

Special Presentation of Letter and Response

A letter to the editor has been submitted to the *Journal* by Dr. Darrel P. Francis and colleagues regarding the paper by Bartunek et al. (1). Due to the nature, detail, and length of the letter and the corresponding reply, the editors have made a decision to waive the usual word limit and timelines for letters and replies so as to provide a full airing of the issues for our readers. However, given the length of the material, we have elected to place the letter and reply in the online version of the issue. We encourage readers to access this material and trust that it contributes to the editorial process.

<http://dx.doi.org/10.1016/j.jacc.2013.09.012>

REFERENCE

1. Bartunek J, Behfar A, Dolatabadi D, et al. Cardiopoietic stem cell therapy in heart failure: the C-CURE (Cardiopoietic stem Cell therapy in heart failURE) multicenter randomized trial with lineage-specified biologics. *J Am Coll Cardiol* 2013;61:2329–38.

APPENDIX

For a list of issues regarding C-CURE and the responses of the authors, please see the online version of this issue.

The C-CURE Randomized Clinical Trial (Cardiopoietic stem Cell therapy in heart failURE)

We read with interest the recent C-CURE (Cardiopoietic stem Cell therapy in heart failURE) trial (1) of stem cells used for the treatment of heart failure. Completing such a multicenter trial is a great achievement, but applying its findings either to clinical care or future trial design might be premature, as there appear to be some inconsistencies in the data. Discrepancies, if left unresolved, can be problematic (2):

- How many patients were randomized? Counts ranged from 45 to 48.
- The authors' corporate website (3) currently states that randomization was 1:1, but Figure 1 in the paper (1) shows counts close to 1:2; conversely, at AHA 2011, the authors said that randomization was 2:1, but reported counts that were close to 1:1. Can the authors please clarify the randomization ratio?
- Once randomized to 1 arm, did any patient's data appear under the heading of the opposite arm? Were some patients allocated to arms by routes other than randomization to those arms? Are baseline characteristics and result data regarding the trial arms, as randomized, available?
- The primary endpoint was pre-specified to be radionuclide ejection fraction, but its results do not appear in the paper. A

new primary endpoint is described in the paper. Did all authors agree on this change, and when?

- Regarding the data presented in the paper (1), its Online Appendix, and the previous trial reports (see the Online Appendix for citations), which of these various conflicting versions are correct regarding ejection fraction, end-systolic volume, end-diastolic volume, New York Heart Association functional class, quality of life, and walk distance? Fewer of certain events, such as arrhythmias, are reported in the current narrative than in previous ones. Could the authors clarify how many stem cell recipients died?

It would be extremely helpful if the authors could resolve these and other uncertainties to aid interpretation (see the Online Appendix for a detailed list of queries, references, and the authors' institutional affiliations).

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Please note: Dr. Olshansky is a consultant for BioControl, Medtronic, Boehringer Ingelheim, Daiichi Sankyo, and Boston Scientific; and is on the DSMB for Amarin and Sanofi Aventis. Dr. Cleland has received research grants from Servier, Novartis, Sorin, and Amgen; is on the advisory boards for Amgen, Novartis, Servier, and Respicardia; and speaker fees from Medtronic and Novartis. All other authors have reported that they have no relationships relevant to the contents of this study to report.

REFERENCES

1. Bartunek J, Behfar A, Dolatabadi D, et al. Cardiopoietic stem cell therapy in heart failure: the C-CURE (Cardiopoietic stem Cell therapy in heart failURE) multicenter randomized trial with lineage-specified biologics. *J Am Coll Cardiol* 2013;61:2329–38.
2. Francis DP, Mielewczik M, Zargarani D, Cole GD. Autologous bone marrow-derived stem cell therapy in heart disease: discrepancies and contradictions. *Int J Cardiol* 2013;168:3381–403.
3. Cardio3 Biosciences. Clinical trials. Available at: <http://www.c3bs.com/en/clinical-trials>. Accessed June 29, 2013.

APPENDIX

For a list of issues regarding C-CURE and the responses of the authors, please see the online version of this issue.