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### Format for ANSWERING REVIEWERS



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6248-review.doc).

**Title:** Duration of Dual Antiplatelet Treatment in the Era of Next Generation Drug-eluting Stents

**Author:** Jong Han Yoo, M.D., Sang Hyuk Seo, M.D., Min Sung An, M.D., Tae Kwun Ha, M.D., Kwang Hee Kim, M.D., Ki Beom Bae, M.D., Chang Soo Choi, M.D., Sang Hun Oh, M.D., Young Kil Choi, M.D

**Name of Journal:** *World Journal of Cardiology*

**ESPS Manuscript NO:** 6248

Dear Reviewer and Editor

Thank you so much for your nice review. We really appreciate the great opportunity you have kindly given to us to resubmit our work to WJC.

First of all, we wish to express our sincere gratitude to you for your kind letter and advice. Your timely encouragement means a great deal to us. It takes you distinguished professors, and three reviewers a lot of time to read our manuscript.

We have revised this manuscript according to the reviewers' comments and the revised parts are marked in blue color in the manuscript. We also responded point by point to each reviewer's comments as listed below, along with a clear indication of the location of the revision. We hope this will make it more acceptable for publication.

Now, we would like to resubmit it for your consideration, and we hope our paper can find a home in your premier journal. Thank you for reviewing it again. We look forward to hearing from you soon.

Yours sincerely,

Seung-Woon Rha,

Korea University Guro Hospital



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Dear Reviewer:

Thank you so much for your very insightful comments on our manuscript! We really appreciate your excellent advice which has helped us a lot in improving our manuscript. According to your comments, we have amended the relevant parts of the manuscript. Your questions are answered below.

Yours sincerely,

Seung-Woon Rha

### 1. Reviewer (#1)

#### COMMENTS TO AUTHORS

This review is a summary of important trials concerning the optimal duration of dual antiplatelet treatment following DES implantation, particularly in patients underwent PCI with next generation DESs. Since the risks and benefits of long-term dual antiplatelet therapy remain unclear such a summary is important. However, the authors:

1. Should add an abstract

; We added an abstract according to your request.

Current percutaneous coronary intervention guidelines recommended that dual antiplatelets (aspirin 100mg+ clopidogrel 75mg daily) for at least 12 months following drug-eluting stent (DES) implantation if patients are not at high risk of bleeding. Several reports have been tried to shorten the dual antiplatelet therapy up to 3-6 months, especially following next-generation DES implantation for cost-effectiveness. However, the clinical results have been inconsistent and the data regarding next-generation DESs are limited. In this report, we summarized recently published important pivotal reports regarding the optimal duration of dual antiplatelets following DES implantation.

2. Should ask for permission for using tables already published in other Journals

; We modified all the tables and left only essential results.

We deleted the figure to avoid conflict.

3. Should add and comment on the recent optimal dual antiplatelet therapy (OPTIDUAL) see Trials 2013 Feb 21;14:56



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; According to your comments, we added the additional published data on the references and on the manuscript.

Another new clinical trial (OPTIDUAL; OPTimal DUAL antiplatelet therapy trial) is ongoing to assess the efficacy and safety of 12 versus 48 months of dual antiplatelet therapy after DES implantation.<sup>[20]</sup>

4. Should add and comment on the Korean "Optimal Duration of Dual Antiplatelet Therapy after Drug-Eluting Stent Implantation: A Randomized Controlled Trial" published this month (October 2013) in "Circulation".

; According to your comments, we added the additional published data on the references and on the manuscript.

Recently, DES-LATE trial was reported that the patients who were on 12-month dual antiplatelet therapy without complications, an additional 24 months of dual antiplatelet therapy versus aspirin alone did not reduce the risk of major composite hard endpoints (cardiac deaths, myocardial infarction or stroke) .<sup>[8]</sup>

5. Should comment on and add as reference the papers (Int J Cardiol. 2012 Apr 19;156(2):125-32 and Thromb Res. 2013 Aug;132(2):312.) emphasizing the hypersensitivity responses following stent implantation in association with thrombosis, bleeding and clopidogrel.

; According to your comments, we added the additional published data on the references and on the manuscript.

Lastly, regarding the clinical events associated with stent thrombosis, P2Y<sub>12</sub> and thromboxane receptor is not the sole therapeutic measure to prevent the thrombotic risk. There must be different pathways leading to thrombotic events including hypersensitivity reactions .<sup>[21, 22]</sup>

Thank you

Dr Seung-Woon Rha

2. Reviewer (#2)

**COMMENTS TO AUTHORS**

Topic of the submitted paper is on the front burner of current cardiology. Essential data have been thoroughly collected and I have no major critical comment. Author should correct typo error on page 10 (abbr. TUMI).

; Thank you so much for your nice comments.

We fixed the typo error and structure according to editor's comments.

3. Reviewer (#3)

**COMMENTS TO AUTHORS**

Rha aims to give an overview on role of the duration of dual antiplatelet treatment in the era of new drug-eluting stents. There are major problems and flaws:

1. The author just copied a couple of summaries of the respective trials in one manuscript  
; We modified tables and added information regarding ongoing clinical trials (OPTIDUAL), limitations and future perspectives on the manuscript.

2. the figures were just taken from the original papers. A general scheme/new summary figure would improve the manuscript.

; According to your comment, we deleted figure to avoid conflict of interests.

All other tables are modified.

3. What about the novel P2Y12 inhibitors? How does the clinical setting (ACS/NSTEMI/STEMI, stable CAD) influence the antithrombotic strategy

; We added following comments on the manuscript according to your comment.

**In this review, we focused on only classical dual antiplatelets aspirin and clopidogrel.**

**However, we have to get more data to define the role of newer generation P2Y12 inhibitors including Ticagrelor and Prasugrel, especially in acute coronary syndrome setting in the future.**

4. what is novel about this paper?



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We added information regarding ongoing clinical trials (OPTIDUAL), limitations and future perspectives on the manuscript for something new.

Thank you

Dr Seung-Woon Rha