

June 22, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: ESPS Manuscript NO 11371-edited.doc).

Title: Lipid-lowering agents in the management of nonalcoholic fatty liver disease

Author: Konstantinos Tziomalos

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 11371

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers

Reviewer 01518980

The review is an accurate summary of the current status of lipid lowering agents in NAFLD.

We thank this Reviewer for his/her positive comments.

Specific comments

1. It is stated that the association between NAFLD and CVD is mostly explained by their shared pathogenesis. However, there is increased CVD with NAFLD even in the absence of DM suggesting that NAFLD is causative in the CVD.

We thank this Reviewer for this important comment. We changed our statement to "Since NAFLD and CVD have many common risk factors (e.g. abdominal obesity, type 2 diabetes mellitus (T2DM), insulin resistance, inflammation and oxidative stress), the increased CVD risk in patients with NAFLD might be partly explained by their shared pathogenesis. However, there is increased CVD risk in patients with NAFLD even in the absence of T2DM, suggesting that NAFLD is directly causative of CVD."

2. The very long paragraph on pages 4-5 should be broken up.

We broke up this paragraph into three shorter paragraphs.

3. Although generally well written, the style of the review needs considerable attention. Too much actual data is provided on every trial - i.e., the number of patients in every study should not be stated, the actual P value not given on every study, etc.

We thank this Reviewer for stating that our Review is "generally well written". We tried to improve the style of the Review. We removed the less important data from the reported trials.

Reviewer 00038721

This review article describes the role of lipid-lowering agents (mainly statins) in the treatment of patients with nonalcoholic fatty liver disease. It is well written and covers the current knowledge of

stain treatment of patients at risk for CVD whom suffer from NAFLD. There are a number misspellings throughout the manuscript. I would suggest adding a section on how current NAFLD drugs might interact with stains. For example, the antifibrotic drugs use to treat liver disease.

We thank this Reviewer for stating that our Review is "well written and covers the current knowledge of stain treatment of patients at risk for CVD whom suffer from NAFLD". We thoroughly edited our manuscript and corrected the misspellings. We also added a section on how current NAFLD drugs might interact with stains in page 5 (last paragraph), where we mention "Importantly, statins do not interact with agents that are used in the treatment of NAFLD (e.g. vitamin E, pioglitazone, metformin, ursodeoxycholic acid, angiotensin receptor blockers) and therefore, can be safely coadministered with the latter agents".

Reviewer 00199528

Author has summarized the role of lipid lowering drugs on treatment of NAFLD. My major comment is that the manuscript does not include any new knowledge or original idea differing from other reviews on this topic.

Indeed, there are several excellent reviews on the topic. However, most other reviews focus on other aspects of the treatment of NAFLD whereas we emphasize the safety and efficacy of lipid-lowering agents in this population. We also include very recently reported and important data on the topic (e.g. the results of the IDEAL trial) and discuss all lipid-lowering agents and not only statins.

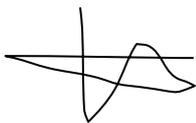
My minor comments are as follow: *abstract: sentence should be corrected as "Nonalcoholic fatty liver disease (NAFLD) is 'the most common' chronic liver" *omega-3 fatty acids section: abbreviation should be added "omega-3 fatty acids (EPA)" *nicotinic acid section sentence should be corrected "...combination of nicotinic acid with a statin does not 'decrease' CVD events more than statin monotherapy".

We thank this Reviewer for pointing out these mistakes. They were all corrected.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Hepatology*.

Sincerely yours,



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