Reviewer's report

Title: Rationale and design of a prospective, randomised study of retrograde application of bone marrow aspirate concentrate (BMAC) through coronary sinus in patients with congestive heart failure of ischemic etiology (The RETRO study)

Version: 0 Date: 28 Sep 2018

Reviewer: Amish Raval

Reviewer's report:

The authors provide an interesting trial design manuscript, that will test a novel therapy/administration approach in a desperate patient population with tremendous unmet needs. The trial will test the safety and possibly efficacy of retrograde transcoronary sinus administration of autologous bone marrow mononuclear cell treatment in chronic ischemic HF with NYHA class 3-4 patients. Few items were noticed:

1. NYHA class 3 patients are fine, but NYHA class 4 patients may not yield data for 6 minute walk distance, and are a rather unstable patient cohort. Further, this can be a challenging patient population to enroll in HF trials. Please discuss the rationale for including class 4 patients.

2. HF stability for 1 month is should be better defined (does this mean no outpatient diuretic variation?). 1 month is rather short to prove stability - perhaps this rationale should be discussed further.

3. The authors should provide the parameters of what would constitute "standard HF treatment", citing recent National Guideline statements, and indicating efforts to optimize standard dosing. Furthermore, how long after a CRT device can a subject be enrolled?

4. There is no effort to blind subjects, which makes the trial results highly susceptible to placebo effect and potential subject drop out. This will be a serious limitation to the study conclusions. Please discuss.

5. What is the sedation/anesthesia protocol for 240mL aspirate?

6. Will right heart catheterization be done before and after treatment?
7. comment on the feasibility and published experience of coronary sinus infusion and cardiac resynchronisation LV lead.

8. How will the investigators evaluate for pulmonary embolism with infusing a platelet rich cell mixture?

9. the study population will be variable consists of recent MI, only excluding patients <1 week post MI. A pt with HF considered for enrollment day 8 post MI would not be chronic heart failure. This should be clarified.

10. There are numerous grammatical and spelling errors throughout.

11. Is there a GFR cutoff for the exclusion criteria?

12. Authors should cite: PMID26217065, PMID29803986 as other relevant un-fractionated BMNC trials completed or on going.

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 recommend additional statistical review
Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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