Author's response to reviews

Title: Comparison of Drug-Eluting Balloon first and then bare metal stent with drug-eluting stent for treatment of de novo lesions (DEB first): A randomized controlled single center clinical trial

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Author's response to reviews:

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Dear Dr. Doug Altman,

Editor-in-Chief

RE: Revision of the manuscript

Manuscript ID: 1768278613755606
Title: “Comparison of Drug-Eluting Balloon first and then bare metal stent with drug-eluting stent for treatment of de novo lesions (DEB first): A randomized controlled single center clinical trial”

Dear Dr. Doug Altman

I, on behalf of all the authors, would like to thank you and the reviewers of Trial: for taking the time and effort to review our manuscript. We appreciate the thoughtful and careful comments of the editor and reviewers. Many of the valuable and constructive points that the reviewers pointed out, were well taken by all the authors. My colleagues and I have tried to address all of the points that
the reviewers have raised. The section below provides a point-by-point response to the issues raised by the reviewers. Each comment is excerpted and addressed in detail with reference made to the locations of any changes in the manuscript. The revised parts in the new manuscript have been underlined and colored for the convenience of the editors and reviewers.

We believe that these major changes have significantly improved the quality of our manuscript and we hope that the revised manuscript better meets the standards of the journal.

Best regards,

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Reviewer and Chief Editor

[Comment #1]
- Major revision of the power calculation and preferably with a superiority design
- "I agree with the reviewer that more information about the choice of a non-inferiority design instead of a superiority design is needed. Why was that choice made? Also, how was the non-inferiority margin selected?"

Response: Thank you for this valuable comment. We definitely agree with you that non-inferior trial have a number of inherent weaknesses that superiority trials do not: no internal demonstration of assay sensitivity, no single conservative analysis approach, lack of protection from bias by blinding, and difficulty in specifying the non-inferiority margin. We thought that setting a group to receive bare metal stent mounted on drug eluting balloon would have an ethical problem because PEPCAD III trial showed a worse result than drug eluting stent. Therefore we designed a non-inferiority trial to show that drug eluting balloon first strategy would be better than bare metal mounted on drug eluting balloon and as effective as a drug eluting stent. The non-inferior margin is defined as an in-segment late luminal loss of 0.1mm which was less than 50% of the difference between bare metal mounted drug eluting balloon and drug eluting stent on PEPCAD III trial (bare metal mounted drug eluting balloon, 0.41 ± 0.51 mm Vs. drug eluting stent, 0.12 ± 0.26 mm, absolute difference 0.29mm). This number of patients would have 85% power to detect superiority with late luminal loss difference of 0.2mm between the groups at a two-sided alpha-level of 0.05. Therefore, we will additionally analyze the superiority as well.

We have precisely described above changes in the manuscript (statistical consideration part). We deeply thank you for this constructive comment.
[Editorial request]
- In addition, if the following are in the manuscript, I missed them:
  The current status of the trial. Some statements about conflicts of interest and the roles of each author in the manuscript.

Response: We thank you for this very important comment. We added the missing part in editorial request on our manuscript (abstract and discussion) and addressed the comments in the revised manuscripts.