Date: 08-02-2023

To,

Editor,

World Journal of Cardiology

Subject: Revision changes in the manuscript no. 80790 in World Journal of Cardiology

Dear Editor,

Thank you for considering our original paper entitled **"Real-world five-year outcomes of FlexyRap® cobalt-chromium rapamycin eluting stents with biodegradable polymer in patients with *de-novo* coronary artery disease".** I am pleased to resubmit for publication the revised version of manuscript no. 80790. We would like to thank the reviewers for their thoughtful review of the manuscript. They raise important issues and their inputs are very helpful for improving the manuscript. We agree with almost all their comments and we have revised our manuscript accordingly. Each comment has been carefully considered a point-by-point response to the comments/queries raised by the reviewers.

Responses to the Editor and changes in the revised manuscript are as follows;

Editor comments:

1. **Resubmit this study as research brief**

RESPONSE: We have revised the manuscript as per the Instructions about research brief

Response to the reviewers' comments:

Reviewer #1: I read with interest the article "Real-world five-year outcomes of FlexyRap® cobalt-chromium rapamycin-eluting stents with biodegradable polymer in patients with de-novo coronary artery disease". It is a retrospective, multi-center, observational, post-market clinical follow-up study of individuals treated with FlexyRap® DES for de novo coronary artery disease (CAD). The results of the study are encouraging and interesting considering the very low MACE rate. There are numerous methodological problems;

1. **cohort of CAD patients is heterogeneous - pts. with stable and unstable AP. 4. basic characteristics of CAD patients are very atypical?!; dyslipidaemia 0%??, DM only 14%, low percentage of smokers?, PAD 0% (how and were they evaluated with CDFI of carotid artery or ABI?**

RESPONSE: We very much appreciate this helpful comment. Having a heterogeneous cohort of patients with both stable and unstable angina in the real-world study of coronary artery disease (CAD) allowed us for a more comprehensive understanding of the disease and its progression. Comparing the two groups provided us the insight into the different risk factors, causes, and outcomes associated with each type of angina, and also helped to identify the potential targets for prevention and treatment of CAD. We have reanalysis the data on the potential errors resulted into the atypical outcomes in the basic characteristics of CAD patients with updating the dyslipidemia (3.4%) and smoking habit (40.6%). However, the patient population with peripheral artery disease (PAD) is 0% as the device being evaluated is intended for the treatment of cardiovascular disease as per our protocol. There are more percentage of patients with previous MI (54.8%) compared to other similar studies. The other risk factors are comparatively low and some not typically seen in CAD Patients. Hence this study has patients with low to medium risk factors

2. **no morphological evaluation of the coronary arteries was performed during the follow-up period either by classic coronary angiography or CCTA, but only MACE was monitored.**

RESPONSE: Thank you for taking it into the consideration. In this real-world study, we made a focus on monitoring major adverse cardiovascular events (MACE) according to our study protocol, rather than performing a morphological evaluation of the coronary arteries at the follow-up period. However, in patients with any evidence or complaint of mild chest pain or burning sensation, exhaustion, the TMT with ECG was performed and analyzed independently to understand the residual cardiac risk.

3. **patients were treated with clopidogrel or prasugrel, and prasugrel is known to be superior to clopidogrel, which could have led to bias. A subanalysis of these groups of patients is needed**

RESPONSE: We are grateful for this comment. However, it has been added according to the cardiologist discretion as it is a retrospective observational study. Thank you for the suggestion for the sub analysis. We will plan specially for the sub analysis of the data for these patients' group for publication. So, we have not included the sub analysis data in this manuscript

4. **Minor comment: check all the data in the tables where there are illogicalities (lower systolic compared to diastolic BP, etc.). Some data in the tables are unnecessary and can be omitted.**

RESPONSE: We are grateful for this helpful comment and we apologize for this error. We have made suggested update in the revised manuscript with correction of data. We have omitted the unnecessary data in the revised manuscript as per the suggestion.

Reviewer #2: The authors evaluated the safety and effectiveness of FlexyRap®DES through a retrospective, multicenter, observational study in the real environment for 5 years. The success implantation rate of FlexyRap® DES was 100%. During the 1-year, 3-year and 5-year follow-up, the incidence of major adverse cardiac events was relatively low, which confirmed that FlexyRap ®DES is safe and effective in patients with new coronary heart disease. However, the research still has the following problems:

1. **Compared with previous RCT studies of rapamycin eluting stent, the incidence of major adverse cardiac events in this study was significantly lower. The difference cannot be explained by product characteristics. The author needs to make a detailed comparison with previous studies in the discussion section.**

RESPONSE: Thank you for your invaluable suggestions. We have added the detailed comparison of the incidence of major adverse cardiac events with the previous studies in the discussion section. During the segregation and analysis of the data it was understood that the risk factors are comparatively low and some not typically seen in CAD Patients when compared to other studies.

2. **The population included in this study is the target vessel disease with diameter stenosis ≥ 50%, which is far less than the surgical indication for stent implantation. Therefore, is it appropriate to evaluate the success rate of the device as 100%**

RESPONSE: We very much appreciate this helpful comment. As per the IFU of the study device, target lesion diameter stenosis ≥ 50% for the patient inclusion was followed in the manuscript. The success rate of the device of 100% which includes the lesions of Type C, where predilatation of the lesion was performed before stent implantation. So proper Lesion preparation contributed to 100% device success rate

3. **Are the patients included in this study all qualified patients, or are they selected artificially? The author should draw a flow chart and specify the inclusion criteria and exclusion criteria.**

RESPONSE: In this retrospective real-world study, the selection of patients was carefully considered and was specifically chosen to provide a clear and accurate evaluation of the device's performance. The chosen population allowed for a thorough examination of the device's capabilities and yielded valuable insights into its effectiveness. The flow chart with the specification of inclusion and exclusion criteria is being updated in the manuscript.

Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, 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. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights.

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RESPONSE: We express our sincere gratitude for the time and effort you took to review and provide feedback. Your comments and suggestions for improvement were extremely valuable and we appreciate the thoughtfulness you put into your review. We have carefully considered your feedback and have incorporated it into the final version of the manuscript. We believe that this will greatly improve the overall quality of the work. The figure of Kaplan Meier graph is provided in the PowerPoint. It is the software generated image and thus cannot be prepared using PowerPoint. The graph of Kaplan Meier is obtained by the software SPSS V 20. The figure of patient selection criteria (Fig. 1.) has been prepared by incorporating your valuable suggestion. Confirming the figures to be original, we have added the copyright information to the bottom right-hand side of the picture in the PowerPoint. The tables have been formatted with the standard three-line format in the revised manuscript submitted. The contents of each cell in the table are added meeting the editing specification with the alignment in the lines of each row and column. We have tried significantly to work on improving the content of the manuscript.

We would like to thank the reviewers for a careful and thorough reading of this manuscript and for the thoughtful comments and constructive suggestions, which have greatly helped to improve the quality of this manuscript. We agree with almost all their comments, and we have revised our manuscript accordingly. We sincerely hope that it would have now met up to your expectations. Please let us know if any further information or clarification is required.

Best wishes,

Thanks, and regards;
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