Author’s response to reviews

Title: Effect of Eicosapentaenoic acid/Docosahexaenoic acid on Coronary High-intensity Plaques Detected with Non-contrast T1-Weighted Imaging (The AQUAMARINE EPA/DHA Study): study protocol for a randomized controlled trial

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Version: 2 Date: 08 Nov 2017

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Reviewer #1: This paper is now a clear account of the design of this trial.

One typo in the title (randomised is spelled incorrectly) needs to be corrected.

(Response)

Thank you for your comment. We have corrected the term.

Randomised→Randomized

On page 8 line 13 the authors have added some detail about the rational for the study suggesting that higher dose EPA could reduce the risk of cardiovascular diseases in patients who "resist LDL-lowering with statins". I think this term could be misleading. Do they mean people who don't take statins? or do they mean that there are a group of people who do not respond to statin therapy when it is taken. Given the controversy around "statin intolerance", and the fact that such a phenomenon is not supported by the randomized evidence, I think the authors would be wise to avoid this area. Furthermore, this trial is including people who have well controlled cholesterol on statin therapy so it seems odd to present the possibility of stabilising plaque in untreated patients as a rational for the study.

I still have reservations about whether a small trial with a surrogate end-point like this one is likely to change practice, but I am not asked to review the study design per se and the study is already underway. I have no further suggestions for this manuscript.

(Response)

Thank you for your comment. In response to your comment, we have revised our manuscript as follows (page8, line 2-3).

Higher dose EPA (1.8g) could reduce the risk of cardiovascular diseases in patients who "resist LDL-lowering with statins"
higher dose EPA (1.8g) could reduce the residual risk of cardiovascular diseases in patients receiving LDL-lowering with statins

Reviewer #2: Interesting work and thank you for sending your work to TRIALS

Thank you for your favorable review.