

Reviewer 2 v.1

Comments to the Author

The sub-study of ETHOS trial to evaluate the impact of triple therapy in comparison to dual therapies on lung function is very well designed, written and addresses an important issue. This study can become foundation for future prospective studies to compare triple therapy to dual therapies in COPD patients.

Minor Comments:

- It mentioned in the article that patients without FEV1 baseline stability (those with >20% or 200 mL change in their FEV1) were excluded from randomization. Given that those with rapid decline in their FEV1 are high risk patients for recurrent and severe exacerbations, they have high likelihood of ending up on triple therapy. Also, being able to have better management of the disease in this subgroup and potentially slow the slope of FEV1 reduction can have significant impact on preventing recurrent admissions. The reason behind this exclusion was not explained in the paper. I suggest authors consider providing the reason in the manuscript.

- Patients with other respiratory diseases including asthma were excluded from the study. However, the reversibility post albuterol with mean of 15-17 and SD of 15-16 in the subgroups raises the question if there were patients with ACOS (asthma COPD overlap syndrome) among the patients. How would that impact the external validity of the results in COPD patients?

- Although the benefits of BGF vs BFF maintained at week 52, in comparison to week 24 the improvement had declined. How would authors explain that specially comparing to BGF vs GFF that the LSM improvement at week 52 were higher than week 24 for BGF vs GFF.