Reviewer’s report

Title: Blood cells for the differentiation of airway inflammatory phenotypes in COPD exacerbations

Version: 3 Date: 18 Dec 2019

Reviewer: Stephen Bourke

Reviewer's report:

The authors have addressed most concerns.

1. I have reservations about stating that measurement of inflammatory cells in sputum is the "Gold Standard" to determine airway inflammatory phenotype. A poor correlation between blood and sputum results may lead to a false conclusion that measurement of blood inflammatory cells is not useful. This is clearly incorrect as blood eosinophil count has been shown to be a reliable predictor of response to inhaled corticosteroids when stable and oral steroids during acute exacerbation (acknowledged in the paper). Instead, I regard both sputum and blood eosinophils as surrogate markers of airway inflammation; the correlation between both of these biomarkers and airway histology is imperfect. What is most important is that the biomarker accurately predicts steroid treatment response. The biomarker in question must also be easy to measure in routine clinical practice; clearly not true of airway histology, and debatable in the case of sputum. I suggest either replace the statement on "Gold Standard" with the above, or at least follow it with this important caveat.

2. The authors have acknowledged that inflammatory cells during exacerbation are likely to differ from stable state and now highlight that blood eosinophil counts during exacerbation should not influence long term ICS decisions - thank you. In the discussion the authors mention eosinophils may be increased if there is overlap with asthma, but in pure COPD approx. 30% of patients have an eosinophilic component to their airway inflammation. Moreover, during sepsis and many severe exacerbations of COPD, blood eosinophils may fall to very low levels (transient eosinopenia) - this latter point is worth acknowledging.

3. All figures should be interpretable without reference to the text; a clear legend is required.

4. Thank you for offering to include an acknowledgement in the paper. As this is an open review process; additional formal recognition is not required (I'm happy either way).

5. Use of English: some further attention is required - perhaps by the copy editor if accepted for publication.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.
I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal