Author's Response to reviewers

The efficacy of adding budesonide/formoterol to ipratropium plus theophylline in managing severe chronic obstructive pulmonary disease: an open- label, randomized study in China

Reviewer: 1

Comments to the Author

Please discuss if a 12-week period of observation was appropriate for documenting the effect of the combined regimen (B/F/I/T) on exacerbations rate.

Response: The reviewer raises an important point, and we have sought to address this in the limitations section of the Discussion. Although a 3-month study is the minimum duration in order to be considered of sufficient sensitivity to detect a treatment effect on exacerbations, it is often thought that they do not provide the level of certainty that longer trials would report. In this study, however, a statistically significant and clinically meaningful difference in exacerbation rate between treatments was demonstrated, so we consider that the observation period of three months had enough sensitivity to assess the effect of the combined regimen on exacerbation rate.

Reviewer: 2

Comments to the Author

Well-written article with implication with a patient cohort different [to] that [of] the majority of studies evaluating budesonide/formoterol combination.

Response: We thank the reviewer for their comment. As noted in the manuscript, the dual combination of ipratropium and theophylline as maintenance therapy is a common treatment modality for COPD in China. Publication of our study, the results of which demonstrate the efficacy of adding budesonide/formoterol to this combination, will therefore improve treatment options and outcomes for such patients in China.