Minor Essential Revisions

1) The authors need to provide more data on the subject characteristics to be able to argue that the low VP1 IgG levels are the cause of frequent exacerbations rather than a marker of a group of patients susceptible to exacerbations. There is already a suspicion of this in that the frequent exacerbation group had worse lung function than the no exacerbation group. In the Discussion the authors have stated that 'Though exacerbation-prone COPD patients had more severe airflow obstruction than the stable COPD patients, the association between lower anti-VP1 IgG1 antibody concentrations and COPD exacerbations appeared to be independent of FEV1'. What they have shown is that there was no statistically significant correlation between antibody levels and FEV1 which is not the same as showing the association between VP1 IgG and exacerbations was independent of FEV1.

The authors should provide data on the number of exacerbations prior to recruitment as, if the frequent exacerbation subjects had more exacerbations previously, then it is likely that they are a group susceptible to exacerbation. This does not exclude low VP1 levels as a mechanism for frequent exacerbations but the authors should provide this data and discuss confounding factors such as lung function and exacerbation frequency.

2) An alternative analysis would have been a multivariate analysis that could have included lung function and previous exacerbation history and would have strengthened their hypothesis if it had shown that low VP1 IgG levels were independently related to exacerbation frequency.

3) To be able to assess the relevance of the data regarding pneumococcal antibodies the pneumococcal vaccine status of the patients should be provided.

4) Influenza vaccination status may also be relevant and should be compared between the groups.

5) No virological sampling was carried out so it is impossible to determine whether the exacerbations were caused by rhinovirus. Evidence of rhinovirus infection would certainly have strengthened the hypothesis. The authors must have data regarding the season of exacerbations. Is there any indirect evidence that these are virus-induced exacerbations by the time of year they occurred? Also from the hospital records can the authors derive any information as to whether the exacerbations were associated with 'viral' symptoms.
6) What proportion of exacerbations had evidence of bacterial infection (sputum purulence, raised inflammatory markers, sputum cultures etc).

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests