Reviewer’s report

Title: The Efficacy and Mechanism Evaluation of Treating Idiopathic Pulmonary Fibrosis with the addition of Co-trimoxazole (EME-TIPAC): study protocol for a randomized controlled trial.

Version: 0 Date: 02 Oct 2017

Reviewer: Melanie Meersch

Reviewer’s report:

- Please specify the term unplanned hospitalization-free survival (abstract). This needs to be explicit to facilitate understanding. And please change the following paragraph Page 2, lines 34 to 43. Precise the outcomes, e.g. "The primary outcome is a composite endpoint consisting of the time to death, transplant or first non-elective hospital admission. Secondary outcomes include the individual components of the composite outcome, respiratory related events, quality of life assessment…"

- When do patients receive folic acid and why?

- Please clearly state for how long patients will receive the investigational product/placebo. This needs to be explicit to be facilitated.

- The 50 patients receiving bronchoscopy, at what time point of the study will those patients be included? At the beginning, at the end, or whenever the patients agree to this procedure?

- Please include an additional table demonstrating the participating centers. Moreover, include an additional table with the members of the TMG, TSC and DMC.

- Page 4, line 43: precise "classical IPF"

- The authors need to precisely describe the standard therapy.

- I assume that patients' data will be documented pseudonymously/anonymously, correct? If yes, please include this statement.

- Inclusion criteria: is there a defined max time point since diagnosis of moderate/severe IPF? Maybe the authors need to precise the screening and inclusion process more precisely. Do I get it right, that hospitalized as well as non-hospitalized patients are included in the trial?

- Please precise the MRC dyspnoea score.

- How do the authors deal with non-compliance with regard to the final analysis? Please explain.
Page 15, line 19: is the sensitivity analysis of patients from TIPAC based only on IPF patients or on the overall cohort?

Page 15, line 19: Are the analyses stratified (e.g. center, gender, severity of IPF)

Discretionary revisions:

- The keywords include the word septrin. However, I cannot find it in the text. Is it really a keyword?

- Page 4, line 24: please add "TIPAC trial" in brackets and describe precisely the results of the TIPAC trial in patients with classical IPF (with numbers)

- Page 4, line 38: please include the p-value.

- Page 4, line 60: the role of infection is becoming more evident. Please include a reference.

- Page 6, line 34: Figures 1 and change the term schematic representation to study flowchart

- Page 6, line 10: participants will remain in the trial. Please change to "participants receive cotrimoxazole or placebo until they meet a primary endpoint…"

- Page 7, line 36 "…characteristic feature of on a thoracic high resolution…”

- Page 9, line 19: change to "Following consent, patients meeting all inclusion and non of the exclusion criteria…”

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