PEER-REVIEW REPORT

Name of journal: World Journal of Cardiology

Manuscript NO: 93255

Title: Establishing delivery route-dependent safety and efficacy of living biodrug
mesenchymal stem cells in heart failure patients

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05196024

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer’s Country/Territory: United States

Author’s Country/Territory: Saudi Arabia

Manuscript submission date: 2024-02-22

Reviewer chosen by: AI Technique

Reviewer accepted review: 2024-03-11 01:10

Reviewer performed review: 2024-03-20 22:40

Review time: 9 Days and 21 Hours

Scientific quality

[ ] Grade A: Excellent [ Y] Grade B: Very good [ ] Grade C: Good
[ ] Grade D: Fair [ ] Grade E: Do not publish

Novelty of this manuscript

[ ] Grade A: Excellent [ Y] Grade B: Good [ ] Grade C: Fair
[ ] Grade D: No novelty

Creativity or innovation of this manuscript

[ ] Grade A: Excellent [ ] Grade B: Good [ Y] Grade C: Fair
[ ] Grade D: No creativity or innovation
SPECIFIC COMMENTS TO AUTHORS
This manuscript is a meta-analysis of the routes of MSC delivery for heart failure in Phase II clinical trials. Similar studies have been performed in the past, but most are several years old and include a variety of pre-clinical and clinical studies. Overall the manuscript is well written and informative. I have a few questions and recommendations for the authors prior to publication. Page 9, Eligibility: Is there a reason the authors limited their analysis to Phase II studies? I can see limiting the study to clinical trials, or even Phase II and III clinical trials, but is there a reason for just Phase II? I’m not saying that this is wrong; it just raises questions from the reader. An explanation would be helpful. I would also recommend adding “Phase II” just before RCTs in the manuscript title. Page 11, Results and Figure 1: The authors state they found narrowed their literature search down to 35 studies, then eliminated 24 to come up with a total of 12 studies to analyze; this is somewhat picky but $35 - 24 = 11$, not 12. Clearly, the authors analyzed 12 Phase II studies; do the authors mean 36 studies? Page 13, last line: A symbol and the word fragment “es” are out of place and should be corrected. Page 14, last 3 lines: The authors say the IM subgroup significantly decreased 6MWD,
but the p value is 0.29, which is not significant. Page 15, Discussion: I would recommend caution in using the terms “engraftment” and “stemness” unless the studies analyzed specifically examined these. There is a paucity of evidence for long term engraftment of MSC, and many researchers believe that the benefits of MSC are due to paracrine stimulation of tissue stem/progenitor cells, or anti-inflammatory effects, and not due to MSC engraftment. Page 15, last line: Several times the authors say “reduction in SAEs”. Since SAEs would probably only increase with an intervention (MSC delivery) it may be better to say something like “change in SAE incidence” or the like. Page 16: The term “most favored” is used; perhaps most common, or most utilized would be better. Once abbreviations are defined, please use them consistently. In the Core Tip, please define HF.