ARTICLE DETAILS

TITLE (PROVISIONAL)	Discontinuation of β-blocker Therapy in Stabilized Patients After Acute Myocardial Infarction (SMART-DECISION): Rationale and Design of the Randomized Controlled Trial
AUTHORS	Choi, Ki Hong; Kim, Juwon; Kang, Danbee; Doh, Joon-Hyung; Kim, Juhan; Park, Yong Hwan; Ahn, Sung Gyun; Kim, Weon; Park, Jong Pil; Kim, Sang Min; Cho, Byung-Ryul; Nam, Chang-Wook; Cho, Jang; Joo, Seung-Jae; Suh, Jon; Jeong, Jin-Ok; Jang, Woo; Yoon, Chang-Hwan; Hwang, Jin-Yong; Lim, Seong-Hoon; Lee, Sang-Rok; Shin, Eun-Seok; Kim, Byung Jin; Yu, Cheol; Her, Sung-Ho; Kim, Hyun Kuk; Park, Kyu Tae; Kim, Jihoon; Park, Taek Kyu; Lee, Joo-Myung; Cho, Juhee; Yang, Jeong Hoon; Song, Young Bin; Choi, Seung Hyuk; Gwon, Hyeon-Cheol; Guallar, E; Hahn, Joo-Yong

VERSION 1 - REVIEW

REVIEWER NAME	Younis, Omar
REVIEWER AFFILIATION	National Heart Institute
REVIEWER CONFLICT OF INTEREST	None
DATE REVIEW RETURNED	02-May-2024

GENERAL COMMENTS	I carefully read your protocol and I do believe it is a SMART DECISION to accept the paper. You were straightforward from the start with a brief introduction on the issue followed by crystal clear methodology and a specific primary endpoint. One perk of this protocol is that you were minded by the cost-effectiveness and economic burden of beta-blockers and put that among the secondary endpoints.
	I am fully aware that not too many changes could be made while the whole work is already complete. However, kindly consider adding to the Strengths & limitations section (in the best way you can):
	1. Time from index myocardial infarction to randomization is not the same for all the patients. However, a prespecified subgroup analysis will include patients randomized at 1-2 years from index MI vs. 2–3 years vs. ≥3 years.
	2. Although patients were regularly followed up from the time of randomization at 6, 12, 24 & 30 months, some patients had an extended follow-up beyond 30 months that was once yearly (i.e. not all patients were followed up to the same extent).
	Finally, I would like to thank you for this research work. I will keep my fingers crossed till the results are published. I will be very keen to read it.

REVIEWER NAME	Wang, Liansheng
REVIEWER AFFILIATION	First Affiliated Hospital of Nanjing Medical University, Department of cardiovascular medicine
REVIEWER CONFLICT OF INTEREST	None
DATE REVIEW RETURNED	06-May-2024

GENERAL COMMENTS	I would like to congratulate the authors on designing a highly significant clinical study, which involves a randomized controlled trial on discontinuing beta-blocker therapy in stable patients after acute myocardial infarction. This study addresses an unresolved question regarding the need for long-term maintenance of beta-blocker therapy in stable coronary artery disease patients. I think the design of this study is rational and holds significant clinical and public health implications.

VERSION 1 – AUTHOR RESPONSE

[Comment #1]
Time from index myocardial infarction to randomization is not the same for all the patients. However, a prespecified subgroup analysis will include patients randomized at 1-2 years from index MI vs. 2–3 years vs. ≥3 years.

Response:
Thank you for your valuable comment. As the Reviewer pointed out, different individual time from index myocardial infarction to randomization might be one of the limitations of the current trial. However, we planned to perform the pre-specified subgroup analysis of time from index myocardial infarction to randomization (1-2 years, 2-3 years, and ≥3 years), to evaluate the efficacy of beta-blocker discontinuation according to the differential periods from myocardial infarction. To respect the Reviewer's opinion, we added the above issue in the Discussion section of the revised manuscript as follows.

Discussion (page 17, line 332)
Furthermore, time from index MI to randomization is not the same for all the patients. However, to evaluate the efficacy and safety of β-blocker discontinuation according to differential period from the index MI, a prespecified subgroup analysis will be performed among patients randomized at 1-2 years from index MI vs. 2–3 years vs. ≥3 years.

[Comment #2]
Although patients were regularly followed up from the time of randomization at 6, 12, 24 & 30 months, some patients had an extended follow-up beyond 30 months that was once yearly (i.e. not all patients were followed up to the same extent).

Response:
Thank you for this comment. As the Reviewer pointed out, every patient has a different follow-up duration. However, all patients had a minimum 30 months of follow-up period. Furthermore, we have calculated the sample size based on the time to event analysis, to consider the different follow-up duration. Our previous paper calculated the study sample size in the same way was published in New England Journal of Medicine without any problems.

[Comment #3]
Finally, I would like to thank you for this research work. I will keep my fingers crossed till the results are published. I will be very keen to read it.

Response:
We really appreciate your positive response of our study. We will do our best to ensure that this research progresses well to the end.

[General Comment]
I would like to congratulate the authors on designing a highly significant clinical study, which involves a randomized controlled trial on discontinuing beta-blocker therapy in stable patients after acute myocardial infarction. This study addresses an unresolved question regarding the need for long-term maintenance of beta-blocker therapy in stable coronary artery disease patients. I think the design of this study is rational and holds significant clinical and public health implications.

Response:
We sincerely appreciate the Reviewer's effort and time in reviewing our manuscript and thank you for all your valuable comments. We will do our best to ensure that this research progresses well to the end.

As you can see, we tried our best to address each of the issues raised by the reviewers. We hope that these revisions greatly strengthen our manuscript and that these better suits the requirements of your prestigious journal.