

University of Genoa

Prof. Fabrizio Montecucco, MD, PhD

Division of Internal Medicine

Department of Internal Medicine

fabrizio.montecucco@unige.it



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Dear Editor-in-chief of World Journal of Cardiology

As corresponding author, I would like to re-submit to World Journal of Cardiology in behalf of my colleagues, the revised (R1) version of the editorial entitled "Facing ethical concerns in the age of precise gene therapy: outlook on inherited arrhythmias" by Carbone and myself.

All the authors have contributed significantly to the revision of the manuscript. All authors have read and approved this revised submission of the manuscript. No persons other than the authors listed have contributed significantly to its preparation.

We would thank the editor for his time in reviewing this submission. We trust that the review process will improve the quality of our manuscript.

My address, phone number, fax number, and e-mail address are on this letterhead. I further confirm that I will serve as corresponding author of this manuscript.

Reviewer #1

This is a well-written editorial. The authors underline that due to the monogenic nature of inherited arrhythmias the disease is a correctly selected target for gene therapy. In addition, they discuss ethically important issues. The very high price of gene therapy, which limits the availability of this type of drugs. They also correctly refer to the inability of insurance policy to adequately manage the reimbursement of such one-time therapies. Finally, they conclude that these problems lead to great inequality in the access to such treatment.

Reply: we thank the reviewer for her/his comment

Editorial Office's comments:

Science editor:

1 Conflict of interest statement: Academic Editor has no conflict of interest.

2 Manuscript's theme: The topic is within the scope of the journal.

3 Scientific quality: The authors submitted a study of facing ethical concerns in the age of precise gene therapy: outlook on inherited arrhythmias. The manuscript is overall qualified. Advantages and disadvantages: The reviewers have given positive peer-review reports for the manuscript. Classification: Grade B; Language Quality: Grade A. The authors underline that due to the monogenic nature of inherited arrhythmias the disease is a correctly selected target for gene therapy. In addition, they discuss ethically important issues. The very high price of gene therapy, which limits the availability of this type of drugs. They also correctly refer to the inability of insurance policy to adequately manage the reimbursement of such one-time therapies. Finally, they conclude that these problems lead to great inequality in the access to such treatment. The author clearly stated the purpose of the study and the research structure is complete. However, the manuscript still requires a further revision according to the detailed comments listed below. Table(s) and

figure(s): There is no Figure and no Table should be improved. A total of 13 references are cited, including 10 published in the last 3 years. The reviewer didn't request the authors to cite improper references published by him/herself.

Reply: we thank the reviewer for her/his comment

4 Language evaluation: The English-language grammatical presentation needs to be improved to a certain extent. There are many errors in grammar and format, throughout the entire manuscript. Before final acceptance, the authors must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Reply: we partially agree with the reviewer's comment. As required, we have carefully reviewed the manuscript to enhance its English language quality. Given that we received a Grade A for language quality from all the referees/editors, we believe it is unnecessary to seek assistance from a professional English language editing company.

5 Specific comments:

a) Please add the author's contribution section. The format of this section will be as follows: Author contributions: Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research; Wang CL, Zou CC, Hong F and Wu XM performed the research; Xue JZ and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed the data; Wang CL, Liang L and Fu JF wrote the paper.

Reply: as required, we added the author's contribution section.

b) The number of key words should be controlled between 4-10.

Reply: as required we implemented the number of Key words as follows: "ethical concerns for gene therapy in inherited arrhythmias; equitable accessibility".

c) The main text of the manuscript must include two parts: "Introduction" and "Conclusion".

Reply: as required we have now introduced paragraphs (introduction, overview and outlook on genome editing for inherited arrhythmias, and conclusion) in this revised (R1) version of the manuscript.

d) The article mentions an article published in the World Journal of Cardiology, but it is not cited in the reference list. Please supplement it in the reference list. (Spartalis M, Spartalis E, Siasos G. Inherited arrhythmias and gene therapy: Are there any ethical considerations to take into account? World J Cardiol 2023; 15(12): 623-626).

Reply: as required we have now introduced the reference.

e) Recommendation: Conditional acceptance. Language Quality: Grade A (Priority publishing) Scientific Quality: Grade B (Very good).

Reply: we thank the editor for her/his comment.

Company editor-in-chief

I have reviewed the Peer-Review Report, full text of the manuscript, all of which have met the basic publishing requirements of the World Journal of Cardiology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. When revising the manuscript, it is recommended that the author supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply PubMed, or a new tool, the RCA, of which data source is PubMed. RCA is a unique artificial intelligence system for citation index evaluation of medical science and life science literature. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at:

<https://www.referencecitationanalysis.com/>, or visit PubMed at:
<https://pubmed.ncbi.nlm.nih.gov/>.

Reply: we thank the editor for her/his comment. As suggested we applied RCA to improve of the latest cutting-edge research results and we have now added to critical references to the manuscript (now Ref 3 and 4 in this revised version of the manuscript).

Yours sincerely,
Fabrizio Montecucco, MD, PhD
for the authors

A handwritten signature in dark ink that reads "Fabrizio Montecucco". The signature is written in a cursive, slightly slanted style.

Prof. Fabrizio Montecucco, MD, PhD
First Clinic of Internal Medicine, Department of Internal Medicine, University of Genoa
School of Medicine, 6 viale Benedetto XV, 13132 Genoa, Italy.
Tel: +39 010 353 8694;
Fax: +39 010 353 8686;
E-mail: fabrizio.montecucco@unige.it