

Format for ANSWERING REVIEWERS

Title: Ulinastatin for Acute Lung Injury and Acute Respiratory Distress Syndrome: Systematic Review and Meta-Analysis

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Name of Journal: *World Journal of Critical Care Medicine*



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The manuscript has been improved according to the suggestions of reviewers. All modification of the manuscript were marked in green:

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer

Reviewer: 00502736

- (1) We have checked our manuscript carefully and had it edited by a native English speaker who is experienced in writing medical papers.
- (2) Reference 39 has been changed.

Reviewer: 02493552

- (1) The spelling errors have been modified.
- (2) Though few studies described randomization, allocation concealment and blindness in detail, they all claimed they were RCT studies. So we can't exclude them but evaluate them objectively.
- (3) Figure 3 has been corrected.
- (4) Discussion about the anti-inflammatory and lung-protective properties of ulinastatin has been added as: It's reported that ulinastatin inhibits pathogenic changes in many factors (including scald, seawater, LPS, phosgene, etc.) induced ALI/ARDS animal models [6-9]. Immunoregulation and the mitigation of excessive inflammatory reaction might be involved. Down-regulation of the human major histocompatibility complex (MHC) class I chain-related antigen A (MICA), mitigation of lipid peroxidation (LPO) and apoptosis may play important roles. Upregulation of MICA in scald induced lung injury can be ameliorated by ulinastatin [6]. What's more, ulinastatin treatment can reduce the level of cytokines like serum E, P-selectin VCAM-1, etc., which are considered to be critical in development of inflammatory responses [41]. Nevertheless, the effect of ulinastatin on pulmonary injury and the molecular mechanism(s) by which ulinastatin exerts its organ-protective activity remained obscurely studied.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Critical Care Medicine*.

Sincerely yours,

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