

Ioannina, 9 December 2016

Dear Editor,

Please find attached our manuscript entitled "Statin escape phenomenon: Fact or fiction?" (manuscript ID: 31260) revised according to the reviewer comments. All changes are highlighted in yellow in the revised text.

Specifically, according to:

**Reviewer 1 (01943305)**

In this retrospective observational study the authors provide additional data on the possible statin escape phenomenon based on their experience and try to elucidate potential risk factors. Considering the small number (n=181) of eligible patients, and the low incidence of cardiovascular disease observed in this study, the results did not have the power to establish an association between statin escape and incidence of cardiovascular disease. Accordingly, the authors stated that statin escape phenomenon, although its clinical significance remains uncertain, should be noticed in clinical practice and the patients with larger than anticipated initial LDL-C lowering should be carefully monitored. This study is well written and the patients have been well selected although several variables could have influenced the results. Just one, have the authors studied the variations of non-HDL cholesterol? They should exclude the diabetic patients and analyze the data of non-HDL in both groups of patients studied. The reference 12 should be completed.

At this point we would like to thank the reviewer for his/her valuable comments. We now present the variations of non-HDL-C in Table 2 and have added a comment in the Discussion section (page 8; lines 2-6, page 10; lines 4-8). Reference #12 has been completed.

**Reviewer 2 (00182548)**

The study is interesting and useful. Unfortunately, the findings are uncertain, as the number of the patient is small. An increased intake of cholesterol in the diet may be suspected if there are intermittent variations in cholesterol levels, determined several times during the trial, not just at baseline, at 6 months and at the end. It would be helpful to study the HMGCoA reductase and PCSK9 activity in future studies. The article sensitizes the researchers with the issue of statin escape phenomenon. This subject deserves to be deepened in the future.

We thank the reviewer for his/her insightful comments. We have added an additional comment on the potential role of a high cholesterol diet in the intermittent variations of cholesterol levels (page 9; lines 20-22)

Furthermore, our manuscript has been updated according to the Guidelines and Requirements for Manuscript Revision-Retrospective Study.

We now hope that our revised manuscript will meet your expectations.

Kind regards,

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