Reviewer's report

Title: Protocol and baseline data for a Prospective open-label explorative randomized single centre comparative study to determine the effects of various intravenous iron preparations on markers of oxidative stress and kidney injury in chronic kidney disease (CKD). (IRON-CKD)

Version: 0 Date: 19 Nov 2018

Reviewer: Natasha Wiebe

Reviewer's report:

This manuscript describes the protocol for a 4-group randomized pilot trial of IV iron preparations for patients with CKD, and some preliminary results on the trial population's accrual and baseline characteristics. The manuscript is decently written (with a few English language errors) and thus fairly clear and easy to read. The list and details of outcomes need to be cleaned up. I have no major essential suggested revisions.

Major Essential Revisions - None

Minor Essential Revisions

1. There a number of English language errors mostly beginning at line 225 in the randomization procedure section but continuing until the end of the manuscript. Most of the manuscript is written in the past tense but the tense changes in a few places.

2. While pilot trials are explorative, I am not sure it is accepted practice to use the term when describing the design. It might be better to use the term pilot throughout and then in the objectives and the sample size section emphasize that pilot trials are explorative and so ...

3. In the Abstract Results, the mean age has an error.

4. Iron needs to be inserted after IV in line 90.

5. The outcomes are described before and after the Iron administration section. The timing of each outcome is laid out in Table 2 and can simply be referenced. The outcomes should be fully described under one section, detailed thoroughly and organized better. Results and timing should not be mixed up with the outcome section.

   a. What specifically is included in the biochemical profile and the full blood count?
b. What measures are included in oxidative stress and what further measures of inflammation will be considered beyond CRP?

c. How was temperature measured?

d. How was blood pressure measured?

e. Are there specific minor adverse events that are expected?

6. In Line 226, were these blocks permuted?

7. The results in lines 257-259 should be moved to the Result section.

8. There needs to be a citation in the sample size section for the cited evidence. Is the confidence interval a 95% interval? Those limits seem unlikely but I cannot check them without the citation.

9. ANCOVA is appropriate for continuous outcomes in RCTs. Are there any dichotomous outcomes?

10. Provide more details for the multiple imputation approach. How many draws? Are you drawing within participant? Or within follow-up visit? Any other considerations?

11. Why are oxidative stress, inflammatory markers and markers of AKI singled out for simple statistics and figures? Why not use ANCOVA?

12. There is a lot of text spent on one compliance issue in lines 334-340. This should be moved to the end of this paragraph and shortened considerably.

13. How will NGAL be analyzed in participants who have baseline markers for heightened inflammation or infection?

14. In Table 1, the inverse of the inclusion criteria need not be listed under exclusion criteria.

15. Table 2 needs footnoted a listing of expanded abbreviations. Will serious adverse events be assessed over the whole follow-up? Can this be added to Table 2.
16. In Table 3, leave (SEM) in the title or as a footnote, and add units for Age and Serum Ferritin. Drop Mean before Age as you are using means throughout the table. Brackets are missing from the uPCR row. The number of decimal places is not always consistent.

17. In Figure 2, 9 are not eligible. Should these be considered screen failures? Or did they not consent? The terminology makes it unclear.

**Level of interest**
Please indicate how interesting you found the manuscript:

An article of importance in its field

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

Needs some language corrections before being published

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**Statistical review**

Is it essential that this manuscript is seen by an expert statistician? If so, please give your reasons in your report.
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No