Reviewer’s report

Title: Role of C-reactive protein as a biomarker for prediction of the severity of pulmonary exacerbations in patients with cystic fibrosis.

Version: 2 Date: 30 June 2014

Reviewer: Bradley Quon

Reviewer’s report:

- Major Compulsory Revisions

The author must respond to these before a decision on publication can be reached. For example, additional necessary experiments or controls, statistical mistakes, errors in interpretation.

1. Exacerbation severity index:
   - Item b) – this index is not practical to apply clinically as it requires the final FEV1 which is not available at the time of admission
   - Item c) - why was this only based on the number of days requiring IV antibiotics in hospital. What about days of IV antibiotics at home?
   - What about including sputum microbiology such as BCC or MDR-PA?

2. It is unclear if each of the 62 exacerbations from 27 unique patients analyzed as separate events? If yes, did the analysis factor in the correlated data as some patients had multiple exacerbations? Consider analyzing just 1 exacerbation per patient. For table 2, the number of exacerbation events should be included.

3. What percentage of patients had oral antibiotics prior to admission and initiation of IV antibiotics? This may influence the admission CRP measurements and mask the relationship between CRP and exacerbation severity.

4. What is known about changes in CRP within the first 48 hours of treatment? If the half-life is short and the patient is responding to treatment, CRP levels might fall quickly and the CRP value might have less ability to predict exacerbation severity if the measurement was delayed. A sensitivity analysis looking at the subgroup with CRP measurements within 24 hours should be considered.

5. How was CRP measured? hsCRP or not? Clinical or research lab? These details should be provided in the Methods.

6. Page 8, line 187: How was larger number of exacerbations defined? Why the focus just on p-values for this comparison.

7. Multivariable analysis should be conducted in the analysis of the association between CRP and baseline characteristics to identify independent baseline factors associated with CRP.

- Minor Essential Revisions
The author can be trusted to make these. For example, missing labels on figures, the wrong use of a term, spelling mistakes.

1. Page 7, line 166: Initial CRP values were associated with FEV1 – which FEV1 measurement does this refer to? Admission or baseline?

2. What were the indications for oral corticosteroid use and were the patients started on this therapy prior to CRP measurement? Were these the same individuals that had ABPA? Multivariable analysis would be useful as mentioned above.

3. Exacerbation severity index – as the authors have acknowledged, this composite score has not been validated and therefore the scoring system might not be comprehensive enough to assess exacerbation severity. This should be mentioned in the limitations.

- Discretionary Revisions

These are recommendations for improvement which the author can choose to ignore. For example clarifications, data that would be useful but not essential.

None

**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