Reviewer’s report

Title: Efficacy and safety of Qing-Feng-Gan-Ke Granules in patients with postinfectious cough: study protocol of a novel design for a phase 3 placebo-controlled, double-blinded randomized trial

Version: 1 Date: 19 April 2015

Reviewer: Anne Elizabeth Vertigan

Reviewer’s report:

MAJOR COMPULSORY REVISIONS

Abstract:
1. Page 2: Third sentence under background. “Optimal treatment in western medicines for PIC has not been known.” This sentence should be changed. There is efficacy of Western medicine for this condition but the treatment effect is often incomplete.
2. Page 2: Why is the upper age limit of 65 years used? Most other cough studies include older patients.
3. Page 4. Most patients with PIC will spontaneously resolve. The authors should include the influence of spontaneous recovery into the study design.

Background
5. There is a contradiction in saying that PIC can last for months but not more than 8 weeks (page 3).
6. Can they authors define what they mean by a ‘meticulous job’? (Page 3)
7. The description of PIC as intractable does not seem accurate if it only lasts for less than 8 weeks.
8. The term general care needs to be defined (page 4).
9. References need to be provided for quality of life (page 4).
10. Examples of adverse outcomes should be provided (page 4).
11. A description of the bias in previous studies should be provided.
12. More information is needed on the integral syndrome differentiation, particularly for readers who are unfamiliar with TCM (page 4). How does the health practitioner arrive at the syndrome differentiation.
13. Page 4 paragraph 2: The phrase “which proved the antitussive and…” should be changed to “which suggests antitussive and…”. Also “subsequent clinical studies underpinned” should be changed to “subsequent clinical studies investigated”.
14. A reference should be provided for the last sentence in paragraph 2 page 4.
Study design
15. How will the symptom differentiation be determined? How consistent are the researchers in making this determination? What criteria is used in making this assessment?
16. The description of table 1 in the text does not seem to match the content of table 1. Table 1 actually lists the inclusion and exclusion criteria for participants in the study.
17. Who will assess the patients? Are the staff assessing the patients different from the staff providing the treatment.
Participants
18. It would be better to separate the description of the participants from the methodology and study design.
19. The content of tables 2 and 3 do not match the description in the text.
20. Page 6: The four time points need to be explained in the text.
21. Page 6: “As long as a little bit difference is observed”. This needs to be more specific.
22. How will the participants be recruited for the study? Who will approach the patients?
Randomization and blinding
23. Blinding needs to be better described. A flowchart might help to outline the process.
24. Stratification needs to be explained in more detail. What is stratification to be based on?
25. It is unclear whether the researchers will know what group the patient is in.
26. Will the placebo medication be matched for taste?
27. If the code is broken will the treating Dr know?
Intervention
28. Figures 1 and 2 are tables rather than figures.
29. Two day follow up is not sufficient. Follow up should be at least one month later.
30. What are the physical properties of the QFGKG.
Outcomes
31. Is the outcome for section A to determine the difference between treatment and placebo groups?
32. More information is needed about the cough symptom score. Is it a questionnaire completed by the patient? Is it obtained in an interview? Does the health practitioner complete it on behalf of the patient?
33. More information is needed about the TCM symptom score.
34. What about patient self report of side effects?
35. No objective cough measures have been included.

**Statistical Analysis**

36. Who will equivalence at baseline between the two groups be ensured?

**Ethics**

37. Page 11 – It is unclear what the authors mean by ‘contentment.

38. Page 11 – Change ‘working on to verify and extend’ to ‘studying’

**Discussion**

39. Page 11 – change great to some.

40. The authors need to comment on the extent to which this methodology has been used in other cough research.

41. Page 12: The sentence ‘Although they are independent for settling different questions…. Is not a complete sentence and the meaning is unclear.

42. Page 12: “has been first proposed…..” The meaning of this sentence is unclear.

43. Page 12: First sentence of the last paragraph needs to be more succinct.

**Tables and figures**

44. Table 1
   a. Are other serious causes ruled out?
   b. How is post infectious cough determined?
   c. Are patients with psychiatric disorders excluded if the disorders are current or if there is any history.
   d. What does legal disability mean?

45. Table 2
   a. Why is the tongue condition relevant?

46. Table 4
   a. Does baseline balance test mean baseline patient characteristics?
   b. Gender and previous treatment should also be included.
   c. What does ‘history’ mean.
   d. More information about the CQLQ is needed including the translation.

**Grammar and verbal expression:** There are many errors with grammar and verbal expression throughout the manuscript. These make the meaning difficult to follow. They include:

47. The meaning of the following sentences is unclear. I suggest that these are reworded or rephrased.
   a. Page 2: “In virtue of different….sections is identical.”
   b. Page 3: “Even though PIC is not bound to….problematic all times”
d. Page 3: “inability of treatment will bring physicians….PIC has not been developed.

e. Page 6: “corresponding treatment will pone to be…..more expected results.

48. Sentence structure: The following suggestions are made.

a. Page 4: Remove however from the second last sentence of paragraph 1.

b. Page 4: Remove always from the first sentence of paragraph 2.

c. Page 4: Paragraph 2 should dioxide-reduced be dioxide-induced?

d. Page 6: Paragraph 2 – deleted nevertheless before section B is designed.

e. Page 7: the phrase ‘recruitment is not allowed’ should be changed to ‘recruitment are not allowed’

f. Page 7: Paragraph 3 - Change ‘of responsible department’ to ‘of the responsible department’

g. Page 7: Paragraph 3 – change ‘harm in patient’ to ‘harm to a patient’

h. Page 7: Paragraph 3 – change ‘patient must be withdrawn’ to ‘the patient must be withdrawn’.

i. Page 7: Paragraph 3 – change ‘breaked code’ for ‘The broken code’

j. Page 7: Paragraph 3 – change ‘filled’ to ‘completed’

k. Page 7: Paragraph 3 – ‘on case report’ should be changed to ‘on the case report.’

l. Page 8: Change the last sentence to read ‘The use of antibiotics, Western or other .....’

m. Page 8: Second last sentence: Delete the words of, are and and last.

n. Page 9: Paragraph 2 – Change ‘both of daytime’ to ‘both daytime’, change ‘reduce one’ to reduced by one and delete and last.

o. Page 9: Paragraph 3 sentence 1; Insert the between is and difference.

p. Page 10: Paragraph 1 – Delete And then before CRFs.

49. Vocabulary

a. Page 5: Under objective change the word safety to safe.

b. Page 5: Last sentence – change trainings to training.

c. Page 6: Change Connective to connected.

d. Page 6: Last sentence - Change suspending to suspension.

e. Page 10: Change input in to entered into a, researching to research, and entering to entered.

f. Page 10: Change on original forms to of the original forms; change records to researching monitor to records to the research monitor; change consistency on data to consistency of data.

g. Page 11: Change ‘Patients’ fully understanding’ to ‘Patients’ full understanding’.
h. Page 11: Change ‘firm a conclusion’ to ‘form a conclusion.
i. Page 12: Change ‘benefits on PIC researching’ to ‘benefits for PIC research’.
j. Page 12: Change allocate participates to allocate participants.

Level of interest: An article of importance in its field

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests