Reviewer’s report

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

Version: 0 Date: 29 Aug 2017

Reviewer: M Rahouma

Reviewer's report:

I would like to thank the authors for their efforts. It was interesting to review this manuscript about "Effect of Eicosapentaenoic acid/Docosahexaenoic acid on Coronary High-intensity Plaques Detected with Non-contrast T1-Weighted Imaging: The AQUAMARINE EPA/DHA Study"

I do have some comments;

Page 7, line 47; "We will study the change in PMR of coronary HIPs detected using CMR after 12 months of EPA/DHA therapy."…. Why 12 months in particular? Could we also report 3 and 5 years. In the prior experimental series, some studies report it at 3 years for effect to appear.

Page 8, line 31-38; "adjusting for age, gender, presence or absence of type 2 diabetes mellitus, and PMR of the primary coronary lesion measured with non-contrast T1WI” and although you mentioned later on page 14 that "dynamic allocation is used in order to ensure an even allocation of factors that may influence the evaluation of the efficacy of anti-hypertensive medications" which is a good point, I would like to include hypertension variable in the randomization process itself as it is a known risk factor for cerebrovascular and cardiovascular events.

Page 9, line 9; Please explain why "presence of bleeding" is exclusion criterion in your manuscript.

Page 9, line 54; "received instructions for lifestyle modification.. Can you add time frame, for example "for at least 3 month"??

Page 11, line 15-19; "inappropriate for study participation in the opinion of the Principal Investigator or Investigator"; What do you mean by the word" inappropriate " as this may represent a bias in itself and What about performance status (PS); did all patients, even with poor PS, will be recruited??

Page 12, line 9-42; I prefer to avoid redundancy in the 2ry endpoints….So we can combine point 5 and 7 to be" Change and Percent change...." Similarly point 4 and 6 together
Page 13, line 9-12; LDL diameter Measured by what??

Page 15, line 15 and 41; please write the meaning of PDF and CRF.

Page 16, line 2; "Plaque to myocardium ratio (PMR): Below 1.1 / 1.1 or higher in non-contrast T1-weighted CMR images of the main lesion".... Why this cutoff point?? please add to the manuscript

Page 18, line 28; what are the adverse events you are looking for? Is there any particular classification for AE eg minor and major...etc. Some papers will report adverse events based on "Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0" that I think will be helpful and more scientific way to represent any adverse events

Page 19, line 9; Typo! "Optimal management", please correct.

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