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: 01 Oct 2018

Reviewer: Joshua Hare

Reviewer's report:

The RETRO study will evaluate the efficacy of BMAC in patients with Ischemic Cardiomyopathy. This randomized, controlled study will evaluate cardiac function and geometry and 6-minute walk test as primary endpoints. Secondary endpoints will evaluate arrhythmogenic adverse events and quality of life parameters.

The author's novel study is based on the cell characteristics of autologous non-selected bone marrow cells delivered by retrograde methodology.

Major comments

-Please provide a more updated description of the current donor sources or state of the art in the stem cell field. Your statement on line 37-38 page 6, until last paragraph is not accurate.

- Please provide reference to studies that have shown efficacy and safety of BMAC on line 54-59 page 6.

- In the Background and Discussion, please provide more clinical trial references and fewer reviews.

- The authors state that cardiac function will be measured by MRI. Please consider including scar size measurement in your parameters as a decrease in fibrosis has been one of the main outcomes in the stem cell field.

- Please include in the Discussion some of previous trials that have utilized retrograde delivery of cells; including the REVIVE Trial: Retrograde Delivery of Autologous Bone Marrow in Patients With Heart Failure (2015), that used a very similar type of cell and methodology of delivery. Others that also used a similar approach albeit in different pathologies:


- In the Discussion please include Heldman et al., Transendocardial Mesenchymal Stem Cells and Mononuclear Bone Marrow Cells for Ischemic Cardiomyopathy: The TAC-HFT Randomized Trial. JAMA. 2014;311:62-73; which compares MSCs vs. BMCs head-to-head in patients with ischemic cardiomyopathy.

- Please provide a more detailed discussion on clinical trials that use BMAC in comparison to the other BMNC.

Minor comments

- Please review the reference style because references in the discussion appear in a different format.

- Page 11 line 44: where the authors mention the increase in dP/dt, are they referring to dp/dt max or min?

- Line 54 of page 11: Transdifferentiation is missing a letter "d".
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.

Not relevant to this manuscript

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Please indicate the quality of language in the manuscript:

Acceptable

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