We thank the reviewer for pointing this out. Thanks for your suggestion and we agree. We have reviewed the included studies carefully and subgroup analysis was performed to find out the statistical gender differences. All the studies provided gender information of enrolled patients. And there was no gender difference between argatroban group and the control group. But the safety and efficacy of argatroban were not assessed according to gender in 4 original studies. Therefore, the impact of gender on the safety and efficacy of argatroban cannot be evaluated. This clarification has been added to the manuscript in the results section.

2. However, the authors can indicate the role of age and comorbidity (renal and liver disease in particular) in the choice of treated population?

Reply:

We thank the reviewer for the insightful comment. We have studied the original data in the literatures carefully. In the studies of Andrew, Kari and Kobayashi the mean age of different groups was described but comparisons were not made. In Marian's study, there was an age difference between the argatroban and control groups but the impacts

were not analyzed. Besides, the safety and efficacy evaluation of argatroban was not performed subgrouped by age. The medical history of enrolled patients was provided in only 1 literature but further analysis was not performed. All the 4 literatures did not mention the abnormal liver and kidney function of patients. Therefore, the metabolism of argatroban cannot be evaluated. So, the role of age and comorbidity in the choice of the treated population can not be evaluated. We have explained it in the results section.